National Surveillance of COVID-19 Infections: Variants, Vaccination Status, and Viral Spread

Update: May 11, 2022

Covid-19 Positivity by Vaccination Status Data Interpretation

Introduction

Beginning in November 2021, the COVID-19 Omicron variant spread rapidly across the United States where new cases have surpassed daily records and changed the trajectory of the pandemic yet again. Individuals infected with this variant presented symptoms similar to other variants with differing symptoms and severity depending on vaccination status, chronic conditions, age, and other factors[1]. Several sources have reported that the Omicron variant demonstrates increased immune evasion leading to more breakthrough infections in vaccinated individuals compared to prior variants[2]. To inform public expectations, vaccine manufacturers and the CDC have reiterated that even if vaccines are less effective at preventing infections, they are proven to prevent and reduce serious illness and death[1].

These findings are further supported by the Walgreens COVID-19 Index, a surveillance system gathering COVID-19 diagnostic data from tests administered at 6,950 pharmacies across the United States and Puerto Rico. Diagnostic tests included drive-through Rapid Nucleic Acid Amplification tests (Rapid) and Polymerase Chain Reaction (PCR) tests; currently however, the Index only displays results from PCR tests. During the pre-Omicron era, the data demonstrated higher positivity rates among the unvaccinated group. However, in early 2022 the data indicated a lower positivity rate among unvaccinated individuals compared to those who have received at least 1 dose of vaccine. On the surface, these results are counterintuitive and may lead to misinterpretation.

Inherently, disease surveillance systems are built on unadjusted observational data and therefore conclusions may be heavily influenced by patient testing behavior. The goal of this analysis is to better understand differences in positivity by vaccination status and identify emerging trends within Walgreens testing population.

Methods

This observational study used best practices to analyze the exposure and non-exposure groups; that is, those who were vaccinated against COVID-19 versus unvaccinated patients. Differences in characteristics between the vaccinated and unvaccinated were analyzed and considered when reporting the outcome, which is a positive or negative COVID-19 test result. Covariates for this analysis included self-reported age, race/ethnicity, location, exposures, chronic condition status, recent positive test, and past COVID-19 infection. Covariates from the data were also derived, including test type (Rapid vs PCR), repeat testing patterns, and positivity rates by county. Finally, self-reported symptoms among those who tested positive were compared between vaccination status groups.

Given the recommendation for all three COVID-19 vaccines available in the United States to include at least two doses (or one dose and one booster), patients reporting only one dose (7.51% of patients) were excluded. Patient testing data from April 3-9, 2022, was included; however, testing trends were examined four weeks prior to this study period in order to identify patients who are weekly repeat testers (3 or more tests in a 4-week time period). Chi-squared statistical test and Student's t-test were used to assess statistical differences between groups with p-values <0.05 generally considered statistically significant.

Research findings

The analysis found several significant differences between vaccination status groups (Table 1). Those who were not vaccinated at the time of testing had a median age 10.83 years younger than those vaccinated (p<0.0001). Among the testing population, the highest percent unvaccinated were in the Midwest region (25.97%), followed by the West (21.47%), Northeast (18.72%), and South (17.62%). Regarding race/ethnicity, the highest percent unvaccinated were among those identified as African American or Black (27.44%) and Hispanic any race (24.28%).

Several of the differences between groups may have led to an apparent decreased probability of unvaccinated patients testing positive for COVID-19.

Patients in the unvaccinated group were:

- 32.51% less likely to report having close contact with someone infected by COVID-19 compared to the vaccinated groups (11.77% vs 17.44%, p<0.0001),
- 23.50% less likely to live in a county with a positivity rate >5% (59.57% vs 77.87%, p<0.0001),
- 61.78% more likely to report a previous COVID-19 infection (32.00% vs 19.78%, p<0.0001), more likely to repeat testing weekly (7.34% vs 0.84%, p<0.0001), and
- less likely to report testing for travel purposes (33.76% vs 62.67%, p<0.0001), and
- more likely to use a Rapid versus PCR test at Walgreens (63.80% vs 59.90%).

Among the unvaccinated who were testing weekly, their positivity rate was significantly lower than those who were not repeat testers (2.55% vs 5.29%, p<0.0001). Patients who reported testing related to travel were less likely to test positive regardless of vaccination status (3.22% vs 14.84%, p<0.0001). Similarly, patients using Rapid tests, were less likely to live in an area with a high positivity rate (73.77% vs 82.18%, p<0.0001) and receive a positive test result (7.22% vs 9.82%, p<0.0001) compared to PCR. Rapid users were less likely to report close contact compared to PCR testers (15.09% vs 18.15%, p<0.0001) and more likely to report testing for travel purposes (59.28% vs 53.00%). The highest proportion of Rapid tests was in the South (69.19%), followed by the Midwest (64.68%), Northeast (53.51%), and West (40.55%). Also, those in rural or suburban areas had a higher proportion of Rapid testing compared to urban areas (70.26% vs 59.60% vs 42.73%, p<0.0001).

Bivariate analyses were limited to patients who reported receiving their last vaccine or booster within the last five months in the vaccinated group. The observed crude difference in positivity was 5.29% for those unvaccinated and 7.53% for those vaccinated (p<0.0001). First, patients who reported a recent positive COVID-19 test (6.50% of testers) were removed due to naturally high positivity among patients who are retesting following a recent positive (19.80% vs 5.77% for those without a recent positive, p<0.0001). The resulting positivity was reduced to 4.77% for those unvaccinated and 6.38% for those vaccinated (p<0.0001). After stratifying by age, no significant differences were found in positivity by vaccination status among patients aged 5-11 (5.34% vs 5.62%, p=0.5665), 12-17 (4.11 vs 4.40, p=0.5738), and 65+ (5.72 vs 5.25, p=0.4888).

Among older adults, 68.07% reported testing for future travel and among these patients, those unvaccinated were more likely to test positive (4.56% vs 2.23%, p=0.0021).

There were no differences in positivity between vaccinated and unvaccinated patients who reported having a chronic condition (20.65% of patients) or who were living in an area with low COVID-19 positivity (23.58% of patients) (6.94% vs 7.01%, p=0.8661 and 2.33% vs 2.17%, p=0.4354). Further, among patients who reported having had previous COVID-19 infection, unvaccinated patients were more likely to test positive than vaccinated (3.08% vs 2.46%, p=0.0042). Patients who did not have previous COVID-19 infection but reported having close contact with a positive patient had no differences in positivity by vaccination status (22.80% vs 22.57%, p=0.8210). Figure 1 shows positivity by vaccination status stratified by previous infection and reported close contact.

Next, the reported symptoms among patients testing positive was analyzed by vaccination status (Figure 2). With the exception of common-cold (cough, sore throat, or congestion), the rest of the self-reported symptoms were found to be significantly higher among unvaccinated patients compared to vaccinated patients ($p<0.05$). Most notably, patients who were unvaccinated compared to those who were vaccinated and received their last vaccination within the last five months were:

- 67.07% more likely to report fever,
- 57.13% more likely to report shortness of breath, and
- 137.75% more likely to report gastrointestinal symptoms.

