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Increasing test specificity without impairing sensitivity: lessons learned from SARS-CoV-2 serology

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With support from BBMRI.at partner Med Uni Wien Biobank researchers from Vienna used samples from Austrian cohorts to investigate sensitivity and specificity of test systems. In their publication, they propose a novel testing strategy to increase the specificity of tests without compromising their sensitivity.

Serological tests are often poor with respect to sensitivity and specificity and leave room for false-positive and false-negative results.

On the example of COVID-19, the researchers from Med Uni Wien & Biobank tested five different serologic antibody SARS-CoV-2 tests. The scientists now propose a novel test algorithm - termed 'sensitivity-improved two-test, SIT²'. For developing and testing the algorithm samples from an Austrian cohort stored at and managed by Med Uni Wien Biobank were used.

Read original article:

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Original research

Increasing test specificity without impairing sensitivity: lessons learned from SARS-CoV-2 serology

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ABSTRACT
 Background: Serological tests are widely used in various medical disciplines for diagnostic and monitoring purposes. Unfortunately, the sensitivity and specificity of test systems are often poor, leaving room for false-positive and false-negative results. However, conventional methods were used to increase specificity and decrease sensitivity and vice versa. Using SARS-CoV-2 serology as an example, we propose here a novel testing strategy: the sensitivity-improved two-test (SIT² algorithm).
 Methods: SIT² involves confirmatory retesting of samples with results falling in a predefined receiving zone of an initial screening test, with adjusted cut-offs to increase sensitivity. We applied and compared the performance of SIT² to single tests and orthogonal testing (OTA) in an Austrian cohort (N=117) negative, 64 post-COVID-positive samples) and validated the algorithm in an independent British cohort (N=576) negative and 539 positive.
 Results: The specificity of SIT² was superior to single tests and non-inferior to OTA. The sensitivity was maintained or even improved using SIT² when compared with single tests or OTA. SIT² allowed correct identification of infected individuals even when a serologic neutralisation assay could not detect antibodies. Compared with single testing (OTA), SIT² significantly reduced test errors to 0.48% (0.24–0.65) or 1.60% (0.94–2.28) at each 5% or 20% seroprevalence.
 Conclusion: For SARS-CoV-2 serology, SIT² proved to be the best diagnostic choice at both 5% and 20% seroprevalence in all tested scenarios. It is an easy to apply algorithm and can potentially be helpful for the serology of other infectious diseases.

WHAT IS ALREADY KNOWN ON THIS TOPIC
 Serological tests are widely used throughout medical disciplines. When a serological assay is to be established, usually a threshold is defined above or below which a result is considered positive or negative. This cut-off comes with a direct sensitivity and specificity. Sensitivity and specificity are conflictingly related—increasing one comes at the cost of the other. Common serological testing algorithms concentrate on confirming positive cases, thereby increasing specificity, but decreasing sensitivity.

WHAT THIS STUDY ADDS
 Here, we propose a novel serological test algorithm applying serological assays with adjusted cut-offs. The reduction of the thresholds for positivity in both the screening and confirmation tests as well as the additional introduction of a high cut-off in the screening test, above which no further confirmation is required, allows to increase the specificity without compromising the sensitivity. This algorithm, which we termed sensitivity-improved two-test, SIT², was derived in an Austrian cohort using five different SARS-CoV-2 antibody tests and validated in an independent UK cohort.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY
 This paper clearly shows that, in the case of SARS-CoV-2 serology, the use of this sensitivity-improved test system allowed for increasing test specificity without impairing its sensitivity. This is of specific interest, when an emerging pandemic looks to be spreading widely—as in this case, serological tests should not be further impaired. Furthermore, we are confident that the principle of SIT² is universally applicable and that this algorithm could also be used with serological assays other than those for SARS-CoV-2.

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