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RT-PCR, COVID-19, SARS-CoV-2, POCT, ID NOW

Abstract
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REVIEW

Innovative technology for rapid molecular diagnostics: COVID-19 and other respiratory tract infections

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Abstract

The outbreak of the COVID-19 pandemic presented the world with many new challenges such as rapid and accurate diagnosis of infected individuals to isolate them and contain the spread of the virus. RT-PCR (reverse transcription [transcriptase] polymerase chain reaction) has become the gold standard in COVID-19 diagnostics, but its major limitations are: long turnaround time and the need to be conducted by specialized staff. The need for rapid and easy-to-use diagnostic tests led to the development of ID NOW — a rapid molecular test that provides a COVID-19 diagnosis in less than 15 minutes and can be performed even by support staff in a variety of point-of-care (POC) locations. It can also detect other infections with similar symptoms, such as influenza or RSV. Due to rapid differentiation between COVID-19 and other infections patients can be isolated quickly and hospital departments operate efficiently. In this publication we present the recommendations for the use of the diagnostic test ID NOW based on clinical research results and opinions of experts in different medical fields, such as epidemiology, cardiology, oncology, pulmonology and microbiology.

Keywords: COVID-19, SARS-CoV-2, ID NOW, RT-PCR, POCT

Introduction

The current SARS-CoV-2 pandemic poses numerous challenges for public health authorities. These include the appropriate use and correct interpretation of the various tests available in different clinical settings. The sudden onset and rapid spread of SARS-CoV-2, with overwhelming public health and economic burden, highlighted the urgent need to effectively diagnose and treat infected patients. Researchers rushed to develop quick and accurate SARS-CoV-2 diagnostic tests that detect specific viral nucleic acids (molecular tests), proteins (antigen tests) or anti-SARS-CoV-2 antibodies, if the patient has previously been exposed to the virus (serological tests). Correct and rapid diagnosis of a SARS-CoV-2 infection is critical both epidemiologically (because many infected individuals are asymptomatic) and clinically (patients should be diagnosed and treated as early as possible). Large-scale diagnostic testing is a key

epidemiological tool used to contain outbreaks such as COVID-19. Technical uncertainties in testing, initial regulatory hurdles, limited resources, and supply chain disruptions have allowed the virus to spread worldwide. These challenges may be more pronounced in low- and middle-income countries.

European Centre for Disease Prevention and Control prepared the document that outlines strategies and objectives for sustainable SARS-CoV-2 testing of populations to achieve specific public health objectives in various epidemiological situations. According to this document implementation of objective-driven and sustainable testing strategies for COVID-19 supports the overall public health response to the pandemic and helps mitigate its impact on vulnerable populations and healthcare systems, while ensuring that societies and economies can continue to function. Ideally, all people with COVID-19 symptoms should be tested as soon as possible after symptom onset. This requires easy access to testing for all, including non-residents. Test turnaround time should be minimised, people testing positive should isolate and timely contact tracing should be carried out, ensuring that all close contacts are tested, irrespective of symptoms. All patients with acute respiratory symptoms in hospitals and other healthcare settings, and all specimens from sentinel primary care surveillance should be tested for both SARS-CoV-2 and influenza during the influenza season to monitor incidence and trends over time [1].

The global disease burden is significant. The United Nations International Labour Organization estimated that there was an 8.3% decline in global labor income in 2020, equivalent to 4.4% of gross domestic product (GDP) or $3.7 trillion. Approximately 8.8% of global working hours were lost in comparison to the fourth quarter of 2019, equivalent of 255 million full-time jobs; this burden is approximately four times greater than the loss of employment seen during the global financial crisis of 2009. The reduction in the number of hours was due to job losses and reductions in working hours [2].

Delayed COVID -19 diagnoses, for example due to prolonged turnaround times or limited capacity of central laboratories performing RT-PCR tests, delay the treatment of severe cases and increase mortality [3]. Understanding the health lost to COVID-19 mortality is important for

policy makers because it can help determine the impact of actions taken to mitigate the consequences of the pandemic. Although COVID-19 also affects the health of survivors, some of whom may have suffered from COVID-19 for a long period of time, the lost health of those who died from this disease accounts for a large proportion of the overall health burden. Wouterse et al. suggest that even when mortality is concentrated among people with poorer health, the average number of QALYs (quality-adjusted life year) lost per COVID-19 death may be substantial. Taking into account the health status of people who died from COVID-19, we arrive at an estimate of approximately 3.9 lost QALYs per male COVID-19 death and 3.5 lost QALYs per female COVID-19 death [3].

