Title

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Journal

Annals of the American Thoracic Society, 18(1)

ISSN

2329-6933

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Publication Date

2021

DOI

10.1513/annalsats.201912-872oc

Peer reviewed

Association of Race and Ethnicity with Sedation Management in Pediatric Intensive Care

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Abstract

Rationale: Racial disparities in pain management have been previously reported for children receiving emergency care.

Objectives: To determine whether patient race or ethnicity is associated with the broader goal of pain management and sedation among pediatric patients mechanically ventilated for acute respiratory failure.

Methods: Planned secondary analysis of RESTORE (Randomized Evaluation of Sedation Titration for Respiratory Failure). RESTORE, a cluster-randomized clinical trial conducted in 31 U.S. pediatric intensive care units, compared protocolized sedation management (intervention arm) with usual care (control arm). Participants included 2,271 children identified as non-Hispanic white (white, $n = 1,233$), non-Hispanic Black (Black, $n = 502$), or Hispanic of any race (Hispanic, $n = 536$).

Results: Within each treatment arm, neither opioid nor benzodiazepine selection, nor cumulative dosing, differed significantly among race and ethnicity groups. Black patients experienced fewer days with an episode of pain (compared with white patients in the control arm and with Hispanic patients in the intervention arm) and experienced less iatrogenic withdrawal syndrome (compared with white patients in either arm or with Hispanic patients in the intervention arm). The percentage of days awake and calm while intubated was not significantly different in pairwise comparisons by race and ethnicity groups in either the control arm (median: white, 75%; Black, 71%; Hispanic, 75%) or the intervention arm (white, 86%; Black, 88%; Hispanic, 85%).

Conclusions: Across multiple measures, our study found scattered differences in sedation management among critically ill Black, Hispanic, and white children that did not consistently favor any group. However, racial disparities related to implicit bias cannot be completely ruled out.

Clinical trial registered with clinicaltrials.gov (NCT 00814099).

Keywords: child; disparities; respiration; artificial; withdrawal

(Received in original form December 3, 2019; accepted in final form August 10, 2020)

A complete list of the RESTORE Study Investigators may be found before the beginning of the References.

Supported by grants from the National Heart, Lung, and Blood Institute and the National Institute of Nursing Research, National Institutes of Health (U01 HL086622 and U01 HL086649). The project described was partially supported by the National Center for Advancing Translational Sciences, National Institutes of Health (UL1 TR000002).

Author Contributions: J.E.N. conceptualized and designed the analyses, interpreted the analyses, drafted the initial manuscript, and reviewed and revised the manuscript. J.G.J. interpreted the analyses and reviewed and revised the manuscript. J.A. and C.B. collected data and critically reviewed the manuscript. L.A.A. and C.U. completed the statistical analysis and reviewed and revised the manuscript. D.W. and M.A.Q.C. designed the study and critically reviewed and revised the manuscript for data accuracy and important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Data sharing statement: De-identified individual participant data (including data dictionaries) that underlie the results reported in this article will be made available to researchers who provide a methodologically sound proposal. Proposals should be submitted jointly to curley@nursing.upenn.edu and david.wypij@cardio.chboston.org until the data are deposited into the Data Repository managed by the National Heart, Lung, and Blood Institute Biological Specimen and Data Repository Information Coordinating Center.

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Ann Am Thorac Soc Vol 18, No 1, pp 93–102, Jan 2021

DOI: 10.1513/AnnalsATS.201912-872OC
Internet address: www.atsjournals.org

There is strong, but not entirely consistent, evidence of racial and ethnic disparities in access to, provision of, and outcomes for clinical care for a wide variety of conditions in both adult and pediatric populations (1–7). Among these well-documented disparities is differential treatment of pain in adult patients (8–11). In pediatric populations, studies exploring treatment of abdominal or appendicitis pain consistently found Black children receive less adequate treatment for pain during emergency care (12–15). Conversely, no racial disparities in pediatric perioperative pain management were detected when white patients were compared with Black patients in one instance and to a broad category of "minority" patients in another (16, 17). Further information is required to better understand pain management disparities in diverse pediatric environments, including the intensive care unit (ICU).

In the context of critical care for mechanically ventilated children, the broader goal is optimal control of both pain and agitation while minimizing sedation-related adverse events, including excessive medication. The importance of this goal is emphasized by emerging evidence that greater exposure to sedation and pain medications in the pediatric ICU is associated with long-term cognitive and functional morbidity (18, 19). To our knowledge, no studies have investigated racial and ethnic disparities in achieving this broader goal. Our aim was to determine whether patient race or ethnicity is associated with the management of pain and sedation among infants and children mechanically ventilated for acute respiratory failure in the pediatric ICU.

