Application Report

Handling Analysis (Charité PST study)

Version 1

SARS-CoV-2 Rapid Antigen Test
Patient Self Testing (Nasal sample)

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SARS-CoV-2 Rapid Antigen Test
Patient Self Testing (Nasal sample)
Handling Analysis –Performance Validation

Handling Analysis

Introduction

The clinical performance of the Rapid Antigen Test by patient self-testing was evaluated at Charité – Universitätsmedizin Berlin (Berlin, Germany), as an manufacturer independent prospective study with support from the Foundation for Innovative Diagnostics (FIND), Charité University Hospital internal funds, and a grant of the Ministry of Science, Research and the Arts of Baden-Württemberg, Germany. (Lindner et al. 2021)

Clinical performance of the Standard™ Q COVID-19 Ag kit (SD Biosensor®, Chuncheongbuk-do, Republic of Korea) was evaluated against the RT-PCR tests Roche cobas® SARS-CoV-2 and TibMolbiol SARS-CoV-2 E-gene assay as the comparator methods. Ethical approval was given by the ethics committee of Charité - Universitätsmedizin (EA1/371/20). Data exchange agreements were signed between study sponsor, SD Biosensor, and Roche as appropriate allowing the usage of the shared data for the Instruction for Use for both the SDB- and Roche-branded products.

Data analysis on the study results was performed as is described in the "Method comparison" application report. This document gives additional insights into the handling of the test by the patients during this study.

Data analyses reported in this document were performed based on the shared line data. In this analysis the test will be referred to by the Roche branded test name "SARS-CoV-2 Rapid Antigen Test Nasal".

Data and Study details

Clinical performance of the SARS-CoV-2 Rapid Antigen Test Nasal was evaluated using nasal swab samples from 146 subjects in a prospective study at Charité – Universitätsmedizin Berlin. The study cohort included symptomatic adults with high suspicion of SARS-CoV-2 infection. This was based on either 1) reported contact with a confirmed case and any compatible symptom, or 2) fever or impaired taste or smell irrespective of exposure. Participants had to be proficient in German or English in order to understand the written instructions. The enrolled patient cohort included adults aged from 18 - 68 years (median, 32 years; IQR, 13 years), and a majority (59.6%) of the participants had a higher education degree.

Study participants followed written and illustrated instructions to obtain a nasal swab sample and perform the testing by themselves in a separate

room. Self-collection and self-testing were observed by health care workers without any intervention*. RT-PCR tests (Roche cobas® SARS-CoV-2 and TibMolbiol SARS-CoV-2 E-gene assay) using combined nasopharyngeal/ oropharyngeal swab (NP/OP) samples were used as the comparator methods as per institutional standard. Nasal sampling always preceded the combined NP/OP sampling. 27.4% of the participants tested positive by RT-PCR.

Detailed comments were recorded by the observing health care taker during the self-testing procedures. These included deviations from the Patient Instructions workflow, and a significant portion were comments on difficulties or remarks patients experienced or made during testing.
A listing of all violations/comments recorded is provided in an attached Excel file (see "Line Data and attached files" section), and an incidence analysis per age and per education category is presented in the "results" section.
Furthermore, patients were asked to rate the self-testing procedure on a scale of 1 (easy) to 5 (difficult), and 114 (80.9%) of the study participants chose Scale 1 or 2, 23 participants (16.3%) chose Scale 3, 4 (2.8%) participants chose Scale 4 and no participants chose Scale 5. Furthermore, while the participants were offered a chance for a second try, no participant opted for this option. (Lindner et al. 2021)

*One intervention by the study physician was necessary because of a possible risk of injury when the patient tried to insert the swab upside down into the nose.

Steps of the Test Workflow (according to Patient Instructions)

The description from the Patient Instructions is copied here for direct reference. It is given in German:

„Lesen Sie die Gebrauchsanweisung für den SARS-CoV-2 Rapid Antigen Test aufmerksam durch. Bitte ziehen Sie auch die beiliegende Kurzanleitung (mit Abbildungen) zu Rate, bevor Sie einen Test durchführen.

Vorbereiten des Tests

Vor Beginn des Verfahrens müssen Teststreifen und Reagenzien auf Arbeitstemperatur (15-30 °C/59-86 °F) gebracht werden.

V1. Überprüfen Sie das Verfallsdatum auf der Rückseite des Verpackungsbeutels. Verwenden Sie den Teststreifen nicht, wenn das Verfallsdatum überschritten ist.
V2. Öffnen Sie den Verpackungsbeutel an der Einrisslinie und entnehmen Sie den Teststreifen sowie die Tüte mit Trockenmittel. Verwenden Sie den Test sofort nach Öffnen des Beutels.
V3. Vergewissern Sie sich, dass der Teststreifen unversehrt ist und dass die Statusanzeige des Trockenmittels gelb ist (= zur Verwendung geeignet).

Entnehmen einer Probe (Nasenabstrich)

P1. Waschen Sie Ihre Hände mit Wasser und Seife oder verwenden Sie ein Handdesinfektionsmittel, bevor Sie den Test durchführen.

