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Emergency medicine is a specialty which closely reflects societal challenges and consequences of public policy decisions. The emergency department specifically deals with social injustice, health and economic disparities, violence, substance abuse, and disaster preparedness and response. This journal focuses on how emergency care affects the health of the community and population, and conversely, how these societal challenges affect the composition of the patient population who seek care in the emergency department. The development of better systems to provide emergency care, including technology solutions, is critical to enhancing population health.

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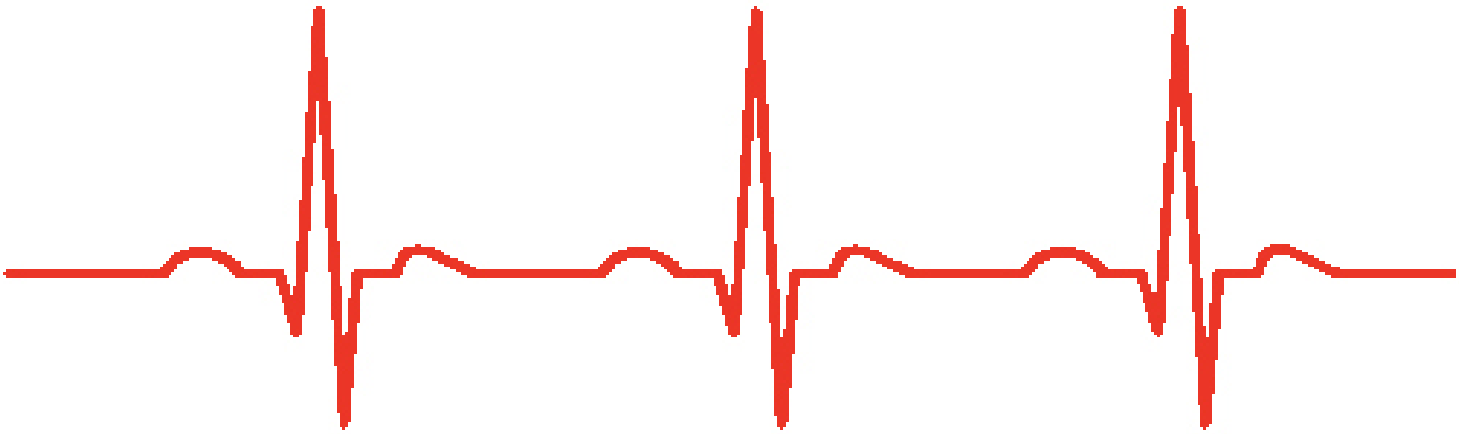

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CPCEM Clinical Practice & Cases

Emergency Department Buprenorphine Quality Improvement and Emergency Physician Knowledge, Attitudes, and Self-Efficacy

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Objective: Buprenorphine is an evidence-based treatment for opioid use disorder that is underused in the emergency department (ED). In this study we evaluated changes in emergency physician knowledge, confidence, and self-efficacy regarding buprenorphine prescribing and working with patients who use drugs after implementation of an ED buprenorphine quality improvement (QI) initiative.

Methods: An anonymous, online survey was administered to emergency physicians staffing four EDs in New England in 2019 and 2020 before and after an ED QI initiative. Survey questions included novel and previously validated questions to assess confidence, knowledge, self-efficacy, and attitudes about buprenorphine and working with patients who use drugs. Confidence, self-efficacy, and attitude responses were assessed on a Likert scale. Participants received a gift card for survey completion. We analyzed pre- and post- survey responses descriptively and compared them using *t*-tests. Using logistic regression we evaluated the factors associated with buprenorphine prescribing.

Results: Of 95 emergency physicians, 56 (58.9% response rate) completed the pre-intervention survey and 60 (63.2%) completed the post-survey. There was an increase in the number of X-waivered adult emergency physicians and ED buprenorphine prescribing after program implementation. Physician confidence increased from a mean of 3.4 (*SD* 0.8) to 3.9 (*SD* 0.7; scale 1–5, $p < 0.01$). Knowledge about buprenorphine increased from a mean score of 1.4 (*SD* 0.7) to 1.7 (*SD* 0.5, $p < 0.01$). Physician attitudes and self-efficacy did not change. Post-initiative, increased confidence was associated with higher odds of buprenorphine prescribing (odds ratio 4.4; 95% confidence interval 1.07–18.4).

Conclusion: After an ED QI initiative, buprenorphine prescribing in the ED increased, as did both physician confidence in working with patients who use drugs and their knowledge of buprenorphine. Increased confidence was associated with higher odds of buprenorphine prescribing and should be a focus of future, buprenorphine implementation strategies in the ED. [West J Emerg Med. 2023;24(6)1005–1009.]

INTRODUCTION

More than one in 20 people treated in an emergency department (ED) after a non-fatal overdose will die within a year, and of those just over two-thirds die from an opioid-related overdose.[1] Visits to the ED by patients with opioid use disorder (OUD) are an important opportunity to prevent overdose deaths and connect patients to evidence-based harm reduction services and treatment.

Buprenorphine treatment for OUD reduces mortality by over 50%[2,3]; however, a minority of people with OUD receive medication. Emergency department-initiated buprenorphine improves engagement in outpatient addiction treatment,[4] is cost effective,[5] and safe.[6,7] Uptake, however, has lagged. Noted barriers include physician comfort in counseling patients and ordering buprenorphine, regulatory concerns, the need for additional training and supports, and robust referral upon ED discharge.[8,9]

Rhode Island has one of the highest rates of opioid overdose deaths in the United States.[10] Since 2014, the Lifespan Opioid Overdose Prevention Program (LOOP) has worked to improve ED OUD care at Lifespan- affiliated EDs in Rhode Island.[11] To increase ED-initiated treatment of OUD, in June 2019 LOOP launched an ED quality improvement (QI) initiative to provide buprenorphine for treatment of OUD and opioid withdrawal. We surveyed attending emergency physicians (EP) before and after implementation to assess changes in their knowledge, attitudes, behaviors, confidence, and self-efficacy regarding ED buprenorphine use. Basing our study on the theory of planned behavior (TPB),[12] we hypothesized that after the initiative, EPs would report more knowledge, self-efficacy, and confidence, and more positive attitudes toward working with patients with OUD and prescribing buprenorphine in the ED.

METHODS

Procedures

This was an anonymous survey of EPs working in a Rhode Island hospital who were recruited through a faculty email listserv. Surveys were completed anonymously on a web platform (Qualtrics Provo, UT). The same survey was administered in June 2019 pre-intervention and again in May 2020 after implementation. Participants received a $20 gift card for each survey. This study was reviewed and deemed exempt by the Lifespan Institutional Review Board.

Intervention

In June 2019, LOOP launched a buprenorphine QI initiative that included educational lectures at faculty retreat and residency conferences, a standardized buprenorphine-prescribing protocol posted in all clinician work areas, and on-shift prescribing support through a physician-staffed 24/7 support warm line. The ED buprenorphine protocol was finalized in October 2019. Clinician education was provided at residency conferences and faculty meetings and via email communications and signage within the ED. Clinician-facing signage included the ED buprenorphine treatment algorithm (Appendix 1). Support was offered through a 24/7 warm line staffed by EPs with ED buprenorphine and addiction medicine expertise.

At the time this study was conducted, clinicians interested in prescribing buprenorphine were required to obtain a federal X waiver to prescribe buprenorphine, which required them to attend an eight-hour Drug Addiction Treatment Act of 2000 (DATA 2000) training and submit an application to the Substance Abuse and Mental Health Services Administration. Attending a training was not required by the study ED, but those who attended waiver training and obtained an X waiver received a $150 incentive. (The waiver requirement has since been removed.[8])

Measures

We developed the survey questions in alignment with the domains of the TPB framework (Appendix 2). The questions included a combination of previously validated and study-specific items about caring for patients who use drugs[13] and buprenorphine prescribing (Appendix 3). Validated questions about attitudes, confidence, willingness, and self-efficacy[13,14] used a five-point Likert scale (1 = strongly disagree, 5 = strongly agree). Knowledge questions were multiple choice with multiple correct responses; each item was scored by summing total correct responses and subtracting total incorrect responses. We calculated total knowledge scores by summing individual knowledge scores. Attitudes, willingness, self-efficacy, knowledge, and confidence were scored by averaging responses across all domain items.

Participants were asked to rate patient, ED, and pharmacy characteristics as barriers or facilitators to ED buprenorphine prescribing on a 10-point Likert scale (1 = not a barrier or facilitator to 10 = significant barrier or facilitator). The survey was pilot tested with clinicians in the ED prior to distribution. We queried the electronic health record (EHR) to examine counts of ED-administered buprenorphine and discharge EPs working in the study EDs.

Outcomes

Primary outcomes included changes in the domains of knowledge, self-efficacy, confidence, and attitudes post intervention. We also examined domains associated with reported buprenorphine prescribing.

Data Analysis

We downloaded survey data from the web platform, excluding from our analysis any missing items. Survey responses and buprenorphine prescribing were analyzed descriptively. We ran independent samples *t*-tests in SPSS statistical software (SPSS Inc, Chicago, IL) to compare ED-wide changes across all domains. A Bonferroni correction was performed to account for multiple comparisons. We conducted independent sample *t*-tests in SPSS to compare pre-post mean differences in 13 barriers to prescription of buprenorphine in the ED. Bonferroni correction was performed to account for multiple comparisons.

Finally, we employed logistic regression to evaluate predictors of reported buprenorphine prescribing. Four

models were run using pre-post initiative X-waiver attainment and pre-post buprenorphine prescription at patient discharge as dependent variables. Theorized predictors tested in the pre-initiative models included pre-implementation self-efficacy, confidence, attitudes, and knowledge. Predictors were identical for the post-implementation models. All logistic regression models controlled for completion of X-waiver training.

RESULTS

Study Subjects

Fifty-six of 95 attending physicians (58.9%) completed the pre-survey while 60/95 (63.2%) completed the post-survey. There were no missing responses in the pre-survey. Two respondents provided partial responses in the post-survey, one not completing knowledge and confidence questions and two not completing questions about attitudes and buprenorphine prescribing. Analysis was completed with all available data. Respondent pre- and post-survey age and gender demographics were similar (Table 1).

Table 1. Respondent demographics and characteristics.

	Pre-intervention n = 56 N (%)	Post-intervention n = 60 N (%)
Gender		
Male	33 (58.9)	28 (46.7)
Female	20 (35.7)	28 (46.7)
Transgender	0 (0)	0 (0)
Not reported	3 (5.3)	11 (18.3)
Age		
20–30 years	2 (3.6)	0 (0)
31–40 years	18 (32.1)	19 (31.7)
41–50 years	19 (33.9)	20 (33.3)
50+ years	15 (26.8)	17 (28.3)
Not reported	2 (3.6)	11 (18.3)
DATA 2000 X-waiver training		
Yes	27 (48.2)	49 (81.7)
No	29 (51.8)	10 (16.7)
Not reported	0 (0)	8 (13.3)
X-waivered	17 (30.4)	42 (70.0)
Ever prescribed buprenorphine upon discharge from ED		
Yes	*4 (7.1)*	*23 (38.3)*
No	*44 (78.6)*	*33 (55.0)*
No, but had someone else	*8 (14.3)*	*2 (3.3)*
Prescribe Missing	*0 (0)*	*9 (15.0)*

DATA 2000, Drug Addiction Treatment Act of 2000.

Pre-Survey Results

Almost half (27/56) of respondents had completed the DATA 2000 waiver training pre-intervention. Of those, only 62.9% (17/27) had received their X-waiver. Respondents reported moderate self-efficacy (mean 3.5 [SD 0.5], scale 1–5) and confidence (mean 3.4 [SD 0.8], scale of 1–5) in caring for people who use drugs. Attitudes were positive, with an average score of 3.8 ([SD 0.8], scale 1–5). Over half (31/56) reported ever administering buprenorphine in the ED; however, only 23.5% (4/17) of X-waivered physicians reported ever prescribing buprenorphine upon discharge. The most selected barriers included patient disinterest in treatment (mean 6.7 [SD 2.7], scale 1-10), availability of outpatient services (mean 5.9 [SD 3.1], scale 1–10), comfort with counseling patients (mean 5.8 [SD 2.9], scale 1–10), lack of knowledge (mean 5.8 [SD 3.1], scale 1–10), and time constraints (mean 5.7 [SD 3.0], scale 1–10). The most selected facilitators included pre-packaged prescription kits (mean 7.0 [SD 3.5], scale 1–10) and presence of an ED-based OUD patient engagement program (mean 6.4 [SD 3.7], scale 1–10). Per EHR data, in 2019 there were 48 prescriptions written for buprenorphine and monthly prescriptions ranged from two to eight (median 4).

Post-Survey Results

Sixty of 95 (63.2%) attendings completed the post-survey. The proportion of respondents who completed X-waiver training increased to 81.7% (60), and the proportion receiving their X-waiver increased from 30.4% (17/56) to 70.0% (42/60) after our intervention. Reported buprenorphine prescribing also increased from 7.1% in 2019 to 38.3% in 2020. Physician confidence increased from a mean of 3.4 (SD 0.8) to 3.9 (SD 0.7; scale 1–5, $P < 0.01$). Overall knowledge was unchanged; however, knowledge about ED buprenorphine use increased from a mean score of 1.4 (SD 0.7) to 1.7 (SD 0.5, $P < 0.01$) (Table 2). Physician attitudes and self-efficacy did not change (Table 2). There were 98 buprenorphine prescriptions in 2020 (median seven monthly prescriptions, range 5–22), almost doubling from 2019. Independent sample *t*-tests were run to evaluate differences in 13 barriers to buprenorphine prescription prior to and post initiative. After performing a Bonferroni correction we found no significant pre-post differences in barriers to buprenorphine prescription.

Logistic Regression Results

Physician confidence was a predictor for both pre- and post -implementation buprenorphine prescribing. Before the intervention, clinician confidence was associated with lower odds of buprenorphine prescribing (odds ration [OR] 0.3; 95% confidence interval [CI] 0.1, 0.9). After the intervention, confidence was a significant predictor of buprenorphine prescribing, such that the odds of prescribing increased more

than four times (OR 4.4; 95% CI 1.1, 18.4) for a one-unit increase in physician confidence.

DISCUSSION

Guided by the TPB,[10] we sought to capture changes in EPs' knowledge of, attitudes toward, and confidence in prescribing buprenorphine following an ED buprenorphine QI initiative. Physicians demonstrated improvements in their knowledge about and confidence in prescribing buprenorphine and treating patients with OUD, while changes in attitudes and self-efficacy were not observed. Previous studies have noted a similar discrepancy between knowledge about buprenorphine and prescribing comfort.[15] Improvements in confidence were observed alongside increases in monthly buprenorphine prescriptions. We also significantly expanded the number of waivered physicians with fewer monetary incentives compared to other institutions, which might suggest that other institutional supports such as education and protocols may be more likely to encourage physicians to provide buprenorphine in the ED.[16]

Identified barriers to ED-administered buprenorphine included need for physician consultation, lay ED overdose engagement specialists, time constraints, comfort in counseling patients, and knowledge. Previous studies have identified similar barriers to prescribing, including the former X-waiver requirement.[8,17] By addressing these and other environmental factors, EPs had the resources and institutional support they needed to successfully change their prescribing behavior. Such organization-wide initiatives are vital to increasing access to evidence-based treatments for OUD.

LIMITATIONS

This study has several limitations. Participant identifiers were not collected; thus, we were unable to link pre- and post-implementation responses, limiting our ability to assess individual changes in attitudes and behaviors over time. Our sample was small and consisted of academic EPs working in Rhode Island; thus, our findings may not be generalizable to other regions or hospital types. Finally, the survey did not capture attitudes, knowledge, and confidence of advanced practice practitioners or resident physicians.

Table 2. Self-efficacy, confidence, attitudes, and knowledge before and after ED intervention (scale 1 to 5) (pre: N = 56; post: N = 60).

	Pre-intervention Mean (SD)	Post-intervention Mean (SD)
Self-efficacy	3.5 (0.5)	3.5 (0.7)
Confidence	3.4 (0.8)	3.9 (0.7)
Attitudes	3.8 (0.8)	3.8 (0.8)
Overall knowledge		
Mean (SD)	11.6 (2.0)[1]	12.3 (2.1)[1]
Range	8 to 15	5 to 15
ED buprenorphine knowledge		
Mean (SD)	1.4 (0.7)[2]	1.7 (0.5)[2]
Range	−1 to 2	1 to 2

[1]Differences were not statistically significant.
[2]$P < 0.01$.

CONCLUSION

Removal of the federal X-waiver requirement will lower barriers to ED buprenorphine prescribing; however, educational and institutional initiatives are needed to reduce prescribing barriers and improve physician confidence in prescribing. Given the increased odds of buprenorphine prescribing with higher confidence, improving physician confidence may be an important target for future buprenorphine-implementation strategies in the ED. Future efforts are needed to improve physician skills, self-efficacy, and attitudes and to continue to minimize barriers to buprenorphine prescribing.

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REFERENCES

1. Weiner SG, Baker O, Bernson D, et al. One-year mortality of patients after emergency department treatment for nonfatal opioid overdose. *Ann Emerg Med.* 2020;75(1):13–7.

2. Larochelle MR, Bernson D, Land T, et al. Medication for opioid use disorder after nonfatal opioid overdose and association with mortality: a cohort study. *Ann Intern Med*. 2018;169(3):137–45.
3. Sordo L, Barrio G, Bravo MJ, et al. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. *BMJ*. 2017;357:j1550.
4. D'Onofrio G, O'Connor PG, Pantalon MV, et al. Emergency department–initiated buprenorphine/naloxone treatment for opioid dependence a randomized clinical trial. *JAMA*. 2015;313(16):1636–44.
5. Busch SH, Fiellin DA, Chawarski MC, et al. Cost-effectiveness of emergency department-initiated treatment for opioid dependence. *Addiction*. 2017;112(11):2002–10.
6. D'Onofrio G, Hawk KF, Perrone J, et al. Incidence of precipitated withdrawal during a multisite emergency department-initiated buprenorphine clinical trial in the era of fentanyl. *JAMA Netw Open*. 2023;6(3):e236108.
7. Herring AA, Vosooghi AA, Luftig J, et al. High-dose buprenorphine induction in the emergency department for treatment of opioid use disorder. *JAMA Netw Open*. 2021;4(7):e2117128.
8. Hawk KF, D'Onofrio G, Chawarski MC, et al. Barriers and facilitators to clinician readiness to provide emergency department-initiated buprenorphine. *JAMA Netw Open*. 2020;3(5):e204561.
9. Kim HS, Samuels EA. Overcoming barriers to prescribing buprenorphine in the emergency department. *JAMA Netw Open*. 2020;3(5):e204996.
10. Centers for Disease Control and Prevention National Center for Health Statistics. Drug Overdose Mortality by State. Available at: https://www.cdc.gov/nchs/pressroom/sosmap/drug_poisoning_mortality/drug_poisoning.htm. Accessed April 2023.
11. Samuels EA, Baird J, Yang ES, et al. Adoption and utilization of an emergency department naloxone distribution and peer recovery coach consultation program. *Acad Emerg Med*. 2019;26(2):160–73.
12. Ajzen I. The theory of planned behavior. In: *Organizational Behavior and Human Decision Processes*. Wuhan, China, Scientific Research Publishing 1991;50(2):179–211.
13. Watson H, Maclaren W, Kerr S. Staff attitudes towards working with drug users: development of the Drug Problems Perceptions Questionnaire. *Addiction*. 2007;102(2):206–15.
14. Samuels EA, Dwyer K, Mello MJ, et al. Emergency department-based opioid harm reduction: moving physicians from willing to doing. *Acad Emerg Med*. 2016;23(4):455–65.
15. Im DD, Chary A, Condella AL, et al. Emergency department clinicians' attitudes toward opioid use disorder and emergency department-initiated buprenorphine treatment: a mixed-methods study. *West J Emerg Med*. 2020;21(2):261–71.
16. Foster SD, Lee K, Edwards C, et al. Providing incentive for emergency physician X-waiver training: an evaluation of program success and postintervention buprenorphine prescribing. *Ann Emerg Med*. 2020;76(2):206–14.
17. Lowenstein M, Kilaru A, Perrone J, et al. Barriers and facilitators for emergency department initiation of buprenorphine: a physician survey. *Am J Emerg Med*. 2019;37(9):1787–90.

Impact of Emergency Department-Initiated Buprenorphine on Repeat Emergency Department Utilization

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Introduction: Recent studies have demonstrated the promise of emergency department (ED)-initiated buprenorphine/naloxone (bup/nx) for improving 30-day retention in outpatient addiction care programs for patients with opioid use disorder (OUD). We investigated whether ED-initiated bup/nx for OUD also impacts repeat ED utilization.

Methods: We performed a retrospective chart review of ED patients discharged with a primary diagnosis of OUD from July 2019–December 2020. Characteristics considered included age, gender, race, insurance status, domicile status, presence of comorbid Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) diagnosis, presenting chief complaint, and provision of a bup/nx prescription and/or naloxone kit. Primary outcomes included repeat ED visit (opioid or non-opioid related) within 30 days, 90 days, and one year. Statistical analyses included bivariate comparison and Poisson regression.

Results: Of 169 participants, the majority were male (67.5%), White (82.8%), uninsured (72.2%), and in opioid withdrawal and/or requesting "detox" (75.7%). Ninety-one (53.8%) received ED-initiated bup/nx, which was independent of age, gender, race, insurance status, presence of comorbid DSM-5 diagnosis, or domicile status. Naloxone was more likely to be provided to patients who received bup/nx (97.8% vs 26.9%; $P < 0.001$), and bup/nx was more likely to be given to patients who presented with opioid withdrawal and/or requested "detox" (63.3% vs 36.7%; $P < 0.001$). Bup/nx provision was associated with decreased ED utilization for opioid-related visits at 30 days ($P = 0.04$). Homelessness and lack of insurance were associated with increased ED utilization for non-opioid-related visits at 90 days ($P = 0.008$ and $P = 0.005$, respectively), and again at one year for homelessness ($P < 0.001$). When controlling for age and domicile status, the adjusted incidence rate ratio for overall ED visits was 0.56 (95% confidence interval [CI] 0.33–0.96) at 30 days, 0.43 (95% CI 0.27–0.69) at 90 days, and 0.60 (95% CI 0.39–0.92) at one year, favoring bup/nx provision.

Conclusion: Initiation of bup/nx in the ED setting was associated with decreased subsequent ED utilization. Socioeconomic factors, specifically health insurance and domicile status, significantly impacted non-opioid-related ED reuse. These findings demonstrate the ED's potential as an initiation point for bup/nx and highlight the importance of considering the social risk and social need for OUD patients. [West J Emerg Med. 2023;24(6)1010–1017.]

INTRODUCTION

According to the Substance Abuse and Mental Health Services Administration, nearly 5.6 million residents of the United States had opioid use disorder (OUD) in 2021, accounting for 2% of the US population.[1] From 2020 to 2021, there were an estimated 1.8 million new users of prescription pain relievers and 26,000 new heroin users, or nearly 5,000 new opioid users per day.[1] Correspondingly, the US Centers for Disease Control and Prevention observed a record high drug overdose mortality in 2021, with over 107,000 drug overdose deaths in the US, more than 80,000 of which involved opioids.[2]

The state of Alabama has been particularly affected by the opioid epidemic. Since 2014, Alabama has led the nation with the highest rate of opioid prescriptions in the country (80.4 prescriptions for every 100 persons in 2020), approximately twofold greater than the national average.[3] Jefferson County, the state's most populous county, had the highest number of opioid overdose deaths in Alabama in 2021, with 342 confirmed opioid overdose deaths, a 44.7% increase from 2020.[4] The opioid epidemic is an ongoing, significant public health emergency as evidenced by the rising incidence of opioid misuse, OUD, and opioid-related deaths in the US.

Emergency physicians are uniquely positioned to help combat the growing opioid crisis by screening and initiating care for patients presenting to the emergency department (ED) with OUD. Opioid-related ED visits have increased, representing nearly one in 80 ED visits, and escalated dramatically during the coronavirus disease 2019 (COVID-19) pandemic when non-opioid-related ED visits decreased.[5,6] Importantly, screening for opioid misuse and dependence in the ED has been proven to positively affect the prognosis of these patients. In a landmark randomized clinical trial in 2015, D'Onofrio and colleagues demonstrated that ED screening, brief intervention, and referral to treatment (SBIRT) for OUD, including ED-initiated medications for OUD (MOUD) with buprenorphine/naloxone (bup/nx), significantly increased 30-day retention in outpatient addiction treatment, decreased the use of opioids, and decreased utilization of inpatient addiction services.[7] As MOUD has been recognized as an effective treatment option to reduce mortality, overdose, and cost, EDs are increasingly engaged in OUD treatment initiation.[8–14] Further, a recent community-based study by Le et al demonstrated decreased subsequent healthcare utilization at 12 months after initiation of MOUD in the ED.[15]

Most ED-initiated MOUD studies have focused on treatment retention in large, urban, academic medical centers outside the Southeast or subsequent healthcare utilization in community hospitals.[7,11,12,15,16] Our large, urban, academic ED in the Southeast offers a unique perspective on the impact of ED-initiated MOUD on healthcare utilization in a resource-limited region characterized by persistent Medicaid non-expansion, high poverty rates, and healthcare access challenges.[13] In this study, we investigated whether ED-initiated bup/nx also impacts acute healthcare utilization, specifically repeat ED visits, for ED OUD patients.

Population Health Research Capsule

What do we already know about this issue?
Emergency department (ED)-initiated buprenorphine/naloxone (bup/nx) improves 30-day retention in outpatient addiction programs for opioid use disorder (OUD).

What was the research question?
Does ED-initiated bup/nx for OUD also impact acute healthcare utilization, specifically repeat ED visits, for OUD patients?

What was the major quantitative finding of the study?
Bup/nx decreased ED utilization at 30 days (37.5% vs. 62.5%, $P < 0.05$). Homelessness and lack of insurance increased ED utilization at 90 days ($P < 0.01$).

How does this improve population health?
Findings show the ED's potential as an initiation point for bup/nx and highlight the importance of social risk and need for OUD patients.

METHODS

Study Design and Setting

We conducted a retrospective chart review of patients who presented to our urban academic medical center ED at the University of Alabama at Birmingham (UAB) and were discharged from the ED with a diagnosis of OUD, using International Classification of Diseases, 10th Revision, (ICD-10) code documentation.[17] We obtained UAB Institutional Review Board approval. Our 48-bed, tertiary care ED evaluates over 75,000 patients annually. The UAB Hospital has 1,157 licensed beds and serves as the primary hospital for north-central Alabama and surrounding areas. We selected the study period July 2019–June 2020 because it marked the inaugural year of the hospital's ED-initiated OUD program, where patients with a diagnosis of OUD were to be discharged with a bridge bup/nx prescription, naloxone take-home kit, and referral to outpatient addiction treatment. However,

emergency clinicians' uptake and utilization of the bup/nx prescription was not universal during that first year. Prior to July 2019, bup/nx was not routinely prescribed from the ED.

Study Variables

The primary outcomes of interest were repeat ED utilization within 30 days, 90 days, and one year of the initial ED visit. Repeat ED visits were further classified as either opioid-related or non-opioid-related, as defined by ICD-10 documentation.[17] When analyzing opioid-related ED visits and non-opioid-related ED visits separately, we considered outcomes at each time point as binary variables. The number of opioid-related repeat ED visits was added to the number of non-opioid-related ED visits within 30 days, 90 days, and one year to obtain the composite outcome of total repeat ED visits at each time point of interest. We used composite value for Poisson regression analysis. The primary exposure of interest was whether the patient was discharged with a bup/nx prescription, which was a binary variable coded as yes or no.

Other variables in the analysis included age, gender, race, health insurance status, domicile status, provision of a naloxone kit, comorbid Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) diagnosis, and presenting chief complaint at the initial ED visit. Age was measured in years and was examined as a continuous variable. Gender was determined by data recorded in the electronic health record (EHR) at the time of ED registration, typically dictated by available legal identification (eg, driver's license) or self-reported in absence of ID. Gender was a nominal variable classified as male, female or other, per EHR limitations. Race was categorized as White or Black. (Other racial categories were not considered due to low numbers.) Health insurance was defined as private, public (Medicare and/or Medicaid), or self-pay (uninsured). Domicile status was a binary variable and classified as either homeless or not homeless. The provision of a naloxone kit upon discharge from initial visit was included as a dichotomous yes or no variable, as was the presence of a comorbid DSM-5 mental health diagnosis. Concomitant mental health diagnosis was determined by presence in "past medical history" during chart review. Chief complaint at the initial ED visit was noted and was manually classified by reviewers as opioid withdrawal/detoxification ("detox") request, opioid overdose, psychiatric complaint, or medical complaint.

Statistical Analysis

We carried out all analyses using SAS 9.4 (SAS Institute, Cary, NC), and $P < 0.05$ was considered statistically significant.[18] Frequencies and proportions were tabulated for categorical variables, which included gender, race, health insurance, naloxone kit provision, buprenorphine prescription, comorbid DSM-5 diagnosis, and ED chief complaint. We calculated mean and standard deviation for age, which was treated as a continuous variable. Chi-square and Fisher exact tests were used to compare the categorical demographic and medical characteristics of those with vs those without a repeat opioid-related ED visit within 30 days, 90 days, or one year. We used *t*-tests to assess differences in age by outcome status. Identical methods were used for the non-opioid-related ED visit outcomes (at 30 days, 90 days, and one year). Crude and adjusted Poisson models were constructed to estimate changes in the number of total repeat ED visits as well as the associated 95% confidence interval (CI) between those who were prescribed bup/nx and those who were not at the index ED visit for each of the time periods (30 days, 90 days, and one year). Separate models were generated for each outcome. Although no overdispersion in the 30-day model was observed, overdispersion in the 90-day and one-year models was detected and was accounted for by scaling by the deviance. Secondary analyses examined whether the association between bup/nx prescription and total number of repeat ED visits varied based on whether the patient also received a naloxone kit at their initial ED visit. To accomplish this, we included an interaction term between bup/nx prescription and naloxone kit in each of the models. All adjusted models included age and domicile status as covariates.

RESULTS

This study included 169 OUD patients. Of these, approximately 67.5% were male and 82.8% were White. Most patients did not have health insurance (72.2%), and 27 (15.9%) were homeless (Tables 1, 2). Additionally, over 75% of patients presented to the ED at their initial visit in opioid withdrawal or requesting "detox." Ninety-one patients (53.8%) received ED-initiated bup/nx (suboxone), and 110 (65.1%) were given a naloxone kit to take home at their initial ED visit. A bup/nx prescription was more likely to be given to patients who presented in opioid withdrawal and/or requested "detox" (63.3% vs 36.7%; $P < 0.001$), but bup/nx prescription did not show significant associations with age, gender, race, insurance status, presence of co-morbid DSM-5 diagnosis, or domicile status. A naloxone kit was more likely to be provided to patients who received bup/nx (97.8% vs 26.9%; $P < 0.001$).

At 30 days, 32 patients (18.9%) had a repeat opioid-related ED visit (Table 1). No significant differences emerged in terms of age, gender, race, health insurance status, homelessness, ED chief complaint, or comorbid DSM-5 diagnosis rates. However, bup/nx prescription and naloxone kit provision were associated with decreased ED utilization for opioid-related visits at 30 days ($P = 0.04$ and $P < 0.001$, respectively). By 90 days, 30.2% of the study sample had a repeat opioid-related ED visit. In this time frame, male patients ($P < 0.05$) and those who did not receive a naloxone kit ($P = 0.001$) were more likely to have a repeat visit;

Table 1. Comparison of patient characteristics by whether the patient had a repeat opioid-related emergency department visit.

	30-Day repeat ED visit			90-Day repeat ED visit			1-Year repeat ED visit		
Variables	No (n = 137)	Yes (n = 32)	*P*-value	No (n = 118)	Yes (n = 51)	*P*-value	No (n = 102)	Yes (n = 67)	*P*-value
Age, mean (SD)	36.5 ± 9.6	37.8 ± 8.0	0.49	36.5 ± 9.6	37.3 ± 8.8	0.62	37.0 ± 10.0	36.4 ± 8.4	0.71
Gender, n (%)									
Female	49 (35.8)	6 (18.8)	0.06	44 (37.3)	11 (21.6)	<0.05*	35 (34.3)	20 (29.8)	0.54
Male	88 (64.2)	26 (81.2)		74 (62.7)	40 (78.4)		67 (65.7)	47 (70.2)	
Race, n (%)									
White	113 (83.7)	27 (84.4)	0.79	97 (83.6)	43 (84.3)	0.64	86 (86.0)	13 (19.4)	0.33
Black	22 (16.3)	5 (15.6)		19 (16.4)	8 (15.7)		14 (14.0)	54 (80.6)	
Health Ins, n (%)									
Private	18 (13.1)	2 (6.2)	0.49	15 (12.7)	5 (9.8)	0.86	14 (13.7)	6 (9.0)	0.43
Public	23 (16.8)	4 (12.5)		19 (16.1)	8 (15.7)		18 (17.6)	9 (13.4)	
Self-pay	96 (70.1)	26 (81.3)		84 (71.2)	38 (74.5)		70 (68.6)	52 (77.6)	
Homeless, n (%)									
No	117 (85.4)	25 (78.1)	0.31	103 (87.3)	39 (76.5)	0.08	90 (88.2)	52 (77.6)	0.07
Yes	20 (14.6)	7 (21.9)		15 (12.7)	12 (23.4)		12 (11.8)	15 (22.4)	
Naloxone kit given, n (%)									
No	39 (28.5)	20 (62.5)	<0.001*	32 (27.1)	27 (52.9)	0.001*	28 (27.4)	31 (46.3)	0.01*
Yes	98 (71.5)	12 (37.5)		86 (72.9)	24 (47.1)		74 (72.6)	36 (53.7)	
Buprenorphine Rx, n (%)									
No	58 (42.3)	20 (62.5)	0.04*	51 (43.2)	27 (52.9)	0.24	45 (44.1)	33 (49.2)	0.51
Yes	79 (57.7)	12 (37.5)		67 (56.8)	24 (47.1)		57 (55.9)	34 (50.8)	
Comorbid DSM-5 Dx, n (%)									
No	116 (84.7)	28 (87.5)	0.68	98 (83.0)	46 (90.2)	0.23	84 (82.4)	60 (89.6)	0.20
Yes	21 (15.3)	4 (12.5)		20 (17.0)	5 (9.8)		18 (17.6)	7 (10.4)	
ED chief complaint, n (%)									
Opioid WD/detox request	102 (74.4)	26 (81.2)	0.52	88 (74.6)	40 (78.4)	0.23	77 (75.5)	51 (76.1)	0.30
Opioid OD	21 (15.3)	2 (6.2)		19 (16.1)	4 (7.8)		15 (14.7)	8 (11.9)	
Psychiatric complaint	9 (6.6)	2 (6.2)		8 (6.8)	3 (5.9)		8 (7.8)	3 (4.5)	
Medical complaint	5 (3.7)	2 (6.2)		3 (2.5)	4 (7.8)		2 (2.0)	5 (7.5)	

Race information was missing for two patients.
ED, emergency department; *Detox*, detoxification; *DSM-5*, Diagnostic and Statistical Manual of Mental Disorders, 5th Edition; *Dx*, diagnosis; *Ins*, insurance; *OD*, overdose; *Rx*, prescription; *WD*, withdrawal.
*Denotes statistical significance where $P < 0.05$.

however, ED-prescribed bup/nx was no longer significantly associated with having a repeat visit ($P = 0.24$).

Within one year, 67 patients (40.0%) had a repeat opioid-related ED visit. In this time frame, the only variable showing a significant association with repeat ED visit was naloxone kit provision ($P = 0.01$). Of those who received a naloxone kit, 32.7% had a repeat visit; however, among those who did not receive a kit, 52.5 % had a repeat visit. Thus, naloxone kit provision was associated with decreased ED utilization for opioid-related visits at 30 days, 90 days, and one year ($P < 0.001$, $P = 0.001$, and $P = 0.01$, respectively). Of the 169 patients, only 11 (6.5%) had a non-opioid-related repeat ED visit within 30 days (Table 2), compared with 32 (18.9%) who had an opioid-related repeat ED visit in that same time frame. Increasing age was associated with a repeat non-opioid-related visit at 30 days (43.8 ± 8.9 years vs 36.3 ± 9.2 years; $P = 0.009$). At this time point, no significant differences emerged in terms of gender, race, health insurance, homelessness, naloxone kit provision, bup/nx prescription, comorbid DSM-5 diagnosis, or ED chief complaint.

By 90 days, the number of patients with a non-opioid-related repeat ED visit increased to 23 (13.6%). Those with a repeat visit were older ($P = 0.004$), more likely to be

Table 2. Comparison of patient characteristics by whether the patient had a repeat non-opioid-related ED visit.

	30-Day repeat ED visit			90-Day repeat ED visit			1-Year repeat ED visit		
Variables	**No (n = 158)**	**Yes (n = 11)**	***P*-value**	**No (n = 146)**	**Yes (n = 23)**	***P*-value**	**No (n = 125)**	**Yes (n = 44)**	***P*-value**
Age, mean (SD)	36.3 ± 9.2	43.8 ± 8.9	0.009*	36.0 ± 9.0	41.9 ± 9.8	0.004*	35.5 ± 9.1	40.3 ± 9.3	0.003*
Gender, n (%)									
Female	53 (33.5)	2 (18.2)	0.51	50 (34.2)	5 (21.7)	0.23	43 (34.4)	12 (27.3)	0.39
Male	105 (66.5)	9 (81.8)		96 (65.8)	18 (78.3)		82 (65.6)	32 (72.7)	
Race, n (%)									
White	130 (83.3)	10 (90.9)	0.75	121 (84.0)	19(82.6)	0.83	103 (83.7)	37 (84.1)	0.70
Black	26 (16.7)	1 (9.1)		23 (16.0)	4 (17.4)		20 (16.3)	7 (15.9)	
Health ins, n (%)									
Private	18 (11.4)	2 (18.2)	0.68	17 (11.6)	3 (13.0)	0.005*	15 (12.0)	5 (11.4)	0.36
Public	25 (15.8)	2 (18.2)		18 (12.3)	9 (39.1)		17 (13.6)	10 (22.7)	
Self-pay	115 (72.8)	7 (63.6)		111 (76.0)	11 (47.8)		93 (74.4)	29 (65.9)	
Homeless, n (%)									
No	134 (84.8)	8 (72.7)	0.39	127 (87.0)	15 (65.2)	0.008*	112 (89.6)	30 (68.2)	0.001*
Yes	24 (15.2)	3 (27.3)		19 (13.0)	8 (34.8)		13 (10.4)	14 (31.8)	
Naloxone kit given, n (%)									
No	55 (34.8)	4 (36.4)	0.92	46 (31.5)	13 (56.5)	0.02*	41 (32.8)	18 (40.9)	0.33
Yes	103 (65.2)	7 (63.6)		100 (68.5)	10 (43.5)		84 (67.2)	26 (59.1)	
Buprenorphine Rx, n (%)									
No	73 (46.2)	5 (45.4)	0.96	64 (43.8)	14 (60.9)	0.13	58 (46.4)	20 (45.4)	0.91
Yes	85 (53.8)	6 (54.6)		82 (56.2)	9 (39.1)		67 (53.6)	24 (54.6)	
Comorbid DSM-5 Dx, n (%)									
No	134 (84.8)	10 (90.9)	0.58	123 (84.2)	21(91.3)	0.53	108 (86.4)	36 (81.8)	0.46
Yes	24 (15.2)	1 (9.1)		23 (15.8)	2 (8.7)		17 (13.6)	8 (18.2)	
ED chief complaint, n (%)									
Opioid WD /detox request	118 (74.7)	10 (90.9)	0.62	109 (74.7)	19 (82.6)	0.29	93 (74.4)	35 (79.6)	0.32
Opioid OD	22 (13.9)	1 (9.1)		21 (14.4)	2 (8.7)		20 (16.0)	3 (6.8)	
Psychiatric complaint	11 (7.0)	0 (0.0)		11 (7.5)	0 (0.0)		8 (6.4)	3 (6.8)	
Medical complaint	7 (4.4)	0 (0.0)		5 (2.4)	2 (8.7)		4 (3.2)	3 (6.8)	

Race information was missing for two patients.
ED, emergency department; *Detox*, detoxification; *DSM-5*, Diagnostic and Statistical Manual of Mental Disorders, 5th Edition; *Dx*, diagnosis; *Ins*, insurance; *OD*, overdose; *Rx*, prescription; *WD*, withdrawal.
*Denotes statistical significance where $P < 0.05$.

uninsured ($P = 0.005$), more likely to be homeless ($P = 0.008$), and less likely to have received a naloxone kit at the initial visit ($P = 0.02$). By one year, 44 patients (26%) had a repeat non-opioid-related ED visit. Again, patients with a repeat visit were older ($P = 0.003$) and more likely to be homeless ($P < 0.001$), although insurance status and naloxone provision no longer showed a significant association ($P = 0.36$).

Next, the total repeat all-cause ED visits were considered. Within 30 days of their index ED visit, 23.1% of patients had at least one repeat all-cause ED visit (range 1–4 visits). By 90 days, this percentage increased to 35.5% (range 1–12 visits). At one year from the initial visit, 50.3% of patients had a repeat visit (range 1–36 visits). In the unadjusted models, bup/nx prescription provision was significantly associated with a reduction in the number of repeat all-cause ED visits at 90 days (but not 30 days or one year) (Table 3). Given that significant association was also observed between older age and homelessness and all-cause repeat ED visits, the bup/nx association findings were re-evaluated after adjusting for age and domicile status. After adjusting for age and domicile status, a stronger association emerged between bup/nx

Table 3. Count ratios and 95% confidence intervals for the association between buprenorphine/naloxone prescription given and number of all-cause repeat emergency department visits.[+]

	Repeat ED visit within 30 days		Repeat ED visit within 90 days		Repeat ED visit within 1 year	
	Crude (95% CI)	Adjusted[1] (95% CI)	Crude (95% CI)	Adjusted[1] (95% CI)	Crude (95% CI)	Adjusted[1] (95% CI)
Overall						
No bup/nx	Ref	Ref	Ref	Ref	Ref	Ref
Bup/nx given	0.60 (0.35–1.02)	**0.56 (0.33–0.96)**	**0.48 (0.29–0.79)**	**0.43 (0.27–0.69)**	0.66 (0.42–1.05)	**0.60 (0.39–0.92)**
No naloxone kit given						
No bup/nx	Ref	Ref	Ref	Ref	Ref	Ref
Bup/nx given	0.95 (0.13–6.97)	1.10 (0.15–8.13)	0.37 (0.03–4.88)	0.50 (0.04–5.68)	0.39 (0.03–5.66)	0.52 (0.04–6.54)
Naloxone kit given						
No bup/nx	Ref	Ref	Ref	Ref	Ref	Ref
Bup/nx given	1.73 (0.52–5.78)	1.50 (0.45–5.07)	3.46 (0.75–15.97)	2.67 (0.63–11.28)	2.38 (0.76–7.44)	1.85 (0.63–5.44)

[+]Estimates of count ratio and 95% CIs generated from Poisson models.
*__Bold face font__ indicates statistical significance where $P < 0.05$.
[1]Adjusted for age and domicile status.
ED, emergency department; *CI*, confidence interval; *bup/nx*, buprenorphine/naloxone; *ref*, reference.

prescription provision and repeat all-cause ED visits, with bup/nx prescription being associated with a 44% reduction in the number of repeat all-cause ED visits at 30 days (adjusted incidence rate ratio [IRR]:0.56, 95% confidence interval [CI] 0.33–0.96), a 57% reduction at 90 days (adjusted IRR 0.43, 95% CI 0.27–0.69), and a 40% reduction at one year (adjusted IRR 0.60, 95% CI 0.39–0.92) (Table 3).

DISCUSSION

This study highlights the impact of OUD and the opioid epidemic in general on the ED. Over half the patients included in this study had a repeat ED visit within one year. This high level of utilization is likely due, in large part, to the overlapping social risk and social need experienced by this cohort. The general demographic characteristics of this study population are similar to the national opioid epidemic landscape, predominantly White (82.8%) and male (67.5%).[19] However, when considering social factors, such as insurance and domicile status, our OUD population was disproportionately affected by negative social determinants of health (SDoH). More than seven in ten OUD patients were uninsured, compared with the average uninsured rate of 12.7% in non-expansion states in 2021.[20] Further, 16% were homeless, which is nearly 100 times the national rate.[21] Homelessness and lack of insurance were independently associated with increased ED utilization for non-opioid-related visits at 90 days ($P = 0.008$ and $p = 0.005$, respectively), and again at one year for homelessness ($P < 0.001$). This underscores the complex social context of the ED OUD population. If co-occurring SDoH domains are not addressed during the ED visit, MOUD may not be successful in decreasing subsequent healthcare utilization. At UAB Hospital, ED social workers and case managers are available 24/7 to provide housing and healthcare access resources to underserved patients; however, referrals to assistance programs are not consistently documented in the EHR.

Although bup/nx provision was associated with decreased ED utilization for opioid-related visits at 30 days ($P = 0.04$), only 53.8% received ED-initiated bup/nx. Further, bup/nx was more likely to be given to OUD patients who presented in opioid withdrawal and/or requesting "detox" (63.3% vs 36.7%; $P < 0.001$). There are many plausible explanations for why 46.2% of OUD patients did not receive bup/nx at the initial ED visit, although this percentage is much lower than a recently published national retrospective cohort study where 91.5% were not prescribed buprenorphine after an ED visit for opioid overdose.[22] First, in July 2019 (study period start date), the UAB Department of Emergency Medicine had just initiated the Drug Addiction Treatment Act of 2000 (DATA 2000) "X-waiver" training requirement to license emergency clinicians for MOUD prescribing bup/nx through an incentive program, which was strongly encouraged but not mandated for all clinicians.[23]

Further, MOUD program uptake was not universal due to several known barriers to MOUD in the ED, including lack of training and experience in SBIRT, lack of availability of close outpatient follow-up in addiction treatment centers, and limited clinician time in a busy ED.[24] Finally, not every OUD patient presenting to the ED was a candidate for MOUD with bup/nx due to lack of motivation to seek and engage in outpatient treatment, concomitant use of illicit depressive agents, hypersensitivity reaction, and concern for diversion.[25] It is standard practice at the UAB ED for

patients receiving ED-initiated MOUD to be referred to community treatment programs; however, outpatient follow-up rates are not easily measured within our current system.

While roughly half of the patients received MOUD at the initial ED visit, nearly two-thirds received a take-home naloxone kit, which, at the time of the study was provided to patients free of charge with an emergency physician (EP) order via a collaborative project with the Jefferson County Health Department. Importantly, naloxone kit provision was associated with decreased ED utilization for opioid-related visits at 30 days, 90 days, and one year ($P < 0.001$, $P = 0.001$, and $P = 0.01$, respectively) and non-opioid-related visits at 90 days ($P = 0.02$). Naloxone is a potentially life-saving, easy-to-use and, in this instance, free intervention. Several factors might have contributed to incomplete provision: 1) The naloxone kit required a specific EP order to be dispensed, which may not have been prioritized due to competing demands for physician focus and time; 2) EPs may have had misperceptions of time-consuming counseling accompanying naloxone provision; and 3) EPs may have been unaware of the availability of naloxone provided as a take-home kit rather than a prescription.

In general, there was significant collinearity between bup/nx and naloxone kit provision. A naloxone kit was more likely to be provided to patients who received bup/nx (97.8% vs 26.9%; $P < 0.001$). Further, bup/nx was more likely to be given to patients who presented in opioid withdrawal and/or requested "detox: (63.3% vs 36.7%; $P < 0.001$). However, patients who presented in the most severe form of OUD, an acute overdose, were not more likely to receive bup/nx. This may be due to the EP's focus on resuscitation of acute decompensation and respiratory depression, rather than engagement of a brief intervention for MOUD to assess a patient's motivation toward behavioral change.

Our study is unique in assessing whether ED-initiated bup/nx impacts subsequent acute healthcare utilization, while also evaluating the impact of SDoH, such as health insurance and domicile status. Our results showed that when controlling for age and homelessness, initiation of bup/nx in the ED setting was associated with decreased subsequent all-cause ED utilization. Further, socioeconomic factors, specifically insurance and domicile status, appear to have significant impact on non-opioid-related ED reuse. These findings demonstrate the ED's potential as an initiation point for OUD treatment and highlight the importance of considering social risk and social need for OUD patients in the ED.

LIMITATIONS

This study had several limitations. First, the study design was a retrospective chart review, which prevents abstractors from being blinded to the study purpose and drawing conclusions of causality. However, to minimize bias, established emergency medicine chart review study methods were adhered to.[26] Further, the study population was obtained from a single site, which limits generalizability. Revisits to EDs in outside healthcare systems were unable to be tracked, preventing complete capture. However, UAB Hospital is the catchment healthcare system for the state of Alabama providing healthcare access to underserved populations, including the Charity Care Program, Equal Access Birmingham free clinic, Providing Access to Healthcare clinic, and a Comprehensive Urban Underserved and Rural Experience program. Finally, ED visit rates for opioid overdose increased by over 25% in 2020 due to the COVID-19 pandemic, despite a decline in overall ED visits.[27] Thus, expanded community- and hospital-based MOUD interventions were needed to support OUD patients during the COVID-19 pandemic; however, many counseling and treatment clinics were unavailable during that time.

CONCLUSION

Initiation of buprenorphine/naloxone in the ED setting can result in decreased subsequent ED utilization. Socioeconomic factors, specifically health insurance and domicile status, also appear to have a significant impact on ED reuse. These findings demonstrate the ED's potential as an initiation point for prescribing medication for opioid use disorder and highlight the importance of considering social risk and social need for OUD patients.

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REFERENCES

1. Key substance use and mental health indicators in the United States: Results from the 2021 National Survey on Drug Use and Health (HHS Publication No. PEP22-07-01-005, NSDUH Series H-57). Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental

Health Services Administration. Available at: https://www.samhsa.gov/data/report/2021-nsduh-annual-national-report. Published December 2022. Accessed March 13, 2023.
2. Spencer MR, Miniño AM, Warner M. Drug overdose deaths in the United States, 2001–2021. NCHS Data Brief, no 457. Hyattsville, MD: National Center for Health Statistics. 2022. Available at: https://www.cdc.gov/nchs/data/databriefs/db457.pdf. Accessed March 13, 2023.
3. U.S. opioid dispensing rate maps. Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/drugoverdose/rxrate-maps/index.html. Published November 10, 2021. Accessed March 13, 2023.
4. Annual 2021 Report Jefferson County Coroner/Medical Examiner's Office. Available at: https://www.jccal.org/Sites/Jefferson_County/Documents/Coroner_Medical%20Examiner%20Office/2021%20annual%20report.pdf. Accessed March 13, 2023.
5. Hall GT, Cruz DS, Lank PM, et al. Opioid-related emergency department visits during COVID-19 in a large health system. *J Addict Med*. 2021;15(4):345–8.
6. Langabeer JR, Stotts AL, Bobrow BJ, et al. Prevalence and charges of opioid-related visits to U.S. emergency departments. *Drug Alcohol Depend*. 2021;221:108568.
7. D'Onofrio G, O'Connor PG, Pantalon MV, et al. Emergency department-initiated buprenorphine/naloxone treatment for opioid dependence: a randomized clinical trial. *JAMA*. 2015;313(16):1636–44.
8. Sordo L, Barrio G, Bravo MJ, et al. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. *BMJ*. 2017;357:j1550.
9. Wakeman SE, Larochelle MR, Ameli O, et al. Comparative effectiveness of different treatment pathways for opioid use disorder. *JAMA Netw Open*. 2020;3(2):e1920622.
10. Fairley M, Humphreys K, Joyce VR, et al. Cost-effectiveness of treatments for opioid use disorder. *JAMA Psychiatry*. 2021;78(7):767–77.
11. Reuter QR, Santos AD, McKinnon J, et al. Long-term treatment retention of an emergency department initiated medication for opioid use disorder program. *Am J Emerg Med*. 2022;55:98–102.
12. Kaucher KA, Caruso EH, Sungar G, et al. Evaluation of an emergency department buprenorphine induction and medication-assisted treatment referral program. *Am J Emerg Med*. 2020;38(2):300–4.
13. Walter LA, Li L, Rodgers JB, et al. Development of an emergency department-based intervention to expand access to medications for opioid use disorder in a Medicaid nonexpansion setting: protocol for engagement and community collaboration. *JMIR Res Protoc*. 2021;10(4):e18734.
14. Melnick ER, Nath B, Dziura JD, et al. User centered clinical decision support to implement initiation of buprenorphine for opioid use disorder in the emergency department: EMBED pragmatic cluster randomized controlled trial. *BMJ*. 2022;377:e069271.
15. Le T, Cordial P, Sankoe M, et al. Healthcare use after buprenorphine prescription in a community emergency department: a cohort study. *West J Emerg Med*. 2021;22(6):1270–5.
16. Edwards FJ, Wicelinski R, Gallagher N, et al. Treating opioid withdrawal with buprenorphine in a community hospital emergency department: an outreach program. *Ann Emerg Med*. 2020;75(1):49–56.
17. Owens PL, Weiss AJ, Barrett ML. Hospital burden of opioid-related inpatient stays: metropolitan and rural hospitals, 2016. 2020 May 26. In: Healthcare Cost and Utilization Project (HCUP) Statistical Briefs [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2006 Feb-. Table 2, ICD-10-CM diagnosis codes defining opioid-related inpatient stays. Available at: https://www.ncbi.nlm.nih.gov/books/NBK559382/table/sb258.tab4/. Accessed March 13, 2023.
18. SAS Institute Inc. 2016. SAS® 9.4 Language Reference: Concepts, Sixth Edition. Cary, NC: SAS Institute Inc.
19. Racial/ethnic differences in substance use, substance use disorders, and substance use treatment utilization among people aged 12 or older (2015–2019) (Publication No. PEP21-07-01-001). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Available at: https://www.samhsa.gov/data/sites/default/files/reports/rpt35326/2021NSDUHSUChartbook.pdf. Accessed March 13, 2023.
20. Health insurance coverage status and type by geography: 2019 and 2021. Available at: https://www.census.gov/content/dam/Census/library/publications/2022/acs/acsbr-013.pdf. Accessed March 13, 2023.
21. De Sousa T, Andrichik A, Cuellar M, et al. The 2022 Annual Homelessness Assessment Report (AHAR) to Congress. Part 1: Point-In-Time Estimates of Homelessness. The U.S. Department of Housing and Urban Development Office of Community Planning and Development. Available at: https://www.huduser.gov/portal/sites/default/files/pdf/2022-AHAR-Part-1.pdf. Issued December 2022. Accessed February 12, 2023.
22. Chua KP, Dahlem CHY, Nguyen TD, et al. Naloxone and buprenorphine prescribing following US emergency department visits for suspected opioid overdose: August 2019 to April 2021. *Ann Emerg Med*. 2022;79(3):225–36.
23. Foster SD, Lee K, Edwards C, et al. Providing incentive for emergency physician X-waiver training: an evaluation of program success and postintervention buprenorphine prescribing. *Ann Emerg Med*. 2020;76(2):206–14.
24. Kim HS and Samuels EA. Overcoming barriers to prescribing buprenorphine in the emergency department. *JAMA Netw Open*. 2020;3(5):e204996.
25. Mackey K, Veazie S, Anderson J, et al. Barriers and facilitators to the use of medications for opioid use disorder: a rapid review. *J Gen Intern Med*. 2020;35(Suppl 3):954–63.
26. Kaji AH, Schriger D, Green S. Looking through the retrospectoscope: reducing bias in emergency medicine chart review studies. *Ann Emerg Med*. 2014;64(3):292–8.
27. Soares WE 3rd, Melnick ER, Nath B, et al. Emergency department visits for nonfatal opioid overdose during the COVID-19 pandemic across six US health care systems. *Ann Emerg Med*. 2022;79(2):158–67.

Characteristics and Outcomes of Patients in the Emergency Department with Left Ventricular Assist Devices

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Introduction: Left ventricular assist devices (LVAD) are increasingly common among patients with heart failure. The unique physiologic characteristics of patients with LVADs present a challenge to emergency clinicians making treatment and disposition decisions. Despite the increasing prevalence of LVADs, literature describing emergency department (ED) visits among this population is sparse. We aimed to describe clinical characteristics and outcomes among patients with LVADs seen in two quaternary-care EDs in a five-year period. Secondarily, we sought to evaluate mortality rates and ED return rates for bridge to transplant (BTT) and destination therapy (DT) patients.

Methods: We conducted a retrospective cohort study of adult patients known to have an LVAD who were evaluated in two quaternary-care EDs from 2013–2017. Data were collected from the electronic health record and summarized with descriptive statistics. We assessed patient outcomes with mixed-effects logistic regression models including a random intercept to account for patients with multiple ED visits.

Results: During the five-year study period, 290 ED visits among 107 patients met inclusion criteria. The median patient age was 61 years. The reason for LVAD implantation was BTT in 150 encounters (51.7%) and DT in 140 (48.3%). The most common presenting concerns were dyspnea (21.7%), bleeding (18.6%), and chest pain (11.4%). Visits directly related to the LVAD were infrequent (7.9%). Implantable cardioverter-defibrillator discharge was reported in 3.4% of visits. A majority of patients were dismissed home from the ED (53.8%), and 4.5% required intensive care unit admission. Among all patients, 37.9% returned to the ED within 30 days, with similar rates between DT and BTT patients (32.1 vs 43.3%; $P = 0.055$). The LVAD was replaced in three cases (1.0%) during hospitalization. No deaths occurred in the ED, and the mortality rate within 30 days was 2.1% among all patients.

Conclusion: In this multicenter cohort study of ED visits among patients with an LVAD, dyspnea, bleeding, and chest pain were the most common presenting concerns. Visits directly related to the LVAD were uncommon. Approximately half of patients were dismissed home, although return ED visits were common. [West J Emerg Med. 2023;24(6)1018–1024.]

Keywords: *emergency department; left ventricular assist device; outcomes; resuscitation.*

INTRODUCTION

With advancements in pharmacotherapy, mechanical devices, and surgical techniques, treatment options for advanced heart failure continue to expand. A left ventricular assist device (LVAD) is a continuous-flow device used in the setting of end-stage heart failure, with the goals of improving quality of life and longevity as destination therapy (DT) or as a cardiac bridge to transplant (BTT). From 2006–2016, a reported 22,866 LVADs were implanted internationally.[1]

Emergency physicians must be aware of the physiologic and anatomic changes inherent to patients with an LVAD and of the complications that may develop.[2–4] Additionally, patients typically begin new heart and anticoagulant medications related to their device, which may result in adverse effects. Patients may seek evaluation in the emergency department (ED) for various LVAD-related concerns, as well as for concerns unrelated to the LVAD.[5] Use of the ED by, and characteristics of, patients with an LVAD have been outlined in only three retrospective reports to our knowledge.[6–8] Although these studies examined ED visits among LVAD patients, few guidelines and only one risk-stratification tool currently exist for identifying high-risk LVAD patients seeking emergency care.[9]

Bleeding, infection, thrombosis, and mechanical complications are among the many reasons for LVAD patients to seek care in the ED.[2,3,10,11] Despite the increasing frequency of implantation of LVADs, relatively little is known regarding the proportion of ED visits that relate to these complications.[7] Furthermore, given the scarcity of literature on this topic, it can be difficult for emergency clinicians to accurately diagnose and treat illness in an LVAD patient and subsequently ensure a safe disposition. Our primary aim in this study was to describe clinical characteristics and outcomes among a large cohort of LVAD patients seeking emergency care during a five-year period. A secondary aim was to compare mortality rates and risk of return to the ED within 30 days between BTT and DT patients.

Population Health Research Capsule

What do we already know about this issue?
Left ventricular assist devices (LVAD) are increasingly common, and therefore are more common among patients in the ED where clinicians face novel treatment concerns.

What was the research question?
We describe characteristics and clinical outcomes of patients with LVADs seen at included centers over a five-year period.

What was the major finding of the study?
There was a 37.9% return to ED rate in 30 days. Destination therapy and bridge to transplant return rates were 32.1% vs 43.3% ($P = 0.055$).

How does this improve population health?
Our study provides background on common chief concerns and outcomes, including rates of ED return, for patients with LVADs.

METHODS

Study Design, Setting, and Participants

We conducted a retrospective cohort study of patients with an LVAD in place who were seen in two geographically distinct EDs of a single institution (Mayo Clinic Hospital-Saint Marys Campus in Rochester, Minnesota, and Mayo Clinic in Jacksonville, Florida) between January 1, 2013–December 31, 2017. All adult patients (≥18 years) who were registered as ED patients with implanted LVADs were eligible for inclusion in the study. The cohort size was determined by the number of encounters occurring during the study period, and each discrete ED visit was recorded. The two EDs are part of a multisite, quaternary-care academic institution with annual censuses of 74,000 and 30,000 during the study period. Our institutional review board approved the study protocol.

Patients were initially identified by searching our electronic health record (EHR) for patients who had *International Classification of Diseases, Ninth Revision* diagnosis code V43.21 (organ or tissue replaced by other means, heart assist device) on or before September 30, 2015, or *International Classification of Diseases, Tenth Revision, Clinical Modification* diagnosis code Z95.811 (presence of heart assist device) on or after October 1, 2015. To ensure that our search criteria identified all eligible patients, we cross-referenced these patients with an internal database of known LVAD patients at our hospital.[12]

We then reviewed data from the discrete ED encounters of patients with identified LVADs. Patients who did not have an LVAD implanted at the time of the ED encounter were excluded from the study. We also excluded patients with implanted LVADs who were directly admitted to the hospital and not evaluated in the ED. As a standard part of our admission process, all evaluated patients were asked for permission to use their documentation for research. Patients who declined research authorization were excluded from the study. We report our data in accordance with the STROBE (Strengthening the Reporting of

Observational Studies in Epidemiology) guidelines for observational studies.[13]

Data Sources and Management

Data were abstracted from the EHR by research team members. We defined all data fields a priori and developed a coding rubric. We used a standardized chart review process. Investigators responsible for abstraction of data (A.S.F., M.M.M., L.V.S., J.G.F., L.E.G.-H., and A.B.K.) were trained by the principal investigator (B.J.S.) and met at regular intervals to reconcile inconsistencies with the principal investigator. A sample of 15 visits was independently extracted by two investigators (M.M.M. and L.V.S.), and the interrater reliability was calculated for key variables and demonstrated with the Cohen κ statistic. The Cohen κ ranged from 0.8–1.0 for most variables and was within 0.6–1.0 for all variables, indicating good interrater reliability. We collected and managed study data by using the Research Electronic Data Capture tool hosted at our institution.[14]

Variables and Outcomes

We reviewed all available data from each ED encounter, and we reviewed prehospital and referring hospital data when available. If a patient was admitted to the hospital from the ED, we reviewed the available inpatient record and dismissal summaries. Specific data that were collected included the following: 1) demographic information; 2) arrival method (emergency medical services vs private vehicle); 3) chief concern; 4) whether the encounter was specifically related to the LVAD; 5) whether the encounter was due to an LVAD-associated factor (eg, anticoagulant medication and bleeding); 6) antiplatelet medications; 7) anticoagulant medications; 8) implantable cardioverter-defibrillator discharge; 9) LVAD information including brand, model, placement date, and placement location; 10) indication for placement (BTT vs DT); 11) cardiac arrest or need for care in the ED; 12) disposition from the ED; 13) admission level of care; 14) duration of hospitalization; 15) 30-day repeat ED visits; 16) one-year repeat ED visits; 17) death within 30 days; and 18) in-hospital death.

Outcome measures were recorded up to one year after each discrete encounter. We categorized encounters as being related to the LVAD if they were specifically associated with a device complication (eg, device alarm, driveline injury, driveline infection).

Statistical Methods

Continuous variables were summarized as mean (SD) or median (IQR); categorical variables were summarized as frequency (percentage). We performed comparisons of demographic characteristics between BTT and DT patients with two-sided Wilcoxon rank-sum tests for continuous features and χ^2 tests for categorical features. We assessed ED visit outcomes with mixed-effects logistic regression models. Random intercepts were included to account for repeat visits to the ED by individual patients, and no random slopes were implemented.

Our main outcome of interest was return visit to the ED within 30 days after the primary visit; secondary outcomes were death in the ED and death within 30 days of patient discharge. For each of these outcomes, we fit independent univariable regression models using disposition (admitted vs dismissed) and therapy type (BTT vs DT) as the predictors of interest. Models were both unadjusted and adjusted for patient age, sex, and race. No variable selection or removal was performed. $P < .05$ was considered statistically significant. We conducted all analyses using R version 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

During the study period, 290 discrete ED encounters among 107 patients met our inclusion criteria. Patients were predominantly men (242; 83.4%), and the median age was 61 years ("IQR," as in Methods 53–67 years). The median number of ED visits per patient was one, and the maximum was 17. Among included patients, 27 patients had one return visit (14 BTT, 13 DT), eight patients had two return visits (four BTT, four DT), three patients had three return visits (three BTT, zero DT), five patients had four return visits (two BTT, three DT), and four patients had five or more return visits (three BTT, one DT). Among discrete encounters, BTT (150 visits, 51.7%) and DT patients (140 visits, 48.3%) were similarly represented. The LVAD devices included HeartMate II (Abbott) (157 visits, 54.1%), HeartWare (Medtronic) (125 visits, 43.1%), and HeartMate 3 (Abbott) (seven visits, 2.4%), with one patient having no LVAD brand listed. Twenty visits (6.9%) were among patients whose LVAD was implanted at an institution other than the study sites.

The most common presenting concerns included dyspnea (21.7%), bleeding (18.6%), and chest pain (11.4%) (Table 1). Visits directly related to the LVAD were infrequent (23 visits, 7.9%). Implantable cardioverter-defibrillator discharges were noted in 19 visits (6.6%). The LVAD team was contacted by the ED team during 177 patient encounters (61.0%), although the LVAD team evaluated the patient in the ED in only 48 encounters (16.6%). Dismissal home from the ED was the most common disposition (53.8%). Only 13 encounters resulted in intensive care unit (ICU) admission (4.5%).

