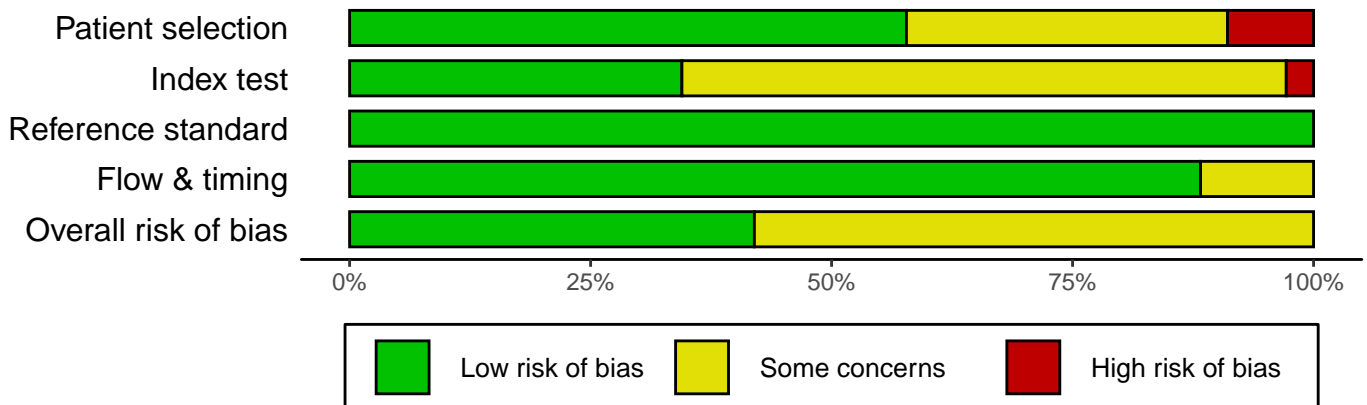


Supplementary Figure 1. Meta-analysis of the sensitivity and negative predictive value using composite reference comparator

