



Philippine COVID-19 Living Clinical Practice Guidelines

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Recommendation A

We recommend the use of saliva drool/spit and oral saliva specimens as an alternative to nasopharyngeal swab for RT-PCR diagnosis of COVID-19 in the following situations:

- Symptomatic and asymptomatic patients with suspected COVID-19
- Hospital and community/outpatient settings

Quality of Evidence: Moderate

Strength of Recommendation: Strong

Recommendation B

We suggest the use of saliva swab and posterior oropharyngeal saliva specimens as an alternative for RT-PCR diagnosis of COVID-19 in the following situations:

- Symptomatic and asymptomatic patients with suspected COVID-19
- Hospital and community/outpatient settings

Quality of Evidence: Low

Strength of Recommendation: Conditional

EVIDENCE SUMMARY

Should RT-PCR of saliva samples be used for diagnosis of COVID-19?

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Key Findings

Based on a meta-analysis of 51 studies, RT-PCR of saliva specimens demonstrated an overall pooled sensitivity and specificity across all studies of 84% (95% CI 0.80, 0.88) and 96% (95% CI 0.94, 0.98) respectively. Subgroup analysis yielded similar pooled sensitivity and specificity to the overall estimates across patients with different COVID-19 status, symptom presence, and settings. Subgroup analysis of confirmed COVID-19 patients yielded similar sensitivity but lower specificity of 65% (95% CI 0.42, 0.83).

Introduction

The current reference standard for establishing the presence of SARS-CoV-2 infection is reverse transcription polymerase chain reaction (RT-PCR) of nasopharyngeal and oropharyngeal swab specimens. However, there are several drawbacks to sample collection, such as pain and discomfort for the patient and a risk of aerosol generation from coughing or sneezing. These



limitations can increase the risk of nosocomial infection and hinder its use in serial monitoring and mass testing programs [1].

Saliva has been suggested as an alternative specimen for SARS-CoV-2 diagnostic testing. SARS-CoV-2 can be present in saliva through at least three possible routes: 1) from the upper respiratory tract to the oral cavity via liquid droplets; 2) from the bloodstream to the oral cavity via exudates from the extracellular fluid and serum; and 3) from infected salivary glands to the oral cavity through the salivary ducts [2]. The use of saliva as a diagnostic specimen has several advantages. Sampling is non-invasive and can be collected with minimal or no healthcare worker assistance, allowing for self-collection and serial sampling. It causes no pain or discomfort, making it suitable for children, the elderly, and the disabled. It is easy to handle and cheap to store and transport, potentially allowing for large-scale population screening. Protocols and kits are also available for extraction of DNA, RNA, and proteins, providing good performance regardless of sampling technique [3,4].

Review Methods

This review involved a literature search for published or preprint studies available on or before December 26, 2020 on MEDLINE, the Cochrane COVID-19 Study Register, and the COVID-19 Living Evidence Database [5]. Assessment for methodological quality was done using the criteria for appraising validity of diagnostic studies published by Dans, Dans, and Silvestre [6]. Diagnostic performance data from each study was extracted to produce 2x2 pooled tables, from which the overall pooled sensitivity and specificity was generated using a bivariate mixed-effects regression model [7]. Pooled sensitivity and specificity data were stratified by COVID-19 diagnostic status (confirmed, suspected, convalescent), presence of COVID-19 symptoms (symptomatic, asymptomatic), setting (hospital, community/outpatient), saliva collection method (drool/spit, swab), saliva collection location (oral saliva, posterior oropharyngeal saliva), and RT-PCR diagnostic kit. Studies that were included in the overall assessment were not included in the subgroup analysis if presenting with incomplete diagnostic accuracy data for that subgroup.

Results

Characteristics of included studies

The database search yielded 1194 results (869 unique), from which 52 studies [9-60] were included in the systematic review and fifty-one [9-59] in the meta-analysis (**Appendix Figure 1**). A total of 22,698 (median=200, range 12-2884) patients were enrolled in the included studies (**Appendix Tables 1 and 2**), from which 19,347 (median = 155, range 16-2884) paired saliva and nasopharyngeal specimens were included in the review. These studies included both pediatric and adult patients, but no study specific to children was included. Since this review did not attempt to discriminate in terms of setting or sample collection, there is a wide variety of included studies (**Appendix Table 3**).

Methodological quality

According to the parameters of the quality assessment in this review, none of the studies showed a high risk of bias, while 80.8% (42/52) of the included studies had a moderate risk and 19.2% (10/52) of the studies had low risk (**Appendix Figure 2**). The acceptability of the reference standard and definition of the index test and reference standard were adequate for all studies, but



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most did not report whether the interpretation of the tests was done independently (i.e., simultaneously or immediately after sample collection).

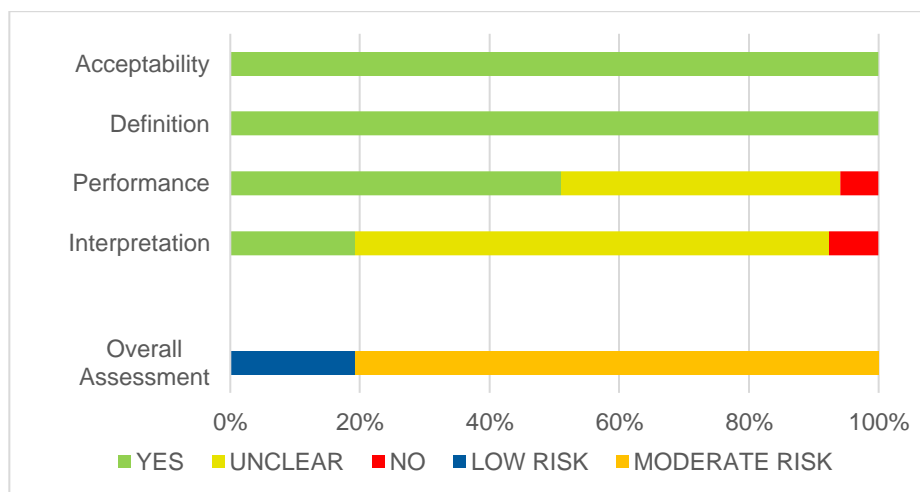


Figure 1. Risk of bias assessment for included studies (n = 52).

Diagnostic accuracy

The pooled sensitivity of saliva RT-PCR using nasopharyngeal with or without oropharyngeal swab RT-PCR as the gold standard is 84% (95% CI 0.80, 0.88), while its pooled specificity is 96% (95% CI 0.94, 0.98) (**Figure 1**).

These results are consistent with those of other recently published meta-analyses. A meta-analysis of 14 studies (n=1118) reported pooled sensitivity of 83.4% and a specificity of 97.7% [61]. Another meta-analysis of 37 studies (n=7822) reported an overall pooled sensitivity of 86.9%. It also stratified the studies according to confirmed COVID-19, symptomatic vs. asymptomatic patients, and inpatient and outpatient settings, with sensitivity ranging from 85.3% to 87.9% across these subgroups [62]. Another meta-analysis of 16 studies (n=5922) reported an overall pooled sensitivity of 83.2% and specificity of 99.2%, with a post hoc meta-analysis yielding a sensitivity of 84.6% and specificity of 99.0% for ambulatory patients [63].

The lower sensitivity of saliva relative to nasopharyngeal PCR may be explained by earlier findings documenting lower SARS-CoV-2 viral load in saliva especially in patients with longer duration of infection [64,65], which may result in a higher rate of false negatives. The variety of populations, sample sizes, and settings of the included studies contributed to the substantial heterogeneity (sensitivity $p < 0.001$, $I^2 = 90.13\%$; specificity $p < 0.001$, $I^2 = 98.14\%$) present in this analysis. These studies also had significant differences in terms of timing and method of collection, use of viral transport medium, and extraction method.



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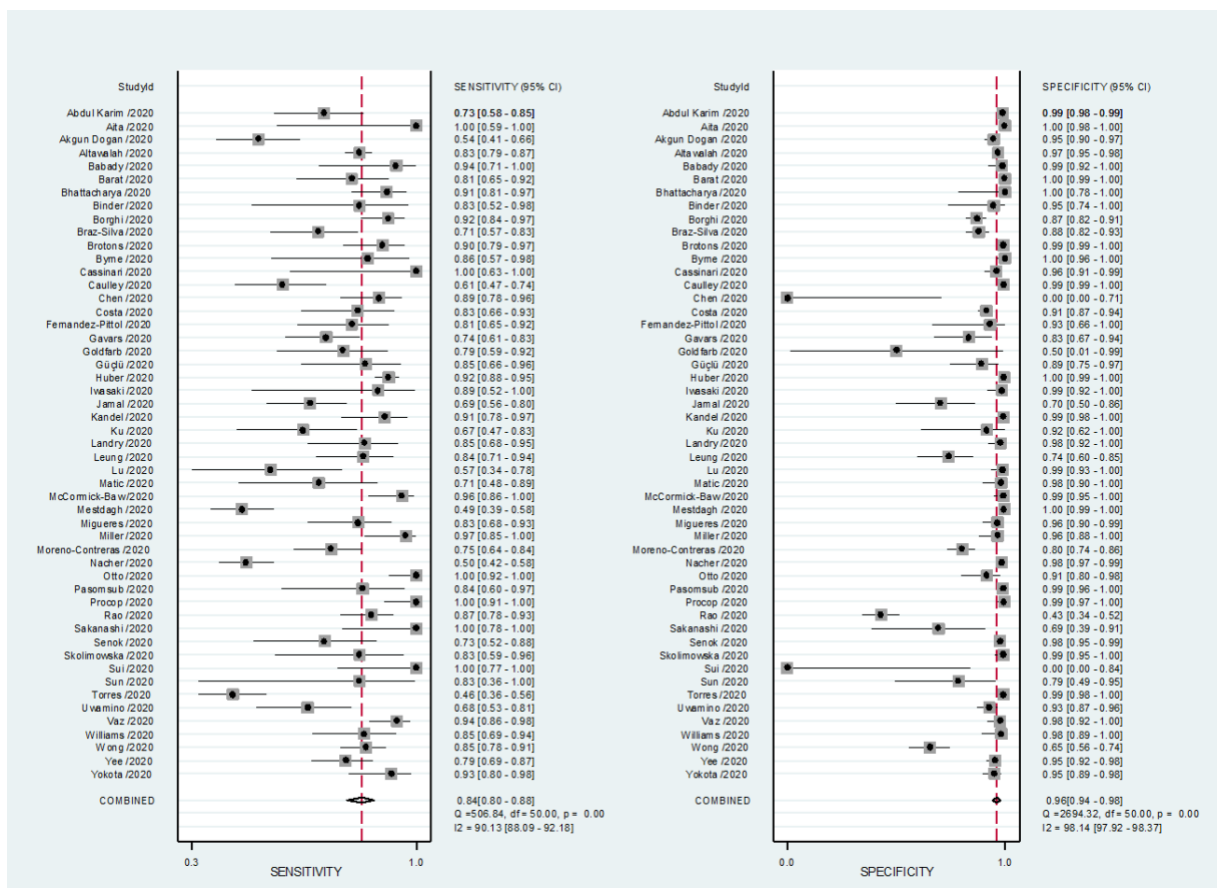


Figure 1. Overall pooled sensitivity and specificity of saliva RT-PCR.

Subgroup analysis

Subgroup analysis was done in anticipation of the expected heterogeneity among the wide range of studies. (Table 1; Appendix Figures 2-11). Pooled sensitivity for each subgroup ranged from 71% to 89% (median=0.83, IQR 0.80-0.85), while pooled specificity ranged from 65% to 98% (median=0.96, IQR 0.885-0.97). All subgroups exhibited substantial heterogeneity ($p < 0.10$).



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Table 1. Pooled sensitivity and specificity per subgroup.