Methods

We report a planned secondary analysis of the RESTORE (Randomized Evaluation of Sedation Titration for Respiratory Failure) study (20), a cluster-randomized trial that evaluated the efficacy and safety of a nurse-directed, goal-driven sedation algorithm. Sedation management of pain and agitation either relied on local usual care methods (14 pediatric ICUs) or a sedation intervention algorithm (17 pediatric ICUs). The methods and results of RESTORE have been comprehensively reported elsewhere (20, 21). Previous reports have also analyzed racial and ethnic differences in trial participant recruitment (22).

Children eligible for enrollment in RESTORE were at least 2 weeks old (42-wk postgestational age) and less than 18 years old who were intubated and mechanically ventilated for acute lung disease. All participating institutions were provided with training in the use of the study methods for the same pediatric-specific, standard, and valid assessment of pain (23–25), sedation (26), and iatrogenic withdrawal (27), for which interrater reliability was demonstrated (28). Reliability was achieved at study initiation and maintained throughout the period of study. The study was approved by each participating hospital's institutional review board, and standard procedures for obtaining consent and assent were followed, including use of appropriate interpretation services for Spanish-speaking families.

Defining Ethnicity and Sedation Management and Ethnicity

Identification of race and ethnicity was obtained from information in the medical record, using site-specific methods or the mother's race and ethnicity if no site-specific recommendations were made. Ethnicity was categorized into three groups: Hispanic, non-Hispanic, or unknown. Race and ethnicity were combined into the three groups compared in analyses reported below: non-Hispanic white (white), non-Hispanic Black (Black), and Hispanic of any race (Hispanic). All races and ethnicities other than these three groups were excluded from the analysis because insufficient numbers were available to permit meaningful analysis.

Outcomes

The primary outcome assessed sedation profiles using four categories of measures: *1*) sedatives administered; *2*) wakefulness, pain, and agitation; *3*) occurrence of iatrogenic withdrawal syndrome; and *4*) sedation-related adverse events through study discharge (72 h after the last opioid dose, hospital discharge, or study Day 28). Additional analyses conducted only in the intervention arm used the State Behavioral Scale (SBS) (26) to examine agreement between achieved scores (daily modal SBS scores) and target scores during the acute, titration, and weaning phases of the trajectory of illness.

Statistical Methods

Primary analyses were conducted in both the control arm, in which sedation practices were left to the discretion of the care providers, and in the intervention arm; because target sedation levels were assigned in the intervention arm, additional analyses were conducted in those patients only. Race and ethnicity groups were compared using linear, logistic, cumulative logit, or proportional hazards regression for log-transformed continuous (except for the percentage-of-study-days variables), binary, ordinal, or time-to-event variables, respectively, controlling for pediatric ICU as a cluster variable using generalized estimated equations with the working-independence assumption. When comparing race and ethnicity groups with repeated days of outcomes (SBS scores) per patient, we controlled for patient as a cluster variable instead. Because of three pairwise comparisons, a Bonferroni correction was applied, and only pairwise P values less than 0.0167 (=0.05 / 3) were deemed to indicate statistically significant differences between the race and ethnicity groups being compared. Comparisons of sedation profiles were adjusted for age group, baseline functional impairment (baseline Pediatric Overall Performance Category score >1), Pediatric Risk of Mortality III score from first 12 hours in the pediatric ICU, and primary reason for intubation. All data analyses were performed using SAS software, version 9.4 (SAS Institute Inc.).

Results

Of the 2,449 individuals who participated in RESTORE, 1,233 were white (50.3%), 502 were Black (20.5%), and 536 were Hispanic (21.9%). For 178 individuals (7.3%), data describing ethnicity or race were unknown or missing, or the individuals identified with some other racial category; these individuals were not included in analyses reported here. Although the control and intervention arms of the cluster-randomized clinical trial enrolled approximately equal numbers of participants (1,139 and 1,132 in these analyses, respectively), there were fewer Black patients enrolled at hospitals implementing the intervention ($n=152$) than in hospitals allocated to the control arm ($n=350$). As reported elsewhere (22),

this reflects, in part, decreased availability and recruitment of Black patients in hospitals where clinical care was going to be modified by active research. As a corollary, more Hispanic patients participated at the intervention hospitals ($n = 349$) than at the usual-care hospitals ($n = 187$).

Males comprised 55% of our cohort, and the mean age was 4.8 years old. There were scattered differences in the sociodemographic and clinical characteristics of patients among the three race and ethnicity groups after stratification by study arm (control vs. intervention) (Table 1). In general, white patients were older and, in the control arm specifically, were also more likely to have baseline cognitive or functional impairment compared with Black patients. In the control arm, white patients were less likely to have airways disease than Black and Hispanic patients.