P2. Nehmen Sie den Abstrichtupfer aus der Verpackung, indem Sie an beiden Laschen der Kunststofffolie ziehen. Achten Sie dabei darauf den Tupfer nur am Griff zu berühren, nicht an der Spitze mit dem „Wattebausch".

P3. Neigen Sie Ihren Kopf leicht nach hinten.

P4. Führen Sie den Tupfer mit dem „Wattebausch" voran in ein Nasenloch ein. Schieben Sie den Tupfer langsam ca. 2 cm vorwärts (parallel zum Gaumen - Richtung Rachen, nicht nach oben), bis Sie einen Widerstand spüren. Üben Sie dabei keinen Druck aus.

P5. Drehen Sie den Tupfer 4-mal (insgesamt ca. 15 Sekunden lang) gegen die Naseninnenseite und entnehmen Sie ihn dann aus der Nase.

P6. Wiederholen Sie Schritt 4 und 5 mit dem gleichen Tupfer im anderen Nasenloch.
Zum Entnehmen einer Probe aus beiden Nasenlöchern wird derselbe Tupfer verwendet.

Testdurchführung

T1. Stellen Sie den Abstrichtupfer in ein Röhrchen mit Extraktionspuffer. Drücken Sie das Röhrchen im unteren Bereich zusammen und drehen Sie den Tupfer mehr als 10-mal hin und her.

T2. Drücken Sie die Seiten des Röhrchens weiterhin zusammen, während Sie den Tupfer entnehmen, um die gesamte Flüssigkeit aus dem Tupfer zu pressen.

T3. Drücken Sie die Spenderkappe fest auf das Röhrchen.

T4. Legen Sie den Teststreifen auf eine ebene Fläche. Halten Sie das Röhrchen vertikal über das runde markierte Feld (nicht das rechteckige Ergebnisfenster). Tropfen Sie genau 4 Tropfen auf das Feld. Drücken Sie dafür falls nötig das Röhrchen leicht zusammen.
Hinweis: Sie können den Test auch fortsetzen, wenn Sie versehentlich 5 Tropfen aufgetragen haben.

T5. Stellen Sie die Stoppuhr und lesen Sie das Testergebnis nach 15-30 Minuten ab.

Interpretation der Testergebnisse

I.
Ungültiges Testergebnis:
Wenn keine Kontrolllinie (C) sichtbar ist, ist das Ergebnis als ungültig zu betrachten (der Test funktioniert nicht richtig). Schauen Sie genau hin: Auch wenn die Kontrolllinie schwach ist, kann der Test als gültig bewertet werden. Möglicherweise haben Sie den Test nicht korrekt durchgeführt. Lesen Sie die Gebrauchsanleitung aufmerksam und wiederholen Sie den Test. Bei weiterhin ungültigen Testergebnissen kontaktieren Sie bitte Ihren Arzt oder ein COVID-19-Testzentrum.

Positives Testergebnis:
Das Vorhandensein einer Testlinie (T), egal wie schwach sie ist, zusammen mit einer Kontrolllinie (C) bedeutet ein positives Testergebnis. Ein positives Ergebnis bedeutet, dass Sie sehr wahrscheinlich an COVID-19 erkrankt sind. Bitte wenden Sie sich umgehend an Ihren Arzt/ Hausarzt oder das örtliche Gesundheitsamt und halten Sie die örtlichen Richtlinien zur Selbstisolation ein. Gegebenenfalls wird Ihr Arzt einen Bestätigungstest mittels PCR verordnen.

Negatives Testergebnis:
Das Vorhandensein einer Kontrolllinie (C) (egal wie schwach sie ist) aber keiner Testlinie (T), bedeutet ein negatives Ergebnis. Es ist unwahrscheinlich dass Sie an COVID-19 erkrankt sind. Auch bei einem negativen Ergebnis, sollten weiterhin alle Schutz- und Hygienemaßnahmen eingehalten werden. Auch bei einem negativen Testergebnis kann eine Infektion vorliegen. Im Verdachtsfall (d.h. wenn Sie anhaltende Symptome haben oder Ihre Symptome schwerwiegender werden) wird empfohlen den Test nach 1-2 Tagen zu wiederholen, da das Coronavirus nicht in allen Phasen einer Infektion genau nachgewiesen werden kann. “

Data analysis

Data analysis was performed on the line data by the Algorithms group in R&D PoC of Roche Diagnostics in Mannheim.

All comments that were captured by the observer during the study were analyzed by the Medical & Scientific Affairs department of Roche Diagnostics in Rotkreuz. The affected step(s) in the test workflow were evaluated. More general comments regarding the workflow are classified in an additional "general" step. The full list is attached to this document.

The number of the study participants that had at least one comments from the observer corresponding to the workflow steps outlined in the Patient Instructions and QRG or the "general" step is counted.
The results are summarized against the age and educational distribution of the study population as corresponding percentages and displayed in a table.
All analyses were done using R v3.6.3, independent verification of the results was performed. All results are given as percentages without additional digits.

