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# Identifying, Understanding, and Managing Patient Safety and Clinical Risks in the Clinical Research Environment

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## IDENTIFYING AND MANAGING CLINICAL RISK IN THE CLINICAL RESEARCH ENVIRONMENT

Clinical research is most often conducted in an environment that is part of a larger health-care system. Both the conduct of clinical research and the practice of clinical medicine involve risk. The extent to which risk is present in the hospital environment has been well documented in recent years. The Institute of Medicine's groundbreaking report "To Err is Human" characterized the magnitude of the occurrence of medical errors during patient care in the United States, estimating that between 44,000 and 98,000 hospital-based deaths per year could be attributed to medical errors.<sup>1</sup> In more than 15 years since this report was released,

multiple studies have provided supporting evidence for these staggering findings.<sup>2</sup> In a 2016 study by Makary and colleagues that analyzed medical death data from four studies conducted from 2000 to 2008, the authors estimated that more than 250,000 deaths each year in the United States result from medical errors.<sup>3</sup> In the study, authors highlighted that these results place medical errors third on the Center for Disease Control and Prevention's list of leading causes of death in the United States—behind the 611,105 deaths that are associated with heart disease and the 584,881 deaths attributable to cancer, and just above the 149,205 patients who die from respiratory diseases. Findings from a study by Van Den Bos et al. estimate that the annual cost of measurable medical errors, in 2008, was over \$17 billion.<sup>4</sup> According to data from the Centers for Disease

Control and Prevention, nearly 2 million health care-associated infections occur each year; costing the United States an estimated \$20 billion dollars.<sup>5</sup> A 2011 study by Magill and colleagues estimated the number of health care-associated infections to be 721,800.<sup>6</sup> These figures are unquestionably daunting; however, they do not include either the scores of near misses or latent errors (errors that never reach the patient or result in harm) or the system failures that influence a patient's health-care experiences negatively. Based on these striking mortality and health care-associated infections data, the fact that the health-care environment is fraught with risks and potential errors that must be identified and deftly managed if patients are to be cared for safely and appropriately seems incontrovertible.

Traditional clinical research is also conducted in the context of these health-care risks. As in the case for clinical care, and as noted by several authors in this text, the conduct of clinical research is inherently associated with risk. During both the scientific and human subjects' protection review processes, great effort is expended to estimate, calculate, and articulate the relative risk associated with each study drug, device, and intervention. This intense scrutiny at the protocol level works to improve the safety of subjects relative to the risks associated with the study question.

Murff et al. describe additional risks that rarely are considered formally during the review of a clinical research protocol, including the clinical environment in which the research will be conducted, as well as system failures that are inherently associated with clinical medicine.<sup>7</sup> The health-care environment—whether an inpatient unit, an ambulatory care clinic, or a community health center—is a complex system that is influenced by multiple factors that contribute to, or mitigate, risk in the conduct of clinical research.

Nolan describes a system as “a collection of interdependent elements that interact to achieve a common purpose.”<sup>8</sup> If one applies this definition to the clinical care environment, examples of interdependent elements that one might consider include such factors as the institution's culture (especially with respect to safety), the skill mix and competence of the staff, the availability of state-of-the-art equipment, and the quality of information systems, to name but a few. The health-care literature is rife with examples of system failures resulting in harm to patients; for example, significant medication errors (e.g., the death of the *Boston Globe* reporter, Betsy Lehman, who died of a massive chemotherapy overdose and the tragic loss of young Josie King),<sup>9–12</sup> wrong site surgeries that often top the Joint Commission's list of reported sentinel events,<sup>13</sup> and the relative epidemic of health care-associated infections.<sup>6,14–16</sup> Whereas any one of these events could be considered an error resulting from an individual provider's negligence, systems

thinking compels us to consider these adverse events as failures in a series of interrelated and/or codependent processes or systems. In truth, in the current complex health-care environment such events almost invariably involve a series of missed opportunities to correct the error—hence they truly represent system failures.<sup>14</sup> This shift in focus—from the individual to the system—forces organizations to broaden their analyses of incidents and, thereby, broaden the impact of any improvements. Because of the endemic nature of errors and system failures in clinical care, investigators and review bodies must collaborate with the health-care practitioners with whom they entrust their participants' safety to assure that the system/environment in which clinical research is conducted is safe and has the necessary infrastructure in place to support the study. Further, the research team must have strategies in place to monitor the clinical research environment to identify risks and clinical events that could contribute to adverse events and/or protocol deviations and to assure that processes are in place to prevent, mitigate, and manage risks.

