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Enrollment Challenges in Critical Care Nursing Research

Mary Lou Sole, RN, PhD, CCNS, Aurea Middleton, RN, BSN, Lara Deaton, RN, BSN, CCRN, Melody Bennett, RN, MN, CCRN, Steven Talbert, RN, PhD, and Daleen Penoyer, RN, PhD, CCRP

Mary Lou Sole is dean and professor and holds the Orlando Health Endowed Chair in Nursing at the University of Central Florida College of Nursing, Orlando, Florida. Aurea Middleton and Lara Deaton are clinical research coordinators and Melody Bennett is the study project coordinator, Orlando Health, Orlando, Florida. Steven Talbert is a clinical assistant professor with the University of Central Florida, Orlando, Florida. Daleen Penoyer is director, Center for Nursing Research and Advanced Practice Nursing, Orlando Health

Abstract

Background—Enrollment challenges for critical care research are common. Contributing factors include short enrollment windows, the crisis nature of critical illness, lack of research staff, unavailable legal proxy, family dynamics, and language barriers.

Objective—To describe enrollment statistics for an ongoing critical care nursing trial, barriers to recruitment, and strategies to enhance enrollment.

Methods—Two years' worth of recruitment and enrollment data from an oral care intervention trial in critically ill adults receiving mechanical ventilation at 1 hospital were analyzed. Recruitment logs include number of patients screened, eligible, enrolled, and declined and patients' sex, race, and ethnicity.

Results—Target enrollment (15.5 patients per month) was based on experience and historical data. Strategies implemented to promote enrollment included providing study personnel at least 18 hours per day for 7 days per week, regular rounds, communication with direct care staff, and Spanish consent processes. In 2 years, 6963 patients were screened; 1551 (22%) were eligible. Consent was sought from 366 (24% of eligible patients). Enrollment averaged 13.3 patients per month (86% of projected target). The main factor impeding enrollment was unavailability of a legal proxy to provide consent (88%). The refusal rates of white (11%), black (13%), and Hispanic (16%) patients did not differ significantly. However, those classified as Asian or as more than 1 race declined significantly more often (35%) than did white or black patients ($P=.02$).

Corresponding author: Mary Lou Sole, RN, PhD, CCNS, FAAN, FCCM, University of Central Florida College of Nursing, 12201 Research Parkway #300, Orlando, FL 32826-2210 (mary.sole@ucf.edu).

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Conclusions—Unavailability of a legal proxy within a short enrollment window was the major challenge to enrollment. Various factors influenced consent decisions. Clinical study design requires more conservative estimates.

Recruitment and retention of eligible participants for clinical studies is often challenging and may create a barrier to successful study completion. Recruitment is further complicated when research takes place in critical care settings, where patients often lack the ability to give consent to participate. Other challenges are the unexpected crisis of critical illness and the stressful environment.

This article describes enrollment statistics for an ongoing federally funded trial of an oral suction nursing intervention to reduce aspiration (clinicaltrials.gov NCT02284178). Our participants are critically ill, adult patients requiring mechanical ventilation who must be enrolled within 24 hours of intubation. The trial is being conducted at a large tertiary care hospital in the southeastern United States. The institutional review board (IRB) has classified the study as expedited, with no more than minimal risk. On the basis of historical data and our success in previous studies with similar inclusion and exclusion criteria, we estimated that we would enroll 560 patients within 24 hours of intubation in 3 years (15.5 participants per month). We believed that we were conservative in our enrollment estimate. In this article, we discuss barriers to recruitment, patients' reasons for declining to participate, and strategies undertaken by the research team to overcome those barriers.

Background

When planning a study, the principal investigator and study team must consider the potential pool of participants and develop enrollment projections to achieve sample size targets. These steps help establish a realistic time line for conducting the study and an appropriate budget for personnel. Grant reviewers assess recruitment and enrollment plans to evaluate the feasibility of completing a successful study.

A gap often exists between the number of eligible patients and the number of consenting participants.^{1,2} Reasons cited for this enrollment gap include limited availability of research staff, limited enrollment time, lack of an available legally authorized representative or proxy, family dynamics, and language barriers.^{1,3–5}

We anticipated some of these issues for our trial and implemented strategies at study inception to help meet enrollment goals. We hired 3 full-time research coordinators along with several part-time research assistants to ensure that study personnel were available 18 to 20 hours each day, 7 days a week. We provided consent forms translated into Spanish, and several of the research assistants are bilingual. We communicate regularly with nursing and respiratory care staff and conduct rounds in 4 critical care units: cardiac, multisystem, neurological, and trauma.

