Ethical Foundations for Critical Care Nursing Research
AACN Mission
Patients and their families rely on nurses at the most vulnerable times of their lives. Acute and critical care nurses rely on AACN for expert knowledge and the influence to fulfill their promise to patients and their families. AACN drives excellence because nothing less is acceptable.

AACN Vision
AACN is dedicated to creating a healthcare system driven by the needs of patients and families where acute and critical care nurses make their optimal contribution.

AACN Core Values
As AACN works to promote its mission and vision, it is guided by values that are rooted in, and arise from, the Association’s history, traditions and culture. AACN, its members, volunteers and staff will honor the following:

- **Ethical accountability and integrity** in relationships, organizational decisions and stewardship of resources.

- **Leadership to enable individuals to make their optimal contribution** through lifelong learning, critical thinking and inquiry.

- **Excellence and innovation** at every level of the organization to advance the profession.

- **Collaboration** to ensure quality patient- and family-focused care.
Ethical Foundations for Critical Care Nursing Research
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AACN’s research vision states that “critically ill patients and their families will have nurses who actively question their practice and base their practice on research.” To fulfill this vision, it is essential to conduct high-quality research to build the scientific foundation of critical care nursing practice. Designing and carrying out research studies salient to the needs of critically ill patients and their families, is challenging because of the nature of the underlying illness or injury, physiologic instability, the complexity of interventions, the rapidity of decisions that must be made, the fleeting nature of patients’ decision-making capacity, and the emotional distress associated with critical illness and injury. All of these factors and many more place critically ill patients and their families in uniquely vulnerable positions, because critically ill patients may be limited in their ability to protect themselves (e.g., unable to make decisions for themselves) in environments rife with external factors that may impact voluntary choice.1 For these reasons, researchers and clinical staff must be exquisitely concerned with designing and carrying out research studies that adhere to the highest ethical standards.

Critical care nurses lead research teams as principal investigators, collaborate as co-investigators on multidisciplinary research teams, serve as research project managers and research staff, and provide clinical care for patients enrolled in research studies. Regardless of their role, all critical care nurses are responsible for committing to the ethical conduct of research. Members of research teams are required to undergo human subjects’ protection training in order to have study protocols approved by human subjects’ boards; clinicians are not held to such a standard. Yet nurses who provide clinical care to critically ill patients are responsible for the quality of the care provided when their patients are enrolled in research studies. It is therefore important that all critical care nurses, whether researchers or clinicians, understand the principles and issues underlying the ethical conduct of research.

The ethical conduct of research is based on core ethical principles that would seem at first to be easily applied to critical care research. Yet the constantly evolving technological world, the rapid pace of knowledge development, and the complexities of patient care make the application of seemingly clear-cut ethical principles challenging. This resource document is based on the premise that the ethical conduct of research is not limited to informed consent or the balance of risks and benefits but extends from study conception through dissemination of results. The ethical conduct of research is structured on a framework developed by Emanuel and colleagues and addresses the requirements necessary for clinical research to be considered ethical.2
Developing a research proposal starts with identifying the research problem. Several broad areas of interest in critical care lend themselves to further research. Such “research areas” can stem from the critical care nurses’ clinical experience, the medical or nursing literature, the National Institutes of Health and National Institutes of Nursing Research priority areas, societal or political issues of importance to the health of the nation, or other external sources. For example, issues of resuscitation, coping with acute illness and disability, family management in intensive care environments, cost-benefit analysis of care in the ICU, and the ethical concerns of caring for critically ill patients and their families are all suitable areas of study. Perhaps a critical care nurse questions the role of aggressive measures in end-of-life care and wonders how he or she might talk to families about an advance directive or other important areas of palliative and end-of-life care. Or, imagine that there are general concerns about communication patterns between nurses and physicians in the critical care setting that affect patient-related outcomes of care, and a clear need exists to identify the facilitators and barriers of communication patterns for improving clinical practice and patient care. Not all research problems lend themselves to research inquiry, however, and many concepts may need further conceptual clarification before beginning an empirical study.

A research problem is usually something that is challenging, problematic, or complex, and it lends itself to investigation through systematic inquiry. Research questions can then be formulated that represent interrogative statements to specifically address the research problem. Finally, research hypotheses provide predictive statements about the research question that the critical care nurse wishes to investigate. Table 1 provides examples of these three key definitions.

