The Research Hospitalist: Protocol Enabler and Protector of Participant Safety

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Background

The Rockefeller University Center for Clinical and Translational Science (CCTS), supported by a Clinical and Translational Science Award (CTSA) from the National Center for Advancing Translational Sciences (NCATS), is the hub for clinical investigation at Rockefeller University. The clinical facilities include an approximately 20-bed inpatient unit and a 4,000 square foot outpatient research center in the Rockefeller University Hospital. Virtually all patients cared for in the Hospital are on a research protocol approved by the Advisory Committee for Clinical and Translational Science (ACCTS), the governing body of the CTSA, and the Rockefeller University Institutional Review Board (IRB). Each laboratory is responsible for the conduct of its research protocols.

The Rockefeller University conducts both basic and clinical research. The University is composed of 75 laboratories, each led by a Head of Laboratory (HOL) who reports directly to the President. Currently, 73% of the HOLs hold PhD degrees, 10% MD degrees, and 17% MD-PhD degrees. The forerunner to the Rockefeller University Hospital opened in 1910 with the mission of integrating both clinical and basic investigation of human disease. In 2002, the senior leadership of the Hospital created the position of Research Hospitalist (RH) with the charge of: (1) promoting patient safety, (2) developing, supporting, and monitoring processes to optimize the scientific integrity of clinical research, (3) providing direct clinical support to nonphysician principal investigators (PIs), (4) educating investigators on current best medical practices, and (5) overseeing resource utilization and prioritization. The overarching goals of creating the position were to lower the barrier to participation in clinical research, especially for PhD investigators and trainee investigators, insure research participant safety, and enhance scientific integrity. The incumbent RH, the lead author on this report (B.O’S.), trained in internal medicine and intensive care medicine and had more than 15 years of clinical experience before joining Rockefeller. This report details the functions and impact of the RH.

Developing, Supporting, and Monitoring Processes to Optimize the Scientific Integrity of Clinical Research

The RH contributes to the scientific integrity of the research conducted at Rockefeller throughout protocol development and conduct (Table 1). As an important member of the CCTS Navigation program¹ the RH participates in helping the PI develop the protocol from its earliest stages. Her expertise is particularly valuable in refining the inclusion and exclusion criteria. Based on the scientific rationale, the RH works with the PI to identify comorbidities that might undermine the scientific goals of the protocol and then to develop precise measures that can be used to decide whether participants should be included in the study.

The RH’s familiarity with validated risk scores and diagnostic algorithms, as well as her appreciation of the limitations in extrapolating from tools developed for clinical care to the clinical research setting, are extremely valuable in deciding the precise diagnostic approach. In addition to medical and diagnostic guidance, the RH works with the Navigation team to identify issues of feasibility in conducting the research. These may include resource use, nonclinical device use, and unconventional methods to deliver investigational agents.

The RH is charged with deciding when standard medical practice can be modified to insure the scientific integrity of a protocol without compromising patient safety. For example, while it is recommended by the Institute for Safe Medication Practice and The Joint Commission that insulin be dispensed in standardized concentrations, the use of these formulations is incompatible with the formulation needed to conduct the euglycemic insulin clamp procedure. This procedure is performed to assess a research participant’s insulin sensitivity and requires a fixed rate of infusion of patient-specific concentrations of insulin based on body surface area. To guard against the potential for increased risk in using these nonstandard formulations, the RH worked with the Research Pharmacist to develop additional safeguards to minimize this risk. Together, they instituted an interdisciplinary process of double-checking at multiple steps in the process, including those involving dose calculation, mixing and labeling of the drug in the pharmacy, and insertion of the drug syringe into the pump.

