Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Microbiological Research 265 (2022) 127185

Contents lists available at ScienceDirect

Microbiological Research

journal homepage: www.elsevier.com/locate/micres

Diagnostic accuracy of rapid antigen test for SARS-CoV-2: A systematic review and meta-analysis of 166,943 suspected COVID-19 patients

Jia-Wen Xie [a,b], Yun He [a,b], Ya-Wen Zheng [a,b], Mao Wang [a,b], Yong Lin [a,b,*], Li-Rong Lin [a,b,*]

[a] Center of Clinical Laboratory, Zhongshan Hospital of Xiamen University, School of Medicine, Xiamen University, Xiamen, China
[b] Institute of Infectious Disease, School of Medicine, Xiamen University, Xiamen, China

ARTICLE INFO

Keywords:
Rapid antigen test
SARS-CoV-2
COVID-19
RT-PCR
Screening

ABSTRACT

To assess the diagnostic accuracy of the rapid antigen test (RAT) compared with RT-PCR (reference standard) for SARS-CoV-2, we searched MEDLINE/PubMed and Web of Science for relevant records. The QUADAS-2 tool was used to assess study quality, and quantitative synthesis was conducted using a bivariate random-effects model. The meta-analysis included 135 studies (166,943 samples). The pooled sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio were 0.76 (95%CI: 0.73–0.79), 1.00 (95%CI: 1.00–1.00), 276.1 (95% CI, 184.1–414.1), 0.24 (95% CI, 0.21–0.27), and 1171 (95% CI, 782–1755), respectively. Compared to other sample types, nasal samples had the best RAT sensitivity [0.79 (95%CI: 0.71–0.85)]. The sensitivities of the different RAT kits ranged from 0.41 (95%CI: 0.23–0.61) to 0.90 (95%CI: 0.70–0.97). Sensitivity was markedly better in samples with lower Ct, and RAT achieved excellent pooled sensitivity at 1.00 (95% CI: 0.70–1.00) among samples with Ct < 20. Testing within 10 days of symptom onset resulted in a high sensitivity. For ≤ 3, ≤ 7, and ≤ 10 days, the sensitivities were 0.91 (95%CI: 0.83–0.96), 0.89 (95%CI: 0.84–0.93), and 0.88 (95%CI: 0.83–0.92), respectively. RAT kits show high sensitivity and specificity in early infection, especially when the viral load is high. Moreover, using nasal samples for antigen testing, which are moderately sensitive and patient-friendly, is a reliable alternative to nasopharyngeal sampling. RAT might be effective for fighting the COVID-19 pandemic; however, it must be complemented by the careful handling of negative test results.

1. Introduction

Coronavirus disease COVID-19 (COVID-19), an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), became a global pandemic within a short period (Lai et al., 2020; "WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020," 2021). The rapid and precise diagnosis of COVID-19 is essential to enable prompt and accurate public health surveillance, prevention, and control (Jin et al., 2020).

Two major types of diagnostic tests for COVID-19 are currently available: a direct method to examine clinical specimens for the presence of viral particles, viral antigens, or viral nucleic acids, and a serological test to detect anti-SARS-CoV-2 antibodies (Borges et al., 2021). Reverse transcription polymerase chain reaction (RT-PCR) is currently the gold standard for detecting SARS-CoV-2 because of its ability to directly measure the genomic portion of the virus (Yüce et al., 2021). However, RT-PCR may be unsuitable in emergency settings because it may take several hours to obtain results. It also requires expensive technology and competent operators, and these may be unavailable in remote health clinics, especially in underdeveloped countries (Khandker et al., 2021). To improve this situation, the rapid antigen test (RAT) for COVID-19, which does not require specific and costly machinery, emerged as an essential alternative tool to aid the clinical diagnosis of COVID-19 (Yamayoshi et al., 2020, p. 1). It is low-cost and straightforward, with a shorter turnaround time. Thus, it can be used as a point-of-care test, allowing for the immediate isolation of infected individuals and permitting the early implementation of appropriate infection control measures, which is critical in a pandemic (Torres et al., 2021).

As numerous COVID-19 antigen tests are rapidly evolving, a growing number of independent validations have been conducted. Studies on the diagnostic accuracy of RAT vary widely in terms of quality, methodology, and results, generally showing excellent specificity but variable sensitivity. The different results may be due to differences in study

* Correspondence to: Centre of Clinical Laboratory, Zhongshan Hospital of Xiamen University, School of Medicine, Xiamen University, Xiamen 361004, China.
E-mail addresses: linyong929@xmu.edu.cn (Y. Lin), linlirong@xmu.edu.cn (L.-R. Lin).

https://doi.org/10.1016/j.micres.2022.127185
Received 8 August 2022; Received in revised form 30 August 2022; Accepted 5 September 2022
Available online 9 September 2022

design, manufacturers of RAT kits, patient selection, type of specimen, and stage of disease at the time of sample collection (Khandker et al., 2021). Therefore, the efficacy of RAT still needs to be thoroughly investigated. This systematic review and meta-analysis aimed to assess the diagnostic accuracy of RAT compared to RT-PCR methods as a reference standard.

2. Materials and methods

This systematic review and meta-analysis were conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, and the protocol of this study was registered in the PROSPERO database (CRD42022339683).

2.1. Literature search

The MEDLINE/PubMed and Web of Science databases were searched for relevant studies published up to 10 May 2022. We used a combination of free text and MeSH terms to identify relevant studies. The main search terms were: "SARS-CoV-2", "COVID-19", "antigen test", "Specificity", and "Sensitivity". The detailed search strategies are presented in Table S1. Two researchers independently conducted a literature search to minimize potential biases.

2.2. Inclusion and exclusion criteria

Any study that satisfied the following requirements was considered eligible for inclusion in our meta-analysis: (i) use of RAT as an index test, (ii) measurement of the performance of RAT against RT-PCR as a reference standard, and (iii) availability of the sensitivity and specificity of RAT. The following were the exclusion standards: (i) duplicate original investigation, reviews, editorials, letters, comments, and meta-analysis articles, and (ii) unavailability of data (by article review or calculation) necessary for a meta-analysis.

2.3. Data extraction and quality assessment

We extracted the following data from the full texts and supplemental materials of all qualified articles: the first author's last name, the publication year, the country of residence of the study participants, and true positive (TP), false positive (FP), false negative (FN), and true negative (TN) values. The diagnostic parameters were calculated using the sensitivity and specificity values if they were unavailable. The risk of bias of each included publication was assessed using The Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool. (Whiting et al., 2011). Two researchers carried out the assessment process independently. A third researcher was invited to reach a settlement in case of disagreement.

2.4. Statistical analysis

The extracted data were recorded for further analysis using STATA software (Stata Corporation, College Station, TX, USA). We used a bivariate random-effects model to perform the quantitative synthesis. We calculated each parameter of individual studies by the following formulas to derive the pooled sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio:

Sensitivity=TP/(TP+FN).

Specificity=TN/(TN+FP).

Positive likelihood ratio=Sensitivity/(1–Specificity).

Negative likelihood ratio= (1–Sensitivity)/Specificity.

Diagnostic odds ratio= Positive likelihood ratio/Negative likelihood ratio.

The forest plots were employed to show the overall effects. The area under the curve (AUC) was calculated using an optimal cutoff value by a summary receiver operating characteristic (SROC) curve. To access interstudy heterogeneity, bivariate boxplots, qualitative Q tests, and quantitative I^2 tests were utilized. Publication bias was evaluated by Deeks' funnel plot. The Fagan nomogram and the likelihood ratio scattergram were used to access the diagnostic value and clinical application value, respectively. All tests were two-sided. A P value < 0.05 was considered statistically significant.

3. Results

3.1. Features of eligible studies

According to our search criteria, 1453 publications were initially selected. A total of 1119 articles were excluded during the initial screening process, including reviews (n = 128), editorials (n = 9), letters (n = 22), commentaries (n = 8), and duplicates (n = 952). A total of 334 articles were selected for full-text review to determine if they qualified for the meta-analysis. Of these, 199 articles including articles irrelevant to the objective of the meta-analysis (n = 143), repetitive studies (n = 12), and articles with insufficient data (n = 44) were excluded. The remaining 135 studies met the eligibility criteria and were included in the meta-analysis. The inclusion and exclusion processes are shown in Fig. 1.

The 135 studies selected for this meta-analysis included 166,943 samples. All included studies were published between 2020 and 2022 and involved 37 countries; the top three countries in terms of the number of studies were Italy (n = 18), the USA (n = 15), and Spain (n = 15). All articles were not pre-prints. Except for three manufacturer-dependent studies, the remaining were all manufacturer-independent studies. Forty different RAT kits were investigated. Different types of specimens (nasal, nasopharyngeal, oropharyngeal, throat, and saliva swabs) were collected from suspected symptomatic or asymptomatic participants (Table 1). Ninety-three studies evaluated the diagnostic efficacy with nasopharyngeal swabs, and 26 studies assessed the performance with nasal swabs. Cycle threshold (Ct) values for positive RT-PCR were provided in 27 studies. Thirteen studies reported the time of symptom onset in RT-PCR-positive patients.