Table 1: Research Terms and Examples

<table>
<thead>
<tr>
<th>Research Terms</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Research Problem</td>
<td>• Evidence suggests that end-of-life care in intensive care environments is costly with questionable benefit, and about 20% of Americans will die in an intensive care unit.</td>
</tr>
</tbody>
</table>
| Research Question    | • Is there a relationship between physician and nurse communication and end-of-life care in the intensive care unit?  
• What are the barriers to effective communication in critical care environments? |
| Hypothesis           | • Families who perceive their communication with physicians and nurses to be positive in the intensive care setting will also indicate positive end-of-life care for their loved one. |
To begin, it is important to know what the literature states about your topic of interest. These are key questions that critical care nurses should consider when thinking about proposing a research study:

- Is it a novel area that the nurse is exploring?
- What contribution does researching the problem add to nursing science and/or to the literature in general?
- Will the area of study add to nursing's knowledge in clinical practice, improve understanding of a theoretical perspective, or develop an innovative intervention?
- What has been done previously, and what more is there to know or learn?
- What are the significant gaps in the literature, and how can you address these gaps?
- What is the overall significance of the problem?
Research is a systematic process that requires rigorous procedures. Critical care nurse researchers often use different types of experimental and nonexperimental methods in their research programs. But regardless of the approach, the processes must convey trustworthiness in the reported outcomes. As stated by Emanuel, Wendler, and Grady, “For a clinical protocol to be ethical, the methods must be valid and practically feasible; the research must have a clear scientific objective; be designed using accepted principles, methods, and reliable practices; have sufficient power to definitively test the objective; and offer a plausible data analysis plan.”

To determine the appropriate number of patient-subjects, the type of sampling methods, levels of measurement of variables under study, and the statistical analysis plan, critical care nurses should work with a statistician during the development phase of their protocols. For quantitative projects, a power analysis determines the number of patient-subjects required to meet the stated research questions. This is important, because researchers don’t want to expose subjects to unnecessary risk without the possibility of benefit. Generally, 80% power at a .05 level of significance allows the researcher to reject the null hypothesis (i.e., null hypothesis states that there are no significant differences) or indicate that differences in fact do exist in the population.

Although there are times when a critical care nurse researcher might need to develop an instrument to measure a new concept, a number of reliable and valid measures (instruments) exist in the literature. Usually the development of an instrument is a study in and of itself. Nurses can adapt measures to meet their stated purposes and retest the reliability and validity as needed. Generally speaking, reliability denotes the consistency of the instrument’s performance across items, people, and time. And, to be valid, the instrument must measure what it is purported to measure (e.g., the attitudes of critical care nurses toward end-of-life issues, coping with illness, nurse job satisfaction). For those critical care nurses who are interested in qualitative work (e.g., phenomenology, grounded theory, ethnography, narrative inquiry) or, for example, understanding the lived experience of seriously ill patients and their families, several prominent qualitative nurse researchers have provided a frame of reference for the number of subjects that one might need for differing qualitative approaches. Generally, however, one collects data until saturation occurs, or when no new themes are derived from the data.
Critical care research builds knowledge to improve the care of critically ill patients; to do so, critically ill patients are asked to participate in research. Patients who agree to enter studies are exposed to the risks and potential benefits of the study protocol. Ethically, therefore, it is important that those patients most likely to bear the benefit of the research should also bear the risks of study participation.

The study aims determine the population of interest and therefore which patients qualify for potential entry into the study and which patients should be excluded. Study sampling criteria not only enhance the scientific rigor but also are developed to minimize the risk to participants. Sampling criteria are central to meet the standard of fair participant selection and should ensure to the greatest degree possible that all patients who fall within the population of interest have equal opportunity to become a study participant. This means that subsets of patients, because of certain characteristics, are not systematically overenrolled or excluded from participation. Thus, all patients who meet the criteria are approached for study entry or have an equal chance of being randomly selected for study entry regardless of insurance status, racial or ethnic background, or other non-study-related factors.

**Case Exemplar:** A study is examining the outcomes of care provided by an acute care nurse practitioner service and a traditional resident staff teaching service. This study is being conducted in an inner city hospital surrounded by communities of intense poverty. Patients with an exacerbation of heart failure qualify for study entry, which entails randomization to one of the two services. Patients who are admitted through the emergency department are approached for consent to enter the study. Patients who meet study criteria but who are directly admitted by private physicians are not approached for consent and are automatically admitted to the teaching service.

This case exemplar highlights a differential enrollment of patients in the research study because of the point of entry and most likely is related to their insurance status (e.g., private insurance for those admitted via private physicians, and Medicaid more likely for those admitted through the emergency department without a private physician). This scenario is ethically problematic in that future patients who will benefit from the study are not fully represented by those patients enrolled in the study and exposed to its risks, and thus, the fair subject selection standard is violated. Such a violation harkens back to Tuskegee, which has become America’s historical touchstone for racism in medical research.13