Clinical research programs must, therefore, embrace a system's approach to managing risk associated with the conduct of clinical research. For the purposes of this chapter, the term “conduct of clinical research” refers both to activities outlined in the research study as well as those intrinsic clinical care activities that are essential to the successful implementation of a study but that may not be explicitly described in the research protocol. Examples of such clinical care activities include infection control measures, medication management procedures, the design of the physical environment, and information management. These critical clinical care functions often are assumed to be present and functioning at an optimal level to support the investigator's study; however, investigators and/or institutional review boards may lack formal processes to assess the capacity of the clinical environment to support the study under review. The research team must engage the clinical care organization proactively to assure that the appropriate infrastructure is in place to provide care safely and efficiently to study participants. In collaboration with the health-care team, the research team should have processes in place to

- identify clinical care functions that are critical to the success of the protocol;
- identify and assess critical risk points of the clinical care processes that might place participants at undue clinical risk and/or compromise the integrity of the study;
- monitor the clinical environment continually for adverse events, errors, near misses, and process failures;
- assess systematically and thoroughly errors that occur;

- establish an armamentarium of process improvement tools with which to manage process and system issues when they are identified; and
- develop robust processes to communicate and learn from untoward events that occur in the clinical care environment in the spirit of organizational learning and continuous improvement.

These processes and the tools and techniques described in this chapter can be implemented and managed at a variety of levels of an organization. If the research program resides in a large health-care system, many of these activities can be managed by the hospital's patient safety and clinical quality enterprise, in collaboration with the research teams. However, these processes and tools effectively can be applied on a much smaller scale (i.e., an individual research unit) with the same degree of success. Regardless of where in the organizational structure these functions reside, the findings from these performance measure, risk mitigation, and improvement strategies should be communicated directly to the leadership and across the organization.

### **BUILDING A ROAD MAP TO SAFE AND HIGH-QUALITY CARE AND RESEARCH SUPPORT: APPLYING THE PRINCIPLES OF HIGH RELIABILITY IN THE CLINICAL RESEARCH ENVIRONMENT**

Nuclear power, aviation, chemical manufacturing, and aerospace are all complex industries in which a single error can result in catastrophic consequences; however, remarkably, these industries are considered incredibly safe. These enterprises adhere to a set of high reliability principles that are aimed at identifying and managing risks in their respective cultures. Sutcliffe describes high reliability organizations (HROs) as having a "collective mindfulness" that supports and promotes a culture in which all staff are encouraged to seek out and share all unsafe conditions or problem before the event compromises operations or service delivery.<sup>15</sup> The five principles of high reliability are

1. Preoccupation with failure
2. Sensitivity to operations
3. Resistance to simplify
4. Commitment to resilience
5. Deference to expertise

The National Institutes of Health Clinical Center (NIH CC) applies these principles to the design and management of complex patient care processes as well as to the design and conduct of clinical research support. An error or lapse in safety in the aforementioned industries' processes can result in tragic outcomes—much like a lapse

in proper infection control in the care of a highly immunocompromised patient or a patient with Ebola virus infection can be catastrophic from a personal as well as an organizational perspective. The NIH CC staff learned a great deal from experiences preparing for and providing care for Ebola patients during the recent epidemic. [Table 36.1](#) provides an overview of each of the principles of high reliability and how the NIH CC leveraged these concepts in the care of acutely ill Ebola patients.

### **LEVERAGING PATIENT SAFETY AND QUALITY IMPROVEMENT TECHNIQUES IN THE CONDUCT OF CLINICAL RESEARCH**

A first step in assuring that appropriate clinical care infrastructure is in place to support a planned study is to examine the research protocol to identify the clinical functions that will be required to support the conduct of the study safely. This process begins with the active engagement of the study investigators, the research team, and the patient care staff who identify, objectively and prospectively, steps in the research process that may place participants at risk. Health-care performance improvement tools such as flowcharting,<sup>16–18</sup> failure mode and effects analysis (FMEA),<sup>18–24</sup> and clinical quality performance measures can be applied effectively to the analysis and management of risk in the context of planning clinical research.

These performance improvement tools are used for this purpose in our institution (NIH CC). We provide this specific information about our own institution to provide context for this discussion. The NIH CC occupies a unique position in the nation's biomedical research establishment. The NIH CC is a distinctive and complex hospital whose primary mission is the support of science. High-quality clinical care is provided at the NIH CC in the context of clinical research, but the primary driver of that care is science. The NIH CC provides clinical research support for, and clinical care to, the research participants enrolled in the more than 1600 active clinical research protocols ongoing at the NIH CC. The NIH CC's research portfolio differs substantially from most academic medical centers. Of the NIH Clinical Center's approximately 1600 clinical research protocols nearly half are designed to study the natural history and pathogenesis of rare, often genetically determined rare diseases. The other half of the NIH Clinical Center's clinical research portfolio is comprised of clinical trials. More than 90% of these clinical trials are phase I or phase II "proof-of-principle" or "first-in-human" translational trials. This unique intersection of clinical care and clinical research mandates that the NIH CC use myriad health-care performance

