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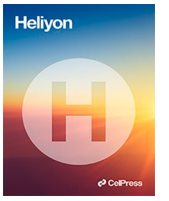

Retrospective and prospective studies evaluating the performance of the SARS-Cov-2 "AQ+ COVID-19 Ag Rapid Test" from InTec on symptomatic and non-symptomatic patients

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ABSTRACT

For the last two years, the SARS-CoV-2 virus spread all around the world and led to the COVID-19 pandemic. The need of methods to control the pandemic and to propose rapid and efficient diagnostic tools has emerged. In this perspective, SARS-CoV-2 rapid antigen detection tests (RADT) have been developed. We performed a retrospective study on 638 collected nasopharyngeal samples used for reference RT-qPCR diagnosis to compare the AQ + COVID-19 Ag Rapid Test" from InTec (AQ + InTec test) performance with other commercially available RADT (Abbott Panbio, Roche SDBiosensor and Siemens Clinitest). We analysed the sensitivity and specificity of the different tests and showed a better overall performance of the AQ + InTec test, which was confirmed on the SARS-Cov-2 Omicron variant. We then conducted a prospective study on 844patients, to evaluate the sensitivity and specificity of the AQ + InTec test on nasal and nasopharyngeal samples in a point of care setting. We showed that sensitivity and specificity reach acceptable criteria (respectively 94.4% and 99.6% on nasal samples) regarding the official recommendations of the MDCG 2021-21 in both symptomatic and asymptomatic patients. Overall, the results of these two studies confirm that the AQ + InTec test is a valuable tool for testing in a pandemic context with a high proportion of asymptomatic patients who are potential carriers for the SARS-CoV-2 virus and is performant on the most current circulating variant Omicron.

1. Introduction

In late 2019, in Wuhan China, a new type of respiratory infection caused by a novel coronavirus strain, the SARS-CoV-2, emerged. The disease was named COVID-19 for CoronaVirus Disease 2019. Since then, it has spread to the entire global population and was given the pandemic status on March 11, 2020 by the World Health Organization (WHO) [1].

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The pandemic has become a major public health problem worldwide and therefore, a rapid and accurate identification of patients requiring supportive care and isolation was important for the management of COVID-19 [2].

The Reverse Transcription-Polymerase Chain Reaction (RT-qPCR) from a nasopharyngeal swab sample became the current gold standard [3,4].

Quickly, rapid antigen detection tests (RADT) have emerged as part of the "Test-Alert-Protect" strategy [5]. In 2020, the French National Authority for Health (HAS) published a favourable opinion on RADT for the diagnosis of symptomatic patients up to 7 days after the onset of symptoms, as an alternative to RT-qPCR on nasopharyngeal swabs, and for asymptomatic individuals in the context of large-scale operations, targeting high-risk of infection populations [6,7]. Furthermore, the HAS supports the deployment of antigenic self-tests based on oropharyngeal or nasal swabs as a complementary tool in the SARS-CoV-2 screening strategy [8]These tests are rapid, inexpensive, easy to use, with an estimated reading time of 15 min but less sensitive than the PCR. During the successive waves of the epidemics, several antigenic rapid tests were developed by manufacturers. It was then crucial, for clinicians and virologists to choose antigenic tests with the highest performances. However, comparison studies are limited and difficult to conduct. InTec PRODUCTS has developed the RADT AQ + COVID-19 Ag Rapid Test (AQ + InTec test).

The present study was divided into three parts. The parts 1 and 2 of the study were comparing RADT kits using archived specimens and serial dilution respectively, the part 3 of the study was evaluating the test performance of the AQ + COVID-19 Ag Rapid Test on fresh nasal and nasopharyngeal samples from patients prospectively recruited according to the European Guidelines for validation of COVID-19 RADTs [9,10].

2. Material and methods

Part one: performance comparison between four RADT kits using archived samples The study was approved by the Orleans regional Hospital ethics committee and notified to the French data protection authority. The study was retrospective, on collected samples and aiming at validating the performances (sensitivity and specificity) of the "AQ + - SARS- CoV-2 Antigen Rapid Qualitative Test" (InTec), compared to the reference method (RT-qPCR) and comparative antigen detection-based tests.