Related and equally problematic is the historical exclusion of women and children from many research studies, although it has improved over the past two decades. Excluding segments of the population is scientifically problematic. Findings from studies conducted solely on men are not easily applied to women, who have a different anatomy and physiologic responses to illness and injury; for example, in studies of cardiac disorders. Similarly, although children deserve special protections, excluding them from research is problematic in that children are not “little adults,” and findings from adult studies cannot simply be applied to the care of critically ill and injured children. Federal funding agencies have specific review processes to ensure that groups previously systematically excluded from research are adequately included in studies. Investigators are required to justify the exclusion of children, women, or minorities from research studies. Peer reviewers of grant applications being considered for funding are specifically asked to comment on the adequacy of the justification.
Favorable Risk-Benefit Ratio

Risks associated with studies of critically ill patients range from very low risk (observation and descriptive studies) to very high risk (innovative treatment in clinical trials). All potential risks to individual participants should be identified and potential participants fully informed. Known risks can be gleaned from the literature, by knowledge of the intervention being tested, and by responses of participants to previous studies of a comparable nature. Risks can be categorized as follows: risks from study treatments, risks of loss of individualized care, risks of other aspects of the research protocol (e.g., loss of confidentiality), psychological risks from participation, and also the risk of nonparticipation.14

Risks can range from emotional feelings from answering questions and skin reactions to study devices on the relatively minor end of the continuum to impaired oxygenation, hypotension, and death on the riskier end of the continuum. Some participants, by virtue of the nature of their illness or injury, are more vulnerable to certain risks than other patients. For example, a woman who is critically wounded in a domestic violence event where one of her children was also injured is likely to be at higher risk for intense psychological distress associated with a research study examining predictors and outcomes of injury than those who were injured in a different manner.15 All risks that are known and likely to arise in a study should be carefully articulated, including the likelihood (if known) of those risks to individual research participants.

New risks may be identified when new or unanticipated adverse events arise during study implementation. These adverse events are typically ranked by their severity. A serious adverse event is an untoward event related to the study protocol that prolongs hospitalization, requires additional treatment, or threatens life. The research team is responsible to document the adverse event and its consequences and report it to the human subjects’ review board and the data safety monitoring board, if one exists. The purpose is not only to report the event, but to protect the safety of current and future research participants.16 New risks may also be identified in newly published research. In either case a new risk-benefit analysis needs to be performed, reviewed by the human subjects’ board, and study participants informed so they can make an informed decision if they will agree to continue in the study.

Whereas the risk assessment focuses on risks to individual research participants, the benefit assessment focuses on benefits to future patients and society in general. Potential benefits accrue primarily for future critically ill patients and not the individual participant, because the goal of research is to develop knowledge and not focus on the needs of an individual patient.

Case Exemplar: A research study seeks to determine if frail older adults who receive early, aggressive mobilization starting in the ICU will have lower mortality and improved function when compared to frail older adults who receive usual care. Mr. Grand agrees to enroll his 85-year-old wife in the study after being informed about the randomization procedure and the potential risks of the treatment arm of the study that include but are not limited to orthostatic hypotension, unintentional extubation, line loss, and falls. Mr. Grand signs the consent form (his wife does not have decision-making ability at this point) after all of his questions are answered. The next day, he tells Mrs. Grand’s primary nurse that he enrolled her in the study, because she would get better care than if she were not in the study.

This case exemplar highlights some well-documented issues on how lay people perceive research. Random assignment is justified when the experimental intervention is not known to be better than current practice. Indeed, if it were known to be better there would not be a need to carry out the research. This balance is called clinical equipoise, and when present, indicates the treatment arm of the trial is not likely to benefit the individual participant over the control arm.17 Despite the clarity with which researchers obtain informed
consent, a subset of patients enters research studies with the belief that by doing so, they will benefit (e.g., receive superior treatment). This is called therapeutic misconception, and such instances include research participants who do not understand that research decisions (e.g., randomization) are not being conducted to meet their individual needs or who hold an unrealistic belief in the potential benefit of participation. Such misconceptions can be a factor in decisions and has been called conditional altruism – where patients decide to enter the study not only for the benefit to future patients but because of their perception of some benefit and with limited risk to themselves. That said, one study of injured children shows that a majority of children (74%) and their parents (77%) report they were glad they participated in research and that 90% of parents felt good about helping others.

There may be potential benefits for patients participating in research studies. The key word here is “potential,” because there is no guarantee that individual participants will benefit from participation. For example, consider a critically ill patient enrolled in a study that includes additional diagnostic scanning designed to test a new anticoagulant medication. In this case, the additional scanning may uncover a thrombus that otherwise would not have been found until it became symptomatic (e.g., an embolus).

The risk-benefit ratio is based on the balance of core ethical principles of nonmaleficence (do no harm) and beneficence (do good). Assessing the risk-benefit ratio is the responsibility of the research team. In principle, studies that pose great risk must also hold the potential for great benefit, or else the risk-benefit ratio cannot be justified. Because the focus of research is on building generalizable knowledge, research participants are exposed to potential harm for the good of others (i.e., future patients). Determining the risk-benefit balance is not a simple numerical calculation, and balancing risk to individual research subjects against the potential benefits to future patients is ethically complex. Therefore, the judgment about risk-benefit is subject to independent oversight.

