

# The fourth wave: vaccination status and intensive care unit mortality at a large hospital system in New York City

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**Background:** We aim to describe the demographics and outcomes of patients with severe disease with the Omicron variant. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus continues to mutate, and the availability of vaccines and boosters continue to rise, it is important to understand the health care burden of new variants. We analyze patients admitted to intensive care units (ICUs) in a large Academic Health System during New York City's fourth surge beginning on November 27, 2021.

**Methods:** All patients admitted to an ICU were included in the primary analysis. Key demographics and outcomes were retrospectively compared between patients stratified by vaccination status. Univariate and multivariate logistic regression was used to identify risk factors for in-hospital mortality.

**Results:** In-hospital mortality for all admitted patients during the fourth wave was significantly lower than in previous waves. However, among patients requiring intensive care, in-hospital mortality was high across all levels of vaccination status. In a multivariate model older age was associated with increased in-hospital mortality, vaccination status of overdue for booster was associated with decreased in hospital mortality, and vaccination status of up-to-date with vaccination showed a trend to reduced mortality.

**Conclusions:** In-hospital mortality of patients with severe respiratory failure from coronavirus disease 2019 (COVID-19) remains high despite decreasing overall mortality. Vaccination against SARS-CoV-2 was protective against mortality. Vaccination remains the best and safest way to protect against serious illness and death from COVID-19. It remains unclear that any other treatment will have success in changing the natural history of the disease.

**Key Words:** COVID-19; mortality; Omicron

## INTRODUCTION

New York City (NYC) was one of the first epicenters of coronavirus disease 2019 (COVID-19) in the United States in early 2020 and has since reported over 2.2 million cases and almost 40,000 deaths [1]. After November 27, 2021, the highly transmissible Omicron variant of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus became prevalent and

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induced NYC's fourth wave of COVID-19. The fourth wave of COVID-19 in NYC differs from prior waves in that over 70% of NYC's population over 5 years of age have been fully vaccinated with either two doses of Pfizer or Moderna or one shot of Johnson & Johnson. There have also been more than 1.1 million additional doses administered (either 3rd dose or booster) [2,3]. Despite this, the Omicron surge resulted in record-high cases per day, reaching a peak of 60,000 in NYC on January 3, 2022 [1], including many breakthrough cases in individuals who completed their initial vaccination series and some who were boosted [4,5].

Over the past 2 years the treatment for COVID-19 has greatly evolved as more research has been conducted on COVID-19. Many aspects of the care of COVID-19 patients have changed, these include timing of intubation [6], Remdesivir [7], steroid use [8], anticoagulation [9], tocilizumab [10], Monoclonal antibodies [11], oral protease inhibitors [12], extracorporeal membrane oxygenation (ECMO) [13], and the covid vaccine [14].

The Omicron variant of SARS-CoV-2 has generally been associated with a milder clinical course and lower mortality as compared to the Alpha variant (0.86% of Omicron patients died vs 5.7% of Alpha patients) [4] and the Delta variant (mortality of patients positive with Omicron was 0.09 fold as high compared to patients with Delta) [15]. Diminished public concern for this strain thus had the potential to lead to greater spread through waning mask usage and social distancing. Given its high prevalence, it is of interest to understand how the admission rates, level of hospital care and outcomes of patients may differ in this fourth surge compared to earlier waves. Given lower reported mortality, it is important to understand the patient population still suffering from the most severe illness.

## MATERIALS AND METHODS

The study was approved by Institutional Review Board of the Mount Sinai Hospital (No. 20-0054). Informed consent was waived. Procedures were followed in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975. Initial inclusion criteria were all adult inpatients admitted to one of five hospitals in a large Urban Academic Health System in NYC, with either a positive SARS-CoV-2 polymerase chain reaction test during admission or clinical documentation of active COVID-19 infection. Patients were grouped into waves with waves 1, 2, 3 consistent with prior literature [16]; the fourth wave was identified as all patients admitted from November

