Estimate false-negative RT-PCR rates for SARS-CoV-2. A systematic review and meta-analysis

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1

Summary

Molecular-based tests used to identify symptomatic or asymptomatic patients infected by SARS-CoV-2 are characterized by high specificity but scarce sensibility, generating false negative results with important implications for the correct identification of infected patients and subsequent repercussions on the entire community. We aimed to estimate, through a systematic review of the literature, the rate of RT-PCR false-negatives at initial testing for COVID-19. We systematically searched Pubmed, Embase, and CENTRAL as well as a list of reference literature. We included observational studies enrolling subject collected samples from respiratory tract to detect SARS-CoV-2 RNA using RT-PCR, reporting the number of false negative subjects and the number of final patients with a COVID-19 diagnosis. Reported rates of false negatives were pooled in a meta-analysis as appropriate. We assessed the risk of bias of included studies and graded the quality of evidence according to the GRADE method. All information in this article is current up to February 2021. We included 32 studies, enrolling more than 18,000 patients infected by SARS-CoV-2. The overall false negative rate was of 0.12 (95%CI from 0.10 to 0.14) with very low certainty of evidence. The impact of misdiagnoses was estimated according to disease prevalence; a range between 2 –58/1,000 subjects could be misdiagnosed with a disease prevalence of 10%,increasing to 290/1,000 misdiagnosed subjects with a disease prevalence of 50%. This systematic review showed that up to 58% of COVID-19 patients may have initial false-negative RT-PCR results, suggesting the need to implement a correct diagnostic strategy to correctly identify suspected cases, thereby reducing false negative results and decreasing the disease burden among the population.

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