SARS-CoV-2 Rapid Antigen Test

Primary and secondary influencers on assay performance

April-2021

Coronaviruses

Virion morphology and structural proteins

Large enveloped RNA viruses (80–120 nm) [1-3]

Lipid bilayer

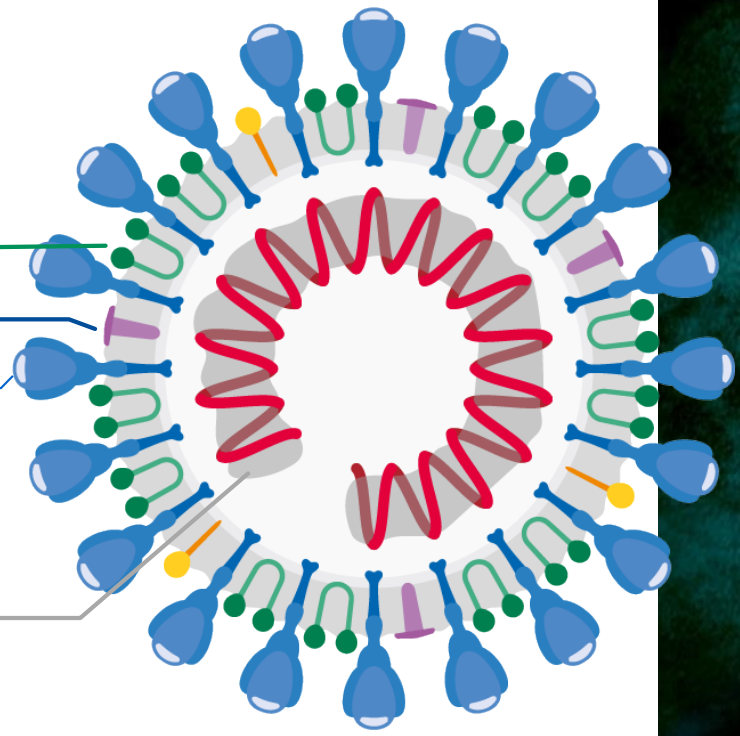
Membrane glycoprotein **(M)**

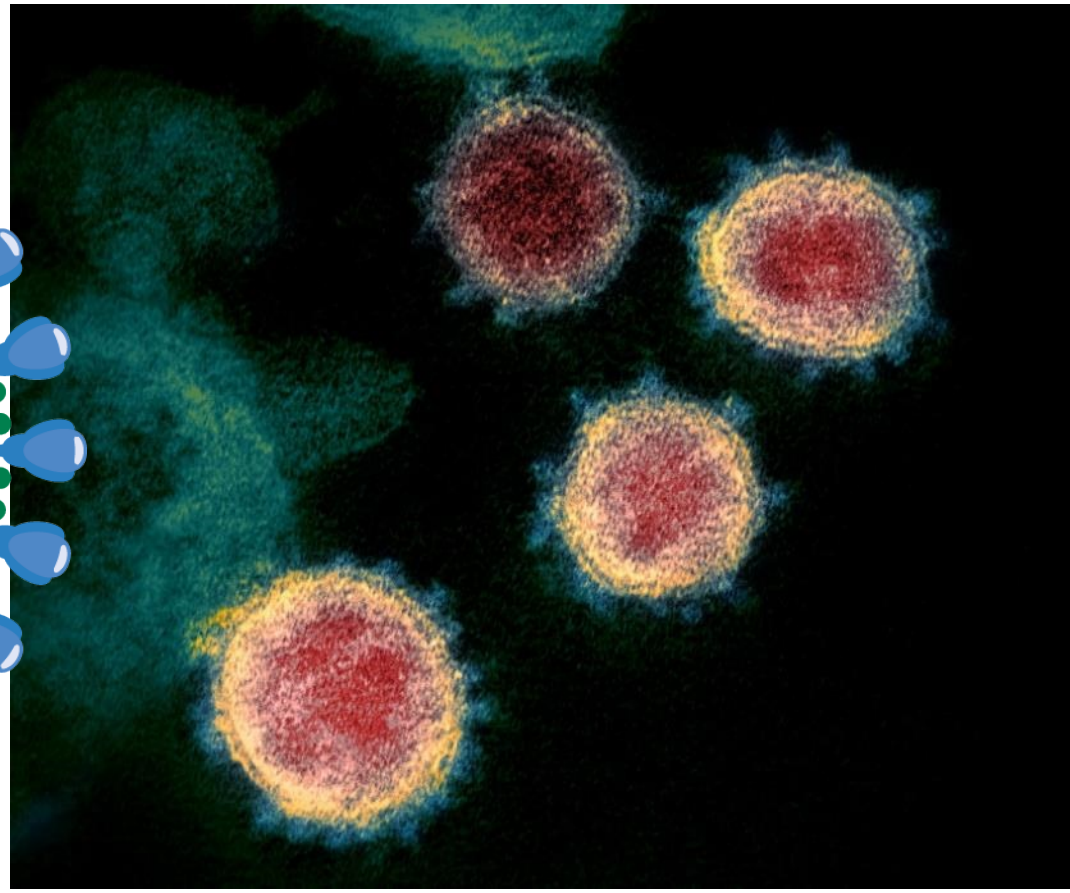
Envelope protein **(E)**

Spike protein **(S)**

Nucleocapsid

Multiple copies of the **nucleocapsid protein** (N) bound to the RNA genome

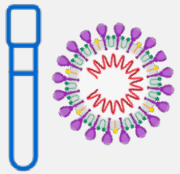




1. Masters PS (2006). Advances in Virus Research. Academic Press. 66: 193–292; 2. Su, S et al. (2016). Trends in Microbiology. 24 (6): 490–502; 3. Paules CI et al. (2020). JAMA. 2020;323(8):707–708

Summary: Factors Impacting on Performance and Test Results of Rapid Antigen Tests

Primary influencer:

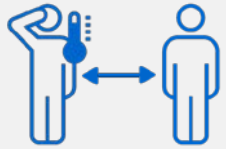


Viral load of the sample, and the **viral load distribution** in the investigated cohort represented by Cycle threshold (Ct) of the PCR

Analytical test performance of the assay: sensitivity & specificity

Secondary influencer:

Days post symptom onset (DPSO) of sampling



Pretest probability or prevalence setting of test

Sampling method, e.g.
- Swabs
- Tubes
- Buffer, Viral Transport Media

Sample Type
- Naso-/Oropharyngeal
- Nasal
- Saliva

Workflow
- Point of Care setting
- Laboratory
- Storage

1. Wölfel R, Corman VM, Guggemos W, et al. Virological assessment of hospitalized patients with COVID-2019. Nature. 2020;581(7809):465-469. doi:10.1038/s41586-020-2196-x
2. Krueger et al, https://www.medrxiv.org/content/10.1101/2020.10.01.20203836v1; 3. Van Beek, J et al:https://doi.org/10.1101/2020.10.13.20211524 ; 4. Lee R. et al. Performance of Saliva, Oropharyngeal Swabs, and Nasal Swabs for SARS-CoV-2 Molecular Detection: A Systematic Review and Meta-analysis medRxiv 2020.11.12.20230748; doi: https://doi.org/10.1101/2020.11.12.20230748

Influencers of Test Performance

Sampling type/ specimen source

Collection device / Transport media and volume

Time to test / transport / storage

Test type / target

Viral load of the sample / distribution in a cohort

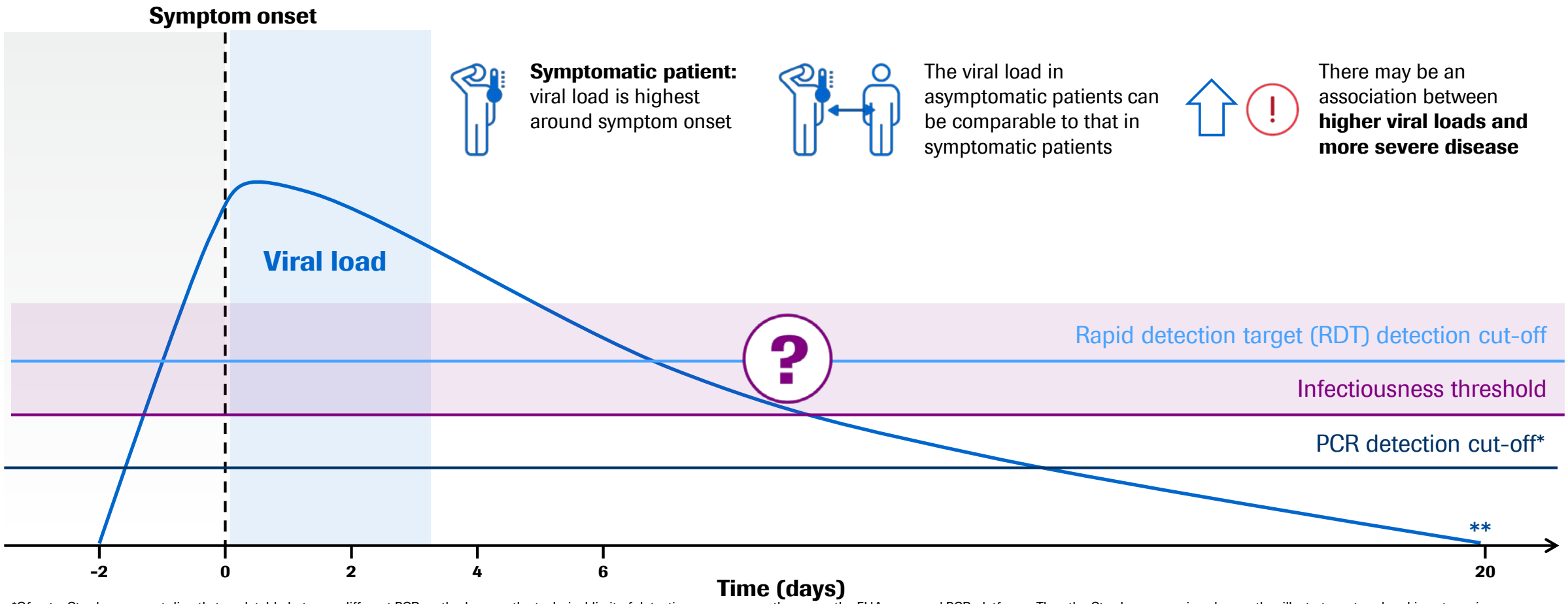
Days from infection to specimen collection

Pre-analytical

Analytical

1. Wölfel R, Corman VM, Guggemos W, et al. Virological assessment of hospitalized patients with COVID-2019. Nature. 2020;581(7809):465-469. doi:10.1038/s41586-020-2196-x
2. Krueger et al, https://www.medrxiv.org/content/10.1101/2020.10.01.20203836v1; 3. Van Beek, J et al:https://doi.org/10.1101/2020.10.13.20211524 ; 4. Lee R. et al. Performance of Saliva, Oropharyngeal Swabs, and Nasal Swabs for SARS-CoV-2 Molecular Detection: A Systematic Review and Meta-analysis medRxiv 2020.11.12.20230748; doi: https://doi.org/10.1101/2020.11.12.20230748

Clinical Sensitivity of a Rapid Test compared to PCR



Symptomatic patient: viral load is highest around symptom onset

The viral load in asymptomatic patients can be comparable to that in symptomatic patients

There may be an association between **higher viral loads and more severe disease**

*Of note, Ct values are not directly translatable between different PCR methods; even the technical limit of detection can vary greatly among the EUA-approved PCR platforms. Thus the Ct value comparison here rather illustrates a trend and is not precise
**Curve is for illustrative purposes only

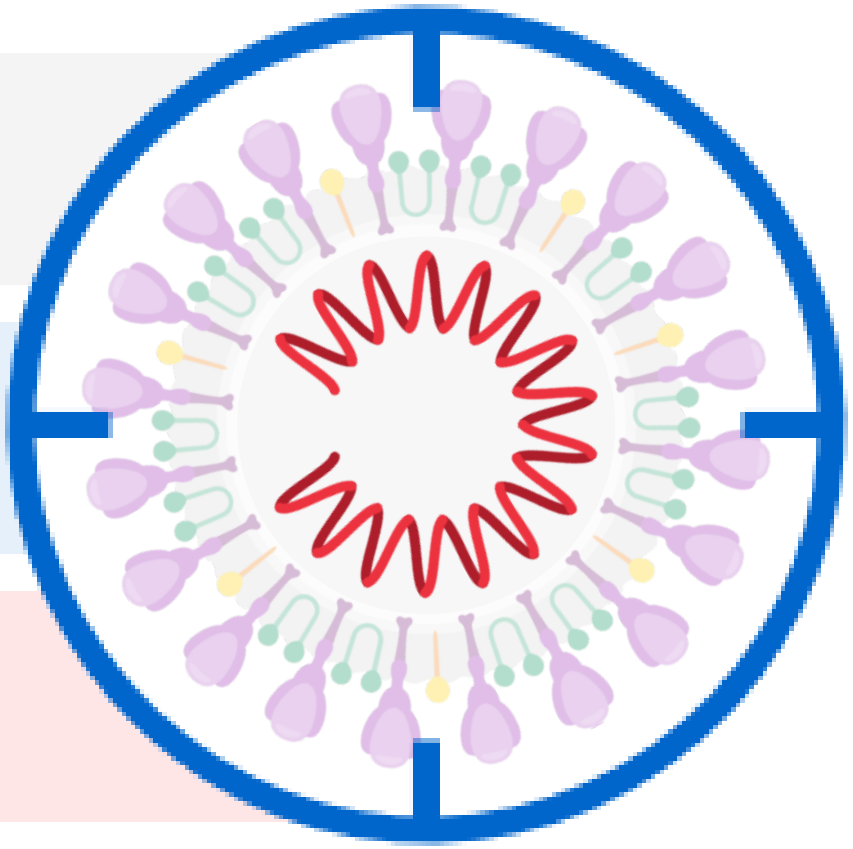
WHO update webinar Sept 11, 2020
Wölfel et al 2020, https://doi.org/10.1038/s41586-020-2196-x

Targets of different Rapid Ag tests

Different assays target different components of the SARS-CoV-2

Targets the **Nucleocapsid**

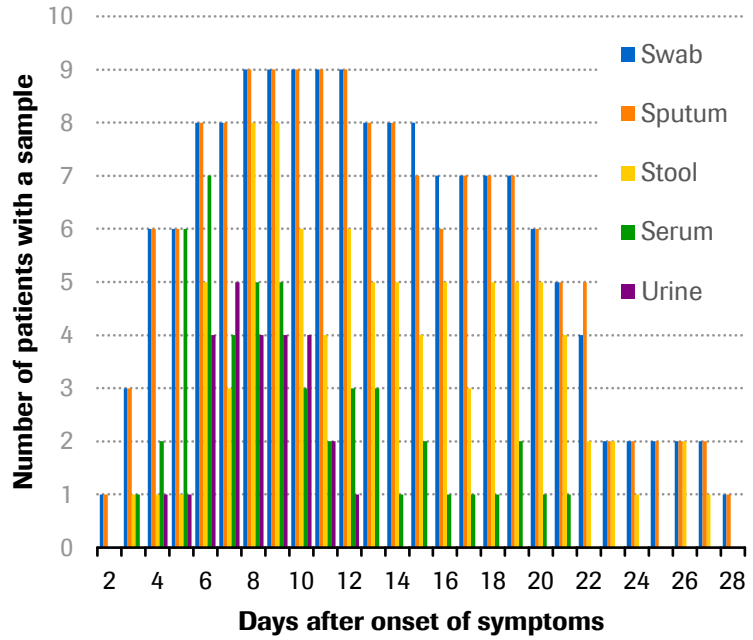
Even with the same target, the antibodies may have **different epitopes and affinites**



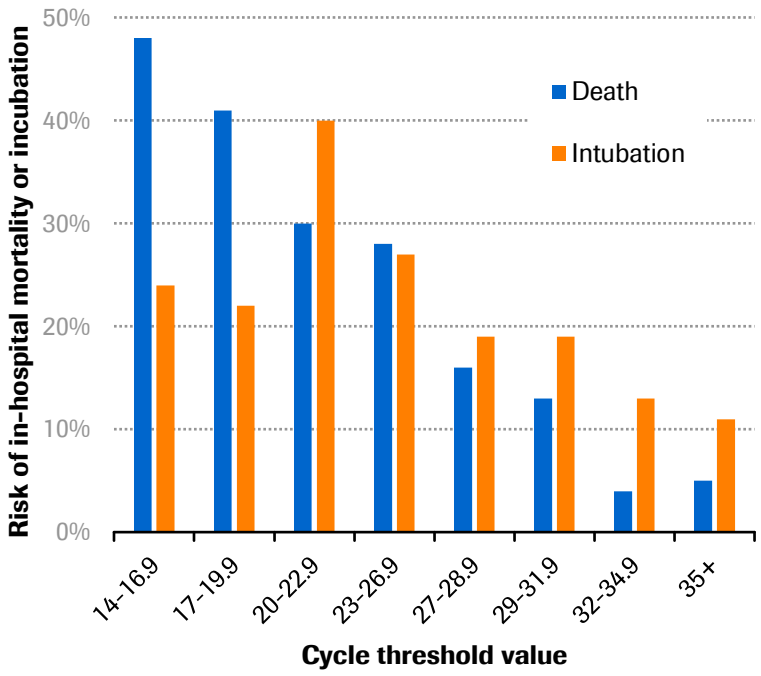
Quality of Samples for COVID-19 Testing

Viral load differs for sample types and different disease severities

Time from symptom onset



Disease severity



Viral load on swabs decreases as symptoms resolve or disease progresses into lungs

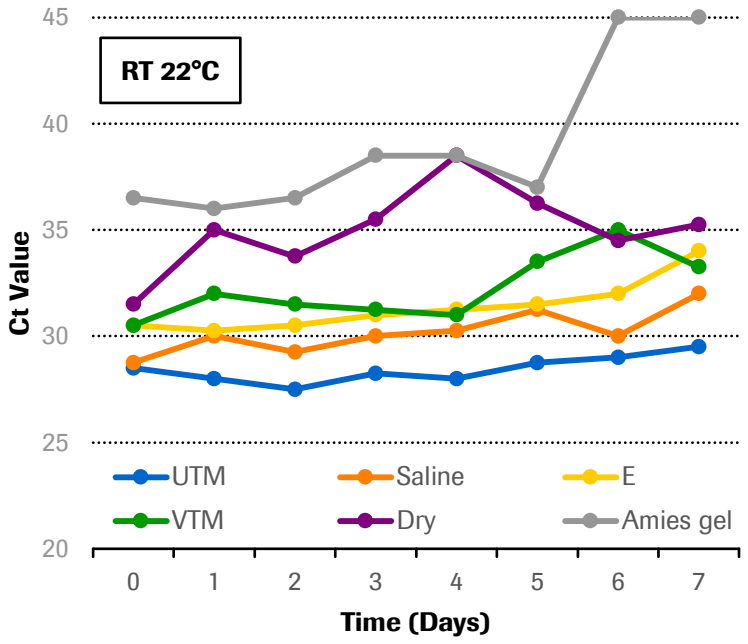
Higher viral loads associated with more severe disease

1. Wölfel R, Corman VM, Guggemos W, et al. Virological assessment of hospitalized patients with COVID-2019. Nature. 2020;581(7809):465-469. doi:10.1038/s41586-020-2196-x | 2. Magleby R, Westblade LF, Trzebucki A, et al. Impact of SARS-CoV-2 Viral Load on Risk of Intubation and Mortality Among Hospitalized Patients with Coronavirus Disease 2019 [published online ahead of print, 2020 Jun 30]. Clin Infect Dis. 2020;ciaa851. doi:10.1093/cid/ciaa851

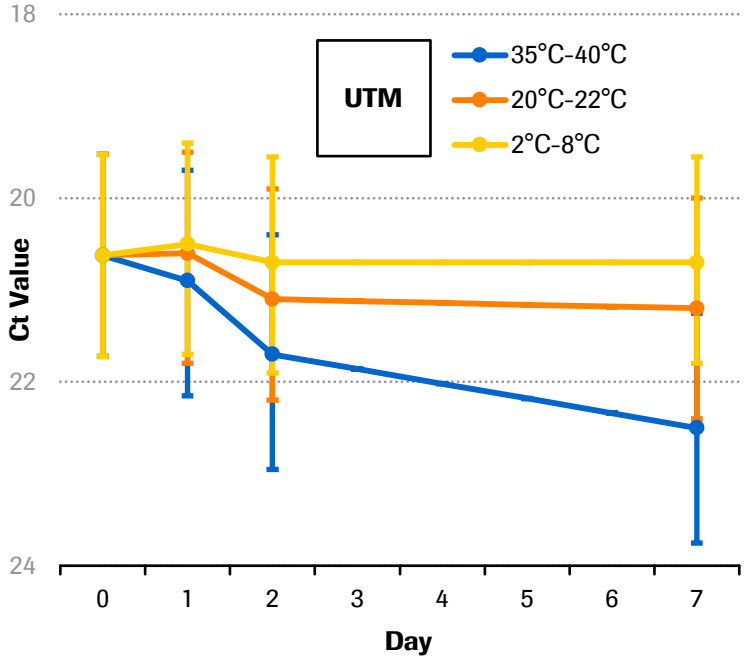
Quality of Samples for COVID-19 Testing

Viral load differs across storage conditions

Collection media and swab



Storage temperature and time



Test samples as soon as possible after collection

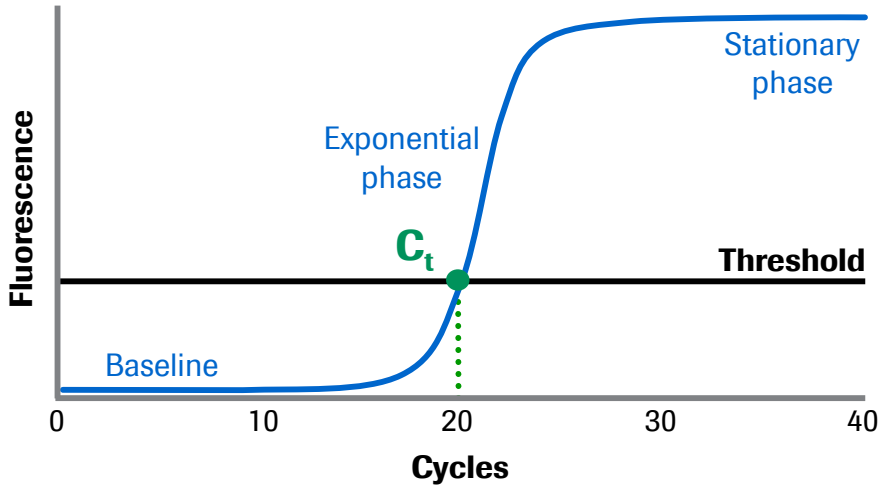
To improve detection, store samples refrigerated and/or in buffered viral transport media containing antibiotics

Stability of viral RNA affected by collection media and storage conditions

| 1. Kim N, Kwon A, Roh EY, et al. Effects of Storage Temperature and Media/Buffer for SARS-CoV-2 Nucleic Acid Detection [published online ahead of print, 2020 Oct 17]. Am J Clin Pathol. 2020;aqaa207. doi:10.1093/ajcp/aqaa207 | 2. Druce J, Garcia K, Tran T, Papadakis G, Birch C. Evaluation of swabs, transport media, and specimen transport conditions for optimal detection of viruses by PCR. J Clin Microbiol. 2012;50(3):1064-1065. doi:10.1128/JCM.06551-11

Is a quantitative test (viral load) useful?

Cycle threshold (Ct): Number of PCR cycles needed to produce a positive result



Lower C_t value = Higher concentrations of viral RNA in the sample

No quantitative SARS-CoV-2 assays have received Emergency Use Authorization (EUA) by the Food and Drug Administration (FDA).

