# Racial and Ethnic Disparities in Parental Refusal of Consent in a Large, Multisite Pediatric Critical Care Clinical Trial

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**Objective** To evaluate whether race or ethnicity was independently associated with parental refusal of consent for their child's participation in a multisite pediatric critical care clinical trial.

**Study design** We performed a secondary analyses of data from Randomized Evaluation of Sedation Titration for Respiratory Failure (RESTORE), a 31-center cluster randomized trial of sedation management in critically ill children with acute respiratory failure supported on mechanical ventilation. Multivariable logistic regression modeling estimated associations between patient race and ethnicity and parental refusal of study consent.

**Result** Among the 3438 children meeting enrollment criteria and approached for consent, 2954 had documented race/ethnicity of non-Hispanic White (White), non-Hispanic Black (Black), or Hispanic of any race. Inability to approach for consent was more common for parents of Black (19.5%) compared with White (11.7%) or Hispanic children (13.2%). Among those offered consent, parents of Black (29.5%) and Hispanic children (25.9%) more frequently refused consent than parents of White children (18.2%, $P < .0167$ for each). Compared with parents of White children, parents of Black (OR 2.15, 95% CI 1.56-2.95, $P < .001$) and Hispanic (OR 1.44, 95% CI 1.10-1.88, $P = .01$) children were more likely to refuse consent. Parents of children offered participation in the intervention arm were more likely to refuse consent than parents in the control arm (OR 2.15, 95% CI 1.37-3.36, $P < .001$).

**Conclusions** Parents of Black and Hispanic children were less likely to be approached for, and more frequently declined consent for, their child's participation in a multisite critical care clinical trial. Ameliorating this racial disparity may improve the validity and generalizability of study findings. *(J Pediatr 2017;184:204-8).*

**Trial registration** ClinicalTrials.gov: NCT00814099.

The external validity of any clinical research study requires the participation of representative groups of subjects. Perhaps nowhere is this more important than in randomized controlled clinical trials (RCTs) where we draw conclusions about the safety and efficacy of new therapies. Both the Food and Drug Administration and National Institutes of Health require investigators to include predicted enrollment tables across race and ethnicity in their grant applications.[1,2] This requirement provides investigators the opportunity to design enrollment schemes to ensure equity and/or provide a scientific rationale justifying an anticipated imbalance.

There are both lingering concerns and contradictory data regarding the ability of RCTs conducted in the US to recruit equitable numbers of diverse racial and ethnic groups, particularly Blacks. A landmark systematic review of studies related to research consent revealed that Blacks were generally as willing as any others to take part in RCTs, that remarkably few studies reported their consent rates by race and ethnicity and that the heterogeneity in how consent rates were reported prevented comparisons across studies.[3] On the other hand, there are studies that document racial and ethnic disparities in health research participation[4-7] and a recent systematic review of barriers and facilitators to minority participation in research identified mistrust, stigma, and competing demands as common barriers.[8]

Unfortunately, there is a paucity of pediatric data on research consent and enrollment and even fewer studies examining this issue in critically ill children. In the previously noted landmark systematic review of research participation by minorities,[3] only 2 of the 17 trials included in the review were relevant to pediatrics.[9,10] Here, we address this gap by analyzing enrollment in the

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| ICUs | Intensive care units |
| RCTs | Randomized controlled clinical trials |
| RESTORE | Randomized Evaluation of Sedation Titration for Respiratory Failure |

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Randomized Evaluation of Sedation Titration for Respiratory Failure (RESTORE) study.[11] Our primary aim was to determine whether race and ethnicity affected the parental consent rates in a pediatric critical care clinical trial.

## Methods

We performed a secondary analysis of existing data from RESTORE, a cluster randomized clinical trial of children under 18 years of age with serious respiratory illness requiring mechanical ventilation (ClinicalTrials.gov: NCT00814099). The purpose of this more than minimal risk trial was to determine the safety and efficacy of a nurse-directed, goal-driven sedation algorithm. The primary study was approved by the Institutional Review Board at each of the 31 collaborating sites across in the US. Pediatric intensive care units (ICUs), rather than individual subjects, were randomized to study protocolized sedation management (intervention group) or to usual unit-based sedation management (control group). Therefore, all parents approached for consent knew the treatment allocation of their child. The primary study and results have been described elsewhere.[11] Here we focus on the methods relevant to this secondary analysis.