Critically ill patients present unique vulnerabilities that may alter the risk-benefit ratio and that should be carefully considered. It is impossible to explore all potential vulnerabilities, but two that cross critical care specialties are particularly salient: the emergent nature of critical illness and physiologic instability. Critical illness and injury are often abrupt in onset and unanticipated by patients and their families. The intense emotional burden that frequently accompanies critical illness may heighten the psychological risks of participating in research studies. In the physiologic realm, an intervention that may be well tolerated by healthy research participants may not be as well tolerated by those who have a physiologically unstable disorder.
Peer review — both formal and informal — is an important component of the research process. Informally, nurses can ask their nurse scientist colleagues or other disciplines to review the research protocol for content and significance, clarity, methodological rigor, human subjects’ protections, data analysis plans, and any other related aspect that critical care nurses might need for clarification and feedback. Formally, however, all research protocols must be approved by an institutional review board (IRB). And, in some cases, this might include several IRBs if the study is being conducted in different locations. Generally, an IRB is an oversight body that consists of at least five members (membership must include at least one nonscientist) who have the responsibility of reviewing institutional research protocols and determining the risk-benefit profile and informed consent procedures.24

Institutional review boards decide whether a protocol is exempt, expedited, or needs full board review; this risk-level determination is not at the investigator’s discretion, and IRB approval must be received before beginning of the study. Table 2 defines research risk-level designations.

Table 2: Research Risk Designation Levels

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<tr>
<th>Research Risk Levels</th>
<th>Definitions</th>
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<tr>
<td>Exempt</td>
<td>A study may be exempt if it is deemed to pose minimal risk. Examples include educational and demonstration projects, and secondary data analysis. This is most likely the case if the sources are available for public use, and subjects are not identifiable.</td>
</tr>
<tr>
<td>Expedited</td>
<td>A study may be expedited if it is deemed to pose no greater than minimal risk and is approved by the IRB chairperson or other designee(s). For example, this may include attitudinal and behavioral surveys, collection of blood samples, and continuing review of an already approved protocol.</td>
</tr>
<tr>
<td>Full-board review</td>
<td>Full board review is required for any protocol that does not meet the exempt or expedited designation.</td>
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See also the Code of Federal Regulations, Title 45, Part 46 (45CFR46).

Data and safety monitoring boards (DSMBs) provide another means of peer review for complex clinical research or clinical trials that require interventions to human participants, especially for those trials that might present considerable risks to participants. These monitoring boards are often commissioned by the sponsoring agency, such as the National Institutes of Health, if the research received federal funding, as well as pharmaceutical sponsorship.25 DSMBs usually consist of independent experts who externally monitor research protocols (clinical trials) on issues of participant safety, recruitment and retention, study operations, data integrity, and other aspects of the trial. DSMB members must remain independent of the study and therefore are required to disclose all possible financial conflicts of interest and links to the study protocol and its investigators. DSMBs make recommendations regarding the continuation of the study; they can agree to continue the study as indicated, suggest minor or major modifications and corrective actions, or terminate the study based on risk-benefit concerns or other patient safety issues. Finally, peer review also plays a critical role in recognizing potential conflicts of interest that are discussed in the next section (and also in the section on scientific integrity).
Informed Consent

Informed consent is the cornerstone of ethical research. Critical care nurses often participate in obtaining informed consent from human subjects (participants) as part of a research team; or individually, as principal investigators of their own research protocols. As critical care bedside nurses, they can also be in a position to witness the informed consent process for their patients and, subsequently, might be asked to clarify research-related questions. Informed consent consists of several important elements: voluntariness and capacity to make decisions, disclosure of information, and comprehension. The following elements are included in the informed consent document:

- Explanation of the nature and purpose of the research
- Outline of the risks and benefits
- Statement of patients’ right to refuse participation without penalty
- Statement of confidentiality and privacy of participants’ information
- Procedural aspects of the research
- Discussion of alternative treatment options, if any
- Voluntary participation
- Name and number of individual to call for any particular issue that might arise during the conduct of the research
- Statement regarding compensation and medical treatments for any research injury that may occur

Additional information might include:

- Amount of remuneration for research participation
- Disclosure of potential conflict of interest, if any
- Pregnancy-related risks
- Notification procedures if any new information arises that impacts research participation
- Instances in which the subject may be withdrawn from the research

See also the Code of Federal Regulations, Title 21, Part 50 (2CFR50.25) for elements of informed consent.