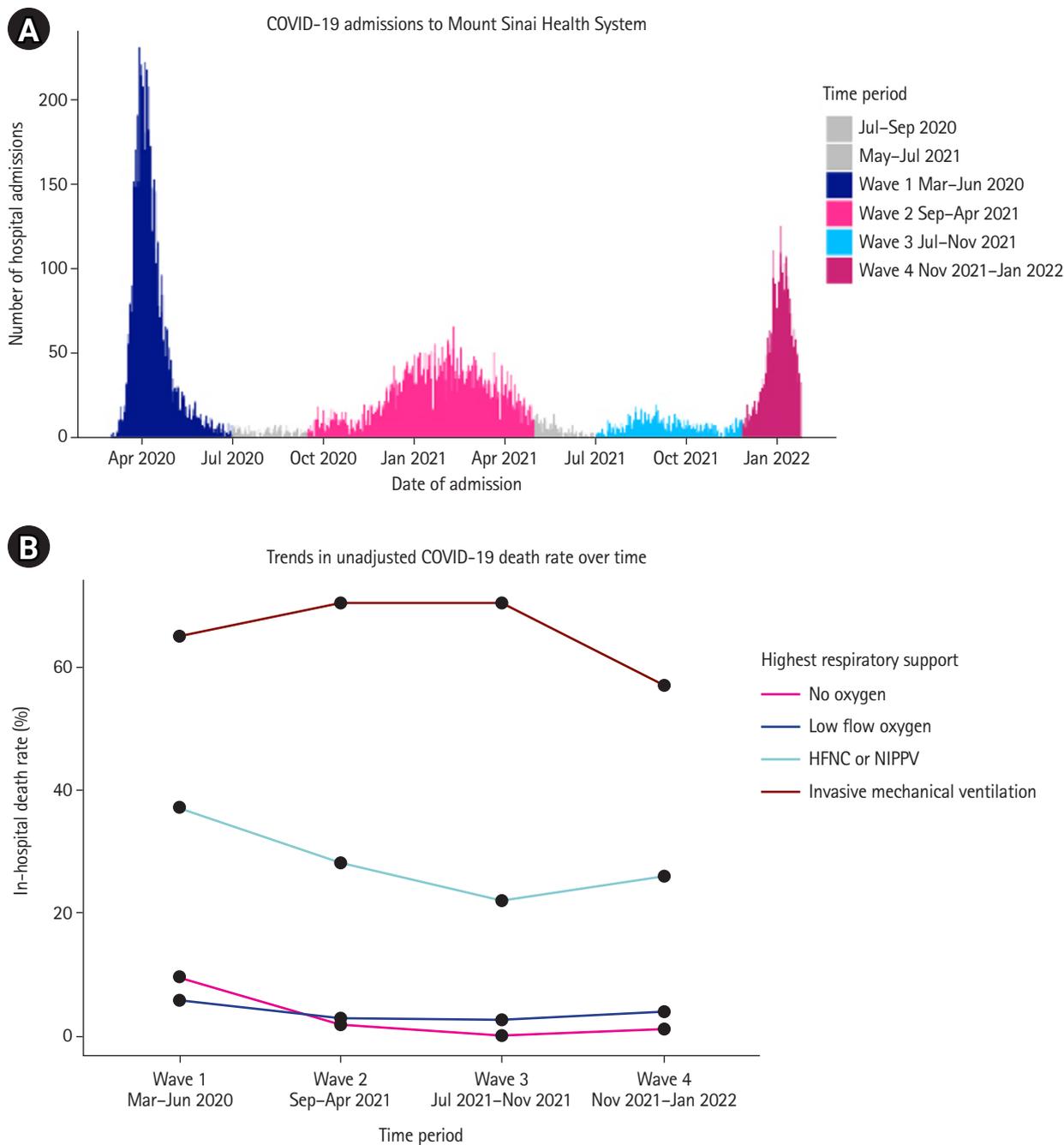
### KEY MESSAGES

- Patients requiring intensive care, in-hospital mortality was high across all levels of vaccination status.
- Up-to-date vaccination remains the best and safest way to protect against serious illness and death from coronavirus disease 2019 (COVID-19).

