Supplemental material

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Diagnostic accuracy of rapid point-of-care tests for diagnosis of current SARS-CoV-2 infections in children: A systematic review and meta-analysis

N. Fujita-Rohwerder, L. Beckmann, Y. Zens, A. Verma

Appendix 4: Quality Assessment – Review-specific guidance to signaling questions of QUADAS-2 tool

DOMAIN 1: Patient selection

A: Risk of Bias

1) Was a consecutive or random sample of individuals enrolled?

Yes	If it is clear that all eligible individuals were asked to participate in the study within a certain recruitment period or if it is stated that the study enrolled a consecutive or random sample of eligible individuals.
No	If a different enrolment method (e.g. via convenience sampling) is described.
Unclear	If the enrolment is not described adequately.

2) Was a case-control design avoided?

Yes	If the study employed a cross-sectional or cohort study design.
No	Not applicable, as "No" would lead to an exclusion of the study.
Unclear	If the design of the study is not described clearly enough, so that a definite judgment cannot be made.

3) Did the study avoid inappropriate exclusions?

Yes	If most (≥90%) eligible individuals were included without unreasonable selection (see applicability).
No	If inappropriate exclusions (>10%) were made that cannot be justified by the test's instructions for use (IFU) (see applicability)
Unclear	If it is not clear whether inappropriate exclusions were made.

Could the selection of individuals have introduced bias?

Low	If all questions are answered "Yes".
High	If ≥ 1 question is answered "No".
Unclear	Either if all questions are answered "Unclear" or if ≥ 1 question is answered "Unclear", and ≥ 1 question is answered "Yes".

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B. Concerns regarding applicability

Is there concern that the included individuals do not match the review question?

Low	If at least 80% of the included paediatric study participants are below the age of 18 and match the review question and no exclusions are made to adhere to intended use in IFU (e.g. due to symptom onset > 7 days)
High	If paediatric study participants are selected in accordance with the described intended use in the instructions for use (IFU), for example symptom onset ≤ 7 days. The presence of exclusions based on IFU does not increase the risk of bias but may affect applicability.
Unclear	If no sufficient information is provided to make a judgment.

DOMAIN 2: Index test

A: Risk of Bias

1) Were the index test results interpreted without knowledge of the results of the reference standard?

Yes	If blinding is explicitly stated or if it is clear that index test was carried out first and the result was read and reported prior to the availability of the result of the reference standard and the process of the read out was described.
No	If no blinding was implemented.
Unclear	If no sufficient information is provided to make a judgment.

2) If a threshold was used, was it pre-specified?

Yes	If a pre-specified threshold was reported in the methods section or if is stated that the test was performed according to the test's IFU.
No	If no pre-specified threshold was used.
Unclear	If no sufficient information is provided to make a judgment.

Could the conduct or interpretation of the index test have introduced bias?

Low	If all questions are answered "Yes".
High	If ≥ 1 question is answered "No".
Unclear	Either if all questions are answered "Unclear" or if ≥ 1 question is answered "Unclear", and ≥ 1 question is answered "Yes".

B. Concerns regarding applicability

Is there concern that the index test, its conduct, or interpretation differ from the review question?

Low	If the test kit was used and if the test was performed according to the IFU.
High	If the test kit was not used (different swab) or if deviations from the IFU occurred (e.g. usage outside defined temperature range or specimen handling not in accordance with IFU)
Unclear	If no sufficient information is provided to make a judgment.

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DOMAIN 3: Reference Standard

A: Risk of Bias

1) Is the reference standard likely to correctly classify the target condition?

Yes	If a validated laboratory-based RT-PCR was used.
No	Not applicable, as "No" would lead to an exclusion of the study.
Unclear	If no sufficient information is provided to make a judgment.

2) Was the general threshold and any additional thresholds that were used pre-specified?

Yes	If all thresholds that were used are reported in the methods section or if is stated that the test was performed according to the laboratory's protocol or the manufacturer's IFU.
No	If no pre-specified threshold(s) was/were used.
Unclear	If no sufficient information is provided to make a judgment.

3) Were the reference standard results interpreted without knowledge of the results of the index test?

Yes	If blinding is explicitly stated.
No	If no blinding was implemented.
Unclear	If no sufficient information is provided to make a judgment.

Could the reference standard, its conduct, or its interpretation have introduced bias?

Low	If all questions are answered "Yes".
High	If ≥ 1 question is answered "No".
Unclear	Either if all questions are answered "Unclear" or if ≥ 1 question is answered "Unclear", and ≥ 1 question is answered "Yes".

B. Concerns regarding applicability

Is there concern that the target condition as defined by the reference standard does not match the review question?

Low	If a SARS-CoV-2 RT-PCR assay was used.
High	Not applicable.
Unclear	If it is not clear, whether a SARS-CoV-2 RT-PCR assay was used.

DOMAIN 4: Flow and timing

A: Risk of Bias

1) Was there an appropriate interval between index test(s) and reference standard?

Yes	If both samples are taken at the same time (concurrently or consecutively) or if it is clear that specimen collection occurred during the same participant encounter in an ambulatory setting.

No	If it is clear that both samples are not taken at the same time (time interval > 12 hours) or during one ambulatory visit.
Unclear	If no sufficient information is provided to make a judgment.

2) Did all study participants receive a reference standard?

Yes	If it is clear that all participants received a reference standard.
No	If it is clear that not all participants received a reference standard.
Unclear	If no sufficient information is provided to make a judgment.

3) Did study participants receive the same reference standard?

Yes	If all participants were tested with a RT-PCR assay.
No	Not applicable, as there is only one reference standard defined.
Unclear	If no sufficient information is provided to make a judgment.

4) Were all *study participants* included in the analysis?

Yes	If the number of enrolled participants matches the total number of included participants reported in the 2x2 table (for cohort studies with repeat testing over time: only initial test is included in the analysis)
No	If number of enrolled participants does not match total number in 2x2 table. "No" does not increase the risk of bias, if difference is ≤ 5 % and reasons for exclusion are reported such as missing data on symptom onset, missing clinical data, missing symptom data, inconclusive/missing index test/reference standard.
Unclear	If it is not possible to determine whether all participants were included in the analysis

Could the patient flow have introduced bias?

Low	If all questions are answered "Yes".
High	If ≥ 1 question is answered "No".
Unclear	Either if all questions are answered "Unclear" or if ≥ 1 question is answered "Unclear", and ≥ 1 question is answered "Yes".

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Unclear	If statement about funding and/or COI is missing.

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