

# **The probability of detection of SARS-CoV-2 in saliva**

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## **MAIN TEXT**

To the editor – It has recently been suggested that saliva tests might provide a useful diagnostic tool for patients infected by the novel coronavirus that has caused over 92,000 cases worldwide (as of 3 March 2020). Diagnosing coronavirus disease (COVID-19) from saliva samples has advantages compared to more invasive procedures based on nasopharyngeal or oropharyngeal samples. We conducted a literature search using PubMed and found nine articles about “saliva AND coronaviruses AND detection”. Out of these, there was a single publication reporting data about the reliability of saliva testing for detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)<sup>1</sup>.

In that study<sup>1</sup>, the authors detected SARS-CoV-2 in the initial saliva specimens of 11 out of 12 patients shown by laboratory confirmation to be carrying the virus. This corresponds to 91.7% of those tested. This indicates positive identification using saliva samples is often likely. However,

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it is important to emphasise the limits to conclusions that can be drawn from such a small cohort of patients. We have therefore constructed a range of intervals characterising the uncertainty in the probability of detection of SARS-CoV-2 in the saliva of infected patients.

If the sensitivity of the test<sup>2</sup> (i.e., the probability of finding the virus in an initial sample from an infected patient, reported as a value between zero and one) is denoted by  $p$ , then various methods allow an interval describing uncertainty in the value of  $p$  to be computed. All depend on the data and, particularly, the number of patients tested. Methods include traditional approaches to find confidence intervals on  $p$ , as well as Bayesian methods to derive credible intervals for  $p$ .

The 95% Clopper-Pearson<sup>3</sup> confidence interval on  $p$  is 0.615-0.998 (Figure 1). The equivalent Wilson score<sup>4</sup> interval is 0.646-0.985. Taking a Bayesian approach<sup>5</sup> with an uninformative prior (see Supplementary Information) leads to a highest density credible interval for  $p$  of 0.681-0.995. The equal-tailed credible interval is 0.640-0.981. The technical details and assumptions of the various methods are unimportant, as are the precise meanings of the different intervals. Our point is simply that positive detection in 11 out of only 12 individuals does not necessarily mean that SARS-CoV-2 will be detected in the saliva of at least 90% of infected patients, or even anything like it. Instead, all that can be said is that the virus will be detected in initial saliva samples of around 60%-99% of infected individuals. Only by testing more infected patients can this uncertainty be resolved.

It is also important to consider how any new test will be used in practice. If saliva samples are being proposed to reduce the risk of nosocomial transmission by confirming that inpatients are

not infected by SARS-CoV-2, then it is at least as important to assess the predictive value of a negative test result (i.e., the proportion of suspected cases with negative tests who are not carrying the virus, as well as the corresponding uncertainty).

Despite these provisos, successful detection of SARS-CoV-2 in the saliva of 11 out of 12 patients is promising. Sampling and testing saliva samples could provide an easy-to-use diagnostic method for COVID-19, and other diagnostic methods do not have perfect sensitivity either. For other respiratory viruses, saliva testing has been found to have similar sensitivity compared to detection using nasopharyngeal swab specimens<sup>6</sup>. However, for SARS-CoV-2, additional data must be collected to reduce the current uncertainty in the sensitivity of saliva tests due to the limited number of patients tested, and to understand the predictive value of a negative test, as well as to explore the effects of other factors (e.g., temporal variations in detectability of the virus in saliva during the course of infection). This is of clear public health importance.

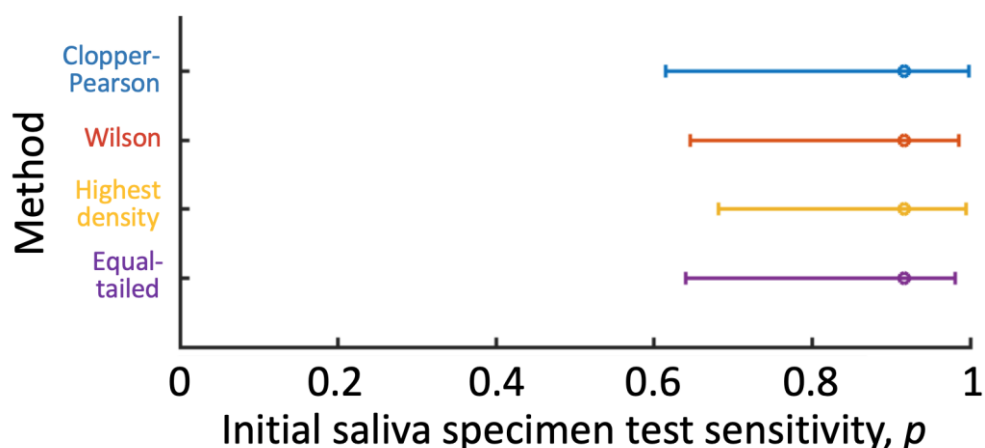


Figure 1. Estimated values of the probability of finding SARS-CoV-2 in the initial saliva sample from an infected patient ( $p$ ). 95% confidence intervals according to the Clopper-Pearson interval (blue) and Wilson score interval

(red), and 95% Bayesian credible intervals according to the highest density (yellow) and equal-tailed (purple) metrics (see Supplementary Information). The observed proportion in the sample ( $11/12 = 0.917$ ) is shown by the circles.

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## CONFLICTS OF INTEREST

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