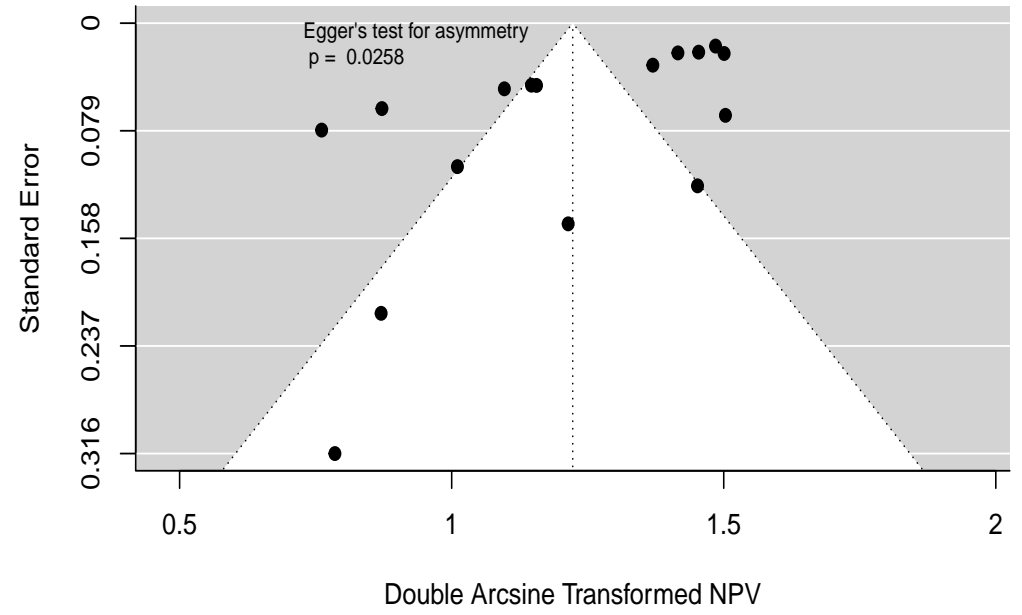
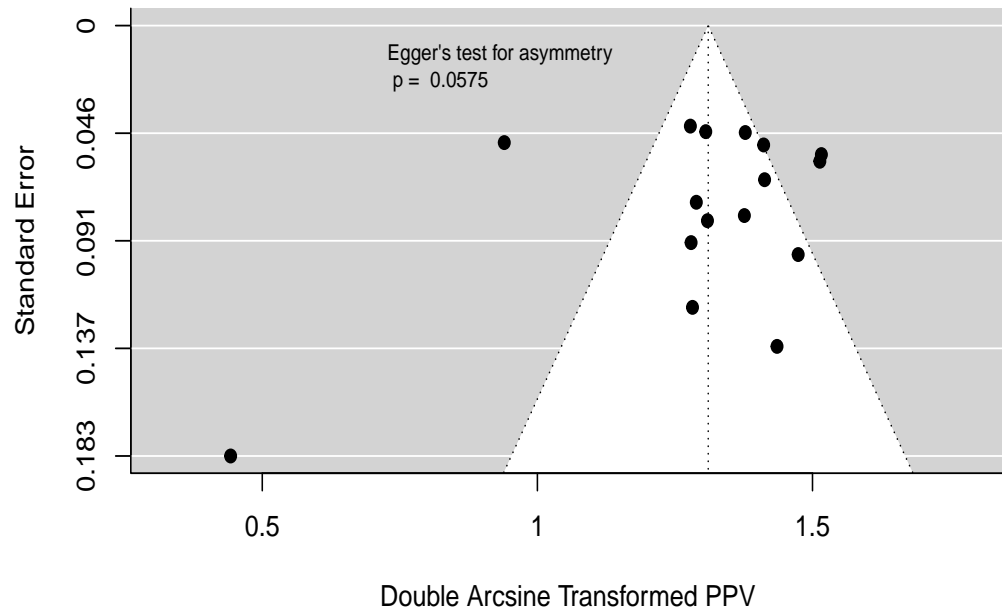
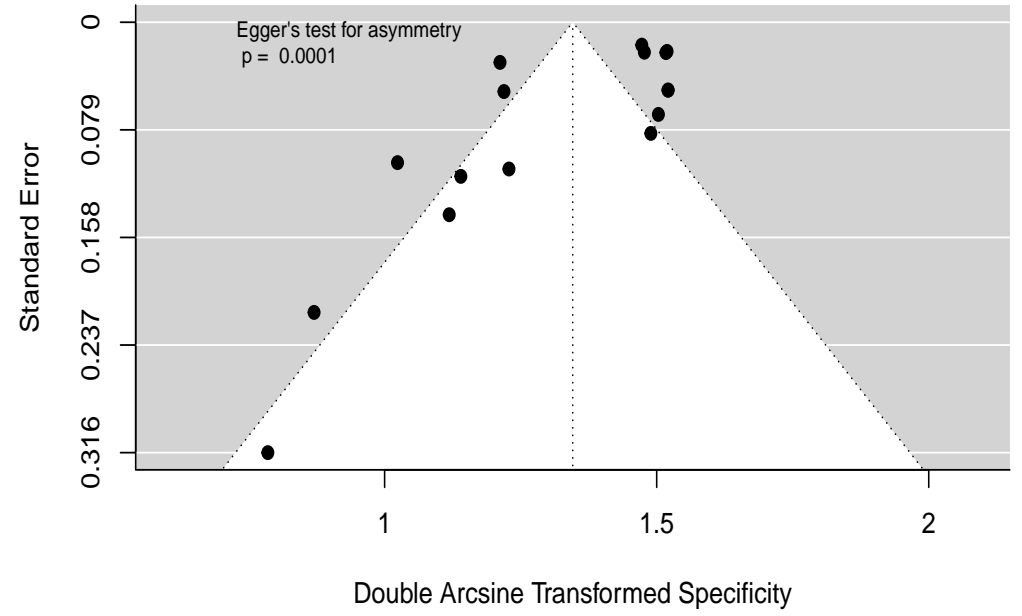
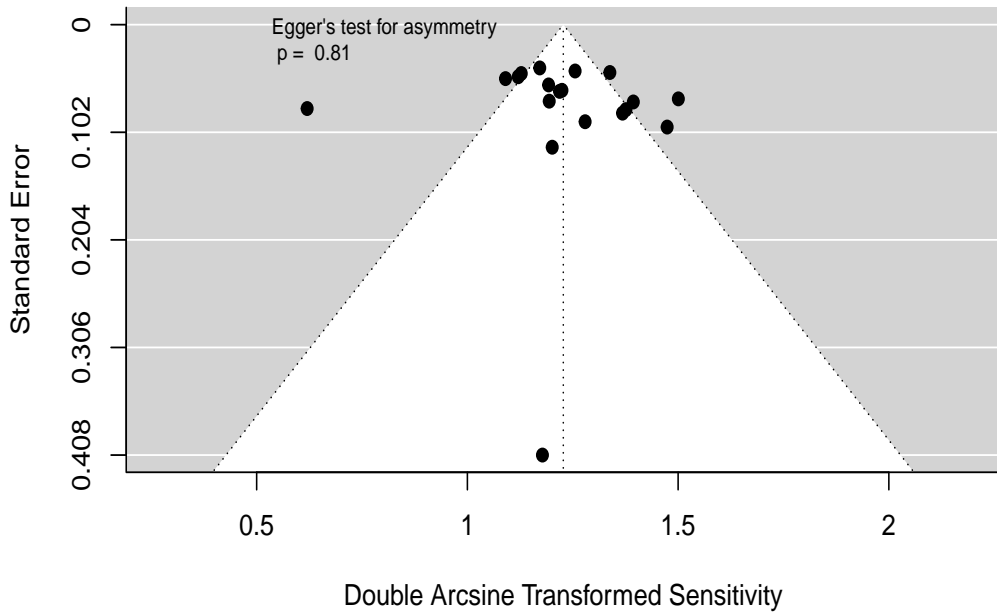
		Risk of bias domains				
		D1	D2	D3	D4	Overall
Study	Kandel et al. (2021)	+	-	+	+	-
	Dumaresq et al. (2021)	+	+	+	+	+
	Mittal et al. (2020)	-	-	+	+	-
	Guo et al. (2020)	-	X	+	+	-
	Goldfarb et al. (2021)	-	-	+	+	-
	Poukka et al. (2021)	-	X	+	+	-
	Michel et al. (2021)	-	-	+	+	-
	Gertler et al. (2021)	-	X	+	+	-
	Olearo et al. (2021)	-	-	+	-	-
	Zander et al. (2021)	-	+	+	+	+
	Kocagoz et al. (2021)	-	-	+	+	-
	Utama et al. (2021)	+	+	+	+	-
	Kwon et al. (2021)	X	-	+	+	-
	Hitzenbichler et al. (2021)	-	-	+	+	-
	Kinshella et al. (2021)	-	-	+	+	-
	Biber et al. (2021)	-	+	+	+	+
	Casati et al. (2021)	X	-	+	+	-
	Benoit et al. (2021)	+	-	+	+	+

