Scope of Clinical Research Nursing Practice

INTRODUCTION TO CLINICAL RESEARCH NURSES AND NURSING

Clinical research nurses (CRNs) are practicing worldwide in diverse roles and settings. Over the past decade, the global landscape of clinical research has become more complex with new patterns of professional practice emerging at a remarkable pace. In addition, the COVID-19 global pandemic introduced a transformative shift, creating unprecedented and complex practice environments. In response to an urgent need to identify effective treatments, vaccines, and long-term impacts of the virus, the clinical research enterprise pivoted to accommodate safe practices and substantial growth in the number of clinical trials (Ellenberg, 2020). CRNs are integral to the success of these clinical research endeavors while at the same time shouldering responsibilities to continue research projects with goals of finding treatments for other diseases affecting global health.

Both healthy people and those with health conditions volunteer their time and their subjective and objective data to advance health sciences. Often, these volunteer participants step outside the mainstream of clinical care, known as the "standard of care," and are willing to give of themselves by participating in clinical research. Persons who volunteer to participate in clinical research deserve specialized nursing care that ensures exceptional, ethical, safe care, yielding high-quality data. The care of the research participant must be consistent with the research protocol, plan of care, and clinical need. The best interest of the participant, along with the integrity of the research protocol, is the primary focus of the clinical research nursing specialty practice.

EVOLUTION OF CLINICAL RESEARCH NURSING

Clinical research is the backbone of international scientific discovery. The use of high-tech procedures, techniques, and laboratories moves discovery quickly from bench to bedside. In the past, physicians were responsible for the day-to-day conduct and management of clinical trials (Fox, 1997). The recent focus on translational research pushes the speed of discovery and places participants in a position of great benefit but also increases their potential risk. The unique skills of the CRN are perfectly suited to foster this rapid discovery while ensuring protection of the participants. Today, nurses play a key role in the clinical research enterprise (Wallen & Fisher, 2018).

Evidence of the CRN's role and specialized practice has appeared in the literature as far back as the mid-19th century with Florence Nightingale's publications. Her ability to collect, collate, and apply statistical calculations, combined with management of the data, enabled her to take steps as a scientist to affect health care reforms and subsequently develop her environmental theory that brought the importance of infection control to the forefront (Gilbert, 2020). Later, Nancy Poultney Ellicott, appointed superintendent of nursing at Rockefeller Institute Hospital in 1910, was an early nurse leader in the new field of clinical research. She recognized that nurses engaged in clinical research had a unique role and impact on the outcomes of clinical trials. Ellicott wrote the following about clinical research nursing: "In order to make possible the realization of the aspirations of the founders of the hospital, the nursing must be of the very highest type. Records must be most carefully and accurately kept, symptoms observed and recorded, reports intelligently and faithfully made, for a lapse in vigilance, or in a specimen lost in a moment of heedlessness, might render worthless the labor of many weeks" (The Rockefeller University, n.d.).

In the 1960s, the clinical trials nurse (CTN), implementing early chemotherapy trials, recognized this nursing role was distinct and required a unique set of knowledge and skills in addition to those outlined for all nurses (Deininger, 2008). Although the term *CTN* is used in oncology nursing, the roles described are represented in CRN practice, which is

inclusive of the oncology-specific role. Throughout the 1980s and 1990s, the literature continued to expand on the concept of clinical research nursing as a professional and specialty nursing practice (Johnson, 1986; McEvoy et al., 1991), and the number of clinical trials in subspecialties grew. The CRN role became more complex with an increasing need for definition. Despite the lack of clear role definition, CRNs were considered crucial to the successful conduct of clinical trials (McKinney & Vermeulen, 2000). The role of the CRN was largely accepted as a career path for nurses by the 1990s (Eaton & Pratt, 1990; McEvoy et al., 1991), and DiGiulio et al. (1996) described the need to expand the role of nurses in clinical trials.

In 1989, nurse managers of the General Clinical Research Center (GCRC) programs were invited, for the first time, by the National Institutes of Health (NIH) to participate in the annual GCRC Program Directors two-day conference in Gaithersburg, Maryland. At this historic meeting, a group of nurse managers volunteered—and were unanimously supported by the program directors—to establish a formal structure for the National Association of GCRC Nurse Managers (GCRCNM). The mission of the association was to exchange knowledge and ideas, to establish nursing standards in the clinical research center settings, and to consult, support, and advance competencies for the GCRC nurse managers. Over time, many hours of dedicated individual and regional work led to the development of an orientation program for new GCRC nurse managers, preparation guidelines for NIH site visits and Joint Commission reviews, and tools for planning nursing services for new protocols. In addition to providing support for nurse managers, the group worked to set standards for CRN education, training, and research procedures common in a variety of settings and address issues of ethical and safe conduct of clinical research. In response to funding changes occurring by 2000 and the apparent need to increase support to a growing base of CRNs, the GCRCNM group expanded their assistance to include CRNs working outside the GCRCs.

In 2003, the NIH accelerated the need for specialty skilled CRNs with the implementation of the NIH Roadmap (Zerhouni, 2003). With research moving rapidly from bench to bedside, studies were becoming more complex and multi-institutional. Focus shifted from research conducted at

centralized research centers to research implemented throughout the health care industry and in communities (NIH, 2014-a). Exploring new ways to speed implementation of clinical trials led to intense growth of the specialty practice in all clinical research areas.

The next decade saw many major advances in defining the specialty. Organizations internationally recognized the need to define competencies and establish a framework for the specialty of clinical research nursing. The GCRCNM put forth a position statement on clinical research nursing (GCRCNM, 2006). This position statement described the unique role of CRNs based on opinions of nurse leaders in the field and spurred further work in describing this role.

In 2009, a group of seven nurse managers of clinical research units throughout the United States founded the IACRN and held the first international meeting. In 2010, the NIH Clinical Center nursing department joined with IACRN for the first joint conference, "CRN2010." This conference became the largest organized effort to share results of work done surrounding CRN domains of practice and role delineation (Bevans et al., 2011; Castro et al., 2011).

