

## Concise Communication

# Benefit and cost of repeating a severe acute respiratory coronavirus virus 2 (SARS-CoV-2) polymerase chain reaction (PCR) test after the second day of hospitalization in five hospitals during various community prevalences and vaccination rates

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### Abstract

At our hospital, universal severe acute respiratory coronavirus virus 2 (SARS-CoV-2) polymerase chain reaction (PCR) testing was performed upon admission and again after 2 inpatient days. As community-wide prevalence, admission, and vaccination rates varied, the number needed to benefit fluctuated between 16 and 769 and the cost per additional detection fluctuated between \$800 and \$29,400. These 2 metrics were negatively associated with new hospital admissions. No other community indicator was associated with the number needed to benefit and cost per additional detection.

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Surges of novel coronavirus 2019 disease (COVID-19) can severely strain healthcare systems. Safe and efficient capacity management is crucial for hospitals, but hospital-acquired COVID-19 frustrates those efforts by increasing lengths of stay, morbidity, and mortality.<sup>1–3</sup> Several issues complicate prevention of nosocomial COVID-19. First, symptoms of congestive heart failure, chronic obstructive pulmonary disease, or other chronic cardiorespiratory conditions can be indistinguishable from those of severe acute respiratory coronavirus virus 2 (SARS-CoV-2). In a recent report, patients with a delayed diagnosis of COVID-19 were more likely to present with heart failure and to have none of the cardinal symptoms of COVID-19 than patients who were diagnosed immediately upon admission (adjusted odds ratio [OR], 2.36; 95% confidence interval [CI], 1.15–4.84).<sup>4</sup> Another issue is the time-dependent nature of the SARS-CoV-2 real-time reverse transcription polymerase chain reaction (RT-PCR) assay. For example, collection and testing 4 days before symptom onset resulted in a false-negative test in 100% of samples, which decreased to 67% the day before symptom onset and 38% on the day of symptom onset.<sup>5</sup>

After fatal nosocomial outbreaks at our facility, we sought (1) to prevent future occurrences and (2) to evaluate the benefit and cost of a testing strategy consisting of retesting all inpatients after the

second day of the hospitalization compared to a single RT-PCR on admission.

### Methods

A nonrandomized intervention was conducted in an accelerated stepped-wedge manner across a 5-hospital (1,029 beds) healthcare system in the 9-county Finger Lakes region of New York. In this system, 19% of rooms (31% of the beds) are semiprivate. Infection control measures at our facility were described previously<sup>6</sup> and mirrored those at other hospitals.<sup>7</sup>

Under the existing testing program (P<sub>1</sub>), all patients were tested upon admission for SARS-CoV-2 infection with nasopharyngeal (NP) swabs that undergo RT-PCR on either the cobas 6800 System (Roche Diagnostics, Indianapolis, IN), the BD SARS-CoV-2 reagents for BD MAX (Becton Dickinson, Franklin Lakes, NJ), or the Simplexa COVID-19 Direct kit (DiaSorin Molecular, Minneapolis, MN) as described previously.<sup>8</sup>

In this study, we evaluated a second testing strategy (P<sub>2</sub>) consisting of automatically retesting all inpatients after their second day of admission on the same platforms. An opt-out clinical decision support (CDS) algorithm was established that activated after 48 hours of admission when any provider opened the patient's chart. This tool consisted of a prewritten order for an NP swab for the RT-PCR. The CDS continued to pose an alarm until it was acted upon by either clicking on a "sign order" button or by opting out and providing a reason (Supplementary Fig. 1 online). The P<sub>2</sub> intervention began with a 3-month

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**Table 1.** Healthcare System–Level COVID-19 Indicators

