SARS-CoV-2 Rapid Antigen Test

Primary and secondary influencers on assay performance

09-Feb-2021

Objectives of this presentation

- The main objective is to summarize key publications that deal with real world performance of the SARS-CoV-2 Rapid Antigen Test
- Secondary objective to showcase factors that influence assay performance
- This presentation will be updated regularly
- Literature search criteria and outcome will be listed
- Publications with results that include comparisons with an CE /EUA approved PCR and the corresponding Ct values will be summarized in this presentation

Roche SARS-CoV-2 Rapid Antigen Test = STANDARD Q-COVID-19 Ag Test

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®

Factors impacting on Performance and Test Results of Rapid Antigen Tests

Coronaviruses

Virion morphology and structural proteins

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

Lipid bilayer

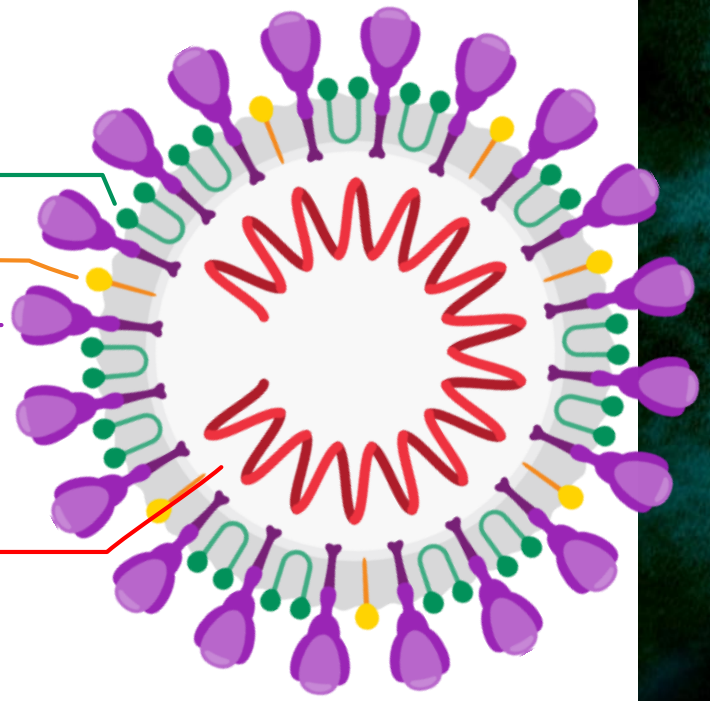
Membrane protein **(M)**