Polish experts point out that more than two years into the COVID-19 pandemic the healthcare system faces its long-term consequences. They include: excess mortality, anxiety and stress, and especially longer waiting times across specialized clinics and for hospital admission [4, 5]. This is due to impeded access to medical services. Unavailability of rapid and reliable tests significantly slows down the operation of hospital departments (e.g., cardiology or oncology), because if a patient shows symptoms of COVID-19 or another infectious disease, the work of the entire hospital department may be stopped until the RT-PCR test result returns. It may be justified to include the rapid molecular diagnostics technology in the guaranteed healthcare benefits package as soon as possible or to change the existing medical procedures to reduce the number of nosocomial infections and improve the health care system in view of the current long-term consequences and the high risk of further pandemics. The psychological aspect is also important, as the possibility of rapid and accurate testing in a hospital or specialty outpatient clinic would help measurably improve the image of the health care system in the eyes of the public, thereby reducing stress and anxiety associated with the pandemic [4, 5].

The spread of the pandemic highlighted the need for diagnostic tests that can distinguish COVID-9 from other infections with similar symptoms. This is especially important in hospitals, where patients with COVID-19 are typically isolated to prevent local outbreaks that can significantly disrupt hospital operations. ID NOW is a rapid *in vitro* molecular diagnostic test using isothermal nucleic acid amplification technology for:

- detection of SARS-CoV-2 (COVID-19) [6],
- detection and differentiation of influenza A and B viral RNA [7],
- detection of RSV [8],
- detection of *Streptococcus pyogenes* [9].

Isothermal technology makes ID NOW one of the fastest POC molecular platforms on the market, with excellent workflow characteristics. ID NOW is easy to use and samples can be collected via nasal or nasopharyngeal swabs. As of the end of 2021 the test was approved in Australia, Canada, Europe, Japan, the UK and the US [1–9].

COVID-19

One of the most important measures to combat the COVID-19 pandemic is to quickly diagnose infected patients and then isolate them. The Center for Disease Control recommends the use of nucleic acid amplification tests (NAAT) (e.g. RT-PCR) and antigen tests to diagnose infection or initiate isolation (e.g. after previous contact with an infected person) or for persons in high-risk settings (nursing homes, medical facilities) [10]. NAAT tests have high sensitivity and specificity. They detect one or more viral RNA genes and indicate current or recent infection. Most NAAT tests are performed in a laboratory and their turnaround times vary (1–3 days). However, some NAAT tests are run in POC environment and their results are available within 15–45 minutes. Most NAATs provide qualitative results. The WHO recommends them as the gold standard for diagnosis of acute SARS-CoV-2 infection. According to the international and Polish guidelines, the RT-PCR is the most reliable method and the gold standard in COVID-19 diagnosis. It is characterized by much higher sensitivity and specificity than antigen tests but has one major limitation: the turnaround time [10–14].

International guidelines also recommend the use of NAATs, including RT-PCR, in certain situations, i.e. when the result of the antigen test needs to be confirmed due to its lower sensitivity compared with molecular tests (NAAT). NAATs (mainly RT-PCR) are also recommended in Poland in the diagnosis of patients with SARS-CoV-2 infection [11–14]. Considering the time-consuming nature and complicated procedure of currently used RT-PCR, rapid molecular tests

(turnaround time: 15-45 min) could become an important diagnostic tool, especially in urgent cases. There is an unmet need for wider use of rapid and accurate POC testing for COVID-19. The diagnostic guidelines highlight that the advantage of antigen tests is their low cost and short waiting time, while their disadvantage is the possibility of cross-reactivity with other common coronaviruses [10–14].

One of the latest NAATs based on nicking enzyme assisted response (N.E.A.R.) is the rapid molecular diagnostic test ID NOW. It uses isothermal nucleic acid amplification technology for qualitative detection of SARS-CoV-2 nucleic acid in nasal and nasopharyngeal swabs from suspected patients. PCR tests require thermocycling, a series of temperature changes for pathogen amplification, which increases time to result. ID NOW N.E.A.R. technology is an isothermal test that uses enzymes and consistent temperature for more rapid amplification and faster molecular results. Both technologies amplify bacterial or viral targets, but NEAR technology makes the ID NOW the fastest POC molecular platform on the market. This speed is in part due to the small size of the amplicon compared to other NAATs (eg. RT-PCR). Fluorescently labeled molecular beacon probes provide a real-time readout. This reaction can be adapted to different temperatures by the use of various primers, polymerases, and nicking enzymes [6].

