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# Application of Abbott ID NOW in the emergency department for SARS-CoV-2 detection: A medical center's perspective

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## ABSTRACT

Testing for SARS-CoV-2 is crucial to tracking and controlling the pandemic. In particular, rapid testing in settings such as the emergency department (ED) could improve time to diagnosis and promote proper infection control measures. Early in the COVID-19 pandemic, we implemented the Abbott ID NOW COVID-19 method for screening symptomatic ED patients. However, due to concerns of suboptimal sensitivity, samples with a negative result were reflexed to the lab for confirmatory testing by the TaqPath COVID-19 Combo RT-PCR method. This study analyzed 6773 ID NOW results from April 2020 to September 2020 in the ED, of which 10% (n = 673) were positive and reported directly. The rest 90% (n = 6100) were negative and reflexed to RT-PCR. Among them, 3% (n = 175) turned positive on RT-PCR while 97% (n = 5925) of the results were consistently negative. The cycle threshold (Ct) values of the false-negative samples (n = 175) showed 90% (n = 158) of them with relatively low viral loads (Ct  $\geq$  30) with median Ct value at 35, while a number of samples (n = 17) had low Ct values (Ct < 30) and no clear explanation for false-negative results. Our study demonstrates that the Abbott ID NOW, despite its sensitivity limitations, was capable of providing near real-time results for 10% of symptomatic patients presenting to the ED allowing for improved management and workflow. However, our study findings emphasize the need to reflex negative specimens to a higher sensitivity method when prevalence is high and false-negative results are intolerable.

## 1. Introduction

Testing for is crucial in helping slow the spread of the virus by identifying those who have the virus and enabling treatment or isolation, and thus controlling the pandemic. Testing is also critical to learn more about how the virus spreads and how prevalent it remains in a given community.

Reverse-transcriptase PCR (RT-PCR) tests remain the gold standard for detecting an active SARS-CoV-2 infection, which was first established by the CDC when the pandemic began in early 2020 [1]. The tests are considered to have good sensitivity and specificity to accurately detect coronavirus disease 2019 (COVID-19) cases. Unfortunately, shortages of testing components have limited access to RT-PCR testing and lengthened turnaround time for results. The need for decentralized testing options with fast turnaround times has led to the development of rapid nucleic acid amplification tests (NAAT) that can be used in a lab or point-of-care (POC) setting. In particular, utilizing rapid NATTs in settings such as the emergency department (ED) could improve time to diagnosis and expedite patient management.

Rapid NAATs, in general, provide good specificity and better sensitivity than antigen tests. The Abbott ID NOW COVID-19 (Abbott Laboratories Chicago, IL) assay performed on the portable ID NOW Instrument is a rapid NAAT test that can produce a qualitative result within 13 min or less if a positive result is acquired [2].

A Cochrane review [3] on rapid SARS-CoV-2 testing (through March 24, 2021) evaluated 21 rapid, POC tests compared with RT-PCR tests for the detection of COVID-19. While the sensitivity varied greatly among the 16 antigen and 5 molecular assays evaluated, it is reported that the average sensitivity of ID NOW was 73.0% (95% CI 66.8% to 78.4%) and average specificity 99.7% (95% CI 98.7% to 99.9%). The authors concluded that prospective and comparative evaluations of rapid NATTs in clinical scenarios, spanning a range of testing indications and inclusive of symptomatology, are needed.

In addition, a number of studies have evaluated the test performance characteristics of ID NOW (i.e.: sensitivity, specificity, negative and positive predictive values). For instance, 7 out of 57 nasopharyngeal samples had been negative by ID NOW but positive by the Hologic Panther Fusion SARS-CoV-2 assay, used as a reference method [4]. In a

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separate study, 101 prospectively collected paired dry nasal swabs were analyzed by ID NOW and Cepheid-Xpert Xpress SARS-CoV-2 (reference method), with a positive percent agreement of 54.8% (95% CI 37.8 to 70.8%) and a negative percent agreement of 98.6% (95% CI, 92.3 to 99.7%) [5]. Smithgall et al. found, compared with Cobas as the reference method, ID NOW has a positive percent agreement 73.9% (95% CI, 63.2–82.3%) and a negative agreement 100% (95% CI, 83.4–100%) [6].

