ORIGINAL ARTICLE

Effectiveness and use of reverse transcriptase polymerase chain reaction point of care testing in a large-scale COVID-19 surveillance system

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Abstract

Background: Rapid COVID-19 testing platforms can identify infected individuals at the point of care (POC), allowing immediate isolation of infected individuals and reducing the risk of transmission. While lab-based nucleic acid amplification testing (NAAT) is often considered the gold standard to detect SARS-CoV-2 in the community, results typically take 2–7 days to return, rendering POC testing a critical diagnostic tool for infection control. The National Football League (NFL) and NFL Players Association deployed a new POC testing strategy using a newly available reverse transcriptase polymerase chain reaction (RT-PCR) rapid test during the 2020 season, and evaluated diagnostic effectiveness compared to other available devices using real-world population surveillance data.

Methods: RT-PCR POC test results were compared to NAAT results from same-day samples by calculation of positive and negative concordance. Sensitivity analyses were performed for three subgroups: (1) individuals symptomatic at time of positive test; (2) individuals tested during the pilot phase of rollout; and (3) individuals tested daily.

Results: Among 4989 same-day POC/NAAT pairs, 4957 (99.4%) were concordant, with 93.1% positive concordance and 99.6% negative concordance. Based on adjudicated case status, the false negative rate was 0.2% and false positive rate was 2.9%. In 43 instances, the immediate turnaround of results by POC allowed isolation of infected individuals 1 day sooner than lab-based testing. Positive/negative concordance in sensitivity analyses were relatively stable.

Conclusion: RT-PCR POC testing provided timely results that were highly concordant with lab-based NAAT in population surveillance. Expanded use of effective RT-PCR POC can enable rapid isolation of infected individuals and reduce COVID-19 infection in the community.

KEYWORDS
agile analytics, COVID-19, diagnostic concordance, diagnostics, emergency use authorization, infectious disease surveillance, point-of-care testing, real-world data, real-world evidence, SARS-CoV-2

Key Points
- Reverse transcriptase polymerase chain reaction (RT-PCR) point of care tests became available later in the 2020 COVID-19 pandemic and demonstrated high concordance with lab-based nucleic acid amplification testing (NAAT), performing significantly better than antigen point of care (POC) assay in broad surveillance settings and presymptomatic individuals.
- Real-world evidence collected through routine surveillance of over 10 000 NFL players and staff in 2020 allowed key insights into the effectiveness of this new diagnostic.
- Point-of-care RT-PCR provided an early signal of infection, allowing for prompt isolation ahead of pending NAAT result.
- Expanded use of effective RT-PCR POC can enable rapid isolation of infected individuals and may reduce community transmission of COVID-19.
- Real-world evidence from this cohort is applicable to other occupational and large-scale surveillance settings.

Plain Language Summary
Lab-based COVID-19 testing in the community can take 2–7 days to return, creating a challenge to prevent spread of infection. Point-of-care (POC) rapid tests allow for immediate detection and isolation of infected individuals. The National Football League (NFL) and NFL Players Association used a newly available RT-PCR rapid test during the 2020 season. Using data from real-world operations, the effectiveness of the rapid testing device was compared to the lab-based nucleic acid amplification testing (NAAT) using positive and negative concordance and comparing to an adjudicated COVID-19 case status. Among 4,989 same-day test pairs, 99.4% were concordant, with 93.1% positive concordance and 99.6% negative concordance. Based on adjudicated case status, the false negative rate was 0.2% and false positive rate was 2.9%. In 43 instances, the immediate turnaround of results by POC allowed isolation of infected individuals one day sooner than lab-based testing. Because of high concordance between lab-based testing and RT-PCR POC, which allowed for immediate isolation, RT-PCR POC is a useful tool for community infection control.

1 | INTRODUCTION

As with many industries, the COVID-19 pandemic significantly impacted professional athletics around the world. Some leagues canceled seasons, some utilized isolated "bubbles,"[1] while others implemented mitigation strategies and proceeded through their seasons with some level of disruption due to canceled or postponed games.