International, commutable standardized reference material is needed AND method specific determination of the threshold for infectiousness

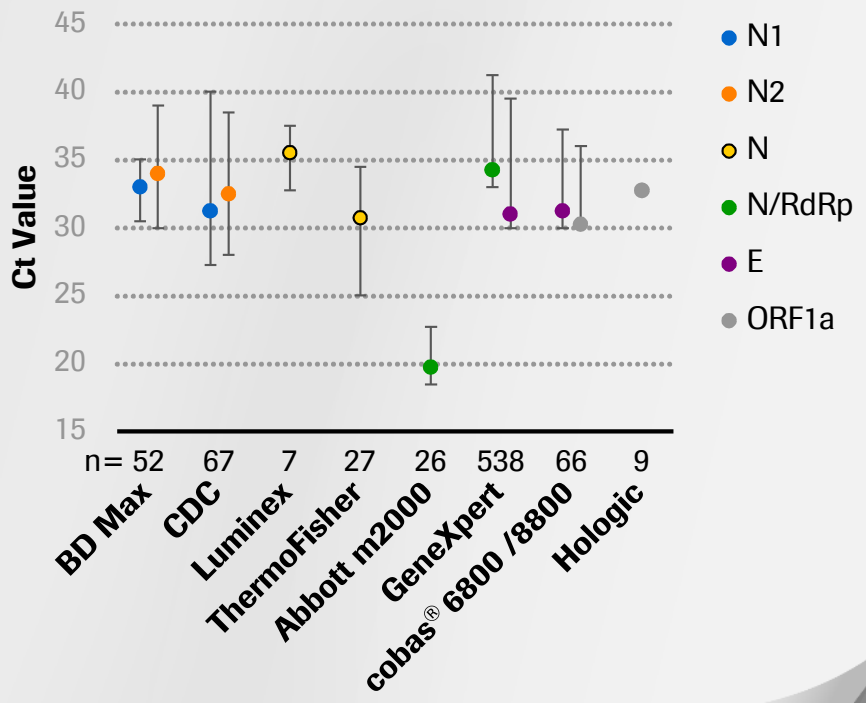
PCR: Polymerase Chain Reaction
Rhoads et al 2020 ; DOI: 10.1093/cid/ciaa1199

Ct-values can vary significantly

There is no "golden PCR standard" and data are hard to compare

CAP survey

>700 laboratories using proficiency testing material produced from the same batch



Different FDA EUA methods:

Median Ct-values for varied by as much as **14 cycles**

14

Different targets – one instrument:

Within a single test performed, the difference in the median Ct-values for different targets was **3.0 cycles**

3

Across all labs:

Within a single gene target for a single method, up to **12.0 cycle** differences

12

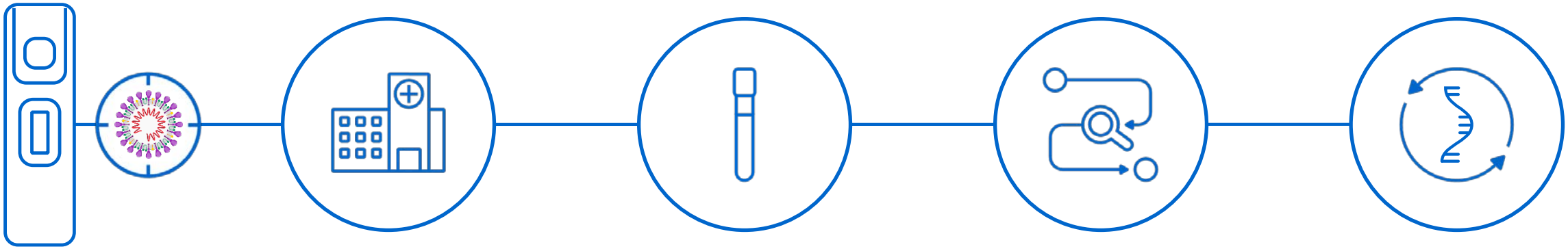
ORF1a detection differed by **6.0 cycles**

6

Rhoads et al 2020 ; DOI: 10.1093/cid/ciaa1199

Comparing sensitivities of SARS-CoV-2 rapid antigen tests

Sensitivities of rapid antigen tests can only be compared:



In a direct Head-to-Head comparison

The same samples
(Identical sample from VTM
e.g., not 1. and 2. swab)
Same cohort size

Identical workflow

The same comparator
(Ct values of different PCRs cannot be compared)

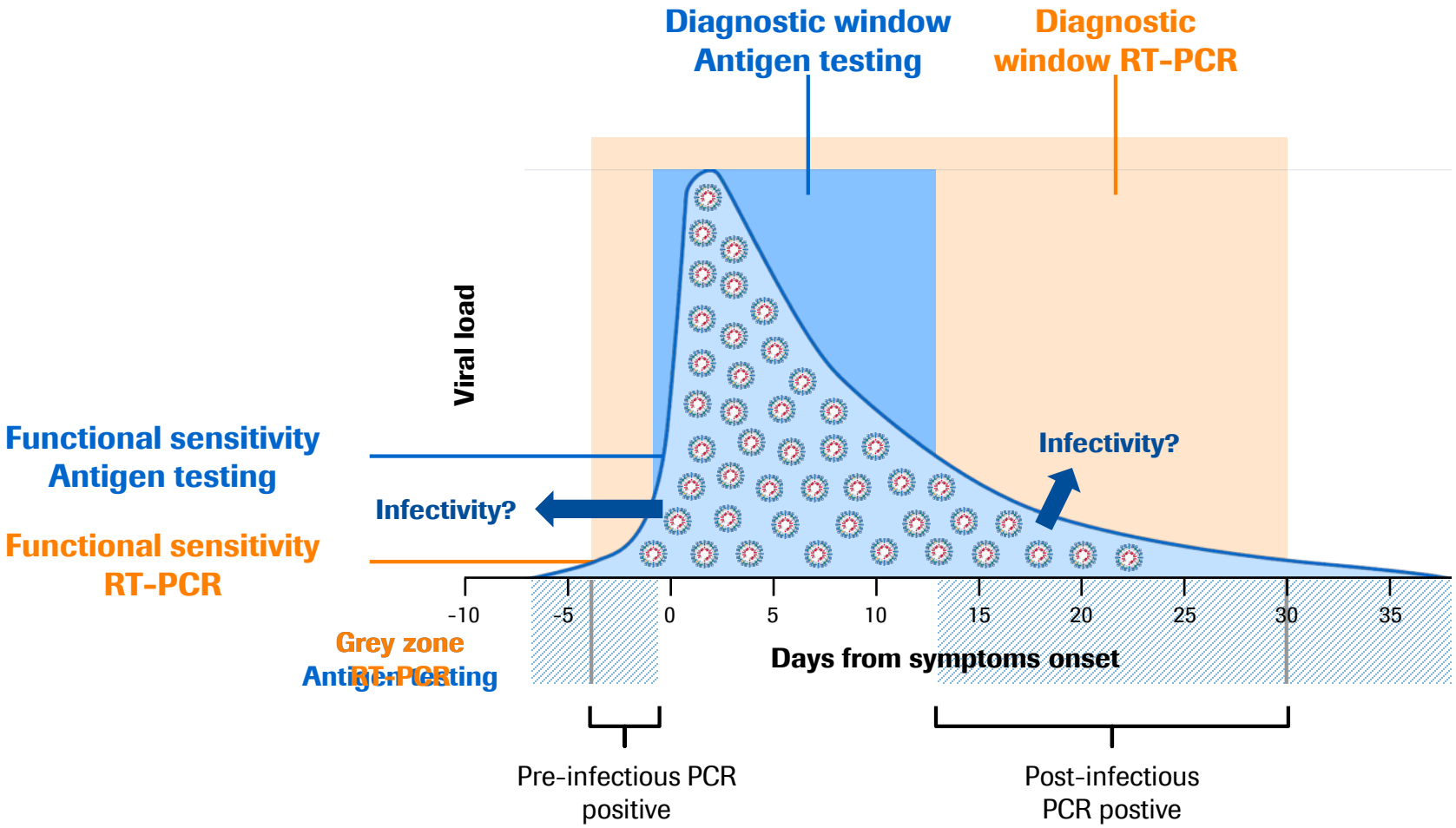
An absolute assessment of **limits of detection** for each test, as well as a strict comparison of **relative sensitivities** is **not possible**

Rhoads et al 2020 ; DOI: 10.1093/cid/ciaa1199

H2H:

Detectability of SARS-CoV-2 PCR vs antigen tests

Antigen test ideal to detect "high spreaders"



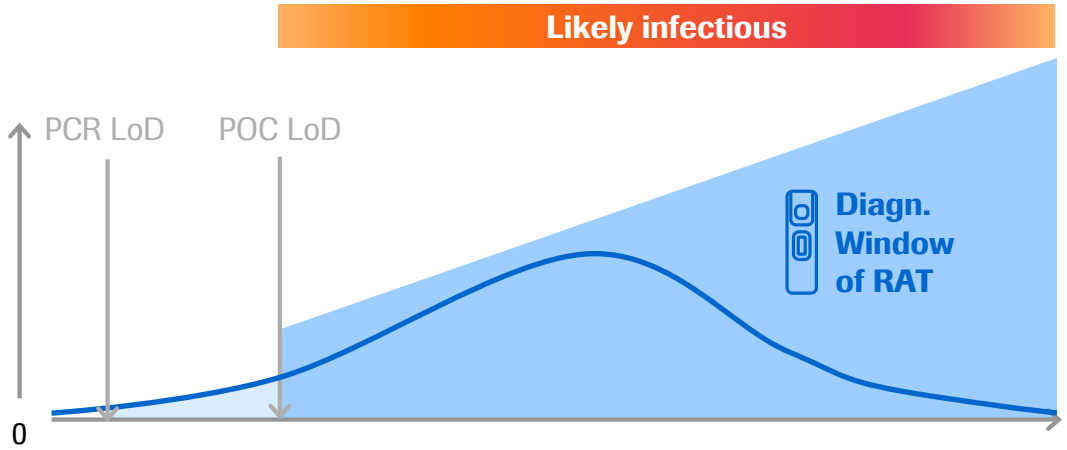
Real Time Polimerase Chain Reaction (RT-PCR)
Rapid antigen testing

Illustrative reference: https://doi.org/10.1515/dx-2020-0131

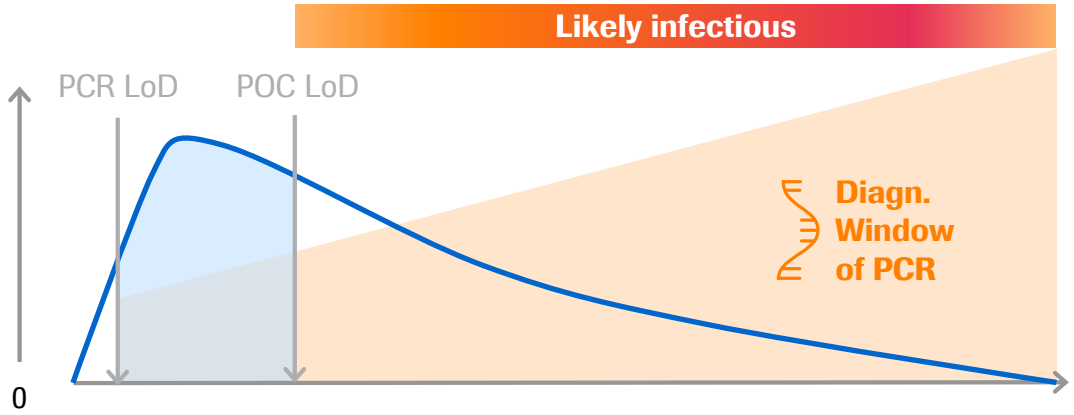
Relative sensitivity of rapid antigen tests

The number of samples with high viral load is crucial

Patients in the study
→ High relative sensitivity of the POC compared to PCR



Patients in the study
→ Lower relative sensitivity of the POC compared to PCR



Illustrative reference: https://www.medrxiv.org/content/10.1101/2020.07.15.20154518v1.full.pdf Van Beek, J et al:https://doi.org/10.1101/2020.10.13.20211524, Igloi et al; https://www.finddx.org/wp-content/uploads/2020/09/SDQ-Ag-Public-Report_20200918.pdf

Relative sensitivity – Choosing the right comparator

Infectivity should be the ultimate comparator

PCR is refered to as golden standard in virus detection

Is virus culture the real gold standard test?

Virus culture is only available in a research setting

The demonstration of infectivity on permissive cell lines *in vitro* is a more reliable surrogate for infectivity and virus transmission

NAAT is **routine reference standard** but accuracy is **not 100%** especially late in the disease

Varies widely across the different non-respiratory samples and **may detect non-viable virus**

This means viral RNA can persist in different body parts and can be detected in specimens for **much longer** than the presence of viable virus

For each PCR the Ct threshold needs to be determined, due to **lack of standarization –** PCR without Ct correlation **overestimates** the number of contagious individuals

Wolfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Muller MA, et al. Virological 343 assessment of hospitalized patients with COVID-2019. Nature. 2020;581:465-9.

SARS-CoV-2 Rapid Antigen Test

External Clinical Validation Studies

May-2021

Objectives of this presentation

- The main objective is to summarize key factors that influence assay performance and test results of rapid antigen tests
- This presentation will be updated regularly

Search strategy; 30 – Nov - 2020

Set#	Searched for	Results
S1	(Ti,Ab(COVID-19 OR "COVID-19" OR COVID19 OR SARS-CoV-2 OR SARSCoV2 OR SARS-CoV2 OR "SARS-CoV-2")) OR (MJEMB.EXACT.EXPLODE("severe acute respiratory syndrome")) OR MJEMB.EXACT.EXPLODE("Coronaviridae") OR MJMESH.EXACT.EXPLODE("Coronaviridae") OR (MJMESH.EXACT.EXPLODE("Severe Acute Respiratory Syndrome"))	179395
S2	emb("coronavirus disease 2019 +")	66193
S3	(((novel NEAR/5 corona NEAR/5 virus) OR (2019 NEAR/2 nCoV) OR ((2019 or novel) NEAR/2 coronavirus*) or "2019-nCoV" or "COVID-19" or (COVID PRE/0 19) or (corona NEAR/5 virus NEAR/5 2019) or (SARS pre/0 CoV pre/0 2) or "SARS-CoV-2"))	170265
S4	S3 OR S2 OR S1	194253
S5	("STANDARD Q COVID-19 Ag")	4
S6	(rapid n/5 antigen* n/5 (test* or assay*))	5886
S7	((S5 or S6) and S4)	70°
S8	(EMB.EXACT.EXPLODE("point of care testing")) OR (MESH.EXACT.EXPLODE("Point-of-Care Testing")) OR (poc or point n/2 care)	90332*
S9	(s4 and s8)	888°
S14	(ti,ab,su,emb,mesh(clinical n/2 perform*)) OR (ti,ab,su,emb,mesh(accuracy* OR sensitiv* OR specific* OR validation* OR concordance* OR “positive agreement” OR “positive percent agreement” OR “negative agreement” OR “negative percent agreement” OR evaluat* OR performance* OR “clinical performances”))	27646286*
S15	(s7 and s14) (ausgeliefert)	48°
S16	(s9 and s14)	471°
S17	((s9 and s14)) and (pd(20190101-20211231))	460°
S18	(s17 not s15) => zusätzliche Publikationen, gefunden mit PoC (Point of Care)	444°

* Duplicates are removed from the search, but included in the result count.
° Duplicates are removed from the search and from the result count.

Databases:

- BIOSIS™ Previews
- Derwent Drug File
- Embase®
- MEDLINE®

FIND REPORT: Summary

Purpose of the study

Independent evaluation of the performance of the test in different patient populations and prevalence settings, performed in three independent sites, two in Germany (Heidelberg and Berlin) and one in Brazil (Macae, state of Rio de Janeiro). Patients included in the study were those that fulfilled the respective national suspect definition at the time of the study.

Main results

Combined overall sensitivity was 84.97% with a specificity of 98.84%.

The combined sensitivity for Ct≤25 was 97.14%.

Specifics

This study was designed according to the requirements of WHO Emergency Use Listing (EUL). The two German cohorts and the Brazilian cohort have to be viewed as one study, as neither site / country would fulfill these criteria alone. The WHO EUL of SD Biosensor is also based on the combined data (Germany & Brazil combined).

Main Conclusions

The Roche SARS-CoV-2 Rapid Antigen Test is a reliable test providing fast answers wherever they are needed

FIND data complement the IFU data and give more information about the performance of the test in different settings.

https://www.finddx.org/wp-content/uploads/2020/09/SDQ-Ag-Public-Report_20200918.pdf

FIND REPORT: Patient Characteristics*

	Germany	Brazil
N, PCR + (%)	1259 (3.7%)	400 (26.5%)
Investigated cohort	symptomatic & asymptomatic meeting national <suspect> definition	symptomatic & asymptomatic meeting national <suspect> definition
Study + sample size	Nasopharygeal and oropharyngeal	Nasopharyngeal
Symptomatics, n (%) DPSO (median (Q1-Q3)) Days < 0-3) Days 4-7 Days 8+	1039 (84.7%) 3 (2-4) 62.7% 30.9% 6.4%	392 (98.7%) 5 (4-6) 21.4% 68.8% 9.8%
PCR Ct (median) CT > 33 (n,%) CT > 30 (n,%) CT >25 (n,%)	**25.3** 6 (12.8%) 11 (23.4%) 26 (55.3%)	**25.5** 7 (6.6) 19 (17.9%) 57 (53.8%)
Reference Method	1. **cobas** 2. Abbott 3. Genesig (Primerdesign) 4. Allplex (Seegane) 5. LightMix (Tib Molbiol)	1. Lab-developed assays based on US CDC protocol, which targets 2 regions (N1+N2) of the NC gene (FDA EUA)

*fullfilling WHO requirements on Emergency Use Listing (EUL)
https://www.finddx.org/wp-content/uploads/2020/09/SDQ-Ag-Public-Report_20200918.pdf

FIND REPORT: Assay Performance

	Combined	Germany	Brazil
Sensitivity Ct ≤ 25	**97.14%** (95% CI 90.1% – 99.65%)	**100%** (95% CI 84.5% – 100%)	**95.9%** (95% CI 86.3% – 95.9%)
Sensitivity Ct ≤ 33	**90.7%** (95% CI 84.6% – 95%)	**87.8%** (95% CI 74.5% – 94.7%)	**91.9%** (95% CI 84.9% – 95.9%)
Sensitivity ≤ 7 days (85% CI)	**87.88%** (95% CI 81.06% – 92.9%)	**80%** (95% CI 64.1% – 90.1%)	**90.7%** (95% CI 74.583.3 – 95.0%)
Sensitivity (95% CI)	**84.97%** (95% CI 78.3% – 90.23%)	**76.6%** (95% CI 62.8% – 86.4%)	**88.7%** (95% CI 81.3% – 93.4%)
Specificity	**98.94%** (95% CI 98.23% – 99.39%)	**99.3%** (95% CI 98.6% – 99.6%)	**97.6%** (95% CI 95.2% – 98.8%)

https://www.finddx.org/wp-content/uploads/2020/09/SDQ-Ag-Public-Report_20200918.pdf

FIND REPORT: Differences between the two cohorts

3,7% of the German cohorts and 26,5% of the Brazilian cohort tested positive by PCR.

84,7% of the German cohorts and 98,7% of the Brazilian cohort were symptomatic.

The median days post symptom onset (DPSO) is slightly lower in the German cohorts (3 DPSO) than in the Brazilian cohort (5 DPSO).

Different PCR reference methods were used (Ct values are not comparable as RT-PCR methods vary across sites with different genome targets, PCR instruments and reagents).

The two sites in Germany had more low viral-load samples (23,4% of Ct > 30; 12,8% Ct > 33) than the site in Brazil (17,9% Ct > 30; 6,6% Ct > 33)

For some patients in the study oropharyngeal swabs were used (not NP) which is not according the IFU.

https://www.finddx.org/wp-content/uploads/2020/09/SDQ-Ag-Public-Report_20200918.pdf

Hospital Universitaires Genève (HUG), Switzerland: Study Summary

Purpose of the study

SARS-CoV-2 antigen rapid diagnostic test (RDT) validation for PanbioTM Covid-19 Ag Rapid Test (Abbott) and Standard Q COVID-19 Rapid Antigen Test (SD Biosensor/Roche), partly done in collaboration with the Foundation for Innovative Diagnostics (FIND), Geneva andsupported by the CRIVE and The Geneva Centre for Emerging Viral Diseases

Main results

RDT test results show highest concordance in samples with low CT values (indicating a high viral load). The overall sensitivity was 89%, for Ct values between <26 it was 90-100%. Despite more samples with lower viral load, Roche Ag Test shows better overall sensitivity and esp. for Ct values 26 – 48 (low viral load).

Specifics

First swab was used for PCR, second for the Rapid Antigen testing. Second swabs might contain lower viral load.

This report will be completed as a full paper rapidly.

Main Conclusions

The results show that the Standard Q (SD Biosensor/Roche), fulfil the criteria as defined by WHO with 80% sensitivity and 97% specificity , which is in line with independent validations from other studies. For individuals presenting with fever 1-5 days post symptom onset, combined Ag-RDT sensitivity was above 95%. Testing criteria focusing on patients with typical symptoms in their early symptomatic period onset could further increase diagnostic value.

https://www.hug.ch/sites/interhug/files/structures/laboratoire_de_virologie/documents/Centre_maladies_virales_infectieuses/ofsp_rdt_report_gcevd_27.10.2020.pdf

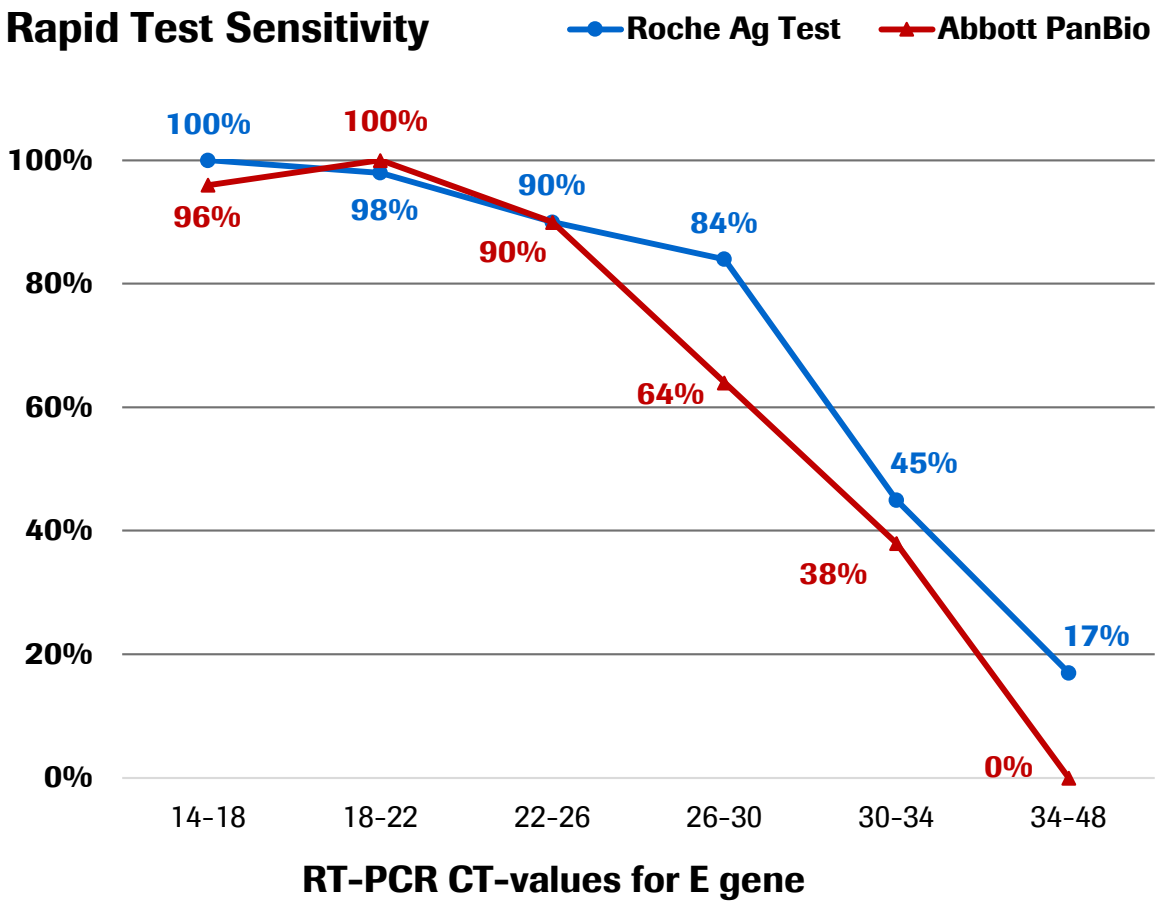
medRxiv preprint doi: https://doi.org/10.1101/2020.11.20.20235341

