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STRATEGIES FOR OVERCOMING SITE AND RECRUITMENT CHALLENGES IN RESEARCH STUDIES BASED IN INTENSIVE CARE UNITS

Linda Chlan, RN, PhD, Jill Guttormson, RN, MS, Mary Fran Tracy, RN, PhD, CCNS, and Karin Lindstrom Bremer, MA, PhD

is an associate professor and **Jill Guttormson** is a project coordinator and doctoral student in the School of Nursing at the University of Minnesota in Minneapolis. **Mary Fran Tracy** is a critical care clinical nurse specialist at the University of Minnesota Medical Center, Fairview, Minneapolis. **Karin Lindstrom Bremer** was a project coordinator and now is an assistant professor for counseling and student personnel at Minnesota State University in Mankato.

Abstract

Although enrolling a sufficient number of participants is a challenge for any multisite clinical trial, recruiting patients who are critically ill and receiving mechanical ventilatory support presents additional challenges because of the severity of the patients' illness and the impediments to their communication. Recruitment challenges related to the research sites, nursing staff, and research participants faced in the first 2 years of a 4-year multisite clinical trial of a patient-directed music intervention for managing anxiety in the intensive care unit were determined. Strategies to overcome these challenges, and thereby increase enrollment, were devised. Individual strategies, such as timing of screening on a unit, were tailored to each participating site to enhance recruitment for this trial. Other strategies, such as obtaining a waiver for a participant's signature, were instituted across all participating sites. Through implementation of these various strategies, the mean monthly enrollment of participants increased by 50%. Investigators are advised to plan well in advance of starting recruitment for a clinical trial based in an intensive care unit, anticipate peaks and valleys in recruitment, and be proactive in addressing issues creatively as the issues arise.

Recruitment of a sufficient number of participants is a challenge for any clinical study that involves humans, and enrollment of participants receiving mechanical ventilatory support in the intensive care unit (ICU) poses particular challenges. The dynamic, fast-paced environment of the ICU; the ever-changing conditions of patients; the need to work with numerous staff members in a complex environment; and the impaired communication of patients due to placement of an endotracheal tube, the nature of the critical illness or injury, heavy sedation, or neuromuscular blockade all affect recruitment efforts. These issues limit the potential recruitment pool from which to obtain a sample for a clinical trial. Innovative strategies are needed to enhance recruitment. We describe the challenges faced in the first 2 years of a 4-

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Corresponding author: Linda Chlan, RN, PhD, School of Nursing, University of Minnesota, 5-160 Weaver-Densford Hall, 308 Harvard St SE, Minneapolis, MN 55455 (chlan001@umn.edu).

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year multisite clinical trial, strategies that successfully addressed those challenges, and recommendations for investigators recruiting critically ill, ventilator-dependent ICU patients.

Overview of the Multisite Clinical Trial and Preparation of Research Sites

The multisite clinical trial on which these observations are based was designed to test a music intervention for self-management of anxiety in patients receiving mechanical ventilation. Approval of the institutional review board (IRB) was obtained from all participating sites (University of Minnesota, School of Nursing; University of Minnesota Medical Center, Fairview; Abbott-Northwestern Hospital; United Hospital; Minneapolis VA Medical Center; North Memorial Medical Center; Regions Hospital). Participants were randomized to 1 of 3 groups: patient-directed music, noise abatement headphones, or usual care. With the strict inclusion criteria necessary to maintain control in an intervention trial, it is imperative to have a sufficient pool from which to recruit participants. Establishing and maintaining access to research sites requires cooperation from many individuals, beginning during development of the proposal and continuing throughout the research project. It is especially important to have access to the site and support from key leaders before applying for IRB approval.

Recruitment Challenges and Recommended Strategies

Environments within each ICU are unique and, as such, can pose challenges when research is conducted with patients receiving mechanical ventilation. Careful selection of ICUs from which to recruit participants is imperative. In selecting sites, many factors were considered: familiarity of the staff nurses with research; support by key leaders on the unit, including the nurse manager and medical director; staff turnover; educational preparation of staff; the anticipated number of potential participants; and site requirements for access by the research team (eg, fees, training). Challenges encountered in the environment included the initial time investment needed to gain access to sites, past experience of unit leaders with clinical research, difficulty in sustaining awareness of the study on the units, unit culture and routines, and unanticipated changes in unit practice at sites.