This ABBOTT ID NOW diagnostic test is performed in health care facilities within the first seven days of symptom onset. This platform-based instrument is a small, portable device that can be used and installed wherever it is needed, for instance in hospital wards or emergency rooms, and delivers results in a very short time (3–15 minutes). Thanks to this technology yielding accurate results, clinicians can quickly make informed decisions. It is a diagnostic test that allows for automatic transmission of results, reducing the administrative burden on the healthcare system. ID NOW diagnostic test also detects influenza A and B, RSV and group A streptococcus. This is particularly important in nosocomial infections, when patients with COVID-19 need to be quickly identified and differentiated for instance from those with influenza or RSV — diseases which produce similar symptoms. Since it is able to detect other pathogens, ID NOW may continue to be used after the pandemic or when COVID-19 is not tested as frequently [6, 12].

ID NOW – Clinical evidence

To achieve the best diagnostic efficacy ID NOW should be used in line with the current protocol approved by the manufacturer, namely:

- the specimen should be a dry swab taken by the investigator — undiluted in universal transport medium (UTM);
- samples for intervention and control (RT-PCR) should be taken from the same site, i.e. nose, nasopharynx, etc.; and
- only fresh (never frozen) specimens should be used, i.e. specimens should be tested shortly (optimally within 1 h) after collection.

The diagnostic efficacy of ID NOW was assessed in 7 prospective studies conducted in line with the current protocol, which showed it in relation to the reference standard in COVID-9 diagnostics: RT-PCR. Detailed study information and main outcomes are presented in the Table 1 below [15–21].

In these 7 prospective studies, the sensitivity and specificity of the diagnostic test ID NOW for the qualitative detection of acute respiratory infectious disease caused by SARS-CoV-2 (COVID-19) infection in symptomatic patients was assessed in relation to the reference standard: RT-PCR. The highest sensitivity of ID NOW in relation to the RT-PCR was reported in the Urgent Care Clinic 2020 study (100%) and the lowest in the Meletis 2021 study (86%). The highest specificity of ID NOW in relation to the the RT-PCR was reported in the Meletis 2021 and Tu 2021 studies (100%) and the lowest in the Stokes 2021 study (64%).

A meta-analysis of prospective studies in symptomatic patients found that the sensitivity of the ID NOW test for the diagnosis of acute infectious respiratory disease due to SARS-CoV-2 infection in symptomatic patients was 95.6% (95% CI: 91.8 - 97.6), while its specificity was 99.5% (95% CI: 94.6 - 99.9) in relation to the the RT-PCR. In symptomatic patients tested COVID-19 within 7 days of symptom onset ID NOW showed sensitivity of 98.7% (95% CI: 91.7 - 99.8) and specificity of 98.9% (95% CI: 98.9 – 98.9) in relation to the the RT-PCR assay.

Other identified systematic reviews evaluating the diagnostic efficacy of ID NOW for qualitative detection of acute infectious respiratory disease caused by SARS-CoV-2 (COVID-19) infection assessed in relation to the RT-PCR assays reported sensitivity of 73% to 78% and a specificity of 99% to 100% [22–26]. However, in the studies included in the systematic reviews ID NOW was not used as intended in the product's directions. Deviations from the recommended protocol included: dilution of samples in UTM, collection of samples from two different anatomical sites, freezing of samples, or testing a long time after sample collection (up to 48 hours). The inclusion of these studies in the meta-analysis significantly undermines the effectiveness of the ID NOW test. Adherence to its instructions for use optimises diagnostic accuracy, as demonstrated by the results of our review of primary studies that included only those in which ID NOW was conducted correctly.

Implementation of the test reduces societal cost by helping to avoid unnecessary isolation and quarantine. Its short turnaround time brings down the number of secondary infections that can occur if patients with suspected infection disregard the rules of self-isolation. ID NOW can streamline hospital operations mainly by reducing the duration of diagnostics and periods of ward closure until the test result in a suspected COVID-19 case arrives.