2.1. Reference method (also used for part 2 and 3)

The reference method was a RT-qPCR test performed on nasopharyngeal sample in subjects who came to the investigative center to perform a COVID-19 molecular test (RT-qPCR, nasopharyngeal swab) with or without symptoms.

The RT-qPCR test for SARS-CoV-2 was performed in the virology unit of the CHR Orléans, France. Nucleic acid extraction was performed with an automated sample preparation system MGISP-960 (MGI, China). Real-time PCR detection of SARS-CoV-2 RNA targeting the ORF1ab, S and N genes was performed with the TaqPath V2 Covid-19 Multiplex RT-PCR kit (Thermofisher). Amplification was performed on QuantStudio5 (Applied Biosystems). The results of the assay were analysed according to the manufacturer's instructions. The assay includes an internal RNA extraction control and an amplification control. The samples were analysed considering the new positivity criteria of the French Microbiology Society's expert committee [11], in particular considering the specific characteristics of the Thermofisher kit used for the RT-qPCR measurement.

2.2. AQ + - SARS- CoV-2 Antigen Rapid Qualitative Test (InTec) and comparative rapid tests

The AQ + COVID-19 Ag Rapid Test (GJ22020185 (25T/Kit)) is a colloidal gold immunochromatographic test for the qualitative detection of SARS-CoV-2 core antigens potentially present in human nasal swabs from individuals suspected of having COVID-19 within the first 7 days of symptom onset or that without symptoms. The test is used as an aid in the diagnosis of SARS-CoV-2 infection. It is suitable for use under healthcare professional supervision. Remote healthcare professional supervision can be used with appropriate clinical governance once training has been completed and verified.

If SARS-CoV-2 antigens are present in the sample, an antibody-antigen complex will form upon contact with anti-SARS-CoV-2 monoclonal antibodies conjugated with coloured particles. This coloured complex migrates by capillary action across the membrane to the test line (T). If no SARS-CoV-2 antigen is present in the sample, no colour appears on the test line (T). The control line (C) is a control that should appear if the test procedures are performed correctly.

Sample collection was performed from subjects who came to the investigative center to perform a COVID-19 molecular test (RT-qPCR, nasopharyngeal swab) with or without symptoms. After testing, sample leftovers were frozen in Viral Transport Media (VTM, Dasky) and subsequently used to carry out the AQ + InTec test and the commercial comparatives RADT.

The following RADT were used as comparatives: Panbio™ COVID-19 Ag Rapid Test Device (Abbott, Chicago, IL, USA), Roche SD BIOSENSOR SARS-CoV-2 Antigen Rapid Test (Roche, Rotkreuz, Switzerland) and CLINITEST® Rapid COVID-19 Antigen Test (Orient Gene, Shanghai, China).

2.2.1. Part 2: limit of detection (LOD) analysis

LOD is defined as the lowest concentration of the analyte that can be reliably detected. A well documented respiratory specimen (delta variant, symptomatic patient, Ct = 20) was used for the LOD analysis. Serial dilutions were made of thes sample collected in VTM, using the leftovers after RT-qPCR reference testing (from 1,00E+06 to 3,20E+01 gcn/mL). Independent swabs were immersed in the diluted sample collected in the VTM, and the RADT test previously described were performed according to each manufacturer instructions, especially the volume of buffer to perform the rapid tests (InTec, Orient Gene, Roche, Abbott). Four different replicates

were performed for each rapid test in the same day.

2.2.2. Part 3: prospective study

The prospective study was approved in April 2022 by the Sud Ouest et Outre Mer ethics committee (N° 2022-A00503040) and was notified to French data protection authority. In accordance with the Declaration of Helsinki, all adult participants or legal representative for participating children provided written informed consent before undergoing any study-specific procedure. The study was prospective, aiming at validating the performances (sensitivity and specificity) of the "AQ + - SARS- CoV-2 Antigen Rapid Qualitative Test" (InTec), compared to the reference method (RT-qPCR).

The study was carried out between April 4th, 2022 and July 30th, 2022 in Orleans University hospital, France. Patients were those attending at the COVID screening center, the emergency unit and hospitalization wards. When a COVID test was indicated for the patient, the study was presented to the patient. After informed consent, the trained study nurses collected a nasal sample from both nostrils to perform the RADT and also asked to the patient if he could accept an additional NP sample for a second RADT, which occurred in two third of patients. Additional data were collected such as age, gender, presence or absence of symptoms, and if any, date of first symptoms declared by the patient himself.