3.2. Quality assessment

Fig. S1 and Table S2 show the quality of the studies in our meta-analysis, based on the QUADAS-2 tool. In the majority (78.5%, 106/135) of the included studies, all patients were consecutively or randomly included, and inappropriate exclusions and case-control designs were avoided. All the studies were judged to have a low risk of bias in the index test and reference standard domains. Regarding the flow and time domains, 73.3% (99/135) of the studies were considered to have a low risk of bias, as they received the same reference standard, and all selected patients were enrolled in the analysis. The patient selection, index tests, and reference standards were considered to meet the objectives of this meta-analysis.

3.3. Publication bias

Deeks' funnel plot (Fig. S2) did not display significant asymmetry on visual inspection; the P-value of 0.78 for the slope coefficient also suggested symmetry in the data and no striking publication bias in this study.

3.4. Analysis of heterogeneity

We found that P values of the Q test for sensitivity and specificity were both < 0.001 based on heterogeneity statistics, suggesting significant interstudy heterogeneity. In addition, as the bivariate boxplot shows in Fig. S3, most studies clustered within the median distribution with 28 outliers, further indicating the presence of interstudy heterogeneity. Thus, a bivariate random-effects model was appropriate for

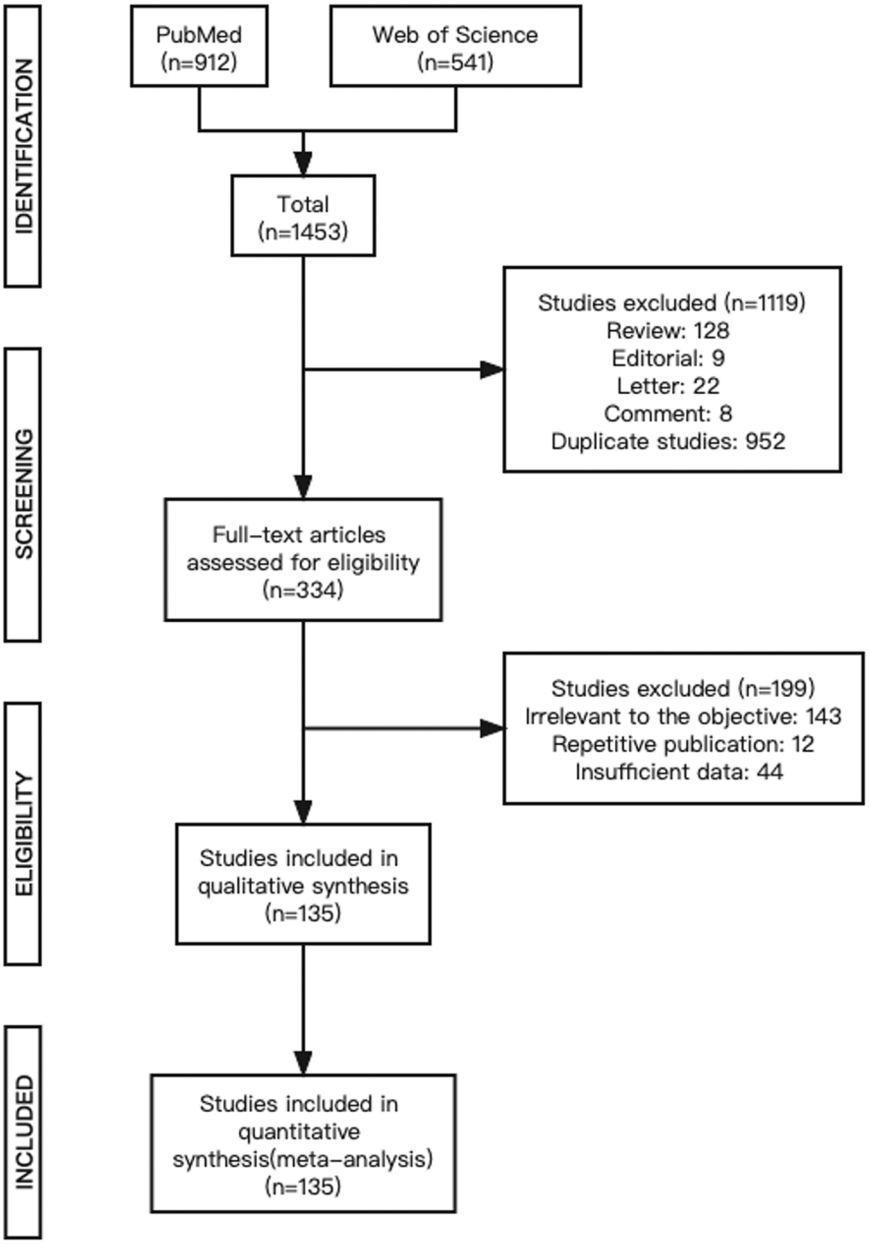

Fig. 1. PRISMA flow diagram.

quantitative synthesis.

3.5. Diagnostic performance

The meta-analysis demonstrated a pooled sensitivity of 0.76 (95% CI: 0.73–0.79) (Fig. 2A) and a pooled specificity of 1.00 (95% CI: 1.00–1.00) (Fig. 2B). The pooled positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio were 276.1 (95% CI, 184.1–414.1), 0.24 (95% CI, 0.21–0.27), and 1171 (95% CI, 782–1755), respectively. Additionally, the summary AUC was 0.97 (95% CI, 0.96–0.98) (Fig. 3), which reveals that RAT is of high diagnostic value for COVID-19. As shown in Fig. 3, there was no shoulder-arm-shaped distribution in the SROC curve, and the proportion of heterogeneity due to the threshold effect was 0.12, indicating that the heterogeneity of this meta-analysis was independent of the threshold effect.

The results of the statistical analysis were used to set the pretest probability to 12%. The Fagan plot presented in Fig. 4A shows that the posttest probability increased to 97% if the antigen test was positive and was as low as 3% if the antigen test was negative. When we assumed a higher pretest probability of infection of 24% (doubling the prevalence rate), both the positive and negative posttest probabilities improved to 99% and 7%, respectively. When the prevalence rate was halved to 6%, the probability of a positive posttest dropped to 95%, and the probability of a negative posttest dropped to 1%.

The likelihood ratio scattergram (Fig. 4B) showed that more than three-quarters of the studies (77.8%, 105/135) along with the summary point of likelihood ratios obtained as functions of mean sensitivity and specificity were in the right upper quadrant. These findings suggest that RAT helps confirm the presence of SARS-CoV-2 when the test result is positive and not for its exclusion when negative.

3.6. Subgroup analyses

In Table 2, all the samples achieved a specificity of 1.00. When assessing studies evaluating nasopharyngeal swab as the sample type for Ag-RDT, the pooled sensitivity from 93 studies with 76,945 samples was

Table 1
Characterization of included studies.