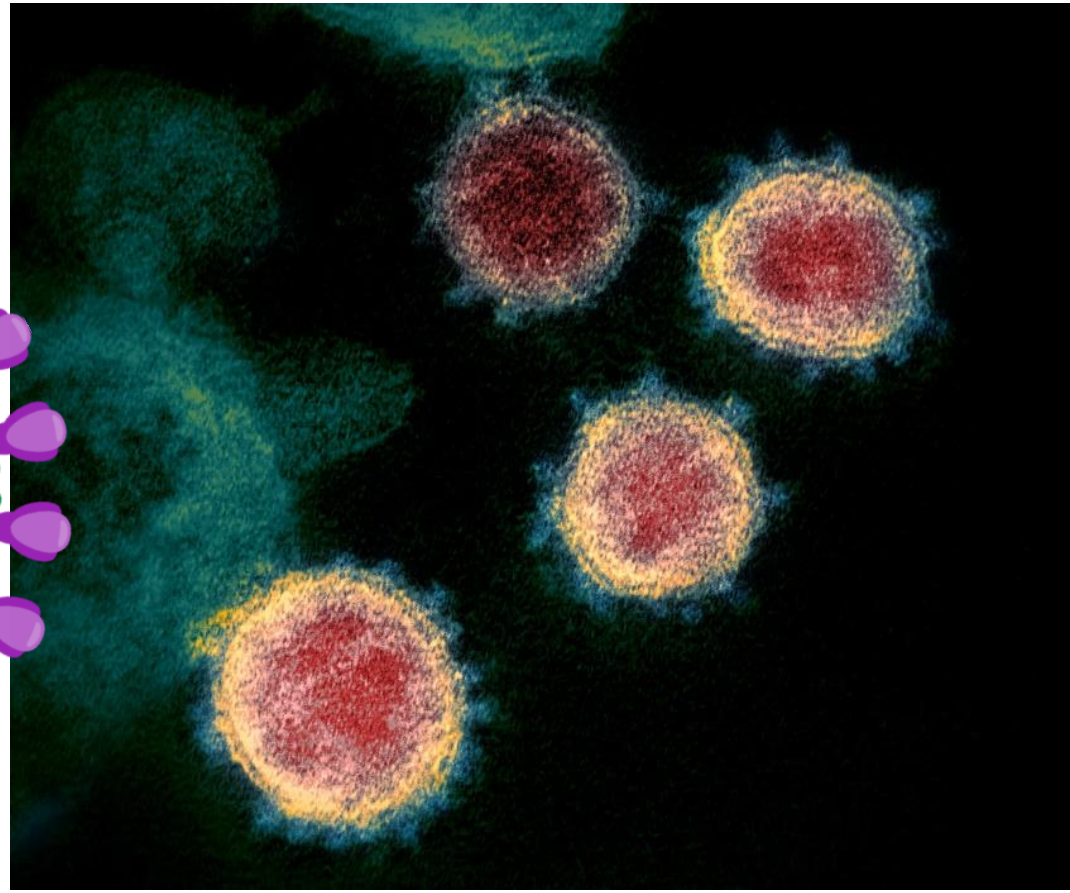
Envelope protein **(E)**

Spike protein **(S)**

Nucleocapsid

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

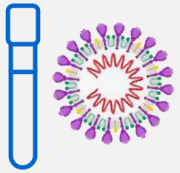




1. Masters PS (2006). Advances in Virus Research. Academic Press. 66: 193–292; 2. Su, S et al. (2016). Trends in Microbiology. 24 (6): 490–502; 3. Paules CI et al. (2020). JAMA. 2020;323(8):707–708

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

Primary influencer:

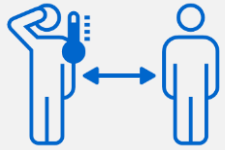


Viral load of the sample, and the **viral load distribution** in the investigated cohort represented by Cycle threshold (Ct) of the PCR

Analytical test performance of the assay: sensitivity & specificity

Secondary influencer:

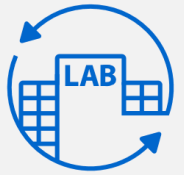
Days post symptom onset (DPSO) of sampling



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

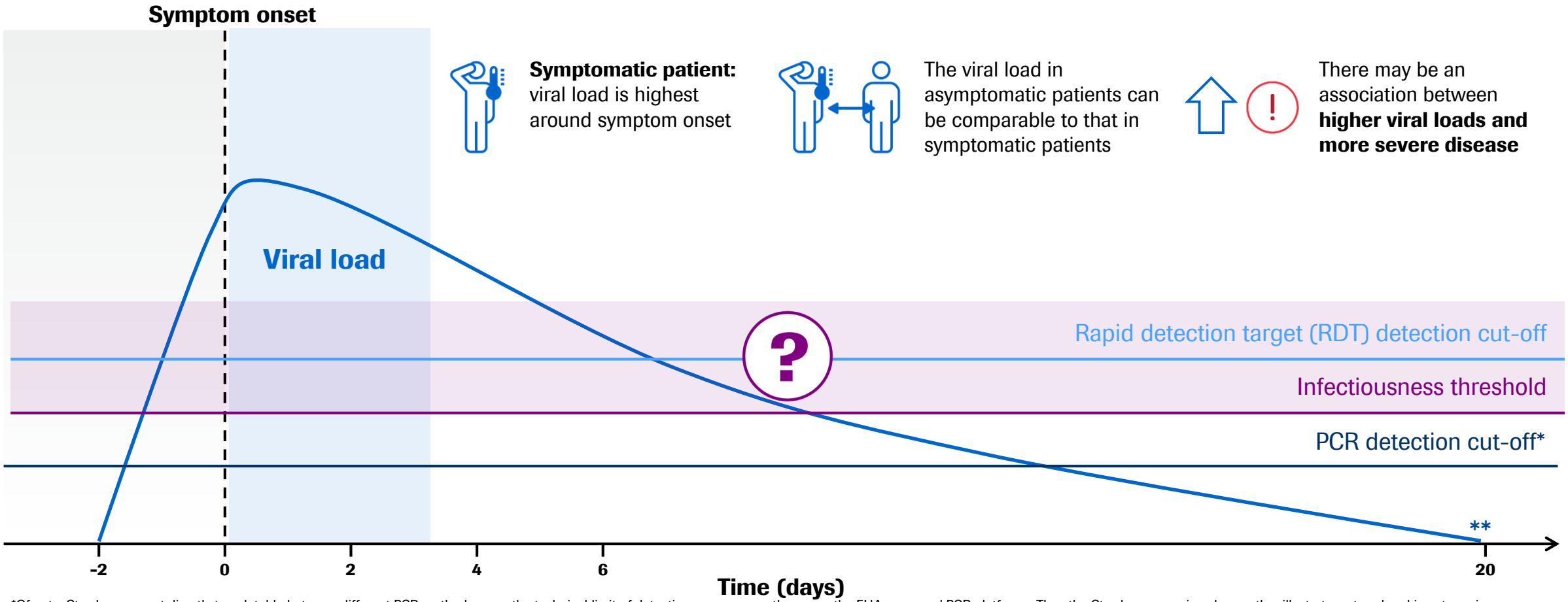
Days from infection to specimen collection