Informed consent documents should be written at a level that is understandable to research participants. In general, this is usually at a 4th to 6th grade reading level. The Office of Human Subjects Research at the National Institutes of Health suggests writing informed consent documents with the use of headings, short concise paragraphs, fewer than three syllables in a word, and easy-to-understand language (the use of non-medical terms as much as possible). To calculate the readability level of informed consent documents, critical care nurses can use the Flesch-Kincaid tools included in Microsoft Word.

**Case Exemplar:** Emily is an 18-year-old who arrives at a level III emergency department following a motor vehicle crash in which she apparently fell asleep at the wheel, crossed the median, and hit another vehicle. She is barely conscious and has a large hematoma to the forehead and other injuries, including possible broken ribs and arm. In addition, she is slurring her speech and has bloody fluid draining from her right ear. An MRI and other tests reveal she has a fractured skull. She is being prepped for the operating room. Following surgery, Emily is transferred to the neurological intensive care unit where she is eligible for a research protocol focused on quality of life and other psychological outcomes in young adults who have head trauma. Her
primary care nurse doesn't feel comfortable that Emily is in a position to understand the research or that her parents should even be approached to discuss the benefits and burdens of the study since they have been seen crying and emotionally distressed when they visit their daughter.

This case exemplar highlights ethical concerns related to research in the critical care environment, surrogate decision making for patients with questionable decision-making capacity, and the difficulties that many nurses might share in regard to clinical care versus research. Nursing’s Code of Ethics\(^{30}\) states that nurses’ primary commitment is to the patient, but a conflict can also arise when the nurse feels that he or she must protect or advocate on behalf of the patient related to the research.

Because of the nature of critically injured patients’ physical and/or psychological trauma, decisional capacity\(^{31}\) or the ability to understand, appreciate, reason and make a decision, or express a choice about what is in their best interest pertaining to research may not be possible. Although it is assumed that hospitalized patients are vulnerable because of their injuries and other associated risks, vulnerability in research is defined differently. In research, **vulnerability** denotes the inability to provide informed consent for various reasons (e.g., incapacity, educational, or emotional burdens). The Code of Federal Regulations (45CFR46)\(^{24}\) discusses several populations that require safeguards or added protections related to informed consent. These include pregnant women, children, prisoners, and adults with capacity concerns (subparts B, C, and D).

Surrogate or proxy decision makers are common in critical care environments and represent those individuals who are legally authorized to act on behalf of patients who are deemed incapacitated in some way.\(^{32}\) Surrogates may include an appointed guardian, spouse, domestic partner, adult children, or other appropriate designee, but it is important to check one’s state of practice to determine who may actually provide consent for an incompetent patient and the order of priority in decision making. Surrogates often use what is called a “substituted judgment standard” and are asked to determine what the patient would have wanted based on his previously expressed wishes (if known) and other relevant factors (e.g., prognosis, wishes of other relatives and friends, risks of harm from the treatment or research, and religious and moral convictions).\(^{32}\) Surrogate consent must be approved by the IRB (see Independent Peer Review section). In addition, a waiver of consent\(^{33}\) can at times be justified by the IRB. In general, research waivers also can be obtained if the following **four criteria** have been met (as outlined in the Code of Federal Regulations for waiving informed consent):

- Research does not pose a greater than minimal risk (minimal risk is defined as when “the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests” [45CFR46.102])\(^{24}\)
- The rights and welfare of the participants will not be altered or harmed by the waiver
- Without the waiver, the research could not be conducted; and
- Additional information will be provided to subjects when appropriate

Waivers for emergency care research\(^{34}\) may be approved in situations where obtaining informed consent is not feasible for patients with a significant life-threatening condition who are in need of immediate intervention that holds out the possibility of direct benefit. In such cases, an appropriate surrogate is not available to obtain informed consent before initiating the intervention. However, researchers must make every effort to obtain consent.
Pediatric critical care nurses who are interested in conducting research with children and their parents must obtain pediatric assent with parental permission as they are essential components of informed consent for pediatric patients. Generally, children about 8 years old have the capacity to understand terms related to research, although they have not reached the legal age for consent to research (check state laws to determine how “children” are defined; generally, it is a person younger than 18). Therefore, pediatric assent is obtained. This means that all elements of the research are discussed with the child at the appropriate age level, and parental permission is also obtained from one or both parents (depending on the requirements of the study). Institutional review boards make determinations regarding the risk level of pediatric protocols, whether assent is needed from all children who participate, and whether permission is required from one or both parents, or whether the requirement can be waived (see subpart D of 45CFR46).
Respect is a core ethical principle. The obligation of the research team to respect begins before interacting with participants who are enrolled in the study. All critically ill patients who are potential study participants should be treated with respect, which entails honoring their right to choose whether to be approached by the research team, the right for health records to be private unless consent for disclosure is provided, and the right to weigh and consider interest in enrolling in and remaining in the research study. The clinical team should ask patients (or surrogates) if they can be approached by the research team, and only when permission is provided should the research team approach patients as potential study participants. The medical record, which includes private health information, is protected legally and ethically, and documentation from the record cannot be extracted for research purposes without the consent of patients (or surrogates).