SUBGROUP	NO. OF STUDIES (SAMPLE SIZE)	SENSITIVITY (95% CI)	SPECIFICITY (95% CI)
COVID-19 diagnostic status			
Confirmed COVID-19	14 (903)	0.81 (0.74, 0.87)	0.65 (0.42, 0.83)
Suspected COVID-19	6 (1699)	0.74 (0.62, 0.82)	0.96 (0.92, 0.98)
Convalescent COVID-19	2 (61)	n/a (inadequate number of observations)	
Presence of symptoms			
Symptomatic	17 (3169)	0.85 (0.76, 0.91)	0.97 (0.90, 0.99)
Asymptomatic	6 (3462)	0.89 (0.83, 0.93)	0.93 (0.73, 0.99)
Setting			
Hospital setting	24 (3573)	0.86 (0.81, 0.90)	0.94 (0.88, 0.97)
Community or outpatient	18 (12637)	0.78 (0.66, 0.86)	0.98 (0.97, 0.99)
Saliva collection method			
Saliva drool/spit	44 (16779)	0.83 (0.78, 0.97)	0.97 (0.94, 0.98)
Saliva swab	6 (3895)	0.71 (0.46, 0.87)	0.98 (0.90, 1.00)
Saliva collection location			
Oral saliva	42 (17309)	0.82 (0.77, 0.86)	0.97 (0.96, 0.98)
Posterior oropharyngeal saliva	7 (829)	0.89 (0.83, 0.93)	0.79 (0.50, 0.93)
RT-PCR kit brand*			
Xpert Xpress SARS-CoV-2 test (Cepheid)	3 (243)	0.95 (0.91, 0.99)	0.99 (0.95, 1.00)
OneStep/COVID-19 Kit (BIOMOL)	1 (122)	0.94 (0.86, 0.98)	0.96 (0.87, 1.00)
Thunderbird Probe One-step qRT-PCR Kit (Toyobo)	1 (161)	0.93 (0.80, 0.98)	0.95 (0.89, 0.98)
Cobas SARS-CoV-2 Assay (Roche)	1 (1187)	0.92 (0.88, 0.95)	1.00 (0.99, 1.00)
SalivaDirect (Yale University)	1 (301)	0.92 (0.84, 0.97)	0.87 (0.82, 0.91)
Real-Q 2019-nCoV detection kit (Biosewom)	1 (217)	0.87 (0.78, 0.93)	0.43 (0.34, 0.52)
Coronavirus Typing (8-well) Assay (AusDiagnostics)	1 (406)	0.85 (0.69, 0.94)	1.00 (0.98, 1.00)
LightMix Modular SARS & Wuhan CoV E-gene kit (TIB-MOLBIOL)	3 (398)	0.84 (0.79, 0.89)	0.80 (0.66, 1.00)
SARS-CoV-2 Nucleic Acid Diagnostic Kit (Sansure)	1 (110)	0.84 (0.60, 0.97)	0.98 (0.91, 1.00)
Panther Fusion SARS-CoV-2 Assay (Hologic)	1 (121)	0.83 (0.68, 0.93)	0.96 (0.90, 0.99)
TaqPath COVID-19 Combo Kit (Thermo Fisher Scientific)	3 (4075)	0.80 (0.73, 0.86)	0.97 (0.95, 1.00)

*Only test kits that demonstrated > 80% sensitivity are shown in this table.

The diagnostic accuracy figures for saliva RT-PCR in symptomatic patients, asymptomatic patients, hospital, samples and community/outpatient samples are similar to those found in recently published literature [62,63]. Neither differences in setting nor differences in patient symptom status seem to affect the accuracy of saliva tests.

The different kits used in the study ranged in sensitivity from 49% to 95%, and specificity from 43% to 100% (**Appendix Table 4**). Among kits used in more than one study, the Xpert Xpress SARS-CoV-2 assay (Cepheid) was the most sensitive at 95% (95% CI 0.91, 0.99), followed by LightMix Modular SARS and Wuhan CoV E-gene kit (TIB-MOLBIOL) at 84% (95% CI 0.79, 0.89). For specificity, Genesig RT-PCR SARS-CoV-2 kit (Primerdesign) was the most specific at 98% (95% CI 0.96, 1.00), followed by TaqPath COVID-19 Combo Kit (Thermo Fisher Scientific) at 97% (95% CI 0.95, 1.00). The Allplex assay was found to be the most suitable assay by one study [60] when compared to the Xpert and Simplexa assays in terms of sensitivity, ease of use, and accuracy relative to nasopharyngeal swabs. Notably, SalivaDirect (Yale University), a direct detection RT-PCR kit not requiring RNA extraction [67], had a sensitivity of 92% (95% CI 0.84, 0.97) and specificity of 87% (95% CI 0.82, 0.91) based on one study [42]; more studies will be needed for confirmation of its diagnostic accuracy.



Recommendations from other groups

European CDC guidelines consider saliva as an alternative specimen for testing if a nasopharyngeal or throat specimen cannot be taken [68]. American CDC interim guidelines also consider saliva specimens to be acceptable for RT-PCR tests depending on the authorized viral test used [69]. Also, on January 25, 2021, Philippine Red Cross officially launched its saliva RT-PCR testing after receiving the approval of the Department of Health [70]. The results of their pilot study have yet to be published.

Research gaps

Further research is needed to confirm the accuracy of saliva RT-PCR in diagnosis of SARS-CoV-2 infection in convalescent patients. To further elucidate the diagnostic accuracy of saliva, there are four clinical trials (**Appendix Table 5**) listed on ClinicalTrials.org as currently ongoing as of January 25, 2021.

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Appendix

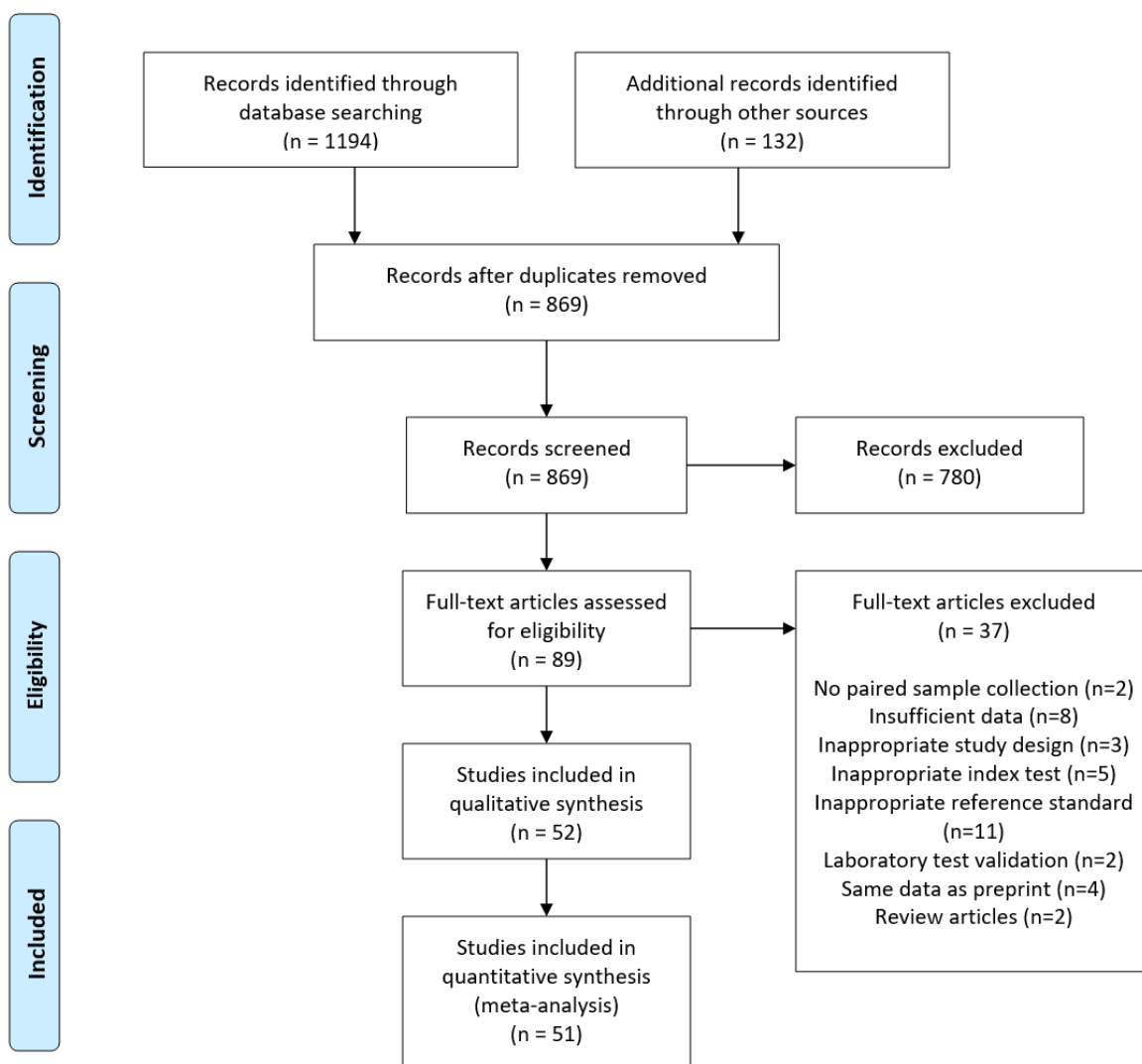


Figure 1. PRISMA study flow diagram.



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Institute of Clinical Epidemiology, National Institutes of Health, UP Manila

In cooperation with the Philippine Society for Microbiology and Infectious Diseases

Funded by the DOH AHEAD Program through the PCHRD

Table 1. Characteristics of included studies.

Study ID	Setting	Index Test	Index Test Specimen	Population	Sample Size	Reference Standard Test	Reference Standard Specimen
Abdul Karim 2020	Bahrain Single-center cross-sectional study	Real-time RT-PCR (Thermo Fisher)	Oral saliva, spit No transport medium	Cases presenting to a COVID-19 hospital clinic; symptomatic individuals, staff, close contacts, pre-operation patients (n=1009)	1019	Real-time RT-PCR (Thermo Fisher)	Nasopharyngeal swab
Aita 2020	Italy Single-center cross-sectional study	<u>Inpatients:</u> Real-time RT-PCR, digital droplet PCR (ddPCR) One-Step RT-ddPCR Advanced Kit for Probes (BioRad) <u>Screening patients:</u> Real-time RT-PCR	Oral saliva, swab Salivette tubes (Sarstedt) No transport medium	Adult inpatients with COVID-19 (n=43); Screening patients (n=326)	369	<u>Inpatients:</u> Real-time RT-PCR, digital droplet PCR (ddPCR) One-Step RT-ddPCR Advanced Kit for Probes (BioRad) <u>Screening patients:</u> Real-time RT-PCR	Nasopharyngeal swab
Akgun Dogan 2020	Turkey Single-center cross-sectional study	RT-PCR Direct Detection of SARS-CoV-2 Detection Kit (Coyote Bioscience) Ct ≤ 29	Oral saliva, drool Viral transport medium (Innomed)	Adult inpatients with possible COVID-19 and moderate-severe disease (n=200)	200	RT-PCR Direct Detection of SARS-CoV-2 Detection Kit (Coyote Bioscience) Ct ≤ 29	Nasopharyngeal and oropharyngeal swabs
Altawalah 2020	Kuwait Multi-center cross-sectional study	Multiplex real-time RT-PCR TaqPath COVID-19 Combo Kit (Thermo Fisher) Ct < 37	Saliva following deep cough Viral transport medium	Admitted patients with suspected COVID-19 (n=891)	891	Multiplex real-time RT-PCR TaqPath COVID-19 Combo Kit (Thermo Fisher) Ct < 37	Nasopharyngeal swab
Babady 2020	USA Single-center cross-sectional study	Real-time RT-PCR CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel Xpert Xpress SARS-CoV-2 (Cepheid) Cobas SARS-CoV-2 test (Roche)	Posterior oropharyngeal saliva, spit Oral rinse No transport medium	Employees with COVID-19 symptoms or exposure to a COVID-19 case (n=275)	87	Real-time RT-PCR CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel Xpert SARS-CoV-2 test (Cepheid) Cobas SARS-CoV-2 test (Roche)	Nasopharyngeal and oropharyngeal swabs