TABLE 36.1 Relating the Principles of High Reliability to the Management of Patients With Ebola Virus Disease

HRO Principle	Description	Application in the Care of Ebola Patients
Preoccupation with failure	All staff are aware of the potential for risk and harm and are encouraged continually to scan the environment for potential and real threats to safety.	<ul style="list-style-type: none"> <li>• Staff were empowered to ask about, and looking for, the untoward outcomes that could result from our care processes.</li> <li>• The team used several tools from high reliability industries to help identify risky processes and behaviors before a catastrophic event occurs (e.g., Failure Mode and Effects Analysis, Root Cause Analysis).</li> <li>• The care team built in multiple layers of redundancy for high risk activities. For instance, the role of “Wat-San” was developed to assure that the critical tasks of donning and doffing personal protective gear were accomplished in a safe manner. The role of the “Wat-San” was to actively and meticulously direct the care providers during each step of the process. The Wat-San had the authority to stop all activity on the spot.</li> <li>• The essential nature of drilling and conducting “Day in the Life” exercises is borne of this “preoccupation with failure”—drills were a central aspect of the care team’s preparation and continual readiness.</li> </ul>
Sensitivity to operations	Maintaining a “situational awareness” is a hallmark of HROs. Leaders and staff need to be constantly aware of how processes and systems affect the organization.	<ul style="list-style-type: none"> <li>• The care team used “safety huddles” liberally. In safety huddles staff gather briefly (5–10 min) to discuss issues/concerns that have developed over the course of their tour of duty</li> <li>• The larger team, led by the hospital and unit medical leadership, “huddled” every day at 3 p.m. to review the events of each day. Unit leaders and staff used this real-time information to drive decisions/process changes.</li> <li>• Leaders and staff evaluated the effectiveness of their care processes continuously to identify opportunities for improvement.</li> </ul>
Resistance to simplify	Staff appreciate that health care is complex, ever-changing and fraught with interdependencies. When faced with challenges, errors, or untoward events HROs seek to understand the “root cause and contributing factors” of these events rather than settle for a more superficial or expedient explanation. And whereas standardization of processes may be useful, HROs understand and actively manage complexity.	<ul style="list-style-type: none"> <li>• Staff were encouraged to resist the risks associated with “painting with broad strokes” when evaluating lapses and failing to dig deeply to find the real source of a particular problem.</li> <li>• When issues were identified in the shift and daily huddles staff and leaders were encouraged to ask “WHY?” at least five times when investigating events and errors to assure that the true nature of the event was identified.</li> </ul>
Commitment to Resilience	This principle is based on the assumption that errors and lapse will occur and organizations must actively design processes that allow an organization to “bounce back” from errors.	<ul style="list-style-type: none"> <li>• Every organization must develop strategies to sustain operations and “bounce back” <i>when</i> (not <i>if</i>) an untoward event occurs</li> <li>• The question, “What if?” needs to end every process step designed in the care of high risk patients.</li> <li>• “What if” a staff experiences an occupation exposure?”</li> <li>• “What if” the public has a negative reaction to our work with Ebola patients?”</li> <li>• <i>What if...</i></li> </ul>

TABLE 36.1 Relating the Principles of High Reliability to the Management of Patients With Ebola Virus Disease—cont'd

HRO Principle	Description	Application in the Care of Ebola Patients
Deference to expertise	Staff closest to, and responsible for, the workflow and care processes is the most knowledge about how best to manage their work. HROs actively solicit input from frontline staff when designing processes of care and, in particular, at time of crisis or during an emergency.	<ul style="list-style-type: none"> <li>• The frontline nursing, infection control, laboratory, transport, housekeeping and other ancillary staff were key members of the planning team from the beginning of the initiative.</li> <li>• Frontline staff were active participants at the daily leadership-led huddles.</li> <li>• A challenge was managing the well-intentioned “directives” of leadership staff who were removed from day to day bedside care but have a vested interest in the care of Ebola patients.</li> </ul>

improvement tools creatively to manage the safe implementation of a broad spectrum of clinical research protocols effectively.

One example of how performance improvement tools have been used to enhance the conduct of clinical research occurred in our institution as the severe acute respiratory syndrome (SARS) epidemic evolved in 2004. At that time, investigators at the NIH Clinical Center authored two protocols designed to gain insight into the epidemiology, pathogenesis, and natural history of this new disease as well as to assess strategies for the clinical evaluation and management of patients with SARS. These protocols perhaps positioned the NIH CC somewhat uniquely as one of the few health-care facilities in the world that was actively recruiting patients with SARS. The research protocols received rigorous scientific and human subject protections vetting and approval, and the principal investigators were poised to enroll their first participant/patient. However, several circumstances caused the NIH CC, as an organization, to pause before the decision was made to open recruitment.