2.3. Reference method

The RT-PCR test for SARS-Co V-2 was performed in the virology unit of the CHR Orleans, France. Nucleid acid extraction was performed with an automated sample preparation system MGISP-960 (MGI, China). Real-time PCR detection of SARS-CoV-2 RNA targeting the ORF1ab, S and N genes was performed with the TaqPath V2 Covid-19 Multiplex RT-PCR kit (Thermofischer, Illkirch, France). Amplification was performed on QuantStudio 5 (Applied Biosystems). The assay included an internal RNA extraction control and an amplification control. The determination of the VOC (variant of concern) was done on each RT-qPCR positive samples which underwent spike protein variant–specific polymerase chain reaction (PCR) to differentiate between present spike protein using the VirSNiP SARS-CoV-2 Spike N501Y, del 69/70, E484K, N501Y, L452R, T478K, and 371L 373P 452R kits (Thermofischer, Illkirch, France).

2.4. AQ + - SARS- CoV-2 Antigen Rapid Qualitative Test (InTec)

The AQ + - SARS-CoV-2 Antigen Rapid Qualitative Test (InTec) was performed on fresh nasal or nasopharyngeal swab collected in subject obtained during the participant's visit for RT-qPCR testing, according to manufacturer instructions.

2.4.1. Statistical methods

Analyses were performed with SAS V9.4, on locked databases, after reviewing the data to identify protocol deviations and their potential impact on the analysis criteria.

The description of all parameters was done on the global population called Full Analysis Set (FAS).

Quantitative parameters have been described using the following statistics: number of non-missing data, mean, standard deviation, median, first and third quartiles, minimum and maximum.

Qualitative parameters have been described using counts and percentages, and were calculated from the number of non-missing observations. The intrinsic performance of each test was assessed by calculating the sensitivity with a 95% confidence interval.

3. Results

3.1. Part 1: performance comparison between four RADT kits using archived samples

The study was conducted on 638 samples from 638 different patients tested with the reference RT-qPCR method: 329 were negative and 309 were positive.

The results obtained with the AQ + InTec test were compared with other SARS-CoV-2 RADT from Orientgene, Roche and Abott (Table 1).

The sensitivity of the AQ + InTec test was higher, with the detection of 218 positive patients out of 309 (70.6%; compared to 168, 51 and 45 respectively with the Orient Gene, Roche, and Abbott tests).

Table 1
Comparison analysis of sensibility and specificity of AQ + Intec test compared with other brand antigenic based rapid tests.

Rapid tests' brands		Intec (1)	Orient Gene (2)	Roche (3)	Abbott (4)
Sensitivity	Overall (n = 309)	70.6% [65.5–75.6]	51.1% [45.6–56.7]	19.7% [15.3–24.2]	14.6% [10.7–18.5]
	Omicron (n = 249)	73.9% [68.4–79.3]	53.4% [47.2–59.7]	20.9% [15.8–25.9]	15.3% [10.8–19.7]
	Delta (n = 51)	51% [37.3–64.7]	33.3% [20.4–46.3]	15.7% [5.7–25.7]	11.8% [2.9–20.6]
Specificity	Overall (n = 309)	100%	100%	100%	100%

Statistical test on overall sensitivity: P value 1 vs 2: <0.0001; P value 2 vs 3: <0.0001; P value 3 vs 4: non-significant.
Chi2: 274; Global p value: P < 0.0001.

This difference of sensitivity was observed for both SARS-CoV-2 Omicron and Delta variants (Fig. 1). Of note, the difference between AQ + Intec test and the other RADT used, especially Roche and Abbott's, was more marked as the CT level was lower (Table 1) (see Fig. 2).

Considering the conditions in which the sample was obtained (storage in VTM and freezing), the sensitivity of the AQ + InTec test was quite high but did not reach the criteria defined in the MDCG 2021–21 [12] which places diagnostic sensitivity threshold higher than 80% (RADT) relative to the SARS-CoV-2 RT-qPCR test.