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



*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

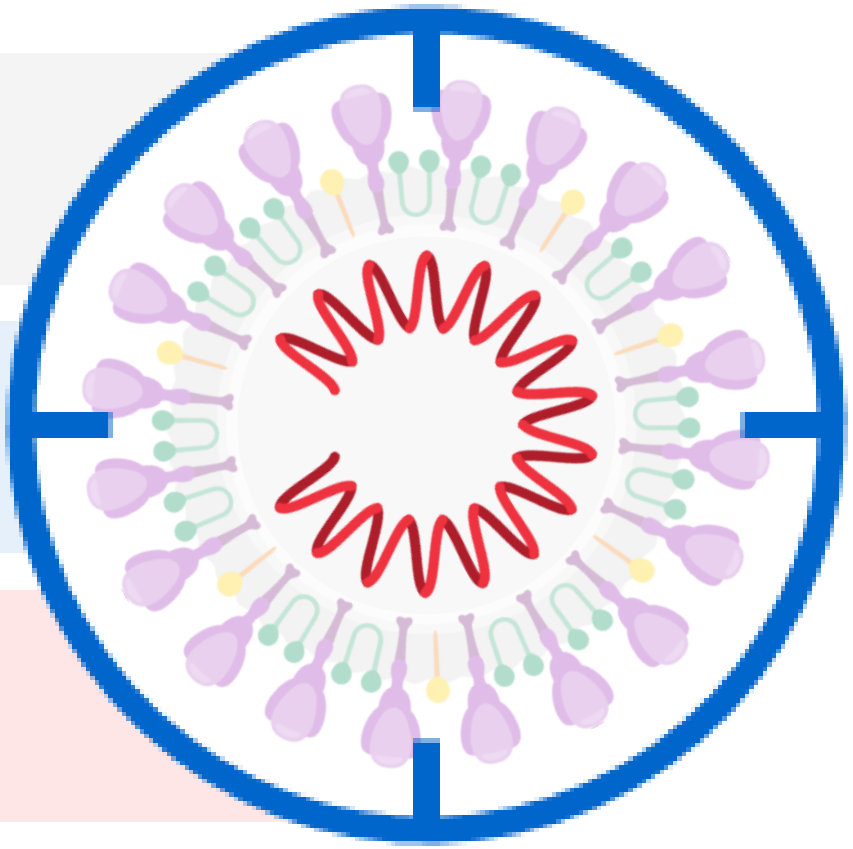
WHO update webinar Sept 11, 2020
Wölfel et al 2020, https://doi.org/10.1038/s41586-020-2196-x

Targets of different Rapid Ag tests

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

Targets the **Nucleocapsid**

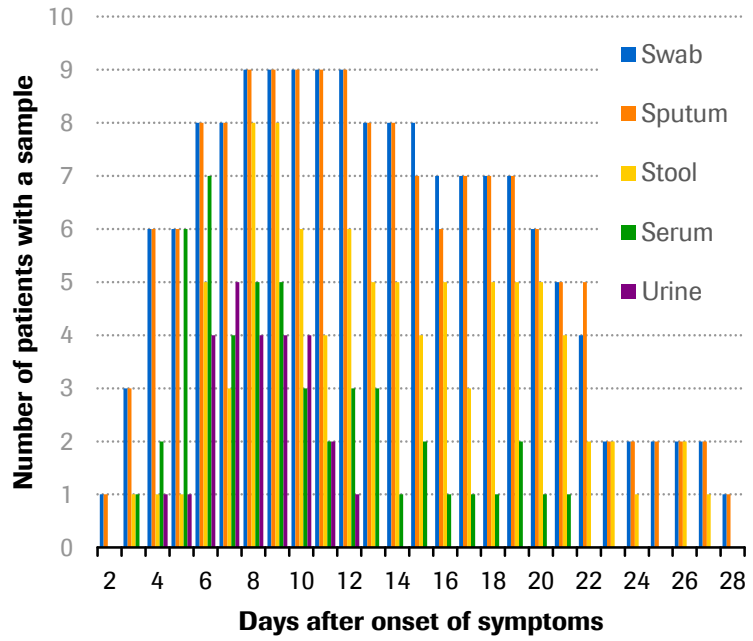
Even with the same target, the antibodies may have **different epitopes and affinites**