Separately, the Oncology Nursing Society (ONS, 2010) began work on the role definition of the CTN in oncology clinical trials. During this time, the ONS Clinical Trials Nursing Special Interest Group developed the CTN Competencies, Clinical Trials Nursing Questionnaire (CTNQ), and the Manual for CTN (Klimaszewski et al., 2008). The CTNQ has been validated as a reliable tool for assessment of the research nurse role in countries throughout the world (Catania et al., 2008; Catania et al., 2012; Ehrenberger & Lillington, 2004; Nagel et al., 2010). Although a valuable resource for role definition, the CTNQ focuses specifically on oncology clinical trials and the role of the research nurse study coordinator, not the broader role of clinical research nursing outside of oncology clinical trials.

At the same time, a workgroup composed of members from the Royal College of Nursing, the National Institute for Health Research United Kingdom Clinical Research Facility Network, and the National Cancer Research Network developed a CRN competency framework to support

the CRN specialty. This was the first time national organizations supported efforts to standardize a framework for this specialty in the United Kingdom (Royal College of Nursing, 2011).

In 2012, the landmark document *Clinical Research Nursing: A Critical Resource in the National Research Enterprise* was published (Hastings et al., 2012). This work, developed over several years by a taskforce of US CRN experts, summarized growth of this specialty practice and outlined anticipated trends and next steps for further work within the specialty. Simultaneously, key research defined the domains of clinical research nursing practice. Agreement from experts across the United States was obtained via a Delphi questionnaire approach, resulting in the articulation of the five domains of practice (Figure 1) that continue to guide the specialty practice (Castro et al., 2011).

In the years following this landmark work, an international workgroup began efforts to formally define the specialty practice that resulted in the publication of *Clinical Research Nursing: Scope and Standards of Practice* (ANA & IACRN, 2016). In 2016, the ANA recognized the specialty nursing practice of Clinical Research Nursing, approved the clinical research nursing scope of practice statement, and acknowledged the standards of clinical research nursing practice. To further support competencies of the specialty practice, IACRN published the *Clinical Research Nursing Core Curriculum* (McCabe & Ness, 2021). In addition, the Clinical Research Nurse Certification Council (CRNCC) was established in 2021 to formally recognize advanced knowledge, skills, and expert attributes of clinical research nurses through specialty certification.

The expansion of clinical research has resulted in a clear demand for nurses specializing in clinical research practice who can best meet the needs of the research participant, adhere to research protocol requirements, and maintain research standards to achieve meaningful results. Over the past 50 years, intense growth in health care, research organizations, academia, and community agencies has contributed to shift the role of the CRN from a supportive role to an active and essential contributor to the clinical research enterprise.

Today, CRNs are members of a wide variety of interprofessional research teams that involve participants, their families, health care providers, researcher investigators, scientists, and other specialists. The CRN provides a consistent participant focus in the midst of managing research protocols. Through specialty practice, the CRN makes important contributions to the clinical research process, facilitating positive outcomes affecting the quality of the research and the participant's safety. The participant's clinical care and the research process are closely related, requiring the CRN to continually balance clinical needs of the participant and requirements of the research. The ability to achieve and maintain this balance is imperative for high-quality outcomes in the clinical research enterprise. CRNs must demonstrate expert clinical skills, be able to think critically, and integrate knowledge of regulatory, ethical, and scientific aspects of clinical research into nursing practice.

Clinical research studies in which CRNs work range from observational and behavioral studies to all phases of clinical research, including first-in-human research. CRNs are often the first to care for participants involved in a clinical trial assessing new therapeutics and devices. Assessments made by CRNs potentially affect the future of the therapeutic/device development or time to market, as well as the appropriate nursing actions and safety profiles for these novel therapeutics and devices. CRNs working in this area of research must closely observe participants and advocate for their safety without the protection of evidence-based clinical practice guidelines.

CRNs care for a wide range of participants, from healthy volunteers to critically ill patients, and in a variety of settings, from the community to critical care units. CRNs care for participants across the age span in every practice specialty, for example, cardiology, oncology, nephrology, and gastroenterology. Clinical research nursing practice requires a unique body of knowledge consisting of specialized training in nursing care, research regulations, scientific process, and data collection, analysis, and interpretation. CRN specialty practice incorporates the five domains of CRN practice. The domains—human subjects protection, care coordination and continuity, contributing to the science, clinical practice, and study management—provide a framework for CRN practice regardless of

the study type, role, or setting. A national panel of CRN experts participated in a Delphi survey that identified these dimensions and related role activities (Castro et al., 2011). These five domains are displayed in Figure 1.

DEFINITION OF CLINICAL RESEARCH NURSING

Clinical research nursing is the specialized practice of professional nursing focused on maintaining equilibrium between care of the research participant and fidelity to the research protocol while ensuring ethical rigor. This specialty practice incorporates human subjects protection, care coordination and continuity, contribution to clinical science, clinical practice, and study management throughout a variety of professional roles, practice settings, and clinical specialties.

Differentiation of Clinical Research Nurse From Nurse Researcher

It is important to clarify the distinction between a *CRN* and a *nurse researcher*. Although there might be role overlap in certain situations, the term *nurse researcher* refers to a doctorally prepared nurse who is "committed to rigorous scientific inquiry that provides a significant body of knowledge to advance nursing practice, shape health policy, and impact the health of people in all countries" (American Association of Colleges of Nursing [AACN], 2006, p. 1). CRNs, in contrast, contribute to science with a focus on the care of research participants and coordination of research activities in a research practice setting (Hastings et al., 2012).

Collateral Definitions

Several additional definitions are important for a complete understanding of the CRN role. The following definitions provide clarity for concepts discussed in this document and are based on background information from the NIH, International Conference on Harmonization's (ICH) Good Clinical Practice (GCP), CenterWatch, and standard research knowledge. (See the Glossary for a complete list of definitions for this publication.)