Hospital Universitaires Genève, Switzerland: Study Details

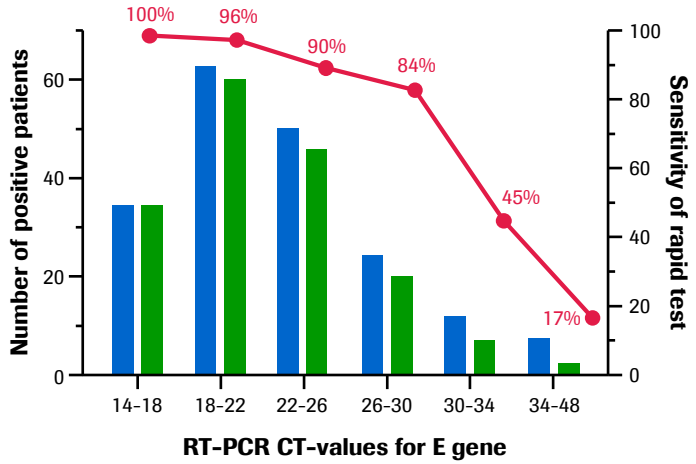
	 Roche Rapid Ag Test	 Abbott PanBio
N, PCR + (%)	529 **(36%)**	535 **(23%)**
Ivestigated cohort	Symptoms for 0-4 days, n (%) 141, (77%) symptomatic & asymptomatic meeting national <suspect> definition	Symptoms for 0-4 days, n (%) 86, (75,4%) symptomatic & asymptomatic meeting national <suspect> definition
Samples	Nasophyryngeal, 1. swab for PCR, 2. swab for POC test	Nasopharyngeal, 1. swab for PCR, 2. swab for POC test
Sensitivity overall Symptoms for 0-4 days Ct 14- 18 Ct 18-22 Ct 22-26 Ct 26-30 Ct 30-34 Ct 34-48	**89.0%** (95% CI 83.69-93.06) 90.85% 100% 98% 90% 84% 45% 17%	**85.48%** (95% CI 78.03-91.16%) 87.21% 96% 100% 90% 64% 38% 0%
Specificity	**99.70% (95%CI 98.36-99.99)**	**100% (95% CI 99.11-100.0)**
Positive Predictive Value	**99.42%** (95%CI 96.00-99.92)	**100%**
Negative Predictive Value	**94.13%** (95%CI 91.47-96.00)	**95.80%** (93.71-97.22)
Reference Method	**cobas**, Roche	**cobas**, Roche

https://www.hug.ch/sites/interhug/files/structures/laboratoire_de_virologie/documents/Centre_maladies_virales_infectieuses/ofsp_rdt_report_gcevd_27.10.2020.pdf
medRxiv preprint doi: https://doi.org/10.1101/2020.11.20.20235341

Hospital Universitaires Genève: Result Details

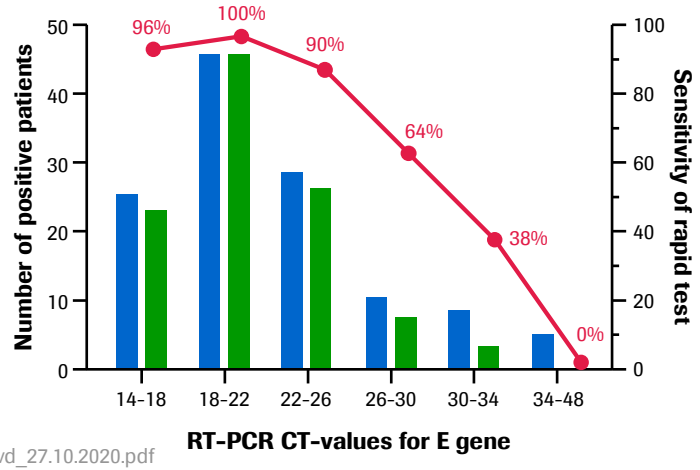


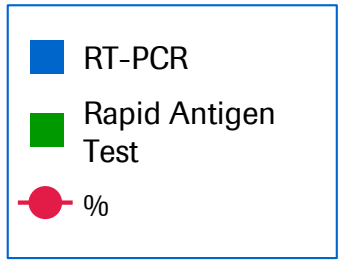
Roche Ag Test



Roche Ag Test with more samples with lower viral load and ghigher sensitivity for Ct values 26 - 48

Abbott PanBio





https://www.hug.ch/sites/interhug/files/structures/laboratoire_de_virologie/documents/Centre_maladies_virales_infectieuses/ofsp_rdt_report_gcevd_27.10.2020.pdf

Cerutti et al., Italy: Study Summary

Purpose of the study

This study evaluated the sensitivity, specificity, negative and positive predictive values (NPV and PPV) of the STANDARD Q COVID- 19 Ag point-of-care diagnostic test (POCT) for the detection of SARS CoV-2 nucleoprotein in nasopharyngeal swab, in comparison with the gold standard RT- PCR

Main results

The STANDARD Q COVID-19 Ag test showed an overall 70.6 % sensitivity and 100% specificity presenting with a Ct between 12.3 - 38.5. For samples with a Ct < 28 the sensitivity was 100%.
Screening of asymptomatic persons without contact to a confirmed case results in lower performance.

Specifics

A major limit of the study was that the test was assessed in suboptimal conditions using UTM samples instead of on-site NP swabs.

Ct values and categories are not comparable with other studies. 3 different PCR methods were used.

Main Conclusions

The POC test shows good sensitivity for investigation of symptomatic patients. POCT (discrepant to PCR) negative results were found in samples with a low viral load, consistent with low viable virus and low infectiousness as confirmed by cell-culture in a subset of samples.

Cerutti F, Burdino E, Milia MG, et al. Urgent need of rapid tests for SARS CoV-2 antigen detection: Evaluation of the SD-Biosensor antigen test for SARS-CoV-2 [published online ahead of print, 2020 Sep 29]. *J Clin Virol*. 2020;132:104654. doi:10.1016/j.jcv.2020.104654

Cerutti et al., Italy: Study Details

	Diagnostic Population 1	Screening Population 2
N, PCR positive (%)	330 **(33%)**	
N, PCR positive (%)	185 **(56%)**	145 **(3.4%)**
Investigated cohort	185 with symptoms and signs consistent with COVID-19	145 asymptomatic travelers returning from EU high risk countries
Samples	Nasopharyngeal (NP), COPAN UTM; A major limit of the study was that the test was assessed in suboptimal conditions using UTM samples instead of on-site NP swabs. 13/185, 7% Ag tests were run on left-over sample stored at −20 ◦C.	
Sensitivity	**72.1%**	**40%**
Sensitivity overall	**70.6%**	
• **Sensitivity at Ct <28**	**100%**	
• Ct 28 - 30	38.5%	
• Ct 30 - 35	26.7%	
• Ct > 35	9.1%	
Specificity, positive/total nr	**100%** (81/81)	**100%** (140/140)
Positive Predictive Value	**100%**	**100%**
Negative Predictive Value	**73.6%**	**97.9%**
Reference Method	SeegeneAllplex (n=159), **cobas**Roche (n=118), DiaSorinSimplexa (n=28)	

Ct values not well comparable with other studies

UTM, viral transort media

Cerutti F, Burdino E, Milia MG, et al. Urgent need of rapid tests for SARS CoV-2 antigen detection: Evaluation of the SD-Biosensor antigen test for SARS-CoV-2 [published online ahead of print, 2020 Sep 29]. *J Clin Virol.* 2020;132:104654. doi:10.1016/j.jcv.2020.104654

Krueger et al., Germany: Study Summary

Purpose of the study

Evaluation of the accuracy, ease of use and limit of detection of novel, rapid, antigen-detecting point-of-care diagnostics for SARS-CoV-2.

Performance of three Ag-RDTs was compared to RT-PCR overall, according to predefined subcategories e.g. cycle threshold (CT)-value, days from symptoms onset. (Berlin, Heidelberg and Liverpool)

Main results

There is large variability on performance of rapid antigen tests.

The Roche / SDB STANDARD Q-CoV test was the best performing, with 100% sensitivity for samples with Ct values < 25 and with 76.6% overall sensitivity.

Specifics

For some patients in the study oropharyngeal samples swabs were used (not nasopharyngeal) which is not according the IFU.
The test was considered easy-to-use and suitable for point-of-care.

Main Conclusions

With a sensitivity of 100% for the STANDARD Q COVID-19 Ag test in infected persons with a high viral load, it is likely to identify highly contagious individuals.

The rapid turn-around time is likely to result in more rapid isolation of cases and effective contact tracing.

Krueger et al, https://www.medrxiv.org/content/10.1101/2020.10.01.20203836v1

Krueger et al., Germany: Study Details

	Roche Rapid Ag Test*	Bioeasy 2019-nCoV Ag	CorisRespi-Strip
N, PCR positive (%)	1263 **(3%)**	729 **(2.9%)**	425 **(1.9%)**
Investigated cohorts	84.4% symptomatics	81.2% sypmtomatics	68.9% symptomatics
Samples	Nasopharyngeal and oropharyngeal	Nasopharynngeal	Nasopharynngeal
Sensitivity (95% CI)	**76.6%** (62.8-86.4)	**66.7%** (41.7-84.8)	**50%** (21.5-78.5)
• **Sensitivity** • Ct <25, (95%CI) • Ct ≥ 25, (95%CI)	 **100%** (82.4-100) **62.1%** (44.0-77.3)	 **88.9%** (56.5-99.4) **33.33%** (9.7-70.0)	 **66.7%** (20.8-98.3) **40%** (11.8-76.9)
Specificity (95%CI)	**99.3%** (98.6-99.6)	**93.1** (91.0-94.8)	**95.8 (93.4-97.4)**
Reference Method	TibMolbiol, Allplex Seegene, Abbott, **cobas**® 6800/8800, Genesig (UK)		

*This is partially the data of the German cohort in the FIND study.
Krueger et al, https://www.medrxiv.org/content/10.1101/2020.10.01.20203836v1

Van Beek et al., The Netherlands: Study Summary

Purpose of the study

Freshly collected nasal and nasopharyngeal samples in viral transport media from people presenting to the drive through test station with a range of Ct values were tested in parallel by RT-PCR, and rapid antigen detection tests (RDT). Detection limits of 5 commercially available RDT's were determined using serial dilutions of freshly harvested SARS-CoV-2 virus stock.

Main results

Rapid antigen tests differ greatly in their ability to detect infectious cases. The test were classified into 3 performance categories without further details
With the most sensitive RDTs, 97.3% of potentially infectious individuals with mild symptoms would be detected, with medium quality tests 92.73% and with the low quality 75.53%.

Specifics

Routine application of rapid antigen testing increased time-to–result at same day from 33% to 97%.
Freshly collected nasal + nasopharyngeal samples in VTM tested by RT-PCR and RDT in parallel. In addition, some samples were also used for virus culture on Vero E6 cells.

Main Conclusions

The use of rapid antigen tests for screening of individuals offers the potential for rapid identification of those individuals at greatest risk of spreading the infection. High quality RDTs offer hope to improve containment by more rapid isolation and contact tracing of the most infectious individuals.

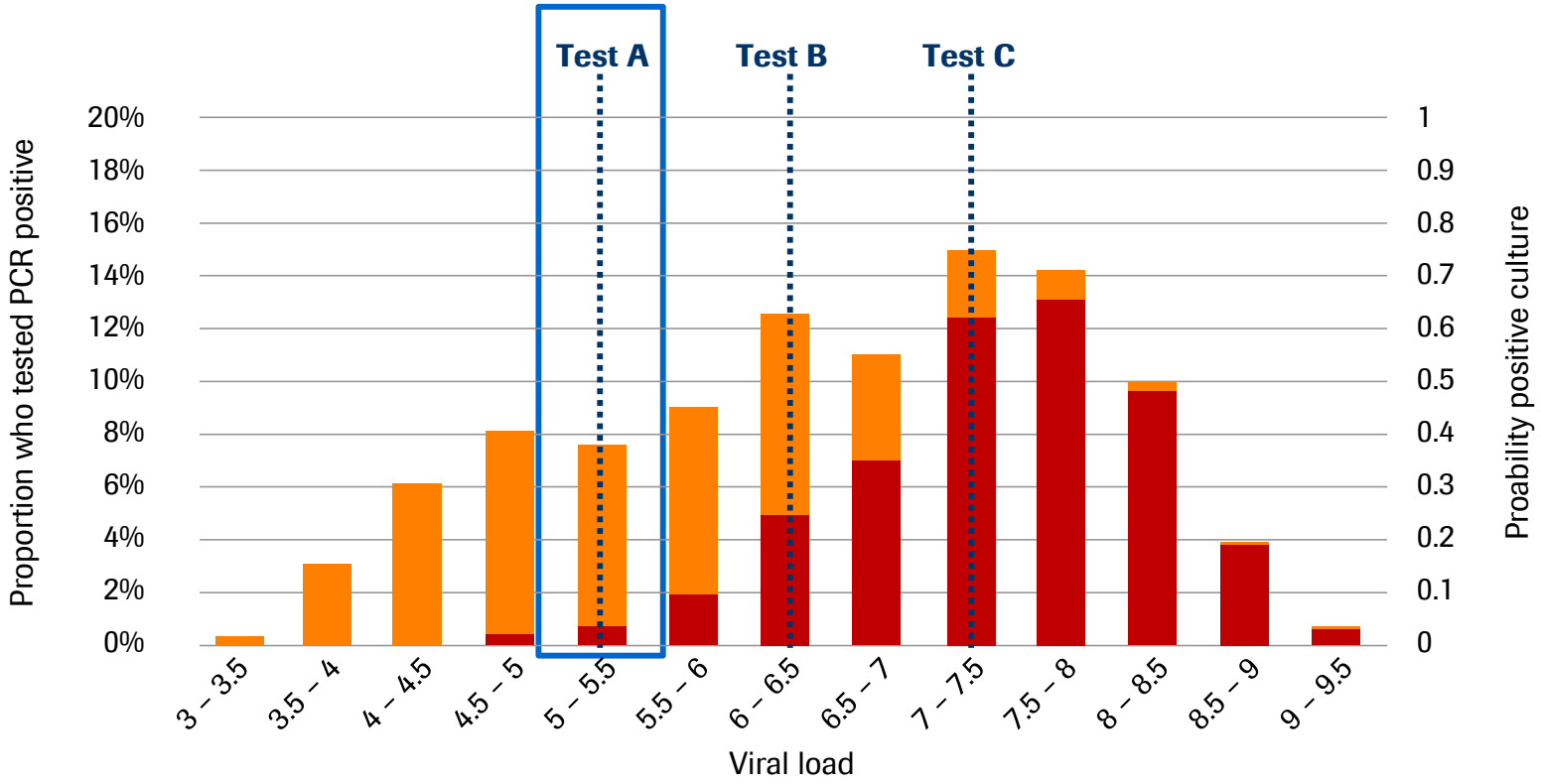
Van Beek, J et al:https://doi.org/10.1101/2020.10.13.20211524

Van Beek et al., The Netherlands: Detection of culture positive (RT-PCR-confirmed) cases by rapid antigen tests depending on severity of symptoms

Rapid Antigen Assay	Mild, outpatient Median (min - max)	Hospitalised, mild Median (min - max)	Hospitalised, severe Median (min - max)	
A - Panbio™ COVID-19 Ag rapid test (Abbott), *and Standard Q COVID-19 Ag (SD Biosensor)*	**94.30%** (88.65% - 99.77%)	**98.68%** (95.79% - 99.81%)	**99.80%** (99.32% - 99.97%)	**Roche & Abbott assays**
B - COVID-19 Ag Respi-Strip (Coris BioConcept, *and GenBody COVID-19 Ag (GenBody Inc)*	**92.73%** (60.30% - 99.77%)	**97.43%** (86.40% - 99.81%)	**99.54%** (97.45% - 99.97%)	
C – Biocredit COVID-19 Ag (RapiGEN)	**75.53%** (17.55% - 99.75%)	**91.70%** (57.90% - 99.81%)	**98.55%** (88.53% - 99.97%)	

Rapid Antigen Tests Performance Comparison including virus culture testing of infectiousness
Van Beek, J et al:https://doi.org/10.1101/2020.10.13.20211524

Van Beek et al., The Netherlands : Correlation of PCR-/AG-test positive and cell-culture positive result for different rapid AG test performance assays



Distribution of viral RNA loads at time of diagnosis with RT-PCR confirmed SARS-CoV-2 infection
N=1754 (of which 78 were tested by virus culture).

Van Beek, J et al:https://doi.org/10.1101/2020.10.13.20211524

Corman et al., Germany: Study Summary

Purpose of the study

7 different Ag POC tests were evaluated on recombinant nucleoprotein, cultured endemic and emerging coronaviruses, stored clinical samples with known SARS-CoV-2 viral loads (n=138), stored samples from patients with respiratory agents other than SARS-CoV-2 (n=100), as well as self-sampled swabs from healthy volunteers (n=35).

Main results

The sensitivity range of most AgPOCT overlaps with viral load figures typically observed during the first week of symptoms, which marks the infectious period in the majority of patients.

All tests x-react with SARS-CoV

Specifics

Specimens were stored in universal transport medium (Copan UTM™) at -20°C. They used stored swabs obtained in universal transport medium (Copan UTM™) or without any medium (dry swabs).

Healthy volunteers (for specificity testing) conducted self-testing. They refer to Krueger that show equivalence of specimen material.

Main Conclusions

In hospitalized patients at the end of their clinical course, negative AgPOCT results may provide an additional criterion to safely discharge patients. Novel public health concepts suggest decisions to isolate or maintain isolation that are based on infectivity testing rather than infection screening.

Drexler, Christian Drosten. Comparison of seven commercial SARS-CoV-2 rapid Point-of-Care Antigen tests. medRxiv 2020; medRxiv preprint doi: https://doi.org/10.1101/2020.11.12.20230292; Van Beek, J et al:https://doi.org/10.1101/2020.10.13.20211524

Corman et al., Germany: Study Details

	 Roche Rapid Ag Test	 Abbott PanBio
N, PCR + (%)	N=529 (archive specimen)	N=535 (archive specimen)
Ivestigated cohort	symptomatic & asymptomatic meeting national <suspect> definition	symptomatic & asymptomatic meeting national <suspect> definition
Samples	Nasophyryngeal, swabs, dry swabs Specimens were stored at -20°C in phosphate-buffered saline (PBS) or universal transport medium (Copan UTM™) at -20°C. For specificity: self-testing	
Sensitivity overall	6.78 x10^6 copies/swab LoD, 95% mean hit rate 4.4 PFU of virus per test	6.55 x10^6 copies/swab 4.4 PFU of virus per test
Specificity **Cumulative Specificity**	**97.12% n= 35** **98.53%**	**100% n=35** **99.26%**
Positive Predictive Value	n.a.	n.a.
Negative Predictive Value	n.a.	n.a.
Reference Method	SARS-CoV-2 E-gene assay Thermofisher Scientific	

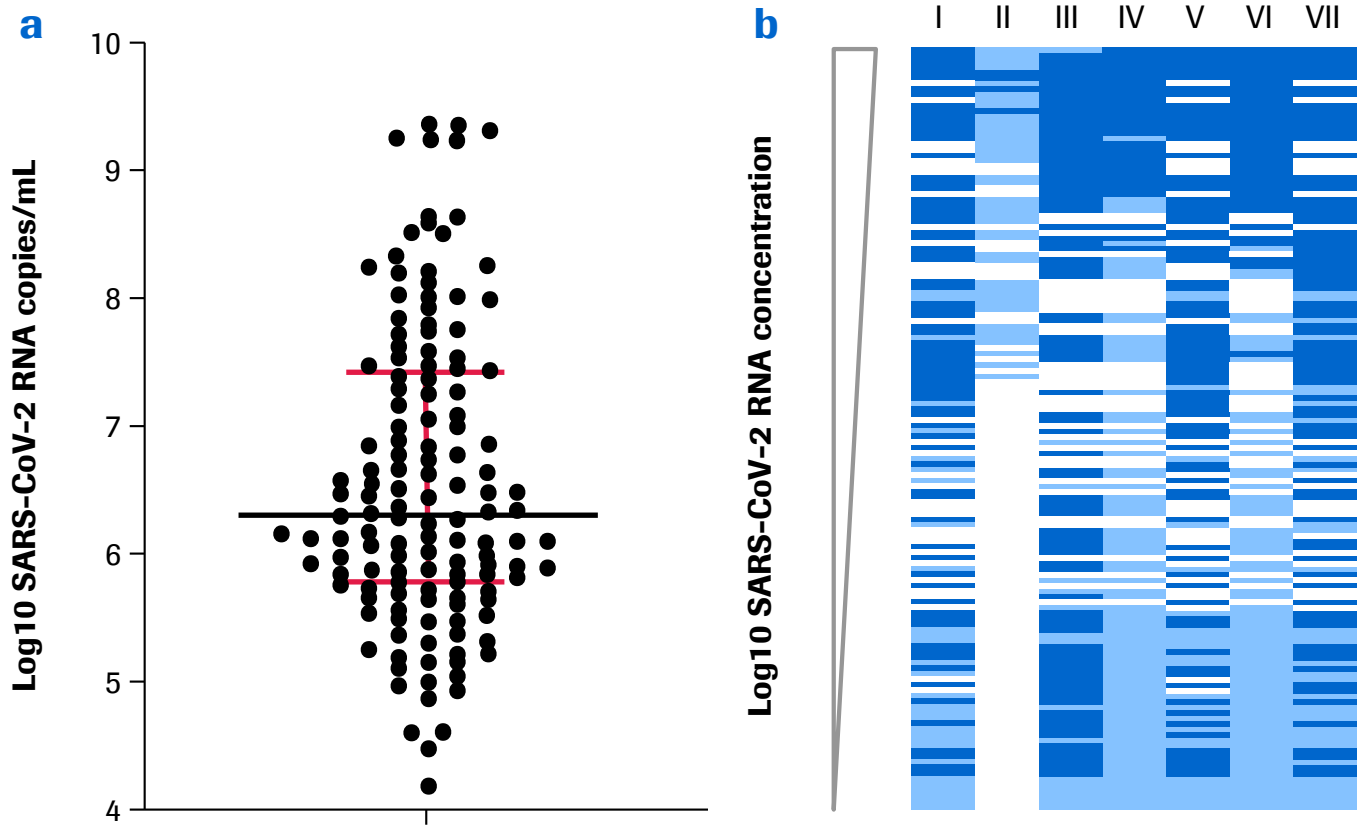
Victor M. Corman VCH, Tobias Bleicker, Marie Luisa Schmidt, Barbara Mühlemann, Marta Zuchowski, Wendy Karen Jó Lei, Patricia Tscheak, Elisabeth Möncke-Buchner, Marcel A. Müller, Andi Krumbholz, Jan Felix Drexler, Christian Drosten. Comparison of seven commercial SARS-CoV-2 rapid Point-of-Care Antigen tests. medRxiv 2020; medRxiv preprint doi: https://doi.org/10.1101/2020.11.12.20230292;

Corman et al., Germany: Result Details

a) Distribution of SARS-CoV-2 viral RNA concentrations across clinical samples used for AgPOCT testing.

b) Overview of tested samples and corresponding outcomes in the seven AgPOCT (per column). Blue fields correspond to a positive AgPOCT result, red fields to a negative result. Empty fields represent samples that were not tested in the corresponding test.

I: Abbott Panbio™ COVID-19 Ag Rapid Test
II: RapiGEN BIOCREDIT COVID-19 Ag
III: Healgen® Coronavirus Ag Rapid Test Cassette (Swab)
IV: Coris Bioconcept Covid.19 Ag Respi-Strip;
V: Biopharm RIDA®QUICK SARS-CoV-2 Antigen;
VI: NAL von minden; NADAL COVID19-Ag Test;
VII: Roche/SD Biosensor SARS-CoV Rapid Antigen Test



Victor M. Corman VCH, Tobias Bleicker, Marie Luisa Schmidt, Barbara Mühlemann, Marta Zuchowski, Wendy Karen Jó Lei, Patricia Tscheak, Elisabeth Möncke-Buchner, Marcel A. Müller, Andi Krumbholz, Jan Felix Drexler, Christian Drosten. Comparison of seven commercial SARS-CoV-2 rapid Point-of-Care Antigen tests. medRxiv 2020. medRxiv preprint doi: https://doi.org/10.1101/2020.11.12.20230292

Corman et al., Germany: Summary

Aim:
To provide a reflection of test performance on analytical properties of 7 newly marketed rapid antigen tests during a low SARS-CoV-2 incidence in summer 2020 in the Northern hemisphere

Sensitivity:
Detection range corresponds to ca. 10 million copies per swab and thus corresponds to a concentration that predicts a virus isolation success of ca. 20% in cell culture*.

