are currently being faced with a barrage of incentives to roll out new predictive CDS systems. At the same time, hospitals that wouldn't approve of their clinicians prescribing new medications with no data behind them shouldn't themselves take up the same practice by deploying unvalidated clinical prediction models. If regulatory authorities don't step in, hospitals and independent researchers like Singh and colleagues will have to keep diving in to pick up the slack. ■

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Historic Abuses, Present Disparities, and Systemic Racism: Threats to Surrogate Decision-making for Critical Care Research Enrollment

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Anyone who has attempted to recruit critically ill patients into clinical trials recognizes the challenges that lie therein. Critically ill patients often lack decisional capacity and must rely on surrogate decision-makers (SDMs) to make both clinical and research enrollment decisions (1). The SDM role is both cognitively and emotionally burdensome (2, 3). Furthermore, it is frequently performed by a close family member who is already under the tremendous stress inherent in having a loved one in the intensive care unit (ICU). Therefore, it may be unsurprising that many SDMs suffer long-term psychological morbidity, including anxiety, depression, and symptoms of post-traumatic stress disorder (4). These effects may be exacerbated by being asked to consider enrollment into research (5). The reliance on SDMs for enrollment decisions may, in part, explain the low enrollment rates of critical care trials (6). To improve enrollment rates and reduce the burden on SDMs, an improved understanding of SDMs' decision-making processes surrounding clinical trial enrollment is imperative.

A previous study in this area identified three phases in SDMs' enrollment decision-making process: *1*) being approached, *2*) reflecting on participation, and *3*) making a decision (7). During each phase, SDMs reported factors related to decisions to move from one stage to the next. Although these findings provided some context for understanding SDM experiences and decision-making processes, the study was

limited by an inconsistent duration between the SDM experiencing the enrollment attempt and qualitative data collection, introducing the possibility of recall bias.

In this issue of *AnnalsATS*, Lane and colleagues (pp. 1185–1190) describe the perspectives of 21 SDMs of critically ill patients about being approached to consider enrolling their family member into research (8). The authors addressed the limitation of previous work in the area by enrolling SDMs within 96 hours of an ICU admission and conducted interviews on a median fifth day of hospitalization. The authors performed a thematic analysis of semistructured interviews of SDMs of critically ill mechanically ventilated patients exploring how they would make a research enrollment decision on behalf of the patient.

The authors found that SDMs focused primarily on themes related to trust when thinking about making enrollment decisions for critically ill family members. They synthesized their findings into a novel conceptual model of ethically sound surrogate decision-making for research consent, the foundation of which is trust in the hospital system and treating physicians, which they label "context-based trust." Without context-based trust, consent is hypothesized to almost assuredly be declined, regardless of the study details. On the opposite end of the spectrum, the authors identify the potential of "blind trust," in which a surrogate trusts the system to such a degree as to blindly consent without much additional thought. Surrogates who have sufficient trust in the hospital system and treating physicians then consider themes the authors label "knowledge-based trust." Knowledge-based trust encompasses issues such as complete transparency to the potential risks and benefits, accountability should complications arise, and rapport with the person seeking consent.

We applaud Lane and colleagues for their well-conducted qualitative study addressing a very important question. Strengths of the study include applying strong qualitative inquiry and data analysis procedures, achieving saturation in qualitative feedback, and providing some context for potential consent decisions. Because of the challenge of conducting research in critical care, we also found the 62% enrollment rate of SDMs to be an impressive proportion. However, we also want to point out a few limitations of this, as well as other research in this area. First, despite the promising enrollment rate, the authors did not report on the characteristics of those who declined participation with those who enrolled. This reduces our understanding of generalizability of the findings relative to groups that are historically less likely to participate in clinical trials. Second, participants were asked to consider research participation in general and had not gone through an enrollment attempt in the recent past, nor were they given a specific hypothetical study to consider.

This second limitation may explain a relative lack of depth in participants' responses. We recently conducted a trial of behavioral nudges using a sham-trial enrollment design to evaluate its effectiveness in increasing trial enrollment among SDMs of critically ill patients (6). Participants were blinded to the sham nature of the trial and believed they were making a real decision to enroll or decline participation in a ventilator weaning trial. After the decision, participants were asked what factors were most important in their decision. Although our qualitative analysis was based on a single question, we identified a wide breadth of themes, including *1*) study characteristics, *2*) the patient's clinical condition, *3*) the decision-making process, *4*) altruism, and *5*) the enrollment attempt (9). Although several factors within these themes are related to trust, we found that participants who believed they were making an actual enrollment decision identified additional factors beyond trust.

Although it may not be sufficient, trust is certainly essential in the process of considering enrollment into research. Burns and colleagues (7) also identified trust in the healthcare system as a prerequisite for SDMs to enroll a critically ill patient into research. Unfortunately, the medical research community's history is rife with race-based research abuses that justify a lack of trust, especially among historically marginalized populations. One example is the Tuskegee study, in which the natural history of untreated syphilis was studied in Black men well after an effective treatment was available. Scientists continue to use the immortal HeLa cell line, which was collected without consent from Henrietta Lacks. However, focusing on these historical research abuses risks missing an opportunity to address the ongoing state of systemic racism and disparities that continue to undermine ethnic and racial minority patients' and SDMs' trust in the healthcare system (10).

Never-ending mistreatment resulting in a reluctance to participate in research, as well as disparities in access, likely contribute to an underrepresentation of ethnic and racial minorities in clinical trials, which threatens the validity and generalizability of trial results. Over the past decade of oncology clinical trials, Black individuals were enrolled at only 22% of their expected representation based on their proportion of U.S. cancer incidence (11). Although the limited available evidence suggests racial disparities are not prevalent among recent critical care trials (12), ICU trialists must remain diligent. Financial and nonfinancial pressures to enroll patients into clinical trials may lead to inadequate disclosure of risks, misrepresentation of potential benefits, enrollment of ineligible subjects, failure to disclose adverse events, data manipulation, and failure to terminate trials when indicated (13).

As if historical abuses, systemic racism, and disparities were not enough, the coronavirus disease (COVID-19) pandemic represents a novel threat that may undermine trust in the healthcare system. The last year has seen multiple assaults on the trustworthiness of the healthcare system, including *1*) conflicting messages, *2*) frequently changing recommendations from governmental leaders and public health departments, *3*) questionable treatments reported in research publications, *4*) the dissemination of pseudoscience and conspiracy theories through social media (14), and *5*) the high-profile retractions of COVID-19–related publications (15, 16). Even the accelerated advances in scientific understanding that have resulted in multiple therapeutics and vaccines have been viewed with skepticism. COVID-19 has further illustrated racial disparities in both clinical outcomes and trial participation. Although Black individuals make up 13% of the U.S. population, they account for 21% of deaths from COVID-19 and only 3% of enrollees in vaccine trials (17).

The short- and long-term impact of COVID-19 on recruitment into critical care trials is yet to be seen. However, the impact of historical abuses, continued disparities, and systemic racism is evident. We must not only recognize the importance of trust in the decision-making process of SDMs considering enrolling their family member in research but also confront and correct our failures that have resulted in a loss of trustworthiness. ■

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