Clinical Research

This is research conducted with human subjects (or on material of human origin such as tissues, specimens, and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that use human tissues that cannot be linked to a living individual. There are two broad categories of clinical research: (1) observational studies and (2) clinical trials (also referred to as interventional studies).

Clinical Trial

This is a research study design in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes (NIH, 2014-b).

Participant

A participant is someone who volunteers to take part in a research study. A participant may be a patient, an individual with a chronic or acute medical or mental health condition, or a healthy volunteer.

There are some instances in this document where the terms *subject* and *patient* are used in place of *participant* when the authors are quoting directly from a source or following document guidelines. It is the intent of the authors that these terms may be used interchangeably. In this document, all three terms refer to a person who volunteers to participate in a research study.

CLINICAL RESEARCH NURSING PRACTICE PROFILE

Prevalence of Clinical Research Nurses

CRNs practice in all venues of the current clinical research enterprise – including federal, academic, industry, and private research settings – as well as non-research-focused settings (Hastings et al., 2012). As early as 1991, publications report nurses as the largest workforce supporting the day-to-day operations of clinical research, as designated by clinical research investigators (Mueller, 2001). Given this, it is reasonable to suggest that

nurses have been a driving force in the conduct and completion of the growing number of research trials registered on Clinicaltrials.gov. At this writing, 436,442 trials in all 50 states and 221 countries around the world have registered on Clinicaltrials.gov since 2000. The number of registered trials in this database of privately and publicly funded clinical studies has doubled since the first edition of this scope and standards document in 2016 (clinicaltrials.gov, n.d.).

Quantifying the number of nurses in this workforce is challenging for several reasons. One is the number of different titles associated with clinical research nursing roles in various settings and in the literature. Another is the number and variety of nontraditional settings that employ CRNs. Finally, clinical research nursing practice continues to evolve globally.

Membership numbers for the IACRN provide some insight into the prevalence of CRNs globally. In 2015, IACRN membership represented 9 countries, whereas in 2022, the membership represented 20 countries: Australia, Belgium, Canada, China, India, Indonesia, Ireland, Jamaica, Japan, Kenya, New Zealand, Nigeria, Philippines, Portugal, Saudi Arabia, South Africa, Spain, Sweden, United Kingdom, and United States. Not only has the number of countries represented increased, but membership in the specialty organization increased by 239% between 2009 and 2022.

In addition to approximately 1,000 nurses employed at the NIH Clinical Center and Institutes, health care organizations, especially academic medical centers, report nurses working in clinical research. There are nursing professional organizations that have specialty interest groups for nurses practicing in clinical research, for example, oncology, cardiology, cardiovascular surgery, and rheumatology. Outside of academia and federally funded centers, the number of CRNs working for industry, private research practices, and regulatory bodies has yet to be identified; it is estimated to be in the thousands. Due to variation in practices at the state and local levels, it is difficult to quantify the total number of CRNs.

Populations Served by Clinical Research Nurses

Persons of all ages are recruited to participate in clinical research. CRNs have expertise in caring for specific groups of participants on the

developmental spectrum from neonates to older adults. An essential component of the CRN specialty practice is the ability to care for the breadth and depth of the unique needs of those participating in research with any health condition at any developmental stage. Independent of age and health status, participants may engage in research in their home, the community, a group developmental setting, or a clinic or health care facility.

Pediatric Population

Children of all ages participate in all types and phases of research. Pediatric participants typically have an acute or chronic condition that requires interface with the health care system. They are often at physical, psychological, or developmental risk due to physical condition and/or the environment. It is not common for healthy pediatric volunteers to participate in research beyond observational and minimal risk studies. As a highly vulnerable population, children participating in clinical research are afforded additional human subjects protection defined in the Code of Federal Regulations (45 CFR 46 Subpart D). Determination as to sufficiency of parental permission from one or both parents is driven by the risk of the study and the Institutional Review Board (IRB). The IRB also determines that adequate provisions are made for soliciting assent of children and "takes into account the ages, maturity, and psychological state of the children involved" (45 CFR 46.408.a).

Adult Population

Adults participating in research encompass a broad spectrum of the population, ranging from healthy volunteers with no preexisting medical conditions to those with specific health conditions or clinical diagnoses. Included in this spectrum is a segment of the population defined, by the Code of Federal Regulations, as "vulnerable populations." Adults who are considered vulnerable include those who are mentally disabled, economically or educationally disadvantaged (45 CFR 46.111.b), pregnant women (45 CFR 46 Subpart B), or prisoners (45 CFR 46 Subpart C). As in the pediatric population, those designated as vulnerable are afforded additional human subjects protection.

Healthy volunteers are most common in the adult study population. These adults would not be in the health care system if they were not volunteering to participate in clinical research. They often serve as a control but may also be exposed to risk as a result of their participation. These healthy volunteers, sometimes referred to as "normal volunteers," may receive research drugs or have interventions performed. This population has no medical condition prompting their participation but may experience greater risk than benefit; therefore, they are entitled to the same protections as all other research participants. CRNs understand that monitoring this population requires a keen awareness for changes in physical and mental status in order to defend against a decline in their health as a result of participation in research.

Older Adult Population

Individuals in advanced age are a unique component of the adult population participating in research. Older persons are frequently underrepresented in research investigations (Elskamp et al., 2012). CRNs understand and consider the additional vulnerabilities that may increase risk of the intervention, limit elder participation, interfere with compliance, or complicate their participation. This group is often restricted by conditions of frailty, mobility, cognition, polypharmacy, and comorbid conditions (Cox et al., 2011). Financial and transportation limitations unrelated to the research may also hinder full participation. In addition, literature demonstrates families and primary physicians discourage this population from participation in clinical trials (Forsat et al., 2020), possibly related to lack of awareness of what trial participation means. CRNs apply knowledge of these limitations to advocate for safety of participants while protecting research efficacy. CRNs are aware that efforts to mitigate these limitations, if appropriate for the specific research study, may allow this segment of the population an opportunity to make important contributions to science and add to the body of knowledge for this age group. When working with older adults, it is important to consider the number of barriers to recruitment and retention in clinical research and proactively design effective methods to address such barriers within the protocol (Forsat et al., 2020).

