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A nationwide analytical and clinical evaluation of 46 rapid antigen tests for SARS-CoV-2 compared to RT-qPCR

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Abstract:	Background The SARS-CoV-2 pandemic has resulted in massive testing by Rapid Antigen Tests (RAT) without solid independent data regarding clinical performance being available. Thus, decision on purchase of a specific RAT may rely on manufacturer-provided data and limited peer-reviewed data. Methods This study consists of two parts. In the retrospective analytical part, 33 RAT and a

	Strand Invasion Based Amplification (SIBA)-rt-PCR test from 26 manufacturers were compared to RT-qPCR on 100 negative and 204 positive deep oropharyngeal cavity samples divided into four groups based on RT-qPCR Cq levels. In the prospective clinical part, 200 individuals found SARS-CoV-2 positive and 200 individuals found SARS-CoV-2 negative by routine RT-qPCR testing were tested within 72 hours with 46 included RAT from 28 manufacturers applying RT-qPCR as the reference method. Results The overall analytical sensitivity differed significantly between the 34 included RAT; from 2.5% (95% CI 0.5-4.8) to 67% (95% CI 60-73). All RAT presented analytical specificities between 93-100%. Likewise, the overall clinical sensitivity varied significantly between the 46 included RAT; from 2.5% (95% CI 0.5-4.8) to 94 % (95% CI 91-97). All RAT presented clinical specificities between 97-100%. Conclusion The study presents analytical as well as clinical performance data for 46 commercially available RAT compared to the same RT-qPCR test. The study enables identification of individual RAT that has significantly higher sensitivity than other included RAT and may aid decision makers in selecting between the included RAT. Funding The study was funded by a participant fee for each test and the Danish Regions.

Conflict of interest

Lars Østergaard has within 36 months received speaker fees from Sanofi-Pasteur and Pfizer. None of the other authors have any personal conflict of interests to report. The project received a participation fee from each of the participating companies to cover the cost of the project.

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A nationwide analytical and clinical evaluation of 46 rapid antigen tests for SARS-CoV-2 compared to RT-qPCR

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- The clinical sensitivity among 46 rapid antigen tests for SARS-CoV-2 varied from 0.03 [95% CI 0.01-0.05] to 0.94 [0.91-0.97]
- 29 rapid antigen tests performed significantly worse than the 17 best performing rapid antigen tests in the study
- The study demonstrates that analytical sensitivity cannot be directly translated to clinical sensitivity for individual SARS-CoV-2 rapid antigen tests

Abstract

Background

The SARS-CoV-2 pandemic has resulted in massive testing by Rapid Antigen Tests (RAT) without solid independent data regarding clinical performance being available. Thus, decision on purchase of a specific RAT may rely on manufacturer-provided data and limited peer-reviewed data.

Methods

This study consists of two parts. In the retrospective analytical part, 33 RAT and a Strand Invasion Based Amplification (SIBA)-rt-PCR test from 26 manufacturers were compared to RT-qPCR on 100 negative and 204 positive deep oropharyngeal cavity samples divided into four groups based on RT-qPCR Cq levels. In the prospective clinical part, 200 individuals found SARS-CoV-2 positive and 200 individuals found SARS-CoV-2 negative by routine RT-qPCR testing were tested within 72 hours with 46 included RAT from 28 manufacturers applying RT-qPCR as the reference method.

Results

The overall analytical sensitivity differed significantly between the 34 included RAT; from 2.5% (95% CI 0.5-4.8) to 67% (95% CI 60-73). All RAT presented analytical specificities between 93-100%. Likewise, the overall clinical sensitivity varied significantly between the 46 included RAT; from 2.5% (95% CI 0.5-4.8) to 94 % (95% CI 91-97). All RAT presented clinical specificities between 97-100%.

Conclusion

The study presents analytical as well as clinical performance data for 46 commercially available RAT compared to the same RT-qPCR test. The study enables identification of individual RAT that has significantly higher sensitivity than other included RAT and may aid decision makers in selecting between the included RAT.

Funding

The study was funded by a participant fee for each test and the Danish Regions.

Introduction

During the current SARS-CoV-2 pandemic, massive testing has been applied with the aim to contain the spread of the virus. The test strategy was emphasized by the WHO in March, 2020 as the backbone of the global pandemic response together with isolation and contact tracing that combined with social distancing and hand hygiene would allow “to extinguish” the pandemic [1].

The unprecedented demand for testing has led to a shortage of reagents and manufactured tests for reverse transcription quantitative polymerase chain reaction (RT-qPCR) and other nucleic acid amplification technology (NAAT) methods including point of care testing (PoCT). Thus, lateral flow based rapid antigen tests (RAT) have been deployed extensively due to delivery of results within minutes, availability, low cost and the ease of use that allow non-healthcare trained individuals to perform the test outside of healthcare facilities [2,3].

Several approaches to evaluate real-life performance of RAT has been applied, including studies on cultured virus, retrospective studies evaluating analytical performance data and clinical evaluations [4–13].

Viral culture studies have shown that limit of detection (LOD) of RAT differs significantly and varies depending on spike variants of SARS-CoV-2 [4,14]. SARS-CoV-2 variants contain several mutations in the nucleocapsid gene together with mutations in the spike gene, which may account for the difference in LOD [15].

Clinical studies have shown that sensitivity of a single RAT may vary at least 20 percentage point between non-symptomatic and symptomatic individuals [9,16–18]. As most clinical studies only include a single or few different RAT and as the tested population varies between different clinical studies regarding SARS-CoV-2 prevalence, proportion of symptomatic versus non-symptomatic individuals, vaccination status and demographic profile, comparing performance data between different studies is difficult [9–11,19,20]. Due to the absence of clinical studies that allow for comparison of the different performances of commercially available RAT and the huge amount of financial resources spent on RAT, the Danish Regions initiated a nationwide clinical study comparing different RAT. This study combines a retrospective analytical sensitivity and specificity study on 100 negative and 204 positive frozen samples with a prospective clinical study on sensitivity and specificity, in which approximately 200 SARS-CoV-2 positive individuals and 200 SARS-CoV-2 negative individuals were tested by routine RT-qPCR and a number of RAT within 72 hours of the initial RT-qPCR test.

Methods

For detailed description of protocol and methods, please refer to Supplementary data and [21].

Study design

A total of 46 tests, 44 RAT and two SIBA-rt-PCR from 28 manufacturers, were included in the study.

Participants

Individuals, who tested positive for SARS-CoV-2 by routine RT-qPCR performed by a public test provider were included in the study.

Retrospective analytical RAT testing

UTM samples from SARS-CoV-2 RT-qPCR positive individuals participating in the prospective arm of the study were collected by out-patient testing teams. All samples were collected as deep oropharyngeal swabs and immediately stored at -80 °C until further processing. In total, 50 samples with Cq <25; 54 samples with Cq between 25 and 30; 50 samples with Cq between 30 and 35 and 50 samples with Cq between 35 and 40 were prepared. One hundred SARS-CoV-2 RT-qPCR negative samples were prepared by pooling ten routine UTM samples that had tested negative for SARS-CoV-2 for each negative sample (Figure 1A).

