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Respiratory Medicine

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Tan SH, Allicock O, Armstrong-Hough M, et al. Saliva as a gold-standard sample for SARS-CoV-2 detection . *Lancet Respir Med* 2021; published online April 19. http://dx.doi.org/10.1016/S2213-2600(21)00178-8.

Table 1. Studies describing salivary diagnosis of SARS-CoV-2 have greatly varying methods with large discrepancies between results. Sample populations also vary in proportion of symptomatic and asymptomatic cases, which can influence reported sensitivities. To encourage standardization in COVID-19 saliva testing, researchers should replicate a method that is high in sensitivity and suited to their available resources. From top to bottom are the newest to oldest papers of 2020 (from 12th Feb - 1st Nov). Across the studies (n=58), saliva sensitivity ranged from 22.4-100% but had a high specificity (negative result agreement), ranging from 95.7-100%, while NPS sensitivity ranged from 52.5-100%. The sensitivities were measured based on the assumption that all positive results were true positives, unless studies indicated the proportion of false positive results. Studies showing greater or similar saliva sensitivities to reference tests are highlighted green (n=40), lower saliva sensitivities are highlighted red (n=14), and mixed-finding studies are highlighted yellow (n=4). These studies (n=44) indicated that a notable proportion of COVID-19 cases (up to 47.5%, median = 10%) were undetected by swabs but detected by saliva alone, indicating that nasopharyngeal swab testing alone may not be a reliable reference standard.
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Date (2020)	Journal / Preprint Server	Title	Authors	Study Type	Cohort	Country	Population		Diagnostic Test Method	Saliva Collection Method	RNA Extraction Method	PCR kit	Vol. Saliva Eluted	Reference Standard Test	No. Positive Cases Based on Reference (% study participants)	No. Matched Sample Pairs	Diagnostic Efficiency	Cases Detected by Saliva Alone (%)
							No. (males / females)	Median Age (Range)										
11/1	MedRxiv	Saliva as a testing specimen with or without pooling for SARS-CoV-2 detection by multiplex RT-PCR test	Sun et al.	Clinical evaluation	Asymptomatic individuals and known positive clinical samples	USA	20	NI	RT-PCR	HCW supervised self-collection of saliva (2 mL) into tube with (2 mL) viral transport media (VTM)	PureLink™ Viral RNA/DNA Mini Kit (Invitrogen, Carlsbad, CA, USA) on the MGISP-960 High-throughput Automated Sample Preparation System	QuantiVirusTM SARS-CoV-2 Multiplex Test kit	Extracted RNA from 200 µL, 5.5 µL used for PCR per test	NPS	17 (85%)	20	Sensitivity: Saliva = 95%, NPS = 85%. Agreement = 80%.	15
10/27	MedRxiv	Performance of At-Home Self-Collected Saliva and Nasal-Oropharyngeal Swabs in the Surveillance of COVID-19	Braz-Silva et al.	Consecutive case series	Suspected positive individuals	Brazil	201 (74m / 126f / 1 NI)	NI	RT-PCR	Home self-collection using cotton pad device (place pad/swab in mouth, chew 1 min to stimulate salivation, place swab in tube)	NucliSENS EasyMag (BioMérieux, Durham, North Carolina, USA) automated DNA/RNA extraction platform	Altona RealStar® SARS-CoV-2 RT-PCR Kit 1.0	Extracted RNA from 200 µL	Combined NPS + OPS	52 (26%) by reference, 70 (35%) by both samples	201	Sensitivity: Saliva = 78.6%, NPS + OPS = 74.2%. Agreement = 83.6%	26
10/27	MedRxiv	Saliva is a promising alternative specimen for the detection of SARS-CoV-2 in children and adults	Yee et al.	Prospective	Suspected positive individuals and family members	USA	300	NI	RT-qPCR	HCW supervised self-collection by spitting (3 mL) in container	MagMAX Viral/Pathogen Nucleic Acid Isolation Kit on the Thermo Fisher KingFisher Flex platform (Thermo Fisher, Waltham, MA, USA)	TaqPath COVID-19 Combo Kit	Extracted RNA from 250 µL, eluted in 50 µL	NPS	87 (29%)	300	Sensitivity (overall): Saliva = 81.4%, NPS = 89.7%. Sensitivity of... Asymptomatic children: both Saliva and NPS = 78.6%; Adults: Saliva = 83.3%, NPS = 90.7%; Symptomatic adults: both Saliva and NPS = 93.8%	10
10/27	MedRxiv	A scalable saliva-based, extraction-free rt-lamp protocol for sars-cov-2 diagnosis	Asprino et al.	Prospective validation	COVID-19 patients	Brazil	244	NI	RT-LAMP	Self-collected by spitting (~1 mL) in container	N/A	N/A	N/A	NPS with RT-PCR	65 (27%)	244	Sensitivity: Saliva = 78.9%, NPS with RT-PCR = 85.5%. Specificity = 100%	14