The National Football League (NFL) successfully played all 269 games of the 2020 season due to risk mitigation strategies applied throughout their facilities, educational efforts for athletes and staff, and a focus on aggressive testing for early identification of COVID-19 infection to limit the risk of large outbreaks through isolation of infected individuals and quarantine of close contacts.[2] As part of the COVID-19 strategies, the NFL and National Football League Players Association (NFLPA) conducted daily nucleic acid amplification (NAAT) tests among players and most staff throughout the 2020 season, with a point of care (POC) test used as an additional tool on a for-cause basis or when NAAT results were not available.[3]

POC testing is an attractive surveillance strategy due to the speed with which results are returned, allowing for interventions to be more rapidly deployed to mitigate the spread of COVID-19. The most prevalent platform for POC testing is antigen testing; however, multiple studies across different populations have demonstrated that antigen testing is not as sensitive as NAAT methods, particularly in early stages of infection and asymptomatic populations.[4–6]

At the beginning of the NFL/NFLPA COVID-192020 monitoring program, an antigen-based platform was used primarily for POC testing for the first 4 months (mid-July through late November) of the NFL season. After observing a low positive predictive value and high rate of false negatives in asymptomatic individuals with a specific antigen-based POC test during this time, the NFL sought to replace antigen POC testing with a rapid reverse transcriptase polymerase chain reaction (RT-PCR) diagnostic device.[3,7,8] Accordingly, the NFL/NFL Players Association transitioned the rapid test method from antigen-based to an RT-PCR POC, utilizing the Mesa Accula platform.[9] This diagnostic was made available under FDA Emergency Use Authorization (EUA), with large-population effectiveness unknown.

The clinical performance of the Accula has been validated and published both in EUA documentation[9] as well as a clinical study with primarily symptomatic patients[10]; however, performance in a real-world setting of a low-prevalence, largely pre/asymptomatic population has not been well established, nor has the impact of having a 1 h turnaround time compared to 24 h. The objective of this study was to measure concordance between an RT-PCR POC platform and same-

day NAAT tests, as well as clinically adjudicated outcomes, evaluating the POC platform's use an effective diagnostic tool for broad population surveillance and case finding.

2 | METHODS

2.1 | Population, time frame and data collection

The NFL/NFLPA COVID-19 testing and monitoring program, conducted within a closed cohort of more than 10 000 individuals, produced curated real-world evidence (RWE) that enables evaluation of newly approved COVID diagnostics.[11]

Briefly, NFL players and Club staff lived at home and underwent frequent, and in most cases, daily, 24-h turnaround NAAT testing for the entirety of the season (mid-July 2020 through playoffs elimination, between January and February 7, 2021).

RT-PCR point-of-care testing using the Accula device was available to Clubs starting on November 5, 2020. The NFL conducted a pilot phase across five Clubs from November 9 to November 18, 2020, at which time RT-PCR POC was used directly alongside NAAT (same-day dual tests). After the pilot phase completed, RT-PCR POC served as the primary POC test for the NFL COVID-19 program starting December 1, 2020, used for-cause in conjunction with the frequent NAAT testing. This study covers November 5, 2020 through the end of the regular season (January 2, 2021).

In an effort to limit infection spread in the event of a COVID-19 case, players and staff were placed into three predefined tiers based on anticipated time of interaction with players and each other; facility access and interaction among individuals was limited by tier. Tier 1 included players and essential personnel whose job function required direct access to players, such as coaches and athletic trainers. Other essential personnel who may be in occasional proximity to players and other tier 1 persons, such as some kitchen staff and video personnel, were categorized as tier 2. Persons who administered facility or event services but did not require regular access and/or close contact with essential personnel were categorized as tier 3.[3] Players and all staff were required to adhere to infection mitigation protocols, including restrictions both inside and outside the Club facility.