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Barat 2020	USA Prospective cross-sectional study	Real-time RT-PCR <u>NIH samples:</u> Panther Fusion SARS-CoV-2 Assay (Hologic) Cobas SARS-CoV-2 real-time RT-PCR test (Roche) Ct < 40 <u>ED samples:</u> BioGX Sars-CoV-2 Reagents for BD MAX System (BD) Xpert Xpress SARS-CoV-2 (Cepheid) Molecular Simplexa COVID-19 Direct (DiaSorin) Ct < 40	Oral saliva, drool No transport medium	Adult NIH employees with COVID-19 symptoms or high-risk exposure (n=390) Adult emergency patients with COVID-19 symptoms or high-risk exposure (n=69)	459	Real-time RT-PCR <u>NIH samples:</u> Panther Fusion SARS-CoV-2 Assay (Hologic) Cobas SARS-CoV-2 real-time RT-PCR test (Roche) Ct < 40 <u>ED samples:</u> BioGX Sars-CoV-2 Reagents for BD MAX System (BD) Xpert Xpress SARS-CoV-2 (Cepheid) Molecular Simplexa COVID-19 Direct (DiaSorin) Ct < 40	Nasopharyngeal swab
Bhattacharya 2020	India Multi-center cross-sectional study	Real-time RT-PCR Cobas 6800 instrument (Roche Molecular Diagnostics)	Oral saliva, spit, 48 hrs after symptom onset	Suspected COVID-19 hospitalized patients having mild-to-moderate symptoms (n=74)	74	Real-time RT-PCR Cobas 6800 instrument (Roche Molecular Diagnostics)	Nasopharyngeal swab, taken 48h after symptom onset
Binder 2020	USA Single-center case series	Real-time RT-PCR SuperScript III Platinum One-Step Real-Time RT-PCR Kit (Invitrogen) CDC 2019-nCoV real-time RT-PCR assay Ct < 40	Oral saliva, drool No transport medium	Adult COVID-19 inpatients (n=20) Adult (n=4) and pediatric (n=2) close contacts of COVID-19 inpatients	31	Real-time RT-PCR SuperScript III Platinum One-Step Real-Time RT-PCR Kit (Invitrogen) CDC 2019-nCoV real-time RT-PCR assay Ct < 40	Nasopharyngeal swab
Borghi 2020	Italy Single-center cross-sectional study	Direct real-time RT-PCR SalivaDirect (Yale University) Ct < 40	Oral saliva, swab No transport medium	Adults (aged 18-85, n=192) Asymptomatic adults (n=80) Pediatric patients (aged 0-17, n=109)	301	Real-time RT-PCR SalivaDirect (Yale University) Ct < 40	Nasopharyngeal swab
Braz-Silva 2020	Brazil Community cross-sectional study	Real-time RT-PCR RealStar® SARS-CoV-2 RT-PCR Kit 1.0 (Altona) Ct < 40	Saliva, swab Salivette (Sarstedt) Morning collection	Patients aged 12 years and older with symptoms and suspected COVID-19 (n=201)	201	Real-time RT-PCR Altona RealStar® SARS-CoV-2 RT-PCR Kit 1.0 (Altona) Ct < 40	Nasopharyngeal swab



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Brotons 2020	Spain Single-center prospective cohort study	Real-time RT-PCR Direct RT-PCR GeneFinder COVID-19 Plus RealAmp kit (Elitech) TaqPath COVID-19 RT-PCR kit (Thermo Fisher)	Oral saliva, spit No transport medium	Asymptomatic children and adults (n=173); Asymptomatic volunteer health workers and staff (n=2709)	2709	Real-time RT-PCR Direct RT-PCR GeneFinder COVID-19 Plus RealAmp kit (Elitech) TaqPath COVID-19 RT-PCR kit (Thermo Fisher)	Nasopharyngeal swab
Byrne 2020	UK Single-center cross-sectional study	Real-time RT-PCR Genesig Real-Time Coronavirus COVID-19 PCR assay (Primerdesign) Ct < 40	Oral saliva, drool No transport medium	Symptomatic adult emergency patients with suspected COVID-19 (n=110)	110	Real-time RT-PCR Genesig Real-Time Coronavirus COVID-19 PCR assay (Primerdesign)	Nasopharyngeal swab
Cassinari 2020	France Single-center cross-sectional study	Real-time RT-PCR Direct detection RT-PCR RealTime SARS-CoV-2 test (Abbott) RealStar® SARS-CoV-2 RT-PCR Kit 1.0 (Altona) One-Step RT-ddPCR Advanced Kit for Probes (BioRad)	Oral saliva, drool No transport medium	Ambulatory patients with COVID-19 symptoms (n=130)	130	Real-time RT-PCR Direct detection RT-PCR RealTime SARS-CoV-2 test (Abbott) RealStar® SARS-CoV-2 RT-PCR Kit 1.0 (Altona) One-Step RT-ddPCR Advanced Kit for Probes (BioRad)	Nasopharyngeal swab
Caulley 2020	Canada Community cross-sectional study	Real-time RT-PCR Allplex 2019-nCoV assay (Seegene) Ct < 37	Oral saliva, drool OMNIGene•ORAL OM-505 (DNA Genotek)	Asymptomatic high-risk adults or adults with mild COVID-19 symptoms (n=1939)	1939	Real-time RT-PCR Allplex 2019-nCoV assay (Seegene) Ct < 37	Nasopharyngeal or oropharyngeal swab
Chen 2020	Hong Kong Single-center cross-sectional study	Real-time RT-PCR In-house SARS-CoV-2 RdRp/Hel real-time RT-PCR assay Xpert Xpress SARS-CoV-2 (Cepheid) CT < 46	Posterior oropharyngeal saliva, spit Viral transport medium	COVID-19 positive inpatients (n=58)	58	Real-time RT-PCR In-house SARS-CoV-2 RdRp/Hel real-time RT-PCR assay Xpert Xpress SARS-CoV-2 (Cepheid) CT < 46	Nasopharyngeal swab
Costa 2020	France Single-center cross-sectional study	Real time RT-PCR Laboratory-developed test Ct < 35	Oral saliva, swab Salivette (Sarstedt)	Adults admitted to the hospital for routine SARS-CoV-2 diagnosis (n=303)	303	Real time RT-PCR Laboratory-developed test Ct < 35	Nasopharyngeal swab



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Delaney 2020	USA Single-center cross-sectional study	Real-time RT-PCR Direct real-time RT-PCR AllPlex 2019-nCoV Assay (Seegene; Ct < 40) ePlex SARS-CoV-2 Test (GenMark) Xpert Xpress SARS-CoV-2 (Cepheid; Ct < 45) Simplexa COVID-19 Direct assay (DiaSorin)	Oral saliva, drool, no transport medium Oral saliva, drool, SpectrumDNA saliva collection kit, with buffer solution	Pediatric and adult patients admitted to the emergency department (n=526)	526	Real-time RT-PCR Direct real-time RT-PCR AllPlex 2019-nCoV Assay (Seegene; Ct < 40) ePlex SARS-CoV-2 Test (GenMark) Xpert Xpress SARS-CoV-2 (Cepheid; Ct < 45) Simplexa COVID-19 Direct assay (DiaSorin)	Nasopharyngeal swab
Fernandez-Pittol 2020	Spain Single-center cross-sectional study	Real-time RT-PCR RNA Process Control Kit (Roche)	Posterior oropharyngeal saliva, spit No transport medium	Emergency department patients with suspected COVID-19 (n=51)	51	Real-time RT-PCR RNA Process Control Kit (Roche)	Nasopharyngeal and oropharyngeal swabs
Gavars 2020	Latvia Community cross-sectional study	Real-time RT-PCR In-house testing kit	Oral saliva, spit No transport medium	Pediatric (n=125) and adult (n=306) ambulatory patients undergoing SARS-CoV-2 testing	104	Real-time RT-PCR In-house testing kit	Nasopharyngeal swab
Goldfarb 2020	Canada Single-center cross-sectional study	Real-time RT-PCR Laboratory-developed test; Xpert Xpress SARS-CoV-2 assay (Cepheid) Ct < 40	Oral saliva, spit; Mouth rinse/gargle No transport medium	Outpatients with known prior positive SARS-CoV-2 tests (n=40), Children 4-12 years with symptoms or household contact with COVID-19 (n=16)	31	Real-time RT-PCR Laboratory-developed test; Xpert Xpress SARS-CoV-2 assay (Cepheid) Ct < 40	Nasopharyngeal swab
Güçlü 2020	Turkey Single-center cross-sectional study	Real-time RT-PCR Genesig RT-PCR SARS-CoV-2 kit (Primerdesign) CT < 45	Oral saliva, spit No transport medium	Inpatients with confirmed COVID-19 (n=30) Inpatients with CT findings compatible with COVID-19 but with negative RT-PCR (n=15) Emergency department patients with COVID-19 symptoms (n=19)	64	Real-time RT-PCR Genesig RT-PCR SARS-CoV-2 kit (Primerdesign) CT < 45	Nasopharyngeal and oropharyngeal swabs



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Huber 2020	Switzerland Multi-center cross-sectional study	Real-time RT-PCR Cobas SARS-CoV-2 assay (Roche) Ct < 40	<u>Study arm 1 (basic):</u> Oral saliva, spit Viral transport medium N=835 <u>Study arm 2 (enhanced):</u> Oral and posterior oropharyngeal saliva, spit Viral transport medium N=352	Adults and children (N = 1187) with COVID-19 symptoms or exposure to an index case	1187	Real-time RT-PCR Cobas SARS-CoV-2 IVD test (Roche) Ct < 40	Nasopharyngeal swab
Iwasaki 2020	Japan Single-center cross-sectional study	Real-time RT-PCR tepOnePlus Real-time PCR System (Thermo Fisher Scientific)	Oral saliva, spit No transport medium	Adult patients with COVID-19 diagnosis (n=10) Patients with suspected COVID-19 (n=66)	76	Real-time RT-PCR tepOnePlus Real-time PCR System (Thermo Fisher Scientific)	Nasopharyngeal swab
Jamal 2020	Canada Multi-center cross-sectional study	Real-time RT-PCR Allplex 2019-nCoV assay (Seegene)	Oral saliva, spit No transport medium	Adult inpatients with confirmed SARS-CoV-2 infection (n=91)	91	Real-time RT-PCR Allplex 2019-nCoV assay (Seegene)	Nasopharyngeal swab
Kandel 2020	Canada Multi-center cross-sectional study	Real-time RT-PCR Cobas SARS-CoV-2 assay (Roche) TaqPath COVID-19 Combo Kit (Thermo Fisher Scientific; Ct < 37)	Oral saliva, drool No transport medium	All adults presenting for SARS-CoV-2 testing at three assessment centers (n=432)	432	Real-time RT-PCR Cobas SARS-CoV-2 assay (Roche) TaqPath COVID-19 Combo Kit (Thermo Fisher Scientific; Ct < 37)	Nasopharyngeal swab
Ku 2020	Singapore Single-center cross-sectional study	Real-time RT-PCR In-house method	Oral saliva, spit (n=42); Buccal swab (n=42) No transport medium	Adult inpatients with confirmed SARS-CoV-2 infection (n=42)	84	Real-time RT-PCR In-house method	Nasopharyngeal swab
Landry 2020	United States Single-center cross-sectional study	Real-time RT-PCR Laboratory-developed assay Ct < 40	Oral saliva, spit No transport medium	Symptomatic outpatients suspected of having COVID-19 (n=124)	124	Real-time RT-PCR Laboratory-developed assay Ct < 40	Nasopharyngeal swab



