# Agreement Between SARS-CoV-2 PCR Test Results Using Nasopharyngeal and Mid-Turbinate Specimens Among Asymptomatic Working-Age Adults

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**Objective:** The aim of this study was to determine whether mid-turbinate specimens reliably detect active infection in asymptomatic adults undergoing regular COVID-19 PCR testing. **Methods:** Qualitative agreement between 2481 paired nasopharyngeal and mid-turbinate PCR results was assessed. Mean cycle threshold values for each positive result were evaluated as an indicator of active infection. **Results:** Overall agreement between nasopharyngeal and mid-turbinate tests was 98.4%. Positive percent agreement was 37.2%, and negative percent agreement was ~100%. Test pairs with lower cycle thresholds (≤30 and ≤25) reached 67% and 100% positive percent agreement, respectively. **Conclusions:** SARS-CoV-2 infections with high viral loads were detected regardless of specimen type. Mid-turbinate swabs reduced staff discomfort and may decrease repeated positive test results weeks or months after initial infection. Discordant pairs generally had high cycle threshold values (>30) indicating low viral load and little risk of transmitting COVID-19.

**Keywords:** PCR testing, nasopharyngeal, mid-turbinate, COVID-19, cycle threshold, asymptomatic

Nasopharyngeal (NP) specimens were considered the criterion standard for use with RT-PCR tests since early in the COVID-19 pandemic. Although less invasive mid-turbinate (MT) swabs were added to FDA Emergency Use Authorizations for PCR testing platforms over time, performance data provided by test manufacturers typically reflect only NP results.[1] Few studies have compared the sensitivity of SARS-CoV-2 RT-PCR test results between NP and MT specimens, and none has assessed comparative performance in an asymptomatic, working population.

During the COVID-19 pandemic, a 5-day quarantine followed by preflight SARS-CoV-2 RT-PCR testing has been routinely required for crew deploying to offshore oil and gas platforms, a setting that includes close proximity work and congregate living quarters. PCR tests are highly sensitive, with the ability to detect not only living virus but viral fragments as well, for up to 3 months after an individual is first infected.[2] However, only living, intact SARS-CoV-2 virus can cause COVID-19; if viral fragments are spread from one person to another, it will not result in disease spread.[3] A drawback of using PCR testing for preflight screening is that it may not distinguish a person who has recovered from COVID-19 but continues to shed viral fragments from a person actively infected and contagious to others. Given this, it is possible that using MT rather than NP specimens for PCR testing may be more fit-for-purpose in this setting; MT tests are less likely to detect very low viral loads, while still using the highly sensitive PCR testing platform.

The objectives of the study were (1) to determine whether MT specimens could reliably identify individuals with high likelihood of active infection, (2) to assess whether MT specimens were better able to discriminate between active and past COVID-19 infection, and (3) to compare reported level of comfort associated with NP versus MT swabbing.

## METHODS

The study population included crew deploying to assets in the Gulf of Mexico between October 2020 and January 2021 who agreed to the collection of an MT specimen in addition to the NP specimen required for preflight testing. Offshore staff members are instructed not to come to the preflight testing site if they are ill, and all are further screened for symptoms or recent SARS-CoV-2 exposure before specimen collection. It was therefore assumed that staff members who passed screening and proceeded to testing were asymptomatic. MT and NP specimens were collected sequentially by the medical service provider contracted to perform preflight COVID-19 testing, using procedures outlined by the US Centers for Disease Control and Prevention.[4] Trained medical personnel collected specimens at nine mobile collection sites, six in Louisiana and three in Texas. Specimens were clearly labeled to identify paired tests and analyzed at two laboratories in Louisiana using the Thermo Fisher Scientific TaqPath RT-PCR platform. Both laboratories hold a Clinical Laboratory Improvement Amendments certificate of accreditation from the US Centers for Medicare and Medicaid Services. To avoid contaminating the nasal cavity, MT specimens were collected first followed by NP specimens. Test results based on the NP specimen continued to serve as the basis of a fly or no-fly determination, regardless of study participation or the result of the MT swab PCR test.