Domains:
D1: Patient selection.
D2: Index test.
D3: Reference standard.
D4: Flow & timing.

Judgement
X High
- Some concerns
+ Low



Supplementary Figure 2. Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) Study Quality Summary



Supplementary Figure 3. Funnel plots

Supplementary Table 1. Patients characteristics of included studies

Author (year)	Setting	Positivity rate of (O)NPS (95% CI), %	Patient characteristics	Symptomology of patients or criteria for suspected infection	Criteria for SARS-CoV-2 infection	Age	Include children
Kandel et al. (2021)	3 outpatient COVID-19 assessment centers	10.53%	Suspected, symptomatic and asymptomatic outpatients	Individual symptoms not reported	NA	Median: 33 IQR: 24-51	Yes
Dumaresq et al. (2021)	Drive-through test center	12.04%	Suspected, symptomatic and asymptomatic individuals	Had symptoms suggestive of COVID-19 or an asymptomatic close contact considered by public health services	NA	Median: 40 Range: 6-91	Yes
Oleairo et al. (2021)	University hospital	3.45%	Asymptomatic HCW	NA	NA	NA	No
Zander et al. (2021)	Doctors' offices	32.50%	Suspected mostly symptomatic outpatients	Cough, coryza, other respiratory symptoms, elevated temperature, loss of smell/taste	NA	Range: 13-89	Yes
Kocagoz et al. (2021)	Hospital	20.94%	Suspected symptomatic inpatients	Symptoms of respiratory infection	NA	Range: ≥18	No
Benoit et al. (2021)	Two COVID-19 screening clinics	20.03%	Suspected, symptomatic outpatients or asymptomatic close contact	Had symptoms of COVID-19 or had contact with a positive case	NA	NA	NA
Utama et al. (2022)	Hospital	60.66%	Suspected symptomatic and asymptomatic outpatients; confirmed symptomatic and asymptomatic COVID-19 inpatients and SARS-CoV-2 negative inpatients	Individual symptoms not reported	Previously diagnosed COVID-19 positive and admitted to hospitals ¹	Mean: 34.3±12.5 (outpatient); 45.4±16.5 (inpatients)	Yes
Goldfarb et al. (2021)	COVID-19 collection center and residence	74.47%	Confirmed and suspected, symptomatic and asymptomatic COVID-19 outpatients	Fever or cough or other symptoms not reported	Had SARS-CoV-2 detected in any clinical sample within a median of 3 days from infection confirmation ¹	Range: 4-71	Yes
Michel et al. (2021)	Refugee facility	51.32%	Confirmed and suspected, asymptomatic individuals	Quarantined close contacts of confirmed cases	Had a previous positive PCR-test for SARS-CoV-2 at a median time of 14 days prior ¹	Mean: 29 Range: 7-59	Yes
Guo et al. (2020)	Hospital	4.17%	Confirmed COVID-19 hospitalised and discharged patients	NA	Laboratory-confirmed COVID-19, met the diagnosis criterial of COVID-19 as per national guideline, within 48-57 days of symptom onset	Range: 26-83	No
Poukka et al. (2021)	Acute COVID-19 outpatients	95%	Confirmed symptomatic and asymptomatic COVID-19 outpatients	Fever, fatigue, headache, cough, anosmia, sore throat, or other symptoms	Had been diagnosed with SARS-CoV-2 infection by RT-PCR on NPS within 1-2 days of diagnosis	Mean: 38.7±12.6 Range: ≥3	-
Gertler et al. (2021)	University hospital and residence	100%	Confirmed symptomatic COVID-19 outpatients	Symptoms compatible with COVID-19, e.g. shortness of breath, fever, chills, fatigue, cough, rhinorrhea, diarrhea, sore throat headache, body aches, or impaired smell and taste	Initial laboratory RT-PCR confirmation of SARS-CoV-2 by professional-collected, combined oronasopharyngeal swab in a testing center, enrolled within 2-15 days from symptom onset	Median: 31.5 Range: 17-66	Yes
Mittal et al. (2020)	Tertiary care hospital	100%	Confirmed symptomatic and asymptomatic COVID-19 inpatients	Fever, sore throat, cough, shortness of breath, or myalgia	RT-PCR confirmed patients with SARS-CoV-2 infection within 72h of diagnosis by a trained HCW, as per the national and hospital policies	Mean: 45.08 ±12.78	No
Kwon et al. (2022)	Medical centers and Hospital	50.50%	Confirmed symptomatic and asymptomatic COVID-19 inpatients and healthy individuals	Cough, sore throat, fever, headache, myalgia, chest pain, chills, fatigue, diarrhea and nausea, dry mouth, and loss of taste or smell	Previously confirmed COVID-19 patients hospitalized in medical centers and hospital ¹	Mean: 43.7, Range: 18-83	No
Hitzenbichler et al. (2021)	Medical Center	85.29%	Confirmed symptomatic and asymptomatic COVID-19 inpatients	Individual symptoms consistent with COVID-19 not reported	Patients with COVID-19 admitted to non-intensive care medical ward, with laboratory-confirmed SARS-CoV-2 infection (defined by a positive RT-qPCR result before inclusion)	Mean: 57.5±14.9, Range: 22-83	No

Kinshella et al. (2021)	Hospital COVID-19 collection centre	100%	Confirmed symptomatic COVID-19 outpatients	NA	Patients with positive RT-PCR result of nasopharyngeal swab	Median: 29.5 IQR: 14-41	Yes
Biber et al. (2021)	Non-hospital facilities dedicated for COVID-19 patients in isolation	84.67%	Confirmed symptomatic and asymptomatic COVID-19 outpatients in isolation	Mild symptoms of fever, headache, malaise, cough, myalgia, and other symptoms	COVID-19 outpatients previously RT-PCR-confirmed by combined oro-nasopharyngeal swab	Range: 18-73	No
Casati et al. (2021)	Medical University	48.72%	Confirmed symptomatic COVID-19 ambulatory patients and negative close contacts	Minimal or mild symptoms or contacts of SARS-CoV-2 infected individuals	Previously tested positive for SARS-CoV-2 via Rt-PCR on nasopharyngeal swab [†]	NA	NA