All the tests had a specificity of 100% and no difference was observed.

3.2. Part 2: limit of detection (LOD) analysis

The limit of detection (LOD) of the AQ + InTec test has been evaluated and compared with the three other RADT. Results are shown in Table 2. The lower LOD was observed with the AQ + InTec test (1.60E+02), followed by Orient Gene (2.00E+04).

In all, the AQ + InTec test showed a higher sensitivity on samples from symptomatic and asymptomatic patients, compared to other RADT commercially available [12–15].

3.3. Part 3: prospective study

Considering the promising results of the retrospective study, it was foreseen to evaluate the performance of the AQ + InTec test, by trained professional in a point of care setting.

Overall, 844 patients attending at the screening centre, the emergency unit and hospitalization wards (Orleans University hospital) were prospectively included in the study. All of them underwent a nasopharyngeal sample for RT-qPCR. In addition, all 844 patients had a nasal sample for antigen rapid testing using AQ + Intec device. Among them 584 underwent an additional nasopharyngeal sampling to perform a second antigen rapid test to compare how nasal or nasopharyngeal sampling could influence the performances of the rapid test. Among the 844 patients included, 391 had a positive rt-qPCR (true positive) and 453 had a negative rt-qPCR (true negative). The AQ + InTec test sensitivity analysis was performed on 391 patients with known SARS-CoV-2 infection (nasopharyngealsample positive with RT-qPCR). The specificity analysis was performed on 453 patients with no SARS-CoV-2 infection (nasopharyngeal sample negative with RT-qPCR).

3.3.1. AQ + InTec test sensitivity: comparison with CT level of the reference test

To evaluate the performance of the AQ + InTec test on nasal and nasopharyngeal samples, the results obtained with the test were compared to the reference RT-qPCR results. Two groups of patients were analysed: nasal and nasopharyngeal samples. In the first group, the sensitivity of the AQ + InTec test was measured on nasal samples of 391 patients. Among these, SArS-Cov2 antigen was detected in 396 patients by the AQ + InTec test compared with the reference method (RT-qPCR), with an overall sensitivity of 94.4% (95% CI [92.1–96.7]). Interestingly, the sensitivity was as high as 99.6% (95% CI [98.9–100.0]) when the CT level was below 25 in the reference test (Table 3) (see Table 4).

The sensitivity of the AQ + InTec test was also measured on nasopharyngeal samples of 269 patients detected positive for SArS-Cov2 by the reference RT-qPCR test. Among these, 262 were positive with the AQ + InTec test, with a sensitivity of 97.4% (95% CI [95.5–99.3]). The sensitivity increased to 100% (95%CI [100−100]) on samples with a CT level below 25.

In both nasal and nasopharyngeal samples, the sensitivity of the AQ + InTec test was lowered when the CT level was high. Nevertheless, the sensitivity was always higher with nasopharyngeal samples compared with nasal samples (Table 3).

3.3.2. AQ + InTec test sensitivity in symptomatic and asymptomatic patients

On nasal samples of the 308 symptomatic positive patients, the sensitivity of the AQ + InTec test was as high as 95.8% and 89.2% on the 83 asymptomatic patients. On nasopharyngeal samples of the 203 symptomatic positive patients, the sensitivity of the test was as high as 97.5% and 97% on the 66 asymptomatic patients.

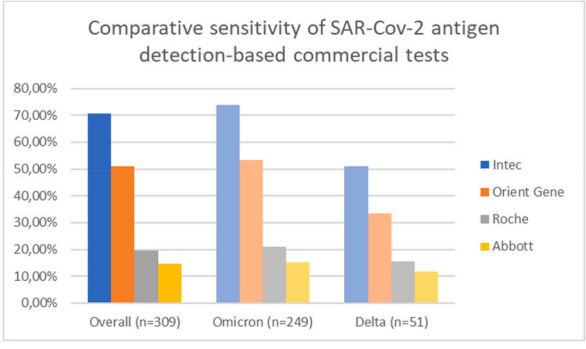

Fig. 1. Comparative sensitivity of SARS-CoV-2 antigen detection-based commercial tests.