Qualitative NP and MT results for each test pair were compared to assess positive percent agreement (PPA) and negative percent agreement (NPA). In addition, laboratories provided cycle threshold (Ct) values for each positive test, reflecting the number of amplifications necessary before SARS-CoV-2 was detected.[5] Ct values are inversely related to viral load; that is, the greater the viral content in the original specimen, the fewer amplifications required before the virus is detectable. In combination with clinical findings, Ct values can also help assess the likelihood of infectiousness,[3] especially when specimen collection follows a quarantine period. At the time of specimen collection, study subjects also scanned a QR code to their smart phone to complete an anonymous single question survey rating their level of discomfort from NP and MT swabbing on a scale of 1 (no discomfort) to 4 (severe discomfort).

### Analysis

Qualitative (positive/negative) NP and MT test results for each test pair were used to calculate an estimate of agreement using an approach recommended by the US Food and Drug Administration when a reference standard is not available; that is, the subject's true infection

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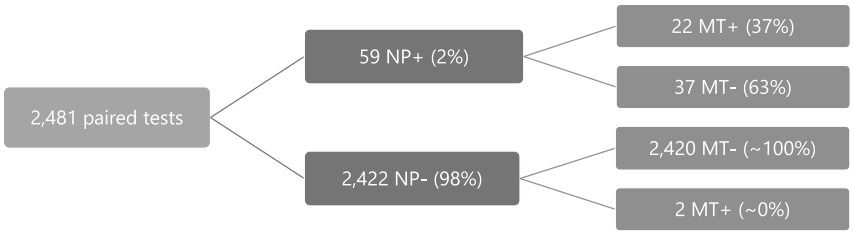


**FIGURE 1.** Summary of nasopharyngeal and mid-turbinate matched pair results.

status is unknown.[6] Results were summarized in a 2 × 2 table, and estimates of overall percent agreement, PPA (the proportion of NP swab positives that were also MT positive), and NPA (the proportion of NP negatives that were also MT negative) were calculated.

We further assessed PPA within high (mean Ct ≤ 25), intermediate (mean Ct = 26–30), and low (mean Ct > 30) viral load categories. In addition, prior preflight test results were checked for each positive subject to determine whether they had tested positive previously, and if so, the number of days between the two positive tests.

## RESULTS

A total of 1844 individuals participated in dual testing, and 637 participated more than once, resulting in 2481 unique testing episodes. Of these, 59 were positive on their NP test (NP+), and of these, 22 were also positive on their MT test (MT+), whereas 37 were MT negative (MT−, see Fig. 1). All but two NP− tests were also MT− (2420 of 2422). Overall agreement between NP and MT tests was 98.4%, whereas PPA was 37.2% and NPA was nearly 100%. Although PPA was moderate for the entire study population (37%), when restricted to those with mean Ct values ≤30 and ≤25, PPA between NP and MT PCR results increased to 67% and 100%, respectively (Table 1).

Full study results are shown in Figure 2, with markers indicating mean Ct values for each of the 59 NP+ subjects, and whether their paired MT tests were also positive (squares) or negative (circles). Among the 59 NP+ subjects, 18 had tested positive (NP+) previously (ie, repeat positives, discussed further below); four of these were MT+ ("POS-REP," light squares), and 14 were MT− ("NEG-REP," light circles).

All NP+ subjects with mean Ct values ≤25 (n = 15) were also MT+; that is, all high viral load individuals prevented from deploying offshore based on their NP specimen would have also been prevented from deploying had their MT specimen been used instead. Conversely, NP+ subjects with low viral loads (mean Ct > 30, n = 29) were MT− except for two repeat positives whose first tests had been 18 and 21 days earlier. These 29 NP+/MT− crew would have been prevented from deploying based on their NP specimens but cleared to fly had MT specimens been used instead.

Fifteen NP+ subjects had mean Ct values between 25 and 30 (ie, intermediate viral load), and the paired MT test for 10 of them was negative. These 10 individuals (circles in Fig. 2) would have been cleared to fly based on their MT test but not on their NP test, and the challenge is discerning whether they were early in their infectious period (detected when viral load was increasing) or late in their infectious period (detected when viral load was decreasing). The former would pose a transmission risk offshore while the latter likely would not.