DOI	Author	Year	Country	Rapid Antigen Test Kit	Specimen Types	TP	TN	FP	FN	SS
10.3390/pathogens10060658	Fiedler	2021	Germany	LIAISON® SARS-CoV-2 Ag assay (Diasorin, Saluggia, Italy),	nasopharyngeal swabs	77	72	0	33	182
10.1016/j.jviromet.2020.114024	Krüttgen	2021	Germany	Roche SARS-CoV-2 antigen assay	nasopharyngeal swabs	53	72	3	22	150
10.1016/j.jcv.2021.104991	Abdelhanin	2021	Belgium	Elecsys® SARS-CoV-2 Antigen assay	nasopharyngeal swabs	81	102	0	42	225
10.1016/j.ijid.2021.09.069	Sberna	2021	Italy	Lumipulse® G SARS-CoV-2 Ag assay	nasopharyngeal swabs	231	212	26	44	513
10.1007/s40121–021–00510-x	Nörz	2021	Germany	Elecsys® SARS-CoV-2 Antigen assay	oro-nasopharyngeal swabs	236	2743	4	156	3139
10.1002/jmv.27459	García-Salguero	2021	Spain	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	30	69	0	8	107
10.1016/j.jcv.2021.104909	Moeren	2021	Netherlands	LIAISON® SARS-CoV-2 Ag assay (Diasorin, Saluggia, Italy),	oro-nasopharyngeal swabs	54	174	0	20	248
10.1016/j.jiac.2020.11.021	Aoki	2021	Japan	Lumipulse® G SARS-CoV-2 Ag assay	nasopharyngeal swabs	22	516	8	2	548
10.1016/j.jviromet.2021.114409	Randriamahazo	2022	Madagascar	STANDARD Q COVID-19 Ag Test	nasopharyngeal swabs	94	106	0	56	256
10.1016/j.ijmmb.2021.07.003	Kanaujia	2021	India	Coris bioconcept COVID-19 ag respi-strip test	nasopharyngeal swabs	136	293	2	53	484
10.1016/j.ijid.2021.05.082	Mayanskiy	2021	Russia	CoviNAg ELISA kit	nasopharyngeal swabs	164	72	23	18	277
10.1128/JCM.00896–21	Korenkov	2021	Germany	STANDARD Q COVID-19 Ag Test	oro-nasopharyngeal swabs	90	1816	2	120	2028
10.3390/vaccines10020198	Lau	2022	Singapore	Elecsys® SARS-CoV-2 Antigen assay	nasopharyngeal swabs	26	288	1	35	350
10.1002/jmv.26830	Ciotti	2021	Italy	Coris bioconcept COVID-19 ag respi-strip test	nasopharyngeal swabs	12	11	0	27	50
10.1016/j.jcv.2021.104838	Bianco	2021	Italy	LumiraDx SARS-CoV-2 Ag Test	nasal swabs	269	561	48	29	907
10.1002/jcla.23745	Peña-Rodríguez	2021	Mexico	STANDARD Q COVID-19 Ag Test	nasopharyngeal swabs	79	265	0	25	369
10.1016/j.jcv.2020.104713	Toptan	2021	Germany	R-Biopharm	oro-nasopharyngeal swabs	45	9	0	13	67
10.1002/jcla.23906	Mueller	2021	Italy	Elecsys® SARS-CoV-2 Antigen assay	nasopharyngeal swabs	12	356	0	35	403
10.3390/v14030468	Salcedo	2022	USA	Rapid antigen tests (E25Bio, Inc., Cambridge, MA, USA)	nasal swabs	51	113	1	8	173
10.1186/s12985–020–01452–5	Chaimayo	2020	Thailand	STANDARD Q COVID-19 Ag Test	nasopharyngeal and throat swabs	59	389	5	1	454
10.1186/s12879–021–06716–1	Mitchell	2021	USA	Sofia SARS rapid antigen	nasal swabs	36	107	0	5	148
10.3390/diagnostics12030650	Polvere	2022	Italy	FAST COVID-19 SARS-CoV-2 Antigen Rapid Test kit	nasal swabs	113	383	3	2	501
10.1016/j.ijid.2021.02.005	Hirotsu	2021	Japan	Lumipulse® G SARS-CoV-2 Ag assay	nasopharyngeal swabs	37	989	0	3	1029
10.3390/jcm10102099	Osmanodja	2021	Germany	Dräger Antigen Test SARS-CoV-2	nasal swabs	62	308	1	8	379
10.1016/j.jcv.2021.105048	Fourati	2022	France	COVID-VIRO® analysis	nasopharyngeal swabs	215	1614	0	77	1906
10.1080/1354750X.2021.1876769	Möckel	2021	Germany	Roche SARS-CoV-2 antigen assay	oro-nasopharyngeal swabs	85	358	1	29	473
10.1016/j.jiac.2021.02.029	Takeuchi	2021	Japan	QuickNavi™-COVID19 Ag	nasopharyngeal swabs	91	1081	0	14	1186
10.1007/s00430–021–00706–5	Häuser	2021	Germany	LIAISON® SARS-CoV-2 Ag assay (Diasorin, Saluggia, Italy),	nasopharyngeal swabs	68	1632	0	101	1801
10.3389/fped.2021.647274	Jung	2021	France	BIOSYNEX Ag-RDT	nasopharyngeal swabs	29	271	4	4	308
10.3390/v14010017	Klajmon	2022	Poland	Humasis COVID-19 Ag Test kit	nasopharyngeal swabs	43	140	2	4	189
10.1093/ajcp/aqab173	Drain	2022	USA	LumiraDx SARS-CoV-2 Ag Test	nasal swabs	23	194	0	5	222
10.1016/j.jcv.2021.104789	Landaas	2021	Norway	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal and throat swabs	186	3738	3	64	3991
10.1016/j.ijid.2021.10.027	Thirion-Romero	2021	Mexico	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	256	579	9	216	1060
10.1515/cclm-2021–0569	Hartard	2021	France	LIAISON® SARS-CoV-2 Ag assay (Diasorin, Saluggia, Italy),	nasopharyngeal swabs	39	330	2	7	378
10.1128/JCM.01742–21	Almendares	2022	USA	BinaxNOW COVID-19 Ag Card test kit	nasal swabs	157	3116	4	142	3419
10.1515/cclm-2021–0182	Menchinelli	2021	Italy	Lumipulse® G SARS-CoV-2 Ag assay	nasopharyngeal swabs	155	397	3	39	594
10.1016/j.heliyon.2021.e08455	Rahman	2021	Bangladesh	STANDARD Q COVID-19 Ag Test	nasopharyngeal swabs	261	593	0	46	900
10.1016/j.jcv.2021.104941	Escrivá	2021	Spain	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	99	331	0	18	448

(*continued on next page*)

Table 1 (*continued*)

DOI	Author	Year	Country	Rapid Antigen Test Kit	Specimen Types	TP	TN	FP	FN	SS
10.1016/j.jcv.2021.104961	Merino-Amador	2021	Spain	Clinitest Rapid COVID-19 Antigen Test (ClinitestRT) (Siemens, Healthineers, Erlangen, Germany)	nasopharyngeal swabs	179	256	2	13	450
10.1016/j.diagmicrobio.2021.115591	Onsongo	2022	Kenya	NowCheck SARS-CoV-2 Ag test	oro-nasopharyngeal swabs	129	845	0	23	997
10.1016/j.jcv.2020.104659	Linares	2020	Spain	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	44	195	0	16	255
10.1016/j.ijid.2020.10.073	Nalumansi	2021	Uganda	STANDARD Q COVID-19 Ag Test	nasopharyngeal swabs	63	159	13	27	262
10.3390/ijerph19073826	Cattelan	2022	Italy	LumiraDx SARS-CoV-2 Ag Test	nasal swabs	174	51	3	54	282
10.1016/j.cmi.2020.11.004	Albert	2021	Spain	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	43	358	0	11	412
10.1097/INF.0000000000003101	González-Donapetry	2021	Spain	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	14	422	0	4	440
10.3201/eid2705.204688	Igloi	2021	Netherlands	Roche SARS-CoV-2 antigen assay	nasopharyngeal swabs	158	780	4	28	970
10.1002/jmv.26896	Courtellemont	2021	France	COVID-VIRO® analysis	nasopharyngeal swabs	117	127	0	4	248
10.1371/journal.pone.0247918	Krüger	2021	Germany	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	92	1001	1	14	1108
10.1016/j.jiac.2021.03.021	Asai	2021	Japan	Lumipulse® G SARS-CoV-2 Ag assay	saliva	49	238	4	14	305
10.3390/v13050818	Cento	2021	Italy	LumiraDx SARS-CoV-2 Ag Test	nasopharyngeal swabs	297	596	17	50	960
10.3389/fpubh.2021.728969	Alqahtani	2021	Bahrain	Panbio COVID-19 Ag Rapid Test Device	nasal swabs	602	3420	30	131	4183
10.3346/jkms.2021.36.e101	Oh	2021	Korea	STANDARD Q COVID-19 Ag Test	nasopharyngeal swabs	7	78	0	33	118
10.1371/journal.pone.0259527	Thell	2021	Austria	Roche SARS-CoV-2 antigen assay	nasopharyngeal swabs	171	325	3	42	541
10.1017/ice.2021.281	Smith	2021	Maryland	Sofia SARS rapid antigen	nasopharyngeal swabs	180	2645	7	55	2887
10.4269/ajtmh.21–0809	Mungomklang	2021	Thailand	STANDARD Q COVID-19 Ag Test	nasopharyngeal swabs	35	1024	3	38	1100
10.1017/ice.2021.20	James	2021	USA	BinaxNOW COVID-19 Ag Card test kit	nasal swabs	86	2184	3	66	2339
10.1016/j.cmi.2020.09.057	Diao	2021	China	FIC assay	nasopharyngeal swabs	152	50	0	49	251
10.1016/j.jiac.2021.07.005	Kiyasu	2021	Japan	QuickNavi™-COVID19 Ag	nasopharyngeal swabs	151	1746	0	37	1934
10.1016/j.cmi.2021.02.001	Merino	2021	Spain	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	325	592	7	34	958
10.3390/v13050796	Kim	2021	Korea	GenBody™ COVID-19 Ag test	nasopharyngeal swabs	121	198	2	9	330
10.1371/journal.pone.0258394	Jo	2022	Korea	STANDARD Q COVID-19 Ag Test	nasopharyngeal swabs	34	110	0	26	170
10.3201/eid2711.211449	Surasi	2021	USA	BinaxNOW COVID-19 Ag Card test kit	nasal swabs	55	642	0	72	769
10.3390/diagnostics11112110	Altawalah	2021	Kuwait	LIAISON® SARS-CoV-2 Ag assay (Diasorin, Saluggia, Italy),	nasopharyngeal swabs	113	150	0	37	300
10.1111/apm.13189	Jakobsen	2021	Denmark	STANDARD Q COVID-19 Ag Test	nasal swabs	32	7008	0	34	7074
10.3390/diagnostics12020447	Yin	2022	Belgium	Lumipulse® G SARS-CoV-2 Ag assay	nasopharyngeal swabs	95	396	4	7	502
10.1007/s15010–021–01723–5	Fitoussi	2021	France	BIOSYNEX Ag-RDT	nasopharyngeal swabs	121	816	3	27	967
10.1371/journal.pone.0260862	Pollreis	2021	USA	BinaxNOW COVID-19 Ag Card test kit	nasal swabs	25	177	0	12	214
10.1016/j.ijid.2021.04.048	Caputo	2021	Italy	Lumipulse® G SARS-CoV-2 Ag assay	nasopharyngeal swabs	436	3661	102	67	4266
10.3201/eid2710.210080	Tinker	2021	USA	BinaxNOW COVID-19 Ag Card test kit	nasal swabs	8	1500	0	32	1540
10.1016/j.jcv.2021.105023	Okoye	2022	USA	BinaxNOW COVID-19 Ag Card test kit	nasal swabs	45	3759	2	4	3810
10.1016/j.jviromet.2021.114299	Paul	2021	India	COVID-VIRO® analysis	nasopharyngeal swabs	72	50	0	26	148
10.1016/j.jiac.2021.10.024	Suzuki	2022	Japan	RapidTesta SARS-CoV-2	nasopharyngeal swabs	53	1045	8	21	1127
10.1080/23744235.2021.1914857	Homza	2021	Czech Republic	ECOTEST Covid-19 Antigen Rapid Test	nasopharyngeal swabs	125	321	9	39	494
10.1002/jmv.27220	Carbonell-Sahuquillo	2021	Spain	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	24	323	0	10	357
10.1016/j.ijid.2021.03.051	Bouassa	2021	France	SIENNA™ COVID-19 Antigen Rapid Test	nasopharyngeal swabs	90	50	0	10	150
	Sazed	2021	Bangladesh		nasal swabs	121	245	2	12	380