Test results were collected directly through a central test provider (BioReference Laboratories) and sent to a curated database linking results to demographic, contact tracing and clinical information (described in detail elsewhere[2,3,12]). Symptom information was collected at the time of a positive test result; symptomology was not systematically collected over the course of infection. Data were reviewed for quality and completeness and adjudicated with the lab provider when missingness or errors were detected.[13]

2.2 | Testing program

During this study's timeframe, players and Tier 1 and 2 staff were tested daily with NAAT. Tier 3 staff tested at least weekly or more frequently if circumstances required (e.g., symptomatic, COVID-19 exposure, schedule/responsibility change). Consistent with CDC guidelines in 2020, individuals with documented NAAT confirmation of prior COVID-19 were not required to test in the 90 days following infection.[3]

NAAT tests (Roche cobas, Hologic Panther, or Thermo Fisher QuantStudio) served as primary testing platforms, with availability within 24 h and similar PPVs in this real-world setting.[3] Throughout the season, either antigen or RT-PCR POC rapid tests were available and used for-cause, as dictated by circumstances for an individual of any Tier such as (1) recent potential exposure based on self-report or contact tracing (e.g., high-risk close contact[2]), (2) receipt of a positive test result (confirmatory as part of adjudication process[3]), (3) prior to facility entry in the event of delayed, invalid or unavailable NAAT results from the prior day's sample or (4) moderate pre-test probability of infection based on cases detected in the team environment or clinical concern for infection from the team's infection control officer or another medical professional. Results were available within 1 h for the POC, with all positive lab samples confirmed with subsequent testing and clinical adjudication.[3] Players and staff who were tested for cause but had a negative RT-PCR POC test were allowed to continue with their duties, when practical and as advised by team medical staff, pending their NAAT results.

2.3 | Pilot phase

The pilot phase of RT-PCR POC (November 9–18, 2020) included 135 individuals across five Clubs. During this time, individuals provided two samples each day, with one run on the RT-PCR POC platform and one on Roche cobas. The RT-PCR POC served as the primary rapid test at this time (instead of an antigen test, which was used prior to the pilot) for for-cause use alongside a NAAT. After the pilot, during which RT-PCR POC testing was observed to be reliable with improved performance over antigen tests, RT-PCR POC was implemented across all Clubs as the primary POC testing platform across the NFL.

The NFL/NFLPA's COVID-19 testing partner, BioReference Laboratories, oversaw virtual and hands-on training of all test operators as well as validation of point-of-care test docks. Competencies evaluated included sample collection, analysis, and results interpretation.[9] Two individuals were required to review and agree upon cassette outputs and result confirmation.

2.4 | Outcome measures

Individuals who tested positive on any test (NAAT or RT-PCR POC) were treated as COVID-19 cases and isolated while cases were medically adjudicated. Symptoms at the time of positive test result were documented by medical staff. COVID-19 case adjudication was performed by a medical committee based on a standardized algorithm (published in detail elsewhere) that considered all of the following: (1) NAAT results (initial positive and systematically collected

subsequent day samples); (2) RT-PCR POC results if available; and (3) symptoms, noting that any positive test with accompanying symptoms was considered a case of COVID-19.[3,13] This medically adjudicated case status using multiple test results was deemed the gold standard in the analysis, rather than a single NAAT test result, due to known imperfect sensitivity and specificity of both the NAAT and RT-PCR POC platforms,[9,14–16] indicating possibility for false negatives and false positives for a single test, and the desire to minimize the isolation of healthy personnel. Any ambiguous combination of positive and negative test results in an individual without symptoms was reviewed by a panel of medical experts and epidemiologists to determine a final case status.

2.5 | Statistical analyses

We compared RT-PCR POC test results to NAAT results from same-day samples collected and calculated both positive concordance (proportion of positive NAAT tests with a positive RT-PCR POC result) and negative concordance (proportion of negative NAAT tests with negative RT-PCR POC) and 95% confidence intervals.[3] NFL/NFLPA testing protocols considered a positive, presumptive positive or inconclusive NAAT result as a positive result.