10/21	Journal of Clinical Microbiology	Self-Collected Anterior Nasal and Saliva Specimens versus Healthcare Worker-Collected Nasopharyngeal Swabs for the Molecular Detection of SARS-CoV-2	Hanson et al.	Prospective	Suspected positive individuals	USA	354 (~ 188m / 166f)	35 mean (18-75)	RT-PCR	HCW supervised self-collection by pooling saliva in mouth (w/o coughing) then repeatedly spitting (min. 1 mL) in tube	Diluted saliva 1:1 in ARUP Laboratories transport medium (ATM) then homogenation using Hologic Aptima lysis tube	Hologic Aptima SARS-CoV-2 transcription-mediated amplification (TMA) assay	NI	NPS	80 (22.5%)	354	Sensitivity: Saliva = 94%. NPS = 93%. Agreement: Positive = 93.8%, Negative = 97.8%	7
10/21	MedRxiv	Saliva as testing sample for SARS-CoV-2 detection by RT-PCR in low prevalence community setting	Gavars et al.	Prospective	General population	Latvia	NI	NI	RT-qPCR	Self-collected by spitting in container	NI	NI	NI	NPS or OPS	68 (65%)	104	Sensitivity (samples taken 0 - 70 days after symptom onset + asymptomatic samples): Saliva = 76%, NPS = 92%. Sensitivity (samples taken 0 - 14 days of symptom onset): Saliva = 90%, Specificity = 100%	6
10/13	MedRxiv	Evaluation of saliva sampling procedures for SARS-CoV-2 diagnostics reveals differential sensitivity and association with viral load	Mestdagh et al.	Prospective	Suspected positive individuals	Belgium	2884	NI, most (59%) participants 31-60 y	RT-qPCR	1. Self-collected by saliva spitting in tube with preservatives (Norgen Biotek's Dx 3800). **or** 2. Self-collected by oral swabbing device (ORE-100).	Total RNA Purification Kit (Norgen Biotek, ON, Canada)	TaqPath COVID-19 Combo Kit	Extracted RNA from 200 µL, eluted in 50 µL	NPS	117 (4.0%)	2884	Sensitivity: spitting = 30.8%, saliva swabbing = 22.4%. Sensitivity of individuals with medium - high viral load: spitting (symptomatic + asymptomatic cases) = 100%, swabbing (symptomatic) = 77.8%, swabbing (asymptomatic) = 100%.	NI
10/5	MedRxiv	Validation of self-collected buccal swab and saliva as a diagnostic tool for COVID-19	Ku et al.	Cross-sectional	Positive health care workers	Singapore	42 (40m, 2f)	45 mean	RT-PCR	Cough deeply x 5, pool saliva in mouth (1-2 mins), then gently spit (1-2 mL) into container	1ml of Cobas Omni Lysis Reagent	Superscript III one step RT-PCR system	NI	NPS	30 (71%)	42	Sensitivity: Saliva = 70%, NPS = 97%. Agreement: Positive = 63.3%, Negative = 91.7%	3.2
10/01	Clinical Virology	Saliva specimens for detection of severe acute respiratory syndrome coronavirus 2 in Kuwait: A cross-sectional study	Altawalah et al.	Prospective, Cross-sectional	Suspected positive individuals	Kuwait	891	NI	RT-PCR	Self-collected by expelling whole saliva (~1.5 mL) after deep cough into container with 300 uL VTM.	MagMax Viral/Pathogen Nucleic Acid Isolation Kit (Thermo Fisher Scientific, Waltham, MA, USA) on KingFisher (Thermo Fisher Scientific, Waltham, MA, USA)	TaqPath™ COVID-19 multiplex RT-PCR	Extracted RNA from 200 µL	NPS	344 (38.6%)	891	Detection rate (based on population) = 89%. Sensitivity (based on positive NPS) = 83.43%. Specificity = 96.71%	NI

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10/01	Infection and Drug Resistance	Saliva as an Alternative Specimen for Molecular COVID-19 Testing in Community Settings and Population-Based Screening	Senok et al.	Prospective	Suspected positive individuals and family members	United Arab Emirates	401 (329m / 72f)	35.5 mean (± SD 9.5)	RT-PCR	Self-collected by pooling in mouth (1-2 mins) then gently spit (2-4 mL) in container	Chemagic viral RNA extraction kit on the automated Chemagic™ 360 Nucleic Acid Extractor (PerkinElmer, Baesweiler, Germany)	NeoPlex COVID-19 kit	Extracted RNA from 300 µL then 5 µL sample added to total vol. 20 µL in PCR tube	NPS	26 (6.5%)	401	Sensitivity: Saliva = 73.1%, NPS = 67.9%. Specificity = 97.6%	26
09/28	Med	SalivaDirect: A simplified and flexible platform to enhance SARS-CoV-2 testing capacity	Vogels et al.	Prospective	COVID-19 patients and healthcare workers	USA	3779	NI	RT-qPCR	Self-collected by pooling in mouth (at least 500 µL) then spit in container	N/A	ThermoFisher Scientific TaqPath COVID-19 combo kit	Extracted RNA from 200 µL, eluted in 50 µL	Anterior nares/OPS	19 (0.5%)	3779	Sensitivity: Saliva = 89.5%, AN/OPS = 89.5%. Agreement: Positive = 89.5%, Negative = >99.9%, Overall = 99.9%	10