Prospective clinical RAT testing

From each included individual, deep oropharyngeal swabs, anterior nasal cavity swabs and saliva were collected for RAT testing together with a deep oropharyngeal swab for RT-qPCR testing. All tests were conducted according to the IFU or according to additional instruction from the manufacturer using the utensils provided for testing by the manufacturer. Samples collected from other anatomical sites than CE-marked were collected and handled as instructed by each manufacturer.

Prospective RT-qPCR

Deep oropharyngeal swabs for RT-qPCR were collected in a NEST disposable sampler inactivation transport medium with an oropharyngeal specimen collection swab (Wuxi NEST Biotechnology Co., Ltd, Wuxi City, China) and sent to RT-qPCR testing.

Analysis

Dual-target RT-qPCR was used as gold standard. In the retrospective part of the study, samples were grouped into four Cq ranges based on the highest Cq level of the two E- and N-targets. In the prospective part of the study, samples were grouped into three Cq ranges based on the average Cq level between the two N-targets.

Sensitivity and specificity were calculated for each individual RAT in relation to RT-qPCR. All p-values less than 0.05 were considered statistically significant.

Role of the funding source

The participating companies had no influence on study design, sample collection, analysis, interpretation, drafting of manuscript, or decision on publishing.

Results

Participants and SARS-CoV-2 variants

A total of 3,797 individuals were included in the prospective part of the study between January 18th, 2021 and September 9th, 2021 to allow each RAT to be tested on 200 SARS-CoV-2 positive and 200 SARS-CoV-2 negative individuals. 2,045 individuals that had just tested positive for SARS-CoV-2 were included in the study within 72 hours and 1,752 SARS-CoV-2 expected RT-qPCR negative individuals were included after screening at a regional test center. Among the newly positive individuals for SARS-CoV-2, twelve individuals were excluded due to missing sample for RT-qPCR (n = 3) or a negative RT-qPCR test including the human control target (n = 9). Among the remaining 2,033 individuals, 140 (6.9%) were negative by the concomitant RT-qPCR at the time of RAT testing (Figure 1B), resulting in inclusion of 1,893 positive individuals among the previous SARS-CoV-2 positive individuals. In the screening group, forty-three individuals were excluded, eight samples were missing for RT-qPCR and thirty-five samples were negative for all targets including the human sampling control. Thus, a total of 1,709 SARS-CoV-2 negative or positive individuals by RT-qPCR were included in the screening group. The SARS-CoV-2 prevalence in the screening group was 0.64%, as 11 out of 1,709 individuals were positive for SARS-CoV-2 by RT-qPCR (Figure 1B). Participating individuals were predominantly between 18 and 70 years of age with few individuals above 70 years of age. Study participants were mainly unvaccinated at the time of inclusion.

The alpha variant (B.1.1.7) was the predominating variant among SARS-CoV-2 positive individuals included in the study and accounted for 90.8% (1,729 of 1,904) of all cases (Supplementary data).

Analytical sensitivity and specificity of RAT

The overall analytical sensitivity differed significantly between the 34 included tests from 26 manufacturers. The SIBA-rt-PCR based assay had the highest overall sensitivity of 67% (95% CI 60-73), but also the lowest specificity of 93% (95% CI 88-98%). The RAT varied from 2.5% (95% CI 0.5-4.8) for the Lituo saliva RAT to 42% (95% CI 35-49) for the Acro RAT. All RAT had a specificity of 100% (Figure 2). The overall mean sensitivity for the tests was 26% (95% CI 21-32), which reflects that RAT detected almost none of the samples with Cq >35 by RT-qPCR (n = 50). For RT-qPCR samples with Cq 30-35 (n = 50), the mean sensitivity was 2.5% (95% CI 1.5-3.8) but increased at Cq 25-30 (n = 54) with a mean sensitivity of 32% (95% CI 21-42) and a mean sensitivity of 71% (95% CI 61-80, range 6.2-99) for samples with RT-qPCR Cq <25 (n = 50) (Supplementary data).

Clinical sensitivity and specificity of RAT

In the prospective part of the study, the overall clinical sensitivity varied significantly among the 46 included tests from 28 manufacturers; from 2.5% (95% CI 0.5-4.8) for the Quidel saliva RAT to 94% (95% CI 91-97) for the Acon Flowflex RAT, with a mean overall sensitivity of 69% (95% CI 63-74). Specificity varied among the RAT from 98% (95% CI 95-99) for the Abbott nasal RAT to 100% for 28 RAT, whereas the Qlife SIBA-rt-PCR Egoo system had the lowest specificity of 97% (95% CI 95-99) for anterior nasal cavity swabs (Figure 3). According to CE-mark, the sensitivities for all tests were reported to be 81% (95% CI 69-89) or above and specificities were reported from 97% (95% CI 91-99) and above (Supplementary data).

The sensitivity of the Acon Flowflex RAT did not differ significantly from 16 of the other RAT from 14 manufacturers, when multiple testing was taken into account. The remaining 29 RAT (including the visual and automated read-out of the BD veritor RAT) had a significantly lower overall sensitivity compared to the Acon Flowflex RAT (Table 1 and Supplementary data).

The mean overall sensitivity was 81% (95% CI 74-87) for strong positive samples with Cq <15, which decreased to 70% (95% CI 62-78) for medium positive samples with Cq 15-20 and 44% (95% CI 31-56) mean sensitivity for weak positive samples with Cq >20 (Supplementary data). Three out of the four included self-test were among the 17 most sensitive tests in the study, whereas the Wantai saliva/buccal RAT was among the five tests with the lowest sensitivity in the study. The sensitivity of RAT with automated readout was distributed over the full range of sensitivities with the Lumira Dx and Quidel nasal RAT performing among the 17 best tests of the study.

Discussion

In our study, we used deep oropharyngeal swabs collected for the analytical sensitivity and specificity study. Thirty-four RAT were compared using the same 204 SARS-CoV-2 positive samples and we anticipated that the analytical sensitivity data would correlate with the ranking in clinical sensitivity among the 46 RAT in the prospective part of the study. The prospective study included a higher number of different RAT compared to the retrospective study, as several manufacturers provided identical RAT to be used on several anatomical sampling sites. Interestingly, we saw similarities between analytical sensitivity and clinical sensitivity on SARS-CoV-2 positive individuals, but several tests performed differently between the retrospective and prospective part of study. As an example, the Qlife SIBA-rt-PCR and the Acro RAT presented the highest analytical sensitivity, but both tests performed significantly worse than the Acon Flowflex RAT in the prospective part of the study. Our data shows that anterior nasal cavity RAT in general had higher sensitivity compared to deep oropharyngeal RAT and RAT using saliva for testing performed the

worst. This may indicate that the Acro RAT using deep oropharyngeal swabs is underperforming in the prospective part of the study as anterior nasal cavity swabs may be a better testing material. Surprisingly, the Qlife SIBA-rt-PCR performed with an unexpected low sensitivity and specificity in the prospective part of the study. This may be due to the small sample volume being used for the test. Furthermore, results were reported by the automated Egoo instrument result-algorithm, which is still under development and previous evaluations of the Qlife SIBA-rt-PCR have been conducted by visual inspection of results instead of the automated result determination [22]. A more general concern regarding the comparison of retrospective and prospective results is that the sampling step, release of material and lysis material from the swab in the lysis buffer are removed from the comparison in retrospective studies, which may lead to underperformance of clinically optimized RAT in analytical studies.