The adjudicated case status was used to determine whether the RT-PCR POC or NAAT result aligned with the true result.[3] We calculated the proportion and 95% confidence intervals for false positives and negatives within same day RT-PCR POC and NAAT discordant pairs based on the adjudicated case status. In instances in which there were multiple pairs of same-day RT-PCR POC and NAAT for the same case, infection status ("diagnosis") was assigned with priority as follows: (1) initial NAAT-positive on same day as RT-PCR POC/NAAT pair; (2) initial NAAT-positive on day prior to RT-PCR POC/NAAT pair; (3) initial NAAT-positive on days subsequent to RT-PCR POC/NAAT pair (with first subsequent day as highest priority and third subsequent day as lowest priority).

In instances of a positive Roche cobas test on the same day as an RT-PCR POC test, we calculated descriptive statistics of cycle threshold (Ct) values for Target 1 (ORF1), stratified by RT-PCR POC result (i.e., true positive, false negative). The Ct is the number of RNA amplification cycles required for the instrument to detect a positive sample (i.e., Ct is inversely correlated with viral load in the sample).[17] The RT-PCR POC/NAAT same-day pair with earliest test date per case was selected for analysis.

To test the robustness of conclusions against in-season evolution of the NFL/NFLPA testing program and potential heterogeneity in the testing population, we performed three sensitivity analyses[13]:
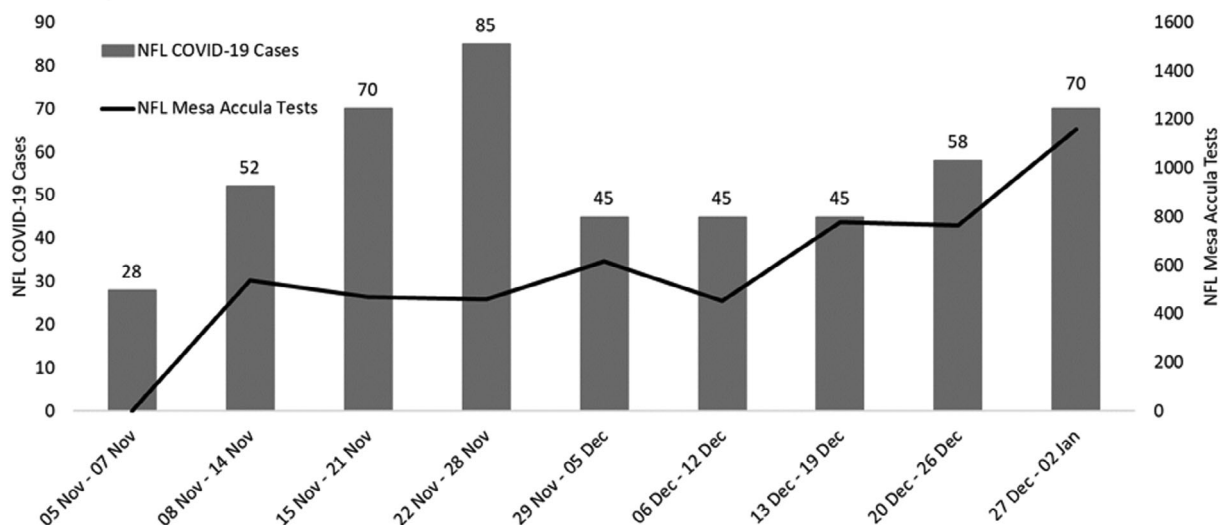

FIGURE 1 COVID-19 incidence and RT-PCR POC testing by week in the NFL (November 05, 2020–January 02, 2021). NFL, National Football League; POC, point of care; RT-PCR, reverse transcriptase polymerase chain reaction

TABLE 1 Same-day RT-PCR POC and NAAT Concordance[a,b] (November 05, 2020–January 02, 2021)

	Positive NAAT N = 204	Negative NAAT N = 4785	Total N = 4989
Positive RT-PCR POC	190 (93.1% [89.7–96.6%])	18 (0.4% [0.2–0.6%])	208 (4.2%)
Negative RT-PCR POC	14 (6.9% [3.4–10.3%])	4767 (99.6% [99.5–99.8%])	4781 (95.8%)

Abbreviations: NAAT, nucleic acid amplification testing; POC, point of care; RT-PCR, reverse transcriptase polymerase chain reaction.
[a]Concordance [95% Confidence Interval] indicates agreement between RT-PCR POC and NAAT. It does not reflect final case status.
[b]These data are restricted to same-day tests; an individual may have had multiple same-day test pairs.

