

Supplementary Materials

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Supplement A

Figure s1. PRISMA Flow Diagram

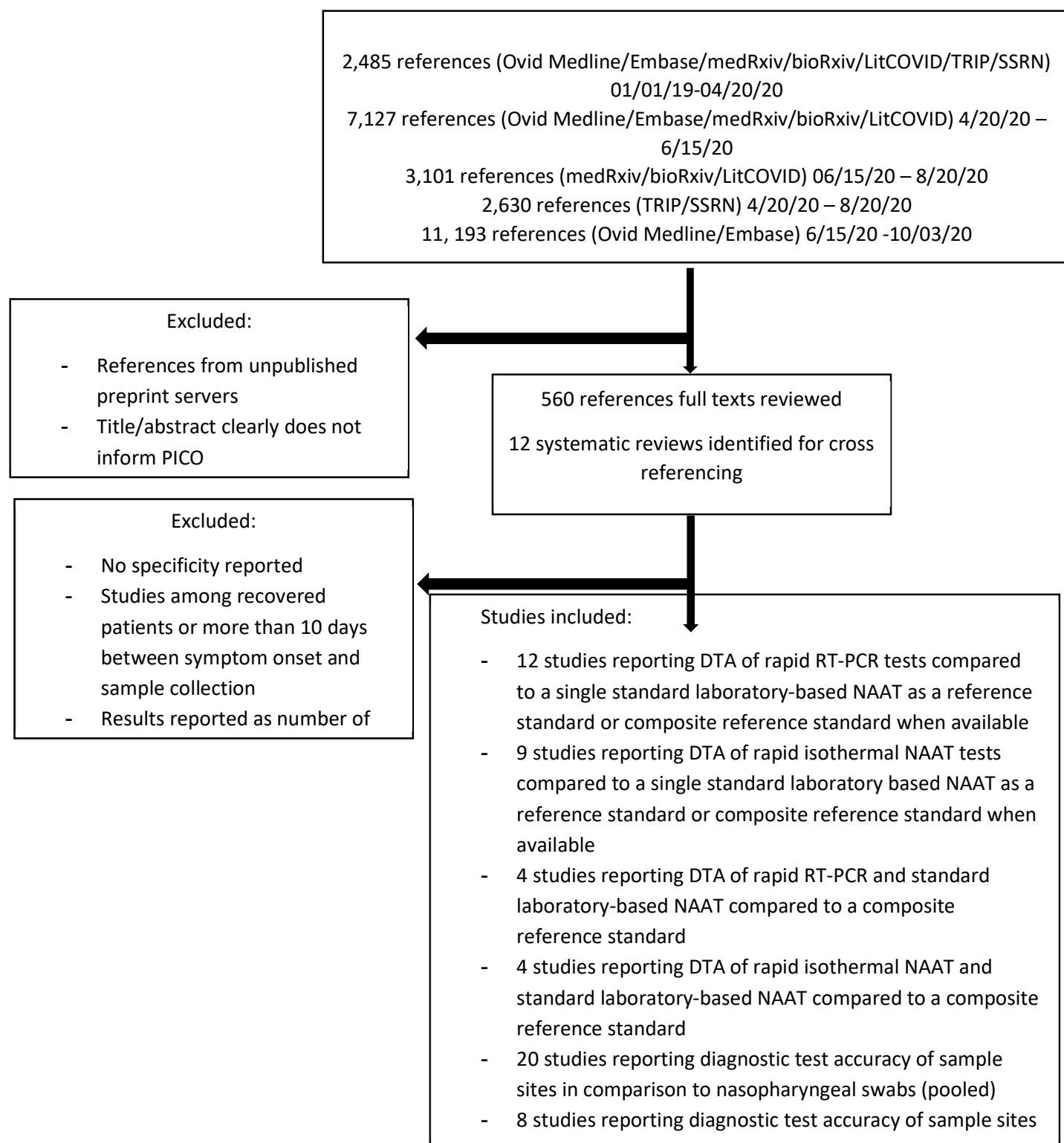


Table s1. PICO Questions Identified by the Panel

The panel identified 14 questions of interest. Of these, 10 were addressed in the first diagnosis guideline, 3 were determined to be important to be addressed in the second diagnosis guideline and one was determined to be important to discuss but not necessary address as a recommendation.

Questions addressed in the first IDSA COVID-19 molecular diagnosis guideline
In symptomatic individuals suspected of COVID-19 • In symptomatic individuals in the community suspected of having COVID-19, should testing vs no testing be done to guide decisions about isolation and contact tracing? • In symptomatic individuals suspected of having COVID-19, is the use of rapid vs lab-based testing (different EUA approved NAATs) affect the diagnostic accuracy of the test? • In symptomatic individuals suspected of having COVID-19, should one test vs repeated testing be done to guide decisions about isolation and going back to work? • In symptomatic individuals with URTI or ILI suspected of having COVID-19, should noninvasive specimens be collected by healthcare providers vs patients? (will collection by HCP vs patients affect the diagnostic accuracy of the test)? • In symptomatic individuals with URTI or ILI suspected of having COVID-19, which of the following specimen types (nasal vs. mid turbinate vs. oral vs. NP vs. combo) should be used to diagnose COVID 19? (will specimen type it affect the diagnostic accuracy of the test)? • In symptomatic individuals with LRTI suspected of having COVID-19, which of the different specimen type (upper vs lower sampling) should be used? (will specimen type (upper vs lower sampling) affect the diagnostic accuracy of the test)? In asymptomatic individuals exposed or not exposed • In asymptomatic individuals who have been exposed to COVID-19, should testing vs no testing be done to diagnose COVID19 (to guide decisions about quarantine and contact tracing). • In asymptomatic individuals, should testing vs no testing be done on admission to the hospital to diagnose COVID19 (to guide decisions about quarantine and contact tracing). • In asymptomatic individuals, should testing vs no testing be done before aerosol generating surgeries or procedures to diagnose COVID19 and inform PPE use. • In asymptomatic individuals, should testing vs no testing be done before immunosuppressive procedures such as solid or stem cell transplantation or cytotoxic chemotherapy to diagnose COVID19 and inform candidacy.
Questions revisited for the update
• In symptomatic individuals suspected of having COVID-19, can specimen types other than a nasopharyngeal swab (i.e., anterior nasal vs. mid turbinate vs. oropharyngeal vs. saliva vs. a combination) should be used to diagnose COVID 19? (will specimen type it affect the diagnostic accuracy of the test relative to an NP swab)? • In symptomatic individuals suspected of having COVID-19, does the use of rapid vs. standard lab-based tests affect the diagnostic accuracy of the test?

- In asymptomatic individuals with cancer or autoimmune disease, should testing vs no testing be done before immunosuppressive procedures to inform management?

Table s2. Search Strategy

Diagnosis of COVID-19 in asymptomatic patients

Database(s): **Embase 1974 to present; OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present**

#	Search	Embase	Medline
1	((((((exp coronavirus/) OR (((corona* or corono*) adj1 (virus* or viral* or virinae*))).ti,ab,kw.)) OR ((coronavirus* or coronovirus* or coronavirinae* or Coronavirus* or Coronovirus* or Wuhan* or Hubei* or Huanan or "2019-nCoV" or 2019nCoV or nCoV2019 or "nCoV-2019" or "COVID-19" or COVID19 or "CORVID-19" or CORVID19 or "WN-CoV" or WNCov or "HCoV-19" or HCoV19 or CoV or "2019 novel*" or Ncov or "n-cov" or "SARS-CoV-2" or "SARSCoV-2" or "SARSCoV2" or "SARS-CoV2" or SARSCov19 or "SARS-Cov19" or "SARSCov-19" or "SARS-Cov-19" or Ncovor or Ncorona* or Ncorono* or NcovWuhan* or NcovHubei* or NcovChina* or NcovChinese*))).ti,ab,kw.)) OR (((((respiratory* adj2 (symptom* or disease* or illness* or condition*)) or "seafood market*" or "food market*") adj10 (Wuhan* or Hubei* or China* or Chinese* or Huanan*))).ti,ab,kw.)) OR (((outbreak* or wildlife* or pandemic* or epidemic*) adj1 (China* or Chinese* or Huanan*))).ti,ab,kw.)) OR "severe acute respiratory syndrome*".ti,ab,kw.) OR exp Coronavirus Infections/	107226	102446
2	((Asymptom*) OR ((Symptomless) OR (no symtom*) OR (Subclinical)).mp.)	302001	204447
3	1 AND 2	3530	2963

Diagnosis of COVID-19 in symptomatic with upper respiratory symptoms/mostly outpatient

Database(s): **Embase 1974 to present; OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present,**

#	Search	Embase	Medline
1	((((((exp coronavirus/) OR (((corona* or corono*) adj1 (virus* or viral* or virinae*))).ti,ab,kw.)) OR ((coronavirus* or oronavirus* or coronavirinae* or Coronavirus* or Coronovirus* or Wuhan* or Hubei* or Huanan or "2019-nCoV" or 2019nCoV or nCoV2019 or "nCoV-2019" or "COVID-19" or COVID19 or "CORVID-19" or CORVID19 or "WN-CoV" or WNCov or "HCoV-19" or HCoV19 or CoV or "2019 novel*" or Ncov or "n-cov" or "SARS-CoV-2" or "SARSCoV-2" or "SARSCoV2" or "SARS-CoV2" or SARSCov19 or "SARS-Cov19" or "SARSCov-19" or "SARS-Cov-19" or Ncovor or Ncorona* or Ncorono*	107226	102446

	or NcovWuhan* or NcovHubei* or NcovChina* or NcovChinese*).ti,ab,kw.)) OR (((respiratory* adj2 (symptom* or disease* or illness* or condition*)) or “seafood market*” or “food market”) adj10 (Wuhan* or Hubei* or China* or Chinese* or Huanan*).ti,ab,kw.)) OR (((outbreak* or wildlife* or pandemic* or epidemic*) adj1 (China* or Chinese* or Huanan*).ti,ab,kw.)) OR “severe acute respiratory syndrome*”.ti,ab,kw.) OR exp Coronavirus Infections/		
2	((upper respiratory OR sneezing OR sore throat OR rhinitis OR sinusitis OR odynophagia OR dysphagia OR pharyngitis OR URTI or URT symptom* OR runny nose OR upper airway or upper airway*).mp.)	273690	140649
3	1 AND 2	2960	1351

Diagnosis of COVID-19 in symptomatic with lower respiratory symptoms/mostly in patient

Database(s): **Embase 1974 to present; OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present,**

#	Search	Embase	Medline
1	((((exp coronavirus/) OR ((corona* or corono*) adj1 (virus* or viral* or virinae*).ti,ab,kw.)) OR ((coronavirus* or oronavirus* or coronavirinae* or Coronavirus* or Coronovirus* or Wuhan* or Hubei* or Huanan or “2019-nCoV” or 2019nCoV or nCoV2019 or “nCoV-2019” or “COVID-19” or COVID19 or “CORVID-19” or CORVID19 or “WN-CoV” or WNCov or “HCoV-19” or HCoV19 or CoV or “2019 novel*” or Ncov or “n-cov” or “SARS-CoV-2” or “SARSCoV-2” or “SARSCoV2” or “SARS-CoV2” or SARSCov19 or “SARS-Cov19” or “SARSCov-19” or “SARS-Cov-19” or Ncovor or Ncorona* or Ncorono* or NcovWuhan* or NcovHubei* or NcovChina* or NcovChinese*).ti,ab,kw.)) OR (((respiratory* adj2 (symptom* or disease* or illness* or condition*)) or “seafood market*” or “food market”) adj10 (Wuhan* or Hubei* or China* or Chinese* or Huanan*).ti,ab,kw.)) OR (((outbreak* or wildlife* or pandemic* or epidemic*) adj1 (China* or Chinese* or Huanan*).ti,ab,kw.)) OR “severe acute respiratory syndrome*”.ti,ab,kw.) OR exp Coronavirus Infections/	107226	102446
2	((EXP acute respiratory distress syndrome/) OR (EXP intensive care/) OR (EXP intensive care unit/) OR (ARDS OR intubat* OR cough* OR	3479525	1919844

	respiratory distress OR hospital* OR inpatient OR ICU OR SOB OR shortness of breath).mp.)		
3	1 AND 2	32024	21262

Study Design Filters

Database(s): OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Search Strategy:

#	Searches	Results
9	limit 8 to human	13574
10	(randomized controlled trial or controlled clinical trial).pt. or (randomized or placebo).ab. or drug therapy.fs. or (randomly or trial or groups).ab.	4848823
11	epidemiologic studies/ or exp case control studies/ or exp cohort studies/ or Cross-sectional studies/	2553129
12	case control.tw.	128954
13	(cohort adj (study or studies)).tw.	218766
14	cohort analy\$.tw.	8470
15	(Follow up adj (study or studies)).tw.	50040
16	(Observational adj (study or studies)).tw.	113247
17	(longitudinal or retrospective or cross sectional).tw.	1133656
18	or/11-16	6987957
19	(registr* or database).mp.	594053
20	(sensitiv: or diagnos:).mp. or di.fs.	6353403
21	10 or 18 or 19 or 20	11498542
22	9 and 21	8665
23	Limit 22 to dt=20190101-20201003	6064
24	Limit 22 to rd=20190101-20201003	5448
25	23 OR 24	6884

Database(s): **Embase 1974 to present**

Search Strategy:

#	Searches	Results
9	limit 8 to human	33191
10	di.fs. or predict:.tw. or specificity.tw.	5520015
11	random*.ab. or random*.ti. or (clinical adj trial*).hw,ab,ti. or exp 'health care quality'/'	5416849
12	exp disease course/ or risk:.mp. or diagnos:.mp. or follow-up.mp. or ep.fs. or outcome.tw.	12797366
13	10 or 11 or 12	16090709
14	9 and 13	25609
15	Limit 14 to dc=20190101-20201003	14508

Table s3a. QUADAS-2 Risk of Bias Assessment (A: Test accuracy data, B: Rapid testing accuracy data)

In symptomatic individuals suspected of having COVID-19, does the use of rapid vs standard laboratory-based testing affect the diagnostic accuracy of the test?				
Author, Year	Patient selection Risk of bias	Index test Risk of bias	Reference standard Risk of bias	Flow and timing Risk of bias
Bulterys, P., 2020	Unclear	Unclear	Low	Low
Smith, E., 2020	High	Unclear	Unclear	Unclear
Lieberman, J., 2020	Low	High	Low	Unclear
Smithgall, M., 2020	High	Low	High	Low
Zhen, W., 2020	High	Low	High	Low
Moore, M., 2020	Unclear	Unclear	Low	Low
Hogan, C., 2020	Unclear	Unclear	Low	Low
Liotti, F., 2020	High	Unclear	Low	Low
Hou, H., 2020	Unclear	Unclear	Low	Low
Loeffelholz, M., 2020	Low	Low	Unclear	Low
Moran, A., 2020	Unclear	Unclear	Low	Low
Stevens, B., 2020	Unclear	High	Low	Low
Wolters, F., 2020	Unclear	Low	Low	Low
Visseaux, B., 2020	Unclear	Low	Low	Low
Harrington, A., 2020	Low	Low	Low	Low
Mitchell, S., 2020	High	Unclear	Low	Low

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Thwe, P., 2020	Low	Low	Low	Low
McDonald, S., 2020	Low	Low	Low	Unclear
Eckel, F., 2020	Low	Low	Low	Low

Table s3b.

In symptomatic individuals suspected of having COVID-19, should one test vs repeated testing be done for better diagnostic accuracy?				
Author, Year	Patient selection Risk of bias	Index test Risk of bias	Reference standard Risk of bias	Flow and timing Risk of bias
Ai J., 2020	Low	Low	High	High
Ai J.W., 2020	Low	Moderate	Moderate	High
Zhou F., 2020	Low	Low	High	High

Table s3c.

In symptomatic individuals with URTI or ILI suspected of having COVID-19, should non-invasive specimens be collected by healthcare providers (HCP) vs patients?				
Author, Year	Patient selection Risk of bias	Index test Risk of bias	Reference standard Risk of bias	Flow and timing Risk of bias
Kojima N., 2020	Low	Low	High	High
Tu YP., 2020	Low	Low	High	Low
Wehrhahn M., 2020	Low	Low	Moderate	Low

Table s3d.

In symptomatic individuals with LRTI suspected of having COVID-19, which of the different specimen type (upper vs lower sampling) should be used?				
Author, Year	Patient selection Risk of bias	Index test Risk of bias	Reference standard Risk of bias	Flow and timing Risk of bias
Fengting Y., 2020	Moderate	Low	Moderate	Low
Gao Y., 2020	Moderate	Low	Moderate	Low
Kojima N., 2020	Low	Low	High	Low
Lin C., 2020	Low	Low	High	Low
Tan W., 2020	Moderate	Low	Moderate	Low
Wang W., 2020	Moderate	Low	High	Moderate
Yang Y., 2020	Moderate	Low	Moderate	Low

Table s3e.

In symptomatic individuals suspected of having COVID-19, are anterior nasal swabs, mid-turbinate/deep nasal swabs, oropharyngeal/throat swabs and/or saliva acceptable alternatives to nasopharyngeal swabs for diagnosis of COVID-19 from the standpoint of diagnostic accuracy?				
Author, Year	Patient selection Risk of bias	Index test Risk of bias	Reference standard Risk of bias	Flow and timing Risk of bias
Studies that used NPS as reference standard				
Migueres, 2020	High	Low	High	Low
Landry, 2020	Low	Low	High	Low
Otto, 2020	Low	Low	High	Low
Azzi, 2020	Low	Low	High	Low
Leung, 2020	Low	Low	High	Low
Iwasaki, 2020	High	Low	High	Low
Williams, 2020	High	Low	High	Low
McCormick, 2020	Low	Low	High	Low
Hanson, 2020	Low	Low	High	Low
Procop, 2020	Low	Low	High	Low
Yokota, 2020	High	Low	High	Low
Pham J., 2020	High	Low	High	Low
Vermeiren, 2020	Low	Low	High	Low
McCulloch, 2020	Low	Low	High	Low

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Patel, 2020	Low	Low	High	Low
Tu YP. 2020	Low	Low	High	Low
Wang X., 2020	Low	Low	High	Low
Le Blanca, 2020	Low	Low	High	Low
Vlek, 2020	Low	Low	High	Low
Péré, 2020	Low	Low	High	Low
Studies that did not use NPS as reference standard				
Skolimowska, 2020	Low	Low	High	Low
Moreno, 2020	Low	Low	High	Low
Pasomsub, 2020	Low	Low	High	Low
Guclu, 2020	Low	Low	High	Low
Byrne, 2020	High	Low	High	low
Vaz, 2020	High	Low	High	Low
Wehrhahn, 2020	Low	Unclear	High	Low
Lin C., 2020	Low	Low	High	Low

Table s4a. Included studies for Recommendation 1

Studies with indirect evidence						
Author (Year)	Study Design	Number of Patients	Patient Selection	Suspicion criteria	Reference Standard	Percentage Diagnosed Based on Suspicion Criteria Used
In symptomatic individuals in the community suspected of having COVID-19, should COVID-19 nucleic acid amplification testing vs no testing be done to guide decisions about isolation?						
Liu R. et al. (2020) ¹	Retrospective Cohort Study	4880	Subjects suspected of or at high risk for infection tested from January 22 to February 14, 2020 in Renmin Hospital of Wuhan University. Among these cases, 2251 were men (46%). The median age was 50 years (IQR = 27).	3173 subjects not in a fever clinic suspected of or at high risk for infection based on (1) respiratory infection symptoms (e.g., cough, dyspnea) but without fever, or (2) close contact with a SARS-CoV-2 patient.	Real-time PCR SARS-CoV-2 positive for both open reading frame 1ab (ORF1ab) and nucleocapsid protein (NP) genes (Shanghai Huirui Biotechnology Co., Ltd).	28% 882/ 3173
				1707 subjects in a fever clinic suspected of or at high risk for infection based on (1) respiratory infection symptoms (e.g., cough, dyspnea) plus fever, or (2) close contact with a SARS-CoV-2 patient.		57% 973/1707
Bordi L. et al. (2020) ²	Cohort Study	126	First suspected cases (patients from different cities), analyzed at Laboratory of Virology at the National Institute for Infectious Diseases 'Lazzaro Spallanzani' (INMI) in Rome from January 21 to February	Considered suspected cases based on clinical and epidemiological grounds, i.e. suspicion of viral etiology, recent travel history to Asia, contact with probable or confirmed case, according to WHO guidelines.	Rapid molecular test for common respiratory pathogens [QIAstat-Dx respiratory panel (QIAGEN, Milan, Italy)] alongside SARS-CoV-2 testing based on World Health Organization protocol.	2.4% 3/124

			7, 2020.			
Pu H. et al. (2020) ³	Cohort Study	73	Adults presenting to hospital with concerns of having COVID-19, inpatients and hospital visitors between January 23 and February 28, 2020 at Shang Jin Nan Fu Hospital (tertiary care teaching hospital, Chengdu, Sichuan province).	1 epidemiological (any single criterion) + 2 clinical manifestations present. OR 3 clinical manifestations present.	Patients excluded from having COVID-19 based on one negative RT-PCR result plus positive results for quick screening tests for influenza or other respiratory viruses, negative routine blood test and radiography based on the "Diagnosis and treatment guideline for novel coronavirus pneumonia (Trial version 6)" Patients excluded based on two consecutive negative test results Patients confirmed positive for COVID-19 based on two consecutive positive RT PCR tests.	2.7% 2/73
Hsieh WH. et al. (2020) ⁴	Cohort Study	43	Patients admitted to China Medical University Hospital Taichung, Taiwan from January 20 to February 19, 2020.	Met Taiwan CDC screening criteria for COVID-19.	SARS-CoV-2 testing of naso-oropharyngeal specimens using RT-PCR targeting RdRP, and E_Sarbeco genes (based on United States Centers for Disease Control and Prevention recommendations), upon and 24 hours after admission.	4.7% 2/43
Ai, J-W. et al. (2020) ⁵	Cohort Study	53	Suspected SARS-COV-2 pneumonia from January 22 to February 9, 2020 in Eastern Chinese cities.	Suspected SARS-COV-2 pneumonia identified by chest CT (with one of the two following criteria met: fever or respiratory symptoms, normal or decreased white blood	Confirmed SARS-COV-2 pneumonia case defined as a positive SARS-COV-2 result by metagenomic	38% 20/53

				cell counts/ decreased lymphocytes counts), and a travel history or contact with patients with fever or respiratory symptoms from Hubei Province or confirmed cases within 2 weeks.	sequencing or RT-PCR assay from nasopharyngeal swab specimens	
Huang G. et al. (2020) ⁶	Single Center, Retrospective observational study	305	Patients with fever, respiratory symptoms, myalgias, fatigue, or other symptoms possibly related to SARS-CoV-2 infection received at the triage reception of a local hospital in Changsha between January 28 and February 20, 2020.	(a) Exposure to Hubei province or local communities with confirmed COVID-19 cases reported; (b) exposure to patients with similar symptoms from regions mentioned in (a); (c) exposure to known COVID-19 patients; (d) association with clustering occurrence. Besides symptoms, clinical and laboratory characteristics suggestive for SARS-CoV-2 infection included: (i) chest computed tomographic results with pneumonia features; (ii) normal or reduced leucocyte count or reduced lymphocyte count of early onset.	SARS-CoV-2 nucleic acid testing by RT-PCR	7% 22/305
Tolia VM et al (2020) ⁷	Retrospective observational study	283	All ED patients who had targeted testing for acute COVID-19 infection at two EDs, located at an urban teaching hospital and academic quaternary medical center in San Diego, California, within the same healthcare system during the initial 10 days	Patients presenting with symptoms concerning for COVID-19 (fever AND cough or shortness of breath); travel within 14 days to countries with high rates of infection (at that time China, Iran, Italy, Japan, and South Korea); or risk factors for infection complications (including age or co-morbid conditions); or the patient was a healthcare worker who could potentially expose others at risk.	Nasopharyngeal swab tested using ePLEX for SARS-CoV-2 nucleic acid.	10.2% 29/283

			of testing (March 10-19, 2020).			
Gudbjartsson D.F. et al (2020) ⁸	Retrospective observational	9199	Patients suspected to have COVID-19	Targeted screening: 9199 patients who were symptomatic (cough, fever, body aches, and shortness of breath) and/or who were returning to Iceland from countries or regions that were classified by the health authorities as being at high risk or who had been in contact with infected persons.	Nasopharyngeal and oropharyngeal samples were collected and were combined into a single tube for each participant before RNA isolation	13.3% 1221/9199

References

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Table s4b. Included studies for Recommendation 2

NP swab reference standard			
Author (Country)	Patient Selection	Index Test	Reference Standard
In symptomatic individuals suspected of having COVID-19, are anterior nasal swabs, mid-turbinate/deep nasal swabs, oropharyngeal/throat swabs, saliva, and/or combination swabs acceptable alternatives to nasopharyngeal swabs for diagnosis of COVID-19 from the standpoint of diagnostic accuracy?			
Migueres ¹ (France) Cohort study	N: 123 Age: Median 43 Gender: 74 females Inclusion: Hospitalized and ambulatory patients Symptomatic vs Asymptomatic: 17 asymptomatic and 27 symptomatic (9 hospitalized)	Sample Site: Saliva without coughing Method of collection: HCW asked patients to salivate, swill their saliva around their mouths for 30 seconds and then spit into a sterile container Test Name: Hologic Panther Fusion Test description: Target: SARS-CoV-2 RNA-dependent polymerase gene (IP2, IP4, Institute Pasteur, Paris, France)	Sample Site: NP swab Method of collection: NR Test Name: Same as index test Test description: Same as index test
Landry ² (USA) Cohort study	N: 124 Age: NR Gender: NR Inclusion: Symptomatic outpatients suspected of having COVID-19 at Yale New Haven Hospital from April 16 to April 28, 2020	Sample Site: Saliva without coughing Method of collection: Patients asked to not eat or drink for 30 minutes, let saliva pool in their mouths and then spit into a sterile container Test Name: CDC 2019 nCoV panel Test description: Targets: N1, N2, and RNase P	Sample Site: NP swab Method of collection: NR Test Name: NR Test description: NR

	Symptomatic vs Asymptomatic: All symptomatic		
Otto ³ (France) Cohort study	N: 253 Age: NR Gender: NR Inclusion: Outpatient adults attending COVID-19 consultation unit; all presented with symptoms consistent with COVID-19 but none had a productive cough Symptomatic vs Asymptomatic: All symptomatic	Sample Site: Saliva with coughing Method of collection: Patients asked to make an effort to cough while wearing a surgical mask and then collect saliva themselves in a sterile container Test Name: LDT primer/probe set using the French National Center protocol on the Light-Cycler 480 Real-Time PCR System Test description: Target: RdRp gene	Sample Site: NP swab Method of collection: HCW-collected Test Name: Same as index test Test description: Same as index test
Azzi ⁴ (Italy) Cohort study	N: 122 Age: Mean 53.5 ±19.8 years Gender: 82 females Inclusion: Patients recruited if scheduled for NP swab collection based on symptoms of COVID-19 Symptomatic vs Asymptomatic: 42 symptomatic, 80 asymptomatic	Sample Site: Saliva without coughing Method of collection: Drooling method used to prevent collection of sputum or throat secretions Test Name: QuantStudio 5 Real-Time PCR System Test description: NR	Sample Site: NP swab Method of collection: NR Test Name: GeneFinder™ COVID-19 Plus Realamp™ NAAT PCR kit (ELITechGroup) Test description: Targets: RdRp E, N

Leung⁵ (China) Cohort study	N: 62 Age: Mean 42 (SD: 17.1) years Gender: 36 females Inclusion: Patients admitted to Prince of Wales Hospital in Hong Kong from February to March 2020 (not all admitted patients COVID-19 confirmed) Symptomatic vs Asymptomatic: NR	Sample Site: Saliva with coughing Method of collection: Patients asked to cough and clear their throat before spitting into a container containing 3 mL viral transport medium Test Name: TIB Molbiol primer/probe set on the ABI 7900 real-time PCR Test description: Target: E gene	Sample Site: NP swab Method of collection: Collected by nursing staff using flocked swab in container with 3 mL viral transport medium Test Name: Same as index test Test description: Same as index test
Iwasaki⁶ (Japan) Cohort study	N: 76 Age: Median 66 (range 23-106) Gender: NR Inclusion: Patients suspicious of having COVID-19 and those with a diagnosis* of COVID-19. *time since symptom onset <10 days Symptomatic vs Asymptomatic: All symptomatic	Sample Site: Saliva without coughing Method of collection: Patients asked to spit into sterile PP Screw cup 50 Test Name: Detection of Pathogen 2019-nCoV 2019 (Japan) primer/probe set using QIAamp Viral RNA Mini Kit/One-Step Real-Time PCR System/tepOnePlus Real Time PCR	Sample Site: NP swab Method of collection: Swab passed through nostril to the posterior nasopharynx and removed while rotating it Test Name: Same as index test

Williams ⁷ (Australia) Case Control	N: 89 Age: NR Gender: NR Inclusion: Patients tested at COVID-19 screening clinic; 600+ patients screened; patients with + NPS test and additional 50 random negative patients included Symptomatic vs Asymptomatic: NR	Sample Site: Saliva without coughing Method of collection: Patients asked to pool saliva in their mouths for 1-2 minutes and then gently spit 1-2 mL of saliva into a 25 mL collection pot Test Name: AusDiagnostics coronavirus typing [8-well] assay Test description: NR	Sample Site: NP swab Method of collection: NR Test Name: NR
McCormick-Baw ⁸ (USA) Cohort Study	N: 156 Age: Mean: 47.8 Gender: 66 females Inclusion: Patients in ED with suspected COVID-19 or randomly selected in the hospital COVID-19 unit from patients not requiring mechanical ventilation Symptomatic vs Asymptomatic: NR ** ED and COVID ward patients, uncertain as to onset of symptoms	Sample Site: Saliva without coughing Method of collection: Patients instructed to avoid food, drink, tobacco, and gum for 30 minutes; staff educated on collecting saliva and not sputum Test Name: Cepheid Xpert Xpress SARS-CoV-2 (Sunnyvale, CA) PCR test Test description: Target: E and N2. Positive if both were positive or N2 alone was positive.	Sample Site: NP swab Method of collection: NR Test Name: Same as index test
Hanson ⁹ (USA) Cohort study	N: 354 Age: Mean: 35 (range 18-75 years) Gender: 167 females	Sample Site: Saliva without coughing Method of collection: Patients instructed to pool saliva in their mouths and repeatedly spit into a tube collecting at least 1.5 ml saliva	Sample Site: NP swab Method of collection: Patients asked to tilt their head back 70°; NP flocked, synthetic fiber mini -tip swab inserted by HCW through nares parallel to palate (not upwards) until resistance