Discussion

Monitoring case counts is important to tracking the epidemiological trends of COVID-19 infection. As the pandemic transitions to the endemic phase, the Walgreens COVID-19 Index should be viewed alongside trends in COVID-19 hospitalizations and deaths in order to glean the full picture of the public health impact of COVID-19, including the impact of vaccination status on severe illness and death. A decrease in vaccine effectiveness has been observed with the emergence of the Omicron variant, which is also evident in the Walgreens COVID-19 index. A limitation of this surveillance system is that severe cases including hospitalizations and deaths are not being measured. Current data shows that recent vaccination or boosters are protective against severe illness and death from the Omicron variant[3].

The results show that the vaccinated and unvaccinated groups vary significantly in their exposure; unvaccinated patients are less likely to report close contact with someone who has confirmed or suspected COVID-19 and less likely to reside in an area with high positivity. COVID-19 positivity is expected to be lower in patients with less exposure. On the other hand, unvaccinated patients repeated testing on a weekly basis more often. Repeat testers were naturally more likely to test negative because their reason for testing was unrelated to exposure. Additionally, unvaccinated patients were more likely to report previous COVID-19 infection. These patients who survived were likely to benefit from natural immunity which provides some protection against future infections, further lowering the reported positivity rate in the unvaccinated group. When the unadjusted positivity was calculated for those with previous COVID-19 infection, unvaccinated patients were significantly more likely to test positive than vaccinated patients. This supports previous findings regarding the 'super immunity' for patients who received the COVID-19 vaccination and had a previous COVID-19 infection[4]. While natural immunity does offer some protection for unvaccinated patients, previous infection and vaccination combined offers even more robust protection.

Among vulnerable groups including children aged 5-17, adults 65+, and patients with chronic medical conditions, there was no difference in positivity between vaccinated and unvaccinated patients in the unadjusted analysis. A majority of older adults reported testing for travel purposes and among that group, unvaccinated patients had significantly higher positivity compared to those vaccinated.

Although all patients testing positive at Walgreens were experiencing a mild, non-hospitalized case at the time of their test, some had elevated symptoms such as fever, chills, and shortness of breath. These symptoms were reported significantly more in unvaccinated patients.

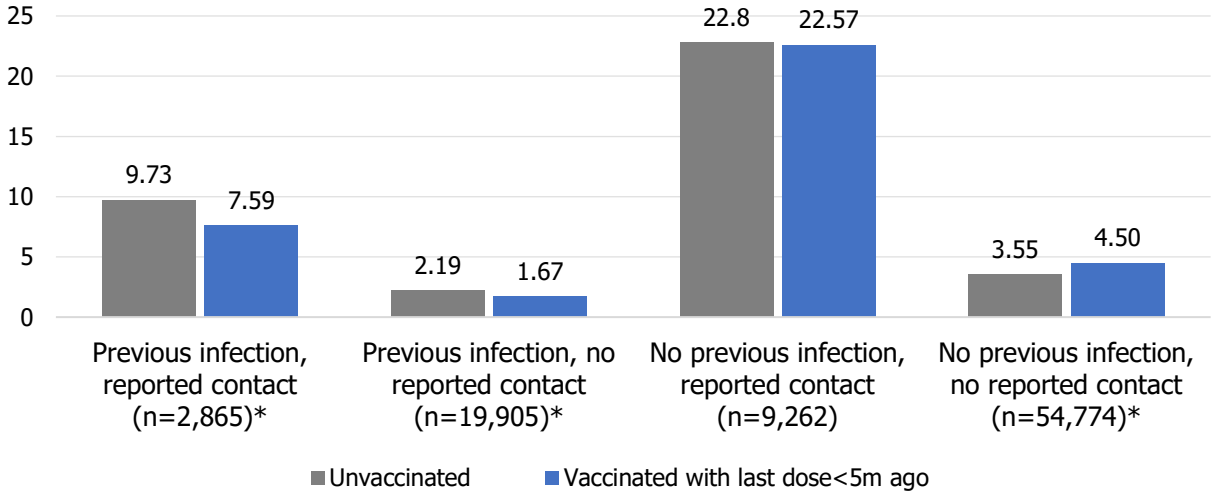
Notably, this study found a significant difference between positivity rates for Rapid versus PCR tests; however, this may be explained in part by the differences in patient behavior and location. Individuals who used Rapid tests were more likely to live in areas with lower positivity rates compared to those who used PCR, more likely to report testing related to travel, and less likely to report close contact with someone who has COVID-19.

Conclusion

Recently, public health officials have made statements that suggest the United States may be trending toward the end of the emergency COVID-19 pandemic phase. With this, there is a growing shift in focus from COVID-19 case counts to severe outcomes including hospitalizations and deaths. COVID-19 vaccine effectiveness is reduced with the Omicron variant compared to prior variants, which explains rising positivity rates, especially among the vaccinated[1]. Importantly, recent studies have demonstrated that the COVID-19 vaccine continues to offer strong protection against the most severe illnesses that result in hospitalizations and deaths[1]. This analysis demonstrated significant differences between unvaccinated and vaccinated patients who are getting tested for COVID-19 at Walgreens pharmacies. These differences help explain the trends in positivity by vaccination status and validates the limitations of drawing conclusions from observational surveillance data.

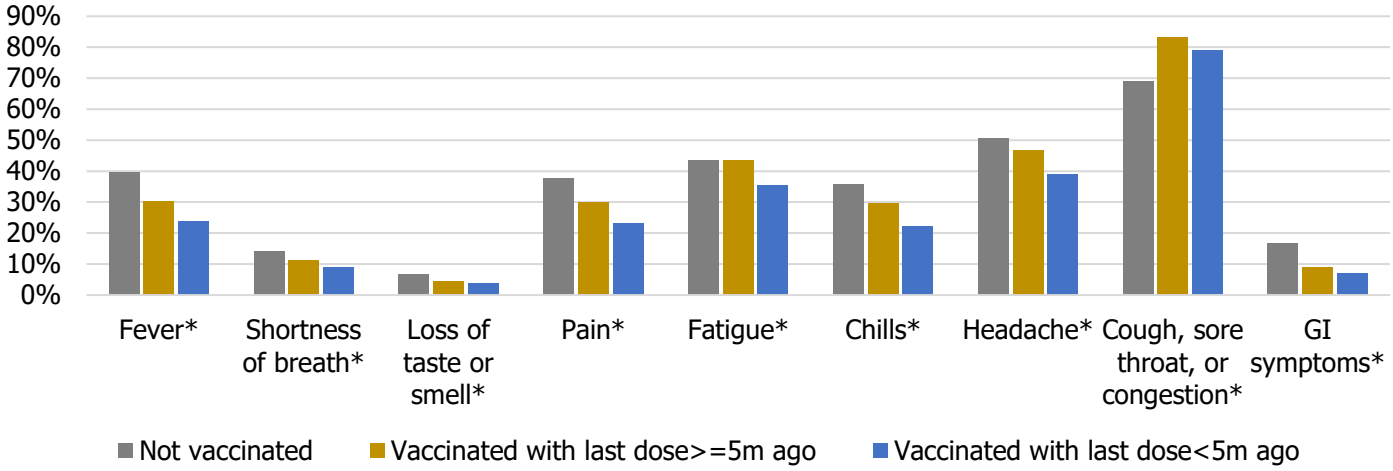
	Not vaccinated	Vaccinated with last dose>=5m ago	Vaccinated with last dose<5m ago	P-value
Number of patients	35,304	81,510	57,532	
Percent positive	5.29%	10.02%	7.53%	<0.0001
Median age	32.66	46.14	39.72	<0.0001
Percent weekly testing	7.34%	0.95%	0.69%	<0.0001
Percent with close contact	11.77%	18.13%	16.47%	<0.0001
Percent with a recent positive COVID-19 test	7.07%	7.75%	6.14%	<0.0001
Percent with past COVID (>90 days ago)	32.00%	19.66%	19.94%	<0.0001
Percent testing for future travel	33.76%	60.64%	65.54%	<0.0001
Percent living in counties with high positivity (>5%)	59.57%	63.61%	65.09%	<0.0001
Percent living in counties with high vaccination (>50%)	17.59%	18.80%	19.92%	<0.0001
Percent with at least one chronic condition	16.68%	31.32%	23.24%	<0.0001
Percent living in a rural area	30.30%	23.09%	22.34%	<0.0001