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Leung 2020	Hong Kong Single-center retrospective study	Real-time RT-PCR lightMix Modular SARS-CoV E-gene detection kit (TIB Molbiol)	Posterior oropharyngeal saliva, spit Viral transport medium	Inpatients with confirmed COVID-19 infection (n=29); Inpatients negative for COVID-19 (n=33)	95	Real-time RT-PCR lightMix Modular SARS-CoV E-gene detection kit (TIB Molbiol)	Nasopharyngeal swab
Lu 2020	USA Multi-center cross-sectional study	Multiplex RT-PCR Genesig RT-PCR SARS-CoV-2 kit (Primerdesign) TaqPath Multiplex RT-PCR COVID-19 Kit (Thermo)	Oral saliva, spit, with kit Oragene OGD-610 (DNA Genotek) Spectrum S-1000 (Spectrum Solutions)	Symptomatic outpatients meeting CDC criteria for COVID-19 testing (n=88) Convalescent COVID-19 patients (n=26)	101	Multiplex RT-PCR Genesig RT-PCR SARS-CoV-2 kit (Primerdesign) TaqPath Multiplex RT-PCR COVID-19 Kit (Thermo)	Nasopharyngeal swab
Matic 2020	Canada Single-center cross-sectional study	Real-time RT-PCR LightMix® ModularDx SARS-CoV E-gene assay (TIB Molbiol)	Oral saliva, spit No transport medium	Patients under investigation for COVID-19: symptomatic inpatients (n=13), residents of long-term care (LTC) facilities (n=20), healthcare workers (n=28), mildly symptomatic outpatients and household contacts (n=13)	74	Real-time RT-PCR LightMix® ModularDx SARS-CoV E-gene assay (TIB Molbiol) Cobas® SARS-CoV-2 Test (Roche)	Nasopharyngeal swab
McCormick-Baw 2020	USA Single-center cross-sectional study	Real-time RT-PCR Xpert Xpress SARS-CoV-2 assay (Cepheid)	Oral saliva, spit No transport medium	Emergency department patients with suspected COVID-19; COVID-19 ward inpatients not requiring mechanical ventilation (n=156)	156	Real-time RT-PCR Xpert Xpress SARS-CoV-2 assay (Cepheid)	Nasopharyngeal swab
Mestdagh 2020	Belgium National multi-center cross-sectional study	<u>Lab 1:</u> Duplex real-time RT-PCR Charite E gene assay (FAM) <u>Lab 2:</u> Multiplex real-time RT-PCR TaqPath COVID-19 Combo Kit (Thermo Fisher Scientific)	Oral saliva, spitting (Norgen) Oral saliva, swab (DNA Genotek)	Ambulatory patients undergoing SARS-CoV-2 testing in triage centers (n=2884)	2884	<u>Lab 1:</u> Duplex real-time RT-PCR Charite E gene assay (FAM) <u>Lab 2:</u> Multiplex real-time RT-PCR TaqPath COVID-19 Combo Kit (Applied Biosystems)	Nasopharyngeal swab



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Migueres 2020	France Single-center consecutive case series	Real-time RT-PCR Panther Fusion SARS-CoV-2 Assay (Hologic)	Oral saliva No transport medium	Hospitalized and ambulatory COVID-19-positive patients (n=123)	123	Real-time RT-PCR Panther Fusion SARS-CoV-2 Assay (Hologic)	Nasopharyngeal swab
Miller 2020	USA Single-center consecutive case series	Real-time RT-PCR In-house real-time RT-PCR test	Oral saliva, spit, kit Oragene-Dx (OGD-510, Orasure)	Symptomatic adults with positive RT-qPCR NP swab within previous 5 days or undergoing testing on day of enrollment; Asymptomatic patients undergoing nasopharyngeal swab RT-PCR (total n=91)	91	Real-time RT-PCR In-house real-time RT-PCR test	Nasopharyngeal swab
Moreno-Contreras 2020	Mexico Single-center cross-sectional study	Real-time RT-PCR StarQ One-Step RT-qPCR (Genes 2 Life) CT ≤ 38	Oral saliva, spit No transport medium	Ambulatory patients (n=250) or hospitalized patients (n=3) undergoing SARS-CoV-2 testing in hospital triage	253	Real-time RT-PCR StarQ One-Step RT-qPCR (Genes 2 Life) CT ≤ 38	Nasopharyngeal or oropharyngeal swab
Nacher 2020	French Guiana Community cross-sectional study	Real-time RT-PCR French national center RT-PCR assay	Oral saliva, spit No transport medium	Persons age 3 or older with mild symptoms suggestive of COVID-19 (n=473); High-risk asymptomatic persons or close contacts (n=303)	776	Real-time RT-PCR French national center RT-PCR assay	Nasopharyngeal swab
Otto 2020	France Single-center cross-sectional study	Real-time RT-PCR GenoXtract (Biocentric)	Posterior oropharyngeal saliva, spit Viral transport medium	Outpatients with symptoms consistent with COVID-19 but without cough (n=92)	92	Real-time RT-PCR GenoXtract (Biocentric)	Nasopharyngeal swab
Pasomsub 2020	Thailand Single-center cross-sectional study	Real-time RT-PCR SARS-CoV-2 Nucleic Acid Diagnostic Kit (Sansure) Ct ≤ 38	Oral saliva, spit Viral transport medium (COPAN)	Adults with COVID-19 symptoms and positive travel or exposure history (n=200)	200	Real-time RT-PCR SARS-CoV-2 Nucleic Acid Diagnostic Kit (Sansure) Ct ≤ 38	Nasopharyngeal and throat swabs
Procop 2020	USA Single-center cross-sectional study	Real-time RT-PCR CDC nCoV Real-Time RT-PCR Diagnostic Panel	Oral saliva, spit, with nasopharyngeal secretions No transport medium	Outpatients with symptoms consistent with COVID-19 (n=216)	216	Real-time RT-PCR CDC nCoV Real-Time RT-PCR Diagnostic Panel	Nasopharyngeal swab



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Rao 2020	Malaysia Single-center cross-sectional study	Real-time RT-PCR Real-Q 2019-nCoV detection kit (Biosewom) Ct < 38	Deep throat saliva, spit, morning sample No transport medium	Asymptomatic adult males with prior positive SARS-CoV-2 tests undergoing quarantine (n=217)	217	Real-time RT-PCR Real-Q 2019-nCoV detection kit (Biosewom) Ct < 38	Nasopharyngeal swab
Sakanashi 2020	Japan Single-center prospective cohort study	Real-time RT-PCR BD MAX open system (BD) N gene	Oral saliva, drool No transport medium	Inpatients with positive SARS-CoV-2 infection (n=5) Outpatients with symptoms consistent with COVID-19 (n=7)	28	Real-time RT-PCR BD MAX open system (BD) N gene	Nasopharyngeal swab
Senok 2020	UAE Single-center cross-sectional study	Real-time RT-PCR Neoplex COVID-19 kit (GeneMatrix) Ct ≤ 40	Oral saliva, drool No transport medium	Adults undergoing COVID-19 testing (n=401)	401	Real-time RT-PCR Neoplex COVID-19 kit (GeneMatrix) Ct ≤ 40	Nasopharyngeal swab
Skolimowska 2020	UK Single-center cross-sectional study	Multiplex tandem RT-PCR (Roche, AusDiagonstics, Thermo Fisher, or Abbott)	Oral saliva, drool	Symptomatic healthcare workers and household contacts (n=132)	132	Multiplex tandem RT-PCR (Roche, AusDiagonstics, Thermo Fisher, or Abbott)	Nasopharyngeal swab
Sui 2020	China Single-center cross-sectional study	RT-digital PCR	Oral saliva	Recovered asymptomatic COVID-19 inpatients with long-term nucleic acid in the respiratory tract (n=35)	27	RT-digital PCR	Nasopharyngeal or oropharyngeal swab
Sun 2020	USA Single-center cross-sectional study	Multiplex real-time RT-PCR QuantiVirus SARS-CoV-2 Multiplex Test (DiaCarta)	Oral saliva, spit QuantiVirus Saliva Collection Kit (DiaCarta) Viral transport medium	Patients with previous positive SARS-CoV-2 test (n=20) Asymptomatic adults (n=389)	20	Multiplex real-time RT-PCR QuantiVirus SARS-CoV-2 Multiplex Test	Nasopharyngeal/or oropharyngeal swab
Torres 2020	USA Community cross-sectional study	Real-time RT-PCR CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel One Step PrimerScript™ III RT-PCR Kit (Takara Bio)	Oral saliva, spit SDNA-1000 saliva collection device (Spectrum Solutions)	Mildly symptomatic or asymptomatic adults at two community testing sites (n=943)	943	Real-time RT-PCR CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel One Step PrimerScript™ III RT-PCR Kit (Takara Bio)	Nasopharyngeal swab



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Uwamino 2020	Japan Single-center cross-sectional study	Real-time RT-PCR 2019 Novel Coronavirus Detection Kit (Shimadzu) N gene Ct < 40	Oral saliva, drool No transport medium	Admitted patients with confirmed COVID-19 (n=32) Symptomatic university staff (n=115)	196	Real-time RT-PCR 2019 Novel Coronavirus Detection Kit (Shimadzu) N gene Ct < 40	Nasopharyngeal swab
Vaz 2020	Brazil Single-center cross-sectional study	Real-time RT-PCR OneStep/COVID-19 Kit (BIOMOL) Ct ≤ 40	Oral saliva, spit No transport medium	COVID ward patients (n=67); Symptomatic healthcare workers (n=82)	155	Real-time RT-PCR OneStep/COVID-19 Kit (BIOMOL) Ct ≤ 40	Nasopharyngeal and/or oropharyngeal swab
Williams 2020	Australia Single-center cross-sectional study	Multiplex RT-PCR Qiagen EZ1 Platform (Qiagen) Coronavirus Typing (8-well) assay (AusDiagnostics)	Oral saliva, drool Liquid Amies media	Ambulatory patients undergoing COVID-19 testing (n=622)	89	Multiplex RT-PCR Qiagen EZ1 Platform (Qiagen) Coronavirus Typing (8-well) assay (AusDiagnostics)	Nasopharyngeal swab
Wong 2020	Hong Kong Multi-center retrospective case series	Real-time RT-PCR LightMix Modular SARS and Wuhan CoV E-gene kit (TIB-MOLBIOL) Ct ≤ 40	Posterior oropharyngeal saliva, spit Viral transport medium (inpatients) No transport medium (outpatients)	Symptomatic COVID-19 patients (n=51) Asymptomatic COVID-19 patients (n=7) Ambulatory patients testing for COVID-19 (n=37)	229	Real-time RT-PCR LightMix Modular SARS and Wuhan CoV E-gene kit (TIB-MOLBIOL) Ct ≤ 40	Nasopharyngeal swab/aspirate ± throat swab
Yee 2020	USA Single-center cross-sectional study	Real-time RT-PCR TaqPath COVID-19 Combo Kit (Thermo Fisher) Ct < 40	Oral saliva, drool No transport medium	Inpatients, outpatients, household members of diagnosed COVID-19 patients (n=300)	300	Real-time RT-PCR TaqPath COVID-19 Combo Kit (Thermo Fisher) Ct < 40	Nasopharyngeal swab



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Yokota 2020	Japan Community cross-sectional study	Real-time RT-PCR <u>CT cohort:</u> Thunderbird Probe One-step qRT-PCR Kit (Toyobo) Loopamp 2019-SARS-CoV-2 Detection Reagent Kit (Eiken Chemical)	Oral saliva, spit No transport medium	<u>CT cohort:</u> asymptomatic persons in close contact with confirmed COVID-19 patients (n=161) <u>AQ cohort:</u> Asymptomatic travellers entering Japan (n=1763)	161	Real-time RT-PCR <u>CT cohort:</u> Thunderbird Probe One-step qRT-PCR Kit (Toyobo) <u>AQ cohort:</u> Thunderbird Probe One-step qRT-PCR Kit (Toyobo) Loopamp 2019-SARS-CoV-2 Detection Reagent Kit (Eiken Chemical)	Nasopharyngeal swab
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Table 2. Diagnostic accuracy data for included studies.

STUDY ID	TRUE POSITIVE	FALSE POSITIVE	FALSE NEGATIVE	TRUE NEGATIVE
Abdul Karim 2020	35	12	13	949
Aita 2020	7	1	0	361
Akgun Dogan 2020	37	10	32	176
Altawalah 2020	287	18	57	529
Babady 2020	16	1	1	69
Barat 2020	30	1	7	421
Bhattacharya 2020	53	0	5	15
Binder 2020	10	1	2	18
Borghi 2020	79	28	7	187
Braz-Silva 2020	37	18	15	131
Brottons 2020	46	23	5	2914
Byrne 2020	12	0	2	96
Cassinari 2020	8	5	0	116
Caulley 2020	34	14	22	1869
Chen 2020	49	3	6	0
Costa 2020	29	23	6	245
Fernandez-Pittol 2020	30	1	7	13
Gavars 2020	50	6	18	30
Goldfarb 2020	22	1	6	1
Güçlü 2020	23	4	4	33
Huber 2020	228	4	20	935
Iwasaki 2020	8	1	1	66
Jamal 2020	44	8	20	19
Kandel 2020	39	3	4	383
Ku 2020	20	1	10	11
Landry 2020	28	2	5	89
Leung 2020	38	13	7	37
Lu 2020	12	1	9	79
Matic 2020	15	1	6	52
McCormick-Baw 2020	47	1	2	105
Mestdaggh 2020	57	12	60	2755
Migueres 2020	34	3	7	79
Miller 2020	33	2	1	55
Moreno-Contreras 2020	60	34	20	139
Nacher 2020	76	10	76	614
Otto 2020	45	4	0	43
Pasomsub 2020	16	2	3	179
Procop 2020	38	1	0	177
Rao 2020	73	76	11	57
Sakanashi 2020	15	4	0	9
Senok 2020	19	9	7	366
Skolimowska 2020	15	1	3	112
Sui 2020	14	2	0	0
Sun 2020	5	3	1	11
Torres 2020	46	8	54	835
Uwamino 2020	32	11	15	138
Vaz 2020	67	2	4	82
Williams 2020	33	1	6	49
Wong 2020	104	37	18	70
Yee 2020	69	10	18	203
Yokota 2020	38	6	3	114



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Appendix Table 3. Definitions of and included studies within subgroups.