(*continued on next page*)

Table 1 (*continued*)

DOI	Author	Year	Country	Rapid Antigen Test Kit	Specimen Types	TP	TN	FP	FN	SS
10.3390/diagnostics11122300				OnSite® COVID-19 Ag Rapid Test						
10.1016/j.ijid.2021.07.010	Jegerlehner	2021	Switzerland	Roche SARS-CoV-2 antigen assay	nasopharyngeal swabs	92	1319	2	49	1462
10.1016/j.jinf.2021.02.014	Bulilete	2021	Spain	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	100	1220	2	40	1362
10.4103/ijmr.IJMR_3305_20	Gupta	2021	India	STANDARD Q COVID-19 Ag Test	nasopharyngeal swabs	63	252	1	14	330
10.1007/s41999–021–00584–3	Paap	2021	Netherlands	Roche SARS-CoV-2 antigen assay	nasopharyngeal swabs	27	363	45	26	461
10.1371/journal.pone.0250886	Moeren	2021	Netherlands	BD Veritor System for Rapid Detection of SARS-CoV-2	nasopharyngeal and throat swabs	16	334	0	1	351
10.1136/bmj.n1637	Fiñana	2021	UK	SARS-CoV-2 antigen rapid lateral flow test (LFT)	nasopharyngeal and throat swabs	28	5431	3	42	5504
10.1128/Spectrum.00342–21	Chiu	2021	USA	LFA-based INDICAID COVID-19 rapid antigen test (INDICAID rapid test)	nasal swabs	158	23462	42	30	23692
10.1016/j.ajem.2021.10.022	Turcato	2022	Italy	STANDARD Q COVID-19 Ag Test	nasopharyngeal swabs	329	3470	32	68	3899
10.3390/diagnostics11122217	Tonen-Wolyec	2021	France	BIOSYNEX Ag-RDT	nasopharyngeal swabs	20	84	0	2	106
10.1007/s11845–021–02863–1	Kolesova	2021	Italy	Elecsys® SARS-CoV-2 Antigen assay	nasopharyngeal swabs	64	34	0	12	110
10.1007/s11845–021–02776-z	Denina	2021	Italy	LumiraDx SARS-CoV-2 Ag Test	nasal swabs	16	160	14	1	191
10.1038/s41598–021–90026–8	Takeuchi	2021	Japan	QuickNavi™-COVID19 Ag	nasal swabs	37	811	0	14	862
10.1002/jcla.24203	Begum	2022	Bangladesh	InTec Rapid SARS-CoV-2 Antigen Test	nasopharyngeal swabs	101	102	0	11	214
10.1016/j.jcv.2021.104878	Ferté	2021	France	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	33	636	0	19	688
10.1128/JCM.03077–20	Pollock	2021	USA	MSD S-PLEX SARS-CoV-2 N assay	nasopharyngeal swabs	112	89	1	24	226
10.3390/ijerph18179151	Kyritsi	2021	Greece	Rapid Test Ag 2019-nCoV (PROGNOSIS, BIOTECH, Larissa, Greece)	nasopharyngeal swabs	141	458	1	24	624
10.1155/2021/3893733	Loconsole	2021	Italy	Lumipulse® G SARS-CoV-2 Ag assay	nasopharyngeal swabs	205	677	18	11	911
10.1016/j.ijid.2021.09.008	Leiner	2021	Germany	Standard F COVID-19 Ag FIA	oro-nasopharyngeal swabs	491	3208	80	297	4076
10.1371/journal.pone.0253321	Nsoga	2021	Switzerland	Panbio COVID-19 Ag Rapid Test Device	oropharyngeal swabs	136	232	2	32	402
10.3390/diagnostics12040847	Ahmed	2022	Malaysia	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	101	51	2	3	157
10.23749/mdl.v112i5.12097	Visci	2021	Italy	LIAISON® SARS-CoV-2 Ag assay (Diasorin, Saluggia, Italy),	nasopharyngeal swabs	78	113	8	10	209
10.1371/journal.pone.0263327	Mori	2022	Japan	Roche SARS-CoV-2 antigen assay	nasopharyngeal swabs	42	1014	0	14	1070
10.1371/journal.pone.0249710	Sood	2021	USA	BinaxNOW COVID-19 Ag Card test kit	nasal swabs	127	539	9	99	774
10.1093/ofid/ofab059	Masiá	2021	Spain	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	118	709	0	77	904
10.1002/jmv.27249	Cassuto	2021	France	COVID-VIRO® analysis	nasal swabs	31	202	0	1	234
10.1007/s15010–020–01542–0	Lanser	2020	Austria	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	31	2	0	20	53
10.1128/JCM.00083–21	Pollock	2021	USA	BinaxNOW COVID-19 Ag Card test kit	nasal swabs	227	2003	12	66	2308
10.3390/diagnostics12030710	Lee	2022	Korea	STANDARD Q COVID-19 Ag Test	nasopharyngeal swabs	58	104	0	13	175
10.1016/j.diagmicrobio.2021.115531	Bräunlich	2022	Germany	Roche SARS-CoV-2 antigen assay	nasopharyngeal swabs	45	2867	21	45	2978
10.1128/Spectrum.01008–21	Siddiqui	2021	USA	BinaxNOW COVID-19 Ag Card test kit	nasal swabs	179	5826	13	43	6061
10.1016/j.ijid.2021.05.063	Leixner	2021	Austria	AMP Rapid Test SARS-CoV-2 Ag	nasopharyngeal swabs	65	297	1	29	392
10.1128/JCM.00991–21	L'Huillier	2021	Switzerland	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	79	703	0	40	822
10.1016/j.jiph.2021.06.002	Amer	2021	Egypt	STANDARD Q COVID-19 Ag Test	oro-nasopharyngeal swabs	54	9	5	15	83
10.3390/jcm10071471	Amendola	2021	Italy	Lumipulse® G SARS-CoV-2 Ag assay	saliva	22	80	5	20	127
10.1016/j.ijid.2021.04.087	Peña	2021	Chile	STANDARD Q COVID-19 Ag Test	nasopharyngeal swabs	51	766	3	22	842
10.1016/j.jiac.2021.07.006	Kurihara	2021	Japan	QuickChaser® Auto SARS-CoV-2	nasopharyngeal swabs	62	1316	2	21	1401
10.1016/j.jcv.2020.104455	Scohy	2020	Brussels			32	42	0	74	148

(*continued on next page*)

Table 1 (*continued*)

DOI	Author	Year	Country	Rapid Antigen Test Kit	Specimen Types	TP	TN	FP	FN	SS
				Coris bioconcept COVID-19 ag respi-strip test	nasopharyngeal swabs					
10.1016/j.cmi.2020.12.022	Torres	2021	Spain	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	38	555	0	41	634
10.1016/j.ijid.2020.05.098	Porte	2020	Chile	Bioeasy 2019-Novel Coronavirus (2019-nCoV) Fluorescence Antigen Rapid Test Kit	oro-nasopharyngeal swabs	77	45	0	5	127
10.1016/j.jcv.2020.104654	Cerutti	2020	Italy	STANDARD Q COVID-19 Ag Test	nasopharyngeal swabs	77	221	0	32	330
10.1002/jmv.27378	Treggiari	2021	Italy	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	282	3741	4	140	4167
10.1002/jmv.27412	Villalba	2021	Cuba	Elecsys® SARS-CoV-2 Antigen assay	nasopharyngeal swabs	288	183	19	33	523
10.1016/j.ijid.2021.11.034	Jian	2022	China	COVID-19 Antigen Rapid Test Kit (Eternal Materials, New Taipei City, Taiwan)	nasopharyngeal swabs	55	2009	15	17	2096
10.1007/s15010–021–01681-y	Krüger	2022	Germany	LumiraDx SARS-CoV-2 Ag Test	nasal swabs	120	611	4	26	761
10.1002/jmv.26855	Veyrenche	2020	France	Coris bioconcept COVID-19 ag respi-strip test	nasopharyngeal swabs	13	20	0	32	65
10.1007/s10096–021–04346–8	Aranaz-Andrés	2022	Spain	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	25	510	1	5	541
10.1016/j.jiac.2021.08.015	Nomoto	2021	Japan	Lumipulse® G SARS-CoV-2 Ag assay	nasopharyngeal swabs	66	19	1	14	100
10.1002/jmv.27033	Holzner	2021	Germany	STANDARD Q COVID-19 Ag Test	nasopharyngeal swabs	379	1816	8	172	2375
10.1002/jmv.27149	Eleftheriou	2021	Greece	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	42	693	0	9	744
10.1016/j.eclinm.2021.100954	Fernandez-Montero	2021	Spain	Roche SARS-CoV-2 antigen assay	nasopharyngeal swabs	35	2486	8	14	2543
10.1016/j.ijid.2021.07.043	Leli	2021	Italy	LumiraDx SARS-CoV-2 Ag Test	nasal swabs	114	596	30	52	792
10.1016/j.jpeds.2021.01.027	Villaverde	2021	Spain	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	35	1540	3	42	1620
10.1093/jpids/piab081	Ford	2022	USA	BinaxNOW COVID-19 Ag Card test kit	nasal swabs	267	1774	2	67	2110
10.1093/labmed/lmab033	Thakur	2021	India	SARS-CoV-2 antigen rapid lateral flow test (LFT)	nasopharyngeal swabs	29	592	1	55	677
10.1016/j.jviromet.2021.114201	Orsi	2021	Italy	FREND™ COVID-19 Ag assay	nasopharyngeal swabs	56	50	0	4	110
10.3390/healthcare9070868	Ifko	2021	Slovenia	NADAL COVID-19 antigen test	nasopharyngeal swabs	20	90	12	3	125
10.1128/JCM.00374–21	Lefever	2021	Belgium	LIAISON® SARS-CoV-2 Ag assay (Diasorin, Saluggia, Italy),	nasopharyngeal swabs	134	210	0	70	414
10.1002/jmv.27505	Roger	2021	France	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	86	4204	33	102	4425
10.37201/req/054.2021	Gras-Valenti	2021	Spain	Panbio COVID-19 Ag Rapid Test Device	nasopharyngeal swabs	58	398	1	37	494