Figure 1: Positivity by previous infection and reported close contact



* P<0.05

Figure 2: Percent reporting symptoms by vaccination status



* P<0.05

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Update Authors:
Tanya Singh, MPH, Senior Analyst, Walgreens Center for Health & Wellbeing Research, Walgreens
Matthew Hardison, PhD, FACMG, Senior VP, Laboratory Operations, Aegis Sciences Corporation
Cyndi R. Clark, PhD, Manager, BioPharma Laboratory, Aegis Sciences Corporation
Josh Schrecker, Pharm.D., Director, Clinical Affairs, Aegis Sciences Corporation
Amy Shah, MPH, Walgreens Center for Health & Wellbeing Research, Walgreens
Liang Feng, PhD, Senior Analyst, Walgreens Center for Health & Wellbeing Research, Walgreens
Renae Smith-Ray, PhD, MA, Manager, Walgreens Center for Health & Wellbeing Research, Walgreens
Michael S. Taitel, PhD, Senior Director, Walgreens Center for Health & Wellbeing Research, Walgreens

For more information contact: info@aegislabs.com or Research@Walgreens.com

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On November 24th, the South African Ministry of Health alerted the World Health Organization about a new variant BA.1 (formerly B.1.1.529) that was quickly classified a variant of concern—Omicron. The increase in mutations along the S-gene allowed for rapid classification of this variant. With the recent identification of the Omicron variant and its initial detection in the United States, Aegis Sciences Corporation has been tracking its emergence via SARS-CoV-2 viral genomic next generation sequencing of COVID-19 positive specimens collected from individuals residing in all 50 states and Puerto Rico. Testing of samples with such broad geographic distribution is able to be performed due to a collaboration between Aegis Sciences Corporation and Walgreens, which has led to the availability of Aegis' real-time reverse transcriptase polymerase chain reaction (RT-PCR) testing at more than 5,200 of the over 7,200 Walgreens locations that provide COVID-19 testing. Together we have completed over 6 million SARS-CoV-2 tests since Fall 2020.

To date, we have confirmed 436 Omicron cases in a subset of sequenced specimens, with a 20-fold increase in the percent of Omicron-confirmed cases over a two-week period. Of these samples, 98.2% had S gene target failure (SGTF) in their RT-PCR results using the ThermoFisher TaqPath™ COVID-19 Combo Kit, a three gene assay that evaluates the N, ORF1ab, and S genes. Our data demonstrate a significant increase in expected Omicron cases based on the rise of SGTF as a proportion of all positive results nationally—25.1% of positive results from 5,091 samples collected on December 16th (Figure U1).

Our analyses support the use of S gene target failure as valid proxy for inferring the spread and impact of the Omicron variant

The S gene encodes the Spike protein that is critical for the virus to enter the host's cells. RT-PCR testing utilizes primers that bind to specific sections of the viral genome and incorporate fluorescent compounds as repeated cycles of replication occur. A sample is considered positive if there is enough fluorescent signal detected above the predetermined threshold in two out of the three gene targets. The Omicron (BA.1) variant has a set of mutations that occur in the TaqPath™ COVID-19 primer binding site within the S gene. These mutations are likely to result in failure to amplify the S gene target, a phenomenon known as S gene target failure (SGTF). Given that the Delta strain, which has been dominant since August, does not exhibit SGTF, tracking the rate of SGTF in COVID-19 positive samples correlates to Omicron emergence and spread. This is particularly important because strain identification through SARS-CoV-2 NGS, while extremely accurate, is a secondary assay that can take an additional week after the identification of a positive sample, whereas SGTF data is generated simultaneously with the determination of a positive result, typically within 12 hours of sample receipt.

To support the validity of SGTF as a proxy, we compared the percent of SGTF samples that were confirmed Omicron versus other lineages by sequencing (Table U1), the N gene and ORF1ab gene average Ct values between confirmed Omicron cases and SGTF positives (Table U2), and the increase of SGTF in positive samples by collection date since Omicron's identification (Figure U1). Sequencing analysis performed on a randomized subset of SGTF samples positively confirmed that 95.5% are Omicron variants with the others being classified as Alpha (0.2%), Delta (2.8%), and other B parental and sub-lineages (1.2%) (Table U1). Comparison of the average Ct values in Omicron-confirmed positives and SGTF positives revealed similar datasets for both the N gene (17.61 vs 18.07) and Orf1ab gene (17.63 vs 18.07) (Table U2). Last, Figure U1 reveals an exponential increase in the national proportion of SGTF COVID-19 positive samples with an average Ct value ≤ 30 for N gene and ORF1ab gene collected from December 5 to December 16 (0.4% to 25.1%). Included in the figure are the daily data points for select high-population states related to prevalence of SGTF amongst positive cases. This includes very recent findings from samples collected on December 16th: California (19.3%), New York

(21.4%), Illinois (29.0%), Texas (52.5%), and Florida (58.5%). In comparison to other states across the country, FL and TX are currently exhibiting some of the highest proportion of SGTF samples amongst positive cases.

These data demonstrate the correlation between SGTF in COVID-19 positive samples and Omicron spread within the population and support the use of SGTF in RT-PCR results as a highly correlative proxy for early detection and surveillance of the emerging Omicron variant.