09/24	MedRxiv	Prospective comparison of saliva and nasopharyngeal swab sampling for mass screening for COVID-19	Nacher et al.	Prospective, Consecutive Cases	Suspected positive individuals and high-risk asymptomatic individuals	French Guiana	776 (478m / 298f)	40 mean (± SD 16.8)	RT-PCR	HCW collected salivary sputum sample in container. Samples taken after eating breakfast and teeth brushing (potential interference)	QIAamp DSP viral kit on the QIAsymphony 96 RGQ (Qiagen GmbH, Germany)	GeneFinderTM COVID-19 kit	Eluates obtained from 200 µL saliva	NPS	152 (20%)	776	Sensitivity: Saliva = 53%, NPS = 94%	6.2
09/25	Clinical infectious Diseases	Mass screening of asymptomatic persons for SARS-CoV-2 using saliva	Yokota et al.	Prospective	Asymptomatic high-risk individuals	Japan	1924 (971 m / 858 f / 95 unknown)	*Contact-tracing (CT) cohort:* 44.9 (IQR 29.8-66.4). *Quarantine Airport (QA) cohort:* 33.5 (IQR 22.6-47.4)	RT-qPCR and RT-LAMP	Self-collected in sputum tube	Saliva was diluted 4-fold with phosphate buffered saline, then was extracted using QIAsymphony DSP Virus/Pathogen kit and QIAamp Viral RNA Mini Kit (QIAGEN, Hilden, Germany)	qRT-PCR: THUNDERBIRD® Probe One-step Kit and 7500 Real-time PCR Systems. RT-LAMP: Loopamp® 2019-SARS-CoV-2 Detection Reagent Kit	Extracted RNA from 200 µL: PCR - 5µL used as a template, RT-LAMP - 10 µL used in reaction tube	NPS	46 (2.4%)	1924	Sensitivity: Saliva = 92%, NPS = 86%. Specificity = >99.9%	16
09/18	MedRxiv	The Accuracy of Healthcare Worker versus Self Collected (2-in-1) Oropharyngeal and Bilateral Mid-Turbinate (OPMT) Swabs and Saliva Samples for SARS-CoV-2	Tan et al.	Prospective	COVID-19 patients and healthy volunteers	Singapore	501 (+ve: n=401, all males. -ve: n=100)	NI	RT-PCR	Self-collected by spitting oropharyngeal sputum into VTM tube	PerkinElmer Nucleic Acid Extraction Kits on the Pre-Nat II Automated Workstation (PerkinElmer®, United States)	PerkinElmer® SARS-CoV-2 Real-time RT-PCR Assay	NI; Extraction involved saliva viscosity-reducing process	Combined OPS + mid-turbinate (OPMT) swab	336 (83.8%)	501	Sensitivity: Saliva = 83.6%, Combined OPMT self-swab + Saliva = 92.3%, Specificity: both OPMT self-swab and Saliva = 100%.	NI
09/16	Clinical Chemistry and Diagnostic Laboratory Medicine	SARS-CoV-2 identification and IgA antibodies in saliva: One sample two tests approach for diagnosis	Aita et al.	Prospective	COVID-19 patients	Italy	369 (+ve: n=43. -ve: n=326)	Pts. +ve: (25 - 94)	RT-PCR	Collected for 1 min using a cotton swab	NI	One-Step RT-ddPCR Advanced Kit for Probes (Bio-Rad)	NI	NPS	9 (2%)	369	Sensitivity: Saliva = 100%, NPS = 87.5%. Specificity = 100%	13
09/14	Clinical infectious Diseases	Saliva is not a useful diagnostic specimen in children with Coronavirus Disease 2019	Chong et al.	Prospective	COVID-19 patients	Singapore	18 (10m / 8f)	6.6 mean (IQR 1.8-11.1)	RT-PCR	Self-collected by spitting into container (min. 0.5 mL) or HCW syringing saliva from mouth for children unable to spit	NI	Superscript III one step RT-PCR system or QIAGEN One-Step RT-PCR Kit	NI	NPS	18 (100%)	53	Sensitivity: Saliva Day 1-3 = 46.7%, Day 4-7 = 52.9%, Day 8-10 = 25%, Day 11-15 = 33.3%. NPS: NI	NI
09/11	MedRxiv	Saliva as a potential clinical specimen for diagnosis of SARS-CoV-2	Bhattacharya et al.	Prospective	Suspected positive individuals	India	74	NI	RT-qPCR	Self-collected by spitting in container	QIAamp Viral RNA Mini Kit (Qiagen)	Assay unknown, used Cobas 6800 instrument (Roche)	NI	NPS	58 (78%)	74	Sensitivity: Saliva = 91.37%. Specificity = 100%	0
09/09	Boletín Médico del Hospital Infantil de México	Saliva as a promising biofluid for SARS-CoV-2 detection during the early stages of infection	López-Martínez et al.	Prospective	COVID-19 patients	Mexico	5 (4m / 1f)	15 (4-56)	RT-PCR	Self-collected by gently spitting (~2 mL) in tube	NI	GeneFinder COVID-19 PLUS RealAmp Kit	NI	NPS	5 (100%)	5 (for just the 1st samples of each Pt.)	Sensitivity = 100%	N/A

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09/03	MedRxiv	Equivalent SARS-CoV-2 viral loads between nasopharyngeal swab and saliva in symptomatic patients	Yokota et al.	Prospective	COVID-19 patients	Japan	42 (25m / 17f)	73 (27-93)	RT-qPCR	Self-collected by spitting in container	Saliva was diluted 4-fold with phosphate buffered saline (PBS) QIAsymphony DSP Virus/Pathogen kit and QIAamp Viral RNA Mini Kit (QIAGEN, Hilden, Germany)	THUNDERBIRD® 79 Probe One-step qRT-PCR Kit	Extracted RNA from 200 µL, 5 µL used for one step PCR	NPS	34 (81%)	42	Sensitivity = 90%	11