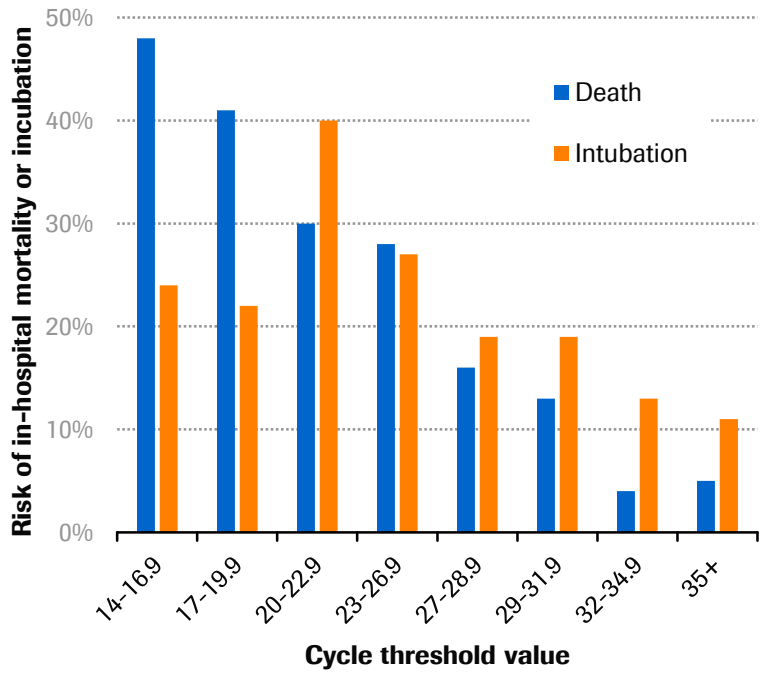
Quality of Samples for COVID-19 Testing

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

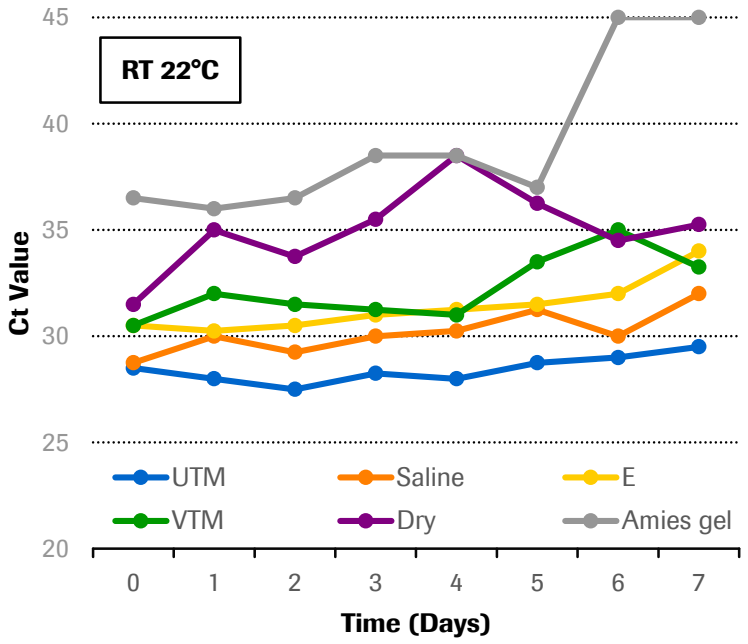
Higher viral loads associated with more severe disease

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

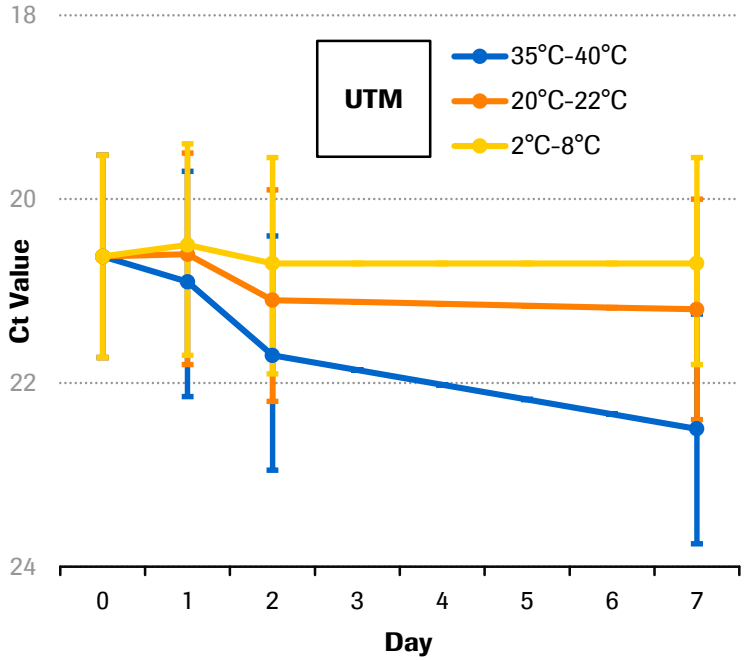
Quality of Samples for COVID-19 Testing

Viral load differs across storage conditions

Collection media and swab



Storage temperature and time



Test samples as soon as possible after collection

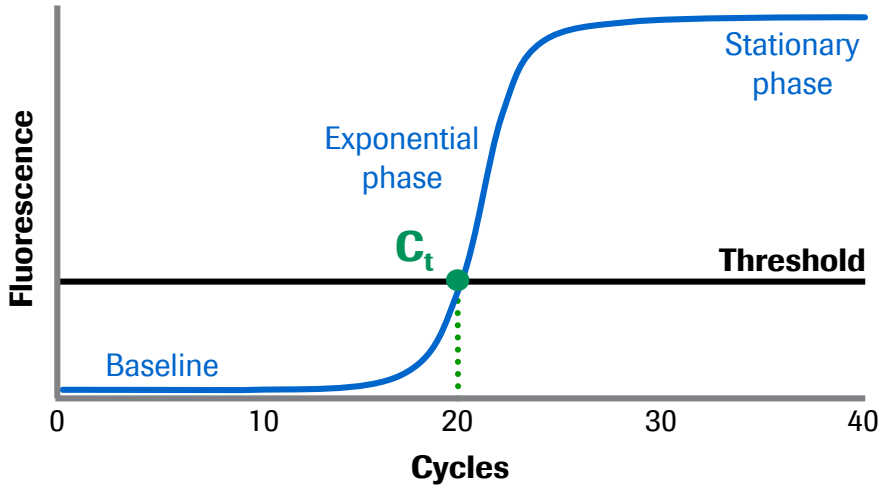
To improve detection, store samples refrigerated and/or in buffered viral transport media containing antibiotics

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).