Because of the nature of the studies conducted at the NIH CC, many of the patients/participants recruited to participate in its clinical research protocols are highly immunocompromised, either as a direct result of their underlying disease or due to the interventions associated with the research studies in which they are enrolled. Further, at the time of the SARS outbreak, the NIH CC's clinical environment was in a building—constructed in the 1950s—that posed significant infrastructural hurdles to providing safe care to patients infected with highly infectious (and in this instance, possibly airborne) pathogens. In this complex clinical context, investigators from the National Institute of Allergy and Infectious Diseases submitted protocols requiring the provision of care for highly infectious SARS patients. Subsequently, these proposals were presented to the NIH community. As one might have anticipated, several investigators who provide care for

patients who have severely compromised immune function were adamantly opposed to admitting patients with SARS or other highly contagious respiratory illnesses electively to the NIH CC. However, because of the clearly urgent public health need, as well as the potential unprecedented scientific opportunities, the leadership of the NIH CC approached the issue not by asking: “Can we safely provide care to patients with SARS?” but rather by asking the question, “How can we care safely for all of our patients?” As the protocols were being reviewed for human subjects' protection, the leadership of the NIH CC set out to identify the critical clinical functions that they felt must be present and operating at optimal levels to admit and care for SARS patients safely. This assessment required the collaboration of the research team, the leadership of the NIH CC, and the active participation of key clinical departments such as hospital epidemiology, nursing, critical care medicine, pharmacy, and housekeeping. Using flow-charting techniques,<sup>17,18</sup> the team carefully cataloged each step in the research process and identified clinical care functions necessary to support the research requirements. Clinical and operational functions that were identified as being essential to the successful care of these patients are outlined in [Table 36.2](#).

This exercise was eye-opening in that both the clinical care providers and the investigators were astounded by the breadth of hospital functions that required flawless orchestration to assure that the protocols could be implemented safely. Following the identification of the key clinical and operational requirements, a team was charged with assuring that appropriate policies, procedures, staff, equipment, and physical infrastructure were in place and functioning optimally and efficiently prior to the admission of the first SARS patient. The clinical care team worked closely with the research team as well as with the community of NIH investigators to assure alignment with the study requirements and to time, appropriately, the admission of the first protocol participant.

**TABLE 36.2** Critical Clinical and Operational Functions Required for the Safe and Effective Management of the Patient With Severe Acute Respiratory Syndrome

- 
- Infection control
    - Isolation rooms
      - Availability
      - Capabilities
    - Appropriateness of current isolation precautions
    - Personal protective equipment (PPE)
      - Availability
      - Staff competence
  - Critical care medicine
    - Intensive care unit capacity
    - Staff competence
  - Respiratory therapy
    - Ventilator availability
    - Staff competence
  - Staff, patient, and family education
    - Personal Protective Equipment
    - Isolation precautions
    - Managing containment/isolation/quarantine
  - Laboratory medicine
    - Availability of tests/assays for clinical research and clinical care
  - Medication management
    - Supply chain issues
  - Equipment and supplies
    - Ventilators
    - Personal protective equipment
  - Social work/emotional support
    - Participant and family support
  - Patient transport
    - To the NIH Clinical Center
    - Within the NIH Clinical Center
  - Security
    - Transportation assistance
    - Crowd control
  - Housekeeping
    - Infection control training
  - Code blue
    - Exposure/transmission mitigation
  - Public relations/Communication
    - For staff, participants, families, public
- 

NIH, The National Institutes of Health.

## **PROACTIVELY ASSESSING CLINICAL AND OPERATIONAL RISK**

The development of a complete listing of the essential clinical processes that need to be in place is a critical first step to prepare for the implementation of a new research protocol. As was the case with the SARS protocol, this process can be daunting. Focusing an organization's finite resources to assure that attention is paid to the most critical and potentially riskiest care processes is a challenge for most organizations. A variety of tools exist to guide the objective prioritization of what may ultimately be a very long list of critical issues that must be addressed. FMEA is a powerful risk assessment tool that provides a systems-based, human-factors-focused,

and objective methodology for identifying and prioritizing risk, with the ultimate aim of reducing patient harm and enhancing clinical research.<sup>19,21–28</sup> Historically, FMEA has been used in the engineering environment to assess high-risk processes associated with power generation in the commercial nuclear power industry; in aviation to assess the acceptability of aircraft designs; and in the automotive industry to establish manufacturing requirements for cars and trucks.<sup>19,22,24</sup> DeRosier and colleagues at the Veteran's Administration's Center for Patient Safety are credited with moving the techniques of FMEA to the bedside, applying the concept of prospective risk analysis to health-care processes.<sup>29,30</sup> In 2002, the use of FMEA in health care further expanded with the issuance of a Joint Commission requirement that all health-care organizations seeking accreditation conduct at least one proactive risk assessment on a high-risk clinical process every 18 months.<sup>31</sup> Clinical care practitioners as well as clinical research professionals can use FMEAs to identify risk and to avert adverse events, errors, and other system failures in a variety of health-care settings.<sup>19,20,22,23,27,28</sup>