	Inclusion: Patients presenting to a drive-through test center with symptoms suggestive of COVID-19 Symptomatic vs Asymptomatic: All symptomatic	Sample Site: Anterior nasal Method of collection: Patients asked to tilt their heads back slightly (20°) and then insert the swab horizontally into their nostril or until resistance was felt, then rotate the swab 3 times and keep it in place for several seconds to absorb secretions, remove the swab from the nostril and repeat the same procedure with the other nostril Test Name: Hologic Aptima SARS-CoV-2 transcription mediated amplification (TMA) assay. Test description: Ct <45 considered positive	met (or distance is equivalent to the distance from the patient's ear to their nostril); swab rotated gently and left in place for several seconds to absorb secretions and then removed while rotating it and immediately placed in sterile tubes containing transport media Test Name: Same as index test
Procop¹⁰ (USA) Cohort study	N: 224 Age: Mean: 44 (range: 18-82) Gender: NR Inclusion: Patients with symptoms suggestive of COVID-19 Symptomatic vs Asymptomatic: All symptomatic	Sample Site: Saliva with coughing Method of collection: Patients instructed to sniff strongly to gather nasal secretions into the oropharynx and then to cough all secretions into a "urine cup" Test Name: CDC 2019 nCoV panel using the ABI 7500 Fast Dx Rt-PCR Test description: NR	Sample Site: NP swab Method of collection: HCW-collected Test Name: Same as index test

Yokota¹¹ (Japan) Cohort study	N: 161 contact tracing (CT) cohort and 1763 airport quarantine (AQ) cohort Age: CT cohort mean 44.9 (range 19-70) and AQ mean 33.5 (range 19-70) Gender: CT 26 females, AQ: 832 females Inclusion: CT: asymptomatic close contacts of confirmed COVID-19 cases. AQ: asymptomatic travelers arriving at Tokyo or Kansai international airports. Symptomatic vs Asymptomatic: All asymptomatic	Sample Site: Saliva without coughing Method of collection: Patients asked to funnel their saliva into a container Test Name: ABI 7500 Real-time PCR System Test description: NR	Sample Site: NP swab Method of collection: FLOQSwabs Test Name: Same as index test
Pham J.¹² (USA) Cohort study	N: 35 Age: NR Gender: NR Inclusion: Clinical sample sets from symptomatic patients suspected of having COVID-19 who had NP, OP and MT swabs Symptomatic vs Asymptomatic: All symptomatic	Sample Site: MT Method of collection: MT swab collected first by inserting swab into the subjects' nostril past the inferior turbinate, twisting the swab in the mid turbinate area for 3 to 5 seconds and placing the swab into a tube of STM Sample Site: OP Method of collection: OP swab samples collected immediately following MT sample collection by swabbing the posterior pharynx for 3-5 seconds and placing the swab into specimen tube containing STM; samples frozen and shipped to Hologic for testing	Sample Site: NP swab Method of collection: NP swabs collected using either BD Universal Viral Transport Nasopharyngeal swab and Universal Viral Transport Medium (VTM) (Becton-Dickinson, San Diego, CA) or Copan Minitip flocced swab and VTM

		Test Name: Fusion SARS CoV-2 RT-PCR assay Test description: NR	
Vermeiren ¹³ (Canada) Cohort study	N: 94 Age: NR Gender: NR Inclusion: COVID-19 symptomatic inpatients, outpatients, and ED patients across five hospitals sampled with both collection systems Symptomatic vs Asymptomatic: All symptomatic	Sample Site: MT Method of collection: Flocked regular nylon tip swab preserved in liquid Amies (ESwab collection system) Test Name: BD Max Rt-PCR Test description:	Sample Site: NP Method of collection: NP sampling technique using FLOQSwab added to universal transport medium (UTM) collection system
McCulloch DJ ¹⁴ (USA) Cohort	N: 185 Age: NR Gender: NR Inclusion: Symptomatic outpatients testing (SARS-CoV-2)-positive and symptomatic HCWs presenting to drive-through clinics Symptomatic vs Asymptomatic: All symptomatic	Sample Site: MT (self) Method of collection: Patients provided with self-collection kit with instructions Test Name: CDC 2019 nCoV panel using the Real-time ABI 7500 instrument Test description: Target genes: N1, N2	Sample Site: NP swab Method of collection: HCW-collected
Patel ¹⁵ (USA)	N: 270 Age: median 40 years (IQR, 24–56)	Sample Site: OP Method of collection: NR	Sample Site: NP Method of collection: NR

Cohort	Gender: 120 females Inclusion: Swabs collected with median of 2 days after symptom onset; if more than 1 sample collected from the same patient, the earliest one used Symptomatic vs Asymptomatic: All symptomatic	Test Name: CDC 2019 nCoV panel Test description: Detects N1, N2, and N3 (nucleocapsid gene); considered positive if Ct <40, or negative if all three genes not identified after 40 cycles	
Tu YP¹⁶ (USA) Cohort	N: 350 Age: NR Gender: NR Inclusion: Patients with symptoms indicative of upper respiratory infection seen in any one of five ambulatory clinics in the Puget Sound region of Washington Symptomatic vs Asymptomatic: All symptomatic	Patients provided instructions and asked to collect tongue, nasal, and mid-turbinate samples, in that order Sample Site: AN swab (self) Method of collection: Gently insert the swab in a vertical position into one nasal passage until there is gentle resistance; leave the swab in place for 10-15 seconds, rotating it; and then repeat the procedure on the other side with the same swab Sample Site: Tongue swab (self) Method of collection: Extend the tongue, and firmly but gently brush the swab along the length of the anterior 2/3rd of the dorsum of the tongue for 10 seconds	Sample Site: NP swan Method of collection: HCW-collected after self-collected swabs

		Sample Site: MT (self) Method of collection: Insert swab in the horizontal position until gentle resistance is met; leave swab in for 10-15 seconds on each side, rotating the swab; and repeat in the other nostril with the same swab Test Name: Not reported. Samples were sent to a reference laboratory for RT-qPCR testing	
Wang X¹⁷ (China) Cohort	N: 192 Age: 49 (IQR: 36 to 61) Gender: 92 females Inclusion: Outpatients presenting with symptoms of COVID-19 Symptomatic vs Asymptomatic: All symptomatic	Sample Site: OP Method of collection: NR Test Name: Tianlong Gentier 96E real-time PCR Test description: Target genes: orf1b and N genes	Sample Site: NP swab Method of collection: HCW-collected
LeBlanc¹⁸ (Canada) Cohort	N: 190 Age: NR Gender: NR Inclusion: Assessment centers, prioritizing areas with suspected community spread of SARS-CoV-2	Sample Site: combined OP/AN swab Method of collection: Insert Aptima Multitest swab in OP first and then insert it in each anterior nares and rotate it for a few times; used 2.9 mL of Specimen Transport Medium. HCW-collected.	Sample Site: NP swab Method of collection: HCW-collected. Collected using a flocked NP swab in 3 mL Universal transport medium TM (Copan Diagnostics Inc.)

	Symptomatic vs Asymptomatic: All symptomatic	Test Name: Cobas 6800 system (Roche Diagnostics)	
Péré ¹⁹ (France) Cohort	N: 44 Age: median 63 (range 18-94) Gender: 21 females Inclusion: Hospitalized patients suspected of having COVID-19 Symptomatic vs Asymptomatic: All symptomatic	Sample site: MT swab Method of collection: nasal swab (Copan Transystem, Copan, Brescia, Italy) inserted in the nostril until it hit an obstacle (the inferior concha), rotated five times, and removed. Test: Allplex 2019-nCoV assay (Seegene, Seoul, Korea)	Sample site: NP swab Method of collection: NP swab (Xpert nasopharyngeal sample collection kit, Cepheid, Sunnyvale, CA, USA) inserted in the nostril until it hit an obstacle (the back of the nasopharyngeal cavity), rotated five times, and removed. Test: Allplex 2019-nCoV assay (Seegene, Seoul, Korea)
Vlek ²⁰ (the Netherlands) Cohort	N: 107 Age: median 34 (range 19-63) Inclusion: Symptomatic healthcare workers from a general hospital Symptomatic vs Asymptomatic: All symptomatic, samples collected between 24-48 hours after symptom onset	Sample Site: OP/AN swab Method of collection: Swabbing the rear wall of the oropharynx and the lower nasal cavity using the same swab. Regular swabs with flocked nylon fiber tip in 1 ml liquid Amies medium (Eswab Collection System, Copan, Italy). Test Name: Magnapure MP24 total NA kit/ ABI Prism 7000 Sequence Detection System Test Description: Target was E gene. Ct value of 40 as cutoff.	Sample Site: NP swab Method of collection: swab inserted in one nostril until reaching the back of the nasopharyngeal cavity and rotated before removal. An ultra-thin applicator swab with flocked nylon fiber tip in 1 ml liquid Amies medium was used (Eswab Collection system, Copan, Italy).
Author (Country)	Patient Selection	Index Test	Reference Standard

Reference standard other than NPS			
Skolimowska ²¹ (England) Cohort study	N: 132 Age: Median: 39 (IQR: 30-51) Gender: 89 females Inclusion: Symptomatic (acute <7 days) HCW and household contacts presenting to outpatient clinic in London between 28 April and 7 May 2020. Disease Severity: Mild (outpatient) Symptomatic vs Asymptomatic: All symptomatic	Sample Site: Saliva without coughing Method of collection: The patients were asked to spit, without preceding cough, into a container that already contained 4.3 mL of Cobas PCR medium. Self vs HCW: Self Test Name: One of the following RT-PCR assays: Roche, AusDiagnostics, ThermoFisher and Abbott Test description: AusDiagnostics: Targeting open reading frame (ORF) 1ab and 8	Sample Site: OP/NP swabs Method of collection: HCW swabbing of both sides of the oropharynx, then nasopharynx, then collection in 4.3 mL of Roche Cobas PCR medium Test Name: Same as index test Test description: Same as index test
Moreno-Contreras ²² (Mexico) Cohort study	N: 253 Age: Median 41 ±14.4 Gender: 137 females Inclusion: Patients with 2 or more symptoms related to COVID-19; all outpatients except 3 inpatients. Symptomatic vs Asymptomatic: All symptomatic	Sample Site: Saliva without cough Method of collection: Self collected by patients who were asked to spit on several occasions into sterile urine cups until collecting roughly 2-3 ml of saliva. Test Name: 2019 nCoV panel QIAamp Viral RNA Mini Kit/StepOnePlus Real-Time PCR System Test description: Samples with Ct value equal or less than 38 classified as positive	2 Reference standards: Initially, OP and NP swabs collected but ran out of swabs so switched to OP swabs only Sample Site: OP and NP swabs Method of collection: NR Test Name: Same as index test Sample Site: OP swab Method of collection: Collected then placed in viral transport medium

			Test Name: Same as index test
Pasomsub ²³ (Thailand) Cohort study	N: 200 Age: median: 36 (IQR: 28-48) year Gender: 131 females Inclusion: Patients presenting to the hospital with clinical suspicion of COVID-19 based on fever or respiratory symptoms in addition to exposure Symptomatic vs Asymptomatic: All symptomatic	Sample Site: Saliva without coughing Method of collection: Patients asked to provide saliva sample, without coughing, in sputum collection container containing UTM Test Name: Sansure SARS-CoV-2 Nucleic Acid Diagnostic Kit using the CFX96 Real-Time Detection System (BioRad) Test description: Target genes: ORF1ab and N gene; positive if Ct value for both targets below 38	Sample Site: NP/OP swabs Method of collection: NR Test Name: NR
Guclu ²⁴ (Turkey) Cohort study	N: 64 Age: Mean: 51.04 ±17.9 years Gender: 27 females Inclusion: Patients presenting to the ED of Sakarya University Training and Research Hospital with COVID-19 symptoms Symptomatic vs Asymptomatic: All symptomatic	Sample Site: Saliva without cough Method of collection: Patients asked to place saliva in sterile dry container and then close it Test Name: Genesis T-PCR SARS-CoV-2 Test description: NR	Sample Site: NP/OP swab Method of collection: Dacron- flocked swab inserted into posterior oropharynx and rotated 2-3 seconds; same swab then inserted through nostrils with rotational movement until the nasopharynx was reached and swab then rotated for 2-3 seconds and removed Test Name: Same as index test
Byrne ²⁵ (UK) Cohort study	N: 110 Age: NR Gender: 61 females	Sample Site: Saliva without coughing Method of collection: Patients asked to funnel their saliva into a container	Sample Site: AN/OP swabs Method of collection: HCW-collected Test Name: Same as index test

	Inclusion: Patients presenting to ED Symptomatic vs Asymptomatic: All symptomatic	Test Name: Genesigal R-Time Coronavirus COVID-19 PCR Test description: NR	
Vaz ²⁶ (Brazil) Cohort study	N: 155 Age: median: 40 (IQR: 33–48.5) Gender: 103 females Inclusion: HCW at C-Hupes presenting with signs and symptoms of COVID-19 and patients on COVID-19 ward Symptomatic vs Asymptomatic: All symptomatic	Sample Site: Saliva without coughing Method of collection: Patients asked to spit repeatedly into a container until 2 mL was collected and to avoid adding pharyngeal or lower respiratory tract secretions Test Name: Applied Biosystems 7500 Real Time PCR. BIOMOL OneStep/ COVID-19 Kit. Test description: Gene targets: RdRp and E genes	Sample Site: NP/OP swabs Method of collection: NP swabs: FLOQSwabs Test Name: BIOMOL OneStep/ COVID-19 Kit
Wehrhahn ²⁷ (Australia) Cohort	N: 236 Age: 40 (range 9–81) Gender: 143 females Inclusion: Patients presenting for SARS-CoV-2 testing at dedicated COVID-19 collection rooms at two sites during a period of one week in March 2020 Symptomatic vs Asymptomatic: NR	Sample Site: AN swab (self) Method of collection: NR Sample Site: OP swab (self) Method of collection: NR Test Name: In-house developed TaqMan assay Test description: NR	Sample Site: Any positive including other HCW-collected nasal, NP, or OP swabs Method of collection: NR
Lin C. ²⁸	N: 52	Sample Site: OP swab	Sample Site: Sputum

(China) Cohort	Age: average 57.3 years (SD, 12.5; range, 34–84 years) Gender: 25 females Inclusion: 52 hospitalized patients suspected of having COVID-19 from February 7 to February 16, 2020, at Jinyintan Hospital. Symptomatic vs Asymptomatic: Symptomatic, unclear timing	Method of collection: Swab posterior pharynx and each tonsil area at least 3 times separately using nylon-flocked swab, avoiding tongue, and immediately place swab into a sterile tube, containing 2-3 mL of sterile saline Test Name: ABI 7500 RealTime PCR System	Method of collection: Sputum collected into sterile 50-mL plastic tube. Sputum added to an equal volume of acetylcysteine (10 g/L) and shaken at room temperature for 30 min to liquefy
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Table s4c. Included studies for Recommendation 3

Diagnostic test accuracy studies					
Author (year)	Study Design	Number of Patients	Patient Selection	Index Test	Reference Standard
In symptomatic individuals with URTI or ILI suspected of having COVID-19, should non-invasive specimens be collected by healthcare providers (HCP) vs patients? (i.e., will collection by HCP vs patients affect the diagnostic accuracy of the test)?					
Tu YP. Et al ¹	Prospective Cohort	504	People seen in any one of five ambulatory clinics in the Puget Sound region with symptoms indicative of upper respiratory infection between the dates March 16 and March 21 were eligible for participation. Inclusion criteria included evidence of symptoms suggestive of an upper respiratory illness (subjective and objective fevers, cough, sore throat, fevers, myalgia, or rhinorrhea, indicating higher risk of COVID-19 in this community).	Participants were provided instructions and asked to self-collect tongue, nasal, and MT samples, in that order*. Tongue samples were collected with a nylon flocked swab. Nasal samples were collected with a foam swab bilaterally. MT samples were collected with a nylon flocked swab. For Nasal sampling patients were instructed to: -Gently inserting the swab in the vertical position into one nasal passage until there is gentle resistance -Leaving the swab in place for 10-15 seconds, rotating the swab -Repeating the procedure on the other side with the same swab.	After patient sampling was completed, Nasopharyngeal samples were collected by a health care worker using a polyester tipped swab on a skinny wire using the following technique: For the HC collected NP swab: 1) The swab was passed along the floor of the nose until meeting gentle resistance as the swab touches the posterior pharynx, in the nostril corresponding to the patient's dominant hand 2) Rotate the swab several times and withdraw the swab Three separate analyses were performed: one comparing tongue samples to NP samples, a second comparing nasal samples to NP samples, and a

					third comparing MT samples to NP samples.
Kojima N. et al ²	Cohort	45	Non-Hospitalized persons that tested for COVID-19 in Los Angeles County, California. The patient population includes symptomatic adults older than age 65, those with a chronic disease, first responders, and law enforcement officers that may have been exposed to SARS-CoV-2	Swabbing technique: For self-collected nasal sampling: Testing kit included a flocked swab (CLASSIQSwabs™, Copan Diagnostics, Murrieta, CA, USA) Self-collected supervised nasal sampling instructions were verbal and were as follows: Insert the swab into one nostril to the depth of 3-4 cm, rotate the swab for 5 to 10 seconds, place the swab into the collection tube, invert the tube 3-5 times, and place the capped tube into a collection bag. To not: Other sampling sites were reported in this study. Supervised Oral fluid sampling** showed the highest positive rate among all other samples with 90%. Unsupervised oral fluid sampling showed lower sensitivity with 66% only (for this category some patients were noticed to not be coughing before sampling, which validate the usage of the supervised oral fluid sampling as sputum sampling).	Positive test on any these types of sampling; supervised self-oral fluid, Supervised self-Nasal sampling, Unsupervised self-oral fluid sampling or health care provider Nasopharyngeal sampling
Wehrhahn M. et al ³	Prospective study		Patients presenting for SARS-CoV-2 testing at dedicated COVID-19 collection rooms at two different sites during a	Self-collected Nasal instructions were written and were as follow:	The reference standard is a positive result on either health care collected or self-collected samples. (The health care workers samples were also

			period of one week in March 2020. Insert swab as far as comfortably possible and at least 2-3 cm inside one nostril, rotating the swab 5 times and leaving in place for 5-10 seconds) Self-collected Throat*** (collected from the posterior throat and tonsil areas) Open-cell polyurethane foam swabs were used in all the self-collected sampling sites. Health care worker sampling was done from nasopharyngeal or the throat but the results were reported combined. HC worker used foam swabs for throat sampling and flocked swabs for NP sampling.	nasal and throat, but the results were reported for both sites together). Results reported as number of patients.
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Table s4d. Included studies for Recommendation 4

Diagnostic test accuracy studies					
Author (year)	Study Design	Number of Patients	Patient Selection	Index Test	Reference Standard
In symptomatic individuals with LRTI suspected of having COVID-19, which of the different specimen type (upper vs lower sampling) should be used? (will specimen type (upper vs lower sampling) affect the diagnostic accuracy of the test?)					
Lin C. (2020) ¹	Retrospective Cohort	52 pt (Throat: 52 pt Sputum: 52 pt)	52 Hospitalized patients suspected of having COVID-19 from February 7 to February 16, 2020, at Jinyintan Hospital. Specimens were collected simultaneously from throat and from the swab.	Sputum and Throat Swab from all 52 patients. qRT-PCR that was performed using a 2019-nCoV nucleic acid detection kit according to the manufacturer's protocol (Shanghai ZJ Bio-Tech Co Ltd)	In the study, the researchers assumed the reference standard to be a positive result in from the throat swab or a positive results from the sputum swab. The diagnostic criteria were based on the recommendation by the national institute for viral disease control and Prevention (China) (http://ivdc.chinacdc.cn/kvjz/202001/t20200121_211337.html)
Yang Y. (2020) ²	Case control	213 pt Throat: 63 pt Sputum: 61 pt	213 Guangdong CDC (Center for Disease Control and Prevention) confirmed 2019-nCoV infected patients who were hospitalized in Shenzhen Third People's hospital between Jan 11 and Feb. 03, 2020 were included. Specimens were studied using qRT-PCR	A total of 866 samples from respiratory tracts of the patients including nasal swabs, throat swabs, sputum and BALF were collected upon admission and at various time-points thereafter. Sample collection dates were divided into 0~7, 8~14 and ≥ 15 d.a.o groups. Data from Sputum and Throat (8-14 days after onset) was used.	CDC confirmed 2019- nCoV diagnosis.

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				(quantitative reverse transcription polymerase chain reaction (qRT-PCR) was performed using a China Food and Drug Administration (CFDA) approved commercial kit specific for 2019-nCoV detection (GeneoDX Co., Ltd., Shanghai, China)) The specimens were considered positive if the CT value was ≤ 37.0, and negative if the results were undetermined.	
Gao Y. (2020) ³	Case control	38 pt Sputum: 38 pt Throat: 38 pt	38 COVID-19 hospitalized patients (aged from 15 years to 75 years) in the Second People's Hospital of Fuyang from January 22, 2020 to February 28, 2020 were collected and retrospectively analyzed.	Sputum and throat swabs collected and viral RNAs of SARS-CoV-2 were measured by qRT-PCR (Real-Time Reverse Transcription Polymerase Chain Reaction Assay) Sample collection dates were divided into any time after d.a.o subdivided into 0~7, 8~14 and ≥ 15 d.a.o groups. Data abstracted from the throat and sputum specimens collected at any time after d.a.o Positive results: amplification curve was S-shaped, and Ct value ≤ 37 Criteria for SARS-CoV-2-infection interpretation: First, both of the two genes (ORF1a / b, N) of SARS-CoV-2 in one specimen were positive; Second, Cases with a single positive gene required confirmation by retesting. If it is still positive for the same single target, it is determined to be positive. If not, it is determined to be negative. These diagnostic criteria were based on the recommendation by the National Institute for Viral Disease Control and Prevention of China	Diagnosis of COVID-19 was based on the New Coronavirus Pneumonia Prevention and Control Program (5th edition) published by the National Health Commission of China.

				(http://ivdc.chinacdc.cn/kyjz/202001/t20200121_211337.html).	
Yu F. et al (2020) ⁴	Prospective cohort	127 pt included 76 confirmed 323 samples Throat: 134 samples Sputum: 116 samples	The enrolled 127 subjects included: 54 confirmed cases, 39 suspected cases, 34 patients: screened due to fever or respiratory symptoms but did not meet the diagnostic criteria for suspected cases, which were as follows: a patient with one exposure history and two clinical conditions (a. Fever and/or respiratory symptoms; b. Imaging features of viral pneumonia; c. Normal or low white blood cell count and reduced lymphocyte in the earlier period of onset), or no clear exposure history but meet three clinical conditions [9]. Among the suspected cases, 17 were found not to be COVID-19, and 22 became confirmed cases with SARS-CoV-2 tested positive in respiratory tract samples. As a result, 76 final confirmed patients from whom swabs were taken.	A total of 323 samples from 76 COVID-19 confirmed patients were analyzed by droplet digital PCR (ddPCR) and RT-PCR based two target genes (ORF1ab and N). Throat and sputum swabs were collected. Data from the RT-PCR analysis was used. In this study the available data is for the number of positive samples and not of positive patients. Reaction system and amplification conditions were performed according to the manufacturer's specifications (Shanghai BioGerm Medical Technology Co. LTD, China). The result was considered positive when the Ct values of both target genes were ≤ 38 , negative when they were both > 38 . If only one of the target genes had a Ct value ≤ 38 and the other > 38 , it was interpreted as a single-gene positive.	The diagnostic criteria was that a suspected case with positive RT-PCR assay or viral gene sequencing that was highly homologous with SARS-CoV-2.
Tan W. (2020) ⁵	Prospective cohort	67 pt Nasopharyngeal: 67 pt	All patients hospitalized transferred into two sections of the Chongqing Public Health Medical Center (CPHMC)) ((one for severe patients, another for mild or moderate patients) between January 26 and February 5, 2020, were enrolled in	Nasopharyngeal and Sputum specimens collected and quantitative real-time reverse-transcriptase polymerase chain reaction (qRT-PCR) for the Orf1ab gene was performed with qRT-PCR kit (BGI-Shenzhen, China).	Laboratory-confirmed as having SARS-CoV-2 infection according to WHO interim guidance

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		Sputum: 61 pt	this cohort study, with final follow-up on February 27, 2020. All of them were laboratory confirmed.	The specimens were considered positive if the cycle threshold (Ct) value was ≤ 38 , and negative if the results were undetermined.	
Wang W. et al (2020) ⁶	Case control	205	COVID- 19 Patients with specimens collected based on clinical indications from 3 hospitals in the Hubei and Shandong provinces and Beijing, China, from January 1 through February 17, 2020, were included. . Most of the patients presented with fever, dry cough, and fatigue; 19% of patients had severe illness.	Nasal Swabs, BAL, Sputum samples collected throughout the illness Pharyngeal Swabs collected from most patients 1 to 3 days after hospital admission. Analyzed using rRT-PCR targeting the open reading frame 1ab gene of SARS-CoV-2 as previously described	No reference standard was provided in the study, the subjects had COVID upon enrollemnet in the study, without further information provided. Results were reported as number of samples.
Kojima N. et al, (2020) ⁷	Cohort	45	Non-Hospitalized persons that tested for COVID-19 in Los Angeles County, California. The patient population includes symptomatic adults older than age 65, those with a chronic disease, first responders, and law enforcement officers that may have been exposed to SARS-CoV-2 Positive test on any these types of sampling; supervised self-oral fluid, Supervised self-Nasal sampling, Unsupervised self-oral fluid sampling or health care provider Nasopharyngeal sampling	Supervised self-collected oral fluid* swab specimen: The testing kit included a sterile swab. Patients had written instructions with real time feedback by a health care worker. Patients had to cough deeply 3-5 times collecting any phlegm or secretions in their mouth, rub the swab on both cheeks, above and below the tongue, both gums, and on the hard palate for a total of 20 seconds to ensure the swab was saturated with oral fluid. Nasopharyngeal sampling: Health care worker collected nasopharyngeal swab specimens with the recommended medical technique using	Positive test on any these types of sampling; supervised self-oral fluid, Supervised self-Nasal sampling, Unsupervised self-oral fluid sampling or health care provider Nasopharyngeal sampling

				nasopharyngeal swabs (Becton, Dickinson and Company, Franklin Lakes, NJ, USA).		
Studies informing baseline risk and patients outcome						
Author (year)	Study Design	Number of Patients	Patient Selection	Tests	Outcome	Results
Woelfel R. et al (2020) ⁸	Case		All patients who were treated in a single hospital in Munich, Germany. Patients acquired their infections upon known close contact to an index case, thereby avoiding representational biases due to symptom-based case definitions.	All patients were initially diagnosed by RT-PCR from oro- or nasopharyngeal swab specimens. Both specimen types were collected over the whole clinical course in all patients.	Difference in viral loads between oropharyngeal or nasopharyngeal sampling/	There were no discernible differences in viral loads or detection rates when comparing nasopharyngeal vs. oropharyngeal swabs
Kim J et al (2020) ⁹	Case series	2	First two patients with COVID-19 in south Korea,	Upper respiratory tract (URT) (Nasopharyngeal and oropharyngeal swabs) and lower respiratory specimen (LRT) (sputum) specimens were collected from confirmed patients.	Viral load	The viral load can be detected in URT samples and LRT samples.

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Table s4e. Included studies for Recommendation 5 and 6

Diagnostic Test Accuracy Studies					
Author (year)	Study Design	Number of Patients	Patient Selection	Index Test	Reference Standard
In symptomatic individuals suspected of having COVID-19, should one test vs repeated testing be done for better diagnostic accuracy?					
Ai JW, et al (2020) ¹	multicenter prospective study	53	53 suspected novel coronavirus pneumonia (NCP) patients, among whom 20 were laboratory-confirmed.	Nasopharyngeal swabs were collected from the patients. The epidemiological characteristics, clinical symptoms, laboratory assessments, and computed tomographic (CT) scans were obtained. Pathogen screen were performed including RT-PCR. If the first RT-PCR result was negative, the second nasopharyngeal sample of observing patients would be collected on DAY 3 for RT-PCR test again.	A confirmed case with NCP was defined as a positive SARS-COV-2 nucleotides result by 14 metagenomic sequencing
Ai J et al. (2020) ²	Cohort	315	All suspected patients that were hospitalized in Xiangyang No.1 People's Hospital until Feb 9th, 2020 with a follow up period until Mar 20th, 2020. The suspicion criteria are not mentioned.	Suspected patients had repeat RT-PCR on throat samples with at least 24 hours between tests.	The tests were repeated up to 5 times and patients were considered positive if they tested positive on any of these.