The primary strength of this study is that we can identify RAT that perform significantly better than other RAT included in the study, as we report analytical as well as clinical performance data for a large number of commercially available RAT and compare the RAT performance to the same RT-qPCR test on the same samples.

This study has several limitations. First, it is important to emphasize that the study was designed to compare performance differences between the included RAT. The data reported in this study cannot be used to predict the sensitivity of a certain RAT in a specific clinical setting. Second, as the out-patient testing teams knew the RT-qPCR result of the included individual prior to sampling and testing by RAT, and as even a weak band should be regarded as a positive test result, the prospective part of the study is biased towards overestimating the sensitivity of each RAT. Third, the current study is likely to overestimate the clinical sensitivity of the included RAT as the study was performed prior to vaccination of the participating age groups. It has previously been shown that vaccination accelerates viral clearance, which may reduce the amount of viral particles released by infected individuals and thereby narrows the time period for a positive RAT [23]. Finally, at the time of the study, the predominant variant of SARS-CoV-2 was the B.1.1.7 alpha variant with few cases of the delta variant (B.1.617.2). It has previously been shown that different SARS-CoV-2 variants may influence the analytical sensitivity of different RAT [14], which may translate to differences in clinical sensitivity of RAT if other SARS-CoV-2 variants are predominant [9].

In conclusion, this study compares analytical and clinical sensitivities to RT-qPCR of 46 commercially available RAT and enables identification of individual RAT that has significant higher sensitivity than other included RAT. The study demonstrates significant differences in analytical as well as clinical sensitivities between the included RAT but cannot be used for prediction of the clinical sensitivity in a specific clinical

setting. The results reported in this study may guide decision makers prior to purchase of RAT for population screening.

Acknowledgments

All participating companies contributed with a participant's fee to cover the costs of the study and delivered all necessary RAT and additional materials free of charge. The authors thank bioinformatician Jose Castruita for assisting with the variant analysis of the SARS-CoV-2 positive samples.

Authors' contributions

UVS, JGL, and JDK conceptuated the study. UVS and JGL were responsible for the funding acquisition. Acquisition of data was conducted by UVS, MWF, TDL, CBJ, KG, CNA, KKM, CSJ, HL, MBJ, US, AK, NSK, The National Danish RAT testing group, MLS, FHJ, RLJ, CMGM, NS, and JGL. Local supervision of research activity was conducted by MWF, CNA, KKM, AC, NS, CSJ, HL, MBH, US, AK, and NSK. Overall project administration was conducted by UVS, MWF, AC, CSJ, JDK, and JGL. Data was curated by CBJ, KG, MWF, CNA, KKM, CSJ, US, NSK, UVS, and JGL. Data was validated by or under supervision of MWF, CBJ, CNA, KKM, CSJ, HL, US, NSK, RLJ, JGL, and UVS. TK and UVS performed the formal analysis of data.

UVS and JGL drafted the manuscript with substantial input from JDK. All authors read and commented on the manuscript and all authors approved the final manuscript prior to submission. All authors agree to be held accountable for all aspects of the work.

Conflict of interest

Lars Østergaard has within 36 months received speaker fees from Sanofi-Pasteur and Pfizer. None of the other authors have any personal conflict of interests to report. The project received a participation fee from each of the participating companies to cover the cost of the project.

Ethics committee approval

The study was evaluated by the National Committee on Health Research Ethics in the Danish Capital Region to be a method validation study without the need of approval of the committee (decision H-20068579). Access to test results for research was granted by the Capital Region of Denmark – Research and Innovation (R-20083753) and contact to participants without prior consent from the individual was granted by the board of directors at the Hospitals at which the participating DCM are situated.

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Table 1

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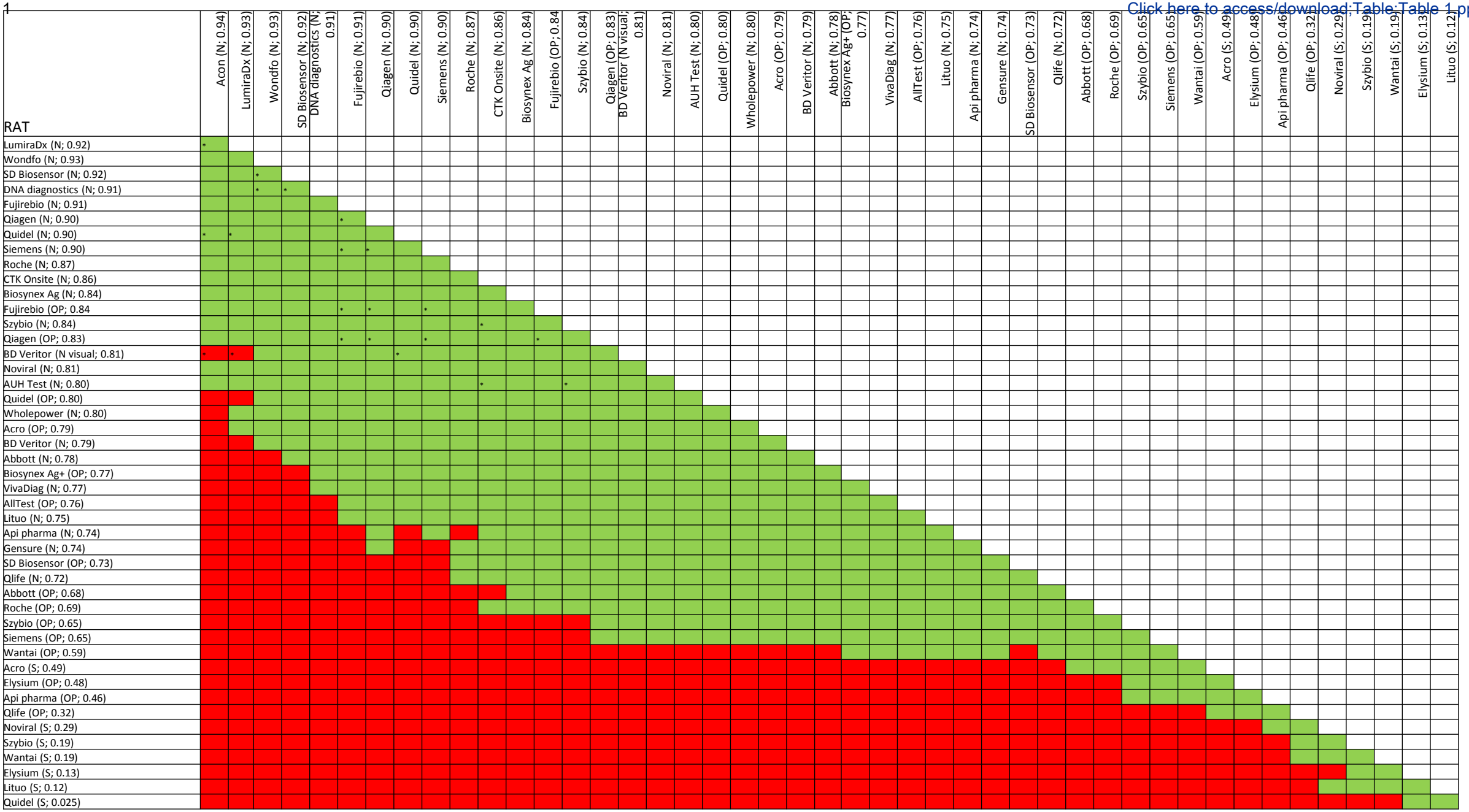
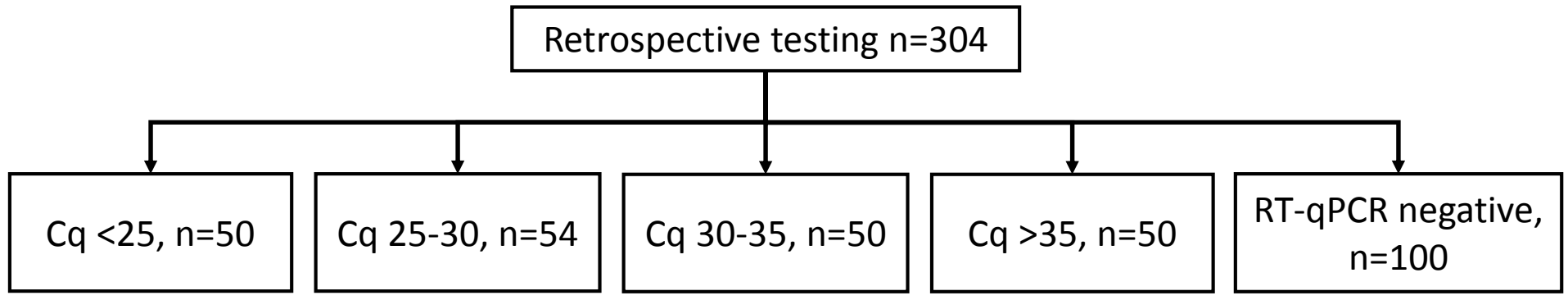