09/01	European Journal of Clinical Microbiology & Infectious Diseases	Practical challenges to the clinical implementation of saliva for SARS-CoV-2 detection	Matic et al.	Prospective	COVID-19 patients and healthcare workers	Canada	NI	NI	RT-PCR	Self-collected saliva by pooling saliva from throat and spitting (~ 1mL) into container	Saliva was diluted 1:2 with sterile phosphate-buffered saline (PBS) then MagNA Pure 96 System (Roche Molecular Diagnostics, CA, USA)	LightMix® ModularDx SARS-CoV (COVID19) E-gene assay	Extracted RNA from 500 µL, eluted in 50 uL	NPS	74 (100%)	74	Sensitvity = 91.9%	1.4
09/01	MedRxiv	SalivaAll: Clinical validation of a sensitive test for saliva collected in healthcare and community settings with pooling utility for SARS-CoV-2 mass surveillance	Sahajpal et al.	Prospective clinical validation	Suspected positive individuals	USA	344	NI	RT-PCR	Self-collected by spitting in container then HCW added VTM	Chemagic 360 instrument, PerkinElmer Inc. OR Omni bead mill homogenizer (Omni International, USA)	TaqMan-based RT-PCR assay + FDA-EUA assay	Extracted RNA from 300µL, eluted in 60µL	NPS	SalivaAll: 75 samples (40%). Other protocol: 61 samples (25%)	429 (n=189 SalivaAll)	SalivaAll (saliva homogenized before RNA extraction) Sensitivity: Saliva = 97.8%, NPS = 78.9%. Agreement = 76.8%. Also showed protocols with more processing challenges can reduce sensitivity: W/o homogenization Saliva = 50.0%, NPS = 89.7%. Positive agreement = 39.7%	21
08/31	Brazilian Journal of Infectious Diseases	Saliva is a reliable, non-invasive specimen for SARS-CoV-2 detection	Vaz et al.	Prospective validation	Suspected positive individuals	Brazil	155 (46m / 109f)	40 (IQR 33−48.5)	RT-PCR	Self-collected by repeatedly spitting (~2 mL) in container, avoiding sputum	Homogenization followed by QIAGEN QIAamp® RNA Mini Kit	BIOMOL OneStep/ COVID-19 Kit	Extracted RNA from 140 µL, eluted in 60 µL	NPS and/or OPS	67 (43%)	155	Sensitivity = 94.4%. Specificity = 97.62%. Agreement = 96.1%	3
08/28	Annals of Internal Medicine	Salivary detection of COVID-19	Caulley et al.	Prospective	Asymptomatic, high-risk and suspected positive individuals	Canada	1939	NI	RT-PCR	Self-collected (at least 1 mL) by spitting in tubes (OMNIgene•ORAL OM-505)	STARMag Universal cartridge kit on a Nimbus or Starlet extractor (Seegene, South Korea)	An RT-PCR assay targeting E gene only	NI	NPS or OPS	70 (3.6%)	1939	Sensitivity: Saliva = 68.6%, NPS = 80.0%. Positive agreement = 48.6%. Disagreement = 31.4%	20
08/28	New England Journal of Medicine	Saliva or Nasopharyngeal Swab Specimens for Detection of SARS-CoV-2	Wyllie et al.	Prospective	Asymptomatic health care workers	USA	70 (41m / 29f) Pts. + 9 asymptomatic healthcare workers (AHW)	61.4 mean (13-91)	RT-qPCR	Self-collected by pooling saliva in mouth then repeatedly spitting in container	MagMAX Viral/Pathogen Nucleic Acid Isolation kit (Thermo Fisher, Waltham, MA, USA) with modifications	US CDC real-time RT-PCR primer/probe sets	Extracted RNA from 300 µL, eluted in 75 µL	NPS and/or OPS	79 (100%)	79 (n=70 Pts., n=9 AHW)	Pts: Sensitivity (1 - 5 d after Dx): Saliva = 81%, NPS = 71%. AHW: Saliva = 9/9 (100%), NPS = 2/9 (22%)	25
08/14	MedRxiv	Validation of Saliva and Self-Administered Nasal Swabs for COVID-19 Testing	Teo et al.	Prospective validation	Asymptomatic and suspected positive individuals	Singapore	200 (all male)	Group 1 (n=149): 32 (18-37). Group 2 (n=51): 38 (IQR 36-41)	RT-PCR	HCW supervised self-collection: 1. Gargling then spitting saliva from back of throat. 2. Clearing nose to expel sputum into container (steps repeated until 1 - 2 mL collected). 3. RNA Stabilization fluid (2 mL) added	GeneAid Biotech Ltd	US CDC real-time RT-PCR primer/probe sets or Fortitude 2.1 kit	Saliva viscosity-reducing process, then xtracted RNA from 200 µL	NPS (PCR kit = CDC)	150 (44.5%)	337	Sensitivity: Saliva (CDC assay) = >100% (209 +ve), Saliva (Fortitude kit) = 100% (167 +ve).	28
08/08	Clinical infectious Diseases	Posterior oropharyngeal saliva for the detection of SARS-CoV-2	Otto et al.	Prospective	Suspected positive individuals	France	92	NI	RT-PCR	Self-collected by coughing in container	MagNA pure compact (Roche, Switzerland) or GenoXtract (Biocentric, France)	Light-Cycler 480 Real-Time PCR System	NI	NPS	45 (49%)	92	Sensitivity: Saliva = 100%, NPS = 92%. Specificity = 100%. Agreement = 91.3%	8