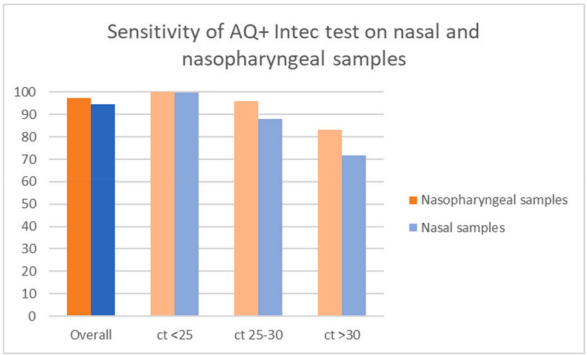

Fig. 2. Sensitivity of the AQ + InTec test on nasal and nasopharyngeal samples and corresponding CT levels of the reference RT-qPCR test.

Table 2
Limit of detection analysis.

		Intec	Orient Gene	Roche	Abbott	Total N = 1
						Estimated gcn/mL
PCR CT (N gene)	25	Positive	Positive	Negative	Negative	1,00E+06
	27	Positive	Positive	Negative	Negative	5,00E+05
	29	Positive	Positive	Negative	Negative	1,00E+05
	31	Positive	Positive	Negative	Negative	2,00E+04
	32	Positive	Negative	Negative	Negative	4,00E+03
	34	Positive	Negative	Negative	Negative	8,00E+02
	36	Positive	Negative	Negative	Negative	1,60E+02
	Undet.	Negative	Negative	Negative	Negative	3,20E+01

Table 3
Sensitivity of the AQ + InTec test on nasal and nasopharyngeal samples and corresponding CT levels of the reference RT-qPCR test.

		Positive RT-qPCR (nasopharyngeal)	Positive AQ + Intec test	Sensitivity % [95% CI]
Nasal samples				
Overall		391	369	94.4 [92.1–96.7]
CT level	<25	259	258	99.6 [98.9–100.0]
	25–30	100	88	88.0 [81.6–94.4]
	>30	32	23	71.8 [56.3–87.5]
Nasopharyngeal samples				
Overall		269	262	97.4 [95.5–99.3]
CT level	<25	168	168	100 [100–100.0]
	25–30	77	74	96.1 [91.8–100]
	>30	24	20	83.3 [68.4–98.2]

Table 4
Sensitivity of the AQ + InTec test on nasal and nasopharyngeal samples in symptomatic and asymptomatic patients.

	Date of symptoms	Positive RT-qPCR	Positive AQ + Intec test	Sensitivity % [95% CI]
Nasal samples				
Asymptomatic		83	74	89.2 [82.5–95.8]
Symptomatic		308	295	95.8 [93.5–98.0]
	<3 days	176	168	95.5 [92.4–98.3]
	3–5 days	100	98	98.0 [95.3–100]
	>5 days	32	29	90.6 [80.5–100]
Nasopharyngeal samples				
Asymptomatic		66	64	97.0 [92.8–100]
Symptomatic		203	198	97.5 [95.4–99.7]
	<3 days	113	111	98.2 [95.8–100]
	3–5 days	67	66	98.5 [95.6–100]
	>5 days	23	21	91.3 [79.8–100]

3.3.3. AQ + InTec test specificity

To evaluate the diagnostic specificity of the AQ + InTec test, an analysis was conducted on 453 subjects with a negative RT-qPCR reference test who had a nasal sample and 315 subjects with a negative RT-qPCR reference test who had a nasopharyngeal sample.

Two subjects out of 453 (nasal sample) had a positive result with the AQ + InTec test with a negative RT-qPCR result, giving a specificity of 99.6%.

All patients with a negative RT-qPCR who had a nasopharyngeal sample were also negative with the AQ + InTec test, giving a specificity of 100% Table 5).