In a complex care environment, where risk is compounded by the interplay of clinical medicine and clinical research, FMEA is a useful tool to guide risk mitigation by identifying critical risk points in clinical care and clinical research processes. In 2016, investigators at the National Institute of Mental Health initiated a clinical research protocol at the NIH CC to study the neurobiology of suicide and to identify risk factors for short and long-term suicidality. One of the study phases involved admitting actively suicidal patients. In response to this research protocol, the NIH CC set in motion a rigorous risk mitigation initiative. An interdisciplinary team comprised of patient safety professionals, research investigators, nurses, social workers, and hospital leadership used FMEA to evaluate potential risk points throughout the clinical research and patient care processes. The analysis was facilitated using QI Path, an FMEA software package. The team segregated the research protocol into three overarching care delivery processes as well as several subprocesses for analysis as illustrated in Fig. 36.1.

Using a consensus decision-making model, Failure Modes were identified for each subprocess and assigned a Hazard Score. Hazard Scores were the product of three factors: the probability of failure occurring (range 1–5), the severity of the outcome (range 1–5), and the failure's detectability (range 1–4). The maximum Hazard Score was 100. The Failure Modes were ranked by Hazard Score to guide prioritization for risk mitigation.

Thirty-nine Failure Modes were identified. Hazard Scores ranged from 0 to 60 with a mean of 18.8. The majority of the Failure Modes skewed to "low risk"—likely due to the NIH CC's existing heightened safety

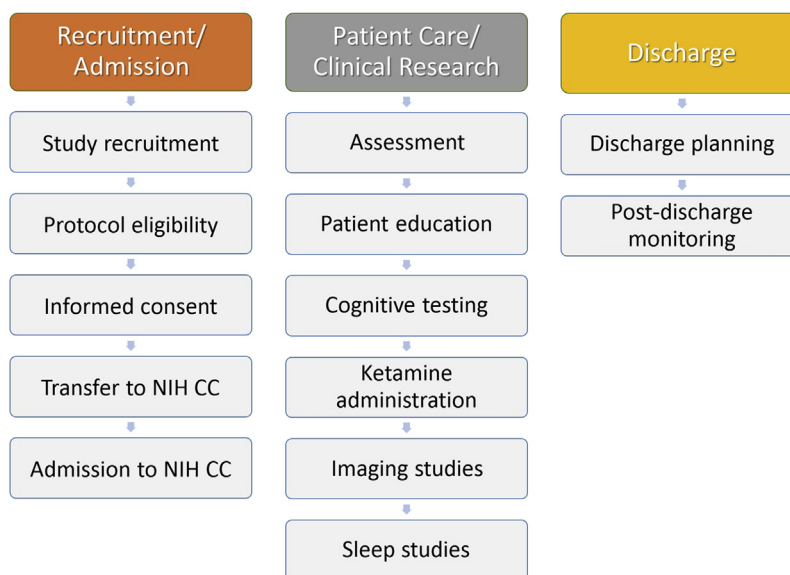


FIGURE 36.1 Neurobiology of suicide protocol process and subprocess steps. *NIH CC*, The National Institutes of Health Clinical Center.

measures that were implemented in response to a past in-hospital suicide. However, nine Failure Modes had Hazard Scores of  $>30$  (the top 20% of all Failure Modes) and were targeted for risk mitigation. Immediate interventions focused on the following Failure Modes with Hazard Scores of 60:

- “Presence of Environmental Risk”
- “Inadequate Nurse Staffing”
- “Undetected Suicidality at Discharge”

Other high-risk Failure Modes included “Inadequate Staff Training” (Hazard Score 45), “Patient Coerced to Enroll” (Hazard Score 36), “Patient Harms Self” (Hazard Score 36), and “Patient Elopement” (Hazard Score 30).

Informed by the data from the FMEA, the patient care and research teams collaboratively developed risk mitigation strategies aimed at reducing the likelihood of patient harm or research lapses: a rigorous environmental assessment process was implemented to identify hazards posed by equipment, sharps, and the physical environment; the nurse skill mix as well as staffing plans were evaluated and adjusted based on evidence from the FMEA; and the medical and research teams developed strategies to assure that patients were thoroughly assessed for suicidality prior to discharge. In addition, two positive “unintended consequences” resulted from this analysis:

- the process provided an effective forum for focused, deliberate discussions between the research team and clinical care staff regarding protocol requirements that otherwise might not have occurred; and
- the care team’s “preoccupation with failure” and focus on the culture of patient safety were reinvigorated.