Hypothesis:
Taken other data into consideration1,2,3,4 positive Ag rapid test results indicate large amounts of virus shedding and may thus indicate the time of infectiousness.

*the numbers are back calculated and inferred from other studies
1Wolfel, R et al. Virological assessment of hospitalized patients with COVID-2019. Nature.2020, 581(7809):465-9; 2van Kampen etal, Shedding of infectious virus in hospitalized patients with coronavirus dsiease-2019 (COVID-19=:duration and key determinants. medRxiv.
2020:2020.06.08.20125310; 3Perera et al. SARS-CoV-2 Virus Culture and Subgenomic RNA for Respiratory Specimens from patients with mild Coronavirus Disease. Emerg Infect. Dis. 2020;26(11):2701-4. 4He X et al: Temporal dynamics in viral shedding and transmissibility
of COVID-19. Nat. Med. 2020;26(5):672-5

Mak et al., Hong Kong: Study Summary

Purpose of the study

- To compare analytical sensitivity and clinical sensitivity for the three commercially available RAD kits.
- Analytical sensitivity for the detection of SARS-CoV-2 virus was determined by limit of detection (LOD) using RT-PCR as a reference method using respiratory specimens from confirmed COVID-19 patients

Main results

- The LOD of Standard Q was 10^{-5}. The corresponding Ct value for LOD at 10^{-5} was 28.67.
- In the cross-reactivity test using virus isolates, all were tested negative by the RAD kits. Review of the Ct values showed that specimens missed by the RAD kits had relatively high Ct values.

Specifics

- To determine LOD between different kits, a respiratory specimen was serially diluted and virus concentrations in each dilution were estimated from Ct value
- Specimen: throat saliva, nasopharyngeal swab and throat swab, nasopharyngeal aspirate and different combinations
- Small number of specimen in the subgoups

Main Conclusions

Although viral culture was not performed in the present study, the Standard Q was 102 fold less sensitive than RT-PCR, it corresponded to the LOD of viral culture based on our results reported previously.
The authors recommended specimens obtained ≤7 days after symptom onset for use with the Standard Q. Then, the RAD kit can serve as a COVID-19 filter (filtered out of the infected persons and prevent spread to the others).

Mak GCK, Lau SSY, Wong KKY, et al. Analytical sensitivity and clinical sensitivity of the three rapid antigen detection kits for detection of SARS-CoV-2 virus. J Clin Virol. 2020;133:104684. doi:10.1016/j.jcv.2020.104684

Mak et al., Hong Kong: Study Details

Standard Q Ag Test

N, PCR + (%)	280 archive specimens (100%)		
Investigated cohort	respiratory specimens from COVID-19 patients collected by the Public Health Laboratory Services Branch (PHLSB) in Hong Kong were retrieved for this evaluation. All of the specimens were confirmed with SARS-CoV-2 infection by RT-PCR as described		
Samples	mainly nasopharyngeal and throat swabs; Samples were mixed in 2 mL of viral transport media (VTM)		
Symptoms	All of the specimens were confirmed with SARS-CoV-2 infection by RT-PCR		
	NP swab & throat swab	**NP swab**	**Throat saliva**
Sensitivity overall	71.4 %	65.7%	71,4%
Ct 12.9-18.4	**(13-18) 100%**	**15-18) 100%**	**(12-18) 100%**
Ct 19.8-28.6	**(20- 29) 93.8 %**	**(19-28) 81.3%**	**(19-29) 88.2%**
Ct 29.0-34.2	(29-34) 10%	(29-35) 10%	(29-33) 11.1
Specificity	**n.a.**		
PPV / NPV	**n.a.**		
Reference Method	PCR method not clear, most probably in house method, see https://doi.org/10.1016/j.jcv.2020.104500		

Calculated sensitivity for Ct <29 is 96%

Mak GCK, Lau SSY, Wong KKY, et al. Analytical sensitivity and clinical sensitivity of the three rapid antigen detection kits for detection of SARS-CoV-2 virus. J Clin Virol. 2020;133:104684. doi:10.1016/j.jcv.2020.104684

Mak et al., Hong Kong: Nasopharyngeal Swab

	Standard Q SD Biosensor	Covid-19 Respi Strip Coris	Nadal Covid-19
Sensitivity Ct (mean)	**(16.38) 100%**	(16.38) 100%	(16.50) 100%
Sensitivity Ct (mean)	**(23.44) 81.3%**	(23.44) 31.3%	(23.31) 56.3%
Sensitivity CT (mean)	**(31.73) 10%**	(31.73) 0%	31.56 0%
Sensitivity (overall)	**65.7%**	40%	51.4%
Specificity	**100%**	100%	100%

Mak GCK, Lau SSY, Wong KKY, et al. Analytical sensitivity and clinical sensitivity of the three rapid antigen detection kits for detection of SARS-CoV-2 virus. J Clin Virol. 2020;133:104684. doi:10.1016/j.jcv.2020.104684

Mak et al., Hong Kong: Nasopharyngeal and Throat Swab

	Standard Q SD Biosensor	Covid-19 Respi Strip Coris	Nadal Covid-19
Sensitivity Ct (mean)	**(15.96) 100%**	(15.96) 100%	(15.81) 100%
Sensitivity Ct (mean)	**(23.72) 93.8%**	(23.72) 31.3%	(23.60) 18.8%
Sensitivity CT (mean)	**(32.04) 10%**	(32.04) 0%	(31.56) 0%
Sensitivity (overall)	**71.4%**	40%	51.4%
Specificity	**100%**	100%	100%

Mak GCK, Lau SSY, Wong KKY, et al. Analytical sensitivity and clinical sensitivity of the three rapid antigen detection kits for detection of SARS-CoV-2 virus. J Clin Virol. 2020;133:104684. doi:10.1016/j.jcv.2020.104684

Chaimayo et al., Thailand: Study Summary

Purpose of the study

Performance characteristics of the rapid SARS-CoV-2 antigen test were evaluated and compared with the gold standard RT-PCR for diagnosis of COVID-19 cases.

Main results

The rapid assay for SARS-CoV-2 antigen detection showed comparable sensitivity and specificity with the RT-PCR assay.

- Sensitivity 98.33%
- Specificity 98.73%

Specifics

Cohort: suspected COVID-19 cases, including pre-operative patients. Mainly combined nasopharyngeal and throat swabs were used.

Main Conclusions

The rapid SARS-CoV-2 antigen test can benefit all healthcare workers in managing infected individuals in time effectively, in high prevalence areas and especially in rural and outbreak areas. The advantage of the Standard Q COVID-19 Ag test as a screening for COVID-19 is its simple procedure and quick results with high NPV, but its disadvantage is low PPV in a low prevalence area.

Chaimayo et al. Virol J (2020) 17:177 https://doi.org/10.1186/s12985-020-01452-5

Chaimayo et al, Thailand: Study Details

Standard Q Ag Test

N, PCR + (%)	454 **(13.2%)**
Ivestigated cohort	suspected COVID-19 cases, including pre-operative patients
Samples	mainly nasopharyngeal and throat swabs; Samples were mixed in 2 mL of viral transport media (VTM)
Symptoms	three days (range 0–14),
Sensitivity overall	**98.33%** (95% CI, 91.06–99.96%) One negative sample had Ct values of E, RdRp, and N with 31.08 / 39.2 / 35.54 (negative RT-PCR is defined as having Ct-values larger than 40)
Specificity	**98.73%** (95% CI, 97.06–99.59%)
PPV / NPV	PPV and NPV of the assay could not be accurately calculated without the present population prevalence of COVID-19.
Reference Method	Allplex™ 2019-nCoV Assay (Seegene®, Korea)

Chaimayo et al. Virol J (2020) 17:177 https://doi.org/10.1186/s12985-020-01452-5

Lindner et al., Germany

Purpose of the study

A manufacturer-independent, prospective diagnostic accuracy study with comparison of a supervised, self-collected anterior nose (AN) swab sample with a professional collected nasopharyngeal swab (NP) sample, using STANDARD Q COVID-19 Ag Test (SD Biosensor)

Main results

The Ag-RDT with AN sampling showed a sensitivity of 74.4% and specificity of 99.2% compared to RT-PCR. The sensitivity with NP sampling was 79.5% and specificity was 99.6%. In patients with high viral load (>7.0 log10 RNA SARSCoV2/swab), the sensitivity of the Ag-RDT with AN sampling was 96% and 100% with NP sampling.

Specifics

A supervised self-collected nasal sample (both nostrils) were taken first, then the combined NP/OP (1 nostril) for PCR, lastly the NP (the other nostril) for the Ag test was taken. Sequence might lead to different viral loads. NP swab was usually rotated against the nasopharyngeal wall for **less** time than recommended by the manufacturer

Main Conclusions

- Supervised self-sampling from the anterior nose is a reliable alternative to professional nasopharyngeal sampling using a WHO-listed SARS-CoV-2 Ag-RDT
- The Ag-RDT frequently did not detect patients with lower viral load or with symptoms >7 days

Lindner et al 2020 doi: https://doi.org/10.1101/2020.10.26.20219600

Lindner et al., Germany: Study Details

Roche Rapid Ag Test

N, PCR + (%)	289 **(13.5%)**	
Ivestigated cohort	Adults at high risk according to clinical suspicion On the day of testing, 97.6% of participants had one or more symptoms consistent with COVID-19.	
Samples	Supervised anterior nose swab (AN) -- > off-label	**Professional NP swab**
Symptoms	Average 4.4 days (SD 2.7)	
Sensitivity overall	**74.4% (CI 58.9-85.4)**	**79.5 (CI 64.5-89.2)**
Sensitivity high viral load (>7.0 log10 RNA SARS-CoV2/swab)	96% (CI 80.5-99.3)	**100% (CI 86.7-100)**
Ct 17.3-23.7	95.7%	**100%**
Ct 17.3-25.3	92.3 %	**96.2%**
Ct 17.3-29.6	87.1%	**90.3 %**
Ct 17.3-30.0	84.4%	**87.5%**
Ct 24.2-35.5	43.8%	**50.0%**
Ct 25.3- 35.5	38.5%	**46.2%**
Specificity	99.2% (CI 97.1-99.8)	**99.6 (CI 97.8-100)**
Pos % agreement AN / NP	**90.6% (Ci 75.8-96.8)**	
Reference Method	The Roche **cobas** SARS-CoV-2 assay or the SARS-CoV-2 E-gene assay from TibMolbiol (Berlin, Germany)	

Sensitivities calculated based on Table in the publication

Lindner et al 2020 doi: https://doi.org/10.1101/2020.10.26.20219600

Igloi et al., The Netherlands: Study Summary

Purpose of the study

The Roche/SD Biosensor lateral flow antigen rapid test was evaluated in a mild symptomatic population at a large drive through testing site.

Main results

Overall sensitivity and specificity were 84.9% and 99.5%
Sensitivity for samples with high loads of viral RNA (ct <30, 2.17E+05 E gene copy/ml) and who presented within 7 days since symptom onset increased to 95.8% .

Specifics

All Ag Rapid Antigen Tests and PCR positive samples were cultured to correlate results with infectivity.
Eligibility for a free of charge test includes either symptoms or close contact with a confirmed SARS-CoV-2 infected person, therefore symptoms may be over-reported.

Main Conclusions

- People with early onset and high viral load were detected with 98.2% sensitivity, 97% of individuals in which virus could be cultured were detected by the rapid test.
- This test is suitable to detect mild symptomatic cases, suggesting screening based on Ag RDT alone in this population would have a high sensitivity for ruling out infectious individuals .

Igloi et al; https://www.finddx.org/wp-content/uploads/2020/09/SDQ-Ag-Public-Report_20200918.pdf

Igloi et al., The Netherlands: Study Details

Roche Rapid Ag Test

N, PCR + (%)	970 (19.2%)		
Investigated cohort	Mild symptomatic population, egilibility for a free of charge test includes either symptoms or close contact with a confirmed SARS-CoV-2 infected person		
Samples	First swab: combined NP + OP for PCR and viral cell culture; in UTM (HiViral™) Nasopharyngeal swabs for Rapid Ag Test as a second swab from the same nostril		
Symptomatics, n (%)	(xx%)		
DPSO (median	4		
Days < 0-3)	44.0%		
Days 4-7	45.7%		
Days 8+	10.3%		
PCR Ct (median; CI)	23.6 (15.6-37.4)		
	0-3 days post onset	**0-7 days post onset**	**All**
Clinical Sensitivity	94.9 (86.1-98.3), 319	90.6 (84.3-94.6), 650	84.9 (79.1-89.4), 970
Sensitivity CT < 30 (95% CI), N	98.2 (90.6-99.9), 316	95.8 (90.5-98.2), 640	94.3 (89.6-0.97), 943
Sensitivity CT < 25 (95% CI)	100 (92.1-100), 305	98.8 (93.7-99.9), 608	99.1 (95.2-100), 897
PPV	98.2 (90.7-99.9)	98.3 (94.0-99.5)	97.5 (93.8-99.0)
Clinical specificity (95% CI), N	99.6 (97.9-100), 319	99.6 (98.6-99.9), 650	99.5 (98.7-99.8), 970
Reference Method	**cobas**® 6800 and Vero cell clone 118; sample material: combined NP + OP swabs		

Igloi et al; https://doi.org/10.1101/2020.11.18.20234104 doi: medRxiv preprint

Krüttgen et al., Germany: Study Summary

Purpose of the study

The sensitivity and specificity of the new Roche SARS-CoV-2 Rapid Antigen Test was evaluated

Main results

- The assay's sensitivity with samples with a cycle threshold of < 25 was 100% and gradually decreases to 22,2% with cycle thresholds >=35.
- They found a specificity of 96%.
- Samples with Ct-values >30 usually do not allow culturing of the virus indicating low infectivity.

Specifics

Using 75 swabs from patients previously tested positive by SARS-CoV-2 PCR and 75 swabs from patients previously tested negative by SARS-CoV-2 PCR,

Main Conclusions

Sensitivity and specificity of the antigen assay is inferior to the PCR assay, but the overall sensitivity is strictly dependent on the distribution of cycle thresholds (Ct) within the population of specimens and does not allow a realistic evaluation of the assay. The new test might be useful to rapidly identify contagious individuals as the authors state that samples with Ct-values >30 usually do not allow culturing of the virus indicating low infectivity.

Krüttgen A, Cornelissen CG, Dreher M, Hornef MW, Im¨ohl M, Kleines M, Comparison of the SARS-CoV-2 Rapid Antigen Test to the Real Star Sars-CoV-2 RT PCR Kit, Journal of Virological Methods (2020), doi: https://doi.org/10.1016/j.jviromet.2020.114024

Krüttgen et al., Germany: Study Details

Roche Rapid Ag Test

N, PCR + (%)	**150 (50%)** (selected samples)
Ivestigated cohort	Using 75 swabs from patients previously tested positive by SARS-CoV-2 PCR and 75 swabs from patients previously tested negative by SARS-CoV-2 PCR
Samples	350 µl of swab transport medium were mixed with extraction buffer provided by the manufacturer
Symptoms	n.a.; sample collection contained clinical specimens only and the SARS-CoV-2 RNA positive subpopulation was characterized by a wide range of Ct-values with medium and low Ct-values dominating.
Sensitivity overall **Sensitivity Ct < 20** **Sensitivity Ct 25-30** Sensitivity Ct 30-35 Sensitivity Ct >35	70,7% **100%** **95%** 44.8% 22.2%,
Specificity	**96%** (previously tested negative by SARS-CoV-2 PCR samples were used, no further details)
Reference Method	Real Star SARS-CoV-2 RT PCR Kit (Altona, Germany)

Krüttgen A, Cornelissen CG, Dreher M, Hornef MW, Im¨ohl M, Kleines M, Comparison of the SARS-CoV-2 Rapid Antigen Test to the Real Star Sars-CoV-2 RT PCR Kit, Journal of Virological Methods (2020), doi: https://doi.org/10.1016/j.jviromet.2020.114024

Nalumansi et al., Uganda: Study Summary

Purpose of the study

- The aim of this study was to evaluate a low cost, easy-to-use rapid antigen test for diagnosing COVID-19 at the point-of-care.
- Ag Test and results compared with the qRT-PCR results

Main results

- Sensitivity and specificity of the antigen test were 70.0% (95% CI: 60 - 79) and 92% (95% CI: 87- 96) respectively; diagnostic accuracy was 84% (95% CI: 79 - 88).
- The antigen test was more likely to be positive in samples with qRT-PCR Ct values ≤29 reaching a sensitivity of 92%.

Specifics

- Nasopharyngeal swabs from suspect COVID-19 cases and from low-risk volunteers were tested on the STANDARD Q COVID-19
- 262 samples incl 90 RT-PCR positives
- The sequence of sampling is not clear

Main Conclusions

- They conclude that the STANDARD Q COVID-19 Ag Test performed less than optimally in this evaluation but that it may still have an important role to play early in infection when timely access to molecular testing is not available but results should be confirmed by qRT-PCR.
- "Unusual" categorization of the Ct values: they were categorized as strongly positive (Ct ≤ 29) (indicative of abundant target nucleic acid in the sample), moderately positive (Ct 30-37) and weakly positive (Ct 38-39)

https://doi.org/10.1016/j.ijid.2020.10.073 IJID 4794

Nalumansi et al., Uganda: Study Details

	Roche Rapid Ag Test
N, PCR + (%)	**262 (34.4%)**
Ivestigated cohort	suspect COVID-19 cases and from low-risk volunteers were tested on the STANDARD Q COVID-19, 262 samples incl. 90 RT-PCR positives
Samples	Nasopharyngeal swabs
Symptoms	n.a., 14% of the positives were mildly symptomatic – no data on symptom onset
Sensitivity overall Ct ≤29-39 **Sensitivity** Ct≤29 **Sensitivity** Ct 30-37 **Sensitivity** Ct 38-39	70% (95% CI: 60 - 79) 92% (95% CI: 87- 96) 55% 56%
Specificity	**92%** (95%CI 87-96)
Reference Method	Berlin protocol for RT-PCR

Ct values not well comparable with other studies

https://doi.org/10.1016/j.ijid.2020.10.073 IJID 4794

Schwob et al., Switzerland: Study Summary

Purpose of the study

A prospective clinical trial in symptomatic patients to investigate analytical (PCR and RDTs) and sampling procedures (saliva and NP swab) and in order to compare the detection rate of SARS-CoV-2 and sensitivities of i) RDT on NP swab, ii) PCR on NP swab and iii) PCR on saliva.

Secondary objectives were to compare detection rates and sensitivities stratified by Viral Load (VL) categories.

Main results

The results of the present study show that the detection rate of positive COVID-19 cases by RDT was high, especially for those with a VL of $\geq 10^6$ copies/ml.

There was a slight variability in performance between the three different RDTs with STANDARD Q® having a higher sensitivity (93%) than those of PanbioTM (86%) and COVID-VIRO® (84%).

Specifics

Very low inter-observer variation in test line reading which confirms user-friendliness.

Well defined population presenting within 7 days after symptom onset.

Results might not apply to hospitalized patients, who tend to present late in the course of the disease, thus with lower viral loads.

Main Conclusions

The high performance of RDTs allows rapid identification of COVID cases with immediate isolation of the vast majority of contagious individuals. Based on the 100% specificity of high quality RDT there is no need to confirm a positive RDT test result by an additional PCR test. A lower sensitivity after the acute phase of disease might be an advantage to prevent unnecessary isolation of patients who are, for most of them, no more contagious, despite a positive PCR result.

Schwob et al https://doi.org/10.1101/2020.11.23.20237057 doi: medRxiv preprint

Schwob et al., Switzerland: Study Details

	Roche Rapid Ag Test	Panbio Abbott	Coivd-Viro Ag tests
N, PCR positive (%)	928 (40.1% (36.9-43.3%) by NP PCR)		
Investigated cohorts	96% of participants had at least one major symptom and 4% at least one minor and a close contact with a documented COVID-19 case. Mean duration of symptoms at the time of swab collection/testing was 2.6 days (SD 2.3, range 0-30).		
Samples	two nasopharyngeal swabs, one for PCR and one for RDT analyses (sequence not described)		
Sensitivity (95% CI)	**92.9%** (86.4-96.9)	86.1% (78.6-91.7%)	84.1% (76.9-89.7%)
Ct ≤26 or VL* ≥ 10^6 (Ct 26), (95%CI)	96.6% (90.5-99.3)	97.8% (92.1-99.7%)	95.3% (89.4-98.5%)
Specificity (95%CI)	100% (99.3-100)		
Reference Method	in-house RT-PCR on the automated molecular diagnostic platform targeting the E gene,13–15 or using the SARS-CoV-2 test of the **cobas**® 6800 instrument (Roche, Basel, Switzerland).		

*The thresholds chosen for analyses by VL were 105 copies/ml (Ct=30) and 106 copies/ml (Ct=26), based on recent and older data investigating the link between viral loads and the presence of culture-competent virus 1-5

Schwob et al https://doi.org/10.1101/2020.11.23.20237057 doi: medRxiv preprint
1. Bullard J et al. Clinical Infectious Diseases 2020;ciaa638. ; 2. Jaafar R, et al. Clinical Infectious Diseases 2020;ciaa1491. 3.L'Huillier AG et al. Emerg Infect Dis 2020;26(10):2494–7. ; 4. Singanayagam A et al. Euro Surveill 2020;25(32). 5. van Beek J et al. https://www.medrxiv.org/content/10.1101/2020.10.13.20211524v2 preprint

Salvagno et al., Italy: Study Summary

Purpose of the study

The purpose of this study was the clinical assessment of the new Roche SARS-CoV-2 Rapid Antigen Test versus a PCR assay in nasopharyngeal swabs.

Main results

The sensitivity was found to range between 97-100% in clinical samples with Ct values <25, between 50-81% in those with Ct values between 25-<30, but low as 12-18% in samples with Ct values between 30-<37.

Specifics

The study population consisted of all consecutive patients referred for SARS CoV- 2 diagnostic testing to the Hospital.

Main Conclusions

The clinical performance of Roche SARS-CoV-2 Rapid Antigen Test is excellent in nasopharyngeal swabs with Ct values <25, which makes it a reliable screening test in patients with high viral load.

Salvagno GL, Gianfilippi G, Bragantini D, Henry BM, Lippi G. Clinical assessment of the Roche SARS-CoV-2 Rapid Antigen Test. Diagnosis (Berl). 2020. doi: 10.1515/dx-2020-0154

Salvagno et al., Italy: Study Details

Roche Rapid Ag Test

N, PCR + (%)	**321 (46.4%)**
Ivestigated cohort	The study population consisted of all consecutive patients referred for SARS CoV-2 diagnostic testing to the Pederzoli Hospital;
Samples	A single swab (Virus swab UTM™, Copan, Brescia, Italy) was collected from each patient and concomitantly used for both Roche SARS-CoV-2 Rapid Antigen testing and molecular testing in 350 µl volume.
Symptoms	n.a.
Sensitivity overall **Sensitivity Ct < 25** **Sensitivity Ct 25-<30** **Sensitivity Ct 30-37**	72.5% **97-100%** 50-81% 12-18%
Specificity	**99.4%**
Reference Method	Seegene AllplexTM2019-nCoV Assay, Seegene, South Korea), targeting three viral genes (N, E and RdRP),

Salvagno GL, Gianfilippi G, Bragantini D, Henry BM, Lippi G. Clinical assessment of the Roche SARS-CoV-2 Rapid Antigen Test. Diagnosis (Berl). 2020. doi: 10.1515/dx-2020-0154

Kohmer et al., Germany: Study Summary

Purpose of the study

Evaluation of the clinical performance of 3 rapid lateral flow assays (Ag-RDT) and one microfluidic immuno-fluorescence assay, and the prescribed lysis buffers for their ability to inactivate SARS-CoV-2.

All clinical samples were tested with rRT-PCR and positive samples were further subjected to cell-culture-based testing to provide a more thorough correlation analysis.

Main results

The overall Ag-RDT sensitivity for rRT-PCR-positive samples ranged from 24.3% (Nadal) to 50% (LumiraDx).

For samples with a viral load of more than 6 log10 RNA copies/mL, typically seen in infectious individuals, Ag-RDT positivity was between 76.2% (Nadal) and 100% (Roche and LumiraDx).

Specifics

Cohort: individuals living in a shared facility regardless of their infection status.