UMass ED have screened patients with the Abbott ID NOW COVID-19 test. ID NOW uses isothermal amplification technology which allows genetic material amplification at a constant temperature, which eliminates the need of a thermocycler and dramatically reduces the reaction time. This assay targets the RNA-dependent RNA polymerase (RdRp) segment of the SARS-CoV-2 viral RNA, with results available in 13 min or less if positive and a reported limit of detection of 125 genomic copy equivalents/mL [2]. Due to the concern of low sensitivity [7], samples with a negative result are then reflexed and analyzed with the Applied Biosystems TaqPath RT-PCR COVID-19 Combo Kit assay (ThermoFisher Scientific, Waltham, MA) for SARS-CoV-2 as a confirmatory test.

This study examines the performance of Abbott ID NOW on patients who were evaluated at UMass ED and the impact on ED operations.

## 2. Methods

### 2.1. Study population and specimen collection

Abbott ID NOW COVID-19 assay results (N = 6773) ordered on patients presenting to UMass ED from April 9th to September 15th 2020 were included in this study, which was approved by UMass Medical School IRB board. The STARD (Standards for Reporting Diagnostic Accuracy) criteria do not apply to this study since the order of ID NOW COVID-19 testing was part of the clinical assessment, based on the caregivers' clinical judgement.

Nasal or nasopharyngeal samples were collected using sterile polyester swabs and transported to the laboratory in 1.5 mL universal viral transport media (VTM). Swabs in VTM were used throughout the study period to accommodate the confirmatory PCR testing required for negative samples, even though ID NOW recommended the use of dry swabs in an effort to increase sensitivity [2].

### 2.2. Abbott ID NOW COVID-19 assay

ID NOW COVID-19 is an automated assay that utilizes isothermal nucleic acid amplification technology for the qualitative detection of SARS-CoV-2 nucleic acids. It consists of a Sample Receiver with the elution/lysis buffer, a Test Base with two sealed reaction tubes, a Transfer Cartridge for transferring the eluted sample to the Test Base. The reaction tubes in the Test Base contain the reagents needed for amplification of SARS-CoV-2 and an internal control. The primers target the RdRp segment of SARS-CoV-2 RNA, and fluorescently-labeled molecular beacons bind to the amplified RNA targets. To perform the assay, a nasal or nasopharyngeal sample collected in viral transport media is added to the Sample Receiver and transferred via the Transfer Cartridge to the Test Base, initiating target amplification. The results are available in 13 min or less if a positive result is acquired [2]. For this study, samples with negative results are reflexed to the TaqPath RT-PCR COVID-19 laboratory method.

### 2.3. TaqPath SARS-CoV-2 RT-PCR

Testing was performed in a 96-well format on nasal or nasopharyngeal specimens collected in viral transport media, which allows for testing of 93 specimens along with a positive, a negative control, and a no-template control per run. Viral RNA was extracted using the King-Fisher Flex System with MagMAX Viral Nucleic Acid Kits. PCR amplification was performed on Applied Biosystems 7500 PCR systems and a QuantStudio 5 PCR system. The assay targets 3 gene sequences: N2,

ORF1ab, and S genes. In addition, MS2 Phage Control was added to all specimens and the Negative Control that served as an internal process control.

Per the manufacturer's instructions for use [8], a specimen was considered positive when 2 or more SARS-CoV-2 gene targets were detected with cycle threshold (Ct) values of  $\leq 37$  on the Applied Biosystems COVID-19 Interpretive Software version 2.3. Samples with Ct value between 37 and 40 on any targets were reported as "Equivocal", and re-testing on a separately collected sample was strongly encouraged. Negative test results had to be negative (Ct  $\geq 40$ ) for all 3 viral genes. All test kits and instruments were purchased from Thermo Fisher Scientific (Waltham, MA). For statistical purpose, equivocal results were considered "positive" in the data analysis of this manuscript.