FMEA has been, and continues to be, a highly effective tool for identifying, characterizing, and prioritizing risk associated with complex patient care and clinical research processes. Findings from this consensus-driven, objective, and quantitative analysis can be used successfully to leverage organizational change and resource allocation.

### Continually Monitoring the Clinical Research Environment for Risk

Using FMEA to identify the clinical risks points associated with the implementation of a clinical care or clinical research process is a critical first step in mitigating patient/participant risk. FMEAs, or other risk assessments, identify process points that are associated with increased risk to the patient/participant, to involved providers, and/or to the scientific integrity of the study. As illustrated in the example above, these risks can be addressed by myriad clinical and organizational interventions that are aimed at reducing those risks.

The next step in mitigating risk is the deployment of strategies to assess the effectiveness of interventions, and to survey the research and care environments continually for other risks to the participants and to the study. Measurement is fundamental to assessment efforts and improvement in the quality of care. The history of health-care quality improvement and measurement dates to Florence Nightingale’s collection of mortality data and infection rates during the Crimean War, as well as to the work of Ernest Codman in establishing standards for hospitals in the early 1900s, including his provocative “end results hypothesis”



that led to a Semmelweis-like estrangement from the health-care establishment (see Chapter 1).<sup>32,33</sup>

In a classic paper in 1968 Avedis Donabedian recommended measuring health-care quality in three areas: structure (the characteristics of a health-care setting); process (what is done in the health-care setting); and outcomes (the status of the patient resulting from specific interventions).<sup>34</sup> This paradigm remains the mainstay of modern health-care performance measurement programs and is the basis for the local, state, and federal programs designed to measure the quality of clinical care and identify health care-associated risks and adverse events. Clinical research programs, too, should implement processes to assess the performance of the clinical research enterprise systematically—primarily to assess for risks to the participants, investigators, and care providers, as well as for threats to the integrity of the study. Collecting and reporting adverse events that occur during the course of a research study is a mandatory component of both the research process and the protection of human subjects. However, event reporting in clinical research focuses on individual protocols, not on how the system of clinical research is performing as a whole. This “protocol-centric” focus fails to identify clinical care and clinical research system failures that potentially might impact participant safety across multiple studies. Murff and his colleagues<sup>35,36</sup> have described the need for research teams to develop reporting systems that collect data about reportable adverse events, as well as “near misses” or “latent failures” in the clinical care and clinical research environments. Near misses or latent failures are errors that do not result in patient/participant harm; however, these events do have the potential to do harm if the circumstances of the event were somewhat different. Identifying and analyzing near misses or system failures provide the care and research teams the luxury of designing and implementing interventions to interrupt the error cycle prior to the occurrence of a serious error. Surveillance for errors, adverse events, and latent errors in the clinical care or research setting can be accomplished using a variety of strategies including<sup>1</sup> event reporting systems<sup>2</sup>; electronic surveillance systems that utilize clinical triggers to identify errors; and<sup>3</sup> analysis of clinical performance measurement data.

### Patient Safety and Clinical Event Reporting Systems

Since the 1980s most health-care patient safety and clinical quality programs have relied on voluntary or mandatory occurrence reporting systems (ORSs) as a critical source of data regarding clinical care errors and/or latent errors and near misses. These reporting systems are readily accessible and have the capacity to

provide detailed information about these kinds of events.<sup>18,34,36–46</sup> The NIH CC has had a hospital-wide electronic ORS since the early 1980s. This voluntary electronic event reporting system captures more than 5000 reports per year. Events entered into the ORS span the spectrum of clinical care and clinical research events—from serious harmful errors to reports of service quality. The NIH CC has found the ORS to be particularly useful as a surveillance tool for identifying trends in latent failures in clinical care and clinical research processes that otherwise would likely not be identified. The following is an example of a potentially harmful near miss or latent failure that could have had a negative impact on clinical research, had the issues not been identified by using data from the NIH CC ORS.