Update Authors:
Matthew Hardison, PhD, FACMG, Senior VP, Laboratory Operations, Aegis Sciences Corporation
Cyndi R. Clark, PhD, Manager, BioPharma Laboratory, Aegis Sciences Corporation
Josh Schrecker, Pharm.D., Director, Clinical Affairs, Aegis Sciences Corporation
Michael S. Taitel, PhD, Senior Director, Walgreens Center for Health & Wellbeing Research, Walgreens
For more information contact: info@aegislabs.com or Research@Walgreens.com

Table U1: Identified Lineages in Subset of S Gene Dropout Cases

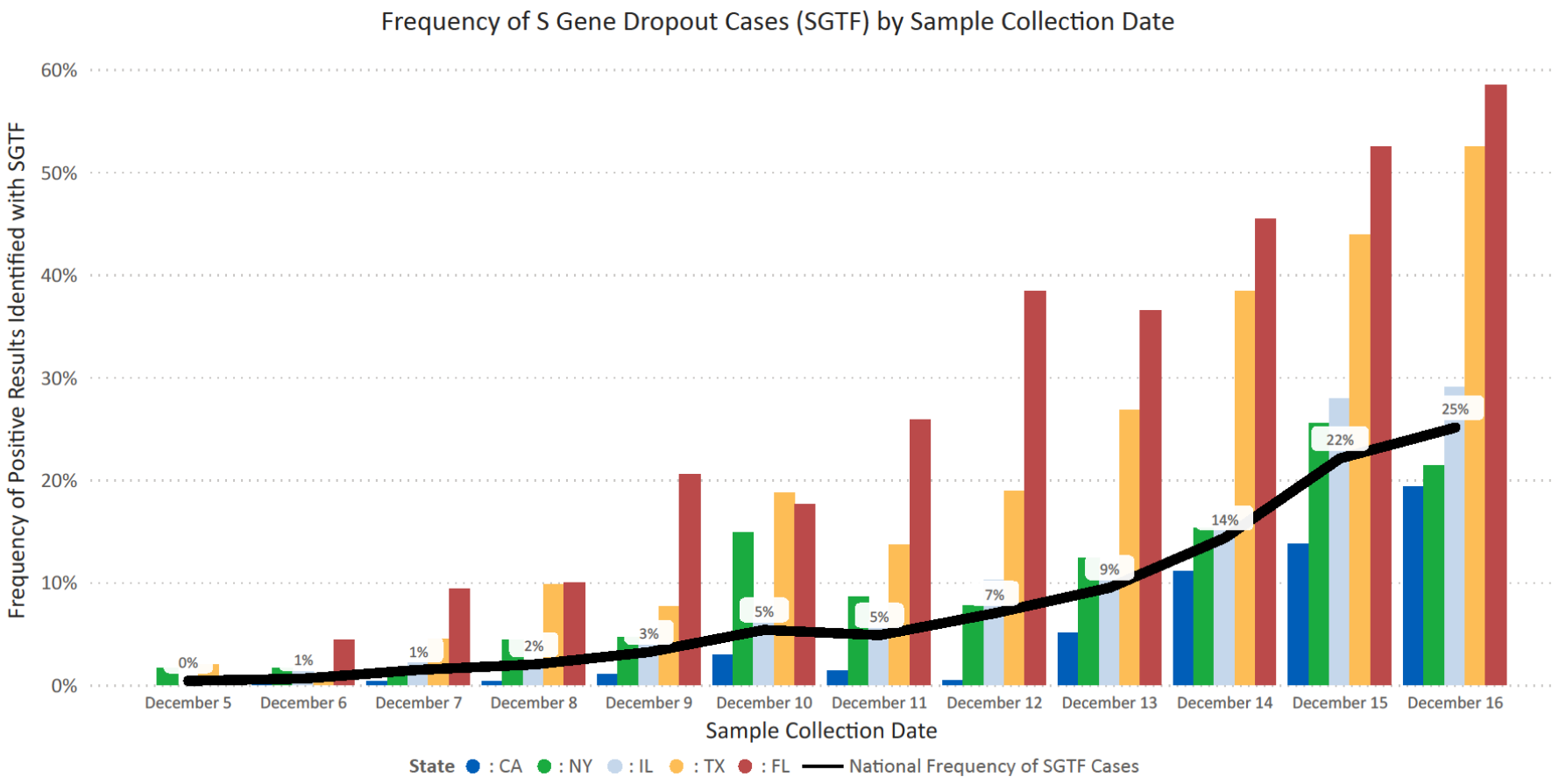
Lineage Call	SGTF Sample Count	% of Total Samples Sequenced
BA.1/B.1.1.529	428	95.5%
AY.44	6	1.3%
AY.103	3	0.7%
B	2	0.4%
AY.25	2	0.4%
B.1	1	0.2%
B.1.1.7	1	0.2%
B.1.177.73	1	0.2%
B.1.1.161	1	0.2%
B.1.637	1	0.2%
B.1.617.2	1	0.2%
AY.3	1	0.2%

Table U2: Comparison of S Gene Dropout cases with Confirmed Omicron Cases

	Total Detected	N Gene Ct Value (Mean)	N Gene Ct Value (Median)	ORF1ab Ct Value (Mean)	ORF1ab Ct Value (Median)
Confirmed Omicron Cases	436*	17.61	16.95	17.63	16.82
S Gene Dropout Cases (Samples collected 12/5-12/16; average Ct ≤ 30 for N-gene and ORF1ab gene)	5836	18.07	17.11	18.07	16.98

*Eight confirmed Omicron case with S gene detected

Figure U1: Frequency of S Gene Dropout by Sample Collection Date



August 2021

For more than 18 months, individuals around the world have dealt with the struggles of an ongoing public health crisis. The impact of the COVID-19 pandemic on daily life cannot be understated, with nearly 210 million cases reported to date and over 37 million cases in the United States alone.[1,2] Diagnostic testing and genome sequencing have been of utmost importance in surveilling and helping control viral spread. Thankfully, multiple vaccines became available for wide distribution earlier this year, and have demonstrated significant benefit in reducing disease progression, hospitalization, and death.[3-6]

Laboratory and Pharmacy Collaboration

In the fall of 2020, Aegis Sciences Corporation and Walgreens began collaborating to significantly improve access to efficient and reliable diagnostic testing throughout the United States. This led to the availability of Aegis's real-time reverse transcriptase polymerase chain reaction (PCR) testing in all 50 states and Puerto Rico at ~3,000 of the more than 6,000 Walgreens locations that provide COVID-19 testing.

Patients schedule drive-thru COVID-19 testing appointments via Walgreens online test scheduling system. They acknowledge the use of their information as described in the Notice of Privacy Practices and then enter demographic and health information such as: location, age, gender, race/ethnicity, chronic conditions, current symptoms, potential COVID-19 exposure, and vaccination status. During the appointment, upper respiratory specimens are collected via a safe, socially distanced mechanism at Walgreens locations. Together, Aegis and Walgreens have completed over 3 million SARS-CoV-2 tests, and Walgreens has administered more than 30 million COVID-19 vaccinations as of August 2021.

In May 2021, Aegis began performing whole genome sequencing on samples identified as positive through diagnostic testing to assist in surveillance of the spread of more transmissible viral variants, such as the Delta variant (B.1.617.2). This has allowed for reporting of viral lineages from over 110,000 samples, accounting for ~15% of all COVID-19 results in the United States found in the GISAID database.[7] The availability of diagnostic testing, genome sequencing, relevant patient information, and vaccination status has allowed for the creation of a sizable, nationally representative database for use in analyses to provide valuable epidemiologic insights. To curtail the pandemic, relationships between laboratories and healthcare organizations are essential to identify infections, surveil viral variants, and administer vaccinations.