FIGURE 2 Target 1 (ORF1) Ct values for same-day NAAT (Roche cobas) by RT-PCR POC test result against adjudicated case status (November 05, 2020–January 02, 2021). Ct, cycle threshold; Max, maximum; Min, minimum; NAAT, nucleic acid amplification testing; ORF1, cycle threshold values for Target 1; POC, point-of-care; RT-PCR, reverse transcriptase polymerase chain reaction; SD, standard deviation
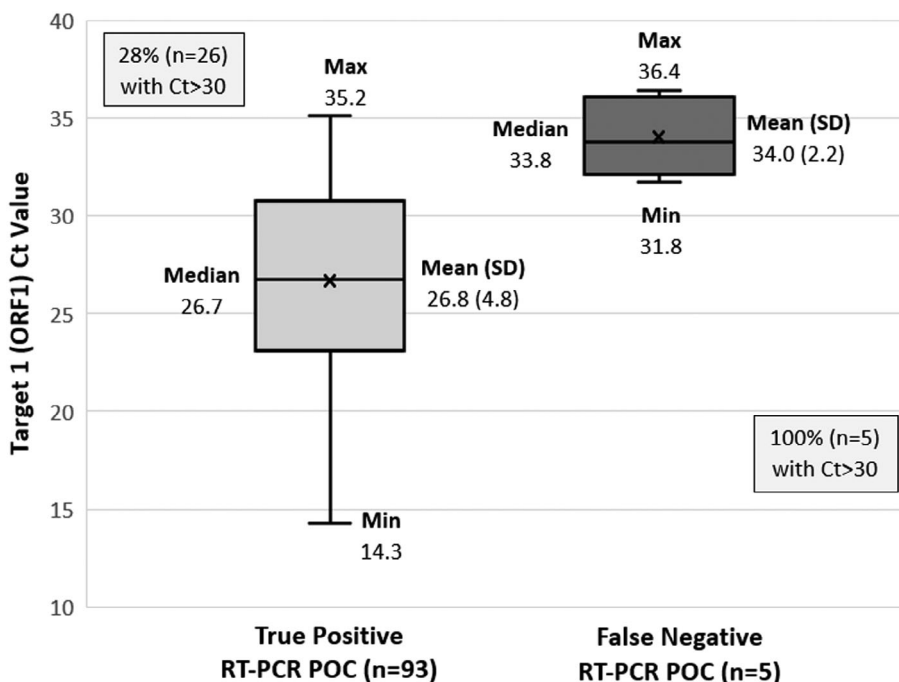

TABLE 2 Sensitivity analyses: comparison of RT-PCR POC and NAAT results for specific subpopulations

Population[a] (Number of same-day RT-PCR POC/NAAT test pairs)	% Positive concordance [95% CI](# positive RT-PCR POC-positive NAAT pairs/# positive NAAT tests)	% Negative concordance [95% CI](# negative RT-PCR POC-negative NAAT pairs/ # negative NAAT tests)	False negatives [95% CI][b] (# negative RT-PCR POC-positive NAAT pairs for true cases/# negative RT-PCR POC tests)	False positives [95% CI][b](# positive RT-PCR POC-negative NAAT pairs for non-cases/# positive RT-PCR POC tests)
entire population	93.1% [89.7–96.6%]	99.6% [99.5–99.8%]	0.2% [0.1–0.3%]	2.9% [0.6–5.2%]
(n = 4989)	(190/204)	(4767/4785)	(10/4781)	(6/208)
Individuals with a positive NAAT test result; Stratified by Symptoms at time of result				
Symptomatic at first positive (n = 77)	97.3% [93.6–100.0%] (72/74)	33.3% [0.0–86.7%] (1/3)	66.7% [13.3–100.0%] (2/3)	N/A[c]
Presymptomatic/ asymptomatic at first positive (n = 143)	90.1% [84.3–95.9%] (91/101)	92.9% [85.1–100.0%] (39/42)	16.3% [6.0–26.7%] (8/49)	N/A[d]
Comparison of pilot testing phase (RT-PCR POC performed alongside NAAT from November 9 to 18, 2020) with non-pilot group testing for cause (November 5, 2020 to January 2 2021)				
Pilot group[e] (n = 851)	100.0% [N/A] (8/8)	100.0% [N/A] (843/843)	0.0% [N/A] (0/843)	0.0% [N/A] (0/8)
Non-pilot group testing performed for-cause[f] (n = 4138)	91.4% [87.5–95.3%] (180/197)	99.5% [99.3–99.8%] (3923/3941)	0.3% [0.1–0.4%] (10/3940)	3.0% [0.6–5.4%] (6/198)
Individuals testing daily on NAAT due to their employment role (Tier)				
Tier 1 & 2 Only (e.g., in daily NAAT testing protocol)[g] (n = 4748)	91.3% [87.3–95.2%] (178/195)	99.6% [99.5–99.8%] (4536/4553)	0.2% [0.1–0.4%] (10/4553)	3.1% [0.7–5.0%] (6/195)