On review of data from the ORS, the Pharmacy Department Quality Officer noted a trend in administration events that was occurring associated with a specific investigational drug in a phase I clinical trial. The reports indicated that drug delivery was delayed on several occasions because the infusion pumps had inexplicably suspended infusion. Each time the infusion would stop, the nursing staff would troubleshoot the problem, requiring the infusions to be restarted several times during a single delivery, potentially resulting in a delay of study drug administration, and potentially adversely affecting drug levels and pharmacokinetics. Alerted to these administration errors via the ORS, the Pharmacy Quality Officer met with the study investigators, the clinical care staff, and the nursing staff. Collectively the group conducted an intensive review of the events. The common factor identified in each incident was that the infusion pumps stopped due to an “air in line” alert, although no air was noted in the tubing. All efforts to determine the cause of the alert generation were futile. Finally, the team contacted the research team who had developed and conducted the initial laboratory testing of the drug in an effort to identify a reason for the alerts. Following the review of the current medication administration procedure for this study, the research team noted that the initial safety testing for the drug was performed using a different brand of intravenous tubing than the brand stocked and used in the NIH Clinical Center. The team changed the procedure for administering the study drug, mandating a change in the brand of intravenous tubing used. No additional reports of misadministrations were reported during the remainder of the study. Whereas these incidents do not appear to have caused any harm to the participant or the study, the potential for harm to the participant and the study are obvious, and any future potential adverse events or protocol deviations were averted as a result of identifying this series of events via the NIH CC’s ORS.

The success of voluntary event reporting is dependent on the organizational culture in which the

reporting system is deployed, as well as on the manner in which the staff and leadership of the organization use the data to drive improvements in care and research. Establishing a nonpunitive “just culture” that encourages the reporting of events, free of reprisal, is essential to maintaining a robust and meaningful reporting system. Equally important is an organizational commitment to using the data provided by staff to understand system and process errors and failures and to develop strategies to mitigate risk and improve care. Finally, organizations should be committed to sharing performance measurement data with the staff to keep them informed and aligned with institutional performance improvement strategies.

### **ELECTRONIC SURVEILLANCE FOR ERRORS AND SYSTEM FAILURES**

The nearly universal deployment of electronic clinical information systems in health-care settings provides a robust platform for identifying adverse events in clinical care as well as in clinical research. Electronic surveillance for adverse events has proven effective in identifying, in real-time, events such as adverse drug toxicities and interactions, health care-associated infections, and other iatrogenic injuries or events. This technology uses clinical triggers to signal the presence of potential errors or adverse events. Clinical triggers can include high-risk medications, select abnormal laboratory values (e.g., abnormal serum potassium levels, microbiology culture results), treatment interventions such as antidotes (e.g., Naloxone (Narcan), vitamin K), corrective procedures (e.g., chest tube insertions and dialysis) and unplanned intensive care unit admissions.<sup>9,47–52</sup> Electronic event surveillance for clinical care and clinical research errors and latent failures provides a tool that administrative institutional leadership, clinicians, and research investigators can use to identify, mitigate, and report these events in a much timelier manner than traditional, voluntary incident reporting systems.

### **PATIENT SAFETY AND CLINICAL QUALITY MEASURES**

Another excellent source of information about the capacity of a hospital or other health-care organization to provide a safe environment in which to conduct clinical research is the organization’s patient safety and clinical quality performance measurement program. These measurement programs collect data that are used to assess the quality of the care and services provided to patients.

All hospitals and other health-care facilities accredited by the Joint Commission must have systems in place to measure, continually, a proscribed list of clinical activities.<sup>53</sup> Most hospitals also participate in a variety of national and/or state clinical performance measurement activities, often as a condition of funding and certification.<sup>54</sup> Regardless of the type of performance indicators used by an organization to monitor patient care processes, these measures, if well designed and appropriately implemented, provide valuable insight into the health-care organization’s management of critical patient care processes. Table 36.3 provides a list of frequently monitored processes of care. Performance measurement activity in the clinical research setting also should take into consideration important clinical metrics associated with the scientific protocol under study. In addition to national and state benchmarks for clinical performance metrics, clinical researchers should be mindful of the specific processes on which their studies depend and create appropriate performance metrics to track the success of those systems.

Data from performance measurement indicators provide investigators with critical information to guide study planning and preparation. For instance, if a clinical research study intervention will be conducted on a highly immunocompromised patient population, the effectiveness of the hospital’s infection control processes becomes highly relevant. Quantitative and objective

**TABLE 36.3** Examples of Clinical Care Performance Indicators

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- Medication management
    - Medication errors
    - Pharmacist Interventions
  - Pain management
    - Reassessment for pain postintervention
  - Treatment delivery
    - Delays in treatment
    - Patient wait times
  - Invasive procedures
    - Complication rates
    - Returns to the operating room
    - Readmissions following outpatient procedures
    - Wrong site/person surgery
  - Infection control
    - Infection rates (e.g., central line-associated bloodstream infection, catheter-associated urinary tract infections, surgical site infections)
    - Hand hygiene compliance
    - Timing of surgical antimicrobial prophylaxis
    - Health-care worker vaccination rates
  - Patient falls
  - Transfusion management
  - Disease/diagnosis-specific measures
    - Acute myocardial infarction
    - Pneumonia
    - Heart failure
    - Stroke
-

data about the organization's health care-associated infection rates and hand hygiene practices provide valuable information about system and process issues that might need to be addressed prior to recruiting and enrolling patients/participants.