SUBGROUP	DEFINITION	NUMBER OF STUDIES (SAMPLE SIZE)	REFERENCES
Confirmed COVID-19	Patients with known COVID-19 infection or SARS-CoV-2 positive test at the time of study enrollment	14 (903)	[9-23]
Suspected COVID-19	Patients with symptoms consistent with COVID-19 AND exposure to a known COVID-19 case OR travel history to a location with COVID-19 at the time of study enrollment OR Patients meeting local criteria for suspected COVID-19 at the time of study enrollment	6 (1699)	[10, 24-28]
Convalescent COVID-19	Patients described as convalescent or recovered at the time of study enrollment	2 (61)	[27,30]
Symptomatic	Patients who have symptoms consistent with COVID-19 infection but with unknown COVID-19 status at the time of study enrollment	17 (3169)	[10,14,20,24-25,27-28,31-41]
Asymptomatic	Patients with unknown COVID-19 status and are asymptomatic at the time of enrollment	6 (3462)	[9,11,19,36,41-45]
Hospital setting	Studies recruiting patients admitted to the hospital or emergency room at the time of enrollment OR Studies with sample collection done in hospitals	24 (3573)	[9-12,14-18,20,22,24,26,28,31-33,38,47,50-54]
Community/outpatient setting	Studies recruiting outpatients, ambulatory patients, or community members at the time of enrollment OR Studies with sample collection done in outpatient clinics, by mobile field teams, or at home	18 (12637)	[9,25,27,31,34-35,37,39,40-41,43-46,55-58]
Saliva drool/spit	Studies involving collection of saliva drool or spit into a vessel	44 (16779)	[10,11-16,18-24,26-41,43-46,48-55,57-58]
Saliva swab	Studies involving the use of a swab to collect saliva	6 (3895)	[9,17,25,42,47,56]
Oral saliva	Studies involving collection of saliva from the oral cavity only	42 (17309)	[10-11,14-17,20-21,23-25,27-37,39-49,51-58]
Posterior oropharyngeal saliva	Studies involving collection of saliva from the posterior oropharyngeal area	9 (3028)	[12,18,19,22,26,38,50]
Viral transport medium	Studies involving addition of viral transport medium to the collected saliva sample*	7 (829)	[9,12,18,21-22,24,28,45,59]
Morning collection	Studies involving morning saliva collection*	4 (705)	[12,19,22,25]

*not included in meta-analysis



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Appendix Table 4. Pooled sensitivity and specificity per RT-PCR kit brand.

BRAND	STUDIES (SAMPLE SIZE)	SENSITIVITY (95% CI)	SPECIFICITY (95% CI)
Xpert Xpress SARS-CoV-2 test (Cepheid)	3 (243)	0.95 (0.91, 0.99)	0.99 (0.95, 1.00)
OneStep/COVID-19 Kit (BIOMOL)	1 (122)	0.94 (0.86, 0.98)	0.96 (0.87, 1.00)
Thunderbird Probe One-step qRT-PCR Kit (Toyobo)	1 (161)	0.93 (0.80, 0.98)	0.95 (0.89, 0.98)
Cobas SARS-CoV-2 Assay (Roche)	1 (1187)	0.92 (0.88, 0.95)	1.00 (0.99, 1.00)
SalivaDirect (Yale University)	1 (301)	0.92 (0.84, 0.97)	0.87 (0.82, 0.91)
Real-Q 2019-nCoV detection kit (Biosewoom)	1 (217)	0.87 (0.78, 0.93)	0.43 (0.34, 0.52)
Coronavirus Typing (8-well) Assay (AusDiagnostics)	1 (406)	0.85 (0.69, 0.94)	1.00 (0.98, 1.00)
LightMix Modular SARS and Wuhan CoV E-gene kit (TIB-MOLBIOL)	3 (398)	0.84 (0.79, 0.89)	0.80 (0.66, 1.00)
SARS-CoV-2 Nucleic Acid Diagnostic Kit (Sansure)	1 (110)	0.84 (0.60, 0.97)	0.98 (0.91, 1.00)
Panther Fusion SARS-CoV-2 Assay (Hologic)	1 (121)	0.83 (0.68, 0.93)	0.96 (0.90, 0.99)
TaqPath COVID-19 Combo Kit (Thermo Fisher Scientific)	3 (4075)	0.80 (0.73, 0.86)	0.97 (0.95, 1.00)
Genesig RT-PCR SARS-coV-2 Kit (Primerdesign)	3 (275)	0.77 (0.61, 0.94)	0.98 (0.96, 1.00)
Neoplex COVID-19 Kit (GeneMatrix)	1 (92)	0.73 (0.52, 0.88)	0.86 (0.76, 0.94)
RealStar SARS-CoV-2 RT-PCR Kit 1.0 (Altona)	1 (201)	0.71 (0.57, 0.83)	0.88, 0.82, 0.93)
Allplex 2019-nCoV Assay (Seegene)	2 (2030)	0.65 (0.57, 0.74)	0.99 (0.99, 1.00)
QuantiVirus SARS-CoV-2 Multiplex Test (DiaCarta)	1 (104)	0.57 (0.34, 0.78)	0.99 (0.93, 1.00)
Charite E-gene Assay (FAM)	1 (308)	0.49 (0.39, 0.58)	0.94 (0.89, 0.97)
Direct Detection of SARS-CoV-2 Detection Kit (Coyote Bioscience)	1 (255)	0.54 (0.41, 0.66)	0.95 (0.90, 0.97)



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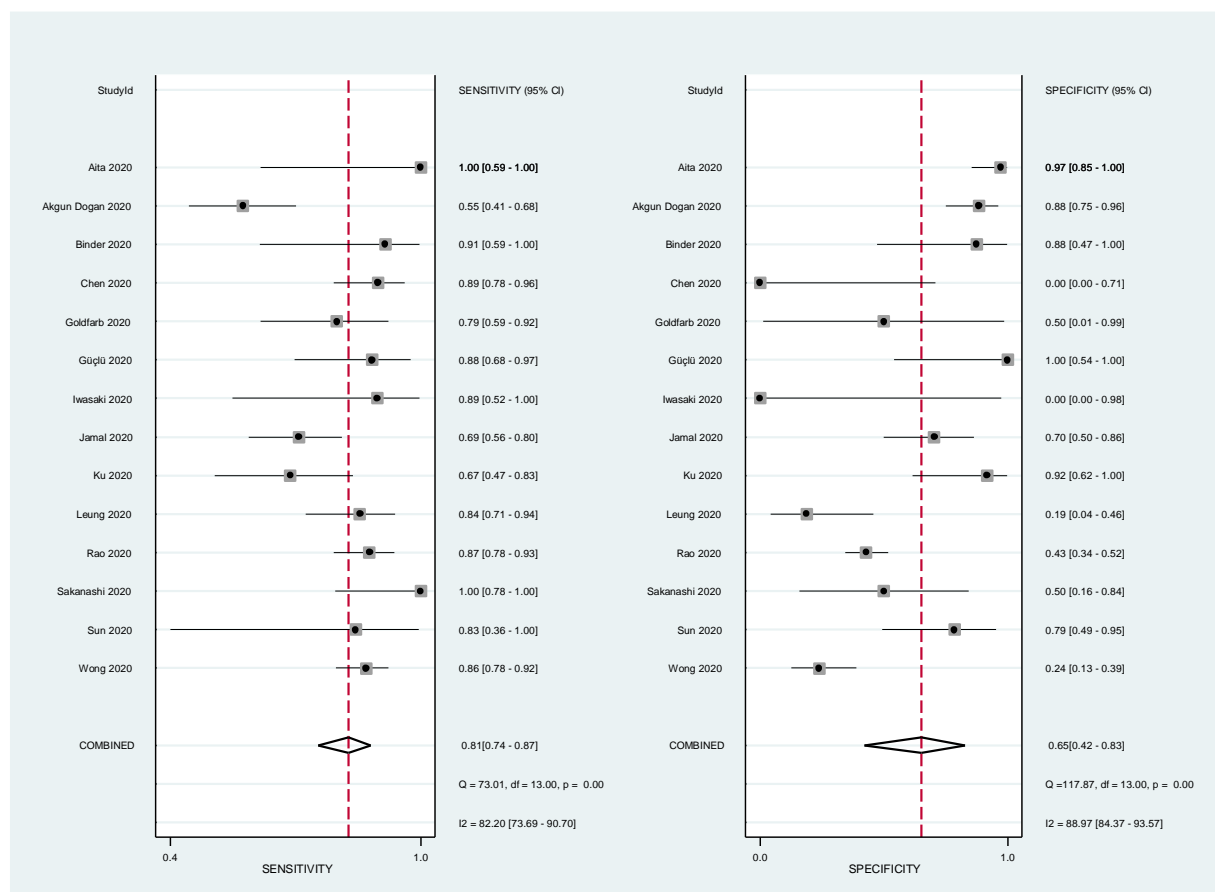


Figure 2. Forest plot of diagnostic accuracy data for confirmed COVID-19 patients.



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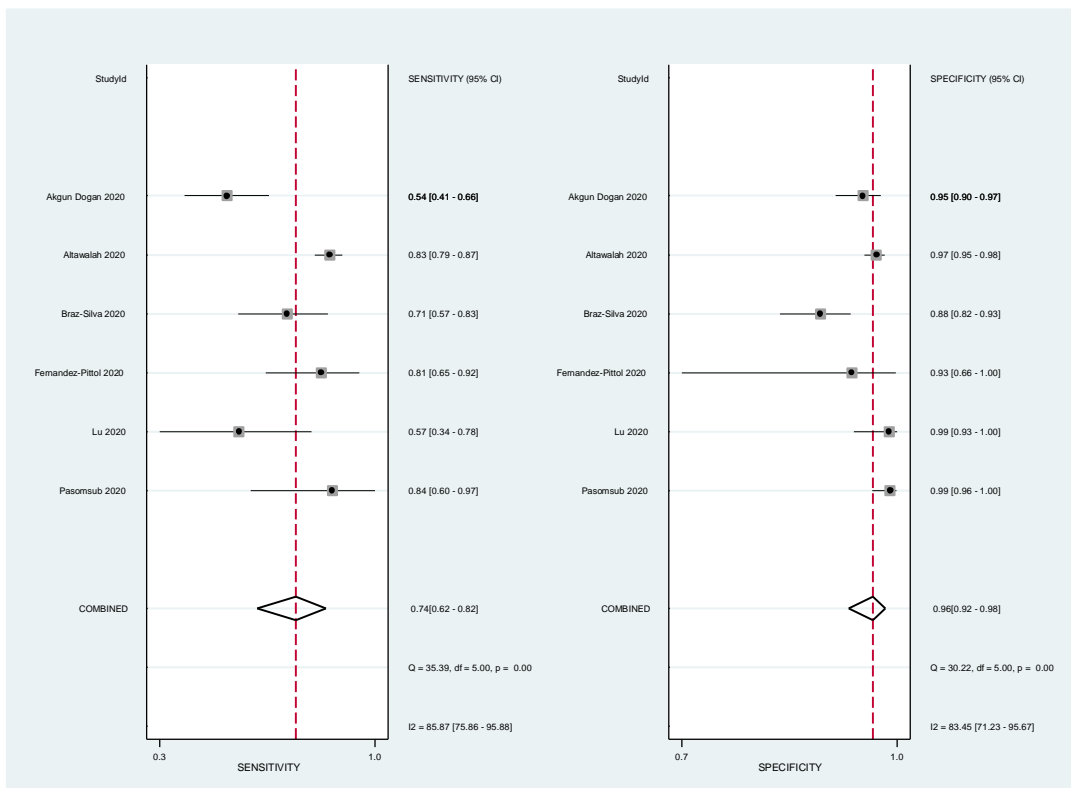


Figure 3. Forest plot of diagnostic accuracy data for suspected COVID-19 patients.