0.76 (95% CI: 0.72–0.79). Analysis of performance with a nasal swab (26 studies, 64,125 samples) showed a higher pooled sensitivity of 0.79 (95% CI: 0.71–0.85). For samples from other parts including combined nasopharyngeal and throat, oropharyngeal, combined oropharyngeal, and nasopharyngeal and saliva swabs (16 studies, 22,372 samples), the pooled sensitivity was 0.76 (95% CI: 0.66–0.84).

Among the 40 RAT kits used in this study, 28 did not provide sufficient data for the bivariate meta-analysis. Of the remaining 12 RAT kits, COVID-VIRO® analysis showed the highest pooled sensitivity of 0.90 (95% CI: 0.70–0.97), followed by Lumipulse® G SARS-CoV-2 Ag assay with a pooled sensitivity of 0.86 (95% CI: 0.79–0.91); the combined sensitivity of BIOSYNEX Ag-RDT, LumiraDx SARS-CoV-2 Ag Test, and QuickNavi™-COVID19 Ag Test were all above 0.80. The Coris bioconcept COVID-19 ag respi-strip test had the lowest pooled sensitivity of 0.41 (95% CI: 0.23–0.61).

The pooled sensitivity decreased as Ct values increased. Samples with a Ct value < 20 achieved excellent pooled sensitivity at 1.00 (95% CI: 0.70–1.00). Ct value using the cutoff of 20–25 also showed a high sensitivity of 0.94 (95% CI: 0.87–0.97). The pooled sensitivity decreased to 0.70 (95% CI: 0.53–0.84) when the Ct value was 25–30. For Ct value > 30, the pooled sensitivity was relatively low at 0.24 (95% CI: 0.16–0.33).

We assessed sensitivity at three different cutoff points on the days after the onset of symptoms. For ≤ 3, ≤ 7, and ≤ 10 days, the summary sensitivities were 0.91 (95% CI: 0.83–0.96), 0.89 (95% CI: 0.84–0.93), and 0.88 (95% CI: 0.83–0.92), respectively. When the number of days after symptom onset exceeded 10 days, the sensitivity notably decreased to 0.36 (95% CI: 0.21–0.55).

4. Discussion

In this meta-analysis, a comprehensive literature search was conducted, and we summarized data from 135 studies, including 163,442 samples, to evaluate the diagnostic performance of RAT in COVID-19. The pooled sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio were 0.76 (95%CI: 0.73–0.79), 1.00 (95%CI: 1.00–1.00), 276.1 (95% CI, 184.1–414.1), 0.24 (95% CI, 0.21–0.27), and 1171 (95% CI, 782–1755), respectively. A positive likelihood ratio > 10 confirms the diagnosis of the disease, while a negative likelihood ratio < 0.1 excludes the possibility of the disease. When the diagnostic odds ratio > 1, the larger the value, the better the ability to distinguish between healthy people and patients. Our results indicated that RAT had a high diagnostic value.

Possibly due to differences in sensitivity, specificity, and patient

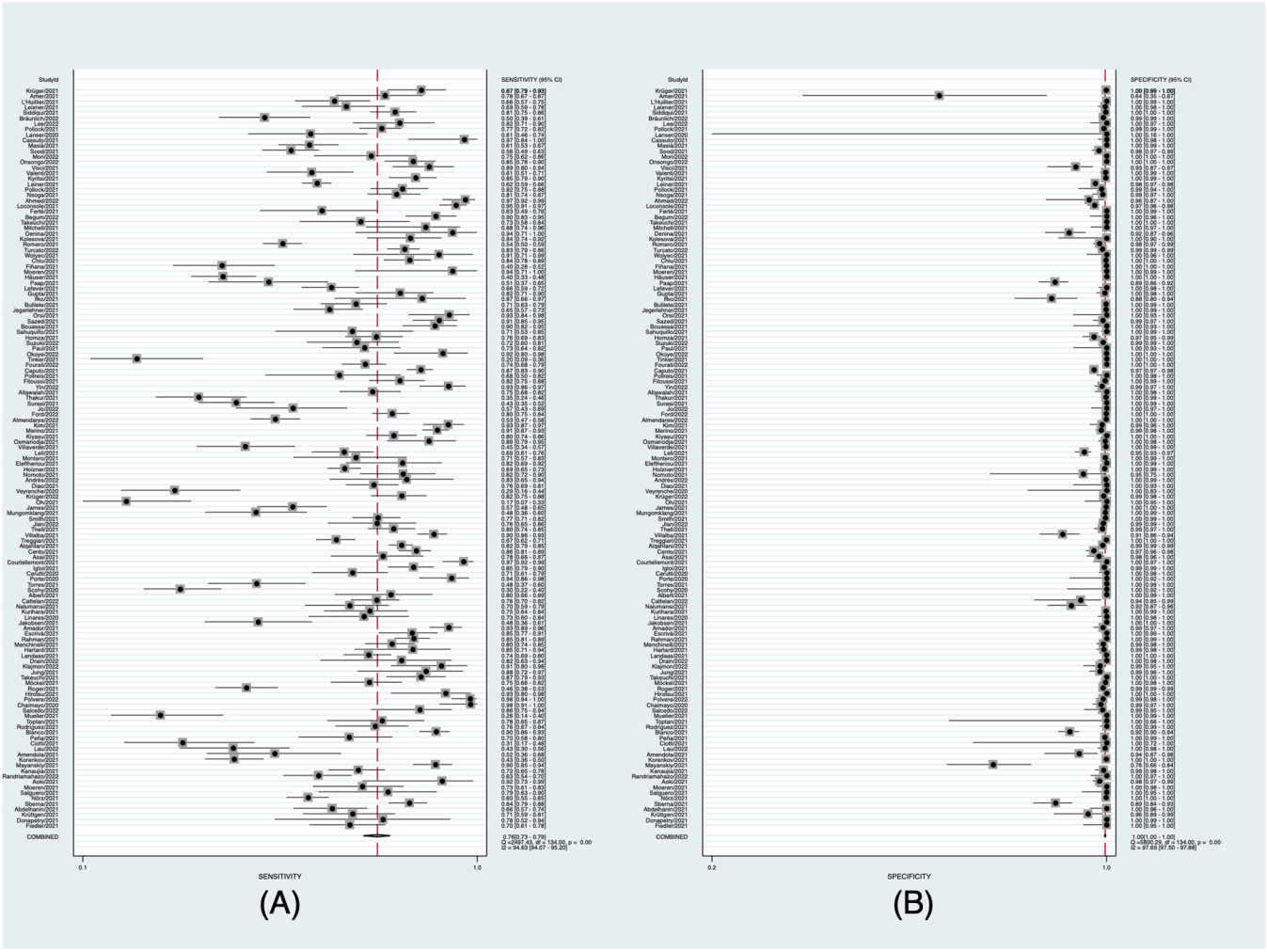

Fig. 2. Pooled sensitivity and pooled specificity of RAT. (A) Forest plots of pooled sensitivity. (B) Forest plots of pooled specificity.