Zhou, F. et al (2020) ³	Retrospective cohort	197	197 cases of COVID-19 discharged from Yichang Central People's Hospital and Yichang Third People's Hospital from Jan 17 to Feb 26, 2020	Throat swab or bronchoalveolar lavage fluid sample were collected from all the suspected patients at admission, and RT-PCR assays were performed at clinical laboratory. If the first RT-PCR result was negative, the second nasopharyngeal sample of observing patients would be collected on DAY 2 for RT-PCR test again.	All cases were confirmed by real-time RT-PCR or chest computer tomography (CT).
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Table s4f. Included studies for Recommendation 7

Test accuracy studies evaluating rapid RT-PCR test vs. standard non-rapid laboratory-based NAAT or composite reference standard when available										
Author	Total Patients	Age	Gender	Patient Characteristics	Rapid Test	Turnaround Time (TAT)	Index Sample Type	Reference Standard	Reference Sample Type	Excluded Results
In symptomatic individuals suspected of having COVID-19, does the use of rapid vs. standard laboratory-based NAAT affect diagnostic accuracy of the test?										
Hogan, C ¹	100	NR	NR	Submitted clinical samples	Accula SARS-CoV2 POCT Test (target N gene)	30 min	NPS in VTM	Stanford Health Care Clinical Virology Laboratory RT-PCR LDT (target E gene)	NPS in VTM	NR
Liotti, F ²	120	NR	NR	Submitted clinical samples	BioFire COVID-19 Test (target ORF1ab and ORF8 genes)	45 min	Nasal Swab, OPS	Quanti COVID-19 Assay (target N1, N2, N3 genes)	Nasal Swab, OPS	NR
Hou, H ³	285	220 patients ≤ 65 years old, 65 patients were >65	126 females	Submitted clinical samples from three medical centers	Cepheid GeneXpert Xpress Assay (target E and N2 genes)	45 min	OPS	Commercially available real-time reverse transcription-PCR (RT-PCR) assays approved by the National Medical Products Administration (NMPA)	OPS	NR
Loeffelholz, M (a) ⁴	99	NR	NR	Convenience sample set to enrich for positive specimen, one site collected samples from symptomatic patients over four days	Cepheid GeneXpert Xpress Assay (target E and N2 genes)	45 min	NPS, combined NPS/OPS, TA, OPS in VTM	New York SARS-CoV-2 Real Time RT-PCR Diagnostic Assay Panel (Modified CDC assay, target N1 and N2 genes) (Hologic Panther Fusion SARS-CoV-2 Assay for discordant results)	NPS, combined NPS/OPS, TA, OPS in VTM	Of total 486 specimen, 1 was invalid, 4 lost due to computer malfunction

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Loeffelholz, M (b) ⁴	88	NR	NR	Convenience sample set to enrich for positive specimen, one site collected samples from symptomatic patients over four days	Cepheid GeneXpert Xpress Assay (target E and N2 genes)	45 min	NPS, combined NPS/OPS, TA, OPS in VTM	Quest SARS-CoV-2 RT-PCR (target N1 and N3 genes) (CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel for discordant results)	NPS, combined NPS/OPS, TA, OPS in VTM	Of total 486 specimen, 1 was invalid, 4 lost due to computer malfunction
Loeffelholz, M (c) ⁴	129	NR	NR	Convenience sample set to enrich for positive specimen, one site collected samples from symptomatic patients over four days	Cepheid GeneXpert Xpress Assay (target E and N2 genes)	45 min	NPS, combined NPS/OPS, TA, OPS in VTM	RealStar SARS-COV-2 RT-PCR (target S and E genes)	NPS, combined NPS/OPS, TA, OPS in VTM	Of total 486 specimen, 1 was invalid, 4 lost due to computer malfunction
Loeffelholz, M (d) ⁴	79	NR	NR	Convenience sample set to enrich for positive specimen, one site collected samples from symptomatic patients over four days	Cepheid GeneXpert Xpress Assay (target E and N2 genes)	45 min	NPS, combined NPS/OPS, TA, OPS in VTM	Allplex 2019-nCoV Assay, GeneFinder COVID-19 plus Realamp Kit (target E, N, RdRp genes)	NPS, combined NPS/OPS, TA, OPS in VTM	Of total 486 specimen, 1 was invalid, 4 lost due to computer malfunction
Loeffelholz, M (e) ⁴	65	NR	NR	Convenience sample set to enrich for positive specimen, one site collected samples from symptomatic patients over four days	Cepheid GeneXpert Xpress Assay (target E and N2 genes)	45 min	NPS, combined NPS/OPS, TA, OPS in VTM	Charite Virology Inhouse (target RdRp gene) (Roche Cobas SARS-CoV-2 Assay when discordant results)	NPS, combined NPS/OPS, TA, OPS in VTM	Of total 486 specimen, 1 was invalid, 4 lost due to computer malfunction
Loeffelholz, M (f) ⁴	18	NR	NR	Convenience sample set to enrich for positive specimen, one site	Cepheid GeneXpert Xpress Assay	45 min	NPS, combined NPS/OPS,	Abbott RealTime SARS-CoV-2 Assay (target N and RdRp genes)	NPS, combined NPS/OPS,	Of total 486 specimen, 1 was invalid, 4 lost due to

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				collected samples from symptomatic patients over four days	(target E and N2 genes)		TA, OPS in VTM		TA, OPS in VTM	computer malfunction
Loeffelholz, M (g) ⁴	3	NR	NR	Convenience sample set to enrich for positive specimen, one site collected samples from symptomatic patients over four days	Cepheid GeneXpert Xpress Assay (target E and N2 genes)	45 min	NPS, combined NPS/OPS, TA, OPS in VTM	Diasorin Simplexa COVID-19 Direct Assay (target ORF1ab and S genes)	NPS, combined NPS/OPS, TA, OPS in VTM	Of total 486 specimen, 1 was invalid, 4 lost due to computer malfunction
Moran, A ⁵	103	NR	NR	Symptomatic inpatient and ambulatory patients	Cepheid GeneXpert Xpress Assay (target E and N2 genes)	45 min	NPS, Nasal Swab	Roche Cobas SARS-CoV-2 Assay (target ORF1ab and E genes)	NPS, Nasal Swab	NR
Stevens, B ⁶	110	NR	NR	Asymptomatic and symptomatic patients	Cepheid GeneXpert Xpress Assay (target E and N2 genes)	45 min	NPS in VTM	Hologic Panther Fusion SARS-CoV-2 Assay (target ORF1ab)	NPS in VTM	6 samples insufficient quantity
Wolters, F ⁷	88	NR	NR	Symptomatic patients	Cepheid GeneXpert Xpress Assay (target E and N2 genes)	45 min	NPS, Mid-turbinate swab, OPS in VTM	RT-PCR (target RdRp and E genes)	NPS, Mid-turbinate swab, OPS in VTM	NR
Visseaux, B (a) ⁸	26	NR	NR	Symptomatic inpatient population	QIAstat-SARS panel (target E and ORF1 genes)	~ 1 hour	23 NPS in VTM, 3 lower respiratory specimen (BAL, tracheal aspirate, bronchial aspirate)	WHO protocol RT-PCR (target E and ORF1 genes)	23 NPS in VTM, 3 lower respiratory specimen (BAL, tracheal aspirate,	NR

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									bronchial aspirate)	
Visseaux, B (b) ⁸	43	NR	NR	Symptomatic inpatient population	QIAstat-SARS panel (target E and ORF1 genes)	~ 1 hour	Dry NPS	WHO protocol RT-PCR (target E and ORF1 genes) (Roche Cobas SARS-CoV-2 Assay when discordant results)	Dry NPS	
Test accuracy studies evaluating rapid isothermal NAAT test vs. standard non-rapid laboratory-based NAAT or composite reference standard when available										
Harrington, A ⁹	524	NR	NR	Symptomatic patients from three emergency departments and two immediate care centers	Abbott ID Now	5-13 min	Nasal swab in VTM	Abbott RealTime SARS-CoV-2 Assay (target N and RdRp genes)	NPS in VTM	NR
Mitchell, S ¹⁰	61	NR	NR	NR	Abbott ID Now	5-13 min	NPS in VTM	CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel, New York SARS-CoV-2 Real Time RT-PCR Diagnostic Assay Panel (Modified CDC assay, target N1 and N2 genes)	NPS in VTM	NR
Moore, M ¹¹	200	Mean: 50 (±17 SD)	108 female	Symptomatic adult and pediatric outpatients, emergency department patients, and inpatients	Abbott ID Now	5-13 min	NPS in VTM	Abbott RealTime SARS-CoV-2 Assay and (target N and RdRp genes), Modified CDC Assay (target N1 and N2 genes), Abbott ID Now *Minimum 2/3 tests agree	NPS in VTM	2 invalid on Abbott RealTime, 2 invalid on CDC
Thwe, P (a) ¹²	129	NR	NR	Symptomatic patients in the emergency	Abbott ID Now	5-13 min	Dry Nasal Swab	Hologic Panther Fusion SARS-CoV-2 Assay (target ORF1ab)	NPS in VTM	NR

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				department and inpatient						
Thwe, P (b) ¹²	10	NR	NR	Symptomatic patients in the emergency department and inpatient	Abbott ID Now	5-13 min	Dry Nasal Swab	Laboratory Derived Test (target E and ORF8 genes)	NPS in VTM	NR
Thwe, P (c) ¹²	22	NR	NR	Symptomatic patients in the emergency department and inpatient	Abbott ID Now	5-13 min	Dry Nasal Swab	Abbott RealTime SARS-CoV-2 Assay and (target N and RdRp genes)	NPS in VTM	NR
McDonald, S ¹³	585	Mean: 53 (±19 SD)	NR	Symptomatic patients in the emergency department. Only negative samples received reference standard (positive patients presumed to be true positive)	Abbott ID Now	5-13 min	Dry Nasal Swab	Abbott RealTime SARS-CoV-2 Assay and (target N and RdRp genes)	NPS in VTM	6 invalid results
Eckel, F ¹⁴	173	Median: 80 (IQR: 70-85)	65 female	Symptomatic patients admitted to the hospital	Variplex SARS CoV-2 test system, Amplex Diagnostics	35 min	Dry NPS, Dry OPS	Laboratory Developed RT-PCR	Dry NPS, Dry OPS	NR
Direct comparative test accuracy studies evaluating rapid RT-PCR test and standard non-rapid laboratory-based NAAT vs. composite reference standard										
Smith, E ¹⁵	150	NR	NR	Symptomatic patient samples	BioFire COVID-19 Test (target ORF1ab and ORF8 genes)	45 min	NPS in VTM	Hologic Panther Fusion SARS-CoV-2 Assay (target ORF1ab gene), Hologic Aptima SARS-CoV-2 Assay (NAAT, target ORF1ab gene), and BioFire COVID-19 (target ORF1ab, ORF8 genes)	NPS in VTM	1 invalid Hologic Panther Fusion result

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								*Minimum 2/3 tests agree		
Lieberman, J ¹⁶	26	NR	NR	Submitted clinical samples	Cepheid GeneXpert Xpress Assay (target E and N2 genes)	45 min	NPS in VTM	UW Laboratory Derived Test (target N2 and E genes), Roche Cobas SARS-CoV-2 Assay (target ORF1ab and E genes), Cepheid GeneXpert Xpress Assay (target E and N2 genes) *Minimum 2/3 tests agree	NPS in VTM	2 patients tested while recovering from covid excluded
Smithgall, M ¹⁷	113	Average age of positive patients 64.9, Average age of negative patients 42.6	52 female	Submitted clinical samples	Cepheid GeneXpert Xpress Assay (target E and N2 genes)	45 min	NPS in VTM	Roche Cobas SARS-CoV-2 Assay (target ORF1ab and E genes), Cepheid GeneXpert Xpress Assay (target E and N2 genes), and Abbott ID Now *Minimum 2/3 tests agree	NPS in VTM	NR
Zhen, W ¹⁸	108	NR	NR	Symptomatic patients	Cepheid GeneXpert Xpress Assay (target E and N2 genes)	45 min	NPS in VTM, Dry Nasal Swab, Midturbinate Swab, Nasal Aspirate	Hologic Panther Fusion SARS-CoV-2 Assay (target ORF1ab), Cepheid GeneXpert Xpress Assay (target E and N2 genes), GenMark ePlex SARS-CoV-2 Assay (target N gene), Abbott ID Now *Minimum 2/4 tests agree	NPS in VTM, Dry Nasal Swab, Midturbinate Swab, Nasal Aspirate	1 Abbott ID Now invalid result
Direct comparative test accuracy studies evaluating rapid isothermal NAAT test and standard non-rapid laboratory-based NAAT vs. composite reference standard										
Bulterys, P ¹⁹	80	NR	NR	Symptomatic patient samples	Atila iAMP COVID-19	~ 1hour	NPS in VTM	Stanford Health Care Clinical Virology	NPS in VTM	1 invalid Atila result

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					(target N and ORF1ab genes)			Laboratory RT-PCR LDT (target E gene), Altona RealStar SARS-CoV-2 RT-PCR (target E and S genes), CDC 2019-nCoV Real-Time RT-PCR (target N1 and N2 genes), Atila iAMP COVID-19 (target N and ORF1ab genes) *Minimum 2/4 tests agree		
Moore, M ²⁰	200	Mean: 50 (±17 SD)	108 female	Symptomatic adult and pediatric outpatients, emergency department patients, and inpatients	Abbott ID Now	5-13 min	NPS in VTM	Abbott RealTime SARS-CoV-2 Assay and (target N and RdRp genes), Modified CDC Assay (target N1 and N2 genes), Abbott ID Now *Minimum 2/3 tests agree	NPS in VTM	2 invalid on Abbott RealTime, 2 invalid on CDC
Smithgall, M ¹⁷	113	Positive samples average = 65 years, Negative samples average = 43 years. Adult age range 23-101.	NR	Submitted clinical samples. Included 111 adult patients (range 23-101 years old) and 2 pediatric patients (age 1 day and 5 days).	Abbott ID Now	5-13 min	NPS in VTM	Roche Cobas SARS-CoV-2 Assay (target ORF1ab and E genes), Cepheid GeneXpert Xpress Assay (target E and N2 genes), and Abbott ID Now *Minimum 2/3 tests agree	NPS in VTM	NR
Zhen, W ¹⁸	108	NR	NR	Symptomatic patients	Abbott ID Now	5-13 min	NPS in VTM, Dry nasal Swab, Throat Swab	Hologic Panther Fusion SARS-CoV-2 Assay (target ORF1ab), Cepheid GeneXpert Xpress Assay (target E	NPS in VTM, Dry nasal Swab, Throat Swab	1 Abbott ID Now invalid result

								and N2 genes), GenMark ePlex SARS-CoV-2 Assay (target N gene), Abbott ID Now *Minimum 2/4 tests agree		
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Table s4g. Included studies for Recommendation 8

In asymptomatic individuals who may have been exposed to COVID-19, should nucleic acid amplification testing vs. no testing be done to diagnose COVID19 (to guide decisions about quarantine and contact tracing)?				
Author (year)	Study Design	Patient Selection/Tests	Outcome	Results
Studies informing baseline risk and patient outcome				
Sutton, D et al. (2020) ¹	Prospective cohort	Between March 22 and April 4, 2020, 215 pregnant women delivered infants at New York–Presbyterian Allen Hospital and Columbia University Irving Medical Center. All women were screened on admission for symptoms of COVID-19. 4 symptomatic patients had COVID-19; 211 were without symptoms and were afebrile on admission. SARS-CoV-2 PCR was performed on nasopharyngeal swabs from 210 of the 211 asymptomatic women (99.5%).	Percentage of asymptomatic patients diagnosed	29 (14%) were positive for SARS-CoV-2. Thus, 29 of the 33 patients who were positive for SARS-CoV-2 at admission (88%) had no symptoms of COVID-19 at presentation.
			Clinical course of asymptomatic patients	In 3/29 (10%) fever developed before postpartum discharge (median length of stay, 2 days). 2 of these received antibiotics for presumed endometritis (although 1 did not have localizing symptoms), and 1 patient was presumed to be febrile due to COVID-19 and received supportive care. 1 patient with initially swab negative results for SARS-CoV-2 on admission became symptomatic postpartum; repeat SARS-CoV-2 testing 3 days after the initial test was positive.
Kimball A et al. (2020) ²	Prospective cohort	On March 13, CDC performed symptom assessment and SARS-CoV-2 testing on 76 (93%) of 82 residents in a skilled nursing facility in King County, Washington. Residents were categorized as asymptomatic or symptomatic at the time of testing, based on the absence or presence of fever, cough, shortness of breath, or other symptoms on the day of testing or during the preceding 14 days. SARS-CoV-2 PCR was performed on nasopharyngeal swabs.	Percentage of asymptomatic patients diagnosed	Among the 76 tested residents, 53 were asymptomatic (70%). 23 (30%) had positive test results for COVID-19; among the 23 residents with positive test results, 10 (44%) were symptomatic, and 13 (57%) asymptomatic. The prevalence of COVID-19 in asymptomatic individuals in this skilled nursing facility was 13/53 (25%).

Supplementary Materials

Hu Z. et al. (2020) ³	Retrospective observational study	Epidemiological investigations were conducted among close contacts of COVID-19 patients (or suspected patients) in Nanjing, Jiangsu Province, China, from January 28 to February 9, 2020, both in a clinic and in the community. Asymptomatic carriers were laboratory-confirmed positive by testing for SARS-CoV-2 nucleic acid in pharyngeal swabs. Clinical records, laboratory assessments, and chest CT scans were reviewed. The median communicable period was defined as the interval from the first day of positive nucleic acid tests to the first day of continuous negative tests.	Clinical course of asymptomatic patients	subjects were studied, none of whom had any obvious symptoms before nucleic acid screening. 5 (21%) developed symptoms (fever, cough, fatigue, etc.) during hospitalization. 12 (50%) showed ground-glass infiltrates on CT chest and 5 (21%) had stripe shadowing in the lungs. The remaining 7 (29%) had normal CT findings and no symptoms during hospitalization; these 7 cases were younger (median age: 14.0 years; $P = 0.012$) than the rest. None developed severe COVID-19 pneumonia or died.
			Median communicable period	9.5 days (up to 21 days)
Gostic K et al. (2020) ⁴	Modeling	Tracked ways in which infected travelers can be detected by screening (fever screen, or risk factor screen at arrival or departure). Additionally tracked ways in which infected travelers can be missed (i.e., missed given fever present, missed given exposure risk present, missed given both present, or missed given undetectable). A gamma distribution was used to model individual incubation times. This was chosen over the Weibull and lognormal distribution for ease of interpretation (gamma shape and scale parameters can be easily transformed to mean and standard deviation)	Upper boundary of subclinical cases	50%: Data from active surveillance of passengers quarantined on a cruise ship off the coast of Japan, and passengers of repatriation flights show that 50–70% of cases are asymptomatic at the time of diagnosis. Due to intensive monitoring, cases in cruise ship passengers will be detected earlier than usual in the course of infection. 50% subclinical cases is a reasonable upper bound.
			Lower boundary of subclinical cases	5%: Estimated from clinical data (where severe cases are likely overrepresented), even among clinically attended cases, 2–15% lack fever or cough, and would be undetectable by symptom screening (Chan et al., 2020; Chen et al., 2020; The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team, 2020; Huang et al., 2020).
			Mean incubation period	5.5 days with a plausible range of 4.5–6.5 days

Supplementary Materials

Wei W. et al. (2020) ⁵	Retrospective observational study	Investigation of COVID-19 cases in Singapore.	2) Number of locally acquired cases at the time in Singapore. 3) Number of possible clusters infected by pre-symptomatic carriers/number of locally acquired at the time in Singapore.	2) At the time, 157 were locally acquired in Singapore 3) 10/157 (6.4%) were identified as caused by pre-symptomatic carriers.
Bi Q. et al (2020) ⁶	Cohort study	1268 Close contacts confirmed before February 9 th of 244 confirmed cases (identified by the Shenzhen CDC between Jan 14, 2020 and Feb 12, 2020) with at least one close contact. 95% of close contacts were followed for at least 12 days. Suspected cases and close contacts were tested for SARSCoV-2 by PCR of nasal swabs at 28 qualified local hospitals, 10 district level CDCs, and 2 third party testing organizations, with final confirmation performed at the Guangdong CDC or Shenzhen CDC (Text S1).	Percentage of positive among contacts. Close contacts were defined as those who lived in the same apartment, shared a meal, traveled, or socially interacted with an index case during the period starting two days before symptom onset.	98/1286 tested positive (7.6%) 17/98 were asymptomatic.
Lu J. et al (2020) ⁷	Retrospective observational	91 customers (83 customers and 8 staff members) who were at a Restaurant in Guangzhou, China that had an outbreak among its customers. None of these patients was symptomatic at the time.	This study reports the number of infected customers among all customers and staff who went to the restaurant during Jan 24.	10/91 (11%) 3 families: A (4 patients) B (3 patients, C (3patients) None of the restaurant staffs got infected.
Folgueira M.D. et al (2020) ⁸	Cohort study	2085 hospital employee from a total of 6800 employees of the Hospital Universitario 12 de Octubre, in Madrid, Spain 2085 (30,6 %) were tested during the period 1-29 March 2020, some of them repeatedly (2286 total samples).	The health care workers were divided into 3 groups based on their risk level: High risk exposure areas: The emergency room, areas with concentrated COVID19	791/2085 (38%) tested positive. High risk: 43.6% Moderate risk: 40.96% Low risk: 41.92%

			patients, ICU, and Anesthesia. Medium risk Areas: Surgery, Oncology, Hematology, Radiology, Ob/Gyn, Pediatrics, Medical areas nonCOVID19 related and outpatient areas. Low risk exposure areas: Laboratory, Pharmacy, Kitchen and administrative personnel.	
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Table s4h. Included studies for Recommendations 9 and 10

Studies informing baseline risk and patient outcome				
Author (year)	Study Design	Patient Selection/Tests	Outcome	Results
In asymptomatic individuals, should nucleic acid amplification testing vs. no testing be done on admission to the hospital to diagnose COVID-19 (to guide isolation, PPE use and contact tracing)?				
Gudbjartsson D.F. et al (2020) ¹	Cohort study	Population screening: 10,797 residents of Iceland who were symptom-free or who had mild symptoms of the common cold (most of them living in Reykjavik, the capital of Iceland.) Random sampling 2283 randomly chosen Icelanders between the ages 20 and 70 years to participate through a telephone text message sent between March 31 and April 1. Nasopharyngeal and oropharyngeal samples were collected and were combined into a single tube for each participant before RNA isolation.	Positive among population screening. Positive among random sampling screening.	87/10,797 (0.8%) 13/2283 (0.6%) (this study also reports the prevalence of COOVDI19 among symptomatic patients 1221/9199 (13.3%))

References

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Table s4i. Included studies for Recommendation 13

Outcome of COVID-19 in Cancer versus No Cancer				
Study	Inclusion/Exclusion Criteria	Cancer Group	No Cancer Group	Cancer vs no cancer
In asymptomatic patients with cancer, should testing vs. no testing for SARS-CoV-2 be performed before initiation of immunosuppressive therapy?				
Hematologic Malignancy				
He 2020 ¹ Union Hospital and Tongji Hospital Wuhan, China Retrospective observational Time: From 1/23 to 2/14	Inclusion: Patients hospitalized with hematological cancer and hospitalized health care providers with COVID-19 Exclusion: NR COVID-19 Diagnosis: Lung CT scans followed by PCR	n = 13 Age: M 35 (IQR 23-53) Gender: 7 males Diseases: 4 AML, 5 ALL, 3 MM, 8 MDS, 18 NHL Treatments: 6 chemotherapy, 3 allotransplant, 1 targeted drug, 2 immunosuppression, 2 proteasome inhibitor Comorbidities: NR COVID-19 severity: 0 mild, 4 common, 4 severe, 5 critical	n = 11 Age: M 32 (IQR 28-36) Gender: 2 males Comorbidities: NR COVID-19 severity: 3 mild, 8 common, 0 severe, 0 critical	Death: 8 (73%) vs 0 (0%) Hospitalization: 13 vs 11 Cured: 5 vs 8 Improved 0 vs 3
Sanchez-Pina 2020 ² Hospital Universitario 12 de Octubre Madrid, Spain Retrospective cohort Time: From 3/7 to 4/7	Inclusion: all symptomatic hematological malignancy patients who tested positive. The control group were selected from the overall COVID-19 patients who were admitted or presented to the emergency room, they were matched in terms of age and severity index values on admission. Diagnosis: Nasopharyngeal swab PCR	n = 39 Age: M 64.7 (range 36-88) Gender: 23 males Diseases: Lymphoma 12, MM 12, CLL 6, acute leukemia and MDS 5, MPN 2, histocytosis 2 Treatments: active treatment 24 (chemotherapy 4, targeted 5, ITK inhibitor 2, proteasome inhibitor 7, monoclonal antibody 5, IMiDs 3, steroids 12), 5 had transplantation or CAR-T within the last year Comorbidities: 19 HTN, 7 DM, 6 cardiac disease, 2 COPD, 4 thrombosis	n = 53 Age: M 65.7 (range 41-89) Gender: 33 males Comorbidities: 26 HTN, 11 DM, 8 cardiac, 9 COPD, 1 thrombosis COVID-19 severity: 6 mild, 18 moderate, 29 severe	Death: 14 (36%) vs 7 (13%) ICU: 1 vs 7 Outpatient treatment: 5 vs 7

		COVID-19 severity: 5 mild, 2 moderate, 18 severe		
Shah 2020 ³ King's College Hospital, UK Case Control Time: NR	Inclusion: Hospitalised COVID-19 patients Exclusion: NR COVID-19 Diagnosis: NR	n = 80 Age: 69.4 (SD: 15.7) Gender: 52 (65.0) Diseases: 14 MM, 14 MGUS, 10 CLL, 8 high grade lymphoma, 5 ALL, 2 follicular lymphoma, 9 others plasma cell neoplasm. Treatments: 6 allotransplant, 3 auto-transplant, 1 CAR-T-cell Comorbidities: 9 DM, 21 HTN, 5 ischemic heart disease, 3 COPD COVID-19 severity: 23 mild, 22 moderate, 35 severe	n = 1,115 Age: median 71 (57- 82) Gender: Males 682 (57.7) Comorbidities: 399 DM, 590 HTN, 147 Ischemic heart disease, COPD 103 COVID-19 severity:	Death: 31 (39%) vs 223 (20%) Hospitalization: 80 vs 1115 Supplemental O2: 496 vs. 38 Association of hematological malignancy with mortality compared to non-cancer patients aHR 1.74 (95%: 1.12-2.71) , adjusted for age and gender. Mortality by cancer type Lymphoid HR: 1.75 (95%: 1.07, 2.87 P: 0.026) Myeloid HR: 1.70 (95%: 0.70, 4.13 P: 0.0244)
Yigenoglu 2020 ⁴ Turkey Retrospective observational Time: From 3/11 to 6/22	Inclusion: All COVID-19 patients with hematological malignancy and age, gender and comorbidity matched COVID-19 patients without cancer (1:1 ratio)	n = 740 Age: M 56 (range 18-94) Gender: 397 males Diseases: HL 27, NHL 223, CLL 54, MM 77, ALL 18, MPN 116, CML 30, MDS 146, AML 40, hairy cell leukemia 9	n = 740 Age: M 56 (range 18-87) Gender: 400 males	Death: 102 (14%) vs 50 (7%) ICU: 140 vs 85 Hospitalization: 452 vs 409 MV: 102 vs 53

	Exclusion: NR COVID-19 Diagnosis: Nasopharyngeal PCR	Treatments: NR Comorbidities: 379 HTN, 198 DM, 156 CVD, 175 respiratory diseases COVID-19 severity: 115 severe, 98 critical	Comorbidities: 378 HTN, 198 DM, 135 CVD, 164 respiratory diseases COVID-19 severity: 96 severe, 49 critical	
Solid Tumors				
Miyashita 2020 ⁵ Mount Sinai Health System New York, USA Retrospective observational Time: From 3/1 to 4/6	Inclusion: Cancer patients with COVID-19	n = 334 Age: 53 <51, 50 < 84 <66, 65 < 143 < 81, 54 >80 Gender: NR Diseases: 57 breast, 56 prostate, 23 lung, 18 urothelial, 16 colon Treatments: NR Comorbidities: NR COVID-19 severity: NR	n = 5354 Age: 2035 <51, 50 < 1557 <66, 65 < 1191 < 81, 571 >80 Gender: NR Comorbidities: NR COVID-19 severity: NR	Death 37 (11%) vs 518 (10%) age <51 3 vs 23 (OR 5.0, 1.5-16.2) age 50 < 4 vs 117 <66 (OR 0.6, 0.2-1.7) age 65 < 15 vs 173 < 81 (OR 0.7, 0.4-1.2) 15 vs 168 age >80 (OR 0.9, 0.6-1.5) MV 37 vs 314
Unspecified Malignancy				
Dai 2020 ⁶ 14 Hubei Province, China Retrospective cohort Time: 01/01 to 02/24	Inclusion: Hospitalized cancer patients with COVID-19. The control group were COVID-19 patients without cancer matched by the hospital, hospitalization time,	n = 105 Age: M 64 (IQR 14) Gender: 57 Male Diseases: 22 lung ca, 13 GI ca, 11 breast ca, 11 thyroid ca, 9 blood ca, 6 cervix ca, 6 esophagus ca.	n = 536 Age: 63.5 (IQR: 14) Gender: 245 Males Comorbidities: 130 HTN, 39 CVD, 29 DM, 21 cerebrovascular disease,	Death: 12 (11%) vs 257 (48%) ICU: 20 vs 402 Hospitalization: 105 vs 536 MV: 10 vs 4

	and age, and were randomly selected. Exclusion: None COVID-19 Diagnosis: WHO interim guidance	Treatments (within 40 days): 8 Surgery, 13 radiotherapy, 17 chemotherapy, 4 targeted therapy, 6 immunotherapy. Comorbidities: 30 HTN, 12 CVD, 7 DM, 5 cerebrovascular disease, 6 CKD, 7 chronic liver disease. COVID-19 severity: 36 severe	22 CKD, 35 chronic liver disease. COVID-19 severity: 83 severe	
Gallo 2020 ⁷ Careggi University Hospital Florence, Italy Retrospective observational Time: From 2/29 to 4/11	Inclusion: Hospitalized patients with confirmed COVID-19 Exclusion: NR COVID-19 Diagnosis: NR	n = 18 Age: M 73.7 Gender: 12 males Diseases: prostate 2, breast 2, multiple myeloma 2, colon 2, lymphoma 2, leukemia 1, larynx 2, urothelial 1, thyroid 1, renal 2, pancreas 1 Treatments: NR Comorbidities: 6 hypertension, 2 chronic heart disease, 1 DM, 2 chronic pulmonary disease, 4 CKD, 1 chronic liver disease COVID-19 severity: NR	n = 101 Age: M 64.2 Gender: 61 males Comorbidities: 28 hypertension, 13 chronic heart disease, 16 DM, 13 chronic pulmonary disease, 4 CKD, 1 chronic liver disease COVID-19 severity: NR	Death: 6 (33%) vs 14 (14%) ICU: 3 vs 19 Hospitalization: 18 vs 101 MV: 0 vs 7 Factors predictive of death (aOR): age 1.1 (1.0-1.2), smoking 2.7 (0.7-10.4), cardiovascular disease 2.9 (0.5-16.0), cancer 2.1 (0.5-9.9).
Li 2020 ⁸ Union Hospital, Wuhan Central Hospital, General Hospital of Central Theater Command PLA, and Wuhan Jinyintan Hospital Wuhan, China	Inclusion: Consecutive subjects with COVID-19 treated at any of the hospitals, they were divided into patients with and without cancer. Exclusion: NR	n = 65 Age: M 63 (54-70) Gender: 31 males Diseases: NR Treatments: NR Comorbidities: 9 CVD, 20 HTN, 12 DM, 1 COPD, 1 CKD, 5 GI disease	n = 1794 Age: M 59 (IQR 45-68) Gender: 903 males Comorbidities: 259 CVD, 559 HTN, 250 DM, 60 COPD, 44 CKD, 93 GI disease	Death: 18 (23%) vs 191 (11%) MV: 7 vs 78 NIPPV: 7 vs 78 ECMO: 0 vs 4 ARDS: 19 vs. 208 High flow O2: 19 vs 214