27, 2021 through January 25, 2022 with follow-up for clinical outcomes through March 1, 2022 (Figure 1A). The study center COVID-19 treatment protocols have been updated as new data and trials have been published. Currently patients undergoing care for COVID-19 receive remdesivir, tocilizumab, high-flow nasal cannula/bilevel positive airway pressure, intubation, prone position ventilation, anticoagulation, and ECMO as needed based on National Institutes of Health guidelines for COVID-19 patients.

The primary analysis was of patients ever admitted to an intensive care unit (ICU) during their stay. The vaccination status of these ICU patients was identified by manual chart review. Patients were considered to be fully vaccinated if they were admitted more than 2 weeks after receiving either the second dose of an mRNA COVID-19 vaccine or 2 weeks after receiving a single dose of the Johnson & Johnson/Janssen COVID-19 or AstraZeneca vaccine. Patients were considered partially vaccinated if they had received any dose of vaccine but did not meet criteria for full vaccination. Patients were considered booster-eligible 5 months after completing their primary mRNA vaccine series or 2 months after getting a single-dose COVID-19 vaccine. Patients were classified according to CDC definition as "up-to-date" if they were fully vaccinated but not yet eligible for booster, or eligible for booster and had a received booster vaccine. Patients were considered "overdue for booster" if they were fully vaccinated and eligible for booster, but had not received any booster vaccine. Patients whose vaccine status was unknown were excluded from vaccine specific analysis.

Patients' Comorbidities were identified using International Classification of Diseases, 10th revision (ICD-10) diagnostic codes. Continuous and categorical variables were compared between groups using the Kruskal-Wallis test or chi-square test as appropriate. Odds ratios (ORs) for in-hospital death were calculated by fitting univariate binomial generalized linear models. All available variables were also included in a multivariable logistic regression. Data extraction and process-



**Figure 1.** (A) Coronavirus disease 2019 (COVID-19) admissions to Mount Sinai Health System. (B) Trend in unadjusted COVID-19 death rate over time. HFNC: high-flow nasal cannula; NIPPV: non-invasive positive pressure ventilation.

ing was done in Python version 3.7.3 (Python Software Foundation, Wilmington, DE, USA; <https://www.python.org/>), and data analysis was done using R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria; <https://www.R-project.org/>) and R studio version 1.2.5001 (RStudio PBC, Boston, MA, USA; <http://www.rstudio.com/>).

## RESULTS

Three thousand fifty-six patients were admitted with COVID-19 during the fourth wave, of which 372 patients (12%) required ICU level of care, significantly lower than previously waves in the pandemic (wave 1: 1,242 (19%), wave 2: 924 (16%), wave 3: 205 (19%);  $P < 0.001$ ) (Table 1). Of these, 43 patients had