Expert's recommendations

Aspects of the medical practice in the diagnosis of COVID-19 in Poland were the subject of a survey conducted among Polish clinical experts and the Medical Advisory Board meeting held in Warsaw on 26 January 2022 . Clinical experts from different fields, including epidemiologists, cardiologists, and oncologists actively involved in COVID-19 prevention and management during the pandemic outbreak in Poland were invited to take part in the panel. The experts participating in the panel represent the largest Polish medical centers in both clinical sciences and public health. All the discussions were carried out in line with the ethical principles expressed in the Declaration of Helsinki and followed the health technology assessment (HTA) guidelines. The clinical experts (co-authors of this manuscript) identified the unmet needs related to COVID-19 diagnostics, as well as discussed the pros and cons of relevant tests. In the experts' opinion the

advantage of antigen tests was their short turnaround time. However, their sensitivity was relatively low and it was often necessary to confirm a negative result using the RT-PCR. Over 30% of experts indicated that it was necessary in symptomatic patients. Since antigen tests sometimes fail to provide reliable results and patients cross paths in the clinic, the infection may spread. The RT-PCR assays have much higher sensitivity and specificity, but their main limitation is long turnaround time, which averages 9 hours in the high-incidence period and about 7 hours in the low-incidence period. Experts also emphasized that the long waiting time for the COVID-19 test result led to complications in hospital surgeries. RT-PCR assay turnaround times also impacted hospital bed occupancy, limiting other patients' access to healthcare. In addition, patients often needed to be tested several times during their stay in the hospital, especially when moving around different clinical departments. The long waiting times hindered clinics' functioning. According to the experts, a rapid, highly sensitive test would greatly improve workflow and restore pre-pandemic clinic conditions. As a rapid molecular diagnostic test ID NOW can respond to these unmet needs by providing reliable results (high sensitivity and specificity) in a very short time (no longer than 15 minutes). Its major advantage is that it can be used by trained support personnel [27].

Influenza A and B

Influenza (flu) is a contagious respiratory disease caused by influenza viruses that infect the nose, throat, and sometimes the lungs [28]. Data from up to 33 countries comprising 57% of the world's population suggest that influenza results in 291,243–645,832 respiratory deaths each year (equivalent to 4.0–8.8 per 100,000 persons) [30]. Hospitalizations represent another important burden of influenza. It is estimated that between 140,000 and 810,000 patients are hospitalized annually in the United States alone since 2010 [29]. A proportion of hospitalized patients requires treatment in the intensive care unit. Infants with influenza are at the greatest risk of requiring intensive care [31]. Even mild cases of influenza are associated with a significant burden as patients are taken off sick for symptoms or to care for children with symptoms [32].

In addition, influenza is associated with serious complications, including pneumonia [33], secondary bacterial infections [34], myocarditis, encephalitis, myositis, rhabdomyolysis, and multiple organ failure [35]. Certain populations are at an increased risk for adverse health consequences of influenza. These include older adults (aged ≥65 years) [36], children younger than 5 years [37], and people with underlying health conditions (e.g., asthma or diabetes) [36]. SARS-CoV-2 could further increase the burden of seasonal influenza [38], although data are currently insufficient. Economically, seasonal influenza is estimated to result in a total societal cost of $11.2 billion in the United States, of which $8.0 billion are indirect costs (e.g., absenteeism) [39]. In the EU, the total annual societal cost of influenza is likely to be between €6 billion and €14 billion per year (2014 estimate) [40].

Several tests are available for the diagnosis of influenza A and B, with rapid molecular tests recommended in guidelines for testing individuals at highest risk for influenza [29]. Nucleic acid amplification tests (NAATs) are considered the gold standard because of their high sensitivity and specificity. Rapid tests are increasingly available and, if sufficiently sensitive, can enable timely clinical management decisions [41]. There is an unmet need for wider use of rapid and accurate POC testing for influenza. Despite the availability of influenza vaccines and effective antiviral medications, seasonal influenza remains a significant burden. Current rapid on-site testing often relies on antigen tests, which are quick but have relatively low sensitivity [42]. Widespread use of rapid and accurate POC molecular testing could improve management and associated resource use, and reduce influenza A & B transmission (through optimized isolation) [43]. Accessible molecular testing can improve disease management by providing both accuracy and speed [42], enabling optimal management, and likely reducing the disease burden [44].

Clinical evidence

The performance and clinical value of the ID NOW Influenza A & B 2 assay have been assessed in a number of studies, demonstrating its high sensitivity, specificity, speed and value in clinical practice. An overview of these studies is provided in Table 2.