Among all patients admitted to the hospital or ICU (122), the median duration of hospitalization was one day. During hospitalization, the LVAD rarely required replacement (two cases, 1.6%; 95% confidence interval [CI] 0.3–6.5%). Among all ED encounters, 110 (37.9%) (95% CI 32.4–43.8%) resulted in return to the ED within 30 days. Among the 156 patient encounters that resulted in dismissal from the ED, 68

Table 1. Emergency department encounter characteristics.

Characteristic	No. of visits (%) (N = 290)
Presenting concern[a]	
Dyspnea	63 (21.7)
Bleeding	54 (18.6)
Epistaxis	25 (8.6)
Hematemesis	1 (0.3)
Hematochezia	13 (4.5)
Melena	25 (8.6)
Other	12 (4.1)
Chest pain	33 (11.4)
Syncope	21 (7.2)
ICD discharged	19 (6.6)
Fall	13 (4.5)
Fever	12 (4.1)
Weakness	9 (3.1)
Leg pain	9 (3.1)
PICC problem	7 (2.4)
LVAD alarm	5 (1.7)
Cough	4 (1.4)
Headache	4 (1.4)
Abdominal pain	4 (1.4)
Altered mental status	3 (1.0)
Rash	3 (1.0)
Back pain	3 (1.0)
Arm pain	3 (1.0)
Stroke/stroke symptoms	3 (1.0)
NPWT not working	2 (0.7)
Other concern (1 occurrence each)	28 (9.7)
Unknown	0 (0)
LVAD directly related to visit	
Yes	23 (7.9)
No	265 (91.4)
Unknown	2 (0.7)
LVAD team involvement	
LVAD team contacted	
Yes	177 (61.0)
No	111 (38.3)
Unknown	2 (0.7)
LVAD team evaluation in ED	
Yes	48 (16.6)
No	220 (75.9)
Unknown	22 (7.6)
Disposition	
External facility	0 (0)
Dismissed home	156 (53.8)
Hospital admission	109 (37.6)
Hospital observation	12 (4.1)
ICU admission	13 (4.5)
Unknown	0 (0)

ED, emergency department; *ICD*, implantable cardioverter-defibrillator; *ICU*, intensive care unit; *LVAD*, left ventricular assist device; *NPWT*, negative pressure wound therapy (wound vac); *PICC*, peripherally inserted central catheter.
[a]Patients could have >1 concern per visit.

(43.6%; 95% CI 35.7–51.8%) returned to the ED within 30 days. After adjusting for patient age, sex, and race, patients dismissed from the ED were nearly twice as likely to return to the ED within 30 days (odds ratio [OR], 1.81; 95% CI 1.01–3.27; $P = 0.047$) than were those admitted to the hospital or ICU (Table 2). Age, sex, and race were not significant predictors of ED return.

Among all patients, no deaths occurred in the ED. The overall 30-day mortality rate for the cohort was six patients (2.1%). No significant difference in 30-day mortality rate was found between the BTT (three, 2.0%) and DT (three, 2.1%) groups after accounting for repeat visits ($P = 0.92$).

The DT patients were significantly older than the BTT patients, with mean ages of 65.4 years and 55.3 years, respectively ($P < .001$) (Table 3). In a univariable analysis, DT patients were 37.4% less likely than BTT patients to return to the ED within 30 days, although the comparison did not reach significance (OR, 0.63; 95% CI 0.39–1.01; $P = 0.056$). Similarly, when accounting for repeat visits to the

Table 2. Multivariable analysis of overall 30-day ED returns.

Characteristic	Odds ratio (95% CI)	*P*-value
Age, per 1-year increase	1.00 (0.97–1.04)	0.84
Sex		0.95
Women	Reference	
Men	1.03 (0.40–2.66)	
Race		0.49
Other than White	Reference	
White	0.77 (0.36–1.63)	
ED disposition		.05
ICU or hospital admission	Reference	
Dismissal or hospital observation	1.81 (1.01–3.27)	

ED, emergency department; *ICU*, intensive care unit.

Table 3. Univariable analysis of emergency department encounters by therapy type.

Characteristic	Therapy type[a]		
	Bridge to transplant (n = 150)	Destination (n = 140)	*P*-value
Age, years	55.3 (9.9)	65.4 (10.3)	<.001
Sex			
Men	117 (78.0)	125 (89.3)	0.01
Women	33 (22.0)	15 (10.7)	
Race			<.001
Black	50 (33.3)	7 (5.0)	
White	86 (57.3)	116 (82.9)	
Other	11 (7.3)	2 (1.4)	
Unknown	3 (2.0)	15 (10.7)	
Visit outcome			
30-day ED return	65 (43.3)	45 (32.1)	0.06
1-year ED return	122 (83.0)	103 (73.6)	0.13
30-day death	3 (2.0)	3 (2.1)	0.92

ED, emergency department.
[a]Values are mean (SD) or No. of visits (%).

ED by discrete patients (OR, 0.59; 95% CI 0.29–1.20; $P = 0.15$) and after accounting for patient age, sex, and race, (OR, 0.51; 95% CI 0.23–1.14; $P = 0.10$), no differences in 30-day return visits to the ED were observed between the BTT and DT groups.

DISCUSSION

Our study describes characteristics of patients with LVADs seen in the EDs of two large quaternary-care centers of the same institution. The BTT and DT patients were evenly represented in our cohort. Unlike in previous studies, which have included only locally implanted devices, 6.9% of patients in our study cohort had LVADs implanted at institutions other than the study sites.[6,7] To our knowledge, we are the first to report return rates among LVAD patients dismissed from the ED: 43.6% within 30 days of the index visit. When patients were admitted, the median duration of admission was brief (one day); however, dismissal from the ED nearly doubled the risk of a return visit to the ED within 30 days. Similar to findings of other investigations,[7] no deaths in the ED were observed.

Regarding disposition from the ED, the proportion of the population dismissed home from the ED (53.8%) was higher than that reported in a previous study (13.4%).[7] This may represent practice site variation or an evolution in the current standard of care for LVAD patients seeking immediate care for acute concerns. However, the high risk of 30-day ED return observed in this cohort, among all encounters (37.9%) and among ED encounters resulting in dismissal (43.6%), suggests that clinicians should be aware of the high likelihood of an ED return visit within 30 days.[15]

Our report is novel in its characterization of ED encounters by BTT and DT groups. Prior studies on this topic specific to the ED have examined LVAD patients only in aggregate.[6,7] Our study expands on previous work, including a recent study of more than 44,000 ED visits in which investigators sought to derive and validate a novel prediction score for death by separating patients into these key subgroups.[9] A patient-centric approach including the intention of device implantation is beneficial in the clinical approach to LVAD patients, and this may be especially useful when characterizing long-term outcomes.[1,16]

No difference in mortality rate was observed between the BTT and DT groups. We found a 30-day mortality rate of 2.1% in the study group, which was lower than that in comparable studies on the topic.[1,16] In comparison, Piffard and colleagues[17] found a 22.9% mortality rate in ICU patients after LVAD implantation, although our study focused on patients admitted through the ED. As can be inferred from these data, LVAD patients are at substantial risk for worsening of clinical status after being hospitalized. We found that ICU admission was uncommon (13, 4.5%), and we identified no predictive factors for ICU admission in our cohort. A clinical implication of our study is that these patients may be safer for dismissal than previously thought, although they remain at risk for death within 30 days. Finally, DT patients were 37.4% less likely than BTT patients to return to the ED within 30 days. Unfortunately, our data do not provide an explanation for this observation, which is an area for potential future study.

In our study, ED encounters were more likely to result from LVAD-associated concerns such as bleeding in the setting of anticoagulation therapy (54, 18.6%) than from concerns directly related to LVAD function, which were uncommon (23, 7.9%). Our findings are consistent with those of other reports on this topic. One study showed bleeding to be the most common presenting concern in their analysis of 620 ED encounters with LVAD patients: 182 visits for bleeding (29.4%) were noted, compared with only 52 device-specific visits (8.4%).[7] Tainter and colleagues[6] similarly found device alarm or malfunction to account for only 4% of visits, whereas chest pain, syncope, and bleeding were common among their patient cohort.

LIMITATIONS

We note important limitations to our study. The retrospective nature of the investigation at our two study sites limited our ability to obtain data, which could only be obtained from the existing EHR. The research team was trained by the principal investigator to minimize variation in data input, as evidenced by high interrater reliability calculations. Although we attempted to broaden the

generalizability of our findings by including two geographically distant sites, all patients were cared for within the same hospital system. Increasing the number and diversity of participating sites would improve future investigations. However, this study is the first, to our knowledge, to include patients with LVADs implanted at institutions other than the study sites, which potentially improves its generalizability compared with the existing literature. Nevertheless, we were unable to determine time from implantation to ED visit, and so we could not assess whether this was an important factor.

A notable feature of our data set is the inclusion of patients with the HeartMate 3 device, which has not been previously reported in other ED-based studies. Additionally, the HeartWare device was better represented in our study than in earlier investigations.[6,7] Furthermore, although BTT and DT encompass most indications for LVAD placement, we did not identify any patients in our cohort with an LVAD implanted as a bridge to recovery. Because our study included patients with LVADs placed at other facilities, this potentially may have affected our admission and outcome data. Additionally, our sites may have a level of expertise with LVADs in general that may not be generalizable to other settings.

Regarding our statistical methods, we did not detect a significant difference between our groups of interest, although our study may have been underpowered to detect a small and true difference in the groups. Although we did evaluate return visits, we could not discern whether a patient visited an outside ED during the subsequent 30 days after the index visit. This is a limitation of our study design, but any additional ED visits that occurred outside of our institutions would only serve to reinforce our findings. Finally, patients were closely followed up by the LVAD coordinator team; therefore, it is unlikely that any patient death would have been unnoticed. It is possible, however, that a patient death could have been missed, particularly for those with devices placed at an outside hospital.

CONCLUSION

Among LVAD patients seen in two quaternary-care EDs of one institution, most visits were for LVAD-associated concerns such as bleeding, as opposed to visits directly related to the device itself. More than half of the cohort was dismissed home, although LVAD patients cared for in the ED had a high rate of return regardless of disposition. Among those who were dismissed, we found a 43.6% rate of return to the ED within 30 days.

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REFERENCES

1. Kirklin JK, Pagani FD, Kormos RL, et al. Eighth annual INTERMACS report: special focus on framing the impact of adverse events. *J Heart Lung Transplant.* 2017;36(10):1080–6.
2. Long B, Robertson J, Koyfman A, et al. Left ventricular assist devices and their complications: a review for emergency clinicians. *Am J Emerg Med.* 2019;37(8):1562–70.
3. Brady W, Weigand S, Bergin J. Ventricular assist device in the emergency department: evaluation and management considerations. *Am J Emerg Med.* 2018;36(7):1295–9.
4. Hockstein MA. Continuous-flow left ventricular assist devices: management in the emergency department. *J Am Coll Emerg Physicians Open.* 2020;1(4):362–70.
5. Trinquero P, Pirotte A, Gallagher LP, et al. Left ventricular assist device management in the emergency department. *West J Emerg Med.* 2018;19(5):834–41.
6. Tainter CR, Braun OO, Teran F, et al. Emergency department visits among patients with left ventricular assist devices. *Intern Emerg Med.* 2018;13(6):907–13.
7. McKillip RP, Gopalsami A, Montoya M, et al. Analysis of patients with ventricular assist devices presenting to an urban emergency department. *West J Emerg Med.* 2018;19(6):907–11.
8. Edelson JB, Edwards JJ, Katcoff H, et al. An increasing burden of disease: emergency department visits among patients with ventricular assist devices from 2010 to 2017. *J Am Heart Assoc.* 2021;10(4):e018035.
9. Edelson JB, Edwards JJ, Katcoff H, et al. Novel risk model to predict emergency department associated mortality for patients supported with a ventricular assist device: the Emergency Department-Ventricular Assist Device Risk Score. *J Am Heart Assoc.* 2022;11(2):e020942.
10. Simeon S, Flecher E, Revest M, et al. Left ventricular assist device-related infections: a multicentric study. *Clin Microbiol Infect.* 2017;23(10):748–51.
11. Robertson J, Long B, Koyfman A. The emergency management of ventricular assist devices. *Am J Emerg Med.* 2016;34(7):1294–301.
12. Worster A, Bledsoe RD, Cleve P, et al. Reassessing the methods of medical record review studies in emergency medicine research. *Ann Emerg Med.* 2005;45(4):448–51.
13. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *PLoS Med.* 2007;4(10):e296.

14. Harris PA, Taylor R, Thielke R, et al. Research Electronic Data Capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform.* 2009;42(2):377–81.
15. Cheng J, Shroff A, Khan N, et al. Emergency department return visits resulting in admission: Do they reflect quality of care? *Am J Med Qual.* 2016;31(6):541–51.
16. McIlvennan CK, Grady KL, Matlock DD, et al. End of life for patients with left ventricular assist devices: insights from INTERMACS. *J Heart Lung Transplant.* 2019;38(4):374–81.
17. Piffard M, Nubret-Le Coniat K, Simon O, et al. Independent risk factors for ICU mortality after left ventricular assist device implantation. *Artif Organs.* 2020;44(2):153–61.

Epinephrine in Cardiac Arrest: Identifying a Potential Limit for Resuscitation

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Introduction: Epinephrine continues to be a fundamental part of the Advanced Cardiac Life Support algorithm despite a lack of evidence that it improves neurologically intact survival. Our aim was both to identify a potential upper limit of epinephrine use in resuscitations and to demonstrate real-world epinephrine use in different patient subgroups.

Methods: This was a single-center, retrospective cohort study, conducted between August 1, 2016–July 1, 2021, of patients with medical cardiac arrest who were administered a known number of epinephrine doses. The primary outcome was neurologically intact discharge defined by a modified Rankin scale ≤3, with secondary outcomes of comparing epinephrine doses by age, rhythm, and emergency medical services vs emergency department administration of epinephrine.

Results: The study included 1,330 patients, with 184 patients (13.8%) surviving to neurologically intact discharge. The primary outcome of neurologically intact discharge was found in 89 (65.4%) patients in the zero epinephrine dose group, 75 (20.0%) in the 1-3 dose group, 15 (4.3%) in the 4-6 dose group, and one (0.002%) in the ≥7 dose group ($P < 0.001$). Patients received similar amounts of epinephrine when stratified by age, while patients with shockable rhythms received more epinephrine than patients with non-shockable rhythms.

Conclusion: There was a significant decrease in neurologically intact discharge with increasing number of epinephrine doses, and our data suggests that seven or more doses of epinephrine is almost always futile. While further prospective studies are needed, clinicians should consider epinephrine doses when weighing the futility or benefit of continued resuscitation efforts. [West J Emerg Med. 2023;24(6)1025–1033.]

INTRODUCTION

Advanced Cardiovascular Life Support (ACLS) has been used for patients in cardiac arrest in both the prehospital and hospital setting following its introduction in 1974.[1] Since that time, the guidelines have undergone several changes. Medications such as bicarbonate and calcium have lost favor,[2,3] while epinephrine remains a mainstay in both shockable (pulseless ventricular tachycardia and ventricular fibrillation) and non-shockable (asystole and pulseless electrical activity) rhythms. The most recent ACLS guidelines recommend epinephrine use in all cardiac arrest patients as a 1 mg dose given every 3–5 minutes, along with high-quality cardiopulmonary resuscitation (CPR), until the patient has return of spontaneous circulation (ROSC).[1] Current research, however, shows epinephrine may improve the rates of ROSC but does not improve rates of survival to hospital discharge or survival with a favorable neurologic outcome.[4–7]

The European Resuscitation Council recommends terminating resuscitative efforts after 20 minutes in the

absence of reversible causes, given the unlikely event of a positive outcome.[8] The American Heart Association recommends cessation of out-of-hospital cardiac arrest resuscitation in patients with unwitnessed, non-shockable rhythms, who do not get ROSC prior to transport.[9]

While previous studies have shown increasing epinephrine doses are associated with worse resuscitation outcomes, the exact dose of epinephrine from which there would be no further benefit is unclear.[6,10–12] It is also unclear how age may play a role in the outcome of resuscitation when taking into account increasing epinephrine dosing. Although epinephrine is a potent inotrope and vasopressor, it is also thought to increase myocardial oxygen consumption as well as increase the risk of arrhythmias during repeated dosing. Often, patients in cardiac arrest with shockable rhythms refractory to management may actually benefit from less epinephrine, to reduce myocardial oxygen demand and to limit adrenergic stimulation, which decreases the risk for dysrhythmia.[13–17] There are, however, no established guidelines regarding when epinephrine dosing should cease during resuscitation, the risk or benefit to neurologically intact ROSC with epinephrine use in shockable rhythms, or the total number of epinephrine doses that would be most beneficial to patients.[18,19]

We set out to conduct a study to determine a point in the resuscitation where further epinephrine dosing is potentially futile. We designed our patient groups and secondary outcomes in an a priori fashion to explore the use of epinephrine by clinicians based on patient age, cardiac rhythm, and location of cardiac arrest. These outcomes provide novel data for this controversial medication. Our a priori hypothesis was that increasing doses of epinephrine are associated with increasing mortality and worse neurologic outcomes. Additionally, we attempted to identify a potential limit of epinephrine use in cardiac arrest within our institution and to describe the use of epinephrine in the emergency department (ED) for various patient populations.

Population Health Research Capsule

What do we already know about this issue?
Epinephrine in cardiac arrest has an unclear survival benefit, and prior studies have shown increasing doses to be associated with increased mortality.

What was the research question?
Is there a point in resuscitation where more epinephrine doses are potentially futile?

What was the major quantitative finding of the study?
Neurologically intact discharge ranged from 65.4% with 0 epinephrine doses to 0.002% in the ≥7 dose group ($P < 0.001$).

How does this improve population health?
Understanding epinephrine and survival rates of cardiac arrest is important to improve outcomes and decrease emergency department resource use.

METHODS

This was a single-center, retrospective cohort study at an academic, Level I trauma and tertiary referral center that sees greater than 100,000 ED visits per year. The study received institutional review board approval. After a joint discussion with all study members, and a one-hour training session, we manually reviewed electronic health records (EHR) for all cardiac arrest patients from August 2016, which marked the institution of our current EHR system, until July 2021. All reviewers were blinded to the study question. Patients were identified using International Classification of Diseases, 10th Revision (ICD-10) codes for cardiac arrest (I46, cardiac arrest; I46.2, cardiac arrest due to underlying condition; I46.9, cardiac arrest, cause unspecified; I49.01 ventricular fibrillation; J98.9 cardiac arrest due to respiratory disorder).

Inclusion criteria were patients ≥18 years old who presented to the hospital in cardiac arrest, had a cardiac arrest in the ED, or were transferred from an outside hospital after a cardiac arrest. Patients were excluded (Figure 1) if they y had a cardiac arrest only after hospital admission, a traumatic cardiac arrest, an advanced directive invoked during resuscitation, or an unknown number of epinephrine doses. Patients were also excluded if we could not determine the actual number of epinephrine doses administered based on chart review.

Definitions

Cardiac arrest was defined as loss of pulses requiring either CPR or a shock delivered by an external defibrillator. We considered ventricular fibrillation or pulseless ventricular tachycardia as shockable rhythms, whereas asystole and pulseless electrical activity were non-shockable rhythms, per ACLS guidelines.[20] Our department's cardiac arrest workflow assigns one ED nurse solely to documentation during every cardiac arrest resuscitation. The nursing documentation was, therefore, the most accurate way to track medication administration, and we used this method to count epinephrine doses. For number of epinephrine doses given by emergency medical services (EMS), we also used the nursing code documentation, which started with a summary of care given by EMS of the patient presentation and

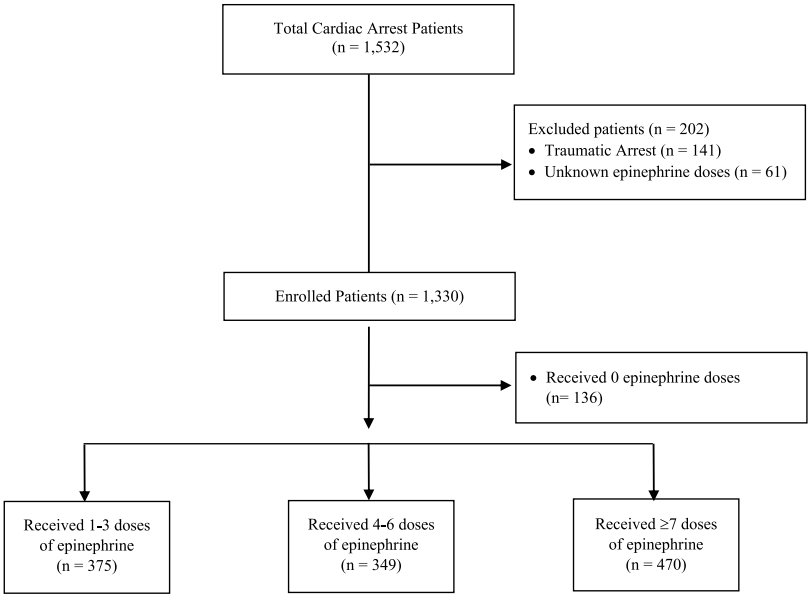

Figure 1. Flow diagram of study enrollment.

transport, including any medications and interventions provided. We unfortunately did not have consistent prehospital records and so opted not to reference these due to large gaps in data collected. A patient was considered to have died in the ED if he or she was pronounced while in the ED without an admission history and physical documented.

We chose to study substance use as a comorbidity and defined it as an existing diagnosis of substance use in the patient's chart based on the patient's past medical history; it was considered separate from a history of alcohol use disorder. The patient population in the area served by the hospital system is medically underserved with a high rate of substance use disorder (with approximately 4% of the total city population receiving substance use disorder treatment over a one-year period),[21] specifically fentanyl and cocaine, which can result in cardiac arrest through arrhythmias or hypoxia.[21–23]

The primary outcome was neurologically intact hospital discharge defined by a modified Rankin scale ≤3, which has been used in previous cardiac arrest literature.[24] The primary outcome was stratified by total number of doses of epinephrine to evaluate for effect of escalating doses. We considered one dose of epinephrine to be 1 mg administered via an intravenous push, the standard dose recommended by ACLS for cardiac arrest. Secondary outcomes included the age of patients receiving epinephrine doses, the number of epinephrine doses administered by EMS vs the ED, and the time to first epinephrine dose.

Patients were stratified by number of epinephrine doses into three groups: 1–3 doses, 4–6 doses, and ≥7 doses. Other studies used smaller groups (1 dose, 2–5 doses, >5 doses), but we found that our grouping resulted in three groups of similar size, allowing for a more balanced analysis.[6] The choice of groups was also determined by an estimate of resuscitation time based on administration of a single epinephrine dose every 3–5 minutes on average. The 1–3 dose group implies at least 10 minutes of resuscitation, 4–6 dose group 20 minutes of resuscitation, and ≥7 dose group above 20 minutes of resuscitation. We chose 20 minutes as our upper cutoff since, as mentioned earlier, this represents the time after which the European Resuscitation Council recommends terminating resuscitative efforts.[8]

Data Collection

We collected data via manual abstraction. The principal investigators (ZB, TS) met to create a standardized method in which data would be abstracted and then held a one-hour session to train the rest of the research team. Each member of the research team (ZB, DD, KD) would collect an equal proportion of data of which 10% was reviewed by a separate investigator (TS) for inter-reviewer reliability and accuracy, and any corrections were made on an ongoing basis. The research team was not blinded to the a priori hypothesis.

We conducted statistical analysis using SPSS version 28 (IBM Corporation, Armonk, NY), using a P-value <0.05 for significance. We first tested for normality with a Shapiro-Wilk test. Non-normal data, such as the grouping of patients by epinephrine dosing and age, was analyzed with either a Mann-Whitney U test (two groups) or Kruskal-Wallis testing (greater than two groups). Normal data such as demographics, comorbidities, EMS vs ED administration, in- vs out-of-hospital cardiac arrest, and shockable vs non-shockable rhythm, was analyzed with either the Student t-test (two groups) or ANOVA testing (greater than two groups).

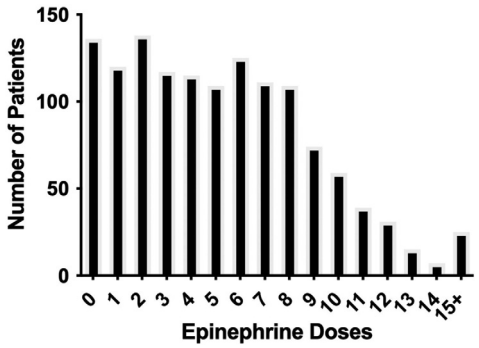

Figure 2. Total epinephrine doses administered.

RESULTS

The study analyzed 1,330 patients, with 136 patients (10.2%) receiving no doses of epinephrine, and 1,194 patients who received at least one dose of epinephrine (Figure 2). The average age of the cohort was 63.3 years old (SD 17.4), and 65.2% male. The total mortality in the study was 1,109 deaths (83.4%) with 653 (58.9%) of those deaths occurring in the ED. The total survival to neurologically intact hospital discharge was 184 patients (13.8%). There were 1,137 (85.5%) out-of-hospital cardiac arrest patients, and 551 patients (41.4%) received at least one defibrillation. Bystander or immediate CPR was initiated in 767 patients (57.6%). Comorbidities were able to be determined for 861 patients (64.7%) from EHR review, while the other patients had no prior visits and no documented comorbidities. Demographics and comorbidities can be found in Table 1, with minor but statistically significant differences between groups. Bystander or immediate CPR was more common if patients received zero or 1–3 doses of epinephrine when compared to higher doses of epinephrine (Table 1).

A total of 136 patients received zero epinephrine doses, with 89 (65.4%) surviving to a neurologically intact hospital discharge. At least one defibrillation was administered to 63.2% of the zero epinephrine patients, compared to 39.8% of patients who received at least one dose of epinephrine. A resuscitation time was able to be calculated for 91 patients with zero epinephrine doses (66.9%), with a mean resuscitation time of 8.2 minutes and median of 5 minutes.

A total of 1,194 patients received at least one dose of epinephrine. They received an average of 5.8 doses epinephrine (SD 3.6). One hundred and fifty-six patients (13.0%) were in-hospital cardiac arrests. A total of

Table 1. Demographics and comorbidities.

	Total cohort (%[a], n)	0 Doses epinephrine (%[a], n)	1–3 Doses epinephrine (%[a], n)	4–6 Doses epinephrine (%[a], n)	≥7 Doses epinephrine (%[a], n)
Total patients	1,330	136	375	349	470
Average age	63.3 years	65.0 years	63.8 years	62.3 years	62.9 years
Male*	65.2 (867)	72.8 (99)	57.6 (216)	67.1 (234)	67.7 (318)
Bystander/immediate CPR*	57.6 (767)	74.3 (101)	63.5 (238)	53.3 (186)	51.5 (242)
Shockable rhythm*	41.9 (557)	60.2 (82)	34.9 (131)	33.5 (117)	48.3 (227)
Non-shockable rhythm*	58.1 (773)	39.7 (54)	65.1 (244)	66.5 (232)	51.7 (243)
In-hospital arrest*	13.5 (180)	17.6 (24)	19.5 (73)	13.1 (46)	7.9 (37)
Out-of-hospital arrest*	88.3 (1,174)	82.4 (112)	80.5 (302)	86.9 (303)	92.1 (433)
Missing comorbidities*	35.3 (469)	17.6 (24)	18.1 (68)	23.2 (81)	28.5 (134)
Cardiac risk factors					
HTN*	48.2 (641)	59.6 (81)	65.9 (170)	60.2 (129)	59.2 (164)
HLD*	29.3 (390)	40.4 (55)	41.0 (106)	34.1 (73)	36.1 (100)
CKD*	11.1 (147)	6.6 (9)	15.5 (40)	15.9 (34)	15.5 (43)
DM*	25.7 (342)	17.6 (24)	31.0 (80)	33.6 (72)	40.4 (112)
CHF*	16.0 (213)	16.2 (22)	24.4 (63)	15.4 (33)	23.5 (65)
MI/CAD*	23.2 (308)	37.5 (51)	32.6 (84)	22.9 (49)	28.2 (78)
Lung disease*	18.6 (248)	19.9 (27)	25.2 (65)	18.7 (40)	27.8 (77)
Substance use*	14.9 (198)	8.8 (12)	20.9 (54)	25.2 (54)	22.0 (61)

*Denotes statistically significant ($P < 0.05$) group difference using an ANOVA test; [a]Percentages calculated based on total patients in each group.

CPR, cardiopulmonary resuscitation; *HTN*, hypertension; *HLD*, hyperlipidemia; *DM*, diabetes mellitus; *CHF*, congestive heart failure; *MI/CAD*, myocardial infarction/coronary artery disease.

91 patients (7.6%) survived to a neurologically intact hospital discharge. Average resuscitation time was 33.4 minutes for this cohort. A resuscitation time could be calculated for 1,007 patients (84.3%), with the other patients having no clear prehospital resuscitation time communicated. Average resuscitation time for the 1–3 dose group was 14.8 minutes (min) (median 10 min), for the 4–6 dose group 32.2 min (median 30 min), and for the ≥ 7 doses group 48.5 min (median 50 min).

The primary outcome of neurologically intact hospital discharge (Figure 3) was found in 89 (65.4%) patients who received zero doses of epinephrine, 75 (20.0%) patients in the 1–3 dose epinephrine group, 15 (4.3%) in the 4–6 dose group, and one (0.2%) in the ≥7 doses group ($P < 0.001$). Patients who did achieve ROSC had an earlier likelihood for mortality with increasing doses of epinephrine (Supplemental Figure 1).

When compared to the 1–3 dose group, the odds of surviving to hospital admission decreased as the number of epinephrine doses increased for both the 4–6 dose group (odds ratio [OR] 0.58. 95% confidence interval [CI] 0.46–0.74; $P < 0.001$)) and the ≥7 doses group (OR 0.27, 95% CI 0.21–0.35; $P < 0.001$)), as well as the odds for survival to neurologically intact hospital discharge (OR 0.26, 95% CI 0.15–0.47; $P < 0.001$) and (OR 0.01, 95% CI 0.002–0.08; $P < 0.001$) respectively.

The single patient in the cohort who survived to neurologically intact discharge with ≥7 doses of epinephrine was a 63-year-old female who had a shockable rhythm. She received 13 doses of epinephrine and 15 defibrillations, all by EMS, and was ultimately found to have severe coronary artery disease and required a coronary bypass.

Secondary Outcomes

Patients who received epinephrine were sub-grouped by age into four cohorts: 18–30 years old; 31–50 years old; 51–70 years old; and ≥71 years old (Figure 4). There was no significant difference between increasing age and increasing doses of epinephrine, as younger patients did not receive ≥7 doses of epinephrine more so than patients ≥71 years old ($P = 0.80$). Patients aged 18-30 years old were also equally likely to receive 1–3 doses of epinephrine when compared to the ≥71 years old group ($P = 0.11$). Overall mortality was also similar between different age groups as well, ranging from 88.4% for the 18–30 group to 92.6% for patients ≥71 years old ($P = 0.23$), and there was no discernible age-based mortality pattern when stratified for epinephrine dosing (Figure 5).

A time to first epinephrine dose was calculated for the 156 in-hospital cardiac arrests who received epinephrine, with those surviving to a neurologically intact hospital discharge (n = 26) receiving their first epinephrine dose on average 1.54 minutes into the resuscitation, compared to those who did not survive to a neurologically intact hospital discharge (n = 130) receiving their first dose at 2.15 minutes, which was statistically significant ($P = 0.02$). Time to first epinephrine dose was not calculated for the out-of-hospital cardiac arrest patients, unfortunately, due to the lack of consistent prehospital data available for retrospective review. Additionally, the survival to neurologically intact hospital discharge for the in-hospital cardiac arrests was 16.0%

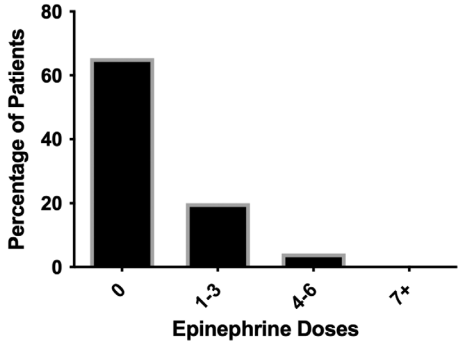

Figure 3. Percentage of patients receiving epinephrine who survived to neurologically intact hospital discharge.

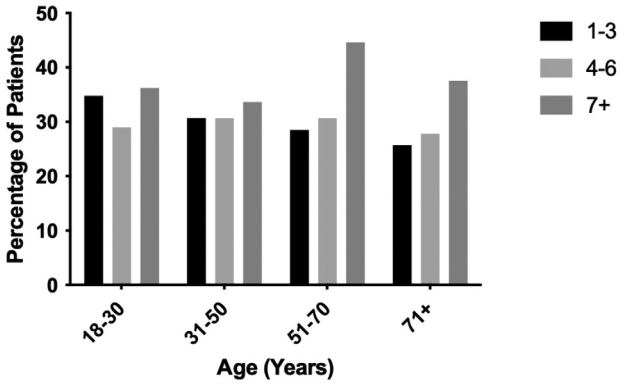

Figure 4. Epinephrine doses distributed by patient age as a percentage of patients within each age group.

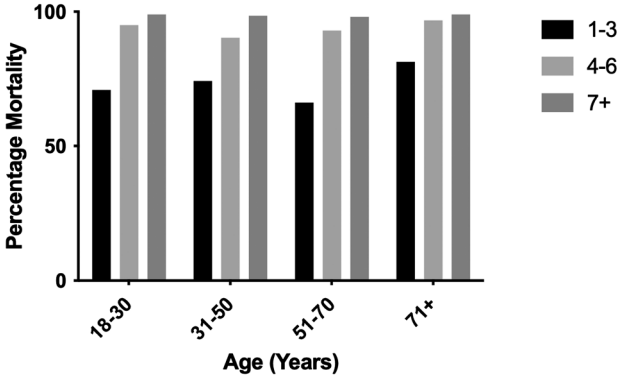

Figure 5. Mortality in patients grouped by age.

(n = 26), compared to 6.3% (n = 65) for the out-of-hospital cardiac arrests ($P < 0.001$).

Patients who received epinephrine and had a shockable rhythm at any time during their arrest (n = 475) received an average of 6.25 doses of epinephrine, compared to 5.49 doses in patients who never had a shockable rhythm ($P < 0.001$). Survival to neurologically intact hospital discharge in this subgroup was 10.4% (49 patients) with a shockable rhythm and 5.8% (42 patients) with a nonshockable rhythm ($P < 0.001$). A shockable rhythm was also seen more in the zero-dose epinephrine group and the ≥7 dose group, and a non-shockable rhythm was seen more in groups receiving epinephrine compared to those who did not receive epinephrine (Table 1).

There were also differences between number of epinephrine doses administered by EMS compared to the ED. Of the out-of-hospital cardiac arrest patients who received epinephrine, the ED was more likely to administer zero doses of epinephrine (34.9%) than EMS (5.9%) ($P < 0.001$). Patients who suffered an in-hospital arrest were more likely to receive zero doses or 1–3 doses, while patients who suffered an out-of-hospital cardiac arrest were more likely to receive ≥7 doses of epinephrine (Table 1). Of 1,036 out-of-hospital cardiac arrests, 162 (15.6%) received ≥7 epinephrine doses by EMS. Of the 158 in-hospital cardiac arrests, 37 patients (23.4%) received ≥7 doses of epinephrine in the ED. A total of 980 patients (82.1%) received their first dose of epinephrine from EMS, with 60 (6.1%) surviving to neurologically intact hospital discharge, compared to 214 patients who received their first dose of epinephrine from the ED, with 31 (14.5%) surviving to a neurologically intact hospital discharge ($P < 0.001$). Sixty-four patients who received their first dose of epinephrine in the ED were defined as out-of-hospital cardiac arrests, with nine (14.0%) patients achieving ROSC by EMS and had subsequent loss of pulses in the ED. Nine (14.0%) of this patient subset survived to a neurologically intact hospital discharge.

DISCUSSION

Our results show a significant decrease in patients with neurologically intact discharges as the number of epinephrine doses increase. In addition, receiving ≥7 doses of epinephrine was associated with a very low probability of achieving ROSC (1/470, 0.2%). This study supports the findings of Jouffroy et al that ≥7 doses of epinephrine decreased the chances of obtaining ROSC.[25] The secondary finding that patients with a shockable rhythm or in-hospital cardiac arrest received more epinephrine doses than their counterparts suggests that physicians may continue giving epinephrine doses due to the known higher survivability of these patient subgroups in prior studies, which our findings corroborated.[26,27] We did not find, however, that younger patients received more epinephrine doses, regardless of how much total epinephrine was given. Patients older than 70 received ≥7 doses of epinephrine in similar proportions to patients 18–30. Mortality was also similar between age groups within each subgroup of epinephrine dosing. This finding, to our knowledge, does not appear in the current literature on epinephrine use in cardiac arrest and suggests that physicians are not taking into consideration patient age during resuscitation, or that the patient's age is less of a factor to cease resuscitation. While the study was not specifically designed to compare patient age and number of epinephrine doses, this novel finding is hypothesis-generating and should be studied in a prospective fashion.

Multiple studies address the futility of increasing the number of epinephrine doses in cardiac arrest, finding that increased epinephrine doses was associated with increased mortality for patients.[6,10,12,28] Our study results agreed with those findings and increase their generalizability to an overall ED population, in that we conducted a secondary analysis of patients by age to show that younger patients did not skew our results and that we included both in-hospital and out-of-hospital cardiac arrests, shockable and non-shockable rhythms, and EMS to ED administration of epinephrine, unlike previous research.

A study by Grunau et al did show survival with neurologically intact discharge in a small number of patients who received >7 doses of epinephrine, but they did not elaborate on these patients as it was not a study outcome.[29] Shi et al showed neurologically intact survival in 23.6% (17/72) of patients receiving ≥7 epinephrine doses, with 12 being shockable rhythms, 14 receiving bystander CPR, and all but one patient receiving targeted temperature management (TTM).[12] This survival rate is much higher than reported in previous literature on cardiac arrest patients receiving large doses of epinephrine and was neither an intended nor a reported final outcome of the study. Because there is some evidence that patients receiving ≥7 epinephrine doses may survive neurologically intact, there may be a subgroup of patients who would benefit from >6 doses of epinephrine, and the true point of epinephrine futility may lie at a higher dose.

While our data suggests the likelihood of neurologically intact hospital discharge decreases as epinephrine doses increase, there are confounders to address which of them affect the conclusions that can be drawn from our data. The average resuscitation time for each group increased with the increasing number of epinephrine doses. Although resuscitation time is directly and inexorably linked with increasing epinephrine use, our study also aimed to evaluate use of epinephrine during cardiac arrest, which is a factor that clinicians have direct control over. The significant difference for the time to first epinephrine for the in-hospital cardiac arrests is also a confounder, as previous studies have shown that a delay to first epinephrine increases mortality and results in worse neurologic outcomes.[30] We had only 14.5% of patients sustain an in-hospital cardiac arrest, which

limited the statistical power of this finding, and only 25% of the in-hospital cardiac arrest patients received ≥7 doses of epinephrine compared to 40% of the out-of-hospital cohort.

Additionally, we found that 64 patients who were classified as out-of-hospital cardiac arrests, who did not receive EMS epinephrine but received epinephrine in the ED, still survived to a neurologically intact hospital discharge at a high rate (14.0%). This finding was either due to a responding EMS crew with emergency medical technicians who were unable to administer medications, an inability to obtain intravenous or intraosseous access, or ROSC being achieved prior to administration of epinephrine with a subsequent cardiac arrest in the ED. We did not include these 64 patients in our time to first epinephrine calculations as no initial time point was available to calculate forward from. If this data was available, it may have changed the association between decreased time to first epinephrine and increased neurologically intact hospital discharge as we would expect the time to first epinephrine to be longer in this population.

We feel that despite these confounders, our data is accurate in showing an association between decreased neurologically intact hospital discharge as the number of epinephrine doses increases. Additionally, there are multiple factors that go into clinicians deciding when to cease resuscitation such as patient age, potential cause of cardiac arrest, initial cardiac rhythm and any defibrillations received. Our novel secondary outcomes attempt to describe these factors to give further insight into which patients receive more epinephrine doses.

Our data showing that ≥7 doses of epinephrine can be considered futile may have an impact not only on resources and duration of ACLS but may also be another tool for guiding goals-of-care conversations with families. If patients received ≥7 doses of epinephrine and achieved ROSC, physicians could better set expectations regarding the exceedingly poor prognosis of these patients. It may also be useful guiding these discussions in patients actively undergoing CPR, relaying the poor outcomes and helping families make decisions on continued resuscitation vs termination of efforts.

LIMITATIONS

The major limitation of this study was the absence of time to first epinephrine, which was due to inconsistent EMS data, as the majority of our cases were out-of-hospital cardiac arrests. This is also due to the retrospective nature of the study, which comes with its own limitations. It would be difficult to perform a prospective trial due to concern regarding the standard of care, and thus it is likely not feasible at this time to evaluate the number, and effect, of epinephrine doses a patient should receive.[31] Additionally, missing data limited our sample size, as we eliminated any patients with missing epinephrine data from the study. We did not have comorbidity data on approximately 37% of the cohort due to patients not having prior ED visits within the hospital system where this data could have been collected.

We do not have access to autopsy or post-mortem health information in our EHR, and so we were unable to effectively screen all patients for comorbidities. There were statistically significant differences between groups for patient comorbidities, but we believe the patient comorbidities may not have had a significant role in the amount of epinephrine patients were administered as they may not have been known to EMS and emergency clinicians at the time. Also, information abstracted from chart review can be inaccurate, but we reduced the possibility of inaccurate data by reviewing both physician and nursing notes along with the code documentation sheet to reconcile all differences.

Our cohort's neurologically intact survival of 13.8% was higher than other reported studies, which we suspect may have been due to us including both in-hospital and out-of-hospital cardiac arrest. We also included patient who received zero doses of epinephrine, who overall had a 65.4% rate of neurologically intact discharge. Finally, we were limited in our assessment of ACLS time as many charts were missing a definitive time of resuscitation, especially for out-of-hospital cardiac arrests, which made up the majority of our dataset. We often found documentation of exact total prehospital ACLS time by emergency physicians often stopped at one hour, which likely led to an underestimation of the duration of resuscitation. When possible, we gathered as much data as possible using the documentation that was available to us via our ED's EHR.

CONCLUSION

This study of epinephrine dosing in cardiac arrest suggests that ≥7 doses of epinephrine is almost always futile within our institution. These results will need to be prospectively studied at other institutions and in different patient populations to confirm their accuracy. Additionally, our data suggests that patients with favorable survival odds from a shockable rhythm or an in-hospital cardiac arrest receive more epinephrine doses, although the difference is small and may not be clinically relevant. In contrast, however, younger adults did not receive more epinephrine doses than older adults, a finding that should be studied further. This study highlights valuable concepts that physicians should be aware of when considering the futility or benefit of continued resuscitation efforts.

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relationships with any companies that are relevant to this study. There are no conflicts of interest or sources of funding to declare.

REFERENCES

1. Panchal AR, Bartos JA, Cabañas JG, et al. Part 3: Adult Basic and Advanced Life Support: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation.* 2020;142(16_suppl_2):S366–468.
2. Velissaris D, Karamouzos V, Pierrakos C, et al. Use of sodium bicarbonate in cardiac arrest: current guidelines and literature review. *J Clin Med Res.* 2016;8(4):277–83.
3. Kette F, Ghuman J, Parr M. Calcium administration during cardiac arrest: a systematic review. *Eur J Emerg Med*. Apr 2013;20(2):72–8.
4. Olasveengen TM, Wik L, Sunde K, et al. Outcome when adrenaline (epinephrine) was actually given vs. not given - post hoc analysis of a randomized clinical trial. *Resuscitation.* 2012;83(3):327–32.
5. Hagihara A, Hasegawa M, Abe T, et al. Prehospital epinephrine use and survival among patients with out-of-hospital cardiac arrest. *JAMA.* 2012;307(11):1161–8.
6. Dumas F, Bougouin W, Geri G, et al. Is epinephrine during cardiac arrest associated with worse outcomes in resuscitated patients? *J Am Coll Cardiol.* 2014;64(22):2360–7.
7. Jacobs IG, Finn JC, Jelinek GA, et al. Effect of adrenaline on survival in out-of-hospital cardiac arrest: a randomised double-blind placebo-controlled trial. *Resuscitation.* 2011;82(9):1138–43.
8. Baskett PJ, Nolan JP, Handley A, et al. European Resuscitation Council Guidelines for Resuscitation 2005. Section 9. Principles of training in resuscitation. *Resuscitation.* 2005;67(Suppl 1):S181–9.
9. Morrison LJ, Kierzek G, Diekema DS, et al. Part 3: ethics: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation.* 2010;122(18 Suppl 3):S665–75.
10. Arrich J, Sterz F, Herkner H, et al. Total epinephrine dose during asystole and pulseless electrical activity cardiac arrests is associated with unfavourable functional outcome and increased in-hospital mortality. *Resuscitation.* 2012;83(3):333–7.
11. Goto Y, Maeda T, Goto Y. Effects of prehospital epinephrine during out-of-hospital cardiac arrest with initial non-shockable rhythm: an observational cohort study. *Crit Care (London, England).* 2013;17(5):R188.
12. Shi X, Yu J, Pan Q, et al. Impact of total epinephrine dose on long term neurological outcome for cardiac arrest patients: a cohort study. *Front Pharmacol.* 2021:12:580234.
13. de Oliveira FC, Feitosa-Filho GS, Ritt LE. Use of beta-blockers for the treatment of cardiac arrest due to ventricular fibrillation/pulseless ventricular tachycardia: a systematic review. *Resuscitation.* 2012;83(6):674–83.
14. Kagawa E, Inoue I, Kawagoe T, et al. Assessment of outcomes and differences between in- and out-of-hospital cardiac arrest patients treated with cardiopulmonary resuscitation using extracorporeal life support. *Resuscitation.* 2010;81(8):968–73.
15. Avalli L, Maggioni E, Formica F, et al. Favourable survival of in-hospital compared to out-of-hospital refractory cardiac arrest patients treated with extracorporeal membrane oxygenation: an Italian tertiary care centre experience. *Resuscitation.* 2012;83(5):579–83.
16. Ristagno G, Sun S, Tang W, et al. Effects of epinephrine and vasopressin on cerebral microcirculatory flows during and after cardiopulmonary resuscitation. *Crit Care Med.* 2007;35(9):2145–9.
17. Rivers EP, Wortsman J, Rady MY, et al. The effect of the total cumulative epinephrine dose administered during human CPR on hemodynamic, oxygen transport, and utilization variables in the postresuscitation period. *Chest.* 1994;106(5):1499–507.
18. Fernando SM, Mathew R, Sadeghirad B, et al. Epinephrine in out-of-hospital cardiac arrest: a network meta-analysis and subgroup analyses of shockable and nonshockable rhythms. *Chest.* 2023;164(2):381–93.
19. Evans E, Swanson MB, Mohr N, et al. Epinephrine before defibrillation in patients with shockable in-hospital cardiac arrest: propensity matched analysis. *BMJ.* 2021;375:e066534.
20. Merchant RM, Topjian AA, Panchal AR, et al. Part 1: Executive Summary: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation.* 2020;142(16_suppl_2):S337–57.
21. Navarretta N. Annual Statistics Report SFY 2019. Connecticut Department of Mental Health and Addiction Services. 2019.
22. Kim ST and Park T. Acute and chronic effects of cocaine on cardiovascular health. *Int J Mol Sci.* 2019;20(3):584.
23. Paredes VL, Rea TD, Eisenberg MS, et al. Out-of-hospital care of critical drug overdoses involving cardiac arrest. *Acad Emerg Med.* 2004;11(1):71–4.
24. Banks JL and Marotta CA. Outcomes validity and reliability of the modified Rankin scale: implications for stroke clinical trials. *Stroke.* 2007;38(3):1091–6.
25. Jouffroy R, Saade A, Alexandre P, et al. Epinephrine administration in non-shockable out-of-hospital cardiac arrest. *Am J Emerg Med.* 2019;37(3):387–90.
26. Bonnin MJ, Pepe PE, Clark PS Jr. Survival in the elderly after out-of-hospital cardiac arrest. *Crit Care Med.* 1993;21(11):1645–51.
27. Grunau B, Reynolds JC, Scheuermeyer FX, et al. Comparing the prognosis of those with initial shockable and non-shockable rhythms with increasing durations of CPR: informing minimum durations of resuscitation. *Resuscitation.* 2016;101:50–6.
28. Fukuda T, Ohashi-Fukuda N, Matsubara T, et al. Effect of prehospital epinephrine on out-of-hospital cardiac arrest: a report from the national out-of-hospital cardiac arrest data registry in Japan, 2011-2012. *Eur J Clin Pharmacol.* 2016;72(10):1255–64.

29. Grunau B, Kawano T, Scheuermeyer FX, et al. The association of the average epinephrine dosing interval and survival with favorable neurologic status at hospital discharge in out-of-hospital cardiac arrest. *Ann Emerg Med.* 2019;74(6):797–806.
30. Hansen M, Schmicker RH, Newgard CD, et al. Time to epinephrine administration and survival from nonshockable out-of-hospital cardiac arrest among children and adults. *Circulation.* 2018;137(19):2032–40.
31. Jung J, Rice J, Bord S. Rethinking the role of epinephrine in cardiac arrest: the PARAMEDIC2 trial. *Ann Transl Med.* 2018;6(Suppl 2):S129.

Sustainable Purchasing Practices: A Comparison of Single-use and Reusable Pulse Oximeters in the Emergency Department

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Background: Delivering healthcare requires significant resources and creates waste that pollutes the environment, contributes to the climate crisis, and harms human health. Prior studies have generally shown durable, reusable medical devices to be environmentally superior to disposables, but this has not been investigated for pulse oximetry probes.

Objective: Our goal was to compare the daily carbon footprint of single-use and reusable pulse oximeters in the emergency department (ED).

Methods: Using a Life Cycle Assessment (LCA), we analyzed greenhouse gas (GHG) emissions from pulse oximeter use in an urban, tertiary care ED, that sees approximately 150 patients per day. Low (387 uses), moderate (474 uses), and high use (561 uses), as well as cleaning scenarios, were modelled for the reusable oximeters and compared to the daily use of single-use oximeters (150 uses). We calculated GHG emissions, measured in kilograms of carbon dioxide equivalents ($kgCO_2e$), across all life cycle stages using life-cycle assessment software and the ecoinvent database. We also carried out an uncertainty analysis using Monte Carlo methodology and calculated the break-even point for reusable oximeters.

Results: Per day of use, reusable oximeters produced fewer greenhouse gases in low-, moderate-, and high-use scenarios compared to disposable oximeters: 3.9 $kgCO_2e$, 4.9 $kgCO_2e$, 5.7 $kgCO_2e$ vs 23.4 $kgCO_2e$, respectively). An uncertainty analysis showed there was no overlap in emissions, and a sensitivity analysis found reusable oximeters only need to be used 2.3 times before they match the emissions created by a single disposable oximeter. Use phases associated with the greatest emissions varied between oximeters, with the cleaning phase of reusables responsible for the majority of its GHG emissions (99%) compared to the production phases of the single-use oximeter (74%).

Conclusion: Reusable pulse oximeters generated fewer greenhouse gas emissions per day of use than their disposable counterparts. Given that the pulse oximeter is an ubiquitous piece of medical equipment used in emergency care globally, carbon emissions could be significantly reduced if EDs used reusable rather than single-use, disposable oximeters. [West J Emerg Med. 2023;24(6)1034–1042.]

INTRODUCTION

The effect of climate change on human health is vast and includes damaging social, economic, and psychological effects.[1] These effects are related to increasing numbers of weather events worldwide. Those extreme weather events are a direct consequence of human-induced climate change.[1] Emergency departments (ED) stand at the front line of the healthcare system, and there is substantial evidence linking climate events such as extreme heat, poor air quality, heavy rainfall, or climate-driven outcomes such as increasing exposure to vector-borne illness, food and housing insecurity, to surges in ED visits.[2] Acute increases in the demand for emergency care also contributes to high ED volumes, prolonged boarding times, a strain on human resources, and adverse patient outcomes.[3] Paradoxically, the delivery of healthcare requires expenditure of significant resources that result in the production of greenhouse gases (GHG), such as carbon dioxide in quantities that will inevitably contribute to further increases in global temperatures.[4] By reducing their carbon dioxide emissions, EDs can decrease their contribution toward human-induced climate change and accrue both short- and long-term benefits for the communities they serve.

GHG emissions are reported in kilograms of carbon dioxide equivalents ($kgCO_2e$), a measure that includes all gases with global warming potential. In Canada, emissions from the healthcare system have been estimated to be responsible for 33 million tons of $kgCO_2e$, or 4.6% of the national total.[5] GHG emissions in healthcare come directly from health facilities; these include anesthetic gases and boilers (referred to as Scope 1), purchased electricity (Scope 2), and indirectly generated GHG from the production and disposal of materials and equipment procured by the organization (Scope 3).[6] Studies have shown that Scope 3 emissions account for four-fifths of the healthcare GHG footprint in the United States.[7]

Healthcare systems, including the ED, have the responsibility to deliver patient care efficiently, fairly, and safely. Not being attentive to the environmental impact associated with healthcare delivery and its consequence on human health violates these duties. Therefore, clinicians and hospital administrators must prioritize initiatives that will reduce emissions and lessen the negative effects of climate change on health. Fortunately, there is a growing body of evidence to support environmentally sustainable operational practices to achieve this end.[5,8–16]

One such method is life cycle assessment (LCA), a tool to quantify the environmental impact of a product or process from cradle to grave. LCA methodology has also been recommended to compare the carbon footprint of medical equipment,[17] allowing healthcare organizations to make environmentally sustainable purchasing decisions. While LCAs have been carried out on numerous surgical devices,[8–10,13,16] this methodology is uncommonly applied to materials in the ED setting.

Pulse oximeters, which are available in single-use or reusable forms, are a piece of medical equipment used in the ED (and other departments) to measure the oxygen saturation of a patient's blood. They are small devices that are applied to the patient, most typically to a finger, for intermittent or continuous monitoring of vital signs and are used on every patient visiting the ED. As such a ubiquitous piece of medical equipment globally, oximeters represent a point of care opportunity to modify healthcare associated GHGs. To our knowledge, the carbon footprint of single-use and reusable oximeters has never been compared. We sought to determine the daily $kgCO_2e$ created in the production, transport, cleaning, and disposal of these two types of oximeters. This comparison will provide baseline data for EDs, and healthcare organization in general, seeking to make informed decisions on sustainable procurement practices for medical equipment.

METHODS

Setting

Our hospital is an urban, tertiary-care centre that provides ED services to approximately 55,000 patients annually, or 150 patients per day, in downtown Toronto, Ontario, Canada.[18]

Study Scope

Life cycle assessment is a tool for mapping the environmental footprint of a product from its raw material extraction to eventual disposal. LCAs evaluate a product across several impact categories including potential to cause global warming, ozone depletion, smog, acidification (production of acid rain), eutrophication (over-accumulation of minerals and nutrients in a body of water), carcinogenics, respiratory effects, ecotoxicity, and fossil fuel depletion. This analysis focussed primarily on global warming potential measured in $kgCO_2e$, although the remaining categories are included in the supplemental information.

An LCA begins with defining the functional unit, which allows products to be compared based on the service they provide. In this project, the functional unit was defined as one day of pulse oximetry measurement in the ED. Both reusable and disposable oximeters are approved for use in our hospital and are thus considered equal in terms of safety and functionality. Reusable oximeters are disinfected between use with a cleaning wipe that has been approved by the infection control service at our hospital and meets the instructions for use from the manufacturer.

Data for the reusable oximeter was scaled per use based on an estimated lifespan of one year, plus one cleaning wipe per patient encounter, and compared to the single-use disposable alternative. A more conservative lifespan was chosen for the reusable oximeter over the manufacturer's estimate of two

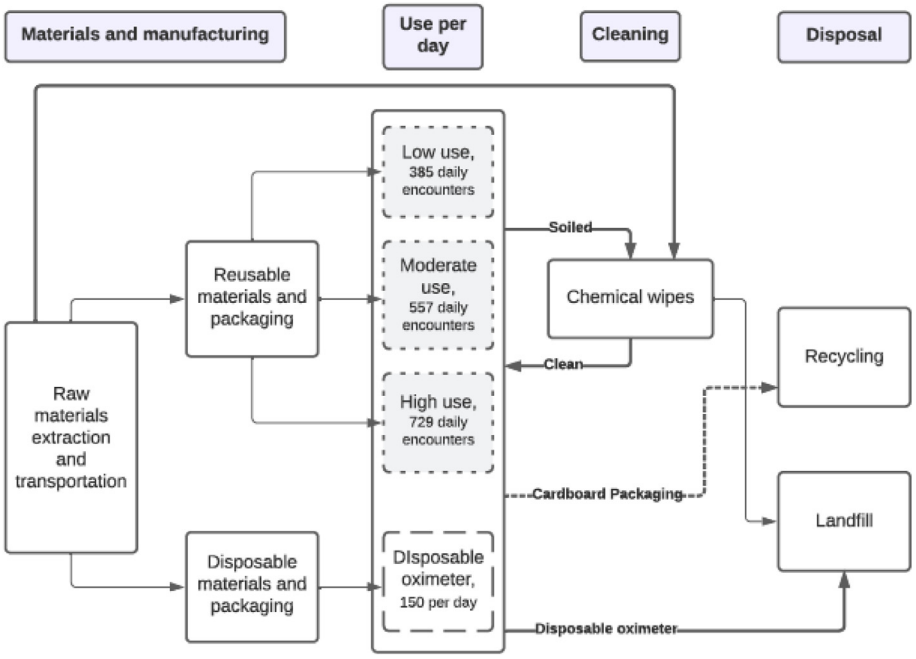

Figure 1. Process map for use of single-use vs disposable pulse oximeters.

years[19] to account for lost or damaged oximeters that would be replaced more frequently. The number of each type of oximeter making up the functional unit was determined by different use scenarios (see modelling parameters below). System boundaries included all materials used in the production of these devices and their associated cleaning products, as well as all energy required for their extraction, packaging, transport, and disposal (Figure 1).

Approval for this project was obtained from the University of Toronto Quality Improvement Review Committee (QI ID 20–0127).

Materials and Manufacturing

We determined the composition and weight of each oximeter by obtaining materials information from the product manufacturers and then deconstructing each device to find the weight in grams of its individual parts. In instances where an exact description of the product's materials was unavailable, such as in the case for LED sensors and cables in both reusable and disposable oximeters, we extrapolated from a similar product by a different manufacturer.[20] Since we were unable to obtain the weights of the individual materials comprising these two items (LED sensor and cable), we assumed the total weight was divided evenly across all their materials. Notably, we excluded the gold plating that covered the pin header of the cable for the following reasons: its contribution was marginal relative to the other materials; it is present in equal amounts on both devices; we could not reliably estimate its weight; and its high global warming impact ran the risk of significantly altering our findings if the estimated weight were to be improperly calculated.

Additionally, the power source to operate each oximeter was drawn in via their cables and was assumed to be equal between devices; therefore, it was also omitted from analysis.

We also included the cleaning wipes used to disinfect the reusable oximeters between each use. This information was collected from the manufacturer's label as well as the material safety data sheet. The generic material compositions of each oximeter and the cleaning wipes are shown in Table 1. As one wipe is often used to disinfect multiple pieces of equipment simultaneously, we modeled one quarter of a wipe and its active ingredients per use. This decision, which was based on direct observation of our staff disinfecting equipment between uses, is in keeping with methodology described in a similar LCA.[8] Since disinfection of pulse oximeters is the same for patients on advanced isolation precaution, we did not need to account for additional cleaning materials used for those patients.

Packaging and Transport

According to the manufacturer, single-use oximeters were packaged as 24 sensors per box and 20 boxes per large carton, whereas the reusable oximeters were packaged one per box and 20 boxes per large carton.[19] We also included individual wrapping around each device. Both devices were manufactured in Tijuana, Mexico, and shipped by truck to Toronto,[19] a distance of approximately 4,180 kilometers (km). As per the manufacturers of the cleaning wipes, there were 160 wipes per container and four containers per box.[19] Cleaning wipes were manufactured in Michigan and shipped by truck to Toronto,[19] approximately 408 km. Packaging

Table 1. Material composition of single-use pulse oximeters, reusable oximeters, and cleaning wipes.

Single-use oximeter	Mass (g)
Packaging	24
Shield	0.08
Sensor top/bottom	1.13
LED sensor	0.07
Cable	15.99
TOTAL	41.27

Reusable oximeter	Mass (g)
Packaging	26.4
Spring	1.43
Plastic housing	10.75
Detector frame and pad	4.49
LED sensor	0.07
Cable	26.4
TOTAL	69.54

Cleaning wipe	Mass (g)
Ammonium chloride	0.0053
Isopropyl alcohol	0.575
Cotton fiber	0.25
Packaging	2.55
TOTAL	3.38

g, gram.

and transport were also included and calculated per one-fourth of a wipe.

Modelling Parameters

Every patient who registered in the ED had their pulse oximetry measured at least once, at triage. Then, depending on their acuity or the clinical scenario, patients may have no further oximetry readings, intermittent or continuous monitoring. Typically, disposable pulse oximeters were used by a single patient throughout the duration of their ED visit and were discarded at discharge. In our setting, this equaled 150 disposable oximeters per day. Alternatively, reusable oximeters were used on multiple patients over the course of a day and cleaned between each encounter. Our department has 34 reusable oximeters divided among the following locations: one in triage; 21 stationary machines located in patient rooms; and 12 attached to portable vital signs machines. Therefore, we compared the GHG emissions associated with 150 disposable oximeters to 34 reusable oximeters. Although the manufacturer's estimated lifespan of the reusables was two years, we conservatively estimated it to be 365 days to account for lost or damaged oximeters that would be replaced more often. As a result, we compared 1/365th of the manufacturing, transportation, and disposal impacts of our 34 reusable oximeters to 150 single-use alternatives.

Table 2. Daily use of reusable oximeters by emergency department location.

	Location			
Uses per day	Triage oximeter (n = 1)	Stationary oximeters (n = 21)	Portable oximeters (n = 12)	Total
Low use	150	63	174	387
Moderate use	150	63	261	474
High use	150	63	348	561

To account for the variable number of disinfectant wipes consumed per day, we added the total daily usage for each of the 34 reusable oximeters (Table 2 and Figure 1). For the triage and stationary oximeters, there were a fixed number of daily uses. The single oximeter at triage was used and cleaned 150 times per day, once for every patient visiting the ED (150 uses). The 21 stationary oximeters were used an average of three times each per day (63 uses). This was based on the assumption that each of the 21 monitored rooms was filled with a new patient every eight hours, as the average ED length of stay in Ontario is 7.8 hours.[21] Finally, for the remaining 87 patients not triaged to a monitored room, the frequency of pulse oximetry readings was highly variable. Therefore, we modeled three use scenarios (low-, moderate-, and high-frequency use) in which different proportions of those 87 patients had their vital signs checked every two hours over an eight-hour visit (Table 2). In the low-use scenario, we assumed that 29 patients (33%) had their vital signs repeated four times, whereas the remaining 58 patients (66%) of patients had their vital signs repeated only once. In the moderate-use scenario, we assumed that 58 patients (66%) had their vital signs repeated four times and 29 (33%) only once. Finally, in the high-use scenario we assumed that all 87 patients had their vital signs repeated four times.

Waste Management

Based on observations of disposal practices, all oximeters, sanitizing wipes, and plastic packaging were modeled as going into municipal waste, whereas cardboard packaging was recycled.

Life Cycle Assessment Modeling

We performed LCA modeling using SimaPro v9.2.0.2 (PRé Consultants, Amersfoort, The Netherlands). We created a life cycle inventory (LCI) in SimaPro by matching materials and processes to those available in the ecoinvent 3.8 database (ecoinvent Association, Zurich, Switzerland).[22] Detailed LCI data and unit process metadata are provided in the supplemental information (Tables 1–4). Environmental impact assessments were carried out using the US

Environmental Protection Agency Tool for the Reduction and Assessment of Chemicals and other environmental Impacts (TRACI) 2.1 V1.06/US-Canada 2008 method.[23] All software, databases, and models employed in this study are widely described and accepted by international standards and guidance.[24–26]

Once the LCA was prepared, we calculated the GHG emissions per day of both devices. For the single-use oximeters, this was simply the GHG emissions from the life cycle phases of production, packaging/transport, and disposal, multiplied by 150 uses per day. For the reusable oximeter, we multiplied its GHG emissions by 34 (to account for all oximeters in our ED) and divided this number by 365 to determine emissions per day. We then added the emissions created by the cleaning wipes to model total emissions by low-, moderate-, and high-use cleaning scenarios. Therefore, the emissions created by the production, packaging/transport, and disposal of the cleaning wipes are represented as the "cleaning phase" for the reusable oximeter.

We performed an uncertainty analysis using Monte Carlo methodology to account for the uncertainty inherent in LCI data and to appreciate the range of potential environmental impacts associated with each type of oximeter. The process of this analysis has been well described in previous literature.[10] In this project, we calculated the resulting distribution from 1,000 random samplings. A 95% confidence interval as well as the median and standard deviation for GHG emissions created by disposable and reusable oximeters (including low-, moderate-, and high-use cleaning) was calculated. We then compared oximeters by life cycle phase (production, transport, cleaning, and disposal) to determine which phases created the highest emissions. Finally, a sensitivity analysis was carried out to estimate the number of reuses needed to make emissions from a reusable oximeter equivalent to the single-use oximeter. This is also known as a break-even analysis.

RESULTS

Life Cycle Assessment

The global warming impact for the production, transport, cleaning, and disposal of reusable and disposable pulse oximeters is displayed in Table 3 and Figure 2. When these devices were compared per day of use (150 disposable oximeters, 34 reusable oximeters), reusable oximeters produced fewer greenhouse gases per day in low-, medium- and high-use scenarios compared to disposable oximeters (3.9 $kgCO_2e$, 4.9 $kgCO_2e$, 5.7 $kgCO_2e$ vs. 23.4 $kgCO_2e$, respectively). This pattern was consistent across every major impact category (See supplemental Tables 1–3), and the results of the uncertainty analysis showed there was no overlap in emissions (Figure 2). To further contextualize this difference, over the duration of one-year, single-use oximeters create between 6,461–7,117 more $kgCO_2$ than reusable oximeters within our department.