4. Discussion

Retrospective studies on SARS-CoV-2 RADT evaluation allow comparison of different tests on the same sample, as multiple sampling from the same patient raises ethical issues. Indeed, as it is compulsory to use the specific test buffer, it would necessitate a number of swabs equal to the number of RADTs to evaluate for each patient. In this retrospective study, four independent swabs were immersed in a previously collected nasopharyngeal samples, then placed in each of the specific buffers before performing the RADTs allowing statistical comparison, which is not possible in independent studies. However, retrospective studies reduce the real sensitivity because the swab is immersed in 3 mL of VTM which dilutes the collected [16]. The present retrospective study revealed an overall better sensitivity of the AQ + InTec test compared to the other commercial tests (Orient Gene, Roche, Abott) included in the analysis. Moreover, the LOD analysis revealed a lower LOD for the AQ + InTec test, followed by Orient Gene, which is consistent with a better sensitivity [17,18]. However, considering the points raised above, these results need to be considered carefully. Of note, in this experimental setup, none of the RADTs, including the AQ + InTec tests reached a satisfying sensitivity regarding of the acceptance criteria defined in the MDCG 2021–21 (sensitivity >80%) [19]. This lack in performance is easily explained by the experimental setup itself, however, it sheds light on the difference of detection limits that exists between the commercially available SARS-CoV-2 RADT as previously reported [18]. Another concern has emerged regarding the potentially different limits of detection for different SARS-CoV-2 variants between the RADTs [17]. Our study supports that the performance of commercially available RADTs for SARS-CoV-2 detection varies with the variant type, but this should also be considered in perspective with the experimental setup.

In the prospective study aiming at evaluating the sensitivity and specificity test in a point of care setting, the AQ + InTec test exhibited high sensitivity on nasal samples (94.4%) and nasopharyngeal samples (97.4%) and high specificity (99.6 to 100%) which fulfil the acceptance criteria defined in the MDCG 2021–21 “Guidance on performance evaluation of SARS-CoV-2 in vitro diagnostic medical devices” [19]:

- - Diagnostic sensitivity: >80% (rapid tests) relative to the SARS-CoV-2 RT-qPCR test;
- - Diagnostic specificity: >98% (rapid tests).

Another point of interest was to compare the results obtained on symptomatic and asymptomatic patients to determine whether the AQ + InTec test was as sensitive when patients were asymptomatic. Indeed, it has been shown in a study comparing the results of 78 studies on SARS-Cov2 antigenic tests, that the sensitivity of this method is reduced by 13.8% points on average for asymptomatic patients [12–15].

It is important to note that the sensitivity of the AQ + InTec test is particularly high on asymptomatic patients compared to other RADTs available on the market. Indeed, an analysis of 12 studies, reported an average sensitivity of 58.1% (95% CI 40.2% to 74.1%) [12], placing the AQ + InTec test above in terms of sensitivity on both nasal and nasopharyngeal samples in asymptomatic patients (respectively 89.2% and 97.0%) and making it a valuable tool for testing in an epidemic context with a high proportion of asymptomatic patients that are potential carriers for the SARS-CoV-2 virus [12–15].

However, the high performance of the results may also be related to the high viral load samples collected, as 369 among the 391 patients (94.3%) having a nasal sample had a viral load Ct 30 or below and 242 among 262 patients (92.4%) having a nasopharyngeal sample had a viral load Ct 30 or below.

5. Conclusion

During these two studies, the AQ + Intec antigen rapid test showed better sensitivity compared with three commercialized antigen tests in the retrospective study and very high performances reaching 95% sensitivity in the prospective study. Nasal and nasopharyngeal samples provide quite equivalent level of antigen detection in terms of sensitivity. Retrospective studies are useful to compare antigen rapid tests but, as samples are diluted compared to fresh samples, they do not give true level of sensitivity.

Author contribution statement

Thierry Prazuck: Conceived and designed the experiments; Analysed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Raphael Serreau: Conceived and designed the experiments.

Aurelie Theillay; Sandra Pallay; Daniela Pires-Roteia: Performed the experiments.

Fanny Prazuck: Analysed and interpreted the data.

Fabien Lesne: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data.

Table 5
Specificity of the AQ + InTec test on nasal and nasopharyngeal samples.

Negative RT-qPCR	Negative AQ + InTec test	Specificity % [95% CI]
Nasal samples		
453	451	99.6 [99.0–100]
Nasopharyngeal samples		
315	315	100 [100–100]

Data availability statement

Data will be made available on request.

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The tests were provided free of charge by InTec Products.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e18088.