Table 2 summarizes the sedation profiles for patients in the control arm. The preponderance of measures quantifying sedation profiles demonstrated no differences by race and ethnicity. There were no differences in opioid and benzodiazepine selection or cumulative dosing, other measures of benzodiazepine exposure, or the use of most secondary sedatives. In addition, the duration of mechanical ventilation in patients extubated by study Day 28 did not differ between race and ethnicity groups (data not shown). The only racial and ethnic differences in sedatives administered were in three measures of opioid exposure and in the use of ketamine as a secondary sedative. The number of opioid exposure days was significantly higher in white patients than in Black patients (median, 11 [interquartile range (IQR), 5–23] vs. 9 [4–20]), whereas the percentage of Black patients receiving continuous infusions of opioids was higher than in white patients (92% vs. 87%). The maximum daily number of one-time or as-needed opioid doses was statistically significantly higher in white patients than in Hispanic patients (7 [5–10] vs. 6 [3–9]), although this difference is unlikely to be clinically important. Ketamine was more frequently used as a secondary sedative in Black patients than in white patients (35% vs. 27%). Measures of wakefulness, pain, and agitation demonstrated some racial and ethnic differences. Specifically, the percentage of study days with an episode of pain defined by a pain score ≥ 4 was higher in white patients than in Black patients (median, 25% [IQR, 6–50%] vs. 19% [0–33%]). The percentage of days awake and calm while intubated was different among race and ethnicity groups in the control arm overall ($P = 0.03$), but none of the pairwise comparisons reached statistical significance at $P < 0.0167$

Table 1. Baseline characteristics of patients by race and ethnicity group and treatment arm

Characteristic	Non-Hispanic White	Non-Hispanic Black	Hispanic of Any Race	*P* Value*
Control arm (usual care)	*n* = 602	*n* = 350	*n* = 187	
Male sex, *n* (%)	323 (54)	198 (57)	111 (59)	0.21
Age, *n* (%)				<0.001†‡
2 wk to 1.99 yr	239 (40)	173 (49)	99 (53)	
2.00 to 5.99 yr	110 (18)	76 (22)	40 (21)	
6.00 to 17.99 yr	253 (42)	101 (29)	48 (26)	
Cognitive impairment (baseline PCPC > 1), *n* (%)	172 (29)	67 (19)	46 (25)	<0.001†
Functional impairment (baseline POPC > 1), *n* (%)	206 (34)	81 (23)	55 (29)	<0.001†
PRISM III-12 score, median (IQR)	9 (5–14)	9 (5–14)	8 (4–13)	0.74
Primary reason for intubation, *n* (%)				<0.001†‡
Airways disease§	148 (25)	124 (35)	74 (40)	
Parenchymal disease‖	454 (75)	226 (65)	113 (60)	
Intervention arm (sedation protocol)	*n* = 631	*n* = 152	*n* = 349	
Male sex, *n* (%)	336 (53)	79 (52)	200 (57)	0.56
Age, *n* (%)				<0.001‡¶
2 wk to 1.99 yr	338 (54)	82 (54)	237 (68)	
2.00 to 5.99 yr	88 (14)	25 (16)	45 (13)	
6.00 to 17.99 yr	205 (32)	45 (30)	67 (19)	
Cognitive impairment (baseline PCPC > 1), *n* (%)	153 (24)	28 (18)	78 (22)	0.20
Functional impairment (baseline POPC > 1), *n* (%)	187 (30)	38 (25)	90 (26)	0.36
PRISM III-12 score, median (IQR)	6 (3–12)	6 (3–12)	6 (3–11)	0.61
Primary reason for intubation, *n* (%)				0.83
Airways disease§	268 (42)	69 (45)	159 (46)	
Parenchymal disease‖	363 (58)	83 (55)	190 (54)	

Definition of abbreviations: IQR = interquartile range; PCPC = Pediatric Cerebral Performance Category; POPC = Pediatric Overall Performance Category; PRISM III-12 = Pediatric Risk of Mortality III score from first 12 hours in the pediatric intensive care unit.

**P* values for the comparisons between groups were calculated using logistic, cumulative logit, and linear regression accounting for pediatric intensive care unit as a cluster variable using generalized estimating equations for binary, ordinal, and log-transformed continuous variables, respectively.

†$P < 0.0167$, non-Hispanic white patients versus non-Hispanic Black patients.

‡$P < 0.0167$, non-Hispanic white patients versus Hispanic patients of any race.

§Airways disease includes bronchiolitis, asthma or reactive airway disease, laryngotracheobronchitis, and pertussis.

‖Parenchymal disease includes pneumonia, acute respiratory failure related to sepsis, aspiration pneumonia, pulmonary edema, thoracic trauma, acute respiratory failure after bone marrow transplant, pulmonary hemorrhage, acute chest syndrome and/or sickle cell disease, and acute exacerbation lung disease (cystic fibrosis or bronchopulmonary dysplasia).