Supplementary Materials

Retrospective observational Time: From 1/20 to 4/4	COVID-19 Diagnosis: Nasal and pharyngeal swabs PCR (1790) and/or lateral flow IgM/IgG antibodies (69)	COVID-19 severity: 1 mild, 29 moderate, 20 severe, 15 critical	COVID-19 severity: 33 mild, 1141 moderate 433 severe, 187 critical	In multivariate Cox model, factors associated with in-hospital death (aHR): age 1.1 (1.0-1.1), male 1.5 (1.1-2.1), severe/critical disease 28.2 (13.8-57.6), cancer 1.6 (0.9-2.7) , smoking 2.0 (1.1-3.6), temperature at admission 1.2 (1.0-1.5), platelet count 0.9 (0.9-0.9), D-dimer 1.0 (1.0-1.1) Cohort was split into those older and younger than 65, and the model re-run to show that cancer was associated with increased risk of death in patients younger than 65 years with a HR 2.5 (1.0-5.8)
Pinto 2020 ⁹ the Provincial Hospital of Reggio Emilia, Italy Cohort study Time: From 02/01 to 04/03	Inclusion: all patients hospitalized at the designated hospital with COVID-19 diagnosis. Exclusion: NR	N = 138 Age: median 76 (45–98) Gender: 86 males	n = 1088 Age: median 73 (23–100) Gender: 647 males Comorbidities: NR	Death: 47 (34%) vs 283 (26%) ICU: 14 vs 73 Hospitalization: 138 vs 1088

	COVID-19 Diagnosis: RT-PCR on NP swab.	Diseases: 27 breast ca, 25 colorectal ca, 30 prostate ca, 12 bladder ca, 9 lung ca, 4 kidney ca, 4 stomach ca, 4 thyroid ca, 3 uterus ca, 1 mesothelioma, 19 other. Treatments: 14 had recent cancer treatment, 12 chemotherapy, 4 antiangiogenic drugs, 1 immunotherapy. Comorbidities: 18 COPD, 105 HTN, 77 CVD, 37 DM COVID-19 severity: NR	COVID-19 severity: NR	Association of risk factors with poor outcome: Mortality risk among cancer patients (aOR): Recent cancer diagnosis (<5 years) aOR 0.31 (0.11-0.84); adjusted for age, sex, metastatic disease. Recent cancer diagnosis (<1 years) 0.13 (0.02-1.04); adjusted for age, sex, metastatic disease. Metastatic disease 3.84 (0.80-17.51); adjusted for age, sex, and time since cancer diagnosis. Bladder cancer 1.80 (0.48-4.75), breast cancer 0.74 (0.21-2.63), colorectal cancer 0.94 (0.34-2.61), lung cancer 0.78 (0.16-3.74); adjusted for age, sex, metastatic
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				disease, and time since cancer diagnosis.
Stroppa 2020 ¹⁰ Piacenza's General Hospital Italy Retrospective observational Time: 2/21 to 3/18	Inclusion: consecutive cancer patients affected by SARS-CoV-2 and hospitalized, and a control group of COVID-19 patients hospitalized during the same period and matched by age, sex, pneumonia and antiviral treatment	n = 25 Age: m 61.6 ± 10.1 Gender: 20 males Diseases: 2 breast, 6 GI, 6 genitourinary, 2 hematologic, 8 lung, 1 undefined Treatment: 8 chemotherapy, 4 immunotherapy, 13 none Comorbidities: 7 COPD, 8 DM, 16 HTN	n = 31 Age: NR Gender: 15 males Comorbidities: NR	Death: 9 (36%) vs 5 (16%) Factors associated with death in the cancer group in univariable assessment: age, female gender, tumor site , CRP elevation
Tian 2020 ¹¹ 9 hospitals in Wuhan, China Retrospective Time: From 01/13 to 03/ 18	Inclusion: Adults patients with COVID-19 and any type of malignant solid tumor or hematological malignancies. Controls were propensity score matched patients (based on age, sex, and comorbidities) at 2:1 ratio. Diagnosis: based on RT-PCR	n = 232 Age: 64.0 (58.0–69.0) Gender: 119 Males Diseases: NR Treatments: 197 Surgery, 214 chemotherapy or radiotherapy, 32 targeted therapy or immunotherapy. Comorbidities: 96 HTN, 55 DM, 22 CHD, 6 CKD, 9 cerebrovascular disease, 6 hepatitis, 3 COPD COVID-19 severity: 84 non severe, 148 severe.	N = 519 Age: 64.0 (56.0–70.0) Gender: 253 Male Comorbidities: 196 HTN, 143 DM, 52 CHD, 21 CKD, 14 CVD, 4 hepatitis, 1 COPD. COVID-19 severity: 353 non severe, 166 severe.	Death 46 (20%) vs 56 (11%) High flow O2: 77 vs 121 NIPPV: 62 vs 99 MV 21 vs 23 Multivariable analyses showed the following variables to be associated with poor outcomes among cancer patients (aOR): Tumor stage IV 2.60 (1.05 to 6.43) ; adjusted for age, sex, comorbidities, cancer

				type, and antitumor treatment.. Chemotherapy or radiotherapy 1.28 (0.85-1.94), and targeted- or immune-therapy 3.29 (1.26-8.61) compared to surgical treatment; adjusted for age, sex, comorbidities, tumor stage, and cancer type.
Abbreviations: NR, not reported; n, number of patients; m, mean; M, median; SD, standard deviation; IQR, interquartile range; AML, acute myeloid leukemia; ALL, acute lymphocytic leukemia; MM, multiple myeloma; MGUS, monoclonal gammopathy of undetermined significance; MDS, myelodysplastic syndrome; HL, Hodgkin's lymphoma; NHL, non-Hodgkin's lymphoma; CLL, chronic lymphocytic leukemia; CML, chronic myeloid leukemia; MPN, myeloproliferative neoplasms; NET, neuroendocrine tumor; NSCLC, non-small cell lung cancer; HCC, hepatocellular carcinoma; IMiD, immunomodulatory drug; mAb, monoclonal antibody; TKI, tyrosine kinase inhibitor; HTN, hypertension; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; CKD, chronic kidney disease; GI, gastrointestinal; GU, genitourinary; CHF, congestive heart failure; ICI, immunecheckpoint inhibitory; ca, cancer; RA, rheumatoid arthritis; HBV, hepatitis B virus; MV, mechanical ventilation; NIPPV, noninvasive positive pressure ventilation; ECMO, extracorporeal membrane oxygenation; ARDS, acute respiratory distress syndrome; OR, odds ratio; aOR, adjusted odds ratio; HR, hazards ratio; aHR, adjusted hazards ratio.				

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Supplementary Materials

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Table s4j. Included studies for Recommendation 13

Outcome of COVID-19 in Cancer Patients				
Study	Inclusion and Demographics	Baseline Characteristics	COVID-19 Diagnosis	Outcomes
In asymptomatic patients with cancer, should testing vs. no testing for SARS-CoV-2 be performed before initiation of immunosuppressive therapy?				
Hematologic Malignancy				
Aries 2020 ¹ Bart's Cancer Institute London, UK Retrospective observational Time: From 3/11 to 5/11	n = 35 Inclusion: adult patients with known diagnosis of hematological malignancy who developed lab confirmed COVID-19 Exclusion: Less than 14 days of follow up. Age: M 69 Gender: 66% males	Diseases: 12 MM, 5 CML, 4 DLBCL, 4 ALL, 3 follicular lymphoma, 2 AML, 1 aplastic leukemia, 1 myelofibrosis, 1 MGUS, 1 mantle cell lymphoma, 1 MDS Treatments: 24 on active treatment Comorbidities: 29% HTN, 14% CKD, 15% DM COVID-19 severity:	COVID-19: 35 PCR+: 35	Death: 14 (40%) Variables associated with death (univariable) included age, number of major comorbidities, admission O ₂ saturation, admission neutrophil count, admission lymphocyte count, and maximum CRP. Factors not associated included being on 3rd line treatment , admission hemoglobin, admission platelets, being on treatment at time of COVID-19 diagnosis, admission neutrophil:lymphocyte ratio
Dufour 2020 ² 30 different cancer centers, Belgium Cross sectional Time: As of April 12, 2020	n = 20 Inclusion: Multiple myeloma patients with confirmed COVID-19 Exclusion: NR Age: Median 68 (57-83) Gender: 60% males (12/20)	Diseases: MM Treatments: Comorbidities: Renal or CVD comorbidities (14/20), diabetes (5/20), another neoplasm (3/20) COVID-19 severity: Mild (5), severe (13), critical (2).	COVID-19: 20 PCR+: NR	Death: 7 (35%) ICU: 5 Hospitalization: 18 MV: 2 Multiple organ failure: 1 Poor outcome in 7 patients: age (median: 77 (58-83), 7 CVD comorbidities or secondary cancer, 7 dexamethasone, 5 progressive cancer, 5 African origin.
Engelhardt 2020 ³ 10 secondary and tertiary Comprehensive Cancer Centers in German pandemic epicenters, Germany	n = 21 (2 asymptomatic) Inclusion: all multiple myeloma in- and outpatients with SARS-COV Exclusion: NR Age: median 59 (46-83)	Diseases: MM Treatments: prior transplant (15), proteasome inhibitors (19), ImiD (12), antibody (10).	COVID-19: 21 PCR+: 21	Death: 0 (0%) ICU: 3 Hospitalization: 17 MV: 2

Supplementary Materials

Retrospective cohort Time: From 03/01 to 05/21	Gender: males (17)	Comorbidities: Cardiac/ HTN (11), renal impairment (3), obesity (1) COVID-19 severity: NR		ARDS: 2
Infante 2020 ⁴ University Hospital Infanta Leonor, Madrid, Spain Case series Time: 03/08 to 04/08	n = 41 Inclusion: patients with hematological cancer and COVID-19 diagnosis Age: Median 76 (37; 92) Gender: 22 Males	Diseases: 14 NHL, 9 CLL, 5 plasma cell dyscrasia, 4 acute leukemia, 4 MDS, 4 MPN, 1 HL. Treatments: 21 active, 5 no treatment. Comorbidities: 22 HTN, 10 COPD, 9 DM, 6 Ischemic heart disease, 6 renal failure, 4 previous ca, 4 atrial fibrillation, 2 venous thromboembolism, 1 asthma, 1 RA	COVID-19: 41 PCR+: 38	Death: 15 (37%) Association of risk factors with death (unadjusted HR) : pneumonia severity 3.76 (1.48-9.54), progressive disease 4.41 (1.17-9.89) , active treatment 1.68 (0.59-4.79) ; ≥ 3 comorbidities 2.22 (0.79- 6.18); ≥ 80 years old 1.92 (0.69-5.32); thromboembolic events 2.14 (0.68-6.76), myeloid vs lymphoid malignancy 1.01 (0.71-1.27) Hospitalization: 41
Lee 2020 (Lancet Oncology) ⁵ UKCCMP database United Kingdoms Prospective cohort Time: 3/18 – 5/8	n = 227 Inclusion: UKCCMP database of cancer patients with symptomatic SARS-CoV2 infection. Data on association of chemotherapy with death was only reported for hematological malignancy, so we only reported the data for patients with hematological malignancy in this report. Exclusion: NR Age: M 69 $\pm$ 4 Gender: 148 men (65%)	Diseases: all hematological malignancy Disease stage/severity: NR Pulmonary involvement: NR Treatments (within 4 weeks): chemotherapy 108 (47.6%), hormone therapy 0, radiotherapy 2 (0.%), surgery 0, targeted treatment 26 (11.5%) Comorbidities: 21 cardiovascular, 7 COPD, 33 DM, 60 HTN, 2 none COVID severity: 103 mild, 19 severe/critical, 5 no data	COVID-19: 227	Death: 82 (36%) Treatment with chemotherapy was associated with death during COVID-19 hospitalization aOR 2.09 (1.09-4.08) , adjusted for age and sex
Passamonti 2020 ⁶ ITA-HEMA-COV group Italy	n = 536 Inclusion: consecutive adult patients with hematological malignancy and	Diseases: 83 MPN, 41 MDS, 51 AML, 16 ALL, 222 NHL, 106 plasma cell neoplasms	COVID-19: 536 PCR+: 536	Death 198 (37%) Predictors of death in multivariable Cox model (aHR): female gender 0.9 (0.6-1.2);

Retrospective observational Time: From 2/25 to 5/18	symptomatic and laboratory confirmed SARS-CoV-2 Exclusion: NR Age: m 66.8 +/- 13.3 Gender: 340 males	Treatments: NR Comorbidities: 82 heart disease, 43 pulmonary disease, 91 vascular disease, 13 connective tissue disease, 34 liver disease, 42 kidney disease, 72 DM, 51 non-hematological cancer COVID-19 severity: 268 mild, 194 severe, 74 critical		age 1.0 (1.0-1.1); Charlson Comorbidity Index 1.1 (0.9-1.2); progressive hematological malignancy 2.1 (1.4-3.1); compared to MPN, MDS 1.6 (0.7-3.6), AML 3.5 (1.6-7.8), ALL 1.6 (0.5-5.9), HL 1.3 (0.4-4.7), chronic lymphoproliferative neoplasms 1.6 (0.8-3.5), indolent lymphoma 2.2 (1.1-4.5), aggressive lymphomas 2.6 (1.3-4.9), plasma cell neoplasm 2.5 (1.3-4.7); time since malignancy diagnosis 1.0 (0.9-1.0); time since last therapy 1.0 (0.9-1.0); severe/critical COVID-19 4.1 (2.7-6.1)
Wang 2020 ⁷ Mount Sinai Hospital, USA Case series Time: 03/01 to 04/30	n = 58 Inclusion: Patients with cancer and confirmed COVID-19 infection. Age: Median 67 years (IQR: 12.5 years) Gender: 30 Males	Diseases: 54 MM, 4 SMM. Treatments: 28 CD38 mAb, 32 ImiD, 22 proteasome inhibitors, 30 corticosteroids, 5 venetoclax, 11 no treatment. Comorbidities: 37 HTN, 36 DL, 16 DM, 14 CKD, 12 lung disease	COVID-19: 58 PCR+: 58	Death: 7 (12%) Hospitalization: 36 ICU: 7 MV: 5 NIPPV: 3 AKI: 12, 7 Shock: 7 Sepsis: 2
Solid Tumors				
Garassino 2020 ⁸ TERAVOLT registry Multinational (Italy, Spain, France, Switzerland, Netherlands, USA, UK, China) Retrospective observational Time: From 3/26 to 4/12	n = 200 Inclusion: Patients with thoracic cancer with COVID-19 diagnosis (PCR, or suspected with clinic evidence) Exclusion: NR Age: 12 <50, 122 >70 Gender: 141 males	Diseases: NSCLC 151, small cell lung cancer, 29, thymoma/thymic carcinoma 8, carcinoid or NET 4, mesothelioma 8 Treatments: 147 on treatment including TKI 28, chemotherapy 48, immunotherapy 34, chemotherapy/immunotherapy 20, other 17	COVID-19: 200 PCR+: 180	Death 66 (33%) Hospitalization 152 ICU 13 MV 9 Multivariable model of factors associated with death (aOR): COPD 1.2 (0.6-2.4), HTN 1.2 (0.6-2.2), female gender 0.7 (0.3-1.4), age >65 1.5 (0.8-3.0), and current/former smoker 3.2 (1.1-9.1)

		Comorbidities: 9 autoimmune diseases, 3 chronic hepatitis, 15 CKD, 51 COPD, 29 DM, 93 HTN, 3 lung fibrosis, 10 CVA, 30 CVD, 3 TB, 8 HBV, 5 HCV, 93 other COVID-19 severity: NR		
Song 2020 ⁹ Zhongnan Hospital of Wuhan University Wuhan, China Case series Time: From 21/12/2019 to 01/31/2020	n = 4 Inclusion: NR Exclusion: NR Age: mean 54 Gender: 50% males	Diseases: Breast cancer, B cell-CLL, rectal cancer, HCC. Treatments: Chemotherapy (2), radiotherapy (1), surgery (3) Comorbidities: HTN (25%), CVD (25%), COPD (25%), HBV (50%) COVID-19 severity: mild (50%), severe (50%)	COVID-19: 4 PCR+: 4	Death: 1 (25%) ICU: 2 Hospitalization: 4 MV: 0 NIPPV: 1 Supplemental O ₂ : 3
Zhang L 2020 ¹⁰ Tongji Sino-French New Town Hospital, Union Red Cross Hospital, and Union West Hospital, Wuhan, China Retrospective cohort Time: 01/13 – 02/26	n = 28 Inclusion: Cancer patients diagnosed with COVID-19 Exclusion: NR Age: median 65 (IQR: 56 – 70) Gender: 11 females	Diseases: 7 lung ca, 11 GI ca, 3 breast ca, 6 GU ca Disease stage/severity: 18 stage 1-3, 10 stage IV. Pulmonary involvement: NR Treatments: 21 surgery, 25 chemo/radiotherapy, 6 target/immunotherapy Comorbidities: DM, COPD, asthma, liver diseases.	COVID-19: 28 PCR+: NR	Death: 8 (29%) Anti-tumor within 14 days of diagnosis association with severe events: aHR 4.079 (1.086-15.322) , adjusted for gender, age, and presence of patchy consolidation on CT scan. Severe events: ICU admission, mechanical ventilation, and death.
Unspecified Malignancy				
Assaad 2020 ¹¹ Comprehensive Cancer Center of Lyon, France Retrospective cohort Time: From 03/01 to 04/15	n = 302 Inclusion: patients presenting to the designated hospital with COVID-19 clinical suspicion and underwent testing.	Diseases: among COVID-19 (+) patients, 35 solid tumor, 20 hematological ca, 7 lung ca Treatments: 29 any ca treatment, 16 cytotoxic, 5 anti-CD20, 3 anti-	COVID-19: 55 (18%) PCR+: 55 Age: mean 63.8 Gender: 36 Males	Death: 8 (14%) Hospitalization: 55 Association of risk factors with death in COVID patients (univariable unadjusted HR): age >60 33.9 (27.4-40.5), male gender 8.19 (6.09-10.3), fever and respiratory

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	Exclusion: NR Age: 58.2 (1.1) Gender: 114 Males	PD1 or -PDL1, 1 anti-proteasomes, 2 anti HER-2 Comorbidities: NR COVID-19 severity: NR		symptoms 36.9 (30.5-43.3), lung ca 4.69 (3.24-6.14), relapsing ca 5.29 (3.19-7.39) . Study assessed for association of variables with death in the entire cohort. Positive SARS-CoV2 PCR was associated with higher risk of death 1.92 (1.12-2.72) in univariable analysis, however, it was not included in the multivariable analysis which included gender, poor performance status, relapsing cancer aHR 3.05 (1.83-4.27) , fever and respiratory symptoms, and lymphopenia.
Jee 2020 ¹² Memorial Sloan Kettering Cancer Center, USA Retrospective cohort Time: 3/8 to 4/13	n = 309 Inclusion: patients with cancer and COVID-19 diagnosis Age: 158 patients < 60 yo, 151 > 60 yo Gender: 159 males	Diseases: 232 any solid malignancy, 74 hematologic, 29 lung ca, 54 breast ca, Treatments: 102 cytotoxic therapy, 49 targeted therapy, 18 immunotherapy, Comorbidities: 92 BMI > 30, 16 COPD, 120 HTN, 36 thromboembolism.	COVID-19: 309 PCR+: 309	Death: 31 (10%) Hospitalization: 309 Association of risk factors with severe COVID-19 disease (aHR) : age >61 1.39 (0.94-2.06), BMI 0.96 (0.62-1.47), male gender 0.73 (0.49-1.08), ECOG ≥2 0.85 (0.58-1.26), current/former smoker 1.42 (0.97-2.09), ≥ 1 comorbidity 1.25 (0.66-2.37), hematologic malignancy 2.1 (1.36-3.24), thoracic malignancy 2.04 (1.16-3.60), cancer in remission 0.78 (0.48-1.27), baseline neutropenia 4.01 (1.52-10.6), lymphopenia at COVID-19 diagnosis 1.92 (1.28-2.89), recent cytotoxic chemotherapy 0.88 (0.57-1.36).
Kuderer 2020 ¹³ USA, Spain, Canada COVID-19 and Cancer Consortium (CCC19) database Prospective cohort Time: 03/17- 04/16	n = 928 Inclusion: Adults with active or previous hematologic malignancy or invasive solid tumor with laboratory confirmed diagnosis of COVID-19.	Diseases: Breast 191, prostate 152, gastrointestinal 108, thoracic 91, gynecological 49, renal cell carcinoma 45, endocrine 39, melanoma 38, head and neck 30, sarcoma 24, nervous system 12, solid tumor NOS 43.	COVID-19: 928 PCR+: 928	Death: 121 (13%) died within 30 days of COVID Treatment (type of anticancer therapy) association with death (aOR) : none in the 4 weeks before COVID 1 (reference), non cytotoxic therapy 1.04 (0.62-1.76), cytotoxic systemic therapy 1.47 (0.84-

	Must be resident of USA, Spain, or Canada. Exclusion: No lab confirmed SARS-CoV-2 infection. Patients with non-invasive cancers including non-melanomatous skin cancer, in-situ carcinoma, or precursor hematological neoplasms. Age: M 66 (IQR 57-76) Gender: 468 males	Hematological malignancies include 102 lymphoid neoplasms (54 low grade NHL, 27 high grade NHL, 6 ALL), 55 multiple myeloma, 42 myeloid neoplasms (13 AML), 6 hematological malignancies NOS. Disease stage/severity: 422 in remission/no evidence of disease, 294 with cancer present, stable, or responding to treatment, 102 with present, progressive disease, 59 with unknown cancer status. 51 with data missing. Pulmonary involvement: NR Treatments: 553 no treatment in the 4 weeks before COVID. 206 on non-cytotoxic therapy (75 targeted therapy, 85 endocrine, 38 immunotherapy, 12 radiotherapy, 2 surgery). 160 on cytotoxic systemic therapy. 9 on unknown therapy. 366 on active anticancer treatment. 32 with recent surgery. Comorbidities: 326 former smoker, 43 current smoker, 172 obese. 202 with 1 comorbidity, 231 with 2 comorbidities, 117 with 3 comorbidities, 192 with ≥ 4 comorbidities.		2.56), unknown 1.60 (0.18-14.14); adjusted for age, sex, smoking status, and obesity. Cancer status association with death (aOR): remission or no evidence of disease 1 (reference), stable or responding to treatment 1.79 (1.09-22.95), progressive disease 5.20 (2.77-9.77), other or unknown 2.71 (1.21-6.09); adjusted for age, sex, smoking status, and obesity Type of malignancy association with death (aOR): solid tumor 1 (reference), hematological malignancy 1.40 (0.83-2.37), multiple cancers 1.34 (0.77-2.34); adjusted for age, sex, smoking status, and obesity
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Lee 2020 (Lancet)¹⁴ UKCCMP database United Kingdom Retrospective cohort Time: From 3/18 to 4/26	n = 800 Inclusion: Patients with active cancer presenting with COVID-19 Exclusion: No PCR Age: M 69 (IQR 59-76) Gender: 449 males	Diseases: 27 lip/oral cavity/pharynx, 150 digestive, 90 respiratory/intrathoracic, 27 melanoma, 102 breast, 45 female genital, 78 male genital, 50 urinary, 15 central nervous system, 60 lymphoma, 109 other hematological, 46 other or unspecified Treatments: 281 chemotherapy, 64 hormone, 44 immunotherapy, 76 radiotherapy, 29 surgery, 72 targeted, 60 other, 272 none, 10 no information Comorbidities: 109 CVD, 61 COPD, 131 DM, 247 HTN, 169 none, 336 other, 123 no information COVID-19 severity: 412 mild, 187 severe, 173 critical, 28 no information	COVID-19: 800 PCR+: 800	Death 226 (28%) Treatment association with death: chemotherapy within the past 4 weeks aOR 1.18 (0.81–1.72), adjusted for age, sex and comorbidities. Similarly for hormone therapy 0.90 (0.49-1.68), immunotherapy 0.59 (0.27-1.27), radiotherapy 0.65 (0.36-1.18), and targeted treatment 0.83 (0.45-1.54). Non-palliative vs palliative chemotherapy 0.40 (0.17-0.96), palliative first line chemotherapy vs other lines 0.84 (0.36-1.98), palliative chemotherapy vs no chemotherapy 1.48 (0.93-2.36), palliative chemotherapy vs no treatment 1.05 (0.63-1.76). ICU 53
Liang 2020¹⁵ 575 hospitals, throughout China. Retrospective cohort Time: Unclear – 01/31	n = 18 Inclusion: Patients with COVID-19 in 575 hospitals. (1590 total COVID-19 patients, 18 had cancer) Exclusion: NR Age: 63.1±12.1 Gender: 7 females	Diseases: 5 lung ca, 3 breast ca, 3 GU ca, 3 GI ca, 1 lymphoma Disease stage/severity: NR Treatments: Surgery, chemotherapy, immunotherapy. Comorbidities: COPD, HTN, DM.	COVID-19: 18 PCR+: NR	Death: 5 (28%) Chemotherapy or surgery in the past month association with severe events (admission to ICU for invasive ventilation, or death): aOR 5.34 (1.80–16.18); adjusted age, smoking history and other comorbidities.
Mehta 2020¹⁶ Montefiore Health System New York, USA Retrospective cohort	n = 218 Inclusion: Cancer patients with COVID Exclusion: NR	Diseases: 164 solid tumors, 57 hematologic malignancies	COVID-19: 218 PCR+: NR	Death 61 (28%); 41/164 (25%) solid tumors and 20/57 (35%) hematologic malignancies ICU 23

Time: From 3/18 to 4/8	Age: M 69 (range 10-92) Gender: 127 male	Treatments: active chemotherapy 42, immunotherapy 5, radiotherapy 49 Comorbidities: 80 DM, 147 HTN, 62 chronic lung disease, 54 CKD, 43 CVD, 33 CHF COVID-19 severity: NR		MV 45 Multivariable analysis of factors associated with death, included if showed $p < 0.05$ on univariable analysis (aOR): younger age 0.2 (0.1-0.6), higher composite comorbidity score 1.5 (1.0-2.3), ICU admission 4.8 (1.5-17.2), and elevated inflammatory markers (increased risk, numbers not reported)
Pinato 2020 (Cancer Discovery) ¹⁷ Multicenter, Europe (UK, Italy, Spain, Germany) Prospective cohort Time: 2/26 – 4/1	n = 890 Inclusion: Confirmed SARS-CoV-2 infection and cancer, the OnCovid registry. Exclusion: NR Age: m 68 ± 12.8 Gender: 503 male	Diseases: GU 132, lung 119, GI 105, breast 162, gynaecological 41, gastro-esophageal 40, hepatobiliary 45, head and neck 29, skin 28, other 52, haematological malignancies 137 Disease stage/severity: advanced 351, non-advanced 539 Pulmonary involvement: NR Treatments: 479 on systemic anticancer therapy (206 were on chemotherapy, 92 on endocrine therapy, 93 on targeted therapies, and 56 on immunotherapy), 403 not on treatment. The mean interval between the last dose of systemic anticancer treatment was 19.3 days (SD 33.3). Comorbidities: 386 HTN, 181 DM, 128 CVD, 110 chronic pulmonary disease, 77 CKD, 54 CVA, 21 CHF, 33 dementia, 28	COVID-19: 890 PCR+: NR	Death: 299 (34%) Treatment with anticancer therapy association with death (aOR): 0.71 (0.53–0.95) , adjusted for age ($\geq$ vs <65 : 2.37, 1.71–3.30), active malignancy (1.81, 1.35–2.44) , having ≥ 2 comorbidities (1.47, 1.13–1.92) Disease complication: 565 (acute respiratory failure, ARDS, acute kidney injury, secondary infection, sepsis, septic shock, acute cardiac injury, acute liver injury, other complication)

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		PVD, 15 liver impairment, 23 immunosuppression, 263 other		
Pinato 2020 (Cancers)¹⁸ Multicenter, Europe (UK, Spain, Italy) Retrospective cohort Time: 02/26 - 04/01	n = 204 Inclusion: Cancer patients with COVID-19 diagnosis. Exclusion: NR Age: 69.3 ± 13.0 Gender: 127 males	Diseases: 43 GU ca, 36 lung, 28 GI, 27 breast, 13 gynecological, 10 Gastro-esophageal, 9 hepatobiliary, 7 head and neck, 3 skin, 6 other Treatments: 96 surgery, 38 chemotherapy, 5 immunotherapy, 5 endocrine therapy, 13 target therapy. Comorbidities: 88 HTN, 46 DM, 44 CVD, 34 COPD, 32 CKD, 16 cerebrovascular, 12 dementia, 8 peripheral vascular disease, 6 liver impairment, 5 immunosuppression. COVID-19 severity: NR	COVID-19: 204 PCR+: 204	Death: 59 (29%) Association of risk factors with death (aHR): age >65 2.2 (1.0-2.60), comorbidities ≥2 1.9 (1.0-3.6), advanced tumor stage 1.5 (0.7-3.2), anticancer therapy 1.3 (0.7-2.6) ICU: 36 Hospitalization: 186 MV: 18 Supplemental O2: 28
Robilotti 2020¹⁹ Memorial Sloan Kettering Cancer Center New York, USA Retrospective cohort Time: 3/10 – 4/7	n = 424 Inclusion: hospitalized cancer patients with COVID-19 Age: 100 ≥ 70, 134 60-69, 101 50-59, 51 40-49, 19 30-39, 11 18-29, and 7<18 Gender: 212 males	Diseases: 32 leukemia, 48 lymphoma, 22 myeloma, 86 breast, 37 colorectal, 35 lung, 26 prostate, 137 other Treatments: 191 systemic chemotherapy, 31 ICI, 66 chronic steroids Comorbidities: 43 asthma, 29 COPD, 84 DM, 84 cardiac dysfunction, 36 CKD, 214 HTN	COVID-19: 423	Death: 51 (12%) Hospitalization: 180 (12 were already hospitalized) On multivariate analysis association with hospitalization (aOR): age >65 (0.96-2.43), nonwhite race 1.62 (1.05-2.51), smoking 1.37 (0.88-2.13), asthma/COPD 1.07 (0.59-1.92), metastatic solid cancer 0.76 (0.43-1.34), hematologic cancer 2.49 (1.35-4.67), cardiac disorder 1.35 (0.77-2.36), HTN/CKD 1.51 (0.96-2.39), chronic lymphopenia or corticosteroids 1.85 (1.06-3.24), ICI 2.84 (1.24-6.72) MV: 40 High flow O2: 47