Enrolling patients receiving mechanical ventilation into research studies is challenging.

Initial Time Investment

Gaining access to sites, fulfilling all the requirements for fees and credentialing, and gaining consensus from all the necessary leaders at institutions is a time-consuming process. Through her past research and her affiliation with the local critical care nurses' association, the principal investigator of this study (L.C.) had established invaluable relationships with clinical nurse specialists and clinical researchers at many sites. The clinical nurse specialists and clinical researchers at each site have served as facilitators and liaisons, assisting in setting up meetings with nursing and medical leaders, identifying practice and culture variations among units, facilitating credentialing issues, and identifying key members of the nursing staff to serve as our primary contact on the unit.

Different sites have different access requirements for investigators outside the organization. These requirements are not always clearly delineated, and often different departments or individuals at sites disagree on the process. Additionally, new requirements are often added during the course of a study. Clinical nurse specialists and clinical researchers can be used to facilitate the process of meeting these requirements. Many hospitals now have electronic medical record systems in place, which require training that must be completed before access will be granted. In addition, many IRBs are requesting fees for review and approval of protocols. The principal investigator may need to negotiate a waiver of fees not budgeted in

the grant application. For this study, the principal investigator was able to secure payment of the IRB review fees from one study site's nursing administration department because of their desire to support nursing research.

Negative past experiences with research are potential roadblocks for clinical research.

Past Experience With Research

Nurse leaders' past negative experiences with research are a potential roadblock for clinical research. During the consensus-building phase for this trial, the principal investigator became aware of a rather "cool" reception from one of the nurse managers who was new to a unit. The principal investigator asked the clinical researcher at the site to facilitate a meeting with the nurse manager to discuss concerns about the conduct of the study. The principal investigator learned from the clinical researcher that the nurse manager had a poor experience with another researcher in the past that "soured" his opinion on research in the ICU. With the facilitation of the clinical researcher, this issue was addressed in an open, professional exchange and did not hinder efforts to begin recruitment on this particular unit. This incident highlights the importance of having key facilitators at each site and being proactive in addressing potential barriers or conflicts before starting to recruit.

Carefully select a unit study champion or liaison.

Awareness of the Study on Units

The research team is advised to use a multifaceted approach to increase awareness and support for the study on each unit, such as production of a study video, flyers, posters, in-service trainings, and attendance at unit meetings. Before starting a study, researchers are advised to attend unit council and staff meetings and to conduct in-service training sessions on all units at various times during a 24-hour period in an effort to accommodate shift routines and encourage attendance. In addition, posters and flyers for each of the participating ICUs with names and contact information announcing the start of the study should be prepared. Periodically placing flyers with a study update in each nurse's mailbox and posting flyers on the units are key strategies for keeping staff engaged. Such flyers also can be used to express gratitude for nurses' cooperation.

Patient and staff exemplars can be used to highlight the positive influence of the study protocol. For example, a patient who had been randomized to the group receiving noise-abatement headphones wrote a note to the research nurse saying, "Best night of sleep I have had since I've been here." Highlighting these comments from patients reassures staff that the research is not a burden and may provide benefit to patients.

Unit Culture and Routines

Attendance at various staff and leadership meetings allows the research team to obtain a clear picture of each unit's practice culture and routines. Awareness of the timing of physician rounds, bedside meetings, weaning trials, shift reports, and staff breaks allows research personnel to adapt screening to the routines on each unit. Research personnel should be cognizant of the milieu every time they arrive on a unit and to be sympathetic and responsive to the ever-changing ICU environment. The continued presence of research personnel on the units helps to increase staff familiarity with a study and promotes partnership between the nurses and the research team.