Table 1 Comparison of clinical sensitivity between RAT. Green fields are non-significant differences, red are significant differences in clinical sensitivity. N anterior nasal cavity swabs, OP deep oropharyngeal swabs, S saliva. Sensitivity is reported in brackets. Details for calculation are included in Supplementary data.

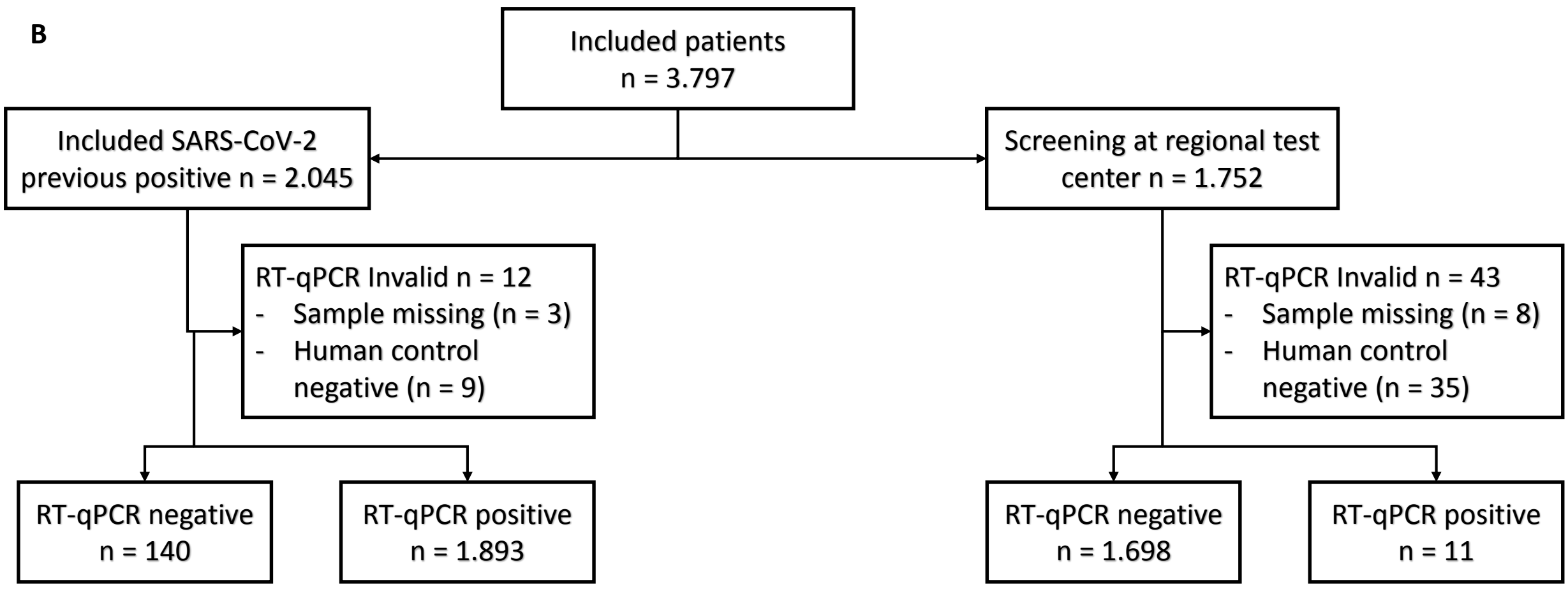
Figure 1A

Click here to access/download;Figure;Figure 1A STARD diagram.pptx

A



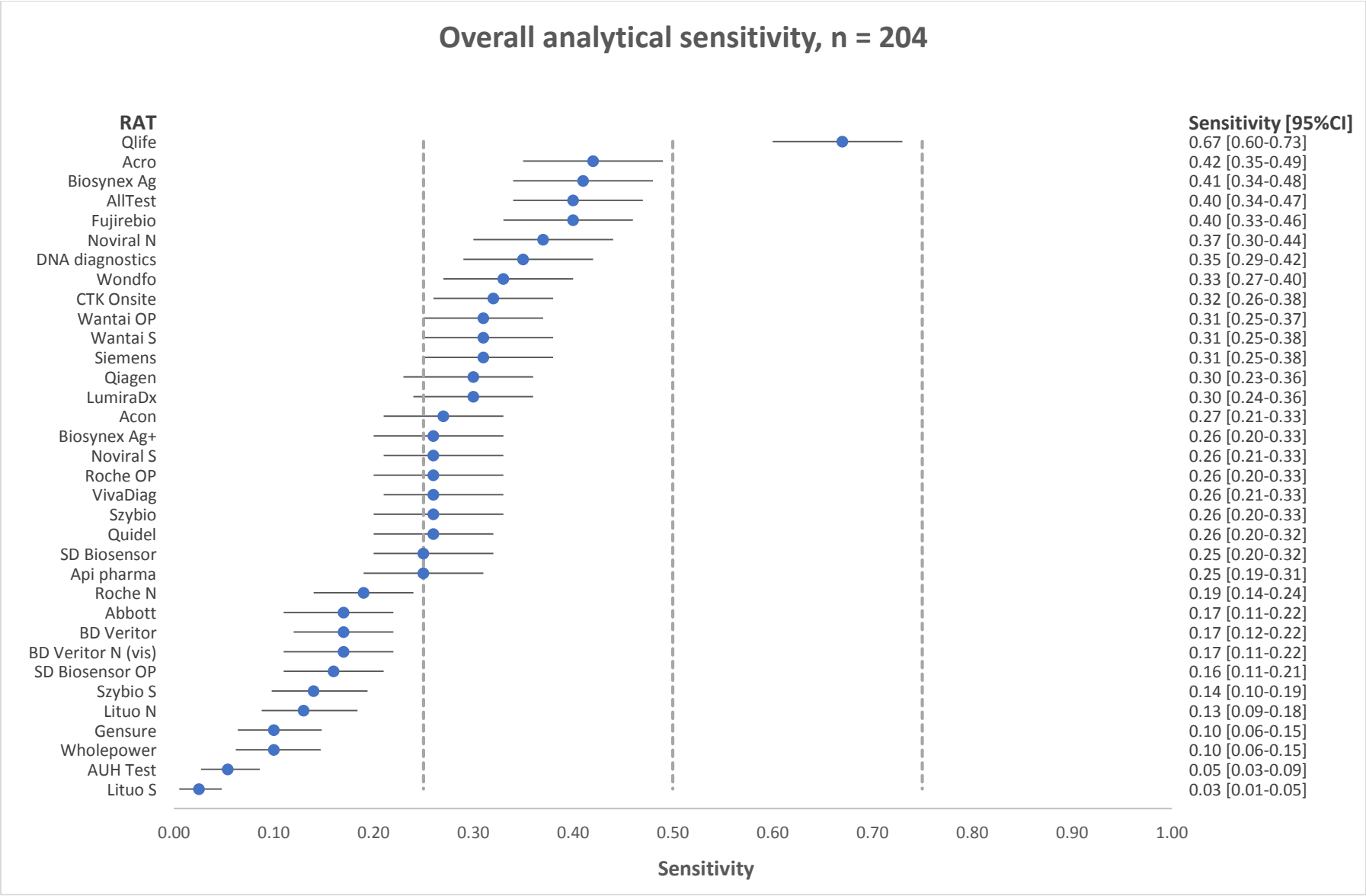
	Cq <25, n=50	Cq 25-30, n=54	Cq 30-35, n=50	Cq >35, n=50	RT-qPCR negative, n=100
Abbott	TP 22, FN 28, Inv 0	TP 12, FN 42, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Acon	TP 38, FN 12, Inv 0	TP 17, FN 37, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Acro	TP 50, FN 0, Inv 0	TP 33, FN 21, Inv 0	TP 3, FN 47, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
AllTest	TP 47, FN 3, Inv 0	TP 35, FN 19, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Api pharma	TP 38, FN 12, Inv 0	TP 13, FN 41, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
AUH Test	TP 9, FN 41, Inv 0	TP 1, FN 53, Inv 0	TP 0, FN 50, Inv 0	TP 1, FN 49, Inv 0	TN 100, FP 0, Inv 0
BD Veritor	TP 25, FN 25, Inv 0	TP 10, FN 44, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
BD Veritor N (visual)	TP 25, FN 25, Inv 0	TP 9, FN 45, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Biosynex Ag	TP 48, FN 2, Inv 0	TP 31, FN 23, Inv 0	TP 5, FN 45, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Biosynex Ag+	TP 41, FN 9, Inv 0	TP 13, FN 41, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
CTK Onsite	TP 42, FN 8, Inv 0	TP 23, FN 31, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
DNA diagnostics	TP 41, FN 5, Inv 4	TP 29, FN 25, Inv 0	TP 1, FN 49, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Fujirebio	TP 50, FN 0, Inv 0	TP 31, FN 23, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Gensure	TP 19, FN 31, Inv 0	TP 2, FN 52, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Lituo N	TP 23, FN 27, Inv 0	TP 4, FN 50, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Lituo S	TP 5, FN 45, Inv 0	TP 0, FN 54, Inv 0	TP 0, FN 49, Inv 1	TP 0, FN 49, Inv 1	TN 100, FP 0, Inv 0
