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LETTER TO THE EDITOR

When To Retest: an Examination of Repeat COVID-19 PCR Patterns in an Ambulatory Population

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Health care facilities have limited supplies for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) amplification/detection, putting them under pressure to optimize reagent use. Repeat testing is a potential source of waste. CDC guidelines list screening criteria but only specify return-to-work criteria for health care providers (HCP), which divides the criteria into symptom-based, time-based, and testing based strategies (1). The testing-based strategy suggests two negative tests at least 24 h apart for clearance. However, these guidelines are for people who have initially tested positive. The Infectious Diseases Society of America (IDSA) recently recommended repeat testing in symptomatic individuals with a sustained clinical suspicion of COVID-19 when the initial test is negative; however, the panel noted the paucity of clinical evidence regarding repeat testing (2). The purpose of this quality improvement study was to see if we could better understand the clinical utility of repeat SARS-CoV-2 PCR testing.

Washington Kaiser Permanente (KPWA) is an integrated health care network with a central laboratory performing testing exclusively for outpatient/ambulatory members following the WHO screening criteria. All SARS-CoV-2 molecular testing has been performed as a send-out to the University of Washington (UW), which uses a combination of the Roche Cobas, Hologic Panther Fusion, and their laboratory-developed test (LDT) (3), or internally at the KPWA central laboratory, which utilizes the Hologic Panther Fusion.

SARS-CoV-2 PCR results between 6 March 2020 and 30 April 2020 were extracted and reviewed. From 6 March 2020 to 20 April 2020, these were exclusively nasopharyngeal swabs ($n = 6,411$); after 20 April 2020, nasal swabs were validated as an additional source. In total, 8,391 tests were performed on 8,084 unique patients ($n = 4,112$ Fusion, $n = 3,492$ UW LDT, and $n = 787$ Cobas; median age, 49 years [interquartile range, 34 to 62]). Of these, 7.1% of testing ($n = 597$ tests) was performed on patients who had more than one SARS-CoV-2 PCR test ($n = 290$ unique patients), with the majority (95.2%) having received 2 tests and the minority having received 3 ($n = 11$; 3.8%) or 4 ($n = 3$; 1.0%) tests. Most testing was ordered by family practice ($n = 4,829$ tests; 57.5%), followed by urgent care ($n = 1,864$; 22.2%), internal medicine ($n = 883$; 10.5%), pediatrics ($n = 175$; 2.1%), and other ($n = 640$; 7.6%). The difference in the distribution of initial tests and repeat tests across departments was not statistically significant ($\chi^2_5 = 10.8$; $P = 0.056$).

For patients who had two tests (276 unique patients), 87.0% of the second tests (240 of 276) were concordant with the first test result (Fig. 1). Of the discordant, 10 unique

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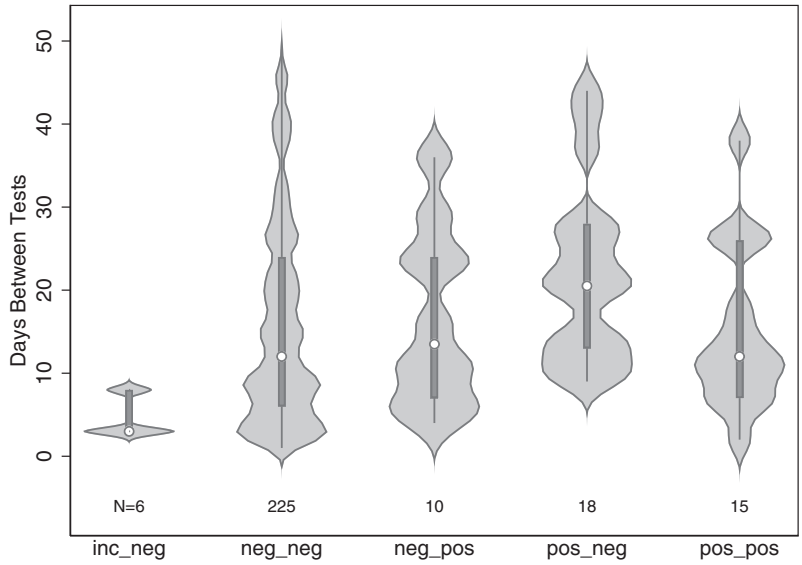

FIG 1 Violin plot illustrating comparison of results between consecutive testing for people with two SARS-CoV-2 PCR tests ($n = 276$). Sample size indicates the number of unique patients who had two tests within each cohort. Hollow circle indicates median. Note that patients with 3 or more tests were excluded from this figure.

patients had a negative result on first swab and a positive result on second swab; of the concordant, 225 unique patients had negative results on first and second swabs; for patients with 3 tests with a negative result on the first swab ($n = 7$), 100% were concordant negative. Only one patient received 4 tests with a negative on the first swab, the second of which was positive, and the following two were negative. The probability that the second test would be positive given that the first test was negative was 4.2% (95% confidence interval [CI], 2.0 to 7.6%). Logistic regression was used to evaluate the impact of time on the probability of a positive second test. Given an initial negative result, the probability of a positive result on a second test increased with the length of time between the initial and subsequent test (odds ratio = 1.04; 95% CI, 1.00 to 1.09; $P = 0.03$). Chart review indicated that 55% of the patients with positive second tests were HCP or had experienced additional exposures, prolonged symptoms, or symptoms that recurred after a resolution period. Thus, repeat testing after a negative result is more likely to be useful when there is strong clinical suspicion of COVID.

Recommendations discourage a testing-based strategy for cure since symptom/time-based strategies are better indicators of resolution (4). In this data set, 37 unique patients ($n = 78$ tests) had at least one follow-up test after a positive result. For these, the mean testing interval was 19.3 days (interquartile range, 10 to 25 days), and 32.4% of the pairs ($n = 12$ patients) were performed on HCP or people with similar high-risk employment; 16.2% ($n = 6$ patients) were performed for preprocedure clearance. Patients whose repeat test was positive were likely retested too soon after initial test result (Fig. 1).

Indeterminate results were defined as samples evaluated on the UW LDT for which one of two amplification products was detected. These are thought to be low-viral-load specimens either due to poor collection and/or resolving or early infection. Here, all samples that were indeterminate on first swab ($n = 8$) were negative on second. Chart review indicated that four of these patients had very mild symptoms and the remaining four were either screened for preprocedure purposes or following low-risk exposure, indicating that the inconclusive result was an incidental finding.

We report the first large data set evaluating the likelihood that repeat testing would provide clinically actionable results in a large ambulatory population. A limitation to this study is that up to three different testing platforms with potentially different performance characteristics were used, prohibiting us from distinguishing if differences

in test results were due to analytic variability. However, the differences in performance characteristics have been shown to be small for the platforms under consideration (3). In this specific data set, the number of tests that could have been reduced by prohibiting subsequent testing was modest ($n = 296$ tests; 3.5% of all tests), only supports decreased testing within the first week of the negative result, and was shown to be diagnostic in a small percentage of cases. However, as testing demands continue to increase, testing supply and operational capacity will continue to be limited. Specific guidance for repeat testing will be critical to mitigate supply with clinical relevance.

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