Methods

We regularly monitor enrollment trends to assess target goals. We maintain recruitment logs that include the number of patients screened, eligible, enrolled, and declined and the

patients' age, sex, race, and ethnicity. For this report, we analyzed data from these logs and calculated frequencies and percentages to identify enrollment trends and challenges for the first 2 years of the intervention trial. The analyses included χ^2 and t tests to compare data between patients who consented and patients who declined to participate.

Results

Recruitment and enrollment data are shown in the Figure. In 2 years, we screened 6963 patients from the 4 critical care units. Of those screened, 1551 (22%) met the inclusion criteria. We approached 366 eligible patients (24% of the eligible pool) or their proxies for consent; 319 (87.2%) of those approached consented to participate. Proxies provided consent in 99% of cases; 4 patients (1%) were cognitively able to sign their own consent. These patients were alert and oriented and signed consent for all aspects of their treatment. To date, we have enrolled 13.3 participants per month, which is 86% of our estimate of 15.5 participants per month.

We missed opportunities for enrolling 1185 potential participants for several reasons. The main reason was that no proxy was available ($n = 1043$; 88%). In some cases, proxies were not identified for the patient or the proxy was not present within the 24-hour enrollment window. Other reasons were that the patient was not screened ($n = 85$; 7%) and patient instability or complex family dynamics ($n=57$; 5%).

Of the 366 patients approached to participate, most (55%) had trauma or neurological diagnoses. Patients for whom consent to participate was granted were a mean of about 5 years younger than patients who declined (57.3 years versus 62.4 years, $P<.001$). The Table shows the sex, race, and ethnicity of patients who consented or declined participation. Neither sex ($P = .71$) nor ethnicity ($P=.42$) differed between patients who consented and patients who did not. A significant difference was noted for the patient's race ($P = .02$). The proxies of the 17 patients classified as "other" (Asian or of more than 1 race) declined 35% of the time, as compared with proxies of white (11.4%) or black (13%) patients. Post hoc analysis showed no difference between consent rates of white patients and black patients. However, both white and black patients had significantly higher consent rates than did patients classified as other.

All 47 refusals were made by proxies; none of the 4 patients who were approached declined participation. Several reasons for declining participation were identified by the proxies and research staff. The most common reason for refusal was that proxies did not believe that their loved ones would want to participate in a research study ($n = 18$; 38%). Other reasons were perceived language or cultural barriers ($n = 12$; 26%), family members being overwhelmed with their loved one's illness ($n = 10$; 21%), and family dynamics that prevented decision-making or delayed the decision beyond the 24-hour enrollment window ($n = 7$; 15%).

Discussion

Overall, 87.2% of patients or proxies whom we approached consented to participate. No differences in consent rates were noted between sexes or across ethnicities. However, white

and black patients were significantly more likely to consent than were patients classified as Asian or other.

Enrollment statistics vary widely in published reports. In the Consent study,¹ a large cross-sectional study of enrollment challenges for critical care research across Canada, 57.3% of all opportunities for recruitment were either missed or not feasible. Our percentage (76%) was even higher. Differences in findings may be attributed to different cultural values for research between Canada and the United States as well as potential differences in patients' demographics or admitting diagnoses.

According to data from various clinical studies,^{2,6} the percentage of patients for whom a proxy is not available to provide consent ranges from as low as 1% to as high as 40%. Our study's inclusion criteria and aims were most similar to those of Grap and Munro,² including recruiting newly intubated patients within 24 hours of intubation and delivering a nursing intervention. However, we noted several differences. Grap and Munro reported that 40% of eligible participants lacked a proxy.² In our study, 67% of proxies were not available (1044 of 1551). Grap and Munro recruited participants from a medical respiratory intensive care unit, whereas we enrolled participants across 4 units. More than half of our participants had a trauma or neurological diagnosis, which is most likely the reason for the higher numbers; family members were often not available within the 24-hour window for many of the trauma patients. In many cases, it took 24 hours to identify patients and notify proxies of admission.