Respect carries through all aspects of the study from the decision by patients to enroll (or not), assurance of privacy during interviews, and patients’ right to withdraw from the study at any point, free from coercion. Freedom from coercion means that patients can choose not to enroll or to withdraw without threat to the nature or quality of clinical care they would receive otherwise. It further means that patients and surrogates to discuss the study with significant others, and to compile additional questions they may want answered.

Respect continues throughout the entire study. As such, consent is not a one-time event but an ongoing responsibility of the research team. Consent is revisited in several situations, including when the risk-benefit ratio changes and when decision-making capacity fluctuates. Frequently, critically ill patients experience temporary loss of decision-making capacity due to physiologic instability (e.g., hypoxemia, hypotension), surgical intervention (e.g., general anesthesia), pharmacologic intervention (e.g., sedation, paralytics), communication impediments (e.g., intubation), and often through a combination of factors. In the case of fluctuating decision-making capacity, it is often necessary to revisit the consent process, because either a surrogate provided initial consent and now the patient has regained decision-making capacity, or the patient does not remember aspects of the study to which he consented. The following case exemplifies this aspect of respect and the responsibility of the research team when consent or assent is withdrawn.

**Case Exemplar:** A study is examining the value of early mobilization of children in a pediatric intensive care unit (PICU). Children are entered in the study within 24 hours of admission to the PICU. Josh is 10 years old and admitted to the PICU with acute respiratory failure for which he is intubated, ventilated and sedated. Josh’s parents consent to enter him in the research study. He has been in the study for five days during which time he is receiving the study protocol and data are being collected. On day six, Josh is no longer sedated and ventilated and is able to understand the nature of the study. He refuses to provide assent to be in the study. He is withdrawn from the study because of his lack of assent, but the data collected to date are used in the analysis, because the parents had provided consent on his behalf.

Welfare of participants is a priority in a research study. The research team carefully monitors participants for adverse events — these may range from known risks to events due to unexpected risks and events that are minor to life-threatening. All adverse events are carefully documented and reviewed by the research team that details the adverse event, determines the severity of that event, and makes a judgment about whether the event was related or unrelated to the research study. Participants experiencing an adverse event that requires treatment (e.g., excess bleeding, hypercarbia, unintended extubation) should have those events managed by clinical treatment regardless of the impact on the research protocol or study. The research team may decide to withdraw the participant from the study if continuing participation exposes the participant to ongoing risk.
Integrity is essential to public trust, and nurses are consistently viewed by the public as trustworthy care providers. In a similar way, nurses who conduct critical care research with human participants must follow regulatory and ethical codes of research conduct (as discussed previously) and commit to intellectual honesty in the research process. The Belmont Report, a historical research ethics document, outlines three basic ethical principles that critical care nurses should be familiar with: beneficence, respect for persons, and justice. In the research context, the principle of beneficence requires that researchers minimize harms and maximize benefits of research participation. Patient-subjects need to be aware of the potential risks and benefits as part of the informed consent dialogue, as discussed earlier; IRBs also make this determination during their deliberations. The principle of respect for persons recognizes the autonomous right of every person to determine what is in his or her best interest and also protects the dignity of those who are not able to make such decisions by authorizing a third party to speak on their behalf. Respect for persons applies to informed consent and its essential elements: voluntariness of the participant, disclosure of information, and comprehension. Finally, the ethical principle of justice obliges researchers to distribute fairly the benefits and burdens of research among research participants; therefore, justifications must be provided for excluding certain groups of subjects.

Researchers make difficult research decisions every day, and honest mistakes or differences of opinion do not imply misconduct. However, research misconduct has been characteristically defined with terms such as fabrication, falsification, and plagiarism (Table 3), although there are other practices that fall outside these terms that can be problematic and ethically questionable. In their study “Scientists Behaving Badly,” Martinson, Anderson, and deVries reported on some of these behaviors including inappropriate authorship credits, self-plagiarism, omitting data points, and inadequate record keeping. Critical care nurses should familiarize themselves with departmental and/or institutional policies on authorship, data management, and other aspects of the research process. It is best to outline these issues a priori and develop a memorandum of understanding among all members of the research team. The responsibilities of critical care nurses conducting research do not differ from those of other disciplines. All researchers have an ethical and regulatory obligation to protect human participants, conducting research with methodological soundness, objectivity, and truthfulness. Nurse researchers can and should seek out senior scholars or designated mentors to gather insights on addressing problems that might arise in the daily work and implementation of research.