				Predictor of severe illness by Cox proportional hazards: age >65 1.67 (1.07-2.6), smoking 1.39 (0.89-2.17), asthma/COPD 1.24 (0.72-2.13), metastatic solid cancer 0.75 (0.40-1.41) , hematologic cancer 1.79 (0.97-3.32) , cardiac disorder 1.44 (0.88-2.37), HTN/CKD 1.18 (0.73-1.89), chronic lymphopenia or corticosteroids 1.42 (0.86-2.34), ICI 2.74 (1.37-5.46) .
Yang, 2020 ²⁰ Renmin Hospital of Wuhan University d Center, France Retrospective Time: From 01/01 to 04/15	n = 52 Inclusion: Cancer patients with COVID-19 diagnosis Age: median 63 (34-98) Gender: Male 28	Diseases: 10 lung ca, 9 breast ca, 8 rectal ca, 5 colon ca, 4 cervical ca, 3 thyroid ca, 2 gastric ca, 2 liver ca, 2 prostate ca, 7 other ca. Treatments: 6 Chemotherapy, 2 resection, 1 catheter ablation, 1 immunotherapy, Comorbidities: 17 HTN, 7 DM, 4 cerebrovascular disease, 4 COPD, 2 hepatitis B, 1 cirrhosis. COVID-19 severity: 33 mild, 19 severe/ critical	COVID-19: 52 PCR+: 52	Death: 11 (21%) Hospitalization: 52 MV: 0 NIPPV: 38
Yarza 2020 ²¹ Hospital Universitario 12 de Octubre Madrid, Spain Retrospective observational Time: From 3/9 to 4/19	n = 63 Inclusion: Consecutive oncologic patients that were admitted Exclusion: NR Age: 4 <50, 23 >70 Gender: 34 males	Diseases: 52 metastatic disease, 36 oligometastatic, 16 polymetastatic, 25 tumor pulmonary involvement Treatments: 61 on active treatment including 36 chemotherapy, 10 endocrine, 7 target, and 8 immunotherapy Comorbidities: 33 HTN, 22 DM, 5 CKD, 12 cardiomyopathy, 14	COVID-19: 63 PCR+: 52	Death: 16 (25%) Treatment with chemotherapy was associated with death during COVID-19 hospitalization aOR 2.09 (1.09-4.08) ; adjusted for age and sex

		chronic pulmonary disease, 13 venous thromboembolic disease COVID-19 severity: NR		
Zhang H 2020²² Zhongnan Hospital, Leishenshan Hospital, the 5th Hospital of Wuhan, the 7th Hospital of Wuhan, and Wuhan Hankou Hospital, Wuhan, China. Retrospective cohort Time: 01/05 - 03/18	n = 107 Inclusion: Patients with diagnosis of COVID-19, prior histological or clinical diagnosis of cancer, and available information about current or prior treatment Exclusion: NR Age: M 66 (37-98) Gender: 60 male	Diseases: 21 lung ca, 20 GI ca, 20 GU ca, 17 head and neck ca, 9 10 breast, hematological, 10 other Disease stage/severity: 84 stage I-III, 23 stage IV. Pulmonary involvement: NR Treatments: 37 anti-cancer treatment (5 surgery/radiotherapy, 15 chemotherapy/targeted therapy, 6 immunotherapy, 5 local treatment). 4/37 continued treatment after COVID-19 diagnosis. 70 patients were on follow-up Comorbidities: HTN, DM, cardiorespiratory diseases. COVID-19 severity: 51 mild, 56 severe	COVID-19: 107	Death: 23 (21%); on treatment: 14/37, during follow-up: 9/70 Active anti-cancer treatment association with death: aHR 3.56 (1.53-8.23), adjusted for age 1.05 (1.01-1.10). MV: 18 ARDS: 21
Abbreviations: NR, not reported; n, number of patients; m, mean; M, median; SD, standard deviation; IQR, interquartile range; AML, acute myeloid leukemia; ALL, acute lymphocytic leukemia; MM, multiple myeloma; MGUS, monoclonal gammopathy of undetermined significance; MDS, myelodysplastic syndrome; HL, Hodgkin's lymphoma; NHL, non-Hodgkin's lymphoma; CLL, chronic lymphocytic leukemia; CML, chronic myeloid leukemia; MPN, myeloproliferative neoplasms; NET, neuroendocrine tumor; NSLCD, non-small cell lung cancer; HCC, hepatocellular carcinoma; IMiD, immunomodulatory drug; mAb, monoclonal antibody; TKI, tyrosine kinase inhibitor; HTN, hypertension; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; CKD, chronic kidney disease; GI, gastrointestinal; GU, genitourinary; CHF, congestive heart failure; ICI, immuncheckpoint inhibitory; ca, cancer; RA, rheumatoid arthritis; HBV, hepatitis B virus; MV, mechanical ventilation; NIPPV, noninvasive positive pressure ventilation; ECMO, extracorporeal membrane oxygenation; ARDS, acute respiratory distress syndrome; OR, odds ratio; aOR, adjusted odds ratio; HR, hazards ratio; aHR, adjusted hazards ratio.				

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Table s4k. Included studies for Recommendation 14

Studies of the Prevalence and Outcomes of COVID-19 in Autoimmune Disease				
Study	Inclusion	Disease characteristics	COVID-19	Outcomes
In asymptomatic patients with autoimmune disease, should testing vs. no testing for SARS-CoV-2 be performed before initiation of immunosuppressive therapy?				
Rheumatologic Disease				
Montero 2020 ¹ Universitario Gregorio Marañon Madrid, Spain Retrospective observational Time: 3/4 to 4/24	n = 62 Inclusion: Patients with any rheumatologic autoimmune or inflammatory disease evaluated at the rheumatology department and who were infected with SARS-CoV2. Age: m 60.9 Gender: 26 males	Diseases: 20 RA, 16 SpA, 9 SLE, 13 other CTD; 4 other inflammatory diseases Treatment: 30 steroids (27 dose greater than or equal to 5mg steroids), 9 HCQ, 12 MTX, 3 leflunomide, 12 anti-TNF, 4 tocilizumab, 2 tofacitinib Comorbidities: 20 obesity, 12 DM, 27 HTN, 31 CVD, 14 lung disease	COVID-19: 62 PCR+: 51	Hospitalization: 42 Associated factors include age 70 or older, male gender, DM, HTN, CVD, and lung disease, baseline therapy with steroids. Factors not associated with hospitalization included nonbiologic DMARDs, biologic DMARDs, and rheumatic disease Death 10 1/20 not hospitalized and 9 /42 hospitalized
Pablos 2020 ² 7 centers of the Research network for the Investigation	n = 26,131 Inclusion: Adult patients under follow-up in rheumatology	Diseases: 10,927 RA, 4,777 PsA, 4,268 SpA, 2,528 non-SLE autoimmune or immune-mediated	Hospital diagnosed-COVID-19: 0.76% (OR 1.32, 95%CI 1.15-1.52) csDMARD 0.53%, (OR 1.1, 95%CI	NA

of Inflammation and Rheumatic Diseases, Spain Retrospective observational Time: 4/7-17	departments diagnosed with chronic inflammatory arthritis or systemic autoimmune or immune-mediated arthritis. Age: M 65 (IQR 53-78) Gender: 56% females	disease, 2,253 SLE, 1,378 PMR-GCA Treatments: 7,558 csDMARD, 5,802 tsDMARD/bDMARD	0.8-1.5) tsDMARD/bDMARD 0.94% (OR 1.6, 95%CI 1.23-2.1) Prevalence was compared to reference population (n = 2,899,935) which had prevalence of 0.58%	
Santos 2020 ³ Complejo Asistencial Universitario de León Leon, Spain Retrospective observational Time: 3/1 – 6/1	n = 38 Inclusion: All patients aged >18 with rheumatic disease with positive COVID admitted to the hospital. Age: m 75.3 Gender: 53% female	Diseases: 16 RA, 8 PMR, 5 SLE, 3 PsA, 2 SpA, 2 GCA, 1 systemic sclerosis, 1 Sjogren's disease Treatment: 22 steroids (mean dose 12.65mg/day), 17 csDMARDs (14 methotrexate, 1 leflunomide, 1 azathioprine, 1 MMF), 2 bDMARDs (1 abatacept, 1 rituximab), 7 hydroxychloroquine Comorbidities: 21 HTN, 15 DM, 21 dyslipidemia, 19 CVD, 12 interstitial lung disease	COVID-19: 38	Death: 10 On multivariable regression, the following factors were associated with mortality: rheumatic disease activity, dyslipidemia, CVD, interstitial lung disease. Factors not associated with death included steroid use and methotrexate.
Scire 2020 ⁴	n = 232	Diseases: 79 RA, 61 SpA, 49 CTD, 26 vasculitis, 17 other	COVID-19: 232	Hospitalizations: 162 Death: 44

CONTROL-19 registry Italy Retrospective observational Time: 3/26 – 5/3	Inclusion: Patients with rheumatic and musculoskeletal disease and COVID-19 Age: m 62.2 ± 13.9 Gender: 149 female	Treatments: 43 HCQ, 120 steroids, 97 csDMARDs, 25 immunosuppressants, 55 TNF-i, 3 tocilizumab, 2 sarilumab, 5 abatacept, 6 rituximab, 2 belimumab, 7 other bDMARDs. 4 baricitinib, 4 tofacitinib, 1 apremilast Comorbidities: 22 smokers, 21 COPD, 27 interstitial lung disease, 21 other lung disease, 103 HTN, 31 obesity, 50 CVD, 28 DM		NIPPV: 12 Mechanical ventilation: 17 Risk ICU/mechanical ventilation or death (aOR, adjusted for sex, age>65, comorbidities): compared to no DMARD, b/ts DMARD only 0.5 (0.13-1.81), cs-DMARD only 0.62 (0.2-1.97), b/tsDMARD and cs-DMARD 0.97 (0.22-4.22); and compared to no prednisone, prednisone 1-9 mg/day 1.73 (0.68-4.43) and >10 mg/day 1.6 (0.40-5.86).
Winthrop 2020⁵ Emerging Infections Network USA and Canada Retrospective observational Time: 4/8 – 5/22	n = 77 Inclusion: COVID-19 patients on immunomodulatory therapy Age: m 60 (range 16-84) Gender: 40 female	Diseases: 64 had autoimmune disease (19 RA, 5 UC, 5 sarcoidosis, 35 other) Treatments: 31 using biologic therapies (16 TNF-i, 6 rituximab, 2 abatacept, 2 tocilizumab, 5 other). Of those 46 patients not using biologics, they were on JAK inhibitors (3), DMARDs (11),	COVID-19: 77	Hospitalization: 63 Mechanical ventilation: 27 ICU: 37 Death: 9 Anti-TNF ± DMARDs and/or corticosteroids 0/16, non-TNF biologic ± DMARDs and/or corticosteroids 2/15, nonbiologic

		prednisone alone (5), or other treatment (27). Comorbidities: 26 HTN, 19 DM, 11 CKD		DMARD alone 2/11, nonbiologic DMARD and corticosteroids 1/3, corticosteroids alone 1/9, JAK inhibitor 0/3, other-immunomodulatory therapy ± DMARDS and/or corticosteroids 2/11
Zen 2020 ⁶ University of Padua Padova, Italy Retrospective observational Time: 4/9-25	n = 916 Inclusion: Telephone conducted survey on rheumatic disease patients Age: m 53.6 ± 14.3 Gender: 720 female	Diseases: 397 SLE, 182 ANCA-associated vasculitis, 176 SSc, 111 RA, 50 idiopathic inflammatory myopathy. Treatments: 91 prednisone (>7.5mg/day), 139 MTX, 11 cyclosporin, 191 MMF, 9 tacrolimus, 61 azathioprine, 4 cyclophosphamide, 336 antimalarial drugs, 17 leflunomide, 5 salazopyrin, 42 anti-TNF, 12 CTLA4-Ig, 9 anti-IL6R, 40 anti-CD20, 21 JAK-i, 47 anti-BLYS	COVID-19: 2 Only 65 were screened	Death: 0/916
Zhao 2020 ⁷	n = 29	Diseases: 15 RA, 5 SLE, 1 hupus, 2 myasthenia gravis, 1 Sjogren's	COVID-19: 29	Mechanical ventilation: 2 Supplemental O2: 20

Huoshenshan Hospital Wuhan, China Retrospective observational Time: 2/4 – 4/9	Inclusion: Patients with COVID-19 and rheumatic disease Age: m 61 Gender: 25 female	syndrome, 1 SpA, 1 dermatomyositis, 1 autoimmune liver disease, 2 undifferentiated CTD Treatment: 5 hydroxychloroquine, 7 steroids. No details on biologics/other immunomodulators		ICU: 1 Death: 1
Emmi 2020 ⁸ Careggi University Hospital Tuscany, Italy Retrospective observational Time: 4/1-14	n = 485 Inclusion: Patients with autoimmune disease followed by the interdisciplinary internal medicine unit who live in the Tuscany were contacted by phone Age: 36-68 Gender: 350 female	Diseases: 121 SLE, Sjogren 38, systemic sclerosis 18, antiphospholipid syndrome 18, myositis 10, SpA 42, RA 24, GCA 63, Behçet syndrome 45, EGPA/GPA/MPA 40, cryoglobulinemia 3, Henoch-Schonlein purpura 2, FMF 16, recurrent idiopathic pericarditis 9, uveitis 14, retroperitoneal fibrosis 4, sarcoidosis 4 Treatment: 253 corticosteroids, HCQ 10, MMF 48, MTX 34, AZA 37, cyclosporine 7, leflunomide 2,	COVID-19: 1 Only 7 tested Symptoms of COVID-19: 13	

		cyclophosphamide 1, anti-TNF 5, tocilizumab 4, elimumab 38, anti-IL5 22, rituximab 17, anti-IL1 13, secukinumab 10, ustekinumab 4, IVIG 44		
Fernandez-Ruiz 2020⁹ New York University New York, USA Prospective cohort Time: 4/13 – 6/1	n = 226 Inclusion: NYU lupus cohort (a convenience registry) who had at least one outpatient visit and a blood sample collected in the last 9 months (176), referral from NYU rheumatology providers as part of WARCOV initiative (33), patients with ICD10 code for SLE and testing for COVID-19 at Bellevue and NYU EMR systems. Age: 41-47 Gender: 210 females	Diseases: SLE Treatments: MMF 45, MTX 13, AZA 18, belimumab 24, cyclophosphamide 4, rituximab 6, abatacept 2, tacrolimus 9, tocilizumab 1, other 4 Comorbidities: 2 pregnancy, 12 active malignancies, 8 organ transplants, 25 HTN, 11 DM, 4 COPD, 7 CHF, 22 asthma	COVID-19: 41 Suspected COVID but not tested: 42	Hospitalization: 24 Supplemental O2: 12 ICU: 4 Mechanical ventilation: 3 Death: 4

Freites Nunez 2020 ¹⁰ Hospital Clinico San Carlos Madrid, Spain Retrospective observational Time: 3/1 – 4/27	n = 123 Inclusion: All patients who attending the rheumatology clinic during the specified period, age >16, ICD10 code of inflammatory rheumatic disease and symptomatic COVID-19 disease, medical or confirmed diagnosis of SARS-CoV-2 Age: m 58.9 ± 14.9 Gender: 86 women	Diseases: 50 RA, 18 axial SpA, 6 PMR, 6 psoriatic arthritis, 8 SLE, 6 MCTD, 9 Sjogren's syndrome, 2 vasculitis, 1 uveitis, 1 systemic sclerosis, 8 inflammatory polyarthritis, 1 polychondritis, 1 polymyositis, 3 Raynaud phenomenon, 3 other Treatments: Glucocorticoid 61, MTX/leflunomide/AZA 68, sulfasalazine 9, antimalarials 27, anti TNF 17, abatacept 1, tocilizumab 2, belimumab 1, rituximab 5, JAKi 1 Comorbidities: 40 HTN, 27 dyslipidemia, 9 depression, 17 DM, 15 heart disease, 8 vascular disease, 7 liver disease, 6 kidney disease, 19 lung disease, 5 cancer, 3 VTE, 17 thyroid disease	COVID-19: 58 Negative PCR in 3 and not performed in 62	
Gartshteyn 2020 ¹¹	n = 450	Disease: SLE	COVID-19: 10	Hospitalization: 7

New York University Presbyterian Hospital- Columbia New York, USA Retrospective cohort Time: until 4/26	Inclusion: Patients from the Columbia Lupus Cohort and NYU Presby- Columbia database of patients who tested positive for COVID Age: NR Gender: NR	Treatments: HCQ 5, nonbiologic immunosuppressant 8, rituximab 1, prednisone 4		
Kumar 2020¹² All India Institute of Medical Sciences New Delhi, India Retrospective cohort Time: 4/20 – 7/20	n = 840 Inclusion: Patients with rheumatological disorders under long term follow up at the Department of Rheumatology and residing in Delhi-NCR. Adult >18 year old with definite rheumatic disease and followed at the department for at least a year. Patients	Diseases: 713 RA, 100 SLE, 14 AS, 6 psoriatic arthritis, 3 systemic sclerosis, 3 Sjogren's syndrome, 1 dermatomyositis Treatments: 203 prednisone, 278 HCQ, 507 MTX, 145 sulfasalazine, 204 leflunomide, 31 MMF, 33 AZA, 7 etanercept, 8 infliximab, 4 adalimumab, 10 golimumab, 11 rituximab, 2 tocilizumab, 5 tofacitinib, 4 filgotinib Comorbidities: 187 HTN, 36 DM, 96 hypothyroidisms, 9 asthma, 24 osteoporosis, 1 CKD, 9	COVID-19: 4 Only 6 tested out of 29 who reported symptoms	

	were contacted by telephone. Age: m 45 ± 13 Gender: 456 females	cardiomyopathy, 1 chronic liver disease		
Huang 2020 ¹³ Tongji Hospital Wuhan, China Retrospective observational Time: 1/29 – 3/8	n = 17 (out of 1255 COVID patient) Inclusion: Patients with COVID-19 and systemic autoimmune disease based on diagnostic codes. Age: m 64 (IQR 60.5-71.5) Gender: 14 females	Diseases: 8 RA, 3 SLE, 2 Sjogren's syndrome, 2 SpA, 1 Behçet's, 1 PMR Treatments: 8 DMARDs, 4 HCQ, 2 MTX, 1 leflunomide, 1 thalidomide, 6 glucocorticoids Comorbidities: 6 HTN, 0 DM, 1 cerebrovascular disease, 2 CKD, 1 infectious disease	COVID-19: 17	ICU 1 Death 1
Dermatologic Disease				
Queiro Silva 2020 ¹⁴ Hospital Universitario Central de Asturias Oviedo, Spain Time: NR	N = 548 Inclusion: Patients on biologic therapy Age: NR Gender: NR	Diseases: psoriasis and peripheral SpA Treatments: 303 apremilast, 209 secukinumab, 36 infliximab	COVID-19: 6 On apremilast 3/303, secukinumab 2/209, infliximab 1/36	Hospitalization: 4 ICU: 2
Strippoli 2020 ¹⁵	n = 139 Inclusion: patients with	Diseases: chronic plaque psoriasis Treatment: biologic therapy	COVID-19: 5 PCR+: 3	Hospitalization: 1 Supplemental O2 (not MV): 1

Alessandro Manzoni Hospital Lecco, Italy Retrospective observational Time: 3/9 – 5/6	chronic plaque psoriasis on biologic therapy followed at hospital Age: range 36-72 Gender: NR			
Fougerousse 2020 ¹⁶ France Retrospective cohort Time: 4/27 – 5/7	n = 1,418 Inclusion: Patients on systemic and biologic treatments Age: NR Gender: 619 female	Diseases: psoriasis (not clear) Treatments: 300 MTX, 26 cyclosporine, 4 acitretin, 48 apremilast, 25 etanercept, 165 adalimumab, 40 infliximab, 8 certolizumab pegol, 240 ustekinumab, 206 secukinumab, 112 ixekizumab, 38 brodalumab, 146 guselkumab, 25 risankizumab, and 35 combination of MTX and biologic Comorbidities: 111 DM, 245 obesity, 232 HTN, 920 none	COVID-19: 12	Hospitalized: 5 on adalimumab, guselkumab, MTX, MTX/etanercept, and ustekinumab ICU: 2 on MTX/etanercept and ustekinumab Death: 0
Gisondi 2020 ¹⁷ Humanitaas and Sand Donato Hospitals Italy	n = 5,206 Inclusion: Patients with psoriasis who were being	Disease: psoriasis Treatments: 1679 anti-TNF, 1996 IL-17 inhibitor, 1389 IL-12/13 inhibitor, 141 IL-23 inhibitor	NR	Hospitalization for COVID-19: 4 Death from COVID-19: 0

Retrospective observational Time: 2/20 - 4/1	regularly followed and treated with a biologic Age: m 53.2 ± 11.2 Gender: 2,823 males	Comorbidities: 1313 obesity, 625 CVD, 1604 HTN, 635 DM		
Inflammatory Bowel Disease				
Norsa 2020 ¹⁸ Papa Giovanni XXIII Hospital Bergamo, Italy Retrospective observational Time: 2/19 to 3/23	n = 552 Inclusion: all IBD patients regularly followed at hospital Age: m 46 Gender: 219 females	Diseases: 186 CD, 336 UC Treatment: 304 salicylates, 89 thiopurines or MTX, 82 biologics (infliximab, adalimumab, ustekinumab, vedolizumab, golimumab), 16 steroids, 11 tacrolimus or cyclosporin or MMF, 20 not on therapy	COVID-19: 0	NA
Scaldaferri 2020 ¹⁹ Centro Malattie Apparato Diferente IBD Centre of the Fondazione Policlinico 'A. Gemelli' IRCCS Rome, Italy Retrospective observational Time: 3/4 - 4/15	n = 1451 Inclusion: IBD patients receiving biotechnological drugs or enrolled in clinical trials and who were regularly followed up at the EMAD IBD Centre. Age: m 44 ± 15	Diseases: 522 UC, 784 CD, 87 IBD-U, 87 pouchitis Treatments: 392 infliximab, 450 adalimumab, 44 golimumab, 218 vedolizumab, 131 ustekinumab, 58 on clinical trials	COVID-19: 5	

	Gender: 609 female			
Allocca 2020²⁰ Humanitas University Hospital and Nancy General Hospital Milan, Italy and Vandœuvre-lès-Nancy, France Retrospective observational Time: NR	n = 6,000 (data reported for 15 infected only) Inclusion: Consecutive IBD patients infected by COVID-19 identified via regular telemedicine and infusion center visits Age: range 26-61 Gender: 4/15 female	Diseases: 6 UC, 9 CD Treatments: 6 infliximab, 2 adalimumab, 1 vedolizumab, 2 ustekinumab, 2 azathioprine, 1 mesalamine, 2 steroid, 1 tacrolimus, 1 everolimus, 1 clinical trial (placebo vs ustekinumab vs guselkimumab) Comorbidities: 1 renal transplantation, 1 PSC, 1 muscular dystrophy, 1 HTN, 1 obesity, 1 SpA, 1 mitral prolapse	COVID-19: 15	Hospitalization: 5 ICU: 0 Death: 0
Brenner 2020²¹ SECURE-IBD registry Multinational Retrospective observational Time: NR	n = 525 Inclusion: All cases of PCR-confirmed COVID-19 occurring in patients with IBD, regardless of severity. After at least 7 days from symptom onset and sufficient time	Diseases: 312 CD, 203 UC, 7 unspecified, 3 missing Treatments: 117 sulfasalazine, 18 budesonide, 37 oral/parenteral steroids, 53 6MP/AZA, 5 MTX, 176 anti-TNF alone, 52 anti-TNF with 6MP/AZA/MTX, 50 anti-integrin, 55	COVID-19: 525	Hospitalized: 161 ICU: 24 MV: 21 Death: 16 Multivariate regression models adjusting for age, gender, CD, active disease, use of steroids, anti-TNF, and 5-ASA product,

	had passed to observe the disease course through resolution of acute illness or death. Age: 42.9 ± 18.2 Gender: 43 female	IL12/23 inhibitor, 8 JAK inhibitor, 22 other, 29 none Comorbidities: 38 CVD, 29 DM, 44 lung disease, 63 HTN, 10 cancer, 4 stroke, 10 chronic renal disease, 26 chronic liver disease, 53 other		smoking, and having 2 or more comorbidities showed increased risk of death with age (aOR 1.07, 1.03-1.11), systemic corticosteroids (aOR 11.6, 2.1-64.7), and 5-ASA/sulfasalazine (aOR 1.71, 0.46-6.38), but not with anti-TNF (aOR 0.99, 0.23-4.23) or active disease (aOR 0.97, 0.26-3.62); composite ICU/ventilator/death with age (aOR 1.04, 1.01-1.06), systemic steroids (aOR 6.87, 2.3-20.5), having 2 or more comorbidities (aOR 2.87, 1.05-7.85), and use of 5-ASA (aOR 3.14, 1.28-7.71); composite hospitalization/death and age (aOR 1.03, 1.01-1.04), systemic steroids (aOR 6.5, 2.7-15.2), and have 2 or more comorbidities (aOR 4.4, 2.2-9.1)
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Rodriguez-Lago 2020 ²² Hospital de Galdakao and Biocruces Bizkaia Health Research Institute, Hospital Universitario Araba, Hospital Universitario de Cruces, and Hospital Universitario de Basurto, Spain Retrospective observational Time: 2/27 to 4/8	n = 40 Inclusion: All patients with IBD and a positive test for SARS-CoV-2 Age: M 40 (IQR 48-68) Gender: 24 male	Diseases: 13 Crohn's disease, 23 ulcerative colitis, 4 IBD unclassified Treatment: 26 mesalamine, 4 systemic steroids, 8 thiopurines, 3 MTX, 2 infliximab, 1 adalimumab, 1 vedolizumab, 3 ustekinumab, 1 thiopurine/anti-TNF, 1 thiopurine/ustekinumab Comorbidities: present in 25 patients	COVID-19: 40	ICU: 0 Hospitalization: 21 Death: 2
Taxonera 2020 ²³ Hospital Clínico San Carlos, Madrid, Spain Retrospective observational Time: up to 4/8	n = 1918 Inclusion: Men and women with an established diagnosis of IBD Age: m 50 ± 14 Gender: 997 males	Diseases: 920 Crohn's disease, 998 ulcerative colitis Treatment: 458 thiopurines, 90 MTX, 6 tofacitinib, 2 tacrolimus, 3 MMF, 110 infliximab, 119 adalimumab, 31 golimumab, 18 vedolizumab, 23 ustekinumab, 157 dual treatment with biologic and immunomodulator, 402 immunomodulator alone, 144 biologic alone	COVID-19: 12 (6.2/1000 crude incidence compared to 6.6/1000 in the general population of Madrid) PCR+: 12 Age: m 52 ± 17 Gender: 9 females Diseases: 7 CD, 5 UC	Hospitalization: 8 ICU: 1 MV: 1 Death: 2

Gubatan 2020 ²⁴ Stanford University Palo Alto, USA Retrospective observational Time: 3/4 to 4/14	n = 168 Inclusion: Patients with diagnosis code of CD, UC or indeterminate colitis who underwent testing for SRAS-CoV-2 Age: m 47.7 ± 16.3 Gender: 80 males	Diseases: 66 Crohn's disease, 86 ulcerative colitis, 16 IBD unclassified Treatment: 34 steroids, 58 5-ASA, 9 thiopurine, 6 MTX, 34 anti-TNF, 10 vedolizumab, 4 ustekinumab, 0 tofacitinb Comorbidities: present in 25 patients	COVID-19: 5	Death: 1
Bezzio 2020 ²⁵ IG-IBD Italy Retrospective observational Time: 3/11 to 3/29	n = 79 Inclusion: Adults with UC or CD with confirmed or likely diagnosis of COVID-19 Age: M 45 (range 18-80) Gender: 35 females	Diseases: 32 CD and 47 UC Treatment: 5 none, 24 5-ASA, 6 thiopurines, 9 steroids, 1 calcineurin inhibitors, 29 anti-TNF, 15 vedolizumab, 3 ustekinumab, 2 investigational Comorbidities: 9 HTN, 5 CHD, 5 COPD, 2 CMV, 2 psoriasis, 2 SpA, 1 MS, 1 RA, 2 undifferentiated CTD, 1 hypothyroidism, 1 Kaposi sarcoma	COVID-19: 79	Death 6 3 5-ASA, 2 steroids, 1 anti-TNF MV 6 Hospitalization 22 Factors associated with death (OR): age >65 19.6 (2.9-130.6), CCI score >1 16.7 (1.8-153.9), active IBD 8.4 (1.3-56.6), UC 2.9 (0.3-27.7), steroids 6.3 (0.9-44.2), anti-TNF 0.4 (0.1-3.8)

Khan 2020 ²⁶ Veterans Affairs Health System USA Retrospective observational Time: 1/1 to 5/15	n = 37857 Inclusion: IBD patients Age: 63 ± 15.8 Gender: NR	Diseases: NR Treatment: 2391 thiopurine, 4920 anti-TNF Comorbidities: NR	COVID-19: 36 Thiopurine 2 Anti-TNF 3	NR
Marafini 2020 ²⁷ Tor Vergata University Hospital Rome, Italy Retrospective observational Time: 3/24 to 4/30	n = 672 Inclusion: IBD patients scheduled for visits. They were called to inquire about symptoms. Age: M 46 (range 16-83) Gender: 311 females	Diseases: 397 Crohn's disease, 269 UC, 6 IBD unclassified Treatment: 56 no therapy, 367 5-ASA, 29 steroids, 43 immune suppressants, 183 anti-TNF, 27 vedolizumab, 31 ustekinumab, 38 antibiotics, 6 experimental Comorbidities: NR	COVID-19 3 Only 10 tested	Hospitalization 2 Death 1
Lukin 2020 ²⁸ NYU Presbyterian Hospital-Weill Cornell Medical Center New York, USA Retrospective observational Time: NR	n = 119 Inclusion: Active IBD patients Age: 53 ± 44.5 Gender: NR	Diseases: 69 Crohn's disease, 46 ulcerative colitis, 4 IBD unclassified Treatment: 84 biologics, 35 steroids, 22 budesonide, 38 5-ASA, 5 immunomodulators. 4 combination therapy Comorbidities: NR	COVID-19: 29 PCR+ 9	NR

Neurologic Disease				
Parrotta 2020²⁹ NYU Multiple Sclerosis Comprehensive Care Center New York, USA Retrospective observational Time: 3/16 to 4/30	n = 76 Inclusion: MS or related disorder who was diagnosed with COVID-19 Age: NR Gender: NR	Diseases: 72 MS, 4 related disorders (neuromyelitis optica spectrum, chronic relapsing inflammatory optic neuropathy, neurosarcoidosis, myelin oligodendrocyte glycoprotein immunoglobulin G associated disorder) Treatments: 34 anti CD20, 10 S1P, 6 glatiramer acetate, 4 natalizumab, 4 dimethyl fumarate, 3 interferon, 3 IVIG, 12 none Comorbidities: 17 HTN, 23 obesity, 8 DM, 4 VTE, 3 CAD, 4 history of cancer, 3 baclofen pump, 3 indwelling foley	COVID-19: 76 PCR+ 37	Hospitalization: 18 Death: 6 5/18 hospitalized and 1/58 not hospitalized died. 2/34 on anti-CD20, 1/6 on glatiramer, 1/4 on natalizumab, 2/12 on no treatment died.
Fan 2020³⁰ Chinese Medical Network of Neuroinflammation China Retrospective observational	n = 4864 Inclusion: Patient with MS or neuromyelitis optica spectrum disorders were surveyed	Diseases: 1804 MS and 3060 neuromyelitis optica spectrum disorders Treatments: 159 interferon beta, 475 teriflunomide, 63 fingolimod,	COVID-19: 2 Both on steroids	Death: 0

Time: 1/15 – 3/15	Age: NR Gender: NR	489 rituximab, 46 dimethyl fumarate, 6 cladribine, 4 alemtuzumab, 759 methylprednisolone, 405 azathioprine, 832 MMF, 403 tacrolimus, 62 tocilizumab, 39 cyclophosphamide		
Abbreviations: n, number of patients; m, mean; M, median; IQR, interquartile range; RA, rheumatoid arthritis; SpA, spondyloarthritis; SLE, systemic lupus erythematosus; CTD, connective tissue disease; PsA, psoriatic arthritis; PMR, polymyalgia rheumatica; GCA, giant cell arteritis; EGPA, eosinophilic granulomatosis with polyangiitis; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; SSc, systemic sclerosis; HCQ, hydroxychloroquine; MTX, methotrexate; AZA, azathioprine; TNF, tumor necrosis factor; DM, diabetes mellitus; HTN, hypertension; CVD, cardiovascular; DMARDs, disease modifying anti-rheumatic drugs; cs-DMARD, conventional synthetic DMARD; tsDMARD, target-synthetic DMARD; bDMARD, biologic DMARD; IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis; PSC, primary sclerosing cholangitis; MMF, mycophenolate; MS, multiple sclerosis; S1P, Sphingosine-1-phosphate receptor modulator; CAD, coronary artery disease; CHF, congestive heart failure; IVIG, intravenous immunoglobulins; VTE, venous thromboembolic disease; ICU, intensive care unit admission; NIPPV, non-invasive positive pressure ventilation; MV, mechanical ventilation; anti-BLys, anti-B-lymphocyte stimulator; NR, not reported; OR, odds ratio; uOR, unadjusted odds ratio; aOR, adjusted odds ratio.				

