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

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Appendix 2: Supplementary methods

Author queries

For studies that did not fully meet the inclusion criteria for the population, index test and/or reference standard, we required that at least 80% of the paediatric (sub-)population matched the population we defined for this systematic review. Studies were excluded if the index test and the reference standard were performed in less than 80% of the paediatric study population. Besides journal articles, reports (including clinical study reports) that adhered to reporting standards such as STARD (Standards for Reporting of Diagnostic Accuracy Studies) [1] or recommendations given by government agencies [2,3] were considered eligible for inclusion. Studies that mentioned the inclusion of paediatric study participants without reporting any corresponding outcome data but otherwise met the eligibility criteria were initially included, and study authors were contacted and asked to provide such data. Further, if the study population's baseline characteristics included information on age, we estimated the proportion of paediatric study participants assuming ages of study participants following a normal distribution and the proportion of PCR-positive paediatric assuming no changes in the PCR positivity rate among age groups. We contacted authors if we estimated at least 10 PCR-positive paediatric study participants in the study population.

Details on the search strategy development and information retrieval process

One researcher performed analyses of simple word frequencies and keywords-in-contexts in R using the "quanteda" package [4]. Because of substantial differences between types of tests, separate test sets were used to identify candidate search terms for antigen tests and molecular tests, respectively. Test sets included 27 potentially relevant studies (irrespective of paediatric study participants) from the Cochrane Review by Dinnes et al. [5] and from a frequently updated website that lists DTA studies on antigen tests [6]. Due to a limited number of potentially relevant references addressing rapid molecular tests for point-of-care usage, the draft search strategy was supplemented by search terms derived from a conceptual approach. Furthermore, brand names of tests included in the Cochrane Review were added to increase sensitivity. The final search strategy achieved 100% completeness against the validation sets with ten studies and relevant references of five studies that

included paediatric participants identified via exploratory searches beforehand. Prior to execution, the search strategy was peer-reviewed by a senior information specialist following the Peer Review of Electronic Search Strategies (PRESS) Guideline statement [7].

We only searched for publications published after December 2019, as we were only interested in literature published after the emergence of SARS-CoV-2. Further, we limited our search to publications written in English or German. Since Embase and MEDLINE provided comprehensive search filters for SARS-CoV-2 related literature via Ovid, our concept addressing the target condition was not used in these two searches.

To acknowledge the unprecedented role of preprints in the rapid dissemination of SARS-CoV-2 related research, we also searched for relevant preprints. Due to the direct availability of full texts of preprints and to increase the efficiency of the information retrieval, a further concept addressing the target population was defined and used in addition to the standard search strategy for identifying potentially relevant preprints directly at the full-text level. We assumed that this approach allowed to increase the precision of the overall search without a relevant reduction of its comprehensiveness.

Endnote X9.3 was used for citation management. Due to the more specific separate search for preprints at full-text level, any preprint records identified from MEDLINE were removed. Duplicates were initially eliminated via Ovid's deduplication feature. After exporting all identified references from Ovid, duplicates were identified in R by comparing digital object identifiers (DOIs) of references from MEDLINE and Embase, and the Embase records of duplicates were removed. Remaining duplicates were manually removed in EndNote X9.3 and by using Endnote's "find duplicates" function. Further, records from ClinicalTrials.gov that were retrieved from the WHO's ICTRP website were removed since directly accessing ClinicalTrials.gov's registry data allows for a more comprehensive search for relevant studies.

Data extraction

At first, a standardized Excel spreadsheet was developed for data extraction. The spreadsheet was piloted before data extraction commenced. Extracted data included information on the general study characteristics, study participant characteristics, index test, reference standard, flow and timing, and reported outcomes. A complete list of data extraction items is presented in Table S2 of Appendix 1.

Meta-analyses

Summary estimates for sensitivity and specificity were derived as follows: if sufficient data was available and the level of heterogeneity allowed meaningful statistical pooling, bivariate meta-analysis with random effects following the approach by Reitsma et al [8–10] was performed. Otherwise, separate univariate meta-analysis was performed. The bivariate approach required a continuity correction to handle zero cells in 2x2 tables. Thus, in studies where zero events were observed in one of the four cells, a continuity correction was applied by adding 0.5 to all four cells.

Depending on the availability of suitable data, subgroup analyses were performed to assess variables that could have an impact on a test's diagnostic accuracy, such as the study participants' presence of symptoms prior to testing and the duration of symptoms prior to testing. The influence of the publication status (preprint vs. peer-reviewed article) was evaluated as well as subgroup analyses with respect to the type of test (antigen vs. molecular; most commonly used antigen tests), setting (community vs. hospital-based), sample type ((oro-) nasopharyngeal vs. anterior nasal for index test and reference standard, respectively), end-user (layperson (self-testing) vs. trained staff/health care worker), and RT-PCR cycle threshold (Ct) value (cut-off values of 25 and 30). Differences between subgroups were assessed within the bivariate model and tested for statistical significance using the likelihood ratio test between the standard model and the model, which includes the corresponding variable. In the case of few studies in a subgroup analysis, univariate analysis for sensitivity and specificity were performed as sensitivity analysis and results were reported if remarkable differences between bivariate and univariate analysis were observed.

All statistical analyses were performed using the statistical platform R version 4.1.0 [11]. Bivariate meta-analysis was performed, along with the construction of the corresponding figures, with the package "mada" [12], while univariate meta-analysis was performed with the package "meta" [13] and "PropCIs" [14]. 95% CIs were computed using the approach proposed by Wilson [15].

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