Risk and Vulnerabilities of Populations Served

Two overarching concepts of significant importance to CRNs are (1) participant risk and (2) participant vulnerability. The research participant's exposure to risk related to study participation ranges from minimal to high, depending on the condition of the participant and the research intervention. Assessment of risk related to research participation is an essential aspect of the nursing process for all populations.

Members of any population or group may be considered vulnerable due to cognitive, institutional, medical, economic, or social variables. These vulnerabilities require attention throughout the development and implementation of the research protocol. Thus, ongoing assessment for risk and vulnerability is central to all clinical research nursing practice.

Clinical Research Nursing Practice Environments

CRNs engage participants in the research process throughout the health care continuum and in a variety of settings and roles. Some of the common settings where CRNs practice include private, public, and academic medical centers; physician or other provider practices within the community; privately owned research centers; and special care facilities. They may also practice in less traditional settings such as pharmaceutical companies, academic institutions, government agencies, and clinical research management organizations. The opportunities for CRN practice settings are endless.

Acute Care and Ambulatory Care

A common CRN practice setting is the hospital-based or academic-based clinical research center. Within the acute care setting, CRNs may work on a discrete unit dedicated to the care of research participants (including inpatient and ambulatory), or they may be part of a research program that provides research support to participants located in departments throughout the institution. The department could be one area of focused specialty or multiple specialty areas. For example, CRNs may work on intensive care units to collaborate with bedside nurses in performing

research-specific activities or in a research support office directing human subjects protection or managing research operations.

Privately Owned Research Centers

Privately owned research facilities typically provide research services to health care industries engaged in pharmaceutical and medical device development. These facilities contract with a variety of sponsors and research organizations to conduct all aspects of clinical trials or a specific component of research. Clinical research conducted within these facilities most often recruits populations with chronic disease or healthy volunteers. CRNs working in these practice environments have a variety of roles and responsibilities similar to those found in acute and ambulatory care facilities.

Community Settings

CRNs coordinate and implement research protocols in community settings through a variety of practice opportunities, such as part of a private physician's practice, other providers' offices, or community engagement of academic medical centers. In these settings, a CRN might be the only research specialist in the practice or may be part of a group of CRNs working in the practice. CRNs practicing in these areas work with research participants in diverse community settings and often lead recruitment of participants by directly engaging members within the communities. For example, research assessments might be completed within the community or at the participant's home for the convenience of the participant or for accurate assessment of the social context of the problem of interest. CRNs skillfully lead these types of decentralized research visits, balancing the needs of the protocol with the safety of the participant.

Research Administration Settings

CRNs practice in various roles in administrative settings. The setting might be part of a pharmaceutical company or other institution where the CRN provides expertise in protocol development and implementation, regulations, and human subjects protection, or an office in a government or contract agency where the CRN reviews protocol data as part of an auditing process or develops and provides education to CRNs.

Special Care Facilities

CRNs encounter research participants in special care facilities. These facilities can include rehabilitation, Alzheimer's or other cognitive impairment care, assisted living, palliative care, and skilled nursing facilities. Expertise in both research and nursing is required when working in these environments to ensure the safety of these vulnerable populations and coordination of care with facility staff.

Ultimately, no matter the practice environment, CRNs directly or indirectly engage with participants in the research process throughout health care environments, in industry settings, and within communities. The CRN understands the importance of the appropriate setting based on the activity being conducted and takes appropriate measures to advance participant safety.

Roles of the Clinical Research Nurse

Over the past 35 years, clinical research has expanded in complexity, regulatory oversight, and workload. As a result, the role of the CRN has developed into a specialty practice in contemporary nursing (ANA & IACRN, 2016; Getz, 2009, 2013; Mueller, 2001). As the clinical research enterprise has matured, clinical research nursing practice has become more clearly delineated. Nurses comprise a significant component of the clinical research workforce, holding a variety of roles commensurate with baccalaureate through doctorate education.

Clinical research is conducted in a wide variety of settings; therefore, it is of utmost importance that nurses caring for participants involved in clinical research are familiar with current ethical, regulatory, fiscal, and clinical issues affecting the conduct of clinical research. Because of the nature of the work and the high-stakes outcomes, it is imperative that nurses practicing in clinical research have training specific to research. The knowledge and expertise of the CRN as they relate to participant care, the conduct of clinical research, protocol activities, and human subjects protection are paramount to the success of the clinical research enterprise. Presently, roles integral to clinical research nursing practice include clinician (direct care provider, CRN study coordinator, and advanced

practice registered nurse [APRN]), administrator/manager, educator, advocate, regulatory specialist, and nurse scientist. The level of practice in each of these roles varies from entry-level generalist to advanced practice and senior leadership, and specific titles and nursing activities in these roles vary across organizations and according to the individual's educational preparation. Positions that CRNs hold may involve elements of some or all of the roles identified. For example, a CRN can be both an administrator/manager and a clinician or an educator and nurse scientist. Most of the current CRN practice is concentrated in these roles; however, nurses will continue to take on new roles within the CRN practice as the specialty continues to evolve.

Clinician

Clinical CRN roles include direct care provider, CRN study coordinator, and advanced clinician (APRN).

Direct care provider. Nurses new to clinical research practice come to the specialty with a solid skillset based on understanding the nursing process and basic developmental, psychosocial, cultural, and physiological aspects that contribute to human health and wellness. Having achieved mastery of the essential basic nursing interventions, they have a focus on clinical practice and care coordination related to protocol activities and care of the research participant. They may not be directly involved in study management but play a crucial role in ensuring correct implementation of study-related activities requiring specific skills, research education, and expertise.