Modifications to allow parallel testing: The specimen swabs were suspended in 2 mL of PBS to allow cell culture (500 L), RT-PCR (500 L) testing along with the Ag-RDTs (~800 L for 4 tests) prior to testing

Main Conclusions

Large-scale SARSCoV- 2 Ag-RDT-based testing can be considered for detecting potentially infective individuals and reducing the virus spread. Ag-RDTs, although less sensitive, align better with cell culture-based testing for infectivity than RT-PCRs. Focusing on the clinical sensitivity within the potential infectious range is a more practicable approach than focusing just on the analytic sensitivity (lower detection limits) of these tests.

Kohmer et al J. Clin. Med. 2021, 10, 328. https://doi.org/10.3390/jcm10020328

Kohmer et al., Germany: Study Details

	Roche SARS-CoV-2 Rapid Ag	NADAL® COVID-19 Ag Test	RIDA®QUICK SARS-CoV-2 Antigen	SARS-CoV-2 Ag Test LumiraDx (needs reader)
N, PCR + (%)	100 (74%)			
Ivestigated cohort	Individuals from shared living facilities – regardless of their symptoms			
Samples	Dry nasopharyngeal swabs in 2 ml PBS, aliquots of specimen-swab dilutions in PBS were tested within 24 h			
Sensitivity	43.2% (37.8–55.3)	24.3% (15.1–35.7)	39.2% (28–51.2)	50% (38.1–61.9)
Sensitivity ≥ 6 log10 RNA copies/mL	100%	76.2%	85.7%	100%
Specificity	100% (86.8–100%)	100% (86.8–100%)	96.2% (80.4–99.9)	100% (86.8–100%)
Reference Method	**cobas**® 6800 system; primers targeting the ORF1 gene; Caco-2 cells (human colon carcinoma cells)			

Kohmer et al J. Clin. Med. 2021, 10, 328. https://doi.org/10.3390/jcm10020328

Favresse et al. 2020, Belgium: Study Summary

Purpose of the study

This study compared and analyzed the clinical performance of 5 antigen tests, 4 rapid antigen (RAT) tests and 1 automated assay from Ortho Clinical Diagnostics.

Main results

RAT tests were most effective to identify RT-PCR positive symptomatic patients or asymptomatic subjects with higher viral loads. Sensitivity for samples with a Ct values <25 was 93.1% for the Biotical and the Panbio assays, while it was **96.6%** for the Healgen and the **Roche** assays.

Specifics

Nasopharyngeal samples were collected using eSwab liquid preservation medium or Vacuette Virus Stabilization tubes.
The same tube was used for both RT-PCR and antigen (RAT) assessments.
Discrepancies were observed between the different reading times.

Main Conclusions

The RAT tests showed an acceptable sensitivity only for samples with Ct values corresponding to higher viral loads (i.e., <25). However, even with such high viral loads, some samples were miscategorized both from symptomatic patients and asymptomatic subjects. RAT tests are not appropriate for mass community screening since they will lead to a high rate of false-positive and negative results.

Favresse et al J. Clin. Med. 2021, 10, 265. https://doi.org/10.3390/jcm10020265

Favresse et al. 2020, Belgium: Study Details

	Roche SARS-CoV-2 Rapid Ag	Biotical SARS-CoV-2 Ag card	Panbio™COVID-19Ag Rapid Test (Abbott)	Coronavirus Ag Rapid Test Cassette (Healgen)
N, PCR + (%)	188 (51.1%), median Ct value 22.23 (min-max 12.6 – 38.2)			
Ivestigated cohort	Nasopharyngeal samples from 188 patients, adult + pediatric (104 females (median age = 54 years; min-max: 5–97 years) and 84 males (median age: 57 years; min-max: 1–94 years))			
Samples	Nasopharyngeal samples were collected using eSwab liquid preservation medium (Copan) or Vacuette Virus Stabilization tubes (Greiner). All tests were performed within a maximum of 24 h after specimen collection.			
Symptoms	118 (62.8%) were symptomatic patients, and 70 (37.2%) were asymptomatic subjects; In symptomatic patients, the median time since symptom onset was three days (interquartile range (IQR): 2–4 days			
Sensitivity Ct<25*	96.6% [88.1%-99.6%]	93.1% [83.3%-98.1%]	93.1% [83.3%-98.1%]	96.6% [88.1%-99.6%] (15 + 30 min)
Sensitivity Ct<33	82.5% [72.4%-90.1%]	76.2% [65.4%-85.1%]	80.0% [69.9%-88.1%]	15 min: 86.3 % [76.6%-92.9%] 30 min: 88.8% [79.7%-94.7%]
Specificity Ct<25	91.5% [85.4%-95.7%]	91.5% [85.4%-95.7%]	91.5% [85.4%-95.7%]	15 min: 114 (87.7%) [80.8%-92.8%] 20 min: 109 (83.9%) [76.4%-89.7%]
Specificity all Ct	100% [96.1%-100%]	98.9% [94.1%-99.9%]	100% [96.1%-100%]	15 min: 90 (97.8%) [92.4%-99.7%] 20 min: 89 (96.7%) [90.8%-99.3%]
Reference Method	The RT-PCR for SARS-CoV-2 determination was performed on a LightCycler® (Roche Diagnostics, Basel, Switzerland)) 480 Instrument II (Roche Diagnostics) using the LightMix® (Roche Diagnostics) Modular SARS-CoV E-gene set			

If the manufacturer recommended reading the result between a certain interval of times, two readings were performed at the lowest and highest recommended times.

- Panbio: 1 result was positive after reading at 15 min (Ct = 28.7) but turned negative at 20 min and 1 result was negative after reading at 15 min (Ct = 26.4) but turned positive after 20 min.
- Healgen: Five negative results at 15 min turned positive at 20 min.
- Roche: No discordance was observed with the Roche assay.

Favresse et al J. Clin. Med. 2021, 10, 265. https://doi.org/10.3390/jcm10020265

* see supplemental data

Lindner et al., Germany Jan-2021

Professional-collected anterior nasal versus nasopharyngeal swab

Purpose of the study

A manufacturer-independent, prospective diagnostic accuracy study comparing professional-collected nasal mid-turbinate (NMT) to nasopharyngeal (NP) swab, using STANDARD Q COVID-19 Ag Test (SD Biosensor)

Main results

The Ag-RDT with NMT sampling showed a sensitivity of 80.5% and specificity of 98.6% compared to RT-PCR. The sensitivity with NP sampling was 73.2% and specificity was 99.3%. In patients with high viral load (>7.0 log10 RNA SARSCoV2/swab), the sensitivity of the Ag-RDT with NMT sampling was 100% and 94.7% with NP sampling.

Specifics

The previous NMT sample collection could have negatively influenced the test result of the NP sample in patients with a low viral load.
The Ag-RDT more frequently did not detect patients with lower viral load or with symptoms >7 days, as commonly observed in studies on Ag-RDTs.

Main Conclusions

This study demonstrates that sensitivity of a WHO-listed SARS-CoV-2 Ag-RDT using a professional nasal-sampling kit is at least equal to that of the NP-sampling kit. NMT-sampling can be performed with less training, reduces patient discomfort, and enables scaling of antigen testing strategies.

Lindner et al 2021 https://doi.org/10.1101/2020.12.03.20243725

Lindner et al., Germany Jan-2021: Study Details

Professional-collected anterior nasal versus nasopharyngeal swab

Roche Rapid Ag Test

N, PCR + (%)	179 **(13.5%)**	
Ivestigated cohort	Adults at high risk according to clinical suspicion On the day of testing, 97.6% of participants had one or more symptoms consistent with COVID-19.	
Samples	Professional-collected nasal mid-turbinate (NMT) swab	Professional nasopharyngeal (NP) swab
Symptoms	Average 4.2 days (SD 2.6)	
Sensitivity overall	**80.5% (CI 66.0-89.8)**	**73.2% CI 58.1-84.3)**
Sensitivity high viral load (>7.0 log10 RNA SARS-CoV2/swab)	**100% (CI 83.9-100)**	**94.7% (CI 76.4-99.7)**
Specificity	98.6% (CI 94.9-99.6)	99.3% (CI 96.0-100)
Pos % agreement AN / NP	93.5% (CI 79.3-98.2)	
Neg % agreement AN / NP	95.9% (CI 91.4-98.1)	
Reference Method	The Roche **cobas** SARS-CoV-2 assay or the SARS-CoV-2 E-gene assay from TibMolbiol (Berlin, Germany)	

Lindner et al 2021 https://doi.org/10.1101/2020.12.03.20243725

Osterman et al., Germany: Study Summary

No sensitivity in correlation with Ct values

Purpose of the study

The diagnostic assessment of the STANDARD F Covid -19 FIA and the Roche SARS-CoV-2 Rapid Antigen Test (RAT) versus div. PCR assays in asymptomatic and symptomatic patient and health care workers.

Main results

For RAT overall clinical sensitivity was **50.3% (n= 445)** and for FIA, 45.4% (n= 381).
For primary diagnosis of asymptomatic and symptomatic individuals, diagnostic sensitivities were 64.5% (RAT) (n= 256) and 60.9% (FIA) (n= 189).
Specificity: 97.78% for FIA and 97.67% for RAT.

Specifics

381 positive and 386 negative respiratory samples
Great pre-analytical variability:

- Original respiratory swabs and transport media were either kept at room temperature for 1–2 h (“fresh”), stored at 4°C for 0–7 days, or stored at - 20°C until SARS-CoV-2 antigen testing was performed
- Different swab types and transport media

A variety of different targets and systems PCR assays was used for quantification.

Main Conclusions

The authors question these tests’ utility for the reliable detection of acute SARS-CoV-2-infected individuals, esp. in high risk setting. Diagnostic single-point measurements do not allow a reliable assessment of the ascending or descending disease state or potentially relevant clinical infectivity on the day of sampling or subsequent days in critical settings.

Osterman et al https://doi.org/10.1007/s00430-020-00698-8

Osterman et al., Germany: Study Details

No sensitivity in correlation with Ct values

Roche Rapid Ag Test

N, PCR + (%)	381 positive and 386 negative respiratory samples (n.a.)
Ivestigated cohort	asymptomatic and symptomatic patients and health care workers.
Samples	Original respiratory swabs and transport media were either kept at room temperature for 1–2 h (“fresh”), stored at 4°C for 0–7 days, or stored at - 20°C until SARS-CoV-2 antigen testing was performed; Different swabs and transport media
Symptoms	Symptomatics and asymptomatics, no further details
Sensitivity overall	50.3% (n=445)
Sensitivity primary diagnosis	61.6% (site 1) and 72.7% (site 2); The median [lower and upper quartile] of Ct/Cp values for antigen-positive samples was 23.8 (20.8–26.4) while values for antigen-negative samples were 34.0 (31.0–36.0), i.e. low viral load; patient’s positive SARS-CoV-2 RNA detection result was classified as “primary diagnosis” when no other SARS CoV-2 positivity had been reported prior to admission or during hospitalization.
Sensitivity follow up	31.2%; Additional samples were analyzed that had been taken from COVID-19 patients at site 1 at “follow-up” during hospitalization, i.e. at variable time points after onset of symptoms or first PCR-positive result. Time points of sampling are not stated, ie. how many >7 days after symptom onset; Median Ct/Cp values of the samples that scored negative was 34.2 (31.8–36.3), ie. low viral load
Specificity	97.67 % (95.63–98.77)
Reference Method	The nucleocapsid (N1) reaction (CDC) protocol, the envelope amplification (Charité protocol), the nucleocapsid amplification (Seegene Allplex 2019-nCoV Assay), the Roche **cobas** SARS-CoV-2 nucleocapsid reaction or the Xpert Xpress SARS-CoV-2 run on the GeneXpert System, Real Accurate Quadruplex SARS CoV-2 PCR Kit, detecting the N gene and RdRp gene and including an inhibitory control run on a Taqman 7500 (Thermo Fisher Scientific, Waltham, USA), and the Xpert Xpress SARS-CoV-2 run on the GeneXpert System.

Osterman et al https://doi.org/10.1007/s00430-020-00698-8

Yamayoshi et al. 2020, Japan: Study Summary

In vitro LOD testing; no sensitivity in correlation with Ct values; off- label sample material; low n

Purpose of the study

Comparison of the sensitivity among four RATs by using severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) isolates and several types of COVID-19 patient specimens and compared their sensitivity with that of RT-qPCR and infectious virus isolation. Evaluation with a small number of several kinds of clinical specimens collected from COVID-19 patients.

Main results

The overall sensitivity of Standard Q COVID-19 Ag and Espline SARS-CoV-2 was better than that of ImmunoAce SARS-CoV-2 and QuickNavi COVID19 Ag. For specimens such as saliva and swabs, Standard Q COVID-19 Ag, Espline SARS-CoV-2, and ImmunoAce SARS-CoV-2 had similar detection sensitivities.

Specifics

- Cell culture: Vero cells expressing human serine protease TMPRSS2 (Vero-TMPRSS2).
- Two SARS-CoV-2 isolate stocks (NC02 and HP72) were diluted to the indicated PFU (isolated from clinical samples)

Main Conclusions

RATs may be suitable for the detection of COVID-19 in individuals who are shedding a large amount of SARS-CoV-2 and they may be useful to identify patients with a high likelihood of transmitting the virus to others.

Yamayoshi et al Viruses 2020, 12, 1420; doi:10.3390/v12121420

Yamayoshi et al. 2020, Japan: Study Details

In vitro LOD testing; no sensitivity in correlation with Ct values; off- label sample material; low n

	Standard Q COVID-19 Ag Test	ImmunoAce SARS-CoV-2	Espline SARS-CoV-2	QickNavi-COVID 19 Ag
N, PCR + (%)	n.a.; in vitro LOD testing			
Ivestigated cohort	Gargle lavage (n = 7), saliva (n = 27), throat (T) swab (n = 2), nasal vestibule swab (n = 1), nasopharyngeal (N) swab (n = 18), sputum (n = 4), and tracheal aspirate (n = 17) samples			
Samples	Two SARS-CoV-2 isolate stocks (NC02 and HP72, isolated form clinical samples) were diluted to the indicated PFU (plaque formation unit)			
Sensitivity **Sensitivity Ct<25**	250 PFU of NC02 250 PFU of HP72 100% (n=8)*	250 PFU of NC02 250 PFU of HP72	500 PFU of NC02 5000 PFU of HP72	750 PFU of NC02 5000 PFU of HP72
Specificity	n.a.	n.a.	n.a.	n.a.
Positive Predictive Value	n.a.	n.a.	n.a.	n.a.
Negative Predictive Value	n.a.	n.a.	n.a.	n.a.
Reference Method	QIAamp Viral RNA Mini Kit (QIAGEN,Tokyo, Japan) and one step RT-qPCR was performed using the LightCycler® 96 System (Roche Diagnostics, Tokyo, Japan) according to the protocol of the National Institute of Infectious Disease, Japan. A Cq value of >40 was considered a negative result.			

Yamayoshi et al Viruses **2020**, 12, 1420; doi:10.3390/v12121420
* Supplemnetal data

Möckel et al., Germany: Study Summary

No sensitivity in correlation with Ct values

Roche

Purpose of the study

The authors implemented rapid antigen (Ag) immunoassay testing in the emergency departments (ED) with the goal of early triage of patients to non-COVID-19 or COVID-19 wards.

They report the first experiences with this strategy in the real life setting of 5 EDs. Test indication was limited to symptomatic suspected COVID-19 patients.

Main results

Adult cohort:
Sensitivity: 75.3 % (95%CI: 65.8/83.4)
Specificity: 100 % (95%CI: 98.4/100)
PPV: 100 %(95%CI: 95.7/100)
NPV: 89.2 % (95%CI: 84.5/93.9)
Pediatric cohort:
Sensitivity: 72.0 % (95%CI: 53.3/86.7)
Specificity: 99.4 % (95%CI:97.3/99.9)
PPV: 94.7 % (95%CI: 78.3/99.7)
NPV: 96.2 % (95%CI:92.7/98.3)

Specifics

Two sequential deep oronasopharyngeal swabs were obtained for viral tests. The first swab was for (rt)-PCR, the second for the rapid Ag test (may impact sensitivity of the rapid test). Rapid test results were available within 15-30 min. The median turnaround time and range (from laboratory registration to digital result communication) of the rt-PCR was 8.2 (3.8-39) hours.

Main Conclusions

The use of rapid Ag test among symptomatic patients in the emergency setting is useful for the early identification of COVID-19, but patients who test negative require confirmation by PCR test and must stay isolated until this result becomes available. Adult patients with a false negative rapid test and symptom onset at least one week earlier have typically a low SARS-CoV-2 RNA concentration and likely passed the infectious period. By combining the rapid test result, the knowledge of time of testing within the course of disease, and further information from patients medical history, a good estimation regarding the potential infectiousness can be made.

Möckel et al https://doi.org/10.1080/1354750X.2021.1876769

Möckel et al., Germany: Study Details

No sensitivity in correlation with Ct values

Roche Rapid Ag Test

N, PCR + (%)	Adults 271 (32.8%), 21-98 years	Children 202 (12.4%), 1-9 years
Ivestigated cohort	Test indication was limited to symptomatic suspected COVID-19 patients.	
Samples	In each suspected COVID-19 patient, two sequential deep oronasopharyngeal swabs were obtained for viral tests. The first swab was collected for (rt)-PCR diagnostic panel in the central laboratory. The second swab was collected to perform the AGTEST	
Symptoms	n.a.	
Sensitivity **PPV** **NPV**	75.3 % (95%CI: 65.8/83.4) 100 %(95%CI: 95.7/100) 89.2 % (95%CI: 84.5/93.9)	72.0 % (95%CI: 53.3/86.7) 94.7 % (95%CI: 78.3/99.7) 96.2 % (95%CI:92.7/98.3)
Specificity	100 % (95%CI: 98.4/100)	99.4 % (95%CI:97.3/99.9)
Reference Method	rt-PCR testing was performed with the Roche **cobas** SARS-CoV-2 assay (Penzberg, Germany) on the Roche **cobas**® 6800 or 8800 system or the Roche MagNA Pure 96 System for RNA purification and the SARS-CoV-2 E-gene assay from TibMolbiol (Berlin, Germany)	

Möckel et al https://doi.org/10.1080/1354750X.2021.1876769

New publications added in this update

Thommes et al. 2021, Austria: Study Summary

Purpose of the study

This single-center study presents a clinical evaluation and comparison of four commercially available COVID-19 antigen tests, using quantitative RT-PCR (**cobas**, Roche) as referbnce. 154 consecutive patients admitted to the department with moderate to severe COVID-19 were tested and antigen test results were linked to Ct (cycle threshold) values as markers for patients' infectivity.

Main results

In patients with a Ct value ≤25, which reflects the population with the highest viral loads and thus the highest infectivity, two tests (Roche and DiaLab) had sensitivities of 100%, whereas Abbott test had a sensitivity of 83.3% and the CLMSRDL of 60%, respectively.

Specifics

The comparative evaluation of the antigen tests was extended to patients being considered non-infectious according to the recommendations of the RKI (Laferl et al., 2020). These investigations showed persistence of positivity in many subjects even with Ct values above 30 and lack of COVID-19 specific symptoms. A limitation of the study: no data on specificity, only hospitalized patients with already confirmed COVID-19.

Main Conclusions

This study indicates that some antigen tests have an excellent sensitivity to identify infected patients with COVID-19 like symptoms needing hospitalization, specifically those with higher viral loads and thus higher infectivity. On the other hand, antigen testing may not be suitable to identify loss of infectivity in COVID-19 subjects during follow-up.

Thommes et al 2021 International Journal of Infectious Diseases 105 (2021) 144–146 https://www.sciencedirect.com/science/article/pii/S1201971221001387

Thommes et al. 2020, Austria: Study Details

	Standard Q COVID-19 Ag Test	Panbio, Abbott	CLMSRDL, Sichuan	Diaquick Covid 19, DIALAB
N, PCR + (%)	154 (100%)			
Ivestigated cohort	Hospitalized patients with moderate to severe COVID-19			
Samples	Oropharyngeal swabs for PCR, nasopharyngeal for Rapid antigen tests			
Sensitivity Ct≤25	100% (66.4–100%, n=9)	83.3% (58.6–96.4%, n=18)	60% (26.2–87.8%, n=10)	100% (73.5–100%, n=12)
Sensitivity Ct≤30	84.4% (67.2–94.7%, n=32)	79.5% (63.5–90.7, n=39)	45.2% (27.3–64.0%, n=31)	88.9% (73.9–96.9%, n=36)
Sensitivity Ct>30	41.0%, n=39	25.6%, n= 43	9.3%, n=54	46.0%, n=63
Specificity	n.a.	n.a.	n.a.	n.a.
Reference Method	RT-PCR **cobas**, Roche Diagnostics: target ORF1a/b and B-CoV target E-Gene			

Thommes et al 2021 International Journal of Infectious Diseases 105 (2021) 144–146 https://www.sciencedirect.com/science/article/pii/S1201971221001387

Jääskjeläinen et al., Finland: Study Summary

Purpose of the study

158 positive and 40 negative retrospective samples collected in saline and analyzed by a laboratory-developed RT-PCR test were used to evaluate Sofia (Quidel), Standard Q (SD Biosensor), and Panbio™ (Abbott) rapid antigen tests (RATs). A subset of the specimens was subjected to virus culture.

Main results

The specificity of all RATs was 100 % and the sensitivity was 84.6% for Sofia, 84.9% for Standard Q, and 86.3 % for Panbio. “Sensitivity” of viral culture was 31%. All three RATs reached 98-99% sensitivity for samples with Ct<25 (high viral load). Virus culture was successful in 80 % of specimens with a Ct value <25. Samples that were negative in virus culture had a median Ct of 29.3.

Specifics

The samples were tested in virus transport medium. All evaluated tests are intended for fresh swab samples, so this is off-label use and leads to dilution of samples. 59 specimens of the PCR positive subset used for analytical performance evaluation was subjected to virus isolation experiments in Vero E6 TMRPSS2 cells.

Main Conclusions

RATs were specific but less sensitive than RT-PCR. However, they benefit from the speed and ease of testing, and lower price as compared to RT-PCR. Repeated testing in appropriate settings may improve the overall performance support repeated testing regimens.

https://doi.org/10.1016/j.jcv.2021.104785

Jääskjeläinen et al., Finland: Study Details

	Roche SARS-CoV-2 Rapid Ag	Quidel Sofia (Instrument)	Panbio Abbott	Virus culture
N, PCR positive (%)	198; 158 positive and 40 negative retrospective samples			
Investigated cohorts	The testing strategy in Finland in November 2020 assumed patients to have at least mild symptoms of SARS-CoV-2 infection.			
Samples	A total of 198 nasopharyngeal swabs in 0.9 % saline, stored - 20◦C			
Sensitivity overall	84.9%	84.6%	86.3%	30.5%
Sensitivity Ct <25	99%	99%	98%	80%
Sensitivity Ct <30	91%	94%	92%	46%
Sensitivity Ct >30	31%	12%	38%	0%
Specificity (95%CI)	100%	100%	100%	/
Reference Method	The samples were originally analyzed with a laboratory-developed RT-PCR test (LDT) based on the method by Corman and others and modified by us to detect the N gene target of SARS-CoV-2.			

https://doi.org/10.1016/j.jcv.2021.104785

Baro et al., Spain: Study Summary

Purpose of the study

Nasopharyngeal specimens from unexposed asymptomatic individuals were used to assess five Ag-RDTs : PanBioTM COVID-19 Ag Rapid test (Abbott), CLINITEST® Rapid COVID-19 Antigen Test (Siemens), SARS-CoV-2 Rapid Antigen Test (Roche Diagnostics), SARS-CoV-2 Antigen Rapid Test Kit (Lepu Medical), and COVID-19 Coronavirus Rapid Antigen Test Cassette (Surescreen).

Main results

For specimens with cycle threshold (Ct) <30 in RT-qPCR, all Ag-RDT achieved a sensitivity of at least 70%, with Siemens, Roche, and Lepu assays showing sensitivities higher than 80%. In models according to population prevalence, all Ag-RDTs will have a NPV >99% and a PPV<50% at 1% prevalence.

Specifics

The study included 101 specimens with confirmed positive PCR results and 185 with PCR negative results.
The reference test (i.e., RT-qPCR) was performed on fresh samples stored at 2 – 8ºC for up to 24 hours; samples were then stored up to 12h at 2-8 ºC until their use for the five Ag-RDTs.