Our rate of patients declining participation was lower than others have reported. However, it is challenging to make comparisons because data are reported differently across studies. Grap and Munro² reported that 27% of those eligible declined participation. In contrast, only 3% of our eligible participants declined (47 of 1551). The Consent study reported a 15.4% refusal rate when study enrollment occurred within 24 hours of admission.¹ Smith et al⁷ reported a 17.8% refusal rate in an international thromboprophylaxis trial. Our rates of decline were lower, as only 13% of patients approached (47 of 366) declined to participate. We worked diligently to foster consent by ensuring a simple-to-read form and by conducting detailed training of all study personnel in the consent process, including practice sessions. We also conduct quarterly retraining and make informed consent processes a priority. We believe that these factors contributed to the higher rate of consent. Additionally, most of the research assistants had extensive experience in facilitating consent for treatment from their earlier experience working as staff nurses in the critical care units.

Our rate of enrollment for patients of Hispanic ethnicity was similar to the rate for patients who were not Hispanic. We attribute these similar rates to our bilingual research staff and the availability of a Spanish consent form. Likewise, we achieved comparable enrollment of white and black patients, which is a strength of our study, because black patients are often underrepresented in clinical studies. Grap and Munro² reported a lower number of black patients who consented relative to the number who were eligible. However, in 2 more recent studies,^{7,8} researchers reported no significant difference in participation rates among various ethnic groups. Our research staff regularly care for and communicate with patients of various cultures because the population of critically ill patients is very diverse. This factor

may also have contributed to our successful recruitment of a diverse group of patients into the study.

Despite our success in enrolling a diverse sample, we identified some issues with language and related cultural barriers to enrollment. Our number of potential participants of Asian or more than 1 race was low ($n = 17$), and more than one-third declined to participate (35%). A systematic review indicated that language-appropriate materials and research staff may facilitate trust and discussion for patients of Asian descent.⁹

Consent may also have been increased because of the minimal-risk nature of the study, which did not change usual care delivery. This fact often reassured the patient and the proxy. Stated and observed reasons for declining to participate were similar to those seen in other studies involving critically ill patients.^{2,10} The proxies of older patients declined more often than did proxies of younger patients. Their focus may have been on simply ensuring that their loved one not receive care or treatment beyond the usual care provided.

According to results of a multicenter cross-sectional study examining recruitment of critically ill participants, the most influential issue in recruitment was missed or unrealized opportunities because of study staffing and short enrollment windows.⁶ The availability of research staffing is reported to be a significant barrier, but our trial minimized its effects with study personnel present around the clock and frequent screening of critically ill patients. Research staff were available 18 to 20 hours per day for 7 days a week, leaving very little time in which research personnel were not available. We communicated to the direct care staff members via staff meetings and huddles. Open communication with the direct care staff is essential for identifying potential participants and allows study personnel to be alerted when the legally authorized representative visits the patient. We routinely leave business cards with the assigned direct care staff member to notify us when the proxy arrives. We use both a department-based wireless phone and personal cellular phones to enhance communication.

The absence of a proxy, the most significant barrier to enrollment, can be attributed to many factors. The study site is a busy level I trauma center, and many patients are admitted without identification. The time required to verify identity and contact family members delays enrollment opportunities. Additionally, we found that many proxies came in for a brief visit but left before research personnel arrived to discuss the study. They may have done so because of the stress of seeing their loved one or as a way to avoid discussing potential research participation. Although direct care staff members alerted study personnel to the availability of the proxies, these situations became missed opportunities.

Researchers in other studies^{1,7} have reported self-consent rates of 9% to 10%. Only 1% of our patients were cognitively able to consent, possibly because of the trauma and neurological diagnoses of most of our participants. These patients often have impaired cognition or are sedated at the time of injury or illness. When planning research studies, it may be helpful to estimate the number of patients able to provide their own consent and to identify screening measures for determining the ability to provide consent.

Gaining the support of unit staff and frequent unit rounding are essential to the enrollment of participants.³ Having a physical presence in the units and keeping direct care nursing staff aware of the study can minimize missed opportunities. If bedside nursing staff know to look for the proxy, they are more apt to call the research staff when the proxy arrives. We ensured regular and frequent communication with direct care staff members and critical care providers, which facilitated notification of potential participants and of availability of the proxy. For example, an acute care nurse practitioner often alerted the team to the presence of patients who were in urgent need of intubation.