08/06	Clinical Infectious Diseases	Comparing nasopharyngeal swab and early morning saliva for the identification of SARS-CoV-2	Rao et al.	Prospective	Asymptomatic COVID -19 individuals	Malaysia	217 (all male)	27 (IQR 18-36)	RT-PCR	Self-collected deep throat saliva in container upon waking	MagNA Pure 96 DNA and Viral NA Small Volume extraction kit on MagNA Pure 96 system (Roche Diagnositc GmBH, Germany)	One-step RT-PCR of Real-Q 2019 nCoV detection	Extracted RNA from 200 µL saliva, eluted in 50 µL	NPS	160 (74%)	217	Sensitivity: Saliva = 93.1%, NPS = 52.5%. Agreement = 45.6%. Disagreement = 47.5%.	47.5

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08/04	MedRxiv	SalivaDirect: Simple and sensitive molecular diagnostic test for SARS-CoV-2 surveillance	Vogels et al.	Prospective diagnostic test validation (granted FDA EUA)	COVID-19 patients and healthcare workers	USA	NI	NI	RT-qPCR	Samples from Yale IMPACT biorepository	N/A	ThermoFisher Scientific TaqPath COVID-19 combo	200 µL input eluted in 50 µL	NPS	37 (55%)	67	Sensitivity: Saliva = 94.1%, NPS = 91.4%. Agreement: positive = 94.1%, negative = 90.9%	8
08/04	MedRxiv	Assessment of multiplex digital droplet RT-PCR as an accurate diagnosis tool for SARS-CoV-2 detection in nasopharyngeal swabs and saliva samples	Cassinari et al.	Prospective validation	Suspected positive individuals	France	130	NI	RT-qPCR and 6 plex RT-ddPCR	Self-collected by drooling (~2 mL) into tube	EZ1 DSP 96 virus kit and EZ1 Advanced XL machine (Qiagen, Hilden, Germany)	RealStar® SARS-CoV-2 **RT-PCR** Kit 1.0. and One-Step **RT-ddPCR** Advanced Kit for Probes	Extracted RNA from 200 µL saliva	NPS	13 (10%)	31	Sensitivity: Saliva (RT-ddPCR) = 87%, NPS = 87%, Saliva (RT-qPCR) = 67%	13
07/31	Clinical Virology	Challenges in use of saliva for detection of SARS CoV-2 RNA in symptomatic outpatients	Landry et al.	Prospective	Suspected positive individuals	USA	NI	NI	RT-PCR	Assisted collection, pool saliva in mouth then spit in container	bioMerieux easyMAG® or EMAG® (bioMerieux Inc, Durham, NC, USA)	US CDC real-time RT-PCR primer/probe sets	Extracted RNA from 200 µL saliva, eluted in 55 µL	NPS	35 (27%)	124	Sensitivity: Saliva = 85.7%, NPS = 94.3%. Agreement = 94.4%	6
07/29	Molecular Sciences	A rapid, simple, inexpensive, and mobile colorimetric assay COVID-19-LAMP for mass on-site screening of COVID-19	Chow et al.	Consecutive case series	COVID-19 patients and asymptomatic COVID -19 individuals	China	40	NI	RT-LAMP	Unspecified, used sputum/deep throat saliva	QIAamp Viral RNA Mini kit (QIAGEN, Hilden, Germany)	N/A	Extracted RNA from 140 µL saliva, eluted in 60 µL	NPS with RT-qPCR	160 samples (98%)	163 unmatched (saliva = 67, NPS = 96)	Sensitivity: Saliva = 97.02%, NPS = 98.96%. Specificity = 100%	NI
07/28	MedRxiv	Does sampling saliva increase detection of SARS-CoV-2 by RT-PCR? Comparing saliva with oro-nasopharyngeal swabs	Dogan et al.	Cross - sectional, consecutive	Suspected positive individuals	Turkey	200 (106m / 94f)	54.9 mean (SD ±16.1)	RT-PCR	HCW sampled by Pts. drooling (~1 mL) into VTM tubes, ensured to collect saliva not sputum	N/A	Direct Detection of SARS-CoV-2 Kit (Coyote Bioscience Co., Ltd)	N/A, kit did not require separate RNA extraction	NPS	98 (49%)	157	Sensitivity (Day 0): Saliva = 63%, NPS = 83%, OPS = 83%. Sensitivity (Day 5): Saliva = 55%, NPS = 55%, OPS = 60%	7
07/16	Experimental Biology and Medicine	Direct on-the-spot detection of SARS-CoV-2 in patients	Ben-Assa et al.	Clinical evaluation	Suspected positive individuals	Israel	4	NI	RT-qPCR and RT-LAMP	Self-collected by spitting in sterile cups	bioMerieux easyMAG® or EMAG® (bioMérieux, Durham, North Carolina, USA), magLEAD 5bL (Precision System Science) or MagEx (STARlet)	Allplex 2019-nCoV (Seegene) or real-time fluorescent RT-PCR Kit for Detecting SARS-2019-nCoV (BGI))	RT-qPCR: Extracted RNA from 0.5 mL saliva, eluted in 50 µL. RT-LAMP: 7 µL inactivated sample used for total reaction vol. 20 µL	Swab (unspecified) with RT-qPCR	3 (75%)	4	Sensitivity = 100%. Positive and negative agreement = 100%	N/A
07/12	Clinical Microbiology and Infection	Non-invasive saliva specimens for the diagnosis of COVID-19: caution in mild outpatient cohorts with low prevalence	Skolimowska et al.	Prospective cross-sectional	Symptomatic healthcare workers and household contacts	UK	132 (43m / 89f)	39 (IQR 30-51)	RT-PCR	Self-collected spitting in container w/o coughing	N/A	Roche, AusDiagnostics, ThermoFisher, and Abbott assays	NI	NPS / OPS	18 (14%)	131	Sensitivity: Saliva = 83.3%, NPS = 93.8%. Specificity = 99.1%	6