The experienced research clinician is generally a baccalaureate-prepared CRN who supports study implementation within the context of a care delivery setting. The CRN practices with a clinical research focus, supporting study implementation, balancing the care of the research participant with the requirements of the study protocol, adhering to human subjects protection standards, ensuring participant safety, contributing to quality data collection, and educating participants and families (Hastings et al., 2012). Examples of positions that a direct care provider CRN may hold include bedside nursing in either a dedicated clinical research hospital or a clinical unit, or ambulatory nursing on a study team providing

care to research participants in a variety of settings, including the community. Specific role activities within these positions will vary; however, a primary focus of the nurse at this level is to provide direct nursing care, support, and education to participants in clinical research, their families, and significant others.

Examples of job titles that could be used for this level of practice are Staff Nurse in a hospital setting, Clinical Research Staff Nurse, Trials Nurse, Outpatient CRN, or Community Research Nurse. The staff nurse practicing as a CRN must be knowledgeable of regulatory accountability consistent with providing nursing care to a research participant. At this level of practice, this regulatory knowledge and resulting advocacy sets CRN practice apart from generalist nursing practice.

Clinical research nurse study coordinator. The CRN study coordinator manages the conduct of multiple clinical trials, including the direct care of participants and data collection for clinical trials. This role requires advanced coordination and management skills. Required training can be achieved through research-specific education or may include master's-level clinical research–focused academic preparation.

Job titles that could be used for this level of practice are clinical research coordinator, study coordinator, clinical trials nurse, or project manager. Nurses in this position are primarily responsible for study coordination and data management, with a central focus on recruitment and enrollment, consistency of study implementation, data management and integrity, and compliance with regulatory requirements and reporting. CRNs with a clinical research coordinator role may or may not participate in direct clinical care of participants but are directly involved with study management and coordination of care; educating participants, families, and members of the research team; and acting as a liaison for sponsors and the IRB.

Advanced clinician. In clinical research, the role of advanced clinician is often held by an APRN. APRNs are well suited to clinical research specialty practice. Their advanced clinical knowledge along with research acumen are valuable assets, especially as APRN entry to practice is

moving toward the doctoral level (AACN, 2015). These APRNs may participate on a research unit or provide advanced nursing care for participants of multiple research protocols. They may hold a leadership position on a research team coordinating and directing care of participants enrolled in a clinical trial. APRNs practicing in clinical research nursing specialty roles incorporate all aspects of the CRN role: educator, manager, clinician, advocate, and regulator at an advanced level of practice.

Administrator

CRN administrators lead discrete clinical research units, private research facilities, research centers, ambulatory research practices, or research hospitals. They may also manage research programs in institutional or industry settings at the regional, national, or global level or hold leadership positions in education departments. Examples of titles for this role include Clinical Research Nurse Manager, Director of Clinical Trials Operations, or Research Administrative Director.

Educator

CRN educators specialize in educating the research staff, participants, or clinical care staff regarding protocol-specific requirements, general research regulations or policies, and best practices for the conduct of clinical research. Additionally, in the industry setting, they may act as recruitment educators, promoting study awareness to aid in recruitment of clinical trials. Examples of titles for this role include Research Nurse Educator, Nurse Consultant, or Recruitment Educator.

Regulatory Specialist

CRN regulatory specialists are research nurses who monitor and oversee the progress of clinical research to ensure that it is conducted, recorded, and reported in accordance with the protocol, standard operating procedures, GCP guidelines, and applicable regulatory requirements. Furthermore, they may direct oversight of the ethical approval of studies through an IRB or Human Research Protections Program. They may conduct their work in the setting of a research practice, center, or hospital, or within industry or governmental agencies. CRN regulatory specialists must have

advanced knowledge of regulatory science. This training is achieved through various research-specific continuing education or master's education with a focus on regulatory science. Examples of titles for this specialist include Clinical Research Associate, Monitor, IRB Director, Director of Human Research Protections Program, and Quality Assurance Manager.

Nurse Scientist

CRNs in the nurse scientist role are prepared at the doctoral level (doctor of philosophy [PhD] or doctorate of nursing [DNSc]) and work in interprofessional teams with a myriad of collaborators. They engage in scientific pursuit of new knowledge to ultimately improve patient outcomes and health care delivery. Their activities include conducting and disseminating original research, participating on advisory boards/appointed committees, and educating/mentoring others. CRN nurse scientists hold senior leadership positions in the clinical research enterprise, as directors, senior scientists, and consultants. Examples of titles for this specialist include Nurse Scientist, Director of Nursing Research, and Director of Clinical Research.

Advocate

All CRNs, regardless of the job title, function in an advocate role. There is, however, a group of CRNs who focus their efforts solely on participant advocacy and safety. The CRN advocate may be an ethics nurse, prepared at the doctoral or master's level, having in-depth knowledge of the ethical principles in the protection of human subjects. The CRN advocate may serve as a consultant to a study team on matters of informed consent, assess voluntariness of research participants when questions of coercion arise, or work with scientific and oversight committees, such as the IRB in review of protocol safety. Some CRN advocates have a standing role on IRB committees. Titles associated with the CRN advocate include Research Participant Advocate, IRB Safety Coordinator, or Research Ethics Director.

Practice Domains of the Clinical Research Nurse

Clinical research is conducted in a wide variety of settings, making it of utmost importance that those caring for research participants are

familiar with the ethical, regulatory, fiscal, and clinical issues surrounding the conduct of clinical research. Because of the emphasis on accurate data collection and adherence to the research protocol in the conduct of clinical research, it is not ideal to task generalist staff nurses with clinical research activities in addition to providing clinical care. The knowledge and expertise of the CRN related to the conduct of clinical research, protocol activities, and human subjects protection are essential to the successful outcome of the clinical research process and best managed by the nurse educated and experienced in the specialty of clinical research nursing (Offnehartz et al., 2008).