Results and Insights

Throughout the pandemic, evaluation of data regarding diagnostic test positivity rates and spread of variants has been important to understand viral transmission. As vaccines continue to be administered and new viral variants are encountered, it will be critical to continue monitoring infection rates in individuals based on age, gender, presence of symptoms, existing healthcare conditions, and vaccination status. Over the past few months, the importance of this evaluation has only grown as we are contending with the spread of the Delta variant within the United States. Aegis and Walgreens have further collaborated with regards to data sharing to provide timely insights amidst the pandemic.

In a recent analysis of 864,607 samples from individuals tested by Aegis (Collection Dates: 5/1/2021-7/31/2021), positive cases were identified at a nearly four-fold higher rate in unvaccinated individuals compared with those who were fully vaccinated. We further analyzed 28,610 positive diagnostic samples that had subsequent genome

sequencing performed (Table 1). Within these results, 78% of specimens were submitted by unvaccinated individuals. This is further characterized in Figure 1 which shows the proportion of cases identified in unvaccinated individuals that underwent successful genome sequencing by state.

During the past few months, emerging viral variants have become a topic of great interest. The CDC defines a "variant of concern" as "A variant for which there is evidence of an increase in transmissibility, more severe disease (e.g., increased hospitalizations or deaths), significant reduction in neutralization by antibodies generated during previous infection or vaccination, reduced effectiveness of treatments or vaccines, or diagnostic detection failures."[8] Throughout 2021, a number of variants of concern have been closely monitored, including Alpha (B.1.1.7), Beta (B.1.351), and Gamma (P.1). Most recently, Delta (B.1.617.2) has garnered the most attention due to increased transmissibility and its risk for evasion of immunity gained through vaccination or previous infection. Currently, results of genome sequencing throughout the United States have identified Delta as the predominant circulating variant (Table 1).

Specimens collected at Walgreens locations and tested at Aegis Sciences Corporation demonstrate a similar pattern to what has been recently reported by the CDC regarding circulating variants. Figure 2 shows the proportion of cases identified in unvaccinated and fully vaccinated individuals (≥14 days from second dose of Moderna or Pfizer vaccine or ≥14 days from dose of Johnson & Johnson vaccine) from May-July 2021. In May, the majority of individuals that tested positive and had samples successfully sequenced were unvaccinated and infected with the Alpha variant. This began to change over time, and by July, the majority of cases were identified in unvaccinated individuals infected with the Delta variant. This change is to be expected based on the known increased transmissibility of Delta and its significantly greater risk to be spread among those who are unvaccinated. Interestingly, despite a significantly lower number of cases occurring in vaccinated individuals, the rate of symptomatic infection that does occur in those who are vaccinated is similar to those who are unvaccinated (Table 2).

Surveillance of Variants and Breakthrough Infections

Since vaccines became widely available, there has been much discussion regarding their effectiveness in preventing both viral transmission and progression to more severe illness, hospitalization, or death. As our data has shown, cases appear to be identified at a higher rate in those who are unvaccinated. As the virus continues to mutate, further evaluation of transmission risk in vaccinated individuals pertaining to breakthrough infections is warranted. Figure 3 shows the prevalence of cases in fully vaccinated individuals by virus lineage over time. As expected, the Delta variant appears to cause more breakthrough cases than other variants of concern. This data is substantiated by a recent CDC publication demonstrating the Delta variant's capability to cause symptomatic and asymptomatic infection in those who were considered fully vaccinated.[9] Additionally, our analysis includes a focus on the prevalence of cases caused by "Other" variants that have not historically been considered variants of concern or have only recently earned this designation (Figure 3, Category: Other). This aggregated grouping of variants shows that approximately 16% of all cases analyzed involved variants that were not Alpha (B.1.1.7), Beta (B.1.351.), Gamma (P.1), or Delta (B.1.617.2) in individuals infected with SARS-CoV-2. Despite almost 100 separate lineages falling into the "Other" category, nearly 60% of cases within this group were identified as the following: AY.3 (only recently considered a Variant of Concern), B.1.621 (first documented in Columbia) and B.1.516 (Iota - CDC Variant of Interest). Often, these lineages contain similar spike protein mutations, or combinations of mutations, to those that are considered variants of concern, such as L452R, E484K, K417N, and N501Y. Furthermore, some of the less frequent "Other" variants appear in a relatively high percent of fully vaccinated individuals. A subset of viral mutations that were identified at a higher frequency

within the "Other" category are further characterized by infection rate and vaccination status in Table 3. Closely observing the trends in "Other" variants will provide an early indication of future variants of concern.

Evaluating New Indicators

Assessment of viral density in samples collected from infected individuals is also of interest as it has been reported that cycle threshold (Ct) values in samples collected from positive individuals may be similar regardless of vaccination status.[9] Cycle threshold values, which are utilized by PCR testing platforms to indicate when viral genetic material is present in a specimen, have been used at times as a marker for transmission risk. Although numerous organizations report that these values should not be used to determine status of infection for those that have been exposed to SARS-CoV-2, it has also been stated that there is some correlation between Ct value and the amount of virus present in a specimen.[10,11] Brown et al. demonstrated similar Ct values in infected individuals regardless of vaccination status. When evaluating our robust national dataset, findings like the CDC publication were identified across all variants of concern. Median Ct values for variants of concern, as well as the aggregate group containing "Other" variants, by vaccination status are reported in Table 4. Ct values included in this table were determined through testing completed via the Thermo Fisher™ TaqPath COVID-19 Combo Kit, an assay containing three probes that are specific to the SARS-CoV-2 target sequenced (ORF1ab, N Gene, S Gene).[12] Although not an absolute measure of transmissibility, the consistency amongst the Ct values between those that are infected regardless of vaccination status appear to demonstrate similar viral load. As more research is completed to aid in potential correlation of viral load and transmission, this may become a key measure in determining risk for spread among vaccinated and unvaccinated individuals.

Conclusion

The COVID-19 pandemic has taken a tremendous toll on both individual lives and the healthcare systems across the nation and world. Non-pharmacologic risk mitigation strategies and vaccinations have made significant progress in reducing viral transmission and deaths associated with SARS-CoV-2. It is essential to be mindful of viral spread to reduce the risk of infection. Aegis Sciences Corporation and Walgreens will continue to provide access to both testing resources and vaccines in the fight against the COVID-19 pandemic, as well as aggregation of available data to assist in public health surveillance. As we continue to fight an ever-changing illness, all available tools will be necessary to move us in a positive direction toward returning to our normal lives.