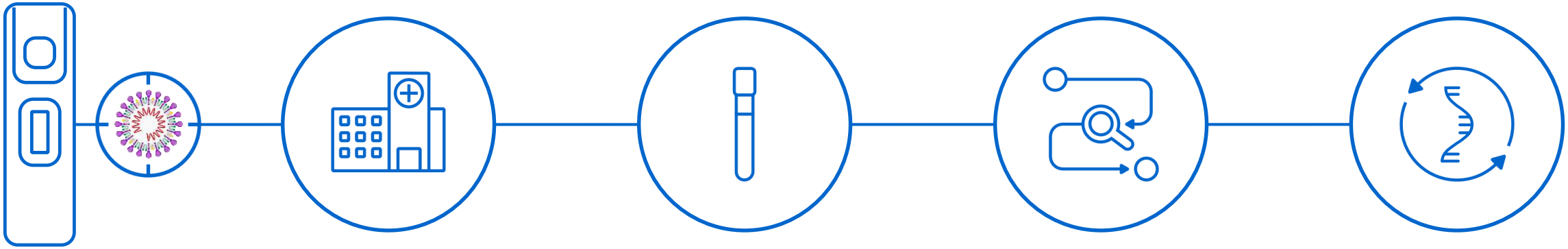
No international, commutable standardized reference material is currently available

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

PCR: Polymerase Chain Reaction

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

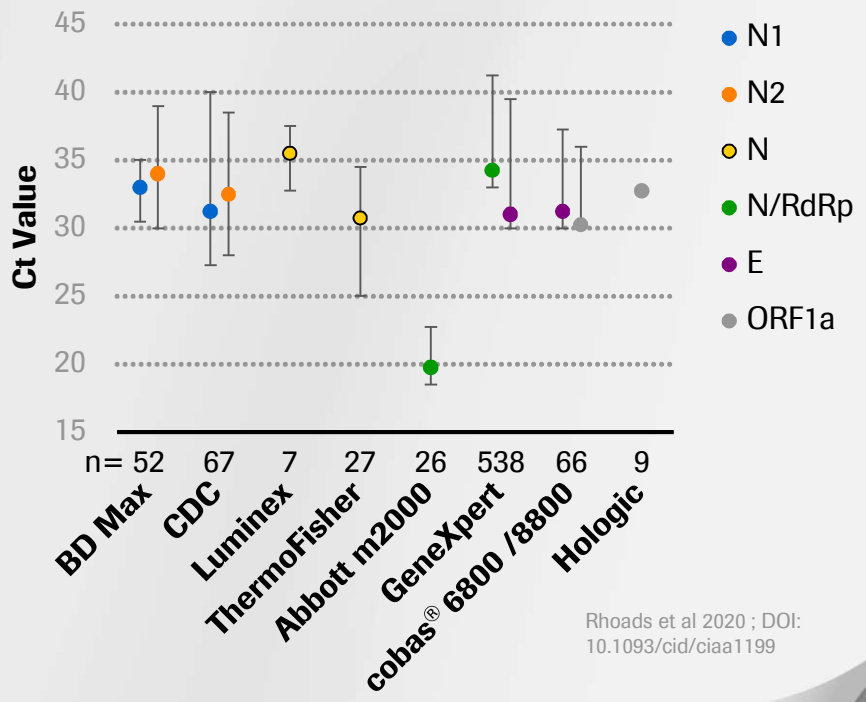
H2H:

Comparing Ct values

Ct-values can vary significantly between and within methods

CAP survey

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



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

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

External Clinical Validation Studies of the Roche SARS-CoV-2 Rapid Antigen Test

(= STANDARD Q-COVID-19 Ag Test)