Promoting Patient Safety

The RH leads a team of clinicians that includes a Research Nurse Practitioner and on-call physicians who provide around-the-clock clinical care. This team reviews the radiology reports, abnormal laboratory results, and electrocardiograms of all research participants in parallel with the reviews performed by the individual laboratory investigators. Since the RH and her colleagues perform their reviews in near real time, they often are the first to identify a new abnormality. This team also responds to medical emergencies when they arise, day or night. These can range from short-lived, mild, unexpected illnesses, to more serious problems, such as withdrawal seizures in participants in studies of drug addiction. The RH strives to manage the acute clinical problems with minimal disruption of the research protocol. This requires unbiased clinical judgment, deep understanding of the research protocol, and the ability to manage clinical problems using diverse approaches. Similarly, the RH works with the investigators to manage chronic medical problems in each research participant. Although most investigators are experts in the clinical condition under study, often participants...
Table 1. Research hospitalist’s role along the path of an active research protocol, starting with the protocol navigation process, indicating the category of involvement by symbol: *safety; †clinical support; §resource use; ‡process oversight.

The RH has primary responsibility for establishing policies and procedures to ensure the safe conduct of research. In this role, she works closely with the Research Nursing and Research Pharmacy departments and has a lead role in continuous performance improvement activities. She monitors protocol deviations, medication variances, and adverse events in research participants in all of the protocols conducted in the Hospital. These real-time, protocol-specific data then form the basis for designing appropriate changes in the protocol and/or processes. The aggregate data are used to develop Hospital-wide standardized clinical research process templates based on observed best practices to enhance patient safety and to harmonize research procedures. For example, when several investigators reported protocol violations because certain laboratory tests were not performed, a root cause analysis led by the RH traced the problem to a unilateral change in the way laboratory requisitions were filled out by the outpatient staff, causing confusion in the clinical laboratory. The process was redesigned and the problem eliminated.

The use of investigational drugs poses unique safety challenges relative to approved medications since there is less information available about their proper dosing and toxicities. This makes them more prone to deviations (variances) in dispensing and administration, calling for heightened vigilance. The RH works closely with nursing and the pharmacy to identify such deviations and to redesign practices to minimize their occurrence. As part of the protocol development process the RH works with the investigator, pharmacy, and nursing to develop procedures that support the scientific goals while adhering as closely as possible to current standards of safe medication use. When the science requires an unconventional process, the RH leads the development of an alternate process with enhanced safety monitoring that differs from, and may go beyond, the established standards for the safe use of medication. In one example, a dose escalation trial required the first study participants to receive a very low dose of the formulation, requiring dilution and admixing of the investigational drug into a solvent. This had to be done immediately before administering the drug. Because the study design required off hours dosing, the pharmacist could not prepare those doses in the pharmacy, which is the current standard practice. Efforts to redesign the timing of drug administration were not successful so the Research Pharmacist requested review of the issue by the Pharmacy and Therapeutics Committee and the RH. They decided that the investigator (an MD) and a backup physician could be trained to prepare and administer the study drug when the pharmacy was closed. The pharmacist trained the physicians to a level of proficiency and the RH worked with the nursing director to identify an appropriate area for this unconventional process.

The RH is also charged with assuring the safety of protocol-specific research devices. Due diligence includes examining the device for potential safety risks, such as electric shock, transmission of infection, exposure to toxins, or physical injury to the user or patient. Based on her examination, the RH may recommend changes to the design or operating procedures. She compares the device to similar devices currently approved for clinical use for guidance on risk reduction. The final prototype is referred for inspection to the biomedical engineers who assess the device for electrical safety. If any substances are used in the device, such as odorsants or other chemicals, the RH consults the Laboratory Safety Officer for guidance. The RH also works with the infection control coordinator to examine the device for potential microbial contamination. Finally, with the nursing director, the RH defines

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the training required by the users. In one example, an investigator (a basic scientist) built a device to deliver tiny puffs of odorants into a mask to test olfaction. The device was electric, contained chemical solutions, and came into direct contact with patients. The RH contacted the biomedical safety service to inspect the electrical integrity, and worked with the infection control coordinator to identify the best method to clean the device to limit the spread of infection. The infection risk analysis led to a redesign of the tubing and face piece to allow for more thorough cleaning of the device between users. The odorants were reviewed by the Laboratory Safety officer for safe use in humans. Input from the director of nursing led to a plan to store the device on the patient care unit, rather than bring it back to the basic science lab, as a way to minimize contamination between uses.