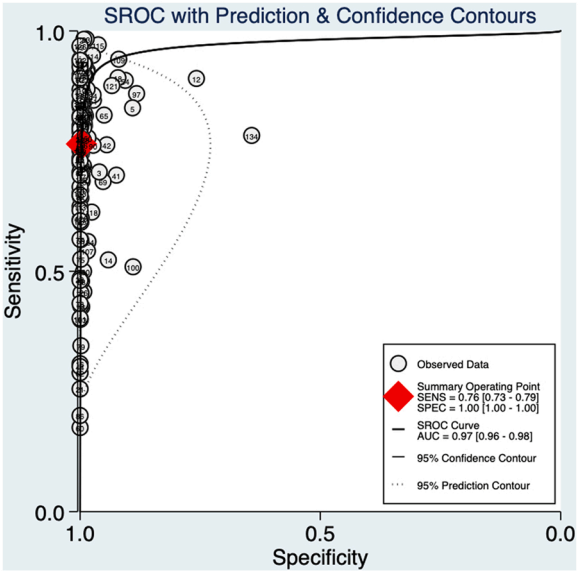

Fig. 3. Summary ROC curve and its area under curve.

population between the studies, we detected a high degree of heterogeneity; however, the bivariate random-effects model we used provided a relatively robust statistical result. Performance between manufacturer-dependent studies and manufacturer-independent studies may differ hugely, but when we removed the 3 manufacturer-dependent studies, the overall effect remained unchanged, (Sensitivity: 0.76 versus 0.76; Specificity: 1.00 versus 1.00; AUC: 0.97 versus 0.97), indicating that our results were not driven by the 3 manufacturer-dependent articles. Furthermore, SROC did not detect marked heterogeneity in the pooled sensitivity and specificity. Tests for publication bias also indicated no noticeable bias. Thus, the statistical analysis of this meta-analysis was reliable to some extent.

By analyzing the data, we hypothesized that the pretest probability was 12%, resulting in a positive posttest probability of 97% and a negative posttest probability of 3%; this suggested a very high probability that a patient with SARS-CoV-2 infection would test positive in the antigen test. According to our findings, pretest probability is positively correlated with posttest probability. This suggests that RAT is more applicable to high-risk populations. Considering that the RAT provided 1.00 specificity in our study along with its rapid turnaround time, it could be used as a screening tool in particular situations, such as highly suspicious contacts, or for triage in an emergency department. A positive antigen test will confirm the infection and prevent the virus from spreading, as well as accelerate and optimize the management of infected individuals. By quickly identifying infected patients, the decision-making process of the entire emergency department is

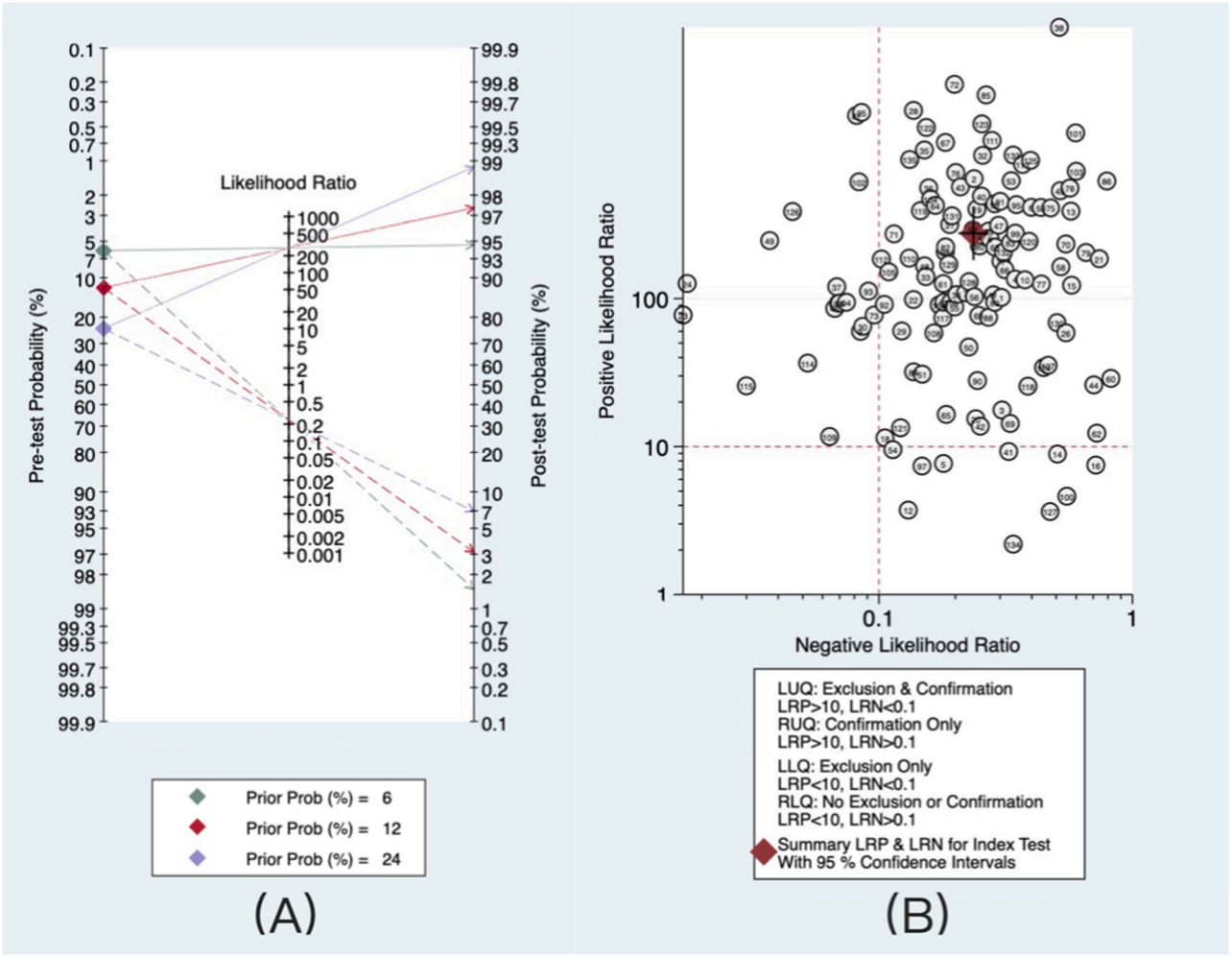

Fig. 4. Diagnostic value and clinical application value of RAT. (A) Fagan plot for evaluating diagnostic value: The solid line represents the positive post-test probability, and the dotted line represents the negative post-test probability. (B) Likelihood ratio scattergram for evaluating clinical application value.

improved.

Nasopharyngeal swabs generally have the highest detection rate for the diagnostic testing of respiratory viruses including SARS-CoV-2 (Lee et al., 2021). However, they must be collected by trained healthcare professionals using protective equipment, and their collection often causes considerable discomfort to patients (Lindner et al., 2021). In comparison, nasal sample collection is notably painless, and self-collection is possible (Lee et al., 2022). Moreover, nasal sampling is associated with less coughing or sneezing during collection, leading to less droplet exposure, thus reducing the transmission risk among healthcare workers (Takeuchi et al., 2021). Recent studies have reported that the diagnostic sensitivity of RT-PCR for nasal specimens is comparable to that for nasopharyngeal specimens (Péré et al., 2020; Tu et al., 2020). Interestingly, our analysis revealed that the sensitivity for nasal swabs (0.79) was higher than that for nasopharyngeal swabs (0.76) for RAT in cases where both swabs reached a specificity of 1.00. Therefore, the results indicate that using a more superficially collected nasal swab specimen is a good alternative for detecting SARS-CoV-2.

The overall sensitivity of the different RAT kits varies widely, ranging from 0.90 (95% CI: 0.70–0.97) to 0.41 (95% CI: 0.23–0.61). Three RAT kits (LumiraDx SARS-CoV-2 Ag Test, Panbio COVID-19 Ag Rapid Test Device, and STANDARD Q COVID-19 Ag Test) in our research have been authorized by the World Health Organization (WHO) for emergency use (Coronavirus Disease (COVID-19) Pandemic — Emergency Use Listing Procedure (EUL) Open for IVDs, 2020). For suspected patients, WHO recommends that a RAT kit reach a minimum performance criterion of 0.80 sensitivity and 0.97 specificity (Antigen-Detection in the Diagnosis of SARS-CoV-2 Infection, 2021). Only the LumiraDx SARS-CoV-2 Ag Test met this criterion, with a sensitivity of 0.83 (95% CI: 0.76–0.88) and specificity of 0.97 (95% CI: 0.94–0.99). The other two kits did not reach a sensitivity of 0.80 (sensitivity of 0.73 for Panbio and 0.70 for Standard Q), although both had a specificity of 1.00. Therefore, these results suggest an urgent need to further validate the performance of RAT kits on the emergency use list.

Previous studies have shown that lower Ct values represent higher viral loads, resulting in significantly higher RAT sensitivity, antigen concentration, and Ct values that are highly correlated (Pollock et al., 2021), and these were confirmed by our study. An outstanding sensitivity of 1.00 was achieved for Ct values < 20, after which the sensitivity of the RAT gradually declined as Ct values increased. Several studies have reported that the infectivity of SARS-CoV-2 persists for only approximately 8–10 days after the onset of symptoms (Bullard et al., 2020; Hirotsu et al., 2021; Million et al., 2020; Perera et al., 2020; van Kampen et al., 2021; Wölfel et al., 2020). Based on the results of the meta-analysis, the sensitivity within 10 days after the appearance of symptoms (0.88) was relatively favorable, which was not much lower than that within 3 days (0.91). Our findings support the use of RAT as an early stage screening tool for symptomatic patients, particularly those with high viral loads.

When Ct values were > 24, Bullard et al. observed that infectious viruses could not be isolated from the diagnostic samples (Bullard et al., 2020). In our research, although the pooled sensitivity was relatively

Table 2
Pooled sensitivity and specificity among subgroups of studies.