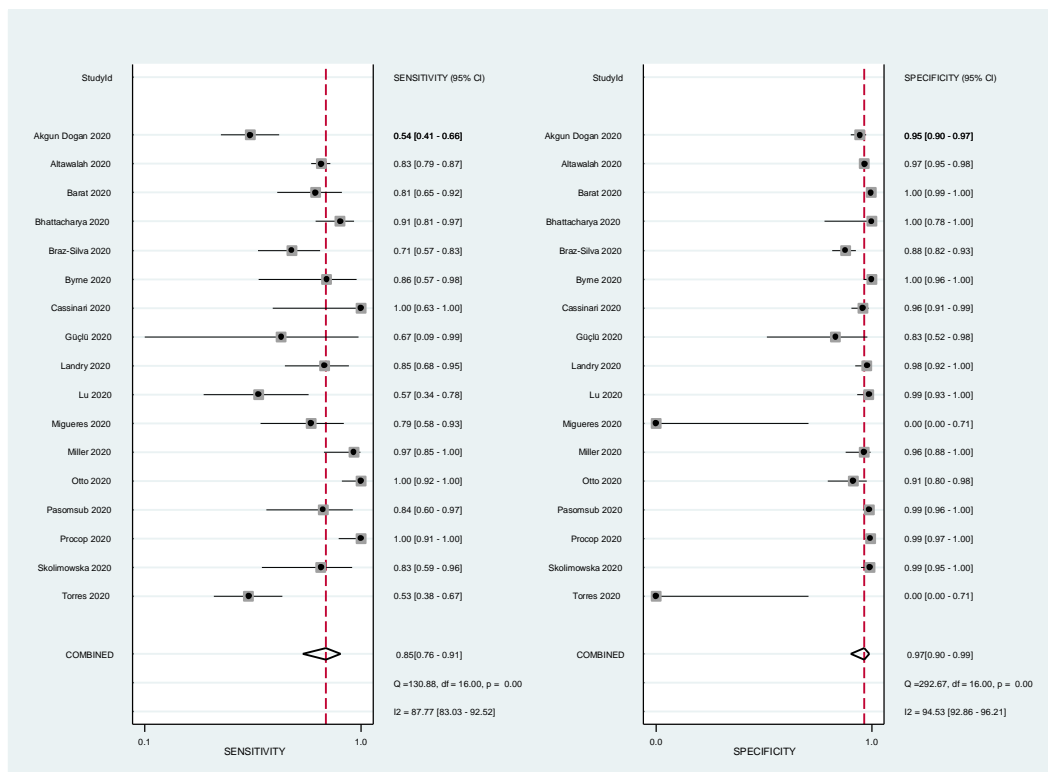


Figure 4. Forest plot of diagnostic accuracy data for symptomatic COVID-19 patients.



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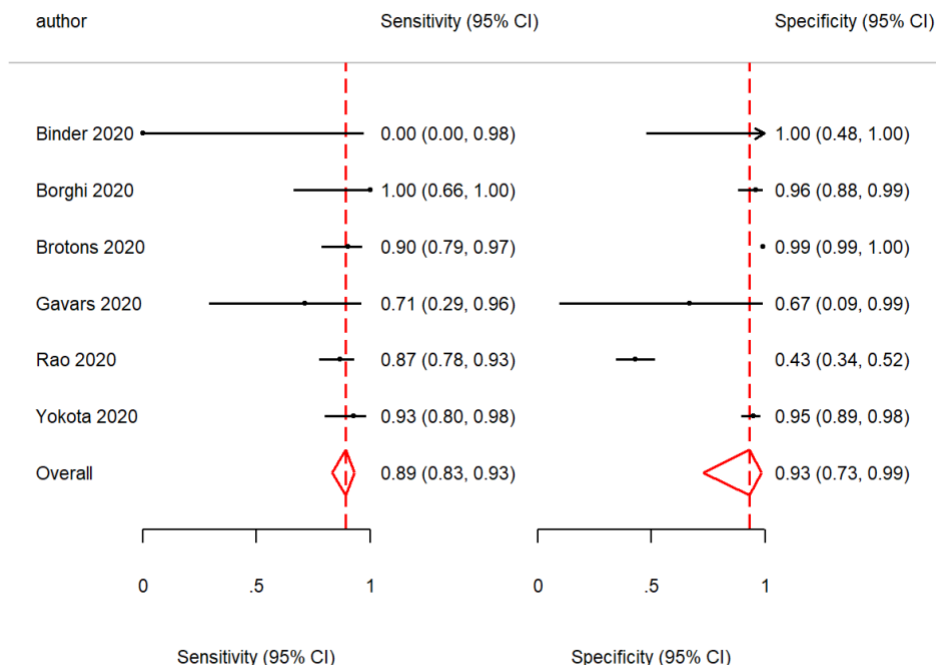


Figure 5. Forest plot of diagnostic accuracy data for asymptomatic COVID-19 patients. Heterogeneity – sensitivity $p < 0.001$, $I^2 = 0.53\%$; specificity $p < 0.001$, $I^2 = 19.61\%$.

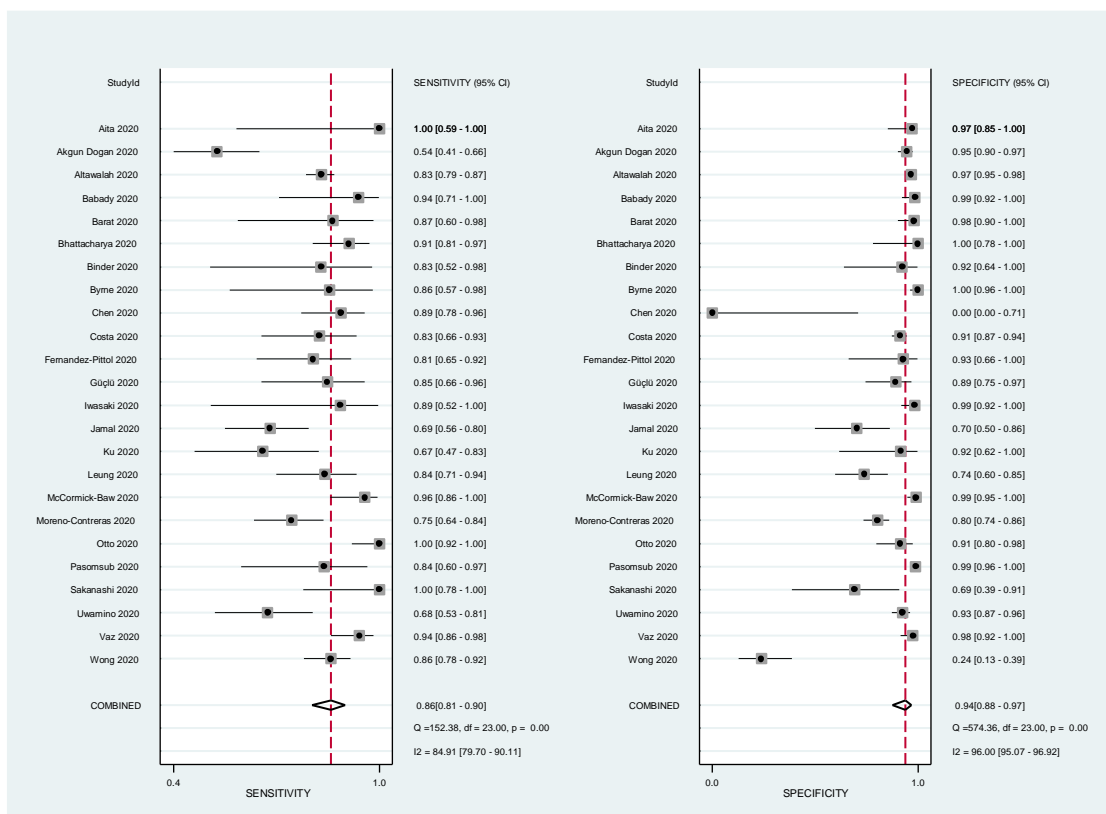


Figure 6. Forest plot of diagnostic accuracy data for hospital setting.



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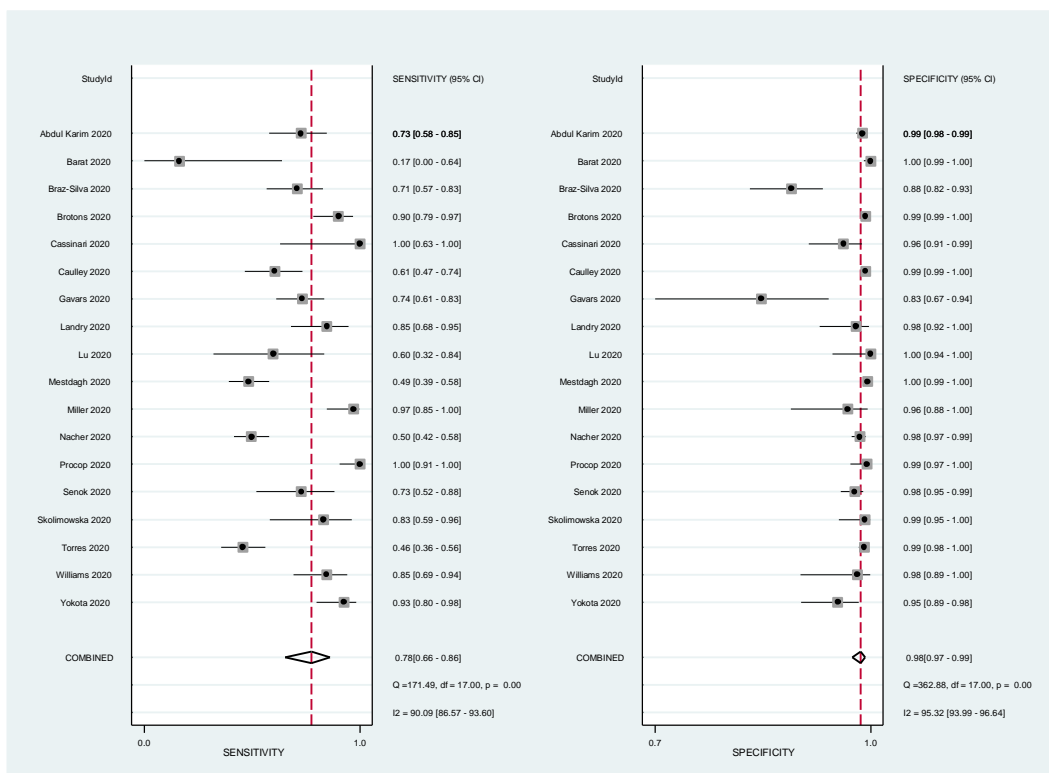


Figure 7. Forest plot of diagnostic accuracy data for community/outpatient setting.