In 2007, a role delineation study of 109 CRNs identified the following distinct roles: nurses at the bedside providing direct care to participants in clinical research trials, nurse managers and supervisors, nurse researchers, clinical research coordinators, educators, and advanced practice nurses (Mori et al., 2007). A recent survey yielded similar responses to validate these findings (Downhour et al., 2022). Further delineation and descriptions of the role of the CRN have been explored in various clinical settings and countries. For example, the role of the CRN in studies is described in practice settings that include oncology and Phase 1 oncology (Fujiwara et al., 2017; Purdom et al., 2017), surgery (Yanagawa et al., 2008), pediatrics (Nagel et al., 2010), nephrology (Micklos, 2016), and perinatology (Salazar et al., 2016). Additionally, the role has been validated in countries such as Australia (Wilkes et al., 2012), the United Kingdom (Kunhunny & Salmon, 2017), Taiwan (Kao et al., 2015), and Korea (Choi & Park, 2018). Literature describing the perceived and demonstrated value of the CRN includes Fell et al. (2016), Jones et al. (2022), McCabe et al. (2019), and Salazar et al. (2016); in addition to the role, descriptions have highlighted the unique and specialized practice of CRNs.

A taxonomy for clinical research nursing has been adopted as the domains of practice for the specialty of clinical research nursing and used to describe the practice elements of the CRN role. As described in Figure 1, the taxonomy includes the domains of human subjects protection, care coordination and continuity, contributing to the science, clinical practice, and study management (Castro et al., 2011). Although each domain

FIGURE 1 Domains of Clinical Research Nursing Practice

Source: Adapted from NIH (2009).

requires a unique set of skills and knowledge, the domains are not necessarily discrete and, depending on the role of the CRN, may overlap either partially or completely in practice.

Human Subjects Protection

Nurses in any setting are patient advocates. This is especially true in the specialty practice of clinical research nursing. The domain of human subjects protection emphasizes this responsibility and the importance of keeping research participants safe in the conduct of clinical research, research interventions, and protocol activities. While there are many entities charged with human subjects protection, in clinical research, the CRN is the person directly involved with the research participant, making the CRN role as advocate even more significant. CRNs are involved in risk assessment from the inception of a research protocol through implementation.

Informed consent is a key element in clinical research, and the CRN facilitates the initial and ongoing informed consent/assent process. The CRN must be knowledgeable of the research protocol in order to facilitate the consent process, answer questions throughout study participation, support the research participant's goal for participating or terminating

participation in a study, ensure ongoing consent, and guard against therapeutic misconception. To that end, CRNs are knowledgeable in human subjects protection principles, federal and global regulations, and research guidelines. CRNs facilitate informed participation of diverse populations, continually assessing risk and coordinating research activities to minimize participant risk. CRNs collaborate with interprofessional teams to address ethical concerns and conflicts, as well as manage potential personal, ethical, and financial conflicts of interest.

Care Coordination and Continuity

This domain focuses on integrating research and clinical activities in order to (1) meet the clinical needs of the research participant across the health care continuum, (2) coordinate and complete protocol activities, and (3) communicate with referring primary providers when necessary. In creating a plan for the research team and research participant, the CRN provides nursing leadership within the interprofessional team (Fisher et al., 2022; Hansen et al., 2022; Purdom et al., 2017). Because CRNs have in-depth knowledge of protocol requirements and expertise in care of research participants, they often facilitate education of research teams related to study requirements. The CRN and the research team ensure that the plan of care for a research participant is safe and allows for effective collection of clinical research data (Castro et al., 2011; Hansen et al., 2022). They also play a pivotal role in educating research participants, their families, and significant others about protocol requirements and any effect research activities may cause. In addition, they coordinate study visits and facilitate resolving research participants' questions and concerns.

Contribution to Science in General and Nursing Science/Practice

As integral members of the research team, CRNs make important contributions to science in general and specifically to nursing science and practice. Established educational and career paths in nursing allow CRNs to work in a variety of roles that are grounded in the holistic care of persons. CRNs engage in specific actions that are essential to the integrity of the scientific process appropriate to their educational background and professional role.

CRNs at all levels may serve as mentors to new study staff and scientists. CRN staff nurses may offer expertise in developing and operationalizing research protocols in the environment, or they may mentor new study staff in the safe conduct of clinical research. CRNs may serve as clinical experts in specialty areas that uphold the integrity and quality of the research. Nurse scientists may advise scientists in methods commonly used in nursing research. CRNs are well positioned to generate practice questions and collect evidence based on the interventions and innovations in the clinical environment, as they are often the first to use an innovation in the patient care context. CRNs are involved in the collection and management, query, and analysis of research data. As a result of their specialized focus, CRNs generate critical questions and fully participate in the research process regarding both clinical practice and nursing research. In addition, CRNs contribute to science through dissemination, publication, and presentation of findings.

Clinical Practice

The domains of practice developed for CRNs define clinical practice as using the nursing process to provide direct nursing care and support to participants in clinical research, their families, and significant others. Care requirements and protocol activities are determined by the scope of study participation, the clinical condition of the participant, and the clinical effects of research procedures and protocol requirements (Castro et al., 2011).

The generalist staff nurse focuses on standards of care, with very different goals and expected outcomes. The generalist staff nurse cares for the patient based on treatment goals, while the CRN incorporates research-specific aims into the care of research participants. Because of their expertise and knowledge of clinical research, CRNs are capable of balancing care needs of the research participant with research protocol requirements. This domain of clinical practice may include specimen collection, data collection, administration of research interventions, operationalization of the research protocol on the clinical unit, and education of research participants, families, and significant others related to the research protocol requirements and the participant's current clinical condition and/or

disease process (Castro et al., 2011). CRNs providing clinical care monitor research participants and are often the first to report adverse events (Catania, 2012; Fisher et al., 2022). Their precise assessment skills and documentation are essential for accurate data analysis, thus ensuring definitive findings of the clinical trial.