Subgroups	No. of study	Total Sample Size	Polled Sensitivity (95% CI)	Polled Specificity (95% CI)
Sample Types				
nasopharyngeal	93	76,945	0.76 (0.72–0.79)	1.00 (1.00–1.00)
nasal	26	64,125	0.79 (0.71–0.85)	1.00 (0.99–1.00)
other	16	22,372	0.76 (0.66–0.84)	1.00 (0.99–1.00)
RATt Kit				
COVID-VIRO® analysis	4	2536	0.90 (0.70–0.97)	1.00 (1.00–1.00)
Lumipulse® G SARS-CoV-2 Ag assay	10	8895	0.86 (0.79–0.91)	0.98 (0.96–0.99)
BIOSYNEX Ag-RDT	3	1382	0.85 (0.77–0.90)	0.99 (0.98–1.00)
LumiraDx SARS-CoV-2 Ag Test	7	4115	0.83 (0.76–0.88)	0.97 (0.94–0.99)
QuickNavi™-COVID19 Ag	3	3982	0.81 (0.76–0.85)	1.00 (1.00–1.00)
Panbio COVID-19 Ag Rapid Test Device	25	30,332	0.73 (0.67–0.79)	1.00 (1.00–1.00)
LIAISON® SARS-CoV-2 Ag assay	7	3532	0.72 (0.60–0.82)	1.00 (0.97–1.00)
Roche SARS-CoV-2 antigen assay	9	10,648	0.71 (0.62–0.78)	0.99 (0.98–1.00)
STANDARD Q COVID-19 Ag Test	17	20,765	0.70 (0.59–0.79)	1.00 (0.99–1.00)
BinaxNOW COVID-19 Ag Card test kit	10	23,344	0.65 (0.50–0.77)	1.00 (1.00–1.00)
Elecsys® SARS-CoV-2 Antigen assay	6	4750	0.65 (0.44–0.81)	1.00 (0.98–1.00)
Coris bioconcept COVID-19 ag respi-strip test	4	747	0.41 (0.23–0.61)	1.00 (0.53–1.00)
Days after symptom onset				
≤ 3 days	10	870	0.91 (0.83–0.96)	/
≤ 7 days	13	1862	0.89 (0.84–0.93)	/
≤ 10 days	13	1918	0.88 (0.83–0.92)	/
> 10 days	4	72	0.36 (0.21–0.55)	/
Ct Values				
< 20	15	368	1.00 (0.70–1.00)	/
20–25	11	342	0.94 (0.87–0.97)	/
25–30	23	579	0.70 (0.53–0.84)	/
> 30	24	715	0.24 (0.16–0.33)	/

low at 0.24 for Ct value > 30, a comparatively high sensitivity of 0.70 was maintained for Ct value using the cutoff of 25–30. Thus, it can be assumed that the missed cases of RAT will not cause a large-scale transmission. Our findings suggest that RAT sensitivity was as low as 0.36 ten days after symptom onset. However, according to the Centers for Disease Control and Prevention, 10 days after the appearance of symptoms can be considered a stage of low contagiousness (CDC, 2020). Hence, patients who have had symptoms for a more extended period may have a low risk of infecting others, even if they are incorrectly classified as negative for the SARS-CoV-2 antigen.

Our findings support the previous studies that RAT had high sensitivity and specificity and performed better in samples with high viral load, but in contrast to the earlier studies, we have a new finding that nasal swabs have a higher sensitivity than nasopharyngeal swabs for RAT. In addition, the strength of the present study lies in the number of studies (and samples) analyzed compared with previous studies (Arshadi et al., 2022; Chen et al., 2021; Hayer et al., 2021). Although our study did not assess the impact of the SARS-CoV-2 variant, RAT may not be influenced by the variant because RAT targets the nucleocapsid antigen whereas the mutant has a variable mutation at the spike antigen (Gupta et al., 2021).

Our study has some limitations, due to the lack of detailed information in the articles, the data of ≤ 10 days included data of both ≤ 7 days and 8–10 days, resulting in some overlap between the data of ≤ 10 days and ≤ 7 days, which may account for the similar sensitivity of the two (Sensitivity: 0.89 versus 0.88), whether the sensitivity of ≤ 7 days was similar with that of 8–10 days after symptom onset need to further study. We did not evaluate all RAT kits, but only part of them because of the limited data.

5. Conclusions

RAT kits show high sensitivity and specificity in the early stages of infection, especially when the viral load is high. In addition, using nasal samples for antigen testing, which is moderately sensitive and patient-friendly, is a reliable alternative to nasopharyngeal sampling. RAT might be an effective tool for the clinical management of patients in hospital settings, especially during the initial triage, as it aids the rapid identification of positive patients to prevent transmission, thus helping disrupt the COVID-19 pandemic. RAT also seems applicable to other areas, such as regular mass screening or airport screening, because it should allow for a more convenient and time-saving experience for people who travel. However, this important epidemiological benefit must be complemented with the thoughtful and responsible handling of negative test results.

Funding

This work was supported by the National Natural Science Foundation of China [Grant numbers 82172331, 81972028, 81802089, 81672094], the Key Projects for Province Science and Technology Program of Fujian Province, China [Grant number 2020D017] and the Natural Science Foundation of Fujian Province, China [Grant number 2020J05285]. The funders played no role in the study design, data collection, or analyses, the decision to publish, or manuscript preparation.

Ethical approval statement

No ethics approval was required for this work.

CRediT authorship contribution statement

Jia-Wen Xie: Methodology, Writing – original draft. **Yun He:** Software, Investigation. **Ya-Wen Zheng**: Formal analysis, Investigation. **Mao Wang:** Validation, Data curation. **Yong Lin:** Visualization, Supervision. **Li-Rong Lin:** Conceptualization, Writing – review & editing.

Conflict of interest

The authors declared that they have no conflicts of interest to this work.

Data availability

Data will be made available on request.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the

online version at doi:10.1016/j.micres.2022.127185.

References

Antigen-Detection in the Diagnosis of SARS-CoV-2 Infection, 2021. [WWW Document]. URL: ⟨https://www.who.int/publications-detail-redirect/antigen-detection-in-the-diagnosis-of-sars-cov-2infection-using-rapid-immunoassays⟩. (Accessed 22 May 2022).

Arshadi, M., Fardsanei, F., Deihim, B., Farshadzadeh, Z., Nikkhahi, F., Khalili, F., Sotgiu, G., Shahidi Bonjar, A.H., Centis, R., Migliori, G.B., Nasiri, M.J., Mirsaeidi, M., 2022. Diagnostic accuracy of rapid antigen tests for COVID-19 detection: a systematic review with meta-analysis. Front. Med. 9, 870738 https://doi.org/10.3389/fmed.2022.870738.

Borges, L.P., Martins, A.F., Silva, B. de M., Dias, B. de P., Gonçalves, R.L., Souza, D.R.V. de, Oliveira, M.G.B. de, Jesus, P.C. de, Serafini, M.R., Quintans, J.S.S., Coutinho, H. D.M., Martins, R.L., Júnior, L.J.Q., 2021. Rapid diagnosis of COVID-19 in the first year of the pandemic: a systematic review. Int. Immunopharmacol. 101, 108144 https://doi.org/10.1016/j.intimp.2021.108144.

Bullard, J., Dust, K., Funk, D., Strong, J.E., Alexander, D., Garnett, L., Boodman, C., Bello, A., Hedley, A., Schiffman, Z., Doan, K., Bastien, N., Li, Y., Van Caeseele, P.G., Poliquin, G., 2020. Predicting infectious SARS-CoV-2 from diagnostic samples. Clin. Infect. Dis. https://doi.org/10.1093/cid/ciaa638 ciaa638.

CDC, 2020. Healthcare Workers [WWW Document]. Centers for Disease Control and Prevention. URL: ⟨https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html⟩. (Accessed 31 May 2022).

Chen, C.-C., Lu, S.-C., Bai, C.-H., Wang, P.-Y., Lee, K.-Y., Wang, Y.-H., 2021. Diagnostic accuracy of SARS-CoV-2 antigen tests for community transmission screening: a systematic review and meta-analysis. Int. J. Environ. Res. Public Health 18, 11451. https://doi.org/10.3390/ijerph182111451.

Coronavirus Disease (COVID-19) Pandemic — Emergency Use Listing Procedure (EUL) Open for IVDs, 2020. [WWW Document]. WHO – Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control). URL: ⟨https://extranet.who.int/pqweb/vitro-diagnostics/coronavirus-disease-covid-19-pandemic-%E2%80%94-emergency-use-listing-procedure-eul-open⟩. (Accessed 20 May 2022).

Gupta, D., Sharma, P., Singh, M., Kumar, M., Ethayathulla, A.S., Kaur, P., 2021. Structural and functional insights into the spike protein mutations of emerging SARS-CoV-2 variants. Cell. Mol. Life Sci. 78, 7967–7989. https://doi.org/10.1007/s00018-021-04008-0.

Hayer, J., Kasapic, D., Zemmrich, C., 2021. Real-world clinical performance of commercial SARS-CoV-2 rapid antigen tests in suspected COVID-19: a systematic meta-analysis of available data as of November 20, 2020. Int. J. Infect. Dis. 108, 592–602. https://doi.org/10.1016/j.ijid.2021.05.029.