ID NOW Influenza A & B 2 is supported by robust clinical data. As a fast and accurate point-of-care test (POCT), ID NOW Influenza A & B 2 offers a variety of benefits to patients and healthcare systems, which include high sensitivity and specificity, a low rate of invalid results [49, 50], a reduction in the administration of antibiotics [49] and increasing appropriate use of antivirals [50]. ID NOW Influenza A & B 2 also reduces the time spent in the emergency department or in hospital, hospitalization rates [49, 51] and resource use [51]. Lower resource consumption leads to cost reductions. From the perspective of United Kingdom National Health Service, introduction of Alere™ Influenza A & B (previous assay generation of POCT) was estimated to lead to savings of £242 per adult presenting with flu-like symptoms [52]. ID NOW Influenza A & B 2 may enable appropriate isolation procedures [53] and thus positively impact epidemiology.

Respiratory Syncytial Virus (RSV)

Respiratory syncytial virus is a common, contagious virus responsible for respiratory illness. Globally, an estimated 199,000 infants die from RSV each year, with 99% of deaths occurring in low- and middle-income countries with limited medical resources [54, 55]. There are no estimates of global RSV-related mortality in adults. RSV kills 11,000 to 17,000 older adults in the United States alone and approximately 8,000 adults per year in the United Kingdom [56]. In children RSV can lead to long-term health effects that include increased risk of asthma [10], clinical allergies, and wheezing [54, 57]. In the elderly RSV is associated with high rates of pneumonia [12] and cardiovascular complications [58]. The clinical burden of RSV results in substantial direct [59] and indirect costs associated with treatment and absenteeism due to illness or the need to care for sick children. The direct costs of treating pediatric RSV infections were estimated at $611 million annually, including 72 low- and middle-income countries [59]. In the United States, the RSV-associated annual cost of hospital care for adults was estimated at approximately $1 billion [60].

Clinical guidelines do not recommend routine testing for RSV [61] and clinicians rarely attempt to identify the pathogen responsible for acute respiratory infection when the illness is mild. Nonetheless, testing offers several benefits, including more appropriate use of antibiotics [62] and shorter stays in emergency departments [63]. Treatment of RSV is generally symptomatic [64]. Until the recent development of rapid molecular POCTs for RSV, testing was based on rapid antigen assays, which lack the sensitivity needed to make confident treatment decisions [65], or reverse transcriptase RT-PCR assays.

Clinical evidence

The performance and clinical value of the ID NOW in testing for RSV have been assessed in prospective studies, which demonstrate its high sensitivity, specificity, speed and value in clinical practice. An overview of these studies is provided in Table 3.

ID NOW RSV is supported by robust clinical data. It performs well when assessed in relation to the standard laboratory RT-PCR tests [66, 68, 69] and shows similar sensitivity for direct swabs and swabs eluted in transport medium [69]. ID NOW RSV delivers results with specificity and sensitivity comparable with other rapid molecular assays (34) and performs well across all pediatric age groups [69]. Its workflow characteristics are excellent in clinical practice [70]. Based on these assay characteristics, it is anticipated that the introduction of the ID NOW RSV assay in POC settings will lead to a number of improvements in the management of RSV.

Group A Streptococcus (GAS)

Group A streptococci (GAS, *Streptococcus pyogenes*) cause a wide range of diseases. Most GAS infections are relatively mild conditions such as pharyngitis and impetigo, but in some patients GAS can cause invasive and immune-mediated disease [71]. If left untreated, GAS pharyngitis can lead to severe disease [73]. Acute rheumatic fever (ARF) and rheumatic heart disease (RHD) — the most serious autoimmune sequelae of GAS infection — cause disability

and death in children worldwide [74]. Group A streptococcal pharyngitis and severe GAS disease impose a significant burden on patients, health care systems, and society. Accurate diagnosis of GAS pharyngitis followed by appropriate antimicrobial therapy is important to improve clinical symptoms, reduce transmission to close contacts, prevent purulent and non-purulent complications, and prevent acute morbidity [75]. An analysis performed for the US showed that the economic burden of GAS pharyngitis is substantial, as the total societal cost ranged from $224 to $539 million annually [76].

In patients who do not present with viral symptoms, clinicians cannot differentiate between viral and GAS pharyngitis based on clinical examination alone [72], and guidelines recommend testing for GAS pharyngitis. A variety of tests are available for this purpose. Traditional methods for detecting GAS infection include rapid antigen tests or 24- to 48-hour bacterial cultures of throat swabs [77]. The sensitivity of rapid antigen tests varies, and several test manufacturers recommend subsequent throat culture to confirm negative results [78].

There is an unmet need for wider use of rapid and accurate POC tests for GAS. More frequent and accurate testing in this setting would inform treatment decisions as well as reduce morbidity and societal burden [79]. Rapid and accurate molecular POC tests, such as highly sensitive nucleic acid amplification tests for GAS, are the latest development in the diagnosis and treatment of GAS pharyngitis [80].