Table 3. Global warming impact or greenhouse gas emissions of pulse oximeters per day of use.

	Global warming impact ($kgCO_2e$)			
		Reusable		
Oximeter	**Single use**	**LU**	**MU**	**HU**
Production	17.35	0.026	0.026	0.026
Transport	4.44	0.0046	0.0046	0.0046
Waste disposal	1.62	0.00219	0.00219	0.00219
Cleaning wipes				
Production	-	2.28	2.79	3.30
Transport	-	0.091	0.112	0.133
Waste disposal	-	1.59	1.95	2.30
Total	23.41	3.96	4.85	5.73

$kgCO_2$, kilograms of carbon dioxide; *LU*, low-use cleaning scenario, reusable (n = 385); *MU*, moderate-use cleaning scenario, reusable (n = 557); *HU*, high-use cleaning scenario, reusable (n = 729).

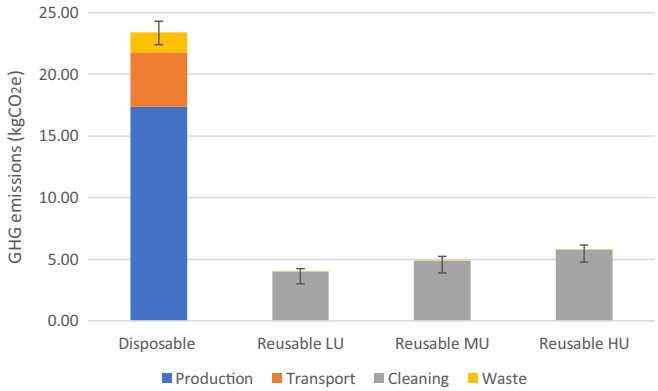

Figure 2. Greenhouse gas emissions per day of use by oximeter type.
$kgCO_2$, kilograms of carbon dioxide; *LU*, low-use cleaning scenario (n = 387); *MU*, moderate-use cleaning scenario (n = 474); *HU*, high-use cleaning scenario (n = 561). Error bars represent a 95% confidence interval from Monte Carlo analysis.

For each device, there were vast differences between which phase of the life cycle contributed the most to GHG emissions per day (Figure 2). The cleaning phase of the reusable oximeter produced most of its GHG emissions (99%) followed by production (0.79%), transport (0.14%), and disposal (0.07%). Alternatively, the production phases of the single-use oximeter had the highest contribution (74%), followed by transport (18.9%) and disposal (6.9%). There was no cleaning phase for the single-use device.

Outside the cleaning scenario, the electric cables on the disposable and reusable oximeters had the highest carbon footprint, 0.073 and 0.144 $kgCO_2$, respectively. (See Supplemental Tables 1 and 2).

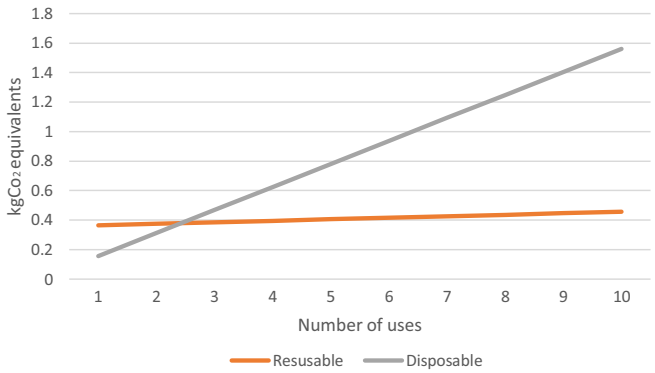

Figure 3. Break-even point of single-use and reusable oximeters. *kgCO*$_2$, kilograms of carbon dioxide.

The results of our sensitivity analysis showed that reusable oximeters produce fewer emissions than disposable oximeters after only 2.3 uses per day with cleaning (Figure 3).

DISCUSSION

In this study, we sought to calculate the environmental impact of single-use vs reusable oximeters in an urban ED. We found that reusable pulse oximeters, regardless of how frequently they were used and cleaned in the ED, created a significantly lower quantity of GHGs per day than is the case for single-use oximeters. This finding was consistent across all major environmental impact categories including ozone depletion, smog, acidification, eutrophication, carcinogenics, non-carcinogenics, respiratory effects, ecotoxicity, and fossil fuel depletion. (See Supplemental Information). Depending on the frequency that reusable oximeters were cleaned (high vs low frequency), the daily emissions created by disposable oximeters was three- to five-fold higher than those created by reusable oximeters in high- vs low-frequency use scenarios. Alternatively, reusable oximeters only needed to be used 2.3 times before they matched the emissions of disposable oximeters. Further, we estimate that if a similar-sized ED that was using disposable oximeters changed entirely to reusable ones, they would reduce their related emissions by up to 7,117.6 kgCO_2 annually. This is nearly equivalent to the energy used by one U.S. household per year.[27]

For single-use oximeters, the production and transportation phases contributed the greatest environmental burden. However, the main source of GHG emissions for the reusable oximeters was due to its cleaning phase, which contributed 99% of its daily GHG emissions, although this still represented a fraction of the GHG emissions created by single-use oximeters. Shared equipment can become colonized with multi-drug resistant bacteria such as methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci[28] Since iatrogenic spread of communicable diseases remains a significant concern in Canadian hospitals,[29,30] thorough cleaning of reusable devices is essential. The methods employed at this hospital are approved by the infection control service and meet the instructions for use from the manufacturer. To our knowledge, there is no practical alternative cleaning process with a lower carbon footprint that could be used.

Beyond the cleaning phase, looking at specific components of the devices themselves, the cable had the greatest environmental impact in the production phase. This may be due to a variety of factors including the large weight of the cable relative to other components of the oximeters or the high proportion of polyvinyl chloride (PVC) used in the cable's jacketing. A 2021 analysis of the environmental footprint of various types of cable jacketing found that PVC has a higher carbon footprint compared to other materials such as high-density polyethylene.[31]

The supply chain is the biggest factor in climate-changing pollution from healthcare services. It is also the hardest to mitigate, as hospitals and healthcare centers need a wide variety of materials and equipment from multiple manufacturers to provide high-quality care, and healthcare professionals have little control over the emissions associated with these materials and equipment. This contrasts with direct on-site Scope 1 GHG emissions from a combustion of fossil fuels and direct emission of waste anesthetic gases, as well as Scope 2 emissions from purchased electricity and other energy. Healthcare organizations have near-complete control over those categories of emissions, with many opportunities for reductions. As a result, we must find any way we can to reduce the impact of our purchased goods and services, which can be achieved by a sustainable approach to device procurement.

Many LCA studies have been published in healthcare comparing reusable and disposable devices. Studies investigating operating room linens,[32] scrubs,[33] laryngoscopes,[9] drug trays,[34] central venous catheter kits,[35] laryngeal mask airways,[36] and vaginal specula[13] have all shown reusable items to have superior environmental performance over single-use disposables. This is the first such study looking at equipment specifically in the ED, and it provides evidence that facilities can greatly reduce their environmental impact from a very commonly used piece of equipment. Further, one previous analysis showed that by switching entirely to reusable oximeters, the cost of providing pulse oximetry was decreased by 56%.[37] Therefore, EDs stand to benefit economically from this change as well.

Healthcare systems, such as Kaiser Permanente in California, have committed to becoming carbon neutral or net-zero in GHG emissions.[38] This will be accomplished in part by setting sustainability targets for their procurement division, including one that 50% of their purchased products meet environmental standards by 2025.[39] This can be a major signal to manufacturers that maintained or increased market share can be achieved by setting and achieving sustainability targets. Over time, this will reduce the healthcare system's

environmental footprint, helping to work toward better planetary health for future generations. As mentioned, reducing Scope 3 emissions from the supply chain will be challenging without effort from manufacturers and vendors. Healthcare institutions can use their power as trusted voices focused on human health to advocate for public policies that lead to improving the environmental performance of the overall energy system, including electricity grids, which will then reduce impacts from the supply chain. In the meantime, healthcare systems can work with their group purchasing organizations to obtain environmental performance data on the products they buy, giving preference to manufacturers that have strong environmental commitments and lower emissions.

LIMITATIONS

There are several limitations in our study that must be acknowledged. First, very few patients triaged to an unmonitored room would have their vital signs repeated four additional times during their ED visit as these are typically low-acuity, stable patients. Therefore, we likely overestimated the true impact of the cleaning phase for the 12 portable monitors in our department. Second, we were unable to obtain the material composition of the cable and LED sensor for either the reusable or disposable pulse oximeters. Therefore, we included materials used in the production of a comparable product from a different manufacturer that was willing to share these data. Since the weights of these materials were also unknown, we assigned an equal weight to each material in the cable. This may have resulted in an over- or underestimation of the contribution of the cable's materials. However, we applied the same methodology to both devices; therefore, it was unlikely to have a significant impact on our comparative results.

In addition, although the product manufacturers were able to provide most of the information for the LCA, the exact details of some of the material specifications needed to be supplemented by other sources.[8,40–43] These production processes are likely representative of typical industrial techniques but may not exactly correspond to the methods and efficiencies of the specific factories in which our pulse oximeters are made. In the future, a more transparent reporting process of material composition and weights would help to facilitate a more robust analysis. Finally, the scope of this project was limited to a single brand of pulse oximeter, delivered to and used in a specific setting, which may limit the generalizability of these findings. Future research comparing the life cycles of multiple brands of oximeters would help to confirm whether reusable devices are universally preferred over disposable ones when it comes to greenhouse gas emissions.

CONCLUSION

In summary, the results of our life cycle assessment found that reusable pulse oximeters in the emergency department have a two- to five-fold lower carbon footprint than their disposable counterparts. Given that the pulse oximeter is such a ubiquitous piece of medical equipment globally, healthcare-associated carbon emissions could be significantly improved with increased use of these devices over disposable oximeters.

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REFERENCES

1. World Health Organization. Climate change and health. Available at: https://www.who.int/news-room/fact-sheets/detail/climate-change-and-health. Accessed June 15, 2022.
2. Sorensen CJ, Salas RN, Rublee C, et al. Clinical implications of climate change on US emergency medicine: challenges and opportunities. *Ann Emerg Med.* 08 2020;76(2):168–78.
3. Salas RN, Solomon CG. The Climate Crisis - Health and Care Delivery. *N Engl J Med.* 2019;381(8):e13.
4. Eckelman MJ, Sherman J. Environmental Impacts of the U.S. Healthcare System and Effects on Public Health. *PLoS One.* 2016;11(6):e0157014.
5. Eckelman MJ, Sherman JD, MacNeill AJ. Life cycle environmental emissions and health damages from the Canadian healthcare system: An economic-environmental-epidemiological analysis. *PLoS Med.* 2018;15(7):e1002623.
6. Eckelman MJ, Huang K, Lagasse R, et al. Healthcare pollution and public health damage in the United States: an update. *Health Aff (Millwood).* 2020;39(12):2071–9.
7. Pichler P, Jaccard I, Weisz U, et al. International comparison of healthcare carbon footprints. *Environ Res Lett.* 2019;14(6)
8. Sanchez S, Eckelman M, Sherman J. Environmental and economic comparison of reusable and disposable blood pressure cuffs in multiple clinical settings. *Conservation & Recycling.* 2020;(155)

9. Sherman JD, Raibley LA, Eckelman MJ. Life cycle assessment and costing methods for device procurement: comparing reusable and single-use disposable laryngoscopes. *Anesth Analg.* 2018;127(2):434–43.
10. Thiel CL, Eckelman M, Guido R, et al. Environmental impacts of surgical procedures: life cycle assessment of hysterectomy in the United States. *Environ Sci Technol.* 2015;49(3):1779–86.
11. Barratt J, Chambers N, Cherrett N, et al *Material Health: A Mass Balance and Ecological Footprint Analysis of the NHS in England and Wales*. Oxford, UK: Best Foot Forward (2004).
12. Townend WK, Cheeseman CR. Guidelines for the evaluation and assessment of the sustainable use of resources and of wastes management at healthcare facilities. *Waste Manag Res*. 2005;23(5):398–408.
13. Donahue LM, Hilton S, Bell SG, et al. A comparative carbon footprint analysis of disposable and reusable vaginal specula. *Am J Obstet Gynecol.* 2020;223(2):225.e1–7.
14. Ison E, Miller A. The use of LCA to introduce life-cycle thinking into decision-making for the purchase of medical devices in the NHS. *J Environ Assess Policy Manage.* 2000;2(4):453–67.
15. Conrardy J, Hillanbrand M, Myers S, et al. Reducing medical waste. *AORN J.* 2010;91(6):711–21.
16. Campion N, Thiel C, Woods NC, et al. Sustainable healthcare and environmental life-cycle impacts of disposable supplies: a focus on disposable custom packs. *J Clean Prod.* 2015;94
17. Coalition for Sustainable Pharmaceutics and Medical Devices. Pharmaceutical and Medical Device Carbon Footpring Guidance. NHS, London, England. Available at: https://shcoalition.org/wp-content/uploads/2019/10/Summary-Document-Pharmaceutical-Product-and-Medical-Device-GHG-Accounting-November-2012.pdf. Accessed June 15, 2022.
18. Univesrity Health Network. University Health Network 2017–2018 year in review. Available at: https://www.uhn.ca/corporate/AboutUHN/Documents/UHN_AR_2018.pdf. Accessed June 15, 2022.
19. Personal communication with manufacturer.
20. Anonymous.
21. Health Quality Ontario. Under pressure: emergency department performance in Ontario. Available at: http://www.hqontario.ca/Portals/0/documents/system-performance/under-pressure-report-en.pdf. Accessed June 15, 2022.
22. Wernet G, Bauer C, Steubing B, et al. The ecoinvent database version 3 (part I): overview and methodology. *Int J Life Cycle Assess,* [online] 2016;21(9):1218–30.
23. Bare J. TRACI 2.0: the tool for the reduction and assessment of chemical and other environmental impacts 2.0. *Clean Technol Envir.* 2011;(13):687–96.
24. Vigon B, Tolle D, Cornaby B, et al. *Life-Cycle Assessment: Inventory Guidelines and Principles*. Columbus, Ohio: Battelle and Franklin Associates Ltd; 1992.
25. Society of Environmental Toxicology and Chemistry. A Technical Framework for Life-Cycle Assessment. Available at: https://cdn.ymaws.com/www.setac.org/resource/resmgr/books/lca_archive/technical_framework.pdf. Accessed June 15, 2022.
26. Society of Environmental Toxicology and Chemistry. Life cycle approaches: the road from analysis to practice. UNEP/SETAC Life Cycle Initiative. Available at: https://www.lifecycleinitiative.org/wp-content/uploads/2012/12/2005%20-%20LCA.pdf. Accessed June 15, 2022.
27. United States Environmental Protection Agency, Greenhouse Gas Equivalencies Calculator. Available at: https://www.epa.gov/energy/greenhouse-gas-equivalencies-calculator#results. Accessed July 28. 2022.
28. Lemmen SW, Häfner H, Zolldann D, et al. Distribution of multi-resistant Gram-negative versus Gram-positive bacteria in the hospital inanimate environment. *J Hosp Infect.* 2004;56(3):191–7.
29. Johnstone J, Garber G, Muller M. Healthcare-associated infections in Canadian hospitals: still a major problem. *CMAJ.* 09 09 2019;191(36):E977–8.
30. Mitchell R, Taylor G, Rudnick W, et al. Trends in healthcare-associated infections in acute care hospitals in Canada: an analysis of repeated point-prevalence surveys. *CMAJ.* 2019;191(36):E981–8.
31. Ozelkan E, Stephens J. Multi-criteria sustainable purchasing decisions using a life cycle analysis approach for fiber optic cable selection in telecommunications industry. *J Cleaner Prod.* 2021;13
32. Vozzola E, Overcash M, Griffing E. Environmental considerations in the selection of isolation gowns: A life cycle assessment of reusable and disposable alternatives. *Am J Infect Control.* 2018;45(8):881–6.
33. Burguburu A, Tanné C, Bosc K, et al. Comparative life cycle assessment of reusable and disposable scrub suits used in hospital operating rooms. *Cleaner Environmental Systems.* 2022;4
34. McGain F, McAlister S, McGavin A, et al. The financial and environmental costs of reusable and single-use plastic anaesthetic drug trays. *Anaesth Intensive Care.* 2010;38(3):538–44.
35. McGain F, McAlister S, McGavin A, et al. A life cycle assessment of reusable and single-use central venous catheter insertion kits. *Anesth Analg.* 2012;114(5):1073–80.
36. Eckelman M, Mosher M, Gonzalez A, et al. Comparative life cycle assessment of disposable and reusable laryngeal mask airways. *Anesth Analg.* 2012;114(5):1067–72.
37. Arciaga Z, Ackerman A, Justice P, et al. Reusable Pulse Oximetry Sensors: A Cost-Saving Quality Improvement Project. *Qual Manag Health Care.* 2020;29(1):35–9.
38. Kaiser Permanente. The first carbon neutral health system in the US. Available at: https://about.kaiserpermanente.org/community-health/news/first-carbon-neutral-health-system-in-us. Accessed June 15, 2022.
39. Healthcare Construction and Operations News. Kaiser Permanente makes aggressive green goals for 2025. Available at: https://hconews.com/2016/06/07/kaiser-permanente-makes-aggressive-green-goals-2025/. Accessed June 15, 2022.

40. Polyethylene plastic HDPE LDPE LLDPE raw plastic resin. Available at: https://www.alibaba.com/product-detail/Polyethylene-Resin-Raw-Plastic-Polyethylene-Plastic_1600205997352.html?spm=a2700.galleryofferlist.normal_offer.d_title.109f66f7vCaG3k&s=p. Accessed June 15, 2022.
41. Retorting liquid polyurethane adhesive plastic laminated polyurethane pu adhesive for laminating. Available at: https://www.alibaba.com/product-detail/Polyurethane-Adhesive-Polyurethane-Retorting-Liquid-Polyurethane_1600433306179.html?spm=a2700.galleryofferlist.normal_offer.d_title.578bc16ediZUwN&s=p. Accessed June 15, 2022.
42. Silicone rubber hot sale including platinum silicone rubber and tin silicone rubber. Available at: https://www.alibaba.com/product-detail/Silicone-Rubber-Molding-Silicone-Rubber-Silicone_1600277899471.html?spm=a2700.galleryofferlist.topad_creative.d_title.68ae5193n8kaj3. Accessed June 15, 2022.
43. Factory Price Manufacturer High Transparency SD831W Epoxy Resin AB Glue For Large Size Wood Table Casting. Available at: https://www.alibaba.com/product-detail/Epoxy-Resin-Epoxy-Resin-Factory-Price_1600181805827.html?spm=a2700.galleryofferlist.normal_offer.d_title.68fd2718hn3t7j&s=p. Accessed June 15, 2022.

Clinical Characteristics of SARS-CoV-2 Acute Pulmonary Embolism and Adjusted D-dimer for Emergency Department Patients

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Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and acute pulmonary embolism (APE) present a diagnostic challenge in the emergency department (ED) setting. We aimed to identify key clinical characteristics and D-dimer thresholds associated with APE in SARS-CoV-2 positive ED patients.

Methods: We performed a multicenter, retrospective cohort study for adult patients who were diagnosed with coronavirus 2019 (COVID-19) and had computed tomography pulmonary angiogram (CTPA) performed between March 17, 2020–January 31, 2021. We performed univariate analysis to determine numeric medians, chi-square values for association between clinical characteristic and positive CTPA. Logistic regression was used to determine the odds of a clinical characteristic being associated with a diagnosis of APE.

Results: Of 408 patients who underwent CTPA, 29 (7.1%) were ultimately found to have APE. In multivariable analysis, patients with a body mass index greater than 32 (odds ratio [OR] 4.4, 95% confidence interval [CI] 1.0 -19.3), a heart rate greater than 90 beats per minute (bpm) (OR 5.0, 95% CI 1.0-24.9), and a D-dimer greater than 1,500 micrograms per liter (μg/L) (OR 5.6, 95% CI 1.6-20.2) were significantly associated with pulmonary embolism. In our population that received a D-dimer and was SARS-CoV-2 positive, limiting CTPA to patients with a heart rate over 90 or a D-dimer value over 1500 μg/L would reduce testing 27.2% and not miss APE.

Conclusion: In patients with acute COVID-19 infections, D-dimer at standard cutoffs was not usable. Limiting CTPA using a combination of heart rate greater than 90 bpm or D-dimer greater than 1,500 μg/L would significantly decrease imaging in this population. [West J Emerg Med. 2023;24(6)1043–1048.]

INTRODUCTION

Since the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Wuhan, China, there have been over one million deaths and over 89 million cases related to coronavirus disease 2019 (COVID-19) in the United States.[1] Although COVID-19 was initially

characterized as a respiratory illness, critically ill patients have proven to have an associated hypercoagulable state.[2] The hypercoagulable state appears to originate in the pulmonary vasculature and evolves into a generalized hypercoagulable state resulting in macro- and microvascular thrombosis such as acute pulmonary embolism (APE).[3,4]

While growing research has documented the incidence of APE in hospitalized patients with COVID-19, few published studies have evaluated patients with SARS-CoV-2 infection and associated diagnosis of APE upon initial presentation to the emergency department (ED). Previous studies of APE risk in ED COVID-19 patients have been either inconclusive and even contradictory.[5–8] The limited information suggests that rates of APE in non-hospitalized COVID-19 patients may be as high as 18%, more than seven-fold higher than in the non-COVID-19 ED population.[9,10] With conflicting evidence on the incidence of APE in the ED setting, there remains a paucity of literature discussing diagnostic algorithms and computed tomography pulmonary angiogram (CTPA) diagnostic yield (the percentage of positive scans) for APE in ED COVID-19 patients. Proposed algorithms using D-dimer levels vary greatly and are not ED-specific.[8]

The diagnosis of APE in COVID-19 patients presents a diagnostic dilemma in the ED. The post-acute SARS-CoV-2 symptoms of dyspnea, chest pain, and tachycardia are all associated with clinical characteristics for APE.[8] Further, traditional methods of ruling out APE, such as using D-dimer in low-risk patients, are not feasible because D-dimer levels are commonly elevated in COVID-19 patients.[9] In particular, a known relationship exists between the level of D-dimer elevation and COVID-19 severity.[10]

In this derivation study, our primary objective was to identify which of the commonly known risk factors for APE were associated with APE in a COVID-19 patient population in the ED. Our secondary objective was to identify D-dimer values associated with APE in the ED setting.

Population Health Research Capsule

What do we already know about this issue?
There is an increased incidence of acute pulmonary embolism (APE) in patients hospitalized with COVID-19.

What was the research question?
Can D-dimer thresholds and clinical characteristics of ED patients be used to determine whether computed tomography pulmonary angiography (CTPA) is indicated to rule out APE?

What was the major finding of the study?
We found that performing CTPA on patients with a heart rate >90 and a D-dimer value over 1,500 μg/L had a sensitivity of 100% (95% CI 80–100%) and would reduce testing 27.2% while being unlikely to miss APE.

How does this improve population health?
In treating COVID-19 patients with suspected APE, emergency physicians should use different D-dimer thresholds in conjunction with patients' heart rates.

METHODS

This retrospective review was approved by our institutional review board. We performed a multicenter, retrospective cohort analysis for adult patients who arrived to any of the five EDs within the Atrium Health Wake Forest Baptist system between March 17, 2020–January 31, 2021. The EDs included one academic medical center and four regional community hospitals.

The inclusion criteria for the study were patients >16 years of age who tested positive for SARS-CoV-2 or had a COVID-19-related diagnosis and had a CTPA study ordered. A COVID-19-related diagnosis was based on International Classification of Diseases, 10th Rev, (ICD-10) codes. (The list of ICD-10 codes used is included in Appendix 1.) Using these criteria, we extracted a patient list from our electronic health record (EHR) via a health analytics software and services company (Roundtable Analytics, Research Triangle Park, NC). Final inclusion was based on confirmation of SARS-CoV-2 based on reverse transcription polymerase chain reaction (RT-PCR) or rapid antigen testing. This article follows the Strengthening and Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[11]

The clinical characteristics we focused on were based on commonly used, ED-specific APE decision rules: pulmonary embolism rule-out criteria, Well's criteria for APE, and the Geneva Score for APE.[12–14] D-dimer values consisted of both fibrinogen equivalent unit (FEU) and D-dimer unit (DDU). To bring parity to the different assays, DDU results were doubled. This was performed in a manner that has been described in prior COVID-19 D-dimer studies.[15] The cut-off for one hospital's FEU assay was 399 micrograms per liter (μg/L), while the other FEU assay cut-offs were 500 μg/L. The cut-off for the DDU assay was 230 μg/L. We calculated chi-square values, odds ratios (OR) with 95% confidence intervals (CI), and Kruskal-Wallis testing of numeric medians, and we used logistic regression to compare characteristics of patients who had APE to those who did not, using $P < 0.05$ as significant.

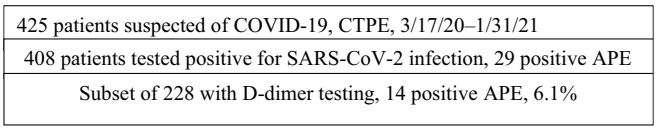

Figure 1. Flow diagram.
COVID-19, coronavirus disease 2019; *CTPE*, computed tomography pulmonary embolus; *SARS-CoV-2*, severe acute respiratory syndrome coronavirus 2; *APE*, acute pulmonary embolism.

RESULTS

We identified 425 patients who underwent evaluation for pulmonary embolism with CTPA in the setting of a suspected COVID-19 infection during the study period. Of this cohort, 408 patients (96%) tested positive for SARS-CoV-2 infection by RT-PCR analysis or rapid antigen testing and were included in our study. Of the CTPAS performed, 72% were done at the four community hospitals and 28% at the academic medical center hospital. Patient demographic and clinical characteristics are summarized in Table 1. Twenty-nine patients (7.1%) were ultimately found to have an APE on CTPA. The diagnostic yield of APE on CTPA varied from a high of 9.9% at one of the medium-sized community hospitals to a low of 2.3% at the smallest community hospital in our system.

Table 1. Characteristics of patient population.

Clinical characteristics	Total N = 408 (%)
Female	224 (54.9)
Male	184 (45.1)
Age	
18–49	126 (30.9)
50–69	169 (41.4)
70+	113 (27.7)
Race/Ethnicity	
White, non-Hispanic	262 (64.2)
Non-White, non-Hispanic	116 (28.4)
Hispanic	30 (7.4)
Clinical features	
Hemoptysis	13 (3.51)
Leg swelling	2 (0.50)
Past history of DVT	24 (6.50)
History of malignancy	11 (2.7)
Estrogens	16 (3.9)
Recent surgery	8 (1.9)
No anticoagulation	273 (66.9)
Aspirin	91 (22.3)
DOAC	15 (3.7)
Warfarin	1 (0.2)
Clopidogrel	4 (1.0)
Two or more anticoagulants	24 (5.9)
Symptom severity	
Asymptomatic	2 (0.5)
Mild	58 (14.2)
Moderate	203 (49.8)
Severe	145 (35.5)
APE on CTPA study	
Positive	29 (7.1)
Negative	379 (92.9)
Heart rate (HR) bpm	
HR ≥90	251 (63.1)
HR<90	147 (36.9)
HR ≥100	223 (56.0)
HR <100	175 (44.0)
Oxygen saturation	
<90	66 (16.1)
<95	156 (38.2)
Supplemental oxygen requirement	170 (41.6)
No supplemental oxygen	238 (58.4)
Date of illness	
0–4	132 (33.7)
5–10	115 (29.3)
>10	145 (37.0)
Excluded no data	5
BMI	
<25	65 (16.4%)
Overweight (BMI 25–29.9)	99 (24.8%)
Obesity (BMI ≥30)	234 (58.8%)

(*Continued on next column*)

Table 1. Continued.

DVT, deep vein thrombosis; *DOAC*, direct oral anticoagulants; *APE*, acute pulmonary embolism; *CTPA*, computed tomography pulmonary angiogram; *bpm*, beats per minute; *BMI*, body mass index.

The heart rate was significantly higher in patients who were found to have APE (median 102 beats per minute [bpm], interquartile range [IQR] 23 compared to 95 bpm (IQR 28), $P = 0.0133$]. Patients with APE were significantly more likely to present with hypoxia or a supplemental oxygen requirement (OR 2.4, 95% CI 1.1–5.3; $P = 0.02$]. Notably, 37.9% of patients found to have APE were not hypoxic. Patients with positive chest radiographs (CXR) experienced significantly more hypoxia (51.7% (89/172) vs 34.1% (46/135), $P = 0.002$). There was no significant

difference between type of PE (saddle, segmental, and subsegmental) and oxygen requirements ($P = 0.43$). There was no significant association between the presence of an infiltrate on CXR and APE ($P = 0.26$).

Median age was observed to be slightly higher in patients with PE (61, IQR 24) compared to 58 (IQR 25), but this difference was not significant ($P = 0.12$). There was no significant difference in body mass index (BMI) between patients who were and were not found to have APE (33, IQR 14 vs 31.5, IQR 11]; $P = 0.91$]. The proportion of patients found to have APE was not significantly different at 0–5, 6–9, and greater than nine days of illness ($P = 0.83$, Table 2). Patients with severe COVID-19 were more likely to have APE (20/145, [13.%] vs 9/263 [3.4%}, OR 4.5, 95% CI 2.0–10.2; $P < 0.0001$). Of the 29 patients with APE, 27 (93.1%) were admitted and followed through their hospital stay.

In patients with D-dimer testing, 204/228 (89.4%) were found to have elevated values as defined by local laboratory normal values. In this cohort, detailed in Figure 1, an abnormal D-dimer had a sensitivity of 93% (95% CI 66–100%) and a specificity of 11% (95% CI 7–16%) for the diagnosis of pulmonary embolism. A positive D-dimer was not significantly associated with a diagnosis of APE ($P = 0.35$). Of patients with D-dimer testing and APE, D-dimer values ranged from 134 μg/L to 38,616 μg/L (Table 3). The median D-dimer value was significantly higher in patients who were found to have PE (4,240 μg/L vs 1,030 μg/L; $P = 0.0048$). Patients with a D-dimer of greater than 1,500 μg/L were significantly more likely to have APE ($P = 0.001$).

Using logistic regression analysis in the cohort with D-dimer results, we found that a BMI greater than 32, (OR 4.4, 95% CI 1.0–19.3; $P = 0.045$), a heart rate >90 bpm, (OR 5.0, 95% CI 1.0–24.9; $P = 0.048$), and a D-dimer greater than 1,500 μg/L (OR 5.6, 95% CI 1.6–20.2; $P = 0.008$) were significantly associated with APE. Using a D-dimer cut-off of 1,500 μg/L yielded the best balance of sensitivity and specificity (Table 4) for diagnosis of APE. In patients where D-dimer was obtained, no patients with a D-dimer <1,500 μg/L and a heart rate <90 bpm were found to have APE. Use of these thresholds for CTPA testing would have decreased testing by 27.2%, representing 62 CTPA scans of the 228 patients for whom D-dimers were drawn.

Table 2. Results of computed tomography pulmonary angiogram by day of illness.

Day of illness	Negative APE number (%)	Positive APE number (%)	Total scans
0–5 days	128 (94.1)	8 (5.8)	136
6–9	110 (92.4)	9 (7.6.)	119
>9 days	135 (92.5)	11 (7.5)	146

APE, acute pulmonary embolism; *CTPA*, computed tomography pulmonary angiogram.

DISCUSSION

The primary finding of this multicenter, retrospective cohort analysis showed that the risk factors of BMI greater than 32, a heart rate >90 bpm and D-dimer >1500 μg/L were

Table 3. Clinical characteristics of patients with D-dimer levels and pulmonary embolism.

D-dimer value (μg/mL)	APE type	COVID-19 severity	Required supplemental O_2	Oxygen saturation % (triage)	Heart rate (triage)	Day of illness
134	Subsegmental	Severe	No	96	93	7
630	Bisegmental	Less than severe	No	96	94	6
652	Segmental	Less than severe	No	95	102	14
720	Segmental	Severe	Yes	97	99	**
1,690	Segmental	Severe	No	99	94	7
3,360	Segmental	Less than severe	Yes	84	117	10
4,200	Subsegmental	Less than severe	Yes	94	97	3
4,280	Segmental	Less than severe	No	95	87	1
4,700	Segmental	Severe	Yes	89	82	11
9,950	Subsegmental	Severe	Yes	95	124	16
11,050	Segmental	Severe	Yes	97	102	12
11,290	Lobar	Severe	Yes	67	111	21
27,412	Segmental	Severe	Yes	93	110	7
38,616	Segmental	Severe	Yes	55	123	5

**Day of illness not documented.
COVID-19, coronavirus 2019; *μg/mL*, micrograms per milliliter; *APE*, acute pulmonary embolism.

Table 4. Test characteristics of different D-dimer cut-points.

D-dimer abnormal cut-point	Chi-square	Sensitivity% (95% CI)	Specificity% (95% CI)
>750 μg/L	0.44	71 (41–92)	39 (32–46)
>1000 μg/L	0.12	71 (41–92)	50 (43–57)
>1500 μg/L	0.001	71 (41–92)	64 (57–71)
>2000 μg/L	0.001	64 (35–87)	77 (71–83)

μg/L, micrograms per liter; *CI*, confidence interval.

significantly associated with APE diagnosis in COVID-19 patients. It was interesting that while median BMI did not significantly differ between those with APE and those without APE (33 vs 31.5), a cut-point of >32 was associated with APE. While patients with hypoxia or supplemental oxygen requirement were more likely to have APE, this cohort still showed that a significant portion of APE patients were not hypoxic. The secondary finding shows that D-dimer levels of 1,500 μg/L were significantly associated with APE, while just having a positive D-dimer level was not. The diagnostic yield of APE in our patient population was 7.1%, contradictory to recent literature that showed dramatic increased incidences of APE in COVID-19 patients.[16,17]

Striking were the clinical characteristics not statistically significant for association with APE. For example, multiple studies have shown an increased risk of APE in the inpatient setting for patients requiring admission for COVID-19.[18] This is thought to be related to elevated pro-inflammatory cytokines and abnormalities in coagulation parameters.[19] We would have expected to find a statistical significance in findings of APE in patients who are later in their illness of COVID-19, after day 6 of illness when symptoms become more pronounced. While we discovered most of our study population (71.4%) was found to have APE after day 5 of COVID-19 illness, this was not statistically significant.

The use of CTPA has associated risks, costs, and staff resources that must be considered when ordering testing. Risks of CTPA include ionizing radiation exposure, contrast nephropathy, and contrast allergies.[20–22] Costs associated with CTPA studies are not just to the patient but to health system capacity, both of which are significant.[23] In a setting of limited healthcare staffing and bed availability, the increased staff resources required for CTPA studies must be considered.[24] Thus, reduction in unnecessary CTPA studies would yield multiple benefits.

Our subset of patients for whom D-dimers were obtained (228) offered the best opportunity for reduction in CTPA studies. With almost 90% of our patient population who had D-dimers drawn having an elevated result, using traditional cut-offs were not helpful in evaluation of APE in COVID-19 patients. However, using elevated D-dimer cut-offs in specific patient populations in the evaluation for APE is not a new concept in emergency medicine. The pregnancy-adapted YEARS algorithm and age-adjusted D-dimer cut-off values for diagnosis of suspected APE are two examples of algorithms that use elevated D-dimer value cut-offs.[25,26]

We found using a D-dimer cut-off of 1,500 μg/L yielded the best balance of sensitivity and specificity (Table 4) for diagnosis of APE. In patients whose D-dimer was obtained, none of them with a D-dimer <1,500 μg/L and a heart rate <90 bpm were found to have APE. Use of these thresholds for CTPA testing would have decreased CTPA usage by 27.2%, potentially eliminating 62 CTPA studies in the 228 patients for whom D-dimers were drawn.

LIMITATIONS

Limitations to our study included the inability to quantify clinician gestalt when choosing to order a CTPA study. A second limitation was the inability to use the same D-dimer assay across all hospitals due to different lab equipment. In our study we included two types of D-dimer assays: FEU and DDU. To achieve parity, our methods used standardization and reporting suggested in COVID-19 D-dimer literature review.[15] While our study covered a regional health system with five EDs, it still lacks generalizability and would require external validation. External validation is particularly important as our study yielded only 14 patients with APE in our D-dimer subset of 228 patients. However, this low yield could potentially be revealing with regard to low overall findings of APE in ED COVID-19 patients.

CONCLUSION

In patients with acute COVID-19 infections, D-dimer at standard cut-offs was not usable; limiting CTPA using a combination of heart rate >90 bpm or D-dimer >1,500 μg/L would significantly decrease the use of imaging in this population. Future prospective studies are needed to determine whether using this D-dimer threshold and heart rate cut-off in the ED COVID-19 patient population can safely reduce the number of CTPA studies performed.

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REFERENCES

1. CDC COVID Data Tracker. Centers for Disease Control and Prevention. 2021. Available at: https://covid.cdc.gov/covid-data-tracker/. Accessed June 10, 2021.
2. Connors JM, Levy JH. Thromboinflammation and the hypercoagulability of COVID-19. *J Thromb Haemost*. 2020;18(7):1559.
3. Abou-Ismail MY, Diamond A, Kapoor S, et al. The hypercoagulable state in COVID-19: incidence, pathophysiology, and management. *Thromb Res*. 2020;194:101–15.
4. Gervaise A, Bouzad C, Peroux E, et al. Acute pulmonary embolism in non-hospitalized COVID-19 patients referred to CTPA by emergency department. *Eur Radiol*. 2020;30(11):6170–7.
5. Miró Ò, Llorens P, Aguirre A, et al. Association between Covid-19 and pulmonary embolism (AC-19-PE study). *Thromb Res*. 2020;196:322–4.
6. Ramadan L, Koziatek CA, Caldwell JR, et al. Pulmonary thromboembolism in COVID-19: evaluating the role of D-dimer and computed tomography pulmonary angiography results. *Am J Emerg Med*. 2021;46:786–7.
7. van Wissen M, Keller TT, Ronkes B, et al. Influenza infection and risk of acute pulmonary embolism. *Thromb J*. 2007;5:16.
8. CDC. Post-COVID conditions: Information for healthcare providers. 2021. Available at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/post-covid-conditions.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fhcp%2Fclinical-care%2Flate-sequelae.html. Accessed June 10, 2022.
9. Kline JA, Nelson RD, Jackson RE, et al. Criteria for the safe use of D-dimer testing in emergency department patients with suspected pulmonary embolism: a multicenter US study. *Ann Emerg Med*. 2002;39:144–52.
10. Yao Y, Cao J, Wang Q, et al. D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study. *J Intensive Care*. 2020;8:49.
11. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol*. 2008;61(4):344–9.
12. Kline JA, Mitchell AM, Kabrhel C, et al. Clinical criteria to prevent unnecessary diagnostic testing in emergency department patients with suspected pulmonary embolism. *J Thromb Haemost*. 2004;2:1247–55.
13. Wells PS, Anderson DR, Rodger M, et al. Excluding pulmonary embolism at the bedside without diagnostic imaging: management of patients with suspected pulmonary embolism presenting to the emergency department by using a simple clinical model and D-dimer. *Ann Intern Med*. 2001;135(2):98–107.
14. Le Gal G, Righini M, Roy PM, et al. Prediction of pulmonary embolism in the emergency department: the revised Geneva score. *Ann Intern Med*. 2006;144(3):165–71.
15. Favaloro EJ, Thachil J. Reporting of D-dimer data in COVID-19: some confusion and potential for misinformation. *Clin Chem Lab Med*. 2020;58(8):1191–9.
16. Freund Y, Drogrey M, Miró Ò, et al. Association between pulmonary embolism and COVID-19 in emergency department patients undergoing computed tomography pulmonary angiogram: the PEPCOV International Retrospective Study. *Acad Emerg Med*. 2020;27(9):811–20.
17. Watchmaker JM, Goldman DT, Lee JY, et al. Increased incidence of acute pulmonary embolism in emergency department patients during the COVID-19 pandemic. *Acad Emerg Med*. 2020;27(12):1340–3.
18. Zanardo M, Martini C, Monti CB, et al. Management of patients with suspected or confirmed COVID-19, in the radiology department. *Radiography (Lond)*. 2020;26(3):264–8.
19. Polo Friz H, Gelfi E, Orenti A, et al. Acute pulmonary embolism in patients presenting pulmonary deterioration after hospitalisation for non-critical COVID-19. *Intern Med J*. 2021;51(8):1236–42.
20. Stals M, Kaptein F, Kroft L, et al. Challenges in the diagnostic approach of suspected pulmonary embolism in COVID-19 patients. *Postgrad Med*. 2021;133(sup1):36–41.
21. Harun HH, Abdul Karim MK, Abbas Z, et al. Association of radiation doses and cancer risks from CT pulmonary angiography examinations in relation to body diameter. *Diagnostics (Basel)*. 2020;10(9):681.
22. Mitchell AM, Jones AE, Tumlin JA, et al. Prospective study of the incidence of contrast-induced nephropathy among patients evaluated for pulmonary embolism by contrast-enhanced computed tomography. *Acad Emerg Med*. 2012;19(6):618–25.
23. Mamlouk MD, vanSonnenberg E, Gosalia R, et al. Pulmonary embolism at CT angiography: implications for appropriateness, cost, and radiation exposure in 2003 patients. *Radiology*. 2010;256(2):625–32.
24. van der Pol LM, Dronkers CEA, van der Hulle T, et al. The YEARS algorithm for suspected pulmonary embolism: shorter visit time and reduced costs at the emergency department. *J Thromb Haemost*. 2018;16(4):725–33.
25. van der Pol LM, Tromeur C, Bistervels IM, et al. Pregnancy-adapted YEARS algorithm for diagnosis of suspected pulmonary embolism. *N Engl J Med*. 2019;380(12):1139–49.
26. Schouten HJ, Geersing GJ, Koek HL, et al. Diagnostic accuracy of conventional or age adjusted D-dimer cut-off values in older patients with suspected venous thromboembolism: systematic review and meta-analysis. *BMJ*. 2013;346:f 2492.

Euglycemic Diabetic Ketoacidosis: Experience with 44 Patients and Comparison to Hyperglycemic Diabetic Ketoacidosis

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Introduction: Euglycemic diabetic ketoacidosis (DKA) (glucose <250 milligrams per deciliter (mg/dL) has increased in recognition since introduction of sodium-glucose co-transporter 2 (SGLT2) inhibitors but remains challenging to diagnose and manage without the hyperglycemia that is otherwise central to diagnosing DKA, and with increased risk for hypoglycemia with insulin use. Our objective was to compare key resource utilization and safety outcomes between patients with euglycemic and hyperglycemic DKA from the same period.

Methods: This is a retrospective review of adult emergency department patients in DKA at an academic medical center. Patients were included if they were >18 years old, met criteria for DKA on initial laboratories (pH ≤7.30, serum bicarbonate ≤18 millimoles per liter [mmol/L], anion gap ≥10), and were managed via a standardized DKA order set. Patients were divided into euglycemic (<250 milligrams per deciliter [mg/dL]) vs hyperglycemic (≥250 mg/dL) cohorts by presenting glucose. We extracted and analyzed patient demographics, resource utilization, and safety outcomes. Etiologies of euglycemia were obtained by manual chart review. For comparisons between groups we used independent-group *t*-tests for continuous variables and chi-squared tests for binary variables, with alpha 0.05.

Results: We identified 629 patients with DKA: 44 euglycemic and 585 hyperglycemic. Euglycemic patients had milder DKA on presentation (higher pH and bicarbonate, lower anion gap; $P < 0.05$) and lower initial glucose (195 vs 561 mg/dL, $P < 0.001$) and potassium (4.3 vs 5.3 mmol/L, $P < 0.001$). Etiologies of euglycemia were insulin use prior to arrival (57%), poor oral intake with baseline insulin use (29%), and SGLT2 inhibitor use (14%). Mean time on insulin infusion was shorter for those with euglycemic DKA: 13.5 vs 19.4 hours, $P = 0.003$. Mean times to first bicarbonate >18 mmol/L and first long-acting insulin were similar. Incidence of hypoglycemia (<70 mg/dL) while on insulin infusion was significantly higher for those with euglycemic DKA (18.2 vs 4.8%, $P = 0.02$); incidence of hypokalemia (<3.3 mmol/L) was 27.3 vs 19.1% ($P = 0.23$).

Conclusion: Compared to hyperglycemic DKA patients managed in the same protocolized fashion, euglycemic DKA patients were on insulin infusions 5.9 hours less, yet experienced hypoglycemia over three times more frequently. Future work can investigate treatment strategies for euglycemic DKA to minimize adverse events, especially iatrogenic hypoglycemia. [West J Emerg Med. 2023;24(6)1049–1055.]

INTRODUCTION

Diabetic ketoacidosis (DKA) is a common and dangerous condition encountered in the emergency department (ED). Severe insulin deficiency triggers increases in counter-regulatory hormones such as cortisol, glucagon, and catecholamines, which results in hyperglycemia and ketoacidosis and requires treatment with exogenous insulin.[1] Standardized, protocolized treatment with intravenous (IV) fluids, insulin, and electrolyte management have led to vastly improved outcomes; however, this requires prompt identification of the clinical entity and initiation of treatment. In certain cases, the body is unable to mount a hyperglycemic response due to either reduced glucose stores (starvation state, chronic liver disease, heavy alcohol use) or is losing glucose more rapidly than can be produced (sepsis, urinary losses, exogenous insulin).[2,3]

This results in a state of euglycemic DKA, which poses a challenge to clinicians, as hyperglycemia, often the first trigger to consider DKA as a potential diagnosis, is not present. It also poses challenges in management with higher attentiveness required to avoid hypoglycemia with use of IV insulin infusion to resolve the ketoacidosis. This condition has gained recognition in recent years given its association with sodium-glucose co-transporter 2 (SGLT-2) inhibitor use, which is only becoming more prevalent as recent American Heart Association guidelines have given a Class 1 recommendation for its use in patients with heart failure.[4] This will also likely increase the prevalence of euglycemic DKA seen in EDs, which currently comprise only 2.6–3.2% of admissions for DKA.[5]

Most of the literature published to date regarding management of euglycemic DKA is centered on using standardized DKA treatments with IV fluids, insulin infusions, and electrolyte management, with the added caveat that glucose will need to be added to fluids early to prevent hypoglycemia. However, very little has been published on the differences in patient demographics and lab values at presentation, approaches to management, or clinical and safety outcomes between euglycemic and hyperglycemic DKA patients. Moreover, many clinicians have built a strong association of euglycemic DKA with SGLT2 inhibitors such that clinical suspicion may be inappropriately lacking in patients who are not taking one of these medications.

Given the challenges in identifying and treating this clinical entity, we sought to analyze our experience with time-matched cohorts of euglycemic and hyperglycemic DKA patients at our institution, both of which were managed with the same two-bag protocol. We also identified etiologies for euglycemia on presentation as risk factors to heighten suspicion for this condition.

Population Health Research Capsule

What do we already know about this issue?
Euglycemic diabetic ketoacidosis (DKA) is often treated with similar protocols as hyperglycemic DKA.

What was the research question?
What are the triggers of euglycemia, and how do treatment and safety outcomes differ between euglycemic and hyperglycemic DKA?

What was the major finding of the study?
Euglycemic DKA patients had more than 3 times the rate of hypoglycemia while on insulin infusion: 18.2% vs 4.8% ($P = 0.02$).

How does this improve population health?
Euglycemic DKA can be present in patients who are not taking SGLT2 inhibitors, and these patients are at increased risk of iatrogenic hypoglycemia during treatment.

METHODS

This was a retrospective review of adults in DKA managed in the ED at a single academic medical center in the United States. The Institutional Review Board at the University of Michigan reviewed this study (HUM00224835). This study is presented in accordance with the STROBE (Strengthening the Reporting of Observational studies in epidemiology) statement.

We conducted a retrospective structured chart review of all DKA patients who presented to our adult ED from August 2015–October 2022. A standardized order set for management of DKA was implemented in August 2015, and defining the study period in this fashion promoted the largest sample size possible. Data points of interest were identified and extracted from the electronic health record using an automated query. Patients were included if they were adult (≥18 years old), met diagnostic criteria for DKA based on initial ED laboratory studies (pH ≤ 7.30, serum bicarbonate ≤18 millimoles per liter [mmol/L], anion gap ≥10), and were managed via a standardized DKA two-bag method order set.[1,6] Patients were subdivided into euglycemic DKA (initial glucose ≤250 milligrams per deciliter [mg/dL]) and hyperglycemic DKA (initial glucose >250 mg/dL). Patients were excluded if more than one insulin infusion order set was used (ie, the two-bag method order set plus an additional

titratable insulin infusion order set used in other areas of our hospital).

Patients in this study were all managed in an ED-based intensive care unit (ED-ICU).[7,8] Our initial search identified 1,160 adult ED patients managed via the two-bag method. We excluded 340 patients for not meeting DKA laboratory criteria, 186 due to use of multiple insulin infusion order sets, and five after chart review identified alcoholic ketoacidosis or starvation ketoacidosis as their ED diagnosis. Starvation ketoacidosis was differentiated from euglycemic DKA primarily by resolution of ketoacidosis with glucose supplementation and lack of diagnosed diabetes mellitus before or during their presenting illness. This resulted in our final cohort of 629 patients, 44 of whom were euglycemic on presentation and 585 hyperglycemic as outlined in Figure 1.

Age, gender, weight, and initial laboratory values were extracted for patient demographics. We assessed resource utilization data including duration of insulin infusion (defined as the interval from the first insulin infusion start time to the last insulin infusion stop time); time from ED presentation to first pH >7.3; time from ED presentation to first bicarbonate >18 mmol/L; lengths of stay (LOS) in (ED, ED-ICU, hospital, ICU); and ED disposition (discharge, admission to ICU, admission to non-ICU, other). Safety outcomes assessed during DKA treatment included incidence of hypoglycemia (glucose <70 and <54 mg/dL, which have been defined as hypoglycemia and clinically important hypoglycemia warranting reporting in clinical trials, respectively), and incidence of hypokalemia (K < 3.3 mmol/L) and severe hypokalemia (K < 3.0 mmol/L).[9]

The time from ED arrival to administration of long-acting subcutaneous insulin (eg, glargine) marked the duration of "DKA treatment" for these safety outcomes, as this transition to long-acting insulin coincides with DKA resolution. The insulin infusion stop time was used as the end time if no long-acting insulin was given, and 24 hours after ED arrival was used as the end time if insulin infusion stop time was missing, which is consistent with the definition of DKA treatment duration used in previous retrospective studies.[6,8] Chart review was conducted for euglycemic patients to identify the most likely etiology for their euglycemia based on ED documentation (insulin administration prior to arrival, SGLT2 inhibitor use, etc). This review was done by a single author who was not blinded to the study hypothesis and did not receive specific training, and we did not assess interobserver reliability.[10]

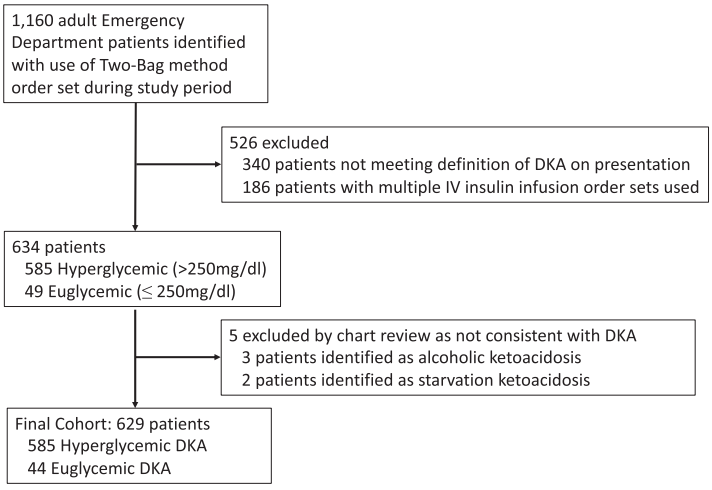

Figure 1. Identification and screening of patients. *IV*, intravenous; *DKA*, diabetic ketoacidosis.

The management of DKA in our ED and ED-ICU has been standardized using the two-bag method. This consists of a fixed-rate IV insulin infusion, constant fluid and electrolyte delivery but titratable dextrose delivery, and frequent lab draws with a nurse-driven fluid titration and electrolyte replacement protocol. With resolution of DKA, defined as pH >7.30, serum bicarbonate >15 mmol/L, glucose <200 mg/dL, anion gap <12, and ability to tolerate by mouth, patients are given subcutaneous insulin with two hours of IV insulin infusion overlap prior to discontinuing the insulin infusion.

Statistical Analysis

For comparisons between the hyperglycemic DKA and euglycemic DKA groups we used independent-groups *t*-tests for continuous variables and chi-squared tests for binary variables. We used an alpha level of 0.05 for all analyses; all hypothesis tests were two-sided, and *P*-values for all test statistics were calculated based on cluster-robust standard errors adjusted for multiple visits clustered within patients. We conducted analyses with the Stata software package (StataCorp LLC, College Station, TX).[11]

RESULTS

We identified 629 adult ED patients with DKA managed from 2015–2022, 44 of whom were euglycemic (initial glucose ≤250 mg/dL) on presentation and 585 hyperglycemic. Patient demographics and presenting metabolic derangements are summarized in Table 1. Mean age was 31.1 vs 39.8 ($P < 0.001$), and gender was 68.2 vs 60.5% female. At the time of ED presentation, mean blood glucose was 195 vs 561 ($P < 0.001$). Euglycemic patients had milder DKA on presentation with pH of 7.17 vs 7.14, bicarbonate of 11.9 vs 10.4, and anion gap of 21.6 vs 26.3 (Ps < 0.05). Presenting potassium was significantly lower in euglycemic patients, 4.3 vs 5.3 ($P < 0.001$).

Resource utilization outcomes are presented in Table 2. The mean time on IV insulin infusion was significantly shorter at 13.5 vs 19.5 hours ($P = 0.003$), whereas the mean time until normalization of serum bicarbonate >18 mmol/L (12.3 vs 12.1 hours) and time to first long-acting subcutaneous insulin (16.7 vs 16.0 hours) were not significantly different. Total hospital LOS was shorter for

Table 1. Patient demographics.

Patient demographics	Hyperglycemic DKA ($n = 585$)[a]	Euglycemic DKA ($n = 44$)[b]	*d* (95% CI)	*P*
Mean age, years (95% CI)	39.8 (36.9, 42.7)	31.1 (27.1, 35.1)	8.7 (4.6, 12.9)	<.001
Female gender, n (%)	354 (60.5)	30 (68.2)	–7.7 (–2.2, 6.6)	0.29
Mean weight, kg (95% CI)	72.0 (68.5, 75.6)	70.2 (63.5, 76.9)	1.8 (–4.5, 8.2)	0.57
Mean presenting laboratory values (95% CI)				
pH	7.14 (7.13, 7.15)	7.17 (7.14, 7.19)	–.03 (–.06, –.004)	0.03
Bicarbonate (mmol/L)	10.4 (9.9, 10.9)	11.9 (10.7, 13.0)	–1.4 (–2.6, –0.2)	0.02
Anion gap	26.3 (25.6, 27.0)	21.6 (19.8, 23.4)	4.7 (2.9, 6.5)	<.001
Glucose (mg/dL)	561 (531, 592)	195 (182, 208)	367 (334, 399)	<.001
Potassium (mmol/L)	5.3 (5.1, 5.4)	4.3 (4.1, 4.6)	1.0 (0.7, 1.2)	<.001

[a]$n = 585$ visits from 370 patients.
[b]$n = 44$ visits from 38 patients.
DKA, diabetic ketoacidosis; *d*, absolute difference; *CI*, confidence interval; *mmol/L*, millimoles per liter; *mg/dL*, milligrams per deciliter.

Table 2. Resource utilization.

Resource utilization	Hyperglycemic DKA ($n = 585$)[a]	Euglycemic DKA ($n = 44$)[b]	*d* (95% CI)	*P*
Mean time on insulin infusion, hours (95% CI)	19.4 (17.6, 21.3)	13.5 (10.1, 16.9)	5.9 (2.1, 5.8)	0.003
Mean hours to first bicarbonate >18 mmol/L (95% CI)	11.9 (11.2, 12.5)	12.3 (10.6, 14.1)	–0.5 (–2.2, 1.2)	0.59
Mean time to first long-acting subcutaneous insulin administration, hours (95% CI)	16.7 (16.0, 17.5)	16.0 (14.4, 17.6)	0.7 (–1.1, 2.5)	0.43
Mean total length of stay, days (95% CI)	3.9 (3.3, 4.4)	2.2 (0.8, 3.6)	1.7 (0.2, 3.1)	0.03
Mean ED-ICU length of stay, hours (95% CI)	16.6 (15.8, 17.4)	16.4 (14.8, 18.1)	0.2 (–1.7, 2.0)	0.85
Emergency department disposition, n (%)				
Admit to ICU	30 (5.1)	0		
Admit to non-ICU	356 (60.9)	19 (43)		
Discharge	193 (33)	25 (57)		
Deceased	1 (0.17)	0		
Other (left against medical advice, send to operating room, transfer to another facility, send to psychiatric emergency department)	5 (0.85)	0		

[a]$n = 585$ visits from 370 patients.
[b]$n = 44$ visits from 38 patients.
DKA, diabetic ketoacidosis; *d*, absolute difference; *CI*, confidence interval; *mmol/L*, millimoles per liter; *ED*, emergency department; *ICU*, intensive care unit.

euglycemic patients at 2.2 vs 3.9 days ($P = 0.03$), whereas mean ED-ICU LOS was similar (16.4 vs 16.6 hours). Admission rates to ICU were 0% vs 5.1%, and ED discharge rates were 57% vs 33% for euglycemic and hyperglycemic patients, respectively.

Key safety outcomes are shown in Table 3. There was a significantly higher rate of hypoglycemia (<70 mg/dL), 18.2 vs 4.6% ($P = 0.02$), and trends toward more clinically important hypoglycemia (<54 mg/dL), 4.5 vs 1.9% ($P = 0.40$),in the euglycemic cohort. The rates of hypokalemia (<3.3 mmol/L) and severe hypokalemia (<3.0 mmol/L) were not significantly different at 27.3 vs 19.1% ($P = 0.23$), and 6.8 vs 6.3% ($P = 0.94$). Hospital mortality was low in both groups at 0 vs 0.9% in euglycemic and hyperglycemic cohorts.

Of the 44 patients who were euglycemic on presentation, etiologies of euglycemia are provided in Table 4. The majority of etiologies, 86%, were related to insulin use and poor oral intake prior to arrival, with only 14% related to SGLT2 inhibitor use.

DISCUSSION

In this study, we present clinical data, resource utilization, and safety outcomes in 629 adult ED patients with DKA, 44

Table 3. Safety outcomes.

	Hyperglycemic DKA ($n = 585$)[a]	Euglycemic DKA ($n = 44$)[b]	*d* (95% CI)	*p*
Hypoglycemia incidence, n (%)				
Glucose <70 mg/dL	28 (4.8)	8 (18.2)	−13.4 (−24.7, −2.1)	0.02
Glucose <54 mg/dL	11 (1.9)	2 (4.5)	−2.7 (−8.8, 3.6)	0.40
Hypokalemia incidence, n (%)				
Potassium <3.3 mmol/L	112 (19.1)	12 (27.3)	−8.1 (−21.4, 5.2)	0.23
Potassium <3.0 mmol/L	38 (6.5)	3 (6.8)	−0.3 (−8.2, 7.5)	0.94
Potassium <2.7 mmol/L	14 (2.4)	1 (2.3)	0.1 (−4.5, 4.7)	0.96
Admission to non-ICU with transfer to ICU within 24 hours, n (%)	1 (0.2)	0	*na*	*na*
Discharge from ED with return and readmission within 72 hours, n (%)	10 (1.7)	0	1.7 (0.5, 2.9)	0.006
Hospital mortality, n (%)	5 (0.9)	0	*na*	*na*

[a]$n = 585$ visits from 370 patients.
[b]$n = 44$ visits from 38 patients.
DKA, diabetic ketoacidosis; *d*, absolute difference; *CI*, confidence interval; *mg/dL*; milligrams per deciliter; *mmol/L*, millimoles per liter; *ED*, emergency department; *ICU*, intensive care unit.

Table 4. Etiologies of euglycemia.

Etiologies of euglycemia	n	%
SGLT2 use	6	14
Insulin prior to arrival	25	57
Insulin pump	5	11
Poor oral intake	8	18

SGLT2, sodium-glucose co-transporter 2.

of whom were euglycemic on arrival. Euglycemic patients had overall milder DKA on presentation, with higher pH and bicarbonate and lower anion gaps. We observed a shorter mean time of IV insulin infusion for euglycemic patients (13.5 vs 19.5 hours); however, there was no difference in mean time until bicarbonate >18 mmol/L or mean time to first long-acting subcutaneous insulin between cohorts. This suggests that patients with hyperglycemic DKA may have been continued on insulin infusions based on continued hyperglycemia as opposed to resolution of acidosis.

We also observed shorter total hospital LOS (2.2 vs 3.9 days) among patients with euglycemic DKA, although without significant differences in ED-ICU LOS. This suggests that the primary driver of increased LOS lies beyond the initial resuscitation and resolution of DKA, which was done primarily in the ED-ICU. This is also reflected by the reduced rates of ICU admission (0% vs 5.1%) and increased rates of ED discharge (57% vs 33%) for euglycemic patients. We hypothesize that this may reflect an association with more severe underlying triggers or stressors precipitating hyperglycemic DKA (ie, infection, ischemia, shock) that require additional time and level of care to address as an inpatient after the initial DKA resuscitation.

Importantly, we observed increased rates of hypoglycemia (<70 mg/dL), 18.2 vs 4.6%, and trends toward more clinically important hypoglycemia (<54 mg/dL), 4.5 vs 1.9%, in euglycemic patients. Hypoglycemia is well known to have neurological manifestations causing coma and seizures in the acute setting, in addition to being associated with higher rates of strokes and cognitive decline in the long term with repeated episodes.[12] Hypoglycemia also acutely increases the risk for life-threatening bradyarrhythmias and tachyarrhythmias due to depolarization and repolarization abnormalities and increased ectopy stemming from alterations in sympathoadrenal activity.[12,13] Iatrogenic hypoglycemia is a crucial adverse event to avoid during management of DKA, and our data suggests that standard DKA treatment protocols may require adjustment and closer glucose monitoring for patients presenting with euglycemic DKA. Future studies can investigate protocol adjustments such as higher concentrations of dextrose while on insulin infusion for patients with euglycemic DKA.

Euglycemic DKA has gained significant recognition after the introduction of SGLT2 inhibitors and their relationship with this condition; however, there is minimal data on the epidemiology of the various causes of euglycemic DKA.[3] We observed only 14% of our euglycemic DKA cohort was taking SGLT2 inhibitors, as opposed to the remaining 86% whose euglycemia was attributable to a combination of exogenous

insulin use and starvation state prior to arrival. This includes insulin self-administered by patients, insulin given by emergency medical services or other outside medical professionals, and insulin pump usage. In most cases the insulin was given subcutaneously immediately prior to leaving for the hospital or en route to the hospital upon patient or caregiver recognition of hyperglycemia. Although SGLT2 inhibitor use is an important cause of euglycemic DKA and becoming more widespread, our data notably shows a low prevalence of SGLT2 inhibitor use among our euglycemic DKA patients. Clinicians should maintain a high suspicion for euglycemic DKA in patients taking these medications, but they should not discount the possibility of euglycemic DKA in patients who are not taking these medications.

There are minimal prior studies describing the care of patients with euglycemic DKA beyond case reports and series related to SGLT2 inhibitor use.[14–19] We present the largest cohort to date of ED patients presenting with euglycemic DKA from a variety of causes, which contributes to increased generalizability. This is also the first direct cohort comparison of patients with euglycemic vs hyperglycemic DKA. This data can help guide emergency clinicians when attempting to diagnose and treat patients with euglycemic DKA and continue to advance the field in caring for this important and growing patient population.

LIMITATIONS

This study was conducted in a unique ED-ICU setting at a single academic medical center in the United States, which may make reproducibility to other settings uncertain. An automated EHR search was used to collect retrospective data for this study and, thus, data points may be prone to human entry error (eg, time of insulin infusion start and stop times). The DKA order set at our hospital has and continues to undergo iterative minor changes, making it possible that safety outcomes measured in this study could have differed over time based on clinical experience and fine tuning of the order set. The sample size of 44 euglycemic patients in this study—while the largest reported cohort of euglycemic DKA ED patients—is relatively small compared to the hyperglycemic cohort (585 patients), which may have increased the possibility of chance contributing to the results and thus the comparisons drawn. Etiologies of euglycemia were discerned from manual chart review by a single author. This left potential for subjectivity in determining the most likely factor contributing to euglycemia for a given patient.

CONCLUSION

We present key clinical and demographic data as well as safety outcomes in 44 adult ED patients with euglycemic DKA and compare it to those with hyperglycemic DKA managed during the same period. Euglycemic DKA patients had milder DKA on presentation based on pH, bicarbonate, and anion gap, were on insulin infusions for shorter amounts of time, had shorter total hospital LOS, and notably had significantly higher rates of hypoglycemia during treatment. The majority of cases of euglycemic DKA were related to insulin use prior to arrival, with only 14% related to SGLT2 inhibitor use. Euglycemic DKA is an important clinical entity that can be difficult to diagnose and requires thoughtful management to avoid adverse events. Future work can investigate treatment strategies for euglycemic DKA to help minimize the rate of adverse events, especially iatrogenic hypoglycemia.

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REFERENCES

1. Kitabchi AE, Umpierrez GE, Miles JM, et al. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care*. 2009;32(7):1335–43.
2. Modi A, Agrawal A, Morgan F. Euglycemic diabetic ketoacidosis: a review. *Curr Diabetes Rev*. 2017;13(3):315–21.
3. Long B, Lentz S, Koyfman A, et al. Euglycemic diabetic ketoacidosis: etiologies, evaluation, and management. *Am J Emerg Med*. 2021;44:157–60.
4. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;145(18):e895–1032.
5. Nasa P, Chaudhary S, Shrivastava PK, et al. Euglycemic diabetic ketoacidosis: a missed diagnosis. *World J Diabetes*. 2021;12(5):514–23.