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

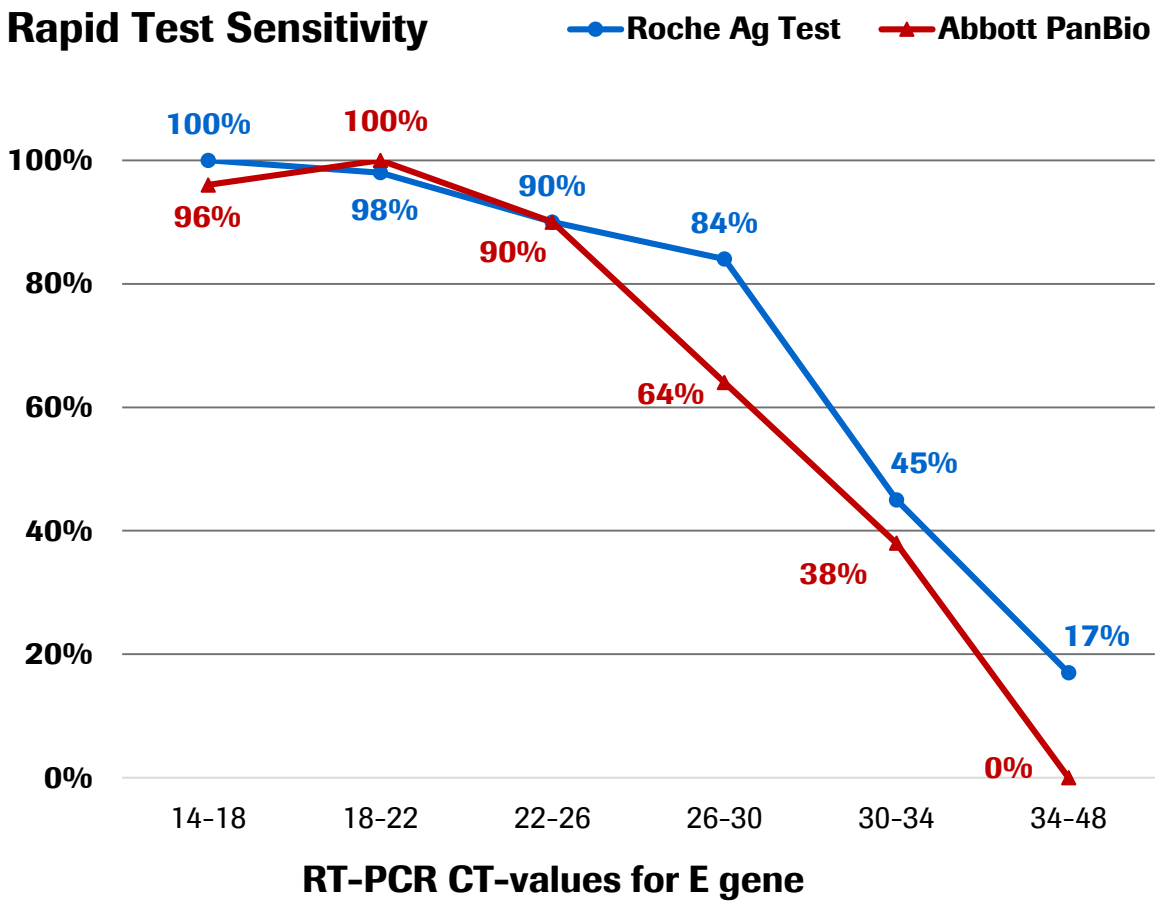
medRxiv preprint doi: https://doi.org/10.1101/2020.11.20.20235341

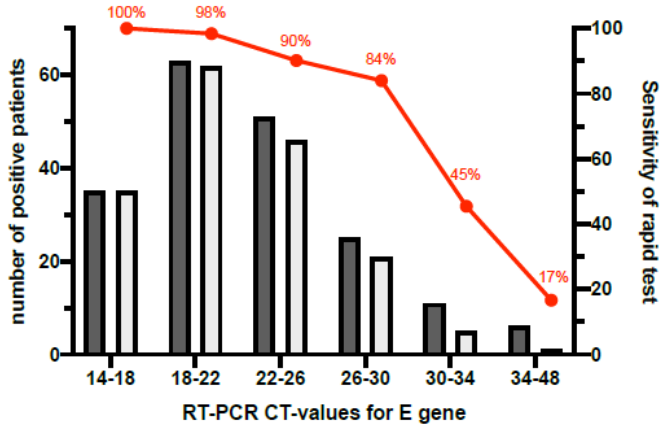
Hospital Universitaires Genève, Switzerland: Study Details

	 Roche 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

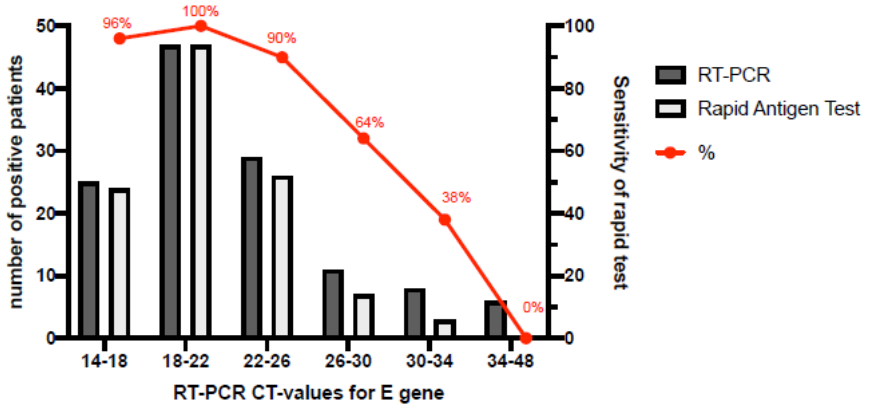
Hospital Universitaires Genève: Result Details





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), cobasRoche (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 SARS-CoV-2*Rapid Ag	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