Table 3: Definition of Terms

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<tr>
<th>Research Misconduct Terms</th>
<th>Definitions</th>
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<tbody>
<tr>
<td>Falsification</td>
<td>Misrepresentation of research through manipulation of data results, such as omitting or changing data.</td>
</tr>
<tr>
<td>Fabrication</td>
<td>Making up data and reporting it in publications, presentations, abstracts, or other areas of scientific inquiry.</td>
</tr>
<tr>
<td>Plagiarism</td>
<td>Using another’s intellectual work, ideas, or results without proper attribution.</td>
</tr>
<tr>
<td>Serious deviation from standards of practice</td>
<td>Egregious practices such as stealing or destroying data, research records, or other aspects of the research process.</td>
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(Adapted from: The Office of Research Integrity and S. Weiss, personal communication, March 19, 2012)
Case Exemplar: Dr. Colleen May is a participating neurologist in a clinical trial to assess the efficacy and toxicity of a new anticonvulsant medication. For the duration of the 2-year study, each neurologist is to meet with each of his or her patients for an average of 30 minutes each month. In Dr. May’s case, this amounts to an average of 20 hours per month. During each visit, the physicians administer a variety of specialized tests, requiring judgments dependent on their experience and training in neurology. At the completion of the study, the results are to be unblended and analyzed by the project leaders. It is anticipated that at least two publications will be prepared for *The New England Journal of Medicine*. Dr. May has just learned that she will be listed in the acknowledgments but not as a coauthor of the manuscript. Dr. May argues that she has provided nearly 500 hours of her expert time, far more than needed to complete a publishable study in her experimental laboratory. Does Dr. May have a case for authorship? [Used with permission of Dr. Francis L. Macrina]

This case exemplar highlights the tensions that exist when individuals associated with a research project expend time and energy toward helping the principal investigator achieve the stated specific aims of the research, yet have attribution expectations that were not fully discussed during initial development of the proposal. Nurses can find themselves in a similar position as they might be part of a team that is using its expertise to obtain informed consent or assist with implementation of research procedures at the bedside or in other settings. However, data collection does not necessarily impart authorship, and these discussions need to occur early so that all members of the team are reasonably satisfied with the deliverables at the end of the project. Primary authorship is generally granted to the individual who provided the greatest overall contribution and intellectual input to the manuscript while coauthorship denotes secondary input for writing, interpretation, and critical review of the manuscript as well as acquisition of data.

Finally, discussions surrounding conflict of interest (COI) have been featured prominently in the literature out of concern for the impact on scientific integrity and the public’s trust of the research enterprise. A COI can occur when researchers have several competing interests that appear to unduly influence their judgment. Thompson defines COI as:

… a set of conditions in which professional judgment concerning a primary interest (such as a patient’s welfare or the validity of research) tends to be unduly influenced by a secondary interest (such as financial gain).

Although the literature and much of the media focus on financial COI, nurse researchers can have other types of conflicts. Such conflicts include the demands placed on their time to allocated projects, educational efforts, attending professional meetings, serving on committees, or paid consultancy. Each institution should have a COI policy to guide researchers in identifying potential COI and disclosure efforts as needed. More recently, the U.S. Department of Health and Human Services and the National Institutes of Health have revised regulations on “Responsibility of Applicants for Promoting Objectivity in Research for Which PHS Funding Is Sought” (42CFR50, subpart F) that address changes in individual and institutional responsibilities regarding financial COI and disclosure requirements. All institutions that receive federal funding must comply with all COI revisions no later than August 24, 2012.
Cross-cutting Information of Importance to Critical Care Nursing Research

The research team is confronted with some significant barriers to consenting critically ill patients in research studies that can negatively affect the ability to carry out the study. The principles and approaches to informed consent whether directly from the patient, the parents of a critically ill child, or from a proxy are explained in the informed consent section. In applying these principles in the emergent setting of critical care, additional complexities surface and in particular, two merit consideration.

First, can informed consent be obtained (from patient, parent or proxy) in the face of the intense emotional distress that accompanies an unanticipated critical illness or injury? Processing the nature of the study, the procedures involved in the study, and in particular the risks posed by the study requires not only intellectual capacity but the psychological ability to focus on and process the information provided by the research team. For the proxy, deciding whether to enter their loved one in a research study may actually be more stressful than the treatment decision that the proxy is asked to make.47

Because of the emotional burden that accompanies a critical illness or injury, some ethicists believe that not all studies require informed consent in critical care, yet this is not a widely shared view, and critical care nurses should expect that consent is obtained from patient, parent or proxy.48 It is recommended that the timing of consent be tailored to the emotional state of the patient or proxy. While ideal, delaying consent until the “time is right” is not possible when testing interventions that are time-sensitive, or if we want to build knowledge about the emergent phase of critical illness or injury. In some instances, deferred consent is a solution to this challenge where study procedures can start until such time as it is appropriate to obtain consent.49 Even later in the phase of care, emotional distress can cloud decision making.50 The case below highlights the importance of answering key research questions, but the challenges of seeking consent during highly emotional times.

