How sensitive are antigen point of care tests towards the end of the first week of symptoms?

A glance at preprints.

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Background

We have been consulted by laboratories and public health entities in Germany regarding our experience with antigen point of care tests (AgPOCT), specifically their sensitivity toward the end of the first week of symptoms. AgPOCT are known to detect infections during the first few days of symptoms with reasonable sensitivity. They identify subjects with high viral load and thereby provide an estimate of infectivity. However, it is unclear up to which day in the course of symptoms AgPOCT may also be useful for provisional guidance regarding presence/absence of infection, such as when using AgPOCT to reduce the waiting time for RT-PCR results, or in settings where RT-PCR is not available.

The purpose of this rapid screen of the literature is thus to obtain an impression of the clinical sensitivity by end of the first week after symptoms onset. Clinical sensitivity in this context is the percentage of RT-PCR positive subjects that test positive by AgPOCT.

We have looked at 25 publications currently available, almost all in preprint form. We found ten contributions that provide insights into the change of sensitivity over the first week of symptoms. The overall impression is that sensitivity toward the end of the first week is only slightly lower than during the first four or five days, with missing data and/or rapid decline of sensitivity during the second week. All studies suggest that sensitivity is mainly determined by viral load (i.e., we could not recognize signs of other influencing factors such as time independent of viral load, although we could not conduct formal analyses).

The following list provides a short summary of findings in the studies evaluated.

1.

Van der Moeren et al. Performance evaluation of a SARS-CoV-2 rapid antigen test: test performance in the community in the Netherlands

https://doi.org/10.1101/2020.10.19.20215202

This study was done in a community care setting in the Netherlands, using the BD Veritor System for Rapid Detection of SARS-CoV-2 assay. 123 RT-PCR-positive and symptomatic subjects were tested in the AgPOCT. AgPOCT positives were detected until day 16, with a good correlation between viral load and AgPOCT detection until day 10. Borderline-positive samples (Ct 25-30) yield a sensitivity of 92.3% if collected before day 7 and 87.0% if collected after day 7. This difference seems to be determined by lower viral loads in samples collected after day 7.

2.

Lindner et al. Head-to-head comparison of SARS-CoV-2 antigen-detecting rapid test with self-collected anterior nasal swab versus professional-collected nasopharyngeal swab

https://doi.org/10.1101/2020.10.26.20219600

Comparison based on 39 RT-PCR-positive patients. Consistent detection up to day 7 (occasionally up to day 10) by using nasopharyngeal swab and the STANDARD™ Q COVID-19 Ag Test. Detection seems to depend on viral load rather than timing.

3.

Lindner et al. Head-to-head comparison of SARS-CoV-2 antigen-detecting rapid test with professional-collected anterior nasal versus nasopharyngeal swab

https://doi.org/10.1101/2020.12.03.20243725

Comparison based on 41 RT-PCR-positive patients. Detection up to day 10 using nasopharyngeal swab and the STANDARD™ Q COVID-19 Ag Test. As in the study above, detection seems to depend on viral load rather than time.

4.

Courtellemont et al. Real-life performance of a novel antigen detection test on nasopharyngeal specimens for SARS-CoV-2 infection diagnosis: a prospective study

https://doi.org/10.1101/2020.10.28.20220657

Testing of nasopharyngeal swabs from 248 individuals using the COVID-VIRO® antigenic rapid test in comparison to RT-PCR in France. 36 patients sampled before symptoms day 4: 94.7% sensitivity. 62 patients sampled after day 4: 95.8% sensitivity. Detection in several cases beyond day 7. Correlation between RT-PCR Ct-value and AgPOCT detection.

5.

Abdulrahman et al. Comparison of SARS-COV-2 nasal antigen test to nasopharyngeal RT-PCR in mildly symptomatic patients

https://doi.org/10.1101/2020.11.10.20228973

The study included 4183 patients who were mildly symptomatic. Nasal samples were used for AgPOCT (Abbott Panbio COVID 19 antigen rapid test) and nasopharyngeal swabs for RT-PCR. Sensitivity in 1290 patients sampled until symptoms day 5: 82.4%. Sensitivity in 1252 patients sampled until symptoms day 7: 82.6% (groups overlapping). Detection seems to be mainly dependent on viral load.

6.

Bulilete et al. Evaluation of the Panbio™ rapid antigen test for SARS-CoV-2 in primary health care centers and test sites

https://doi.org/10.1101/2020.11.13.20231316

Nasopharyngeal samples from 1,369 patients (close contact with a confirmed COVID-19 individual or due to symptoms suggestive of COVID-19) were tested by Panbio™ Ag-RDT in comparison to RT-PCR, in Mallorca, Spain. Sensitivity in 101 PCR-positive patients sampled until 5 days after onset: 79.2%. Sensitivity in 120 PCR-positive patients sampled on any day: 78.3%. Strong dependence of AgPOCT sensitivity on viral load.

7.

Iglói et al. Clinical evaluation of the Roche/SD Biosensor rapid antigen test with symptomatic, non-hospitalized patients in a municipal health service drive-through testing site

https://doi.org/10.1101/2020.11.18.20234104

This study applied the Roche/SD Biosensor lateral flow antigen rapid test on nasopharyngeal swabs obtained from mildly-symptomatic individuals in the Netherlands. 186 SARS-CoV-2 positives by RT-PCR. Sensitivity in patients sampled up to day 3, 7, and unlimited: 94.9, 90.6, and 84.6%. When restricting patients to those with Ct<25: Sensitivities 100, 98.8, and 99.1%. Sensitivity seems to be strictly dependent on viral load. Interesting: in 140 culture-positive samples, only 5 are missed by AgPOCT while among 149 AgPOCT-positive samples, 14 are culture-negative.