Discussion and Conclusion

The steps with the highest occurrence of comments are T4 (for 38% study participants), P4 (for 27% study participants), or P5 (for 27% study participants). These three steps each comprises several actions, thereby more content to comment on. Additionally, they each contain (an) explicit number(s), making them easier to quantify and comment on. Furthermore, multiple individual features derived from each of these three steps were explicitly asked to the observers, potentially prompting more comments.

Performance of patient self-testing was statistically indifferent from professional testing using nasopharyngeal swab samples, despite of the comments collected during the study. Importantly, most study participants did handle the test as intended, and considered the sampling and testing relatively easy to perform.
The study investigators concluded that the study participants were able to reliably perform the Rapid Antigen Test by themselves, and that self-testing, when paired with appropriate public information and education, could have a significant impact on pandemic management (Lindner et al. 2021).

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Results

Sample Description

The number of samples is summarized in the following table.

Table 1 – Overview of sample size and sample type for the study

Sample Type	# negative PCR results	# positive PCR results
Nasal PST	106	40

The following tables give a description of the age distribution and the educational distribution of the study population.

Table 2 – Age and educational distribution for the study population

	Hochschul-abschluss	Abitur/ Fachabitur	Mittlere Reife	unknown	Total
[18-30]	26	21	12	3	62
[31-40]	33	8	3	3	47
[41-50]	12	1	3	1	17
[51-60]	8	1	2	3	14
61 and above	5	0	1	0	6
Total	84	31	21	10	146

Handling analysis - overall result

The handling analysis can be found in the following tables. It gives the details what percentage of study participants grouped by age or education category had at least one comments from the observer corresponding to the workflow steps outlined in the Patient Instructions.
"General" means that it was a comment to the general workflow of the patient. Columns "V1" through "I" correspond to the respective steps in the workflow (see "Steps of the Test Workflow (according to Patient Instructions)" section). The percentage in column "Any" indicates the percentage of study participants that had a comment for any of the workflow steps:

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Table 3 – Percentage of study participants per age that had at least one comment corresponding to the stated workflow step from the Patient Instructions

Age	N	General	V1	V2	V3	P1	P2	P3	P4	P5	P6	T1	T2	T3	T4	T5	I	Any
		% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes
[18-30]	62	8%	3%	5%	13%	0%	0%	13%	29%	31%	6%	18%	16%	3%	34%	0%	3%	82%
[31-40]	47	6%	6%	4%	13%	0%	2%	13%	26%	21%	0%	19%	17%	6%	47%	0%	0%	79%
[41-50]	17	0%	0%	6%	24%	0%	0%	12%	29%	24%	0%	24%	0%	12%	29%	0%	0%	82%
[51-60]	14	0%	21%	14%	21%	0%	0%	43%	14%	21%	0%	7%	14%	21%	36%	0%	0%	93%
61 and above	6	0%	17%	17%	50%	0%	0%	17%	50%	50%	17%	33%	17%	0%	33%	0%	0%	100%
overall	146	5%	6%	6%	16%	0%	1%	16%	27%	27%	3%	18%	14%	7%	38%	0%	1%	83%

Table 4 – Percentage of study participants per education that had at least one comment corresponding to the stated workflow step from the Patient Instructions

Education	N	General	V1	V2	V3	P1	P2	P3	P4	P5	P6	T1	T2	T3	T4	T5	I	Any
		% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes	% Yes
Hochschulabschluss	84	4%	7%	5%	20%	0%	1%	20%	25%	20%	4%	20%	8%	8%	33%	0%	1%	80%
Abitur/Fachabitur	31	6%	6%	13%	13%	0%	0%	6%	26%	35%	0%	13%	16%	6%	48%	0%	3%	84%
Mittlere Reife	21	10%	5%	5%	5%	0%	0%	10%	33%	43%	10%	19%	24%	5%	33%	0%	0%	90%
unknown	10	10%	0%	0%	20%	0%	0%	20%	40%	20%	0%	20%	40%	0%	50%	0%	0%	90%
overall	146	5%	6%	6%	16%	0%	1%	16%	27%	27%	3%	18%	14%	7%	38%	0%	1%	83%

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Line Data and attached files

Table 5 – References

Document Reference	Document Title
Patient Instructions	Gebrauchsanweisung für Patienten BfArM
Application Report Method Comparison	Application Report Method Comparison (Charité PST study)
(Lindner et al. 2021)	Lindner, Andreas K., et al. "SARS-CoV-2 patient self-testing with an antigen-detecting rapid test: a head-to-head comparison with professional testing." *medRxiv* (2021). https://www.medrxiv.org/content/10.1101/2021.01.06.20249009v1

The list of all comments from the study and how they were categorized to certain workflow steps from the Patient Instructions is summarized in the following Excel file.
"Berlin_Selftest_allCommentsList.xlsx"

Table 6 – Change history of document versions

Version	Author	Date	Comment
1	5.1.2e	24-Feb-2021	Initial Version