Predominant Lineage	Control Period 10/20–2/21	FEB 2021	MAR 2021	APR 2021	MAY 2021	JUN 2021	JUL 2021	AUG 2021	SEP 2021	OCT 2021	NOV 2021
		Alpha Variant	Alpha Variant	Alpha Variant	Alpha Variant	Alpha Variant	Alpha Variant	Delta Variant	Delta Variant	Delta Variant	Delta Variant
<b>Community Level COVID-19 Indicators for the 9-County Finger Lakes Region, New York</b>											
% Positive <sup>a</sup>	9.6	2.4	1.8	3.1	2.8	0.6	0.8	4.2	5.0	5.0	8.6
New cases <sup>b</sup>	70.0	19.2	15.5	32.2	20.0	2.4	1.7	18.9	28.9	33.8	61.9
New hospitalizations <sup>c</sup>	8.2	2.6	2.2	1.5	2.5	0.6	0.5	1.3	2.0	2.3	4.0
% completed vaccine series	0.2	13	19	34	48	53	55	57	59	61	63
<b>Healthcare system–level COVID-19 indicators, Rochester Regional Health</b>											
Electronic reminders, no. <sup>d</sup>		2,887	21,269	19,840	20,796	20,675	21,493	21,844	19,485	18,572	17,876
Signed orders, no. <sup>e</sup>		292	2,000	1,906	2,033	1,955	2,005	1,977	1,806	1,741	1,622
Patients tested, no.		282	1,661	1,358	1,512	1,659	1,585	1,199	1,484	1,399	1,348
Patients available for testing, no. <sup>f</sup>		5,246	6,726	6,567	6,427	6,593	6,503	6,452	5,799	5,736	5,856
Patients positive, no.		18	16	12	10	5	3	2	17	20	12
Detection rate		6.38	0.963	0.883	0.661	0.301	0.189	0.167	1.146	1.429	0.890
Testing efficiency, also P2 <sup>g</sup>		0.0638	0.0096	0.0088	0.0066	0.0030	0.0019	0.0017	0.0115	0.0143	0.0089
NNT (1/E) <sup>h</sup>		16	104	113	152	333	526	588	87	70	112
Yield <sup>i</sup>		335	65	58	42	20	12	11	67	82	52
HO-COVID-19 rate, also P1 <sup>j</sup>	1.5 0.0015	0.5 0.0005	0.1 0.0001	0.5 0.0005	0.7 0.0007	0.1 0.0001	0.5 0.0005	0.4 0.0004	0.8 0.0008	103 0.0013	0.8 0.0008
P2 – P1 = D <sup>k</sup>		0.0633	0.0095	0.0083	0.0059	0.0029	0.0014	0.0013	0.0107	0.0130	0.0081
NNB = 1/D <sup>l</sup>		16	105	120	169	345	714	769	93	77	123
Cd, USD <sup>m</sup>		800	5,200	5,650	7,600	16,650	26,300	29,400	4,350	3,500	5,600

Note. NNB, the number needed to benefit; NNT, test the number needed to test; Cd, cost per additional detection. Sources for the table: <https://www.flvaccinehub.com/regional-data> and <https://forward.ny.gov/early-warning-monitoring-dashboard>.

<sup>a</sup>% positive tests, 7-day rolling average.

<sup>b</sup>New cases per 100,000 population, 7-day rolling average.

<sup>c</sup>New hospitalizations per 100,000 population 7 day rolling average.

<sup>d</sup>No. of times the best practice advisory fired for ordering a SARS-CoV-2 PCR on second day of hospital admission

<sup>e</sup>No. of signed orders for SARS-CoV-2 PCR tests on second day of hospital admission.

<sup>f</sup>Number of patients eligible/available for testing based on inpatient census.

<sup>g</sup>Expected testing efficiency = the proportion of SARS-CoV-2-positive cases identified out of all individuals tested (cases detected per test); also P2.

<sup>h</sup>NNT = 1/Efficiency.

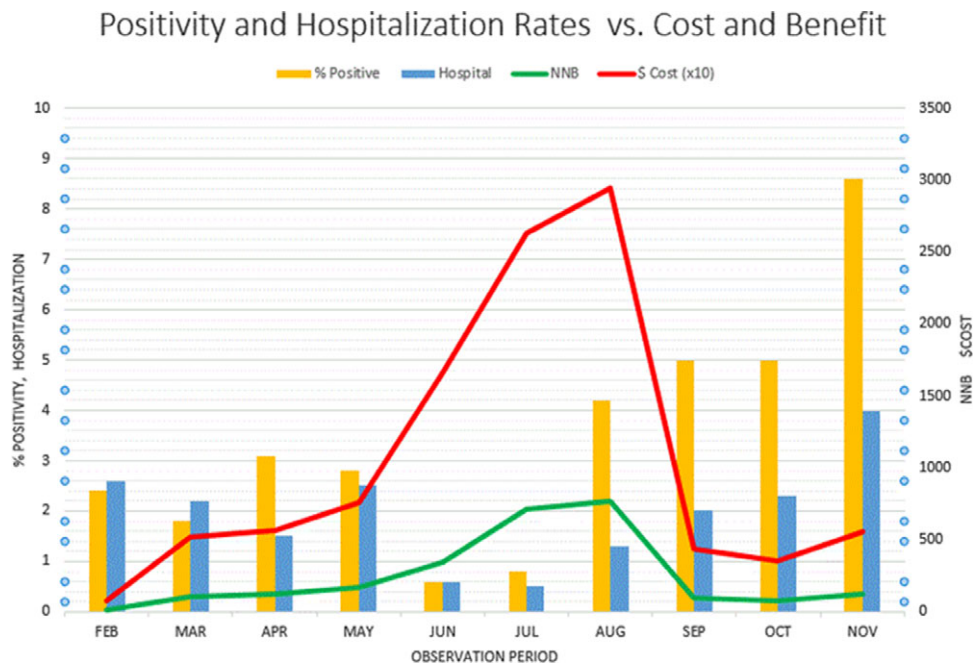
<sup>i</sup>Yield = total number of cases under a given testing strategy (eligible population × efficiency).