### Repeat Positives

Eighteen of the 59 NP+ subjects had a previous preflight positive test, and 14 of these 18 were negative on their paired MT test during the study period (Fig. 3). There was little difference in mean Ct values between MT− and MT+ for these repeat positives; MT− (n = 14) mean Ct values ranged from 29 to 33, and MT+ (n = 4) mean Ct values ranged from 28 to 31. More than 10 days had passed between the first and second PCR tests for 17 of the 18 repeat positives, which at the time of the study was recommended by the Centers for Disease Control and Prevention for safely ending quarantine.[2] One individual was MT− only 9 days after first testing positive; however, mean Ct for both tests was 31.

### Questionnaire Results

Forty-three percent (n = 784) of subjects rated their level of comfort associated with the two specimen collection methods, and there was a strong preference for MT over NP swabs. As shown in Figure 4, 83% rated MT samples as having no or little discomfort, compared with 22% for NP samples. Conversely, 78% rated NP sample collection as moderately or severely uncomfortable, compared with 17% for MT sample collection.

## DISCUSSION

Based on our results, PCR testing in asymptomatic working-age adult populations has a high likelihood of detecting actively contagious individuals with either NP or MT specimens when combined with a 5-day quarantine, and the use of MT swabs may decrease the number of individuals repeatedly testing positive weeks or months after their initial infection. Those with the highest viral loads and likelihood of transmitting COVID-19 to others were detected regardless of whether an NP or MT swab was used. Individuals who were NP+ but MT− generally had high mean Ct values (>30), indicating low viral load and little risk of transmitting COVID-19 to others.

Although Ct values are inversely correlated with viral load, two issues complicate their use as a definitive indicator of infectiousness. First, high Ct values can be seen in both very early and late-stage infection. SARS-CoV-2 replicates quickly inside the body, and the amount of virus is already increasing exponentially once detected. As a result, COVID-19 has a short, early period of transmissibility,[5] with peak viral load at or just after the onset of symptoms, on average, 3 to 5 days postexposure.[7] However, although possible in the early days after exposure, a high Ct positive result is much more likely during the "long tail" after the infectious period has ended.[8] This underscores the importance of a robust quarantine period to reduce the potential for exposure just before testing.

Second, there is no definitive Ct cutoff to distinguish contagious and noncontagious individuals, although a Ct value 30 has been suggested.[9,10] Comparative studies of the Thermo Fisher TaqPath PCR platform indicate this cutoff may be even lower (Ct 25–27).[11,12] Thus, we

**TABLE 1.** Positive Percent Agreement Between Matched Testing Pairs, Overall, and by Mean Ct Subgroup

| | NP+ (all) | NP+ (Ct ≤ 30) | NP+ (Ct ≤ 25) |
|---|---|---|---|
| MT+ | 22 | 20 | 15 |
| MT− | 37 | 10 | 0 |
| Total | 59 | 30 | 15 |
| PPA | 37% | 67% | 100% |

Ct, cycle threshold; NP, nasopharyngeal specimens; MT, mid-turbinate specimens; PPA, positive percent agreement.

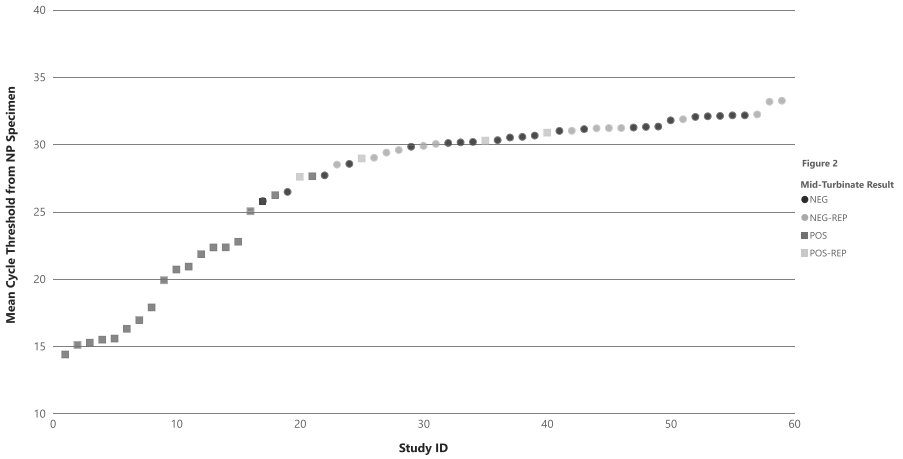


**FIGURE 2.** Qualitative results and mean Ct values of paired PCR tests for all subjects who were NP positive (n = 59). Squares indicate pairs for whom both the NP and MT tests were positive. The circles indicate pairs for whom the NP test was positive, but MT test was negative. Lighter shades indicate those who tested positive in an earlier preflight NP PCR.