Abbreviations: NAAT, nucleic acid amplification testing; POC, point of care; RT-PCR, reverse transcriptase polymerase chain reaction.

[a]See Figure S1.

[b]Based on adjudicated case status.

[c]The case adjudication algorithm classified any symptomatic individual testing positive on a NAAT platform as a confirmed case of COVID-19 (noting that individuals who had recently recovered from COVID-19 were not in the testing pool). Therefore, no positive NAAT results for symptomatic individuals were considered false positives.

[d]Due to differential missingness in symptom information for cases compared to non-cases, rate of false positives not calculated.

[e]Pilot group testing includes RT-PCR POC tests done alongside NAAT (same day) across five select Clubs from November 9 to November 18, 2020.

[f]Non-pilot group testing includes RT-PCR POC tests performed for-cause when RT-PCR POC was in operational use after the pilot phase ended on November 18, 2021 (all 32 Clubs) or use at any time in the study period among the non-pilot Clubs.

[g]Tier 1 & 2 only included RT-PCR POC tests for-cause (n = 3897) and daily during the pilot study (n = 851); these represent individuals likely tested earlier in infection (i.e., likely with lower viral load).

(1) symptomatic vs. asymptomatic at the time of positive NAAT result; (2) pilot testing phase (described above); and (3) individuals in Tier 1/Tier 2 only (i.e., daily testers with a likely low viral load at the time of testing).

This analysis was conducted in accordance with the NFL/NFLPA Medical Research Approval Protocol[3] and determined exempt by Advarra Institutional Review Board.

3 | RESULTS

From November 5, 2020 through January 2, 2020, 10 634 players and staff were tested by NAAT or RT-PCR POC, with 498 cases of COVID-19 identified during the time frame (Figure 1). There were 4989 same-day pairs of NAAT and RT-PCR POC tests among 2127 individuals; 203 individuals with an adjudicated case of COVID-19 had at least one same-day pair of NAAT and RT-PCR POC; 3271 (66%) of the same-day pairs were performed on a Roche cobas platform, vs. 34% that were on qualitative platforms (Hologic or Thermo Fisher); these 3271 same-day pairs had Ct values if the test was positive, allowing examination of approximate viral load.[18]

3.1 | Same-day concordance

Among the 4989 same-day RT-PCR POC/NAAT pairs, 4957 (99.4%) were concordant, with positive concordance of 93.1% [89.7–96.6%] (190/204) and negative concordance 99.6% [99.5–99.8%] (4767/4785) (Table 1). Thirty-two same-day pairs (0.6%) were discordant. In the 14 instances in which NAAT was positive and RT-PCR POC was negative, 10 were adjudicated as confirmed COVID-19 cases and 4 were determined not to have COVID-19, meaning 10 of 4781 negative RT-PCR POC results (0.2% [0.1–0.3%]) were false negatives. In the 18 instances in which RT-PCR POC was positive and NAAT was negative, 12 were determined to be true COVID-19 cases, and six (2.9% [0.6–5.2%] of all positive RT-PCR POC tests) were false positive results.