Hirotsu, Y., Maejima, M., Shibusawa, M., Amemiya, K., Nagakubo, Y., Hosaka, K., Sueki, H., Hayakawa, M., Mochizuki, H., Tsutsui, T., Kakizaki, Y., Miyashita, Y., Omata, M., 2021. Prospective study of 1308 nasopharyngeal swabs from 1033 patients using the LUMIPULSE SARS-CoV-2 antigen test: Comparison with RT-qPCR. Int. J. Infect. Dis. 105, 7–14. https://doi.org/10.1016/j.ijid.2021.02.005.

Jin, Y., Wang, M., Zuo, Z., Fan, C., Ye, F., Cai, Z., Wang, Y., Cui, H., Pan, K., Xu, A., 2020. Diagnostic value and dynamic variance of serum antibody in coronavirus disease 2019. Int. J. Infect. Dis. 94, 49–52. https://doi.org/10.1016/j.ijid.2020.03.065.

Khandker, S.S., Nik Hashim, N.H.H., Deris, Z.Z., Shueb, R.H., Islam, M.A., 2021. Diagnostic accuracy of rapid antigen test kits for detecting SARS-CoV-2: a systematic review and meta-analysis of 17,171 suspected COVID-19 patients. J. Clin. Med. 10, 3493. https://doi.org/10.3390/jcm10163493.

Lai, C.-C., Shih, T.-P., Ko, W.-C., Tang, H.-J., Hsueh, P.-R., 2020. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): the epidemic and the challenges. Int. J. Antimicrob. Agents 55, 105924. https://doi.org/10.1016/j.ijantimicag.2020.105924.

Lee, R.A., Herigon, J.C., Benedetti, A., Pollock, N.R., Denkinger, C.M., 2021. Performance of saliva, oropharyngeal swabs, and nasal swabs for SARS-CoV-2 molecular detection: a systematic review and meta-analysis. e02881-20 J. Clin. Microbiol. 59. https://doi.org/10.1128/JCM.02881-20.

Lee, S., Widyasari, K., Yang, H.-R., Jang, J., Kang, T., Kim, S., 2022. Evaluation of the diagnostic accuracy of nasal cavity and nasopharyngeal swab specimens for SARS-CoV-2 detection via rapid antigen test according to specimen collection timing and viral load. Diagnostics 12, 710. https://doi.org/10.3390/diagnostics12030710.

Lindner, A.K., Nikolai, O., Kausch, F., Wintel, M., Hommes, F., Gertler, M., Krüger, L.J., Gaeddert, M., Tobian, F., Lainati, F., Köppel, L., Seybold, J., Corman, V.M., Drosten, C., Hofmann, J., Sacks, J.A., Mockenhaupt, F.P., Denkinger, C.M., 2021. Head-to-head comparison of SARS-CoV-2 antigen-detecting rapid test with self-collected nasal swab versus professional-collected nasopharyngeal swab. Eur. Respir. J. 57, 2003961. https://doi.org/10.1183/13993003.03961-2020.

Million, M., Lagier, J.-C., Gautret, P., Colson, P., Fournier, P.-E., Amrane, S., Hocquart, M., Mailhe, M., Esteves-Vieira, V., Doudier, B., Aubry, C., Correard, F., Giraud-Gatineau, A., Roussel, Y., Berenger, C., Cassir, N., Seng, P., Zandotti, C., Dhiver, C., Ravaux, I., Tomei, C., Eldin, C., Tissot-Dupont, H., Honoré, S., Stein, A., Jacquier, A., Deharo, J.-C., Chabrière, E., Levasseur, A., Fenollar, F., Rolain, J.-M., Obadia, Y., Brouqui, P., Drancourt, M., La Scola, B., Parola, P., Raoult, D., 2020. Early treatment of COVID-19 patients with hydroxychloroquine and azithromycin: a retrospective analysis of 1061 cases in Marseille. Fr. Travel Med. Infect. Dis. 35, 101738 https://doi.org/10.1016/j.tmaid.2020.101738.

Péré, H., Podglajen, I., Wack, M., Flamarion, E., Mirault, T., Goudot, G., Hauw-Berlemont, C., Le, L., Caudron, E., Carrabin, S., Rodary, J., Ribeyre, T., Bélec, L., Veyer, D., 2020. Nasal swab sampling for SARS-CoV-2: a convenient alternative in times of nasopharyngeal swab shortage. e00721-20 J. Clin. Microbiol. 58. https://doi.org/10.1128/JCM.00721-20.

Perera, R.A.P.M., Tso, E., Tsang, O.T.Y., Tsang, D.N.C., Fung, K., Leung, Y.W.Y., Chin, A. W.H., Chu, D.K.W., Cheng, S.M.S., Poon, L.L.M., Chuang, V.W.M., Peiris, M., 2020. SARS-CoV-2 virus culture and subgenomic RNA for respiratory specimens from patients with mild coronavirus disease. Emerg. Infect. Dis. 26, 2701–2704. https://doi.org/10.3201/eid2611.203219.

Pollock, N.R., Savage, T.J., Wardell, H., Lee, R.A., Mathew, A., Stengelin, M., Sigal, G.B., 2021. Correlation of SARS-CoV-2 nucleocapsid antigen and RNA concentrations in nasopharyngeal samples from children and adults using an ultrasensitive and quantitative antigen assay. e03077-20 J. Clin. Microbiol. 59. https://doi.org/10.1128/JCM.03077-20.

Takeuchi, Y., Akashi, Y., Kato, D., Kuwahara, M., Muramatsu, S., Ueda, A., Notake, S., Nakamura, K., Ishikawa, H., Suzuki, H., 2021. Diagnostic performance and characteristics of anterior nasal collection for the SARS-CoV-2 antigen test: a prospective study. Sci. Rep. 11, 10519. https://doi.org/10.1038/s41598-021-90026-8.

Torres, I., Poujois, S., Albert, E., Álvarez, G., Colomina, J., Navarro, D., 2021. Point-of-care evaluation of a rapid antigen test (CLINITEST® rapid COVID-19 antigen test) for diagnosis of SARS-CoV-2 infection in symptomatic and asymptomatic individuals. J. Infect. 82, e11–e12. https://doi.org/10.1016/j.jinf.2021.02.010.

Tu, Y.-P., Jennings, R., Hart, B., Cangelosi, G.A., Wood, R.C., Wehber, K., Verma, P., Vojta, D., Berke, E.M., 2020. Swabs collected by patients or health care workers for SARS-CoV-2 testing. N. Engl. J. Med. https://doi.org/10.1056/NEJMc2016321. NEJMc2016321.

van Kampen, J.J.A., van de Vijver, D.A.M.C., Fraaij, P.L.A., Haagmans, B.L., Lamers, M. M., Okba, N., van den Akker, J.P.C., Endeman, H., Gommers, D.A.M.P.J., Cornelissen, J.J., Hoek, R.A.S., van der Eerden, M.M., Hesselink, D.A., Metselaar, H. J., Verbon, A., de Steenwinkel, J.E.M., Aron, G.I., van Gorp, E.C.M., van Boheemen, S., Voermans, J.C., Boucher, C.A.B., Molenkamp, R., Koopmans, M.P.G., Geurtsvankessel, C., van der Eijk, A.A., 2021. Duration and key determinants of infectious virus shedding in hospitalized patients with coronavirus disease-2019 (COVID-19). Nat. Commun. 12, 267. https://doi.org/10.1038/s41467-020-20568-4.

W.H.O. Director-General's Opening Remarks at the Media Briefing on COVID-19 – 11 March 2020, (n.d.). [WWW Document]. URL: ⟨https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19—11-march-2020⟩. (Accessed 19 May 2022).

Whiting, P.F., Rutjes, A.W.S., Westwood, M.E., Mallett, S., Deeks, J.J., Reitsma, J.B., Leeflang, M.M.G., Sterne, J.A.C., Bossuyt, P.M.M., QUADAS-2 Group, 2011. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann. Intern. Med., 155, pp. 529–536. ⟨https://doi.org/10.7326/0003-4819-155-8-201110180-00009⟩.

Wölfel, R., Corman, V.M., Guggemos, W., Seilmaier, M., Zange, S., Müller, M.A., Niemeyer, D., Jones, T.C., Vollmar, P., Rothe, C., Hoelscher, M., Bleicker, T., Brünink, S., Schneider, J., Ehmann, R., Zwirglmaier, K., Drosten, C., Wendtner, C., 2020. Virological assessment of hospitalized patients with COVID-2019. Nature 581, 465–469. https://doi.org/10.1038/s41586-020-2196-x.

Yamayoshi, S., Sakai-Tagawa, Y., Koga, M., Akasaka, O., Nakachi, I., Koh, H., Maeda, K., Adachi, E., Saito, M., Nagai, H., Ikeuchi, K., Ogura, T., Baba, R., Fujita, K., Fukui, T., Ito, F., Hattori, S., Yamamoto, K., Nakamoto, T., Furusawa, Y., Yasuhara, A., Ujie, M., Yamada, S., Ito, M., Mitsuya, H., Omagari, N., Yotsuyanagi, H., Iwatsuki-Horimoto, K., Imai, M., Kawaoka, Y., 2020. Comparison of rapid antigen tests for COVID-19. Viruses 12, 1420. https://doi.org/10.3390/v12121420.

Yüce, M., Filiztekin, E., Özkaya, K.G., 2021. COVID-19 diagnosis—a review of current methods. Biosens. Bioelectron. 172, 112752 https://doi.org/10.1016/j.bios.2020.112752.