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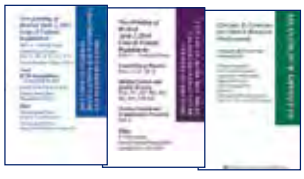

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99 Canal Center Plaza, Suite 200,
Alexandria, VA 22314

+1.703.254.8102 (fax)
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GUEST EDITOR'S MESSAGE

Steven Ziemba, PhD, MBA, CRCP, CIP, FACHE, CCRC

Integrating Research into Healthcare

It gives me great pleasure to serve as guest editor for this issue of *Clinical Researcher,* and to engage our focus on a topic of great interest not just to me, but to a growing extent of professionals across our field: namely, the ever-developing relationship between clinical research and the healthcare industry.

Clinical research has evolved in dramatic fashion. To some extent, this evolution has been in sync with the overall healthcare industry, and has not always moved in a single direction. The two have steadily become more intertwined, with a diverse array of interactions, changes, and applications of thinking. This edition of *Clinical Researcher* steps back and explores the various means by which clinical research has become more involved in the general healthcare industry, with the diversity of this relationship being reflected in the array of articles presented.

Beyond the Basics

Research is having a greater impact on the care of patients beyond the determination of the safety and efficacy of novel investigational agents and medical devices. The growth of translational research and its ability to rapidly alter patient care is one dramatic example investigated by Drs. Richard Dart and Robert Haws in their discussion on barriers and opportunities among clinician researchers. This topic has been explored before, but here the authors address the matter in terms of the need for clinicians to remain current in their practice—a task for which the conduct of research is an important component.

The field of medicine is growing in ways that could not even be considered only a few decades or even years ago, and this growth increases the value of research and its resulting knowledge to healthcare. However, a disconnect exists between science and medicine, a topic explored in the commentary by Drs. Ayaka J. Iwata, Christine Johnson, and Steven S. Chang. The authors discuss the slow application of new knowledge to medicine, including its impact on advancing healthcare in the day-to-day care of patients, and some of the reasons for a lack of rapid integration of research-generated knowledge.

A more basic overview of the variety of clinical study design is also provided by me, demonstrating how this variety can address the myriad of questions in healthcare.

This is a good place to note that this edition of *Clinical Researcher* differs from most in that its peer-reviewed content presents aspects of our environment not directly tied to clinical research, but describe the progressing influence of research on healthcare operations.

A significant aspect of such nature is the need for performance and quality data by clinicians, administrators, and other healthcare professionals. Such need stems from patient care, payment and reimbursement, quality measures, and enhancement of productivity.

The movement to a pay-for-performance approach brings with it the need to better

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understand the complexities of healthcare across the industry and its individual hospitals, clinics, and providers. Readers may find the article on colorectal cancer screening and Medicaid to be seemingly out of place in a journal focused on clinical research; however, Dr. Gloria Coronado and her team present a practical application of research to a healthcare issue. The authors describe the application of research via a coordinated care organization to determine if quality improvement measures were being met. This approach demonstrates the changing face of clinical research and how it is applied to healthcare. In doing so, the authors describe a way that those engaged in research can demonstrate additional value to healthcare organizations, and help to integrate what they do more readily into the overall field.

Dr. Farhan Huq and colleagues also describe the use of quality measures, patient satisfaction scores, and other aspects in head and neck cancer management, highlighting the role that research provides healthcare in understanding the current environment, studying what improvements are necessary, and assessing if, indeed, such improvements succeed.

Going in Depth

A growing field of research in healthcare, and one that is engaging more in the clinical research realm, is health services research. A prime example of the increasing prominence of this area of study is seen in the cancer care delivery research (CCDR) component of the National Cancer Institute (NCI) Community Oncology Research Program (NCORP), the successor to the Community Clinical Oncology Program of the NCI. Originally designed to provide cancer treatment clinical trials to academic and community cancer centers and others that treat cancer patients, the new NCORP will design and conduct studies on cancer prevention, screening, control, treatment, and post-care management. CCDR takes the mission of the NCORP studies further by investigating social factors, costs, technologies, and provider and patient behavior on treatment outcomes and quality of care.

To some extent, the works on cancer screening point to the increase in clinical trial–related research. Dr. Andrew Masica and colleagues delve further into health services research, investigating its integration into the healthcare infrastructure. Clearly, it can be seen how health services research can become an even greater, and diverse, component of clinical research.

Viewing clinical research as a fundamental component of healthcare presents another aspect for our consideration, in recognizing clinical research as a profession in the healthcare industry. The success of changes described herein, and the role of clinical researchers in those changes, may depend on how clinical research is regarded. Terri Hinkley, Dr. Jeff Kingsley, and I explore the aspect of clinical research as a profession. We encourage our readers to take the concepts discussed in the article further by attending an interactive session on this topic at ACRP's 2015 Global Conference & Exhibition in Salt Lake City, Utah, in April.

Conclusion

The Editorial Advisory Board of *Clinical Researcher* has stepped back to view clinical research against the background of healthcare. This is not an easy task, and the articles in this issue provide only a brief glimpse at how extensive such a relationship can be.

Healthcare as a whole relies on research to advance and improve patient care. The changes in healthcare, bringing with them a combination of improvement and uncertainty, render clinical research all the more important to the overall field. I hope you enjoy this issue's varied and interesting discussions.

> The field of medicine is growing in ways that could not even be considered only a few decades or even years ago, and this growth increases the value of research and its resulting knowledge to healthcare.

Steven Ziemba, PhD, MBA, CRCP, CIP, FACHE, CCRC, (steven.ziemba@gmail.com) is associate director of Marshfield Clinic Research Foundation, Marshfield, Wis., and a member of the ACRP Board of Trustees and Editorial Advisory Board.

BY THE NUMBERS

Summing up recent facts and figures on patient centricity that will be evident in the next issue of *Clinical Researcher*.

In a recent survey, almost **75%** of senior individuals with responsibility for or a special interest in clinical trials agreed that "putting the patient at the heart of the clinical trial" is the top priority for their organization going into 2015.

Source: eyeforpharma white paper on "An End to Trial by Ordeal and a Shift to Patient-Centricity," released in 2014 and available at www.eyeforpharma.com/patient-clinical-trials-europe/docs/clinical-trials-whitepaper.pdf

In 2014, concerning the nonprofit Patient-Centered Outcomes Research Institute (PCORI), **35** articles were published in journals by PCORI awardees, **26** articles were published by or about PCORI, and **82** articles were published that cite or mention PCORI work.

Source: PCORI Dashboard Review: End of FY 2014, released December 8, 2014 and available at www.pcori.org/sites/default/files/PCORI-Dashboard-Presentation-from-Board-Meeting-Slides-120814.pdf

In 2009–13, just **25%** of patients who were screened for Phase II–IV trials remained as participants through to the completion of the study, compared to 49% in 1999–2003 and 29% in 2004–08.

Source: 2014 Tufts Center for the Study of Drug Development presentation on "A Critical Need to Support Patient Centricity in Clinical Research" to Clinical Trials Ontario, available at www.ctontario.ca/wp-content/uploads/2014/03/Getz_Kenneth_session4_a.pdf

About **90%** of respondents to a 2013 survey reported that they found their clinical trial medicine packaging and instructions either "Very Easy" or "Somewhat Easy" to use.

Source: "Report on the ISPE Project Concerning Patient Experiences with Clinical Trial Materials," released in November 2013 and available at www.ISPE.org/Patient-Initiatives/2013NovReport

ACRP
ASSOCIATION OF CLINICAL RESEARCH PROFESSIONALS

EDITOR-IN-CHIEF
A. Veronica Precup
editor@acrpnet.org
(703) 254-8115

ASSOCIATE EDITOR
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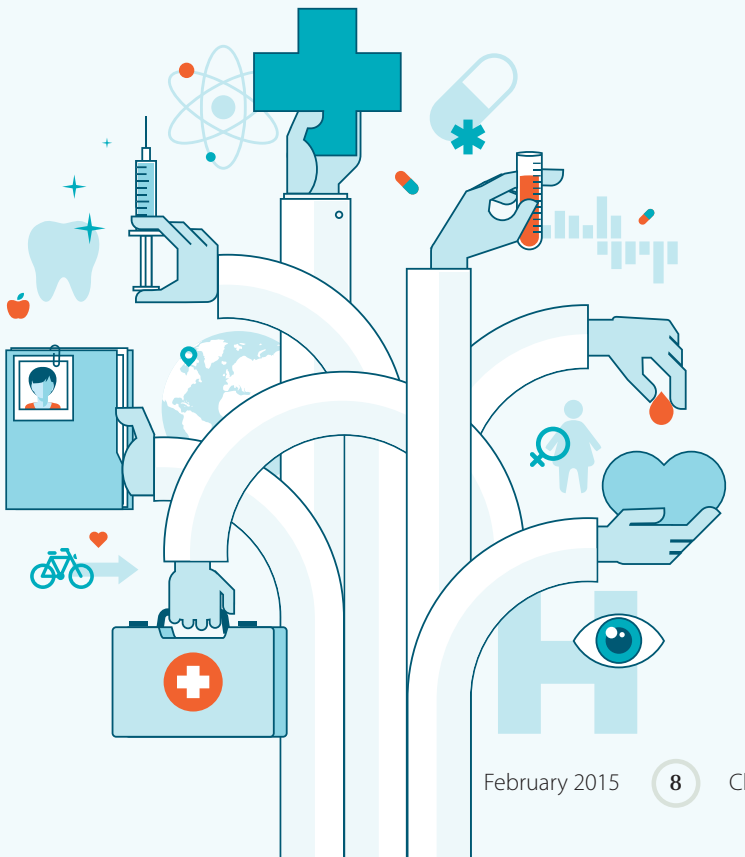
Michael R. Hamrell, PhD, RAC, FRAPS, RQAP-GCP, CCRA

I Never Thought of That!

In this issue's column, the questions raise several seldom-considered and/or complicating issues that can make managing clinical trials as much an art as a science.

Q: Is it permissible to have clinical trial branding under the tenets of good clinical practice (GCP)?

A: The U.S. Food and Drug Administration's (FDA's) GCP program has noted that the regulations and guidance do not specifically mention clinical trial names or acronyms. Sponsors are prohibited from representing "in a promotional context" the notion that an investigational product is safe or effective for the purposes for which it is under study, or otherwise promoting the product.[1]



If a clinical trial name or acronym could appear to be promotional, FDA could ask the sponsor to change it. In addition, an institutional review board (IRB) would be within its authority to ask that a promotional study name be changed to avoid the appearance of trying to unduly influence subjects to participate in a trial.[2]

According to my *Clinical Researcher* colleague-columnist Beth D. Harper, founder and president of Clinical Performance Partners, Inc., "When used in the context of clinical trial awareness and education for subjects, there is a possibility that a clinical trial acronym may be coercive by subliminally enticing or outwardly promising something that the trial may not be able to deliver. Some researchers have suggested, for example, that acronyms such as 'ALIVE' (Adenosine Lidocaine Infarct zone Viability Enhancement trial) or 'CURE' (Clopidogrel in Unstable angina to prevent Recurrent ischemic Events) are coercive, but that 'COMET' (Carvedilol Or Metoprolol European Trials) would be neutral and non-coercive."[3]

Although these clinical trial acronyms may not be "advertising" per se, some experts claim that IRBs and ethics committees should, by extension, not only review advertisements and other recruitment-related materials, but clinical trial acronyms as well to ensure that an acronym is not misleading or potentially coercive. This would seem particularly true when a trial acronym will be used prominently in recruitment advertising, the informed consent form, and other key study-related materials to be provided to prospective study subjects.

Do you have a GCP question or an issue that has come up at your site or company? If you are not sure of how to proceed, please send an e-mail to: gcp@moriahconsultants.com and I will answer it in an upcoming column.

Q: Do any FDA requirements or standards establish the length of time a study participant must wait after leaving one drug study before beginning the screening process for another drug study?

A: The FDA regulations do not specify a timeframe that should elapse between a subject's enrollment in two successive trials. However, there must be an adequate washout and recovery period to ensure that subjects are appropriately protected (against product interactions) and risks are minimized. Information about pharmacokinetics (e.g., absorption, dissolution, metabolism, excretion) of the drug would be needed to determine the appropriate interval.

Although a 30-day washout is common, many study protocols specify a longer time period (60 or 90 days). For a device trial, this interval should be guided by good science and consideration of the safety of the subjects.

Q: Are there any plans to update the International Conference on Harmonization (ICH) GCP guideline (E6), which is now roughly 18 years old?

A: In June 2014, the ICH Steering Committee adopted a proposal and work plan to add an addendum to this well-referenced guideline. According to ICH, since the adoption of the ICH GCP (E6) guideline, clinical trials have evolved substantially, with increases in globalization, study complexity, and technological capabilities. The Working Group is charged with developing an addendum to supplement ICH E6 with recommendations to facilitate innovative approaches to clinical trials, including quality risk management and quality-by-design processes, which emphasize upfront assessment of risks specific to a study design and protocol.

Study operational procedures to facilitate innovative approaches should be addressed, including those focused on risk-based monitoring, critical study elements, and use of technological tools to ensure robust conduct, oversight, and reporting.

Some of the discussions regarding the need to update the ICH E6 guideline were prompted by a recent member poll conducted by the Institute of Clinical Research, which found that 84% of the respondents were in favor of updating the E6 guideline, at least in some areas.

It is expected that this addendum will be completed and reach Step 4 (ready for adoption by parties) by November 2016. No other details are available at this point.

References

1. See 21 CFR 312.7 and 812.7 in the *Code of Federal Regulations*.
2. 21 CFR 56.108(a).
3. Orlowski JP, Christensen JA. The potentially coercive nature of some clinical research trial acronyms. *CHEST* 2002;121:2023-8.

Michael R. Hamrell, PhD, RAC, FRAPS, RQAP-GCP, CCRA, (gcp@moriahconsultants.com) is president of MORIAH Consultants (a regulatory affairs/clinical research consulting firm), holds appointments at several major universities, is a member of the ACRP Editorial Advisory Board, and serves similarly for several other leading clinical research and regulatory affairs journals.

Judith L. Forman, MPH

When Should Informed Consent Begin?

About 15 years ago, when I was the project manager for a large, federally funded, multicenter clinical trial, a patient who had been offered enrollment called to express his horror that we were randomizing people into different treatment arms. He had never heard of such a thing. How could we let someone's treatment be decided by chance? Surely this was illegal!

I explained that a randomized controlled trial is the gold standard for learning about whether treatments were effective, and that the study had been approved by a committee whose job it is to make sure studies are ethical. "I really doubt that!" he said, adding that he had a PhD in history. I gently told him that, because participation was voluntary, he was under no obligation to enroll in the study if it made him uncomfortable.

The informed consent process for this study included a 50-minute video that explained the disease, what prior studies had shown about treatment effectiveness, the study and its purpose, and the options of enrolling in either a randomized trial or an observational cohort. Following the video, volunteers had a discussion with the study coordinator before signing the consent form.

I thought we had a robust informed consent process; yet we still had an outraged history professor and an older woman who verbally agreed to be randomized and happily signed the consent form, but only after crossing out the sentence that said she agreed to have her treatment chosen by chance (she wrote "no" in the margin).