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Table s4I. Included studies for Recommendation 14

Studies that Compared the Outcome of COVID-19 in Patients with and without Autoimmune Disease				
Study	Inclusion criteria	Autoimmune Disease Group	No Autoimmune Disease	Outcomes
In asymptomatic patients with autoimmune disease, should testing vs. no testing for SARS-CoV-2 be performed before initiation of immunosuppressive therapy?				
Outcome of COVID in Rheumatologic Patients				
Pablos 2020 ¹ 5 centers of the Research network for the Investigation of Inflammation and Rheumatic Diseases, Spain Retrospective observational Time: up to 4/17	Inclusion: Hospital PCR+ COVID-19 rheumatic patients matched by age, sex, and PCR date to non-rheumatic controls (randomly sampled 1:1)	n = 228 Age: M 63 (IQR 54-78) Gender: 87 males Diseases: 136 inflammatory arthritis, 65 RA, 35 SpA, 36 PsA, 92 CTD Treatments: steroids 91 (dose >10 15), MTX 64, antimalarial 28, leflunomide 20, sulfasalazine 17, MMF 12, azathioprine 7, cyclophosphamide 2, calcineurin 7, TNF inhibitor 35, rituximab 5, IL 17/IL 23 antagonist 4, abatacept 3, tocilizumab 2, sarilumab 1, tofacitinib 3 Comorbidities: 71 obesity, 46 DM, 111 HTN, 64 CVD, 45 lung disease	n = 228 Age: M 65 (IQR 53-77) Gender: 95 males Comorbidities: 38 obesity, 39 DM, 99 HTN, 42 CVD, 48 lung disease	Death: 41 vs 30 ICU: 15 vs 16 Hospitalization: 162 vs 175 MV: 8 vs 6 NIPPV: 11 vs 13 Supplemental O2: 106 vs. 113 Significant complications (subcategories of heart failure, encephalopathy, thrombotic event, kidney failure, septic shock): 63 vs 55 Association of risk factors with poor outcome (adjusted OR): chronic inflammatory arthritis (1.82, 1-3.3), age > 60 (4.8, 2.8-8.4), male sex (1.9, 1.2-3.1), obesity (1.5, 0.9-2.5), DM (0.8, 0.5-1.5), heart failure (1.6, 0.9-2.7),

				glucocorticoids (1.1, 0.6-2.01), antivirals (2.1, 1.3-3.2).
Silva 2020 ² MGH and BWH Boston, USA Retrospective observational Time: 1/30 – 4/8	Inclusion: age >17, positive PCR. Identified patients with rheumatic diseases and matched them to patients with not rheumatic diseases (1:2 ratio, based on date of PCR, age, sex)	n = 54 Age: m 62.5 ± 15.1 Gender: 39 females Disease: 19 RA, 10 SLE, 7 PMR, 7 seronegative SpA, 3 myositis, 1 GCA, 2 small vessel vasculitis, 1 sarcoidosis, 1 JIA, 1 Kikuchi's disease Treatments: 9 HCQ, 7 anti-TNF, 1 IL-6 inhibitor, 2 belimumab, 3 rituximab, 2 IL- 12/IL-23 inhibitor, 1 abatacept, 3 tofacitinib, 9 MTX, 4 leflunomide, 3 MMF, 5 prednisone Comorbidities: 20 former smokers, 2 current smokers, 34 HTN, 13 DM, 12 CAD, 4 CHF, 3 ILD, 14 asthma, 2 COPD, 7 OSA	n = 104 Age: m 63.1 ± 14.9 Gender: 72 female Comorbidities: 20 former smoker, 6 current smoker, 50 HTN, 29 DM, 10 CAD, 11 CHF, 17 asthma, 7 COPD, 4 OSA	Death: 3/52 vs 4/104 ICU: 11/52 vs 7/104 Supplemental O2: 17/52 vs. 26/104 Hospitalization: 23/52 vs 42/104 Association of rheumatic disease with: hospitalization aOR1 (age and BMI) 1.27 (0.61-2.6), aOR2 (age, BMI, smoking, #comorbidities) 1.22 (0.56-2.6) and aOR3 (age, HTN, CAD, lung disease) 1.1 (0.5-2.4) MV/ICU aOR1 (age and BMI) 3.3 (1.2- 9.1), aOR2 (age, BMI, smoking, #comorbidities) 3.1 (1.1-9.1) and aOR3 (age, HTN, CAD, lung disease) 2.9 (1.0- 8.5) death aOR1 (age and BMI) 1.6 (0.3- 8.03)
Outcome of COVID in IBD				
Lukin 2020 ³	Inclusion: All confirmed or highly	n = 80 Age: m 48.3 ± 18.3	n = 160 Age: m 48.7 ± 17.7	Hospitalization 17 vs 34 Death 0 vs 2

NYU Presbyterian Hospital-Weill Cornell Medical Center New York, USA Retrospective observational Time: NR	suspected COVID-19 patients at the hospital. Patients with IBD were matched with patients without IBD based on decade of age and gender (1:2)	Gender: 45 males Diseases: IBD Treatments: 10 steroids, 22 immunosuppressants Comorbidities: 14 HTN, 4 DM, 5 CKD, 5 CVD, 2 COPD, 9 cancer, 5 chronic liver disease, 1 solid organ transplant	Gender: 90 males Comorbidities: 38 HTN, 20 DM, 7 CKD, 10 CVD, 19 COPD, 4 cancer, 2 chronic liver disease, 1 solid organ transplant	MV 2 vs 11 ICU 3 vs 11
Outcome of COVID in Dermatologic Diseases				
Damiani 2020 ⁴ San Donato Hospital Milan, Italy Retrospective cohort Time: 2/21 – 4/09	Inclusion: adult patients, moderate to severe plaque psoriasis for more than 1 year, approved anti-psoriasis monotherapy (biologics or small molecules), being in the maintaining phase. The control	n = 1,193 Age: m 55 Gender: 68% males Diseases: moderate/severe plaque psoriasis Treatments: 262 anti-TNF, 238 anti-IL12/23, 542 anti-IL17, 62 anti-IL23, 89 small molecules Comorbidities: 215 obesity, 167 CVD, 346 HTN, 143 DM, 197 COPD, 53 OSA, 298 PsA	n = 10,060,574 Age: m 65 Gender: 48.9% males Comorbidities: NR	COVID-19 22 vs 54,901 Patients on biologics were at higher risk of developing COVID-19 (uOR 3.4, 2.3-5.7) Home quarantine 17 vs 16,042 (OR 9.1, 5.6-14.6) Hospitalization 5 vs 11,796 Risk of ICU admission (uOR 3.4, 0.2-54.6) Death 0 vs 10,222 (uOR 0.4, 0.03-6.6).

	group was the Lombardi population.			
n, number of patients; m, mean; M, median; IQR, interquartile range; RA, rheumatoid arthritis; SpA, spondyloarthritis; SLE, systemic lupus erythematosus; CTD, connective tissue disease; PsA, psoriatic arthritis; PMR, polymyalgia rheumatica; GCA, giant cell arteritis; HCQ, hydroxychloroquine; MTX, methotrexate; AZA, azathioprine; TNF, tumor necrosis factor; DM, diabetes mellitus; HTN, hypertension; CVD, cardiovascular; CAD, coronary artery disease; CHF, congestive heart failure; OSA, obstructive sleep apnea; IBD, inflammatory bowel disease; MMF, mycophenolate; NIPPV, non-invasive positive pressure ventilation; MV, mechanical ventilation; ICU, intensive care unit admission; -ILD, interstitial lung disease; NR, not reported; OR, odds ratio; uOR, unadjusted odds ratio; aOR, adjusted odds ratio.				

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Table s4m. Included studies for Recommendations 15-17

Studies informing baseline risk and patient outcome				
Author (year)	Study Design	Patient Selection/Tests	Outcome	Results
In asymptomatic individuals, should nucleic acid amplification testing vs. no testing be done before aerosol generating surgeries or procedures to diagnose COVID19 and inform PPE use?				
Lei S. et al (2020) ¹	Retrospective observational study	Retrospective review of patients charts who had undergone elective surgeries admitted from January 1 to February 5, 2020, the early stage of COVID-19 epidemic in Wuhan, China. 37 asymptomatic patients developed symptoms after operation and were diagnosed with COVID-19 according to WHO interim guidance.	Patients requiring ICU admission Patients death	15 (44.1%) patients 7 (20.5%) patients died
Gudbjartsson D.F. et al (2020) ²	Cohort	22279 patients. Targeted screening: 9199 patients who were symptomatic (cough, fever, body aches, and shortness of breath) and/or who were returning to Iceland from countries or regions that were classified by the health authorities as being at high risk or who had been in contact with infected persons. Population screening: 10,797 residents of Iceland who were symptom-free or who had mild symptoms of the common cold (most of them living in Reykjavik, the capital of Iceland.) Random sampling 2283 randomly chosen Icelanders between the ages 20 and 70 years to participate	Positive among Targeted screening. Positive among population screening. Positive among random sampling screening.	1221/9199 (13.3%) 87/10,797 (0.8%) 13/2283 (0.6%)

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		through a telephone text message sent between March 31 and April 1. Nasopharyngeal and oropharyngeal samples were collected and were combined into a single tube for each participant before RNA isolation.		
Folgueira M.D. et al (2020) ³	Cohort	2085 patients from a total of 6800 employees of the Hospital Universitario 12 de Octubre, in Madrid, Spain 2085 (30,6 %) were tested during the period 1-29 March 2020, some of them repeatedly (2286 total samples).	The health care workers were divided into 3 groups based on their risk level: High risk exposure areas: The emergency room, areas with concentrated COVID19 patients, ICU, and Anesthesia. Medium risk Areas: Surgery, Oncology, Hematology, Radiology, Ob/Gyn, Pediatrics, Medical areas nonCOVID19 related and outpatient areas. Low risk exposure areas: Laboratory, Pharmacy, Kitchen and administrative personnel.	791/2085 (38%) tested positive. High risk: 43.6% Moderate risk: 40.96% Low risk: 41.92%

Zhong O. et al (2020) ⁴	Cohort	Patients with radiologically confirmed COVID-19 undergoing spinal anesthesia (45 C-section, and 4 orthopedic surgery) were enrolled if they had clinically confirmed COVID-19, in accord with current diagnostic criteria (13/49 had confirmed RT-PCR). Anesthesiologists who delivered clinical care to patients confirmed as having COVID-19 during surgery, but who had no contact with confirmed COVID-19 patients beyond the operating theatre.	Post-op severe pneumonia or death RT-PCR positive among anesthesiologist / type of PPE	0/49 had post op severe pneumonia or death 5/44 anesthesiologist developed COVID-19 1/37 anesthesiologists were using level 3 PPE 4/7 anesthesiologists were using level 1 PPE
Chen R. et al (2020) ⁵	Cohort	17 pregnant women undergoing C-section Three patients received general anesthesia Fourteen patients had epidural anesthesia.	Number of post c- section recovered Number of Neonates discharged Number of medical staff infected.	Fourteen patients quickly recovered from COVID-19 and were discharged from hospital after six to 13 days in the hospital. The three patients remaining are still in the hospital as of 1 March 2020 recovering from their Cesarean delivery and COVID-19 17 neonates discharged No medical staff were infected.

References

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Supplement B

Recommendation 1: In symptomatic individuals in the community suspected of having COVID-19, should COVID-19 nucleic acid amplification testing vs. no testing be done to guide decisions about isolation?

Table s5. GRADE evidence profile, recommendation 1

Certainty assessment							Impact	Certainty
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		

Percent diagnosed based on suspicion criteria

8	observational studies	serious ^a	serious ^b	very serious ^c	not serious	none	For this question, "In symptomatic individuals in the community suspected of having COVID-19, should COVID-19 nucleic acid amplification testing vs. no testing be done?", we referred to 8 studies. Each of these studies reported the positivity rate of COVID-19 among patients suspected of having COVID-19 based on specific criteria, clinical and/or epidemiological. The COVID-19 positivity rate ranged from 2.4 to 57% among studies. The clinical scenarios were variable among the included studies, including respiratory infection symptoms such as cough, shortness of breath, fever, and pneumonia, alongside radiologic and biomarker indicators of having the disease.	⊕○○○ VERY LOW
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Explanations

- There is serious concern about how different studies defined and assessed the clinical characteristics of patients suspected of having COVID-19. This concern prohibited us from assessing how these characteristics affect the prediction of positive cases. There is also a serious concern about the reference standard used to confirm COVID-19 cases in many of the included studies.

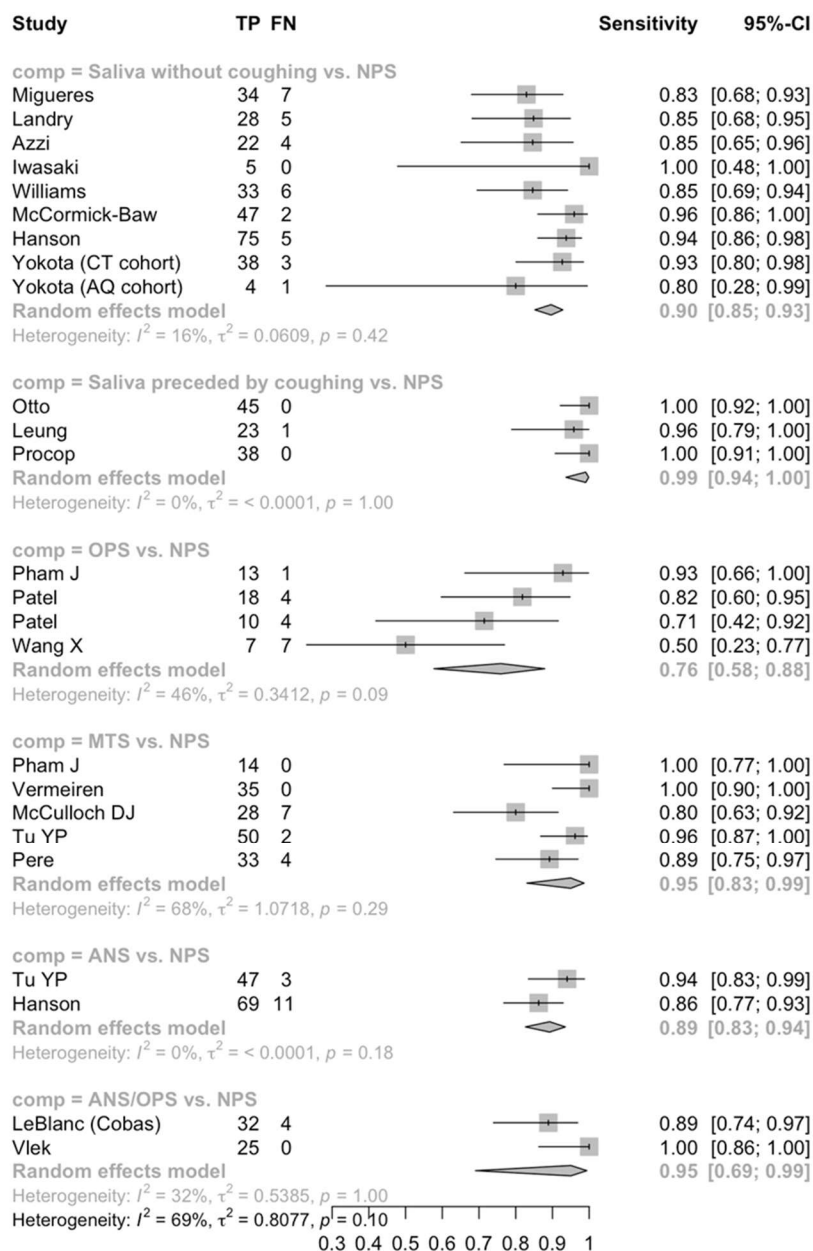
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- b. There is serious unexplained inconsistency in the results.
- c. The included studies do not directly compare a strategy of testing vs relying on clinical judgment. However, the indirect information from observational studies estimating the proportion of people who were confirmed out of all those who were suspected based on their clinical presentation provided indirect estimates about the false positive rates. Furthermore, four of these studies included patients presenting to the hospital which is a different population than a community-based symptomatic population.

Supplement C

Recommendation 2: In symptomatic individuals suspected of having COVID-19, are anterior nasal swabs, mid-turbinate/deep nasal swabs, oropharyngeal/throat swabs and/or saliva acceptable alternatives to nasopharyngeal swabs for diagnosis of COVID-19 from the standpoint of diagnostic accuracy?

Figure s2a. Sample Sensitivity/Specificity by Proportion



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Figure s2b. Sample Sensitivity/Specificity by Proportion

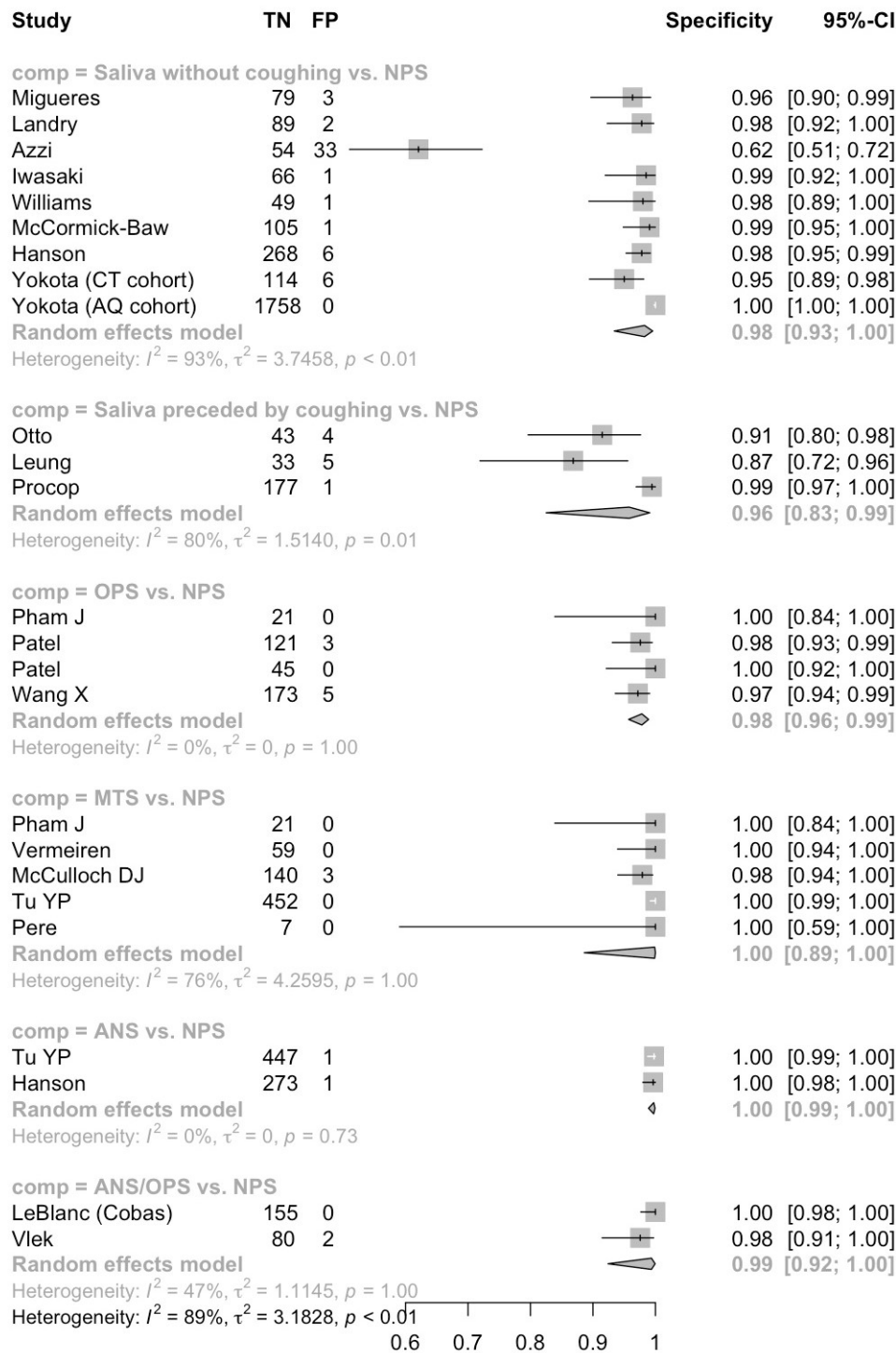


Table s6. GRADE Summary of Findings of test accuracy results for prevalence/pre-test probability of 1% for different specimen types

Sample site	Saliva without coughing	Saliva with coughing	OP swab	AN swab	MT swab	Combined AN/OP swab
Sensitivity	0.90 (95% CI: 0.85 to 0.93)	0.99 (95% CI: 0.94 to 1.00)	0.76 (95% CI: 0.58 to 0.88)	0.89 (95% CI: 0.83 to 0.94)	0.95 (95% CI: 0.83 to 0.99)	0.95 (95% CI: 0.69 to 0.99)
Specificity	0.98 (95% CI: 0.93 to 1.00)	0.96 (95% CI: 0.83 to 0.99)	0.98 (95% CI: 0.96 to 0.99)	1.00 (95% CI: 0.99 to 1.00)	1.00 (95% CI: 0.89 to 1.00)	0.99 (95% CI: 0.92 to 1.00)
Outcome	Effect per 1,000 patients tested					
	Pre-test probability of 1%^{a, f}					
True positives (patients with COVID-19)	9 (9 to 9)	10 (9 to 10)	8 (6 to 9)	9 (8 to 9)	10 (8 to 10)	10 (7 to 10)
False negatives (patients incorrectly classified as not having COVID-19)	1 (1 to 1)	0 (0 to 1)	2 (1 to 4)	1 (1 to 2)	0 (0 to 2)	0 (0 to 3)
Quality of the evidence	9 studies 387 patients ⊕⊕○○ LOW ^b	3 studies 137 patients ⊕⊕○○ LOW ^b	4 studies 64 patients ⊕○○○ Very LOW ^{b,e}	2 studies 130 patients ⊕⊕○○ LOW ^b	5 studies 855 patients ⊕⊕○○ LOW ^b	2 studies 61 patients ⊕○○○ Very LOW ^{b,e}
True negatives (patients without COVID-19)	970 (921 to 990)	950 (822 to 980)	970 (950 to 980)	990 (980 to 990)	990 (881 to 990)	980 (911 to 99)

False positives (patients incorrectly classified as having COVID-19)	20 (0 to 69)	40 (10 to 168)	20 (10 to 40)	0 (0 to 10)	0 (0 to 109)	10 (0 to 79)
Quality of evidence	9 studies 2662 patients ⊕⊕○○ LOW ^{b,c}	3 studies 316 patients ⊕○○○ Very LOW ^{b,d}	4 studies 368 patients ⊕⊕○○ LOW ^b	2 studies 722 patients ⊕⊕○○ LOW ^b	5 studies 682 patients ⊕○○○ Very LOW ^{b,d}	2 studies 237 patients ⊕⊕○○ LOW ^b

Explanations: This table is based on applying the sensitivity and specificity estimates to calculate true and false positives and negatives in a hypothetical population of 1000 individuals

- Typically seen in general population in areas that are not hotspots
- Using the NP swab as the only reference standard increases the risk of bias for all the studies due to its imperfect accuracy.
- One study with unexplained inconsistent results noted. However, a sensitivity analysis without this study showed robustness of the overall pooled estimate of specificity.
- Considering the upper and lower limits of the confidence interval might lead to different clinical decisions.
- The test of interest was conducted in a small number of patients which might lead to imprecise results.
- The different sample types were not assessed directly in the same studies.

Table s7. GRADE Summary of Findings of test accuracy results for prevalence/pre-test probability of 10% for different specimen types

Sample site	Saliva without coughing	Saliva with coughing	OP swab	AN swab	MT swab	Combined AN/OP swab
Sensitivity	0.90 (95% CI: 0.85 to 0.93)	0.99 (95% CI: 0.94 to 1.00)	0.76 (95% CI: 0.58 to 0.88)	0.89 (95% CI: 0.83 to 0.94)	0.95 (95% CI: 0.83 to 0.99)	0.95 (95% CI: 0.69 to 0.99)
Specificity	0.98 (95% CI: 0.93 to 1.00)	0.96 (95% CI: 0.83 to 0.99)	0.98 (95% CI: 0.96 to 0.99)	1.00 (95% CI: 0.99 to 1.00)	1.00 (95% CI: 0.89 to 1.00)	0.99 (95% CI: 0.92 to 1.00)
Outcome	Effect per 1,000 patients tested					
	Pre-test probability of 10%^{a, f}					
True positives (patients with COVID-19)	90 (85 to 93)	99 (94 to 100)	76 (58 to 88)	89 (83 to 94)	95 (83 to 99)	95 (69 to 99)
False negatives (patients incorrectly classified as not having COVID-19)	10 (7 to 15)	1 (0 to 6)	24 (12 to 42)	11 (6 to 17)	5 (1 to 17)	5 (1 to 31)
Quality of the evidence^{b,c,d}	9 studies 387 patients ⊕⊕○○ LOW ^b	3 studies 137 patients ⊕⊕○○ LOW ^b	4 studies 64 patients ⊕○○○ Very LOW ^{b,d,e}	2 studies 130 patients ⊕⊕○○ LOW ^b	5 studies 855 patients ⊕⊕○○ LOW ^b	2 studies 61 patients ⊕○○○ Very LOW ^{b,d,e}
True negatives (patients without COVID-19)	882 (837 to 900)	864 (747 to 891)	882 (864 to 891)	900 (891 to 900)	900 (801 to 900)	891 (828 to 900)

False positives (patients incorrectly classified as having COVID-19)	18 (0 to 63)	36 (9 to 153)	18 (9 to 36)	0 (0 to 9)	0 (0 to 99)	9 (0 to 72)
Quality of Evidence	9 studies 2662 patients ⊕⊕○○ LOW ^{b,c}	3 studies 316 patients ⊕○○○ Very LOW ^{b,d}	4 studies 368 patients ⊕⊕○○ LOW ^b	2 studies 722 patients ⊕⊕○○ LOW ^b	5 studies 682 patients ⊕○○○ Very LOW ^{b,d}	2 studies 237 patients ⊕⊕○○ LOW ^b

Explanations: This table is based on applying the sensitivity and specificity estimates to calculate true and false positives and negatives in a hypothetical population of 1000 individuals

- Typically seen in general population in high risk population
- Using the NP swab as a reference standard increases the risk of bias for all the studies.
- One study with unexplained inconsistent results noted. However, a sensitivity analysis without this study showed robustness of the overall pooled estimate of specificity.
- Considering the upper and lower limits of the confidence interval might lead to different clinical decisions.
- The test of interest was conducted in a small number of patients which might lead to imprecise results.
- The different sample types were not assessed directly in the same studies.