<sup>j</sup>HO-COVID-19 = hospital-onset infections per 1,000 non-COVID-19 patient days; also P1.

<sup>k</sup>P1, case rate identified by existing methods = nosocomial infection rate used as surrogate for established strategy (a single admission PCR) as surrogate. P2, case rate using new testing strategy (a repeat PCR on day 2).

<sup>l</sup>NNB = 1/(P2 – P1).

<sup>m</sup>Cd, NNT × \$50 in USD.



**Fig. 1.** Positivity and hospitalization rates versus cost and benefit. Note. % Positive, % positive tests 7 day rolling average; Hospital, new hospitalizations per 100k population 7 day rolling average; NNB, number needed to benefit; S cost (x10) = cost in USD x10.

preimplementation or ‘control’ phase from October 2020 to February 2021 on several units at the main hospital. Over the next month, it was sequentially implemented across all hospitals in the system.

Hospital-onset (HO) COVID-19 was defined according to the CDC definition: a negative admission test followed by a positive test  $\geq 7$  days (probable HO) or  $\geq 14$  days later (definite HO). HO-COVID-19 rates were reported as the proportion of nosocomial cases per 1,000 SARS-CoV-2-negative patients. The cost per additional detection was calculated as cost per subject screened ( $\$50$ )  $\times$  the number needed to test. The number needed to test was the average number of individuals who must be tested under a given strategy to identify a single case of SARS-CoV-2, also calculated as the inverse of efficiency.<sup>9</sup> Efficiency was the proportion of positive cases identified among all individuals tested.<sup>9</sup> Using only the number needed to test would overestimate the impact of the new testing strategy because it does not account for the cases already detecting by the existing strategy.<sup>10</sup> Therefore, we calculated the number needed to benefit as previously described and summarized below.<sup>10</sup>

First, because identification of newly positive cases would trigger immediate enhanced isolation precautions and theoretically thwart further transmission, we defined ‘successful outcome’ (or benefit) as the identification of a conversion from negative to positive in an asymptomatic inpatient that would otherwise not have been retested. Second, we denoted the proportion of successful outcomes using the established mode of diagnosis (a single admission PCR test) as  $P_1$ , and the proportion of successful comes under the new strategy (test efficiency of repeated PCR test on day 2) as  $P_2$ . The inverse of the difference in success rates or  $1/(P_2 - P_1)$  equals the number needed to benefit from the change to the new testing strategy.<sup>10</sup> Linear regression was used to analyze associations between community metrics and the outcome variables (the number needed to benefit and cost per additional detection).

## Results

Community-level indicators such as positivity, vaccination, and new hospitalization rates are presented in Table 1 and Figure 1.

The 7-day rolling average transmission rate fluctuated between 0.6% to 8.6%, and the vaccination rates ranged from 0.2% to 63%. The SARS-CoV-2  $\alpha$  (alpha) and  $\delta$  (delta) variant lineages predominated in the first and last 5 months of the study period, respectively.

Healthcare system-level COVID-19 indicators, including the number of electronic reminders, the number of signed orders, and detection rates, are presented in Table 1. The mean monthly number of times the electronic reminder was triggered in patients’ charts and resulted in an order was 20,202 (range, 2,887–21,844), or 9.4% of the time. The 3 most common reasons for a day-2 order not resulting were (1) not part of treatment team, (2) patient will be discharged within 24 hours, and (3) patient refused test. Also, >90% of the repeated PCR tests were performed between inpatient days 2 and 4. The mean turnaround time for PCR results was 16.5 hours.