Study Management

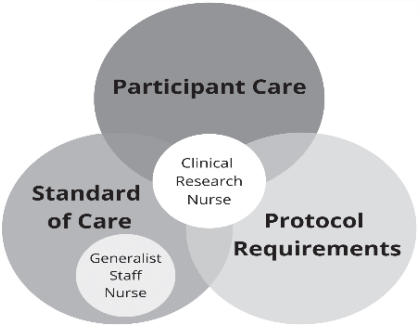
Study management is defined as management of clinical and research support activities to ensure participant safety, address clinical needs, and safeguard protocol integrity and accurate data collection (Castro et al., 2011). Some activities associated with this domain include study development, participant recruitment, identification of clinical care implications during study development, and recording and managing data to ensure data integrity. Figure 2 graphically represents this domain of clinical research nursing.

The study management domain comprises the largest set of activities within the CRN domains of practice. Activities associated with this domain most closely represent the specialized knowledge of clinical research. The CRN brings together the specialty knowledge of the research enterprise with that of clinical nursing knowledge and skills to expertly carry out those tasks associated with study management. The CRN is well situated to support the intersection of protocol management and participant safety.

The generalist staff nurse and the CRN have different objectives when approaching a participant in a clinical trial. While the generalist staff nurse without specialized research knowledge provides care with a goal of treatment, the CRN must manage the care of the participant with a focus on the objectives of the research that are not necessarily treatment focused. It is this balance between participant safety and protocol fidelity that demonstrates the value of the specialty practice.

Implementation of a study protocol alone is a complex process. A clinical protocol that engages healthy controls or participants with the target disease requires critical thinking skills to implement the protocol within the health care framework. CRNs' specialty knowledge allows them to

FIGURE 2 CRN Study Management Domain of Practice



assess the protocol for areas that might affect participant safety and develop processes to protect the participant while still collecting the necessary data in an accurate and timely manner.

An unfortunate reality in clinical research, serious adverse events (SAEs) may occur during the conduct of a clinical trial. The CRN manages the safety of the participants by adequately addressing their acute medical needs while collecting and reporting the necessary data mandated by research regulations. The CRN's "unique contributions and skills allow him or her to be an integral component to the safety-reporting process" (Catania, 2012, p. 18). In addition, high-quality data often require CRNs to develop methods for data collection not previously used or tested. Understanding the nuances of protocol implementation and potential pitfalls, in addition to clinical expertise, is essential to the successful implementation of clinical research.

Adequate recruitment of participants in clinical research is essential to accurate findings. An appropriate informed consent process during the recruitment phase is important to protect participants, ensure participants' autonomy in decision-making, and increase retention. It has been repeatedly demonstrated that CRNs are central to achieving successful recruitment (Fisher et al., 2022; Salazar et al., 2016) and ensuring an appropriate informed consent process (Fisher et al., 2022; Isaacman & Reynolds, 1996). CRNs are able to integrate foundational knowledge of their nursing practice with a thorough understanding of the research

process, research regulations, and research protocol to safeguard the participant.

While the domains of practice outline the work of the CRN, titles and roles specific to the practice vary. All CRNs, regardless of title, ensure human subjects protection and contribute to the science. The study management, coordination of care, and clinical practice domains are dependent on the specific roles and responsibilities of the CRN. While there is often overlap in the roles and responsibilities among position titles, the focus of each title is unique. CRNs are essential to the efficacious conduct of clinical research with humans because of their skills, education, and expertise related both to nursing and to clinical research.

Tenets of Clinical Research Nursing

1. Caring and health are central to the practice of the CRN

The specialty of clinical research nursing integrates caring, health, and clinical research with the aims of human subjects protection and improving health care globally. Promoting a healing environment and building positive relationships between the nurse and individual participants and their families are central to the CRN's practice of caring and the guiding principles of research. CRNs extend the values of caring to self, society, and the environment and consider the impact of research on each. More specifically, the nurse scientist promotes health through investigations of ways of caring (Institute of Medicine [IOM], 2011). The ultimate reward for CRNs is the awareness that the research they are contributing to is likely to have "a positive benefit for patients both now and in the future" (Gibbs & Lowton, 2012, p. 39).

2. Clinical research nursing practice is individualized

CRNs support advancement of health equity in research through respect for diversity and a focus on identifying the unique needs of the individual research participant or situation. CRNs individualize practice using knowledge of the core ethical principles of research involving human subjects: respect for person, beneficence, and justice (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1978). The research participant can be an individual, a family, a group, a

community, or a population who is the focus of investigation and to whom the CRN is providing services, as sanctioned by regulatory bodies.

3. CRNs use the nursing process to plan and provide individualized care for research participants

In collaboration with research participants and interprofessional research teams, CRNs apply the nursing process to individualize health care plans with thoughtful consideration to preserving fidelity to the research protocol. CRNs advocate for the best interest of research participants and continuously assess their condition, needs, and outcome responses to appropriately evaluate effectiveness of care, research interventions, and the participant's situation in relation to identified goals and outcomes. CRNs employ critical thinking to synthesize the current body of evidence, protocol information, knowledge of research regulations, and clinical research experience to make informed decisions and individualized care throughout the nursing process.

4. CRNs coordinate care of research participants by establishing partnerships

"The CRN coordinates research and clinical activities to meet clinical needs, complete study requirements, and manage linkage with referring and primary care providers" (Castro et al., 2011, p. 78). As strategic members of the research team, CRNs establish effective and equitable partnerships with research participants, families, groups, and populations, as well as research colleagues and interprofessional health care providers, to meet the needs of those being served. Engaging in transformative clinical research partnerships capitalizes on each partner's respective strengths and develops greater partnership synergy (Whitney et al., 2022).

In all interactions, the CRN demonstrates qualities of emotional intelligence and selects the most effective communication approach and/or system by which to conduct discussions and convey shared goals. Further, the CRN uses appropriate, effective communication strategies to assess the potential research participant's comprehension of risks and benefits associated with specific research activities, from which to make an informed decision to take part in research or continue participation. CRNs observe

for therapeutic misconception and take appropriate action when it is identified.