Table 1: Patient Demographic and Positive Genome Sequencing Results by State

State	Samples Sequenced	% of Total Sequenced	Median Age	% Male	% White	% Fully Vaccinated	% Not Vaccinated	% Symptomatic	% Delta Variant (B.1.617.2)
FL	7578	26.5%	34	47.0%	61.6%	18.4%	79.8%	72.0%	70.7%
CA	6774	23.7%	31	47.5%	44.6%	22.4%	75.9%	76.8%	74.6%
TX	2580	9.0%	33	48.6%	60.1%	22.3%	75.9%	75.8%	66.7%
IL	1007	3.5%	35	50.0%	57.3%	21.3%	76.3%	72.5%	34.8%
GA	773	2.7%	32	44.8%	37.0%	12.8%	85.3%	71.2%	54.9%
NC	673	2.4%	31	48.1%	47.3%	13.8%	83.8%	75.2%	55.7%
TN	576	2.0%	30	46.5%	53.3%	13.4%	84.9%	76.6%	47.2%
CO	573	2.0%	33	53.2%	72.8%	14.0%	83.9%	79.2%	41.0%
NJ	542	1.9%	33	47.8%	52.6%	19.9%	77.1%	64.9%	50.9%
MO	501	1.8%	33	46.9%	60.1%	20.6%	77.0%	76.8%	47.7%
MA	469	1.6%	31	50.5%	57.4%	26.9%	70.1%	74.8%	49.5%
AL	453	1.6%	31	45.5%	58.3%	14.6%	83.4%	80.8%	66.0%
MI	432	1.5%	33	46.3%	74.8%	11.8%	85.9%	74.8%	22.7%
MN	372	1.3%	33	46.8%	66.4%	14.8%	81.7%	77.2%	30.4%
LA	360	1.3%	34	45.6%	61.1%	21.1%	76.1%	78.3%	58.9%
OR	351	1.2%	33	48.4%	75.5%	19.9%	78.1%	77.8%	37.9%
UT	347	1.2%	36	45.0%	77.8%	20.2%	79.3%	83.6%	70.6%
NV	341	1.2%	34	42.2%	51.0%	14.7%	84.2%	80.6%	78.9%
MD	315	1.1%	33	46.7%	37.5%	23.8%	74.6%	70.5%	45.4%
AZ	307	1.1%	35	46.6%	61.2%	15.3%	81.4%	75.9%	59.0%
NY	248	0.9%	31	42.7%	56.0%	22.6%	75.8%	65.7%	34.7%
OH	247	0.9%	32	52.2%	61.5%	14.2%	81.8%	74.1%	32.4%
PR	246	0.9%	29	52.4%	48.8%	32.1%	65.9%	49.2%	43.9%
WI	245	0.9%	33	45.7%	78.0%	29.0%	70.6%	80.0%	54.3%
IN	237	0.8%	36	46.4%	63.3%	15.6%	83.5%	84.0%	46.0%
AR	211	0.7%	29	50.2%	52.1%	14.7%	83.9%	75.4%	64.5%
PA	172	0.6%	32	51.2%	57.6%	12.2%	83.7%	75.0%	30.2%
WV	166	0.6%	33	55.4%	92.8%	11.4%	85.5%	75.9%	18.1%
MS	160	0.6%	30	45.6%	44.4%	11.3%	87.5%	75.6%	36.3%
OK	147	0.5%	32	47.6%	64.6%	20.4%	78.9%	79.6%	51.0%
SC	138	0.5%	35	45.7%	61.6%	13.8%	85.5%	77.5%	65.2%
KS	129	0.5%	30	48.1%	69.8%	19.4%	76.0%	85.3%	54.3%
KY	123	0.4%	34	47.2%	74.8%	17.9%	80.5%	82.9%	48.0%
VA	100	0.3%	33	44.0%	67.0%	39.0%	59.0%	70.0%	65.0%
NM	92	0.3%	31.5	48.9%	75.0%	19.6%	80.4%	82.6%	47.8%
IA	90	0.3%	35.5	51.1%	75.6%	21.1%	78.9%	83.3%	60.0%
NE	75	0.3%	30	37.3%	68.0%	18.7%	78.7%	86.7%	30.7%
MT	64	0.2%	32	51.6%	78.1%	18.8%	79.7%	76.6%	48.4%
CT	56	0.2%	27.5	37.5%	69.6%	32.1%	67.9%	82.1%	53.6%
HI	49	0.2%	23	51.0%	36.7%	2.0%	98.0%	16.3%	55.1%
RI	46	0.2%	29	37.0%	58.7%	30.4%	67.4%	78.3%	45.7%
WY	43	0.2%	35	51.2%	86.0%	7.0%	90.7%	88.4%	37.2%
ID	41	0.1%	38	56.1%	87.8%	17.1%	78.0%	65.9%	56.1%
ME	39	0.1%	35	53.8%	94.9%	20.5%	76.9%	64.1%	43.6%
DE	27	0.1%	30	44.4%	66.7%	11.1%	88.9%	70.4%	40.7%
AK	21	0.1%	36	71.4%	71.4%	23.8%	71.4%	76.2%	52.4%
WA	21	0.1%	31	71.4%	85.7%	19.0%	81.0%	57.1%	61.9%
NH	20	0.1%	25	50.0%	80.0%	35.0%	60.0%	70.0%	30.0%
SD	16	0.1%	34.5	37.5%	56.3%	18.8%	81.3%	93.8%	75.0%
DC	<10	0.0%	39	44.4%	22.2%	33.3%	66.7%	33.3%	44.4%
VT	<10	0.0%	34	0.0%	57.1%	28.6%	71.4%	28.6%	57.1%
VI	<10	0.0%	17	0.0%	0.0%	0.0%	100.0%	0.0%	0.0%