Image Problems and Process Pitfalls

In 2002, *Time* magazine published a cover story on "Human Guinea Pigs" featuring the now iconic picture of a woman curled up in a cage equipped with a water bottle meant for a rodent. PowerPoint slides of this image still appear in research ethics presentations at conferences, symbolizing the ubiquitous problem of the public's perception of clinical research. Bad press continues to be the primary source of public information about what we do, with stories of our missteps and questionable behaviors eclipsing what we do well. The public is not getting a fair and balanced education.

As researchers based within academic medical centers (AMCs), we educate clinicians and our communities through events, courses, and public service announcements. We also educate researchers and conduct research in the context of the healthcare we provide, but we do little to educate patients about research prior to presenting them with a consent form.

When we begin the enrollment process in the clinic, we might be speaking with someone who has just received a troubling diagnosis and is upset, anxious, confused, and consequently functionally illiterate when presented with a consent form. Improving the readability of the form is a noble gesture, but there is no sweet spot that will make

a consent form accessible to people who cannot focus on and digest written information regardless of how educated they are. Randomization, a difficult concept at the best of times, is probably more difficult to learn in study enrollment than in a purely educational context, where nothing personal at stake.

The Hits and Misses of Outreach

AMCs offer community education programs focused on health and wellness topics, attracting a self-selected population with a pre-existing interest in a specific topic and opening up opportunities for discussing research participation when appropriate. As another kind of outreach, the nonprofit Center for Information and Study on Clinical Research Participation (CISCRP), based in Boston, Mass., holds "Aware for All" events celebrating clinical research volunteers and educating the community about such participation.

In the same spirit, in 2007 a group of concerned study coordinators at Dartmouth College developed a program called "Research Revealed," aimed at bringing people from the community into the medical center for a fun day of learning about clinical research. The members of Dartmouth's institutional review board (IRB) had a novel creative activity explaining what they do by giving cookies to people who signed an informed consent form: "Consent to Eat a Cookie." Unfortunately, many people who attended just happened to be there that day for an appointment, rather than having planned their day around attending the research fair.

Dartmouth staff next focused on improving the informed consent process by educating study coordinators, most of whom had never been trained on how to conduct an informed consent discussion. The Valid Informed Consent Education (VoICE) program has been teaching study coordinators how to use the "teach back" technique, which involves asking prospective participants to summarize in their own words the key points in the consent form, to ensure that coordinators have done their job in explaining the study.

VoICE has been incorporated into the semiannual "Introduction to Clinical Research" course at Dartmouth's Geisel School of Medicine and presented at conferences and hospitals across the country. Since the program targets research professionals and their interactions with patients, more education is needed at the community level *before* people become patients.

Laying the Groundwork

To produce quality research, we should foster public knowledge about what clinical research is and the role it plays in improving all our lives as early in the education system as feasible. What about setting our sights on a long-range goal of developing fun and informative programs for our schools? CISCRP is planning a large-scale, traveling museum exhibit called "Medical Heroes," which aims to teach school-age children about clinical research (see https://www.ciscrp.org/programs-events/museum-exhibit/).

I envision a program offered directly to schools through presentations to health and science classes, or through a curriculum written for teachers to carry out on their own. Let's teach kids about the research that goes on at the nearest AMC, because they or someone they know may one day be asked to participate in a study. Let's help them understand that research is how treatments get discovered in a way that benefits everyone.

We could engage students by using examples that relate to them, such as treatments for asthma or acne. We could make it fun by conducting a mini mock clinical trial with them. We also could teach a little about the history of human subjects research and the regulations and procedures in place to protect all of us. Older students could even participate in a mock process from idea to grant writing to IRB review.

Conclusion

This is where the informed consent process should begin: out in the community and with our children. Let's create a population of people who know something about clinical research and the role it plays in everyone's healthcare. This might lead to a better and more valid informed consent process. As a bonus, it might inspire kids to pursue the roles of coordinators, monitors, investigators, managers, recruiters, IRB members, and all the other team members the clinical research enterprise will need and deserve in the future.

Judith L. Forman, MPH, (judith.l.forman@dartmouth.edu) is research director for the Center for Genomic Medicine at the Geisel School of Medicine at Dartmouth, a research associate in the Department of Orthopaedics and the Center for Surgical Innovation, a member of the Committee for the Protection of Human Subjects (the IRB for Dartmouth College), and a member of the team that developed VoICE (Valid Informed Consent Education).

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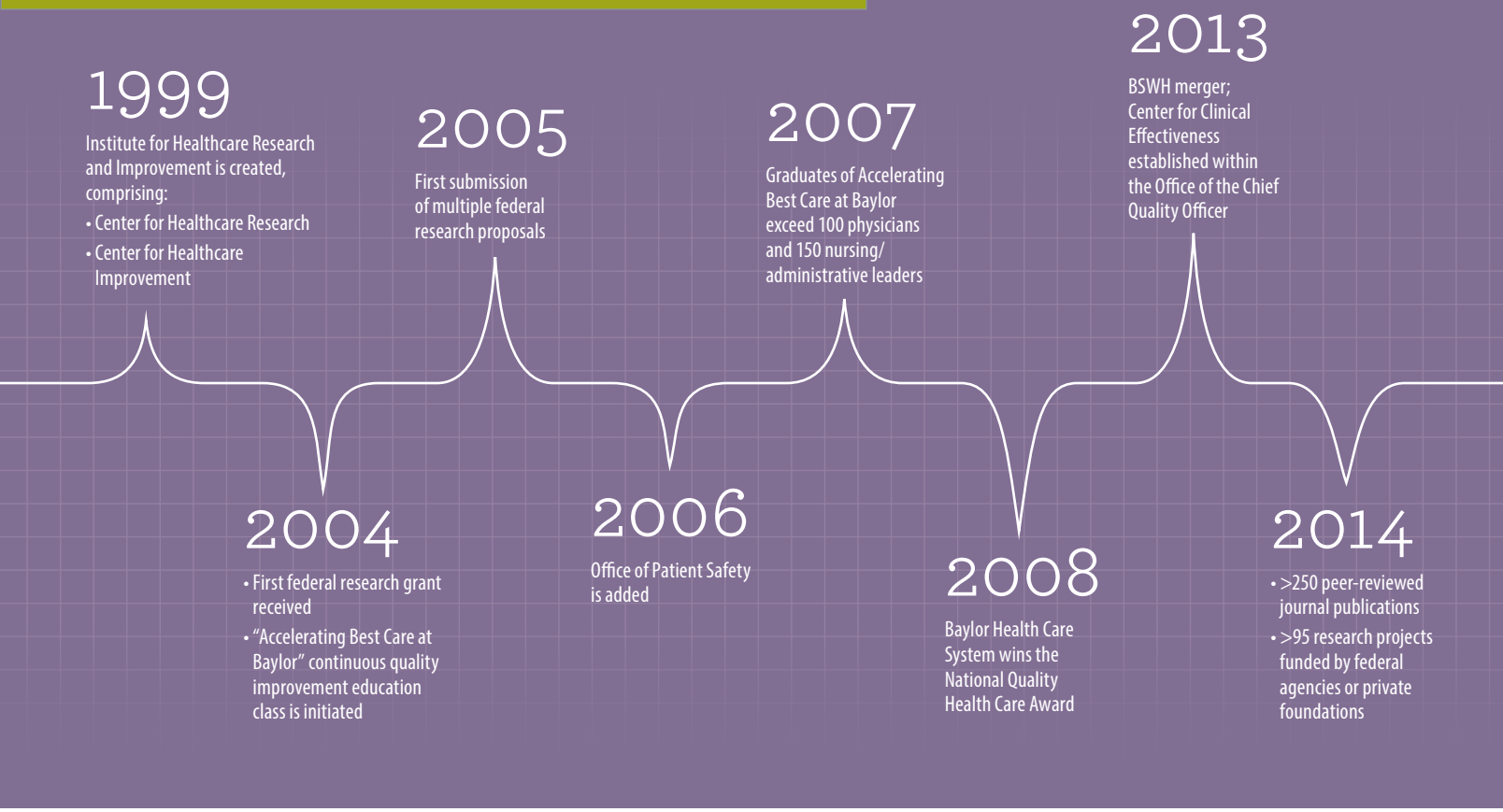
Health Services Research as Operational Infrastructure Within an Integrated Care Delivery System: *A Case Study*

PEER REVIEWED | Andrew L. Masica, MD, MSCI | Ashley W. Collinsworth, MPH, ELS
Elisa L. Priest, DrPH | Giovanni Filardo, MPH, PhD | Brett D. Stauffer, MD, MHS, FHM
Susan H. Smith, DNP, APRN, ACNS-BC | Marygrace Hernandez Leveille, PhD, RN, ACNP-BC
Susan Houston, PhD, RN | Neil S. Fleming, PhD | David J. Ballard, MD, MSPH, PhD

[DOI: 10.14524/CR-14-0041]

Health services research is "a multidisciplinary field of scientific investigation that studies how social factors, financing systems, organizational structures and processes, health technologies, and personal behaviors affect access to healthcare, the quality and cost of healthcare, and ultimately, our health and well-being."[1]

FIGURE 1: Evolution of the Health Services Research Operational Resource within BSWH



The role of research in supporting healthcare operations is becoming increasingly important, particularly with adoption of the triple aim of healthcare improvement—to provide better quality care, to improve the health of populations, and to reduce costs of quality care.[2] There is also a heightened recognition that delivery organizations must embrace a "culture of participation," in terms of actively engaging the development of new evidence delineating effective care practices.[3]

Despite the growing demand for health services research and its potential contribution to operational success, many healthcare delivery systems lack capacity in this area. Here, in a case study format, we describe our 15 years of experience leveraging a research group as operational infrastructure in a not-for-profit, integrated healthcare delivery system.

Setting

Baylor Health Care System (BHCS) was a nonprofit organization dedicated to serving all people through exemplary healthcare, education, research, and community service. In 2013, BHCS merged with Scott & White Healthcare to form Baylor Scott & White Health (BSWH), one of the largest nonprofit healthcare systems in the United States.

The Baylor Research Institute works with entities within BSWH to develop and promote medical research from the bench to the patient, administer research contracts, and ensure regulatory compliance. The Office of Research Subject Protection within the Baylor Research Institute oversees the Baylor Institutional Review Board (IRB).

Evolution and Operational Functionality of a Health Services Research Resource

The Institute for Healthcare Research and Improvement (IHCRI) was established within BHCS in 1999.[4] Over its 15-year lifespan, the IHCRI underwent substantial transformation, including a shift in focus from the research interests of individual scholars to organizational priorities for improving patient care and outcomes (see Figure 1).

With the 2013 formation of BSWH, the IHCRI was reconfigured into the Office of the Chief Quality Officer (CQO). Health services research activities in BSWH's north region were consolidated into the Center for Clinical Effectiveness (CCE) within the Office of the CQO; integration with similar activities in the BSWH central region is in its early phases. The reorganization provided an opportunity to connect research data management and analytics in the CCE more directly to operational

HS

LEARNING OBJECTIVE
After reading this article, participants should be able to describe the challenges of performing health services research in a healthcare delivery organization.

DISCLOSURES
Susan H. Smith, DNP, APRN, ACNS-BC: *Consultant for Fisher & Paykel*
Andrew L. Masica, MD, MSCI; Ashley W. Collinsworth, MPH, ELS; Elisa L. Priest, DrPH; Giovanni Filardo, MPH, PhD; Brett D. Stauffer, MD, MHS, FHM; Marygrace Hernandez Leveille, PhD, RN, ACNP-BC; Susan Houston, PhD, RN; Neil S. Fleming, PhD; David J. Ballard, MD, MSPH, PhD: *Nothing to Disclose*

This research is a crucial step on the research translation pathway, as it tests whether findings shown to have clinical efficacy demonstrate similar results when applied in care delivery settings across heterogeneous patient populations.

initiatives. The research group's present organizational structure is shown in Figure 2.

The CCE is funded primarily (80 to 85% in a given year) by the BSWH operational budget; the balance is covered by external grants. Under this framework, the CCE supports efforts ranging from continuous quality improvement projects run by individual clinicians to multisite research projects with collaborations reaching across the country. Table 1 breaks down the essential skills and functions needed in the CCE to provide health services research capacity for the organization.

Examples of Studies and Operational Support Provided

The wide range of care settings (from community care clinics to tertiary care academic medical centers) and of types of care (ambulatory care, emergency care, acute inpatient care, and rehabilitation) that BSWH encompasses, combined with rapid technological advances and new models for healthcare delivery and financing, has provided the CCE with an extensive substrate for both research and operational projects.

Such projects form a crucial step on the research translation pathway, as they test whether findings shown to have clinical efficacy demonstrate similar results when applied in care delivery settings across heterogeneous patient populations.[5] CCE investigators have received research funding from federal agencies, private foundations, and national nonprofit organizations largely owing to their capacity to extract and transform real-world data into an analytical format, and have received recognition through such honors as the 2013 *Health Services Research* John M. Eisenberg Article-of-the-Year Award.[6]

The symbiotic relationship between system operations and health services research has

FIGURE 2: Simplified Organizational Chart for the Health Services Research Operational Resource within BSWH

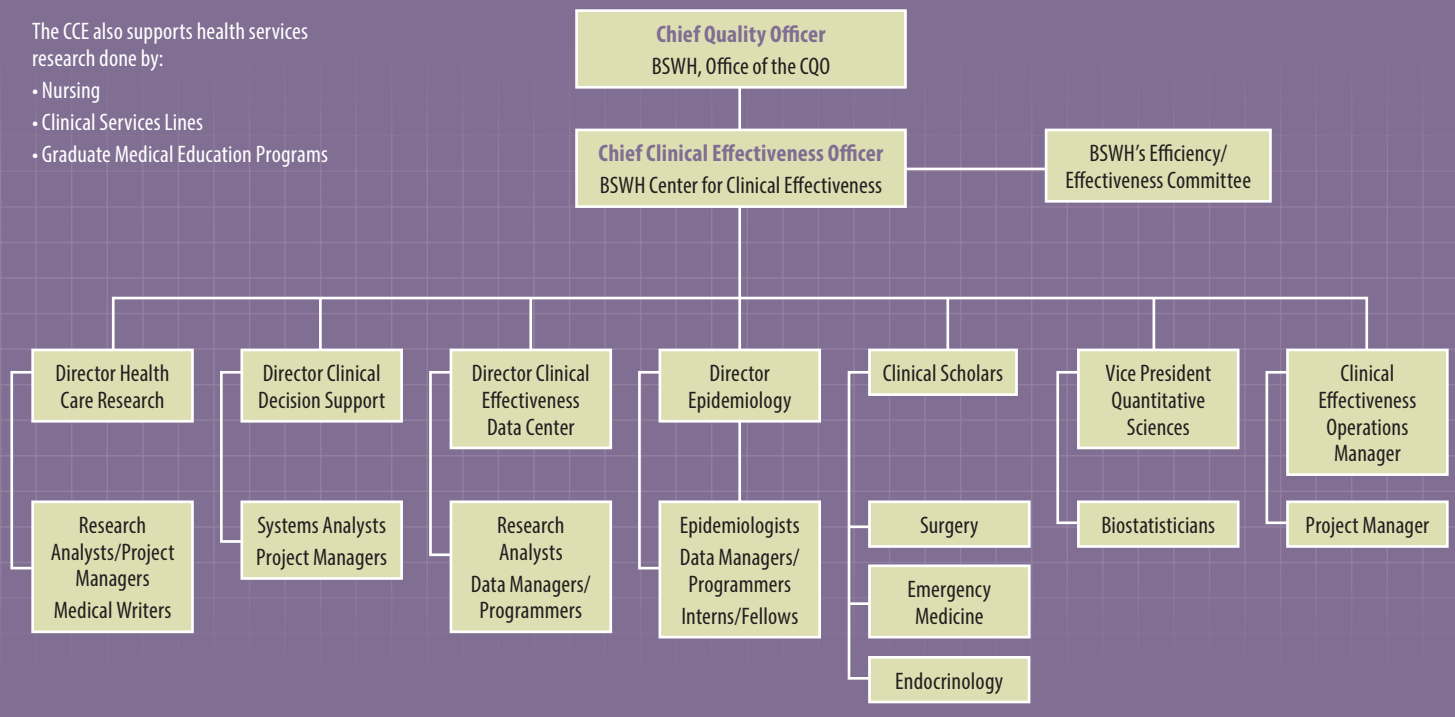


TABLE 1: Essential Roles in Health Services Research Infrastructure Within an Integrated Healthcare Delivery System