Main Conclusions

The estimated NPV for a screening performed in an area with 1% prevalence would be >99% for all tests, while the PPV would be <50%. These findings support the idea that Ag-RDTs can be used for mass screening in low prevalence settings and accurately rule out a highly infectious case in such setting.

medRxiv preprint doi: https://doi.org/10.1101/2021.02.11.21251553

Baro et al., Spain: Study Details

	Roche SARS-CoV-2 Rapid Ag	Panbio Abbott	Clinitest Siemens	SARS-CoV-2 Ag Rapid Test Lepu	COVID-19 Surescreen
N, PCR positive (%)	The study included 101 specimens with confirmed positive PCR results and 185 with PCR negative results.				
Investigated cohorts	Mass testing of unexposed asymptomatic individuals living in areas at high risk of an outbreak.				
Samples	Nasopharyngeal swabs were placed in sterile tubes containing viral transport media (DeltaSwab Virus, Deltalab; or UTM Universal Transport Medium, Copan)				
Sensitivity overall (95%CI)	43.56% (33.72-53.8)	38.61% (29.09-48.·82)	51.49% (41.33-61.55)	45.54% (35.6-55.76)	28.71% (20.15-38.57)
Sensitivity Ct <30 (95%CI)	83.33% (65.28-94.36)	76·67% (57.72-90.07)	86.67% (69.28-96.24)	83.33% (65.28-94.36)	70% (50.6-85.27)
Specificity (95%CI)	96.22% (92.36-98.47)	99.46% (97.03-99.99)	98.38% (95.33-99.66)	89.19% (83.8-93.27)	97.84% (94.56-99.41)
NPV / PPV	The estimated NPV for a screening performed in an area with 1% prevalence would be >99% for all tests, the PPV would be <50%.				
Reference Method	viral RNA/Pathogen Nucleic Acid Isolation kit for the Microlab Starlet or Nimbus platforms (Hamilton, USA) Allplex™ 2019-nCoV assay (Seegene, South Korea) on the CFX96 (Bio-Rad, USA)				

medRxiv preprint doi: https://doi.org/10.1101/2021.02.11.212515530

Jakobsen et al., Denmark: Study Summary

Purpose of the study

The aim of this study was to determine the accuracy of the STANDARD Q COVID-19 Ag test (SD BIOSENSOR) by comparison with RT-PCR in a public setting. Sensitivity, specificity, positive and negative predictive values of the antigen test were calculated with test results from RT-PCR as reference.

Main results

The overall sensitivity and specificity of the antigen test were 69.7% and 99.5%, the positive and negative predictive values were 87.0% and 98.5%. Ct values were significantly higher among individuals with false negative antigen tests compared to true positives. Changing the criteria of positive RT-PCR to Ct ≤ 30 increased the sensitivity of the RAT to 81.1%.

Specifics

This study comprises a non-selected population with a 4.6% prevalence of SARS-CoV-2 infection.
The individuals with disconcordant negative results of the RAT had significantly higher Ct value corresponding to a lower viral load. This indicates that individuals with false negative RATs are less infectious in general.

Main Conclusions

In agreement with WHO's recommendation of testing for SARS-CoV-2 as intensively as possible, the STANDARD Q COVID-19 Ag test and other RATs with similar accuracy (sensitivity, specificity, and predictive values) seem to be a good supplement to RT-PCR testing.

medRxiv preprint doi: https://doi.org/10.1101/2021.01.22.21250042

Jakobsen et al., Denmark: Study Details

	Roche Rapid Ag Test
N, PCR + (%)	4811(4.6%)
Ivestigated cohort	Non-selected population; Individuals aged 18 years or older who had booked an appointment for a RT-PCR test. 4697 individuals were included (female n=2456, 53.3%; mean age: 44.7 years, SD: 16.9 years); 196 individuals were tested twice or more
Samples	Oropharyngeal (OP) for RT-PCR and nasopharyngeal (NP) for RAT
Symptoms	144 reported symptoms, 4667 without symptoms, but not all participants responded to the online questionnaire
Sensitivity overall (Ct≤38) **Sensitivity Ct ≤30** **Sensitivity with symptoms (n=144)** **Sensitivity withut symptoms**	69.7% 81.1% 78.8% 49.2%
Specificity overall	99.5%
Reference Method	Not specified. The criteria for positive RT-PCR test result were cycle threshold (Ct) ≤38

medRxiv preprint doi: https://doi.org/10.1101/2021.01.22.21250042

Schuit et al., The Netherlands: Study Summary

Purpose of the study

Pre-/asymptomatic close contacts of SARS-CoV-2 infected individuals were tested at day 5 after contact by real-time reverse transcriptase polymerase chain reaction (RT-PCR). Prospective cross-sectional diagnostic test accuracy study for antigen-detecting rapid diagnostic tests (Ag-RDT) BD Veritor System Ag-RDT , and Roche/SD Biosensor Ag-RDT.

Main results

Overall sensitivity for BD was 63.9% and for SD-B 62.9%. When applying an infectiousness viral load cut-off ≥ 5.2 log10 gene copies/mL, the sensitivity was 90.1% for BD, 86.8% for SD-B overall. For those still asymptomatic at the actual time of sampling the sensitivity was 88.1% for BD and 85.1% for SD-B Specificity was >99% for both Ag-RDTs in all analyses.

Specifics

Trained personnel took two combined oropharyngeal-nasal (West-Brabant) or oro-nasopharyngeal (Rotterdam) swabs from each study participant: the first for an RT-PCR test and the second for an Ag-RDT.
BD results were determined visually instead of using a BD Veritor Plus Analyzer.

Main Conclusions

The sensitivity for detecting SARS-CoV-2 of both Ag-RDTs in pre- /asymptomatic close contacts is over 60%, increasing to over 85% after applying an infectiousness viral load cut-off. Dutch policy allows testing of close contacts using Ag-RDTs from day 5 onwards, even when they have not (yet) developed symptoms. Accordingly, positive test results are known and communicated earlier such that the use of Ag-RDTs in pre-/asymptomatic close contacts has the potential to help prevent onward SARS-CoV-2 transmission.

medRxiv preprint doi: https://doi.org/10.1101/2021.03.18.21253874

Schuit et al., The Netherlands: Study Details

	Roche Rapid Ag Test	BD VeritorTM System Ag-RDT
N, PCR + (%)	N=1‘596 (8.3%)	N=2‘678 (8.7%)
Ivestigated cohort	asymptomatic when requesting a test, test-and-trace program or contact tracing app, aged 16+	
Samples	Trained personnel took two combined oropharyngeal-nasal (West-Brabant, BD) or oro-nasopharyngeal (Rotterdam, SD-B) swabs from each study participant: the first for an RT-PCR test and the second for an Ag-RDT	
Sensitivity overall	62.9% (54.0%-71.1%)	63.9% (57.4%-70.1%)
Sensitivity 5.2 log10 E-gene copies/mL	86.8% (78.1% to 93.0%)	90.1% (84.2% to 94.4%)
Sensitivity Asymptomatics at infectious viral load cutoff	85.1% (74.3-92.6%)	88.1% (80.5% to 93.5%)
Specificity	>99% in all analyses	>99% in all analyses
Positive Predictive Value	n.a.	n.a.
Negative Predictive Value	n.a.	n.a.
Reference Method	Roche **cobas**® 6800/8800 RT-PCR; Virus culture was performed in RT-PCR positive individuals to determine the viral load cut-off above which 95% was culture positive, as a proxy of infectiousness.	

medRxiv preprint doi: https://doi.org/10.1101/2021.03.18.21253874

Pena et al., Chile: Study Summary

Purpose of the study

The study compared a SARS CoV-2 rapid antigen test (RAT) and RT-PCR in 842 asymptomatic individuals from Tarapacá, Chile.

Main results

Sensibility of 69.86%, a specificity of 99.61%, PPV of 94.44% and NPV of 97.22%. Individuals with false-negative results of the RAT had significantly higher Ct values (Ct > 27), which can be related to lower viral loads and less infectiousness in general.

Specifics

Two nasopharygeal swabs were taken, sequence not described.

Main Conclusions

The high predictive values supports the fact that RAT might have a significant impact in the identification of asymptomatic carriers in areas that lack well-equipped laboratories to perform SARS-CoV-2 real-time RT-PCR diagnostics or the results take more than 24-48 hours, as well as zones with high traffic of individuals, such as border/customs, airports, interregional bus, train stations or in any mass testing campaign requiring rapid results.

https://doi.org/10.1101/2021.02.12.21251643 doi:

Pena et al., Chile: Study Details

	Roche Rapid Ag Test
N, PCR + (%)	842 (8.64%)
Ivestigated cohort	Asymptomatics, workers (n=56; 6.7%), sanitary residence (n=239; 28.4%), and general public (n=547; 65 65%)
Samples	Naspopharyngeal swabs
Symptoms	Asymptomatics
Sensitivity overall	Antigen testing sensitivity was 69.86% (58.56% to 79.18%)
Specificity	Specificity was 99.61% (98.86% to 99.87%)
NPV	97.22 (95.81-98.15)
PPV	94.44% (84.89-98.09)
Accuracy	97.04% (95.66 to 98.08%)
Reference Method	RT-PCR was performed using the GenomeCov19 Detection Kit ABM (Applied Biological Materials, Ct) values ≤40 considered positive for the N and S viral gene regions

https://doi.org/10.1101/2021.02.12.21251643 doi:

Pena-Rodriguez et al., Mexico: Study Summary

Purpose of the study

The aim of this study was to evaluate a chromatographic immunoassay's performance for the rapid diagnosis of SARS-CoV-antigen.

Main results

In 28.2% of the patients was detected the SARS-CoV- 2 RNA, and 21.4% were positive for antigen detection. The rapid antigen test showed a sensitivity and specificity of 75.9% and 100%, respectively, with a positive predictive and negative values of 100% and 91%.

Specifics

Two sampels were taken, the NP fo RAT as a second which may have lead to lower viral loads.

Main Conclusions

There is an urgent need for rapid diagnosis so that the transmission burden is dampened. SD BIOSENSOR is a useful assay, but some caveats must be considered before the general implementation.

https://doi.org/10.1101/2021.02.12.21251643

Pena-Rodriguez et al., Mexico: Study Details

	Roche Rapid Ag Test
N, PCR + (%)	369 (28.2%)
Ivestigated cohort	A cross-sectional study included 369 adults from Western México with diagnosis or suspicion of SARS-CoV-2 infection
Samples	A naso-oropharyngeal sample was used for a molecular determination of SARS-CoV-2 RNA.The second sample was retrieved from a nasopharyngeal rub and used for the rapid diagnosis of SARS-CoV-2 antigen employing the commercial STANDARD™ Q COVID-19 Ag Test
Symptoms	With and without symptoms
Sensitivity overall (CI) **Ct <25**	75.9% (66.5–83.8%) 88%
Specificity	100% (98.6–100%)
NPV (CI)	91% (88.2–93.7)
PPV (CI)	100% (NA)
Reference Method	DeCoV19 Kit Triplex (Genes2life S.A.P.I de C.V., Mexico), which is based on the CDC diagnostic panel for SARS-CoV2 detection, Ct <35 were considered as positive

https://doi.org/10.1101/2021.02.12.21251643

Olearo et al. 2021, Germany: Study Summary

Purpose of the study

The analytic performance and handling of four CE-labeled rapid Antigen Point of Care Tests (AgPOCTs) were evaluated in a single center non-interventional study: (I) Roche, (II) Abbott, (III) MEDsan and (IV) Siemens

Main results

The overall relative sensitivity was 49.4%, 44.6%, 45.8% and 54.9 % for tests I, II, III and IV, respectively. In the high viral load subgroup (containing $>10^6$ copies of SARS-CoV-2 /swab, n=26), AgPOCTs reached sensitivities of 92.3% or more (range 92.3%-100%). Specificity was 100% for tests I, II and IV and 97% for test III.

Specifics

100 RT-PCR negative and 84 RT-PCR positive oropharyngeal swabs were prospectively collected in UTM and used to determine performance and accuracy of these AgPOCTs. Handling was evaluated by 10 healthcare workers/ users through a questionnaire.

Main Conclusions

All tests were able to detect 10^6 or more copies/swab with high reliability (95%), implying that patients with high viral loads can be identified with acceptable accuracy. RT-qPCR remains the gold standard to definitively confirm or rule out infections due to its significantly higher sensitivity and specificity.

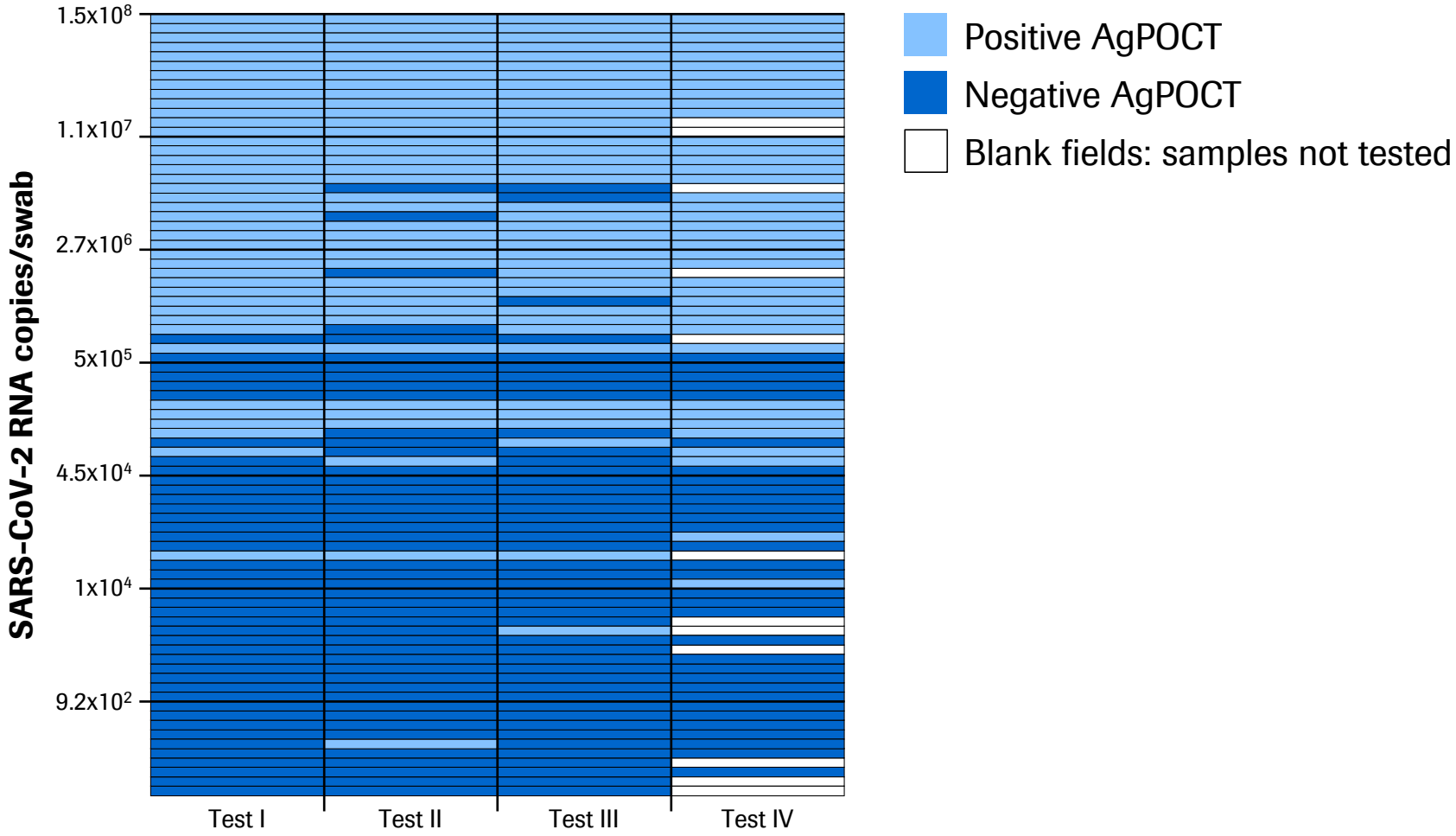
medRxiv preprint doi: https://doi.org/10.1101/2020.12.05.20244673

Olearo et al. 2021, Germany: Study Details

	SARS-CoV-2 Rapid Antigen Test, Roche (I)	Panbio COVID-19 Rapid Test Device, Abbott (II)	MEDSan SARSCoV-2 Antigen Rapid Test (III)	CLINITEST Rapid COVID.19 Antigen Test, Siemens IV
N, PCR + (%)	184 (45.7%)	184 (45.7%)	184 (45.7%)	170 (less clinical samples, inroducing a bias*)
Ivestigated cohort	100 RT-qPCR negative and 84 positive respiratory samples. The median duration from symptom onset to sampling was 6 days (IQR 2-12 days).			
Samples	**Oropharyngeal** swabs were prospectively collected using UTM based collection kits by Copan or Iclean following routine diagnostics. Swabs supplied with the AgPOCT kits were immersed in patient oropharyngeal samples for approximately 10 seconds before tests were carried out according to instructions of the manufacturer.			
Overall Clinical Sensitivity (CI95)	49.4% (38.9%-59.9%)	44.6% (34.3% - 55.3%)	45.8% (35.5% - 56.5%)	54.9 % (43.4% - 65.9%)
>10^6copies/swab	100% (87% -100%)	92.3% (CI95: 75.8% - 97.8%)	92.3% (CI95: 75.8% - 97.8%)	100% (85.7% -100%)
Specificity	100% (96.3-100%)	100 % (96.3-100%)	97% (CI95: 91.5% - 98.9%),	100% (96.3-100%)
Handling	Regarding handling, test I obtained the overall highest scores, while test II was considered to have the most convenient components. Of note, users considered all assays, with the exception of test I, to pose a significant risk for contamination by drips or spills			
Reference Method	**cobas**® 6800 SARS-CoV-2 IVD assay in conjunction with quantitative external control material by Instand e.V. (Düsseldorf, Germany) to allow for absolute quantification			

medRxiv preprint doi: https://doi.org/10.1101/2020.12.05.20244673
*Less clinical samples were tested with Test IV as it only became available when experiments were already underway, thus introducing a bias.

Olearo et al. 2021: AgPOCT results vs SARS-CoV-2 RNA copies/swab



medRxiv preprint doi: https://doi.org/10.1101/2020.12.05.20244673

Olearo et al. 2021, Germany: Usability

Evaluation of the ease of handling and implementation of AgPOCTs into clinical routine

- User survey employing a questionnaire with 10 participants representing different clinical specialties and professions (3 ICU medical doctors, 2 ICU nurses, 3 microbiologists and 2 lab technicians)

Results:

- Test I was considered the overall easiest to use while test II had the easiest to use test components.
- Test III scored lowest overall.
- Users considered all assays, with the exception of test I, to pose a significant risk for contamination by drips or spills.

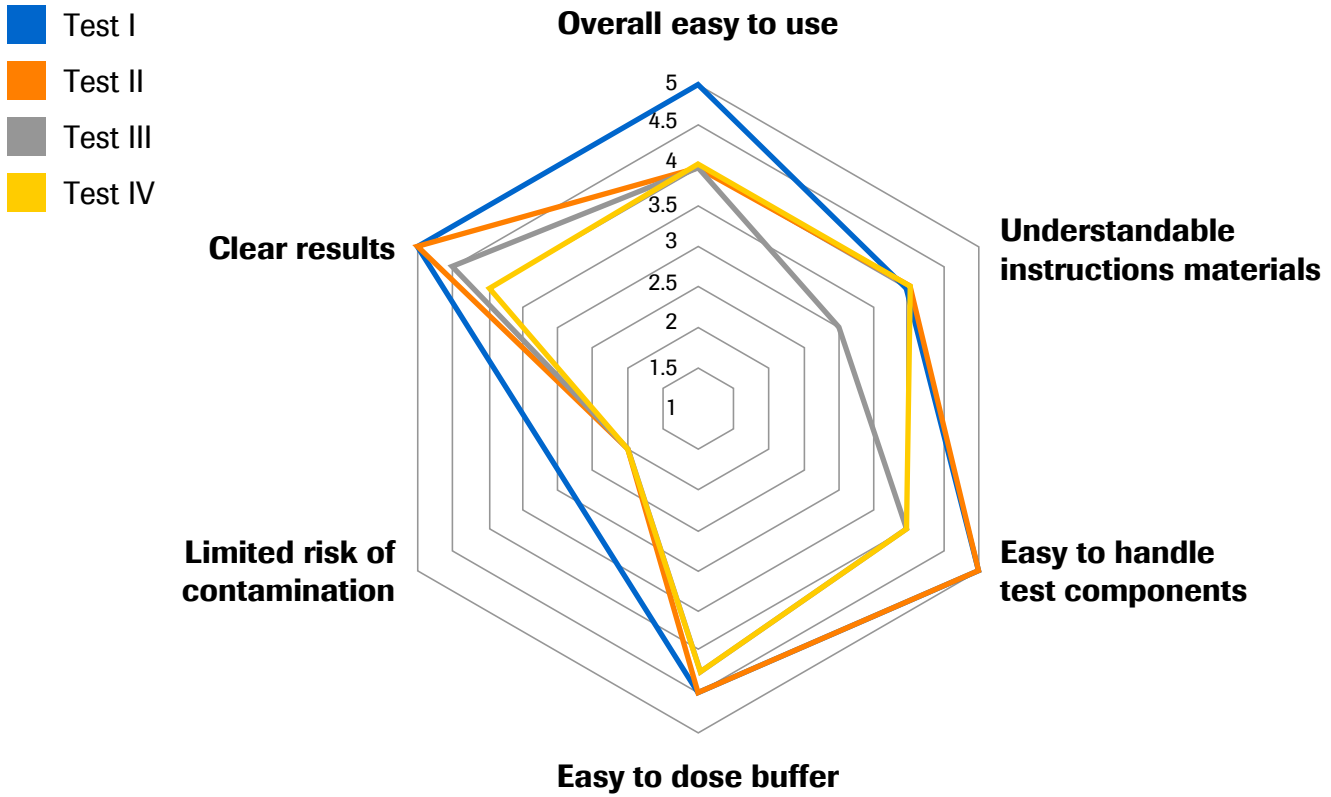


Figure 1: Scores vary from 1 ("do not agree at all") to 5 ("absolutely agree"). The median of the results for each usability item is illustrated in the figure.

medRxiv preprint doi: https://doi.org/10.1101/2020.12.05.20244673

Caruana et al. 2021, Switzerland: Study Summary

Purpose of the study

RAT were implemented in the emergency ward of the university hospital for rapid patients' triaging and compared performances of four different antigen tests. All results were compared to SARS-CoV-2 specific RT-PCR (reference standard).

Standard Q® COVID-19 Rapid Antigen Test (SD Biosensor/Roche, Panbio COVID-19 Ag Rapid Test (Abbott), One Step Immunoassay for Exdia COVID-19 Ag (Precision Biosensor Inc.) and the BD Veritor System for Rapid Detection of SARS-CoV-2 (Becton Dickinson)

Main results

Among 532 patients, overall sensitivities were 48.3% for One Step Exdia and 41.2% for Standard Q, Panbio and BD Veritor. All four antigen tests exhibited specificity above 99%. Sensitivity increased up to 100%, 97.8%, 96.6% and 95.6% for viral loads above 10^6 copies/ml and 100% (for all tests) when considering viral loads above 10^7 copies/ml. Sensitivity was significantly higher for patients presenting with symptoms onset within 4 days (74.3%, 69.2%, 69.2% and 64%, respectively). The low overall sensitivity is due to the lower viral load among hospitalized subjects.

Specifics

Dedicated RAT laboratory with two lab technicians receiving nasopharyngeal samples taken from every patient consulting the ER the evaluation was done using a wet swab procedure, by suspending the nasopharyngeal swabs in 2.5 to 3 ml of viral transport media (VTM) solution. Then, 300 µl (for Panbio , BD Veritor and One Step Immunoassay) or 350 µl (for Standard Q) were mixed with the buffer.

Main Conclusions

For the RAT the time from the patients' registration to result was 0.6 hours (mean SD ± 1.8), as compared to a mean of 4.5 hours (SD ± 6.4) for the result of RT-PCR; a mean delay of 3.9 hours (SD ± 6.8) was observed between the result of antigen test and the one of RT-PCR (n=375). Short time to results might also play a pivotal role in early placement of SARS-CoV-2 positive patients into COVID units, thus reducing risks of cross-transmission in emergency departments. RAT can represent a useful resource in the context of massive screening among outpatients, if not used in subjects with more than 4 days of symptoms and in subjects considered vulnerable. Antigen tests may also prove to be useful at hospitals' emergency rooms for patients' cohorting, especially when rapid RT-PCR reagents are not available in sufficient numbers due to reagent shortage. RATS can be a valuable complementary tool, especially during outbreaks, when patient flow to the emergency department is particularly high and early orientation and effective cohorting is crucial.