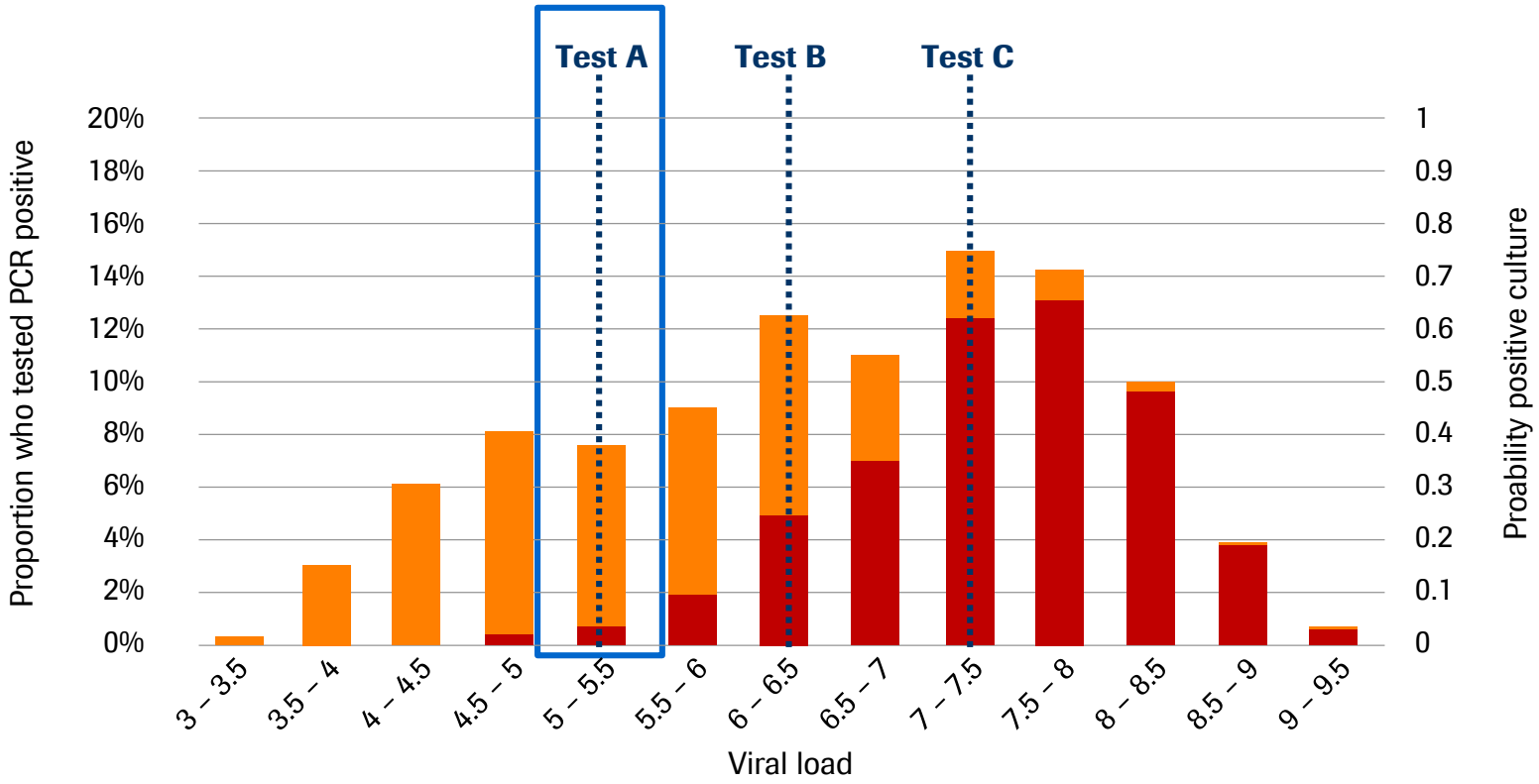
Van Beek et al., The Netherlands: Detection of culture positive (RT-PCR-confirmed) cases by rapid antigen tests depending on severity of symptoms

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.