Among the 190 instances in which RT-PCR POC and NAAT were both positive, 43 (23%) had no positive NAAT in the prior 7 days, meaning RT-PCR POC was the first signal of infection due to the 24-h turnaround of NAAT testing (i.e., NAAT result was still pending at time of RT-PCR POC receipt).

Among the 93 true positive RT-PCR POC tests with a NAAT on Roche, Ct values ranged from 14.3 to 35.2, with a median of 26.8 and mean (SD) of 26.7 (4.8). In the five instances where RT-PCR POC did not detect infection (i.e., false negatives) on the same day that the Roche sample tested positive, sample Ct values ranged from 31.8 to 36.4, with a median of 33.8 and mean (SD) of 34.0 (2.2) (Figure 2).

3.2 | Sensitivity analyses

RT-PCR POC was positive in 72 of the 74 RT-PCR POC-NAAT pairs among symptomatic individuals with a positive NAAT test result, yielding 97.3% [93.6%–100.0%] positive concordance (Table 2). Of the 101 RT-PCR POC-NAAT pairs among pre/asymptomatic individuals with a positive NAAT test result, 91 were RT-PCR POC positive, yielding 90.1% [84.3%–95.9%] positive concordance; however, the false negative rate was higher in this subsample of tests among individuals who already had a positive NAAT test compared to the full population, a metric which is limited by small sample size. All 851 test pairs in the pilot group (routine surveillance testing) agreed (100% RT-PCR POC-NAAT concordance), and there were no false negative or false positive tests. Among the 4138 RT-PCR POC-NAAT pairs performed for-cause, typically due to potential exposure, 180 had positive RT-PCR POC out of 197 positive NAATs, yielding 91.4% [87.5%–95.3%] positive concordance; negative concordance was higher at 99.5% [99.3%–99.8%].

Among test pairs in individuals testing with NAAT daily (e.g., those likely caught earlier infection with potentially lower viral load at time of first positive test; $n = 4748$), 178 had positive RT-PCR POC out of 195 total positive NAATs for 91.3% [87.3%–95.2%] positive concordance; negative concordance was 99.6% [99.5%–99.8%]. This subgroup's false negative and false positive rate was similar to the full population. In the 17 instances where RT-PCR POC was negative but NAAT was positive, the RT-PCR POC was a false negative for 10 and was a true negative (i.e., NAAT result was a false positive) for 7. In the 17 instances where RT-PCR POC was positive but NAAT was negative, the RT-PCR POC was a false positive for 6 and was a true positive (i.e., NAAT result was a false negative) for 11.

4 | DISCUSSION

The RT-PCR POC test provided timely and accurate results and had high concordance with traditional NAAT in the NFL cohort. In cases where the RT-PCR POC and NAAT platforms were concordant, the ability for the RT-PCR POC to provide results within 1 h compared to a 12–24 h wait time for NAAT results in the NFL setting—and often longer in population-based settings—almost certainly reduced the transmission of disease and enabled business continuity for the majority of individuals who tested negative on both.

Of particular importance, for the 43 instances where both RT-PCR POC and NAAT platforms were positive among individuals with seven consecutive days of negative tests prior to the initial positive, RT-PCR POC provided an early signal of infection, allowing for prompt isolation of the infected individual when they otherwise would have been in-facility due to unreturned positive NAAT result. This number of "early catches" may have even higher impact when RT-PCR POC replaces NAAT in routine monitoring settings (vs. for-cause based on exposure or symptom reports).

Sensitivity analyses restricted to individuals tested daily, and likely early infection at first positive, suggest that RT-PCR POC is a useful and accurate diagnostic tool for individuals with low-to-moderate pre-test probability of infection. RT-PCR POC was able to identify individuals with low CT values with similar sensitivity as traditional NAAT. This is particularly relevant in settings where individuals can wait for test results prior to engaging in activities that have high

transmission risk. The high concordance between RT-PCR POC and traditional NAAT, along with a low false negative rate for RT-PCR POC, suggests that RT-PCR POC results can be acted upon in place of NAAT.