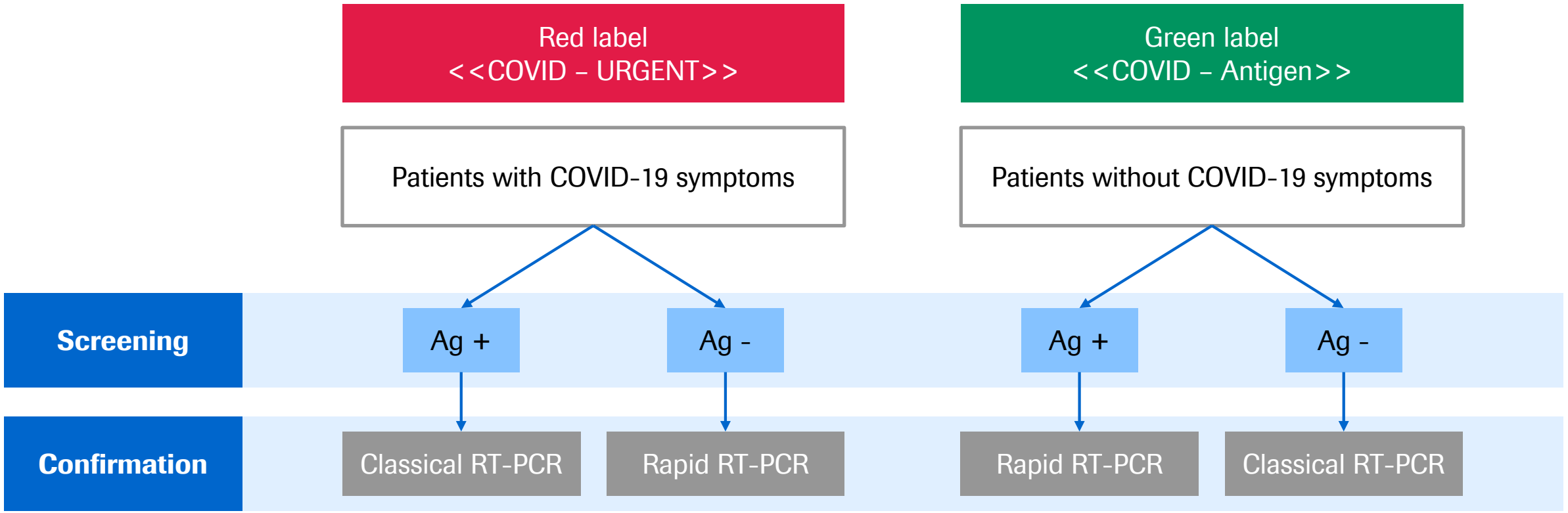
https://doi.org/10.1101/2021.02.10.21250915 doi: medRxiv preprint

Caruana et al. 2021, Switzerland: Study Details

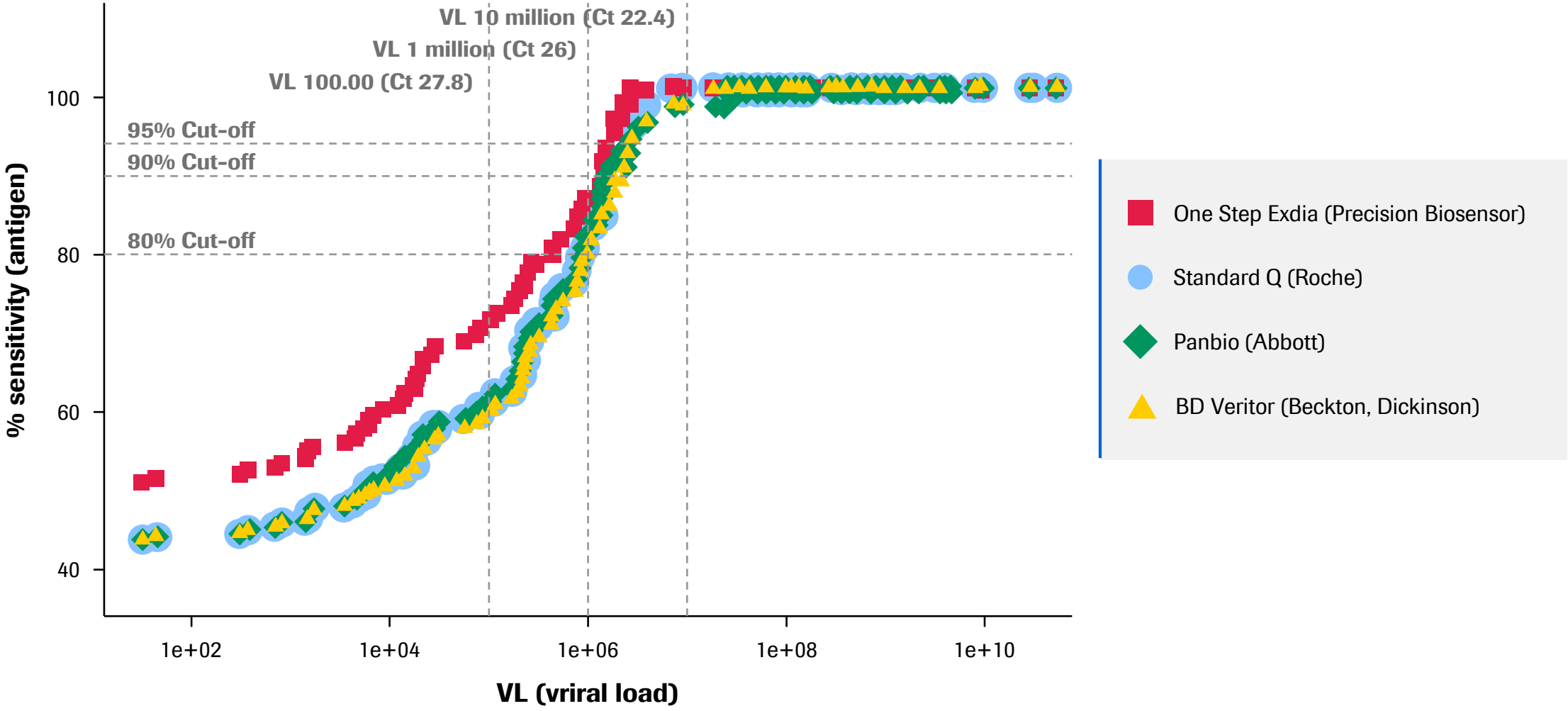
	Roche Rapid AgTest	Panbio, Abbott	BD Veritor (reader needed)	One Step Exdia Immunoassay (reader)
N, PCR + (%)	532 (21.4%)			
Ivestigated cohort	all patients presenting at the emergency department, with or without suspected of SARS-CoV-2 infection; 293 (55.1%) had symptoms consistent with COVID-19, the rest was admitted for other reasons			
Samples	Nasopharyngeal swabs were transported in a VTM to be able to perform both RAT and RT-PCR analyses on the same sample, the 2.5-3 ml dilution of the sample might have affected the sensitivity			
Overall Sensitivity	41.2%	41.2%	41.2%	48.3%
VL>10^5	66.2%	66.2%	64.8%	74.6%
VL>10^6	97.8%	96.6%	95.6%	100%
VL>10^7	100%	100%	100%	100%
Without symptoms	33%	33%	33%	33%
Specificity	Specificity was greater than 99% for all the antigen tests			
PPV	97.9%	97.9%	98.9%	96.5%
NPV	86.2%	86.2%	86.1%	87.6%
Reference Method	i) VIASURE SARS-CoV-2 (N1 + N2) Real Time PCR Detection Kit for BD MAX™ (Becton Dickinson, USA) or GeneXpert SARS-CoV-2 test (Cepheid) as rapid systems, ii) test **cobas**® 6800 SARS-CoV-2 (Roche) or our automated high-throughput molecular diagnostic (MDx) platform as classic systems			

https://doi.org/10.1101/2021.02.10.21250915 doi: medRxiv preprint

Caruana et al.: Diagnostic algorithm for managing tests flow according COVID-19 symptoms



Caruana et al.: Sensitivity according to the viral load



Ristić et al., Serbia: Study Summary

Purpose of the study

The performance of the STANDARD Q COVID-19 Ag Test for the detection of SARS-CoV-2 antigen was evaluated in comparison to RT-qPCR results in 120 symptomatic patients in the early and late phase of the disease who presented to health care facility.

Main results

The overall sensitivity was 58.1% (95% CI 42.1–73.0) but it was higher in the early days of disease, when the highest viral loads were detected. During the first five days after the symptom onset, the sensitivity was 88.6%.

Specifics

Only patients with mild or moderate clinical signs and symptoms of COVID-19 were included in the study.

Main Conclusions

A strong agreement between performance of STANDARD Q COVID-19 Ag Test and RTqPCR was observed during the first five days of illness, suggesting that this rapid antigenic test can be very useful for COVID-19 diagnosis in the early phase of disease through accelerating clinical decision making in majority of suspected patients.

https://doi.org/10.1371/journal.pone.0247606

Ristić et al., Serbia: Study Details

Roche Rapid Ag Test

N, PCR + (%)	120 (35.8%)
Ivestigated cohort	120 symptomatic patients (median age 49, 14-91), presented to health care facility, only patients with mild or moderate clinical signs and symptoms were included
Samples	nasopharyngeal
Symptoms	The average period between signs/symptoms onset and swab collection was 9.4 days (ranging between 1 and 45 days) and the median time was 5 days (IQR 3–15): 52.5% cases were tested within the first five days after symptoms onset.
Sensitivity overall (95% CI) (day 1-16)	58.1% (42.1–73.0)
Sensitivity day 1-5	79.2% (57.9-92.9%)
Specificity	100% (n.a.)
NPV (CI) overall **NPV day 1-5**	81.1% (75.1-85.9%) 88.6% (78.2-94.5%)
PPV (CI)	100% (n.a.)
Reference Method	Argene1, SARS-COV-2 R-GENE assay (bioMerieux), 3 targets: ORF1ab region, the E gene (envelope protein gene), and the N gene (nucleocapsid protein gene); Applied Biosystems 7500 Real-Time PCR System (Life Technologies)

https://doi.org/10.1371/journal.pone.0247606

Homza et al., Czech Republic: Study Summary

Purpose of the study

In a screening setting for mildly symptomatic or asymptomatic patients with high COVID-19 prevalence (30–40%), 1141 patients were tested using one of five RAts and RT-PCR.

Main results

Sensitivities of the RATs compared to RT-PCR ranged from 42% to 76%. Corrected on the virus viability, sensitivities grew to 81–97%. In the best performing RAT tests, almost 90% of samples with “false negative” AGT results contained no viable virus.

Specifics

The number of samples per RAT shows big variances.
Two (one from each nostril) nasopharyngeal swabs were taken, sequence not described.
RATs were performed immediately.
Viral culture: CV-1 cells (African green monkey kidney fibroblasts)

Main Conclusions

A well-performing antigen test could in a high-prevalence setting serve as an excellent tool for identifying patients shedding viable virus. We also propose that the high proportion of RT-PCR-positive samples containing no viable virus in the group of “false negatives” of the antigen test should be further investigated with the aim of possibly preventing needless isolation of such patients.

https://doi.org/10.3390/v13040684

Homza et al., Czech Republic: Study Details

	Roche Rapid Ag Test
N, PCR + (%)	**139 (30.2)**
Ivestigated cohort	screening setting with asymptomatic (48.3%) and/or mildly symptomatic (51.7%) patients
Samples	Two (one from each nostril) nasopharyngeal swabs were taken
Symptoms	
Sensitivity vs PCR (95% CI) **Sensitivity vs viral culture**	61.9 (45.6–76.4) 86.7 (69.3–96.2)
Sensitivity symptom. vs PCR **Sensitivity asymptom. vs viral culture**	63.6 (45.1–79.6) 87.5 (67.6–97.3)
Sensitivity symptom vs PCR **Sensitivity asymptom. vs viral culture**	50.0 (15.7–84.3) 80.0 (28.4–99.5)
Specificity vs PCR **Specificity vs viral culture**	99.0 (94.4–100) 99.1 (95–100)
NPV (CI) vs PCR **NPV vs viral culture**	85.7 (77.8–91.6) 96.4 (91.1–99)
PPV (CI) vs PCR **PPV vs viral culture**	96.3 (81-99.9) 96.3 (81-99.9)
Reference Method	PCR detection kit COVID- 19 Multiplex RT-PCR Kit (DIANA Biotechnologies); positive if Ct <40

The number of samples between different RATs varies significantly therefore only the Roche assay is shown. https://doi.org/10.3390/v13040684

External Clinical Performance Study Results Overview

Roche SARS-CoV-2 Rapid Antigen Test

Study	#Sample	# PCR+ (%)	Sensitivity (95% CI) Ct ≤ x	Sensitivity (CI)	Specificity (CI)
FIND, BRA & D	1659	9.2%	**97.14%** (90.1-99.65) **Ct≤25**	84.97% (78.3-90.23)	**98.94%** (98.23-99.39)
HUG (Berger) CH	529	36%	**98%** (n.a.) **Ct≤22**	89.0% (83.69-93.06)	**99.70%** (98.36-99.99)
Cerutti, I	330	33%	**100%** (n.a.) **Ct≤28**	72.1% (83.69-93.06)	**100%** (98.36-100)
Krueger, D & UK	1263	3%	**100%** (82.4-100) **Ct≤25**	76.6% (62.8-86.4)	**99.3%** (98.6-99.6)
Van Beek, NL	1754	100%	Detection of culture positive and RT-PCR-confirmed: **94.3-99.8%**		
Mak, HK	280	100%	**96% Ct<29**	**71.4%**	**n.a.**
Chaimayo, THAI	454	13.2%	**98.3%** (91.06–99.96%) Ct n.a.	98.3% (95% CI, 91.06–99.96%)	98.7% (97.06–99.59%)

CT-values cannot be compared 1:1 as RT-PCR methods vary across sites with different genome targets, PCR instruments and reagents

External Clinical Performance Study Results Overview

Roche SARS-CoV-2 Rapid Antigen Test

Study	#Sample	# PCR+ (%)	Sensitivity (95% CI) Ct ≤ x	Sensitivity (95% CI)	Specificity (95% CI)
Lindner 2020, D	289	13.5%	**96.2%** **Ct 17.3-25.3**	74.4% (CI 58.9-85.4)	99.6 (CI 97.8-100)
Igloi, NL	970	19.2%	**99.1%** (95.2-100) **Ct < 25**	84.9 (79.1-89.4)	99.5 (98.7-99.8)
Krüttgen, D	150	50%	**100%** **Ct <25**	70.7%	96%
Nalumansi; UG	262	34.4%	**92%** **Ct ≤29**	70%	92% (95%CI 87-96)
Schwob, CH	928	40.1%	**96.6%** (90.5-99.3) **Ct ≤26**	92.9% (86.4-96.9)	100%
Salvagno, I	321	46.4%	**97-100%** **Ct < 25**	72.5%	99.4%
Favresse, B	188	51.1%	**96.6%** **Ct < 25**	82.5% (Ct <33)	All Ct: 100% Ct <25: 91.5%
Lindner 2021, D	179	13.5 %	**Nasal: 100%, NP: 94.7%** **>7.0 log10 RNA SARS-CoV2/swab**	Nasal: 80.5%, NP: 73.2%	98.6% (94.9-99.6)

CT-values cannot be compared 1:1 as RT-PCR methods vary across sites with different genome targets, PCR instruments and reagents

Roche SARS-CoV-2 Rapid Antigen Test

No or limited sensitivity evaluation based on Ct values available

Study	#Sample	# PCR+ (%)	Sensitivity (95% CI) Ct ≤ x	Sensitivity (95% CI)	Specificity (95% CI)
Corman, D	115	n.a.	6.78 copies/swab LoD, 95% mean hit rate detected as little as 4.4 PFU (plaque forming units) of virus per test.		97.12% n= 35 Cumulative Spec. 98.53%
Osterman, D	454	n.a.	n.a.	«pimary diagnosis» 64.45 (58.42–70.06)	97.67% (95.63–98.77)
Möckel, D	271 adults 202 children	32.8% 12.4%	n.a	75.3 % (95%CI: 65.8-83.4) 72.0 % (95%CI: 53.3-86.7)	100 % (95%CI: 98.4-100) 99.4 % (95%CI:97.3-99.9)
Yamayoshi, JAP	8	n.a.	100% **Ct <25 ***	250 PFU of NC02 250 PFU of HP72	n.a.
Pena, CHL	842	8.6%	false-negative results had significantly higher Ct values (Ct > 27);	69.9% (58.56-79.18)	99.6%

* Supplemental data
CT-values cannot be compared 1:1 as RT-PCR methods vary across sites with different genome targets, PCR instruments and reagents

External Clinical Performance Study Results Overview

Roche SARS-CoV-2 Rapid Antigen Test

Study	#Sample	# PCR+ (%)	Sensitivity (95% CI) Ct ≤ x	Sensitivity (95% CI)	Specificity (95% CI)
Thommes, A	154	100%	100% (66.4–100%, n=9) **Ct≤25** 84.4% (67.2–94.7%, n=32) **Ct≤30** 41.0%, (n=39) CT>30	/	n.a.
Jääskeläinen, FIN	198	79.8%	99% CT<25 91% Ct<30 31% Ct>30	84.9%	100%
Baro, E	286	54.3%	83·33% (65.28-94.36) Ct<30	43·56% (33.72-53.8)	96.22% (92.36-98.47)
Jakobsen, DK	4811	4.6%	81.1% Ct≤30	69.7% Ct≤38	99.5%
Schuit, NL	1596	8.3%	86.8% (78.1-93.0%) 5.2 log10 E-gene copies/mL 85.1% (74.3-92.6%) Asymptomatcis at infectiousness cutoff	62.9% (54.0%-71.1%)	>99%
Pena-Rodriguez, CH	369	28.2%	88% Ct<25	75.9% (66.5–83.8%)	100% (NA)

* Supplemental data
CT-values cannot be compared 1:1 as RT-PCR methods vary across sites with different genome targets, PCR instruments and reagents

External Clinical Performance Study Results Overview

Roche SARS-CoV-2 Rapid Antigen Test

Study	#Sample	# PCR+ (%)	Sensitivity (95% CI) Ct ≤ x	Sensitivity (95% CI)	Specificity (95% CI)
Olearo D	184	45.7	100% (87% -100%) **>10^6copies/swab**	49.4% (38.9%-59.9%)	100% (96.3-100%)
Caruana, CH	532	21.4	66.2% **VL>10^5** 97.8% **VL>10^6** 100% **VL>10^7**	41.2%	>99%
Ristic, SER	120	35.8	79.2% (57.9-92.9%) d1-5	58.1% (42.1–73.0)	100%
Homza, CZ	139	30.2	86.7 (69.3–96.2) vs viral culture	61.9 (45.6–76.4) vs PCR	99.0 (94.4–100) vs PCR 99.1 (95–100) vs viral culture

* Supplemental data
CT-values cannot be compared 1:1 as RT-PCR methods vary across sites with different genome targets, PCR instruments and reagents

Conclusions: systematic meta-analysis of real-world performance of SARS-CoV-2 rapid antigen tests

- > 40 studies presented with over 25'000 patient samples investigated detection rates and sensitivities stratified by CT (viral load) categories.
- The sensitivity of the Roche / SD Biosensor POC Antigen assay was between 96.2 to 100% with a CT that is considered to be associated with culture positive results. *
- If the specimens are obtained ≤7 days after symptom onset for use with the Rapid Antigen test, it can help to filter out the infected persons and prevent spread to the others.
- Focusing on the clinical sensitivity within the potential infectious range is a more practicable approach than focusing only on the analytic sensitivity (lower detection limits) of POC antigen tests.
- By combining the rapid test result, the knowledge of time of testing within the course of disease, and further information from patients medical history, a good estimation regarding the potential infectiousness can be made.
- First real world performance data confirms the primary use case for POC assay, however, more and larger studies are needed.

*The data from Uganda are not considered due to great discrepancy of the Ct values and categorization compared to all other republications.

Reviews / Meta-analyses

Hayer et al.: Real-world clinical performance of SARS-CoV-2 rapid antigen tests: a systematic meta-analysis of available data as per November 20, 2020

Introduction: Immunochromatographic rapid antigen tests (RATs) emerged onto the COVID-19 pandemic testing landscape to aid in the rapid diagnosis of people with suspected SARS-CoV-2 infection. RATs are particularly useful where RT-PCR is not immediately available and symptoms suggestive of a high viral load and infectiousness are assumed. Several lateral flow immunoassays have been authorized for use under EUA and/or the CE mark, presenting varying overall clinical performance data generated by the manufacturer or by independent investigators. To compare the real-world clinical performance of commercially available rapid chromatographic immunoassays intended for the qualitative detection of SARS-CoV-2, we performed a systematic meta-analysis of published data.

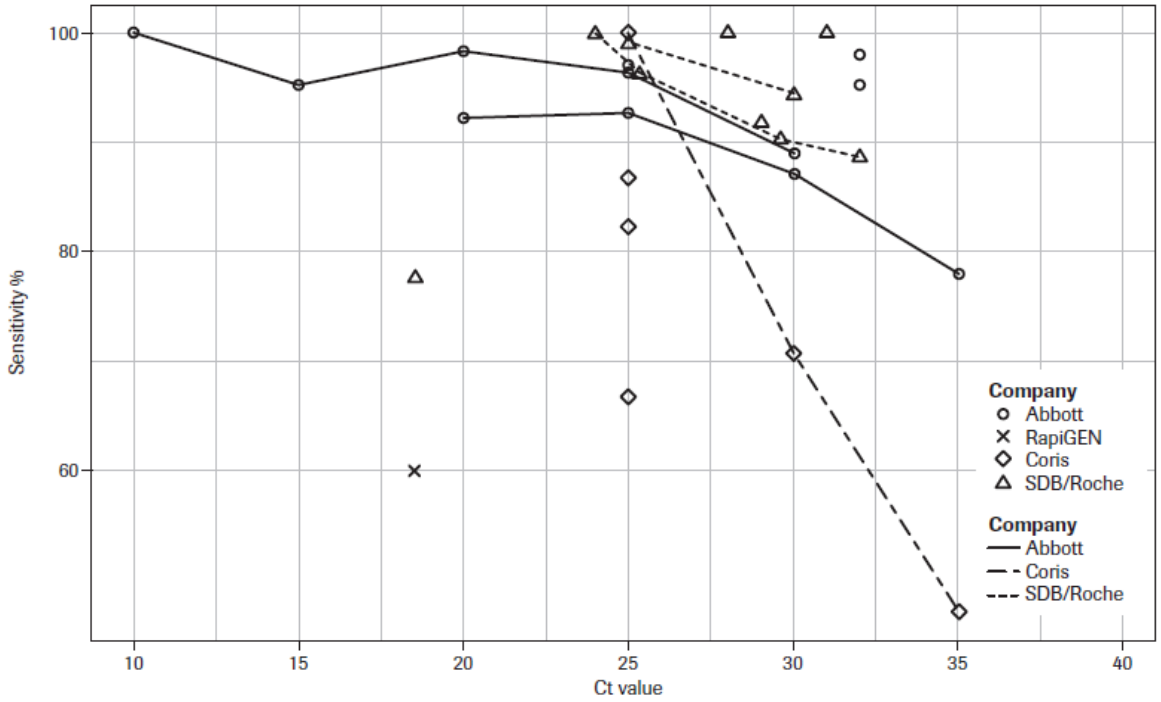
Methods: We searched MEDLINE®, Embase®, BIOSIS™ and Derwent Drug File (ProQuest®) for manufacturer-independent prospective clinical performance studies comparing SARS-CoV-2 RATs and RT-PCR assays. Only studies on lateral flow assays not needing a separate reader for retrieving the result were included, if data were available on viral load, patients' symptom status, sample type, and PCR assay used. For better data comparability, recalculation of the studies' single performance data confidence intervals using the exact Clopper–Pearson method was applied.

Results: We could include 19 studies (ten peer-reviewed) presenting detailed clinical performance data on 11,209 samples with 2,449 RT-PCR-positives out of study prevalence rates between 1.9–100% and between 50–100% symptomatic samples. Four studies directly compared two to three different RATs and 15 studies compared one RAT to RT-PCR. Overall specificity ranged, with one test outlier, between 92.4% (87.4–95.9) and 100% (99.7–100), and overall clinical sensitivity varied between 28.9% (16.4–44.3) and 98.3% (91.1–99.7), depending on assay, population characteristics, viral load, and symptom status. Sensitivity in high-viral-load samples (cycle threshold ≤25) showed a considerable heterogeneity among the assays ranging from 66.7% to 100%.