Role	Skills/Functions
Principal Investigator (PI)/ Health Services Research	A doctoral-level subject matter expert, with masters-level training or commensurate experience in research methods
Epidemiologist	A masters- or PhD-level epidemiologist with rigorous training in research design
Project Manager/ Research Coordinator or Research Analyst	Overlapping roles include such tasks as IRB applications and maintenance of required regulatory records, tracking the research budget, subject recruitment/ enrollment, data collection, coordinating between study sites, and assisting with grant proposal and manuscript preparation
Data Manager/Programmer	Knowledge of database development and data extraction, and of the creation of analytic datasets
Statistician	Masters- or PhD-level training in statistics for a rigorous evaluation of study data
Medical Writer (optional)	Depends on the skills and time demands of the other members of the research team

also led to other national acknowledgments of leadership in this research discipline for BSWH. Likewise, the success of using these methodologies to support and guide operational quality improvement can be seen in the external recognition for high-quality care received by BSWH components that have followed this model.[7–10]

Challenges to and Applied Solutions in an Integrated Healthcare Delivery System

Leveraging health services research as operational infrastructure in a healthcare delivery organization is also associated with challenges. Although individual projects often raise their own unique issues, the following are some recurring themes.

Few data are collected specifically with research goals in mind

Unlike clinical trials, health services research projects seldom have the luxury of data sources and collection procedures designed specifically with the research aims in mind. Instead, much of this research relies on combining data from existing sources—most commonly, clinical records, healthcare providers' administrative and billing data, and survey data.

There are several barriers frequently encountered in working with these data sources. Clinical records are not always complete and/or accurate,[11–14] and manual data collection from these records is expensive, which can severely affect sample sizes under budget pressures. Although widespread adoption of electronic health records (EHRs) may eliminate or mitigate these data challenges,[4] problems such as data being recorded in free text notes or scanned documents, as well as poor capture of valid reasons for not providing recommended care, have limited use of data from these systems.[15,16] Additionally, in multisite studies, issues related to data incompatibility between sites and EHR systems are common.[17]

Administrative databases provide readily available sources due to the routine collection of data for provider billing and insurance claims. However, administrative databases and collection processes are intended primarily to support reimbursement, and thus generally lack the clinical detail needed for rigorous evaluations; this paucity of clinical data hampers the ability to risk-adjust outcomes.[18]

> Unlike clinical trials, health services research projects seldom have the luxury of data sources and collection procedures designed specifically with the research aims in mind.

The third common data source is surveys.[18] Although survey data offer the opportunity to elicit information from perspectives not typically captured in the routine delivery of care, they can also be expensive to collect, do not capture all variables of interest, and are prone to recall and nonresponse biases.[18]

To counter the array of data-related issues, we established an interdisciplinary team that relies heavily on experienced, highly skilled data managers.[19] Pairing subject matter experts with specific data systems helps as well, because they develop in-depth technical knowledge of the system and understand the nuances of the data. Further, we have found a project manager role essential in maintaining communication and documenting the data challenges, decisions made, and lessons learned within and across projects.

Unfamiliarity of clinical, administrative, and research personnel with health services research

In a healthcare organization with a research history focusing on drug and device clinical trials, health services research projects can create confusion because many of the traditional issues, such as risk of physical harm to participants or intellectual property rights in the products of the work, simply do not apply. Moreover, multisite collaborative projects require the involvement of legal units, compliance officers, the IRB, and the information systems group responsible for evaluating and planning data transfer security. Successfully navigating these waters can require substantial time and effort, and must be accounted for in project planning.

As an example, Figure 3 shows the time taken for each of these steps for BHCS's participation in an industry-healthcare delivery organization

Pairing subject matter experts with specific data systems helps as well, because they develop in-depth technical knowledge of the system and understand the nuances of the data.

collaboration (MEDIC: the Multisite Electronic Data Infectious Diseases Consortium). Addressing barriers in this category requires clear and consistent communication. A precise explanation of intent (i.e., what would constitute project success), what the project entails, what particular risks each stakeholder entity is trying to mitigate, and what regulatory measures the project falls under can help identify the adaptations needed in either the health services project or the organizational policy or procedure that will produce a workable solution.

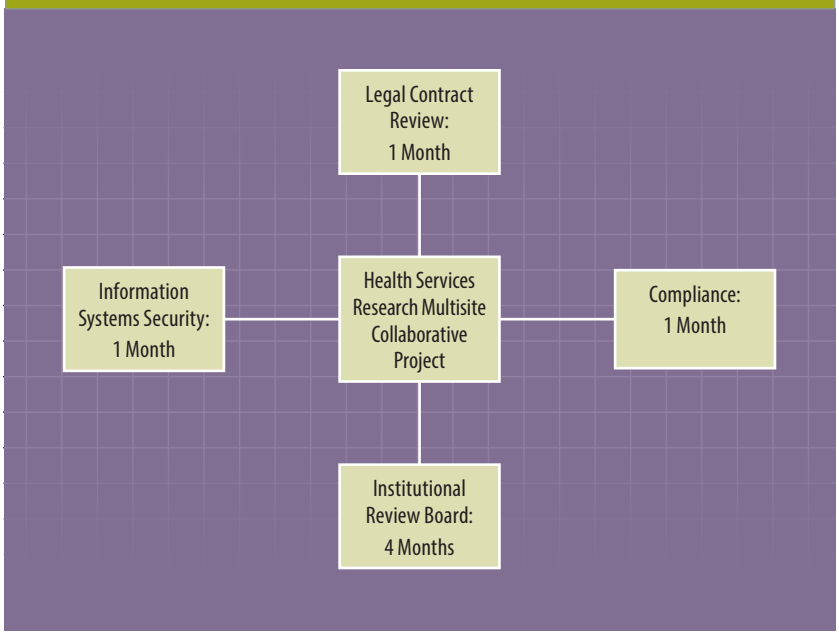
Competing organizational priorities

When conducted as operational infrastructure, health services research activities face competition in the organizational prioritization process.

For example, when the planned implementation of an EHR system across all practices in the BHCS-affiliated physician network, HealthTexas Provider Network, presented an opportunity to study the impact on the quality of ambulatory care provided, a proposal was made to conduct a randomized controlled trial, with practices being randomized to receive the EHR immediately vs. at the end of the study. However, to optimize efficiency, HealthTexas Provider Network needed to implement the EHR on a sequential, staggered schedule, starting with the practices that were most prepared for launch. Implementation of the EHR in this manner necessitated redesign of the evaluation, moving to interrupted time series and cohort studies that accommodated the "real world" nature of the intervention.[20,21] Similar considerations applied in the inpatient setting when decisions were being made regarding the optimal manner in which to roll out and evaluate the impact of standardized order sets.[22,23]

Another example of aligning research and operational priorities relates to the use of information technology (IT) resources. For a grant-funded project studying the impact of a bundled care process on practice adoption and clinical outcomes related to delirium in intensive care unit (ICU) settings, the research intervention was designed so the required IT modifications directly addressed other important patient safety and clinical workflow needs (particularly for frontline nursing staff). In that context, the EHR modification request could be prioritized, allowing the designation of specific IT personnel to carry out the changes in an expedited production cycle. Building a business case that demonstrates how a request associated with a research effort can support other operational interests is crucial to the work being moved up in the priority queue.

FIGURE 3: Example of Interactions (with Associated Process Times) Between Health Services Research Projects and Oversight Entities within BSWH



Conclusion

As demonstrated by the CCE at BSWH, a health services research resource functioning as operational infrastructure within an integrated healthcare delivery organization can make meaningful contributions to both the individual organization's quality improvement enterprise and evaluations, and to the broader clinical research community. Achieving this synergy requires:

- support from the executive leadership to establish and organize the infrastructure in a manner that allows the research entity to integrate its work into operational initiatives;
- investment in the personnel and skill sets required to conduct rigorous health services research investigations;
- a "hard money" budget that covers the majority of the costs of having this resource available to support operations; and
- a collaborative environment that values health services research and facilitates its conduct within the system.

When conducted as operational infrastructure, health services research activities face competition in the organizational prioritization process.

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Andrew L. Masica, MD, MSCI, (andrewma@baylorhealth.edu) is vice president and chief clinical effectiveness officer, Baylor Scott & White Health, and clinical assistant professor of medicine, Texas A&M Health Science Center.

Ashley W. Collinsworth, MPH, ELS, is director of health care research, Baylor Scott & White Health.

Elisa L. Priest, MPH, DrPH, (elisa.priest@baylorhealth.edu) is director, Clinical Effectiveness Informatics, Baylor Scott & White Health, and adjunct clinical assistant professor, Department of Internal Medicine, Texas A&M Health Science Center.

Giovanni Filardo, MPH, PhD, is Endowed Chair in Cardiovascular Epidemiology, Baylor University Medical Center, Dallas, Texas; director of epidemiology, Office of the Chief Quality Officer, Baylor Scott & White Health; adjunct professor of medicine, University of Louisville, Louisville, Ky.; adjunct associate professor of epidemiology, University of North Texas, Fort Worth; and research associate professor of statistics, Southern Methodist University, Dallas, Texas.

Brett D. Stauffer, MD, MHS, FHM, is vice president of Hospital Care Quality Improvement, Baylor Scott & White Health, and clinical assistant professor, Department of Internal Medicine, Texas A&M Health Science Center.

Susan H. Smith, DNP, APRN, ACNS-BC, is adult clinical nurse specialist, Critical Care Services, Baylor University Medical Center, and adjunct professor, Texas Christian University.

Marygrace Hernandez Leveille, PhD, RN, ACNP-BC, is nurse scientist, Baylor University Medical Center.

Susan Houston, PhD, RN, is director of nursing research, Baylor Scott & White Health-North Division, and interim associate dean of research, Baylor University School of Nursing.

Neil S. Fleming, PhD, is vice president, Quantitative Sciences, Baylor Scott & White Health, and clinical professor of health services research, Robbins Institute for Health Policy & Leadership, Hankamer School of Business, Baylor University.

David J. Ballard, MD, MSPH, PhD, is chief quality officer, Baylor Scott & White Health, and president, STEEEP Global Institute.

Standardizing Principal Investigator Delegation Records: *An Alternative Approach for Sites*

PEER REVIEWED | Staci Horvath, BS, CCRA

[DOI: 10.14524/CR-14-0028]

Principal investigator (PI) delegation and the records associated with delegation form an important aspect of clinical research trial management. Although the PI has the ultimate responsibility for the conduct of a trial at his/her site, it takes a team of individuals to carry out the specific duties required for compliance with the trial and regulations. Depending on the organization, the team could include sub-investigators, nurses, clinical research coordinators, regulatory specialists, data coordinators, and more. This list can be lengthy, but each individual plays a role in performing significant duties in the conduct of a trial, under the direction of the PI.

All sites are faced with the need to maintain delegation records; however, a one-size-fits-all approach in the industry may not be feasible, and can actually present a challenge for some sites. Strategizing internally on alternative methods for maintaining these records can benefit the site and potentially bring some efficiency to site operations.

Background

In 2009, the U.S. Food and Drug Administration (FDA) released a guidance document on "Investigator Responsibilities—Protecting the Rights, Safety, and Welfare of Study Subjects."[1] This guidance was written to help investigators better meet their responsibilities and to clarify for investigators and sponsors FDA's expectations concerning the investigator's responsibility to supervise a clinical trial in which some study tasks are delegated to employees or colleagues.[1] Although the document provides explanations regarding appropriate delegation and adequate training and supervision, this article focuses on the records maintained to support PI delegation.

The guidance document is a reminder that the FDA regulations are silent on how to maintain delegation records; however, the guideline for Good Clinical Practice from the International Conference on Harmonization specifies that the investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.[2] Further FDA guidance notes that this list should also include a description of the delegated tasks and the dates of involvement.[3]

Thus, the investigator is accountable for documenting delegation or "a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties." However, documenting delegation can be a challenge to accomplish when considering the expectations of sponsors and site management as well as striving to adhere to FDA guidance.

Traditional Delegation Documentation

Sponsors often design a form that sites may use when documenting delegation; in many cases, they require use of this specific form rather than any the site may already have developed. The form is commonly presented in a log format that incorporates many elements, including a listing of staff with start and stop dates; signatures, initials, and writing samples from each involved person; an outline of delegated duties per person; and PI acknowledgment per person. Although these forms often look similar, the expectations for their completion vary from sponsor to sponsor.

Sponsors that require this format are likely looking for consistency in records across all sites participating in a trial. The study-specific nature of the form, however, may create a burden for high-volume research sites, especially in situations when some of the information contained does not change from study to study. Additionally, these traditional forms may prove to be a burden for the sponsor if the form is completed incorrectly, which then triggers a query process for corrections.

Ultimately, the PI is responsible for delegation documentation; therefore, if the sponsor's method is not ideal for the site, site representatives should consider proposing an alternative approach to the sponsor.

Introducing an Alternative Approach to Delegation

Although varying site organizational structure is a noteworthy factor in creating standardized delegation records, the alternative method described in this article is currently in use at a dedicated research site with research staff in multiple locations. The site has research staff who perform the same tasks regardless of which trial they are working on, as well as research staff who perform identical tasks, but on specific trials.

As an example of the first scenario, the site employs multiple treatment nurses. The PI has delegated administration of study drug to these nurses, and this delegation is applicable to all trials that are active at the site.

As an example of the second scenario, the site employs multiple regulatory specialists. The PI has delegated the handling of submissions to the institutional review board (IRB) to all research staff with the title regulatory specialist, but these individuals are assigned to specific trials and are delegated this task only for those trials.