Our analysis demonstrates that RT-PCR POC performed significantly better than antigen POC assay in this population with moderate pre-test probability. Taken in conjunction with our previously published study on our testing protocols,[3] our analysis demonstrates that RT-PCR POC testing was more sensitive to infection detection compared to antigen POC testing in this population with moderate pre-test probability. 42.3% of COVID-19 positive individuals in the NFL had a false negative antigen POC, but only 0.2% [0.1%–0.3%] had a false negative RT-PCR POC when collected at the same timepoint.[3] Additionally, although not a direct comparison, the false positive rate of antigen POC testing in the NFL was 35% compared to 2.9% [0.6%–5.2%] for the RT-PCR POC.[3]

Throughout the 2020 NFL season, scientific knowledge of COVID-19 detection and transmission evolved, with NFL/NFLPA protocols evolving accordingly, based both on CDC guidance, as well as real-time findings based on these data. For the POC test platforms, these frequent analytics and the resulting RWE around platform performance directly changed the on-the-ground testing protocols. For RT-PCR POC in particular, the observed high concordance performance in the November 2020 pilot led to the adoption of this test as the primary POC test for the remainder of the regular season. At the inception of the postseason (January through February), the RT-PCR POC test was used even more broadly, eventually serving in a pre-travel and broad surveillance capacity.

There are limitations to this study. Many individuals were tested "for-cause," and therefore had a moderate pre-test probability; PPV and NPV may not generalize to asymptomatic surveillance populations. Additionally, symptoms were not collected throughout course of illness; individuals labeled as pre/asymptomatic in this analysis may have developed symptoms. Due to differential missingness in symptom information for cases compared to non-cases (30%/60% missingness, respectively), the false positive rate for the asymptomatic subgroup may be biased. This 2020 study was prior to the prevalence of COVID-19 variants and availability of vaccinations; therefore, we cannot comment on RT-PCR POC performance specific to 2021 variants or among vaccinated individuals.

5 | CONCLUSION

RT-PCR POC testing was an effective POC test and performed well in this daily surveillance setting, allowing fast turnaround of accurate results very early in infection. RT-PCR rapid testing was an improvement from antigen point-of-care, as it was able to detect COVID-19 in both symptomatic and asymptomatic individuals, and in many cases, likely prevented transmission by providing a test

result within an hour, 1 day earlier than a NAAT test was able to be reported. We observed a low rate of false positives in this infection-naive population with a moderate pre-test probability of infection. The availability of this device and its observed high performance in 2020 are be extendable to other occupational and large-scale surveillance settings.

CONFLICT OF INTEREST

Christina D. Mack, Erin B. Wasserman, and Kalyani Hawaldar are full-time employees of IQVIA, which is in a paid consultancy with the NFL. Emily Myers and Allen Sills are full-time employees of the NFL, Gary Solomon is an NFL consultant and Thom Mayer is a full-time employee of the NFL Players Association. Deverick J. Anderson and Deverick J. Anderson are paid consultants to the NFL through Infection Control for Major Sports, LLC. Patti Walton, Michele Best, and Daniel Eichner are paid consultants of the NFL. No author received direct, individual payment for this work. No authors have financial or other interest in Mesa Biotech, any parent companies, or other conflicts of interest to report that are not listed here.

AUTHOR CONTRIBUTIONS

Christina D. Mack and Erin B. Wasserman designed the work and were responsible for data collection, analysis, and interpretation, and drafted the article. Kalyani Hawaldar was responsible for analysis and manuscript editing. Allen Sills designed and led the Program and contributed critical direction and major revisions to the work. Gary Solomon contributed critical direction and major revisions to the work. Deverick J. Anderson, Deverick J. Anderson, Emily Myers, Patti Walton, Michele Best, Daniel Eichner and Thom Mayer contributed to program design and operations, results interpretation, and editorial contributions to this manuscript.

ETHICS STATEMENT

This analysis was conducted in accordance with the NFL/NFLPA Medical Research Approval Protocol3 and determined exempt by Advarra Institutional Review Board.

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SUPPORTING INFORMATION

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