HCW: Healthcare worker

NA: Not available

[†]For confirmed cases only

Supplementary Table 2. Stratified pooled estimates on diagnostic indicators for SARS-CoV-2 using gargle as an alternative sampling approaches among population with suspected infection by study characteristics

Study Characteristic	Studies, n	Sensitivity Est (95% CI)	I² (95% CI), %	Specificity Est (95% CI)	I² (95% CI), %	PPV Est (95% CI)	I² (95% CI), %	NPV Est (95% CI)	I² (95% CI), %
Suspected population only	7	91 (87-95)	56 (33-71)	98 (94-100)	96 (95-97)	93 (85-99)	90 (86-92)	98 (93-100)	96 (95-97)
Reference standard									
Nasopharyngeal swab	4	92 (84-98)	58 (26-76)	98 (92-100)	97 (95-97)	92 (74-100)	91 (87-94)	99 (97-100)	78 (62-87)
Oropharyngeal-nasopharyngeal swab	3	91 (84-95)	73 (50-85)	97 (89-100)	97 (95-98)	94 (91-97)	26 (0-55)	95 (80-100)	99 (98-99)
Gargle medium*									
Saline	2	96 (80-100)	-	100 (100-100)	-	99 (95-100)	-	99 (98-100)	-
Water	4	92 (87-95)	39 (0-64)	98 (92-100)	97 (97-98)	89 (73-99)	93 (89-95)	99 (97-100)	86 (77-91)
Sterility of gargle									
<u>Saline gargle (n=2)</u>									
Sterile	0	-	-	-	-	-	-	-	-
Non-sterile / not mentioned	2	96 (80-100)	-	100 (100-100)	-	99 (95-100)	-	99 (98-100)	-
<u>Water gargle (n=4)</u>									
Sterile	0	-	-	-	-	-	-	-	-
Non-sterile / not mentioned	4	92 (87-95)	39 (0-64)	98 (92-100)	97 (97-98)	89 (73-99)	93 (89-95)	99 (97-100)	86 (77-91)
Volume of gargle Δ									
≤5mL	6	92 (87-96)	61 (39-75)	99 (96-100)	94 (91-96)	96 (93-98)	27 (0-53)	98 (93-100)	97 (96-98)
>5mL	0	-	-	-	-	-	-	-	-
Duration of gargling#									
≤10 seconds	1	87 (78-94)	-	88 (84-91)	-	65 (56-74)	-	96 (93-98)	-
>10 seconds	4	95 (90-98)	42 (0-67)	100 (99-100)	15 (0-55)	96 (93-99)	10 (0-32)	99 (98-100)	69 (46-82)

Positivity rate of (O)NPS

<20%	3	93 (87-97)	36 (0-63)	100 (99-100)	50 (5-73)	96 (92-99)	17 (12-21)	99 (99-100)	9 (0-40)
≥20%	4	91 (84-96)	73 (54-85)	96 (87-100)	95 (93-96)	91 (74-100)	95 (92-96)	95 (86-100)	95 (93-97)

Region

European countries	3	93 (81-100)	69 (42-83)	98 (88-100)	96 (95-97)	90 (62-100)	91 (85-94)	99 (96-100)	81 (67-89)
North America	3	92 (88-95)	28 (0-57)	99 (99-100)	36 (0-64)	96 (93-98)	12 (0-34)	99 (98-99)	68 (40-83)
Asia	1	85 (79-90)	-	89 (81-94)	-	92 (87-96)	-	79 (71-87)	-
Middle East	0								

Symptomology

Symptomatic	1	87 (78-94)	-	88 (84-91)	-	65 (56-74)	-	96 (93-98)	-
Symptomatic and asymptomatic	5	92 (87-96)	70 (51-81)	99 (95-100)	95 (92-96)	96 (93-98)	37 (0-62)	97 (90-100)	97 (96-98)
Asymptomatic	1	89 (69-100)	-	100 (99-100)	-	94 (76-100)	-	100 (99-100)	-