Conclusion: Only two RATs, Roche SARS-CoV-2 Rapid Antigen Test and Abbott Panbio™ COVID-19 Ag Test, offered sufficient manufacturer-independent, real-world performance data supporting use for the detection of current SARS-CoV-2 infection in symptomatic or high-viral-load patient populations. Reliable positive predictive values require testing of symptomatic patients or asymptomatic individuals only in case of a high pre-test probability. If RATs are used for screening of asymptomatic cases in low-prevalence scenarios, a high negative predictive value and a low positive predictive value of the result have to be considered.

Hayer et al 2021 medRxiv preprint doi: https://doi.org/10.1101/2020.12.22.202486140

Hayer et al., 2020: Forest plot of studies evaluating rapid antigen test sensitivity, grouped by test



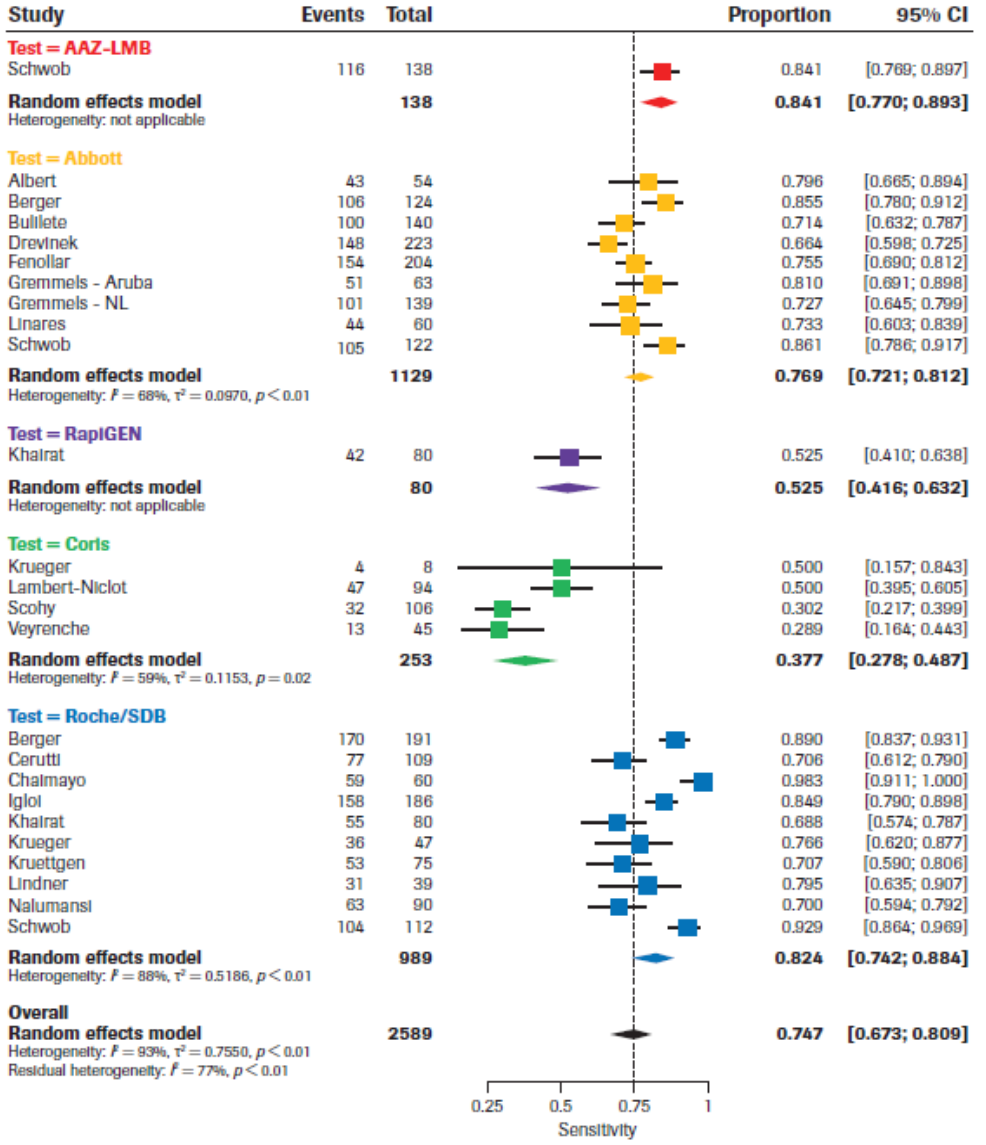
Sensitivity in high-viral-load samples (cycle threshold ≤25) showed a considerable heterogeneity among the assays, ranging from 66.7–100%

Hayer et al 2021 medRxiv preprint doi: https://doi.org/10.1101/2020.12.22.202486140

Hayer et al., 2020: Forest plot of studies evaluating rapid antigen test sensitivity

The individual and pooled sensitivities of the assays:

- Overall clinical sensitivity varied between 28.9% (95% CI: 16.4–44.3)[1] and 98.3% (95% CI: 91.1–99.7)[2]
- Depending on assay, population characteristics, viral load, and symptom status.



1. Scohy A, et al. J Clin Virol 2020;129:104455; 2. Chaimayo C, et al. Virol J 2020;17:177
Hayer et al 2021 medRxiv preprint doi: https://doi.org/10.1101/2020.12.22.202486140

Dinnes et al. 2021 Cochrane Database of Systematic Reviews

Rapid antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Version 24th March 2021 includes evidence published up to 30 September 2020

Antigen tests

- Forty-eight studies reported 58 evaluations of antigen tests.
- Sensitivity differed between symptomatic (72.0%, 95% CI 63.7% to 79.0%; 37 evaluations; 15530 samples, 4410 cases) and asymptomatic participants (58.1%, 95% CI 40.2% to 74.1%; 12 evaluations; 1581 samples, 295 cases).
- Average sensitivity was higher in the first week after symptom onset (78.3%, 95% CI 71.1% to 84.1%; 26 evaluations; 5769 samples, 2320 cases) than in the second week of symptoms (51.0%, 95% CI 40.8% to 61.0%; 22 evaluations; 935 samples, 692 cases).
- Sensitivity was high in those with cycle threshold (Ct) values on PCR <25 (94.5%, 95% CI 91.0% to 96.7%; 36 evaluations; 2613 cases) compared to those with Ct values >25 (40.7%, 95% CI 31.8% to 50.3%; 36 evaluations; 2632 cases).
- Using data from instructions for use (IFU) compliant evaluations in symptomatic participants, summary sensitivities ranged from 34.1% (95% CI 29.7% to 38.8%; Coris Bioconcept) to 88.1% (95% CI 84.2% to 91.1%; SD Biosensor STANDARD Q).
- Average specificities were high in symptomatic and asymptomatic participants, and for most brands (overall summary specificity 99.6%, 95% CI 99.0% to 99.8%).
- In people who did not have COVID-19, antigen tests correctly ruled out infection in 99.5% of people with symptoms and 98.9% of people without symptoms.
- **Only one assay (SD Biosensor STANDARD Q) met the WHO acceptable criterion for sensitivity based on pooled results of several studies for confirming and ruling out COVID-19 in people with signs and symptoms of COVID-19. Two more tests met the WHO acceptable standards (Abbott Panbio and BIONOTE NowCheck) in at least one study.**

https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013705.pub2/full#CD013705-abs-0002

Dinnes et al. 2021 Cochrane Database of Systematic Reviews

Roche SARS-CoV-2 Rapid Antigen Test

"Only one assay (SD Biosensor STANDARD Q) met the WHO acceptable criterion for sensitivity based on pooled results of several studies." …

"Some antigen tests are accurate enough to replace RT-PCR when used in people with symptoms.

This would be most useful when quick decisions are needed about patient care, or if RT-PCR is not available.

Antigen tests may be most useful to identify outbreaks, or to select people with symptoms for further testing with PCR, allowing self-isolation or contact tracing and reducing the burden on laboratory services.

People who receive a negative antigen test result may still be infected.

We need more evidence on rapid testing in people without symptoms, on the accuracy of repeated testing, testing in non-healthcare settings such as schools (including self-testing), and direct comparisons of test brands, with testers following manufacturers' instructions." …

https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013705.pub2/full#CD013705-abs-0002

Dinnes et al. 2021 Cochrane Database of Systematic Reviews

Limitations

- Deviations from the IFU and intended use
- Deviations in workflow: Tests were not performed as POC test
- 97% of the studies relied on a single negative RT-PCR result as evidence of no COVID-19 infection
- Results from different test brands varied
- Few studies directly compared one test brand with another (head-to-head comparison).
- Not all studies gave enough information about their participants how long they had had symptoms, or even whether or not they had symptoms.

https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013705.pub2/full#CD013705-abs-0002

Dinnes et al. 2021 Cochrane Database of Systematic Reviews

Examples of pooled results for individual antigen tests using data for evaluations compliant with manufacturer instructions for use according to symptom status

	Tests	Evaluations	Samples	SARS-CoV-2	Sensitivity (95% CI)	Specificity (95% CI)
Symptomatic participants	Coris Bioconcept – COVID-19 AG Respi-Strip	3	780	414	34.1 (29.7, 28.8)	100 (99.0, 100)
	Abbott – Pabio Covid-19 AG	3	1094	252	75.1 (57.3, 87.1)	99.5 (99.5, 99.8)
	SD Biosensor – STANDARD Q COVID-19 Ag	**3**	**1947**	**336**	**88.1 (84.2, 91.1)**	**99.1 (97.8, 99.6)**
Asymptomatic participants	Coris Bioconcept – COVID-19 AG Respi-Strip	2	45	14	28.6 (8.4, 58.1)	100 (88.8, 100)
	Abbott – Pabio Covid-19 AG	1	474	47	48.9 (25.1, 62.9)	98.1 (98.1, 99.1)
	SD Biosensor – STANDARD Q COVID-19 Ag	**1**	**127**	**13**	**69.2 (28.6, 90.9)**	**99.1 (95.2, 100)**

https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013705.pub2/full#CD013705-abs-0002

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	Tests	Prevalence	TP (95% CI)	FP (95% CI)	FN (95% CI)	TN (95% CI)	PPV	1-NPV
Symptomatic participants average sensitivity and specificity (and 95% CIs) applied to a hypothetical cohort of 1000 patients where 50, 100 and 200 have COVID-19 infection	Coris Bioconcept	5%	17 (15 to 19)	0 (0 to 10)	33 (31 to 35)	950 (941 to 950)	100%	3.4%
		10%	34 (30 to 39)	0 (0 to 9)	66 (61 to 70)	900 (891 to 900)	100%	6.8%
		20%	68 (59 to 78)	0 (0 to 8)	132 (122 to 141)	800 (792 to 800)	100%	14.1%
	Abbot – Pabio Covid-19 AG	5%	38 (29 to 44)	5 (2 to 12)	12 (6 to 21)	945 (938 to 948)	89%	1.3%
		10%	75 (57 to 87)	5 (2 to 12)	25 (13 to 43)	896 (888 to 898)	94%	2.7%
		20%	150 (115 to 174)	4 (2 to 10)	50 (26 to 85)	796 (790 to 798)	97%	5.9%
	SD Biosensor – STANDARD Q COVID-19 Ag	5%	44 (42 to 46)	9 (4 to 21)	6 (4 to 8)	941 (929 to 946)	84%	0.6%
		10%	88 (84 to 91)	8 (4 to 20)	12 (9 to 16)	892 (880 to 896)	92%	1.3%
		20%	176 (168 to 182)	7 (3 to 18)	24 (18 to 32)	793 (782 to 797)	96%	2.9%
Asymptomatic participants average sensitivity and specificity (and 95% CIs) applied to a hypothetical cohort of 1000 patients where 50, 100 and 200 have COVID-19 infection	Coris Bioconcept	5%	14 (4 to 29)	0 (0 to 114)	36 (21 to 46)	9950 (8836 to 9950)	100%	0.4%
		10%	29 (8 to 58)	0 (0 to 1109)	71 (42 to 92)	9900 (8791 to 9900)	100%	0.7%
		20%	57 (17 to 116)	0 (0 to 1098)	143 (84 to 183)	9800 (8702 to 9800)	100%	1.4%
	Abbot – Pabio Covid-19 AG	5%	24 (18 to 31)	189 (90 to 368)	26 (19 to 32)	9761 (9582 to 9860)	11%	0.3%
		10%	49 (35 to 63)	188 (89 to 366)	51 (37 to 65)	9712 (9534 to 9811)	21%	0.5%
		20%	98 (70 to 126)	186 (88 to 363)	102 (74 to 130)	9614 (9437 to 9712)	34%	1.0%
	SD Biosensor – STANDARD Q COVID-19 Ag	5%	35 (19 to 45)	90 (0 to 478)	15 (5 to 31)	9860 (9472 to 9950)	28%	0.2%
		10%	69 (39 to 91)	89 (0 to 475)	31 (9 to 61)	9811 (9425 to 9900)	44%	0.3%
		20%	138 (77 to 182)	88 (0 to 470)	62 (18 to 123)	9712 (9330 to 9800)	61%	0.6%

https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013705.pub2/full#CD013705-abs-0002

Brümmer et al., 2021: A living systematic review

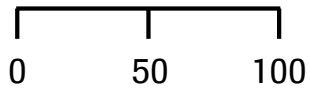
Status December 11th 2020

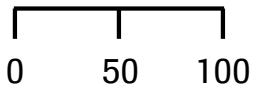
- 98 data sets for performance of SARS-CoV-2 Ag-RDTs compared to RT-PCR
- Best-performing tests achieved a sensitivity of C (SD Biosensosor).
- Highest sensitivity was found in patients within seven days of symptom onset when NP swabs were utilized.
- Across all meta-analyzed samples, the pooled Ag-RDT sensitivity was 73.8% (CI 68.6 to 78.5).
- If analysis was restricted to studies that followed the Ag-RDT manufacturers' instructions using fresh upper respiratory swab samples the sensitivity increased to 79.1% (95%CI 75.0 to 82.8).
- The best Ag-RDT performance was found with nasopharyngeal sampling (77.3%, CI 72.0 to 81.9) in comparison to other sample types (e.g., anterior nasal or mid turbinate 63.5%, CI 49.5 to 75.5).
- Testing in the first week from symptom onset resulted in higher sensitivity (87.5%, CI 86.0 to 89.1) compared to testing after one week (64.1%, CI 54.4 to 73.8).
- The tests performed markedly better on samples with lower Ct values, i.e., <30 (87.9%, CI 86.7 to 88.8), in comparison to those with Ct ≥ 30 (47.8%, CI 41.1 to 54.5).
- **Ag-RDTs detect most cases within the first week of symptom onset and those with high viral load, thus they can have high utility for screening purposes in the early phase of disease, and can be a valuable tool to fight the spread of SARS-CoV-2.**

medRxiv preprint doi: https://doi.org/10.1101/2021.02.26.21252546; this version posted March 1, 2021

Brümmer et al., 2021

Test	N	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Coris	679	168	1	209	301	41.9 (29.9, 54.8)	99.9 (79.5, 100.0)
Panbio	15735	3001	60	865	11809	72.7 (63.7, 80.2)	99.9 (99.4, 100.0)
Rapigen	771	190	8	95	478	65.8 (44.4, 82.3)	98.3 (92.2, 99.7)
Standard F	1467	310	14	169	974	70.9 (52.0, 84.6)	98.5 (97.7, 99.2)
Standard Q	5891	1043	72	250	4526	81.7 (74.8, 87.0)	99.2 (97.0, 99.8)



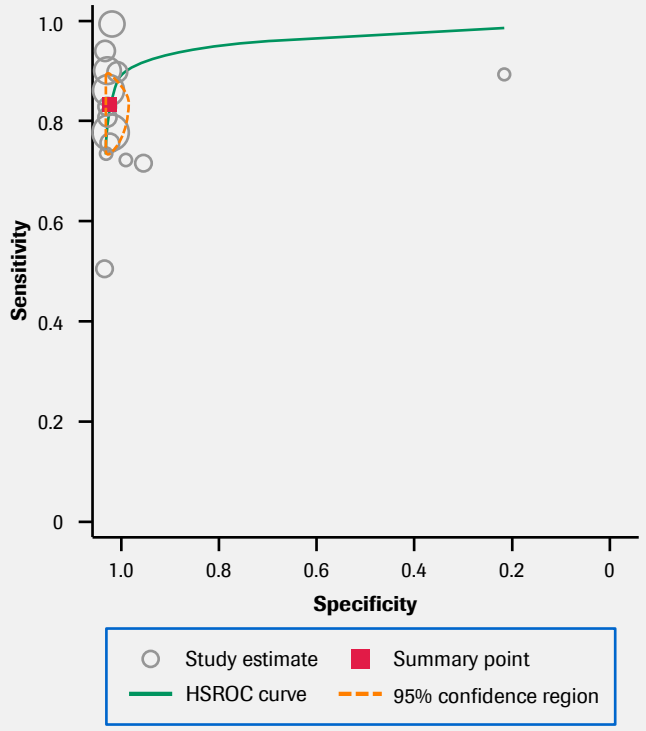


medRxiv preprint doi: https://doi.org/10.1101/2021.02.26.21252546

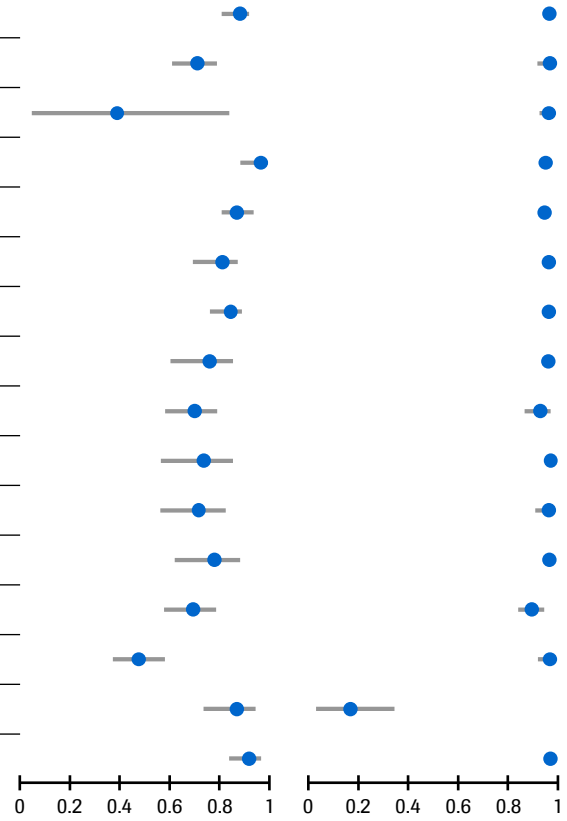
Brümmer et al. 2021

S6 HSROC curves for top-performing Ag-RDTs

Figure 8 – HSROC curve Standard Q Ag-RDT



Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Berger, NP	170	1	21	337	0.89 [0.84, 0.93]	1.00 [0.98, 1.00]
Cerutti, NP, ER	75	0	29	81	0.72 [0.62, 0.80]	1.00 [0.96, 1.00]
Cerutti, NP, tr*	2	0	3	140	0.40 [0.05, 0.85]	1.00 [0.97, 1.00]
Chaimao, NP/OP	59	5	1	389	0.98 [0.91, 1.00]	0.99 [0.97, 1.00]
FIND, NP	94	7	12	287	0.89 [0.81, 0.94]	0.98 [0.95, 0.99]
Gupta, NP	63	1	144	252	0.82 [0.71, 0.90]	1.00 [0.98, 1.00]
Igloi, NP	158	4	28	780	0.85 [0.79, 0.90]	0.99 [0.99, 1.00]
Kreuger, NP/OP	36	9	11	1207	0.77 [0.62, 088]	0.99 [0.99, 1.00]
Kruettgen, NP	53	3	22	72	0.71 [0.59,0.81]	0.96 [0.89, 0,99]
Lindner, AN	29	2	10	248	0.74 [0.58, 0.87]	0.99 [0.97, 1.00]
Lindner, NP, pc	30	1	11	138	0.73 [0.57, 0.86]	0.99 [0.96, 1.00]
Lindner, NP, sc	31	1	8	249	0.79 [0.64, 0.91]	1.00 [0.98, 1.00]
Nalumansi, NP	63	13	27	159	0.70 [0.59, 0.79]	0.92 [0.87, 0.96]
Olearo, OP	41	0	43	100	0.49 [0.38, 0.60]	1.00 [0.96, 1.00]
Schildgen, LRT	37	25	5	6	0.88 [0.74, 0.96]	0.19 [0.07, 0.37]
Schwob, NP	104	0	8	221	0.93 [0.86, 0.97]	1.00 [0.98, 1.00]



HSROC = Hierarchical summary receiver-operating characteristic

medRxiv preprint doi: https://doi.org/10.1101/2021.02.26.21252546

Conclusions: systematic meta-analysis of real-world performance of SARS-CoV-2 rapid antigen tests

- Up to 98 data sets with >24'000 samples were analyzed regarding the performance of SARS-CoV-2 Ag Rapid Antigen tests compared to RT-PCR [1.2.3]
- Highest sensitivity was found in patients with high viral load or within seven days of symptom onset when NP swabs were utilized, followed by nasal swabs [1.2.3]
- Rapid antigen tests can have high utility for screening purposes in the early phase of disease, and can be a valuable tool to fight the spread of SARS-CoV-2 [1.2.3]
- Average specificities were high in symptomatic and asymptomatic participants, and for most brands (overall summary specificity 99.6%, 95% CI 99.0% to 99.8%).[1]
- Using data from instructions for use (IFU) compliant evaluations in symptomatic participants, summary sensitivities ranged from 34.1% (95% CI 29.7% to 38.8%; Coris Bioconcept) to 88.1% (95% CI 84.2% to 91.1%; SD Biosensor Standard Q).[1]

1. Dinnes et al 2021 https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013705.pub2/full#CD013705-abs-0002
2. Brümmer et al 2021 medRxiv preprint doi: https://doi.org/10.1101/2021.02.26.21252546
3. Hayer et al 2021 medRxiv preprint doi: https://doi.org/10.1101/2020.12.22.202486140

Conclusions: systematic meta-analysis of real-world performance of the Roche SARS-CoV-2 Rapid Antigen Test

Roche SARS-CoV-2 Rapid Antigen Test (= SD Biosensor Standard Q)

- All three meta-analysis show Roche Rapid Antigen test with the highest pooled average sensitivity: 88.1% (95% CI 84.2% to 91.1%)[1], 81.7 (CI 74.8 to 87.0%)[2] and 82.4 (74.2-88.4%)[3]
- The overall pooled specificity was 99.2% (CI 97.0 to 99.8%) (Brümmer), 99.1% (CI 97.8 to 99.6%) in symptomatics and 99.1% (CI 95.2 to 100%) in asymtptomatics[1]
- Only one assay (Roche Rapid Antigen Test) met the WHO acceptable criterion for sensitivity based on pooled results of several studies for confirming and ruling out COVID-19 in people with signs and symptoms of COVID-19.[1]
- Roche SARS-CoV-2 Rapid Antigen Test offers sufficient real-world and manufacturer-independent performance evaluations

1 Dinnes et al 2021 https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013705.pub2/full#CD013705-abs-0002
2 Brümmer et al 2021 medRxiv preprint doi: https://doi.org/10.1101/2021.02.26.21252546
3. Hayer et al 2021 medRxiv preprint doi: https://doi.org/10.1101/2020.12.22.202486140

Meta- analysis show

High quality RATs offer sufficient manufacturer-independent, real-world performance data supporting use for the detection of current SARS-CoV-2 infection in symptomatic or high-viral-load patient populations.

Ruling in or out

Ruling in: High positive predictive values require testing of symptomatic patients or asymptomatic individuals in case of a high pre-test probability

Ruling out: Screening of asymptomatic cases in low-prevalence scenarios, the negative predictive value is high but the low positive predictive value suggests confirmation testing for the positives

Specificity

Average specificities were high in symptomatic and asymptomatic participants, >99%

Sensitivity

Best performance during the **early stages of SARS-CoV-2** infection when the **viral load is higher**

Higher sensitivities in IFU-compliant studies with fresh upper respiratory swab samples

Ag-RDTs detect most cases within the first week of symptoms meaning they are useful for screening

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https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013705.pub2/full#CD013705-abs-0002

Doing now what patients need next