Unit Practice Changes

Researchers must remain flexible and proactive in regard to practice changes at sites, over which they have no control. Although infrequent, situations such as labor strikes, changes in medical record keeping, and new equipment purchases such as ventilators and infusion pumps can have devastating consequences for a research protocol if the situations are not actively addressed. Having a key contact at each site is invaluable; this liaison can inform the research team about upcoming changes and assist in problem solving to minimize disruption of the protocol and the unit. Although nurse managers may seem an obvious choice for key contacts, a more useful strategy is to have a staff nurse, charge nurse, or assistant nurse manager serve as the contact because they more readily hear comments from staff about concerns or barriers to study engagement and may identify practical solutions to enhance cooperation. For example, one of the participating sites was converting from paper medical records to a new electronic medical records system. Personnel were participating in lengthy training and nursing staff had great anxiety about the conversion. The study liaison at that site suggested that a screening hiatus be taken during this particularly stressful time. The implementation of a short screening hiatus at that site did not interrupt the nurses, and the research team gained further respect and cooperation from the nursing staff when screening resumed.

Recruitment Challenges Related to ICU Nursing Staff and Recommended Strategies

Issues surrounding the personnel employed on the ICUs also are a challenge for research. These recruitment challenges can emanate from the unit's charge nurses and from patient-care nurses. Challenges include the nurse serving as protector of the patient, the multiple demands on nurses, and the terminology used by nurses when presenting the study to the patient.

Nurse as Patient's Protector

Nurses who choose to work in the ICU take their role as protectors of patients and advocates for patients seriously. Although these roles are admirable, they create barriers for research personnel in accessing potential research participants. Research nurses must maintain constant vigilance to ensure that nurses do not impede access to potential participants. Research nurses can frequently remind the nurses about the study routine and requirements and can clarify details with staff who may not be as engaged with the unit culture, who work infrequently, who have not cared for a study participant recently, or who simply misunderstand the conduct of the study. At the beginning of a study, nurses may be hesitant to have a patient approached for consent. Nurses may express concern about the burden on the patient and question the patient's ability to provide consent. To allay these concerns, a commitment to ensure that patients understand the consent process, minimize the burden, and have nurses witness the research nurse's interactions with patients are effective and can promote a more collegial relationship with nursing staff.

To ensure equal opportunity for patients, research personnel must keep in mind that it is not the nurses' prerogative to decide which patients who meet eligibility criteria should be approached about participating in the study. Having the nurse make that decision violates the patient's right to self-determination and introduces bias that could limit the generalizability of study findings. Research personnel must be trained to seek more information from a nurse who says, "Don't bother him now" or "He isn't eligible for your study." A brief conversation with the nurse will inform the research nurse of the patient's condition and show whether it might be more appropriate to return later in the day, or whether the nurse simply needs more information about the study.

Highlighting positive comments from patients reassures staff that research may provide benefits.

Demands on ICU Nurses

ICUs are busy, hectic settings in which to conduct clinical research. Given the highly complex ICU environment, ongoing efforts are necessary to minimize the demands placed on the nursing staff while still obtaining enough preliminary information to determine which patients receiving mechanical ventilation might be eligible. Because of stringent restrictions from the Health Insurance Portability and Accountability Act (HIPAA) at the participating ICUs, research personnel in this study could not access patients' medical records to determine study eligibility until the patient consented to participate. Nurses are key informants who can assist research nurses to determine whether a potential participant meets eligibility requirements. So as not to impede the work flow on the units, research nurses should be trained to be efficient in obtaining screening information. Strategies include providing a brief explanation for nurses unfamiliar with the study; focusing on key criteria; asking quick screening questions; using a checklist focusing on most likely exclusion criteria first, such as altered cognition, hemodynamic status, or mental status; and providing guidance to staff nurses on the most efficient way to obtain the information requested (eg, inspect the last day's progress note or problem list for a pulmonary component).

Tailor recruitment strategies to the unit's culture and routine.

Careful selection of a "unit champion" can be invaluable in addressing the recruitment barriers set up by overprotective nurses and minimizing the demands on ICU nursing staff. Since the inception of the study, a lead nurse role has been instituted on each participating ICU. Lead nurses are selected for their interest in research and their desire to improve patient care on the unit. The unit's lead nurse is a liaison between the research team and the nursing staff, and the lead nurse serves as a resource to nursing staff when members of the research team are not available. Lead nurses also alert research personnel to potential patients on their unit who might be appropriate for the study. Each lead nurse identifies approaches specific to his or her unit to engage staff (if that is a barrier to access to potential participants), and serves as a role model in establishing a culture for the study on the unit. For example, one charge nurse initially was less than cooperative in providing research nurses with basic information on the ventilator-dependent patients on her unit. She was rather abrupt with a research nurse one afternoon. This exchange was witnessed by the unit's lead nurse, who promptly approached her colleague in a professional manner, reminded her that the unit was participating in the study and had an agreement to collaborate by exchanging necessary information. Since that time, research nurses have developed a collegial working relationship with that charge nurse.