**Case Exemplar:** A study is designed to examine the decision-making processes and experiences of families as they determine whether to withdraw life-sustaining therapy from a loved one in critical care. Mr. Jones is 64 years old and has been in the critical care unit for one week following a car crash resulting in massive injuries. He has been comatose since the injury, has adult respiratory distress syndrome, acute renal failure and is now septic. The clinical team has approached Mrs. Jones to initiate discussions about changing goals of care and possible withdrawal of treatment. From the research team’s perspective, this is the optimal time to enroll Mrs. Jones in its study. The following day, a member of the clinical team asks Mrs. Jones if the researcher can speak with her. She agrees, and the researcher explains the study and answers questions about the nature of the study and the interviews that will take place over the course of the coming week, and Mrs. Jones consents to participate.

The second challenge common to critical care research is the “popular patient” population that qualifies for multiple research studies. This is especially true in research-intensive academic health centers and in specialty centers caring for highly specialized patient populations (e.g., patients with spinal cord injury). The challenge is twofold: 1) Scientifically, it is important to determine if enrollment in more than one study would compromise the methodologic validity of either study; and 2) humanistically, it is confusing and emotionally burdensome for patients and families to be approached by uncoordinated teams for multiple research consents. Clinicians cannot expect that the human subjects’ boards that provide ethical approval for studies will address the issues of multiple studies at any given time in the same population. Systems and processes need to be put in place that address the issue and that equitably balance the needs of the research teams involved.
The clinical team is also confronted with significant challenges. Research studies have the potential to add to the workload of critical care nurses. For example, a study protocol that requires scans may require transport of critically ill patients off the unit and will consume resources since critical care nurses transport such patients. Some protocols require nursing care that exceeds usual care, requires additional documentation, requires education for the staff and may add to the workload. For example, a study that is testing an aggressive mobilization protocol for critically ill patients requires learning the protocol, and the additional staff nurse time for implementing the protocol may impact staffing. Ethically, the just distribution of resources indicates that care be taken that patients not enrolled in a given research study suffer as a result of such workload issues. For this reason, when research studies are planned, requirements of the nursing staff should be discussed before study implementation. If the study will consume nurse resources, the research team should consider compensating the nursing department for the time and effort, or consider providing financial support for supplemental staff.

A second challenge is the potential for conflicting goals between clinicians and researchers. Nurses’ primary duty is to patients, thus to make the best decision for individual patients to achieve the goals of care. The research teams’ primary focus is to build knowledge, and although researchers are ethically bound to identify and minimize the risks of the study, their duty is distinctly different from the clinician’s duty. Such differences can at times create tensions when managing critically ill patients. Clinicians should be as fully aware as possible of the research protocol and its potential for adverse effects since that can impact clinical care. As such, all critical care nurses should be aware if their patients are enrolled in studies and the nature of those studies. For this reason, a copy of the informed consent should be part of the medical record that can be reviewed by the clinical team. Further, the clinical team may be required to step in and deal with any negative consequences that occur as a result of the research protocol. Ultimately, the well-being of patients takes precedence over the requirements of the research protocol.
For those critical care nurse researchers working with animals, specific federal regulations and professional guidelines dictate standards for research with animals, recognizing the need to minimize pain and suffering imposed on them. The 1966 Animal Welfare Act (revised several times and addresses only those animals defined as “warm blooded”), the 1985 Health Research Extension Act, Section 495, and the Guide for the Care and Use of Laboratory Animals (1996) provide references for researchers and institutions on animal care and use. Researchers must provide appropriate housing, feed, and care of animals as well as the involvement of veterinary personnel; and they must be qualified to carry out the research. Animals are defined by the Public Health Service Policy on Humane Care and Use of Laboratory Animals, more commonly known as the PHS Policy, as “any live, vertebrate animals used or intended for use in research, research training, experimentation, or biological testing or for related purposes.”

Each institution that conducts research with animals must have an Institutional Animal Care and Use Committee as mandated by the federal government. These committees are responsible for monitoring the humane treatment of animals in research, addressing any concerns that might arise related to the use and care of animals, inspecting the animal facilities, and reporting any deficiencies to the appointed institutional officer. At a minimum, committee members must include a scientist conducting research with animals, a doctor of veterinary medicine, and a lay person who is not affiliated with the institution. In some cases, an ethicist might also be a member of this committee.


49 Jansen TC, Kompanje EJO, Bakker J. (2009). Deferred proxy consent in emergency critical care research: Ethically valid and practically feasible. Critical Care Medicine, 37, S65-S68.