6. Haas NL, Gianchandani RY, Gunnerson KJ, et al. The two-bag method for treatment of diabetic ketoacidosis in adults. *J Emerg Med*. 2018;54(5):593–9.
7. Gunnerson KJ, Bassin BS, Havey RA, et al. Association of an emergency department–based intensive care unit with survival and inpatient intensive care unit admissions." *JAMA Network Open*. 2019;2(7):e197584.
8. Haas NL, Whitmore SP, Cranford JA, et al. An emergency department-based intensive care unit is associated with decreased hospital and intensive care unit utilization for diabetic ketoacidosis. *J Emerg Med*. 2020;58(4):620–26.
9. International Hypoglycaemia Study Group. Glucose concentrations of less than 3.0 mmol/l (54 mg/dl) should be reported in clinical trials: A Joint Position Statement of the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care*. 2016;40(1):155–7.
10. Worster A, Bledsoe RD, Cleve P, et al. Reassessing the methods of medical record review studies in emergency medicine research. *Ann Emerg Med*. 2005;45(4):448–51.
11. StataCorp. 2017. *Stata Statistical Software: Release 15.1*. College Station, TX: StataCorp LLC.
12. Frier BM. Hypoglycaemia in diabetes mellitus: epidemiology and clinical implications. *Nat Rev Endocrinol*. 2014;10(12):711–22.
13. Chow E, Bernjak A, Williams S, et al. Risk of cardiac arrhythmias during hypoglycemia in patients with type 2 diabetes and cardiovascular risk. *Diabetes*. 2014;63(5):1738–47.
14. Diaz-Ramos A, Eilbert W, Marquez D. Euglycemic diabetic ketoacidosis associated with sodium-glucose cotransporter-2 inhibitor use: a case report and review of the literature. *Int J Emerg Med*. 2019;12(1):27.
15. Fukuda M, Nabeta M, Muta T, et al. Euglycemic diabetic ketoacidosis caused by canagliflozin: a case report. *Int J Emerg Med*. 2020;13(1):2.
16. Mendelsohn RA, Taveras AN, Mazer BA, et al. Euglycemic diabetic ketoacidosis precipitated by SGLT-2 inhibitor use, pericarditis, and fasting: a case report. *Clin Pract Cases Emerg Med*. 2020;4(3):389–92.
17. Puls HA, Haas NL, Franklin BJ, et al. Euglycemic diabetic ketoacidosis associated with SGLT2i use: case series. *Am J Emerg Med*. 2021;44:11–3.
18. Karakaya Z, Topal FE, Topal F, et al. Euglisemic diabetic ketoacidotic coma caused by dapagliflozin. *Am J Emerg Med*. 2018;36(11):2136.e1–e2.
19. Brown F, McColl T. Euglycemic diabetic ketoacidosis secondary to dapagliflozin use: a case report. *J Emerg Med*. 2018;54(1):109–11.

Prognostic Accuracy of SpO_2-based Respiratory Sequential Organ Failure Assessment for Predicting In-hospital Mortality

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Introduction: In this study we aimed to investigate the prognostic accuracy for predicting in-hospital mortality using respiratory Sequential Organ Failure Assessment (SOFA) scores by the conventional method of missing-value imputation with normal partial pressure of oxygen (PaO_2)- and oxygen saturation (SpO_2)-based estimation methods.

Methods: This was a single-center, retrospective cohort study of patients with suspected infection in the emergency department. The primary outcome was in-hospital mortality. We compared the area under the receiver operating characteristics curve (AUROC) and calibration results of the conventional method (normal value imputation for missing PaO_2) and six SpO_2-based methods: using methods A, B, PaO_2 is estimated by dividing SpO_2 by a scale; with methods C and D, PaO_2 was estimated by a mathematical model from a previous study; with methods E, F, respiratory SOFA scores was estimated by SpO_2 thresholds and respiratory support use; with methods A, C, E are SpO_2-based estimation for all PaO_2 values, while methods B, D, F use such estimation only for missing PaO_2 values.

Results: Among the 15,119 patients included in the study, the in-hospital mortality rate was 4.9%. The missing $PaO_2$was 56.0%. The calibration plots were similar among all methods. Each method yielded AUROCs that ranged from 0.735–0.772. The AUROC for the conventional method was 0.755 (95% confidence interval [CI] 0.736–0.773). The AUROC for method C (0.772; 95% CI 0.754–0.790) was higher than that of the conventional method, which was an SpO_2-based estimation for all PaO_2 values. The AUROC for total SOFA score from method E (0.815; 95% CI 0.800–0.831) was higher than that from the conventional method (0.806; 95% CI 0.790–0.822), in which respiratory SOFA was calculated by the predefined SpO_2 cut-offs and oxygen support.

Conclusion: In non-ICU settings, respiratory SOFA scores estimated by SpO_2 might have acceptable prognostic accuracy for predicting in-hospital mortality. Our results suggest that SpO_2-based respiratory SOFA score calculation might be an alternative for evaluating respiratory organ failure in the ED and clinical research settings. [West J Emerg Med. 2023;24(6)1056–1063.]

Keywords: *Sequential Organ Failure Assessment scores; pulse oximetry; sepsis; respiratory failure.*

INTRODUCTION

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection.[1] A recent analysis estimated 11 million sepsis-related deaths worldwide, accounting for almost 20% of all global deaths.[2] Sepsis continues to be a major burden to healthcare systems including emergency departments (ED), affecting one of every 120 ED visits.[3–6] The most recent revision of the sepsis definition (Sepsis-3) stresses the defining feature of sepsis as a "dysregulated host response to infection" and emphasizes focus on quantification of organ dysfunction.[1,7] The Sepsis-3 definition adopts the Sequential Organ Failure Assessment (SOFA) score as a measure of organ failure, and the clinical criteria of sepsis included acute change in SOFA score.[7,8]

While various scoring systems can be used for prognostication of suspected sepsis patients, the SOFA score is the most validated system and an essential component of a clinical sepsis definition.[9] The SOFA score was initially designed to provide population-level insights into acute morbidity in intensive care unit (ICU) patients, but it has become integrated into many aspects of critical care in both ICU and non-ICU settings including the ED.[10] The SOFA score is based on six organ categories, one for each of the respiratory, cardiovascular, hepatic, coagulation, renal, and neurological systems, each scored from 0 to 4, with an increasing score reflecting worsening organ dysfunction.[11]

The severity of respiratory dysfunction is measured with the SOFA score based on the ratio of partial pressure of oxygen (PaO_2) to fraction of inspired oxygen (FiO_2) (PF). The PF ratio provides information about pulmonary gas exchange adjusted for the quantity of oxygen delivered.[12] Although PaO_2 is a reference variable, invasive arterial blood gas (ABG) measurements are infrequently performed, and PF ratios are often unavailable for patients outside the ICU.[1] Furthermore, PaO_2 is often measured once rather than multiple times, which reduces clinical utility in non-ICU settings. In clinical studies, missing PaO_2 values are usually considered normal. As a noninvasive alternative to PaO_2, peripheral oxygen saturation (SpO_2)-based estimation and the SpO_2/FiO_2 (SF) ratio have been proposed, but comparative data of estimation methods including simplified or mathematical models in non-ICU settings are limited and require further validation.[12]

In this study we aimed to investigate the prognostic accuracy for predicting in-hospital mortality of respiratory SOFA scores by the conventional method of missing value imputation with normal PaO_2- and SpO_2-based estimation methods.

Population Health Research Capsule

What do we already know about this issue?
Although PaO_2 is a reference value in the Sequential Organ Failure Assessment (SOFA) score, it is often unavailable for non-ICU patients.

What was the research question?
Are respiratory SOFA scores estimated by SpO_2 comparable to the conventional method for predicting in-hospital mortality?

What was the major quantitative finding of the study?
The AUROC of the SpO_2-based respiratory SOFA (0.772; 95% CI 0.754–0.790) was higher than that of the conventional method.

How does this improve population health?
Respiratory SOFA scores estimated by SpO_2 might be an alternative way to evaluate respiratory organ failure in the emergency department and clinical research.

METHODS

Study Design

This was a single-center, retrospective cohort study of patients with suspected infection who presented to the ED of a tertiary-care hospital located in a metropolitan city between December 2017–November 2019. This study was approved by the Institutional Review Board of Samsung Medical Center (No. SMC 2022-08-158-001). The requirement for informed consent was waived given the study's retrospective nature and anonymized patient data. We followed the guidelines of the Strengthening the Reporting of Observational Studies in Epidemiology Statement (Appendix 1).

Study Population and Definitions

We included patients ≥18 years old with suspected infection who presented to the ED. Suspected infection was defined as cases in which blood culture and antibiotic administration were conducted in the ED.[1,13] We excluded patients who had limitations on invasive care (eg, patients who had terminal malignancy or who had previously signed a do-not-resuscitate [DNR] order), who presented with cardiac arrest, who had obvious non-infectious conditions such as trauma or bleeding, who were without SpO_2 or FiO_2, or had inadequate data due to our inability to access their electronic health record (EHR).

Data Collection and Outcome Measurements

We collected retrospective cohort data by extraction from the hospital's clinical data warehouse and review of EHR.

Eligible cases were electronically identified by the aforementioned definition. Data extraction was carried out by two designated research coordinators trained on the definition of each variable by the investigator and who were blinded to the study hypothesis. To ensure high quality, one investigator reviewed the EHRs and verified the final data to resolve data conflicts. The following data were retrieved: demographic characteristics including age and gender; comorbidities; vital signs; laboratory data including platelet count, bilirubin, creatinine, lactate, and ABG analysis; vasopressor use; SOFA score; FiO_2 and mechanical ventilation support; infection focus; and outcome-related data including in-hospital mortality and 28-day mortality. For collecting mortality data, we used visit history after discharge, mortality data provided by Statistics Korea, and telephone interviews. The primary endpoint was in-hospital mortality.

Respiratory SOFA Score Assessment

Detailed equations for assessing respiratory SOFA score are shown in Table 1. As a conventional method, we calculated respiratory SOFA by PaO_2 value and imputation as a normal value for missing PaO_2. We used estimated PaO_2 values from SpO_2 based on two previously suggested methods (from Madan et al and Sauthier et al).[14,15] We replaced all PaO_2 (methods A and C) with estimated values regardless of the presence of measured PaO_2, or we imputed missing PaO_2 with estimated values (methods B and D). We also estimated respiratory SOFA scores by SpO_2 and respiratory support use in all cases (method E) or in cases with missing PaO_2 values (method F). We used a modified model from Valik et al because the original study did not incorporate use of respiratory support.[16] All SOFA score components were calculated using maximum values during the 24 hours after ED arrival. Estimation of FiO_2 in patients receiving supplementary oxygen is shown in Table S1.

Statistical Analyses

Results are presented as median values with interquartile ranges (IQR) for continuous variables and numbers of patients with percentages for categorical data. Continuous and categorical variables were analyzed by the Kruskal-Wallis test and chi-square test, respectively. We compared prognostic performance of estimated respiratory SOFA score from each method with conventional respiratory SOFA score calculation for predicting in-hospital mortality. The estimated total SOFA scores from estimation methods for respiratory SOFA were compared to the total SOFA score by the conventional method. Discrimination was measured using the area under the receiver operating characteristic curve (AUROC). We also calculated the exact binominal 95% confidence interval (CI) for the AUROC. We measured the differences between conventional respiratory

Table 1. Respiratory SOFA assessment methods.

	Description	PaO_2 and respiratory SOFA estimation	Reference
Conventional method	Missing PaO_2 as normal	Normal value imputation	
Method A	SpO_2-based estimation for all PaO_2 values	1. For the first 10% reduction in SpO_2 from 100% to 90%, decrease PaO_2 by 4 mmHg for every percentage reduction in SpO_2, with the resultant PaO_2 decreasing from 100 to 60 mmHg	Madan et al.[14]
Method B	SpO_2 based estimation for missing PaO_2 values	2. For the next 10% reduction in SpO_2 from 90% to 80%, decrease PaO_2 by 1.5 mm Hg for each percentage reduction in SpO_2, which will result in PaO_2 decrease from 60 to 45 mm Hg. 3. For SpO_2 levels below 80%, divide the value by 2.	
Method C	SpO_2-based estimation for all PaO_2 values	$PaO_2 = \left(\frac{27.8^{2.8}}{\frac{1}{SpO_2}-0.99}\right)^{\frac{1}{2.8}}$	Sauthier et al.[15]
Method D	SpO_2-based estimation for missing PaO_2 values		
Method E	Respiratory SOFA score estimation using SpO_2 and respiratory support for all values	Respiratory SOFA calculation: Score 0: SpO_2 >94% Score 1: 90 < SpO_2 ≦94% Score 2: 85 < SpO_2 ≦90% Score 3: SpO_2 ≦85% *Add one point in each case for respiratory support such as oxygen or ventilator	Modified from the respiratory SOFA model of Valik et al.[16]
Method F	Respiratory SOFA score estimation using SpO_2 and respiratory support for missing PaO_2 values		

SOFA, Sequential Organ Failure Assessment; *PaO_2*, partial pressure of oxygen in arterial blood; *SpO_2*, peripheral oxygen saturation; *mm Hg*, millimeters of mercury.

SOFA score AUROC and estimated respiratory SOFA score AUROC using the method proposed by DeLong et al.[17] Calibration was assessed using calibration plots based on 100 bootstrap replicates. A *P*-value less than 0.05 was considered significant. We used R version 4.1.3 (R Foundation for Statistical Computing, Vienna, Austria; http://www.R-project.org/) for statistical analysis.

RESULTS

Study Population

We assessed the eligibility of 17,736 adult patients who underwent blood culture and antibiotic administration in the ED from December 2017–November 2019. After excluding patients who had limitations on invasive care (eg, patients who had terminal malignancy or who had previously signed a DNR order), presented with cardiac arrest, had obvious non-infectious conditions such as trauma or bleeding, were missing data on SpO_2 or FiO_2, or had inadequate data due to inability to access the EHR, 15,119 patients were included in the analyses (Figure 1). As shown in Table 2, the overall median age was 63 years, and 8,248 of patients (54.6%) were male. Respiratory tract infection was the most common diagnosis, found in 4,523 patients (29.9%). The median PF ratio was 324.3 (IQR 255.2–388.1). The proportion of patients with missing PF ratio was 56.0%, and patients with data on PF ratio had higher in-hospital mortality (9.3% vs 1.4%; Table S2). The median SF ratio was 452.4 (IQR 443.0–461.9). Overall, the total conventional SOFA score was 2.0 (IQR 1.0, 4.0), and in-hospital mortality was 740 patients (4.9%).

Calibration of Respiratory SOFA Scores

Incidence and in-hospital mortality according to respiratory SOFA scores by the conventional method and the six estimation methods are shown in Figure 2. In-hospital mortality increased as estimated respiratory SOFA score increased in all methods. The calibration curve for in-hospital mortality showed similar calibration for all methods (Figure S1).

Discrimination of Respiratory and Total SOFA Scores

The AUROCs of respiratory SOFA scores for predicting in-hospital mortality by the conventional method and by the six estimation methods are shown in Table 3 and Figure S2. The AUROC for method C (0.772; 95% CI 0.754–0.790) was significantly higher than that of the conventional method (0.755; 95% CI 0.736–0.773). The AUROCs of method B (0.739; 95% CI 0.719–0.759) and method D (0.735; 95% CI 0.715–0.755) were lower than that of the conventional method. The AUROCs of methods A (0.760; 95% CI 0.741–0.779), E (0.761; 95% CI 0.742–0.780), and F (0.758; 95% CI 0.739–0.777) were not significantly different from that of the conventional method.

The AUROCs for total SOFA scores for predicting in-hospital mortality are shown in Table 4. The AUROC for total SOFA score from method E (0.815; 95% CI 0.800–0.831) was statistically higher than that for the conventional method (0.806; 95% CI 0.790–0.822). The AUROCs for methods B and D were lower than that of the conventional method. The AUROCs for methods A, C, and F were similar to that of the conventional method.

DISCUSSION

In this single-ED study of 15,119 patients with suspected infection, PaO_2 values were commonly missing. Compared with a conventional missing value imputation with normal PaO_2, SpO_2-based estimation methods for missing PaO_2 did not improve the prognostic accuracy for predicting in-hospital mortality. In contrast, respiratory SOFA scores estimated by SpO_2, instead of measured and missing PaO_2, yielded higher discrimination for respiratory SOFA assessment (method C using the equation from Sauthier et al)

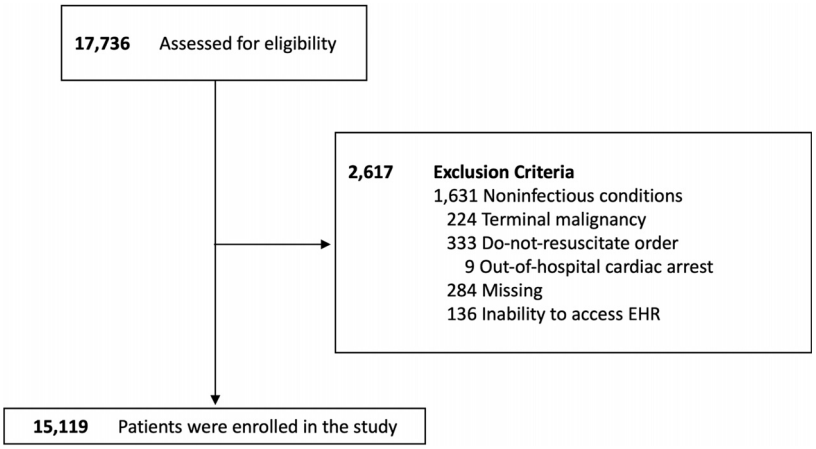

Figure 1. Study flowchart.
EHR, electronic health record.

Table 2. Baseline characteristics.The data are presented as median [IQR] for continuous variables or as number (%) for categorical variables.

Variables	Overall (N = 15,119)	In-hospital survival (n = 14,379)	In-hospital death (n = 740)	*P*-value
Age, years	63 [52, 73]	63 [52, 73]	66 [57, 75]	<0.01
Gender, female	6,871 (45.4)	6,597 (45.9)	274 (37.0)	<0.01
Comorbidities				
Hypertension	4,638 (30.7)	4,384 (30.5)	254 (34.3)	0.03
Diabetes	3,154 (20.9)	2,980 (20.7)	174 (23.5)	0.08
Cardiac disease	1,991 (13.2)	1876 (13.0)	115 (15.5)	0.06
Cerebrovascular disease	1,324 (8.8)	1,243 (8.6)	81 (10.9)	0.04
Chronic lung disease	1,370 (9.1)	1,277 (8.9)	93 (12.6)	<0.01
Hematologic malignancy	1,295 (8.6)	1,166 (8.1)	129 (17.4)	<0.01
Metastatic cancer	2,847 (18.8)	2,580 (17.9)	267 (36.1)	<0.01
Chronic renal disease	1,646 (10.9)	1,564 (10.9)	82 (11.1)	0.91
Chronic liver disease	1,316 (8.7)	1,233 (8.6)	83 (11.2)	0.02
Infection focus				
Respiratory tract	4,523 (29.9)	4,118 (28.6)	405 (54.7)	<0.01
Urinary tract	2,451 (16.2)	2,360 (16.4)	91 (12.3)	<0.01
Gastrointestinal	2,213 (14.6)	2,100 (14.6)	113 (15.3)	0.66
Hepatobiliary	2,633 (17.4)	2,562 (17.8)	71 (9.6)	<0.01
Bone or soft tissue	986 (6.5)	969 (6.7)	17 (2.3)	<0.01
Other focus	3,029 (20.0)	2,889 (20.1)	140 (18.9)	0.47
Unclear focus	662 (4.4)	630 (4.4)	32 (4.3)	1.00
Laboratory findings				
Platelets, 10^3/L	197.00 [122.00, 273.00]	198.00 [127.00, 273.00]	130.00 [43.00, 249.00]	<0.01
Bilirubin, mg/dL	0.70 [0.40, 1.20]	0.70 [0.40, 1.20]	0.90 [0.50, 1.90]	<0.01
Creatinine, mg/dL	0.985 [0.766, 1.216]	0.84 [0.766, 1.14]	1.00 [0.71, 1.765]	<0.01
Lactate, mmol/L	1.56 [1.215, 2.325]	1.53 [1.14, 2.218]	2.42 [1.61, 4.34]	<0.01
Mean arterial blood pressure, mm Hg	75.00 [67.00, 83.00]	75.00 [68.00, 83.00]	67.50 [53.875, 78.00]	<0.01
Vasopressor use	1210 (8.0)	983 (6.8)	227 (30.7)	<0.01
PaO_2, mm Hg	72.20 [61.40, 84.80]	72.90 [62.10, 85.30]	64.10 [54.70, 77.327]	<0.01
Missing PaO_2	8462 (56.0)	8340 (58.0)	122 (16.5)	<0.01
PaO_2/FiO_2 ratio	324.329 [255.24, 388.10]	330.00 [264.876, 391.82]	248.657 [137.61, 326.43]	<0.01
SpO_2	95.00 [93.00, 97.00]	95.00 [94.00, 97.00]	91.00 [85.00, 95.00]	<0.01
SpO_2/FiO_2 ratio	452.438 [442.986, 461.90]	452.438 [442.986, 461.90]	387.50 [219.876, 447.62]	<0.01
Mechanical ventilation	419 (2.8)	282 (2.0)	137 (18.5)	<0.01

(*Continued on next page*)

Table 2. Continued.

Variables	Overall (N = 15,119)	In-hospital survival (n = 14,379)	In-hospital death (n = 740)	*P*-value
Conventional respiratory SOFA (%)				<0.01
0	9,875 (65.3)	9,688 (67.4)	187 (25.3)	
1	2,581 (17.1)	2,433 (16.9)	148 (20.0)	
2	1,805 (11.9)	1,630 (11.3)	175 (23.6)	
3	580 (3.8)	450 (3.1)	130 (17.6)	
4	278 (1.8)	178 (1.2)	100 (13.5)	
Total conventional SOFA	2.00 [1.00, 4.00]	2.00 [1.00, 4.00]	6.00 [3.00, 10.00]	<0.01

INR, interquartile range; *SOFA*, Sequential Organ Failure Assessment; *L*, liter; *mg*, milligram; *dL*, deciliter; PaO_2, partial pressure of oxygen in arterial blood; SpO_2, peripheral oxygen saturation; *mm Hg*, millimeters of mercury; FiO_2, fraction of inspired oxygen.

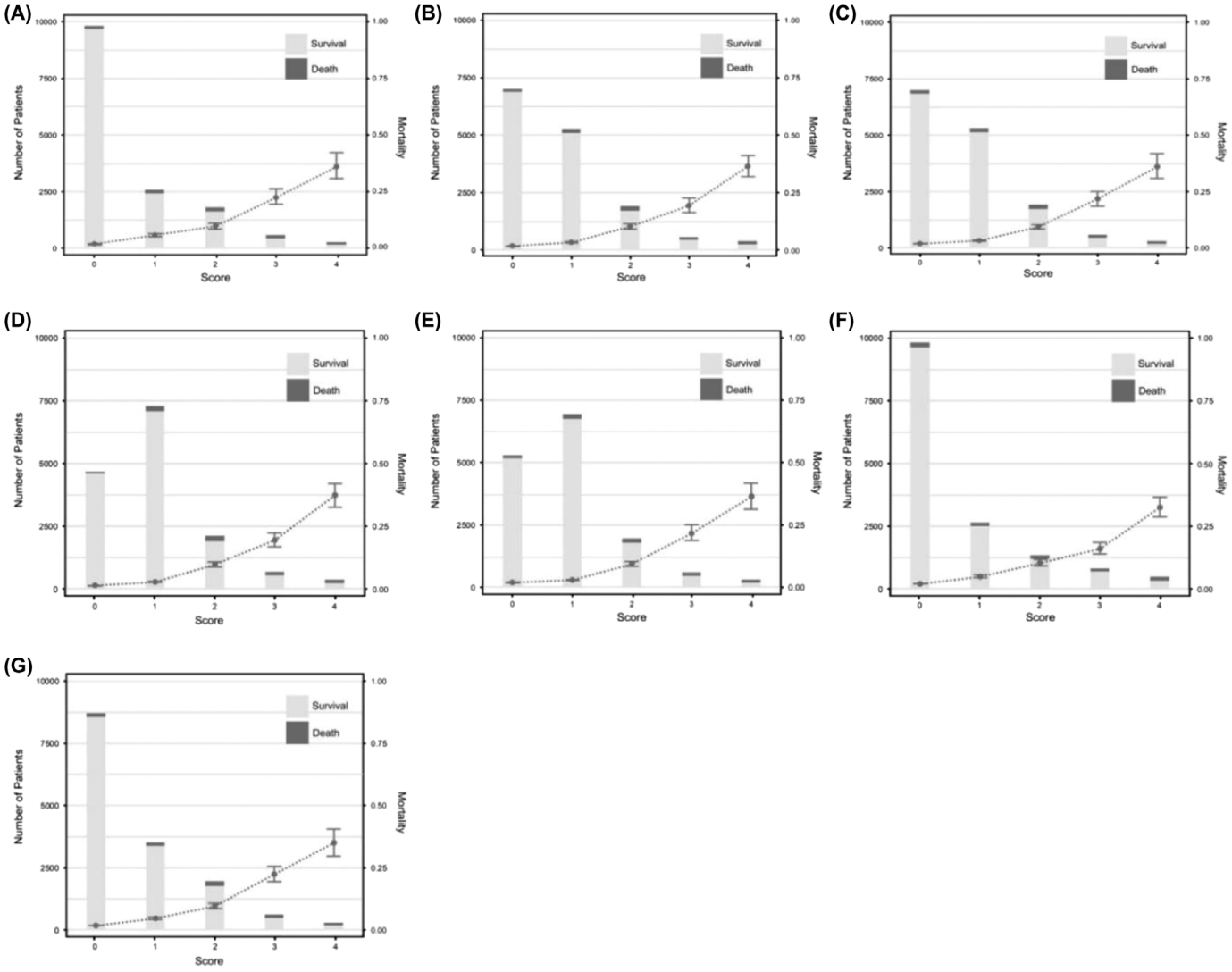

Figure 2. Distribution and in-hospital mortality according to respiratory SOFA scores by the conventional method and six estimation methods. Bar graphs represent number of patients, and points with error bars indicate in-hospital mortality with 95% confidence interval: (A) Conventional respiratory SOFA score. (B) Estimated respiratory SOFA score from method A. (C) Estimated respiratory SOFA score from method B. (D) Estimated respiratory SOFA score from method C. (E) Estimated respiratory SOFA score from method D. (F) Estimated respiratory SOFA score from method E. (G) Estimated respiratory SOFA score from method F.
SOFA, Sequential Organ Failure Assessment.

Table 3. Area under the receiver operating characteristic curve for respiratory SOFA* scores for predicting in-hospital mortality by the conventional method and six estimation methods. *Conventional method respiratory SOFA score vs estimated respiratory SOFA score.

Respiratory SOFA score	AUROC	95% CI	*P*-value*
Conventional method	0.755	0.736–0.773	
Estimated methods			
Method A	0.760	0.741–0.779	0.47
Method B	0.739	0.719–0.759	0.02
Method C	0.772	0.754–0.790	0.02
Method D	0.735	0.715–0.755	0.01
Method E	0.761	0.742–0.780	0.38
Method F	0.758	0.739–0.777	0.42

**SOFA*, Sequential Organ Failure Assessment; *AUROC*, area under the receiver operating characteristic curve; *CI*, confidence interval.

or total SOFA assessment (method E using a modified model from Valik et al). Our study showed that respiratory function assessment based on estimated respiratory SOFA scores from SpO_2 is comparable to the conventional scoring system and could facilitate respiratory dysfunction assessment in the ED. Our study is important because we included patients with suspected infection in a non-ICU setting, where PaO_2 measurement is limited but acute management of sepsis and septic shock usually take place.

The SOFA score is a validated tool for organ failure assessment and for defining clinical sepsis.[1,7] The association of SOFA score with clinical outcomes has led many investigators to propose it as a potentially valid surrogate in clinical trials.[3,9] However, accurate respiratory SOFA score evaluation requires an invasive ABG measurement, which is not routinely ordered in patients outside the ICU due to limited resources and substantial risk of failure or complications.[3] Jakobsen et al and Gadrey et al addressed the issue that multiple imputations of large proportions of missing data lead to unreliable outcomes.[18,19] SpO_2 measured by pulse oximetry is a non-invasive, surrogate marker for tissue oxygenation that is routinely applied to most ED patients, and it can be monitored continuously.[20,21] Previous studies introduced methods for imputing PaO_2 from SpO_2. Rice et al found that the SF ratio correlates with a simultaneously obtained PF ratio in acute respiratory distress syndrome.[22] Sauthier et al developed and validated a method to filter SpO_2 streams to estimate PaO_2 using only continuous and noninvasive data.[15] Valik et al showed that discrimination of mortality causes using SOFA score with respiratory function assessment based on SpO_2 is comparable with that of conventional respiratory function assessment.[16]

Table 4. Area under the receiver operating characteristic curve for total SOFA* scores for predicting in-hospital mortality by the conventional method and six estimation methods. *Conventional method total SOFA score vs. estimated methods total SOFA score.

Total SOFA score	AUROC	95% CI	*P*-value*
Conventional method	0.806	0.790–0.822	
Estimated methods			
Method A	0.807	0.791–0.823	0.77
Method B	0.796	0.779–0.814	<0.01
Method C	0.808	0.792–0.824	0.52
Method D	0.794	0.776–0.812	<0.01
Method E	0.815	0.800–0.831	<0.01
Method F	0.807	0.790–0.823	0.75

**SOFA*, Sequential Organ Failure Assessment; *AUROC*, area under the receiver operating characteristic curve; *CI*, confidence interval.

All six estimated methods in our study replaced PaO_2 regardless of the presence of measured PaO_2 and yielded higher AUROCs for predicting in-hospital mortality. It is unclear why replacement of all PaO_2 values with estimated SpO_2 yielded better mortality-discriminant power than imputation of only missing PaO_2 values. It may be because it is difficult to perform ABG sequentially in the ED. As it suggests, sequential increases in SOFA score are associated with organ dysfunction.[23]

Selection of the lowest SpO_2 values from continuous monitoring might reflect deterioration in respiratory function better than does one-time PaO_2 measurement. SpO_2 measurement could identify more high-risk patients, including less severe patients, in the absence of PaO_2 values (Table S2). An optimal strategy or equation to assess respiratory SOFA score can be selected considering the clinical settings, severity of patients, and number of PaO_2 measurements. For example, we suggest that a simplified equation might be useful in resource-limited, urgent clinical settings like EDs. Among the six methods, Method E might be a good option for use in an ED. For clinical research, Method C would be preferred to show detailed data about estimated PaO_2 and betted discrimination performance of respiratory SOFA score.

LIMITATIONS

This study has several limitations. First, this was a single-center study conducted in the ED. Second, we were unable to assess pulse oximetry accuracy. There was the possibility that patient factors, such as skin pigmentation and peripheral circulation, affected SpO_2 measurement. Third, there might have been a selection bias in acquiring ABG measurements. For generalizability, further studies including representative patients in non-ICU settings are needed to determine the proper relationship between PaO_2 and SpO_2.

CONCLUSION

Our study shows that respiratory SOFA scores estimated by SpO_2 might have acceptable or higher prognostic

accuracy for predicting in-hospital mortality in ED patients with suspected infection who had not routinely undergone arterial blood gas analysis for PaO_2 measurement. These findings suggest that SpO_2-based respiratory SOFA score calculation might be an alternative way to evaluate respiratory organ failure in the ED and clinical research. Further studies for validation and modification of SpO_2-based respiratory SOFA are needed.

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REFERENCES

1. Singer M, Deutschman CS, Seymour C, et al. The Third International Consensus Definitions ror Sepsis and Septic Shock (sepsis-3). *JAMA* 2016;315(8):801–10.
2. Rudd KE, Johnson SC, Agesa KM, et al. Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. *Lancet.* 2020;395(10219):200–11.
3. Gupta T, Puskarich MA, DeVos E, et al. Sequential Organ Failure Assessment component score prediction of in-hospital mortality from sepsis. *J Intensive Care Med.* 2020;35(8):810–7.
4. Wang HE, Jones AR, Donnelly JP. Revised national estimates of emergency department visits for sepsis in the United States. *Crit Care Med.* 2017;45(9):1443–9.
5. Moore JX, Donnelly JP, Griffin R, et al. Defining sepsis mortality clusters in the United States. *Crit Care Med.* 2016;44(7):1380–7.
6. Namgung M, Ahn C, Park Y, et al. Mortality of adult patients due to sepsis and septic shock in South Korea: a systematic review and meta-analysis. *Clin Exp Emerg Med*. Published online March 7, 2023.
7. Seymour CW, Liu VX, Iwashyna TJ, et al. Assessment of clinical criteria for sepsis for the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* 2016;315(8):762–74.
8. Vincent JL, Ferreira F, Moreno R. Scoring systems for assessing organ dysfunction and survivaL. *Crit Care Clin.* 2000;16(2):353–66.
9. Thodphetch M, Chenthanakij B, Wittayachamnankul B, et al. A comparison of scoring systems for predicting mortality and sepsis in the emergency department patients with a suspected infection. *Clin Exp Emerg Med.* 2021;8(4):289–95.
10. Lambden S, Laterre PF, Levy MM, et al. The SOFA score: development, utility and challenges of accurate assessment in clinical trials. *Crit Care.* 2019;23(1):1–9.
11. Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med.* 1996;22(7):707–10.
12. Patel S, Singh G, Zarbiv S, et al. Mortality prediction using SaO_2/FiO_2 ratio based on eICU database analysis. *Crit Care Res Pract.* 2021;2021:6672603
13. Kim DS, Park JE, Hwang SY, et al. Prediction of vasopressor requirement among hypotensive patients with suspected infection: usefulness of diastolic shock index and lactate. *Clin Exp Emerg Med.* 2022;9(3):176–86.
14. Madan A. Correlation between the levels of SpO_2 and PaO_2. *Lung India.* 2017;34(3):307–8.
15. Sauthier M, Tuli G, Jouvet PA, et al. Estimated PaO_2: A continuous and noninvasive method to estimate PaO_2 and oxygenation index. *Crit Care Explor.* 2021;3(10):e0546.
16. Valik JK, Mellhammar L, Sundén-Cullberg J, et al. Peripheral oxygen saturation facilitates assessment of respiratory dysfunction in the Sequential Organ Failure Assessment Score with implications for the Sepsis-3 Criteria. *Crit Care Med.* 2022;50(3):e272–83.
17. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics.* 1988;44(3):837–45.
18. Jakobsen JC, Gluud C, Wetterslev J, et al. When and how should multiple imputation be used for handling missing data in randomised clinical trials: a practical guide with flowcharts. *BMC Med Res Methodol.* 2017;17(1):1–10.
19. Gadrey SM, Lau CE, Clay R, et al. Imputation of partial pressures of arterial oxygen using oximetry and its impact on sepsis diagnosis. *Physiol Meas.* 2019;40(11):115008.
20. Chan ED, Chan MM, Chan MM. Pulse oximetry: understanding its basic principles facilitates appreciation of its limitations. *Respir Med.* 2013;107(6):789–99.
21. Jubran A. Pulse oximetry. *Intensive Care Med.* 2004;30(11):2017–20.
22. Rice TW, Wheeler AP, Bernard GR, et al. Comparison of the SpO_2/FiO_2 Ratio and the PaO_2/FiO_2 ratio in patients with acute lung injury or ARDS. *Chest.* 2007;132(2):410–17.
23. Ferreira FL, Bota DP, Bross A, et al. Serial evaluation of the SOFA Score to predict outcome in critically ill patients. *JAMA.* 2001;286(14):1754–8.

Simulation-based Comparison of British and Australian Advanced Life Support Guidelines

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Introduction: Cardiac arrest is a major health concern that has been linked to poor disease outcomes. Cardiopulmonary resuscitation (CPR) is a critical protocol for restoring spontaneous circulation. The guidelines used by medical staff differ across different countries. A comparison of these guidelines can help in designing more efficient Advanced Life Support (ALS) protocols. The goal in this study was to compare the guidelines for interruption of compression during CPR (hands-off time) for ALS protocols provided by Australian and United Kingdom (UK) resuscitation councils.

Methods: The author designed a simulation-based study using a mannequin and a defibrillator, and then recruited six participants. Three participants were certified ALS practitioners who followed UK guidelines, and three were certified ALS practitioners who followed Australian guidelines. Each participant received a random task assignment for each scenario, as a team leader, performer of cardiopulmonary resuscitation, or assistant. The team leader and the chest compressor were unaware of the shockability of each case's rhythm. Eight minutes total were spent on 10 CPR trials, each lasting four cycles. A video of the simulation was recorded for automated timekeeping. An independent sample *t*-test was used to compare the amount of hands-off time (seconds) throughout each cycle between two procedures. For purposes of calculating statistical significance, a 0.05 *P*-value was employed.

Results: The mean duration of second cycle hands-off time (seconds) in the UK ALS protocol was statistically significantly longer than the Australian ALS ($t = -2.100$; $P = 0.05$). For shockable rhythms, the hands-off time of the UK ALS protocol was significantly longer than Australian ALS protocol, as reflected in the second cycle ($t = -0.621$; $P < 0.001$), third cycle ($t = -8.083$; $P < 0.001$), and fourth cycle ($t = -5.814$; $p < 0.001$), while the difference in the first cycle between groups was not statistically significant. ($t = -0.258$; $P = 0.803$).

Conclusion: This simulation-based study demonstrated that the UK ALS guidelines led to an increased duration of hands-off time during the second cycle. The hands-off time in the shockable rhythms was also higher during the second, third, and fourth cycles in the UK ALS protocol compared to the Australian ALS protocol. These points must be focused on in future revisions of the UK ALS guidelines. For better results, it is critical to limit hands-off time between chest compression cycles. [West J Emerg Med. 2023;24(6)1064–1068.]

Keywords: *cardiopulmonary resuscitation; Australian Resuscitation Council; Resuscitation Council United Kingdom; Adult Life Support.*

INTRODUCTION

Cardiac arrest is a serious public health concern that has been linked to a high incidence of mortality.[1] Both out-of-hospital and in-hospital cardiac arrests are associated with poor disease outcomes.[2,3] Chest compression qualities, including proper depth and pace, appropriate chest recoil and, critically, minimal interruptions, are necessary to increase the survival rates of cardiac arrest patients. When treating a person experiencing shockable cardiac arrest, interruptions typically refer to the time required to monitor their rhythm, pulse, intravenous cannulation, intubation, and administration of a shock if necessary.[4] The cardiac output produced by effective chest compressions is roughly 30% of the average value. It has been demonstrated that stopping chest compressions reduces coronary perfusion pressures, cardiac output, and brain perfusion pressures.[5]

High-quality cardiopulmonary resuscitation (CPR) is an established practice crucial for the restoration of spontaneous circulation and effective outcomes in cardiac arrests. CPR can deliver blood to the major organs at an adequate level of coronary perfusion pressure.[6] More recent guidelines have focused on improving survival rates by improving CPR quality.[7] Edelson et al found that performing high-quality CPR, defibrillation as soon as possible and reducing hands-off time—defined as the total number of breaks between chest compressions during each cycle of CPR—improved survival rates.[8]

Recent guidelines advise a maximum hands-off time per cycle of ≈5 seconds.[9] Prior research has shown that a shorter hands-off period enhances the likelihood of survival.[10] More recent studies emphasize the need to minimize interruptions between chest compressions cycles to improve the chest compression quality and attain better outcomes.[4,11] Duration of peri-shock pause—defined as the time consumed before and after delivering the shock—was found to be inversely related to outcomes in animal studies.[12]

Advanced Life Support (ALS) guidelines from the Resuscitation Council United Kingdom (RCUK) state that the rescuer should continue CPR until the defibrillator is retrieved and pads applied. The shocks must be given with minimal interruptions to minimize the pre- and post-shock pauses.[13] In contrast, the adult ALS guidelines of the Australian Resuscitation Council (ARC) recommend charging the shock immediately while performing chest compressions, so that the defibrillator is charged and ready upon rhythm check if deemed necessary.[14]

The effectiveness of charging the manual defibrillator during chest compressions before pausing to monitor the rhythm has been assessed in several human and mannequin trials.[15,16] Depending on whether a shockable heart rhythm is discovered, the defibrillator may be armed or disarmed. Pre-charging technique minimises pauses and hands-off time overall.[15,17,18] The difference in pre-charging protocols can affect the hands-off time, which can determine the harm during chest compressions.[15] The variation in these protocols warrants a comparison to develop consensus guidelines. In this study, the author for the first time compared the hands-off time duration in a cardiac arrest between the ALS protocols provided by British and Australian resuscitation guidelines.

Population Health Research Capsule

What do we already know about this issue?
Cardiopulmonary resuscitation (CPR) is critical in restoring spontaneous circulation in cardiac arrest, but national protocols vary.

What was the research question?
The goal was to compare the hands-off time recommended by the Australian and UK resuscitation councils and identify more efficient advanced life-saving protocols.

What was the major finding of the study?
The mean duration of the hands-off time in shockable rhythms in the UK ALS guidelines was significantly longer than in the Australian ALS guidelines ($t = -2.100$; $P = 0.05$).

How does this study improve population health?
By minimizing hands-off time between chest compression cycles, the quality of chest compressions can be enhanced, leading to improved outcomes in cardiac arrest cases.

METHODOLOGY

The author conducted a simulation-based study in a medical simulation facility, where the experiments were run using a Resusci Anne mannequin (Laerdal Medical Corporation, Stavanger, Norway) and a LIFEPAK 20 (Physio-Control Inc., Redmond, WA) defibrillator. Six participants were enrolled from a tertiary-care hospital in Riyadh, Saudi Arabia. Participants' cohort allocation was based on ALS certification, either by the RCUK or the ARC. They were allocated to one of two groups, with three participants in each group. The first group followed RCUK protocols, and the second group followed the protocols established by the Australian Resuscitation Council (ARC). Each participant, whether a team leader, CPR performer, or defibrillator assistant, was randomly assigned a specific task for every scenario.

Commands and rhythm checks fell under the purview of the team leader. The assistant oversaw administering

medication, defibrillation, and ventilation. To eliminate bias, the defibrillator assistant retained 10 cards with various rhythms (pulseless electrical activity, pulseless ventricular tachycardia, asystole, and ventricular fibrillation), and participants were asked to choose one card for each situation. A brief patient history was given at the beginning of each case to mimic genuine cases. Ten CPR attempts lasting four cycles and a total of eight minutes were made. A video of the simulation was recorded for automated timekeeping.

STATISTICAL ANALYSIS

The author used mean and standard deviation for the presentation of descriptive statistics. Hands-off time (seconds) in each cycle between Australian and UK ALS protocols was contrasted employing an independent sample *t*-test. For purposes of calculating statistical significance, a 0.05 *P*–value was employed. SPSS version 26 was used for all data analysis (IBM Corporation, Armonk, NY).

RESULTS

Table 1 compares hands-off time in seconds between Australian and UK ALS protocols. We found that the mean duration of the second cycle hands-off time (seconds) following the RCUK protocol was statistically significantly longer than Australian ALS protocol ($t = -2.100$; $P = 0.05$), while the difference in the hands-off times of the first cycle, third cycle, and fourth cycle were not substantially different in Australian and UK ALS ($P > 0.05$). Table 1 presents the comparison of hands-off time in seconds between Australian and UK ALS protocols. We found that the mean duration of the second cycle hands-off time (seconds) in UK ALS was statistically significantly longer than Australian ALS ($t = -2.100$; $P = 0.05$), while the difference in the hands-off times of the first, third, and fourth cycles were not significantly different in Australian and UK ALS ($P > 0.05$).

Table 2 compares hands-off tine in shockable rhythms between Australian and UK ALS. It can be observed that the hands-off time (seconds) of the UK ALS protocol was statistically significantly longer than the Australian ALS, which was reflected in the second cycle ($t = -0.621$; $P < 0.001$), third cycle ($t = -8.083$; $P < 0.001$), and fourth cycle ($t = -5.814$; $P < 0.001$) while the difference in the first cycle was not statistically significant between the groups ($t = -0.258$; $P = 0.803$).

Table 3 shows the comparative analysis of the hands-off time in the non-shockable rhythms between the Australian and British ALS. The mean ± SD hands-off times are lower for the first and fourth cycles in Australian ALS as compared to the UK ALS (5.20 ± 0.84 vs 5.40 ± 1.34 and 6.00 ± 1.22 vs 6.20 ± 2.59, respectively) and higher in the second and third cycles (5.80 ± 1.30 vs 5.60 ± 1.67 and 6.00 ± 1.00 vs 5.20 ± 1.92, respectively). However, none of these differences were statistically significant (*P*-value > 0.05).

DISCUSSION

To the best of our knowledge, this is the first simulation-based study to compare hands-off time between the ALS

Table 1. Descriptive statistics of the hands-off time between Australian and United Kingdom Advanced Life Support protocols.

	Hands-off time in seconds			
Cycle level	Australia ALS Mean ± SD	UK ALS Mean ± SD	*t*-test	*P*-value[§]
First cycle	5.20 ± 1.23	5.40 ± 0.97	−0.405	0.691
Second cycle	4.80 ± 1.39	6.10 ± 1.37	−2.100	0.050**
Third cycle	4.80 ± 1.48	5.80 ± 1.48	−1.515	0.147
Fourth cycle	4.80 ± 1.55	6.20 ± 1.81	−1.856	0.080

[§]*P*-value calculations are based on an independent sample *t*-test.
**Significance threshold at $P \leq 0.05$.
ALS, Advanced Life Support; *UK*, United Kingdom.

Table 2. Comparison of hands-off time in shockable rhythms between Australian and United Kingdom Advanced Life Support protocols.

	Hands-off time in seconds			
Cycle level	Australia ALS Mean ± SD	UK ALS Mean ± SD	*t*-test	*P*-value[§]
First cycle	5.20 ± 1.64	5.40 ± 0.55	−0.258	0.803
Second cycle	3.80 ± 0.45	6.60 ± 0.89	−6.261	<**0.001****
Third cycle	3.60 ± 0.55	6.40 ± 0.55	−8.083	<**0.001****
Fourth cycle	3.60 ± 0.55	6.20 ± 0.84	−5.814	<**0.001****

[§]*P*-value calculations are based on an independent sample *t*-test.
**Significance threshold at $P \leq 0.05$.
ALS, Advanced Life Support; *UK*, United Kingdom.

Table 3. Comparison of hands-off time in non-shockable rhythms between Australian and United Kingdom Advanced Life Support protocols.

	Hands-off time in seconds			
Cycle level	Australia ALS Mean ± SD	UK ALS Mean ± SD	*t*-test	*P*-value[§]
First cycle	5.20 ± 0.84	5.40 ± 1.34	−0.283	0.784
Second cycle	5.80 ± 1.30	5.60 ± 1.67	0.211	0.838
Third cycle	6.00 ± 1.00	5.20 ± 1.92	0.825	0.433
Fourth cycle	6.00 ± 1.22	6.20 ± 2.59	−0.156	0.880

[§]*P*-value calculations are based on an independent sample *t*-test. In comparing time off-chest in non-shockable rhythms between Australian and UK ALS, it was found that all cycle levels were not significantly different in both Australian and UK ALS ($P > 0.05$).
ALS, Advanced Life Support; *UK*, United Kingdom.

guidelines provided by the UK and Australian resuscitation councils. This study demonstrated that the mean duration of second cycle hands-off time (seconds) in the UK ALS was statistically significantly longer than in the Australian ALS protocol ($t = -2.100$; $P = 0.050$. However, the difference in hands-off times of the first, third, and fourth cycles were not significantly different when comparing both Australian and UK ALS protocols ($P > 0.05$). The hands-off time is an important contributor to the overall success of CPR and can have life-saving importance.[2] This finding clearly suggests that the Australian guidelines are more efficient at reducing the time between cycles, as interruptions between chest compressions can reduce the overall quality of CPR.[19]

Cardiac arrest is usually classified into shockable vs non-shockable. This classification is based on the electrocardiograph rhythm. The non-shockable rhythms are asystole and pulseless electrical activity (PEA). The two shockable rhythms are ventricular fibrillation and pulseless ventricular tachycardia. Administering CPR or a defibrillator to shock the heart within a few minutes may be used to reverse cardiac arrest in patients with shockable rhythms. Comparing hands-off time in shockable rhythms showed that these times were longer in the UK than in the Australian guidelines. The correlation was found to be statistically significant ($P < 0.001$). These more prolonged interruptions were evident in the second ($P < 0.001$), third ($P < 0.001$), and fourth ($P < 0.001$) cycles. However, the difference in the first cycle was not statistically significant when comparing both groups ($P = 0.803$). The difference was not found to be statistically significant for non-shockable rhythms ($P > 0.05$). These findings suggest that the Australian ALS guidelines address the time-off chest more closely by defibrillator pre-charging approach. To increase the effectiveness of the UK ALS protocol, the time-off chest may need to be addressed.[20]

LIMITATIONS

Our study has certain limitations, including its single-center setting and simulation-based design, which hampered the measurement of mortality and morbidity. Another limitation was the unavailability of means to directly measure coronary perfusion pressures while performing CPR.

CONCLUSION

The guidelines for ALS are based on the systemic analysis of the published evidence and grading of overall confidence in evidence and the strength of recommendations. A consensus is then developed through the participation of global stakeholders and clinicians. Analysis of these guidelines from time to time can lead to improvement in these protocols and enhance their overall efficiency. We found that the hands-off times in shockable rhythms were higher during the second, third, and fourth cycles in the UK ALS protocol compared to the Australian protocol. These points must be focused on in future revisions of UK ALS guidelines. Chest compression interruptions should be kept to a minimum for improved outcomes.

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REFERENCES

1. Martinell L, Nielsen N, Herlitz J, et al. Early predictors of poor outcome after out-of-hospital cardiac arrest. *Crit Care.* 2017;21(1):1–10.
2. Andersen LW, Holmberg MJ, Berg KM, et al. In-hospital cardiac arrest: a review. *JAMA.* 2019;321(12):1200–10.
3. Wilber DJ, Garan H, Finkelstein D, et al. Out-of-hospital cardiac arrest. *N Engl J Med.* 1988;318(1):19–24.
4. Meaney PA, Bobrow BJ, Mancini ME, et al. Cardiopulmonary resuscitation quality: improving cardiac resuscitation outcomes both inside and outside the hospital: a consensus statement from the American Heart Association. *Circulation.* 2013;128(4):417–35.
5. Berg RA, Sanders AB, Kern KB, et al. Adverse hemodynamic effects of interrupting chest compressions for rescue breathing during cardiopulmonary resuscitation for ventricular fibrillation cardiac arrest. *Circulation.* 2001;104(20):2465–70.
6. Czapla M, Zieli ska M, Kubica-Cieli ska A, et al. Factors associated with return of spontaneous circulation after out-of-hospital cardiac arrest in Poland: a one-year retrospective study. *BMC Cardiovasc Disord.* 2020;20(1):1–7.
7. Nadkarni VM, Nolan JP, Billi JE, et al. Part 2: International collaboration in resuscitation science: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. *Circulation.* 2010;122(16_suppl_2):S276–82.
8. Edelson DP, Abella BS, Kramer-Johansen J, et al. Effects of compression depth and pre-shock pauses predict defibrillation failure during cardiac arrest. *Resuscitation.* 2006;71(2):137–45.
9. Koster RW, Sayre MR, Botha M, et al. 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

Science with Treatment Recommendations, Part 5: Adult Basic Life Support. *Resuscitation.* 2010;81(1, suppl. 1):E48–70.

10. Eftestøl T, Sunde K, Steen PA. Effects of interrupting precordial compressions on the calculated probability of defibrillation success during out-of-hospital cardiac arrest. *Circulation.* 2002;105(19):2270–3.
11. Monsieurs KG, Nolan JP, Bossaert LL, et al. European Resuscitation Council guidelines for resuscitation 2015: section 1. Executive summary. *Resuscitation.* 2015;95:1–80.
12. Cheskes S, Schmicker RH, Christenson J, et al. Perishock pause: an independent predictor of survival from out-of-hospital shockable cardiac arrest. *Circulation.* 2011;124(1):58–66.
13. Soar J, Deakin C, Nolan JP, et al. Adult Advanced Life Support Guidelines. *Resuscitation Council UK.* 2021;161:115–51.
14. Walker T, Morley P. Australian Resuscitation Council: Adult Advanced Life Support (ALS) Guidelines 2006. *Crit Care Resusc.* 2006;8(2):129–31.
15. Edelson DP, Robertson-Dick BJ, Yuen TC, et al. Safety and efficacy of defibrillator charging during ongoing chest compressions: a multi-center study. *Resuscitation.* 2010;81(11):1521–6.
16. Kramer-Johansen J, Edelson DP, Abella BS, et al. Pauses in chest compression and inappropriate shocks: a comparison of manual and semi-automatic defibrillation attempts. *Resuscitation.* 2007;73(2):212–20.
17. Hansen LK, Folkestad L, Brabrand M. Defibrillator charging before rhythm analysis significantly reduces hands-off time during resuscitation: a simulation study. *Am J Emerg Med.* 2013;31(2):395–400.
18. Koch Hansen L, Mohammed A, Pedersen M, et al. The stop-only-while-shocking algorithm reduces hands-off time by 17% during cardiopulmonary resuscitation–a simulation study. *Eur J Emerg Med.* 2016;23(6):413–7.
19. Krarup NH, Terkelsen CJ, Johnsen SP, et al. Quality of cardiopulmonary resuscitation in out-of-hospital cardiac arrest is hampered by interruptions in chest compressions—a nationwide prospective feasibility study. *Resuscitation.* 2011;82(3):263–9.
20. Oving I, de Graaf C, Karlsson L, et al. Occurrence of shockable rhythm in out-of-hospital cardiac arrest over time: a report from the COSTA group. *Resuscitation.* 2020;151:67–74.

Quality Improvement Curriculum for Intensive Care Unit Upgrades

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Patients admitted to the hospital ward from the emergency department (ED) occasionally decompensate and require transfer to the intensive care unit (ICU). An emergency medicine (EM) curriculum focused on review of these ICU upgrade cases could improve resident knowledge related to patient acuity, critical illness, and appropriate disposition. Furthermore, initial identification of critical pathology in the ED and earlier admission to the ICU could reduce delays in care and improve patient outcomes.

We performed a retrospective analysis to determine the effectiveness of a resident quality improvement curriculum evaluating cases where patients require transfer from the inpatient floor to the ICU within 12 hours of admission from the ED. We compared postgraduate year 2 (PGY-2) EM residents who participated in the ICU upgrades curriculum during their first year to PGY-2 EM residents who did not participate in the curriculum.

Analysis of the 242 qualifying ICU upgrade cases from July 2019–October 2021 showed post-curriculum residents were responsible for an average of 1.0 upgrades per resident compared to an average of 1.54 upgrades per resident ($P = 0.12$) for pre-curriculum residents. Although there was no statistically significant difference in ICU upgrades between the groups, there was a trend toward decreased ICU upgrade cases for residents who participated in the curriculum. Common reasons for ICU upgrade included worsening respiratory distress requiring higher level of respiratory support, recurrent hypotension after initial intravenous fluid resuscitation requiring vasopressor support, and declining mental status.

This retrospective study showed no significant difference in the number of ICU upgrades for residents who completed the ICU upgrades curriculum compared to residents who were not enrolled in the course. However, the study was likely underpowered to detect a significant difference in the groups, and there was a trend toward reduced ICU upgrades for residents who completed the curriculum. ICU upgrade cases were frequently associated with worsening respiratory status, hypotension, and mental status. These findings highlight the importance of reassessment of vital signs and mental status prior to determining disposition from the ED. Additional, larger studies are needed to better determine the curriculum's impact on resident proficiency in recognizing critical illness and reducing ICU upgrades. [West J Emerg Med. 2023;24(6)1069–1072.]

BACKGROUND

Emergency physicians care for undifferentiated patients with a wide range of acuity. Making the correct diagnosis and determining the appropriate disposition can be challenging, especially for resident physicians in training. However, appropriately determining patient disposition, such as discharge vs floor admission vs intensive care unit (ICU) admission, is one of the most important roles of an

emergency physician. Patients initially triaged as stable for hospital ward admission occasionally decompensate and require rapid upgrade in care to the ICU setting. These ICU upgrades can lead to disjointed and delayed patient care, inefficient resource utilization, and undesirable outcomes for the patient, clinician, and healthcare system.[1,2,3]

Initial identification of critical pathology in the emergency department (ED) and earlier admission to the ICU could reduce delays in care and improve patient outcomes. A residency quality improvement (QI) curriculum focused on reviewing these ICU upgrade cases could improve resident proficiency in determining appropriate patient disposition, reduce the number of ICU upgrades, and enhance the quality of patient care.

Population Health Research Capsule

What do we already know about this issue?
Patients admitted from the ED occasionally decompensate and require transfer to the ICU. These upgrades to ICU care can be associated with delayed care and worse outcomes.

What was the research questions?
What was the impact of a resident quality improvement course on the number of ICU upgrades within 12 hours of admission from the ED?

What was the major finding of the study?
Post-course residents averaged 1.0 upgrades/resident vs 1.54 upgrades/resident ($P = 0.12$) for pre-course residents.

How does this improve population health?
While we did not detect a significant difference between groups, there was a trend toward reduced ICU upgrades for residents who completed the course.

OBJECTIVES

The purpose of this educational initiative was to create a QI curriculum focused on structured case reviews and root cause analyses for patients who were initially admitted from the ED to the inpatient floor and subsequently required transfer to the ICU within 12 hours of admission. We chose a 12-hour window by consensus opinion, as this was considered a reasonable time frame in which clinical deterioration might be anticipated and not so long as to be significantly impacted by floor interventions or lack thereof. The curriculum was implemented at a large, urban, academic tertiary-care facility with an established emergency medicine (EM) residency program. After implementation, we performed a retrospective, observational analysis of the educational initiative, comparing the incidence rate ratio of ICU upgrade cases for postgraduate year 2 (PGY-2) post-curriculum EM residents to PGY-2 pre-curriculum EM residents.

CURRICULAR DESIGN

The UT Southwestern Medical Center Emergency Medicine Residency Program developed a QI curriculum called Residents Enhancing Safety and Quality (RES-Q). This curriculum allows residents the opportunity to rotate through different QI-focused subgroups every six months. The current project addresses the ICU-upgrades aspect of this curriculum and the impact of this program on the likelihood of resident physicians being involved in ICU upgrade cases.

Each ICU upgrade was identified in the electronic health record (EHR) system with the help of EHR query tools and information technology staff. We excluded cases if the patient went directly from the ED to the operating room, if the patient had an ICU specialty consult in the ED prior to admission, or if the patient was cared for by only an attending physician or an advanced practice practitioner.

At the beginning of each month, the residents in the ICU Upgrades RES-Q group received a report with all the ICU upgrade cases from the previous month. The upgrade cases were then divided among the residents in the RES-Q group. Residents were instructed to thoroughly review all notes and documentation related to each ICU upgrade case, including clinician notes, nursing notes, diagnostic study results, vital signs, and medication administration reports. Residents were tasked with identifying any indications of the patients' impending decompensation during their time in the ED and potential root causes for the upgrade to ICU care.[4]

Finally, the residents made note of any opportunities for improvement in diagnosis or management that could have affected the clinical course and possibly negated the need for an ICU upgrade. Faculty were available to discuss the cases and possible learning points, but the exercise was primarily resident driven. Cases that were deemed to be of high learning potential by the faculty were subsequently presented to the entire residency program during weekly academic conference.

We submitted this study as an educational process improvement project. It was reviewed by a QI committee at UT Southwestern, and institutional review board approval was deemed unnecessary.

IMPACT/EFFECTIVENESS

After the RES-Q ICU upgrades curriculum was implemented, we performed a retrospective, observational

analysis. This study took place at a large, urban, academic tertiary-care facility in Dallas, Texas, associated with an EM residency program. The duration of the study was July 2019–October 2021.

The primary outcome of the study was a quantification of the number of cases in which patients seen by PGY-2 EM residents required an upgrade to ICU care. We chose PGY-2 residents to reduce the variability in clinical experience that would result from including residents of all academic years. By comparing residents of the same year randomly assigned to complete the ICU upgrades curriculum, confounding variables were minimized.

Our analysis compared PGY-2 EM residents who participated in the ICU upgrades curriculum their first year to PGY-2 EM residents who did not participate in the curriculum their first year. We then estimated the method of maximum likelihood by fitting a generalized Poisson linear regression model to the data.

Analysis of the 242 qualifying resident ICU upgrade cases from July 2019–October 2021 showed that 19 PGY-2 EM residents who completed the curriculum were responsible for 19 ICU upgrades, and 26 PGY-2 EM residents who had not yet completed the curriculum were responsible for 40 ICU upgrades. The incidence rate ratio of ICU upgrade cases for PGY-2 pre-curriculum residents was 1.54 (95% confidence interval 0.89–2.66; $P = 0.122$) compared to PGY-2 post-curriculum residents. See Figure 1 for a breakdown of the number of ICU upgrade cases.

Although we found no statistically significant difference in ICU upgrades between the groups, there was a trend toward decreased ICU upgrade cases for residents who participated in the curriculum. Over the study period, residents who completed the ICU upgrades curriculum had a 35% relative risk reduction in ICU upgrades compared to their pre-curriculum colleagues.

During review of ICU upgrade cases, we identified several circumstances associated with an ICU upgrade. Common reasons for transfer from the floor to the ICU after initial ED evaluation included worsening respiratory distress requiring intubation or higher level of respiratory support; recurrent hypotension after initial intravenous (IV) fluid resuscitation requiring vasopressor support; and declining mental status. Specifically, those patients who needed high-flow nasal cannula or non-invasive ventilation for respiratory support and those who required multiple liters of IV fluids for hypotension were at high risk for subsequent ICU upgrade. Another common reason for ICU upgrade was development or worsening of alcohol withdrawal. These common reasons for ICU upgrade suggest that deteriorating clinical status from initial ED evaluation is a frequent root cause of ICU upgrades. These cases highlight the importance of frequent patient reassessment prior to determining final disposition.

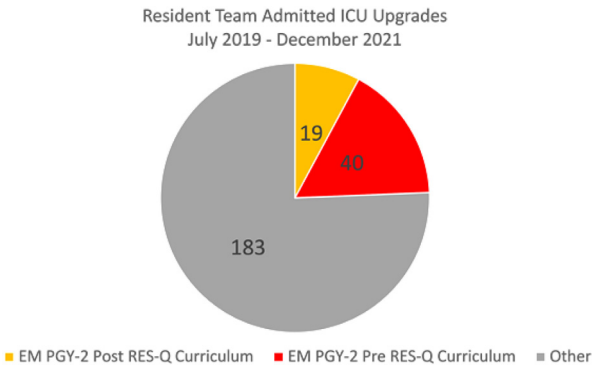

Figure 1. Breakdown of upgrades to intensive care unit care. *EM*, emergency medicine; *PGY*, postgraduate year; *RES-Q*, Residents Enhancing Safety and Quality.

Although not statistically significant, this data is promising. A simple educational intervention with minimal cost to the healthcare system was potentially associated with reduced patient transfers from the floor to the ICU. Similar QI programs could improve resident training in identifying critical illness and potentially lead to improved patient outcomes, more appropriate resource utilization, and decreased healthcare costs. Additional time periods and residency classes are currently under review to better determine the effect of the RES-Q ICU upgrades curriculum.

LIMITATIONS

This study had several limitations. This was a retrospective, observational study that was conducted at a single academic medical center. The smaller sample size specifically reduced the power of the study and decreased the likelihood of detecting a significant difference between the groups. In addition, although only the residents in the RES-Q group went through the structured case review of ICU upgrades, all residents at the program were exposed to teaching points from the monthly RES-Q conference lectures. We were not able to control for the attending on shift or other unidentified factors that may have taken the medical decision-making responsibility away from the resident. We did not account for patient volume or ED boarding of inpatient admissions, which could have influenced length of stay and impacted the number of ICU upgrades. Patient and resident demographic data was not collected during this study, which could be an area of subsequent research. Future studies could investigate the effect of the RES-Q ICU upgrades QI curriculum at other EM programs. This would increase the sample size and provide external validity across other programs and patient populations.

CONCLUSION

This study demonstrated that completion of the RES-Q ICU upgrades curriculum was not associated with a significant difference in the number of patients who required transfer from the inpatient floor to the ICU within 12 hours

of admission. However, completion of the quality improvement curriculum was associated with a trend toward decreased ICU upgrades. The ICU upgrade cases were frequently associated with worsening respiratory status, hypotension, and mental status. These findings highlight the importance of reassessment of vital signs and mental status prior to determining disposition from the ED. Additional, larger studies are needed to determine whether the curriculum has a significant impact on ICU upgrades and can improve resident proficiency in recognizing critical illness and appropriately triaging the clinical acuity of patients. With tools in the electronic health record and appropriate buy-in from residents and program leadership, this curriculum could be easily replicated at other EM residency training programs.

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REFERENCES

1. Werline L, Young A. Emergency department to ICU time is associated with hospital mortality: a registry analysis of 14,788 patients from six university hospitals in the Netherlands. *J Emerg Med.* 2019;58(2):368–9.
2. Goldhill DR, Sumner A. Outcome of intensive care patients in a group of British intensive care units. *Crit Care Med.* 1998;26(8):1337–45.
3. Huang DT. Clinical review: impact of emergency department care on intensive care unit costs. *Crit Care.* 2004;8(6):498–502.
4. Long B. The ED floor admit that later requires ICU care: What are we missing and how can we improve? emDOCs.net - Emergency Medicine Education. 2017. Available at: http://www.emdocs.net/ed-floor-admit-later-requires-icu-care-missing-can-improve/. Accessed October 21, 2022.

Survey of Vaccine Hesitancy in Patients Visiting Three Tertiary-care Emergency Departments in Southeast Louisiana

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Objectives: Vaccine hesitancy has been a barrier to achieving herd immunity during the coronavirus 2019 (COVID-19) pandemic. Having low socioeconomic status and education levels, and being a person of color, are associated with higher COVID-19 infection risk and worse outcomes. These same groups are associated with higher vaccine hesitancy. The state of Louisiana has one of the lowest vaccination rates in the country. In this study we aimed to identify demographic, perspective, and health behavior factors associated with vaccine hesitancy in emergency departments (ED) in Southeast Louisiana.