**Table 1.** Characteristics of patients separated by wave

Characteristic	Wave 1 (n=6,495)	Wave 2 (n=5,849)	Wave 3 (n=1,062)	Wave 4 (n=3,056)	P-value <sup>a</sup>
Age	65±17	65±18	61±19	64±20	<0.001
Sex					<0.001
Female	2,816 (43)	2,786 (48)	505 (48)	1,546 (51)	
Male	3,679 (57)	3,063 (52)	557 (52)	1,510 (49)	
Unknown	0	0	0	0	
BMI (kg/m <sup>2</sup> )	29±9	29±11	30±17	28±12	<0.001
Race					<0.001
White	1,611 (25)	1,868 (32)	331 (31)	909 (30)	
Black	1,663 (26)	1,246 (21)	319 (30)	930 (30)	
Hispanic	1,515 (23)	1,081 (18)	181 (17)	540 (18)	
Asian	332 (5.1)	407 (7.0)	42 (4.0)	118 (3.9)	
Native American or Pacific Islander	23 (0.4)	14 (0.2)	5 (0.5)	8 (0.3)	
Other	1,351 (21)	1,233 (21)	184 (17)	551 (18)	
History of diabetes	2,652 (41)	2,222 (39)	344 (34)	568 (29)	<0.001
History of hypertension	4,072 (63)	3,679 (65)	571 (56)	1,022 (53)	<0.001
History of chronic lung disease	1,154 (18)	1,130 (20)	207 (20)	394 (20)	0.01
History of chronic liver disease	455 (7.1)	436 (7.7)	76 (7.5)	125 (6.5)	0.3
History of renal failure	1,343 (21)	1,175 (21)	195 (19)	367 (19)	0.2
History of heart failure	1,030 (16)	1,035 (18)	178 (17)	341 (18)	0.01
HIV/AIDS	154 (2.4)	123 (2.2)	36 (3.5)	56 (2.9)	0.04
History of alcohol or substance use disorder	313 (4.9)	275 (4.9)	52 (5.1)	194 (10)	<0.001
BMI ≥30.0 kg/m <sup>2</sup>	1,776 (37)	1,930 (36)	333 (34)	784 (30)	<0.001
Highest level of respiratory support					<0.001
No oxygen	1,846 (28)	1,515 (26)	286 (27)	1,350 (44)	
Low flow oxygen	1,851 (28)	2,396 (41)	393 (37)	1,016 (33)	
HFNC or NIPPV	1,967 (30)	1,464 (25)	279 (26)	485 (16)	
Invasive mechanical ventilation	831 (13)	474 (8.1)	104 (9.8)	205 (6.7)	
Received ICU level of care	1,242 (19)	924 (16)	205 (19)	372 (12)	<0.001
Ever intubated	831 (13)	474 (8.1)	104 (9.8)	205 (6.7)	<0.001
Hospital length of stay (day)	7 (3–12)	7 (4–14)	7 (4–14)	6 (3–13)	<0.001
Died	1,550 (24)	840 (14)	145 (14)	303 (9.9)	<0.001
Discharged out of hospital	4,938 (76)	5,005 (86)	915 (86)	2,697 (88)	<0.001

Values are presented as mean±standard deviation, number (%), or median (interquartile range). Wave 1: Mar–Jun 2020; Wave 2: Sep–Apr 2021; Wave 3: Jul 2021–Nov 2021; Wave 4: Nov 2021–Jan 2022.

BMI: body mass index; HIV: human immunodeficiency virus; HFNC: high-flow nasal cannula; NIPPV: non-invasive positive pressure ventilation; ICU: intensive care unit.

<sup>a</sup>The Kruskal-Wallis rank sum test and Pearson's chi-square test were used for continuous and categorical variables, respectively.

unknown vaccine status and were excluded from primary analysis. Among the remaining 329 fourth wave ICU patients, 124 (37.7%) were never or partially vaccinated, 117 (35.6%) were fully vaccinated but overdue for a booster vaccine, and 88 (26.7%) were up-to-date with COVID-19 vaccination (Table 2). Unvaccinated patients were younger (mean age of 64 years vs. 69 years for patients overdue for booster and 67 years for up-to-date patients,  $P<0.047$ ) and had the highest BMI (31 kg/m<sup>2</sup> vs. 27 kg/m<sup>2</sup> in overdue for booster patients, and 29 kg/m<sup>2</sup> in

up-to-date,  $P<0.01$ ). There was no significant difference in race or gender between groups. In all groups between 50%–60% required invasive mechanical ventilation and 20%–30% required noninvasive positive pressure ventilation or high-flow nasal cannula.