07/11	MedRxiv (and CDC)	Saliva offers a sensitive, specific and non-invasive alternative to upper respiratory swabs for SARS-CoV-2 diagnosis. Peer-reviewed version: Saliva Alternative to Upper Respiratory Swabs for SARS-CoV-2 Diagnosis	Byrne et al.	Prospective	Suspected positive individuals	UK	110 (49m / 61f)	NI	RT-qPCR	Self-collected pooling in mouth then spitting in tube (~200 µL)	RNA using the QIAamp Viral RNA Mini Kit (QIAGEN)	Genesig® Real-Time Coronavirus COVID-19 PCR assay	NI	Nasal/throat (NT) swabs	19 samples (13%)	145	Sensitivity = 100%. Agreement: positive = 85%, negative = 97.6%	13
07/07	Clinical Microbiology	Clinical evaluation of self-collected saliva by RT-qPCR, direct RT-qPCR, RT-LAMP, and a rapid antigen test to diagnose COVID-19	Nagura-Ikeda et al.	Clinical evaluation	COVID-19 patients	Japan	103 (66m / 37f)	46 (18-87)	RT-qPCR + RT-LAMP	Self-collected by spitting in tube (~0.5 mL)	QIAsymphony RNA kit (Qiagen, Hilden, Germany)	QuantiTect® Probe RT-PCR Kit (QIAGEN)	RNA extracted from 140 µL. If w/o RNA extraction, Method A: 8 µL sample + 2 µL prep buffer. Method B: 5 µL sample + 5 µL buffer	NPS	103 (100%)	103	Sensitivity of various methods: RNA extraction = 81.6%, Automated PCR = 80.6%, A = 76.7%, B = 78.6%, RT-LAMP = 70.9%	NI

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							No. (males / females)	Median Age (Range)										
07/04	Medical Virology	Deep throat saliva as an alternative diagnostic specimen type for the detection of SARS-CoV-2	Leung et al.	Retrospective	COVID-19 patients	China	62	NI	RT-PCR	Self-collected deep throat saliva into container	MagMAX Viral RNA isolation kit (Applied Biosystems, Foster city, CA, US)	LightMix Modular SARS-CoV E-gene detection kit	Extracted 50 µL RNA from 200 µL sample	NPS	29 (47%)	95 (n=61 positive, n=36 negative)	Sensitivity: Saliva = 83.6%, NPS = 73.8%. Agreement: positive = 67.2%, negative = 100%	21
07/01	bioRxiv	Saliva sampling is an excellent option to increase the number of SARS CoV2 diagnostic tests in settings with supply shortages	Moreno - Contreras et al.	Prospective	COVID-19 patients and healthcare workers	Mexico	253 (115m / 137f)	41 (IQR 26-55)	RT-qPCR	Self-collected by spitting (2-3 mL) on several occasions in containers	N/A	StarQ One-Step RT-qPCR (Genes 2 Life)	50 µL saliva mixed with 50 µL DNA extraction Quick Extract reagent	NPS and/or OPS	114 (45%)	253	Sensitivities: One-swab group (n=182) Saliva = 86.2%, OPS = 65%. Two-swab group (n=71) Saliva = 73.5%, NPS+OPS = 82.3%.	30
06/25	Clinical Infectious Diseases	Sensitivity of nasopharyngeal swabs and saliva for the detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)	Jamal et al.	Prospective	COVID-19 patients	Canada	91 (52m / 39f)	66 (23-106)	RT-PCR	Self-collected by spitting 1 tsp (5 mL) saliva in container. Diluted with 2.5 mL of PBS	NI	Allplex™ 2019-nCoV Assay (100T)	NI	NPS, midturbinate, or NS	91 (100%)	91	Sensitivity: Saliva = 72%, NPS = 89%. Positive agreement = 61%	9
06/21	Clinical Infectious Diseases	Posterior oropharyngeal saliva for the detection of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)	Wong et al.	Retrospective cohort	COVID-19 patients	China	95 (57m / 38f)	36 (4-92)	RT-PCR	Self-collected deep throat saliva by clearing saliva from back of throat into container	MagNA Pure LC 2.0 or MagNA Pure 96 (Roche, Switzerland)	LightMix® Modular SARS + Cobas z480 real-time PCR analyzer (Roche)	20 µL reaction mixture containing 10 µL extracted RNA from saliva received in 1 mL VTM	NPS	51 (54%)	229	Sensitivity: Saliva = 100% NPS = 86.5%. Agreement = 76.0%	23
06/18	MedRxiv	Evaluation of specimen types and saliva stabilization solutions for SARS-CoV-2 testing	Griesemer et al.	Cross-sectional	Suspected positive individuals	USA	227	(14-77)	RT-PCR	HCW assisted saliva collection in tubes	bioMerieux easyMAG® or EMAG® (BioMérieux, Durham, North Carolina, USA)	CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel	System 1 (EMAG®): 110 µL added to 2 mL lysis buffer, extracted into 110 µL eluate. System 2 (MagNA Pure 96): 100 µL added to 350 µL lysis buffer, eluted into 100 µL	NPS	93 (41%)	227	Sensitivity: Saliva = 87.1%, NPS = 97.9%, NS = 87.1%, Combined saliva + NS = 94.6%	1