Methods: A cross-sectional survey was distributed at three tertiary-care hospital EDs. Patients >18 years old and not in acute distress were recruited between April–July 2021. The 37-item questionnaire addressed socioeconomic demographics, social determinants of health, COVID-19 safety practices, thoughts and perceptions on COVID-19 and vaccines, sources of COVID-19 and vaccine information, and trust in the healthcare system.

Results: Overall, 247 patients completed our survey. Of those, 29.6% reported they were vaccine hesitant. These respondents were significantly more likely, when compared to vaccine-acceptant respondents, to never have married, to have some college education, make less than <$25,000 in household earnings yearly, be unsure whether vaccines prevent disease, not have discussed the COVID-19 vaccine with their primary care doctor, and to prefer to do their own research for COVID-19 vaccine information. We observed no statistically significant differences based on gender, race/ethnicity, parental status, area of living, or their perceived risk of needing hospitalization for treatment or dying from the virus.

Conclusion: Vaccine hesitancy was associated with multiple socioeconomic factors, perspectives, and beliefs. Vaccine-hesitant individuals were more uncertain about the safety of the COVID-19 vaccine, the feasibility of obtaining the vaccine, and its efficacy. Public health interventions aimed at these findings and improving public trust in healthcare systems are needed to increase vaccine acceptance. [West J Emerg Med. 2023;24(6)1073–1084.]

INTRODUCTION

As of April 2022, the number of global severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) cases surpassed 486 million, with over 6.1 million deaths. The United States has more cases than any other country, with nearly 79 million confirmed cases reported and 972,000

deaths.[1] Despite the development of multiple vaccines for SARS-CoV-2, the coronavirus 2019 (COVID-19) pandemic continues to spread across the globe.

The COVID-19 vaccine rollout began in the United States in December 2020 with the US Food and Drug Administration (FDA) emergency-use authorization of the Pfizer and Moderna vaccines. Currently, 77.0% of individuals living in the US have received their first dose of the vaccine, and 65.6% are fully vaccinated.[2] The number of vaccinations, however, is inconsistent across the US as there is widespread reluctance to receive a vaccine, also known as vaccine hesitancy.[3]

Vaccine hesitancy is not a new phenomenon. It dates back to the 1800s with the introduction of the smallpox vaccine and has played a factor in several vaccine rollouts thereafter, including diphtheria, tetanus, pertussis, mumps, and polio.[4] An Associated Press poll in May 2020 found that only 50% of US residents reported an intent to receive the COVID-19 vaccine once available.[5] While breakthrough cases have been reported,[6] receiving a vaccine remains the most effective way individuals are protected from COVID-19.[7–9] Identifying and mitigating factors related to vaccine hesitancy is crucial to increasing vaccination rates. Vaccine hesitancy can be attributed to multiple factors including the rapid development of novelty mRNA vaccines.[10,11] Misinformation spread via social media platforms is also a contributing factor.[12,13] Several studies found that persons with low socioeconomic status, low levels of education, being a person of color, and living in a rural area are associated with vaccine hesitancy as well.[14–17] Consequently, these factors are also associated with higher risk of COVID-19 infection and poorer outcomes.[18–21]

Research in COVID-19 vaccine hesitancy remains limited. While papers early in the COVID-19 pandemic evaluated factors related to the intent of becoming vaccinated, few have investigated hesitancy since the vaccine became available. It is important to note that reported intentions may not always correspond with vaccine uptake.[22] Additionally, prior vaccine-hesitancy studies focused on nationwide data. Vaccination hesitancy gaps exist among geographic locations, with the states having the most vaccine-hesitant residents concentrated in the Southeast, Midwest, and Alaska, and the least hesitant concentrated in the West and New England.[23] The state of Louisiana has one of the lowest rates of vaccinated residents in the US, with 53.0% of its population fully vaccinated, compared to the national average of 65.6%.[24] Given these geographic gaps, we sought to identify the demographic factors, perspectives, beliefs, and health behaviors related to vaccination hesitancy in patients presenting to emergency departments (ED) in Southeast Louisiana.

Emergency departments routinely treat the most vulnerable patient populations, including those with higher levels of adverse social determinants of health and minority communities.[25–27] Notably, these populations are historically the most vaccine hesitant.[28–30] By identifying determinants of COVID-19 vaccine hesitancy in the ED, public health campaigns can tailor communication efforts to address the concerns of the unvaccinated. To date, this is the first ED-based, in-person survey that investigates vaccine hesitancy as it relates to trust in the medical system. We also expand on current ED literature on COVID-19 vaccine hesitancy and social health behaviors.

METHODS

This manuscript adheres to the EQUATOR guideline, Consensus-Based Checklist for Reporting of Survey Studies.[31]

Study Design and Population

We conducted this cross-sectional study in the EDs at three tertiary-care hospitals within a multi-hospital system. The study was approved by our organization's institutional review board. The questionnaire used for this research was developed using expert knowledge in emergency medicine, COVID-19, and public health, following extensive literature review. The questionnaire (Appendix 1) contains 37 questions within two sections:

- Section 1: Questions designed to collect self-reported socioeconomic demographics and social determinants of health.
- Section 2: Questions regarding COVID-19 safety practices, the respondents' thoughts on and perceptions of COVID-19 specific vaccines, self-perceived risk, trust of the healthcare system, and sources of COVID-19 vaccine information.

Questionnaires were multiple choice but did include space for additional information if the provided answers were insufficient to the participant.

Surveys were administered in the ED between April–July 2021 by trained research staff following verbal consent. Participants were asked to participate and had the option to complete the survey on paper. Additional research information and relevant contacts were included in a cover page and provided to the participant. The completed questionnaires were transferred to and managed using REDCap, (Research Electronic Data Capture) hosted at Ochsner Main Campus, Ochsner Baptist, and Ochsner Kenner. Source documents were stored securely on site. REDCap is a secure, web-based software platform designed to support data capture for research studies.[32,33] Only authorized, IRB-approved study team members extracted research data from source documents, entered it into the research database, and/or accessed secure patient information.

During the periods of data collection, research staff approached all adults who checked in to the ED and

completed triage. Patients were excluded if they were 1) not in the waiting room of the ED, 2) were in any clear and apparent distress per discretion of research staff, or 3) had any impaired decision-making ability. If any participants needed accommodation secondary to illiteracy or visual deficiencies, a research staff member was available to read and record answers with the patient. During the research period, we did not have any participants who required additional accommodations. Patients were chosen to participate based on convenience sampling.

Survey Context and Administration

Originally, the surveys were to be offered to patients by ED registration and nursing staff following triage at seven sites in SE Louisiana. When using this protocol, there were low rates of participation. Adjustments to the research protocol were made and surveys were only collected by available research staff at limited sites. We used ED sites for this research to collect a diverse sample of the SE Louisiana region. Table 1 reports patient demographics of the research sites, using 2020 data. Demographics of the study population are recorded in Table 2.

The optimal sample size for this research based on a population of approximately 80,000 patients served at the three ED sites was 400 participants, calculated using a 5% margin of error and 95% confidence interval. However, a high non-participation rate was expected per literature review on similar research.[34] Additionally, due to the third and fourth wave of COVID-19 and the emergence of the delta variant, we stopped survey collection with a sample size of 294 to keep research conditions relatively constant.

Data Analysis

We used means, standard deviations, frequencies, and percentages to describe the cohort's sociodemographic characteristics, opinions and health behaviors related to COVID-19 and vaccines. Respondents were categorized as *vaccine hesitant* if they answered "No" or "Unsure" to the question: "Do you plan to receive a COVID-19 vaccine?" and as *vaccine accepting* if they answered "I have already received the vaccine" or "Yes" to the same question. We examined comparisons of respondents' sociodemographic characteristics, opinions and health behaviors related to the COVID-19 virus and vaccines between the vaccine-hesitant and vaccine-accepting groups with *t*-tests, chi-square, or Fisher exact tests. We used SAS version 9.4 (SAS Institute Inc, Cary, NC) to perform all analyses.

RESULTS

Overall, 247 patients participated in our survey, with most responses coming from ED #1 (115) and ED #2 (105). Tables 2–4 describe the results of the demographic, perspective/opinions, and health behavior portions of the questionnaire. Of those who participated, 246 answered our primary question, "Do you plan to receive the COVID-19 vaccine?"; 70.3% indicated that they planned to receive or had already received the COVID-19 vaccine and 29.55% reported they had no plans to receive the vaccine or were unsure whether they were going to receive the vaccine. Most participants in this study were female (63.2%), Black (56.0%), never married (35.7%), were parents (71.0%), employed (53.3%), had a household income of <$25,000, and lived in the city (65.0%) (Table 2).

Among sociodemographic characteristics, we found significant associations between vaccine hesitancy and age, marital status, education level, work status, and household income ($P < 0.05$). On average, vaccine-hesitant individuals were younger than those in the vaccine-acceptant cohort (33.88 vs 52.10, $P < 0.001$). Respondents who were vaccine hesitant were more likely to never have been married

Table 1. Emergency department patient demographics.

Variable	All sites* N (%)	ED #3 n (%)	ED #2 n (%)	ED #1 n (%)
Population served	77,573	20,924	17,714	43,527
Gender				
Male	34,437 (44.39)	9,343 (44.65)	6,738 (38.04)	20,248 (46.52)
Female	43,122 (55.59)	11,580 (55.34)	10,971 (61.93)	23,271 (53.46)
Unknown/Other	14 (.02)	1 (.01)	5 (.03)	8 (.02)
Race/Ethnicity				
White	36,638 (47.23)	10,839 (51.80)	5,224 (29.49)	22,419 (51.51)
Black	36,485 (47.03)	8,331 (39.82)	11,841 (66.84)	18,908 (43.44)
Non-Black minority	2,744 (3.54)	1,329 (6.35)	313 (1.77)	1,012 (2.32)
Unknown	1,706 (2.20)	425 (2.03)	336 (1.90)	1,188 (2.73)

*Not an accumulation of all three sites, patients may be counted in the demographic statistics at more than one site.
ED, emergency department.

Table 2. Participant sociodemographics.

Variable	Total sample N = 247 N (%)	Vaccine accepting n = 173 n (%)	Vaccine hesitant n = 73 n (%)	*P*-value
Age (mean years of age)	46.9	52.1	33.9	<**0.001**
Gender				0.4
Male	82 (36.0)	59 (36.2)	23 (35.4)	
Female	144 (63.2)	103 (63.2)	41 (63.1)	
Race/Ethnicity				0.2
White	77 (34.2)	60 (37)	17 (27.0)	
Black	126 (56.0)	85 (52.5)	41 (65.1)	
Non-Black minority	22 (9.8)	17 (10.5)	5 (7.9)	
Marital status				<**0.001**
Never married	79 (35.8)	44 (28.0)	34 (54.0)	
Living with partner	24 (10.9)	14 (8.9)	10 (15.9)	
Married	69 (31.2)	59 (37.6)	10 (15.9)	
Divorced or separated	39 (17.7)	32 (20.4)	7 (11.1)	
Widowed	10 (4.5)	8 (5.1)	2 (3.2)	
Children				0.3
Have children	154 (71.0)	114 (73.1)	40 (65.6)	
No children	63 (29.0)	42 (26.9)	21 (34.4)	
Education				**0.04**
Some education but non-high school graduate	27 (12.1)	16 (10.1)	10 (15.6)	
High school graduate	55 (24.6)	36 (22.6)	19 (29.7)	
Some college/university	65 (29.0)	43 (27.0)	22 (34.4)	
College/university graduate or above	77 (34.4)	64 (40.3)	13 (20.3)	
Employment status				<**0.001**
Working	120 (53.3)	86 (53.1)	34 (54.0)	
Retired	46 (20.4)	43 (26.5)	3 (4.8)	
Laid off	20 (8.9)	9 (5.6)	11 (17.5)	
Other	39 (17.3)	24 (14.8)	15 (23.8)	
Average household income				**0.003**
<$25,000	88 (43.1)	58 (40.9)	30 (48.4)	
$25,000–$74,999	73 (35.8)	45 (31.7)	28 (45.2)	
≥$75,000	43 (21.1)	39 (27.5)	4 (6.5)	
Area of living				0.2
Small town/rural	35 (15.9)	24 (15.4)	11 (17.5)	
Suburban	42 (19.1)	35 (22.4)	7 (11.1)	
City	143(65.0)	97 (62.2)	45 (71.4)	
Political orientation				**0.002**
Republican	31 (14.6)	23 (14.9)	8 (13.6)	
Democrat	95 (44.6)	82 (53.3)	13 (22.0)	
Libertarian	3 (1.4)	2 (1.3)	1 (1.7)	
Green	0 (0)			
Independent	20 (9.4)	12 (7.8)	8 (13.6)	
No political orientation	27 (12.7)	15 (9.7)	12 (20.3)	
Prefer not to answer	33 (15.5)	18 (11.7)	15 (25.4)	
Other	4 (1.7)	2 (1.3)	2 (3.4)	

(53.97 vs 28.03, $P < 0.001$), to have some college/university education without graduating (34.38 vs 27.04, $P < 0.042$), were less likely to be retired (4.76 vs 26.54, $P < 0.001$), and made less than $25,000 in household earnings (48.39 vs 40.85, $P < 0.003$), compared to respondents who were vaccine acceptant. Vaccine-acceptant individuals were more likely to be Democrat (53.25 vs 22.03, $P < 0.002$). This study did not find any statistically significant differences between vaccine-acceptant and vaccine-hesitant groups based on gender, race/ethnicity, parental status, or area of living (Table 2).

Survey questions concerning perceived difficulty accessing the COVID-19 vaccine, chances of being infected with COVID-19, and overall state of health were significantly associated with vaccine hesitancy. Respondents who were vaccine hesitant were more unsure about their ease of obtaining the vaccine (40.28 vs 3.64 $P < 0.001$) and perceived a higher chance of being infected with the COVID-19 virus (29.17 vs 13.10, $P < 0.01$), compared to those who were vaccine hesitant. In general, more vaccine-hesitant individuals thought of themselves as being in great health (28.57 vs 12.57, $P < 0.02$), compared to respondents who were vaccine acceptant. There were no significant associations between vaccine hesitancy and perceived risk of contracting the virus in the following six months, needing hospitalization for treatment, or dying from the virus (Table 3).

We found significant associations between vaccine hesitancy and perceived vaccine effectiveness. Vaccine-hesitant respondents did not believe that vaccines in general help prevent disease (30.43 vs 2.37, $P < 0.001$) and believed in general that vaccines were harmful (40.58 vs 18.71, $P < 0.001$), compared to non-vaccine-hesitant respondents. Vaccine-hesitant individuals were more likely to be unsure whether the COVID-19 vaccine prevented COVID-19 disease (51.47 vs 27.98, $P < 0.001$), compared to those who were not vaccine hesitant.

Vaccine-hesitant respondents believed they did not have enough information to decide on the COVID-19 vaccine (53.85% vs 7.10%, $P < 0.001$) and preferred to receive COVID-19 vaccine information by doing their own research (24.66% vs 5.20%, $P < 0.001$) or waiting to see how others reacted after being vaccinated (23.29% vs 4.62%, $P < 0.001$) (Table 3). Vaccine-hesitant respondents were more unsure whether healthcare clinicians had their best interests in mind when recommending the COVID-19 vaccine (39.39% vs 7.06%, $P < 0.001$), compared to vaccine-acceptant individuals. There was no significant difference in other forms of receiving COVID-19 vaccine information (Table 3).

Vaccine-hesitant individuals were less likely to wear masks in public (84.93% vs 93.64%, $P < 0.029$) and to have gotten the flu vaccine the previous year (36.23% vs 64.12%, $P < 0.001$), compared to vaccine-acceptant individuals (Table 4). Furthermore, vaccine-hesitant respondents were less likely to have discussed the COVID-19 vaccine with their primary care doctor (30.74% vs 73.43%, $P < 0.001$), compared to vaccine-acceptant individuals (Table 4).

We did not find associations between vaccine hesitancy and previous positive COVID-19 test, social distancing, or having a primary care doctor. There was also no statistically significant difference between vaccine-acceptant and vaccine-hesitant participants regarding medical insurance status and the number of people respondents interacted with mask-less (Table 4).

DISCUSSION

Currently, approximately 65% of the US population is fully vaccinated against COVID-19.[2] Although the national vaccination rate has improved, the local vaccination rate at the state level lags in certain areas. Louisiana has one of the lowest vaccination rates (53%) in the country and one of the highest mortality rates secondary to COVID-19.[35] The vaccine gap threatens to unnecessarily prolong the COVID-19 pandemic. This study demonstrates an association between vaccine hesitancy and multiple demographic factors, health attitudes, opinions, and behaviors.

The majority of our respondents self-identified as Black and female and had an average age of 46. (Table 2). Prior research shows a connection between Black race, female gender identity, and vaccine hesitancy.[36–38] The lack of race and gender association seen in this investigation could be due to the small census numbers across multiple ethnicities. Larger studies using electronically distributed surveys show differences based on ethnicity and race.[39] We halted our study prematurely due to the higher risk of exposure during the Sars-CoV-2 delta-variant surge. Further subgroup analysis was considered; however, smaller sample sizes make results less generalizable. Moreover, the intersectionality of gender and race was not investigated in this study. Previous research shows higher vaccine hesitancy in respondents who identify as both Black and female compared to others.[39] Larger surveys in the future could evaluate subgroup associations with vaccine hesitancy in men and women of different ethnicities and races.

The observations in this research are consistent with prior studies finding that vaccine-hesitant individuals were younger than the vaccine acceptant (Table 2). The difference in overall mortality and morbidity of COVID-19 seen across ages may explain this discrepancy. Older patients have worse outcomes, higher risk of hospitalization, and higher risk of death compared to younger patients.[40,41] Potentially, younger individuals believe they are at lower risk for worse outcomes and, therefore, do not see a need for vaccination. Even though younger individuals have a lower risk of severe disease, the risk is not zero. Additionally, younger patients can still serve as asymptomatic carriers and infect susceptible friends and family. A message tailored to younger populations focusing on the hazards of transmitting the virus

Table 3. Perspective/opinion questions and responses.

Variable	Total sample N (%)	Vaccine accepting n (%)	Vaccine hesitant n (%)	*P*-value
When available to you, how difficult do you think it will be to get access to the COVID-19 vaccine?				<**0.001**
Very/somewhat difficult	5 (2.1)	2 (1.2)	3 (4.2)	
Neutral	8 (3.4)	4 (2.4)	4 (5.6)	
Easy/Very easy	71 (30.0)	35 (21.2)	36 (50)	
Unsure	35 (14.8)	6 (3.6)	29 (40.3)	
I have already received the COVID-19 vaccine	118 (49.8)	118 (71.5)	0 (0)	
What do you think are your chances of being infected by the COVID-19 virus?				**0.01**
Low	186 (77.2)	138 (82.1)	47 (65.3)	
Medium	43 (17.8)	22 (13.1)	21 (29.2)	
High	12 (5.0)	8 (4.8)	4 (5.6)	
What do you think are your chances of needing to be hospitalized for treatment for COVID-19?				0.1
Low	212 (88.0)	152 (90.5)	59 (81.9)	
Medium	20 (8.30)	12 (7.1)	8 (11.1)	
High	9 (3.7)	4 (2.4)	5 (6.9)	
What do you think are your chances of dying from COVID-19 virus				0.2
Low	217 (92.0)	157 (94.0)	60 (87.0)	
Medium	10 (4.2)	6 (3.6)	4 (5.8)	
High	9 (3.8)	4 (2.4)	5 (7.3)	
What is your best guess as to whether you will get the coronavirus within the next 6 months?				1.0
I don't think I will get the coronavirus.	196 (83.1)	138 (82.6)	58 (84.1)	
I think I will get a mild case of the coronavirus.	17 (7.2)	12 (7.2)	5 (7.3)	
I think I will get seriously ill from the coronavirus.	17 (7.2)	13 (7.8)	4 (5.8)	
I already had the coronavirus, and I don't think I will get it again.	6 (2.5)	4 (2.4)	2 (2.9)	
Which best describes your overall state of health?				**0.02**
Great health	41 (17.3)	21 (12.6)	20 (28.6)	
Good health	88 (37.1)	63 (37.7)	25 (35.7)	
Average health	86 (36.3)	65 (38.9)	21 (30)	
Poor health	22 (9.3)	18 (10.8)	4 (5.7)	
Do you believe vaccines, in general, help prevent disease?				<**0.001**
Yes	168 (70.6)	147 (87.0)	21 (30.4)	
No	25 (10.5)	4 (2.4)	21 (30.4)	
Unsure	45 (18.9)	18 (10.7)	27 (39.1)	
Do you believe vaccines, in general, are harmful?				<**0.001**
Yes	28 (11.6)	14 (8.2)	13 (18.8)	
No	153 (63.5)	125 (73.1)	28 (40.6)	
Unsure	60 (24.9)	32 (18.7)	28 (40.6)	
Do you believe the COVID-19 vaccine can prevent COVID-19 disease?				<**0.001**
Yes	121 (51.1)	115 (68.5)	5 (7.4)	
No	34 (14.4)	6 (3.6)	28 (41.2)	
Unsure	82 (34.6)	47 (28.0)	35 (51.5)	
Do you think you have enough information to make a decision on the COVID-19 vaccine?				<**0.001**
Yes	187 (79.9)	157 (92.9)	30 (46.2)	
No	47 (20.1)	12 (7.1)	35 (53.9)	

(*Continued on next page*)

Table 3. Continued.

Variable	Total sample N (%)	Vaccine accepting n (%)	Vaccine hesitant n (%)	*P*-value
Preferred method of receiving COVID-19 vaccine information				
Discussion with healthcare practitioner	84 (34.0)	59 (34.1)	24 (32.9)	0.9
Pamphlets, flyers, articles	16 (6.5)	12 (6.9)	4 (5.5)	0.7
Videos	14 (5.7)	9 (5.2)	5 (6.9)	0.6
Own research	27 (10.9)	9 (5.2)	18 (24.7)	**<0.001**
Waiting to see how others do after being vaccinated	25 (10.1)	8 (4.6)	17 (23.3)	**<0.001**
Discussion with people who are vaccinated	31 (12.6)	20 (11.6)	11 (15.1)	0.5
Other	14 (5.7)	13 (7.5)	1 (1.4)	0.1
Unsure	13 (5.3)	4 (2.3)	9 (12.3)	**0.001**
Do you trust that healthcare practitioners have your best interest in mind when recommending the COVID-19 vaccine?				**<0.001**
Yes	185 (78.4)	154 (90.6)	31 (47.0)	
No	13 (5.5)	4 (2.4)	9 (13.6)	
Unsure	38 (16.1)	12 (7.1)	26 (39.4)	

COVID-19, coronavirus 2019.

to higher risk friends and family should be a public health goal.

The research on vaccine hesitancy and marital status is unclear. This study documents an association between vaccine hesitancy and respondents who were never married (Table 2). Prior studies show an association between being in a relationship and vaccine hesitancy.[42] Conflicting research has shown that married couples were more likely to accept the vaccine.[36,43] Married people engage in healthier daily behaviors and live longer lives compared to unmarried.[44,45] It is possible that having a significant other provides a healthier support network and pressure to retain healthier behaviors. This could also be explained by nepotism; however, our study did not demonstrate an association with vaccine acceptance and having children (Table 2). This is puzzling as one would think having children to care for would convince respondents to get the vaccine either for one's own well-being or to reduce the risk of transmitting the virus to family members. Conceivably the low morbidity and mortality in the pediatric population had study participants less concerned about transmitting the virus to younger children.[46,47]

Similar to prior studies, lower household income and education levels were associated with vaccine hesitancy. Multiple socioeconomic factors may influence overall health literacy.[36,42,48] Lower levels of education may result in a decreased chance of learning and developing skills necessary to critically appraise health information.[20,36–38,42,46,47] Both lower education levels and lower income can lead to fewer opportunities to understand health information and less access to health care.[49,50] Additionally, lower education levels may cause individuals to be more easily swayed by misinformation.[51] The ED often offers the most timely access to the healthcare system for vulnerable populations in lower socioeconomic classes.[52,53] The ED is a prime location to intervene and offer educational materials and teachings about the COVID-19 vaccine.

Political affiliation is strongly correlated with vaccine acceptance.[54] People who identify as Democrat are more likely to be vaccine acceptant while Republicans are more likely to be vaccine hesitant. This study found Democrats to be vaccine acceptant but lacked the hesitant association with Republicans. A portion of respondents preferred not to answer, which could have affected outcomes. Additionally, respondents may have been apprehensive about sharing their political affiliation given the current, divisive political climate or they feared it could have affected the quality of their care.

Individual attitudes, beliefs, and perceptions are the most influential predictors of vaccine acceptance.[55] Our study expands on the 2021 work of Fernandez-Penny et al, which delved into vaccine hesitancy as it relates to attitudes/perceptions of the COVID-19 virus and disease and trust in the medical system. Vaccine-hesitant individuals in this survey felt they were in better health compared to vaccine-acceptant individuals, which falls in line with previous studies.[56] Presumably if respondents believed they were in good or great health, they did not consider themselves to be at risk of being hospitalized or dying from COVID-19 disease and, therefore, did not wish to have the vaccine.

Equitable vaccine access is one of the cornerstones of proper vaccine distribution. Hospitals throughout the nation have formed health equity committees to ensure equitable allocation. Despite the number of vaccine distribution centers in SE Louisiana, respondents to this survey were

Table 4. Health behavior questions and responses.

Variable	Total sample N (%)	Vaccine accepting n (%)	Vaccine hesitant n (%)	*P*-value
Have you had a positive test for COVID-19?				0.2
Yes	43 (17.7)	35 (20.5)	8 (11.1)	
No	183 (75.3)	124 (72.5)	59 (81.9)	
I have never been tested for COVID-19	17 (7.0)	12 (7.0)	5 (6.9)	
Do you generally wear masks in public and around other people?				**0.03**
Yes	224 (91.1)	162 (93.6)	62 (84.9)	
No	22 (8.9)	11 (6.4)	11 (15.1)	
How many people do you interact with, mask-less and without social distancing, in a typical week?				0.1
0	35 (14.3)	26 (15.3)	8 (11.0)	
Between 1 to 5	123 (50.4)	85 (50)	38 (52.1)	
Between 6 to 10	48 (19.7)	37 (21.8)	11 (15.1)	
Between 11 to 20	11 (4.5)	5 (2.9)	6 (8.2)	
Between 21 to 30	6 (2.5)	2 (1.2)	4 (5.5)	
30 or more	21 (8.6)	15 (8.8)	6 (8.2)	
In the past week, how often did you practice social distancing, that is, you maintained a distance of at least 6 feet between you and other people?				0.7
Never	16 (6.5)	9 (5.3)	6 (8.2)	
Some of the time	50 (20.4)	33 (19.3)	17 (23.3)	
Most of the time	87 (35.5)	62 (36.3)	25 (34.3)	
All the time	92 (37.6)	67 (39.2)	25 (34.3)	
Do you have medical insurance?				0.3
Yes	211 (89.8)	153 (91.1)	58 (86.6)	
No	21 (8.9)	14 (8.3)	7 (10.5)	
Unsure	3 (1.3)	1 (0.6)	2 (3.0)	
Did you get the flu vaccine last year?				<**0.001**
Yes	134 (55.8)	109 (64.1)	25 (36.2)	
No	105 (43.8)	61 (35.9)	43 (62.3)	
Unsure	1 (0.4)	0 (0)	1 (1.5)	
Do you have a primary care doctor?				0.4
Yes	201 (84.5)	145 (86.3)	55 (79.7)	
No	31 (13.0)	20 (11.9)	11 (15.9)	
Unsure	6 (2.5)	3 (1.8)	3 (4.4)	
If yes, have you discussed the COVID-19 vaccine with your primary care doctor?				<**0.001**
Yes	125 (63.8)	105 (73.4)	20 (30.7)	
No	71 (36.2)	38 (26.6)	33 (62.3)	

COVID-19, coronavirus 2019.

unsure of their ability to access the vaccine. One potential reason is that vaccine distribution centers were not set up in the areas of greatest need. Access can be stifled by geographic barriers. Low socioeconomic areas have been overlooked while organizing vaccine distribution centers around the country.[57] A second reason behind perceived poor access could be a lack of advertisement of existing distribution centers in these areas. To meet the needs of the community, planned access and equitable distribution of vaccine centers should be organized with community engagement in mind.

One of the most prevalent reasons for vaccine hesitancy is the perceived overall safety of the vaccine.[34,38,42] Respondents were unsure whether vaccines in general were harmful. Many believe that the COVID-19 vaccine was

developed too quickly, bypassing safety protocols for economic incentives.[34] Although the COVID-19 vaccine is novel, the technological and scientific basis of the vaccine has been well studied.[58] Strategies for public education regarding vaccine safety should consider communication surrounding unprecedented global partnership and rigorous testing before and during vaccine rollout.

This investigation was performed during the advent of the SARS-CoV-2 delta variant. Despite the increased transmissibility of the delta variant, most respondents believed they had a low chance of contracting the SARS-CoV-2 virus.[59] Vaccine-hesitant individuals believed they had a higher chance of contracting the virus compared to the vaccine acceptant. One explanation behind this discrepancy is that the vaccine-acceptant group may contain individuals who have already gotten the vaccine. These same individuals believe in the protective effects of the vaccine and perceive a lower chance of contracting the virus. Also, despite a perceived higher risk of contracting the virus, most vaccine-hesitant respondents did not believe that vaccines prevented disease. These results are in line with prior vaccine-hesitancy literature.[37,38,59,60] Public health interventions may need to focus on the clearly established benefit vs very low risk of vaccination, while also highlighting the effectiveness of COVID-19 vaccines in preventing hospitalization and death.[61]

The survey findings show respondents who were vaccine hesitant would like to do more of their own research or wait until others have had the vaccine before getting it themselves (Table 3). COVID-19 vaccine information has been distributed in multiple formats. Public health advocates should focus on continuously disseminating information on the vaccine in different formats to encourage vaccine uptake. Social media, for example, is an important avenue to encourage positive health behaviors.[62] Hospitals could partner with organizations that cater to at-risk and socially vulnerable populations to form creative educational resources.

This is the first ED-based, in-person survey study to measure vaccine hesitancy as a dependent factor of medical mistrust. Respondents who were vaccine hesitant did not believe that health practitioners had their best interest in mind when recommending the vaccine (Table 3). Multiple media outlets falsely reported that clinicians were taking monetary incentives for inappropriately diagnosing COVID-19 infections and for distributing the vaccine.[63,64] Medical mistrust, in certain populations, is based on years of mistreatment by the medical community. Healthcare professionals should be given the tools to suspend judgment regarding the vaccine hesitant and understand the historical, political, and social context that has disproportionally disparaged vulnerable populations. Public health officials may need to rethink ideas of encouraging vaccine acceptance by investing in ways to build trust within the medical community.[65] Emergency physicians can promote changes in health behaviors and should use their limited time to engage in a patient-centered discussion on the utility of vaccines.[66]

This study adds to the current research on vaccine hesitancy in the ED setting. The ED is a unique context as it serves vulnerable populations. The COVID-19 pandemic has preferentially affected racial minorities and people in a lower socioeconomic class. Prior research shows these same populations are less likely to accept the vaccine. Our investigation can help elucidate target populations to deliver health messages. A televised public health intervention using health practitioners could grow more vaccine acceptance over time. In the ED, vaccination discussions during ED visits give health access to lower socioeconomic classes and provides an opportunity to speak with a clinician. Continuing an ED-based vaccination effort could increase the proportion of vaccinated vulnerable peoples.

Future directions could expand on our research by using longitudinal survey and logistical regression models. Previous studies support the transtheoretical model of change: behavioral change does not occur at one point but at various stages in a cycle.[67] Vaccine hesitancy is a labile trait and can change overtime.[68] Longitudinal studies can discover changing opinions over time with each variant surge and the need for further booster shots. Additionally, discovering the strength of association with vaccine hesitancy and changing opinions can help tailor public health interventions. Future survey studies can also focus on a more diverse group of respondents. Occupations that place individuals at higher risk of COVID-19 disease are often performed by economically and socially disadvantaged populations.[20] Prior investigations highlight that these same individuals are more vaccine hesitant. Workers in the healthcare sector can organize interventions that speak to these communities to obtain novel perspectives.

LIMITATIONS

The present study is not without limitations. The survey was conducted in person with patients in the ED. Social desirability bias may have influenced our study as it took place in a healthcare facility, around health practitioners, during a time when the vaccine became more widely available. Respondents may have wanted to be falsely agreeable to vaccine acceptance while they were in a healthcare setting. This research focused on vaccination hesitancy solely in the adult population. The pediatric vaccination rate is lower than the adult rate in some age groups in Louisiana.[69] The reasons surrounding pediatric vaccination hesitancy may not coincide with that of the adult population. This study was also limited to the answer choices we provided in the survey, which did not give space for novel perspectives, attitudes, and opinions from our respondents. A qualitative or a mixed-methods approach could reveal new

factors associated with vaccine hesitancy that have not yet been published.

Geographic context is associated with vaccine hesitancy. Our study took place at three different sites. Few respondents were taken from ED #3, a location at a considerable distance from a major city that was noted to have lower vaccination rates.[69] This may have influenced the results of the survey as each hospital was not represented proportionately.

CONCLUSION

This study demonstrates that, despite the finding that vaccine-hesitant patients perceive a higher risk of contracting COVID-19, they feel more uncertain about the safety of the COVID-19 vaccine, the feasibility of obtaining the vaccine, and its efficacy. Many vaccine-hesitant patients felt as though they did not have enough information to make the decision to accept or decline the COVID-19 vaccine, while at the same time many preferred to do their own research and were unsure how much trust to place in their physicians. Further studies should focus on what platforms could be used and trusted by this patient population to provide scientifically sound education to the vaccine-hesitant population.

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REFERENCES

1. World Health Organization. WHO Coronavirus (COVID-19) Dashboard. Available at: https://covid19.who.int/. Accessed April 2, 2022.
2. Centers for Disease Control and Prevention, U.S. Department of Health and Human Services. COVID Data Tracker. Available at: https://covid.cdc.gov/covid-data-tracker/#vaccinations_vacc-total-admin-rate-total. Accessed April 5, 2022.
3. Mayo Foundation for Medical Education and Research. U.S. coronavirus map: What do the trends mean for you? Available at: https://www.mayoclinic.org/coronavirus-covid-19/map. Accessed September 6, 2021.
4. Dubé E, Vivion M, MacDonald NE. Vaccine hesitancy, vaccine refusal and the anti-vaccine movement: influence, impact and implications. *Expert Rev Vaccines* 2015;14(1):99–117.
5. Neergaard L, Fingerhut H. AP-NORC poll: Half of Americans would get a COVID-19 vaccine. *AP News* 2020. Available at: https://apnews.com/dacdc8bc428dd4df6511bfa259cfec44. Accessed August 22, 2021.
6. Bergwerk M, Gonen T, Lustig Y, et al. Covid-19 breakthrough infections in vaccinated health care workers. *N Engl J Med* 2021;385(16):1474–84.
7. Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med* 2021;384(5):403–16.
8. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 2020;383(27):2603–15.
9. Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet* 2021;397(10269):99–111.
10. Shah A, Marks PW, Hahn SM. Unwavering regulatory safeguards for COVID-19 vaccines. *JAMA* 2020;324(10):931–932.
11. Solís Arce JS, Warren SS, Meriggi NF, et al. COVID-19 vaccine acceptance and hesitancy in low- and middle-income countries. *Nat Med* 202;27(8):1385–94.
12. Ball P, Maxmen A. The epic battle against coronavirus misinformation and conspiracy theories. *Nature* 2020;581(7809):371–4.
13. Islam MS, Sarkar T, Khan SH, et al. COVID-19-related infodemic and its impact on public health: a global social media analysis. *Am J Trop Med Hyg* 2020;103(4):1621–9.
14. Guidry JPD, Laestadius LI, Vraga EK, et al. Willingness to get the COVID-19 vaccine with and without emergency use authorization. *Am J Infect Control* 2021;49(2):137–42.
15. Kelly BJ, Southwell BG, McCormack LA, et al. Predictors of willingness to get a COVID-19 vaccine in the U.S. *BMC Infect Dis* 2021;21(1):338.
16. Khubchandani J, Sharma S, Price JH, et al. COVID-19 vaccination hesitancy in the United States: a rapid national assessment. *J Community Health* 2021;46(2):270–7.
17. Ruiz JB, Bell RA. Predictors of intention to vaccinate against COVID-19: results of a nationwide survey. *Vaccine* 2021;39(7):1080–6.
18. Lakhani HV, Pillai SS, Zehra M, et al. Systematic review of clinical insights into novel coronavirus (CoVID-19) pandemic: persisting challenges in U.S. rural population. *Int J Environ Res Public Health* 2020;17(12):4279.
19. McLaughlin JM, Khan F, Pugh S, et al. County-level predictors of coronavirus disease 2019 (COVID-19) cases and deaths in the United States: What happened, and where do we go from here? *Clin Infect Dis* 2021;73(7):e1814–21.
20. Price-Haywood EG, Burton J, Fort D, et al. Hospitalization and mortality among Black patients and White patients with Covid-19. *N Engl J Med* 2020;382(26):2534–43.
21. Tai DBG, Shah A, Doubeni CA, et al. The disproportionate impact of COVID-19 on racial and ethnic minorities in the United States. *Clin Infect Dis* 2021;72(4):703–6.

22. McEachan RRC, Conner M, Taylor NJ, et al. Prospective prediction of health-related behaviours with the theory of planned behaviour: a meta-analysis. *Health Psychology Review* 2011;5(2):97–144.
23. Beleche T, Ruhter J, Kolbe A, et al. COVID-19 Vaccine Hesitancy: Demographic Factors, Geographic Patterns, and Changes Over Time. Washington, DC: Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services, May 2021. Available at: https://aspe.hhs.gov/sites/default/files/private/pdf/265341/aspe-ib-vaccine-hesitancy.pdf. Accessed August 20, 2021.
24. Johns Hopkins Coronavirus Resource Center, Johns Hopkins University & Medicine. Understanding vaccination progress. Available at: https://coronavirus.jhu.edu/vaccines/international. Accessed April 5, 2022.
25. Anderson ES, Lippert S, Newberry J, et al. Addressing social determinants of health from the emergency department through social emergency medicine. *West J Emerg Med* 2016;17(4):487–9.
26. Burt CW, Arispe IE. Characteristics of emergency departments serving high volumes of safety-net patients: United States, 2000. *Vital Health Stat 13* 2004(155):1–16.
27. Davis CI, Montgomery AE, Dichter ME, et al. Social determinants and emergency department utilization: findings from the Veterans Health Administration. *Am J Emerg Med* 2020;38(9):1904–9.
28. Burger AE, Reither EN, Mamelund SE, et al. Black-White disparities in 2009 H1N1 vaccination among adults in the United States: a cautionary tale for the COVID-19 pandemic. *Vaccine* 2021;39(6):943–51.
29. Gatwood J, McKnight M, Frederick K, et al. Extent of and reasons for vaccine hesitancy in adults at high-risk for pneumococcal disease. *Am J Health Promot* 2021;35(7):908–16.
30. Gilbert RM, Mersky JP, Lee CP. Prevalence and correlates of vaccine attitudes and behaviors in a cohort of low-income mothers. *Prev Med Rep* 2021;21:101292.
31. Sharma A, Minh Duc NT, Luu Lam Thang T, et al. A Consensus-Based Checklist for Reporting of Survey Studies (CROSS). *J Gen Intern Med* 2021;36(10):3179–87.
32. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009;42(2):377–81.
33. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: building an international community of software platform partners. *J Biomed Inform* 2019;95:103208.
34. Momplaisir FM, Kuter BJ, Ghadimi F, et al. Racial/ethnic differences in COVID-19 vaccine hesitancy among health care workers in 2 large academic hospitals. *JAMA Netw Open* 2021;4(8):e2121931.
35. Johns Hopkins Coronavirus Resource Center, Johns Hopkins University & Medicine. All state comparison of testing efforts. Available at: https://coronavirus.jhu.edu/testing/states-comparison. Accessed January 24, 2022.
36. Kricorian K, Civen R, Equils O. COVID-19 vaccine hesitancy: misinformation and perceptions of vaccine safety. *Hum Vaccin Immunother* 2022;18(1):1950504.
37. Rodriguez RM, Torres JR, Chang AM, et al. The rapid evaluation of COVID-19 vaccination in emergency departments for underserved patients study. *Ann Emerg Med* 2021;78(4):502–10.
38. Fernández-Penny FE, Jolkovsky EL, Shofer FS, et al. COVID-19 vaccine hesitancy among patients in two urban emergency departments. *Acad Emerg Med* 2021;28(10):1100–7.
39. Willis DE, Andersen JA, Bryant-Moore K, et al. COVID-19 vaccine hesitancy: race/ethnicity, trust, and fear. *Clin Transl Sci* 2021;14(6):2200–7.
40. Biswas M, Rahaman S, Biswas TK, et al. Association of sex, age, and comorbidities with mortality in COVID-19 patients: a systematic review and meta-analysis. *Intervirology* 2021;64(1):36–47.
41. Boehmer TK, DeVies J, Caruso E, et al. Changing age distribution of the COVID-19 pandemic - United States, May-August 2020. *MMWR Morb Mortal Wkly Rep* 2020;69(39):1404–9.
42. Freeman D, Loe BS, Chadwick A, et al. COVID-19 vaccine hesitancy in the UK: the Oxford coronavirus explanations, attitudes, and narratives survey (Oceans) II. *Psychol Med* 2020:1–15.
43. Badr H, Zhang X, Oluyomi A, et al. Overcoming COVID-19 vaccine hesitancy: insights from an online population-based survey in the United States. *Vaccines (Basel)* 2021;9(10):1100.
44. Lillard LA, Panis CW. Marital status and mortality: the role of health. *Demography* 1996;33(3):313–27.
45. Valkonen T, Martikainen P, Blomgren J. Increasing excess mortality among non-married elderly people in developed countries. *Demographic Research* 2004;2(12):305–30.
46. Alsohime F, Temsah MH, Al-Nemri AM, et al. COVID-19 infection prevalence in pediatric population: Etiology, clinical presentation, and outcome. *J Infect Public Health* 2020;13(12):1791–6.
47. Delahoy MJ, Ujamaa D, Whitaker M, et al. Hospitalizations associated with COVID-19 among children and adolescents - COVID-NET, 14 States, March 1, 2020-August 14, 2021. *MMWR Morb Mortal Wkly Rep* 2021;70(36):1255–60.
48. Fisher KA, Bloomstone SJ, Walder J, et al. Attitudes toward a potential SARS-CoV-2 vaccine: a survey of U.S. adults. *Ann Intern Med* 2020;173(12):964–73.
49. Jacobson HE, Hund L, Mas FS. Predictors of English health literacy among U.S. Hispanic immigrants: the importance of language, bilingualism and sociolinguistic environment. *Lit Numeracy Stud* 2016;24(1):43–64.
50. Castro-Sánchez E, Chang PWS, Vila-Candel R, et al. Health literacy and infectious diseases: Why does it matter? *Int J Infect Dis* 2016;43:103–10.
51. Aw J, Seng JJB, Seah SSY, et al. COVID-19 vaccine hesitancy: a scoping review of literature in high-income countries. *Vaccines (Basel)* 2021;9(8):900.
52. Rust G, Ye J, Baltrus P, et al. Practical barriers to timely primary care access: impact on adult use of emergency department services. *Arch Intern Med* 2008;168(15):1705–10.
53. Sarver JH, Cydulka RK, Baker DW. Usual source of care and nonurgent emergency department use. *Acad Emerg Med* 2002;9(9):916–23.

54. Fridman A., Gershon R., Gneezy A. COVID-19 and vaccine hesitancy: a longitudinal study. *PloS one.* 2021;16(4),e0250123.
55. Castner J. Infection control and vaccine hesitancy in the emergency department. *J Emerg Nurs* 2020;46(6):731–8.
56. Soares P, Rocha JV, Moniz M, et al. Factors associated with COVID-19 vaccine hesitancy. *Vaccines (Basel)* 2021;9(3):300.
57. Hardeman A, Wong T, Denson JL, et al. Evaluation of health equity in COVID-19 vaccine distribution plans in the United States. *JAMA Netw Open* 2021;4(7):e2115653.
58. Dolgin E. The tangled history of mRNA vaccines. *Nature* 2021;597(7876):318–24.
59. Centers for Disease Control and Prevention, U.S. Department of Health and Human Services. What you need to know about variants. Available at: https://www.cdc.gov/coronavirus/2019-ncov/variants/delta-variant.html. Accessed November 3, 2021.
60. Hussain A, Ali S, Ahmed M, et al. The anti-vaccination movement: a regression in modern medicine. *Cureus* 2018;10(7):e2919.
61. Lin DY, Gu Y, Wheeler B, et al. Effectiveness of Covid-19 vaccines over a 9-month period in North Carolina. *N Engl J Med* 2022;386(10):933–41.
62. Goodyear VA, Armour KM, Wood H. Young people and their engagement with health-related social media: new perspectives. *Sport Educ Soc* 2018;24(7):673–88.
63. Pollack R. AHA continues to debunk false claims about COVID-19 deaths and payments. American Hospital Association 2020. Available at: https://www.aha.org/news/blog/2020-11-02-aha-continues-debunk-false-claims-about-covid-19-deaths-and-payments. Accessed November 3, 2021.
64. Staff Reuters. Fact check: payments for delivery of COVID-19 vaccines are to ensure general practices can afford to offer the service. Reuters 2020. Available at: https://www.reuters.com/article/uk-factcheck-gp-vaccines-idUSKBN28D39G. Accessed November 3, 2021.
65. Quinn SC, Andrasik MP. Addressing vaccine hesitancy in BIPOC communities - toward trustworthiness, partnership, and reciprocity. *N Engl J Med* 2021;385(2):97.
66. Rollnick S, Butler CC, Kinnersley P, et al. Motivational interviewing. *BMJ* 2010;340:c1900.
67. Prochaska JO, Norcross JC. Stages of change. *Psychother Theor Res Pract Train* 2001;38(4):443–8.
68. Siegler AJ, Luisi N, Hall EW, et al. Trajectory of COVID-19 vaccine hesitancy over time and association of initial vaccine hesitancy with subsequent vaccination. *JAMA Netw Open* 2021;4(9):e2126882.
69. Louisiana Department of Health. COVID-19 information. Available at: https://ldh.la.gov/Coronavirus. Accessed November 3, 2021.

Large-scale Implementation of a COVID-19 Remote Patient Monitoring Program

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Introduction: We implemented a large-scale remote patient monitoring (RPM) program for patients diagnosed with coronavirus 2019 (COVID-19) at a not-for-profit regional healthcare system. In this retrospective observational study, patients from nine emergency department (ED) sites were provided a pulse oximeter and enrolled onto a monitoring platform upon discharge.

Methods: The RPM team captured oxygen saturation (SpO_2), heart rate, temperature, and symptom progression data over a 16-day monitoring period, and the team engaged patients via video call, phone call, and chat within the platform. Abnormal vital signs were flagged by the RPM team, with escalation to in-person care and return to ED as appropriate. Our primary outcome was to describe study characteristics: patients enrolled in the COVID-19 RPM program; engagement metrics; and physiologic and symptomatic data trends. Our secondary outcomes were return-to-ED rate and subsequent readmission rate.

Results: Between December 2020–August 2021, a total of 3,457 patients were referred, and 1,779 successfully transmitted at least one point of data. Patients on COVID-19 RPM were associated with a lower 30-day return-to-ED rate (6.2%) than those not on RPM (14.9%), with capture of higher acuity patients (47.7% of RPM 30-day returnees were subsequently hospitalized vs 34.8% of non-RPM returnees).

Conclusion: Our program, one of the largest studies to date that captures both physiologic and symptomatic data, may inform others who look to implement a program of similar scope. We also share lessons learned regarding barriers and disparities in enrollment and discuss implications for RPM in other acute disease states. [West J Emerg Med. 2023;24(6)1085–1093.]

INTRODUCTION

Coronavirus 2019 (COVID-19) created an urgent need for rapid adoption of telehealth. Hospital systems, faced with unprecedented demand on limited resources, needed a means to maximize inpatient capacity while minimizing infectious spread, and to redistribute care safely from the hospital to the community setting. Remote patient monitoring (RPM) offered one potential solution. Remote patient monitoring is the use of digital medical devices to collect and electronically transmit patient data from a remote site to drive care management.[1] Frequently used devices include pulse oximeters, blood pressure cuffs, glucometers, and weight scales.[1]

Historically, RPM has been used to manage chronic diseases such as diabetes, hypertension, and chronic obstructive pulmonary disease,[2] with demonstrated decrease

in return-to-ED and hospital readmission rates.[3–5] Due to its versatility, RPM emerged as a promising tool for COVID-19 management. It allows for timely detection of disease progression (as denoted by hypoxemia or tachycardia) and provides a venue for patients to report worsening symptoms. All together, these data points help clinicians identify when return to acute care is necessary.

Currently, little is known about the use of RPM in acute disease states for large populations. Baseline care inequity due to health disparities such as insurance status, English-speaking proficiency, and technologic fluency may be exacerbated in RPM. This study contributes knowledge on logistics for deploying a program that incorporates two often marginalized patient populations in RPM: patients with limited English proficiency, and those without smartphones. Furthermore, we share information regarding enrollment process, device supply and management, and staffing for a large-scale program deployed across a multiregional patient population. Our primary purpose in this retrospective observational study was to describe the methodology of deploying a COVID-19 RPM program at a multiregional hospital system and quantify its patient and program characteristics. We also share the return-to-ED rate and disposition of patients who return to acute care following COVID-19 RPM.

Population Health Research Capsule

What do we already know about this issue?
Remote patient monitoring (RPM) is a versatile tool for management of patients with chronic disease states (eg, hypertension).

What was the research question?
Is a large-scale implementation of RPM feasible for patients with COVID-19? What are the associated barriers?

What was the major finding of the study?
With 3,457 patients enrolled in the COVID-19 RPM program, RPM was associated with a lower 30-day return-to-ED rate (6.2% vs 14.9% for controls).

How does this improve population health?
Remote patient monitoring is a lightweight and scalable tool to manage care for large populations with acute diseases states such as COVID-19.

METHODS

Study Design and Patient Selection

This study was approved by the hospital system's institutional review board. The two vendors used in this study entered into a master security agreement with the institution, and both entered a business associate agreement to maintain private health information and ensure Health Insurance Portability and Accountability Act of 1996 compliance. This was a retrospective, qualitative study conducted at a not-for-profit healthcare system with nine acute care hospitals in the Mid-Atlantic Region, including tertiary-care, urban academic hospitals and rural community hospitals, with a combined annual ED volume of 430,000 visits. Any ED patient who was diagnosed with COVID-19 between December 2020–August 2021 was considered for monitoring. Qualifying patients were identified by their treating physician, physician assistant, or nurse. Patients were offered enrollment 24 hours a day, and the enrollment population consisted of patients residing in both metropolitan and rural geographies. Clinicians were instructed to be insurance agnostic; all patients were eligible regardless of insurer or insurance status.

Criteria for inclusion in the RPM program were as follows:

- Patient in the ED had new diagnosis of COVID-19 within the prior seven days
- Disposition from ED visit was characterized as "discharge to home"
- Patient consented to monitoring (or parent/legal guardian consented if the patient was <18 years old)
- Patient had reliable access to a mobile phone or land line (did not need to be the patient's own phone; could belong to family member or friend)
- Patient interested in program enrollment
- Clinician discretion (They were encouraged but not required to enroll all eligible patients)

Criterion for exclusion:

- Patient not interested in, or not consenting to, monitoring

Two forms of consent were obtained: verbal consent (clinician discussed the program with the patient and determined patient interest) and written consent (embedded within the RPM mobile app, prior to initialization). For patients <18 years old, the parent or legal guardian consented to and operated the app and transmitted data on behalf of their child. No patient under the age of 18 handled the device independently.

Patients received a kit containing a pulse oximeter and thermometer. Once a patient consented to monitoring, the clinician placed an order for "COVID Home Monitoring" in

the electronic health record (EHR), which assigned the patient an RPM enrollment ID number (matched to the ID number on the pulse oximeter). On the RPM platform, patient identifiers were removed, and patients were referred to by enrollment ID number only. If needed, the RPM clinician could reference a secure report of all patients who had received a "COVID Home Monitoring" order (generated within the EHR) to match a patient's enrollment ID number back to their medical record number.

Two RPM platforms were used for this program, which we will refer to as Platform 1 and Platform 2. The two platforms differed in design. Active monitoring on Platform 1 was introduced in December 2020; patients were asked to self-report oxygen saturation and symptomatology on the platform using the mobile app. Platform 2 was introduced in March 2021 to simplify the data collection process: its Bluetooth-integrated pulse oximeter automatically uploaded oxygen saturation and heart rate data to Platform 2 as soon as the pulse oximeter was applied to the patient's finger, eliminating the need for manual entry. Patients without smartphones were issued a traditional (non-Bluetooth) pulse oximeter and vital sign data was solicited and entered manually by the monitoring team. Patients who met inclusion criteria but did not enroll, or patients who enrolled but did not submit any data, were considered the non-RPM group.

The RPM team was comprised of nurse practitioners and medical assistants, with coverage seven days a week from 9 AM to 5 PM. Patients were monitored for a maximum of 16 days, with the option to disenroll at any time during that period. During that time, patients uploaded vital signs as frequently as desired. Any patients with ongoing COVID-19 symptoms after 16 days (but without vital sign abnormalities) were referred to our institution's COVID-19 Recovery Program. Participants kept the pulse oximeter after completion of the program.

Participation was insurance-agnostic and free of charge to the patient. A subset of patients identified a primary language other than English; for these, we used interpreter services during interactions. The default language on both RPM apps could be toggled to English or Spanish.

Interventions and Measurements

Oxygen saturation and heart rate data were collected each time the patient applied the pulse oximeter. With each check-in, patients also had the option of reporting temperature and symptoms. Alert parameters were embedded within the digital platform; the RPM team received an alert when a concerning symptom (ie, chest pain or dyspnea) or vital sign reading (ie, $SpO_2 < 94\%$ or heart rate >100) was submitted, and contacted the patient via video call, phone call, or in-app message. If appropriate, patients were referred back to the ED. We encountered several spurious SpO_2 readings due to poor contact between the pulse oximeter and the patient's finger; these values improved after adjustment of pulse oximeter placement with coaching from the RPM clinician.

Alerts received after hours triggered an automatic reply advising ED precautions. The RPM care team followed up with these patients the next day. Alerts were set for "missed vitals"—several days without data transmission—which prompted a call from the RPM team. Any technologic difficulties were addressed with troubleshooting via phone call from the RPM team. Throughout the monitoring period, patients could initiate communication with the RPM team at any time via the chat function or by calling the RPM support number.

Outcomes and Analysis

Our primary outcome was a descriptive analysis of patients enrolled in the COVID RPM program (including total number of patients, patient age, patient gender, racial distribution, their engagement (number of SpO_2 readings uploaded per patient, average SpO_2 reading, and number of days of engagement per patient). Our secondary outcomes were descriptions of 30-day returns to ED, number of days between discharge and return visit, ED diagnosis at return visit, and disposition from return visit for the RPM vs non-RPM group, using an as-treated analysis.

RESULTS

Population characteristics are noted in Table 1. The RPM group was comprised of younger patients (median age of 47 years vs 52 in non-RPM group) and a higher percentage of female patients (61.1% female vs 55.4% in the non-RPM group). There was a slight predominance of patients

Table 1. Study population characteristics.

	RPM	Non-RPM
Median age in years (IQR)	47 (23)	52 (32)
Female gender	61.1%	55.4%
Male gender	38.9%	44.6%
Racial distribution		
Black	64.4%	60.6%
White	21.0%	28.1%
Other	14.6%	11.3%
Insurance at emergency department visit		
Unknown	36%	4%
Medicaid	21%	35%
Managed care	25%	22%
Medicare	10%	24%
Self-pay	6%	10%
Commercial	1%	4%

RPM, remote patient monitoring; *IQR*, interquartile range.

Table 2. Remote patient monitoring enrollment following COVID-19 emergency department visits.

	Patient volume	% of Total
Total COVID+ ED visits 12/1/2020–8/31/2021	16,013 (14,127 unique patients)	
Discharged to home	8,357	52.2%
Enrolled on RPM	3,457	41.4%
Active on RPM[1]	1,779	51.4%
Non-RPM[2]	6,578	78.7%
Admission	5,749	35.9%
Observation	1,101	6.9%
Other (transfer, discharge to rehabilitation or skilled nursing facility, elopement, against medical advice, or deceased)	806	5.0%

[1]Reported at least one vital sign or symptom during the monitoring period.
[2]Met inclusion criteria but not enrolled or referred but not active.
COVID-19, coronavirus 2019; *ED*, emergency department; *RPM*, remote patient monitoring.

identifying as Black in the RPM group (64.4% vs 60.6% in the non-RPM group). Fewer RPM patients were enrolled in Medicaid (21% vs 35% in non-RPM group) and more enrolled in a managed care plan (25% vs 22% in the non-RPM group). Gender was extracted from the EHR, and there were no participants who identified as non-binary.

Overall, 52.2% of patients with a new diagnosis of COVID-19 were discharged home, of whom 41.4% were enrolled on RPM (Table 2). The remaining patients were predominantly placed in inpatient admission, followed by observation and transfer. Of those enrolled, 51.4% were active and engaged, reporting at least one vital sign or symptom during the monitoring period.

Further examination of the active patient population revealed differing engagement between platforms (Figure 1). The Bluetooth-enabled platform demonstrated a higher percentage of active patients (uploading at least one point of data) and longer duration of engagement (5 days vs 3.8 days). Patients using the non-Bluetooth-enabled platform uploaded more points of data on average. The percentage of patients with SpO_2 reading < 92% was similar on both platforms.

In the RPM group, we observed a lower rate of 30-day return to ED compared to the non-RPM group (Table 3). Mean number of days between discharge and return and mean number of return-to-ED episodes within 30 days were similar. Of 30-day returns to the ED, a higher percentage of patients in the RPM group required admission or observation at the second visit (47.7% vs 34.8%). Most 30-day returns were coded with diagnoses of sepsis, chest pain, urinary tract infection, and pulmonary embolism. The non-RPM group had a higher percentage of patients diagnosed with viral diseases complicating third trimester pregnancy.

RPM referrals peaked in December 2020 and January 2021 (Figure 2). In March 2021, we adopted a Bluetooth-enabled device (Figure 2, Platform 2) and phased out the

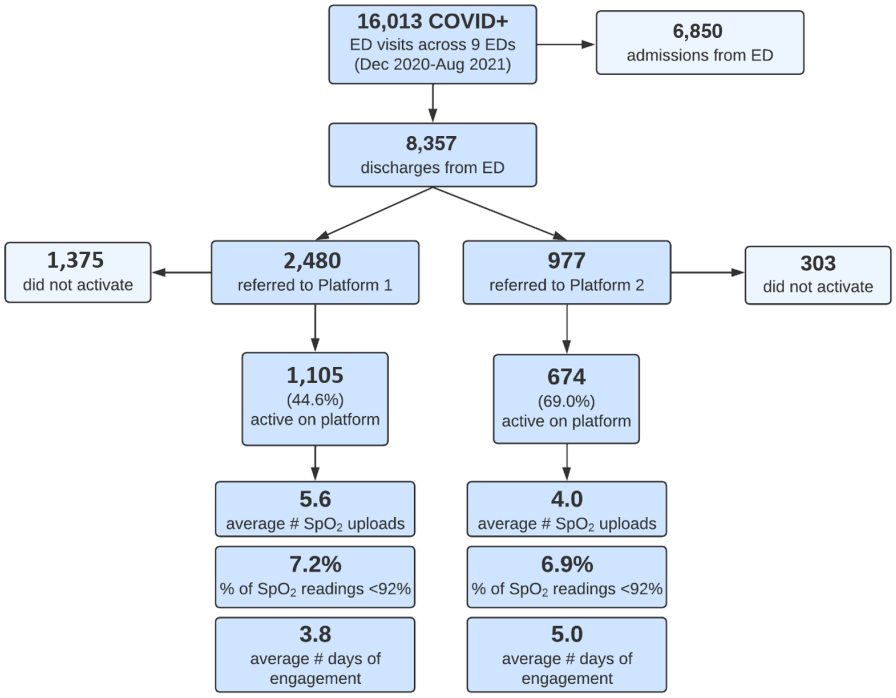

Figure 1. Study size and engagement by platform.
COVID-19, coronavirus 2019; *ED*, emergency department; *SpO_2*, oxygen saturation.

Table 3. 30-day returns for patients with COVID-19 diagnosis.

	RPM	Non-RPM
Patients with 30-day return to ED	111/1779 (6.2%)	980/6578 (14.9%)
Mean days between discharge and return	5.1 ± 4.4	5.2 ± 4.6
Mean return-to-ED episodes within 30-day period	1.0 ± 0.2	1.1 ± 0.4
Disposition of 30-day return-to-ED visit		
Discharge to home	55 (49.5%)	581 (59.3%)
Admission or observation	53 (47.7%)	341 (34.8%)
Other	3 (2.7%)	58 (5.9%)
Diagnosis for 30-day ED returns		
COVID-19	91	723
Other specified sepsis	9	43
Other viral diseases complicating pregnancy, third trimester	0	6
Other chest pain	2	5
Urinary tract infection, site not specified	0	5
Other pulmonary embolism without acute cor pulmonale	0	5
Contact with and (suspected) exposure to COVID-19	0	4
Bacteremia	0	3
Unspecified abdominal pain	0	3
Other viral diseases complicating pregnancy, first trimester	0	3
Anxiety disorder, unspecified	1	0
Other viral diseases complicating pregnancy, first trimester	1	0
Cerebral edema	1	0
Other fatigue	1	0
Type 2 diabetes mellitus with hyperglycemia	1	0
Single subsegmental pulmonary embolism without acute cor pulmonale	1	0
Hypertensive chronic kidney disease with stage 5 chronic kidney disease or end stage renal disease	1	0
Calculus of gallbladder and bile duct with acute cholecystitis without obstruction	1	0
Other	0	180

COVID-19, coronavirus 2019; *ED*, emergency department; *RPM*, remote patient monitoring.

non-Bluetooth device. Geographically, participants were distributed widely across the metropolitan Washington, DC, and Baltimore areas as well as surrounding rural regions (Figure 3). The RPM activity was not limited to geographies adjacent to hospitals where enrollment took place.

DISCUSSION

RPM expands the scope of available "clinical space" beyond the brick-and-mortar constraints of the hospital, which was especially useful given rapid variation in inpatient capacity during the pandemic surge. Given the highly individual trajectory of COVID-19 disease progression, patients can remain stable for several days before decompensation;[6] it may be in the patient's best interest to recover at home during this latent period, due to risk of nosocomial infection, deconditioning, and financial and social burden associated with hospital admission.[7] For patients with deteriorating clinical status, physiologic monitoring prompts them to return to the ED sooner than with symptomatic monitoring only,[8] due to higher sensitivity of oxygen saturation reading compared to self-reported dyspnea.[9] In particular, patients with COVID-19 often experience "silent hypoxemia"[10]—hypoxemia in the absence of symptoms—which can lead to delayed care.

Of the 8,357 COVID-19 positive patients in our study who met inclusion criteria, 3,457 were referred to RPM, and 1,779 enrolled onto the platform. Our enrollment of 1,779 patients made this one of the largest published COVID-19 RPM programs to date with physiologic monitoring, a demonstration of an innovative post-acute digital patient

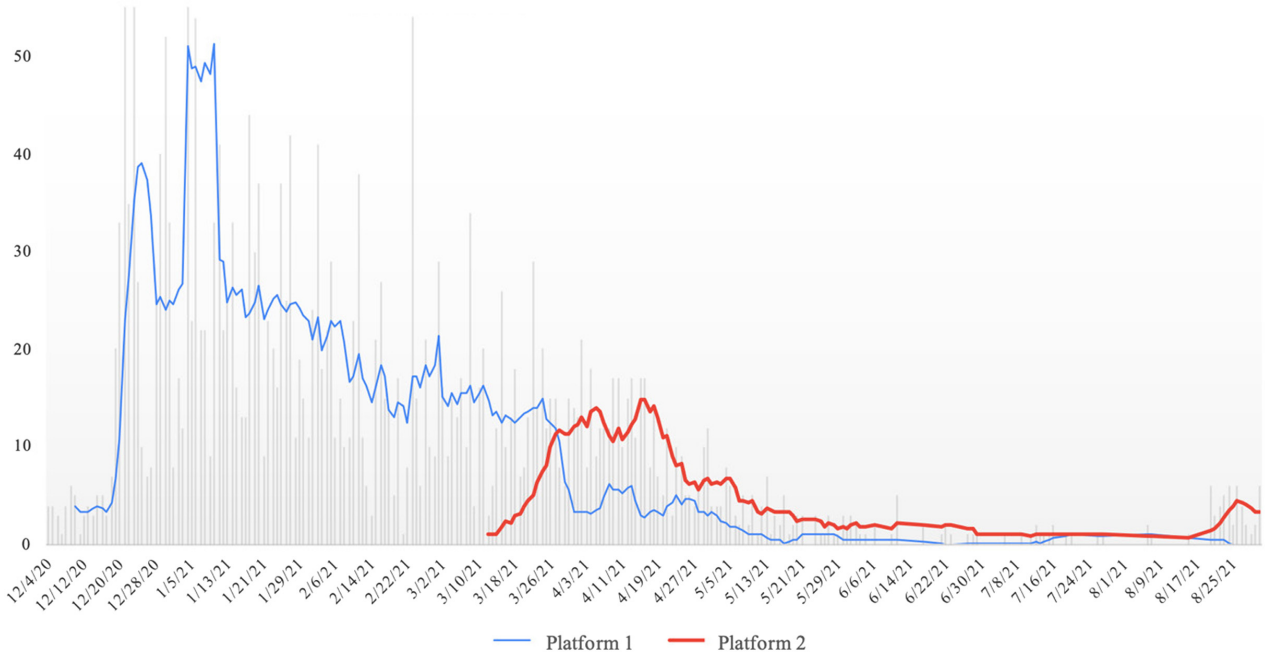

Figure 2. Remote patient monitoring referrals, 7-day rolling average, December 2020–August 2021.