Figure 1: Percent of Unvaccinated Among Positive Cases by State

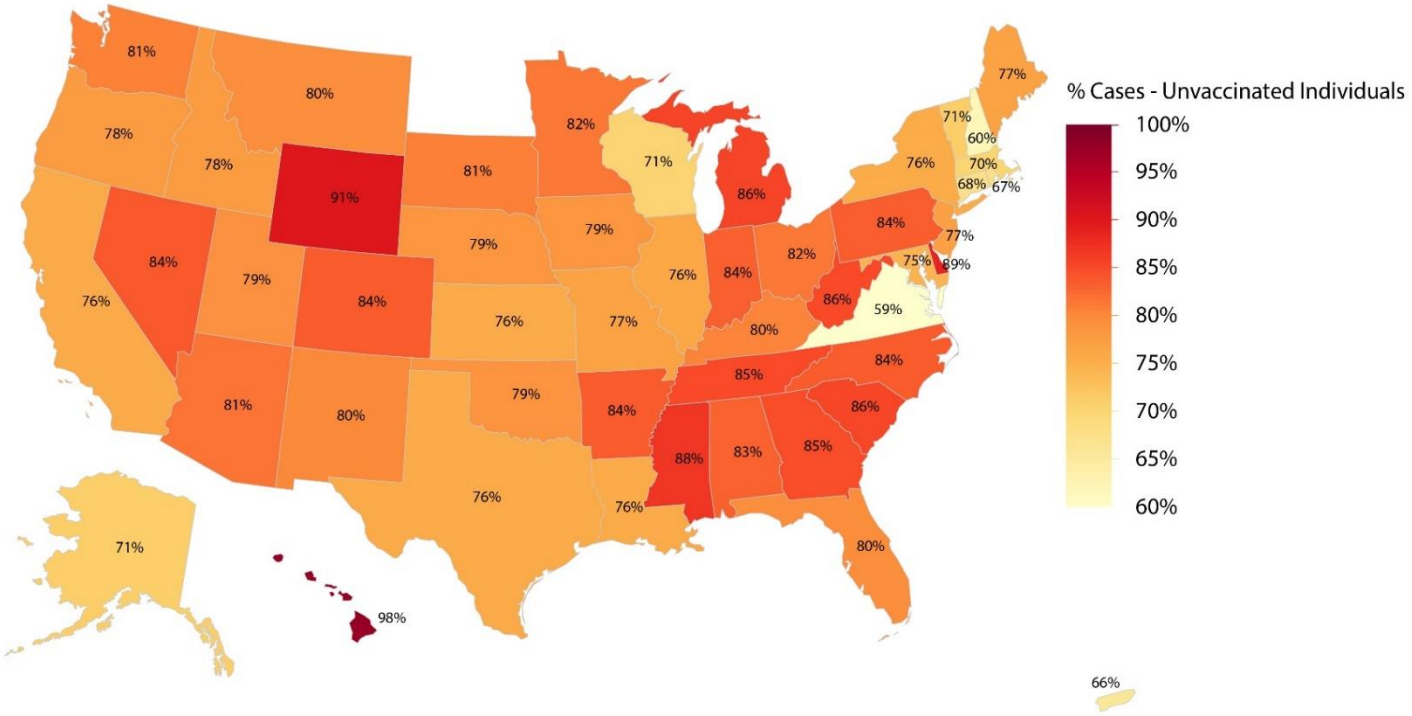
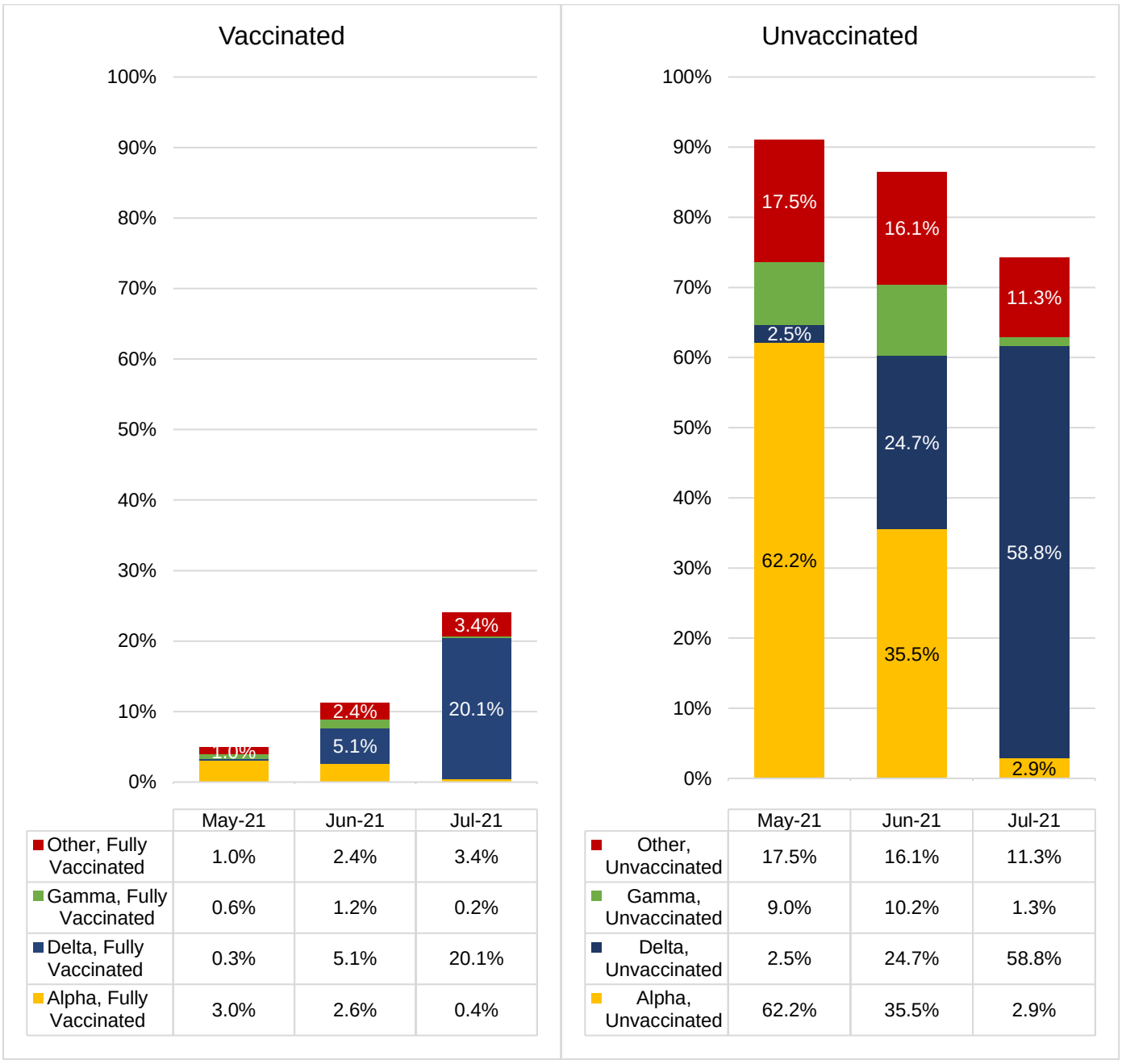


Figure 2: Prevalence of Cases Identified by Month, Lineage, and Vaccination Status



	May-21	Jun-21	Jul-21
Other, Fully Vaccinated	1.0%	2.4%	3.4%
Gamma, Fully Vaccinated	0.6%	1.2%	0.2%
Delta, Fully Vaccinated	0.3%	5.1%	20.1%
Alpha, Fully Vaccinated	3.0%	2.6%	0.4%

	May-21	Jun-21	Jul-21
Other, Unvaccinated	17.5%	16.1%	11.3%
Gamma, Unvaccinated	9.0%	10.2%	1.3%
Delta, Unvaccinated	2.5%	24.7%	58.8%
Alpha, Unvaccinated	62.2%	35.5%	2.9%