In-hospital mortality for all admitted patients during the fourth wave was significantly lower than in previous waves (295 [10%] in wave 4 vs. 1,550 [24%] in wave 1, and 840 and 145 [14%] in waves 2 and 3, respectively;  $P<0.01$ ) (Table 2). When strat-

**Table 2.** Characteristics of fourth wave patients based on vaccination status

Characteristic	Never or partially vaccinated (n=124)	Overdue for booster (n=117)	Vaccination up to date (n=88)	P-value <sup>a</sup>
Age	64±18	69±16	67±16	0.05
Sex				0.3
Female	57 (46)	44 (38)	42 (48)	
Male	67 (54)	73 (62)	46 (52)	
Unknown	0	0	0	
BMI (kg/m <sup>2</sup> )	31±10	27±7	29±17	0.01
Race				0.2
White	28 (22.6)	35 (22.9)	31 (35.2)	
Black	52 (41.9)	34 (29.1)	25 (28.4)	
Hispanic	20 (16.1)	17 (14.5)	10 (11.4)	
Asian	4 (3.2)	2 (1.7)	4 (4.5)	
Native American or Pacific Islander	0	0	0	
Other	20 (16.1)	29 (24.8)	18 (20.5)	
History of diabetes	26 (46)	18 (33)	11 (28)	0.1
History of hypertension	30 (54)	34 (62)	20 (50)	0.5
History of chronic lung disease	11 (20)	14 (25)	9 (22)	0.8
History of chronic liver disease	5 (8.9)	2 (3.6)	2 (5.0)	0.5
History of renal failure	15 (27)	14 (25)	8 (20)	0.7
History of heart failure	15 (27)	21 (38)	10 (25)	0.3
HIV/AIDS	1 (1.8)	1 (1.8)	1 (2.5)	1.0
History of alcohol or substance use disorder	6 (11)	4 (7.3)	3 (7.5)	0.8
Highest level of respiratory support				0.7
No oxygen	8 (6.5)	4 (3.4)	6 (6.8)	
Low flow oxygen	19 (15.3)	20 (17.1)	19 (21.6)	
HFNC or NIPPV	26 (21.0)	30 (25.6)	19 (21.6)	
Invasive mechanical ventilation	71 (57.3)	63 (53.8)	44 (50)	
Ever intubated	71 (57)	63 (54)	44 (50)	0.6
Hospital length of stay (day)	15 (8–22)	18 (9–27)	13 (6–24)	0.1
Died	56 (45)	37 (32)	33 (38)	0.1
Discharged out of hospital	55 (44)	73 (62)	48 (55)	0.02
Primary vaccination series type				<0.001
AstraZeneca	0	1 (0.9)	1 (1.1)	
Johnson & Johnson	0	14 (12)	6 (6.8)	
Moderna	3 (2.4)	38 (32.5)	27 (30.7)	
Never vaccinated	111 (89.5)	0	0	
Pfizer	9 (7.3)	58 (49.6)	52 (59.1)	
Unknown	1 (0.8)	6 (5.1)	2 (2.3)	
Booster vaccination type				<0.001
Moderna	0	0	18 (20.5)	
No booster	123 (99)	108 (92.3)	35 (39.8)	
Pfizer	0	0	32 (36.4)	
Unknown	1 (0.8)	9 (7.7)	3 (3.4)	

Values are presented as mean±standard deviation, number (%), or median (interquartile range).

BMI: body mass index; HIV: human immunodeficiency virus; HFNC: high-flow nasal cannula; NIPPV: non-invasive positive pressure ventilation.

<sup>a</sup>The Kruskal-Wallis rank sum test and Pearson's chi-square test were used for continuous and categorical variables respectively.

ified by highest level of oxygen support required, in-hospital mortality remained similar throughout the pandemic. Patients requiring invasive mechanical ventilation had more than a 50% mortality rate in all waves (Figure 1B).

Among patients requiring intensive care, in-hospital mortality was high across all levels of vaccination status. There was no significant difference in in-hospital mortality among different vaccination status (38% in up-to-date patients, 32% in overdue for booster patients, and 45% in never or partially vaccinated patients;  $P=0.1$ ). In univariate analysis only age showed a significant relationship with in-hospital mortality (OR, 1.05;  $P<0.001$ ), though vaccination status had a non-significant trend towards decreasing mortality when compared with Never or Partially Vaccinated patients (overdue for booster: OR=0.62,  $P=0.075$ ; vaccination up-to-date: OR=0.65,  $P=0.14$ ). In a multivariate model incorporating all collected data elements increasing age (OR, 1.08; 95% CI, 1.05–1.12 per year;  $P<0.001$ ) was associated with higher in-hospital mortality and vaccination status of overdue for booster (OR, 0.21; 95% CI, 0.07–0.59;  $P=0.005$ ) was associated with lower in-hospital mortality (Table 3).