The alternative approach to delegation was developed with the above structure in mind, and demonstrates the ability to capture the PI's delegation of duties, broadly, in addition to the PI's delegation to a specific trial.

Two Forms to Capture PI Delegation

This alternative delegation method includes one position-specific form and one trial-specific form.

The position-specific form is referred to as a **Delegation of Responsibility** (DOR) form. The DOR encompasses the specific tasks within a research staff member's job description that are relevant to trial and regulatory responsibilities as delegated by the PI. These relevant responsibilities are often referred to as "significant trial-related duties"; however, duties related to involvement in a specific trial are not reflected on this form. The intent of the DOR is to be applicable as long as the staff member is in the position reflected on the form.

The DOR form captures the following elements:

- Position title
- Name
- Employment start date (as well as position start date, if applicable)
- Stop date
- Signature
- Initials
- Handwriting sample, requiring the numbers 0 to 9 to be written
- Description of the significant trial-related duties
- PI signature

The second form applies to specific trials and is referred to as the **Delegation of Authority Form** (DAF). The DAF is used to reflect who is involved in a trial, when they are involved in the trial, and the

Documenting delegation can be a challenge to accomplish when considering the expectations of sponsors and site management as well as striving to adhere to FDA guidance.

HS

LEARNING OBJECTIVE

After reading this article, participants should be able to discuss principal investigator delegation requirements, analyze site practices in their program, and provide a starting point for implementation of an alternative approach to delegation documentation.

DISCLOSURES

Staci Horvath, BS, CCRA: *Nothing to Disclose*

PI's agreement. With this form, the PI is documenting his or her delegation for the listed research staff members to a specific trial with use of their titles, which can be tied back to the DOR.

The DAF captures the following elements:

- Protocol title
- Trial location
- PI signature and date
- Log format of:
  - Staff member name
  - Staff member title
  - Staff member dates, including affiliated date and nonaffiliated date

How the Two Forms Work Together

When a new research staff member joins a team, he or she completes the DOR form, which is then signed by the PI. The new research staff member is now delegated to perform the tasks listed on the DOR, but not yet delegated to perform those duties on an actual trial. Once the new research staff member is trained to his or her new position and trained to the trials, he or she is added to the DAF, thereby being included as someone delegated those duties to specific trials.

Using the previous example of the treatment nurse and regulatory specialist, each would have a DOR for his or her position. Through inclusion on DAFs, the treatment nurse may be added to all of the site's trials, whereas the regulatory specialist is added only to the DAFs of the trials to which he or she is assigned. The treatment nurse can now perform delegated duties on all trials, but the regulatory specialist can perform delegated duties on only a smaller number of trials.

Maintenance of Documents

The documents can be maintained in several ways; described here is the method followed by the research site using the alternative delegation approach.

First, files are maintained for each person. These files contain the CV, medical license (if applicable), Good Clinical Practice training documentation, and the completed DOR form. These files are not trial specific, and are shared across all studies. If a monitor, sponsor, or auditor is reviewing a specific trial, these files are provided as reference.

Second, the trial-specific regulatory file contains the completed DAF and the trial-specific training documentation for each person listed on the DAF. Although the DAF could be maintained in various ways, the research site uses a clinical trial management system (CTMS) to house the data. For each staff member, the site is able to track trial assignment, training completion, and affiliated and nonaffiliated dates, and subsequently generate a new DAF.

> Ultimately, the PI is responsible for delegation documentation; therefore, if the sponsor's method is not ideal for the site, site representatives should consider proposing an alternative approach to the sponsor.

The process developed at this research site specifies that a DAF is generated from the CTMS and signed by the PI at the time the trial opens and at the time the trial closure visit is coordinated/completed. Changes that occur during the trial are reflected in the CTMS and by reviewing the DOR and the training files. If discrepancies are seen that would not be evident through this automated system, a Note to File is created to further explain. A working copy of the DAF is generated and provided, if requested, but this working copy is not signed and does not become part of the regulatory file.

Implementing the Alternative Delegation System

As with any new process at a site, it is important to roll out the use of an alternative approach like this one strategically. Developing a standard operating procedure (SOP) to document the new process prior to implementing it is essential. Keeping the initial SOP in draft and piloting the process on a limited number of studies may help different sites in better defining the process and fine tuning it to their individual needs in final SOP form.

Based on the approach described in this article, the following should be addressed in the SOP:

- DOR Subheading:
  - What is the DOR?
  - When is the DOR completed (e.g., during new hire process)?
  - Content/required elements for completion of the DOR.
  - What necessitates DOR updates (e.g., change in title, change in significant trial-related duties)?
  - When updates are necessary, when is the DOR completed?
  - Where and by whom is each DOR maintained?
- DAF Subheading:
  - What is the DAF?
  - What are the content/required elements for completion of the DAF?
  - When is the DAF initially completed (e.g., at trial "onset")?
  - Where, how, and by whom is the DAF maintained (e.g., original DAF with copies of DOR)?

» When is the DAF finalized (e.g., at the time of clinical trial completion)?

Once the SOP is developed, implementation can occur, but it's important to think through how this will be managed. Note the following considerations:

- Assess if implementation will be done for new trials or if ongoing trials will be switched to the new method.
- Create DOR profiles for each person/position.
- Have each person complete his/her DOR form.
- Have PI sign each DOR form (date not needed).
- Review personnel records to ensure training records are complete and available.
- Create a DAF for each trial, and include all designated research staff and their start and stop dates, as applicable. Maintain this document electronically.
- Have the PI sign and date the completed DAF.

Troubleshooting Q&A

Each site has its own organizational structure and, if considering evaluating an alternative method for delegation records, there are a few additional components to this system that may be helpful. It is important to keep in mind that this is based on a single research site's process.

What if a research staff member changes positions within the organization and will be working on the same trials in the new position? In this situation, the previous position DOR is updated to reflect the end date of that position. The system used to generate the DAF is updated as well, to reflect the end date of the role. This person then completes a DOR for the new position and, once trained to that new position, is added to the DAF. The DAF now reflects two entries for this person: a start and stop date for the first position and a start date for the second position.

How is the DOR maintained if there is more than one PI? The original DOR is left unsigned, and copies are made for each PI to sign. The file then contains an unsigned version as well as a number of PI-signed copies, depending on the number of PIs at the site. This shows that each PI has delegated the tasks listed to that person.

What if a research staff member is performing more than one role? There are numerous reasons a research staff member may be performing tasks across multiple positions. For example, in transitioning from one position to another, there may be a period of time where the person is closing up one position while also splitting time in performing duties of the new position. This scenario is usually temporary, and the position the person is leaving can remain open on the DOR and DAF until he or she has officially ended it.

If a person is performing a dual role, the site can have two DORs active at once, which would then mean there would be two entries on the DAF if that person is performing both roles on the same trial. Alternatively, the site could create a new DOR for that person to reflect all of his/her responsibilities, though the important thing to keep in mind with this scenario is to make sure the title on the DAF matches the title on the DOR.

How can a DAF be maintained without a CTMS? Although a CTMS does help in the management of this delegation documentation approach, it is certainly not required. The site used as an example in this article started this system using MS Excel in managing the records and generating the DAFs.

Do sponsors accept this alternative delegation method? During the development of a trial, the delegation method is described in detail to the sponsor, and a Note to File that describes the process is provided for its records, as well as kept in the study-specific regulatory file. Additionally, the site SOP on this process is available upon request during onsite visits throughout the trial. Although some sponsors are not initially receptive to the method, after talking through the concept by personnel at the study site described here, all sponsors have agreed to its use.

A sponsor's lack of receptiveness is more geared toward understanding the process and ensuring it is in line with regulatory requirements, and does not reflect an argument against its compliance. The site has been successfully using this method for more than 10 years; during that time, it has developed and opened more than 400 studies, for which there have been 64 sponsor-driven quality audits and one FDA audit. Audits to date have not included any actions or official findings directly related to the delegation process.

Conclusion

PI delegation can be a challenge to maintain due to turnover or position/function fluctuations within the research site. Using sponsor-provided paper logs for delegation records can be burdensome for site operations. Finding a balance between site operations and regulatory requirements using an alternative strategy that will work best for the site is recommended. Because delegation is a PI responsibility, when a sponsor may provide a tool to help, the PI does not have to use that tool.

The alternative approach described in this article has been proven to be successful to record and document the PI's responsibility for adequate delegation and, at the same time, provide the site some efficiencies. The traditional method and this alternative method do require a need for coordination, but the alternative approach can be applied in a way that is less burdensome and prevents some duplicative work.

During the development of a trial, the delegation method is described in detail to the sponsor, and a Note to File that describes the process is provided for its records, as well as kept in the study-specific regulatory file.

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Staci Horvath, BS, CCRA, (shorvath@marycrowley.org) is an operations manager at Mary Crowley Cancer Research Centers in Dallas, Texas.

Clinical Research as a Profession: *Are We There Yet?*

PEER REVIEWED | Teresa-Lynn Hinkley, RN, BScN, MBA, CCRC
Jeff Kingsley, DO, MBA, MS, CPI, FAAFP
Steven Ziemba, PhD, MBA, CRCP, CIP, FACHE, CCRC

[DOI: 10.14524/CR-14-0056]

Clinical research has developed as a complement to the world of healthcare, but remains a young field. Clinical trials are conducted in patients, and are most often completed by physicians, either as an adjunct to their clinical practice or, more recently, as freestanding businesses of their own. Over time, research has become more complex, and the associated needs and expectations of researchers increasingly large.

Discussions among those in clinical research regarding how to move forward are occurring everywhere. We in the research community recognize and accept the need to raise the bar of performance and standards, but two looming questions remain: What is a profession? And how do we know if clinical research is one?

LEARNING OBJECTIVE
After reading this article, participants should be able to define the concept of "profession" and how clinical research fits into this definition.

DISCLOSURES
Teresa-Lynn Hinkley, RN, BScN, MBA, CCRC: *Employee of ACRP*
Jeff Kingsley, DO, MBA, MS, CPI, FAAFP; Steven Ziemba, PhD, MBA, CRCP, CIP, FACHE, CCRC: *Members of the ACRP Board of Trustees*

Defining a Profession

The term "profession" is not to be confused with such terms as "job" or "career," although these may be components of a profession. One definition is "a calling requiring specialized knowledge and often long and intensive academic preparation" (merriam-webster.com). Even more broadly, Google defines profession as "a paid occupation, especially one that involves prolonged training and formal qualification" and "a body of people engaged in a particular profession."

Key characteristics of a profession include a body of knowledge, qualification (licensure/certification), establishment of professional associations, development of a code of ethical conduct, and achievement of support of law.[1]

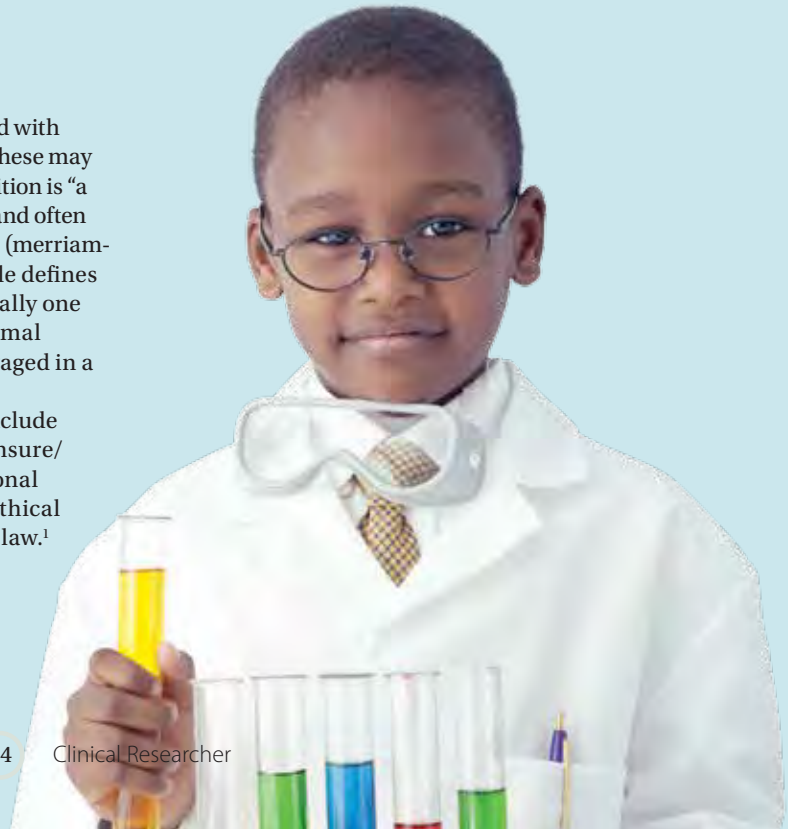

FIGURE 1: Process Model of Professionalization

Adapted from Curnow and McGonigle[2]

Several methods can be used to develop a profession. The process model offers a means of defining the sequence of events in the evolution of a profession. Figure 1 illustrates the process model of professionalization as described by Curnow and McGonigle.[2]

Each stage is sequential; however, a later stage can influence a prior one. For example, when stage 5 occurs and legal recognition is obtained, the regulations developed as a result may lead to a required change in the training or education programs developed in stage 2.

The maturity of a profession also evolves over time. The elements of a mature profession are based on the stages of professionalization, but are expanded to include items such as professional development, licensure, and certification as indicators of maturity.

To illustrate, consider the profession of law, in which the five stages of professionalization have been achieved and the practices of the profession have been well established and recognized. Further, the legal profession is mature, with all eight elements of maturity achieved (see sidebar).

Having explored both the process of evolution of a profession and the elements of a mature profession, we now move to our second question. Is clinical research a profession? Are we there yet? To start this discussion, let us explore the evolution of clinical research as an occupation.

Evolution of Clinical Research

The field of clinical research did not emerge in a wholly formed fashion; rather, it developed gradually from various sources into a cohesive and readily recognizable field. The initial barrier to entry was (and often still is) incredibly low.

Sponsor organizations approached physicians, in a variety of practice settings, to conduct clinical trials because of their access to the patient populations needed for the studies. No specialized knowledge or expertise was required; this was simply something a physician did in addition to his or her clinical practice. Often, the physician did not employ specially trained research staff to assist in the conduct of the study, but would use existing employees, such as a nurse or receptionist, to complete study activities and documentation.

The development of the various roles in clinical research came in step with scientific methodology, cultural interpretation, and ethical thinking. These components have been critical in the practice's evolution toward professionalism.

In the United States, applying scientific thought to medical care came about because of public demand for better government oversight of supposed "cures."[4] As our understanding of molecular, genetic, and population aspects of healthcare improved, we required more sophisticated scientific models. Advancements in statistical applications, including formulas and software, created new opportunities and demands for unique roles.

Elements of a Mature Profession[3]

- Initial professional education
- Accreditation of education programs
- Skills development (work experience prior to certification)
- Certification
- Licensing
- Professional development
- Professional societies
- Code of ethics

Clinical research has begun to develop into a formal profession, although there is much work still to be done to solidify it.

The field of clinical research did not emerge in a wholly formed fashion; rather, it developed gradually from various sources into a cohesive and readily recognizable field.