Minimize demands on nursing staff while still obtaining enough preliminary information.

Terminology for Approaching Potential Participants

The manner in which the study is initially presented to patients can significantly influence participation. The research protocol for this study requires that the staff nurse be the first contact with potential participants. The experimental arm tests patient-directed music listening; therefore, nurses tend to refer to the study as the "music study." If the nurse initially presents the study in this way, it introduces a specific treatment expectation. To address this challenge, nurses are given a written script to use when approaching patients that simply states that a study is being conducted for patients receiving mechanical ventilation, looking at ways to help with

rest and relaxation. Use of the script reduces the chance that nurses will incorrectly say to patients that a “music study” is being conducted when only 33% of participants are randomized to the arm of the study that uses the patient-directed music intervention. Reading from a written script also makes it easier for nurses to know exactly what to say, alleviating some of the stress in their busy day.

Consistent and regular presence of the research team on the unit is critical.

Recommended Strategies for Recruiting Research Participants Receiving Mechanical Ventilation

Although many of the challenges to recruitment are interrelated, the foremost challenge comes from the potential participants themselves. Appreciation of the dignity and respect due to individuals requires that investigators maximize the decision-making opportunities for research participants.¹ Not only must patients’ rights and protection from risk be considered, but patients should have equal opportunities to participate in research. Although research personnel work cooperatively with the nursing staff, patients themselves must be provided the opportunity to decide whether they want to participate in the study, because patients in our study are required to provide their own informed consent. Research personnel must work closely with nurses to identify appropriate patients who meet the eligibility criteria for the study and to assess if an individual is capable of providing informed consent. Research nurses can use a checklist of inclusion and exclusion criteria to efficiently screen all potential participants. Use of the checklist ensures that no patients are burdened by the consent process if they are not eligible to participate in the study.

Investigators should closely monitor recruitment efforts and specifically track reasons for exclusion and reasons that patients decline. All of that information can be used to provide direction about needed changes or adjustments to the protocol. Some particular challenges that may be encountered related to patients receiving mechanical ventilation include muscle weakness, fatigue, and the influence of patients’ family members on the decision to participate.

Muscle Weakness

A major challenge encountered in recruiting patients receiving mechanical ventilation to participate in research is peripheral muscle weakness that makes it impossible for the patient to hold a pen and sign the consent form. Muscle weakness involving peripheral limbs is increasingly common in critically ill patients receiving prolonged mechanical ventilation.² In the early phase of recruitment for the study, 25 patients who were otherwise eligible could not participate because they did not have sufficient muscle strength and fine motor movement in their hands to sign the consent form. This situation was terribly frustrating to the patients, nurses, and research personnel. Two solutions to overcome this potential enrollment barrier included use of adaptive writing aids to facilitate obtaining a participant’s signature (www.lifesolutions.com) and approval by participating IRBs of an amendment to the protocol to waive having an actual signature on the consent form or to allow a witness to sign for the patient when the patient is physically unable to do so. Since the implementation of the writing aid and institution of the signature waiver, 40 participants have been recruited into the protocol who otherwise could not have been enrolled.

Fatigue

The fatigue that critically ill patients experience related to their illness, stress, and sleep disturbances is very challenging during the consent process. The consent form and HIPAA documents can be 3 to 8 pages, depending on the specifications of the IRB at the site. A number

of patients are too weak or tired to read the consent forms themselves; therefore, research personnel may need to read the documents aloud. The time that it takes to read these documents can make the consent process arduous. Research personnel must balance the patient's desire to participate in the study with level of fatigue and ability to tolerate the consent process. Experienced research nurses can determine whether the discussion of the consent process should continue and ensure that the patient understands what is being read to him or her by rephrasing key points of the consent documents. A set of yes/no questions are asked of each patient to ensure comprehension of the study protocol and what is required of participants to allay fatigue.