**Table 3.** Multivariable model for in hospital mortality in 4th wave patients requiring critical care

Characteristic	Odds ratio	95% CI	P-value
Age	1.08	1.05–1.12	<0.001
BMI	1.03	0.98–1.09	0.2
Race			-
White	-	-	
Black	0.61	0.22–1.65	0.3
Hispanic	0.57	0.11–2.76	0.5
Asian	0.41	0.01–6.71	0.6
Other	1.47	0.50–4.45	0.5
History of diabetes	0.88	0.34–2.27	0.8
History of chronic lung disease	1	0.37–2.66	1.0
History of renal failure	0.93	0.32–2.66	0.9
History of heart failure	0.77	0.29–2.01	0.6
History of chronic liver disease	0.72	0.08–4.64	0.7
History of alcohol or substance use disorder	0.20	0.02–1.22	0.1
HIV/AIDS	0		1.0
Vaccination status			
Never or partially vaccinated	-	-	
Overdue for booster	0.21	0.07–0.59	0.01
Vaccination up to date	0.54	0.18–1.51	0.2

CI: confidence interval; BMI: body mass index; HIV: human immunodeficiency virus.

## DISCUSSION

As the COVID-19 pandemic reaches its 2-year anniversary, NYC has seen four distinct waves of infection. New strains have emerged and disappeared with changes in transmissibility and lethality. Treatments and protocols have also emerged and waned, with none as efficacious as the as the multiple approved vaccines. With the emergence of the Omicron variant, the 4th wave rapidly spread around the world. Much has been written in the lay press about the Omicron variant being less virulent than prior strains; and indeed in our population there was a large group of hospitalized patients who have no or low oxygen requirements and a low mortality rate during the 4th wave [17]. However, even in a vaccinated and Omicron predominant population, patients requiring invasive mechanical ventilation or intensive care have high mortality rate that is similar to the prior waves. While variance in absolute mortality rate between centers in patients receiving non-invasive or invasive mechanical ventilation may be in part due to patient selection for these therapies, it remains clear that the patients with most severe respiratory failure have high mortality despite decreasing death rate overall.

When modeling patient factors related to in hospital mortality, older age remains associated with mortality, and completed primary vaccination status was protective. While patients who were fully boosted had a trend towards lower mortality, it did not reach the level of significance most likely related to sample size; regardless the data are consistent with the protective effect of vaccination against developing severe illness and death, consistent with other studies [4,5,15,18,19]. The ORs for mortality for other comorbid conditions may be underestimated in the current study because of low sample size and wide confidence interval. In our experience, even though the proportion of patients not requiring respiratory support has risen, the in-hospital mortality for those patients requiring supplemental oxygen and mechanical ventilation has not changed throughout the pandemic; and patients who ultimately progress to critical illness do not have much better outcome currently than they did earlier in the pandemic.

In an Omicron predominant 4th wave of COVID-19 in NYC, in hospital mortality and requirement for advanced respiratory support is lower than earlier in the pandemic; however, mortality has not fallen in the population of patients who ultimately develop critical illness. It is important to remember that as public health measures ease COVID-19 remains a highly lethal disease in those patients who become critically ill. Vaccina-

tion remains the best and safest way to protect against serious illness and death from COVID-19. It remains unclear that any other treatment will have success in changing the natural history of the disease.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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Conceptualization: PT, EL, AH, KM, MAL, RKS. Data curation: PT, AH, KM, KL. Formal analysis: PT. Methodology: EL, MAL, RKS. Project administration: KM. Writing—original draft: PT, EL, AH, KM, KL, MAL. Writing—review & editing: PT, EL, MAL, RKS.

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