Those who conducted early applications of medical research, such as Jenner with smallpox, were often isolated in their efforts. This has since evolved into studies that span the globe—an increase in capability that has been possible only with advancing statistical concepts to develop large studies and the technology to handle them.

Such advancement has increased the number and diversity of roles involved in clinical research. Besides the investigator who develops a hypothesis, designs a protocol, and oversees a study, we now have research coordinators to assist in the conduct of the study, data managers to collect and aggregate data, and statisticians to interpret results.

Such a simple example of additional roles does not demonstrate those who are not directly involved in the study. These may include research compliance officers, institutional review board (IRB) or research ethics committee (REC) members, project managers, research administrators, monitors, and others.

Voluntary education and certification for various research roles have existed for years; however, organizations are only beginning to grapple with the need for mandatory formal education, certification, and competence-based training, and the roles have yet to be standardized. Today, those employees with the title of "study coordinator" may have different responsibilities in different organizations, and differing criteria for their education and experience.[5]

TABLE 1: Elements of Maturity as a Profession in Clinical Research

Element	Present in Clinical Research
Initial professional education	Yes (but not mandatory for the practice of clinical research)
Accreditation of education programs	Yes for some programs, but not all
Skills development (work experience prior to certification)	Yes
Certification	Yes (but not mandatory for the practice of clinical research)
Licensing	No
Professional development	Yes
Professional societies	Yes
Code of ethics	Yes

Clinical research has not only grown in this context, but has evolved in several ways. Some were mentioned earlier, and include the incorporation of the basic science of statistical study design, the maturation of ethical guidance, and the diversification of roles. It has also evolved, and greatly, to transcend industries; clinical research, in one form or another, can be found either within or as a component of industries as far-ranging as healthcare, law, engineering, pharmaceuticals, molecular biology, communication, nonprofit and for-profit organizations, and education, among many others.

The extension of clinical research into the modern form of industries where transactions can be measured in billions of dollars abruptly demonstrates what this field, if taken as a profession, has become. It also outlines the importance of defining clinical research as a profession. In the next section, we'll investigate the concepts of professionalism discussed earlier in this context.

Clinical Research as a Profession

Several items related to defining what a profession is, and how it is greater than the concepts of job or career, were discussed earlier. To evaluate clinical research as a profession, what follows considers its components in the light of the five-stage process model of professionalization seen in Figure 1.

Clinical research has clearly defined roles, although this aspect is filled with complexity. There are more roles in clinical research than there are in the legal profession, for example. Also, the roles in clinical research differ from organization to organization, and even from country to country. There needs to be international collaboration to establish more consistent definition of the roles within clinical research.

Is there application of rigorous academic standards for those practicing clinical research? We could argue that the training of physicians is rigorous, and would be expected to transfer into the field. However, the tenets of clinical research are not necessarily presented in medical school, residency, or fellowship.

Formal education or professional development (via classroom instruction, conferences, symposia, online services, mentoring programs, and more) in clinical research has been developing, including the availability of courses geared toward a topic of interest, and undergraduate- and graduate-level

degrees in research, clinical research, and research administration. Although more opportunities for training and education are growing increasingly complex and sophisticated, formal training is not yet a requirement to practice.

Aligned with research education is the development of professional associations and formal certification in clinical research. In these associations, the ongoing development of best practices, which are informally shared among research organizations through networking and communication, is seen as a priority, as is the continued enforcement of codes of ethical conduct.

A prime example of formalization in clinical research is seen in how many organizations have achieved accreditation through the Association for the Accreditation of Human Research Protection Programs, which seeks to consolidate ethical standards across the industry. A second example is the Joint Task Force for Clinical Trial Competency, through which representatives of industry, professional associations, and educational providers developed eight core competencies for clinical research, to define the minimum competencies required for practitioners in this field.[6] Additional areas of best practices that have garnered interest include business practices, contract and budget development, metrics and benchmarks, and job roles and functions.

Lastly to consider, there is support of law as applied to clinical research. The conduct of clinical trials is highly regulated, as evidenced by the regulations and guidelines of such entities as the U.S. Food and Drug Administration and the Office for Human Research Protections, both within the U.S. Department of Health and Human Services, and similar bodies in other countries.

Some of the roles in clinical research are defined and recognized according to local law, such as the investigator and clinical research associate in the U.S., but others are not—the clinical research coordinator, data manager, project manager, and regulatory specialist, to name a few—and overall support of law is lacking for clinical research as a profession.

Interestingly, the following list of terms was generated by a largely experienced audience of individuals in clinical research attending a session at the Association of Clinical Research Professionals' 2014 Global Conference and Exhibition on defining clinical research as a profession:

- Code of conduct
- Ownership of the role
- Caring
- Self-governing
- Unique body of knowledge
- Training and education
- Expertise
- Ethical standards
- Competencies
- Liability and repercussions
- Talent
- Academic standards
- Requirements of training
- Coming from within

This list presents features that the audience members thought would begin to define a profession, and they were not far off the mark. Our assumption is that clinical research practitioners clearly understand the requirements of a profession, most likely because many clinical researchers come from established professions in healthcare and medicine. They came into clinical research with an established comfort with and an understanding of how a profession feels and behaves.

Conclusion

We are not yet a full-fledged profession, but we are on the road to clinical research professionalization. Table 1 reflects our perception of the elements of a mature profession that are currently established, or are being established, in clinical research.

We are witnessing the birth of a profession. Clinical research has begun to develop into a formal profession, although there is much work still to be done to solidify it. The array of formally recognized roles, presence of academic requirements, use of ethical standards, and existence of associations tailored to the ideals of a profession are a few of the factors pointing to this conclusion.

However, not all of these elements is mandatory, and the barrier to entry remains low because our industry still allows novice practitioners to engage in research with privileges equal to veteran practitioners. Until accredited professional education and certification are mandatory, this will continue to be the case.

As the practitioners of an emerging profession, it is our responsibility to grow clinical research into a profession of great purpose, all the while garnering the respect of already established professions, whose support is vital to our own maturation.

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Teresa-Lynn Hinkley, RN, BScN, MBA, CCRC, (thinkley@acrpnet.org) is the deputy executive director of the Association of Clinical Research Professionals (ACRP), based in Alexandria, Va.

Jeff Kingsley, DO, MBA, MS, CPI, FAAFP, (jeffkingsley@serrg.com) is chief executive officer of the Columbus Regional Research Institute in Columbus, Ga., and is treasurer of the ACRP Board of Trustees.

Steven Ziemba, PhD, MBA, CRCP, CIP, FACHE, CCRC, (steven.ziemba@gmail.com) is associate director of Marshfield Clinic Research Foundation, Marshfield, Wis., and a member of the ACRP Board of Trustees and Editorial Advisory Board.

HOME STUDY HS

Integrating Research into Healthcare

OPEN BOOK TEST

This test expires on February 29, 2016

(original release date: 02/01/2015)

Health Services Research as Operational Infrastructure Within an Integrated Care Delivery System: A Case Study

1. **What are two main outcomes studied in health services research?**

1. Access to healthcare
2. Development of new clinical treatments
3. Quality and cost of healthcare
4. Efficacy of a new drug

A. 1 and 2 only
B. 1 and 3 only
C. 1 and 4 only
D. 2 and 4 only

2. **Health services research can support the triple aim of healthcare improvement, which includes:**

1. Development of innovative treatments
2. Improvement of the health of populations
3. Reduction of the costs of quality of care
4. Provision of better quality of care

A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

3. **What are three main sources of data for health services research?**

1. Administrative and billing data
2. Survey data
3. Patient population selected by the investigator
4. Clinical records

A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

4. **What are three limitations of using electronic health record (EHR) data to mitigate the problems of using clinical records?**

1. Data are often recorded in free text notes or in scanned documents
2. The data are prone to recall or nonresponse biases
3. Poor capture of valid reasons for not providing recommended care
4. Data incompatibility between multiple sites and EHR systems

A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

5. **What is the main challenge of using administrative databases for health services research?**

A. Databases are expensive.
B. The data are not always complete or accurate.
C. The data generally lack clinical detail.
D. The data are prone to recall or nonresponse biases.

6. **What is an advantage of using survey data for health services research?**

A. It is relatively inexpensive.
B. It captures all variables of interest.
C. It is least prone to recall or nonresponse biases.
D. It can elicit information not captured in the routine delivery of care.

7. **What is one way to alleviate some of the data challenges of health services research?**

A. Use only clinical records for a data source.
B. Organize an interdisciplinary team that relies on data managers.
C. Rely only on data managers for research support.
D. Rely only on clinical personnel for research support.

8. **What are two advantages of pairing subject matter experts with specific data systems to help counteract data challenges?**

1. They understand the nuances of the data.
2. They document all of the data challenges and decisions made across projects.
3. They maintain communication within and across projects.
4. They develop in-depth technical knowledge of the system.

A. 1 and 2 only
B. 1 and 3 only
C. 1 and 4 only
D. 2 and 4 only

9. **The solution to some of the challenges associated with unfamiliarity with the methods and purposes of health services research begins with:**

A. communication about the specifics of the project.
B. using only one type of data source.
C. incorporating a standardized process for every project.
D. relying only on a research team with specific knowledge of health services research.

10. **What is one way for health services research activities to advance in the priority queue in the organizational prioritization process?**

A. Build a business case that demonstrates how a request associated with a research effort can support other operational interests.
B. Organize an interdisciplinary team to conduct and handle all the operational needs of the activities.
C. Incorporate a standardized process for every project.
D. Allow for a flexible budget to cover all operational costs for each project.

Standardizing Principal Investigator Delegation Records: An Alternative Approach for Sites

11. **Although the principal investigator (PI) is responsible for clinical research trial management at his/her site, the team that typically assists in carrying out the specific delegated duties may include which of the following?**

1. Research coordinator
2. Nurse
3. Monitor
4. Data coordinator

A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

12. **What is the main focus of the FDA's Guidance for Industry document titled "Investigator Responsibilities—Protecting the Rights, Safety, and Welfare of Study Subjects"?**

A. Discussing adverse event assessments and reporting requirements to ethics committees
B. Summarizing expectations regarding an investigator's supervision of a clinical trial
C. Outlining specific financial interest in research by an investigator that may affect the rights and welfare of human subjects
D. Discussing clinical trial oversight and the risk-based approach to monitoring

Find the most current online test at **www.acrpnet.org/homestudy**, including any revisions made after publication of this issue of *Clinical Researcher*.

13. **Which resource specifies that an investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties?**
- **A.** Health and Human Services
- **B.** ICH Guideline for Good Clinical Practice
- **C.** FDA regulations
- **D.** National Institutes of Health

14. **Who is ultimately responsible for delegation documentation?**
- **A.** PI
- **B.** Research coordinator
- **C.** Sponsor
- **D.** FDA

15. **In the alternative delegation documentation method described in this article, which form can document PI delegation for the research staff members in a specific trial?**
- **A.** Delegation of Authority Form (DAF)
- **B.** Curriculum Vitae
- **C.** Delegation of Responsibility (DOR) form
- **D.** Financial Disclosure form

16. **Which of the following elements are contained in the DOR form?**
- **1.** Position title
- **2.** Handwriting sample requiring the numbers 0-9 to be written
- **3.** Description of the significant trial-related duties
- **4.** Protocol title

A. 1, 2, and 3 only **C.** 1, 3, and 4 only
B. 1, 2, and 4 only **D.** 2, 3, and 4 only

17. **When a new research staff member joins a team, which form in the article is completed first?**
A. DAF **C.** DOR
B. Curriculum Vitae **D.** Financial Disclosure

18. **At the research site represented in this article, where is the final signed DAF maintained at the end of a trial?**
- **A.** Pharmacy
- **B.** Clinical trial management system
- **C.** Personnel files
- **D.** Trial-specific regulatory file

19. **Per the author, what activity should be considered prior to implementation of the standard operating procedure for a new delegation process?**
- **A.** DOR form is defined.
- **B.** Process for maintenance of the DAF is determined.
- **C.** DOR profile for each person/position is created.
- **D.** Requirements for a DOR update are determined.

20. **How does the article suggest maintaining the DOR form if a site has more than one PI?**
- **A.** This alternative delegation system works only for sites with one PI.
- **B** The research staff member must complete an original DOR form for each PI.
- **C.** This is not an issue as the PI does not need to sign the DOR form.
- **D.** The original DOR form is left unsigned and each PI signs a copy of the DOR form.

Clinical Research as a Profession: Are We There Yet?

21. **A profession may be described as:**
- **A.** synonymous with the term "job."
- **B.** synonymous with the term "career."
- **C.** a paid occupation with training and qualification.
- **D.** a paid job or career regardless of training or qualification.

22. **What are key characteristics of a profession?**
- **A.** The same job responsibilities for the same pay
- **B.** A specific body of knowledge qualification, professional associations, and an ethical code
- **C.** Responsibilities determined by the organization's Human Resources department
- **D.** Identical education and credentialing requirements

23. **What are some elements of a mature profession?**
- **1.** Initial professional education
- **2.** Established job descriptions
- **3.** Professional certification
- **4.** Professional societies

A. 1, 2, and 3 only **C.** 1, 3, and 4 only
B. 1, 2, and 4 only **D.** 2, 3, and 4 only

24. **What is the first stage of the process model of professionalization?**
- **A.** Determining whether an occupation exists
- **B.** Developing training and educational programs
- **C.** Obtaining the support of law
- **D.** Establishing a code of ethics

25. **What is the last stage of the process model of professionalization?**
- **A.** Determining whether an occupation exists
- **B.** Developing training and educational programs
- **C.** Establishing a code of ethics
- **D.** Obtaining the support of law

26. **Stages 2, 3, 4, and 5 of the process model of professionalization indicate which of the following?**
- **A.** That a code of ethics is required
- **B.** That later stages can also affect earlier stages
- **C.** That professionals make up a common group
- **D.** That work activities may vary greatly from one occupation to another

27. **The field of clinical research:**
- **A.** has always existed in its present form.
- **B.** is a fully formed and recognized profession.
- **C.** remains immature because of the low barriers to entry.
- **D.** has very rigorous standards and high barriers to entry.

28. **The roles of those engaged in clinical research developed along with:**
- **A.** scientific methodology, but have yet to be standardized.
- **B.** standardized ethical thinking.
- **C.** the demands of regulatory agencies.
- **D.** standardized demands of the healthcare industry.