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

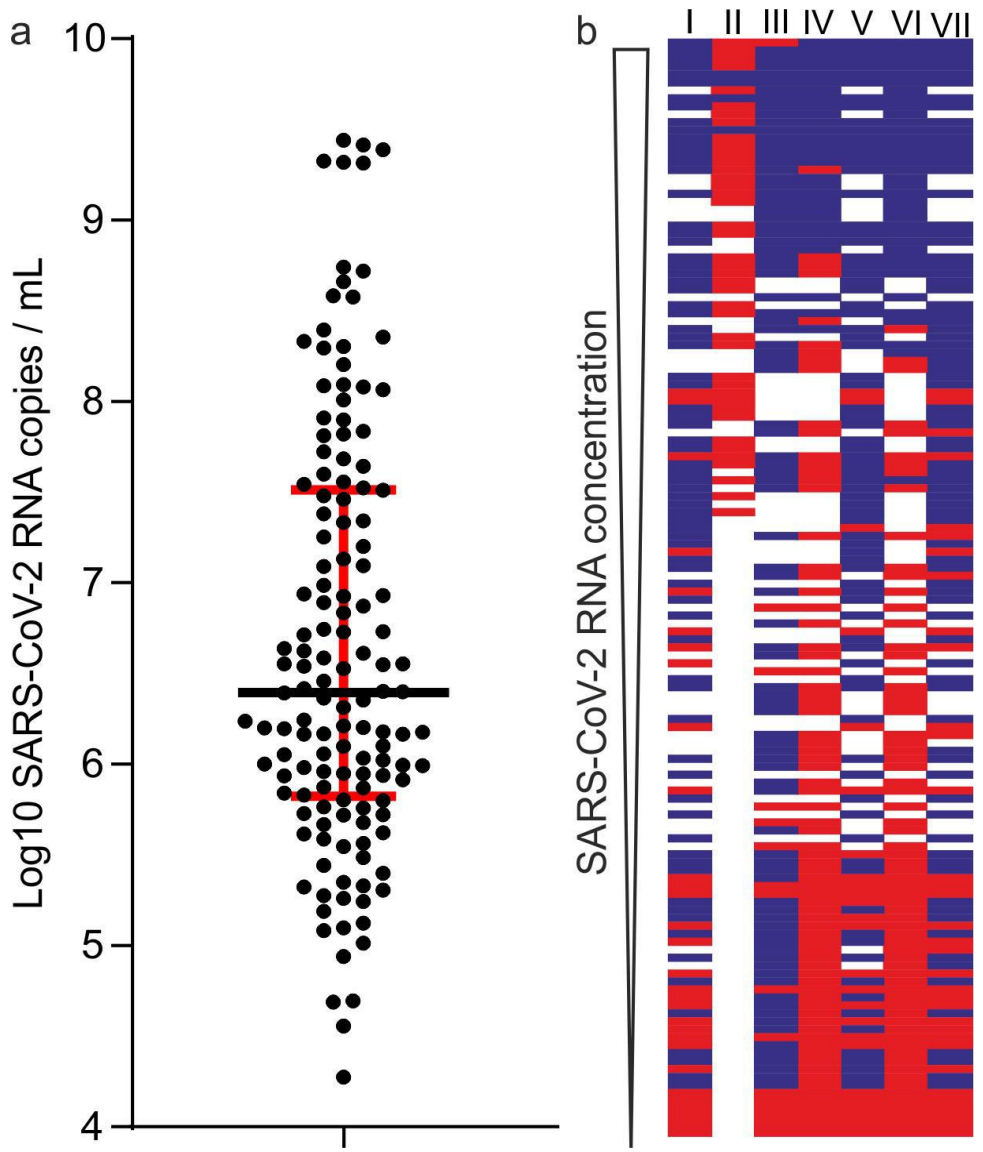
Corman et al., Germany: Study Details

	 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 consideration[1,2,3,4] 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 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 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 (%) DPSO (median Days < 0-3) Days 4-7 Days 8+	(xx%) 4 44.0% 45.7% 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 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 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 SARS-CoV-2 Rapid Ag	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 10^5 copies/ml (Ct=30) and 10^6 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 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.

x

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

Roche

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 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 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

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, TAI	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 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.

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

* Supplemental data

Conclusions

- 15 studies presented with over 9’500 patient samples investigated detection rates and sensitivities stratified by CT (viral load) categories. (4 studies had no corresponding Ct data and symptom status)
- 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.

Doing now what patients need next

Backup: Off label use, not analyzed further

Schildgen et al., Germany: Study Summary

Off-label sample material, low n

Preanalytics

- In order to determine if SARS-CoV-2 antigen could be detected in specimens other than nasopharyngeal swabs, applied. bronchoalveolar lavage (BALF) and throat washes (TW), either a diluted or an original PCR positive specimen were used
- To increase the probability of antigen detection, samples with Ct values <16 for E and S-gene were used

Main results

- Overall sensitivities of 33.3% (RapiGEN), 50% (Abbott), and 88.1% (Roche) with opposite overall specificities of 87.1% (RapiGEN), 77.4% (Abbott), and 19.4% (Roche)

Specifics

- Very small N: In total, 11 of 13 BALFs, and 31 of 60 (TWs) were tested as PCR positive and compared to Rapid AG tests
- solution of NaCl (0.9% w/v) without any additional potentially interfering chemicals
- Pre-dilution of samples not specified per sample
- sample volumes: 55 µl (Roche), 110 µl (Abbott), and 150 µl (RapiGen) BALF/TW, instead of extracted swab material

Main Conclusions

In off-label sample material, rapid Ag test cannot replace PCR and they are not appropriate for screening of asymptomatic individuals. They should additionally be used to gain deeper insights into infectivity and the course of infection to develop more advanced testing strategies and their benefit has to be carefully evaluated for the respective

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Schildgen et al., Germany: Study Details

Off-label sample material, low n

	Roche SARS-CoV-2 Rapid Ag	Panbio Abbott	Biocredit RapiGEN
N, PCR positive (%)	9 (out of 11 bronchoalveolar washes) and 31 (out of 60 throat washes)		
Investigated cohorts	Pilot sample panel		
Samples	bronchoalveolar lavage and throat washes, either a diluted or an original PCR positive specimen		
Sensitivity overall (95% CI) Ct ≤16	88.1 (75-95)	50.0 (35-64)	33.3 (21-48)
BAL N=13	72.7	72.7	54.6
TW symptomatic N=23	100	40.0	30.0
TW asymptomatic N=27	84.6	38.5	33.3
Specificity overall (95%CI)	19.4 (9-36)	77.4 (60-89)	87.1 (71-95)
BAL N=13	100	100	100
TW symptomatic N=23	7.7	84.6	76.9
TW asymptomatic N=27	19.4	71.4	92.9
Reference Method	RealStar® SARS-CoV-2 RT-PCR Kit, Altona, Germany, two targets PCR validated and certified with INSTAND external survey		

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TW: throat wash