06/18	BioRxiv	Saliva based molecular testing for SARS-CoV-2 that bypasses RNA extraction	Ranoa et al.	Prospective	Healthy individuals	USA	100	NI	RT-qPCR	Self-collected by drooling (1 mL) into container	Heat inactivation OR MagMax Viral/Pathogen II Nucleic Acid Isolation Kit (Applied Biosystems, Foster city, CA, US)	TaqPath RT-PCR COVID-19 Kit	W/o RNA extraction: buffer addition for final [sample] of 0.5%. RNA extraction: 200 µL saliva, eluted with 50 µL	NPS	9 (9%)	100	Single sample testing: Sensitivity = 88.9%. Specificity = 98.9%. Duplicate testing: Sensitivity = 100%. Specificity = 100%. Agreement: positive = 88.9%, negative = 98.9%	N/A
06/16	MedRxiv	Field-deployable, rapid diagnostic testing of saliva samples for SARS-CoV-2	Wei et al.	Prospective diagnostic test validation	Suspected positive individuals	USA	149 NPS samples	NI	High-Performance LAMP	Collected from mouth directly or by spitting in container	N/A	N/A	NI	NPS	4 Pts. (2.7%)	18	Pt samples: Sensitivity = 100%. Specificity = 100%. Spiked saliva samples (n=30 +ve, n=30 -ve): Sensitivity = 98.3%. Specificity = 100%. Agreement: positive = 96.7%, negative = 100%	20
06/10	Infection and Chemotherapy	A case report of SARS-CoV-2 confirmed in saliva specimens up to 37 days after onset: Proposal of saliva specimens for COVID-19 diagnosis and virus monitoring	Tajima et al.	Case Report	COVID-19 patient	Japan	1 (1m)	71	RT-PCR	Self-collected early morning saliva by spitting in container (600 µL)	SMGNP to concentrate the virus, then 0.1% sodium lauryl sulfate aqueous solution was added to elute the RNA	NI	NI	NPS	1 (100%)	6	Sensitivity (of samples taken days 28 - 37 after symptom onset): Saliva = 4/6, NPS = 5/6	0

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06/09	MedRxiv	Validation of a Self-administrable, Saliva-based RT-qPCR Test Detecting SARS-CoV-2	Miller et al.	Clinical and analytical validation (granted FDA EUA)	Suspected positive individuals	USA	91 samples	NI	RT-qPCR	HCW observed self-collection by spitting in OGD-510 tube	MagMAX Viral/Pathogen Nucleic Acid Isolation Kit (ThermoFisher Scientific) or Maxwell HT Viral TNA Kit using the Maxwell RSC TNA Viral Kit (Promega Corporation)	CFX384 Touch Real-Time PCR Detection System with 2019-nCoV CDC EUA Authorized qPCR Probe Assay primer/probe mix	NI	NPS	34 (37%)	91	Sensitivity = 97.1%. Specificity = 96.5 - 98.2%. Agreement: positive = 97.1%, negative = 96.5-98.2%	N/A
06/04	Infection	Comparison of SARS-CoV-2 detection in nasopharyngeal swab and saliva	Iwasaki et al.	Prospective cohort	Suspected positive individuals and COVID patients	Japan	76	69 (30-97)	RT-qPCR	Self-collected by spitting in container	HT Viral TNA Kit (Promega Corporation) and automated extraction using the Maxwell RSC TNA Viral Kit (Promega Corporation)	TepOnePlus Real Time PCR System (Thermo Fisher Scientific)	200 µL saliva added to 600 µL PBS, then 140 µL supernatant used as sample	NPS	10 (13%)	76	Sensitivity: Saliva = 80%, NPS = 80%. Agreement = 97.4%	10
06/04	Clinical Infectious Diseases	The natural history and transmission potential of asymptomatic SARS-CoV-2 infection	Chau et al.	Prospective	COVID-19 patients and high risk individuals	Vietnam	30 (15m / 15f)	29 (16-60)	RT-PCR	Self-collected by spitting in container	QIAamp viral RNA kit (QIAgen GmbH, Hilden, Germany)	Superscript III one step RT-PCR system (ThermoFisher)	Extracted RNA from 140 µL saliva, eluted with 50 µL	NPS	30 (100%)	27	Sensitivity: Saliva = 74%. (asymptomatic = 64%, symptomatic = 81%)	4
05/30	MedRxiv	EasyCOV : LAMP based rapid detection of SARSCoV-2 in saliva	L'Helgouach et al.	Prospective diagnostic test validation	Symptomatic healthcare worker and COVID patients	France	123 (42m / 81f)	43 mean (19-84)	RT-LAMP	Assisted collection by pipette under tongue (200 µL)	N/A	N/A	3 µL treated saliva added to 17 µL reaction mix	NPS with RT-PCR	19 (15%)	123	Sensitivity = 78.9%. Specificity = 95.7%	N/A
05/22	FDA EUA Summary	P23 Labs TaqPath SARS-CoV-2 Assay	FDA.gov	Prospective diagnostic test authorization	Clinical samples	USA	42	NI	RT-PCR	At-home self-collection and/or HCW assisted collection in OM-505 tube	MagMAX Viral/Pathogen Nucleic Acid Isolation Kit on the KingFisher Duo Primer Purification System (Thermo Fisher, Waltham, MA, USA)	Applied Biosystems (AB) TaqPath COVID-19 Combo Kit	Extracted RNA from 400 µL saliva, eluted with 50 µL	NPS	31 (74%)	42	Sensitivity: Saliva = 100%, NPS = 100%. Agreement = 100%	N/A