¶$P < 0.0167$, non-Hispanic Black patients versus Hispanic patients of any race.

Table 2. Sedation profiles for control arm (usual care) patients by race and ethnicity group

Variable	Non-Hispanic White (*n* = 602)	Non-Hispanic Black (*n* = 350)	Hispanic of Any Race (*n* = 187)	*P* Value*
Sedatives administered				
Primary opioid agent, *n* (%)				0.47
Morphine	102 (17)	51 (15)	39 (21)	
Fentanyl	488 (81)	291 (83)	145 (78)	
Hydromorphone	6 (1)	4 (1)	0	
None	6 (1)	4 (1)	3 (2)	
Opioid exposure				
Peak daily dose, median (IQR), mg/kg	3.9 (1.9–6.9)	4.2 (2.3–7.0)	4.5 (2.0–7.5)	0.77
Cumulative dose, median (IQR), mg/kg	18.6 (5.6–54.9)	16.0 (5.1–47.9)	19.2 (5.9–62.4)	0.51
Number of exposure days, median (IQR)	11 (5–23)	9 (4–20)	11 (5–20)	0.02†
Continuous infusions, *n* (%)	526 (87)	322 (92)	165 (88)	0.001†
Scheduled intermittent doses, *n* (%)	278 (46)	144 (41)	95 (51)	0.15
Maximum daily number of one-time or PRN doses, median (IQR)	7 (5–10)	7 (4–10)	6 (3–9)	0.02‡
Primary benzodiazepine agent, *n* (%)				0.24
Midazolam	515 (86)	287 (82)	145 (78)	
Lorazepam	83 (14)	61 (17)	41 (22)	
None	4 (<1)	2 (<1)	1 (<1)	
Benzodiazepine exposure				
Peak daily dose, median (IQR), mg/kg	3.3 (1.5–6.6)	3.0 (1.6–6.6)	3.6 (1.7–7.4)	0.53
Cumulative dose, median (IQR), mg/kg	14.3 (4.6–45.3)	13.3 (3.6–35.1)	14.9 (5.6–47.7)	0.16
Continuous infusions, *n* (%)	487 (81)	268 (77)	143 (76)	0.87
Scheduled intermittent doses, *n* (%)	308 (51)	161 (46)	101 (54)	0.32
Maximum daily number of one-time or PRN doses, median (IQR)	7 (4–9)	6 (4–9)	5 (3–8)	0.07
Secondary sedatives, *n* (%)				
Dexmedetomidine	300 (50)	166 (47)	90 (48)	0.58
Propofol	77 (13)	36 (10)	16 (9)	0.57
Barbiturates	108 (18)	60 (17)	45 (24)	0.12
Ketamine	163 (27)	122 (35)	58 (31)	0.01†
Methadone	177 (29)	114 (33)	53 (28)	0.68
Clonidine	88 (15)	42 (12)	26 (14)	0.44
Number of different sedative classes received, median (IQR)	3 (2–4)	3 (2–4)	3 (2–4)	0.78
Antidelirium medications, *n* (%)	19 (3)	5 (1)	2 (1)	0.64
Measures of wakefulness, pain, and agitation, median (IQR)				
Percentage of study days awake and calm (modal SBS score of −1 or 0)	75 (50–100)	71 (50–100)	75 (43–100)	0.03
Days to first awake and calm state	2 (1–4)	2 (1–4)	2 (1–5)	<0.001†
Percentage of study days with an episode of pain (highest pain score ⩾ 4)	25 (6–50)	19 (0–33)	25 (0–50)	0.002†
Percentage of study days with an episode of agitation (highest SBS score of +1 or +2)	40 (11–67)	33 (11–65)	43 (14–71)	0.45
Occurrence of iatrogenic withdrawal§				
Iatrogenic withdrawal syndrome (WAT-1 score ever ⩾3), *n*/*N* (%)	183/247 (74)	84/142 (59)	47/77 (61)	<0.001†‡
Peak WAT-1 score, median (IQR)	4 (2–6)	3 (2–5)	3 (2–5)	<0.001†‡
Percentage of study days with WAT-1 score ⩾ 3, median (IQR)	33 (0–57)	15 (0–40)	22 (0–46)	<0.001†
Sedation-related adverse events, *n* (%)				
Inadequate pain management (pain score > 4 for 2 consecutive h)	103 (17)	35 (10)	28 (15)	0.11
Inadequate sedation management (SBS score > 0 for 2 consecutive h)	130 (22)	58 (17)	40 (21)	0.68
Clinically significant iatrogenic withdrawal (rescue therapy used to manage an increase in WAT-1 symptoms)	73 (12)	17 (5)	16 (9)	0.02†