Electronic consent is a potential option for obtaining consent from the proxy. Our IRB policy permits electronic consent; however, the process is very detailed. For example, the consent form must be sent electronically via text or email, discussed with those obtaining consent, signed, and scanned or faxed back to the facility. We found this process to be an unsuccessful way to recruit participants. One research coordinator attempted this process with 111 proxies. Most proxies (101) were either unable to or chose not to complete the additional steps (scanning or faxing a signed form) required to enroll electronically. The remaining 10 proxies declined enrollment outright. The critical nature of the patient's illness, the need to make a decision at a distance, and the extra steps involved in the process may all have contributed to our lack of successful electronic enrollment. Telemedicine approaches may be an alternative in future studies. In a recent study, researchers found noninferior informed consent using telemedicine for remote study enrollment; understanding of consent and accrual rates of participation were similar between face-to-face and telemedicine groups.¹¹

IRBs require consent except for life-threatening situations and studies that have low risk and foreseeable benefit.⁵ In emergency research, delayed consent (enrolling participants and obtaining consent within a specified time period) is sometimes granted. Per our IRB policies, our study did not meet the criteria for waiver of consent or delayed consent. Patients and their families value the granting of consent for research. In a study of survivors of critical illness, nearly half of patients found waiver of informed consent to be unacceptable. Several (15%–20% depending on the scenario) also believed that delayed consent was not acceptable.¹² These findings support the importance of securing consent before enrollment.

We missed screening 85 participants within the 24-hour enrollment window. We are actively addressing this issue. Most of these missed events occurred at the start of participant recruitment. We minimized them by implementing more detailed processes for maintaining the screening log and by educating study personnel to screen and update the log multiple times per shift. We conduct regular education of the study team to ensure that all are trained and comfortable in the informed consent process. Several potential participants were identified as not meeting criteria (that is, not intubated or receiving mechanical ventilation) and subsequently were intubated for deteriorating respiratory status. Preemptive consenting, the gaining of consent upon admission to the critical care unit and before intubation, is one strategy to potentially address this barrier. Cognitively intact patients or their proxies can potentially provide pre-consent if they are at high risk for intubation based on their admission diagnosis. Pinder et al¹³ reported success in obtaining preconsent from potential

participants on admission to a critical care unit in South Africa. We have recently obtained IRB approval to initiate this process.

Conclusions

Although we believed that our enrollment estimates were conservative and we developed processes to facilitate recruitment of participants, we have not achieved our enrollment goals. However, we are retaining a higher number of participants than projected, which has enhanced our ability to complete the study as initially planned. We believe that enrolling more than 13 critically ill patients per month is very good.

Issues that can affect enrollment, such as inadequate study personnel staffing and unit involvement,^{3,6,10} did not influence the results of this study. The unavailability of proxies was the most unsurpassable barrier.^{3,6} Within the critical care environment, informed consent is increasingly difficult to obtain because the nature of patients' illnesses often renders them incapable of making decisions regarding their care. When this occurs, the proxy is consulted to make care decisions. If the proxy is not present or not known, efforts to enroll the patient in research studies are impeded.^{2,4} We have found that having a short enrollment window in a setting where most patients are unable to provide consent creates a challenging barrier when waiver of consent is not permissible. Working with IRBs to facilitate innovative methods to obtain consent (eg, secure online approaches) while ensuring that the proxy clearly understands the risks and benefits should be a goal.

To ensure the success of clinical studies, adequate planning and resources must be invested to determine the feasibility of participant recruitment.¹⁴ We completed this step but underestimated the impact of not having proxies available. Based on this analysis, it may be unrealistic to expect a higher percentage of enrollment within a short window in critical care studies. We believe that the results of our analysis and other studies may help researchers identify accurate recruitment targets.

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Figure.
Enrollment flowchart.

Table

Comparison of decline rates on the basis of patient's sex, race, and ethnicity

Characteristic	No. approached, N = 366	No. of patients (% approached)		P
		Enrolled, n = 319 (87.2%)	Declined, n = 47 (12.8%)	
Sex				.71
Male	209	181 (86.6)	28 (13.4)	
Female	157	138 (87.9)	19 (12.1)	
Race				.02
White	272	241 (88.6)	31 (11.4)	
Black	77	67 (87)	10 (13)	
Other	17	11 (65)	6 (35) ^a	
Ethnicity				.42
Hispanic	70	59 (84)	11 (16)	
Non-Hispanic	296	260 (88.1)	36 (12.2)	

^aSignificantly higher decline rate than white or black patients.