Research personnel must be astute in their assessment of patients and be willing to explore reasons for hesitancy so that any concerns can be addressed immediately and reassurances can be given to potential participants. Research personnel responsible for enrollment need to know when to defer the consent process and reassess a particular patient later rather than continuing with the process. The goal is to avoid having patients decline to participate for reasons related to timing of the interaction or other issues that could easily be resolved. For example, some patients seem hesitant to give consent, yet they do not formally decline participation. Rather than simply saying they will return the following day to discuss the project again, research nurses for this study have discovered that encouraging patients to try the protocol for 24 hours, while reassuring them they can withdraw at any time, has resulted in enrolling several participants who have gone on to complete the protocol.

Influence of the Patient's Family

Hospitalization of a loved one in an ICU is a stressful time for family members. For purposes of research, family members can positively or negatively influence the patient's decision to participate in a study. Family members can encourage participation if they see the study as a positive opportunity for the patient or for future ICU patients. However, family members can subtly or overtly discourage participation if they feel protective of their loved one or are feeling overwhelmed themselves. They may view study participation as one more thing to do or as an invasion of privacy. Although the patient is the central focus in the consent process, research nurses must be skilled at addressing concerns and questions of patients' family members in an effort to promote the patient's family supporting the patient's participation in the study. Most family members accept their loved one's participation in the study after receiving information and learning that the protocol does not involve testing an experimental drug or device.

The fatigue that critically ill patients experience is very challenging to the process.

Summary of Strategies to Overcome Recruitment Challenges and Recommendations

As with any clinical trial, accrual of sufficient participants is a challenge. Based on the experiences just described, the following strategies are recommended to enhance recruitment:

- Careful selection of research sites based on trusted relationships with nurse leaders and strong familiarity or interest of the nursing staff in research
- Multifaceted and frequent education of staff nurses about the research protocol
- Awareness of the culture and routine on each participating unit, with screening and recruitment strategies tailored to these complex environments
- Consistent and regular presence of the research team on the unit
- Careful selection of a unit liaison or study champion

- Close tracking of screening and recruitment efforts to identify the need to modify aspects of the protocol or procedures

Select lead nurses who are interested in research and want to improve patient care.

These strategies for enhancing recruitment are interrelated and center on a cohesive, highly functioning research team with a principal investigator who proactively addresses barriers with practical solutions. Strategies to enhance recruitment in clinical trials should be tailored to each participating unit and balanced with each unit's priorities; ICUs in the same hospital can have very different cultures and routines for dealing with the many demands of the complex critical care environment.

A number of the strategies presented to enhance recruitment are similar to those discussed by other investigators; others are unique to the ICU setting and patients receiving mechanical ventilation. The authors of a recent Cochrane review³ discussed 5 strategies to improve recruitment: alerting or providing some form of information to potential participants before approaching them, providing extra information about the study to potential participants, making changes in the study design, changing the consent method, and providing research incentives. Although offering monetary incentives for participation is controversial, limited evidence indicates that doing so actually enhances recruitment.⁴ Alerting potential participants was done consistently in this study, with the staff nurse first approaching the patient with basic information about the study. Other strategies employed that were similar to the Cochrane review suggestions include changes in the requirements for consent and obtaining a signature waiver from IRBs for patients with peripheral muscle weakness.

Strategies used to maximize recruitment for this clinical trial include using writing aids, obtaining a waiver of a patient's signature on consent documents if the patient had peripheral muscle weakness, and careful selection of unit champions. All research sites were fully operational by September 2006. From June 2007 to December 2007, strategies to address recruitment barriers were instituted and resulted in overall improved recruitment (see Figure).

Conclusion

Investigators conducting research with ICU patients receiving mechanical ventilation are advised to implement multifaceted strategies to enhance recruitment of participants, including careful preparation of the site before the start of the study, creatively balancing the numerous demands of ICU patients and personnel, and tailoring specific strategies mentioned in this article to the patients and respective cultures of the research sites in a proactive manner.

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Figure.
Total number of participants enrolled in the study by month (July 2006-March 2008).