(Continued)

Table 2. (*Continued*)

Variable	Non-Hispanic White (*n* = 602)	Non-Hispanic Black (*n* = 350)	Hispanic of Any Race (*n* = 187)	*P* Value*
Unplanned endotracheal tube extubation (≥1 event)	24 (4)	24 (7)	6 (3)	0.08
Unplanned removal of any invasive tube (≥1 event)	23 (4)	16 (5)	9 (5)	0.82
Unplanned endotracheal tube extubation or unplanned removal of any invasive tube (≥1 event)	46 (8)	36 (10)	14 (7)	0.11

Definition of abbreviations: IQR = interquartile range; PRN = as needed; SBS = State Behavior Scale; WAT-1 = Withdrawal Assessment Tool-1.
**P* values for the comparisons between groups were calculated using logistic, linear, and proportional hazards regression accounting for pediatric intensive care unit as a cluster variable using generalized estimating equations for binary variables, log-transformed continuous variables (except percentage of study days variables), and time-to-event variables, respectively. Analyses were adjusted for age group, functional impairment, Pediatric Risk of Mortality III score from first 12 hours in the pediatric intensive care unit, and primary reason for intubation.
†$P < 0.0167$, non-Hispanic white patients versus non-Hispanic Black patients.
‡$P < 0.0167$, non-Hispanic white patients versus Hispanic patients of any race.
§WAT-1 scores range from 0 to 12; higher WAT-1 scores indicate more withdrawal symptoms; WAT-1 scores ≥3 are associated with clinically significant withdrawal symptoms. Occurrence of iatrogenic withdrawal was calculated for 466 survivors in the control arm who completed weaning from ≥5 days of opioids and had at least 1 WAT-1 assessment.

(median: white, 75%; Black, 71%; Hispanic, 75%). Three measures describing iatrogenic withdrawal symptoms (any Withdrawal Assessment Tool-1 [WAT-1] score of at least 3, peak WAT-1 score, and percentage of study days with WAT-1 score of at least 3) were significantly more disadvantageous in white patients than Black patients. In addition, the first two measures were also significantly more disadvantageous in white patients than in Hispanic patients. Of the six sedation-related adverse events compared across race and ethnicity groups, only clinically significant iatrogenic withdrawal demonstrated any differences, occurring more frequently in white patients than in Black patients (12% vs. 5%).

These same sedation profile measures are described in Table 3 for the intervention arm. As noted for the control arm, sedation profiles were generally the same across all race and ethnicity groups, and the duration of mechanical ventilation in patients extubated by study Day 28 did not differ between race and ethnicity groups (data not shown). With respect to sedatives administered, the maximum daily number of one-time or as-needed benzodiazepine doses was statistically significantly higher in Hispanic patients than in white patients (median, 8 [IQR, 5–11] vs. 7 [4–10]), but this difference is not likely clinically significant. Dexmedetomidine was more frequently used as a secondary sedative in white patients than in either Black or Hispanic patients (29% vs. 16% or 17%, respectively). The percentage of study days with an episode of pain was higher in Hispanic patients than in Black patients (median, 50% [IQR, 33–67%] vs. 45% [18–60%]), whereas the percentage of study days awake and calm while intubated was similarly attained in all three groups (median: white, 86%; Black, 88%; Hispanic, 85%). There were racial and ethnic differences between groups for all three measures of iatrogenic withdrawal symptoms in the intervention arm. Iatrogenic withdrawal syndrome was more common in white and Hispanic patients than in Black patients. Similarly, the peak WAT-1 score was higher in white and Hispanic patients than in Black patients, and the percentage of study days with a WAT-1 score of at least 3 was higher in Hispanic patients than Black patients. Unplanned removal of any invasive tube and unplanned removal of any invasive tube or an endotracheal tube were more common in Black patients than in white patients (7% vs. 4% and 12% vs. 7%, respectively).

In an additional analysis within the intervention arm only in which the sedation algorithm was applied, we examined whether sedation targets as measured by the SBS were differentially achieved across the three race and ethnicity groups during the acute, titration, and weaning phases of the trajectory of illness (Table 4). During the acute phase only, both white and Hispanic patients had a higher percentage of study days for which their modal SBS score was the same as their target SBS score than Black patients (76% and 74%, respectively, vs. 68%). No racial and ethnic differences were observed in the agreement between daily modal SBS score and SBS target score during the titration and weaning phases.