LumiraDx	TP 39, FN 11, Inv 0	TP 21, FN 33, Inv 0	TP 1, FN 49, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Noviral N	TP 50, FN 0, Inv 0	TP 25, FN 29, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Noviral S	TP 43, FN 7, Inv 0	TP 0, FN 54, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Qiagen	TP 45, FN 5, Inv 0	TP 0, FN 54, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Qlife	TP 50, FN 0, Inv 0	TP 50, FN 4, Inv 0	TP 30, FN 20, Inv 0	TP 6, FN 44, Inv 0	TN 93, FP 7, Inv 0
Quidel	TP 37, FN 13, Inv 0	TP 16, FN 38, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Roche N	TP 27, FN 23, Inv 0	TP 12, FN 42, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Roche OP	TP 43, FN 7, Inv 0	TP 10, FN 43, Inv 1	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
SD Biosensor	TP 40, FN 10, Inv 0	TP 12, FN 42, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
SD Biosensor OP	TP 23, FN 27, Inv 0	TP 10, FN 44, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Siemens	TP 44, FN 6, Inv 0	TP 20, FN 34, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Szybio	TP 40, FN 10, Inv 0	TP 14, FN 40, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Szybio S	TP 23, FN 27, Inv 0	TP 6, FN 48, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
VivaDiag	TP 37, FN 13, Inv 0	TP 16, FN 38, Inv 0	TP 1 FN 49, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Wantai OP	TP 40, FN 10, Inv 0	TP 23, FN 31, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Wantai S	TP 42, FN 8, Inv 0	TP 21, FN 33, Inv 0	TP 1, FN 49, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Wholepower	TP 14, FN 36, Inv 0	TP 7, FN 47, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0
Wondfo	TP 43, FN 7, Inv 0	TP 25, FN 29, Inv 0	TP 0, FN 50, Inv 0	TP 0, FN 50, Inv 0	TN 100, FP 0, Inv 0