The diagnostic and financial impacts of the new testing strategy are presented in Table 1 and Figure 1. Testing efficiency ranged from 0.002% to 0.064%. The number needed to test ranged from 16 to 588. Cost per additional detection ranged from  $\$800$  to  $\$29,400$ , and the number needed to benefit ranged from 16 to 769. Of the 3 community-level indicators evaluated, only the number of new hospitalizations was associated (negatively) with the number needed to benefit and the cost per additional detection ( $P = .04$ ; adjusted  $R^2$ , 0.35 and  $P = .03$ ; adjusted  $R^2$ , 0.39, respectively).

## Discussion

The benefit and cost of a repeated RT-PCR testing on or after the second day of admission compared to a single admission test fluctuated as community prevalences and vaccination rates changed. Our healthcare system that has a mean daily census of 1000, and a mean length of stay of 5 days. Thus, applying these testing strategy performance characteristics (efficiency, <1%–9%) to day 2 testing could detect <10–90 HO-COVID-19 cases per month that would have otherwise been missed. These direct costs may seem excessive, but they are offset by having prevented additional nosocomial COVID-19 hospital days, staff exposures with the

corresponding workforce effects, and additional morbidity and mortality.

This study had several limitations. Linear regression was applied to the few community factors that were available at the time. Therefore, the insight provided is incomplete because a number of factors are related to the properties of the healthcare system, such as staffing levels, that could not be captured in that analysis. Second, the true number needed to benefit and cost per additional detection could be less than reported due to the large number of opt-out responses.

Despite these limitations, these results could help other system administrators decide when repeat testing of asymptomatic inpatients might be most cost-effective. A provisional threshold for such an approach could be to test all inpatients until the vaccine coverage or level of immunity in the community reaches 50%. After that, only retest the asymptomatic when the 7-day rolling average of the new hospitalization rate is  $\geq 2$  per 100,000 residents.

**Supplementary material.** To view supplementary material for this article, please visit <https://doi.org/10.1017/ice.2022.157>

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#### References

1. Elkrief A, Desilets A, Papneja N, *et al.* High mortality among hospital-acquired COVID-19 infection in patients with cancer: a multicentre observational cohort study. *Eur J Cancer* 2020;139:181–187.
2. Khonyongwa K, Taori SK, Soares A, *et al.* Incidence and outcomes of healthcare-associated COVID-19 infections: significance of delayed diagnosis and correlation with staff absence. *J Hosp Infect* 2020;106:663–672.
3. Lessells R, Moosa Y, de Oliveira T. Report into a nosocomial outbreak of coronavirus disease 2019 (COVID-19) at Netcare St. Augustine's Hospital. University of Kwazulu-Natal website. [https://www.groundup.org.za/media/uploads/documents/staugustineshospitaloutbreakinvestigation\\_finalreport\\_15may2020.pdf](https://www.groundup.org.za/media/uploads/documents/staugustineshospitaloutbreakinvestigation_finalreport_15may2020.pdf). Published May 2020. Accessed January 26, 2021.
4. Pfoh ER, Hariri EH, Misra-Hebert AD, Deshpande A, Jehi L, Rothberg MB. Late diagnosis of COVID-19 in patients admitted to the hospital. *J Gen Intern Med* 2020;35:2829–2831.
5. Kucirka LM, Lauer SA, Laeyendecker O, Boon D, Lessler J. Variation in false-negative rate of reverse transcriptase polymerase chain reaction-based SARS-CoV-2 tests by time since exposure. *Ann Intern Med* 2020;173:262–267.
6. Lesho E, Walsh E, Gutowski J, *et al.* A cluster-control approach to a SARS-CoV-2 outbreak on a stroke ward with infection control considerations for dementia and vascular units. *Infect Control Hosp Epidemiol* 2021;42:1333–1339.
7. Rhee C, Baker M, Vaidya V, *et al.* Incidence of nosocomial COVID-19 in patients hospitalized at a large US academic medical center. *JAMA Netw Open* 2020;3:e2020498.
8. Lesho E, Reno L, Newhart D, *et al.* Temporal, spatial, and epidemiologic relationships of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) gene cycle thresholds: a pragmatic ambidirectional observation. *Clin Infect Dis* 2020;ciaa1248.
9. In COVID-19 testing, what does yield mean? University of North Carolina website. <https://gillingscovid19.unc.edu/coronavirus-questions/covid-19-testing-yield>. Accessed December 8, 2021.
10. Honorio MR, Benzon HT, Molloy RE. Membrane stabilizers, in essentials of pain medicine and regional anesthesia, second edition. Science Direct website. <https://www.sciencedirect.com/topics/medicine-and-dentistry/numbers-needed-to-treat>. Published 2005. Accessed December 8, 2021.