Discussion

In this large, multisite, cluster-randomized trial of sedation management in the pediatric ICU, we found scattered and largely inconsistent differences in the sedation profiles of white, Black, and Hispanic children treated in hospitals randomized to usual care or a sedation-intervention algorithm. Such inconsistent findings included more frequent use of ketamine among Black patients than among white patients in the control arm and more frequent use of dexmedetomidine among white patients than among Black patients and Hispanic patients in the intervention arm. Similarly, although unplanned removals of an invasive tube, including endotracheal tubes, were uniformly uncommon, these occurred more frequently in Black patients than in white patients in the intervention arm. By examining measures of iatrogenic withdrawal symptoms, in both the control and intervention arms, more adverse WAT-1 scores were observed in white patients than in Black patients. Taken together, there was no evidence of consistent disparities in sedation profiles indicating a systematic disadvantage for Black or Hispanic children. These results are encouraging and can

Table 3. Sedation profiles for intervention arm (sedation protocol) patients by race and ethnicity group

Variable	Non-Hispanic White (*n* = 631)	Non-Hispanic Black (*n* = 152)	Hispanic of Any Race (*n* = 349)	*P* Value*
Sedatives administered				
Primary opioid agent, *n* (%)				0.52
Morphine	413 (65)	90 (59)	222 (64)	
Fentanyl	212 (34)	62 (41)	121 (35)	
Hydromorphone	2 (<1)	0	0	
Remifentanil	0	0	1 (<1)	
None	4 (<1)	0	5 (1)	
Opioid exposure				
Peak daily dose, median (IQR), mg/kg	3.1 (1.5–6.0)	3.5 (2.1–6.7)	3.3 (1.6–6.0)	0.21
Cumulative dose, median (IQR), mg/kg	12.4 (4.7–35.8)	16.0 (6.5–40.5)	15.9 (5.7–40.9)	0.29
Number of exposure days, median (IQR)	9 (5–15)	10 (5–14)	10 (5–16)	0.53
Continuous infusions, *n* (%)	569 (90)	145 (95)	317 (91)	0.41
Scheduled intermittent doses, *n* (%)	191 (30)	40 (26)	107 (31)	0.81
Maximum daily number of one-time or PRN doses, median (IQR)	7 (5–10)	7 (5–10)	8 (5–10)	0.18
Primary benzodiazepine agent, *n* (%)				0.14
Midazolam	559 (89)	141 (93)	308 (88)	
Lorazepam	67 (11)	9 (6)	38 (11)	
None	5 (<1)	2 (1)	3 (<1)	
Benzodiazepine exposure				
Peak daily dose, median (IQR), mg/kg	2.7 (1.4–5.6)	3.3 (1.8–7.7)	3.1 (1.6–6.2)	0.23
Cumulative dose, median (IQR), mg/kg	13.1 (5.0–36.5)	16.4 (6.3–52.8)	14.6 (5.5–47.3)	0.46
Continuous infusions, *n* (%)	523 (83)	139 (91)	299 (86)	0.15
Scheduled intermittent doses, *n* (%)	379 (60)	89 (59)	207 (59)	0.68
Maximum daily number of one-time or PRN doses, median (IQR)	7 (4–10)	7 (5–11)	8 (5–11)	0.03†
Secondary sedatives, *n* (%)				
Dexmedetomidine	183 (29)	24 (16)	59 (17)	0.006†‡
Propofol	92 (15)	23 (15)	42 (12)	0.86
Barbiturates	67 (11)	18 (12)	47 (13)	0.51
Ketamine	147 (23)	37 (24)	59 (17)	0.40
Methadone	76 (12)	18 (12)	44 (13)	>0.99
Clonidine	80 (13)	16 (11)	40 (11)	0.78
Number of different sedative classes received, median (IQR)	3 (2–3)	2 (2–3)	2 (2–3)	0.33
Antidelirium medications, *n* (%)	12 (2)	2 (1)	4 (1)	0.40§
Measures of wakefulness, pain, and agitation, median (IQR)				
Percentage of study days awake and calm (modal SBS score of −1 or 0)	86 (67–100)	88 (67–100)	85 (71–100)	0.92
Days to first awake and calm state	2 (1–4)	2 (1–4)	2 (1–3)	0.05
Percentage of study days with an episode of pain (highest pain score ⩾ 4)	50 (27–67)	45 (18–60)	50 (33–67)	0.02‖
Percentage of study days with an episode of agitation (highest SBS score of +1 or +2)	58 (30–80)	50 (25–80)	60 (33–75)	0.37
Occurrence of iatrogenic withdrawal¶				
Iatrogenic withdrawal syndrome (WAT-1 score ever ⩾3), *n*/*N* (%)	233/332 (70)	43/81 (53)	136/194 (70)	0.001‡‖
Peak WAT-1 score, median (IQR)	4 (2–5)	3 (1–5)	4 (2–5)	0.005‡‖
Percentage of study days with WAT-1 score ⩾ 3, median (IQR)	29 (0–50)	17 (0–40)	25 (0–50)	0.03‖
Sedation-related adverse events, *n* (%)				
Inadequate pain management (pain score > 4 for 2 consecutive h)	104 (16)	22 (14)	56 (16)	0.92
Inadequate sedation management (SBS score > 0 for 2 consecutive h)	155 (25)	33 (22)	86 (25)	0.80
Clinically significant iatrogenic withdrawal (rescue therapy used to manage an increase in WAT-1 symptoms)	77 (12)	12 (8)	45 (13)	0.17