TN 7, FP 0, Inv 0	TP 143, FN 64, Inv 1	Abbott (OP) n=390	TN 171, FP 0, Inv 0	TP 0, FN 4, Inv 0
TN 6, FP 1, Inv 0	TP 163, FN 44, Inv 0	Abbott (N n=390	TN 169, FP 3, Inv 0	TP 0, FN 3, Inv 1
TN 5, FP 0, Inv 0	TP 187, FN 12, Inv 0	Acon (N) n=414	TN 210, FP 0, Inv 0	TP 0, FN 0, Inv 0
TN 13, FP 1, Inv 0	TP 172, FN 46, Inv 0	Acro (OP) n=429	TN 196, FP 0, Inv 0	TP 0, FN 1, Inv 0
TN 13, FP 1, Inv 0	TP 100, FN 106, Inv 12	Acro (S) n=428	TN 174, FP 1, Inv 20	TP 0, FN 1, Inv 0
TN 31, FP 0, Inv 0	TP 155, FN 49, Inv 1	Alltest (OP) n=407	TN 169, FP 0, Inv 0	TP 1, FN 1, Inv 0
TN 11, FP 0, Inv 0	TP 92, FN 109, Inv 4	Api pharma (OP) n=413	TN 196, FP 0, Inv 0	TP 1, FN 0, Inv 0
TN 10, FP 1, Inv 0	TP 146, FN 53, Inv 6	Api pharma (N) n=412	TN 195, FP 0, Inv 0	TP 1, FN 0, Inv 0
TN 7, FP 0, Inv 0	TP 145, FN 36, Inv 3	AUH Test (N) n=376	TN 184, FP 1, Inv 0	TP 0, FN 0, Inv 0
TN 5, FP 0, Inv 0	TP 158, FN 41, Inv 0	BD Veritor (N) n=411	TN 207, FP 0, Inv 0	TP 0, FN 0, Inv 0
TN 5, FP 0, Inv 0	TP 165, FN 39, Inv 1	BD Veritor (N) vis n=422	TN 212, FP 0, Inv 0	TP 0, FN 0, Inv 0
TN 13, FP 1, Inv 0	TP 183, FN 35, Inv 0	Biosynex Ag (N) n=434	TN 201, FP 0, Inv 0	TP 0, FN 1, Inv 0
TN 14, FP 0, Inv 0	TP 165, FN 51, Inv 0	Biosynex Ag+ (OP) n=414	TN 183, FP 0, Inv 0	TP 0, FN 1, Inv 0
TN 9, FP 0, Inv 0	TP 184, FN 30, Inv 1	CTK onsite (N) n=420	TN 193, FP 0, Inv 2	TP 0, FN 1, Inv 0
TN 23, FP 1, Inv 0	TP 202, FN 18, Inv 1	DNA diagnostic (N) n=418	TN 169, FP 0, Inv 0	TP 1, FN 1, Inv 2
TN 7, FP 0, Inv 0	TP 101, FN 107, Inv 1	Elysium (OP) n=391	TN 171, FP 0, Inv 0	TP 1, FN 3, Inv 0
TN 7, FP 0, Inv 0	TP 27, FN 179, Inv 3	Elysium (S) n=388	TN 167, FP 1, Inv 0	TP 0, FN 4, Inv 0
TN 22, FP 0, Inv 0	TP 172, FN 30, Inv 0	Fujirebio (OP) n=465	TN 229, FP 0, Inv 10	TP 0, FN 2, Inv 0
TN 22, FP 0, Inv 0	TP 183, FN 18, Inv 1	Fujirebio (N) n=441	TN 196, FP 0, Inv 19	TP 0, FN 1, Inv 1
TN 13, FP 4, Inv 0	TP 150, FN 54, Inv 1	Gensure (N) n=424	TN 200, FP 0, Inv 1	TP 0, FN 1, Inv 0
TN 13, FP 1, Inv 0	TP 160, FN 54, Inv 4	Lituo (N) n=450	TN 216, FP 0, Inv 2	TP 0, FN 0, Inv 0
TN 13, FP 0, Inv 1	TP 26, FN 184, Inv 8	Lituo (S) n=447	TN 206, FP 2, Inv 7	TP 0, FN 0, Inv 0
TN 5, FP 0, Inv 0	TP 193, FN 15, Inv 0	Lumiradx (N) n=416	TN 202, FP 0, Inv 0	TP 1, FN 0, Inv 0
TN 6, FP 1, Inv 0	TP 169, FN 39, Inv 1	Noviral (N) n=389	TN 168, FP 1, Inv 0	TP 1, FN 1, Inv 2
TN 7, FP 0, Inv 0	TP 59, FN 147, Inv 3	Noviral (S) n=384	TN 162, FP 1, Inv 1	TP 1, FN 3, Inv 0
TN 21, FP 0, Inv 1	TP 167, FN 35, Inv 0	Qiagen (OP) n=430	TN 206, FP 0, Inv 0	TP 0, FN 0, Inv 0
TN 22, FP 0, Inv 0	TP 180, FN 21, Inv 1	Qiagen (N) n=430	TN 206, FP 0, Inv 0	TP 0, FN 0, Inv 0
TN 16, FP 1, Inv 0	TP 66, FN 142, Inv 0	Qlife (OP) n=389	TN 162, FP 2, Inv 0	TP 0, FN 0, Inv 0
TN 11, FP 6, Inv 0	TP 150, FN 59, Inv 0	Qlife (N) n=447	TN 220, FP 1, Inv 0	TP 0, FN 0, Inv 0
TN 5, FP 0, Inv 0	TP 160, FN 40, Inv 7	Quidel (OP) n=392	TN 176, FP 0, Inv 4	TP 0, FN 0, Inv 0
TN 5, FP 0, Inv 0	TP 185, FN 20, Inv 3	Quidel (N) n=368	TN 145, FP 0, Inv 10	TP 0, FN 0, Inv 0
TN 4, FP 1, Inv 0	TP 5, FN 199, Inv 3	Quidel (S) n=366	TN 146, FP 0, Inv 8	TP 0, FN 0, Inv 0
TN 11, FP 0, Inv 0	TP 140, FN 65, Inv 0	Roche (OP) n=406	TN 190, FP 0, Inv 0	TP 0, FN 0, Inv 0
TN 10, FP 1, Inv 0	TP 177, FN 28, Inv 0	Roche (N) n=403	TN 187, FP 0, Inv 0	TP 0, FN 0, Inv 0
TN 24, FP 0, Inv 0	TP 162, FN 60, Inv 0	SD Biosensor (OP) n=441	TN 194, FP 0, Inv 0	TP 0, FN 1, Inv 0
TN 22, FP 2, Inv 0	TP 204, FN 17, Inv 0	SD Biosensor (N) n=440	TN 194, FP 0, Inv 0	TP 0, FN 1, Inv 0
TN 31, FP 0, Inv 0	TP 132, FN 72, Inv 1	Siemens (OP) n=407	TN 169, FP 0, Inv 0	TP 1, FN 1, Inv 0
TN 22, FP 0, Inv 0	TP 182, FN 20, Inv 0	Siemens (N) n= 450	TN 225, FP 0, Inv 0	TP 0, FN 1, Inv 0
TN 9, FP 0, Inv 0	TP 140, FN 75, Inv 0	Szybio (OP) n=411	TN 187, FP 0, Inv 0	TP 0, FN 0, Inv 0
TN 9, FP 0, Inv 0	TP 178, FN 34, Inv 3	Szybio (N) n=411	TN 187, FP 0, Inv 0	TP 0, FN 0, Inv 0
TN 9, FP 0, Inv 0	TP 40, FN 170, Inv 5	Szybio (S) n=396	TN 172, FP 0, Inv 0	TP 0, FN 0, Inv 0
TN 30, FP 0, Inv 0	TP 158, FN 47, Inv 0	VivaDiag (N) n=406	TN 166, FP 0, Inv 3	TP 1, FN 1, Inv 0
TN 23, FP 1, Inv 0	TP 130, FN 91, Inv 1	Wantai (OP) n=469	TN 214, FP 3, Inv 4	TP 0, FN 2, Inv 0
TN 23, FP 0, Inv 0	TP 39, FN 170, Inv 0	Wantai (S) n=449	TN 206, FP 2, Inv 7	TP 0, FN 2, Inv 0
TN 6, FP 1, Inv 0	TP 166, FN 41, Inv 1	Wholepower (N) n=417	TN 200, FP 0, Inv 1	TP 0, FN 1, Inv 0
TN 21, FP 2, Inv 1	TP 204, FN 14, Inv 3	Wondfo (N) n=468	TN 217, FP 0, Inv 4	TP 0, FN 2, Inv 0