Include children†

Yes	4	93 (85-98)	78 (63-87)	98 (93-100)	95 (93-97)	96 (92-98)	46 (5-69)	97 (87-100)	98 (97-98)
No	2	88 (80-94)	-	96 (77-100)	-	80 (47-99)	-	98 (93-100)	-

Peer-review

Yes	7	91 (87-95)	56 (33-71)	98 (94-100)	96 (95-97)	93 (85-99)	90 (86-92)	98 (93-100)	96 (95-97)
No	0	-	-	-	-	-	-	-	-

Target gene

1 gene	2	95 (76-100)	84 (67-92)	96 (77-100)	94 (88-96)	88 (39-100)	96 (93-98)	98 (93-100)	69 (33-85)
≥2 genes	5	90 (86-94)	50 (17-70)	99 (95-100)	96 (94-97)	95 (92-97)	22 (0-46)	97 (90-100)	98 (97-99)

n, number of studies; Est, estimate; PPV, positive predictive value; NPV, negative predictive value; US, United States; HCW, healthcare worker; (O)NPS, oropharyngeal-nasopharyngeal swab.

Others in region included European countries, Mediterranean countries and Asian countries.

Target gene referred to number of gene regions tested by the RT-PCR assays, i.e. assays detecting both N1 and N2 were counted as dual targets.

*One study did not specify the gargling medium (water or saline).

ΔOne study did not specify the volume of gargling solution.

#Three studies did not report the duration of gargling.

†One study did not specify the inclusion of children population.

Supplementary Table 3. Stratified pooled estimates on diagnostic indicators for SARS-CoV-2 using gargle as an alternative sampling approaches among population with confirmed infection by study characteristics

Study Characteristic	Studies, n	Sensitivity Est (95% CI)	I² (95% CI), %	Studies, n	Specificity Est (95% CI)	I² (95% CI), %	PPV Est (95% CI)	I² (95% CI), %	NPV Est (95% CI)	I² (95% CI), %
Confirmed and suspected population	12	91 (80-98)	91 (89-93)	9	94 (81-100)	86 (81-90)	95 (84-100)	91 (88-94)	78 (63-90)	86 (80-89)
Reference standard										
Nasopharyngeal swab	8	97 (90-100)	79 (71-85)	6	92 (68-100)	91 (87-94)	93 (70-100)	95 (93-97)	89 (84-93)	0 (0-38)
Oropharyngeal-nasopharyngeal swab	4	75 (49-94)	95 (92-96)	3	94 (79-100)	72 (48-85)	98 (93-100)	17 (13-20)	58 (46-70)	43 (0-69)
Gargle medium†										
Saline	6	98 (87-100)	85 (79-90)	4	91 (73-100)	84 (75-90)	88 (45-100)	97 (96-98)	83 (57-99)	91 (86-94)
Water	3	78 (34-100)	97 (95-98)	2	95 (20-100)	78 (54-90)	99 (92-100)	0 (0-98)	60 (45-74)	0 (0-99)
Sterility of gargle										
<u>Saline gargle (n=6)</u>										
Sterile	5	100 (90-100)	81 (72-88)	3	91 (64-100)	89 (82-93)	82 (20-100)	97 (96-98)	92 (78-100)	64 (31-81)
Non-sterile / not mentioned	1	82 (74-88)	-	1	90 (73-100)	-	98 (94-100)	-	47 (32-63)	-
<u>Water gargle (n=3)</u>										
Sterile	1	33 (19-49)	-	1	100 (95-100)	-	100 (87-100)	-	59 (46-71)	-
Non-sterile / not mentioned	2	93 (83-99)	58 (12-80)	1	50 (0-100)	-	97 (89-100)	-	50 (0-100)	-
Volume of gargle Δ										
≤5mL	4	91 (82-98)	75 (58-85)	3	94 (73-100)	83 (71-90)	97 (90-100)	72 (49-85)	84 (77-90)	0 (0-26)
>5mL	7	87 (66-100)	94 (92-95)	5	93 (75-100)	88 (82-92)	91 (60-100)	96 (94-97)	74 (49-93)	92 (88-94)