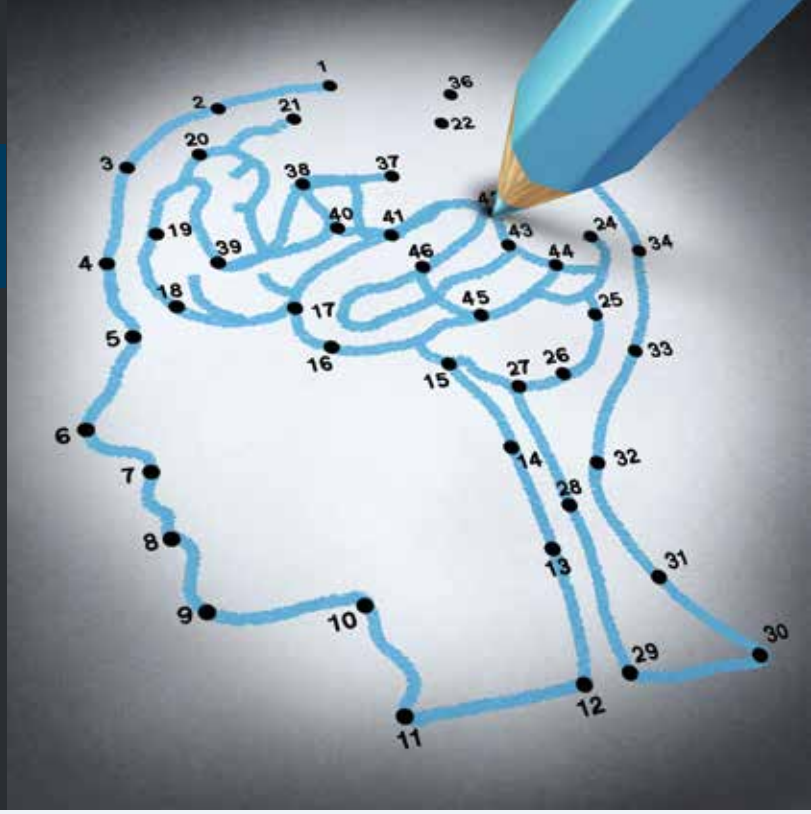
29. **The development of best practices in clinical research:**
- **A.** has been successfully achieved.
- **B.** can be achieved only via academic programs.
- **C.** is mandated by federal regulation.
- **D.** can be achieved via professional associations and formal certification.

30. **Which of the following elements of maturity is not present in clinical research?**
- **A.** Professional education
- **B.** Professional licensing
- **C.** Professional certification
- **D.** Professional societies

ETHICALLY SPEAKING

Stuart Horowitz, PhD, MBA | Jeffrey Cooper, MD, MMM

Integrating Social-Behavioral Research into Healthcare: *Proposed Revisions to the Common Rule*



This issue of *Clinical Researcher* focuses on integrating clinical research into healthcare. From a regulatory perspective, a seamless integration is challenging. On the one hand, researchers hope to transform huge clinical datasets in a way that produces generalizable knowledge and improves healthcare. On the other hand, current regulations require a distinct separation of research from treatment.

In addition to clinical/biomedical research, vitally important social/behavioral knowledge can be gained in healthcare. Although we tend to view this research as distinct, over time the lines between biomedical and social science research become blurred. Many social and behavioral scientists believe we need to change the regulations to more effectively and efficiently conduct social and behavioral research—especially in the healthcare environment.

In April 2014, the National Academies Press published a report entitled "Proposed Revisions to the Common Rule for the Protection of Human Subjects in the Behavioral and Social Sciences."[1,2] The report, developed by the Division of Behavioral and Social Sciences and Education of the National Research Council, made the following major recommendations:

General recommendation: Clarify the definition of "human subjects research" and create a new category of "excused research."

a. Combine the definitions of "research" and "human subject" into one "human subjects research" definition.

b. Clarify that many forms of scholarship considered "research" are not "human subjects research."

c. Do not apply the regulations to the use of publicly available information or observation in public contexts where there is neither interaction nor intervention with human subjects.

d. Do not consider research on public-use data to be human subjects research if the data are de-identified and protected against disclosure.

e. Include a new category of "excused" research, as proposed in the 2011 Advanced Notice of Proposed Rulemaking (ANPRM) regarding the Common Rule.

f. Include pre-existing research and non-research data that contain private information or "benign" interactions or interventions in excused research.

g. Clarify that excused research has only minimal risk, even if it involves questions about human subjects' physical or psychological well-being.

h. Require consent for excused research only when there is interaction or intervention with subjects.

i. Include procedures for excused research review that require a timely institutional review board (IRB) response.

These recommendations reflect the frustration researchers often feel with IRBs that expand their authority beyond the regulations and create additional burden without value. However, the

current regulations apply only to research that involves human subjects and already establish a set of nonregulated (exempt) categories.

Knowledgeable and experienced IRB professionals have no problem correctly and quickly determining whether an activity is subject to IRB review. Most IRB staff and members, however, misread the regulations, apply them to nonregulated activities, and create time-consuming bureaucracies for nonregulated research.

General recommendation: Clarify the definition of "minimal risk."

a. Adopt a definition of "minimal risk" with a "general population" (not "healthy individual") standard.
b. Eliminate regulatory language related to populations "vulnerable to coercion and undue influence."[3]
c. IRBs should consider whether protections will be implemented to reduce the magnitude and probability of harm or discomfort to no more than minimal.
d. Clarify when excused research should undergo expedited review to afford special protections to specific populations.
e. Eliminate continuing review for expedited research.

These recommendations flow from the frustration of researchers with IRBs that are risk averse. Knowledgeable and experienced IRB professionals can correctly and quickly determine that research is minimal risk, understand that vulnerable populations do not need additional protections from the risks of minimal risk research, and rarely find minimal risk research ineligible under the current expedited categories.

However, most IRB staff and members misread the regulations to require a "search and destroy" mission for every risk, focus on the magnitude of risk without considering probability, ignore the risks of daily life, and find excuses not to apply the expedited categories.

General recommendation: Encourage IRBs to emphasize the process of informed consent over its documentation, facilitate the use of a waiver of permission by the guardians of adolescents participating in minimal risk research, and facilitate the process of consent for the participation of children.

a. Eliminate requirements for specific elements of consent as a default, including removing ambiguous language found in the *Code of Federal Regulations* in 45 CFR 46.116(d).
b. Eliminate language preferring written documentation of consent and add language permitting nonwritten consent.
c. Require institutional or sponsor liability statements to be separate from information related to research participation.
d. Reject the proposal that excused research should be restricted to "competent adults."
e. Reject the proposal in the ANPRM requiring reconsent for future use of pre-existing, de-identified, nonresearch data.

These recommendations are inspired by the frustration of researchers with IRBs that focus on consent documents. Knowledgeable and experienced IRB professionals focus on the consent process, recognize when the regulations require disclosures only in cases "if any" of a list of conditions are present, waive written documentation of consent for almost all minimal risk research, remove "liability" statements from consent disclosures for minimal risk research, and guide researchers on how to conduct future research in a way that does not involve human subjects.

Still, most IRB staff and members over-apply the regulations because they are unaware of the regulatory flexibility regarding informed consent for minimal risk research.

General recommendation: Clarify informational risk in the social and behavioral sciences. Keep the purview of the Common Rule within its current boundaries.[4]

a. Endorse the ANPRM recommendation to use a single IRB to review and oversee multisite research on a voluntary, phased-in basis with the IRB and local body sharing responsibility.
b. An authoritative body should be established to appeal IRB decisions.

These recommendations are tied to the frustration of researchers with IRBs that are risk averse regarding informational harms. Knowledgeable and experienced IRB professionals understand the low probability of information risk compared to the informational risks of daily life. Most IRB staff and members, however, do not consider the probability of informational risks and underestimate the probability and magnitude of information breaches in daily life.

With all the above general recommendations and their associated sub-recommendations, it is unclear whether one should expect those who do not follow the current regulations to follow any rewritten regulations.

Conclusion

Whether any of these recommendations will ever be implemented is unclear. Although it is already three years since the ANPRM was published—with no changes to the Common Rule—we may yet see the ANPRM advance to the next stage (NPRM). Ultimately, some regulatory revisions may occur. If there are changes, it will be an open question whether they can affect positive changes in the behaviors of those who already have difficulty interpreting and following existing regulations.

Many social and behavioral scientists believe we need to change the regulations to more effectively and efficiently conduct social and behavioral research—especially in the healthcare environment.

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Stuart Horowitz, PhD, MBA, (shorowitz@wcgclinical.com) is president for institutions and institutional services at WIRB-Copernicus Group.

Jeffrey Cooper, MD, MMM, is vice president for global consulting at WIRB-Copernicus Group.

THE CLINICIAN AND CLINICAL RESEARCH: *Barriers and Opportunities*

PEER REVIEWED | Richard A. Dart, MD, FACP, FCCP, FAHA, FASN, FASH | Robert M. Haws, MD

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In 1999, the Institute of Medicine defined quality patient care as that which "increases the likelihood of desired health outcomes and is consistent with current professional knowledge."[1] Seen in this light, the need to stay consistent and current brings with it the need for research; as a result, the corresponding knowledge base has continued to explode. In addition, the demand to integrate new information into healthcare, as well as the rapid transfer of new information via electronic means, presents challenges in satisfying this demand using results vetted through research.

To address these issues, the National Institutes of Health (NIH) recently published recommendations and proposals to enhance and improve the integration and translation of new discoveries into clinical practice.[2-4] Complicating matters is the fact that research is varied, and can range from drug trials to introduction of new medical devices or processes. It can occur both in outpatient and inpatient settings, and may involve a myriad of disciplines. Further, research is not static, though it can be done alone or in larger collaborations and may be clinically based or in collaboration with basic science or related fields of medicine (epidemiology).

The need to stay consistent and current brings with it the need for research; as a result, the corresponding knowledge base has continued to explode.

The complexity of why collaborative research and innovation in translation of new discoveries, and desired outcomes, does not happen more easily is the subject of many reviews, but is not the focus of this commentary. Under discussion here are some of the suggested factors that may impede the undertaking of collaborative research and implementation of new approaches, and those elements that may need to be in place to encourage and sustain clinical research.

Background

In a comprehensive review, Nembhard et al.[5] noted several key elements in clinical practice that make innovative implementation much more difficult to accomplish. This wide variety of elements includes workforce aversion to the experimentation needed to bring successful implementation, aversion to the collaborative learning needed to master interdisciplinary innovations, overall lack of interest in participation, and issues of leadership and organizational structure.

Although the desire or interest to do clinical research may be present, many factors also impinge on the basic challenge of attracting physicians to engage in clinically related research. Time, support (financially, collegially, administratively), and resistance to encouraging patients to want to be study subjects are all factors. The time and energy required by providers to work on protocols or ideas, whether in their group, their clinic, in collaboration with internal, basic science–oriented colleagues or with others (such as in bioinformatics or epidemiology), or even with externally located colleagues may also be impediments.

Further, for clinicians, the ancient admonition of Hippocrates—"make a habit of two things—to help, or at least to do no harm"—is a deeply held conviction.[6] Since this admonition urges doing something that may help, herein lies the door to doing clinical research as a very valid undertaking. Indeed, the purpose of research is to enhance knowledge, even though it may not necessarily help the immediate patient, which might be considered a conflict to "first do no harm."

Conversely, the opposite may be true, because a patient might be helped. The guard mechanisms in place—institutional review boards and patient (or data) safety monitoring boards—are well defined in their role to oversee and effect, to the greatest extent possible, that any potential harm from research is minimized. Thus, what are some ways or means to improve clinical research participation by clinicians?

Solberg[7] notes few studies that address strategies to enhance physician recruitment to do research. Additionally, there is a paucity of information on how to engage an entire medical group practice in research studies aimed at organizational aspects of quality improvement.[7] Based on a collaborative effort focused on patients with depression, among 41 medical groups in a region of Minnesota, Solberg summarizes the "lessons learned" as to what components are important to a successful practice-based research network. The elements he identified are "relationships, reputation, requirements, rewards, reciprocity, resolution, and respect"[7]—all relevant factors to any collaborative undertaking.

Applying What We Know

So, where and how does this translate into the persistent difficulties in garnering clinician interest in doing clinical research?

Research as a part of medical residency is mandated in many, but not all, programs. It is not a "mandatory" requirement for the American Board of Internal Medicine or the American Board of Pediatrics, unless it is a part of the program for a trainee planning on a career in both research and clinical practice.[8,9] However, recently, a very ambitious program to address this point involves a University of Texas Southwestern group's efforts to integrate electronic medical records and clinical research systems into a means to "facilitate research protocol development and management."[10] The Texas report highlights the makeup of a broad-based research team that includes residents. By its design, this model may provide a basis for improved collaborative work and eventually be a model for replication elsewhere.

Furthermore, Hershenberg et al. recently proposed a framework that applies evidence-based practice into curriculum development meant to bridge the gap between research and practice.[11]

As the pressure and need to see patients are foremost in practices, the question involves how to make the opportunity to do research feasible and achievable. Although many examples of collaborative research exist and have been studied, the results are mixed.[12] Recently, however, Kottke et al.[13] elucidated five broad principles that bear on improving one aspect of research results and optimizing outcomes:

- Patient and population needs are the research agenda determinants;
- The agenda addresses both context and implementation, including systems to develop delivery;
- Accountability, because the research agenda determines research methods, not vice versa;
- Researcher and clinician collaboration defines the research agenda, resources, and implementation of findings; and
- Funding of implementation research equals the task.

As the pressure and need to see patients are foremost in practices, the question involves how to make the opportunity to do research feasible and achievable.

Although the desire or interest to do clinical research may be present, many factors also impinge on the basic challenge of attracting physicians to engage in clinically related research.

To the extent these principles, and those of Solberg,[7] have been applied in more recent research, several studies now demonstrate the incorporation of such elements aimed at improving a very desired outcome: translation from science into clinical practice. In particular, family medicine, psychiatry, and nursing have demonstrated the effective use of collaborative approaches to integrating translation of scientific evidence into clinical practice.[14–20]

Further Forays

In a report that yielded mixed findings on collaborative research, Blevins et al.[12] studied a Veterans Health Administration program designed to encourage clinician-driven research. It focused on the extent to which funded projects maintained integrity to the original proposals, remained methodologically rigorous, and resulted in a sustained clinical impact via the collaboration between researchers and clinicians. Though successful in achieving clinician-directed collaboration, the program did not produce sustainable interventions due to a lack of resources and administrative support.

Elsewhere, despite many unsubsidized costs, McAlearney et al. recently found that, in the National Cancer Institute's Community Clinical Oncology Program trials, clinicians were motivated by "altruism" and "self-interest," but the overall benefits followed translational research goals, and participation contributed value to providers by way of access to innovation in patients' medical care.[21]

Furthermore, as Pickler and Tubbs-Cooley recently noted, the Patient-Centered Outcomes Research Institute, a nonprofit, nongovernmental organization authorized by Congress through the Patient Protection and Affordable Care Act of 2010, may provide, at least for several years, an excellent funding source in the U.S. for the collaborative research needed on large populations.[22]

Similar issues seem to face nations besides the United States, with many examples of comparative differences and similarities of support, policy linkage, and collaborative research and integration into translation to clinical practice.[23–27]

Other Considerations

Restifo and Phelan[28] provide a very important insight to the "cultural divide" that exists between the basic science researcher and clinicians. However, they also provide some important suggestions on how to remedy these impediments.

The point of developing mutual respect, as also noted by Solberg,[7] arises from the need to communicate more clearly on points of information, such that there is a mutual understanding of meaning, when and where that may occur.[12] Other points include motivation, being curious and asking questions, reforming curricula to focus more on research as a core part of the medical educational experience, and encouraging researchers and clinicians to be more proactive in getting the NIH to do more for public education, including explaining why taxpayer-funded research is beneficial.[12]

Recently, Wolfe[29] discussed the major issues separating the researcher from the clinician and suggested possible solutions. Although his focus is on the specialty of psychiatry, his dialogue approach bears merit for any research/clinician situation: how to break down barriers between a researcher and the clinician—the "language barrier" issue.