Providing Direct Clinical Support to Nonphysician PIs

One of the goals of the Rockefeller CCTS is to encourage basic scientists to engage in translational research, including research involving human participants. To help achieve this, the RH and the clinical team she leads are available to provide needed medical evaluations and/or medical care in protocols developed by basic investigators. In addition, the RH supervises the hospital research clinician, a Nurse Practitioner, who provides direct clinical support to both physician and nonphysician investigators to conduct human subjects’ studies.

The investigators conducting translational research range from the most senior investigators on campus to newly minted postdoctoral scientists. They include established physician-scientists, as well as early career physicians in training in the KL2 Clinical Scholar’s program, and a growing number of nurse practitioners. The RH has enabled a dramatic increase in the number of human subjects protocols led by basic science investigators as shown in Table 2, using statistics from 2001 and 2014.

In addition to their oversight roles, the RH and the research Nurse Practitioner serve as key study personnel on protocols. The RH, the Nurse Practitioner overseen by the RH, or both together serve as key study personnel on 33 protocols.

Educating Investigators on Best Medical Practices and Emergency Preparedness

The breadth of the RH’s clinical expertise makes her an important resource for investigators whose clinical expertise may be more narrowly focused. This includes both informal advice and formal recommendations as part of the ACCTS review process. The RH also holds the title of Medical Director of the Hospital, in which role she provides ongoing education to the entire medical staff.

The RH also leads ongoing disaster planning for the Hospital, including contingency plans for pandemic diseases and natural disasters, such as hurricanes. In this role, in addition to medical and safety issues, she focuses on research integrity. For example, the Hospital’s disaster plan contains specific provisions to insure that research samples are protected and that special arrangements are made to insure that study medications are dispensed and administered according to specifications in the protocol. The RH also developed a clinical research utility matrix to quickly identify the impact of any utility failure on the conduct of critical research processes.

Overseeing Resource Utilization and Prioritization

The RH works closely with investigators to assess the resources and special needs required to conduct research protocols. This includes the repurposing of space and the redesign of participant rooms to accommodate unusual requirements. Thus, the RH directed the creation of a sleep study unit and a unit for very intensive around-the-clock electronic monitoring of patients in the minimally conscious state, including new cabling and the creation of a separate data control center room. The RH is also charged with monitoring protocol-specific use of CCTS resources to insure their equitable distribution and appropriate prioritization. This information is reported to the ACCTS for its review and final determination.

Conclusions

At the Rockefeller University CCTS, the RH plays a vital role in achieving the patient care, research, and education missions of the Center. While our model builds on the hospitalist movement that began more than 20 years ago to enhance the quality and efficiency of inpatient care, the RH position at Rockefeller is broader in function in that it includes oversight responsibilities in both the inpatient and ambulatory settings as well as protocol-specific and high-level policy responsibilities. Since Rockefeller differs from most academic health centers in its size, academic organization, and research-focused range of medical services, it is unlikely that the model we have developed will be directly applicable to larger and more complex academic medical centers. It may, however, be suitable for a smaller unit, such as a clinical department or a dedicated clinical research center. In addition, even if the RH position per se is not applicable to larger or more complex institutions, charging one or more individuals with the specific functions of the RH detailed in this report may be valuable for institutions of all sizes.

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Conflict of Interest

The authors have no conflicts of interest to disclose.

| Principal Investigator Category | 2001 (N = 125 protocols) | 2014 (N = 188 protocols) |
|-------------------------------|--------------------------|--------------------------|
| PhD                          | 28                       | 48                       |
| MD-PhD                       | 21                       | 70                       |
| MD                           | 76                       | 63                       |
| Other: RN, NP, BS            | 0                        | 7                        |

Table 2. Protocols by principal investigator category, 2001 and 2014.

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