5. A strong link exists between the professional work environment and the CRN's ability to provide quality health care and achieve optimal outcomes

CRNs endorse the ANA's Nurses Bill of Rights, which ensures a healthy practice environment for the nurse that allows full and meaningful nursing practice (ANA, 2022). CRNs recognize their role in creating, advancing, and sustaining healthy and ethical work environments in which to conduct clinical research and the mounting evidence that links healthy work environments to the quality aims of safe, effective, efficient, timely, patient-centered, and equitable care (IOM, 2001). The work environment not only affects outcomes in the current work environment but also influences health care decisions of the future, through the accuracy and quality of data collected. Healthy work environments encourage retention of nurses with advanced clinical research nursing experience and expertise, in addition to fostering a more ethnically and multigenerational diverse workforce (Cohen et al., 2009; Dols et al., 2019).

Principles That Guide Clinical Research Practice

The principles that guide CRN practice in the research setting are advocacy, safety and self-determination, research informed consent, fidelity to the research protocol, and regulatory compliance. When these principles are rigorously combined with exceptional participant care, they result in safe environments for conducting research and producing reliable, valid data on which to base future health care decisions, treatments, and interventions.

Advocacy

Clinical research nursing practice is a synthesis of nursing practice and the ICH's GCP guidelines (2018). All aspects of the CRN's education, training, and skill integrate knowledge of GCP to expand the role of advocate to include both the research participant and fidelity to the protocol. The amalgamation of GCP guidelines and fundamentals of nursing practice includes advocacy for human subjects protection, protocol fidelity, and adherence to research guidelines and regulations to establish

principles that guide CRN practice. It is the CRNs' knowledge of how research dovetails precisely into clinical practice that enables them to expertly manage the delicate balance of patient advocate and research advocate simultaneously, when others may see only aspects of conflict between the two.

Safety and Self-Determination

Each research participant encounter deserves utmost care, compassion, and professionalism to embrace the core values of respect, beneficence, and justice (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1978).

- Each research participant is recognized as an autonomous being, free to make decisions for themselves and to enter into research voluntarily. CRNs follow ethical guidelines and regulatory requirements that protect those unable to make a decision in their own best interest, guarding against coercion, undue risk, and potential for harm.
- Research protocol plans maximize benefits and minimize risk to the individual participant to ensure harm does not come to one person in the pursuit of possible benefits to others.
- Research participants are selected for reasons directly related to the research problem being studied, not because they are easily manipulated, available, or vulnerable. Benefits and burdens in a research study are justly distributed through fair procedures.

Research Informed Consent

The process of informed consent is composed of three essential elements: (1) provision of complete and accurate information, (2) assessment of comprehension, and (3) safeguards to protect voluntary participation. Employing these elements ensures participants' adequate opportunity to choose what will or will not happen to them.

- The participant understands the information and volunteers to participate in clinical research free from coercion.

- The potential participant has sufficient time to consider information provided on all available options in order to make an informed decision to participate or not.
- The informed consent process is ongoing throughout the participant's enrollment in a research study; additional information is provided as the participant requests it or as the situation requires it. The participant has the opportunity to ask questions and receive a response at any point, from initial consenting throughout the remainder of participation in the study.
- Information is provided in such a way as to avoid therapeutic misconception. When instances of therapeutic misconception are suspected or identified, information is provided to clarify the participant's understanding of the purpose of the research and their wish to continue or withdraw consent is verified.

Participants with diminished capacity are entitled to additional protections, per the stipulations of the Belmont Report – see Glossary – (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1978; US Department of Health and Human Services 45 CFR 46.102her; US Food and Drug Administration [FDA] [21 CFR 50.3(l)]), and regulations mandate that potential participants lacking decision-making capacity may participate in minimal risk research or research that has the potential of direct benefit through use of a surrogate decision maker, known as a legally authorized representative (LAR). Local and state laws define who may fulfill the role of a LAR in a given locality. In addition to a LAR's authorization for the individual to participate, the participant's initial and continuing assent is often required. Change in capacity during the study may influence research obligations to the participant. CRNs monitor and report the participant's gain or loss of capacity to give assent or consent during the course of the study and report findings to the interprofessional research team

Fidelity to the Research Protocol

Research studies are conducted as planned, with strict adherence to the design to reduce or eliminate protocol deviations.

- All essential elements of interventions are delivered in a comparable manner, thereby advancing the study's aim(s) (FDA, 2021-b; ICH, 2018).
- Confidence in the study's findings is dependent on strict adherence to the protocol plan and internal validity, thus facilitating the accurate association between the intervention and study outcomes (FDA, 2021-b; ICH, 2018).

Regulatory Compliance

All human subjects research is conducted in compliance with international regulations (International Compilation of Human Research Standards, n.d.), federal regulations, state laws, and institutional policies. Federal regulations governing the protection of human subjects participating in biomedical and behavioral research are codified in the Federal Register in 45 CFR 46, including Subparts A (also known as the common rule) B, C, and D (Department of Health and Human Services [HHS], 2018), and 21 CFR 50 and 56 (FDA, 2022). For example, it is a regulatory requirement that the IRB or institutional ethics committee (IEC) should consist of a reasonable number of members with varied and diverse backgrounds, who collectively have the qualification and experience to review and evaluate the science, medical aspects, and ethics of the proposed research in relation to the protections of human subjects. It is required in the United States for IRBs and often recommended for IECs to include at least the following:

- Five members
- One member whose primary area of interest is scientific and one member in a nonscientific area
- One of those members must not be affiliated with the institution where the research will be conducted.
- If research with prisoners is being reviewed, a prisoner advocate must be present during the meeting.

It is also of increasing importance to ensure that some of the members are sensitive to the culture and attitudes of communities where the research is being conducted and any vulnerable groups engaged. Only