(Continued)

Table 3. (*Continued*)

Variable	Non-Hispanic White (*n* = 631)	Non-Hispanic Black (*n* = 152)	Hispanic of Any Race (*n* = 349)	*P* Value*
Unplanned endotracheal tube extubation (≥1 event)	21 (3)	9 (6)	12 (3)	0.15
Unplanned removal of any invasive tube (≥1 event)	25 (4)	11 (7)	21 (6)	<0.001†‡
Unplanned endotracheal tube extubation or unplanned removal of any invasive tube (≥1 event)	45 (7)	18 (12)	31 (9)	0.006‡

Definition of abbreviations: IQR = interquartile range; PRN = as needed; SBS = State Behavior Scale; WAT-1 = Withdrawal Assessment Tool-1.
**P* values for the comparisons between groups were calculated using logistic, linear, and proportional hazards regression accounting for pediatric intensive care unit as a cluster variable using generalized estimating equations for binary variables, log-transformed continuous variables (except percentage of study days variables), and time-to-event variables, respectively. Analyses were adjusted for age group, functional impairment, Pediatric Risk of Mortality III score from first 12 hours in the pediatric intensive care unit, and primary reason for intubation.
†$P < 0.0167$, non-Hispanic white patients versus Hispanic patients of any race.
‡$P < 0.0167$, non-Hispanic white patients versus non-Hispanic Black patients.
§This *P* value does not adjust for covariates because of small cell sizes.
‖$P < 0.0167$, non-Hispanic Black patients versus Hispanic patients of any race.
¶WAT-1 scores range from 0 to 12; higher WAT-1 scores indicate more withdrawal symptoms; WAT-1 scores ⩾ 3 are associated with clinically significant withdrawal symptoms. Occurrence of iatrogenic withdrawal was calculated for 607 survivors in the intervention arm who completed weaning from ⩾5 days of opioids and had at least 1 WAT-1 assessment.

contribute to our emerging understanding of health disparities in the acute care environment. To the best of our knowledge, this is the first available report examining potential disparities in clinical care in this number and complexity of measurements.

Although racial disparities in sedation management have received little attention in the literature, the effect of race and ethnicity on acute pain management has been explored in pediatric care, specifically in the emergency department and in perioperative arenas. Although not uniform, the majority of findings emerging from pediatric emergency department care provide evidence that Black children receive less adequate pain management, an effect that appears to be particularly pronounced with respect to opioid analgesia (12–15, 29). This contrasts with the emerging negative findings from the perioperative environment (16, 17, 30) and suggests the need for data from other care environments, such as reported here.

To integrate findings reported here into this broader literature regarding potential disparities in management of pediatric pain and sedation, it is necessary to recognize the features of the current investigation that broadly distinguish it from previously reported studies. First, data reported here were obtained from the highly specialized and uniquely structured care environment of pediatric ICUs, in which potential disparities in pain and sedation management have not, to our knowledge, been previously examined. Second, the care delivered in such intensive care environments is characterized by high levels of interprofessionalism and team-based management (31, 32), rather than by individual decision-making. Third, the participating patients were cared for continuously over a sustained period of multiple days rather than episodically for a briefer period, as is the case with emergency or perioperative care. Fourth, the goal of sedation management was more global than pain control. Rather, it was to achieve pharmacological management of wakefulness, pain, and agitation so that pediatric patients were both awake and calm, although intubated and mechanically ventilated. Fifth, both clinical care and its effectiveness were assessed in multiple ways and longitudinally, using validated scales for which interrater reliability was demonstrated. Finally, the mean age of participating patients in this investigation was younger than that of children described in studies of pediatric pain management in the emergency department (mean ages ranging from 11.5 to 14.5 yr) (13–15).

Given these multiple features of the current investigation, it would be inappropriate to suggest that the absence of systematic disparities disadvantaging racial and ethnic minorities documented here arose solely or even principally from the characteristics of the pediatric ICU clinical environment when compared with other pediatric care. There are simply too many potentially relevant differences in the provision of care and in the type, complexity, and quality of the analyzed data to draw conclusions regarding explanations for this difference.