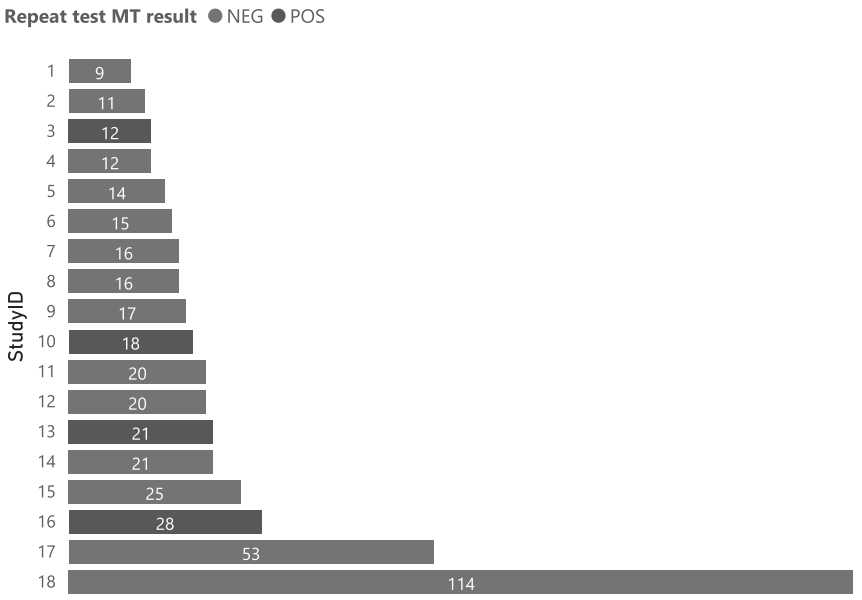


**FIGURE 3.** Days between repeat positive tests and MT test result during study period.

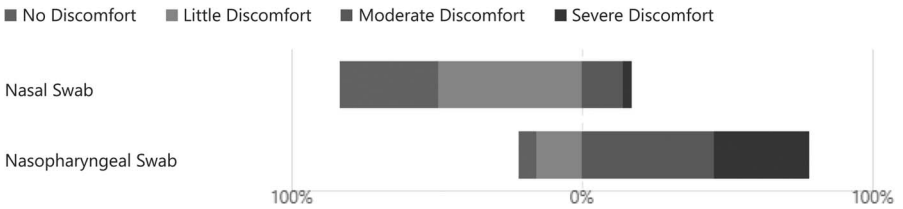


**FIGURE 4.** Self-reported level of comfort with NP and MT specimen collection.

 

also calculated PPA restricted to NP+ with mean Ct values <30 and <25. Although PPA overall was moderate (37%), it was much higher when limited to individuals believed to be actively infected, based on Ct values from their NP tests.

Preflight quarantine combined with COVID-19 testing can effectively prevent deployment of actively infected, contagious individuals. However, due to high sensitivity, PCR tests also capture those with past infection, keeping crew from deploying when it was likely safe for them to do so. A question we sought to answer was whether discordant test pairs were limited to NP tests with high Ct values at the time of testing. Our results confirmed this, indicating that MT specimens can reliably detect high viral load/infectious individuals, with less discomfort for those undergoing testing. When quarantine compliance is high, the likelihood of low or intermediate viral load individuals posing a risk for ongoing transmission is negligible. Crew who do not adhere to a 5-day quarantine and are infected just before testing pose a higher risk of false-negatives regardless of whether NP or MT swabs are used, but this becomes particularly important when a slightly less sensitive test is used. A robust quarantine of 5 days for all crew before testing would minimize any added risk of false-negatives resulting from the use of MT swabs.

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