Table s8. GRADE Summary of Findings of test accuracy results for prevalence/pre-test probability of 40% for different specimen types

Sample site	Saliva without coughing	Saliva with coughing	OP swab	AN swab	MT swab	Combined AN/OP swab
Sensitivity	0.90 (95% CI: 0.85 to 0.93)	0.99 (95% CI: 0.94 to 1.00)	0.76 (95% CI: 0.58 to 0.88)	0.89 (95% CI: 0.83 to 0.94)	0.95 (95% CI: 0.83 to 0.99)	0.95 (95% CI: 0.69 to 0.99)
Specificity	0.98 (95% CI: 0.93 to 1.00)	0.96 (95% CI: 0.83 to 0.99)	0.98 (95% CI: 0.96 to 0.99)	1.00 (95% CI: 0.99 to 1.00)	1.00 (95% CI: 0.89 to 1.00)	0.99 (95% CI: 0.92 to 1.00)
Outcome	Effect per 1,000 patients tested					
	pre-test probability of 40%^{a,f}					
True positives (patients with COVID-19)	360 (340 to 372)	396 (376 to 400)	304 (232 to 352)	356 (332 to 376)	380 (332 to 396)	380 (276 to 396)
False negatives (patients incorrectly classified as not having COVID-19)	40 (28 to 60)	4 (0 to 24)	96 (48 to 168)	44 (24 to 68)	20 (4 to 68)	20 (4 to 124)
Quality of the evidence^{b,c,d}	9 studies 387 patients ⊕⊕○○ LOW ^b	3 studies 137 patients ⊕○○○ Very LOW ^{b, d}	4 studies 64 patients ⊕○○○ Very LOW ^{b,e}	2 studies 130 patients ⊕⊕○○ LOW ^b	5 studies 855 patients ⊕○○○ Very LOW ^{b,d}	2 studies 61 patients ⊕○○○ Very LOW ^{b,d,e}
True negatives (patients without COVID-19)	588 (558 to 600)	576 (498 to 594)	588 (576 to 594)	600 (594 to 600)	600 (534 to 600)	594 (552 to 600)

False positives (patients incorrectly classified as having COVID-19)	12 (0 to 42)	24 (6 to 102)	12 (6 to 24)	0 (0 to 6)	0 (0 to 66)	6 (0 to 48)
Quality of Evidence	9 studies 2662 patients ⊕⊕○○ LOW ^{b,c}	3 studies 316 patients ⊕○○○ Very LOW ^{b,d}	4 studies 368 patients ⊕⊕○○ LOW ^b	2 studies 722 patients ⊕⊕○○ LOW ^b	5 studies 682 patients ⊕⊕○○ LOW ^b	2 studies 237 patients ⊕⊕○○ LOW ^b

Explanations: This table is based on applying the sensitivity and specificity estimates to calculate true and false positives and negatives in a hypothetical population of 1000 individuals

- Typically seen in general population in exposed and nursing homes
- Using the NPS as a reference standard increases the risk of bias for all the studies.
- One study with unexplained inconsistent results noted. However, a sensitivity analysis without this study showed robustness of the overall pooled estimate of specificity.
- Considering the upper and lower limits of the confidence interval might lead to different clinical decisions.
- The test of interest was conducted in a small number of patients which might lead to imprecise results.
- The different sample-types were not assessed directly in the same studies.

Supplement D

Recommendation 3: In symptomatic individuals with URTI or ILI suspected of having COVID-19, should non-invasive specimen be collected by healthcare providers (HCP) vs patients (i.e., will collection by HCP vs patients affect diagnostic accuracy of the test)?

Figure s3. Sensitivity of Self-Collected and Healthcare Collected Nasal Sampling

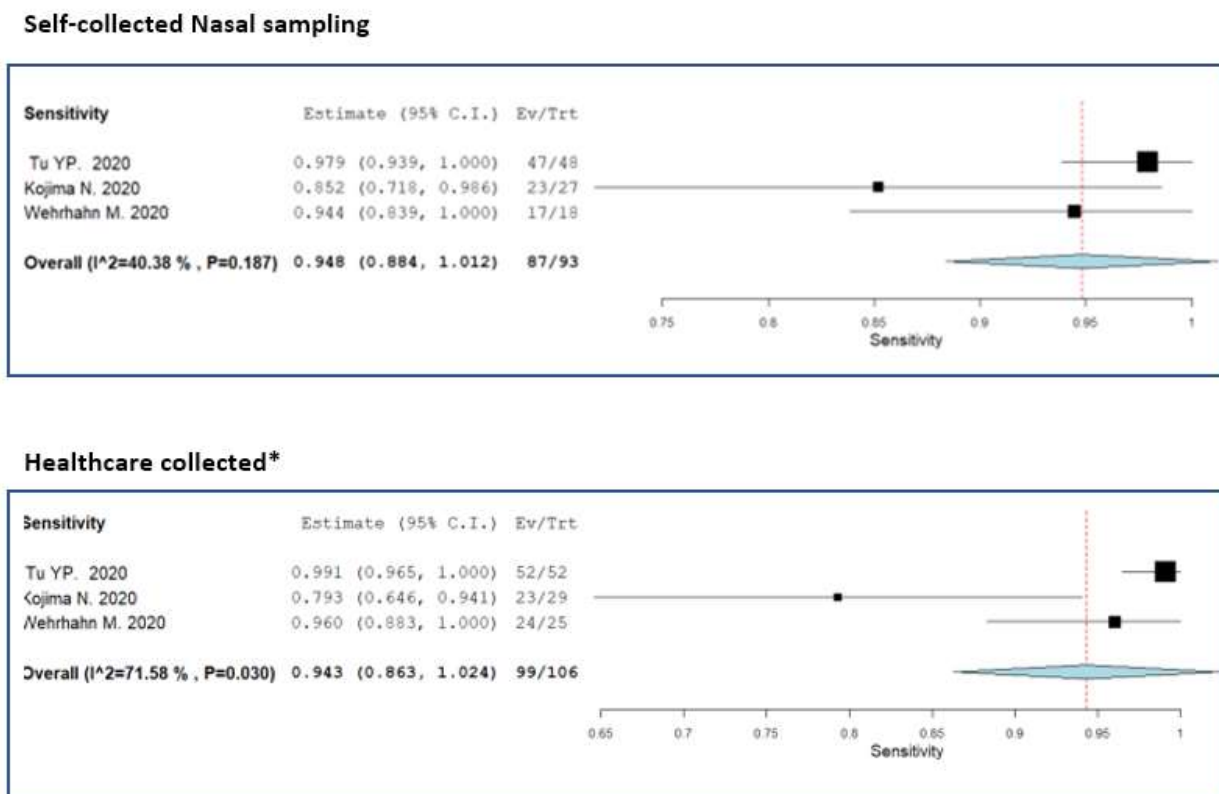


Table s9. Sensitivity and Specificity of Self-Collected versus Healthcare-Collected Samples

	Self-collected nasal						Healthcare worker collected			
Sensitivity	0.95 (95% CI: 0.88 to 1.00)						0.94 (95% CI: 0.86 to 1.00)			
Specificity	1.00 (95% CI: 0.99 to 1.00)						1.00 (95% CI: 0.99 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
								pre-test probability of 10% ^c		
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Self-collected nasal	Health care worker collected	
True positives (patients with COVID-19)	3 studies 200 patients	cross-sectional (cohort type accuracy study)	serious ^a	serious ^b	not serious	not serious	none	95 (88 to 100)	94 (86 to 100)	⊕⊕○○ LOW
								1 more TP in Self-collected Nasal		
False negatives (patients incorrectly classified as not having COVID-19)								5 (0 to 12)	6 (0 to 14)	
								1 fewer FN in Self-collected Nasal		
True negatives (patients without COVID-19)	3 studies 600 patients	cross-sectional (cohort type accuracy study)	serious ^a	serious ^b	not serious	not serious	none	900 (891 to 900)	900 (891 to 900)	⊕⊕○○ LOW
								0 fewer TN in Self-collected Nasal		
False positives (patients incorrectly classified as having COVID-19)								0 (0 to 9)	0 (0 to 9)	
								0 fewer FP in Self-collected Nasal		

Explanations: This table is based on applying the sensitivity and specificity estimates to calculate True and false positives and negatives in a hypothetical population of 1000 individuals

a. There is a high risk of bias in regard to the reference test that is considered to be the healthcare provider collected swab result.

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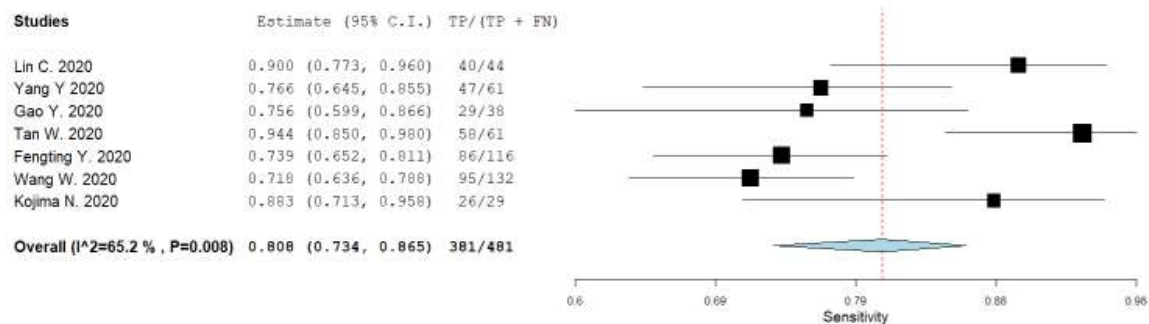
- b. The studies provide test accuracy results or concordance results but do not provide patient-important outcomes based on those results.
- c. Typically seen in symptomatic outpatients who have not reached a hospital facility.

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Recommendation 4: In symptomatic individuals with LRTI suspected of having COVID-19, which of the different specimen types (upper vs lower sampling) should be used [i.e., will specimen type (upper vs lower sampling) affect the diagnostic accuracy of the test]?

Figure s4. Forest plots of bivariate pooling of the DTA results from the seven studies

LRT Sampling:



URT Sampling:

Sens Forest Plot

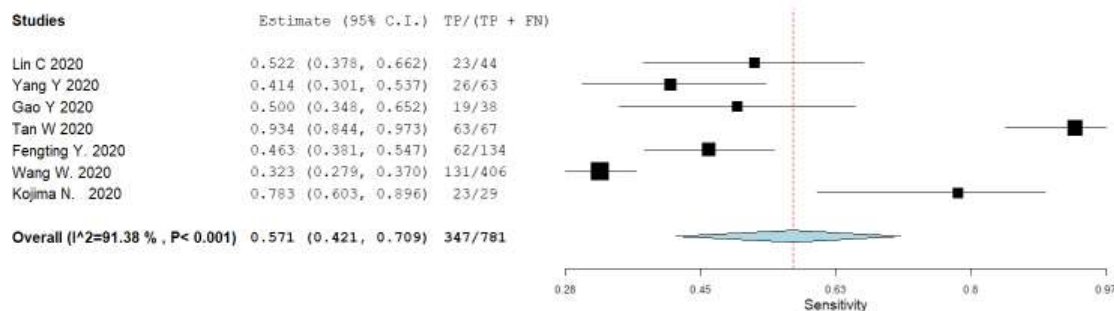


Table s10. GRADE Evidence Profile of Test Accuracy Results for Prevalence/Pre-Test Probability of 40% and 80% for URT vs LRT Sampling (7 studies)

	Upper respiratory tract sample							Lower respiratory tract sampling				
Sensitivity	0.57 (95% CI: 0.42 to 0.71)							0.81 (95% CI: 0.73 to 0.86)				
Specificity	1.00 (95% CI: 0.99 to 1.00)							1.00 (95% CI: 0.99 to 1.00)				
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
								pre-test probability of 40% ^a		pre-test probability of 80% ^b		
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	URT sampling	LRT sampling	URT sampling	LRT sampling	
True positives (patients with COVID-19)	7 studies 1244 patients	cohort & case-control type studies	serious ^{a,b}	serious ^c	serious ^d	serious ^e	none	228 (168 to 284)	324 (292 to 344)	456 (336 to 568)	648 (584 to 688)	⊕○○○ VERY LOW
False negatives (patients incorrectly classified as not having COVID-19)								96 fewer TP in URT sampling		192 fewer TP in URT sampling		
								172 (116 to 232)	76 (56 to 108)	344 (232 to 464)	152 (112 to 216)	
								96 more FN in URT sampling		192 more FN in URT sampling		
True negatives (patients without COVID-19)	1 study 8 patients	cross-sectional (cohort type accuracy study)	not serious	serious ^c	not serious	very serious ^f	none	600 (594 to 600)	600 (594 to 600)	200 (198 to 200)	200 (198 to 200)	⊕○○○ VERY LOW
False positives (patients incorrectly								0 fewer TN in URT sampling		0 fewer TN in URT sampling		
								0 (0 to 6)	0 (0 to 6)	0 (0 to 2)	0 (0 to 2)	

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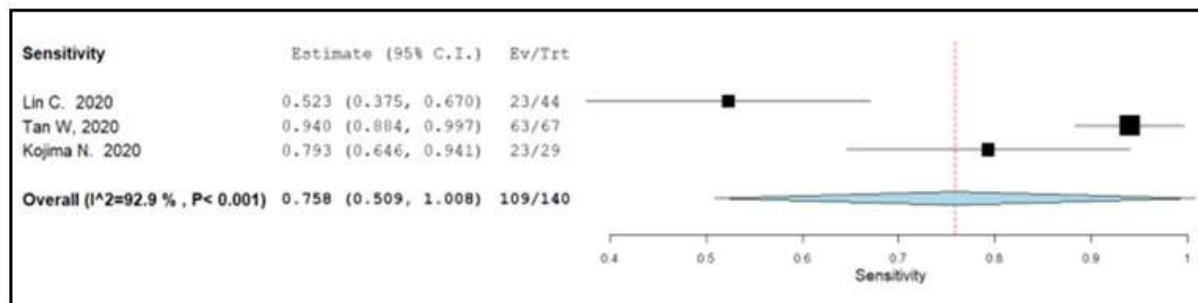
classified as having COVID-19)								0 fewer FP in URT sampling	0 fewer FP in URT sampling	
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Explanations: This table is based on applying the sensitivity and specificity estimates to calculate True and false positives and negatives in a hypothetical population of 1000 individuals

- a. The case-control design leads to a serious study population bias.
- b. The Fengting Y. (2020) study showed results as the number of samples and not the number of patients.
- c. There was no direct evidence comparing the accuracy of a strategy with starting with upper sample and then conducting a lower sample if the upper sample is negative. Additionally, studies reported test accuracy results but did not report on patient-important and population-important outcomes based on the results.
- d. There is serious unexplained heterogeneity.
- e. Considering the upper vs lower limits of the sensitivity's confidence interval would lead to different clinical decisions.
- f. A very low number of patients.
- g. Typically seen in patients meeting clinical definition for COVID-19 who were hospitalized.
- h. Typically seen in patients meeting clinical definition for COVID-19 who were admitted to intensive care units.

Figure s5. Forest plots of sensitivity for upper and lower respiratory tract sampling

Forest Plot of sensitivity pooled by proportion for the URT sampling from the 3 cohort studies.



Forest Plot of sensitivity pooled by proportion for the LRT sampling from the 3 cohort studies.

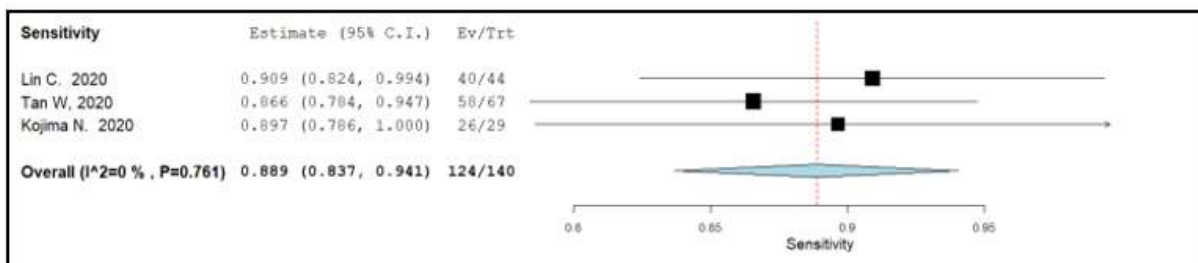


Table s11. GRADE Evidence Profile of Test Accuracy Results for Prevalence/Pre-Test Probability of 40% and 80% for URT vs. LRT Sampling (3 studies)

	Upper respiratory tract sample							Lower respiratory tract sampling				
Sensitivity	0.76 (95% CI: 0.51 to 1.00)							0.76 (95% CI: 0.51 to 1.00)				
Specificity	1.00 (95% CI: 0.99 to 1.00)							1.00 (95% CI: 0.99 to 1.00)				
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
								pre-test probability of 40% ^d		pre-test probability of 80% ^e		
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	URT sampling	LRT sampling	URT sampling	LRT sampling	
True positives (patients with COVID-19)	3 studies 280 patients	cross-sectional (cohort type accuracy study)	not serious	serious ^a	serious ^b	serious ^c	none	304 (204 to 400)	356 (336 to 376)	608 (408 to 800)	712 (672 to 752)	⊕○○○ VERY LOW
								52 fewer TP in URT sampling		104 fewer TP in URT sampling		
False negatives (patients incorrectly classified as not having COVID-19)								96 (0 to 196)	44 (24 to 64)	192 (0 to 392)	88 (48 to 128)	
								52 more FN in URT sampling		104 more FN in URT sampling		
True negatives (patients without COVID-19)	1 study 8 patients	cross-sectional (cohort type accuracy study)	not serious	serious ^a	not serious	Very serious ^c	none	600 (594 to 600)	600 (594 to 600)	200 (198 to 200)	200 (198 to 200)	⊕○○○ VERY LOW
								0 fewer TN in URT sampling		0 fewer TN in URT sampling		
False positives (patients incorrectly								0 (0 to 6)	0 (0 to 6)	0 (0 to 2)	0 (0 to 2)	

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classified as having COVID-19)								0 fewer FP in URT sampling	0 fewer FP in URT sampling	
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Explanations: This table is based on applying the sensitivity and specificity estimates to calculate True and false positives and negatives in a hypothetical population of 1000 individuals

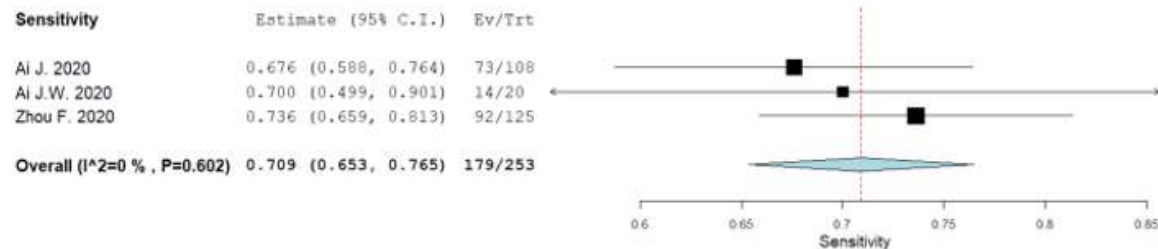
- a. There was no direct evidence comparing the accuracy of a strategy with starting with upper sample and then conducting a lower sample if the upper sample is negative. Additionally, studies reported test accuracy results but did not report on patient-important and population-important outcomes based on the results.
- b. There is serious unexplained heterogeneity.
- c. Considering the upper vs lower limits of the sensitivity's confidence interval would lead to different clinical decisions. Also, only one study informed specificity with only 8 patients.
- d. Typically seen in patients meeting clinical definition for COVID-19 who were hospitalized.
- e. Typically seen in patients meeting clinical definition for COVID-19 who were admitted to intensive care units.

Supplement F

Recommendations 5 and 6: In symptomatic individuals suspected of having COVID-19 with a negative test, should additional testing be done for better diagnostic accuracy?

Figure s6. DTA pooled by proportion

DTA pooled by proportion for first testing



DTA pooled by proportion for cumulative testing

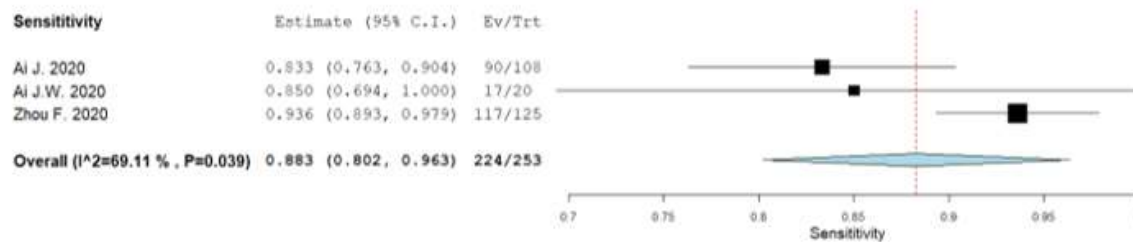


Table s12. GRADE Evidence Profile of Test Accuracy Results for Prevalence/Pre-Test Probability of 10% and 40% for single versus repeat testing

	RT-PCR single testing							RT-PCR repeat testing				
Sensitivity	0.71 (95% CI: 0.65 to 0.77)							0.88 (95% CI: 0.80 to 0.96)				
Specificity	1.00 (95% CI: 0.99 to 1.00)							1.00 (95% CI: 0.99 to 1.00)				
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
								pre-test probability of 10% ^c		pre-test probability of 40% ^d		
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	RT-PCR Single testing	RT-PCR Repeat testing	RT-PCR single testing	RT-PCR Repeat testing	
True positives (patients with COVID 19)	3 studies 253 patients	cross-sectional (cohort type accuracy study)	not serious	serious ^a	not serious	serious ^b	none	71 (65 to 77)	88 (80 to 96)	284 (260 to 308)	352 (320 to 384)	⊕⊕○○ LOW
								17 fewer TP in RT-PCR rapid testing		68 fewer TP in RT-PCR rapid testing		
False negatives (patients incorrectly classified as not having COVID 19)								29 (23 to 35)	12 (4 to 20)	116 (92 to 140)	48 (16 to 80)	
								17 more FN in RT-PCR rapid testing		68 more FN in RT-PCR rapid testing		
True negatives (patients without COVID 19)	2 studies 105 patients	cross-sectional (cohort type accuracy study)	not serious	serious ^a	not serious	serious ^b	none	900 (891 to 900)	900 (891 to 900)	600 (594 to 600)	600 (594 to 600)	⊕⊕○○ LOW
								0 fewer TN in RT-PCR rapid testing		0 fewer TN in RT-PCR rapid testing		

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
								pre-test probability of 10% ^c		pre-test probability of 40% ^d		
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	RT-PCR Single testing	RT-PCR Repeat testing	RT-PCR single testing	RT-PCR Repeat testing	
False positives (patients incorrectly classified as having COVID 19)								0 (0 to 9)	0 (0 to 9)	0 (0 to 6)	0 (0 to 6)	
								0 fewer FP in RT-PCR rapid testing		0 fewer FP in RT-PCR rapid testing		

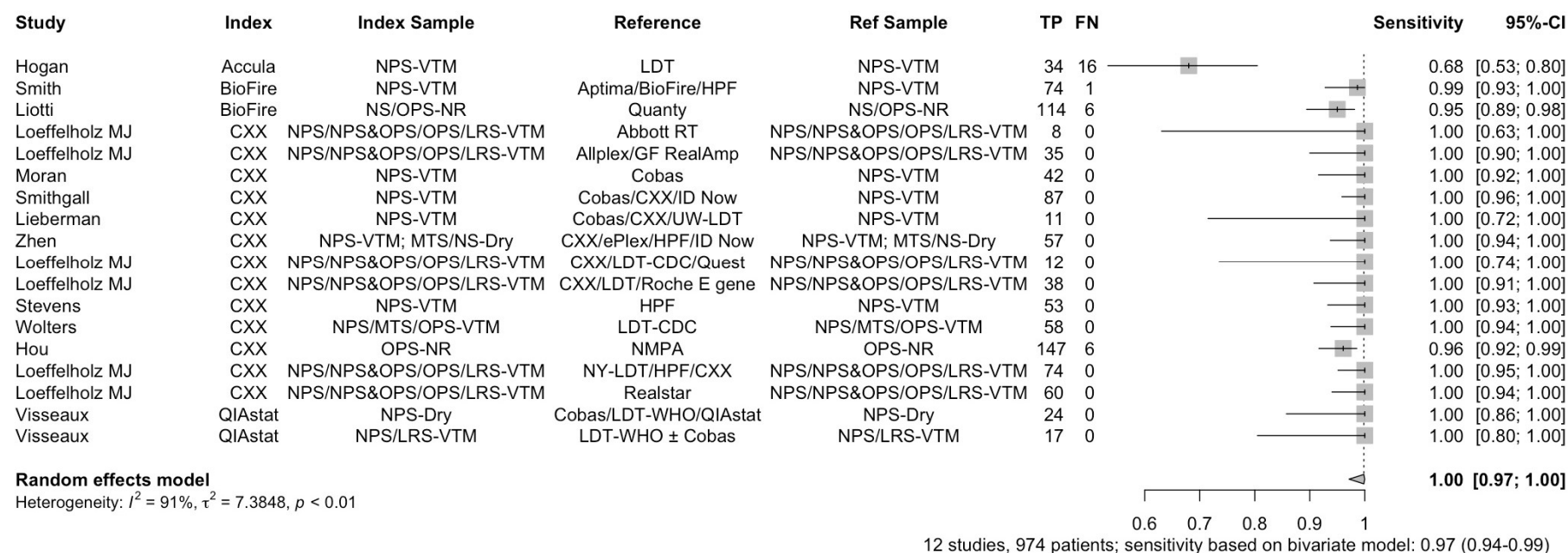
Explanations: This table is based on applying the sensitivity and specificity estimates to calculate True and false positives and negatives in a hypothetical population of 1000 individuals

- Studies reported test accuracy results but did not report on patient-important and population-important outcomes based on the results.
- Considering the lower vs upper limit of the sensitivity confidence interval may lead to different clinical decision, and the low number of patients lead to very serious imprecision.
- Typically seen in symptomatic outpatients who have not reached a hospital facility.
- Typically seen in patients meeting clinical definition for COVID-19 who were hospitalized.

Supplement G

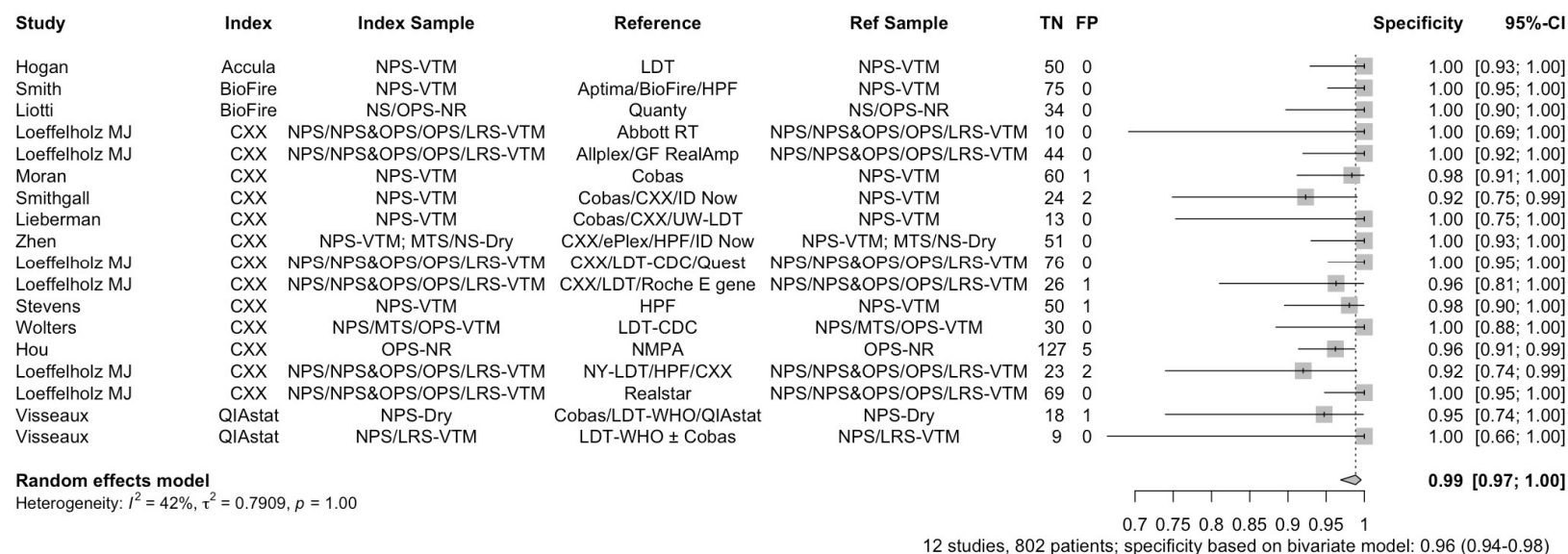
Recommendation 7: In symptomatic individuals suspected of having COVID-19, does the use of rapid vs. standard lab-based nucleic acid amplification testing (NAAT) affect diagnostic accuracy of the test?

