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False-Positive Results in Rapid Antigen Tests for SARS-CoV-2

Concerns have been raised whether rapid antigen tests for SARS-CoV-2 can result in false-positive test results[1,2] and undermine pandemic management for COVID-19. This study investigated the incidence of false-positive results in a large sample of rapid antigen tests used to serially screen asymptomatic workers throughout Canada.

Methods | Rapid antigen tests for SARS-CoV-2 were implemented as an extra layer of protection to control transmission in workplaces throughout Canada by the Creative Destruction Lab Rapid Screening Consortium (CDL RSC). Asymptomatic employees were screened twice weekly. Workplace participation was voluntary. From January 11 to October 13, 2021, tests were conducted by employees, with some workplaces providing at-home screening and others on-site screening programs. Over this period, Canada experienced 2 significant Delta variant–driven waves from March to June and August to October. Screening results were recorded, including a deidentified record identifier, the place of employment, the test, and (optionally) the lot number. If a test result was positive, the patient was immediately referred for a confirmatory polymerase chain reaction (PCR) test to be completed within 24 hours. Initial data validation was completed at the point of collection. All data collected before June 26 and presumptive positive screen results and PCR test results reported before September 15 were externally verified through an audit process by participant organizations. False-positive results were matched to lot number and test manufacturer. A false-positive result was defined as a positive screen on a rapid antigen test and a subsequent negative confirmatory PCR.

The data from the CDL RSC were collected to inform the operational requirements of deploying rapid antigen screens in workplaces. All participants provided written consent to participate in the screening program and to share their deidentified data with the CDL RSC, including for publication, and with public health authorities. This study was approved by the University of Toronto Research Ethics Board.

Results | There were 903 408 rapid antigen tests conducted for 537 workplaces, with 1322 positive results (0.15%), of which 1103 had PCR information. Approximately two-thirds of screens were trackable with a lot number. The number of false-positive results was 462 (0.05% of screens and 42% of positive test results with PCR information). Of these, 278 false-positive results (60%) occurred in 2 workplaces 675 km apart run by different companies between September 25 and October 8, 2021. All of the false-positive test results from these 2 workplaces were drawn from a single batch of Abbott's Panbio COVID-19 Ag Rapid Test Device.

Discussion | The overall rate of false-positive results among the total rapid antigen test screens for SARS-CoV-2 was very low, consistent with other, smaller studies.[3] The cluster of false-positive results from 1 batch was likely the result of manufacturing issues rather than implementation. These results inform the discussion of whether rapid antigen tests will result in too many false-positives that could overwhelm PCR testing capacity in other settings.[1,2] Also, the results demonstrate the importance of having a comprehensive data system to quickly identify potential issues. With the ability to identify batch issues within 24 hours, workers could return to work, problematic test batches could be discarded, and the public health authorities and manufacturer could be informed. Aside from issues with the batch, false-positives are possible due to the timing of the test (ie, too early or too late in the infectious stage) or quality issues in how the self-test was completed.

Limitations of the study include the convenience sample of workplaces and that reporting of PCR confirmatory results and identification of lot number was not compulsory. In addition, these results reflect the epidemiology experienced in Canada and may not generalize to other countries experiencing different COVID-19 incidence.

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COMMENT & RESPONSE

Vasopressin and Methylprednisolone vs Placebo and Return of Spontaneous Circulation in Patients With In-Hospital Cardiac Arrest

To the Editor The recent study[1] about patients with in-hospital cardiac arrest demonstrated that administration of vasopressin and methylprednisolone, compared with placebo, significantly increased the return of spontaneous circulation but did not result in increased survival at 30 days. We would like to raise an ethical concern about the use of a therapeutic intervention that could lead to return of spontaneous circulation without achieving a meaningful clinical benefit. The results can be stated another way: that the intervention achieved return of spontaneous circulation but prolonged death in a statistically significant number of patients, as shown by transition to comfort care in 27% in the intervention group vs 12% in the placebo group. When stated this way, the concept of nonmaleficence was possibly violated.[2]

In addition, while not reported, there is a high likelihood that most, if not all, of the patients who achieved return of spontaneous circulation were admitted to an intensive care unit and received invasive and potentially painful interventions (such as mechanical ventilation, deep suctioning, and central line and arterial line placement). As shown in Supplement 2 of the article,[1] among patients who achieved return of spontaneous circulation, more patients in the intervention group vs placebo group required insulin infusions (37% vs 28%) and developed mesenteric (3% vs 2%) and peripheral (5% vs 3%) ischemia, although these numbers were low. However, we also note that patients in the placebo group who achieved return of spontaneous circulation received higher rates of certain invasive interventions (eg, percutaneous coronary interventions, kidney replacement therapy, and venoarterial extracorporeal membrane oxygenation). We acknowledge that many of these interventions may be necessary in the postresuscitation phase of care, especially if thought to be clinically beneficial and concordant with patient and family wishes, but it is important to acknowledge that attainment of return of spontaneous circulation is not always benign and may lead to burdensome care.

Randomized clinical trials investigating interventions that may improve meaningful outcomes following cardiac arrest are a worthwhile endeavor, especially because earlier studies suggested clinical benefit of vasopressin and methylprednisolone.[3] However, while return of spontaneous circulation is clearly the first step to eventual recovery, we are concerned that if the likelihood of return of spontaneous circulation is increased without downstream beneficial outcomes, it may lead to a prolonged death—which may, in fact, be worse.

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To the Editor A recent study[1] reported a significant increase in likelihood of return of spontaneous circulation among patients administered vasopressin and methylprednisolone compared with placebo. However, as the authors pointed out, the trial was powered only to the primary outcome of return of spontaneous circulation and not for the secondary outcomes of survival and favorable neurologic outcomes at 30 days. Furthermore, this study used Cerebral Performance Category measurements at 30 days, which may be an insufficient amount of time to predict positive longer-term outcomes because cognitive function is susceptible to many physiologic and pharmacologic perturbations that may occur during the early period after cardiac arrest.[2]

Second, the time to drug delivery in this trial[1] was longer than that in prior studies of vasopressin, steroids, and epinephrine for patients with cardiac arrest.[3] It appears the delay