Limitations

We recognize limitations in the analyses reported here. For one, these secondary analyses did not allow us to determine the reasons for the absence of systematic racial and ethnic disparities in pediatric ICU sedation management. For example, it is not possible to exclude the potential contribution of implicit bias and differential scoring on the observed results. However, a recent report finds that provider-related implicit pain attitudes did not significantly moderate their pain assessment and treatment decision in video virtual scenarios for pediatric chronic abdominal pain (33). On the other hand, although sustained interobserver reliability in observational assessments was achieved (28), this does not rule out the possibility of shared implicit bias in such assessment. Furthermore, we recognize the possibility of systematic bias in study methods that could arise from use of instruments incompletely reflecting behavioral expressions of pain and distress in Black or Hispanic children. Although the WAT-1 was developed in patient samples that included approximately equal numbers of Black and white children (27), the SBS was developed in a study group that included less than 10% Black children (26). It is also important to consider the

Table 4. Agreement between daily modal SBS score and SBS target score by trajectory of illness and by race and ethnicity group for intervention arm (sedation protocol) patients

Phase	Variable	Non-Hispanic White (*n* = 631)	Non-Hispanic Black (*n* = 152)	Hispanic of Any Race (*n* = 349)	*P* Value*
Acute	Total study days, *n*	1,208	315	768	
	Target SBS score, *n* (%)				0.01†
	−3/−2	652 (54)	179 (57)	335 (44)	
	−1/0	556 (46)	136 (43)	433 (56)	
	+1/+2	0	0	0	
	Modal SBS score, *n* (%)				0.02‡§
	Below target	78 (6)	12 (4)	60 (8)	
	Same as target	918 (76)	215 (68)	566 (74)	
	Above target	212 (18)	88 (28)	142 (18)	
Titration	Total study days, *n*	2,266	430	1,092	
	Target SBS score, *n* (%)				0.008†§
	−3/−2	86 (4)	22 (5)	16 (2)	
	−1/0	2,180 (96)	408 (95)	1,076 (99)	
	+1/+2	0	0	0	
	Modal SBS score, *n* (%)				0.50
	Below target	103 (5)	12 (3)	47 (4)	
	Same as target	2,050 (91)	392 (91)	989 (91)	
	Above target	113 (5)	26 (6)	56 (5)	
Weaning	Total study days, *n*	543	139	367	
	Target SBS score, *n* (%)				0.18
	−3/−2	9 (2)	3 (2)	1 (<1)	
	−1/0	534 (98)	136 (98)	366 (99.7)	
	+1/+2	0	0	0	
	Modal SBS score, *n* (%)				0.95
	Below target	9 (2)	2 (1)	3 (<1)	
	Same as target	512 (94)	131 (94)	353 (96)	
	Above target	22 (4)	6 (4)	11 (3)	

Definition of abbreviation: SBS = State Behavioral Scale.
**P* values for the comparisons between groups were calculated using cumulative logit regression accounting for patient as a cluster variable using generalized estimating equations.
†$P < 0.0167$, non-Hispanic white patients versus Hispanic patients of any race.
‡$P < 0.0167$, non-Hispanic white patients versus non-Hispanic Black patients.
§$P < 0.0167$, non-Hispanic Black patients versus Hispanic patients of any race.

possibility that Black or Hispanic children may confront a variety of barriers to care, thereby requiring more prolonged ventilation. If this were the case, such children would require longer sedation and higher cumulative dosing, implying that equivalence in these outcomes represents a disparity in care. However, we found no racial or ethnic differences in the duration of ventilation in children who were successfully extubated by study end, Day 28. Taken together, it is clear that we cannot exclude all possibility that we have failed to detect a disparity in the sedation management of Black or Hispanic children. However, in a study characterized by uniquely multifaceted and longitudinal data, our analyses reveal scattered and rare differences between Black, Hispanic, and white children that do not consistently favor any one group across multiple measures.

Recognizing that care standardization has been associated with racial parity (34–36), it is possible that the study procedures themselves promoted consistency of care across racial and ethnic groups, at least for the intervention-arm patients. Furthermore, although nearly half of study participants were Black and Hispanic children, there were insufficient numbers to support detailed subgroup analyses that might reveal groups more vulnerable to disparities in sedation management. We also recognize that data analyzed here were obtained as part of a rigorously designed and implemented cluster-randomized trial, and pediatric ICUs participating in this trial may not be representative of all pediatric critical care, given the multiple demanding study procedures. Lastly, we have no information on the race or ethnicity of care providers, which may have affected decisions they made regarding management of pain and sedation.

Conclusions

Overall, our data provide reassuring information that, at least in the sedation management of critically ill, ventilated children, clinical care does not systematically disadvantage minority children. Future investigations of clinical care and its effectiveness are warranted in various, well-characterized care environments. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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