Conclusion

Many barriers exist and are complex, multifactorial, and not easily resolved. However, the key issues identified and addressed, as reviewed, may and should provide insight and potential means to address barriers to collaborative research in a given institution. Such approaches may offer an institution ways to enhance the important components of collaborative research and to encourage, sustain, and support both basic science researchers and clinicians who need and desire to undertake research projects.

The support for research starts with a fundamental commitment to the importance research holds in advancing knowledge and in its place on the continuum from new discoveries to actual implementation of applicable discoveries into clinical practice, with the goal being improved outcomes.

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Richard A. Dart, MD, FACP, FCCP, FAHA, FASN, FASH, (dart.richard@mcrf.mfldclin.edu) is emeritus research clinician (active), Center for Human Genetics, Marshfield Clinic Research Foundation; staff nephrologist (retired), Marshfield Clinic; and adjunct clinical professor of medicine, University of Wisconsin School of Medicine and Public Health, Marshfield Campus (active).

Robert M. Haws, MD, (haws.robert@marshfieldclinic.org) is a physician in pediatric nephrology and director, Clinical Research Center, Marshfield Clinic Research Foundation, Marshfield Clinic, Marshfield, Wis.

Martin Robinson, PhD

What Makes a SUCCESSFUL PARTNERSHIP?

Clinical research is a sector where working in partnerships is a commonplace, and often essential, practice for the successful conduct of a clinical study. The relationship may occur at the micro level (e.g., between a clinical research associate and an investigator's site team) or at the macro level (e.g., between organizations forming strategic partnerships). In addition, pharmaceutical companies may form alliances such as licensing agreements, which may include the clinical development, manufacture, and marketing of therapeutic agents. The question remains: What makes a successful partnership, and why do organizations form these associations, particularly when sometimes they appear to be competitors?

Why Do Organizations Form Partnerships?

The fundamental principle of any partnership is that it has to be mutually beneficial for all parties. When commercial organizations form alliances, there has to be a financial return. There are usually short-term benefits to be gained first, but the partnership may also be forged with long-term goals in mind.

Organizations may partner because it gives them access to new markets and more customers. They may also form alliances because each organization has mutually complementary products or services in the same or related sectors, giving each party the opportunity to offer new products and services to existing customers.

Organizations may partner because they have different skills and expertise, and combining the two sets of capabilities makes a good fit for an enhanced offer to their respective sets of customers. Further, a new business opportunity may arise so that the organizations—working together—may have a better chance of exploiting than if they operated separately.

In terms of partnerships in clinical research, one of the most common is the relationship between pharmaceutical companies and contract research organizations (CROs). Outsourcing by pharmaceutical companies to CROs has become commonplace, and this sector is likely to continue growing.

Trust and transparency are essential ingredients, and alliances have a better chance of thriving when all parties have similar values and ethics.

Pharmaceutical and biotechnology companies are increasingly entering into global partnerships, such as strategic alliances with large CROs, as they seek to improve their financial returns in developing new therapies. The CROs, of course, make their money by selling a variety of services to the pharmaceutical sector.

What Form Do Partnerships Take?

Partnerships come in all shapes and sizes. One of the simplest alliances is when organizations agree to refer business to each other, usually for a percentage of the revenue of the piece of business referred. This straightforward arrangement holds a low risk, and may form the platform for a more in-depth partnership in the future.

At the other end of the scale, organizations can form strategic alliances that may involve sharing goals, visions, plans, and even staff.

Sometimes, a new company may be formed, such as Boots-Celltech Diagnostics. Both parent companies, Boots and Celltech, were based in the U.K. Boots had, and still has, a retail pharmacy business, and Celltech was a biotechnology company specializing in producing monoclonal antibodies for medical use. The organizations combined their expertise to produce novel medical diagnostic kits, some of which could be sold over the counter at Boots' retail outlets while others were designed for use by clinical testing laboratories. Those were exciting times, but eventually the relationship ended when Boots withdrew to focus on its core business.

What Makes a Successful Partnership?

Not all alliances succeed, as with Boots-Celltech; they require plenty of hard work and commitment from all sides. So what is the recipe for a prosperous relationship? I suggest :

- There should be mutual benefit for all the players. In simplest terms, this equates to increased revenue through access to more customers, or through new or enhanced offerings to both longstanding and new customers. This may include new products or innovative combinations of related products and services that customers may find more attractive.
- Trust and transparency are essential ingredients, and alliances have a better chance of thriving when all parties have similar values and ethics. Much of it comes down to the individual people involved in setting up and maintaining the partnership; they must be like-minded and enjoy doing business together.
- A joint business plan for the partnership should be agreed upon and drawn up, defining roles and responsibilities, revenue projections, sales targets, joint marketing strategies, and short- and long-term goals. Going for a small short-term project is a good way to test how the partnership will work when it's time to go for the bigger fish!
- Open communication is vital, and a regular schedule of meetings and teleconferences should be set up. These get-togethers should monitor progress, exchange ideas and views, and check that each party is comfortable with its respective role in the partnership.

Martin Robinson, PhD, (mrobinson@iaocr.com) is principal director of IAOCR.

OPINION:

The Importance of the Physician-Scientist to Healthcare Advancement

PEER REVIEWED | Ayaka J. Iwata, MS, MD | Christine C. Johnson, MPH, PhD
Steven S. Chang, MD

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Today, there is a daunting disconnect at the core of biomedical research and patient care. At one end of the spectrum, the basic life sciences and healthcare research have made dramatic and celebratory leaps forward. True scientific inquiry has led to exciting advances in our understanding of molecular biology and complex human diseases, and we've witnessed the emergence of powerful technological methodologies such as high-throughput screening, sequencing, genomics, proteomics, imaging, and bioinformatics.

Physician-scientists are uniquely equipped to translate scientific discoveries into population health benefits.

Our knowledge base has also expanded explosively. The Big Data era of the 21st century has offered a wealth of information derived from multiple levels of sources—from genome and molecular data, to electronic medical records, to social networks.[1] Funding has kept pace as well. Even during the current post-sequestration era, the National Institutes of Health (NIH) in fiscal year 2013 invested more than $29 billion toward research, about three times the annual funding seen just two decades prior.[2]

However, as agreed upon by numerous voices—from the NIH medical director to public media—the relative impact of scientific progress on patients and population health is dismal.[3–5] The data are sobering; according to Contopoulos-Ioannidis and colleagues, out of 101 major basic science articles with clear clinical application published between 1979 and 1983, only five led to licensed interventions by 2002, and only one of the five had been adopted widely into clinical practice.[6]

Along those same lines, the drug development world has not kept up its production, despite experiencing rapid scientific advances. The rate of new pharmaceutical drug introductions to the market has remained stubbornly flat.[7,8] New cures and therapies are not only hard to come by, but involve increasingly expensive, risky, and time-consuming development cycles.[7,9]

Finally, in public health, the evidence behind ways to prevent common chronic diseases has long been clear: smoking cessation, physical activity, cancer screening, and improved diet will address the core leading causes of death in this country. Again, progress has been slow in translating this knowledge to decrease the global burden of disease.[10]

Basic research and clinical research have now become distinct entities, each with its own dauntingly complex databases, infrastructure, and technologies. The gulf between these two disciplines has widened, and they seldom communicate with each other.

Physician-scientists, broadly defined as those medically trained who devote a portion of their professional career to research anywhere along the spectrum from basic biomedical investigations to applied clinical epidemiology to outcomes research, are uniquely equipped to translate scientific discoveries into population health benefits.

A Growing Sense of Detachment

The disconnect between science and clinical application is a relatively new phenomenon. Up until the 1970s, biomedical research was carried out by physicians who treated patients regularly.[11] Observations made in the hospital or clinics led to controlled laboratory experiments or other methodical studies. Science, in other words, was directly relevant to patient care.

Gradually, however, medical research started marching toward elucidating more basic mechanisms. As the philosophy of reductionist physical sciences became incorporated into the biological disciplines, and as more nonclinically trained PhD scientists entered the medical world with opportunities and funding, progress in biomedical research became more and more detached from patient care.[11]

The explosion of discoveries and progress in molecular biology and genetics in the 1970s drastically catalyzed this separation. Basic research and clinical research have now become distinct entities, each with its own dauntingly complex databases, infrastructure, and technologies. The gulf between these two disciplines has widened, and they seldom communicate with each other.

What is also worrisome is that the pool of physician-scientists who led the biomedical research field in the past has dramatically shrunk from 4.6% of all physicians in 1985 to only 1.8% in 2003.[12] This is due to both a steady increase in the number of physicians overall as well as a decline in the absolute number of physician-scientists.

Furthermore, in the context of the biggest explosion of the number of PhDs in the life sciences, there is a discordant lack of increase in the number of MDs who are applying for R01 grants in the past two decades.[13,14] These NIH-funded MD scientists are consistently less persistent, and therefore less successful, than their PhD counterparts, and exit the NIH grant cycle at a higher rate.[14,15]

Grants are also increasingly difficult to obtain. With the NIH sequestration of 2013 resulting in across-the-board budget cuts, combined with more costly requirements in terms of maintaining "big data," technology, and basic science, supporting clinician scientists is an ongoing challenge that just gets worse with time.

Parsing the Roles of Different Scientific Callings

All these challenges aside, physician-scientists offer valuable merit to biomedical research that nonclinician scientists and pure clinicians cannot provide. Basic scientists are expertly trained to focus on biological discoveries and mechanisms as ends in themselves. There is no question as to how essential this is; basic science breakthroughs provide the very foundation for solutions to human disease, and have radically revolutionized our understanding of modern medicine.

The basic scientific community, however, fails on one important front: It stops pursuing the potential applications of its work in people. Once a fundamental scientific question has been answered and published, scientists have every reason to return to a related basic problem, and no reason to recognize or push its application in patients. They are expertly equipped to work within their own intellectual niches, being neither trained, paid, nor motivated to enter the foreign and messy realities of patients, where matters are complicated by ethics, regulations, and lack of controlled settings.

Physician-scientists offer valuable merit to biomedical research that nonclinician scientists and pure clinicians cannot provide.

By understanding science in the expanded context of social relevance, access, cultural value, and patient priorities, physician-scientists help focus the scientific community to prioritize problems that are most valuable to patients.

In short, having very little experience with the nuances of delivering patient care and clinical practice, basic scientists are generally unsuited to integrate their data into medicine.

In a similar fashion, pure epidemiological researchers and biostatisticians without clinical training are constrained. On the one hand, their methodologies and tools are certainly powerful; they can establish patterns of disease in a given population, identify risk factors and determinants of disease, and demonstrate the efficacy of interventions. Factor analysis, dynamic systems models, and other complex methodologies arm them with the potential to uncover previously unimagined interactions.

However, not all epidemiologic concepts are created equal. In order to have the most merit, public health researchers must be able to ask relevant clinical questions. These questions stem from insights gathered from practicing medicine and standing at the bedside of sick patients. The most sophisticated epidemiological tools and those who use them, therefore, are blind without clinical input.

Pure clinicians are isolated as well; many are inadequately trained to understand and appreciate the vocabulary of the modern scientific disciplines and stay up to date with preclinical advancements that may affect their field. Furthermore, by being too unfamiliar with the capabilities of basic research, they fail to identify pertinent observations of their patient populations that may have the potential to provide new scientific insights.

In addition, clinicians are often taught to adhere to, not challenge, standards of care and existing paradigms of medicine. The distinct mentality necessary for delivering quality clinical care becomes an antagonizing force against participating in the creative and critical process that defines biomedical research.

Appreciating a Unique Role

Thus we find that physician-scientists are essential in spanning the divide between the increasingly specialized and compartmentalized worlds of basic research and clinical practice. They bring unique personal skills and perspectives to biomedical research that pure researchers or pure clinicians alone cannot provide.[16–19]

Clinical epidemiologists, for instance, can discern patterns from large aggregates of scientific datasets and integrate them with their understanding of disease and health determinants. Outcomes researchers systematically study the impact of therapeutic interventions on pertinent health issues of large patient populations. Further, more molecularly oriented physician-scientists possess scientific priorities that are guided by clinically relevant issues.

Most importantly, physician-scientists are equipped to be leaders of collaborative teams that drive healthcare research and translational science. Translational research, as a discipline that transforms scientific discoveries into effective health outcomes, is increasingly recognized as a critical discipline, and one that Dr. Elias Zerhouni, the former director of the NIH, says needs to be "more and better… for the sake of our patients."[20]

Within translational research is the relatively new field of dissemination and implementation (D&I), which specifically aims to transform scientific evidence into everyday, real-world settings.[21] It is a multidisciplinary science that draws from a variety of public health, social science, clinical, and health policy disciplines that physician-scientists are most well-equipped to integrate.

As a recent example, a randomized clinical trial published in 2011 showed that screening for lung cancer of an at-risk population with low-dose helical computed tomography (LDCT) decreases lung cancer mortality by 20%.[22] Two years later, the U.S. Preventive Services Task Force put forth guidelines for annual lung cancer screening with LDCT in line with the evidence.

However, integrating a new cancer screening service into the primary physician's visit is challenging, and will require multiple interdisciplinary steps.[23,24] Barriers for nationwide implementation include financial constraints on accessing sophisticated CT scanners and analytic software, staff, and qualified radiologists; the complexity of integrating a costly cancer screening to an already busy workflow limited in time and resources; the need to diffuse screening especially to underserved populations who are disproportionately affected by lung cancer; and overcoming cultural concerns for patients, such as stigmatization or lack of trust in the medical system.

Physician-scientists who are proficient with both the human aspects of clinical practice as well as the scientifically rigorous disciplines of epidemiology and biostatistics can actively lead the necessary collaborative approach to make progress in D&I research. In essence, by understanding science in the expanded context of social relevance, access, cultural value, and patient priorities, physician-scientists help focus the scientific community to prioritize problems that are most valuable to patients.

Conclusion

The numerous challenges that face the making of physician-scientists have been briefly mentioned here, and have been thoughtfully discussed elsewhere.[25–28] Possible solutions proposed include:

- increasing the number of postgraduate research training and medical scientist training programs[29];
- securing increased funding from the NIH toward relevant centers (e.g., the National Center for Advancing Translational Sciences)[30];
- expanding loan forgiveness programs to reduce debt burden[31]; and
- exploring mechanisms to shorten research training for physician-scientists.[31]

Finally, what may be most meaningful to aspiring physician-scientists are mentorships facilitated to encourage, train, and push them to create the level of research that will genuinely touch the core beneficiary: our patients.

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Ayaka J. Iwata, MS, MD, (aiwata1@hfhs.org) is a resident in the Department of Otolaryngology Head and Neck Surgery, Henry Ford Health System, Detroit, Mich.

Christine C. Johnson, MPH, PhD, is chair of the Department of Public Health Sciences, Henry Ford Health System, Detroit, Mich.