Duration of gargling#										
≤10 seconds	5	86 (53-100)	93 (90-95)	5	88 (63-100)	78 (65-86)	90 (60-100)	94 (91-96)	70 (39-95)	86 (79-91)
>10 seconds	4	96 (86-100)	84 (75-90)	2	97 (67-100)	86 (72-93)	99 (89-100)	77 (51-89)	86 (79-92)	0 (0-98)
Positivity rate of (O)NPS										
<20%	1	100 (0-100)	-	1	74 (54-90)	-	14 (0-52)	-	100 (90-100)	-
≥20%	11	88 (78-96)	92 (90-94)	8	96 (84-100)	85 (79-90)	98 (96-100)	50 (24-67)	73 (60-85)	79 (71-85)
Region										
European countries	5	81 (58-97)	94 (92-96)	4	95 (61-100)	91 (85-94)	99 (94-100)	45 (4-68)	72 (49-90)	74 (57-84)
North America	2	98 (92-100)	0 (0-99)	1	83 (56-100)	-	94 (84-100)	-	91 (65-100)	-
Asia	4	98 (81-100)	84 (75-90)	3	91 (65-100)	90 (83-94)	81 (20-100)	98 (96-98)	88 (68-99)	81 (66-90)
Middle East	1	82 (74-88)	-	1	90 (73-100)	-	98 (94-100)	-	47 (32-63)	-
Symptomology†										
Symptomatic	2	94 (82-100)	69 (34-86)	0	-	-	-	-	-	-
Symptomatic and asymptomatic	8	91 (83-96)	82 (75-87)	7	94 (78-100)	86 (80-90)	98 (95-100)	56 (32-71)	76 (61-89)	78 (68-85)
Asymptomatic	1	33 (19-49)	-	1	100 (95-100)	-	100 (87-100)	-	59 (46-71)	-
Include children‡										
Yes	5	85 (60-99)	94 (92-96)	3	93 (74-100)	75 (54-86)	95 (90-99)	0 (0-87)	72 (53-87)	61 (26-79)
No	5	96 (83-100)	85 (77-90)	4	89 (64-100)	87 (80-92)	88 (45-100)	97 (96-98)	79 (47-99)	91 (87-94)
Peer-review										
Yes	11	92 (80-99)	91 (89-93)	8	91 (76-100)	81 (74-86)	94 (80-100)	91 (88-94)	76 (58-91)	84 (78-88)
No	1	79 (70-87)	-	1	100 (98-100)	-	100 (98-100)	-	83 (76-90)	-
Target gene										
1 gene	3	90 (77-99)	77 (59-87)	3	87 (31-100)	82 (69-90)	98 (92-100)	61 (26-79)	80 (53-98)	37 (0-63)
≥2 genes	9	90 (75-100)	93 (91-95)	6	93 (80-100)	82 (74-88)	92 (70-100)	95 (93-96)	78 (59-92)	89 (85-92)

n, number of studies; Est, estimate; PPV, positive predictive value; NPV, negative predictive value; US, United States; HCW, healthcare worker; (O)NPS, oropharyngeal-nasopharyngeal swab.

Others in region included European countries, Mediterranean countries and Asian countries.

Target gene referred to number of gene regions tested by the RT-PCR assays, i.e. assays detecting both N1 and N2 were counted as dual targets.

†Two studies did not specify the gargling medium (water or saline), and one study used bean extract gargle. One study used sterile gargle, without specifying water or saline gargle.

ΔOne study did not specify the volume of gargling solution.

#Three studies did not report the duration of gargling.

‡One study did not report the symptomatic status of the population.

§Two studies did not specify the inclusion of children population.

Supplementary Table 4. Sensitivity and NPV of gargling using (oropharyngeal-)nasopharyngeal swab as the reference comparator or a composite reference comparator

	(O)NPS as reference comparator				Any positive specimen as composite reference comparator			
	Sensitivity Est (95% CI)	I² (95% CI), %	NPV Est (95% CI)	I² (95% CI), %	Sensitivity Est (95% CI)	I² (95% CI), %	NPV Est (95% CI)	I² (95% CI), %
Gargle	91 (85-96)	88 (86-91)	91 (81-98)	98 (97-98)	90 (85-95)	89 (87-91)	91 (81-98)	98 (97-98)
(O)NPS	100 (ref)	-	100 (ref)	-	97 (92-99)	89 (87-91)	97 (92-100)	96 (95-96)

Est, estimate; (O)NPS, oropharyngeal-nasopharyngeal swab