## 3. Results

During the period of April to September 2020, there were over 6,700 ID NOW COVID tests performed at UMass clinical laboratory, primarily ordered on symptomatic patients in the ED. Among those, 10% (n = 673) were positive and the rest were reflexed to TaqPath RT-PCR as the confirmatory test. Of those reflexed, 97% (n = 5925) of the samples remained negative, and the false-negative rate of ID NOW was roughly at 3% (n = 175) (Fig. 1).

We analyzed the Ct values of the 175 false-negative results on ID NOW (Fig. 2). Ninety percent of them had a Ct  $\geq 30$  (n = 158) with the median at Ct 35. The limit of detection is roughly 50 genomic copy equivalents/mL at Ct 34 based on the TaqPath package insert [8], so the majority of these samples (n = 113; 65%) were considered to have relatively low viral counts. On the other hand, a few samples with low Ct values (Ct < 30) (n = 17) were missed by ID NOW.

## 4. Discussion

In this study, we reported the Abbott ID NOW COVID-19 assay has a fairly low false-negative rate (3%) and high specificity [2], especially when performed on symptomatic patients. The specificity persists, even through the delta variant surge [11] due to the assays targets the the RdRp segment, instead of the S gene, of SARS-CoV-2 RNA. One limitation to our study is that because the positive ID NOW samples were not tested by the TaqPath method, we were unable to confirm the positive percent agreement. Furthermore, there may be selection biases inherent in the algorithm which may further influence the data, since the order was part of the clinical assessment in the ED.

It was surprising that the limited sensitivity of the ID NOW method was observed to include samples (n = 17) with low Ct values (<30) by the confirmatory TaqPath method. This was most possibly due to a sample issue (i.e., collection/transportation) rather than an analytical issue, because ID NOW is reported to be highly specific from the literature [4–6]. Rapid NAAT platforms involving nucleic acid amplification have been shown to be vulnerable to even slight variation in collection/transportation process (i.e., nasal spray treatment, temperature fluctuation) [12]. Respiratory tract samples include tissue residues and respiratory secretions, with endogenous and exogenous factors, initially deposited in the respiratory mucosa or lung parenchyma which, in high concentrations, can inhibit inexpertly conducted or low-sensitivity PCR tests.

When the Abbott ID NOW COVID-19 assay first became available in April 2020, there were some concerns about the low sensitivity according to a media report from the Cleveland Clinic [7], which might lead to a risk of intra-hospital spread. The actual sensitivity was much lower than the package insert claimed at 125 genomic copy equivalents/mL [2]. To avoid false-negative results, we implemented a reflexing algorithm that all negative samples on the ID NOW were tested again by the TaqPath SARS-CoV-2 RT-PCR, and the ED and infectious disease clinicians were educated on this matter.

A few things have since been recommended to improve the

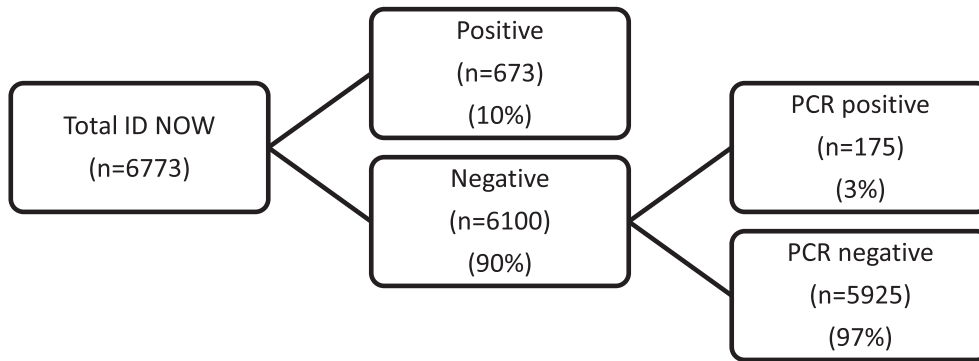


Fig. 1. Breakdown analysis of the ID NOW results in this study.