Figure s7a. Test accuracy studies evaluating rapid RT-PCR test vs. single standard non-rapid lab-based NAAT or composite reference standard when available

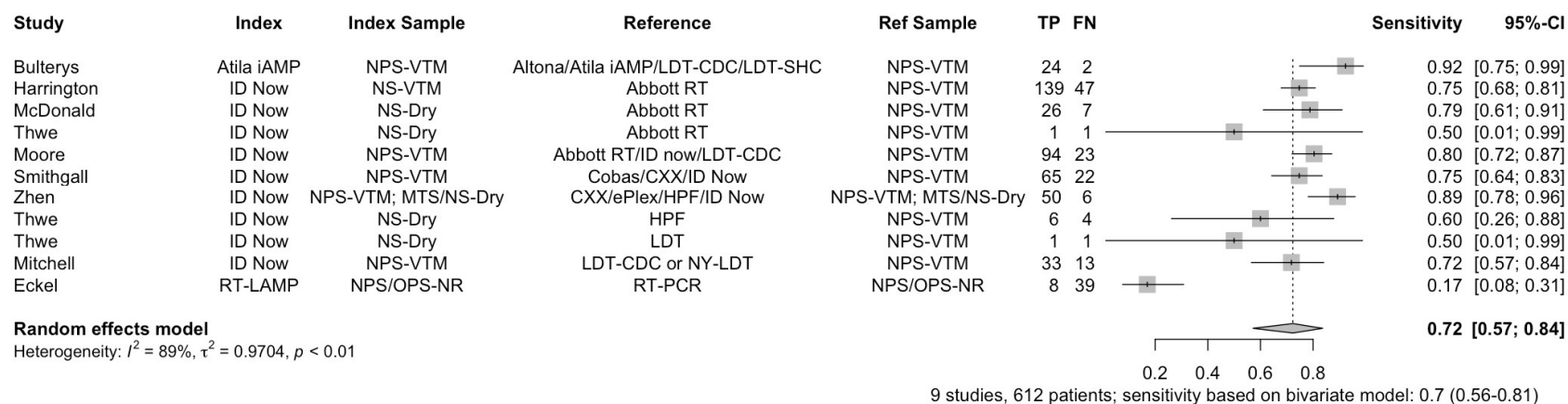


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Figure s7b. Test accuracy studies evaluating rapid RT-PCR test vs. single standard non-rapid lab-based NAAT or composite reference standard when available

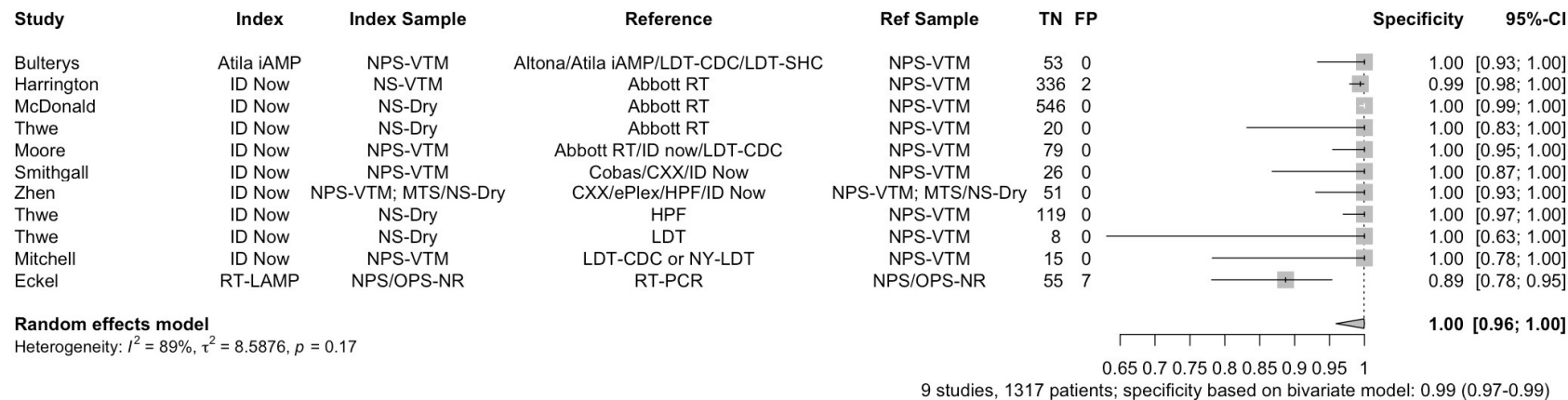


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Figure s8a. Test accuracy studies evaluating rapid isothermal NAAT test vs. single standard non-rapid lab-based NAAT or composite reference standard when available

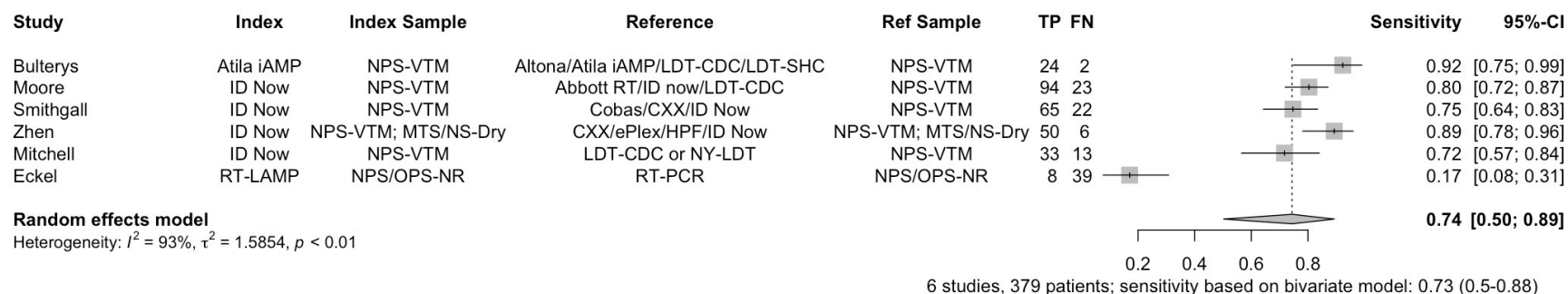
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Figure s8b. Test accuracy studies evaluating rapid isothermal NAAT test vs. single standard non-rapid lab-based NAAT or composite reference standard when available



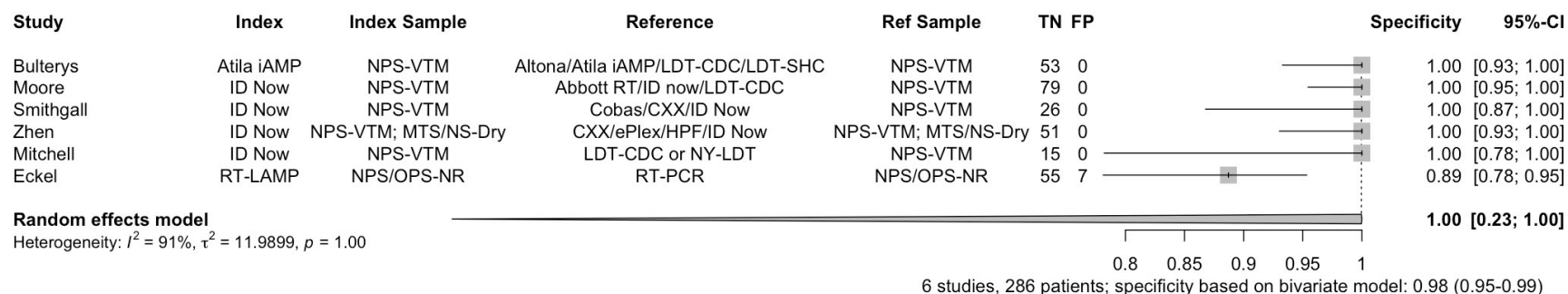
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Figure s8c. Test accuracy studies evaluating rapid isothermal NAAT test vs. single standard non-rapid lab-based NAAT or composite reference standard when available, sensitivity analysis excluding studies that used different sample source and/or transport media in index sample compared to reference sample



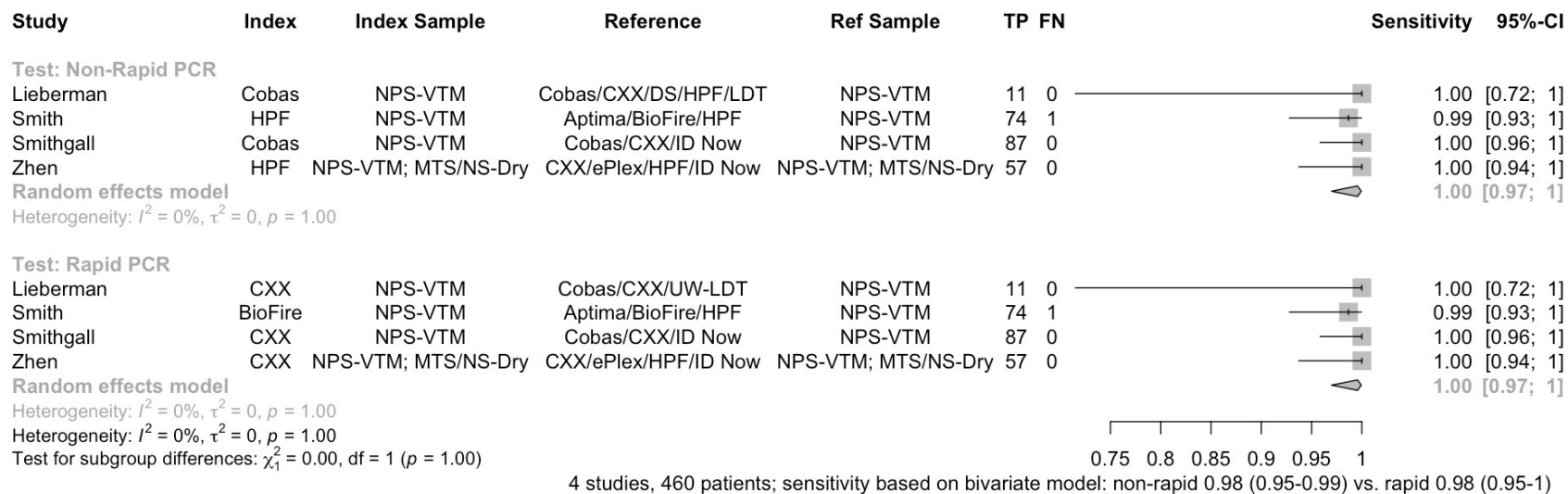
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Figure s8d. Test accuracy studies evaluating rapid isothermal NAAT test vs. single standard non-rapid lab-based NAAT or composite reference standard when available, specificity analysis excluding studies that used different sample source and/or transport media in index sample compared to reference sample

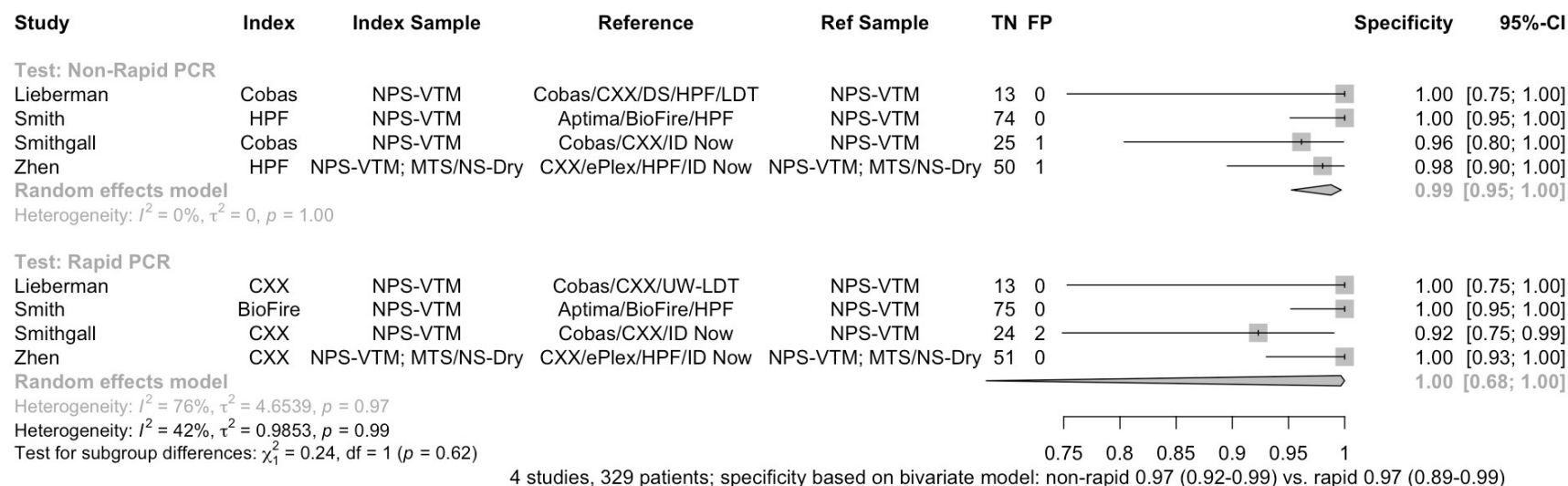


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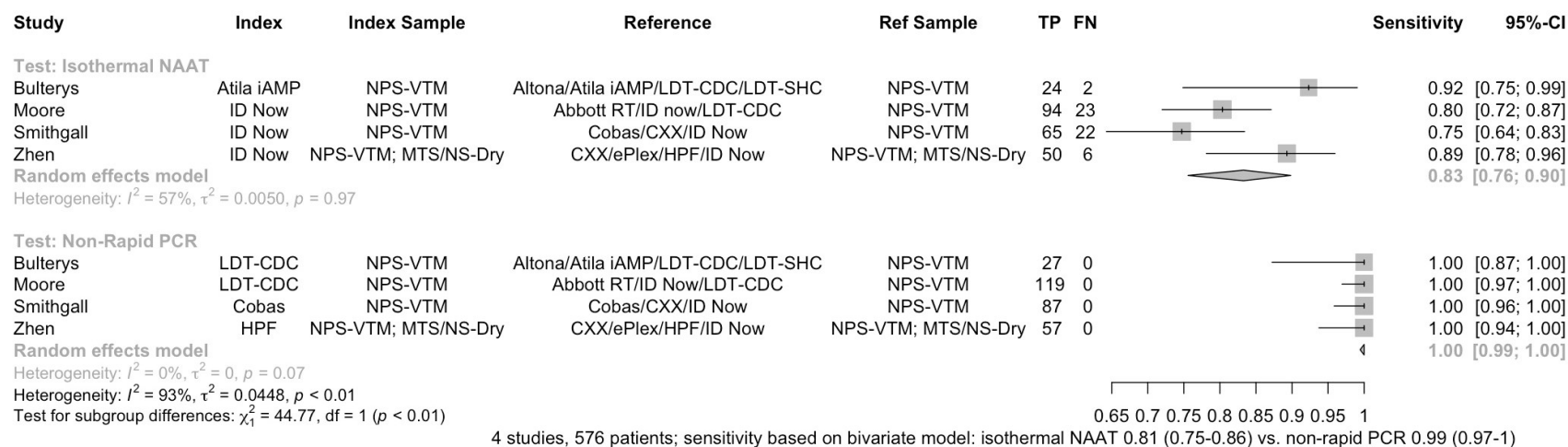
Figure s9a. Direct comparative test accuracy studies evaluating rapid RT-PCR test and standard non-rapid laboratory-based NAAT vs. composite reference standard



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Figure s9b. Direct comparative test accuracy studies evaluating rapid RT-PCR test and standard non-rapid laboratory-based NAAT vs. composite reference standard

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Figure s10a. Direct comparative test accuracy studies evaluating rapid isothermal NAAT test and standard non-rapid lab-based NAAT vs. composite reference standard

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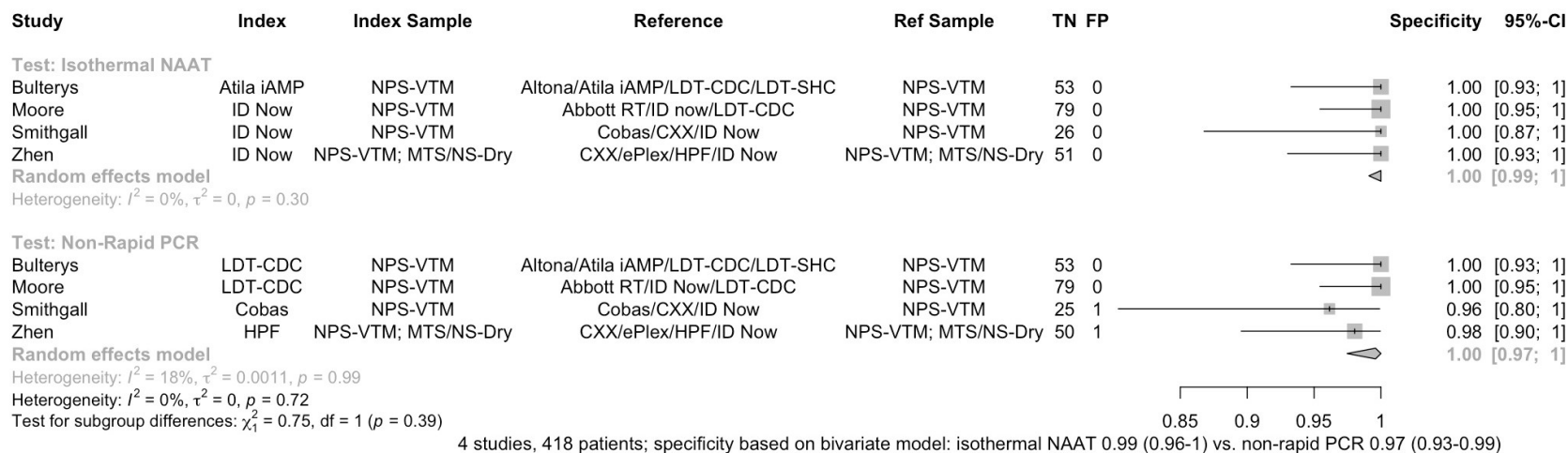
Figure s10b. Direct comparative test accuracy studies evaluating rapid isothermal NAAT test and standard non-rapid lab-based NAAT vs. composite reference standard

Table s13. GRADE Evidence Profile of Test Accuracy Results for Prevalence/Pre-Test Probability of 1%, 10%, and 40% for rapid RT-PCR vs. standard non-rapid lab-based NAAT or composite reference standard when available

Rapid RT-PCR											
Sensitivity	0.97 (95% CI: 0.94 to 0.99)										
Specificity	0.96 (95% CI: 0.94 to 0.98)										
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 1%	pre-test probability of 10%	pre-test probability of 40%	
True positives (patients with SARS-CoV2 infection)	12 studies 974 patients	cohort & case-control type studies	Not serious ^a	not serious	serious ^b	serious ^c	none	10 (9 to 10)	97 (94 to 99)	388 (376 to 396)	⊕⊕○○ LOW
False negatives (patients incorrectly classified as not having SARS-CoV2 infection)								0 (0 to 1)	3 (1 to 6)	12 (4 to 24)	
True negatives (patients without SARS-CoV2 infection)	12 studies 802 patients	cohort & case-control type studies	not serious ^a	not serious	serious ^d	not serious	none	950 (931 to 970)	864 (846 to 882)	576 (564 to 588)	⊕⊕○○ LOW
False positives (patients incorrectly classified as having SARS-CoV2 infection)								40 (20 to 59)	36 (18 to 54)	24 (12 to 36)	

Explanations

- The reference test used in many of the studies was a single non-rapid test with no second test for discordant results. However, sensitivity analysis limited to studies with multiple reference tests showed that the results did not change.
- There was evidence of some inconsistency, it was driven mainly by one study that used a lab-developed test as a reference standard.
- This specially applies to the 40% probability.
- The point estimates ranged from 0.92 to 1.00

Table s14. GRADE Evidence Profile of Test Accuracy Results for Prevalence/Pre-Test Probability of 1%, 10%, and 40% for rapid isothermal NAAT vs. standard non-rapid lab-based NAAT or composite reference standard when available

Rapid Isothermal NAAT											
Sensitivity	0.70 (95% CI: 0.56 to 0.81)										
Specificity	0.99 (95% CI: 0.97 to 0.99)										
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 1%	pre-test probability of 10%	pre-test probability of 40%	
True positives (patients with SARS-CoV2 infection)	9 studies 612 patients	cohort & case-control type studies	serious ^a	not serious	very serious ^b	serious ^c	none	7 (6 to 8)	70 (56 to 81)	280 (224 to 324)	⊕○○○ VERY LOW
False negatives (patients incorrectly classified as not having SARS-CoV2 infection)								3 (2 to 4)	30 (19 to 44)	120 (76 to 176)	
True negatives (patients without SARS-CoV2 infection)	9 studies 1317 patients	cohort & case-control type studies	serious ^a	not serious	serious ^d	not serious	none	980 (960 to 980)	891 (873 to 891)	594 (582 to 594)	⊕⊕○○ LOW
False positives (patients incorrectly classified as having SARS-CoV2 infection)								10 (10 to 30)	9 (9 to 27)	6 (6 to 18)	

Explanations

- The reference test used in most of the studies was a single non-rapid test with no second test for discordant results. In a sensitivity analysis, the results were robust when studies that used different sample source and/or transport media for the rapid isothermal NAAT test and standard laboratory based NAAT test were excluded.
- The point estimates ranged from 0.17 to 0.89.
- This specially applies to the 10% probability.
- The point estimates ranged from 0.89 to 1.00.

Table s15. GRADE Evidence Profile of Test Accuracy Results for Prevalence/Pre-Test Probability of 1%, 10%, and 40%, for rapid RT-PCR and standard non-rapid laboratory-based NAAT vs. composite reference standard

Rapid RT PCR			Standard laboratory based NAAT												
Sensitivity	0.98 (95% CI: 0.95 to 1.00)		Sensitivity	0.98 (95% CI: 0.95 to 0.99)											
Specificity	0.97 (95% CI: 0.89 to 0.99)		Specificity	0.97 (95% CI: 0.92 to 0.99)											
Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested						Test accuracy CoE	
								pre-test probability of 1%		pre-test probability of 10%		pre-test probability of 40%			
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	rapid PCR tests	standard NAAT	rapid PCR tests	standard NAAT	rapid PCR tests	standard NAAT		
True positives (patients with SARS-CoV2 infection)	4 studies 460 patients	cohort & case-control type studies	not serious	not serious	serious ^b	not serious ^b	none	10 (10 to 10)	10 (10 to 10)	98 (95 to 100)	98 (95 to 99)	392 (380 to 400)	392 (380 to 396)	⊕⊕⊕○ MODERATE	
False negatives (patients incorrectly classified as not having SARS-CoV2 infection)								0 fewer TP in rapid PCR test		0 fewer TP in rapid PCR test		0 fewer TP in rapid PCR test			
								0 (0 to 0)	0 (0 to 0)	2 (0 to 5)	2 (1 to 5)	8 (0 to 20)	8 (4 to 20)		
								0 fewer FN in rapid PCR test		0 fewer FN in rapid PCR test		0 fewer FN in rapid PCR test			
True negatives (patients without SARS-CoV2 infection)	4 studies 329 patients	cohort & case-control type studies	not serious	not serious	serious ^c	not serious ^c	none	960 (881 to 980)	960 (911 to 980)	873 (801 to 891)	873 (828 to 891)	582 (534 to 594)	582 (552 to 594)	⊕⊕⊕○ MODERATE	
False positives (patients incorrectly classified as having SARS-CoV2 infection)								0 fewer TN in rapid PCR test		0 fewer TN in rapid PCR test		0 fewer TN in rapid PCR test			
								30 (10 to 109)	30 (10 to 79)	27 (9 to 99)	27 (9 to 72)	18 (6 to 66)	18 (6 to 48)		
								0 fewer FP in rapid PCR test		0 fewer FP in rapid PCR test		0 fewer FP in rapid PCR test			

Explanations

- The study by Bulterys et al which used the Atila iAMP test had a lower sensitivity compared to the other studies, making the range of point estimates 0.92-1.00. Borderline judgment, combined with concerns about imprecision due to the small number of patients, we rated down once only.
- The study by Smithgall et al which used the Cepheid Xpert Xpress test had a lower sensitivity compared to the other rapid tests, making the range of point estimated 0.92-1.00. Borderline judgment, combined with concerns about imprecision due to the small number of patients, we rated down once only

Table s16. GRADE Evidence Profile of Test Accuracy Results for Prevalence/Pre-Test Probability of 1%, 10%, and 40% for rapid isothermal NAAT and standard non-rapid laboratory based NAAT vs. composite reference standard

Rapid isothermal NAAT			Standard laboratory based NAAT											
Sensitivity	0.81 (95% CI: 0.75 to 0.86)		Sensitivity	0.99 (95% CI: 0.97 to 1.00)										
Specificity	0.99.(95% CI: 0.96 to 1.00)		Specificity	0.97 (95% CI: 0.93 to 0.99)										
Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested						Test accuracy CoE
								pre-test probability of 1%		pre-test probability of 10%		pre-test probability of 40%		
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	rapid isotherm al NAAT	Standard NAAT	rapid isotherm al NAAT	Standard NAAT	rapid isotherm al NAAT	Standard NAAT	
True positives (patients with SARS-CoV2 infection)	4 studies 576 patients	cohort & case-control type studies	serious ^a	not serious	serious ^b	not serious ^c	none	8 (8 to 9)	10 (10 to 10)	81 (75 to 86)	99 (97 to 100)	324 (300 to 344)	8 (8 to 9)	⊕⊕○○ LOW
								2 fewer TP in rapid isothermal NAAT tests		18 fewer TP in rapid isothermal NAAT tests		72 fewer TP in rapid isothermal NAAT tests		
False negatives (patients incorrectly classified as not having SARS-CoV2 infection)								2 (1 to 2)	0 (0 to 0)	19 (14 to 25)	1 (0 to 3)	76 (56 to 100)	2 (1 to 2)	
								2 more FN in rapid isothermal NAAT tests		18 more FN in rapid isothermal NAAT tests		72 more FN in rapid isothermal NAAT tests		
True negatives (patients without SARS-CoV2 infection)	4 studies 418 patients	cohort & case-control type studies	serious ^a	not serious	not serious	not serious ^c	none	980 (950 to 990)	960 (921 to 980)	891 (864 to 900)	873 (837 to 891)	594 (576 to 600)	980 (950 to 990)	⊕⊕⊕○ MODERATE
								20 more TN in rapid isothermal NAAT tests		18 more TN in rapid isothermal NAAT tests		12 more TN in rapid isothermal NAAT tests		
False positives (patients incorrectly classified as having SARS-CoV2 infection)								10 (0 to 40)	30 (10 to 69)	9 (0 to 36)	27 (9 to 63)	6 (0 to 24)	10 (0 to 40)	
								20 fewer FP in rapid isothermal NAAT tests		18 fewer FP in rapid isothermal NAAT tests		12 fewer FP in rapid isothermal NAAT tests		

Explanations

- The studies varied on swab type used for patient population. The studies by Smithgall et al and Moore et al used nasopharyngeal swabs in viral transport media for both index test and reference standard. The study by Zhen et al used a combination of nasopharyngeal swab in viral transport media, dry nasal swab, throat swab for index test and reference standard.
- The point estimate of sensitivity ranged from 0.75 to 0.89
- Borderline judgment due to the small number of patients. There was evidence of imprecision for the 10% group.

Supplement H

Recommendation 8: In asymptomatic individuals who may have been exposed to COVID-19, should nucleic acid amplification testing vs. no testing be done to diagnose COVID19 (to guide decisions about quarantine and contact tracing)?

Forest Plots for the sensitivity of URT sampling among symptomatic patients. (This was used to indirectly to determine the sensitivity of URT sampling among asymptomatic patients)

Figure s11. Sensitivity pooled by proportion from the 6 studies reporting comparative data

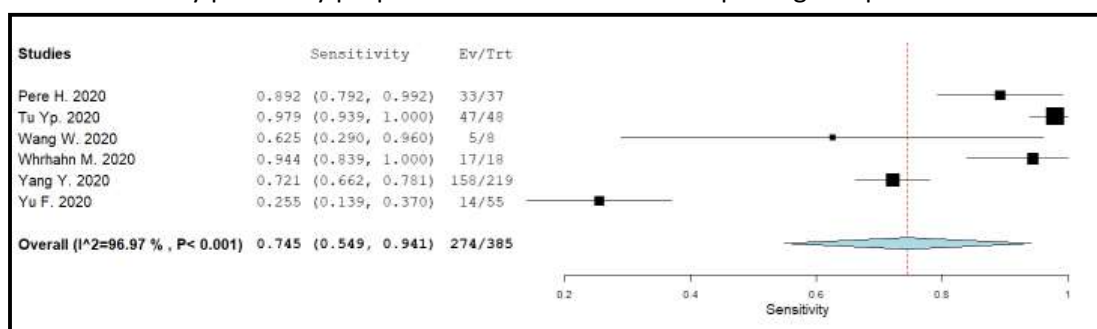


Figure s12. Specificity Pooled by Proportion from 2 studies that reported specificity

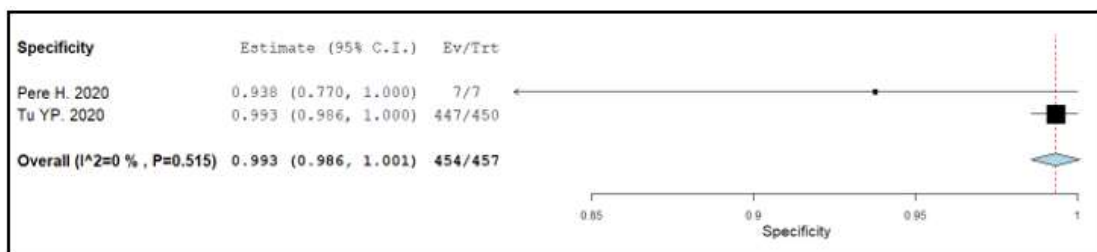


Figure s13. Sensitivity pooled by proportion from the two studies that used NP as a reference standard

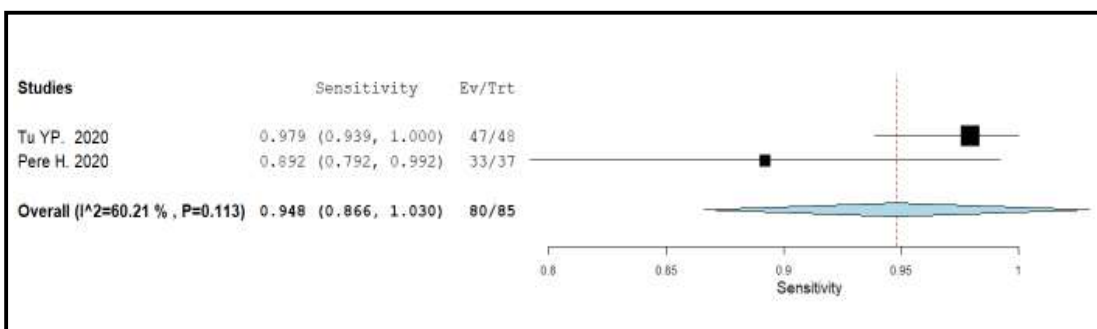


Table s17. GRADE Summary of Findings of Test Accuracy Results for Prevalence/Pre-Test Probability of 40% and 80% for URT vs LRT Sampling (7 studies)

Outcome	Effect per 1,000 patients tested				No of patients (studies)	Test accuracy CoE		
	pre-test probability of 40% ^g		pre-test probability of 80% ^h					
	URT sampling	LRT sampling	URT sampling	LRT sampling				
True positives (patients with COVID-19)	228 (168 to 284)	324 (292 to 344)	456 (336 to 568)	648 (584 to 688)	1244 (7)	⊕○○○ VERY LOW a,b,c,d,e		
	96 fewer TP in URT sampling		192 fewer TP in URT sampling					
False negatives (patients incorrectly classified as not having COVID-19)	172 (116 to 232)	76 (56 to 108)	344 (232 to 464)	152 (112 to 216)				
	96 more FN in URT sampling		192 more FN in URT sampling					
True negatives (patients without COVID-19)	600 (594 to 600)	600 (594 to 600)	200 (198 to 200)	200 (198 to 200)	8 (1)	⊕○○○ VERY LOW ^{c,f}		
	0 fewer TN in URT sampling		0 fewer TN in URT sampling					
False positives (patients incorrectly classified as having COVID-19)	0 (0 to 6)	0 (0 to 6)	0 (0 to 2)	0 (0 to 2)				
	0 fewer FP in URT sampling		0 fewer FP in URT sampling					

Explanations: This table is based on applying the sensitivity and specificity estimates to calculate True and false positives and negatives in a hypothetical population of 1000 individuals

- The case-control design leads to a serious study population bias.
- The Fengting Y. (2020) study showed results as the number of samples and not the number of patients.
- There was no direct evidence comparing the accuracy of a strategy with starting with upper sample and then conducting a lower sample if the upper sample is negative. Additionally, studies reported test accuracy results but did not report on patient-important and population-important outcomes based on the results.
- There is serious unexplained heterogeneity.
- Considering the Upper vs Lower limits of the sensitivity's confidence interval would lead to different clinical decisions.
- A very low number of patients.
- Typically seen in patients meeting clinical definition for COVID-19 who were hospitalized.
- Typically seen in patients meeting clinical definition for COVID-19 who were admitted to intensive care units.