* Beta Variant (B.1.351) not included due to low frequency of detection

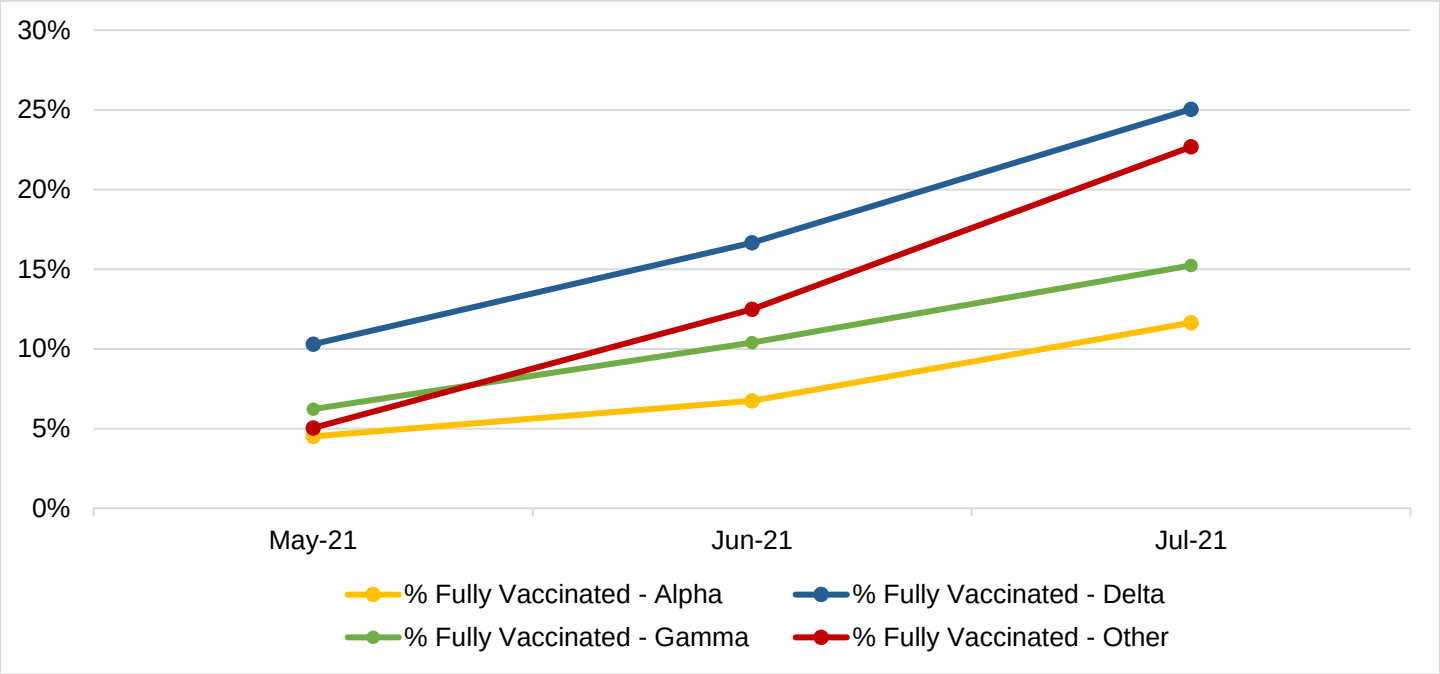
** Does not include proportion of cases in partially vaccinated individuals (Unvaccinated: n=22,469, Partially Vaccinated: n=555, Fully Vaccinated: n=5,586)

Table 2: Symptom Frequency and Percent by Lineage and Vaccination Status

Lineage Category	Fully Vaccinated, Asymptomatic	Fully Vaccinated, Symptomatic	Unvaccinated, Asymptomatic	Unvaccinated, Symptomatic
Alpha (B.1.1.7)	100 (32.7%)	206 (67.3%)	1,335 (28.7%)	3,315 (71.3%)
Beta (B.1.351)	2 (100%)	0 (0%)	8 (21.6%)	29 (78.4%)
Delta (B.1.617.2)	911 (21.0%)	3,426 (79.0%)	3,093 (23.6%)	9,996 (76.4%)
Gamma (P.1)	32 (27.6%)	84 (72.4%)	288 (28.5%)	724 (71.5%)
Other	210 (25.5%)	615 (74.5%)	1,114 (30.3%)	2,567 (69.7%)

* Does not include proportion of cases in partially vaccinated individuals (Unvaccinated: n=22,469, Partially Vaccinated: n=555, Fully Vaccinated: n=5,586)

Figure 3: Prevalence of Infections by Lineage in Vaccinated Individuals



* Beta Variant (B.1.351) not included due to low frequency of detection

Table 3: Other Variants by Frequency and Vaccination Status

Lineage	Samples Sequenced	% of Total in Other" Category	% Identified in Fully Vaccinated Patients	% Identified in Unvaccinated Patients
AY.3	1,656	36.2%	**23.0%**	75.2%
B.1.526	568	12.4%	6.7%	91.4%
B.1.621	388	8.5%	**26.3%**	70.1%
B.1	247	5.4%	8.9%	88.7%
AY.2	166	3.6%	12.7%	86.7%
AY.3.1	164	3.6%	**22.0%**	77.4%
B.1.575	136	3.0%	**24.3%**	71.3%
B	136	3.0%	19.1%	80.1%
B.1.526.1	115	2.5%	2.6%	93.9%
B.1.526.2	92	2.0%	1.1%	95.7%
B.1.621.1	89	1.9%	**24.7%**	73.0%
C.37	79	1.7%	8.9%	91.1%
B.1.623	64	1.4%	**21.9%**	75.0%
B.1.36.10	63	1.4%	**20.6%**	76.2%
B.1.628	60	1.3%	6.7%	88.3%
B.1.1.318	50	1.1%	16.0%	84.0%
AY.1	48	1.1%	**52.1%**	47.9%
B.1.429	46	1.0%	2.2%	91.3%
B.1.427	45	1.0%	11.1%	80.0%
B.1.1.519	43	0.9%	4.7%	90.7%

***Bold ≥ 20%**

** Does not include proportion of cases in partially vaccinated individuals (Unvaccinated: n=22,469, Partially Vaccinated: n=555, Fully Vaccinated: n=5,586)

Table 4: Ct values by Genome Target and Vaccination Status

Lineage Category	ORF1ab, Fully Vaccinated (Median)	ORF1ab, Unvaccinated (Median)	N Gene, Fully Vaccinated (Median)	N Gene, Unvaccinated (Median)
Alpha (B.1.1.7)	18.31	17.66	17.66	17.36
Beta (B.1.351)	21.93	16.94	23.30	17.94
Delta (B.1.617.2)	15.93	15.99	16.26	16.41
Gamma (P.1)	18.37	18.11	18.47	17.98
Other	17.73	17.64	18.24	18.27

* Does not include proportion of cases in partially vaccinated individuals (Unvaccinated: n=22,469, Partially Vaccinated: n=555, Fully Vaccinated: n=5,586)

** TaqPath RT-PCR COVID-19 Kit - containing the COVID-19 Real Time PCR Assay Multiplex, that include the three primer/probe sets specific to different SARS- CoV-2 genomic regions (Gene Orf-1ab, N Protein, S Protein); Ct values for S protein not included due to dropouts caused by certain variants (especially Alpha)

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Authors:
Josh Schrecker, Pharm.D., Director, Clinical Affairs, Aegis Sciences Corporation
Michael S. Taitel, PhD, Senior Director, Walgreens Center for Health & Wellbeing Research, Walgreens

For more information contact:
info@aegislabs.com or Research@Walgreens.com