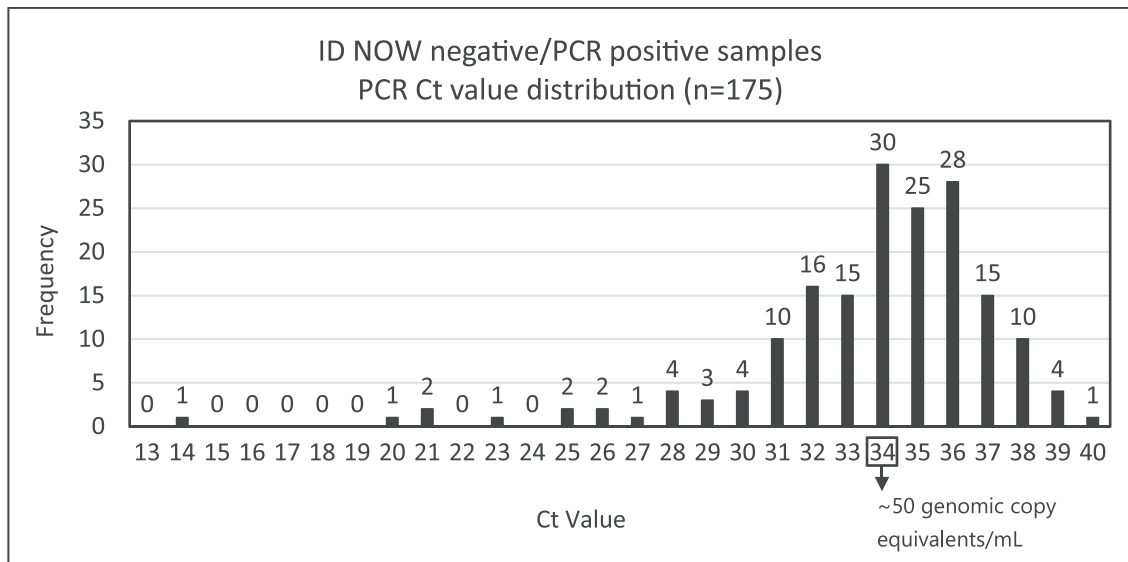


Fig. 2. RT-PCR Ct value distribution of the false-positive samples on ID NOW.

sensitivity if using ID NOW. ID NOW has updated the specimen type to perform the tests on dry swabs directly, rather than on the transport media [2]. The theory was that the transport media might dilute the viral concentration that result in a lower sensitivity. According to a study that applied logistic regression model and paired swab study to predict ID NOW performance in dry swab and VTM samples, VTM samples would have a theoretically higher Ct value by about 4 cycles [13]. Their findings also suggest that nasopharyngeal samples have higher positive percent agreement with a RT-PCR method than nasal swabs [13], although it is difficult to tease apart the percentage of nasal and nasopharyngeal samples used in our study. Other recommendations, such as waiting for 5–7 days to get tested after last exposure or until symptomatic [9] or serial testing [10], can also be very helpful in identifying a true positive case.

The data in this study were collected in the first 6 months of the pandemic, during which majority of patients seeking medical attention in the ED were presented with COVID-/flu-like symptoms. Although there was only 10% positivity rate, the ID NOW still made a significant difference to be able to report positive results in minutes, rather than the analysis on the TaqPath RT-PCR, which would take more than 8 h for result. While there is a great variation in Ct values correlating with a person being infectious, most studies demonstrate a low infectivity with a RT-PCR method at Ct value > 30 [14], which coincides with most of the missed samples on ID NOW (90%, n = 158). As we learned more from our experience with the performance of the ID NOW assay in suspected COVID-19 patients and additional studies were available in

the literature increasing the comfort level of providers with potential false-negative results, we have decided to stop reflexing negative samples.

A robust and responsive testing infrastructure is essential to our success in stopping the spread of SARS-CoV-2. Our study showed that the Abbott ID NOW, if used appropriately, is very effective on the symptomatic patient population.

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