Figure 1 STARD diagram. A, retrospective study part reporting RAT results compared to RT-qPCR stratified into Cq ranges. B, prospective clinical study part reporting data from individuals, who were either included due to a positive RT-qPCR test for SARS-CoV-2 or being tested as part of screening for SARS-CoV-2. For each RAT the total number of tests is reported together with the distribution compared to RT-qPCR. FN false negative, FP false positive, Inv invalid RAT, TN true negative, TP true positive. N anterior nasal cavity sampling, OP deep oropharyngeal sampling, S saliva.

Figure 2



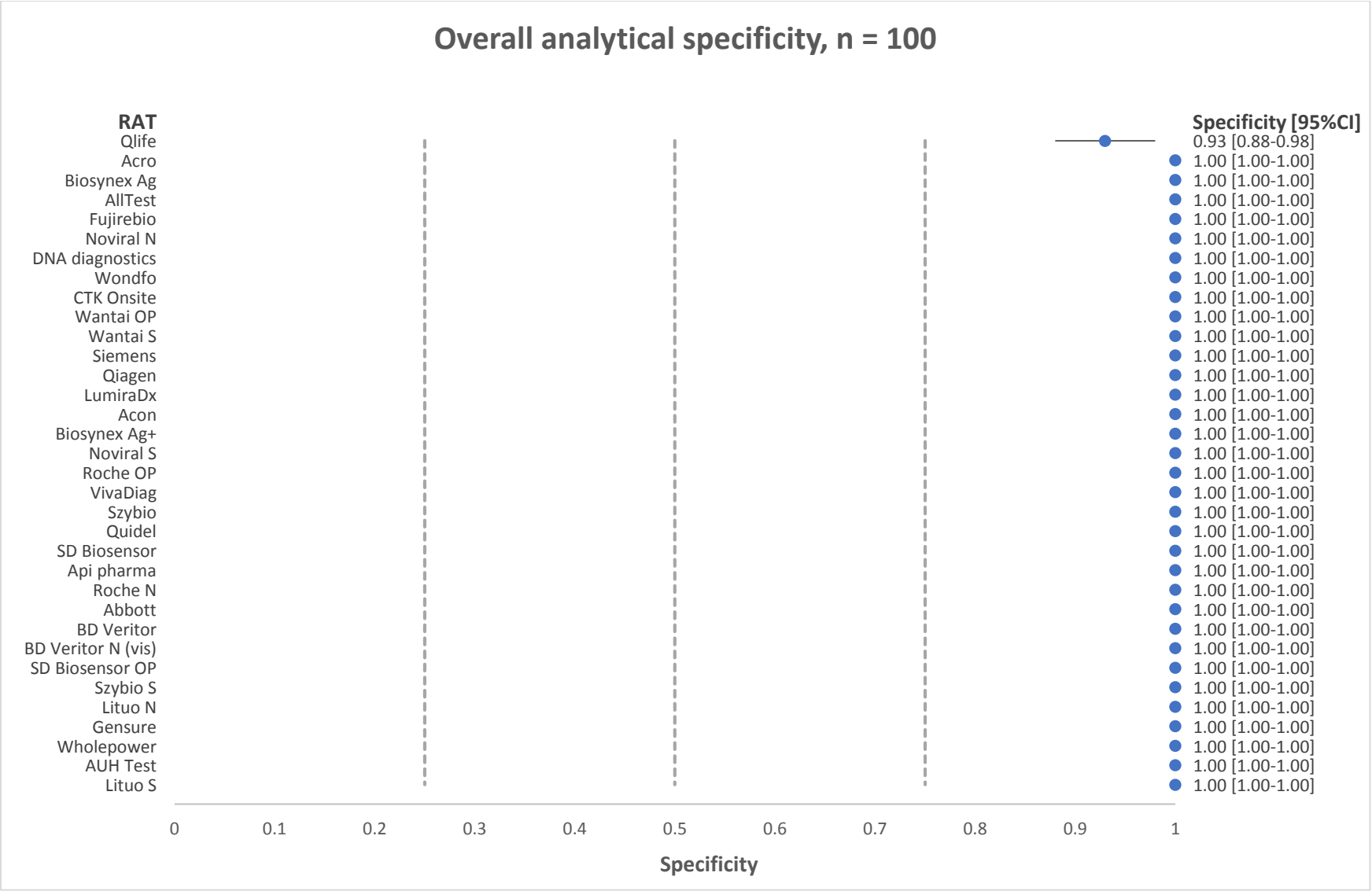
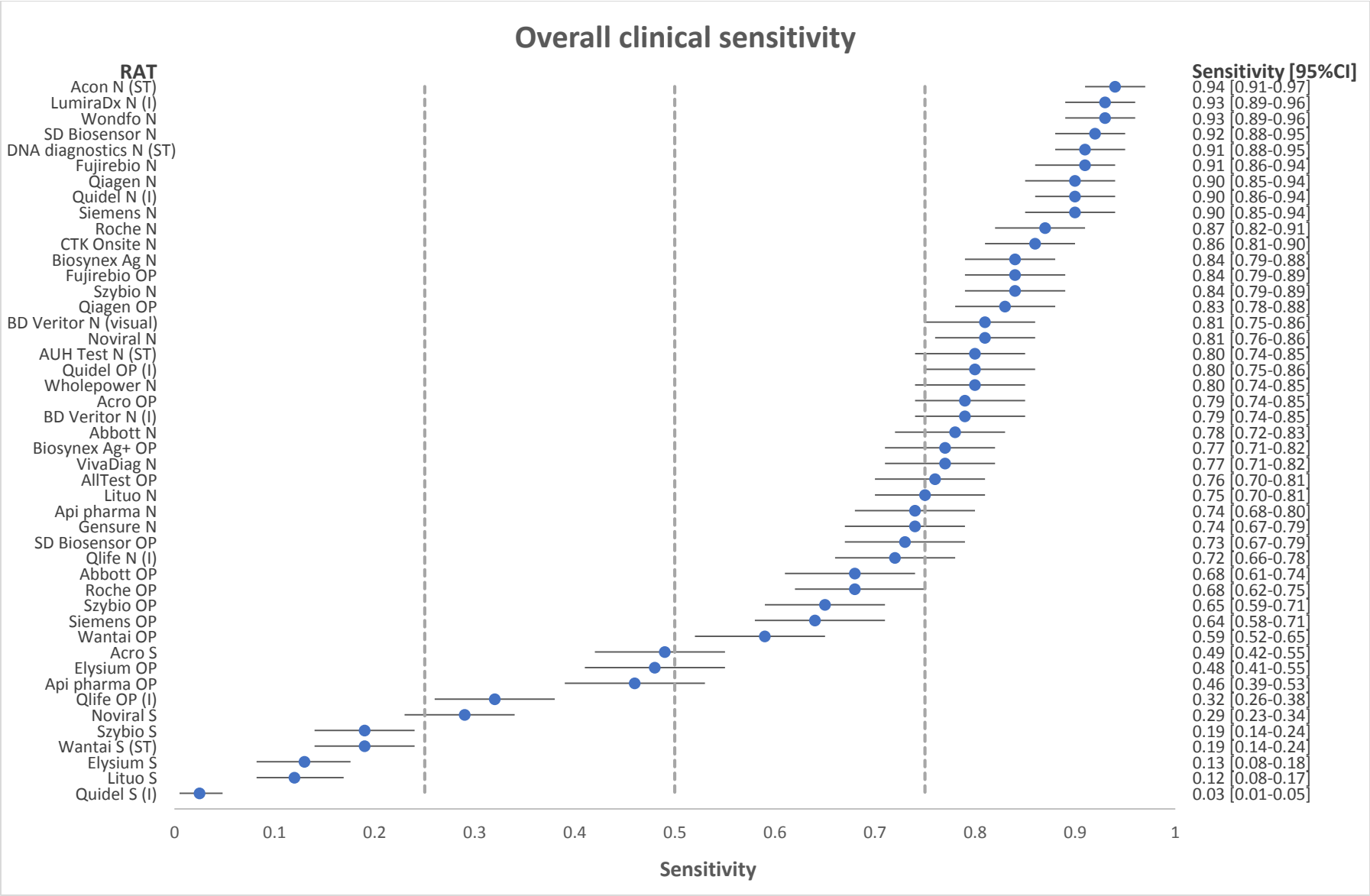