8.

Berger et al. Diagnostic accuracy of two commercial SARS-CoV-2 antigen-detecting rapid tests at the point of care in community-based testing centers

https://doi.org/10.1101/2020.11.20.20235341

Panbio™ Covid-19 Ag Rapid Test device was validated in 535 participants and the Standard Q Ag-RDT (SD Biosensor, Roche) was validated in 529 participants.

315 RT-PCR-positives. Strong correlation of AgPOCT sensitivity with viral load, weak correlation with day of symptoms (most patients sampled during first week, individual samples positive during second week up to day 14).

9.

Schwob et al. Antigen rapid tests, nasopharyngeal PCR and saliva PCR to detect SARS-CoV-2: a prospective comparative clinical trial

https://doi.org/10.1101/2020.11.23.20237057

Three antigen-based RDTs were applied, STANDARD Q® COVID-19 Ag Test from Biosensor/Roche, Panbio™ COVID-19 Ag Test from Abbott, and COVID-VIRO® from AAZ-LMB in comparison to RT-PCR.

372 PCR-positive subjects. Sensitivity in samples taken before symptoms day 4: 87.8%. Sensitivity in samples taken after symptoms day 4: 85.7%. Sensitivity in samples taken during first week of symptoms: 87.7%. Sensitivity in samples taken after first week of symptoms: 81.3%.

10.

Krüger et al. Evaluation of the accuracy and ease-of-use of Abbott PanBio - A WHO emergency use listed, rapid, antigen-detecting point-of-care diagnostic test for SARS-CoV-2

https://doi.org/10.1101/2020.11.27.20239699

This study used the Abbott PanBio antigen-detecting rapid diagnostic test in 1108 participants. 106 RT-PCR-positive subjects. Positive AgPOCT detection up to day 13. Sensitivity in samples taken before symptoms day 8: 90.8%. Sensitivity in samples taken from symptoms day 8: 61.5%. Difference seems to be mainly explained by viral load.

Additional preprints screened, not containing sufficient information with regards to timing:

Real-life evaluation of a rapid antigen test (Panbio COVID-19 Ag Rapid Test Device) for SARS-CoV-2 detection in asymptomatic close contacts of COVID-19 patients

https://doi.org/10.1101/2020.12.01.20241562

COVID-19 Antigen Rapid Test as Screening Strategy at the Points-of-Entry: Experience in Lazio Region, Central Italy, August-October 2020

https://doi.org/10.1101/2020.11.26.20232728

Multicenter evaluation of the Panbio™ COVID-19 Rapid Antigen-Detection Test for the diagnosis of SARS-CoV-2 infection

https://doi.org/10.1101/2020.11.18.20230375

Nasopharyngeal Panbio COVID-19 antigen performed at point-of-care has a high sensitivity in symptomatic and asymptomatic patients with higher risk for transmission and older age

https://doi.org/10.1101/2020.11.16.20230003

Correlation of SARS-CoV-2 nucleocapsid antigen and RNA concentrations in nasopharyngeal samples from children and adults using an ultrasensitive and quantitative antigen assay

https://doi.org/10.1101/2020.11.10.20227371

Performance of qualitative and quantitative antigen tests for SARS-CoV-2 in early symptomatic patients using saliva

https://doi.org/10.1101/2020.11.06.20227363

Analytical and Clinical Performance of the Panbio COVID-19 Antigen-Detecting Rapid Diagnostic Test

https://doi.org/10.1101/2020.10.30.20223198

Field evaluation of a rapid antigen test (Panbio™ COVID-19 Ag Rapid Test Device) for the diagnosis of COVID-19 in primary healthcare centers

https://doi.org/10.1101/2020.10.16.20213850

Antigen-based testing but not real-time PCR correlates with SARS-CoV-2 virus culture

https://doi.org/10.1101/2020.10.02.20205708

Panbio antigen rapid test is reliable to diagnose SARS-CoV-2 infection in the first 7 days after the onset of symptoms

https://doi.org/10.1016/j.jcv.2020.104659

Clinical evaluation of BD Veritor SARS-CoV-2 point-of-care test performance compared to PCR-based testing and versus the Sofia 2 SARS Antigen point-of-care test.

https://jcm.asm.org/content/early/2020/10/05/JCM.02338-20

A handheld point-of-care system for rapid detection of SARS-CoV-2 in under 20 minutes

https://doi.org/10.1101/2020.06.29.20142349

Clinical evaluation of self-collected saliva by RT-qPCR, direct RT-qPCR, RT-LAMP, and a rapid antigen test to diagnose COVID-19

https://doi.org/10.1101/2020.06.06.20124123

Field Evaluation of the Performance of a SARS-CoV-2 Antigen Rapid Diagnostic Test in Uganda using Nasopharyngeal Samples

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

Urgent need of rapid tests for SARS CoV-2 antigen detection: Evaluation of the SD-Biosensor antigen test for SARS-CoV-2

https://doi.org/10.1016/j.jcv.2020.104654