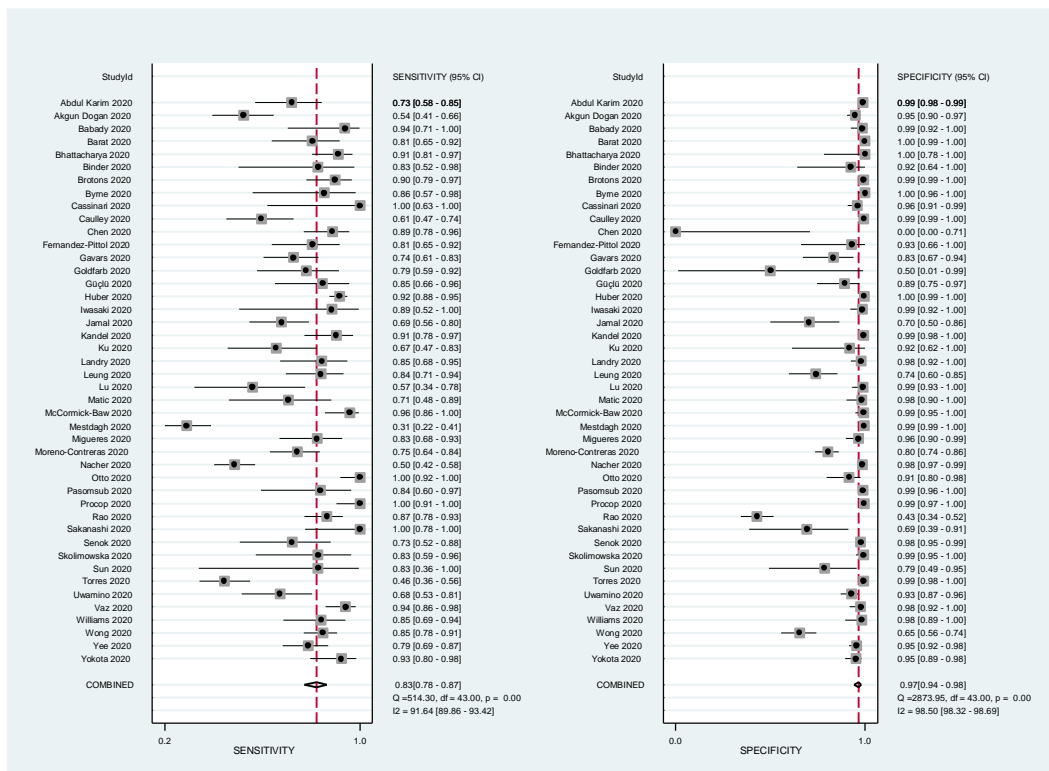


Figure 8. Forest plot of diagnostic accuracy data for saliva drool/spit sample.



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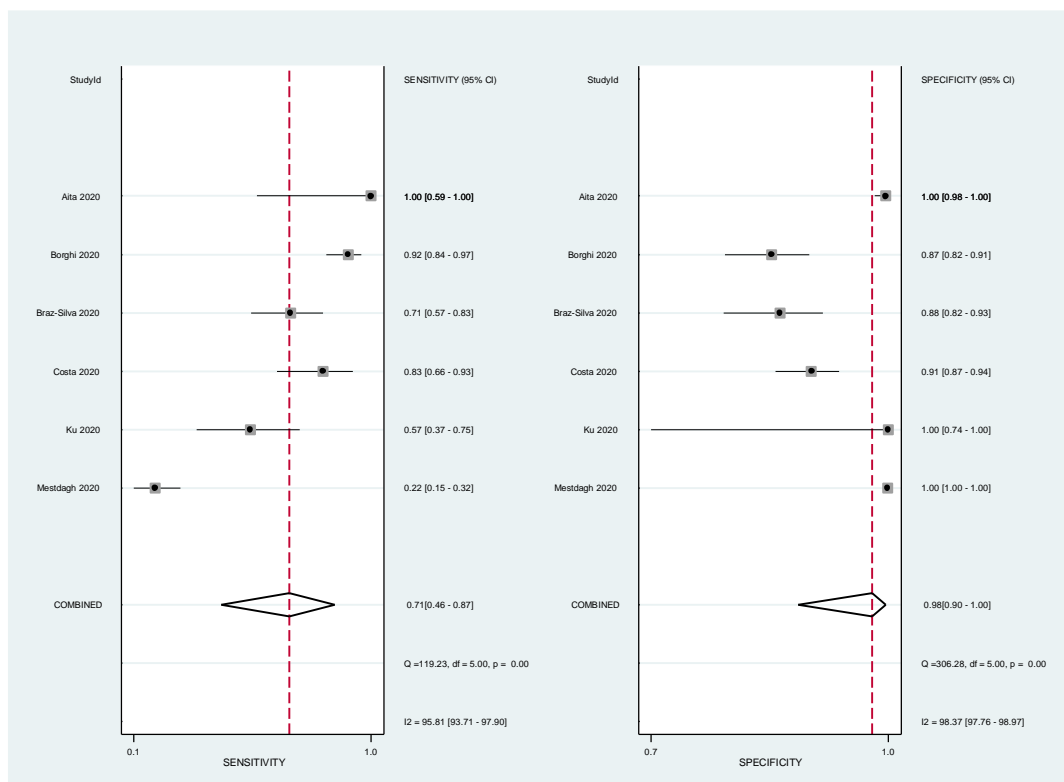


Figure 9. Forest plot of diagnostic accuracy data for saliva swab sample.

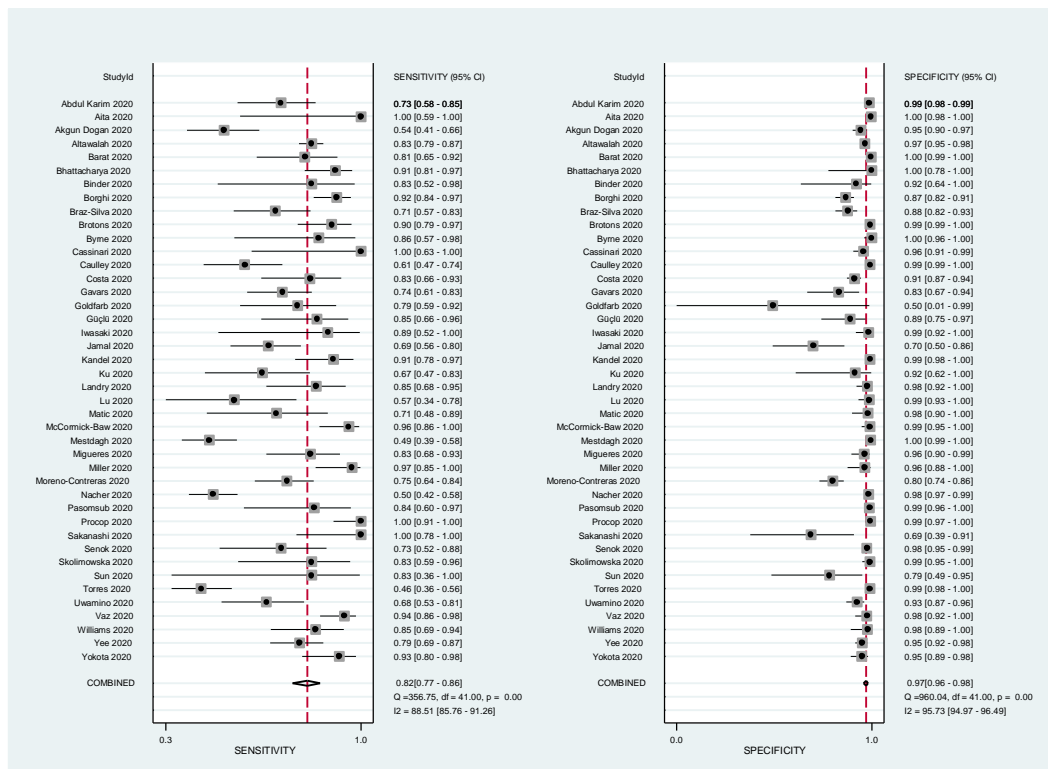


Figure 10. Forest plot of diagnostic accuracy data for oral saliva sample.



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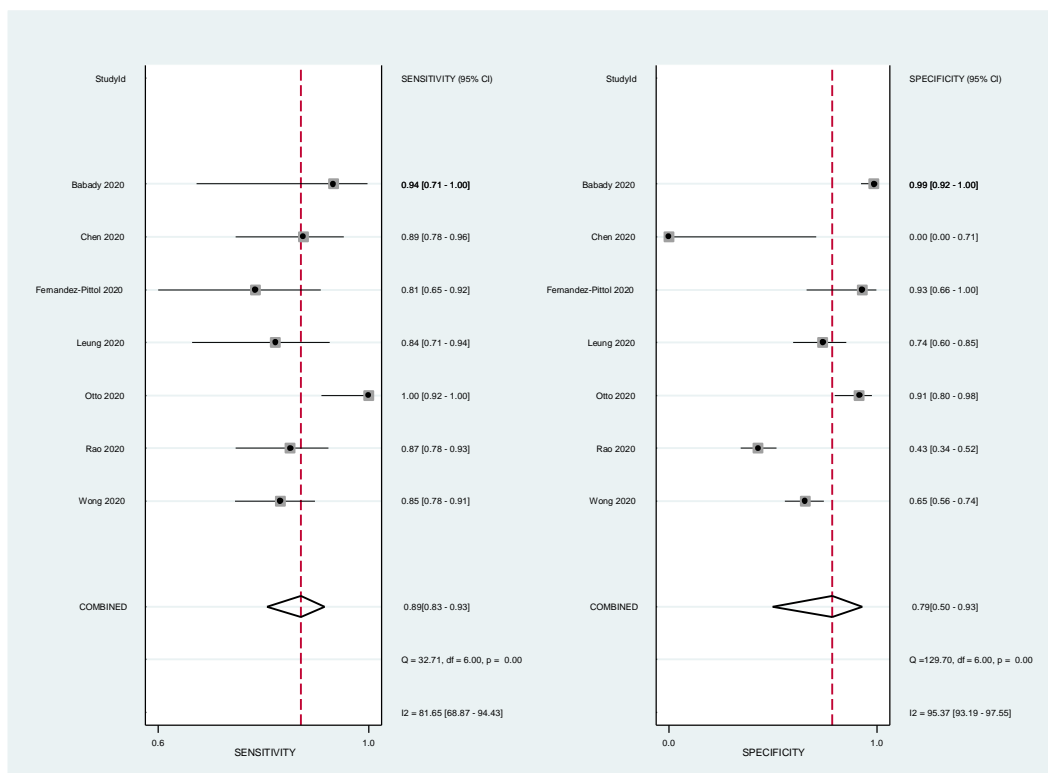


Figure 11. Forest plot of diagnostic accuracy data for posterior oropharyngeal saliva sample.



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Figure 12. Forest plots of sensitivity (left) and specificity (right) of RT-PCR diagnostic kits.



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Table 5. Characteristics of ongoing saliva RT-PCR trials.

Clinical Trial Identifier (Location)	Official Title	Methodology	Outcome Measures	Population	Estimated Date of Completion
NCT04715607 Denmark	COVID-19: SARS-CoV-2 Detection in Saliva, Oropharyngeal and Nasopharyngeal Specimens	Interventional diagnostic study Randomized Double-blind Parallel assignment	SARS-CoV-2 detection rates for oropharyngeal swabs (OPS) compared with nasopharyngeal swabs and saliva collection; SARS-CoV-2 RT-PCR cycle threshold (Ct) values; OPS, NPS and saliva test discomfort and likelihood to get retested; Ratio of mutations in SARS-CoV-2	n=22000 16 years and older	February 10, 2021
NCT04604145 United States	Evaluation of Self Collected Saliva Samples Without Viral Transport Media for SARS-CoV-2 Testing Via RT-PCR	Interventional diagnostic study Non-randomized Open label Parallel assignment	Percent positive agreement between self-collected saliva samples and healthcare-worker collected nasopharyngeal samples; Percent negative agreement between self-collected saliva samples and healthcare-worker collected nasopharyngeal samples; Percent overall agreement between self-collected saliva samples and healthcare-worker collected nasopharyngeal sample	n=600 18 years and older	February 2021
NCT04567953 United States	COVID-19 Tests With Saliva Specimens	Interventional screening study Open label Single group assignment	The clinical evaluation of saliva as specimen for COVID-19 molecular test	n=2000 18 years and older	June 27, 2021
NCT04424446 United States	Saliva as a Source of Detection for SARS-CoV-2	Observational cross-sectional study	Saliva SARS-CoV-2 RTPCR test results Saliva and midturbinate swab SARS-CoV-2 RTPCR test result	n=5000 18 years and older	June 1, 2021



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Question: Should saliva RT-PCR be used to diagnose SARS-CoV-2 infection in the general population?