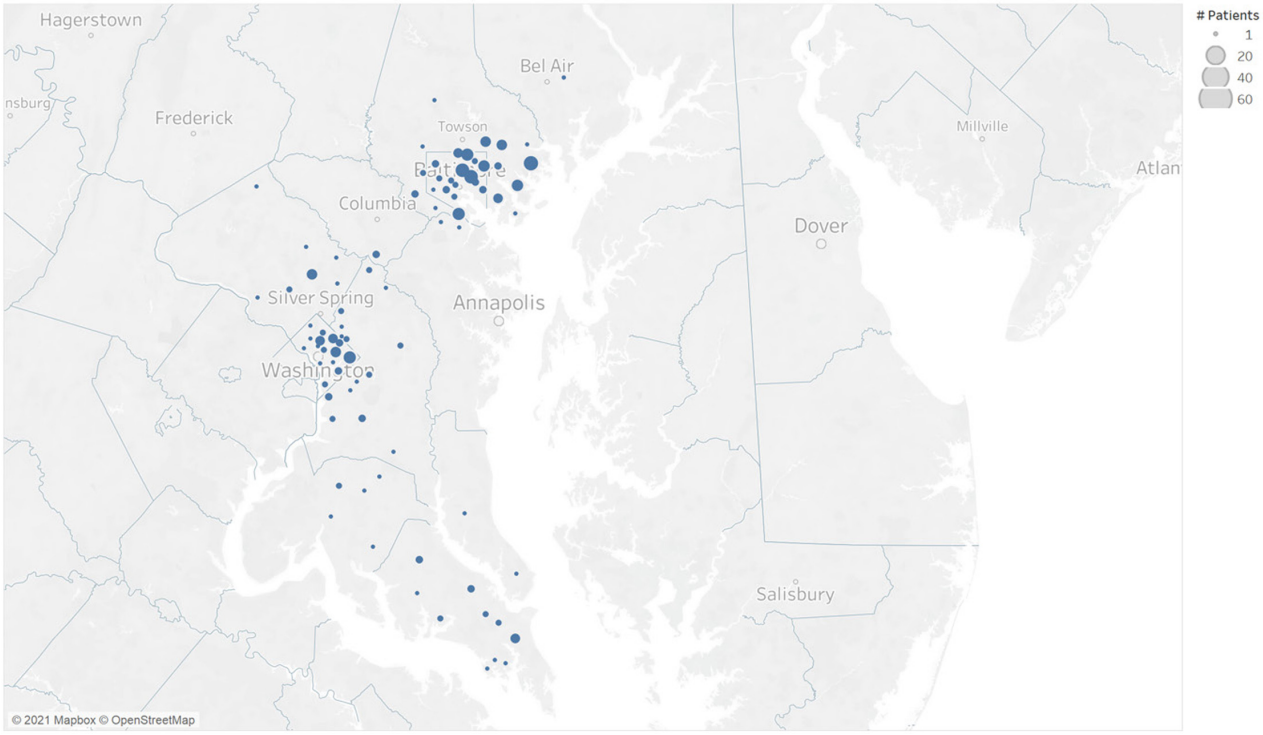

Figure 3. Geographic distribution of patient population by ZIP Code.

engagement at multihospital system scale. A COVID-19 RPM program at Kaiser Permanente Southern California, which also monitored a large population of patients,[11] had two primary differences: insurance status of participants and the use of Bluetooth-enabled devices. Kaiser enrolled patients from within its insurance program, while our study enrolled all comers regardless of insurance status, including patients with Medicaid or who were uninsured. Our use of Bluetooth-enabled devices led to increased engagement on the platform (69.0% vs 44.6% engagement on the Bluetooth

vs non-Bluetooth-enabled platform), presumably due to a simplified process for uploading vital signs. However, our overall compliance was lower compared to Kaiser (51% vs 94%). This may be due to Kaiser's more thorough patient education at the point of enrollment.

Our study is one of the few to examine both physiologic and symptomatic data in an all-comer ED population, agnostic to insurance.[11–17] In addition, we built workflows to accommodate patients who have historically been excluded from RPM: patients without smartphones or with limited English proficiency.[7,18–20] This was done to decrease a selection bias commonly seen in technology-based interventions. Of 1,779 enrollees, 120 did not own a smartphone. For these patients, the RPM team dedicated time to calling patients daily, with the goal of providing the same level of monitoring and virtual care that was available to patients with smartphones. For this population, RPM nurse practitioners manually recorded patient-reported physiologic and symptom data, in lieu of automatic data upload from Bluetooth-enabled pulse oximeters. We additionally encouraged the use of RPM via surrogate (ie, recruiting a family member, friend, or home health aide to input data on behalf of a patient who was not facile with the digital platform). Forty-three patients spoke a primary language other than English (including Spanish, Portuguese, and Thai). Both platforms were made available in Spanish; all other non-English interactions were undertaken with the assistance of an interpreter service. We acknowledge that despite a dedicated effort to lessen these disparities, we did not fully eliminate them. Bias that persisted was due in part to clinician discretion in patient enrollment.

Of note, the median age of those in the RPM program (47 years old) was lower than their non-RPM counterpart (52 years old). This may be due to clinician enrollment bias, higher likelihood of admission or observation on index ED visit for older patients (rather than discharge to home), or higher technologic fluency among younger patients. Both the RPM and non-RPM groups included a greater percentage of patients identifying as female as opposed to male.

We observed a lower 30-day return-to-ED rate for patients on RPM (6.2%) compared to patients not on RPM (14.9%), and the average number of return-to-ED episodes within that 30-day period was lower for RPM (1.0 ± 0.2) than for non-RPM (1.1 ± 0.4). Additionally, we observed a higher rate of admission or observation at return ED visit (47.7%) for the RPM group (47.7% vs 34.8%).

Compared to the non-RPM cohort, we saw greater enrollment from patients insured by Blue Cross Blue Shield. While the RPM cohort was smaller than the non-RPM cohort, which could have led to distortion of payer distribution, we must also consider the effect of enrollment bias. Insurance status (specifically Medicaid) is commonly used as a proxy for socioeconomic status. Although we aimed to enroll patients regardless of insurance status, it is possible that other factors dissuaded against RPM enrollment, including the lack of reliable access to a phone number and Wi-Fi or data plan, technologic fluency, or housing. While unintended, these biases affect healthcare delivery. Future RPM interventions should implement an enrollment process that identifies and counteracts any categorical barriers posed by technical or medical literacy, access to Wi-Fi or data, and age.

Finally, we learned lessons in supply management. We instated a Cerner order for "Referral to COVID-19 Home Monitoring"; this was essential for tracking device distribution at each ED site. Our supply management was overseen centrally; a logistics coordinator contacted each ED site monthly to determine device supply needs. In designing the program, we opted for an entirely virtual care team, which allowed for easy scalability in work force and more agility in staffing in response to epidemiologic trends. Remote staffing of one nurse practitioner and one medical assistant was sufficient to monitor all enrollees.

There is ample opportunity for future research. Interesting questions include the following: Are participants less likely to return to the ED for non-urgent COVID-19 symptoms, with the knowledge that their SpO_2 was in the acceptable range? Does immediate access to a virtual clinical team change a patient's return-to-ED behavior? Does the presence of an RPM program change clinician behavior in deciding discharge vs admission? For participants who did not stay enrolled for the full duration of monitoring, what factors led to disenrollment? All these questions bear further investigation.

The COVID-19 RPM program was retired in April 2022. In the interim between this study period and completion of the program, we expanded enrollment to include patients from our outpatient monoclonal antibody infusion clinics and select inpatient COVID-19 units. In total, we referred 6,294 patients to RPM and enrolled 2,937. While the focus of this study was RPM in the context of COVID-19, we can apply lessons learned and workflows to other acute disease states (eg, pneumonia, acute decompensated heart failure, chronic obstructive pulmonary disease exacerbation). From February–April 2022, we implemented a parallel ED RPM program for patients with pneumonia and non-COVID-19 respiratory viral illness, using the same clinical protocols. We have received overwhelmingly positive responses from patients and their families, as well as from clinicians.

LIMITATIONS

This study has several limitations. First, as a non-matched retrospective observational study, we cannot conclude that any difference in return-to-ED or readmission rate was attributable to the use or non-use of RPM. Patient enrollment was not blinded, and not all patients who qualified for RPM were enrolled, thus creating opportunity for bias in enrollment. Variables that introduce bias include

the following: patient selection (individual clinician determines which patients would benefit most from RPM); shift mechanics (clinicians are less likely to enroll a patient during a particularly busy shift); and patient's preferred language (patients with limited English proficiency may be less likely to be enrolled due to the additional step of using an interpreter service.) Another limitation due to our study design was information bias; some patients sought additional care at a different medical system and thus were lost to our 30-day return-to-ED data collection. Therefore, we were not able to fully account for the outcomes of all patients.

There were also external confounding factors. With rapid shifts in ED practice patterns (threshold determination of which patients are safe for discharge), hospital inpatient capacity, and community prevalence of COVID-19, the number of patients who were discharged and enrolled on RPM varied widely during our study period. Therefore, the population characteristics of both the RPM-enrolled and non-enrolled groups varied. During our nine-month enrollment period, we acknowledged the need to iterate on both hardware and workflow in response to rapidly changing COVID-19 and RPM landscapes. For example, the increasing prevalence of Bluetooth-enabled pulse oximetry led to our pivot from manual data entry to automated Bluetooth-enabled data upload. Consequently, patients were offered one of two different RPM pulse oximeter devices and platforms depending on their time of enrollment.

We recognize as well that using an as-treated analysis may overestimate the difference in 30-day return-to-ED calculations. For example, patients who do not engage with the platform and pulse oximeter may also be more likely to return to the ED due to underlying medical or social factors. However, many patients who were "enrolled but not active" did not receive a pulse oximeter kit or download the app. In these cases, the emergency physician placed a "Refer to RPM" EHR order, but the patient did not have the opportunity to use the pulse oximeter or communicate with our team.

Finally, while we were able to capture the majority of patients who were referred to our program, a subset (1,678 of 3,457 patients referred) did not successfully connect to the platform. This was due to several reasons, including lack of pulse oximeter distribution or app download at discharge; technologic difficulty (with either the pulse oximeter or app); lack of consistent phone access; or loss of patient interest. Patients with higher technologic and medical fluency were more facile with operating the app, which contributed to self-selection bias in enrollment. While outside the scope of this study, further analysis of causes for lack of patient engagement would be valuable.

CONCLUSION

Remote patient monitoring is a versatile tool to expand our scope of care delivery. There is a paucity of data on the long-term significance of at-home monitoring, especially as it relates to engagement with care and return-to-ED patterns in patients commonly excluded from RPM. This study does not imply causation and may not apply broadly, due to differences in study population. However, it contributes to our current knowledge of large-scale RPM implementation and can be used as a building block to continue exploring the functionalities and clinical strengths of RPM.

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REFERENCES

1. Hood C, Sikka N, Van CM, Mossburg SE. Remote patient monitoring; 2023. Available at: https://psnet.ahrq.gov/perspective/remote-patient-monitoring. Accessed May 20, 2023.
2. Vegesna A, Tran M, Angelaccio M, et al. Remote patient monitoring via non-invasive digital technologies: a systematic review. *Telemed e-Health*. 2017;23(1):3–17.
3. Gordon WJ, Henderson D, Desharone A, et al. Remote patient monitoring program for hospital discharged COVID-19 patients. *Appl Clin Inform*. 2020;11(5):792–801.
4. Kotb A, Cameron C, Hsieh S, et al. Comparative effectiveness of different forms of telemedicine for individuals with heart failure (HF): a systematic review and network meta-analysis. *PLoS One*. 2015;10(2).
5. Palaniswamy C, Mishkin A, Aronow WS, et al. Remote patient monitoring in chronic heart failure. *Cardiol Rev*. 2013;21(3):141–50.
6. Kilaru AS, Lee K, Snider CK, et al. Return hospital admissions among 1419 COVID-19 patients discharged from five U.S. emergency departments. *Acad Emerg Med*. 2020;27(10):1039–42.

7. Aalam AA, Hood C, Donelan C, et al. Remote patient monitoring for ED discharges in the COVID-19 pandemic. *Emerg Med J*. 2021;38(3):229–31.
8. Medina M, Babiuch C, Card M, et al. Home monitoring for COVID-19: Posted April 18, 2020. *Cleve Clin J Med*. 2020;87(5):1–4.
9. Lee KC, Morgan AU, Chaiyachati KH, et al. Pulse oximetry for monitoring patients with Covid-19 at home - a pragmatic, randomized trial. *N Engl J Med*. Published online April 6, 2022.
10. Rahman A, Tabassum T, Araf Y, et al. Silent hypoxia in COVID-19: pathomechanism and possible management strategy. *Mol Biol Rep*. 2021;48(4):3863–9.
11. Huynh DN, Millan A, Quijada E, et al. Description and early results of the Kaiser Permanente Southern California COVID-19 home monitoring program. *Perm J*. 2021;25.
12. Annis T, Pleasants S, Hultman G, et al. Rapid implementation of a COVID-19 remote patient monitoring program. *J Am Med Inform Assoc*. 2020;27(8):1326–30.
13. Morgan AU, Balachandran M, Do D, et al. Remote monitoring of patients with Covid-19: design, implementation, and outcomes of the first 3,000 patients in COVID watch. *NEJM Catal*. Published online 2020.
14. Watson AR, Wah R, Thamman R. The value of remote monitoring for the COVID-19 pandemic. *Telemed e-Health*. 2020;26(9):1110–2.
15. Steinberg R, Anderson B, Hu Z, et al. Associations between remote patient monitoring programme responsiveness and clinical outcomes for patients with COVID-19. *BMJ Open Qual*. 2021;10(3):e001496.
16. Patel H, Hassell A, Cyriacks B, et al. Building a real-time remote patient monitoring patient safety program for COVID-19 patients. *Am J Med Qual*. 2022;37(4):342–7. Published online 2022.
17. Medina M, Babiuch C, Card M, et al. Home monitoring for COVID-19: posted April 18, 2020. *Cleve Clin J Med*. 2020;87(5):1–4.
18. Fritz BA, Ramsey B, Taylor D, et al. Association of race and neighborhood disadvantage with patient engagement in a home-based COVID-19 remote monitoring program. *J Gen Intern Med*. 2022;37(4):838–46.
19. Oh SM, Nair S, Casler A, et al. A prospective observational study evaluating the use of remote patient monitoring in ED discharged COVID-19 patients in NYC. *Am J Emerg Med*. 2022;55:64–71.
20. Gordon WJ, Henderson D, Desharone A, et al. Remote patient monitoring program for hospital discharged COVID-19 patients. *Appl Clin Inform*. 2020;11(5):792–801.

Beyond the Basics: A Novel Approach to Integrating a Social Determinants of Health Curriculum into an Emergency Medicine Course

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Background: Our aim was to implement and evaluate a novel social determinants of health (SDoH) curriculum into the required fourth-year emergency medicine (EM) course at the University of Vermont Larner College of Medicine with the goal to teach students how to assess and address SDoH in clinical practice. The objectives were as follows:

1. Assess the SDoH, risk factors, and barriers to healthcare facing patients from diverse socioeconomic and cultural backgrounds in the ED.
2. Examine how social work consult services operate in the ED setting and how to identify appropriate referrals, resources, and treatment plans for patients in the ED.
3. Examine and interpret the impact health disparities have on patients in the ED and develop potential solutions to reduce these disparities to improve health outcomes.
4. Analyze the experiences and lessons learned and use them to inform future patient interactions.

Curricular Design: The curriculum was developed by a workgroup that considered the following: scope; target learners; overall structure; instructional and delivery methods; and session scheduling. The curriculum consisted of four components that took place over the four-week EM course. Students completed a required end-of-course survey. Survey results underwent a mixed-methods analysis to assess student attitudes and the impact of the curriculum.

Impact/Effectiveness: We received a 78.7% (74/94) completion rate for the 2021-2022 academic year. Of all respondents, 92% (68/74) indicated that they would apply lessons learned from the SDoH components of the curriculum; 74% (54/74) rated the SDoH curriculum as good, very good, or excellent; and 81% (60/74) felt that the EM course increased their understanding of diversity, equity, and inclusion as it relates to the practice of medicine. The thematic analyses revealed four main themes: 1) general comments; 2) course design; 3) interprofessional collaboration; and 4) expanding the scope of the curriculum.

Conclusion: Social medicine integration into core EM courses is a generalizable approach to experiential and collaborative exposure to the social determinants of health. Of student respondents, 92% indicated they will use lessons learned from this curriculum in their future practice. This can improve the way future generations of physicians identify SDoH and address the social needs that affect their patients, thereby advancing and promoting health equity. [West J Emerg Med. 2023;24(6)1094–1103.]

BACKGROUND

Social determinants of health (SDoH) are the conditions in which people are born, grow, live, work, and age.[1] The SDoH contribute to about 80% of a person's overall health and underlie many health disparities that exist in different groups of people based on class, gender, and ethnicity.[2,3] As health inequities continue to widen, the calls for teaching the SDoH and health equity to the new generations of health professionals become more urgent.[4,5,6]

Traditionally, medical education has focused primarily on the biomedical approach, which overlooks the urgent need to keep pace with the evolution of medicine's social contract with humanity—our commitment to advocate for social, economic, educational, and political changes that ameliorate suffering and contribute to human well-being.[7,8,9] Despite the growing obligation of medical schools to cultivate awareness and understanding of the SDoH and social inequalities, undergraduate medical education (UME) has been slow to prioritize these needs at the same level as foundational science material.[8,9,10,11] This omission has led to the perpetuation of structural racism, transphobia, and many other forms of structural violence in medicine that exacerbate inaccessibility to basic medical care and contribute to health inequities.[12,13,14] Moreover, the persistent health inequities in the US, especially those worsened by the COVID-19 pandemic, necessitate intentional and sustainable approaches to teaching equity-informed care. The next generation of physicians needs UME training that addresses the forces that drive health inequities such as the SDoH, social needs, and adverse structural factors such as systemic discrimination.[15]

A growing number of US medical schools have started to incorporate the SDoH into their curricula; however, many obstacles remain that prevent meaningful integration.[9,10,11,14] These obstacles include an ideology that addressing SDoH is outside the realm of physician responsibility, limited space in the curriculum, lack of faculty knowledge, and lower prioritization due to lack of representation of the concepts on certifying examinations.[9,10,11] Historically, pedagogical approaches in UME aimed at the SDoH have been mostly siloed into a few lecture-based sessions with few longitudinal options, and the material is often heterogeneous outside of basic definitions.[10,11]

The 24/7 accessibility of the ED and the enactment of the Emergency Medical Treatment and Labor Act in 1986, a federal law requiring that anyone coming to the ED be stabilized and treated regardless of ability to pay, solidified the role of the ED as a safety net for medical and psychosocial emergencies.[16] As such, the ED is a unique environment to engage students in understanding and critically addressing the SDoH, as a patient's presentation is quite often influenced by the impacts of social factors on their health.[17,18,19,20] Currently, there is a paucity of literature on incorporating SDoH training at the UME level within emergency medicine (EM) courses.[10,11,21]

We designed a novel SDoH curriculum to address gaps and limitations of teaching SDoH that goes beyond an introductory approach and challenges students to assess SDoH and address them in clinical practice. The curriculum is incorporated into the required University of Vermont Larner College of Medicine (LCOM) fourth-year EM course, building off the foundation developed in the pre-clinical longitudinal social medicine curriculum. The pre-clinical curriculum includes the utilization of year-long, small-group discussion space for critical reflection on social medicine topics, the creation of social medicine learning objectives, cross-curricular integration with foundational sciences, and adjunctive events such as SDoH rounds.[22,23]

Our curriculum uses students' prior knowledge of SDoH and applies that knowledge in a real-time clinical context. This allows for the contextualization and recognition of the interplay between SDoH and clinical medicine by ensuring students are encountering the SDoH in conjunction with their patients' presenting clinical complaints rather than learning about SDoH in isolation. In this article, we explain the development of the SDoH curriculum and how we assessed its impact using a mixed-methods approach.

OBJECTIVES

Four educational objectives were designed and mapped to LCOM competencies and programmatic objectives that are specific to LCOM and based on the standards set by the Liaison Committee on Medical Education. The core competencies at LCOM include the following: 1) patient care; 2) medical knowledge; 3) practice-based learning and improvement; 4) interpersonal and communication skills; 5) professionalism; and 6) systems-based practice[25] (Table 1).

CURRICULAR DESIGN

SDoH Curriculum Development

The concept for the SDoH curriculum was curated using the Instructional Design Framework of Analysis, Design, Development, Implementation, and Evaluation.[32] We first completed a literature search. We then reviewed the titles and abstracts of approximately 268 publications related to medical education, SDoH, and teaching social medicine. A singular publication was identified that specifically addressed the incorporation of a SDoH curriculum into an EM course. That curriculum takes more of an introductory approach to teaching the SDoH as opposed to our experiential and collaborative approach[21] (Table 2).

Next, we designed the curriculum considering the following: scope; target learners; overall structure; instructional and delivery methods; and session scheduling. The SDoH curriculum then underwent a rigorous approval process by the LCOM Medical Curriculum Committee and

Table 1. Educational objectives of a social determinants of health curriculum and the corresponding University of Vermont Larner College of Medicine competencies each objective is linked to.

Educational objective	Corresponding LCOM competency
Assess the SDoH, risk factors, and barriers to health care facing patients/families from diverse socioeconomic and cultural backgrounds in the ED.	1-Patient care 2-Medical knowledge 4-Interpersonal and communication skills
Using ICP, examine how social work consult services operate in the ED setting and how to identify appropriate referrals, resources, and treatment plans for patients in the ED.	4-Interpersonal and communication skills 6-Systems-based practice
Examine and interpret the impact health disparities have on patients in the ED and develop potential solutions to reduce these disparities to improve health outcomes.	2-Medical knowledge 3-Practice-based learning and improvement 6-Systems-based practice
Analyze the experiences and lessons learned and use them to inform future patient interactions.	2-Medical knowledge 3-Practice-based learning

LCOM, Larner College of Medicine; *SdoH,* social determinants of health; *ICP*, interpersonal collaborate practice; *ED*, emergency department.

was approved and implemented for the 2021–2022 academic cycle. The EM course director, the director for health equity, and two other faculty members oversaw and facilitated the components of the SDoH curriculum. The social work team played an integral role in assisting with curricular design and scheduling. Lastly, an end-of-course survey was completed. The EM course materials were provided to students through the LCOM online platform. We created a separate SDoH syllabus that detailed each of the components of the curriculum and provided a list of resources for students to use. Other materials provided were a SDoH screening questionnaire for use during the structured patient interviews and a scoring rubric for the reflection.[26,27,28]

SDoH Curriculum Structure

The components of the SDoH curriculum were 1) a SDoH shift; 2) SDoH structured patient interviews; 3) written reflection; and 4) a solutions-focused group project.

Each student completes 14 clinical shifts over the course of four weeks. In addition to these clinical shifts, the students were assigned a four-hour SDoH shift during their first 10 days in the ED where they engaged in interprofessional collaborative practice with a social worker. The social work team is consult-driven and serves the ED and inpatient services. Our social work team volunteered to have students

Table 2. Search strategy including all search terms for literature search performed at the start of the analysis process for the social determinants of health curriculum.

Database	Strategy	Date	Number of unique publications
PubMed	"Education, medical"[mh] OR "Education, medical, undergraduate"[mh] OR "clinical clerkship"[mh] OR "schools, medical"[mh] OR "emergency medicine"[mh] OR "medical school*"[tiab] OR "medical education"[tiab] OR "medical training"[tiab] OR "emergency medicine"[tiab] OR "medical student*"[tiab] OR "clinical clerkship*"[tiab] OR "medicine clerkship*"[tiab] AND Curriculum[tiab] OR curricula*[tiab] OR curriculum[mh] AND "social determinants of health"[tiab] OR "social determinants of health"[mh]	2/2/2022	229 unique items
CINAHL	(MH "Education, Medical") OR (MH "Education, Emergency Medical Services") OR (MH "Schools, Medical") OR (TI ("medical school*" OR "medical education" OR "medical training" OR "emergency medicine" OR "medical student*" OR "clinical clerkship*" OR "medicine clerkship*")) OR (AB ("medical school*" OR "medical education" OR "medical training" OR "emergency medicine" OR "medical student*" OR "clinical clerkship*" OR "medicine clerkship*")) AND (MH Curriculum) OR (TI (curricula* OR curriculum)) OR (AB (curricula* OR curriculum)) AND (MH "social determinants of health") OR (TI ("social determinants of health")) OR (AB ("social determinants of health"))	2/2/2022	24 unique items
Scopus	TITLE-ABS-KEY(((("medical school*" OR "medical education" OR "medical training" OR "emergency medicine" OR "medical student*" OR "clinical clerkship*" OR "medicine clerkship*") W/10 (Curriculum OR curricula*)) AND ("social determinants of health"))	2/2/2022	15 unique items

work with them. The social workers chose dates for the student shifts based on their availabilities, and these shifts were assigned to students at the start of the course. During the SDoH shifts, students applied their pre-clinical understanding of the SDoH along with the knowledge obtained from the social work team to help develop a plan of home care, follow-up care, or transition care dependent upon the patient's situation.

In the first two weeks of the course, students also conducted a minimum of four structured SDoH patient interviews that were focused on understanding the patient's needs beyond the scope of the disease process with which they were presenting. These interviews took place at the convenience of the student either during their SDoH shift with the help of the social work team, during regular clinical shifts, or on their own time. Students asked the patients questions using a questionnaire guide that we adapted from several validated screening tools.[29,30,31] The questions involved learning about the patient's social situation including utilization of primary care, housing insecurity, food insecurity, language barriers, bias (racial, economic, sexual orientation, etc), transportation, and alcohol or substance use.

Prior to the interview, students introduced themselves and obtained consent from the patients to discuss their social circumstances. The goal of the interview was to provide students with the time to ask questions to their patients relating to social needs. Often this was the first time students were asking these specific questions to real patients. Because we did not want time constraints to impact building rapport and trust with patients, students were not timed on the interviews. When a patient screened positive the student could either report back to social work, if this was during their SDoH shift, inform the patient's physician of the need for a social work consult, or the student could directly place a consult through the secured social work consult email.

The second week of the course provided dedicated time for students to meet in their assigned small groups (3–5 students) to discuss patient cases identified during the SDoH shift or from their individual patient interviews. Each rotation there were approximately three to five small groups. The small group then selected one case to explore further by identifying a problem, barrier, or major health-equity issue related to the case and then developing solutions to prevent and possibly mitigate it. Students were expected to develop an action plan in collaboration with the ED faculty, residents, and social workers. Students were provided with contact information for faculty and social workers to whom they could reach out for guidance as needed. The last week of the course each small group presented to an audience of their peers, faculty, and social workers through a virtual meeting.

Finally, the individual students submitted a written reflection on their personal experience and expanded upon lessons learned, unexpected aspects involving the social side of EM, and how these concepts could be implemented into their future delivery of patient care. A scoring rubric was provided to students for reference.

IMPACT/EFFECTIVENESS

To understand the impact on and the attitudes of the medical students toward the SDoH curriculum, we used a mixed-methods approach to analyze the end-of-course survey results. The survey questions assessing the SDoH course consisted of one "yes" or "no," two free-response, and three Likert scale (1–5) items. There were additional questions about the overall EM course, and many students included specific comments about the SDoH curriculum when answering those questions as well. Data was collected throughout the 2021–22 academic year as each cohort of students completed the EM course. The demographics of the survey respondents consisted of fourth-year medical students at LCOM who had completed the EM course.

We tabulated quantitative responses and displayed them numerically, using percentages where appropriate. Qualitative feedback was analyzed using thematic analysis rooted in grounded theory.[24] We selected this approach because of its compatibility with our goal of exploring individual narrative comments to understand the impact and attitudes of students toward the SDoH curriculum. Analysis of de-identified narrative comments was initially independently reviewed and iteratively coded by two authors. The authors compared codes and discussed their findings. Recurring codes were organized into categories of similar content and then further discussed and arranged into broader themes.

Coders reflected on potential biases that could influence interpretation. The first coder was a medical student at the time of analysis who completed the EM course in the 2021–22 academic year and had a scholarly interest in health disparities and curriculum development to improve the quality of care delivered to historically marginalized populations. The second coder was an attending emergency physician who was part of facilitating the EM course in the 2021–22 academic year and had an interest in improving the quality and culture of care for underserved communities.

It was not possible to individually identify any of the de-identified comments. Data management and analysis was facilitated with the use of Microsoft Excel (Microsoft Corp., Redmond, WA). The qualitative reporting was conducted in compliance with the standards for qualitative research reporting.[29] We received 74/94 completed surveys, a 78.7% completion rate for the 2021–2022 academic year. Of all respondents, 92% (68/74) indicated that they would apply lessons learned from the SDoH components of the curriculum (Table 3).

The two narrative-response questions underwent thematic analyses that revealed a variety of themes and sub-themes. For the narrative response question, "how can we improve

Table 3. Quantitative results for the social determinants of health end-of-course survey questions.

Question/Statement				Yes	No
Will you apply lessons learned from your Health Equity Experience to your future practice?				68 (92%)	6 (8%)
	Likert scale				
	Strongly Disagree (1)	Disagree (2)	Neutral (3)	Agree (4)	Strongly Agree (5)
This course helped increase my understanding of how diversity, equity, and inclusion relate to the practice of medicine.	2 (3%)	–	12 (16%)	34 (46%)	26 (35%)
I had an opportunity to participate in the care of a variety of different patients in this course. Examples of variety include different medical conditions, diverse cultures, ethnicities, socioeconomic backgrounds, sexual orientations, and belief systems.	–	–	4 (5%)	27 (36%)	43 (58%)
	Poor (1)	Fair (2)	Good (3)	Very Good (4)	Excellent (5)
Rate the overall quality of the Health Equity Experience during your course (social determinants of health shift, small-group experience, and large-group discussion).	5 (7%)	15 (20%)	25 (34%)	16 (22%)	13 (18%)

the health equity component of the curriculum," we found four main themes: 1) general comments; 2) course design; 3) interprofessional collaboration; and 4) expanding the scope of the curriculum. For the narrative response question, "please comment on how this course addressed issues of diversity, equity, and inclusion (DEI)," we found two themes: 1) acknowledgment of how the SDoH curriculum addressed DEI training; and 2) awareness of how attitudes of attendings affect DEI and SDoH training (Table 4).

Based on our results, we posit that the lessons learned through the SDoH curriculum can translate to improved patient care and health outcomes as 92% of students indicated they would apply these lessons to their future patients. We found that students are receptive to incorporating social medicine topics into standard clinical training courses and expressed desire to see further integration in the future. Students felt our SDoH curriculum could be improved by reducing the number of its components, primarily focusing on the SDoH social work shifts and the collaborative project, thus making structural changes in the course design to increase the impact for both students and patients.

The SDoH curriculum provided students with an opportunity to develop interdisciplinary skills through dedicated time to explore the role of social work for patients in the ED setting. We recognize that because social work is a consult-driven service in our hospital, this resulted in varying opportunities for students. Thus, this may have created a disparity in the experience of the SDoH shift for certain students where the focus was more on patient follow-up than consults. This is one area we intend to work on increasing the standardization for all students. Despite some variability, working with the social workers increased students' ability to learn and understand the role of social work in the ED and how to work with them efficiently as future physicians. The SDoH shift also exposed students to some of the local community resources available to patients. These are useful skills for students to learn as they will be more adept at being able to navigate finding resources and working with social work for their future patients in new locations.

Our SDoH curriculum went further than many introductory courses because the students in the class of 2022 had completed a longitudinal social medicine course during their pre-clinical years. Students were able to apply their knowledge to develop solutions for their selected patient encounters. The small groups generated a myriad of solutions, several of which are being explored as improvements to ED systems processes. The small groups presenting their solutions elicited robust discussions with our faculty facilitators and social workers. The presentations cultivated an interest in population health, public health, advocacy and health policy, medical education, and more.

For example, because the first iteration of the curriculum occurred in the 2021–2022 academic year there were many social factors impacting patients related to the impact of the COVID-19 pandemic. One group recognized that non-domiciled patients were at risk of losing stable housing as a Vermont policy for providing hotels during COVID-19 pandemic would soon be ending.[34] The group solution proposed was to organize meetings with members of the Legislature of the State of Vermont to advocate for the continuation of this policy. The group discussion led to additional ideas around how to navigate using media and other outlets for advocacy. Another small group also

Table 4. Qualitative results of the thematic analysis performed on the results of the social determinants of health end-of-rotation narrative responses provided with exemplar quotes for each of the sub-themes.

How can we improve the Health Equity Component of the Clerkship?		
Theme	**Sub-theme**	**Exemplar quotes**
General comments	Positive	I thought this part was great. Much more than I've had in any other rotation (clinical or non-clinical) thus far in med school. I was surprised by that, but very pleasantly surprised by how much I got out of it even in a short time.
		It was the best health equity clerkship course so far.
	Negative	Remove it (SDoH curriculum), we do this during family med rotation, so it is repetitive.
	Neutral	I really thought it was great and can't think of any improvements to be made at this time.
Course design	Structure of patient interviews	Encourage asking the SDoH questions to patients the student has already been building a relationship with. It's so awkward going up to a random patient or asking the attending . . . if there are any patients with SDoH barriers.
		The questionnaire can be improved - it is very objective and the whole concept of SDoH is subjective; that extends beyond simple questions like "do you have housing/food?"
	Structure of SDoH shift	Work with social work when they are consulted when it is a patient that we saw during a normal shift so that we can better understand when social work is needed and how it is incorporated into better healthcare for our patient. It would make integrating the medicine and the social pieces more powerful and tangible.
	Reduce components	The SDoH curriculum is great and a fundamental aspect of what we should be learning as EM students. That being said, it was more work than expected, and tough during a stressful time of the year to have several added requirements. A panel where peers can talk thoughtfully about their experiences (vs a project and essay) would have been less stressful and more fulfilling.
	Variability of SDoH shift	I think shadowing the social workers is a little challenging. Often they are on the phone calling consults or are in meetings and there is little engagement for us. I think it was helpful to see all that they do and how they are integrated into patient care in the ED.
	Remove SDoH shift	I don't think there needs to be an extra SDoH shift. I think it would be sufficient to provide students with the questionnaire and seek patients out during their shifts.
	Improve guidance for group project	I feel like we didn't focus on solutions enough. It would have been more helpful to have longer case discussions with social work instead of shadowing them.
Interprofessional collaboration	SDoH shift was impactful	I personally thought I got more out of shadowing the social worker than the interview portion.
		The half-day with social work was awesome.
	Want more time with social work	I don't think there needs to be an extra SDoH shift. I think it would be sufficient to provide students with the questionnaire and seek patients out during their shifts.
		Include more time for screening for SDoH and working with the social work team to provide patient care.
	Exposure to community resources	We talked about a lot of the resources that are offered at UVM when I was on my rotation, but there are so many it is easy to forget. It would be helpful to compile a list of resources that address each determinant of health to have a quick reminder of ways in which we can assist our patients if they screen positively for social determinants of health.

(*Continued on next page*)

Table 4. Continued.

How can we improve the Health Equity Component of the Clerkship?		
Theme	**Sub-theme**	**Exemplar quotes**
Expand the scope of curriculum	Want to have more of an impact	Work with social work when they are consulted when it is a patient that we saw during a normal shift, so that we can better understand when social work is needed and how it is incorporated into better healthcare for our patient. It would make integrating the medicine and the social pieces more powerful and tangible.
	Teach attendings	Make the preceptors aware of the health equity clerkship so they are on the lookout for appropriate patients and engaged in that side of learning.
		Teach doctors too.
	Exposure to mental health topics	More robust conversation about mental illness given its prevalence in the ED (especially in winter 2022 with many boarding psych patients). Eg, mental illness as a social determinant, stigma surrounding mental illness. Could also include how COVID-19 has magnified such disparities (also very apparent in the ED).
	Integrate with EM patients during regular shifts	Please allow students to complete the interviews during their time on shift. There was never a shift that was without a quiet period at some point, and patients who will screen positive aren't always waiting for you to be done with your shift to interview them.
	Add more patient encounters	Continue to have students interview patients for SDoH.
Please comment on how this course addressed issues of diversity, equity, and inclusion. Some examples include how the course dealt with race/ethnicity, gender, sexual orientation, religion, age, disability, political affiliation, and veteran status. Include what worked well for you along with any suggestions for improvement.		
Theme	**Sub-theme**	**Exemplar quotes**
SDoH curriculum addressing DEI training	Impactful	Honestly awesome part of this course was getting to work with the social workers for an afternoon - I was pleasantly surprised by how much I got out of it and how much more I was thinking about SD[o]H afterwards with further patient encounters.
	Diversity of ED population	The social determinants of health shift was really beneficial in making us aware of some patients from all different walks of life. The ED is the place where we possibly see the most diverse patients, so overall it was an awesome experience.
	Increased awareness of DEI topics	This course had a full section/syllabus designated to SD[o]H that correlated with diversity, equity and inclusion in medicine. I really enjoyed the SD[o]H components and know the experiences will assist me as a future physician.
	Did not address DEI	Not a focus of this course.
Attending attitudes affect DEI and SDoH training		SD[o]H curriculum was okay but was superseded by the way some faculty speak about patients. I heard one doctor say "There is a drug addict in room XX" before saying "no way is she getting pain meds" the doctors are the biggest model for our behavior.
		I would like to see attendings encourage us to take on patients with different backgrounds and who speak languages other than English so that we can get that experience and practice. Sometimes they discourage us from seeing such patients.

DEI, diversity, equity, and inclusion; *SdoH*, social determinants of health; *ED*, emergency department.

discussed housing insecurity and worked with a social work team to develop an easy-to-use flow chart for emergency clinicians to follow when discharging non-domiciled patients who were COVID-19 positive. The real-world application of the SDoH curriculum is providing an environment where students can develop skills in critical appraisal, peer-to-peer teaching, and ultimately foster lifelong learning.

Another salient point noted by students in both narrative response questions was the impact that the attitudes of physicians and other health professionals have on the

significance of teaching the SDoH. This is an astute observation made by students because a 2014 qualitative study assessing the determinants of empathy during medical education found that interactions with colleagues can both promote and inhibit empathy through their role modeling of empathic and non-empathic behavior.[30] This was one of six themes that emerged from their survey of practicing physicians. It is not hard to extrapolate that when adding in a power difference between an attending physician and a medical student, the attending physician's role-modeling behavior will have a greater impact on the student. When those whom the students look up to are acting in opposition to what is being expected of students it can negate some of the impacts of what we are trying to accomplish.

While most of the feedback toward the SDoH curriculum was positive, we faced several challenges with the implementation of this curriculum. We encountered many of the same challenges described in the literature around incorporating social medicine topics into UME, such as differing opinions on the relevance of SDoH despite the exhaustive evidence of their impact on health equity, an already dense curriculum, and varying levels of expertise from faculty.[9,10,11,14,33] To overcome some of the challenges both faculty and students advocated for the inclusion of the SDoH curriculum, and ultimately it was approved after rigorous review by the LCOM Medical Curriculum Committee. There was also no protected time or funding for the additional workload on the administrators, faculty, or the social work team. Faculty facilitators and the social work team volunteer their time to bring this curriculum to students. We recognize volunteering additional time of already busy faculty and social workers is not sustainable. although after years of relentless advocacy from LCOM medical students, LCOM now has a director for social medicine who is responsible for leading the efforts in addressing social medicine with LCOM medical education programs.

As with any curriculum, ours is continuously evolving. For the following academic year, we implemented changes based on student feedback. For example, students felt they did not have adequate time to meaningfully engage in each of the components of the curriculum on top of their clinical schedule. Therefore, we removed the reflection component and shortened the social work shift to three hours. As we continue to improve the curriculum, we are also working to further integrate social medicine concepts into existing lectures and sessions that have not typically made these connections in the past.

We recognize that although 92% of respondents indicated they would use lessons learned, we did not assess past a Kirkpatrick level 1 outcome.[35] Therefore, we are continuing to improve the curriculum and our assessments by developing a delayed post-survey regarding students' impression of how important and relevant this subject is regardless of specialty in attempts to identify any gaps in the curriculum as well as assessing pre- and post-knowledge related to SDoH before and after completion of the curriculum.[14]

There are also several limitations to be addressed for generalization to other institutions. First, our curriculum builds off the LCOM pre-clinical longitudinal social medicine curriculum, which we recognize most institutions do not have in place. This could increase the difficulty for some institutions if there is no formal SDoH teaching prior to their EM course/clerkship. However, we feel that our curriculum could easily be modified if this is the case. For example, the small-group projects could instead focus on students learning about a particular SDoH they identified instead of solutions. Second, the results for our study were subjective to each student's experiences, and we had a small sample size of 74 respondents. Future analyses for this curriculum would benefit from the use of a validated course survey.

CONCLUSION

Social medicine or health equity integration into core courses is a generalizable approach to experiential and collaborative exposure to the social determinants of health. We believe this is a model for a SDoH curriculum in an EM course that can be generalized to other institutions even with different baseline SDoH curricula. This represents an opportunity for UME to expand pedagogic practices beyond the specialty to include and encourage interprofessional partnerships. We found 92% of student respondents indicated they will use lessons learned from this curriculum in their future practice. And while our work is not finished, we intend to evaluate downstream impacts on the transfer of students' SDoH knowledge to clinical care; this approach takes students further than before. This type of curriculum can improve the way future generations of physicians identify social determinants of health and address the social needs that affect their patients, thereby advancing and promoting health equity among the population.

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REFERENCES

1. Social determinants of health. WHO. Available at: https://www.who.int/health-topics/social-determinants-of-health#tab=tab_1. Accessed on August 4, 2022.
2. National Conference of State Legislatures: racial and ethnic health disparities what state legislators need to know. Available at: https://www.ncsl.org/portals/1/documents/health/HealthDisparities1213.pdf. Accessed on August 4, 2022.
3. Social determinants of health. *NEJM Catalyst.* Available at: https://catalyst.nejm.org/doi/full/10.1056/CAT.17.0312#d3e166. Accessed on August 4, 2022.
4. Taira BR, Hsieh D. Advancing the biosocial perspective in the clinical training environment: surmounting the barriers and constructing the framework. *Acad Med* 2019;94(8):1094–8.
5. Skochelak S, Stack S. Creating the medical schools of the future. *Acad Med* 2017;92(1):16–9.
6. Brown IM, Khan A, Slocum J, et al. COVID-19 disparities and the Black community: a health equity-informed rapid response is needed. *Am J Public Health* 2020;110(9):1350–1.
7. American Medical Association Declaration of Professional Responsibility. Available at: https://www.ama-assn.org/delivering-care/public-health/ama-declaration-professional-responsibility. Accessed on August 4, 2022.
8. Mullan F, Chen C, Petterson S, et al. The social mission of medical education: ranking the schools. *Ann Intern Med* 2010;152:804–11.
9. Mangold KA, Bartell TR, Doobay-Persaud AA, et al. Expert consensus on inclusion of the social determinants of health in undergraduate medical education curricula. *Acad Med* 2019;94(9):1355–60.
10. Doobay-Persaud A, Adler MD, Bartell TR, et al. Teaching the social determinants of health in undergraduate medical education: a scoping review. *J Gen Intern Med*. 2019;34(5):720–30.
11. Lewis JH, Lage OG, Grant BK, et al. Addressing the social determinants of health in undergraduate medical education curricula: a survey report. *Adv Med Educ Pract* 2020;11:369–77.
12. Bailey ZD, Feldman JM, Bassett MT. How structural racism works — racist policies as a root cause of U.S. racial health inequities. *N Engl J Med* 2021;384(8):768–73.
13. Stroumsa D, Shires DA, Richardson CR, et al. Transphobia rather than education predicts provider knowledge of transgender health care. *Med Educ* 2019;53(4):398–407.
14. Sharma M, Pinto AD, Kumagai AK. Teaching the social determinants of health: a path to equity or a road to nowhere? *Acad Med* 2018;93(1):25–30.
15. Stillman K, Owen DD, Mamtani M, et al. A social emergency medicine curriculum: bridging emergency care and health equity. *AEM Educ Train* 2021;5(Suppl 1):S154–7.
16. Emergency medical treatment and labor act. Available at: https://www.cms.gov/Regulations-and-Guidance/Legislation/EMTALA. Accessed on May 18, 2022.
17. Axelson DJ, Stull MJ, Coates WC. Social determinants of health: a missing link in emergency medicine training. *AEM Educ Train* 2018;2(1):66–8.
18. Richardson LD, Hwang U. America's health care safety net: intact or unraveling? *Acad Emerg Med*. 2001;8(11):1056–63.
19. Behr JG, Diaz R. Emergency department frequent utilization for non-emergent presentments: results from a regional urban trauma center study. *PLoS One* 2016;11(1).
20. Marcozzi D, Carr B, Liferidge A, et al. Trends in the contribution of emergency departments to the provision of health care in the USA. *Int J Health Serv* 2017;48(2):267–88.
21. Moffett SE, Shahidi H, Sule H, et al. Social determinants of health curriculum integrated into a core emergency medicine clerkship. *MedEdPORTAL* 2019;15:10789.
22. Goyal RK, Dawson CA, Epstein SB, et al. The design and implementation of a longitudinal social medicine curriculum at the University of Vermont's Larner College of Medicine. *BMC Med Educ* 2021;21(1):131.
23. Finnie SM, Brach RJ, Dawson CA, et al. A new roadmap for social medicine curriculum design based on mixed methods student and faculty evaluations of the preclinical curriculum. *BMC Med Educ* 2021;21(1):442.
24. Chun Tie Y, Birks M, Francis K. Grounded theory research: a design framework for novice researchers. *SAGE Open Med* 2019;7.
25. The University of Vermont Larner College of Medicine Competencies and Medical Education Programmatic Objectives. Available at: https://www.med.uvm.edu/mededucation/VIC/medical_education_competencies. Accessed August 4, 2022.
26. American Academy of Family Physicians Social Needs Screening Tool. Available at: https://www.aafp.org/dam/AAFP/documents/patient_care/everyone_project/hops19-physician-form-sdoh.pdf. Accessed on August 4, 2022.
27. Centers for Medicare and Medicaid Services Accountable Health Communities Health-Related Social Needs Screening Tool. Available at: https://innovation.cms.gov/files/worksheets/ahcm-screeningtool.pdf. Accessed on August 4, 2022.
28. North Carolina Department of Health and Human Services Standardized Social Determinants of Health Screening Questions. Available at: https://files.nc.gov/ncdhhs/documents/SDOH-Screening-Tool_Paper_FINAL_20180405.pdf. Accessed on August 4, 2022.
29. O'Brien BC, Harris IB, Beckman TJ, et al. Standards for reporting qualitative research: a synthesis of recommendations. *Acad Med*. 2014;89(9):1245–51.
30. Ahrweiler F, Neumann M, Goldblatt H, et al. Determinants of physician empathy during medical education: hypothetical conclusions from an exploratory qualitative survey of practicing physicians. *BMC Med Educ* 2014;14(122).
31. Lett E, Adekunle D, McMurray P, et al. Health equity tourism: ravaging the justice landscape. *J Med Syst* 2022;46(17).

32. Kurt S. ADDIE Model: Instructional Design. Available at: https://educationaltechnology.net/the-addie-model-instructional-design/ Accessed on August 2, 2022.
33. Cleveland Manchanda E, Sivashanker K, Kinglake S, et al. Training to build antiracist, equitable health care systems. *AMA J Ethics*. 2023;25(1):E37–47.
34. Bendavid I. Homeless hotel program undergoing changes this summer. Available at: https://www.wcax.com/2022/03/31/vt-homeless-hotel-program-undergoing-changes-this-summer/. Accessed on May 3, 2023.
35. The Kirkpatrick Model. Available at: https://kirkpatrickpartners.com/the-kirkpatrick-model/. Accessed on May 3, 2023.

Implementation and Impacts of California Senate Bill 1152 on Homeless Discharge Protocols

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Introduction: In recent decades, there has been a growing focus on addressing social needs in healthcare settings. California has been at the forefront of making state-level investments to improve care for patients with complex social and medical needs, including patients experiencing homelessness (PEH). Examples include Medicaid 1115 waivers such as the Whole Person Care pilot program and California Advancing and Innovating Medi-Cal (CalAIM). To date, California is also the only state to have passed a legislative mandate to address concerns related to the hospital discharge of PEH who lack sufficient resources to support self-care. To this end, California enacted Senate Bill 1152 (SB 1152), a unique legislative mandate that requires hospitals to standardize comprehensive discharge processes for PEH by providing (and documenting the provision of) social and preventive services. Understanding the implementation and impact of this law will help inform California and other states considering legislative investments in healthcare activities to improve care for PEH.

Methods: To understand health system stakeholders' perceived impact of SB 1152 on hospital discharge processes and key barriers and facilitators to SB 1152's implementation, we conducted 32 semi-structured interviews with key informants across 16 general acute care hospitals in Humboldt and Los Angeles counties. Study data were coded and analyzed using thematic analysis informed by the Consolidated Framework for Implementation Research.

Results: Participants perceived several positive impacts of SB 1152, including streamlined services, increased accountability, and more staff awareness about homelessness. In parallel, participants also underscored concerns about the law's limited scope and highlighted multiple implementation challenges, including lack of clarity about accountability measures, scarcity of implementation supports, and gaps in community resources.

Conclusion: Our findings suggest that SB 1152 was an important step toward the goal of more universal safe discharge of PEH. However, there are also several addressable concerns. Recommendations to improve future legislation include adding targeted funding for social care staff and improving implementation training. Participants' broader concerns about the parallel need to increase community resources are more challenging to address in the immediate term, but such changes will also be necessary to improve the overall health outcomes of PEH. [West J Emerg Med. 2023;24(6)1104–1116.]

INTRODUCTION

In the context of compelling evidence that social and economic circumstances influence health and healthcare utilization, healthcare systems are increasingly exploring ways to address adverse social determinants of health. Much of the attention in this evolving area has centered on improving care for patients experiencing homelessness (PEH), since homelessness is strongly associated with barriers to healthcare access, worse physical and mental health outcomes, increased mortality, and higher healthcare utilization costs.[1,2] For example, various healthcare screening tools have emerged to assess homelessness and other social needs in clinical settings.[3] In some states, screening and documentation of homelessness have been incentivized with reimbursement models that risk-adjust payments based on social adversity.[4] Beyond screening, other healthcare investments have focused on care coordination and discharge planning for PEH. Some initiatives such as Chicago's Better Health through Housing and the national Healthcare for the Homeless program have shown improved patient health outcomes and decreased hospital costs.[5,6]

In California, several state initiatives have been implemented in an attempt to improve care for patients with complex social and medical needs, including PEH. These include successive Medicaid 1115 waivers such as the Whole Person Care (WPC) pilot programs and California Advancing and Innovating Medi-Cal (CalAIM).[7,8] Studies of the WPC pilots, which in many participating counties were targeted to PEH, showed reduced healthcare expenditures, decreased readmission rates, improved availability of services, and improved mental health of participants.[9] Despite these state-level investments, concerns have persisted about PEH being discharged from acute care settings without sufficient resources to maintain wellbeing,[10] with recent high-profile media coverage drawing attention to particularly egregious examples of what has been called "patient dumping."[11,12] In response to these concerns, in 2019 the California State Legislature enacted into law Senate Bill 1152 (SB 1152), a unique legislative mandate that requires a written plan to coordinate medical and social care upon discharge of PEH from hospital emergency departments (ED) and inpatient settings. Until its temporary suspension in March 2020 due to the COVID-19 pandemic, the law required hospitals to meet the following criteria to maintain licensure[13]:

1. Effective January 1, 2019, hospitals must offer and document services prior to discharging any PEH. These services include providing a meal, weather-appropriate clothing, referrals, medications, appropriate infectious disease screenings, and vaccinations; contacting the primary care clinician or coordinated entry system; conducting health insurance screening; and transporting the patient to the discharge destination within a 30-mile or 30-minute radius of the hospital.
2. Effective July 1, 2019, hospitals must create a written plan for care coordination between behavioral health, social service, healthcare, and appropriate non-profit service agencies. Hospitals must also maintain a log of discharged PEH with their discharge location and evidence of completing the discharge protocol.

Population Health Capsule

What do we already know about this issue?
In 2019 California enacted Senate Bill 1152 (SB1152), a novel hospital mandate to standardize discharge protocols for patients experiencing homelessness.

What was the research question?
We explored the law's implementation facilitators and barriers, and impact on hospital discharge protocols.

What was the major finding of the study?
SB1152 helped systematize discharge protocols, but had implementation barriers.

How does this improve population health?
Findings can inform future legislative efforts to improve health care services for patients experiencing homelessness.

To date, California is the only state to have passed such a law. However, the Healthcare Association of Hawaii implemented discharge guidelines akin to California's in anticipation of a similar proposal passing through the Hawaii State Legislature.[14] Understanding the implementation and impact of this law on hospital procedures (and ultimately on patient outcomes) is critical both to California's future investments in this area and to other states considering similar legislation to improve the health of PEH. This qualitative study begins to address these evidence gaps by exploring the following research questions:

1. What are hospital staff and leaders' perceptions of SB 1152 and the law's impact on hospital discharge processes?
2. What are the principal facilitators and barriers hospitals have faced in meeting the law's requirements?

METHODS

We conducted a qualitative research study using semi-structured interviews with key informants. Key informants, defined as individuals involved in the implementation of SB 1152, included leaders, managers, and frontline healthcare workers from hospitals subject to the law. We focused on two California counties that we anticipated would be strongly impacted by the legislation: Humboldt County, which in 2019 had the highest per capita rate of homelessness in the state, and Los Angeles (LA) County, which had the highest number of individuals experiencing homelessness in the state.[15,16] Because Humboldt is a rural, northern county and LA County is a mostly urban Southern California county, this approach also offered an opportunity to understand the law's impacts in geographically diverse settings. In both counties, study staff used emails and phone calls to reach leaders of general acute care hospitals with EDs. In Humboldt County, we recruited at least one participant from each of its four hospitals. In LA County, 69 hospitals met our inclusion criteria, and the local hospital association also circulated our study invitation. Key informants from 10 LA County hospitals agreed to participate.

After interviewing the first key informant at each hospital, we used snowball sampling to recruit additional participants. Participant outreach efforts included a maximum of three rounds of follow-up emails or phone calls. The study protocol was approved by the Institutional Review Board at the University of California, San Francisco.

Between September 2020–May 2021, a medical student (HA) trained in qualitative research methods conducted 24 interviews with 28 participants. Interviews lasted approximately one hour, were conducted via Zoom (Zoom Video Communications, Inc, San Jose, CA) and recorded. Interviews were conducted with each participant individually when possible; four interviews were conducted in dyads to accommodate informants' schedules. For all conducted interviews, HA developed and used an interview guide specific to this study (see Appendix A), which included questions about hospital protocols in place for PEH prior to the enactment of SB 1152; changes made after the law was enacted; perceived implementation factors, including the impacts of COVID-19; and overall impressions regarding discharge planning for PEH.

During hospital recruitment, our team became aware of a concurrent research effort focused on SB 1152 that was being conducted in LA County between June 2020–March 2021. That study was a mixed-methods evaluation that combined quantitative analysis of data extracted from the electronic health record, manual chart review, and interviews with patient-facing clinicians and staff.[17] That concurrent study focused only on county-affiliated hospitals, three of which met our inclusion criteria. There was considerable overlap between the study goals and the interview guides used in both research projects (see Appendix B). Based on these similarities and to minimize the interview burden for participants from the LA County-affiliated hospitals, the teams developed a shared data use agreement that enabled us to review transcripts from semi-structured interviews conducted with eight leaders at three additional hospitals in LA County. Investigators from the other study joined our study team as collaborators in data interpretation and co-authored this paper.

In summary, we conducted 24 interviews and received access to eight additional interviews for a total of 32 interviews from two California counties across 16 participating hospitals (Table 1). The number of participants from each hospital ranged from one to five. All interviews were anonymized, professionally transcribed, and analyzed using qualitative analytic software Dedoose version 9.0.17 (SocioCultural Research Consultants, LLC, Manhattan Beach, CA).[18] HA and a senior research associate on the study team, YC, developed a preliminary codebook by open coding the first four transcripts together. Subsequently, HA analyzed the remaining transcripts and reapplied new codes to previous transcripts; YC reviewed the coded excerpts. Both team members refined the codebook through weekly reconciliation and analysis meetings and received feedback from other team members. There were no significant discrepancies in the code application.

Throughout the process, we also reflected on how our backgrounds and perspectives influenced our interpretation of the data. We used the Consolidated Framework for Implementation Research (CFIR) as a framework to build the interview guide and to guide our thematic analyses of interview data. This consisted of reviewing the applied codes to generate analytic memos for each hospital, which were then synthesized into analytic memos that reflected each construct within CFIR. The CFIR identifies constructs across five interactive domains to influence implementation effectiveness: 1) outer setting; 2) inner setting; 3) intervention characteristics;

Table 1. Summary of participating hospitals.

	Non-profit	For profit	University owned	County owned	Total
Humboldt	2 hospitals	1 hospital	—	1 hospital	4 hospitals
Los Angeles	5 hospitals	2 hospitals	2 hospitals	3 hospitals* *data collected from LA county study	12 hospitals
Total	7 hospitals	3 hospitals	2 hospitals	4 hospitals	16 hospitals

4) individuals involved; and 5) implementation process.[19] In this study, the *outer setting* included community resource availability, the impact of COVID-19 on such resources, and guidance by government agencies. *Inner setting* included hospital characteristics and internal resource availability. *Individuals involved* focused on staff roles with regard to SB 1152 and staff perceptions of social care for PEH. *Intervention characteristics* focused on perceived positive and negative impacts of SB 1152, and the staff's beliefs about the law itself. Finally, the *implementation process* domain focused on the execution of changed workflows, initial responses to the law, and coordination among staff and hospitals.

RESULTS

Overall Perceived Impact of SB1152

While participants described many shortcomings to SB 1152, when asked about their overall perceptions of the law, many shared positive perceptions. They noted that being held accountable by the state law prompted a wide range of hospital changes that helped to systematize discharge planning for PEH (Table 2).

Table 2. Perceived positive impacts of Senate Bill 1152: examples from key informant interviews.

Perceived positive impacts of SB 1152 on hospital processes	
Increased accountability and consistency in documentation and service delivery	"I feel as if there has been a difference between before SB 1152 and now. In that there's much more accountability in terms of all individuals that are touching a patient throughout their stay. Whether it's the doctor, the nurse, the licensed vocational nurse or certified nurse assistant. Then social work and case management. There's definitely more accountability." – Clinical Social Work Supervisor, non-profit, LA County
	"I think our biggest learning curve was just how we were tracking and documenting the individuals that were presenting into the hospital, where before that was kind of hit or miss if we even asked them if they were homeless." – Manager of Care Transitions, non-profit, Humboldt County
	"I don't want to be super critical of SB 1152, because I think it gives guidance and I think it helps. And I like the collaborative effort that it really does pull different services responsible to make sure that they have clothing and they have some food and they have their immunizations that they need. I think these types of bills are very necessary to make sure that there's some accountability. But at the same time, we need to work with the community as well." – Clinical Social Work Supervisor, county, LA County
	"[SB 1152] probably put [discharge planning] more to the forefront and kind of forced us to evaluate every one of our discharges for homeless [patients] to make sure they're safe. So, I can't say that that's a bad thing." – Director of EM and Trauma Services, non-profit, Humboldt County
	"We're proud of the fact that we're very consistent. If we do it once, we do it 100 times and everybody gets the same" – ICU/ED Nurse Manager, for profit, Humboldt County
Improved quality of resources	"We also wanted to make sure that everyone had an identified place for their clothing . . . we actually ordered clothing from a local vendor who offered it at a discounted price. What ended up happening is we were able to provide that vendor's contact information to all of the other ministries. Now that is our contact for all six to eight ministries to order their clothing. It's weather appropriate clothing. T-shirts, sweatshirts, sweatpants, sweat shorts, socks, shoes. We also have ponchos and underwear. The essentials basically." – Clinical Social Work Supervisor, non-profit, LA County
	"Another change for us is that we provide more cab rides. We always provide bus tickets, but now we will provide a cab ride just depending on their situation. If [patients] are having a difficult time with accessing the bus, then we provide cab rides, and we meet the [SB1152] criteria [of providing transportation] within a 30-mile distance." – Social Worker and Nurse Case Manager, for profit, Humboldt County

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Table 2. Continued.

Perceived positive impacts of SB 1152 on hospital processes	
	"SB 1152 made us more responsible for making sure the patient gets their medication. So when the pharmacy is open, we'll fill them and make sure that the patient has them in hand when they leave, . . . even after hours now . . . rather than just [giving] them a prescription and say[ing], 'Go to the next free clinic and go get it filled.'. [Instead], what patients are being told is, come back to the emergency room in the morning, the social worker will help you get it filled . . . So that was one thing that SB 1152 did for us, made us make sure that our patients have the proper treatment and prescriptions filled." – ED Social Worker, university, LA County
Streamlined processes	"I think what's changed is there's a lot more tracking and a more streamlined approach to it, and also now it's the hospital or the nursing staff or physician initiation [to provide services], rather than patient requesting for services." – Nurse Manager, non-profit, Humboldt County
	"And the Box . . . setting up this resource system for everybody that's much more friendly to navigate and we're updating it always in real time has really helped to streamline resources and update resources." – Associate Chief of Clinical Social Work, university, LA County
Improved awareness of homelessness	"Through this law, we realize more that there's people that live in their cars, that are couch surfing. When they come to the hospital they might look like a normal patient, they have proper clothes . . . like there's nothing wrong with them. But then when we look into their story, then we find out they're living in their car, they're just bouncing between friends . . . it brought the spotlight into this population, and even if [people like hospital security guards] don't know the specifics of the law, people [at the hospital] know that someone's required to do something." – ED Social Worker and Homeless Care Coordinator, university, LA County
Respect and funding for social care staff	"It made it to where we have more support to do our job from our own organization . . . I think that we have more professional respect in what we do." – Clinical Social Work Supervisor, non-profit, LA County
	"I think it was the pressure of SB 1152 that came that made [our hospital administrators] say, okay, we really should look at this [request for hiring homeless care coordinators], and . . . get on board with that." – ED Social Worker, university, LA County

SB 1152: California Senate Bill 1152; *LA*: Los Angeles; *ED*: emergency department.

Increased accountability

Many participants noted that their hospitals had already established protocols for some of the requirements of SB 1152 prior to the enactment of the law (such as providing meals and clothing and linking patients with community resources). However, the same participants remarked that the law increased staff accountability to ensure that PEH were more consistently identified and provided with resources prior to discharge.

Improved quality of resources

Participants noted that prior to SB 1152, the quality of discharge resources offered to PEH did not consistently meet the law's standard. The law's requirements led staff to standardize both the provision and acquisition of resources. One hospital, for instance, changed the type of clothing being provided and improved the distribution efficiency by using its materials management department. Three other hospitals began an initiative to collect clothing in bulk from local vendors. In another example, to comply with the requirement to provide appropriate medications before discharge, two hospitals developed new protocols for patients to obtain medications from the hospital pharmacy, which was a change from pre-SB 1152, when they had been referring PEH to local free clinics.

Streamlined processes

Many participants also noted that SB 1152 led to more streamlined discharge processes. Two hospitals developed a centralized, up-to-date database of information on shelter options and community programs for social workers to use during discharge planning. In contrast, another hospital developed accessible resource packets that provided similar information for patients. Participants from two other hospitals reported that SB 1152 led them to make improvements in their referral systems (one began using a centralized calling system, and the other developed a shared online resource folder) that helped staff procure beds for PEH in shelters and recuperative care centers.

Improved awareness of homelessness and social care staff

Informants also expressed that the law led staff to better appreciate the complexity of issues about homelessness and the role that hospitals can play in helping address some of those issues. Furthermore, several social workers felt that the law strengthened the respect and support they received at their hospitals. In one hospital, informants indicated that the law served as a catalyst for funding new social care staff specifically to coordinate care for PEH.

In parallel, participants shared perspectives about the negative impacts of SB 1152. This included increased staff burden and consumption of hospital resources, and limitations in the scope of the law. (Table 3).

Increased initial staff burden and stress

Participants across hospital departments and positions described an initial increase in stress, reluctance to participate, and concerns about the division of responsibilities required under SB 1152. They reported lack of clarity about which staff members (eg, social workers, nurses, or other staff) would be assigned the different requirements outlined in the law. Some reported hesitancy about assuming new tasks since they already felt overburdened with existing responsibilities. Still, those

Table 3. Perceived shortcomings of California Senate Bill 1152: examples from key informant interviews.

Perceived shortcomings of SB 1152	
Increased initial staff burden and stress	"The biggest panic came from the social workers who work in the ED. They hit the ground running. So, it was quite overwhelming for them for a while. We had to do a lot of care in there just to calm the nerves." – Care Coordination Director, Non-Profit, LA County
	"The IT people had to build into the nursing progress notes, the whole part about homelessness. It was rough in the beginning, but I think [nurses] do it okay now. A lot of grumbling about it like, 'Don't we do enough?'" – Social Worker & Nurse Case Manager, for profit, Humboldt County
Increased utilization of resources and time	"We do as much as we can, but some of the testing and the assessment that we do are maybe wasteful, because it's a repeat of everything, but it's a new presentation. So, the physician has to do everything, the testing, we do lab work, and the whole nine yards. So, I don't know if some of that is redundant and wasteful." – Social Work Manager, non-profit, LA County
	"Again, we have a lot of homeless people. So, it's gotten to the point that our social worker and our seasoned staff kind of know all our homeless people that visit the ED frequently. And they kind of know that they'll either accept or deny whatever resources we have to offer. So, it's almost to the point where we already know what they're going to say as soon as we see them. And, you know, I mean, but we still have to go through hoops. It is a mandated requirement." – Nurse, county, LA County
	"We have a lot of homeless populations showing up in our emergency rooms. Some of them are pretty savvy with the Senate bill, so we have to provide food and clothing and then find a destination point. And so our resources get heavily consumed, going through this populous of patients . . . But they have [been savvy] even without the Senate bill." – CNO, non-profit, Humboldt County
Limited scope of the law	"Say, there's a homeless person, police will pick them up, bring him to the hospital, drop them off. And it's really not an appropriate place to drop off . . . in [theory], [SB 1152] is a good idea, but it

(*Continued on next page*)

Table 3. Continued.