Clinical evidence

The performance and clinical value of the ID NOW Strep A and A2 tests have been assessed in several studies, which demonstrate their high sensitivity, specificity, speed and value in clinical practice. An overview of these studies is provided in Table 4.

ID NOW Strep A 2 is supported by clinical data. As a fast and accurate POC test, ID NOW Strep A 2 offers a variety of benefits to patients and healthcare systems: high sensitivity and specificity [9, 81], and a low rate of invalid results, which may reduce the need for backup testing on negative results. ID NOW Strep A 2 compares well with PCR for accuracy and is more sensitive than rapid antigen tests for GAS [81]. It is easy to use by non-laboratory personnel in a Clinical

Laboratory Improvement Amendments (CLIA)-waived setting. ID NOW Strep A 2 avoids the false negative results obtained with POC rapid antigen tests, leading to earlier appropriate treatment [81].

Published studies demonstrate that Alere™ (previous generation point-of-care test) reduces resource use by optimising antibiotic therapy [81] and eliminating the need for additional cultures [83].

Expert's recommendations — summary

Clinical experts from different fields, including epidemiologists, cardiologists or oncologists, pointed out that ID NOW can be used not only to detect COVID-19 but also other respiratory pathogens such as influenza viruses, RSV and Strep A [Figure 1], especially to differentiate between infections with similar symptoms. Quick and accurate COVID-19 diagnosis makes it possible to isolate the patient and prevent local outbreaks that significantly disrupt hospital operations [27]

Conclusion

Clinical experts in Poland highlight a great unmet need for a rapid and sensitive diagnostic test to detect COVID-19. Currently, the long turnaround time of RT-PCR assays disrupts hospital operations, forcing patients to wait many hours before admission. Experts believe this unmet need could be eliminated by the introduction of rapid yet sensitive molecular diagnostic tests such as ID NOW, which is based on the N.E.A.R. method. The highest sensitivity and specificity of ID NOW was achieved in the population of symptomatic patients tested within the first seven days of symptom onset. This is the population in which this test should be used for the highest diagnostic efficiency according to the manufacturer's recommendations.

ID NOW diagnostic test can also be used to detect influenza A and B, RSV, and group A streptococci. This is particularly important in nosocomial infections, when patients with COVID-19 need to be quickly identified and differentiated for instance from those with influenza and RSV — diseases that cause similar symptoms. Since it is able to detect other pathogens, ID NOW may continue to be used after the pandemic or when COVID-19 is not tested as frequently.

Widespread use of ID NOW rapid molecular test for COVID-19 diagnostics may:

- improve access to the health care system,
- speed up medical processes and decisions,
- enable faster detection of local outbreaks caused by common respiratory pathogens,
- enable point-of-care testing, also by support staff (better allocation of human resources),
- streamline hospital workflow (e.g. reduce patient waiting times for hospital admission).

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Disclosure

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Innovative technology for rapid molecular diagnostics: COVID-19 and other respiratory tract infections

Introduction

The outbreak of the COVID-19 pandemic presented the world with many new challenges such as rapid and accurate diagnosis of infected individuals to isolate them and contain the spread of the virus.

PCR

RT-PCR (reverse transcription [transcriptase] polymerase chain reaction) has become the gold standard in COVID-19 diagnostics, but its major limitations are: long turnaround time and the need to be conducted by specialized staff.

15 MIN

The need for rapid and easy-to-use diagnostic tests led to the development of ID NOW - a rapid molecular test that provides a COVID-19 diagnosis in less than 15 minutes and can be performed even by support staff in a variety of point-of-care (POC) locations.

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Results

The current protocol for the use of ID NOW in the diagnosis of COVID-19 is following:

- dry swab collected by investigator – undiluted in universal transport media
- samples for intervention and control taken from the same anatomic site
- „fresh" samples - tested shortly after collection, without freezing

✓ 7 prospective studies that met the requirements of the current ID NOW usage protocol were identified as a result of conducted systematic literature review (SLR).

Sensitivity of 98.7%
Specificity of 98.9%

of COVID-19 diagnosis using ID NOW was calculated based on studies (n=3) in symptomatic patients with symptoms appearing within 7 days, compared to RT-PCR as a reference standard

ID NOW use was also examined in robust clinical studies to **detect other pathogens, like influenza A and B, RSV, and group A streptococci.**

✓ During the Advisory Board meeting Polish clinical experts discussed the position of ID NOW in Polish clinical practice, where the unmet needs are most urgent.