Assuring that the clinical care environment in which clinical research participants will receive safe and high-quality care that supports clinical research is a shared responsibility of the health-care organization's leadership, the care providers, and the research team. Basic quality improvement tools such as flowcharting, prospective risk assessment methodologies (e.g., FMEA), and clinical quality and patient safety performance measures provide objective data to guide protocol planning and implementation strategies.

### ASSESSING CLINICAL RESEARCH PARTICIPANTS' PERCEPTIONS OF THE CLINICAL RESEARCH EXPERIENCE

One aspect of quality that has been far less intensely addressed in the literature is the assessment of the quality of the care and services provided to research participants. In particular, few studies have addressed participants' perceptions of their experiences with clinical research processes. In this section, we focus on the assessment of participants' perceptions of their clinical research experiences.

The clinical research community can look to the health-care industry for guidance in determining how to assess participants' experiences as research subjects. Although the processes of providing patient care in a hospital and the conduct of a clinical research study often differ, investigators and the care teams supporting the research must be mindful that at the center of these processes is a human being interacting with a health-care delivery system whether in a community hospital, a Clinical Translational Science Award unit, or an outpatient setting. How research subjects perceive the clinical research experience provides valuable insights for future improvement of both the clinical and scientific processes.

The NIH CC has surveyed patient/participants using a Picker-derived survey instrument<sup>55</sup> since the mid-1990s. The NIH CC is motivated to understand how patient/participants perceived the care they receive during their participation in studies conducted at the NIH CC as one method to assure that the needs and expectations of this special group of individuals who volunteer to contribute to scientific discovery are met. In 1995, the Clinical Center partnered with the Picker Institute (the National Research Corporation (NRC) acquired the Picker Institute in 2001) to develop a method of eliciting patient/participant feedback about critical aspects of their clinical research experience at the NIH CC. The Picker Institute's philosophy

of eliciting information from patients about their experiences was used to develop the NIH CC's survey. The survey was tailored to the unique clinical research environment of the Clinical Center and was designed to include several questions addressing the experience of participating in clinical research.

For the past 15 years, the NIH CC used these data to identify opportunities to improve our patient/participants' experiences. Issues such as communication with clinical staff, attention to emotional support, and the participant's understanding about the point at which he or she can cease participation in a study were identified as areas requiring focused review and attention. These issues and others were addressed using the NIH CC's organizational performance improvement structure. Interventions were implemented and improvements were measured. Many of these issues would not have been identified as problematic had the NIH CC leadership not actively queried their research participants about their perceptions of these processes.

In 2003, the leadership of the Rockefeller University Hospital Center for Clinical and Translational Science expressed interest in the NIH Clinical Center's survey and, subsequently, partnered with the NIH Clinical Center and the NRC–Picker to develop a valid and reliable survey instrument specifically to measure participants' perceptions of their clinical research experiences.<sup>56</sup>

### CONCLUSION

Patient safety, clinical quality, and efficient and effective processes of care delivery are of equal import to clinical care and clinical research. Irrespective of the approach taken, we believe that researchers and institutions involved in clinical research must collect data from a variety of sources, including the solicitation of perceptions from participants and staff input about their research experiences, to improve the conduct of clinical research continually.

Developing clinical research programs that include structured approaches to collecting reliable information about factors that contribute to process failures and adverse events (including careful root cause analyses); mechanisms for assessing trends in process and outcome failures, structured approaches to identifying risk points prior to study implementation (e.g., FMEA); and obtaining participant insights about their perceptions of the clinical research experience will provide the necessary data to allow institutions and investigators to improve the clinical research experience. We believe these approaches to patient safety, clinical quality, and clinical research quality and safety will increase substantially the likelihood of successful completion of clinical studies.

## SUMMARY QUESTIONS

Which of the following is not a characteristic of an HRO?

1. Preoccupation with failure
2. Punitive approach to managing untoward events
3. Resistance to simplify
4. Commitment to Resilience
5. Deference to expertise

Which of the following tools is used prospectively to identify risk in processes, procedures, and protocols?

1. Root Cause Analysis
2. FMEA
3. Ishikawa Diagram
4. Pareto Chart

The evaluation of a hospital's Central Line-Associated Bloodstream Infection rate is considered to be what type of measure?

1. Structure measure
2. Process measure
3. Outcome measure

The person credited with establishing standards for evaluating hospitals is

1. Donald Berwick
2. Florence Nightingale
3. Ernest Codman
4. Ignaz Semmelweis

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