05/17	MedRxiv	Saliva is less sensitive than nasopharyngeal swabs for COVID-19 detection in the community setting	Becker et al.	Prospective cohort	Suspected positive individuals and COVID patients	USA	112	NI	RT-PCR	Self-collected by spitting in tubes containing different preservatives (OM-505 or OGD-610 DNA) for Pts. to add after	Acid Isolation Kit on the automated KingFisher Duo Primer Purification System (v4.0)	TaqPath Multiplex RT-PCR COVID-19 kit (Thermo) and PrimerDesign COVID-19 assay	Extracted RNA from 400 µL, eluted with 50 µL	NPS	Diagnostic cohort = 88 (100%). Recovering cohort (>8 d, <21 d since 1st symptom) = 9 (37.5%)	112	Diagnostic cohort Sensitivity: Saliva = 69.2%, NPS = 98.9%. Recovering cohort Sensitivity: Saliva = ~50%.	1
05/15	Clinical Microbiology and Infection	Saliva sample as a non-invasive specimen for the diagnosis of coronavirus disease 2019: a cross-sectional study	Pasomsub et al.	Cross-sectional	Suspected positive individuals	Thailand	200 (69m / 131f)	36 (28-48)	RT-PCR	Self-collected saliva sample (no coughing) into container	Lysis buffer for viral inactivation (bioMerieux, Marcy-l'Etoile, France), then extracted using MagDEA® Dx reagents and platform (Precision System Science, Chiba, Japan)	CFX96 Real-Time Detection System	Extracted RNA from 200 µL	NPS + throat swab	19 (9.5%)	200	Sensitivity: Saliva = 84.2%, NPS = 88.9%. Specificity = 98.9%. Overall agreement = 97.5%	11
05/07	FDA EUA Summary	Rutgers Clinical Genomics Laboratory TaqPath SARS-CoV-2 Assay	FDA.gov	Prospective diagnostic test (granted FDA EUA)	Clinical samples	USA	60	NI	RT-PCR	Self-collected under HCW observation by spitting in tube containing preservatives (SDNA-1000)	PerkinElmer Chemagic 360 automated specimen processing system with the Chemagic Viral DNA/RNA 300 Kit H96.	Applied Biosystems TaqPath COVID-19 Combo Kit	Extracted RNA from 300 µL, eluted in 50 µL	NPS / OPS	30 (50%)	60	Sensitivity = 100%. Agreement = 100%	N/A
04/22	MedRxiv	Saliva is more sensitive for SARS-CoV-2 detection in COVID-19 patients than nasopharyngeal swabs	Wyllie et al.	Consecutive case series	COVID-19 patients and healthcare workers	USA	29 (16m / 13f)	59 mean (23-91)	RT-PCR	Self-collected by pooling saliva in mouth then repeatedly spitting in container	MagMAX Viral/Pathogen Nucleic Acid Isolation kit (ThermoFisher, Waltham, MA, USA)	US CDC real-time RT-PCR primer/probe sets	Extracted RNA from 300 µL, eluted in 75 µL	NPS and/or OPS	29 (100%)	38	Sensitivity: Saliva = 86.8%, NPS = 73.7%. Agreement: positive = 65.8%, negative = 100%	21

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04/21	Clinical Microbiology	Saliva as a non-invasive specimen for detection of SARS-CoV-2	Williams et al.	Consecutive case series	Suspected positive individuals	Australia	622	NI	RT-PCR	Pool saliva in mouth 1-2 mins then gently spit (1-2 mL) in container	Saliva diluted 1:1 with Amies solution, then extracted on Qiagen EZ1 platform (QIAGEN, Hilden, Germany).	Coronavirus Typing (8-well) assay	Extracted RNA from 200 µL, eluted in 60 µL	NPS	39 (6%)	522	Sensitivity = 84.6%	2
04/14	Infection	Saliva is a reliable tool to detect SARS-CoV-2	Azzi et al.	Consecutive case series	COVID-19 patients	Italy	25 (17m / 8f)	61.5 mean (39-85)	RT-PCR	Drooling saliva samples or collected by physician with pipette if Pt. compromised	QIAmp Viral RNA mini kit (Qiagen, Hilden, Germany)	Abi Prism 7000 sequence detection system (Applied Biosystems)	Extracted RNA from 140 µL, eluted in 60 µL	NPS	25 (100%)	33	Sensitivity = 100%	8
03/23	Lancet Infectious Diseases	Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2	To et al.	Observational Cohort	COVID-19 patients	China	23 (13m / 10f)	62 (37-75)	RT-qPCR	Self-collected coughed up deep throat saliva by clearing throat	NUCLISENS® easyMAG® (bioMérieux, Durham, North Carolina, USA)	NI	NI	NPS / sputum	23 (100%)	173 unmatched samples	Sensitivity = 87%	NI
03/21	Infection	Comparisons of viral shedding time of SARS-CoV-2 of different samples in ICU and non-ICU patients	Fang et al.	Consecutive case series	COVID-19 patients	China	32 (16m / 16f)	41 (34-54)	RT-PCR	NI	NI	NI	NI	NS	32 (100%)	NI	Sensitivity: Saliva = 78.1%, NS = 100.0%	0
02/12	Clinical Infectious Diseases	Consistent detection of 2019 novel coronavirus in saliva	To et al.	Prospective diagnostic test validation	COVID-19 patients	China	12 (7m / 5f) COVID patients + 33 non-COVID	62.5 (35-75)	RT-PCR	Self-collected by coughing out saliva (0.5 - 1 mL) from throat in container	NucliSENS easyMAG (bioMérieux, Durham, North Carolina, USA)	QuantiNova SYBR Green (Qiagen) Kit	Extracted RNA from 250 µL, eluted in 55 µL	NPS / sputum	12 (23%)	45	Sensitivity = 91.7% (11/12 Pts.). Specificity = 100%	0