References

[1] World Health Organization, WHO Director-General's Opening Remarks At The Media Briefing On COVID-19 - 11 March 2020, 2020. https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19—11-march-2020.
[2] H.A. Rothan, S.N. Byrareddy, The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak, J. Autoimmun. 109 (2020).
[3] N. Sethuraman, S.S. Jeremiah, A. Ryo, Interpreting diagnostic tests for SARS-CoV-2, JAMA 323 (2020) 2249–2251.
[4] Gorbalenya A. E., et al. Severe acute respiratory syndrome-related coronavirus: The species and its viruses-a statement of the Coronavirus Study Group. doi: 10.1101/2020.02.07.937862.
[5] https://www.ameli.fr/hauts-de-seine/assure/covid-19/tester-alerter-proteger-comprendre-la-strategie-pour-stopper-lepidemie, 2021.
[6] La HAS positionne les tests antigéniques dans trois situations, 2020. https://www.has-sante.fr/jcms/p_3212125/fr/covid-19-la-has-positionne-les-tests-antigeniques-dans-trois-situations.
[7] Les tests antigéniques sont performants chez les patients symptomatiques, 2020. https://www.has-sante.fr/jcms/p_3203094/fr/covid-19-les-tests-antigeniques-sont-performants-chez-les-patients-symptomatiques.
[8] Quelle place pour les tests antigéniques nasaux dans la stratégie de dépistage ?, 2021. https://www.has-sante.fr/jcms/p_3243463/fr/covid-19-quelle-place-pour-les-tests-antigeniques-nasaux-dans-la-strategie-de-depistage.
[9] Options for the use of rapid antigen tests for COVID-19 in the EU/EEA and the UK. Preprint at, 2020. https://ec.europa.eu/health/sites/default/files/preparedness_response/docs/covid-19_rat_common-list_en.pdf.
[10] A common list of COVID-19 rapid antigen tests and a common standardized set of data to be included in COVID-19 test result certificates. Preprint at, 2021. https://ec.europa.eu/health/sites/default/files/preparedness_response/docs/covid-19_rat_common-list_en.pdf.
[11] J. Salomon, B. Worms, Avis du 25 septembre 2020 de la Société Française de Microbiologie (SFM) relatif à l'interprétation de la valeur de Ct (estimation de la charge virale) obtenue en cas de RT-PCR SARS-CoV-2 positive sur les prélèvements cliniques réalisés à des fins diagnostiques ou de dépistage Version 4 _ 14/01/2021 Mise à jour, 2021. https://www.sfm-microbiologie.org/wp-content/uploads/2021/01/Avis-SFM-valeur-Ct-excre%CC%81tion-virale-_-Version-def-14012021_V4.pdf.
[12] J. Dinnes, et al., Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection, Cochrane Database Syst. Rev. 2021 (2021).
[13] I.W. Pray, et al., Performance of an antigen-based test for asymptomatic and symptomatic SARS-CoV-2 testing at two university campuses — Wisconsin, September–October 2020, MMWR (Morb. Mortal. Wkly. Rep.) 69 (2021) 1642.
[14] S.L. Mitchell, et al., Performance of SARS-CoV-2 antigen testing in symptomatic and asymptomatic adults: a single-center evaluation, BMC Infect. Dis. 21 (2021) 1–7.
[15] A. Brihn, et al., Diagnostic performance of an antigen test with RT-PCR for the detection of SARS-CoV-2 in a hospital setting — Los Angeles county, California, June–August 2020, MMWR (Morb. Mortal. Wkly. Rep.) 70 (2021) 702.
[16] H. Zhou, et al., The impact of sample processing on the rapid antigen detection test for SARS-CoV-2: virus inactivation, VTM selection, and sample preservation, Biosaf Health 3 (2021) 238–243.

[17] S. Stanley, et al., Limit of detection for rapid antigen testing of the SARS-CoV-2 omicron and delta variants of concern using live-virus culture, J. Clin. Microbiol. 60 (2022) 165–170.
[18] A.I. Cubas-Atienzar, et al., Limit of detection in different matrices of 19 commercially available rapid antigen tests for the detection of SARS-CoV-2, Sci. Rep. 11 (2021), 18313.
[19] Guidance on performance evaluation of SARS-CoV-2 in vitro diagnostic medical devices, 2021. https://ec.europa.eu/health/sites/default/files/md_sector/docs/mdcg_2021-21_en.pdf.