Perceived shortcomings of SB 1152
really [is] a Band-Aid. Because it sticks the hospital with making this plan, and the hospital is really not an appropriate place to make a long-term plan for someone. Even when we connect the patient to . . . agencies . . . it's still lacking. Mental health is a huge piece that's missing because we don't have the resources to really treat people like we should treat them. So, I think really, what we're just creating is like the cyclical, patient relationship with the hospital. We do our discharge properly, they possibly get housing if they wanted, many say no . . . a lot of times, they don't fit the criteria to go to these recuperative cares, and then they end up coming back again." – Clinical Social Worker, non-profit, LA County
"[The law] helped with something more immediate. But it didn't really help with something long term, which I think is a drawback with the law . . . there could be other long-term solutions that may need to be addressed." – Social Worker, county, LA County
"SB 1152, I think comes from the feeling that we need to intervene and we need to hold somebody accountable. And the hospitals in this case are the ones that were chosen to be accountable. Do I really think that's the answer? No, but do I think that we can and should be involved? Yes. So that's where it stands." – Nurse Administrator, county, LA County
"[I want the state legislators] to know that it's an interdisciplinary approach, and then it's not just something that we could fix in the hospital. We have to be able to work with community partners and just along the continuum of care to meet the need. So, I think that if hospitals are held to such a high standard, then I feel like every other agency before and after should be held to a high standard." – Social Work Manager, non-profit, LA County

we spoke with reported that most of these concerns abated after the initial phase of their hospital's implementation efforts.

Increased hospital resource consumption

Participants also expressed concern that the law's requirements would lead to hospital resource strains. Interpretations of SB 1152's requirements led some hospitals to conduct the full discharge protocol for each PEH encounter regardless of how recently the patient had last presented, which some informants, especially in the ED, noted was time consuming and redundant. Others anecdotally noted that SB 1152 led to an influx of patients using the hospital for social services and were concerned about the increased consumption of hospital resources and staff time. While the resource and time constraints were a concern across most hospital informants, several participants suggested alternative explanations for the law's impact on patient numbers. They suggested that the perceived influx of patients may have reflected an increase in homelessness in the county overall, increasing medical complexity of PEH, and lack of access to social services in the community, rather than being a consequence of SB1152. As one social worker noted:

> *"[SB1152] has made the ED very impacted because homeless people will come and say, 'I know I can get resources here.' Which I get it . . . we're open 24 hours a day, and it's a one-stop shop for everything that you need, and no one's going to turn you away, versus having to go to one of the community centers, and stand in line or possibly be turned away . . . It also goes back to if more time and resources can be put into making the community resource centers better, it would create a better flow and a better system for us." (ED social worker, university, LA County)*

Limited scope of the law

Participants expressed concerns that SB 1152's narrow focus on hospital discharge processes overlooked broader, community-level barriers to addressing homelessness, such as the lack of affordable housing and poorly coordinated systems of care for PEH. They described how this contributed to difficulties in implementing changes to meet the law's requirements and to frustration among staff that their work amounted to providing only short-term solutions to meet the very complex needs of PEH.

Implementation Barriers and Facilitators

Various factors influenced hospitals' capacity to make changes to meet the law's requirements (Table 4). Participants noted that discharge processes for PEH were

Table 4. Implementation barriers and facilitators: examples from key informant interviews.

	Implementation barriers
Limited community resources	"We still are dealing with lack of resources in order to satisfy the law. I think even after SB 1152 was [put in place], it was as if nothing had changed. We still have the same limited women's shelters, men's shelters. [We need] more recuperative care [and] more long-term housing options . . . those options should have been available as of January 1st, 2019. It's almost like having family come over for Thanksgiving but all you have is Top Ramen and half a jug of water in your refrigerator. Like, okay. Well, do what you can, you know." – Clinical Social Worker, non-profit, LA County
	"Eureka has [a] psychiatric hospital . . . and I think it's only 16 beds. However, it's the only one from Santa Rosa to Brookings, Oregon. That's four hours in each direction. There are no towns around us to absorb it. It's all wilderness between north, south, east, then there's the ocean." – Social Worker and Nurse Case Manager, for profit, Humboldt County
	"For someone who is experiencing homelessness, those patients are just much, much harder to find a place for, because facilities don't want to accept them, unless they know in the beginning that there's a discharge plan waiting for them at the end of their course there." – ED Social Worker, non-profit, LA County
Limited hospital funding	"So, it's like one size does not fit all and small rural facilities, especially like ours, we're a privately owned for-profit. We ride the ragged edge of financial disaster every single day and sometimes we can't afford to buy [even] angiocaths. So, kick a little money our way . . . And the cudgel that you want to beat these large urban centers with, is just like Godzilla's footprint on the small rural facilities." – ICU/ED Nurse Manager, for profit, Humboldt County
	[SB 1152] has caused hospital more money in some way because we do the increase in number of meals, each meal may cost $10–$12 because it has to be a meal, not a sandwich. So, you know, and then when you multiply by 10 to 20 and 365 days, that could add up." – ED Physician Administrator, county, LA County
Limited staffing	"But I would say one of the main limitations is just the fact that we don't have 24-hour social work and case management . . . and there are only two acute medical social workers. They can't always call when we have a homeless patient who's discharging." – Clinical Social Work Supervisor, non-profit, LA County
Limited state support	"[The] law is up to interpretation . . . it will be nice to clarify if this was intended for inpatient [discharges]. And then what are some of the things that need to be done from the emergency department. What about urgent care, what about from the clinics[?] Clinics . . . they don't follow any of these [SB 1152] rules, or even urgent care, while the patient goes to [the] ED then [for us] to do things, including making arrangements for transportation and document all this need. So, I think the clarification of the law would help." – Emergency Physician Administrator, county, LA County
	"I guess for me personally, a better understanding of, if someone doesn't want medication, are we still obligated to get it to them? There are some questions we still have . . . where I get tripped up a little bit is like, well, how much are we supposed to bend over to get someone medication if they don't want it? Can we just say, we don't need to do that if they don't want it? That's the one hiccup that I get chipped up about." – Clinical Educator, university, LA County
	"Well, maybe a toolkit of 'Oh, these are options' could have been [helpful] . . . It's like, 'Here's what hospital A is doing and has done, and this meets our criteria. Are you doing this? Here's some ideas.' Something like that probably would have been helpful." – Manager of Care Transitions, non-profit, Humboldt County

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Table 4. Continued.

	Implementation barriers
Implementation facilitators	
Strong community partnerships	"We continue to have strong partnerships with the local rescue mission and a number of sober living houses and places like that, where patients could go at discharge." – Nurse Manager, non-profit, Humboldt County
	"We've also established some really great relationships with community entities that really worked to address homelessness in the South Bay. We have one entity called Harbor Interfaith Services that recently opened up two Bridge Home sites, which is interim housing. They've been really diligent in making sure to keep in contact with us to identify some of our homeless individuals that are constantly coming back to the ED and the hospital. That way they can get them into the Coordinated Entry System and get them connected to long-term housing . . . They'll come to the hospital. Assess the patient. Put them in the Coordinated Entry System . . . Then we can potentially have them discharged to that interim housing. As opposed to discharging to an emergency shelter or back to the streets." – Clinical Social Work Supervisor, non-profit, LA County
Donor funding	"There should be more support . . . we're lucky that we're at [this hospital], and [we have] funding for us to pay for recuperative care. We've been using recuperative care to place the homeless, but the hospital's paying for that. For the hospitals that don't have that much money, they don't have that luxury." – Homeless Care Coordinator, university, LA County
Hospital staff for PEH	"Everybody should have a point person that's building the relationship and really has the bandwidth to get out there for the resources. Adding [the homeless care coordinator] has been the best thing that's happened for us. Just all around, because he's been able to make the relationship within the community, and really tell us, 'No, this is an existing resource, this doesn't work,' so we're all in touch and not out of date." – ED Social Worker, university, LA County

SB 1152, California Senate Bill 1152; *LA*, Los Angeles; *ED*, emergency department; *CNO*, chief nursing officer; *ICU*, intensive care unit.

facilitated by strong community partnerships with shelters and sober living houses, as well as by Medicaid plan coverage for recuperative care costs. However, a more consistent barrier that emerged was an overall lack of community resource capacity, particularly in mental health facilities, discharge locations (skilled nursing facilities [SNF], recuperative care centers, shelters), long-term housing, and navigation centers. In rural Humboldt County, community facilities were scarce; in LA County, these facilities existed but were already over capacity and functionally inaccessible. In both counties, lack of capacity limited hospitals' ability to provide discharge location options for PEH. Additionally, interviewees from both counties described the specific challenge of getting PEH accepted into SNFs, as *"SNFs have the ability to say no, just because they don't want to deal with the process of trying to safely discharge them." (Clinical social work supervisor, non-profit, LA County)*.

The coronavirus 2019 pandemic exacerbated community resource constraints in both counties, posing another barrier to safely discharging PEH. While many participants noted the initial increase in resources as a result of initiatives such as Project Roomkey,[20] one participant noted that by pandemic year two, those resources were no longer available.

Another significant implementation barrier was the limited funding for required services and social care staff. Without funding, hospitals had difficulty covering expenses, including for patient clothing, food, and transportation vouchers. Many hospitals also noted difficulty covering recuperative care costs, which hospitals were forced to absorb if the patient was unable, or insurance declined, to cover related expenses. While many hospital leaders in both counties expressed concern about hospital resource limitations, informants from smaller hospitals in Humboldt County more strongly emphasized the negative impacts of the service and staffing shortages.

Nurses and social workers from one of the Humboldt County hospitals reported sometimes paying out of their own wallets to provide supplies for PEH at discharge, including for items such as tents, sleeping bags, blankets, and backpacks. Not surprisingly, hospitals that endorsed institutional resources to support social care commitments for PEH reported that this support facilitated efforts to meet SB 1152's stipulations. Examples included having a homelessness task force and staff explicitly hired (eg, homeless care coordinators) to ensure patients were discharged with appropriate resources and referrals to

community agencies. Yet even in these instances, many interviewees underscored that they could not hire or maintain adequate staff to continue meeting the law's requirements. The lack of staff capacity delayed discharges for PEH, particularly when discharges were outside regular business hours.

Furthermore, although the California Department of Public Health and professional organizations such as the California Hospital Association offered some guidance to hospitals about the law's requirements,[21] other barriers noted by participants in both counties related to ambiguity about the law's requirements. The ambiguity contributed to different interpretations of the law. For example, one hospital noted that they decided that the discharge requirements would not apply if a patient had been discharged from the same hospital within the prior 48 hours. Another hospital chose to follow the discharge protocol each time a PEH was hospitalized or in the ED.

The law's ambiguity also confused community partners and patients. According to participants from five hospitals, some community advocates and patients initially misinterpreted the statute as requiring hospitals to provide housing when needed, leading at least one hospital ED to experience a surge of housing requests from PEH. In that more rural hospital, a participant described, *"There was definitely a learning curve, and dialogue had to happen with community members too." (Manager of Care Transitions, non-profit, Humboldt County).* While this was less of a concern for participants compared to the lack of community resources and funding, the law's ambiguity still added complexity to the implementation process for many hospitals.

DISCUSSION

SB 1152 is a novel California law that aims to improve health outcomes for PEH by mandating standardized hospital discharge protocols. Mandates for care delivery specific to PEH are unique; prior government-led efforts in this realm have focused on other ways to support PEH using Medicaid expansion and programs such as Healthcare for the Homeless.[22–24] Our findings highlight that SB 1152 had several positive effects, including more systematic discharge processes for PEH, increased awareness of and accountability for addressing homelessness, and increased support for social work in some California hospitals. However, our study informants also shared critical concerns that affect implementation and sustainability, including concerns about the lack of funding for hospital social care staff and related services, insufficient state guidance about the law's provisions and enforcement, and limited investments in community resources that are needed to support PEH.

Although little data specific to SB 1152's impacts have been published, our nuanced findings are consistent with overarching findings from the mixed-methods study in LA County.[17] That study revealed several barriers to SB 1152 implementation, including resource limitations in hospital and community environments and ongoing ambiguity about the bill's requirements. Our study included different types of hospitals and more informants across two counties with different resource capacities, yet it underscored the same significant implementation barriers. Future policymaking can address these concerns by 1) increasing hospital funding for social care services, 2) strengthening implementation guidance, and 3) better integrating healthcare mandates with efforts to expand available community-level resources for PEH.

Increase Hospital Funding

Successful implementation of state-level initiatives requires financial resources. For example, California's WPC pilot program was funded under a Medicaid 1115 waiver, and implementation studies of the program have concluded that its success was contingent on adequate funding and community partnerships.[25,26] In contrast to funded programming, unfunded legislative mandates often lead to increased financial strain on health systems. A salient example is the Emergency Medical Treatment and Active Labor Act (EMTALA), which requires hospitals to provide emergency care to patients regardless of their ability to pay.[27] While EMTALA has led to improved emergency care for vulnerable populations, compliance across hospitals has varied in part due to the financial challenges of providing uncompensated care.[28–30] Similarly, our study of SB 1152 highlights challenges hospitals face implementing new protocols without new funding. Attaching funding to SB 1152's requirements would enable hospitals to cover costs associated with hiring more social care staff and obtaining needed resources for PEH, including meals, clothing, transportation, and recuperative care beds.

Strengthen Guidance, Education, and Training

In addition to highlighting funding needs, many informants emphasized that implementation would have been streamlined with more guidance, education, and training about the law and strategies for meeting the mandate's requirements. This echoes findings from a systematic review on common hospital implementation barriers[31] and hospital experiences with other mandates: for instance, complaints about EMTALA's ambiguity similarly posed barriers to initial implementation efforts.[30,32] In the case of SB 1152, informants suggested that the state offer more guidance on how frequently to conduct screening for homelessness, what screening measures should be used, and the appropriate intensity of interventions. As data accrues, these supports should include detailed information about best practices (eg, toolkits), which can help standardize

hospital practices and allay hospital concerns about compliance. Training and education materials about the law should also be directed to community advocates and resource centers to ensure communities are accurately informed about the law's requirements.

Facilitate Action on Upstream Solutions

Finally, while laws like SB 1152 ideally will improve hospital discharge processes, healthcare experiences, and outcomes for PEH, study participants emphasized that hospital-focused policies enacted without simultaneous expansion of community resources are inadequate for meeting long-term, complex needs of PEH. These findings are consistent with scoping reviews that describes how integrated community care and support services are critical to improve outcomes for PEH.[33,34]

To move in this direction, any legislation intending to improve care for PEH must be accompanied by the expansion of community-based health and social service resources across the state—both in rural areas where these resources are scarce and in urban areas that may have resources that are over capacity. Discharge facilities such as SNFs, recuperative care centers, and shelters are sorely needed. These institutions must also be held accountable for accepting PEH who require care; that accountability is likely to require new policies, such as Medicaid reimbursement reforms or coverage mandates. Expansion of psychiatric facilities, sobering centers, and general navigation centers can also help to reduce the reliance of PEH on ED services and, concurrently, improve care and outcomes post-discharge for PEH. Overall, reforms and policy incentives across other sectors that have many touchpoints with PEH are necessary to better support well-meaning initiatives like SB1152 and address the long-term, complex needs of PEH.

LIMITATIONS

Findings should be interpreted considering three key study limitations. First, there may be selection bias as we interviewed informants who responded to our outreach attempts and thus may have been more likely than non-respondents to hold strong opinions about SB 1152. However, to mitigate selection bias, we conducted multiple outreach efforts and relied on hospital associations to circulate our study invitation to hospitals that met our inclusion criteria. Second, our findings may be influenced by the fact that some study data came from a concurrent study in LA County. However, prior to incorporating the LA County data, the analysis team reviewed all transcripts to ensure that the same topics had been covered at a similar level of detail as done in the primary study. Other published research has also combined data from similar studies when the content was similar.[35] As a result, we believe the addition of the concurrent study data enriches this study by increasing the number of knowledgeable participants. A third potential limitation is that enforcement of SB 1152 was suspended in March 2020 due to the COVID-19 pandemic. Therefore, we included questions in the interview guide that focused on pandemic-related protocol changes; most informants indicated that the pandemic did not lead them to abandon their SB 1152 protocols.

CONCLUSION

This study provides insight into the implementation process and perceived impacts of SB 1152 from hospitals across Humboldt County in northern California and Los Angeles County in the south. Future research should aim to examine the law's impacts on a broader array of hospitals and how PEH have personally experienced hospital changes. Overall, SB 1152 helped hospitals focus on the safe discharge of PEH. But high-quality care for PEH will also require more community resources and other care system investments. While hospitals found creative ways to interpret and implement this unfunded mandate, they faced significant challenges in meeting the law's requirements. Future policies that refine or expand on SB 1152 to improve care for PEH should focus on strengthening implementation supports, including funding, training, community investments, and reforms both within and outside of health systems.

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REFERENCES

1. Fazel S, Geddes JR, Kushel M. The health of homeless people in high-income countries: descriptive epidemiology, health consequences, and clinical and policy recommendations. *The Lancet*. 2014;384 (9953):1529–40.
2. Horwitz LI, Chang C, Arcilla HN, et al. Quantifying health systems' investment in social determinants of health, by sector, 2017–19. *Health Affairs*. 2020;39(2):192–8.

3. Billioux A, Verlander K, Anthony S, et al. Standardized screening for health-related social needs in clinical settings: the accountable health communities screening tool. *NAM Perspect*. 2017;7(5):1–9.
4. Ash AS, Mick EO, Ellis RP, et al. Social determinants of health in managed care payment formulas. *JAMA Intern Med*. 2017;177(10):1424–30.
5. Kuehn BM. Hospitals turn to housing to help homeless patients. *JAMA*. 2019;321(9):822–4.
6. Cousineau MR, Wittenberg E, Pollatsek J. A Study of the Health Care for the Homeless Program, Executive Summary. U.S. Department of Health and Human Services; 1995. Accessed October 19, 2020. http://archive.org/details/studyofhealthcar00cous.
7. Chuang E, Pourat N, Haley LA, et al. Integrating health and human services in California's Whole Person Care Medicaid 1115 waiver demonstration. *Health Affairs*. 2020;39(4):639–48.
8. *California Advancing and Innovating Medi-Cal (CalAIM) High Level Summary*. California Dept of Health Care Services. Accessed May 24, 2022. https://www.dhcs.ca.gov/provgovpart/Documents/CalAIM/CalAIM-High-Level-Summary.pdf.
9. Pagel L, Backstrom C, Haycock H. Whole Person Care Pilot Program: A Mid-Point Check-In. chcf.org. Published March 29, 2019. Accessed September 9, 2020. https://www.chcf.org/publication/whole-person-care-pilot-program-mid-point-check/.
10. Canham SL, Davidson S, Custodio K, et al. Health supports needed for homeless persons transitioning from hospitals. *Health Soc Care Community*. 2019;27(3):531–45.
11. Reyes-Velarde A. Silver Lake Medical Center to pay $550,000 settlement in patient-dumping case, L.A. officials say. *Los Angeles Times*. Published July 2, 2018. Accessed June 21, 2022. https://www.latimes.com/business/la-me-patient-dumping-20180702-story.html.
12. Regardie J. The ugly history of downtown patient 'dumping.' *Los Angeles Downtown News.* Published July 9, 2018. Accessed June 21, 2022. http://www.ladowntownnews.com/news/the-ugly-history-of-downtown-patient-dumping/article_05fa6cea-8165-11e8-96aa-dbaced2025ed.html.
13. Hernandez E.*SB-1152 Hospital patient discharge process: homeless patients.* California State Legislature; 2018. Accessed February 13, 2020. https://leginfo.legislature.ca.gov/faces/billNavClient.xhtml?bill_id=201720180SB1152.
14. Shannon FA. Implementation of a Standardized Workflow for the Discharge of Patients Who Are Homeless at a Tertiary Medical Center. Thesis. University of Hawai'i at Manoa; 2020. Accessed December 30, 2020. http://scholarspace.manoa.hawaii.edu/handle/10125/69035.
15. *PIT and HIC Data Since 2007*. US Dept of Housing and Urban Development; 2021. Accessed November 2, 2021. https://www.hudexchange.info/resource/3031/pit-and-hic-data-since-2007.
16. *County Population Totals: 2010-2019*. US Census Bureau; 2021. Accessed November 2, 2021. https://www.census.gov/data/datasets/time-series/demo/popest/2010s-counties-total.html.
17. Taira BR, Kim H, Prodigue KT, et al. A mixed methods evaluation of interventions to meet the requirements of California Senate Bill 1152 in the emergency departments of a public hospital system. *Milbank Q*. 2022;100(2):464–91.
18. Dedoose Version 9.0.17, cloud application for managing, analyzing, and presenting qualitative and mixed method research data *(2021)*. Los Angeles, CA: SocioCultural Research Consultants, LLC. www.dedoose.com.
19. Damschroder LJ, Aron DC, Keith RE, et al. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. *Implement Sci*. 2009;4(1):50.
20. *Project Roomkey/Housing and Homelessness COVID Response*. California Dept of Social Services. Accessed February 28, 2022. https://www.cdss.ca.gov/inforesources/cdss-programs/housing-programs/project-roomkey.
21. Vivona S. *All Facilities Letter Senate Bill (SB) 1152 - Homeless Patient Discharge Planning Policy and Process*. California Dept of Public Health; 2019. Accessed April 17, 2022. https://calhospital.org/wp-content/uploads/2019/01/afl-19-01.pdf.
22. Piel L, Boyd E, Duff J, et al. *Homelessness: targeted federal programs.* Congressional Research Service; October 18, 2018. 1-29. Accessed September 7, 2020. https://sgp.fas.org/crs/misc/RL30442.pdf.
23. Institute of Medicine (US) Committee on Health Care for Homeless People. Access to health care services for homeless people. In: *Homelessness, Health, and Human Needs*. Washington, DC: National Academies Press. 1988:1–16.
24. Zlotnick C, Zerger S, Wolfe P. Health care for the homeless: What we have learned in the past 30 years and what's next. *Am J Public Health*. 2013;103(Suppl 2):S199–205.
25. Potter AJ, Wilking J, Nevarez H, et al. Interventions for health: Why and how health care systems provide programs to benefit unhoused patients. *Popul Health Manag*. 2020;23(6):445–52.
26. Alderwick H, Hood-Ronick CM, Gottlieb LM. Medicaid investments to address social needs in Oregon and California. *Health Affairs*. 2019;38(5):774–81.
27. American College of Emergency Physicians. EMTALA Fact Sheet. Accessed September 9, 2020. https://www.acep.org/life-as-a-physician/ethics–legal/emtala/emtala-fact-sheet/.
28. *Emergency Care: EMTALA Implementation and Enforcement Issues*. Washington, DC: US General Accounting Office. Published June 22, 2001. 1-38. Accessed November 10, 2021. https://www.gao.gov/products/gao-01-747.
29. Rosenbaum S, Cartwright-Smith L, Hirsh J, et al. Case studies at Denver Health: 'patient dumping' in the emergency department despite EMTALA, the law that banned it. *Health Affairs*. 2012;31(8):1749–56.
30. Hsuan C, Horwitz JR, Ponce NA, et al. Complying with the Emergency Medical Treatment and Labor Act (EMTALA): challenges and solutions. *J Healthc Risk Manag*. 2018;37(3):31–41.
31. Geerligs L, Rankin NM, Shepherd HL, et al. Hospital-based interventions: a systematic review of staff-reported barriers and

facilitators to implementation processes. *Implementation Sci*. 2018;13(36):1–17.

32. Stieber J and Spar L. EMTALA in the 90's – enforcement challenges. *Health Matrix*. 1998;8(1):57–81.
33. Jego M, Abcaya J, tefan DE, et al. Improving health care management in primary care for homeless people: a literature review. *Int J Environ Res Public Health*. 2018;15(2):309.
34. Hwang SW, Tolomiczenko G, Kouyoumdjian FG, et al. Interventions to improve the health of the homeless: a systematic review. *Am J Prev Med*. 2005;29(4):311–19.
35. Shields-Zeeman L, Gadbois E, Tong M, et al. How Medicare Advantage plans use data for supplemental benefits decision-making. *AJMC*. 2022;28(4):132–9.

Prospective Cohort Study of Emergency Department Visit Frequency and Diagnoses Before and During COVID-19 Pandemic in Urban, Low-Income, US- and Foreign-Born Mothers in Boston, MA

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Background: The coronavirus 2019 (COVID-19) pandemic fundamentally changed how populations interface with the healthcare system. Despite historical spikes in US mortality during the pandemic, emergency department (ED) visits were paradoxically low. This is a concerning phenomenon that raises a red flag regarding access to care, especially among vulnerable populations. In this study we sought to understand how ED utilization evolved during the COVID-19 pandemic among traditionally understudied, low-income, racially diverse US- and foreign-born mothers.

Methods: This is a secondary analysis of a pre-existing dataset of 3,073 participants enrolled in the Boston Birth Cohort at birth and followed prospectively. We obtained ED visit diagnoses from 2019 and 2020 via electronic health records, categorized according to the International Classification of Diseases, 10th Revision, and compared them using graph plots, chi-square, and negative binomial regression.

Results: The number of ED visits decreased by 29.1% ($P < 0.001$) from 2019 (1,376) to 2020 (976). However, visits for infectious and parasitic diseases, including COVID-19, increased by 90.6% (32:61) with COVID-19 accounting for 77% of those visits in 2020 (47/61). Mental health-related visits increased by 40.9% (44:62), with diagnoses of alcohol use disorder increasing by 183% (6:17). Regression analysis showed 50% less ED utilization among foreign- vs US-born participants; however, the increase in infectious diseases visits was greater among foreign-born compared to US-born mothers (185% vs 26%, $P = 0.01$), while the increase in mental health diagnoses was greater among US-born mothers (69% vs −33%, $P = 0.10$).

Conclusion: Despite a decrease in total ED visits during the pandemic, there was an increase in COVID-19- (immigrant > US born) and mental health- (US-born only) related visits. Our findings demonstrate that EDs remain a critical access point for care for minority populations and have implications for preparedness, resources, and services of EDs in urban settings to better address the needs of communities. However, alternative avenues for healthcare services for these populations, particularly during health crises, warrant further investigation. [West J Emerg Med. 2023;24(6)1117–1127.]

INTRODUCTION

Coronavirus 2019 (COVID-19) disease has caused significant morbidity and mortality; according to the World Health Organization (WHO), there have been over 91 million reported cases of COVID-19 with over a million deaths.[1] The pandemic affected not only physical health but had a profound effect on mental health, social interactions, education, economic growth, and overall well-being.[2–5] Prior literature has shown that COVID-19 impacted how communities interface with the healthcare system; specifically, one study in Minnesota demonstrated a 49.3% decline in emergency department (ED) visits,[3] while another in Germany demonstrated a 63.8% decrease in ED pediatric visits[6] as a result of the COVID-19 pandemic.

Despite this decrease in ED utilization, people still have healthcare needs, particularly for mental health services. More recent evidence found an increase in outpatient adult mental health visits,[7] particularly among low-income and urban populations[8]; however, there is limited evidence of a similar pattern in large-scale studies or ED settings. A study by Rusk et al on pediatric utilization within a similar population also showed an increase in outpatient visits for mental health despite an overall decrease in other kinds of outpatient healthcare encounters.[9]

While emerging studies highlight the impact of COVID-19 on mental health,[2,10] less is known regarding the mental health implications of COVID-19 as it relates to ED presentations, particularly among people of color, immigrants, and those of lower socioeconomic status who were disproportionately affected by the COVID-19 pandemic.[11,12] Black and Hispanic populations are more likely to be infected with and die from COVID-19 infection.[11–14] Similar trends have been observed as it relates to mental health: Research has shown higher rates of psychological stress and substance abuse disorders among minority populations in relation to the COVID-19 pandemic.[15–17] These findings were largely based on survey data and data from non-ED settings; thus, it is important that we study trends among this population to improve their health outcomes. Additionally, prior studies have documented lower rates of psychological disorders and substance use disorder among those born outside of the US[18,19]; however, data is limited as it relates to ED populations and presentations for mental health-related complaints.

While recent studies have looked at changes to ED visit patterns around the world, there is a paucity of data examining both the trends and reasons for changes in ED visits as it relates to maternal and mental health, especially among low-income minority, immigrant populations. In this study we aimed to evaluate changes in both the numbers and diagnoses for ED visits, particularly for mental health-related visits, during the COVID-19 pandemic (2020) compared to baseline (2019) among a sample of US- and foreign-born, urban, low-income, racially diverse, underrepresented mothers.

Population Health Research Capsule

What do we already know about this issue?
The early COVID-19 pandemic, which disproportionately affected people of color, was associated with significant mortality and decreased ED utilization.

What was the research question?
How did ED utilization patterns among minority mothers change during the COVID-19 pandemic?

What was the major finding of the study?
Despite a 29% decrease in overall ED visits, there was a 41% increase in ED mental health visits; diagnoses of alcohol use disorder increased by 183% ($P = 0.003$).

How does this improve population health?
The increased psychological burden associated with COVID-19 among minority mothers highlights the need to expand supportive services for this population.

METHODS

Study Design

Participants for this study came from the Boston Birth Cohort (BBC), which was initiated in 1988 in response to rising pre-term birth rates in the US particularly among minority populations. This ongoing birth cohort enrolls mother-child dyads shortly after delivery at Boston Medical Center (BMC). Mothers and their children who continue to receive medical care at BMC were invited to participate in the postnatal follow-up study, which includes electronic health record (EHR) surveillance. Further details regarding recruitment have been published in a profile of the BBC.[20]

Boston Birth Cohort

The full BBC follow-up cohort is comprised of 3,073 racially diverse and primarily low-income women who continue to receive care at BMC and consented to postnatal follow-up.[8] This cohort included a robust dataset to track ED utilization among a diverse population and, thus, was the focus of our study. In this study we analyzed ED utilization among the 796 women who visited the ED in 2019 and/or

2020. This created two datasets for analysis. The first dataset is comprised of ED encounters from 2019 and 2020; the observations are ED encounters. The second dataset contains demographic information on participants, where observations correspond to individuals. For the primary analysis we used the ED encounters dataset. The second dataset with demographic information was used to provide additional context about participants. The BBC received institutional review board approval from both Johns Hopkins Bloomberg School of Public Health and BMC. For clarification, the term "women" in this study refers specifically only to women who have given birth to children as defined in our cohort and for the remainder of the paper will be referred to as "mothers."

Data Collection

Enrollment into the BBC is performed at BMC by research assistants. Eligible mothers are approached and consented within 1–3 days postpartum, and a baseline questionnaire interview is administered. Mothers and children beginning at six months old are invited to consent to enrollment in the longitudinal, follow-up study, which allows for EHR surveillance. The BMC field team extracts relevant clinical data and diagnoses for the follow-up study from the Clinical Data Warehouse (CDW) at BMC. For our study, the CDW was then queried by field directors for ED visits and filtered by year. We then collated this data into International Classification of Diseases, 10th Rev, Clinical Modification (ICD-10-CM) system categories, which we used for our study analysis. Further details on data collection have been previously published.[20]

We evaluated all ED visits among study mothers from January to December of 2019 and 2020. Information regarding visit diagnoses was collected from the BMC CDW, which holds the EHR for research. All maternal ED visits resulting in at least one diagnosis in 2019 (before the pandemic) and 2020 (intra-pandemic period) were analyzed. We excluded visits where participants "eloped," "left without being seen," or did not receive a diagnosis. Each encounter resulted in at least one visit diagnosis with a maximum of three, and there were secondary and tertiary diagnoses in 50% and 25% of ED encounters, respectively (Supplemental Table 1 and 2). Secondary and tertiary diagnoses were most likely representative of additional or incidental diagnoses. Upon examination of secondary diagnoses, 50% were categorically similar to the primary diagnosis; thus, we chose to use the primary diagnosis alone for analysis as this was present for all participants and would represent the most pertinent reason for the ED visit.

Statistical Analysis

We performed sensitivity analysis of perinatal characteristics of mothers (Table 1). The total number of ED visits for the entire study cohort, as well as by nativity (eg, US- and foreign-born mothers) is shown in Table 2, and we calculated percentage change from 2019 to 2020 (Table 3). Data is also presented as a line graph to reflect the longitudinal patterns for 2019 and 2020, respectively (Figure 1). To understand how pre- and intra-pandemic periods and participant demographics predict the count of ED visits, we fit two negative binomial regression models to our full sample data. Model 1 includes the following: a pandemic period indicator; foreign-born, race/ethnicity (Hispanic and non-Hispanic White, Black and other, with non-Hispanic White as the reference); level of education (lower than high school, high school, with college-educated as the reference); low family income level (lower than $65,000 vs otherwise); and age of delivery <35 years. Model 2 added an interaction term between immigrant status and the pandemic indicator. The coefficients, standard errors, and significance levels for both Model 1 and Model 2 are represented in Supplemental Table 3.

We categorized ED visit diagnoses from 2019 and 2020 using the ICD-10-CM Tabular List of Diseases and Injuries. Visit diagnoses that could not be characterized into any of the ICD-10-CM systems categories were listed as un-codable. We tabulated the frequency of each category and calculated the percentage change between 2019 and 2020; this was done for both foreign- and US-born subgroups (Table 3). The visit categories that showed a positive percentage increase from 2019 to 2020 (with cell count $N > 10$) are bolded. Visit categories that displayed a divergent utilization pattern between the study cohort—US- and/or foreign-born mothers—were also bolded. We calculated the frequency of the top 14 diagnoses and analyzed the percentage change using chi-square analysis. The Bonferroni correction method was used to lower the significance threshold due to multiple comparisons. We also compared the top 15 ED visit diagnoses, as well as top mental health diagnoses, between 2019 and 2020 and graphically present them (Figure 2). For all analyses, $P < 0.05$ was considered to be statistically significant.

RESULTS

ED Utilization

A sensitivity analysis of ED vs. non-ED users found significant differences with respect to maternal birthplace, race, education, and smoking status (Table 1; Supplemental Table 4). Of the 3,073 mothers enrolled in the full maternal BBC cohort, almost 60% reported being born outside the US (1,841/3,073). Of the 796 in our sample, 51.1% (407/796) of mothers reported being foreign-born (Table 1). Almost 65% of our study sample participants identified as Black, while 19.1% identified as Hispanic. In the full maternal cohort, 58.1% and 22.3% of mothers identified as Black and Hispanic, respectively (Table 1). Only 7.5% of mothers in our study sample reported having a college degree compared to 13.8% in the full maternal cohort. A larger majority (30.9%)

Table 1. Summary of preconception and perinatal characteristics of the participating mothers in total sample and by maternal place of birth.

Characteristic (% or mean [SD])	Full maternal BBC cohort	ED users in 2019 and/or 2020			p-value[1]
		Study sample ED users in 2019 and/or 2020	Mothers born outside US	Mothers born in US	
Total n	3,073	796	407	382	
Maternal demographic characteristics					
Maternal race					***
Non-Hispanic White	232 (7.5)	34 (4.3)	4 (1.0)	29 (7.6)	
Non-Hispanic Black	1,786 (58.1)	514 (64.6)	224 (55.0)	286 (74.9)	
Hispanic	686 (22.3)	152 (19.1)	112 (27.5)	39 (10.2)	
All others[2]	369 (12.0)	96 (12.1)	67 (16.5)	28 (7.3)	
Maternal age at delivery	28.55 (6.6)	28.04 (6.8)	30.15 (6.56)	25.76 (6.3)	***
Maternal age in March 2020	41.54 (7.7)	40.6 (8.0)	42.36 (7.8)	38.72 (7.8)	***
Maternal birthplace					N/A
Outside US	1,841 (59.9)	407 (51.1)	407 (100)	0 (0.0)	
US	1,191 (38.8)	382 (48.0)	0 (0.0)	382 (100.0)	
NA	41 (1.3)	7 (0.9)	0 (0.0)	0 (0.0)	
Highest level of education					***
Less than high school	859 (28.0)	261 (32.8)	145 (35.6)	114 (29.8)	
High school degree	1757 (57.2)	465 (58.4)	213 (52.3)	249 (65.2)	
College degree	425 (13.8)	60 (7.5)	42 (10.3)	17 (4.5)	
NA	32 (1.0)	10 (1.3)	7 (1.7)	2 (0.5)	
Household income at delivery					**
<$15,000	812 (26.4)	246 (30.9)	104 (25.6)	140 (36.6)	
$15,000–$30,000	520 (16.9)	127 (16.0)	79 (19.4)	48 (12.6)	
$30,000–$60,000	256 (8.3)	59 (7.4)	27 (6.6)	32 (8.4)	
$60,000+	108 (3.5)	13 (1.6)	5 (1.2)	8 (2.1)	
Don't know	1040 (33.8)	262 (32.9)	140 (34.4)	121 (31.7)	
NA	337 (11.0)	89 (11.2)	52 (12.8)	33 (8.6)	
Maternal clinical characteristics					
Maternal BMI category at delivery				*	
Overweight/obese	1475 (48.0)	411 (51.6)	211 (51.8)	198 (51.8)	
Underweight/normal	1424 (46.3)	334 (42.0)	163 (40.0)	169 (44.2)	
NA	174 (5.7)	51 (6.4)	33 (8.1)	15 (3.9)	
Maternal chronic hypertension					NS
No	2854 (92.9)	741 (93.1)	381 (93.6)	355 (92.9)	
Yes	204 (6.6)	48 (6.0)	24 (5.9)	24 (6.3)	
NA	15 (0.5)	7 (0.9)	2 (0.5)	3 (0.8)	
Maternal PEH					NS
0	2699 (87.8)	690 (86.7)	361 (88.7)	324 (84.8)	
1	346 (11.3)	97 (12.2)	44 (10.8)	53 (13.9)	
NA	28 (0.9)	9 (1.1)	2 (0.5)	5 (1.3)	
Maternal diabetes					NS
GDM or DM	369 (12.0)	101 (12.7)	60 (14.7)	41 (10.7)	

(*Continued on next page*)

Table 1. Continued.

Characteristic (% or mean [SD])	Full maternal BBC cohort	ED users in 2019 and/or 2020			p-value[1]
		Study sample ED users in 2019 and/or 2020	Mothers born outside US	Mothers born in US	
No	2697 (87.8)	692 (86.9)	347 (85.3)	340 (89.0)	
NA	7 (0.2)	3 (0.4)	0 (0.0)	1 (0.3)	
Maternal cardiometabolic disorders[3]					NS
0	1,788 (58.2)	421 (52.9)	210 (51.6)	207 (54.2)	
1	771 (25.1)	225 (28.3)	116 (28.5)	109 (28.5)	
2	265 (8.6)	77 (9.7)	36 (8.8)	41 (10.7)	
3	53 (1.7)	13 (1.6)	9 (2.2)	4 (1.0)	
N/A	196 (6.4)	60 (7.5)	36 (8.8)	21 (5.5)	
Maternal smoking status					***
Continuous	343 (11.2)	114 (14.3)	12 (2.9)	100 (26.2)	
Never	2,471 (80.4)	606 (76.1)	386 (94.8)	217 (56.8)	
Quitter	227 (7.4)	71 (8.9)	6 (1.5)	65 (17.0)	
N/A	32 (1.0)	5 (0.6)	3 (0.7)	0 (0.0)	

[1]*P*-value reflects birthplace-stratified comparison among ED users.
[2]"All others" includes Asian, Pacific Islander, mixed, and other.
[3]Maternal cardiometabolic disorders include chronic hypertension or preeclampsia, diabetes, and obesity.
ED, emergency department; *BBC*, Boston Birth Cohort; *BMI*, body mass index; *PEH*, preecampsia, eclampsia and/or HELLP Syndrome; *GDM*, gestational diabetes; *DM*, diabetes mellitus; *NA*, not available.

Table 2. Number of emergency department encounters in 2019 and 2020 among US and foreign-born mothers (column percentages in parentheses).

# of encounters	2019	2020	Total
US born	843 (61.3%)	624 (63.9%)	1467 (62.4%)
Foreign born	526 (38.2%)	347 (35.6%)	873 (37.1%)
N/A[1]	7 (0.5%)	5 (0.5%)	12 (0.5%)
Total	1376	976	2,352

A chi-square test of independence revealed no statistically significant relationship between place of birth and year (P = 0.20).
[1]N/A refers to individuals for whom information regarding birthplace was not available.

of our study sample participants reported a household income of <$15,000 compared to 26% of mothers in the full cohort. Most mothers in our study sample reported never having been smokers (76.1%), with just over 50% of mothers being overweight/obese.

Foreign-born mothers made up over 50% of participants in the study cohort; however they only accounted for 38.2% of ED encounters in 2019 and 35.6% in 2020. Mothers born in the US represented a higher percentage (63.9%) of ED encounters in 2020 compared to 2019 (61.3%), while the proportion of ED encounters completed by foreign-born mothers decreased by 3% (Table 2).

Figure 1 depicts the COVID-19 timeline overlayed with the change in ED visit encounters from 2019 to 2020 for the study cohort—foreign-born mothers and US-born mothers. Across all groups, the largest decline in ED visits was observed in March of 2020 when the stay-at-home order was issued.[21] Visit frequency slowly increased (without ever reaching pre-pandemic rates) over the following months up until August, when ED visits declined in conjunction with rising COVID-19 cases.[21] There were a total of 1,376 visit diagnoses in 2019 and 976 in 2020, an absolute decrease of 29.1%. A greater decrease was observed among foreign-born mothers (34.0%) compared to US-born mothers (26.0%), despite foreign-born mothers making up a smaller proportion of ED visits at baseline (Table 2, Figure 1).

Even when controlling for other variables, the results from the negative binomial regression (Supplemental Figure 1, Supplemental Table 3) indicate the decrease in ED visits from 2019 to 2020 was significant (−0.4−1 = 29.7%). The model showed that immigrant status, race/ethnicity, level of education, and low-income are significant predictors of ED visits: foreign-born mothers experienced a 49.4% reduction in utilization rate compared to US-born mothers. Black and Hispanic mothers experienced a 158.1% and 100.7% increase in utilization rate, respectively, compared to White mothers. Mothers with a high school degree and less than high school education had a 77.0% and 142.2% increase in utilization rates, respectively, compared to mothers with a college

Table 3. International Classification of Diseases, 10th Revision, systems categories of primary diagnoses among mothers who visited the emergency department, stratified by year.

	All mothers			Foreign-born mothers			US-born mothers		
ICD-10 systems diagnosis categories	2019 (n)	2020 (n)	% change '19–'20	2019 (n)	2020 (n)	% change '19–'20	2019 (n)	2020 (n)	% change '19–'20
Certain infectious and parasitic diseases	**32**	**61**	**90.6**	**13**	**37**	**184.6**	**19**	**24**	**26.3**
Complications of pregnancy, childbirth, and the puerperium	78	34	–56.4	38	16	–57.9	40	18	–55.0
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	212	127	–40.1	2	1	–50.0	210	126	–40.0
Diseases of the circulatory system	67	43	–35.82	32	18	–43.75	35	25	–28.6
Diseases of the digestive system	**131**	**98**	**–25.2**	**63**	**28**	**–55.6**	**67**	**69**	**3.0**
Diseases of the ear and mastoid process	10	7	–30.0	5	1	–80.0	5	6	20.0
Diseases of the eye and adnexa	22	13	–40.9	4	8	100.0	18	5	–72.2
Diseases of the genitourinary system	105	80	–23.8	47	30	–36.2	58	50	–13.8
Diseases of the musculoskeletal system and connective tissue	165	96	–41.8	72	41	–43.1	89	54	–39.3
Diseases of the nervous system	9	9	0.0	2	4	100.0	7	5	–28.6
Diseases of the respiratory system	92	49	–46.7	36	21	–41.7	55	28	–49.1
Diseases of the skin and subcutaneous tissue	101	67	–33.7	48	38	–20.8	53	29	–45.3
Endocrine, nutritional, and metabolic diseases	11	13	18.12	8	6	–25.0	3	7	133.3
External causes of morbidity	47	36	–23.4	20	16	–20.0	27	19	–29.6
Factors influencing health status and contact with health services	9	16	77.8	4	5	25.0	5	11	120.0
Injury, poisoning, and certain other consequences of external causes	65	42	–35.4	30	17	–43.3	35	23	–34.3
Mental, behavioral, and neurodevelopmental disorders	**44**	**62**	**40.9**	**12**	**8**	**–33.3**	**32**	**54**	**68.8**
Neoplasms	4	1	–75.0	0	1	NA	4	0	–100.0
Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified	163	119	–27.0	88	50	–43.18	74	69	–6.8
Un-codable	9	3	–66.7	2	1	–50.00	7	2	–71.4
Total	1376	976	**–29.1**	526	347	**–34.03**	843	624	**–26.0**

Categories with divergent utilization patterns between the overall cohort, foreign-born mothers, and/or US-born mothers are bolded. Categories with positive percent increases from 2019 to 2020 and with an n > 10 are also bolded.
ICD-10, International Classification of Diseases, 10th Rev.

degree;. Mothers with an annual household income <$60,000 had a 20.6% increase in utilization rate compared to those with incomes >$60,000 per year, all else being equal.

Although nearly significant ($P = 0.10$), the magnitude of the interaction between pandemic indicator by immigrant status in Model 2 suggests there may be a difference in the reduction of ED visits from 2019 to 2020 between foreign- and US-born mothers. The Supplementary Figure 1 shows that the marginal effect of immigrant status is nearly significant for Blacks; ie, immigrant Blacks had a greater reduction in ED visits from 2019 to 2020 than their native-born counterparts.

Disease-specific Diagnoses in the Emergency Department

We characterized ED visit diagnoses for the study cohort, US- and foreign-born mothers, into one of 15 ICD-10-CM system categories represented in Table 3. Although baseline numbers within each category were small, visits with a large increase or a divergent pattern between the study cohort (n > 10) were bolded. The most common system diagnosis category in both 2019 and 2020 was "diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism" with a frequency of 15.4% (212/1,376) and 13.0% (127/976) in 2019 and 2020, respectively, with US-born mothers making up almost 100% of those visits

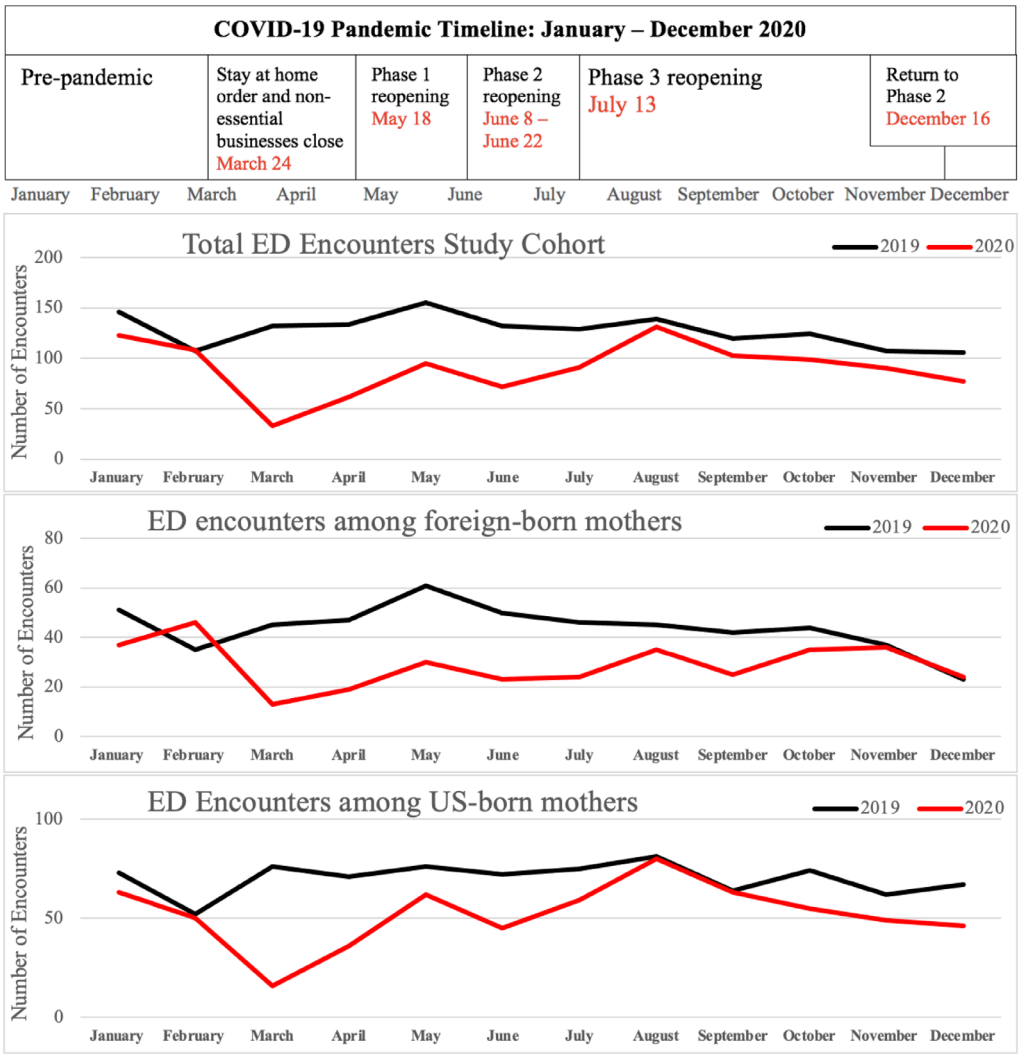

Figure 1. The number of monthly emergency department visits among foreign-born and US-born mothers in the study sample from the full Boston Birth Cohort before and during COVID-19.
ED, emergency department.

(210/212, 126/127). While there was an overall decrease from 2019 to 2020, visits for sickle cell crisis were the most common diagnosis within that category both before and during the pandemic (Figure 2).

Within the "certain infectious and parasitic diseases" category, there was a meaningful increase in visits between 2019 and 2020 of 90.7% ($P = 0.01$, Supplemental Table 5). This included visit diagnoses for COVID-19, of which there were zero visits in 2019, but they accounted for 77% of visit diagnoses within that category in 2020 (47/61). Interestingly, the number of visit diagnoses within the "mental, behavioral and neurodevelopmental disorders" category showed a noteworthy increase of 40.9% from 2019 to 2020; however, this was not statistically significant ($P = 0.10$, Supplemental Table 6). This was solely driven by US-born mothers, where there was a 68.8% increase in visits; among foreign-born mothers there was a 33.3% decrease. For the study cohort within this category, ED visits for substance use disorder were the most common in 2019 (13/44) with a modest increase in visits by 23.1% in 2020, while not statistically significant ($P = 0.20$, Figure 3, Supplemental Table 7 and 8). There were zero visits under the behavioral category (which includes diagnoses related to eating and sleep disorders) in 2019; this number increased to four in 2020. Notably, the largest increase of 183.3% was seen in visit diagnoses for alcohol use disorder ($P = 0.003$, Figure 3, Supplemental Table 7 and 8).

DISCUSSION

Our study demonstrates that the ED continues to serve as a safety net for minority mothers. However, there exists a differential in service needs between our immigrant vs non-immigrant population. In our cohort of urban, low-income, US- and foreign-born mothers, we found a decrease in ED

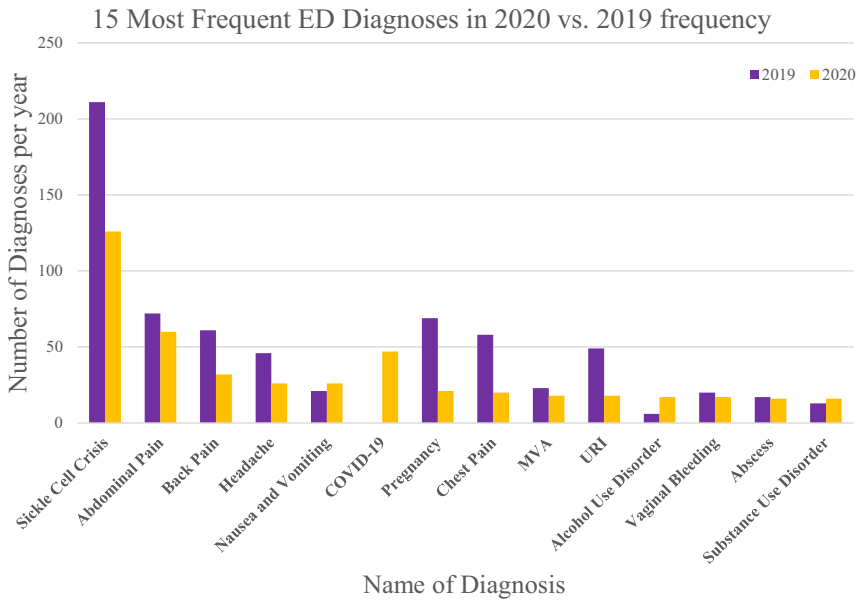

Figure 2. Most frequent emergency department diagnoses among study mothers in 2020 shown with their frequency in 2019.

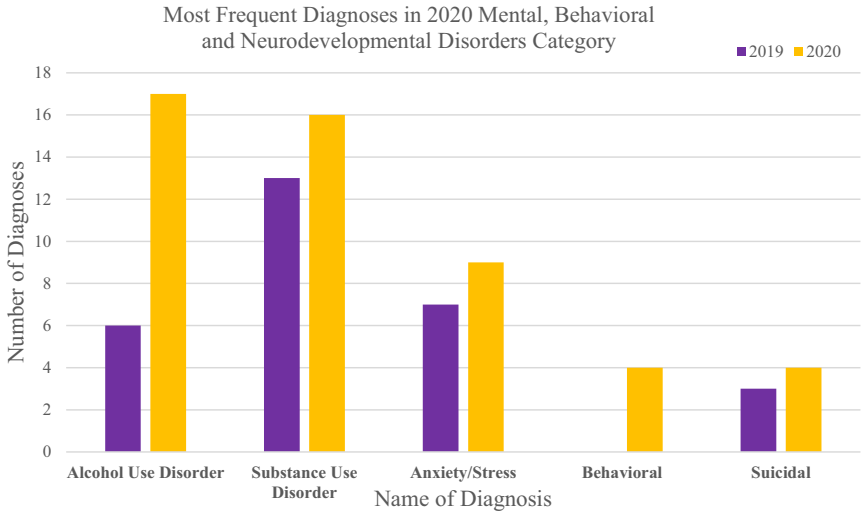

Figure 3. Top five most frequent diagnoses among all mothers in the study, foreign-born and US-born mothers in 2020 within the mental, behavioral, and neurodevelopmental disorders category, as defined by the International Classification of Diseases coding scheme and displayed next to their frequency in 2019.

visits of almost 30% from 2019 to 2020. This is less than what has been reported in the current literature, which documented reductions ranging from 40% to over 60%[3,22–24]; however, these studies examined changes in ED patterns over the first few months of the COVID-19 pandemic as opposed to the entire year. Our results offer a more longitudinal view of changes in ED patterns reflecting the various waves of the COVID-19 pandemic. The parent study also similarly found a reduction in outpatient clinic visits among the same maternal cohort,[8] consistent with current literature showing declining outpatient visits across the country.[25–27]

This raises the question of where the patients who would normally present to the ED went and how they received care. Many institutions expanded their outpatient telemedicine services during the pandemic, which served as one potential avenue to capture missing patients who would otherwise have presented to the ED. However, studies have found that the increase in telemedicine visits was not sufficient to offset the decline observed in the outpatient setting,[25,26] thus challenging the theory as to where ED visits were captured. The observed decrease in total ED visits during the pandemic without a comparable increase in alternative healthcare

services could have lingering effects on the continuity and accessibility of healthcare and subsequent health outcomes among this cohort of mothers.

Additionally, we found foreign-born mothers were underrepresented in ED encounters based on their baseline frequency in the full BBC cohort. They also had a greater percentage reduction in ED visits compared to US-born mothers. Results from the negative binomial regression confirmed this trend, again raising the question of where and how this population received care during the pandemic. The BBC participants born inside the US, who are Black or Hispanic, have a high school degree or less, or who are low income have higher rates of ED utilization, regardless of the year. Patterns of ED use among foreign-born individuals vary. Reasons for decreased use could be due to lack of access, fear due to undocumented status, and/or distrust or unfamiliarity with navigating the US healthcare system.[28,29]

Despite the overall decrease, the distribution of ED diagnoses did not change dramatically from 2019 to 2020. However, it is important to note that the baseline number of visits for some of the specific ED visit diagnoses was small, which had a larger impact on the relative percentage change. Visits for sickle cell-related crises remained the most common, followed by visits for abdominal pain and back pain in both 2019 and 2020. However, visits related to infectious disease, particularly those for COVID-19, showed an unsurprising increase. While the observed increase among foreign-born mothers was from 13 to 37, it did coincide with the beginning of the first wave of the pandemic, which is consistent with other studies.[24]

Interestingly, our study did demonstrate a trend of increasing ED visits for mental behavioral and neurodevelopmental disorders among mothers, specifically alcohol and substance use disorders. While the observed change was based on relatively smaller baseline numbers, emerging studies have demonstrated a higher incidence of stress, anxiety, and depression among the general population secondary to the COVID-19 pandemic,[5,30,31] and women particularly have been reported to be more susceptible to psychological distress.[17,32] Theories for the increased psychological strain are multifaceted; there is the direct impact of the disease itself including fear of infection, disease progression, death, and loss of loved ones.[32,33] There is also the associated stigma, stress related to job loss/security, and issues surrounding prevention, which includes social isolation, school closures, and lack of social support.[32] Our study reinforces these findings. While our study showed a trend toward increasing visits for substance use disorder and anxiety among mothers, there was a statistically significant increase in visits for alcohol use disorder consistent with other studies,[15,34] with one potential explanation of increased substance and alcohol use as a mechanism for coping with stress and anxiety related to the COVID-19 pandemic.[15] A recent study by Anderson et al also demonstrated a similar increase in mental health-related ED presentations during the pandemic, particularly among minority populations[35]; however, they did not specifically look at immigration status or a maternal population.

Notably, our study's observed increase in mental health-related visits was solely driven by US-born mothers, as visits for mental and behavioral disorders for foreign-born mothers were lower at baseline and demonstrated a decline compared to before the pandemic. Similar results were also seen in a study evaluating the effect of COVID-19 on outpatient mental health visits, with US-born mothers showing higher rates of visits.[8] This is consistent with research that has shown that despite the stress of migration, immigrants tend to experience fewer negative mental and behavioral health outcomes, often termed the "healthy migrant hypothesis," particularly when they immigrate at younger ages.[18,19,36] While there are nuances based on ethnicity and generational status, foreign-born individuals have been found to have lower rates of depressive disorders, anxiety disorders, and substance abuse disorder, with increased social support networks being theorized as one of the reasons for improved mental health outcomes,[18] which likely contributed to the pattern observed among mothers in our study.

COVID-19 has disproportionately affected people of color,[12,14] and based on our study this pattern remains true as it relates to mental health and substance use disorder. To our knowledge, no previous research has examined changes in ED utilization particularly as it pertains to visits for mental health and substance use disorder, among a minority maternal population. In contrast, a few studies have reported similar disproportionate rates of mental health and substance use disorders among Black and Hispanic patients in relation to the COVID-19 pandemic.[15] However, they do not differentiate between US- vs foreign-born individuals.

Through an analysis of ED utilization and diagnoses, our study suggests a correlation between the COVID-19 pandemic and increased psychological burden and substance use disorder among minority, low-income, primarily US-born mothers at greater risk for infection and indirect psychological/behavioral disturbance. Furthermore, results from our negative binomial regression model suggest that a larger sample size may help identify the differences in ED utilization among various race/ethnicity and birthplace combinations within our cohort. Further research should be done to determine specific ED patterns related to the immigrant population.

As health systems continue to face additional waves of the COVID-19 pandemic, our study suggests the need to invest in more substance use disorder and mental health resources as we simultaneously expand the capacity to manage those infected with COVID-19. Clinicians should remain vigilant in screening for signs of depression, anxiety, and increased

substance dependence in both inpatient and outpatient settings, particularly in low-income and minority populations. The ED should focus efforts on improving the care for a population that has already seen worse outcomes related to COVID-19 and traditionally encounter barriers to receiving treatment for mental health and substance use disorders. This means increasing the availability of substance use disorder counselors, counseling services, social workers, and rehabilitation programs and bolstering systems that refer ED patients to these services. Institutions should also expand the availability of outpatient services to capture these patients upstream of the ED visit to allow for timely intervention and to reduce ED utilization. Additionally, our findings show that the ED remains a critical access point for vulnerable populations, and there are significant differences in service needs among immigrant vs non-immigrant mothers; thus, we as practitioners must take a nuanced approach in both evaluating ED utilization and addressing the needs of these populations in our community.

LIMITATIONS

Our study focuses explicitly on low-income, urban, minority mothers; thus, our findings may not be generalizable to the larger US population or other populations with different demographic distributions. Nor is it representative of women as a whole, given that our cohort is comprised specifically of women who had given birth to children. Our data overall also relies on small baseline numbers, which had a greater impact on reported percentage changes. Additionally, our intra-pandemic period ran from January to December 2020, including two months that preceded the official declaration of the COVID-19 pandemic by the WHO. Thus, changes in ED utilization in those months may not solely reflect COVID-19. Of note, our study was conducted prior to the onset of widespread vaccination, which also would have impacted ED utilization. Finally, our data relies on the EHR records of study participants who presented to BMC. While unlikely, given that BMC is a comprehensive health system integrated within the Medicaid system, we cannot guarantee that this was the sole facility used by the participants. They may have received services or interacted with the healthcare system outside BMC; therefore, that data would not be represented.

CONCLUSION

Our study illustrates the importance of the ED as a safety net for healthcare access for minority maternal populations. It supports findings of the psychological burden of the COVID-19 pandemic, showing a need, particularly in minority US-born mothers, for expansion of substance use disorder resources, including inpatient and outpatient treatment centers, rehabilitation programs, and housing support. Our study also shows that immigrant populations have significantly different healthcare service needs and that alternatives for increased care access in the face of pandemics, such as telemedicine, may not be sufficient to appropriately address the needs of those in this community. Therefore, we must take a nuanced approach to better prepare our EDs and communities to handle the consequences of the ongoing pandemic and better plan to face future pandemics.

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REFERENCES

1. WHO. WHO Coronavirus (COVID-19) Dashboard. 2021. Available at: https://covid19.who.int/region/amro/country/us. Accessed August 12, 2022.
2. Golberstein E, Wen H, Miller BF. Coronavirus disease 2019 (COVID-19) and mental health for children and adolescents. *JAMA Pediatr*. 2020;174:819–20.
3. Westgard BC, Morgan MW, Vazquez-Benitez G, et al. An analysis of changes in emergency department visits after a state declaration during the time of COVID-19. *Ann Emerg Med*. 2020;76:595–601.
4. WHO. Impact of COVID-19 on people's livelihoods, their health and our food systems. 2020. Available at: 'https://www.who.int/news/item/13-10-2020-impact-of-covid-19-on-people's-livelihoods-their-health-and-our-food-systems. Accessed January 3, 2022.
5. Cullen W, Gulati G, Kelly BD. Mental health in the COVID-19 pandemic. *QJM:International J Med*. 2020;113:311–2.

6. Dopfer C, Wetzke M, Zychlinsky Scharff A, et al. COVID-19 related reduction in pediatric emergency healthcare utilization - a concerning trend. *BMC Pediatr*. 2020;20:427.
7. Lo J, Rae M, Amin K, et al. Telehealth has played an outsized role meeting mental health needs during the COVID-19 pandemic. 2022. Available at: https://www.kff.org/coronavirus-covid-19/issue-brief/telehealth-has-played-an-outsized-role-meeting-mental-health-needs-during-the-covid-19-pandemic/. Accessed August 30, 2022.
8. DiBari JD, Rusk SA, Li M, et al. The impact of COVID-19 on clinical encounters among minority women in Boston, MA [Conference Presentation]. APHA 2021 *Annual Meeting and Expo.* Denver, CO, USA 2021.
9. Rusk SA, DiBari J, Mason DM, et al. The impact of COVID-19 on psychiatric clinical encounters among low-income racially-diverse children. *J Child Psychol Psychiatry.*
10. Shim RS, Tierney M, Rosenzweig MH, et al. Improving behavioral health services in the time of COVID-19 and racial inequities. *NAM Perspect.* 2021.
11. Jung J, Manley J, Shrestha V. Coronavirus infections and deaths by poverty status: the effects of social distancing. *J Econ Behav Organ*. 2021;182:311–30.
12. Tai DBG, Shah A, Doubeni CA, et al. The disproportionate impact of COVID-19 on racial and ethnic minorities in the United States. *Clin Infect Dis*. 2021;72:703–6.
13. Finch WH and Hernández Finch ME. Poverty and Covid-19: rates of incidence and deaths in the United States during the rirst 10 weeks of the pandemic. *Front Sociol*. 2020;5.
14. Raifman MA and Raifman JR. Disparities in the population at risk of severe illness from COVID-19 by race/ethnicity and income. *Am J Prev Med*. 2020;59:137–9.
15. Czeisler M, Lane RI, Petrosky E, et al. Mental health, substance use, and suicidal ideation during the COVID-19 pandemic - United States, June 24–30, 2020. *Morb Mortal Wkly Rep*. 2020;69:1049–57.
16. McKnight-Eily LR, Okoro CA, Strine TW, et al. Racial and ethnic disparities in the prevalence of stress and worry, mental health conditions, and increased substance use among adults during the COVID-19 pandemic - United States, April and May 2020. *Morb Mortal Wkly Rep*. 2021;70:162–6.
17. Qiu J, Shen B, Zhao M, et al. A nationwide survey of psychological distress among Chinese people in the COVID-19 epidemic: implications and policy recommendations. *Gen Psychiatr*. 2020;33:e100213.
18. Alegría M, Álvarez K, DiMarzio K. Immigration and mental health. *Curr Epidemiol Rep*. 2017;4:145–55.
19. Salas-Wright CP, Vaughn MG, Goings TC, et al. Immigrants and mental disorders in the United States: new evidence on the healthy migrant hypothesis. *Psychiatry Res*. 2018;267:438–45.
20. Pearson C, Bartell T, Wang G, et al. Boston Birth Cohort profile: rationale and study design. *Precision Nutrition*. 2022;1:e00015.
21. CDC. CDC Museum COVID-19 Timeline. Available at: https://www.cdc.gov/museum/timeline/covid19.html. Accessed February 17, 2022.
22. Jeffery MM, D'Onofrio G, Paek H, et al. Trends in emergency department visits and hospital admissions in health care systems in 5 states in the first months of the COVID-19 pandemic in the US. *JAMA Intern Med*. 2020;180:1328–33.
23. Pines JM, Zocchi MS, Black BS, et al. Characterizing pediatric emergency department visits during the COVID-19 pandemic. *Am J Emerg Med*. 2021;41:201–4.
24. Hartnett KP, Kite-Powell A, DeVies J, et al. Impact of the COVID-19 pandemic on emergency department visits - United States, January 1, 2019-May 30, 2020. *Morb Mortal Wkly Rep.* 2020;69:699–704.
25. Cortez C, Mansour O, Qato DM, et al. Changes in short-term, long-term, and preventive care delivery in us office-based and telemedicine visits during the COVID-19 pandemic. *JAMA Health Forum*. 2021;2:e211529.
26. Patel SY, Mehrotra A, Huskamp HA, et al. Trends in outpatient care delivery and telemedicine during the COVID-19 pandemic in the US. *JAMA Internal Medicine*. 2021;181:388–91.
27. Whaley CM, Pera MF, Cantor J, et al. Changes in health services use among commercially insured US populations during the COVID-19 pandemic. *JAMA Network Open*. 2020;3:e2024984.
28. Tarraf W, Vega W, González HM. Emergency department services use among immigrant and non-immigrant groups in the United States. *J Immigr Minor Health*. 2014;16:595–606.
29. Derose KP, Escarce JJ, Lurie N. Immigrants and health care: sources of vulnerability. *Health Aff (Millwood)*. 2007;26:1258–68.
30. Talevi D, Socci V, Carai M, et al. Mental health outcomes of the CoViD-19 pandemic. *Riv Psichiatr*. 2020;55:137–44.
31. Vindegaard N and Benros ME. COVID-19 pandemic and mental health consequences: systematic review of the current evidence. *Brain Behav Immun*. 2020;89:531–42.
32. Semo BW and Frissa SM. The mental health impact of the COVID-19 pandemic: implications for Sub-Saharan Africa. *Psychol Res Behav Manag*. 2020;13:713–20.
33. Park SC and Park YC. Mental health care measures in response to the 2019 novel coronavirus outbreak in Korea. *Psychiatry Investig*. 2020;17:85–6.
34. Sun Y, Li Y, Bao Y, et al. Brief report: increased addictive internet and substance use behavior during the COVID-19 pandemic in China. *Am J Addict*. 2020;29:268–70.
35. Anderson KN, Radhakrishnan L, Lane RI, et al. Changes and Inequities in adult mental health–related emergency department visits during the COVID-19 pandemic in the US. *JAMA Psychiatry*. 2022;79:475–85.
36. Marks AK, Ejesi K, García Coll C. Understanding the U.S. immigrant paradox in childhood and adolescence. *Child Dev Perspect*. 2014;8:59–64.