Sensitivity	0.84 (95% CI: 0.80 to 0.88)		<div>Prevalences</div> <div>4.0671%</div> <div></div> <div></div>			
Specificity	0.96 (95% CI: 0.94 to 0.98)					

Outcome	No of studies (No of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy <div>CoE</div>
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 4.0671%	
True positives (patients with SARS-CoV-2 infection)	51 studies 2705 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious *	not serious	none	34 (33 to 36)	<div>⊕⊕⊕○</div> <div>MODERATE</div>
False negatives (patients incorrectly classified as not having SARS-CoV-2 infection)								7 (5 to 8)	
True negatives (patients without SARS-CoV-2 infection)	51 studies 16602 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious *	not serious	none	921 (902 to 940)	<div>⊕⊕⊕○</div> <div>MODERATE</div>
False positives (patients incorrectly classified as having SARS-CoV-2 infection)								38 (19 to 57)	

Explanations

a. Substantial heterogeneity across all studies ($p=0.00$, $I^2=90.13\%$)

Figure 13. Summary of evidence table for saliva RT-PCR diagnosis in the general population.



Philippine COVID-19 Living Clinical Practice Guidelines

Question: Should saliva RT-PCR be used to diagnose SARS-CoV-2 infection in patients with confirmed COVID-19?

Sensitivity	0.81 (95% CI: 0.74 to 0.87)	Prevalences 55%		
Specificity	0.65 (95% CI: 0.42 to 0.83)			

Outcome	No of studies (No of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 55%	
True positives (patients with SARS-CoV-2 infection)	14 studies 548 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious ^a	not serious	none	446 (407 to 479)	⊕⊕⊕○ MODERATE
False negatives (patients incorrectly classified as not having SARS-CoV-2 infection)								104 (71 to 143)	
True negatives (patients without SARS-CoV-2 infection)	14 studies 355 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious ^a	serious ^b	none	293 (189 to 373)	⊕⊕○○ LOW
False positives (patients incorrectly classified as having SARS-CoV-2 infection)								157 (77 to 261)	

Explanations

a. Substantial heterogeneity ($p < 0.10$, $I^2 > 75\%$)

b. Wide confidence interval

Figure 14. Summary of evidence table for saliva RT-PCR monitoring in patients with confirmed COVID-19.



Philippine COVID-19 Living Clinical Practice Guidelines

Question: Should saliva RT-PCR be used to diagnose SARS-CoV-2 infection in patients with suspected COVID-19?

Sensitivity	0.74 (95% CI: 0.62 to 0.82)				
Specificity	0.96 (95% CI: 0.92 to 0.98)				
		Prevalences	31.9%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 31.9%	
True positives (patients with SARS-CoV-2 infection)	6 studies 469 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious ^a	not serious	none	236 (198 to 262)	⊕⊕⊕○ MODERATE
False negatives (patients incorrectly classified as not having SARS-CoV-2 infection)								83 (57 to 121)	
True negatives (patients without SARS-CoV-2 infection)	6 studies 1230 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious ^a	not serious	none	654 (627 to 667)	⊕⊕⊕○ MODERATE
False positives (patients incorrectly classified as having SARS-CoV-2 infection)								27 (14 to 54)	

Explanations

a. Substantial heterogeneity ($p < 0.10$, $I^2 > 75\%$)

Figure 15. Summary of evidence table for saliva RT-PCR diagnosis in patients with suspected COVID-19.



Philippine COVID-19 Living Clinical Practice Guidelines

Question: Should saliva RT-PCR be used to diagnose SARS-CoV-2 infection in patients with COVID-19 symptoms?

Sensitivity	0.85 (95% CI: 0.76 to 0.91)	Prevalences 35.8% 0% 0%		
Specificity	0.97 (95% CI: 0.90 to 0.99)			

Outcome	No of studies (No of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 35.8%	pre-test probability of 0%	pre-test probability of 0%	
True positives (patients with SARS-CoV-2 infection)	17 studies 772 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious ^a	not serious	none	304 (272 to 326)	0 (0 to 0)	0 (0 to 0)	⊕⊕⊕○ MODERATE
False negatives (patients incorrectly classified as not having SARS-CoV-2 infection)								54 (32 to 86)	0 (0 to 0)	0 (0 to 0)	
True negatives (patients without SARS-CoV-2 infection)	17 studies 3169 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious ^a	not serious	none	623 (578 to 636)	970 (900 to 990)	970 (900 to 990)	⊕⊕⊕○ MODERATE
False positives (patients incorrectly classified as having SARS-CoV-2 infection)								19 (6 to 64)	30 (10 to 100)	30 (10 to 100)	

Explanations

a. Substantial heterogeneity ($p < 0.10$, $I^2 > 75\%$)

Figure 16. Summary of evidence table for saliva RT-PCR diagnosis in symptomatic patients.



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Question: Should saliva RT-PCR be used to diagnose SARS-CoV-2 infection in asymptomatic patients?

Sensitivity	0.89 (95% CI: 0.83 to 0.93)	Prevalences 28.25% 0% 0%		
Specificity	0.93 (95% CI: 0.73 to 0.99)			

Outcome	No of studies (No of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 28.25%	pre-test probability of 0%	pre-test probability of 0%	
True positives (patients with SARS-CoV-2 infection)	6 studies 280 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious ^a	not serious	none	251 (234 to 263)	0 (0 to 0)	0 (0 to 0)	⊕⊕⊕○ MODERATE
False negatives (patients incorrectly classified as not having SARS-CoV-2 infection)								32 (20 to 49)	0 (0 to 0)	0 (0 to 0)	
True negatives (patients without SARS-CoV-2 infection)	6 studies 3182 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious ^a	not serious	none	669 (524 to 710)	933 (730 to 990)	933 (730 to 990)	⊕⊕⊕○ MODERATE
False positives (patients incorrectly classified as having SARS-CoV-2 infection)								49 (8 to 194)	67 (10 to 270)	67 (10 to 270)	

Explanations

a. Substantial heterogeneity ($p < 0.10$)

Figure 17. Summary of evidence table for saliva RT-PCR diagnosis in asymptomatic patients.



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Question: Should saliva RT-PCR be used to diagnose SARS-CoV-2 infection in the hospital setting?

Sensitivity		0.86 (95% CI: 0.81 to 0.90)						<div>Prevalences</div> <div>45.12%0%0%</div>			
Specificity		0.94 (95% CI: 0.88 to 0.97)									
Outcome	No of studies (No of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 45.12%	pre-test probability of 0%	pre-test probability of 0%	
True positives (patients with SARS-CoV-2 infection)	24 studies 1236 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious *	not serious	none	388 (365 to 406)	0 (0 to 0)	0 (0 to 0)	⊕⊕⊕○ MODERATE
False negatives (patients incorrectly classified as not having SARS-CoV-2 infection)								63 (45 to 86)	0 (0 to 0)	0 (0 to 0)	
True negatives (patients without SARS-CoV-2 infection)	24 studies 2337 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious *	not serious	none	516 (483 to 532)	940 (880 to 970)	940 (880 to 970)	⊕⊕⊕○ MODERATE
False positives (patients incorrectly classified as having SARS-CoV-2 infection)								33 (17 to 66)	60 (30 to 120)	60 (30 to 120)	

Explanations

a. Substantial heterogeneity ($p < 0.10$, $I^2 > 75\%$)

Figure 18. Summary of evidence table for saliva RT-PCR diagnosis in the hospital setting.



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Question: Should saliva RT-PCR be used to diagnose SARS-CoV-2 infection in the community/outpatient setting?

Sensitivity	0.78 (95% CI: 0.66 to 0.86)
Specificity	0.98 (95% CI: 0.97 to 0.99)

Prevalences	20.3%	0%	0%
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Outcome	No of studies (No of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 20.3%	pre-test probability of 0%	pre-test probability of 0%	
True positives (patients with SARS-CoV-2 infection)	18 studies 733 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious ^a	not serious	none	158 (134 to 175)	0 (0 to 0)	0 (0 to 0)	⊕⊕⊕○ MODERATE
False negatives (patients incorrectly classified as not having SARS-CoV-2 infection)								45 (28 to 69)	0 (0 to 0)	0 (0 to 0)	
True negatives (patients without SARS-CoV-2 infection)	18 studies 11904 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious ^a	not serious	none	781 (773 to 789)	980 (970 to 990)	980 (970 to 990)	⊕⊕⊕○ MODERATE
False positives (patients incorrectly classified as having SARS-CoV-2 infection)								16 (8 to 24)	20 (10 to 30)	20 (10 to 30)	

Explanations

a. Substantial heterogeneity ($p < 0.10$, $I^2 > 75\%$)

Figure 19. Summary of evidence table for saliva RT-PCR diagnosis in the community/outpatient setting.



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Question: Should saliva drool/spit RT-PCR be used to diagnose SARS-coV-2 infection in the general population?

Sensitivity	0.83 (95% CI: 0.78 to 0.97)	Prevalences 25.7%		
Specificity	0.97 (95% CI: 0.94 to 0.98)			

Outcome	No of studies (No of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 25.7%	
True positives (patients with SARS-coV-2 infection)	44 studies 2286 patients	cohort & case-control type studies	not serious	not serious	serious	not serious	none	213 (200 to 249)	⊕⊕⊕○ MODERATE
False negatives (patients incorrectly classified as not having SARS-coV-2 infection)								44 (8 to 57)	
True negatives (patients without SARS-coV-2 infection)	44 studies 14493 patients	cohort & case-control type studies	not serious	not serious	not serious	not serious	none	721 (698 to 728)	⊕⊕⊕⊕ HIGH
False positives (patients incorrectly classified as having SARS-coV-2 infection)								22 (15 to 45)	

Figure 20. Summary of evidence table for saliva drool/spit RT-PCR.



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Question: Should saliva swab RT-PCR be used to diagnose SARS-coV-2 infection in the general population?

Sensitivity	0.71 (95% CI: 0.46 to 0.87)	<div>Prevalences</div> <div>0%</div> <div></div> <div></div>							
Specificity	0.98 (95% CI: 0.90 to 1.00)								
Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 0%	
True positives (patients with SARS-coV-2 infection)	6 studies 317 patients	cohort & case-control type studies	not serious	not serious	serious	serious	none	0 (0 to 0)	⊕⊕○○ LOW
False negatives (patients incorrectly classified as not having SARS-coV-2 infection)								0 (0 to 0)	
True negatives (patients without SARS-coV-2 infection)	6 studies 3578 patients	cohort & case-control type studies	not serious	not serious	not serious	not serious	none	980 (900 to 1000)	⊕⊕⊕⊕ HIGH
False positives (patients incorrectly classified as having SARS-coV-2 infection)								20 (0 to 100)	

Figure 21. Summary of evidence table for saliva swab RT-PCR.



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Question: Should oral saliva RT-PCR be used to diagnose SARS-coV-2 infection in the general population?

Sensitivity	0.82 (95% CI: 0.77 to 0.86)	Prevalences 0%		
Specificity	0.97 (95% CI: 0.96 to 0.98)			

Outcome	No of studies (No of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 0%	
True positives (patients with SARS-coV-2 infection)	42 studies 2201 patients	cohort & case-control type studies	not serious	not serious	serious	not serious	none	0 (0 to 0)	⊕⊕⊕○ MODERATE
False negatives (patients incorrectly classified as not having SARS-coV-2 infection)								0 (0 to 0)	
True negatives (patients without SARS-coV-2 infection)	42 studies 15108 patients	cohort & case-control type studies	not serious	not serious	not serious	not serious	none	970 (960 to 980)	⊕⊕⊕⊕ HIGH
False positives (patients incorrectly classified as having SARS-coV-2 infection)								30 (20 to 40)	

Figure 22. Summary of evidence table for oral saliva RT-PCR.



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Question: Should posterior oropharyngeal saliva RT-PCR be used to diagnose SARS-coV-2 infection in the general population?

Sensitivity	0.89 (95% CI: 0.83 to 0.93)	Prevalences 44.5%		
Specificity	0.79 (95% CI: 0.53 to 0.93)			

Outcome	No of studies (No of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 44.5%	
True positives (patients with SARS-coV-2 infection)	7 studies patients	cohort & case-control type studies	not serious	not serious	not serious	serious	none	396 (369 to 414)	⊕⊕⊕○ MODERATE
False negatives (patients incorrectly classified as not having SARS-coV-2 infection)								49 (31 to 76)	
True negatives (patients without SARS-coV-2 infection)	7 studies patients	cohort & case-control type studies	not serious	not serious	serious	serious	none	438 (294 to 516)	⊕⊕○○ LOW
False positives (patients incorrectly classified as having SARS-coV-2 infection)								117 (39 to 261)	

Figure 23. Summary of evidence table for posterior oropharyngeal saliva RT-PCR.