Figure 2 Overall analytical sensitivity and specificity of 33 RAT and one SIBA-rt-PCR test. Sensitivity and specificity are reported as mean with 95% CI and is based on 50 samples with Cq <25, 54 samples with Cq between 25 to 30, 50 samples with Cq between 30 to 35 and 50 samples with Cq >35 by RT-qPCR.

Figure 3

Click here to access/download;Figure;Figure 3 JCV.docx



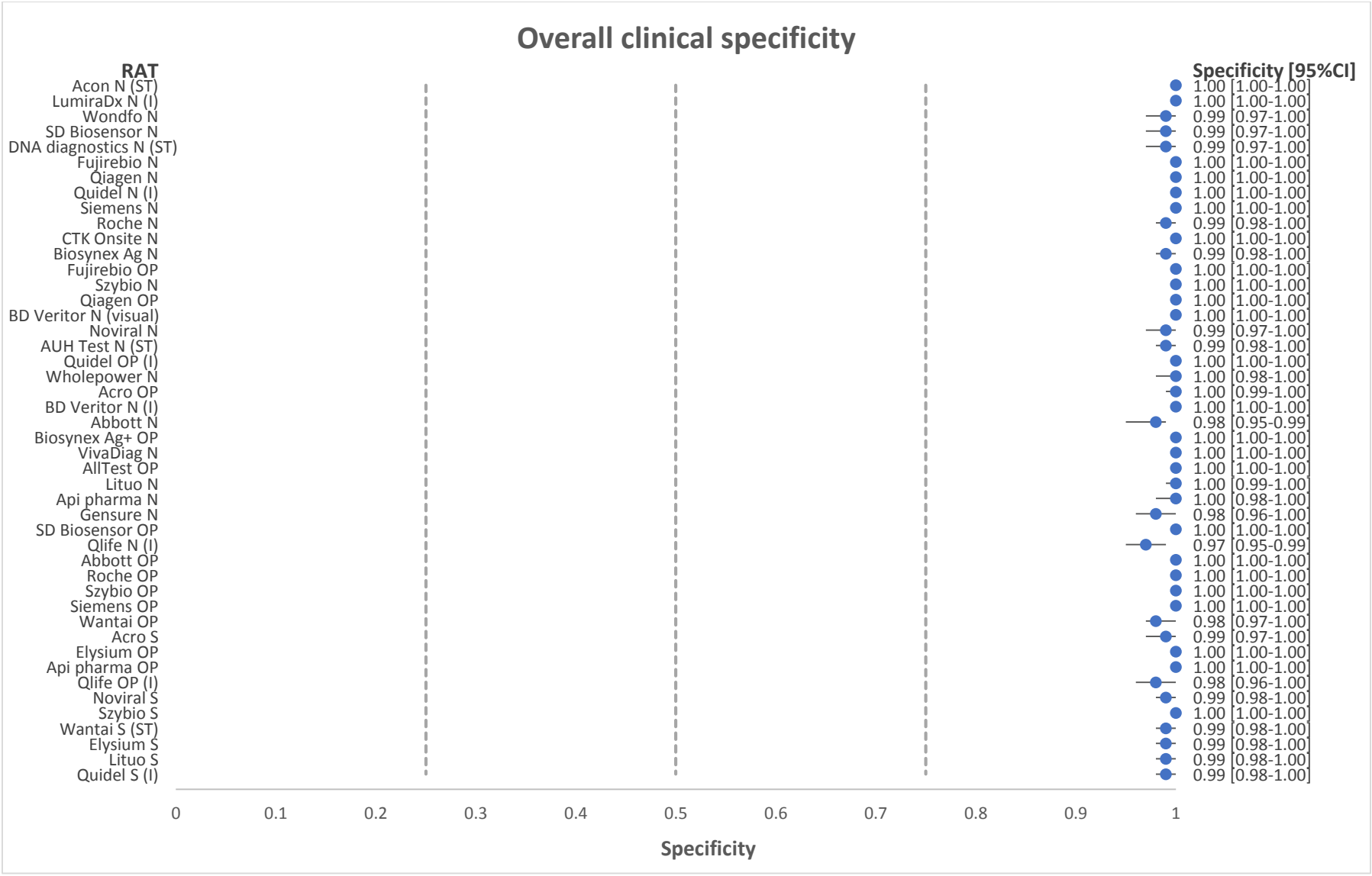


Figure 3 Overall clinical sensitivity and specificity of 44 RAT and two SIBA-rt-PCR tests. Sensitivity and specificity are reported as mean with 95% CI. N are anterior nasal cavity swabs, OP are deep oropharyngeal swabs and S are saliva based RAT. ST are self-test, I are instrument read-out tests and visual means that the RAT was evaluated visually instead of by instrumental read-out.