Conclusions

Clinical experts in Poland highlighted an urgent unmet need for a rapid and sensitive diagnostic test to detect COVID-19.

Widespread use of **ID NOW** rapid molecular test for COVID-19 diagnostics may:

- improve access to the health care system,
- speed up medical processes and decisions,
- enable faster detection of local outbreaks caused by common respiratory pathogens,
- enable point-of-care testing, also by support staff (better allocation of human resources),
- streamline hospital workflow (e.g., reduce patient waiting times for hospital admission).

(line 180) Table 1. Studies assessing ID NOW diagnostic efficacy in relation to the RT-PCR in symptomatic patients suspected of COVID-19 infection and their main outcomes

Study	Study design	Reference standard	Setting	Time from symptom onset till testing	Number of samples	ID NOW Sensitivity	ID NOW Specificity
Urgent Care Clinic study 2020 [17]	prospective	Roche Cobas® SARS-CoV-2	Urgent care clinics	Less than 7 days	256	100%	99.6%
Graham 2021 [18]	prospective	Xpert Xpress SARS-CoV-2	Academic hospitals	Less than 7 days	1043	NaN[1]	99.9%
Mahmoud 2021 [19]	prospective	Roche Cobas® SARS-CoV-2	COVID-19 quarantine facilities	NR[2]	686	95.2%	96.9%
Meletis 2021 [20]	prospective	Abbott RealTime SARS-CoV-2	Emergency department	NR	30	85.7%	100%
NguyenVan 2021 [21]	prospective	Simplexa COVID-19	Emergency department	NR	395	98.1%	97.5%
Stokes 2021[3] [22]	prospective	Roche Cobas® SARS-CoV-2	Community and hospital	Less than 7 days	62	98%	63.6%
Tu 2021 [23]	prospective	Hologic Panther Fusion® SARS-CoV-2	Ambulatory	NR	965	91.3%	100%

[1] NaN: Uncountable value (cannot be calculated: no patients with COVID-19)
[2] NR – not reported
[3] Results for the subpopulation of patients in whom symptoms occurred within 7 days with samples analyzed within 1 hour of swab collection (population selected according to the manufacturer's instructions)

(line 277) Table 1. Overview of clinical studies evaluating the ID NOW Influenza A & B 2 assay

Study name (Ref)	Design	Reference standard	ID NOW Sensitivity	ID NOW Specificity
Farfour 2020 [49]	Test performance	GeneXpert®	96.6%	96.1%
Kanwar, 2020 [50]	Prospective clinical trial	RT-PCR[1]	93.2% (Type A) 97.2% (Type B)	-
Mitamura, 2021 [51]	Analysis of current samples and retrospective results (Japan)	RT-PCR	2016/2017 to 2019/2020: 97.3% (Type A) 100% (Type B) 97.8% (Type A and Type B)	-
Mitamura, 2020 [52]	Prospective multicenter study	RT-PCR	Type A: 95.9% (NPS[2]) 95.7% (NPA[3]) Type B: 100% (NPS) 98.7% (NPA)	100% (Type A/B) (NPS/NPA)
O'Connell, 2020 [53]	Prospective study	GeneXpert®	92% (Type A)	100% (Type A/B)