Time to Treat the Climate and Nature Crisis as One Indivisible Global Health Emergency

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Over 200 health journals call on the United Nations, political leaders, and health professionals to recognise that climate change and biodiversity loss are one indivisible crisis and must be tackled together to preserve health and avoid catastrophe. This overall environmental crisis is now so severe as to be a global health emergency.

The world is currently responding to the climate crisis and the nature crisis as if they were separate challenges. This is a dangerous mistake. The 28th Conference of the Parties (COP) on climate change is about to be held in Dubai while the 16th COP on biodiversity is due to be held in Turkey in 2024. The research communities that provide the evidence for the two COPs are unfortunately largely separate, but they were brought together for a workshop in 2020 when they concluded that: "Only by considering climate and biodiversity as parts of the same complex problem…can solutions be developed that avoid maladaptation and maximize the beneficial outcomes."[1]

As the health world has recognised with the development of the concept of planetary health, the natural world is made up of one overall interdependent system. Damage to one subsystem can create feedback that damages another—for example, drought, wildfires, floods and the other effects of rising global temperatures destroy plant life, and lead to soil erosion and so inhibit carbon storage, which means more global warming.[2] Climate change is set to overtake deforestation and other land-use change as the primary driver of nature loss.[3]

Nature has a remarkable power to restore. For example, deforested land can revert to forest through natural regeneration, and marine phytoplankton, which act as natural carbon stores, turn over one billion tonnes of photosynthesising biomass every eight days.[4] Indigenous land and sea management has a particularly important role to play in regeneration and continuing care.[5]

Restoring one subsystem can help another—for example, replenishing soil could help remove greenhouse gases from the atmosphere on a vast scale.[6] But actions that may benefit one subsystem can harm another—for example, planting forests with one type of tree can remove carbon dioxide from the air but can damage the biodiversity that is fundamental to healthy ecosystems.[7]

The Impacts on Health

Human health is damaged directly by both the climate crisis, as the journals have described in previous editorials,[8,9] and by the nature crisis.[10] This indivisible planetary crisis will have major effects on health as a result of the disruption of social and economic systems—shortages of land, shelter, food, and water, exacerbating poverty, which in turn will lead to mass migration and conflict. Rising temperatures, extreme weather events, air pollution, and the spread of infectious diseases are some of the major health threats exacerbated by climate change.[11] "Without nature, we have nothing," was UN Secretary-General António Guterres's blunt summary at the biodiversity COP in Montreal last year.[12] Even if we could keep global warming below an increase of 1.5°C over pre-industrial levels, we could still cause catastrophic harm to health by destroying nature.

Access to clean water is fundamental to human health, and yet pollution has damaged water quality, causing a rise in water-borne diseases.[13] Contamination of water on land can also have far-reaching effects on distant ecosystems when that water runs off into the ocean.[14] Good nutrition is underpinned by diversity in the variety of foods, but there has been a striking loss of genetic diversity in the food system. Globally, about a fifth of people rely on wild species for food and their livelihoods.[15] Declines in wildlife are a major challenge for these populations, particularly in low- and middle-income countries. Fish provide more than half of dietary protein in many African, South Asian and small island nations, but ocean acidification has reduced the quality and quantity of seafood.[16]

Changes in land use have forced tens of thousands of species into closer contact, increasing the exchange of pathogens and the emergence of new diseases and pandemics.[17] People losing contact with the natural environment and the declining loss in biodiversity have both been linked to increases in noncommunicable, autoimmune, and inflammatory diseases and metabolic, allergic and neuropsychiatric disorders.[10,18] For Indigenous people, caring for and connecting with nature is especially important for their health.[19] Nature has also been an important source of medicines, and thus reduced diversity also constrains the discovery of new medicines.

Communities are healthier if they have access to high-quality green spaces that help filter air pollution, reduce air and ground temperatures, and provide opportunities for physical activity.[20] Connection with nature reduces stress, loneliness and depression while promoting social interaction.[21] These benefits are threatened by the continuing rise in urbanisation.[22]

Finally, the health impacts of climate change and biodiversity loss will be experienced unequally between and within countries, with the most vulnerable communities often bearing the highest burden.[10] Linked to this, inequality is also arguably fuelling these environmental crises. Environmental challenges and social/health inequities are challenges that share drivers and there are potential co-benefits of addressing them.[10]

A Global Health Emergency

In December 2022 the biodiversity COP agreed on the effective conservation and management of at least 30% percent of the world's land, coastal areas, and oceans by 2030.[23] Industrialised countries agreed to mobilise $30 billion per year to support developing nations to do so.[23] These agreements echo promises made at climate COPs.

Yet many commitments made at COPs have not been met. This has allowed ecosystems to be pushed further to the brink, greatly increasing the risk of arriving at 'tipping points', abrupt breakdowns in the functioning of nature.[2,24] If these events were to occur, the impacts on health would be globally catastrophic.

This risk, combined with the severe impacts on health already occurring, means that the World Health Organization should declare the indivisible climate and nature crisis as a global health emergency. The three pre-conditions for WHO to declare a situation to be a Public Health Emergency of International Concern[25] are that it: 1) is serious, sudden, unusual or unexpected; 2) carries implications for public health beyond the affected State's national border; and 3) may require immediate international action. Climate change would appear to fulfil all of those conditions. While the accelerating climate change and loss of biodiversity are not sudden or unexpected, they are certainly serious and unusual. Hence we call for WHO to make this declaration before or at the Seventy-seventh World Health Assembly in May 2024.

Tackling this emergency requires the COP processes to be harmonised. As a first step, the respective conventions must push for better integration of national climate plans with biodiversity equivalents.[3] As the 2020 workshop that brought climate and nature scientists together concluded, "Critical leverage points include exploring alternative visions of good quality of life, rethinking consumption and waste, shifting values related to the human-nature relationship, reducing inequalities, and promoting education and learning."[1] All of these would benefit health.

Health professionals must be powerful advocates for both restoring biodiversity and tackling climate change for the good of health. Political leaders must recognise both the severe threats to health from the planetary crisis as well as the benefits that can flow to health from tackling the crisis.[26] But first, we must recognise this crisis for what it is: a global health emergency.

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This Comment is being published simultaneously in multiple journals. For the full list of journals see: https://www.bmj.com/content/full-list-authors-and-signatories-climate-nature-emergency-editorial-october-2023

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REFERENCES

1. Otto-Portner H et al. Scientific outcome of the IPBES-IPCC co-sponsored workshop on biodiversity and climate change. 2021. Available at: https://zenodo.org/record/4659159.
2. Ripple WJ, Wolf C, Lenton TM, et al. Many risky feedback loops amplify the need for climate action. *One Earth.* 2023;6:86–91.
3. European Academies Science Advisory Council. Key Messages from European Science Academies for UNFCCC COP26 and CBD COP15.2021. Available at: https://easac.eu/publications/details/key-messages-from-european-science-academies-for-unfccc-cop26-and-cbd-cop15 . Accessed September 15, 2023.
4. Falkowski P. Ocean Science: The power of plankton. *Nature.* 2012;483(7387):S17-20.
5. Dawson NM, Coolsaet B, Sterling EJ, et al. The role of Indigenous peoples and local communities in effective and equitable conservation. *Ecology and Society.* 2021;26(3):19.
6. Bossio DA, Cook-Patton SC, Ellis PW, et al. The role of soil carbon in natural climate solutions. *Nature Sustainability.* 2020;3:391–8.
7. Levia DF, Creed IF, Hannah DM, et al. Homogenization of the terrestrial water cycle. *Nat Geosci.* 2020;13:656–8.
8. Atwoli L, Baqui AH, Benfield T, et al. Call for emergency action to limit global temperature increases, restore biodiversity, and protect health. *BMJ.* 2021;374:1734.
9. Atwoli L, Erhabor GE, Gbakima AA, et al. COP27 climate change conference: urgent action needed for Africa and the world. *BMJ.* 2022;379:02459.
10. WHO, UNEP, Convention on Biological D. Connecting Global Priorities: Biodiversity and Human Health: A State of Knowledge Review. 2015. Available at: https://www.cbd.int/health/SOK-biodiversity-en.pdf. Accessed January 10, 2023
11. Magnano San Lio R, Favara G, Maugeri A, et al. How Antimicrobial Resistance Is Linked to Climate Change: An Overview of Two Intertwined Global Challenges. *Int J Environ Res Public Health.* 2023;20(3):1681.
12. Jelskov U. 'Without nature, we have nothing': UN chief sounds alarm at key UN biodiversity event. UN News. 2022. Available at: https://news.un.org/en/story/2022/12/1131422. Accessed September 15, 2023.
13. WHO. State of the world's drinking water: an urgent call to action to accelerate progress on ensuring safe drinking water for all. 2022. Available at: https://apps.who.int/iris/rest/bitstreams/1474551/retrieve. Accessed July 25, 2023.
14. Comeros-Raynal MT, Brodie J, Bainbridge Z, et al. Catchment to sea connection: Impacts of terrestrial run-off on benthic ecosystems in American Samoa. Marine Pollution Bulletin. 2021;169:112530.
15. IPBES. Assessment report on the sustainable use of wild species. 2022. Available at: https://www.ipbes.net/sustainable-use-assessment. Accessed October 14, 2023.
16. Falkenberg LJ, Bellerby RGJ, Connell SD, et al. Ocean Acidification and Human Health. *Int J Environ Res Public Health.* 2020;17(12):4563.
17. Dunne D. Climate change 'already' raising risk of virus spread between mammals. 2022. Available at: https://www.carbonbrief.org/climate-change-already-raising-risk-of-virus-spread-between-mammals/. Accessed September 15, 2023.
18. Altveş S, Yildiz HK, Vural HC. Interaction of the microbiota with the human body in health and diseases. *Biosci Microbiota Food Health.* 2020;39:23–32.
19. Schultz R, Cairney S. Caring for country and the health of Aboriginal and Torres Strait Islander Australians. *Med J Aust.* 2017;207(1):8–10.
20. MacGuire F, Mulcahy E and Rossington B. The Lancet Countdown on Health and Climate Change - Policy brief for the UK. 2022. Available at: https://s41874.pcdn.co/wp-content/uploads/Lancet-Countdown-2022-UK-Policy-Brief_EN.pdf. Accessed September 15, 2023.
21. Wong FY, Yang L, Yuen JWM, et al. Assessing quality of life using WHOQOL-BREF: a cross-sectional study on the association between quality of life and neighborhood environmental satisfaction, and the mediating effect of health-related behaviors. *BMC Public Health.* 2018;18:1113.
22. Simkin RD, Seto KC, McDonald RI, Jetz W. Biodiversity impacts and conservation implications of urban land expansion projected to 2050. *Proc Natl Acad Sci U S A.* 2022;119: e2117297119.
23. Secretariat of the Convention on Biological Diversity. COP15: Nations Adopt Four Goals, 23 Targets for 2030 In Landmark UN Biodiversity Agreement. Convention on Biological Diversity. 2022. Available at: https://www.cbd.int/article/cop15-cbd-press-release-final-19dec2022. Accessed 15 September 2023.
24. Armstrong McKay DI, Staal A, Abrams JF, et al. Exceeding 1.5°C global warming could trigger multiple climate tipping points. *Science.* 2022;377(6611):eabn7950.
25. WHO guidance for the use of Annex 2 of the International Health Regulations (2005). In: World Health Organization [Internet]. [cited 5 Oct 2023]. Available at: https://www.who.int/publications/m/item/who-guidance-for-the-use-of-annex-2-of-the-international-health-regulations-(2005). Accessed January 10, 2023.
26. Consultation on Australia's first National Health and Climate Strategy. Available at: https://www.health.gov.au/news/consultation-on-australias-first-national-health-and-climate-strategy. Accessed July 25, 2023.

Is Two Better Than Three? A Systematic Review of Two-bag Intravenous N-acetylcysteine Regimens for Acetaminophen Poisoning

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Introduction: Acetaminophen poisoning is commonly treated by emergency physicians. First-line therapy is N-acetylcysteine (NAC), traditionally administered intravenously via a US Food and Drug Administration (FDA)-approved three-bag protocol in which each bag has a unique concentration and infusion duration. Recently, simplified, off-label two-bag NAC infusion protocols have become more common. The purpose of this review is to summarize the effectiveness and safety of two-bag NAC.

Methods: We undertook a comprehensive search of PubMed, EMBASE, and MEDLINE from inception to December 13, 2022, for articles describing human acetaminophen poisonings treated with two-bag NAC, defined as any regimen involving two discrete infusions in two separate bags. Outcomes included effectiveness (measured by incidence of liver injury); incidence of non-allergic anaphylactoid reactions (NAAR); gastrointestinal, cutaneous, and systemic reactions; treatments for NAARs; incidence of NAC-related medication errors; and delays or interruptions in NAC administration.

Results: Twelve articles met final inclusion, 10 of which compared two-bag NAC to the three-bag regimen. Nine articles evaluated the two-bag/20-hour regimen, a simplified version of the FDA-approved three-bag regimen in which the traditional first and second bags are combined into a single four-hour infusion. Nine articles assessed comparative effectiveness of two-bag NAC in terms of liver injury, most commonly assessed for by incidence of hepatotoxicity (aspartate aminotransferase or alanine aminotransferase >1,000 international units per liter). No difference in liver injury was observed between two-bag and three-bag regimens. Of nine articles comparing incidence of NAARs, eight demonstrated statistically fewer NAARs with two-bag regimens, and one showed no difference. In seven articles evaluating treatment for NAARs (antihistamines, corticosteroids, epinephrine), all showed that patients received fewer medications for NAARs with two-bag NAC. Three articles evaluated NAC-related medication errors; two demonstrated no difference, while one study evaluating only children showed fewer errors with two-bag NAC. Two studies evaluated delays and/or interruptions in NAC infusions; both favored two-bag NAC.

Conclusion: For patients with acetaminophen poisoning, two-bag NAC regimens appear to have similar outcomes to the traditional three-bag regimen in terms of liver injury. Two-bag NAC regimens are associated with fewer adverse events and fewer treatments for those events than the three-bag regimen and fewer interruptions in antidotal therapy. [West J Emerg Med. 2023;24(6)1131–1145.]

INTRODUCTION

Acetaminophen poisoning is frequently seen by emergency physicians in the United States and is commonly reported to US poison centers. In 2021, US poison centers advised in over 87,000 cases of acetaminophen poisoning.[1] Morbidity and mortality from acetaminophen poisoning are substantial. In the National Poison Data System (NPDS)—the national database owned and managed by America's Poison Centers (formerly known as the American Association of Poison Control Centers), containing data from all 55 accredited US poison centers—acetaminophen was the most common substance associated with poisoning fatalities in 2021, contributing to 419 deaths.[1] Acetaminophen is responsible for 50% of cases of acute liver failure (ALF) in the US each year, and acetaminophen-associated ALF accounts for approximately 7% of US liver transplants annually.[2,3]

N-acetylcysteine (NAC) has been the treatment of choice for acetaminophen poisoning for over four decades.[4,5] Originally developed as an oral antidote, NAC is now most commonly administered via the intravenous (IV) route after its approval by the US Food and Drug Administration (FDA) in 2004.[5] In the 2021 NPDS Annual Report, 29,377 patients received IV NAC, while only 1,909 received NAC via the oral route.[1] Controversy remains, however, on the optimal IV NAC regimen. The FDA-approved IV NAC regimen involves administering 300 milligrams per kilogram (mg/kg) of IV NAC over 21 hours via three separate IV infusion bags, each with its own unique concentration and infusion rate (Table 1). While this regimen is time-tested, it leads to interruptions in antidote infusion and is associated with dosing errors.[6] In addition, non-allergic anaphylactoid reactions (NAAR) frequently occur as a function of the large NAC dose administered in the first bag of the traditional protocol (Table 1).[7]

Over the past decade, evidence has emerged that a simplified two-bag IV NAC regimen is both safe and effective.[8–12] A two-bag regimen is appealing as it may minimize interruptions in care, medication errors, and the incidence of dose-related NAARs.[7] The traditional three-bag regimen, developed by Prescott and colleagues and first reported in 1977, involves a large initial bolus (150 mg/kg) of IV NAC over the first 15–60 minutes of treatment (which is when NAARs typically occur), whereas two-bag regimens generally extend the initial bolus of NAC over multiple hours (Table 1).[7,13] Since NAARs are typically dose-related, reducing the infusion rate from the initial 150 mg/kg bolus in the traditional three-bag protocol may contribute to a reduction in NAARs. Multiple two-bag regimens have been studied, but an up-to-date summary of the evidence supporting their use is lacking. The purpose of this report was to review and summarize the effectiveness and safety of

Table 1. Comparison of traditional three-bag intravenous N-acetylcysteine (NAC) regimen with two-bag NAC regimens.

Traditional 3-bag FDA-approved regimen ("Prescott protocol")	Bag 1 (administered over 15–60 minutes)	Bag 2 (administered over 4 hours)	Bag 3 (administered over 16 hours)
Dose	150 mg/kg in 200 mL D5W	50 mg/kg in 500 mL D5W	100 mg/kg NAC in 1,000 mL D5W
Simplified 2-bag, 20-hour regimen	Bag 1 (administered over 4 hours)		Bag 2 (administered over 16 hours)
Dose	200 mg/kg in 500 mL D5W		100 mg/kg in 1,000 mL D5W
SNAP* 12-hour IV NAC regimen	Bag 1 (administered over 2 hours)		Bag 2 (administered over 10 hours)
Dose	100 mg/kg in 200 mL D5W		200 mg/kg in 1,000 mL D5W

IV, intravenous; *NAC*, N-acetylcysteine; *FDA*, US Food and Drug Administration; *mL*, milliliter; *D5W*, dextrose 5% in sterile water; *mg*, milligram; *kg*, kilogram; *SNAP*, Scottish and Newcastle Antiemetic Pre-treatment for Paracetamol Poisoning, used in the United Kingdom with a unique treatment threshold (four-hour [APAP] = 100 mcg/mL nomogram line) compared to the United States (four-hour [APAP] = 150 mcg/mL nomogram line).

two-bag NAC regimens for acetaminophen poisoning. In the interest of precise pharmacologic nomenclature, we defined "two-bag NAC regimens" as any NAC regimen involving two discrete infusions in two separate bags (Table 1).[14] Regimens involving a single bag of NAC with the rate adjusted at various times were not included for analysis.

METHODS

Search Strategy

Three searches were undertaken. The first search, performed by the primary author (JBC) on December 13, 2022, duplicated a previously published search strategy by searching PubMed using the following terms: (((Acetylcysteine) OR (NAC) OR (n-acetylcysteine)) AND ((novel) OR (alternative) OR (simplified) OR (off-label))) AND (overdose).[15] The references of relevant articles were also reviewed by JBC for inclusion.

To ensure all relevant articles were included, we consulted a professional research librarian who performed two additional searches. First, PubMed was searched on December 14, 2022, using the following terms: (acetylcysteine) AND (acetaminophen poisoning) AND (safety). Second, a comprehensive search for English language articles was conducted using the EMBASE and MEDLINE libraries (separately, via EBSCOhost) (EBSCO Information Services, Ipswich, MA) from inception through December 14, 2022. The librarian crafted a search strategy to cover synonymous terms and phrases to retrieve pertinent articles related to human acetaminophen poisoning and NAC. The search strategy included the keywords noted above. Last, an outside expert in acetaminophen poisoning was also contacted to

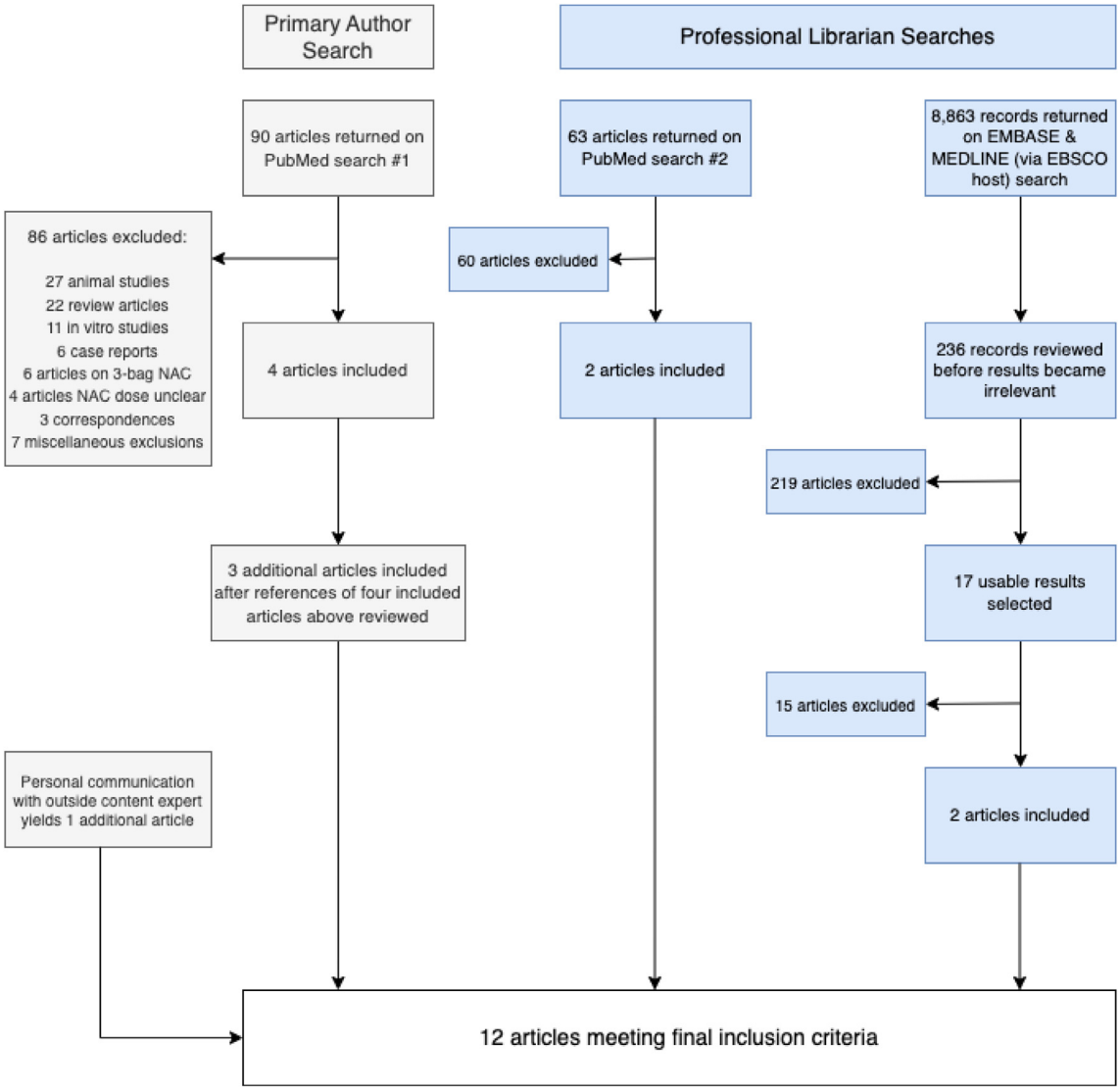

Figure 1. Screening process for article inclusion.
NAC, N-acetylcysteine.

ensure the three searches returned all relevant articles. The complete search strategy is outlined in Figure 1.

Inclusion Criteria

We sought to include articles containing data solely in human acetaminophen poisonings treated with two-bag NAC infusions. Editorials, commentaries, letters, case reports, and laboratory or animal data were excluded, as were articles on one- or three-bag NAC infusions. A single, board-certified emergency physician and medical toxicologist, working independently, reviewed the articles for inclusion and collected data from the articles. No automated tools were used.

Outcomes

Outcomes of interest assessed for included effectiveness (measured by liver injury), incidence of NAARs (gastrointestinal, cutaneous, and systemic), medications used to treat NAARs, incidence of medication errors, and delays or interruptions in NAC administration. Effects were measured in absolute differences, odds ratios, and number needed to treat (NNT) as reported by the authors. When not reported, NNT was calculated from raw data in the articles. Similarly, we manually calculated unadjusted odds ratios with 95% confidence intervals for NAARs based on data from the included articles (if available), and from this a forest plot was generated to better define the reported effect of two-bag vs three-bag NAC regimens on NAARs.

RESULTS

After initial searches and exclusion of irrelevant references (Figure 1), 11 articles met final inclusion criteria. Consultation with an outside expert yielded one additional article leaving 12 articles for final inclusion (Table 2), 10 of which compared 2-bag NAC regimens to the 3-bag regimen and two single-arm observational studies.[10,16] Nine articles evaluated the 2-bag/20-hour regimen, a simplified version of the FDA-approved 3-bag regimen in which the traditional first and second bags are combined into a single four-hour 200 mg/kg infusion (Table 1).[9–12,17–21] Two articles evaluated the Scottish and Newcastle Anti-emetic Pre-treatment for Paracetamol Poisoning (SNAP) protocol (Table 1).[8,22] A single case series of 40 children evaluated a unique regimen not elsewhere reported.[16]

Seven articles evaluated the incidence of NAARs as the primary outcome.[8–10,17–19,21] Three studies evaluated the incidence of hepatotoxicity as the primary outcome.[11,20,22] One study each evaluated delays in treatment and serum sodium as the primary outcome.[12,16] (Table 2) Nine articles assessed comparative effectiveness of two-bag NAC in terms of liver injury; liver injury was most commonly assessed for by incidence of hepatotoxicity (aspartate aminotransferase or alanine aminotransferase >1,000 international units per liter).[8,9,11,12,17,18,20–22] In all nine articles no difference in liver injury was observed between groups; in two articles, subgroup analyses favored the two-bag regimen.[12,21]

Nine articles assessed comparative effectiveness of two-bag NAC regarding incidence of NAARs (Table 3).[8,9,11,12,17–19,21,22] The definition of NAARs varied between studies; each study's NAARs definition is displayed in Table 3. All but one article demonstrated statistically fewer NAARs with two-bag regimens.[21] The single article demonstrating no difference in NAARs between two-bag and three-bag regimens studied 243 children (age <18 years) and reported fewer cutaneous NAARs associated with two-bag NAC in subgroup analysis.[21] Reductions in cutaneous and systemic NAARs were more common than reductions in gastrointestinal (GI) NAARs (Table 3). Eight comparative studies evaluated GI NAARs, three favored two-bag NAC while five showed no difference when comparing two-bag and three-bag regimens.[8,9,11,12,17–19,21] In contrast, seven studies evaluated cutaneous NAARs; all but one favored two-bag NAC regimens.[9,11,12,17–19,21,22] Seven articles evaluated use of anti-allergy medications to treat NAARs (antihistamines, corticosteroids, and epinephrine); all seven studies favored two-bag NAC regimens.[9,12,17–19,21,22] Four studies reported granular data on the use of anti-allergy medications; all four studies favored two-bag NAC.[9,19,21,2] A summary of calculated unadjusted odds ratios with 95% confidence intervals for NAARs, comparing two-bag and three-bag regimens, is displayed as a forest plot in Figure 2.

Three articles evaluated medication errors related to NAC; two demonstrated no difference, while one study evaluating only children showed fewer errors with two-bag NAC.[9,18,21] Two studies evaluated delays and/or interruptions in NAC infusions; both favored two-bag NAC.[12,18]

DISCUSSION

This systematic review demonstrates that two-bag NAC regimens have similar and, in some studies, non-inferior outcomes to the traditional three-bag regimen in terms of liver injury from acetaminophen poisoning while resulting in fewer adverse reactions, fewer treatments for adverse reactions, and fewer delays or interruptions in NAC infusions. Two-bag NAC regimens are associated with fewer adverse events, including cutaneous (eg, flushing, itching) and systemic (eg, bronchospasm, hypotension, angioedema) reactions.[8–12,17–19,22] Fewer GI side effects were observed with two-bag NAC as well, although this finding was less common.[8,11,12] Two-bag NAC infusion regimens may also result in fewer medication errors. Of the published two-bag regimens, the two-bag/20-hour regimen that combines bags one and two of the traditional FDA-approved three-bag regimen is the most studied (Table 1).

All but one study with comparative data favored two-bag NAC regimens over the traditional three-bag Prescott protocol, and the single negative study evaluated only

Table 2. Evidence for improved outcomes with two-bag intravenous N-acetylcysteine regimens.

Study (Total n = 14,618)	Study type	2-bag NAC regimen studied	Primary outcome	Outcomes			
				NAARs	Hepatotoxicity	Dosing errors	Delays in treatment
Studies evaluating NAARs as primary outcome							
Bateman et al. 2014 ("SNAP Trial")[8] (n = 217)	RCT (adults)	SNAP (n = 108) vs. Prescott Protocol (n = 109)	Reduction in vomiting (including retching or need for antiemetics) in first 2 hours (36.1% vs. 65.1%; aOR = 0.26, [97.5% CI: 0.13–0.52], NNT = 3)	Reduction in clinically relevant severe* NAARs (4.6% vs. 31%; aOR = 0.23, [97.5% CI: 0.12–0.43], NNT = 4)	No difference in 50% increase in ALT between the groups (12.9% vs. 9%; aOR = 0.60, [97.5% CI: 0.20–1.83])	NA	NA
Wong & Graudins. 2016[9] (n = 599)	Retrospective cohort	2-bag/20-hours (n = 210) vs. Prescott Protocol (n = 389)	Fewer overall NAARs (4.3% vs 10%, OR = 2.5, [95% CI: 1.1–5.8], NNT = 18)	Fewer severe** NAARs (0.5% vs. 1.8% [p < 0.01], NNT = 76)	No difference in hepatotoxicity (ALT >1,000 IU/L) (5.2% vs. 4.3%, p = 0.68, OR = 1.2, [95% CI: 0.55–2.63])	NA	NA
Isbister et al. 2016[10] (n = 654)	Prospective observational (no comparison except to historical data)	Modified 2-bag based on ingestion time (n = 654)	Frequency of systemic hypersensitivity reactions = 8% (95% CI: 6–10%), lower than most previously published prospective studies of the Prescott protocol.	GI side effects similar to historic rates	16 patients had an ALT >1,000 IU/L	Four errors related to NAC; three of which involved incorrect infusion rate of bag #1.	NA
McNulty et al. 2018[17] (n = 476)	Prospective data compared to historic controls	2-bag/20-hours (n = 163) vs. Prescott Protocol (n = 313)	Fewer NAARs; 14% vs 5% (difference: 9.4% [95% CI: 4.3–14.6%], p = 0.002, NNT = 11)	Fewer severe*** NAARs; 8% vs. 2% (difference: 6.1% [95% CI: 2.5 –9.8%], p = 0.007, NNT = 17) Fewer anti-allergy medications; 11% vs. 4% (difference: 6.9% [95% CI: 2.4–11.3%], p = 0.01, NNT = 15)	No difference in incidence of hepatotoxicity (4.8% vs. 3.7%)	NA	NA

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Table 2. Continued.

Study (Total n = 14,618)	Study type	2-bag NAC regimen studied	Primary outcome	Outcomes			
				NAARs	Hepatotoxicity	Dosing errors	Delays in treatment
Schmidt et al. 2018[18] (n = 767)	Retrospective cohort	2-bag/20-hours (n = 493) vs. Prescott Protocol (n = 274)	Fewer NAARs; 17% vs 4% (difference = −12.8%, 95% CI:−17.6%—8.0%, p < 0.01, NNT = 8)	Fewer severe NAARs (hypotension, edema, respiratory symptoms); 0.6% vs. 4% (p = 0.003, NNT = 30) Fewer cutaneous NAARs: 2% vs. 14% (p < 0.001, NNT = 9)	No difference in hepatotoxicity (4% vs. 4%, difference: 0%, 95% CI:−2.9%–3.0%)	Medication errors were rare (1%)	Fewer interruptions or delays in NAC; 5% vs. 12% (difference: 6.6% [95% CI: 2.2–10.9%], p = 0.002, NNT = 15)
Daoud et al. 2020[19] (n = 4,315)	Retrospective cohort	2-bag/20-hours (n = 2,951) vs. Prescott Protocol (n = 1,364)	2-bag/20 hour NAC protocol associated with significantly fewer NAARs requiring treatment. (OR = 0.36 [95%CI: 0.28–0.46], 4% vs. 10.4%, NNT = 16)	Fewer life-threatening reactions (severe hypotension or airway-threatening angioedema): 0.6% vs. 0.14% Meta-analysis conducted revealed fewer NAARs with 2-bag regimens published to date.	NA	NA	NA
Sudanagunta et al. 2023[21] (n = 243)	Retrospective cohort (children age <18 years)	2-bag/20-hours (n = 93) vs. Prescott Protocol (n = 150)	No overall difference in NAARs: 19% 2-bag vs. 23% 3-bag (p = 0.54)	NAARs Sub-analyses favoring 2-bag/20-hour protocol: Cutaneous NAARs: 2% vs. 10% (p = 0.02, NNT = 13) Fewer antihistamines administered for NAARs: 8% vs. 16% (p = 0.05, NNT = 13)	NA	Fewer NAC medication errors: 23% vs. 39% (p = 0.01, NNT = 7)	Majority of medication errors were due to timing defined as delays or pauses in NAC >1 hour
Studies evaluating hepatotoxicity as primary outcome							
Pettie et al. 2019[22] (n = 3,340)	Prospective observational	SNAP (n = 1,852) vs. Prescott Protocol (n = 1,488)	No difference in liver injury, synthetic dysfunction, or hepatotoxicity (peak ALT >1,000 IU/L)	Fewer antihistamines given for NAARs; 11.0% vs. 2.0% (difference 9.0% [95% CI: 7.3–10.7], NNT = 10)	4.3% Prescott Protocol vs. 3.6% SNAP (difference −0.7%; 95% CI: −2.1–0.6%)	NA	NA

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Table 2. Continued.

Study (Total n = 14,618)	Study type	2-bag NAC regimen studied	Primary outcome	Outcomes			
				NAARs	Hepatotoxicity	Dosing errors	Delays in treatment
Wong et al. 2020 ("2NAC study")[11] (n = 2,211*) *Single, acute ingestions included in non-inferiority analysis. 2,763 patients received NAC, however in 552 cases the dosing regimen was not specified	Retrospective cohort	2-bag/20-hours (n = 1,300) vs. Prescott Protocol (n = 911)	No difference in acute liver injury (peak ALT > 150 IU/L), regardless of time of presentation or peak [APAP].	Fewer NAARs; 7.1% vs. 1.3% (difference: 5.8% [95% CI: 4.0–7.6%], p < 0.0001, NNT = 18) Fewer GI side effects; 31% vs. 19% (p < 0.0001, NNT = 9)	No difference in hepatotoxicity (1.2% 2-bag vs. 1.6% 3-bag, difference: –0.4%, 95% CI: –1.75–0.91)	NA	NA
Syafira et al. 2022[20] (n = 887)	Retrospective cohort (only patients receiving NAC within 8 hours of ingestion	2-bag/20-hours (n = 191) vs. Prescott Protocol (n = 696)	No difference in acute liver injury (peak aminotransferase > 150 IU/L): 1.6% 2-bag vs. 2.2 – 2.9% 3-bag (difference, 0.6%, OR 0.7 [95%CI: 0.2–2.6])	NA	No difference in hepatotoxicity (peak ALT >1,000 IU/L) between groups. Significantly higher proportion of patients with elevated aminotransferases (peak aminotransferase > 40 IU/L) in one of two 3-bag regimen cohorts: 14.8% vs. 3.7% (difference, 11.1%, OR = 0.2 [95% CI: 0.01–0.5], NNT = 10)	NA	NA
Studies evaluating delays in treatment as primary outcome							
O'Callaghan et al. 2022[12] (n = 869)	Retrospective cohort	2-bag/20-hours (n = 598) vs. Prescott Protocol (n = 271)	Shorter median cumulative delays in NAC administration: 35 vs. 65 minutes (absolute difference: 30 minutes [95%CI: 20 – 33], p < 0.01)	Fewer GI side effects: 76% vs. 56% (p < 0.0001, NNT = 5) Fewer cutaneous NAARs: 4.2% vs. 10% (p < 0.0001, NNT = 18) Fewer systemic NAARs: 4.1% vs. 0.8% (p < 0.001, NNT = 31)	Higher median ALT (40 IU/L vs. 19 IU/L) in patients receiving the 3-bag regimen with delays > 3 hours	NA	Delays in NAC administration > 1 hour less common with 2-bag (31% vs. 51%, p < 0.01, NNT = 5)

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Table 2. Continued.

Study (Total n = 14,618)	Study type	2-bag NAC regimen studied	Primary outcome	Outcomes			
				NAARs	Hepatotoxicity	Dosing errors	Delays in treatment
Studies evaluating serum sodium levels as primary outcome							
Oakley et al. 2011[16] (n = 40)	Case series (children ≤17 years)	150 mg/kg over one hour, then 10 mg/kg/hr for 20 hours (n = 40)	Serum sodium remained in normal range using 0.45% saline as the NAC diluent rather than D5W to prevent iatrogenic hyponatremia in children.	18 patients (49%) had any adverse reaction.	NA	NA	NA

*Clinically significant NAARs: requiring drug treatment or interruption of NAC infusion.
**Severe NAARs: angioedema, bronchospasm, or hypotension.
***Severe NAARs: hypotension, dyspnea, swelling.
RCT, randomized controlled trial; *SNAP*, Scottish and Newcastle Antiemetic Pre-treatment for Paracetamol Poisoning; *NAC*, N-acetylcysteine; *OR*, odds ratio; *aOR*, adjusted odds ratio; *CI*, confidence interval; *NNT*, number needed to treat; *NAARs*, non-allergic anaphylactoid reactions, which in some studies include both gastrointestinal and systemic effects; *ALT*, alanine aminotransferase; *GI*, gastrointestinal; *D5W*, dextrose 5% in sterile water.

Table 3. Studies evaluating non-allergic anaphylactoid reactions in two-bag intravenous N-acetylcysteine regimens.

Study (Total N = 13,731)	Study type	2-bag NAC regimen studied	NAARs definitions	Specific NAARs			
				GI effects	Total NAARs and/or systemic NAARs	Skin-only reactions	Anti-allergy medications administered as treatment
Studies with comparative data evaluating NAARs as primary outcome							
Bateman et al 2014 ("SNAP Trial")[8] (n = 217)	RCT (adults)	SNAP (n = 108) vs. Prescott Protocol (n = 109)	Reduction in vomiting (including retching or need for antiemetics) in first 2 hours Anaphylactoid reactions, defined as need for treatment or NAC interruption; self-reported flushing, itchy skin, rash, chest pain, dyspnea, wheezing, tongue/lip swelling	Reduction in vomiting (including retching or need for antiemetics) in first 2 hours (36.1% vs. 65.1%; aOR = 0.26, [97.5% CI: 0.13–0.52], NNT = 3)	Reduction in clinically relevant severe* NAARs (4.6% vs. 31%; aOR = 0.23, [97.5% CI: 0.12–0.43], NNT = 4) Fewer total anaphylactoid reactions (54% vs. 75%)	NA	NA
Wong and Graudins. 2016[9] (n = 599)	Retrospective cohort	2-bag/20-hours (n = 210) vs. Prescott Protocol (n = 389)	NAARs classified into cutaneous (flushing, rash, urticaria. Wheals, itch) and more severe reactions including respiratory symptoms (bronchospasm, wheeze, dyspnea) and angioedema or cardiovascular instability (i.e., hypotension) GI symptoms included nausea or vomiting.	No difference in gastrointestinal side effects (2-bag = 41%, 3-bag = 39%)	Fewer severe** NAARs (0.5% vs. 1.8% [p < 0.01], NNT = 76) Fewer overall NAARs (4.3% vs 10%, OR = 2.5, [95% CI: 1.1–5.8], NNT = 18)	Fewer reactions (8%) with 2-bag compared to 3-bag (33%)	Assessed for but not reported
McNulty et al 2018[17] (n = 476)	Prospective data compared to historic controls	2-bag/20-hours (n = 163) vs. Prescott Protocol (n = 313)	Cohorts compared for adverse reactions to NAC (not further defined), or use of anti-allergy medications	No difference in gastrointestinal side effects (3-bag = 37%, 2-bag = 31%).	Fewer NAARs; 14% vs 5% (difference: 9.4% [95% CI: 4.3 – 14.6%], p = 0.002, NNT = 11) Fewer severe*** NAARs; 8% vs. 2% (difference: 6.1% [95% CI: 2.5 –9.8%], p = 0.007, NNT = 17)	No difference in skin-only reactions (3-bag = 6%, 2-bag = 3%, p = 0.12)	Fewer anti-allergy medications; 11% vs. 4% (difference: 6.9% [95% CI: 2.4 – 11.3%], p = 0.01, NNT = 15)

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Table 3. Continued.

Study (Total N = 13,731)	Study type	2-bag NAC regimen studied	NAARs definitions	Specific NAARs			
				GI effects	Total NAARs and/or systemic NAARs	Skin-only reactions	Anti-allergy medications administered as treatment
Schmidt et al 2018[18] (n = 767)	Retrospective cohort	2-bag/20-hours (n = 493) vs. Prescott Protocol (n = 274)	Cutaneous (flushing, rash, urticaria, wheals, itch), severe reactions (bronchospasm, wheeze, dyspnea) and angioedema or cardiovascular instability (i.e., hypotension). Intensity of symptoms rated as mild (aware of signs/ symptoms but easily tolerated), moderate (discomfort to interfere with usual activity), severe (incapacitating with inability to work or do usual activity) or unknown.	No difference in gastrointestinal side effects (3-bag = 1%, 2-bag = 0%).	Fewer NAARs; 17% vs 4% (difference = −12.8%, 95% CI:−17.6% – −8.0%, $p < 0.01$, NNT = 8) Fewer severe NAARs (hypotension, edema, respiratory symptoms); 0.6% vs. 4% ($p = 0.003$, NNT = 30)	Fewer cutaneous NAARs: 2% vs. 14% ($p < 0.001$, NNT = 9)	Assessed for but not reported
Daoud et al 2020[19] (n = 4,315)	Retrospective cohort	2-bag/20-hours (n = 2,951) vs. Prescott Protocol (n = 1,364)	Defined as a reaction requiring treatment with IV antihistamine and/or glucocorticoids	GI effects rare for both groups, no difference found: 2-bag = 0.24%, 3-bag = 0.51%, $p = 0.14$	2-bag/20 hour NAC protocol associated with significantly fewer NAARs requiring treatment. (OR = 0.36 [95%CI: 0.28 – 0.46], 4% vs. 10.4%, NNT = 16) Fewer life-threatening reactions (severe hypotension or airway-threatening angioedema): 0.6% vs. 0.14%	Fewer cutaneous reactions with 2-bag (2.9%) vs. 3-bag (7.7%), $p < 0.0001$	Fewer medications needed to treat NAARs with 2-bag (6.9%) vs. 3-bag (19.7%), $p < 0.0001$
Sudanagunta et al 2023[21] (n = 243)	Retrospective cohort (children age <18 years)	2-bag/20-hours (n = 93) vs. Prescott Protocol (n = 150)	NAARs divided into 4 organ systems (cutaneous, cardiovascular, GI, respiratory), keywords searched for in chart (e.g., urticaria, wheal, edema, bronchospasm, wheeze, nausea, vomiting, hypotension)	No difference in GI symptoms: (3-bag = 11%, 2-bag = 11%)	No overall difference in NAARs: 19% 2-bag vs. 23% 3-bag ($p = 0.54$)	Fewer cutaneous NAARs: 2% vs. 10% ($p = 0.02$, NNT = 13)	Fewer antihistamines administered for NAARs: 8% vs. 16% ($p = 0.05$, NNT = 13)

(*Continued on next page*)

Table 3. Continued.

Study (Total N = 13,731)	Study type	2-bag NAC regimen studied	NAARs definitions	Specific NAARs			
				GI effects	Total NAARs and/or systemic NAARs	Skin-only reactions	Anti-allergy medications administered as treatment
Studies with comparative data evaluating NAARs as a secondary outcome							
Pettie et al 2019[22] (n = 3,340)	Prospective observational	SNAP (n = 1,852) vs. Prescott Protocol (n = 1,488)	Antihistamine prescribing was used to estimate the rate of anaphylactoid reactions.	NA	Fewer antihistamines given for NAARs; 11.0% vs. 2.0% (ARR = 9.0% [95% CI: 7.3–10.7], NNT = 10)	NA	See total NAARs; sub-analysis of 37 patients receiving both regimens for multiple overdoses (198 admissions, 81 received 3-bag, 117 received SNAP), found NAARs occurred in 6.2% of 3-bag admissions and in 0.9% of SNAP admissions (ARR = 5.3%, 95% CI: 0.1–12.8%)
Wong et al 2020 ("2NAC study")[11] (n = 2,211*) *Single, acute ingestions included in non-inferiority analysis. 2,763 patients got NAC, however in 552 cases the dosing regimen was not specified	Retrospective cohort	2-bag/20-hours (n = 1,300) vs. Prescott Protocol (n = 911)	NAARs classified into cutaneous (flushing, rash, urticaria, itch), more severe reactions (bronchospasm, wheeze, dyspnea, angioedema, cardiovascular instability [i.e., hypotension]), and GI symptoms (nausea, vomiting, or both)	Fewer gastrointestinal side effects; 31% vs. 19% (p < 0.0001, NNT = 9)	Fewer Cutaneous and Systemic NAARs: combined data 7.1% vs. 1.3% (difference: 5.8% [95% CI: 4.0–7.6%], p < 0.0001, NNT = 18)	Fewer Cutaneous NAARs: (2-bag, 1.1% vs. 3-bag, 6.4%)	NA
O'Callaghan et al 2022[12] (n = 869)	Retrospective cohort	2-bag/20-hours (n = 598) vs. Prescott Protocol (n = 271)	Adverse reactions assessed in three categories: gastrointestinal (nausea/vomiting/ retching), cutaneous (rash/itch/flushing), and systemic (bronchospasm/ hypotension/ angioedema or administration of medications)	Fewer gastrointestinal side effects: 76% vs. 56% (p < 0.0001, NNT = 5)	Fewer systemic NAARs: 4.1% vs. 0.8% (p < 0.001, NNT = 31)	Fewer cutaneous NAARs: 4.2% vs. 10% (p < 0.0001, NNT = 18)	Assessed for but not reported individually

(*Continued on next page*)

Table 3. Continued.

Study (Total N = 13,731)	Study type	2-bag NAC regimen studied	NAARs definitions	Specific NAARs			
				GI effects	Total NAARs and/or systemic NAARs	Skin-only reactions	Anti-allergy medications administered as treatment
Single-arm studies evaluating non-allergic anaphylactoid reactions.							
Oakley et al 2011[16] (n = 40)	Case series (children ≤17 years)	150 mg/kg over one hour, then 10 mg/kg/hr for 20 hours (n = 40)	Not defined	11 patients (30%) had vomiting.	18 patients (49%) had any adverse reaction. One patient each (2.5%) had breathlessness, abdominal pain, and cough.	Four (11%) patients developed rash.	NA
Isbister et al 2016[10] (n = 654)	Prospective observational (no comparison except to historical data)	Modified 2-bag based on ingestion time (n = 654)	Primary outcome was proportion of patients with adverse reactions, including only GI symptoms (not further defined) and the proportion with systemic hypersensitivity reactions, defined as either skin only or non-immune mediated anaphylaxis as defined by NIAID-FAAN. Severe anaphylaxis reactions were defined by hypotension or hypoxia	Gastrointestinal side effects similar to historic rates (26.5%)	Frequency of systemic hypersensitivity reactions = 8% (95% CI: 6–10%), lower than most previously published prospective studies of the Prescott Protocol. 0.5% had severe anaphylaxis	8% had skin-only reactions	NA

*Clinically significant NAARs: requiring drug treatment or interruption of NAC infusion.
**Severe NAARs: angioedema, bronchospasm, or hypotension.
***Severe NAARs: hypotension, dyspnea, swelling.
RCT, randomized controlled trial; *SNAP*, Scottish and Newcastle Antiemetic Pre-treatment for Paracetamol Poisoning; *NAC* = N-acetylcysteine; *GI*, gastrointestinal, *OR*, odds ratio; *aOR*, adjusted odds ratio; CI, confidence interval; *NNT*, number needed to treat; *NAARs*, non-allergic anaphylactoid reactions, which in some studies include both gastrointestinal and systemic effects; *ALT*, alanine aminotransferase, *ARR*, absolute risk reduction, *NIAID-FAAN*, National Institute of Allergy and Infectious Diseases/ Food Allergy and Anaphylaxis Network.

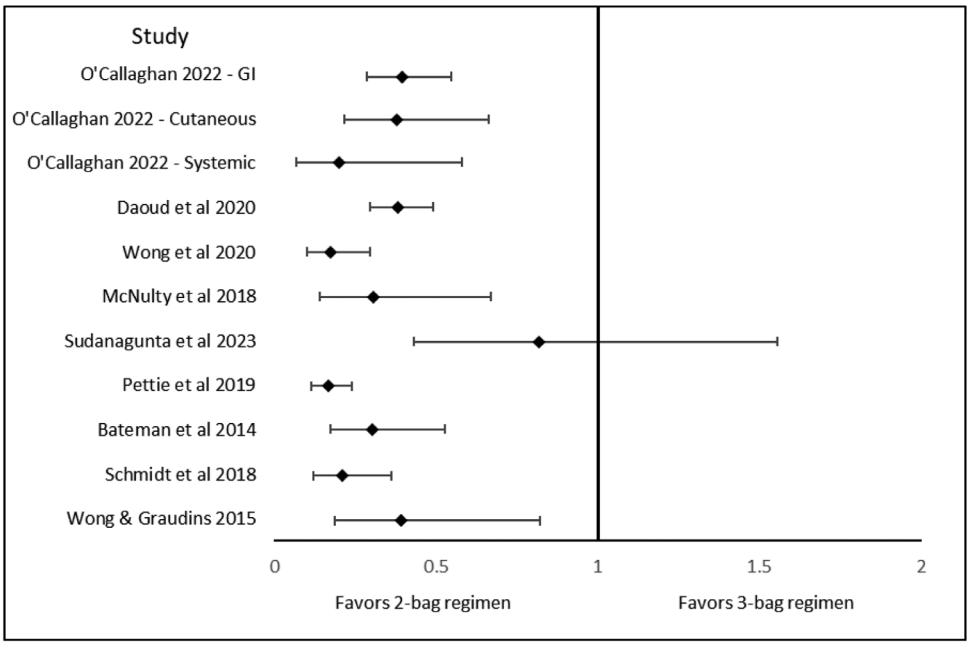

Figure 2. Forest plot of non-allergic anaphylactoid reactions (NAARs) reported in studies that compare two-bag to three-bag N-acetylcysteine infusions for acetaminophen poisoning.
Aggregate data for NAARs are displayed for all studies with the exception of O'Callaghan et al, as that study's data was reported by the individual organ system.

children, was relatively small in terms of enrollment, and did favor two-bag NAC when considering both cutaneous NAARs and anti-allergy medications administered.[21] Although NAARs definitions varied from study to study (Table 3), a decrease in both mild and severe effects was routinely associated with two-bag NAC regimens. For instance, the Scottish and Newcastle Antiemetic Pre-treatment for Paracetamol Poisoning (SNAP) trial (Table 1) demonstrated a reduction in severe NAARs from 31% to 4.6% when a two-bag protocol was used.[8] Follow-up data from implementation of the SNAP protocol saw a reduction in antihistamine use from 11% with the traditional three-bag protocol to 2% when SNAP was used in a study of 3,340 patients.[22] Similarly for the two-bag/20-hour protocol, prospectively collected data showed this protocol's implementation was associated with a reduction in severe NAARs from 8% with the three-bag regimen to 2%.[17] Multicenter implementation data evaluating the two-bag/20-hour protocol showed a drop in overall NAARs from 7.1% with the three-bag regimen to 1.3%.[11] Significant reductions in GI (76% to 56%), cutaneous (10% to 4.2%), and systemic (4.1% to 0.8%) NAARs were also seen after implementation of the two-bag/20-hour protocol.[12]

Because of the advantages noted above, many toxicologists and poison centers have adopted a two-bag NAC regimen as their first-line therapy for treating acetaminophen poisoning.[4,11,14,19,22,23] For practice in the United States, when considering a two-bag NAC regimen, a logical choice is the two-bag/20-hour protocol. While data on the SNAP protocol is robust, his data was generated in the United Kingdom, where the treatment threshold for NAC in acute acetaminophen poisoning is typically based upon a nomogram with a treatment line set at a four-hour acetaminophen concentration of 100 micrograms per milliliter (mcg/mL).[8,22] In comparison, in the US, a 150 mcg/mL threshold is commonly used, making the SNAP data less generalizable to US practice. The 2-bag/20-hour protocol is now a reliable international standard; it is now the first-line recommended regimen in Australia, New Zealand, Denmark, and Sweden.[19,24,25] We also believe the two-bag/20-hour regimen has the most robust body of supporting evidence, as its introduction in multiple studies results in consistent reductions in NAARs. To put this in clinical context, in 2021 987 patients reported to our regional poison center received IV NAC for acetaminophen poisoning. The NNT to reduce the incidence of various NAARs for the two-bag/20-hour regimen (Tables 2 and 3) is as low as five. Using a more conservative NNT of 11 from one study, if the two-bag/20-hour regimen were applied to our population of 987 patients, almost 90 fewer people would experience NAARs in one year.[17]

The adoption of the two-bag/20-hour protocol has several advantages for emergency physicians at the local level. Most IV NAC in the US is started in emergency departments (ED).[26] Beyond the obvious advantage of a simpler regimen with half the number of additional orders to place, fewer orders for pharmacy departments to process and bags to prepare, and fewer bags for nurses to hang, the two-bag/20-hour protocol is associated with a significant reduction in

NAARs (as noted above). Most NAARs with the traditional three-bag regimen occur in the first hour or two of the infusion, while the patient is in the ED.[7] A reduction in NAARs during this time period not only results in a better patient experience, it results in fewer interruptions for the emergency physician, nurse, and pharmacist to attend to a patient's adverse reaction, including reactions that require additional medication administration such as antihistamines, antiemetics, corticosteroids, and even epinephrine. Particularly important for the practice of emergency medicine, any systemwide change to the two-bag/20-hour NAC regimen will disproportionately affect the emergency medicine team, as all the changes from the traditional three-bag regimen occur in the first four hours of the infusion when the patient is likely to still be in the ED. Appropriate resource utilization and decreasing unnecessary treatments and interventions are increasingly important as ED boarding has become more common since the COVID-19 pandemic.[27] Regardless, for US emergency physicians adopting a two-bag NAC regimen, poison centers remain available 24 hours a day, 365 days a year, at 1-800-222-1222 to answer questions regarding modified NAC protocols.

LIMITATIONS

This review has several limitations. We searched only for English language articles. Our search may have been incomplete. For example, unlike some toxicologic reviews, we did not search academic meeting abstracts for data published only in abstract form, preferring to review only data that had undergone peer-review and was published in indexed journals.[28] We also did not include editorials, commentaries, letters, or individual case reports. We excluded editorials, commentaries, and letters because they were unlikely to include original data. Individual case reports were excluded because claims about effectiveness and safety are difficult to infer from single cases, and because case reports focusing on two-bag NAC regimens are exceedingly rare. Nevertheless, it is possible that meaningful data was missed in any of these forms of articles that could have affected our results.

Two-bag regimens are not adequately studied in unusual or extreme circumstances, such as massive overdoses.[29] The safety and effectiveness of two-bag NAC regimens in these uncommon circumstances are still understudied; however the same is true for the standard three-bag regimen. In large overdoses, such as overdoses of 30 grams or more, commensurate larger doses of NAC may be required, and consultation with a poison center or medical toxicologist is advised as tailored NAC dosing may be needed to prevent or treat liver injury.[30]

Additionally, we only evaluated two-bag NAC regimens. Data exists to support the use of a one-bag regimen in which the infusion rate of a single bag and concentration of NAC is changed at various points during treatment.[31–33] While we understand the rationale for this unique approach, evaluation of one-bag regimens was not the purpose of our review.

Last, NAARs may have been inadequately documented in some of the studies we reviewed. The detection of adverse drug reactions is often under-reported in retrospective studies when compared with subsequent clinical trials.[34,35] We suspect this may be the case with the present data. For example, GI side effect rates in the present studies range from 76% to <1%, suggesting they were under-reported in some studies, particularly those that are retrospective in nature. If GI side effects are poorly documented (or undocumented) in the medical records of study subjects, it may be difficult to detect a difference in nausea or vomiting after implementation of a two-bag NAC regimen. Such bias could lead to over- or under-estimating the effect of two-bag NAC regimens.

CONCLUSION

For patients with acetaminophen poisoning, two-bag NAC regimens appear to have similar outcomes to the traditional three-bag regimen in terms of liver injury while resulting in fewer adverse reactions, fewer treatments for adverse reactions, and fewer delays or interruptions in NAC infusions. A two-bag infusion may also result in fewer medication errors. Of the published two-bag regimens, the two-bag/20-hour regimen that combines bags one and two of the traditional three-bag regimen is the most studied.

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REFERENCES

1. Gummin DD, Mowry JB, Beuhler MC, et al. 2021 Annual Report of the National Poison Data System© (NPDS) from America's Poison Centers: 39th Annual Report. *Clin Toxicol*. 2022;60(12):1381–643.

2. Khan R, Koppe S. Modern management of acute liver failure. *Gastroenterol Clin North Am*. 2018;47(2):313–26.
3. Mendizabal M, Silva MO. Liver transplantation in acute liver failure: a challenging scenario. *World J Gastroenterol*. 2016;22(4):1523–31.
4. Hoyte C, Dart RC. Transition to two-bag intravenous acetylcysteine for acetaminophen overdose: a poison center's experience. *Clin Toxicol*. 2019;57(3):217–8.
5. Rumack BH, Bateman DN. Acetaminophen and acetylcysteine dose and duration: past, present and future. *Clin Toxicol*. 2012;50(2):91–8.
6. Hayes BD, Klein-Schwartz W, Doyon S. Frequency of medication errors with intravenous acetylcysteine for acetaminophen overdose. *Ann Pharmacother*. 2008;42(6):766–70.
7. Kerr F, Dawson A, Whyte IM, et al. The Australasian Clinical Toxicology Investigators Collaboration randomized trial of different loading infusion rates of N-acetylcysteine. *Ann Emerg Med*. 2005;45(4):402–8.
8. Bateman DN, Dear JW, Thanacoody HKR, et al. Reduction of adverse effects from intravenous acetylcysteine treatment for paracetamol poisoning: a randomised controlled trial. *Lancet*. 2014;383(9918):697–704.
9. Wong A, Graudins A. Simplification of the standard three-bag intravenous acetylcysteine regimen for paracetamol poisoning results in a lower incidence of adverse drug reactions. *Clin Toxicol*. 2016;54(2):115–9.
10. Isbister GK, Downes MA, Mcnamara K, et al. A prospective observational study of a novel 2-phase infusion protocol for the administration of acetylcysteine in paracetamol poisoning. *Clin Toxicol*. 2016;54(2):120–6.
11. Wong A, Isbister G, McNulty R, et al. Efficacy of a two bag acetylcysteine regimen to treat paracetamol overdose (2NAC study). *EClinicalMedicine*. 2020;20:100288.
12. O'Callaghan C, Graudins A, Wong A. A two-bag acetylcysteine regimen is associated with shorter delays and interruptions in the treatment of paracetamol overdose. *Clin Toxicol*. 2022;60(3):319–23.
13. Prescott LF, Park J, Ballantyne A, et al. Treatment of paracetamol (acetaminophen) poisoning with N-acetylcysteine. *Lancet*. 1977;2(8035):432–4.
14. Stanton M, Feldman R, Gummin D. Excess baggage in describing acetylcysteine regimens. *Clin Toxicol*. 2023;61(1):88–9.
15. Burnham K, Yang T, Smith H, et al. A review of alternative intravenous acetylcysteine regimens for acetaminophen overdose. *Expert Rev Clin Pharmacol*. 2021;14(10):1267–78.
16. Oakley E, Robinson J, Deasy C. Using 0.45% saline solution and a modified dosing regimen for infusing N-acetylcysteine in children with paracetamol poisoning. *Emerg Med Australas*. 2011;23(1):63–7.
17. McNulty R, Lim JME, Chandru P, et al. Fewer adverse effects with a modified two-bag acetylcysteine protocol in paracetamol overdose. *Clin Toxicol*. 2018;56(7):618–21.
18. Schmidt LE, Rasmussen DN, Petersen TS, et al. Fewer adverse effects associated with a modified two-bag intravenous acetylcysteine protocol compared to traditional three-bag regimen in paracetamol overdose. *Clin Toxicol*. 2018;56(11):1128–34.
19. Daoud A, Dalhoff KP, Christensen MB, et al. Two-bag intravenous N-acetylcysteine, antihistamine pretreatment and high plasma paracetamol levels are associated with a lower incidence of anaphylactoid reactions to N-acetylcysteine. *Clin Toxicol*. 2020;58(7):698–704.
20. Syafira N, Graudins A, Yarema M, et al. Comparing development of liver injury using the two versus three bag acetylcysteine regimen despite early treatment in paracetamol overdose. *Clin Toxicol*. 2022;60(4):478–85.
21. Sudanagunta S, Camarena-Michel A, Pennington S, et al. Comparison of two-bag versus three-bag N-acetylcysteine regimens for pediatric acetaminophen toxicity. *Ann Pharmacother*. 2023;57(1):36–43.
22. Pettie JM, Caparrotta TM, Hunter RW, et al. Safety and efficacy of the SNAP 12-hour acetylcysteine regimen for the treatment of paracetamol overdose. *EClinicalMedicine*. 2019;11:11–7.
23. Stanton MT, Kostic MA, Theobald JL, et al. Wisconsin Poison Center intravenous N-acetylcysteine dosing recommendations in acetaminophen toxicity. *J Pharm Society of Wisconsin*. 2018;47–9.
24. Chiew AL, Reith D, Pomerleau A, et al. Updated guidelines for the management of paracetamol poisoning in Australia and New Zealand. *Med J Aust*. 2020;212(4):175–83.
25. Nordmark Grass J, Lindeman E, Höjer J, et al. [Simplified N-acetylcysteine treatment after paracetamol overdose - new recommendations from Swedish Poisons Information Centre]. *Lakartidningen*. 2019;116.
26. Ershad M, Naji A, Vearrier D.N-acetylcysteine. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing; 2023.
27. Janke AT, Melnick ER, Venkatesh AK. Hospital occupancy and emergency department boarding during the COVID-19 pandemic. *JAMA Netw Open*. 2022;5(9):e2233964.
28. Gosselin S, Juurlink DN, Kielstein JT, et al. Extracorporeal treatment for acetaminophen poisoning: recommendations from the EXTRIP workgroup. *Clin Toxicol*. 2014;52(8):856–67.
29. Hoffman RS. Acetylcysteine for paracetamol: Will one size ever fit all? *EClinicalMedicine*. 2020;20:100314.
30. Hendrickson RG. What is the most appropriate dose of N-acetylcysteine after massive acetaminophen overdose? *Clin Toxicol*. 2019;57(8):686–91.
31. Johnson MT, McCammon CA, Mullins ME, et al. Evaluation of a simplified N-acetylcysteine dosing regimen for the treatment of acetaminophen toxicity. *Ann Pharmacother*. 2011;45(6):713–20.
32. Shah KR, Beuhler MC. Single bag high dose intravenous N-acetylcysteine associated with decreased hepatotoxicity compared to triple bag intravenous N-acetylcysteine in high-risk acetaminophen ingestions. *Clin Toxicol*. 2022;60(4):493–8.
33. Baumgartner K, Filip A, Liss D, et al. N-acetylcysteine for acetaminophen toxicity: The one-bag regimen. *Br J Clin Pharmacol*. 2021;87(5):2399–400.

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