RESTORE enrolled children more than 42 weeks postconceptional age and less than 18 years old who were intubated and mechanically ventilated for acute lung disease. Excluded were children whose length of mechanical ventilation was thought to be unaffected by sedation management; specifically, children with cyanotic heart disease, congenital diaphragmatic hernia, primary pulmonary hypertension, a critical airway, an obstruction of the lower airway, chronic-assisted ventilation, neuromuscular respiratory failure, spinal cord injury, or pain managed by patient-controlled analgesia. Also excluded were children in whom care was considered futile as evidenced by the presence of a "do not resuscitate" order.

At the start of the trial, the lead investigators at each enrolling site received training on best practices in obtaining informed consent using the RESTORE study's practice guideline.[12] This training tool described the ethical and administrative requirements for informed consent and the study procedures for doing so. Because all eligible patients were intubated and sedated, assent for those over 8 years of age could only be sought after endotracheal extubation and after 72 hours after the last sedative dose. Therefore, this report focuses on parental decision making regarding their child's participation in this research.

RESTORE's best practices consent guideline recommended that parents be introduced to study personnel by a treating physician, the informed consent discussions by study personnel be family-centered, and the discussions include careful attention to the distress experienced by parents of critically ill children. Consent discussions were to include thoughtful, open-ended and nondirective questions (eg, "what more would you like to know about this study?").[12] Consent needed to be obtained within 24 hours of a child meeting eligibility criteria and was typically obtained 7 days per week during the day or evening hours. If the parent was not onsite in the pediatric ICU, the enrollment window could be extended to 48 hours or further with the permission of the clinical coordinating center. Provisions were made for obtaining consent by judicially approved guardians whenever possible. In instances where no parent or guardian was present, procedures did include telephone conversations, especially during the H1N1 influenza epidemic when parent visitation was limited in several centers in symptomatic parents. In these cases, the study was presented to the parent on the telephone and the executed consent was returned by fax or signed remotely using Docu*Sign* (San Francisco, California).

Interpretation services were used in recruiting, interacting with and obtaining consent from a parent whose preferred language was not English. However, use of non-English consent required approval by the local institutional review board of a professionally translated and certified informed consent documents, thereby limiting the ability to recruit parents speaking languages other than the dominant non-English local language, typically Spanish.

Because this was a cluster randomized trial, parents were consenting for their child to receive either algorithm-based sedation management (intervention) or to continued usual sedation management (control) that only involved data extraction from the medical record. There were no special procedures or guidelines for recruitment of particular racial or ethnic groups, nor was the race/ethnicity of those obtaining consent matched to the race/ethnicity of the parent.

Quality monitoring throughout the trial included tracking site-specific consent rates. These data were reviewed during separate intervention and control site conference calls and during yearly site-specific dashboard calls. Discussion of opportunities to improve consent rates was a standing agenda item on study conference calls and included site-to-site sharing of expertise.

For this analysis, we included all patients eligible to participate in the study. All data were extracted as directed by standardized study protocols from medical records review. Data elements included the clinical site, study arm, child's race, ethnicity (Hispanic vs non-Hispanic), sex, age, and primary reason the patient required endotracheal intubation. Identification of race and ethnicity was based on information provided in the medical record, using site-specific methods or the mother's race/ethnicity if no site-specific recommendations were made. Standard National Institutes of Health definitions were used.[13] We categorized ethnicity with respect to 3 groups: Hispanic, non-Hispanic, or unknown. Ethnicities noted as unknown were treated as non-Hispanic. This allowed us to combine race and ethnicity into 3 main groups: Non-Hispanic White, Non-Hispanic Black, and Hispanic of any race. All race and ethnicities other than these 3 groups were excluded from the analysis because of insufficient numbers to adequately analyze these groups.

### Statistical Analyses

The primary aim of the study was to compare refusal rates across race/ethnicity groups. We also compared rates for being unable to approach for consent to the families, refusal rates by treatment group, and baseline characteristics of subjects