[1] RT-PCR, reverse transcription [transcriptase] polymerase chain reaction

[2] NPS, nasopharyngeal swab

[3] NPA, nasopharyngeal aspirate

(line 315) Table 1. Overview of clinical trials evaluating the ID NOW RSV assay

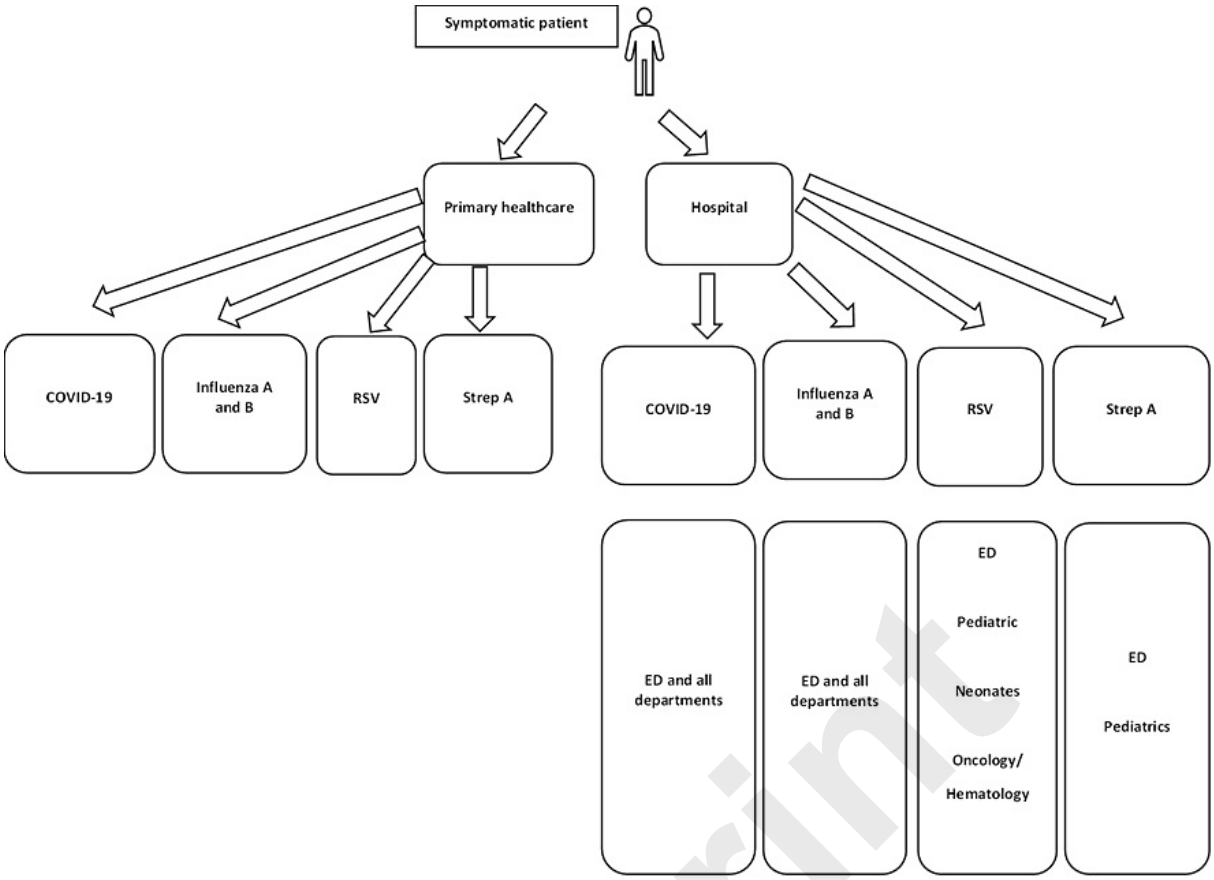
Study name (Ref)	Design	Reference standard	ID NOW Sensitivity	ID NOW Specificity
Hassan, 2018 [72]	Prospective, multicenter trial	RT-PCR	98.6% (direct NPS[1]) 97.8% (UTM[2] NPS)	98.0% (direct NPS) 97.8% (UTM NPS)
Leonardi, 2019 [73]	Prospective, single center	RT-PCR	94.7%	96.5%
Peters, 2017 [74]	Prospective, single center	RT-PCR	100%	97%
Schnee, 2017 [75]	Prospective study	RT-PCR	93% 98% (children <6 months) 87% (children ≥2 years)	96% 98% (children ≥2 years)

[1] NPS, nasopharyngeal swab

[2] UTM, universal transport medium

(**line 352)** Table 1. Overview of clinical studies evaluating the ID NOW Strep A and A2 tests

Study name (Ref)	Design	Reference standard	ID NOW Sensitivity	ID NOW Specificity
Berry, 2018 [88]	Laboratory-based comparison study	Reference: bacterial culture Discrepant samples analysis: RT-PCR	100%	91.3%
Cohen, 2015 [89]	Prospective, multicenter clinical trial	Reference: bacterial culture	95.9% Following PCR adjudication of discrepant results: 98.7% 98.5%	94.6% Following PCR adjudication of discrepant results: 98.5%
Weinzierl, 2018 [90]	Laboratory-based comparison	Reference: bacterial culture	98%	100%
Abbott Laboratories [8]	Multi-center, prospective study	Reference: bacterial culture	98.5%	93.4%
Demkowicz and Reineks, 2018 (Abstract) [91]	Review of electronic medical records	Reference assay: bacterial culture	99.3%	-



(line 373) Figure I. Position of ID NOW diagnostic test in the healthcare pathways (ED – emergency department)