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# SARS-CoV-2 RT-qPCR Test Detection Rates Are Associated with Patient Age, Sex, and Time since Diagnosis



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Quantifying the detection rate of the widely used quantitative RT-PCR (RT-qPCR) test for severe acute respiratory syndrome coronavirus 2 and its dependence on patient demographic characteristics and disease progression is key in designing epidemiologic strategies. Analyzing 843,917 test results of 521,696 patients, a “positive period” was defined for each patient between diagnosis of coronavirus disease 2019 and the last positive test result. The fraction of positive test results within this period was then used to estimate detection rate. Regression analyses were used to determine associations of detection with time of sampling after diagnosis, patient demographic characteristics, and viral RNA copy number based on RT-qPCR cycle threshold values of the next positive test result. The overall detection rate in tests performed within 14 days after diagnosis was 83.1%. This rate was higher at days 0 to 5 after diagnosis (89.3%). Furthermore, detection rate was strongly associated with age and sex. Finally, the detection rate with the Allplex 2019-nCoV RT-qPCR kit was associated, at the single-patient level, with viral RNA copy number ( $P < 10^{-9}$ ). These results show that the reliability of the test result is reduced in later days as well as for women and younger patients, in whom the viral loads are typically lower. (*J Mol Diagn* 2022, 24: 112–119; <https://doi.org/10.1016/j.jmoldx.2021.10.010>)

The ongoing coronavirus disease 2019 (COVID-19) pandemic has already infected tens of millions of individuals worldwide. A major tool in combating the pandemic is testing for viral carriage, which is used for both diagnostic and epidemiologic purposes. The most commonly used viral detection tests are based on quantitative RT-PCR (RT-qPCR) of viral genes. This nucleic acid test is of high specificity (ie, very low false-positive rate).<sup>1–4</sup> In contrast, the false-negative rate of these tests has often been reported as high.<sup>5–9</sup> High false-negative rates may impede local and global efforts to slow down disease spread, as patients incorrectly diagnosed as noncarriers might pose an obstacle for efforts such as contact tracing.<sup>10–12</sup> Systematically quantifying the rate of detection and its dependencies on disease progression and patient demographic characteristics is therefore critical for disease spread modeling and public health policy-making.

Various approaches have been taken to estimate the false-negative rate of COVID-19 RT-qPCR tests. Measuring the rate of false-negative results in a population of patients with highly specific pathologies (eg, chest CT imaging) has initially alerted physicians and epidemiologists of the high false-negative rate, estimated at approximately 30%.<sup>3–6,8,13–16</sup> A meta-analysis of multiple such studies found that the reported rates were highly variable, with a mean false-negative rate of 11%.<sup>17</sup> However, and as noted previously,<sup>17,18</sup> these meta-analysis studies were necessarily based on a combination of variable studies of nonuniform

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