Steven S. Chang, MD, is a senior staff surgeon in the Department of Otolaryngology Head and Neck Surgery and a research scientist in public health sciences, Division of Cancer Epidemiology Prevention and Control, Henry Ford Health System, Detroit, Mich.

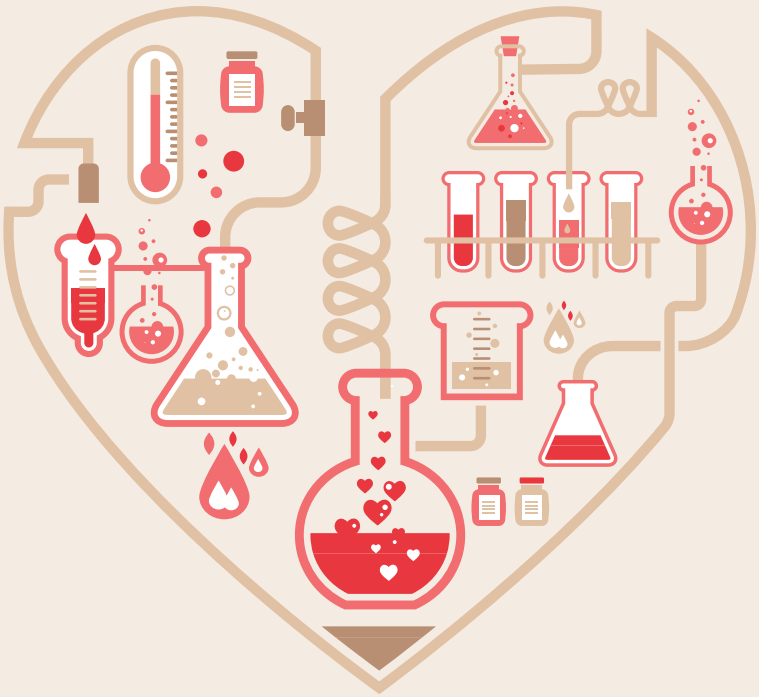
Jamie Meseke, MSM, CCRA

Relationships 101:

The Dating Game Between CRAs and Research Site Staff

Clinical research associates (CRAs) play a vital role in the partnership between sponsors/contract research organizations (CROs) and sites, and project success may depend on how well the site staff works with their assigned CRAs/monitors. Collaboration, flexibility, and professionalism are key factors in fostering and maintaining an effective working paradigm.

For this issue's column, several questions were presented to a long-time clinical research coordinator (CRC) and to a site study manager (SM) to understand their perceptions and assessments of today's CRA-site relationships.



Q: Preparing for monitor visits can be frustrating and stressful for study teams. What actions do you take prior to the monitoring visit to ensure things run smoothly?

CRC: We ask our monitors to send us confirmation letters at least seven working days prior to the visit. This allows us time to follow up on outstanding issues.

SM: I am copied on communications between the study coordinators and the monitors. By being kept in the loop, I can quickly step in and assist with resolving issues. However, I would stress that more is not always better. It can be overwhelming when monitors send multiple e-mails over a short period of time. It helps when e-mails are limited to those that are relevant and necessary.

Q: We all have pet peeves. What are some things monitors do that drive you crazy? Is there any advice you'd like to give from your perspective?

CRC: It can be annoying when monitors run back and forth every time they have a question or want us to correct something. Questions and correction requests should be batched for more efficient use of visit time. Monitors should save their questions for the end of the visit, if there aren't many or if the issues are not urgent. If there are a lot of questions, it helps to break them up; cover some just after lunch and then again toward the end of the day. Also, since we receive large volumes of e-mails daily, sending queries for resolution via e-mail is not always effective.

Also, excessive or loud talking can be disruptive; therefore, phone calls should be taken outside the facility.

We appreciate when monitors schedule their next appointment while still at the facility, rather than waiting until a week before they want to come.

Finally, regarding essential documents, monitors should check with the regulatory manager during the visit to determine if any issues may be resolved while still at the site.

SM: It's bothersome when monitors do not fully discuss issues with me or the principal investigator prior to leaving the site, and instead put everything into the follow-up letter. Often, we could have resolved the issues prior to the monitor's departure.

Also, pick up the phone and call us! E-mail is a wonderful tool, but urgent issues really should be brought to our attention by phone. It's easy to overlook e-mails, and sometimes technology fails.

Q: What characteristics or actions displayed by some monitors do you wish other monitors would adopt?

CRC: I appreciate it when monitors e-mail general study reminders, such as weekly reminders to check whether there are unresolved queries in the electronic data capture (EDC). Also, it really helps with query resolution when monitors provide a reference to where they found the information in our source, by inserting a flag or sticky note, for example, or adding the query within the EDC system.

SM: Some monitors are very conscientious about e-mailing summaries of phone discussions, which helps us ensure communications were understood the same way on both sides. Also, it provides formal documentation for our records that we can refer back to, if necessary.

Q: Do you have any advice or tips for monitors on how to improve the relationship between monitors and site staff?

CRC: Monitors should take the time to become familiar with the systems being used for each study (e.g., EDC, interactive voice response systems, lab portals). It makes working together easier if they know what the system looks like on our end, as the views may be different.

Also, it is so much easier to communicate with the monitor when he or she thoroughly understands the protocol.

Most of all, come with a positive attitude!

SM: The best way to foster a good relationship is through open communication. It helps tremendously when monitors come prepared and take the time to talk with us before, during, and after completing the visit. No one likes surprises buried in follow-up letters.

Also, be flexible. Remember, site staff often juggle multiple protocols and have to switch gears quickly if patient issues arise during monitoring visits.

In Summary

A healthy partnership between sponsors/CROs and sites may take considerable effort, yet is essential for study success. All parties should understand the value of open and continuous communication. Monitors and site staff should be able to discern early the most appropriate method for delivering messages. Applying this best practice can limit tension between parties when unresolved issues or data entry backlogs exist.

Research has shown that people tend to read e-mails multiple times and often misinterpret messages as being more aggressive than intended.[1] If the issue is complex, or immediate feedback is needed, it should be addressed by phone or in person during an onsite visit. E-mail communications should be succinct and limited to only the information that is relevant and necessary.[2] As the study manager keenly pointed out earlier, more communication is not always better; there can be a fine line between too much and too little.

The last takeaway point raised by both individuals is the need for professionalism and positive attitude. Business relationships require give and take from all parties. Sometimes a simple smile and "thank-you" can break tension and quell conflict before it escalates.

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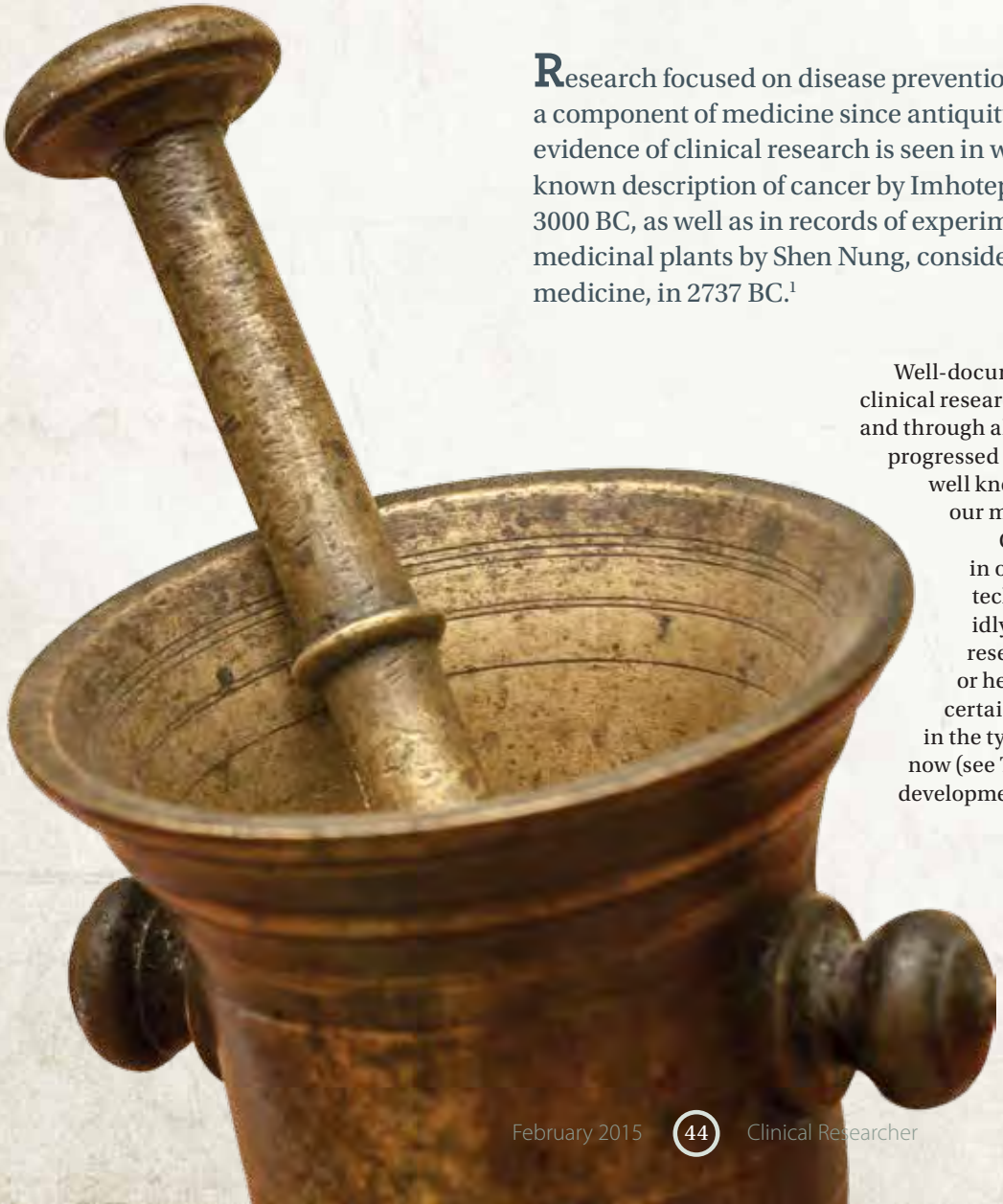
Jamie Meseke, MSM, CCRA, (jamie.meseke@ppdi.com), is a clinical trial manager for PPD, Inc., and a member of the ACRP Editorial Advisory Board.

The Evolution of Research Design: NEW WAYS OF THINKING

PEER REVIEWED | Steven Ziemba, PhD, MBA, CRCP, CIP, FACHE, CCRC

[DOI: 10.14524/CR-14-0046]



Research focused on disease prevention and treatment has been a component of medicine since antiquity. Some of the earliest evidence of clinical research is seen in what may be the earliest known description of cancer by Imhotep in Egypt from around 3000 BC, as well as in records of experimentation with poisons and medicinal plants by Shen Nung, considered the father of Chinese medicine, in 2737 BC.[1]

Well-documented evidence of the progress of clinical research is seen in other parts of the world and through all of history. The ethical factors that progressed hand-in-hand with the practice are well known, and provide the mainstay of our modern regulatory system.

Clinical research has also advanced in other ways—most notably in its techniques, which have changed rapidly in just the past decade. A clinical research professional that started his or her career more than 10 years ago has certainly experienced significant changes in the types of studies that are present now (see Table 1 for a brief overview of these developments).

Further, much of what is seen changing in these approaches is not necessarily about the designs themselves, but about how the research designs are used. Key to this is the use of these design types in mainstream healthcare; in fact, such research designs have promoted the advancement of research in the greater world of general healthcare. To that end, an understanding of the research designs is insufficient; bending their application to healthcare provides a greater appreciation.

Is This the Real World?

One criticism of clinical research is that it does not truly reflect the real world of medicine.[2] Clinical studies incorporate experimental design and are not intended to benefit the study participant directly, but rather to generate new knowledge. A caveat of this aspect is the need to minimize variables, to be able to draw conclusions based on the collected data.

Hence, the strict eligibility criteria of many studies are often seen as representing a barrier to achieving target enrollments.[3] The study may have additional requirements that can be difficult for a participant to adhere to, resulting in increased risk, loss of data, and reduced enrollments that risk the completion of a study.

A strategy developed to address such concerns is known as patient-centered outcomes research (PCOR). In this approach, the input of patients, caregivers, and other stakeholders is used in study design, conduct, and amendments. Such input is also used in the assessment and rewarding of grants through the federally supported Patient-Centered Outcomes Research Initiative (PCORI), demonstrating the extent to which patient focus is considered important.

The inclusion of input from actual patient populations in terms of formulating research designs is a milestone in study development. Previously, patient influence would have been minimal or even nonexistent, based on the thought that those without scientific training would not be able to understand the nuances of scientific research or make sense of the data and results.[4]

However, patient-centered research does not seek to train the lay population on these and related topics. Rather, its purpose is to use the patient experience in determining if a proposed scientific approach, no matter how well crafted, is indeed feasible and practical. The approach has met with successes, as evidenced by the awarding of over $670 million in grants by PCORI as of 2014 (pcori.org).

As a healthcare advancement, PCOR provides insight to observers on the focus of the industry in general. The emphasis seen today on prevention, patient satisfaction, and a more holistic approach demonstrates the acceptance of this research paradigm to the healthcare industry.

What's Behind Bench to Bedside

Translational research is another area that has moved clinical research in a new direction. Popularly termed as "bench to bedside," the intent of translational research is to rapidly translate the discoveries of basic science into medical care. It also uses the lessons learned from medical care in guiding subsequent bench science work.

Taken further, translational research seeks to ensure that new treatments and knowledge do indeed reach the intended patient populations at large.[5] In a broad sense, when applied to the healthcare setting, it provides the means to use results of both basic and clinical research to affect decisions and behaviors of providers and patients alike.

Add Research…and Mix

Healthcare is more than the diagnosis and treatment of injury and disease. The industry as a whole is complex, with a myriad of philosophies and methodologies, billing rules, regulatory requirements, accreditation guidelines, and costs. Inserting research into this environment introduces additional layers of complexity.

The clinical research enterprise has taken note of broad trends in healthcare and, in an attempt to stay relevant, responded by enhancing the visibility of health services research either as standalone research or as a component of clinical trials. This field of research is a multidisciplinary area of

A clinical research professional that started his or her career more than 10 years ago has certainly experienced significant changes in the types of studies that are present now.

TABLE 1: Study Design Types and Characteristics

Study Design Type	Defining Characteristic
Patient-Centered Outcomes Research	Provides patient and stakeholder input in study design, conduct, data analysis, and determining conclusions
Translational	Attempts to integrate the discoveries of bench science with medical outcomes
Health Services	Clinical research beyond that of treatment or prevention, such as health economics, patient satisfaction, others
Comparative Effectiveness	Evaluation of efficacy or other attributes of two or more approved and marketed treatments
Adaptive Design	Ability to alter the design in response to changes in the environment during the course of a study
Big Data	Analysis on the accumulated data on thousands or tens of thousands of individuals

The inclusion of input from actual patient populations in terms of formulating research designs is a milestone in study development.

investigation that incorporates various factors, including social, financial, organizational structure and processes, technology, and personal behavior, in understanding the quality and cost of healthcare.[6]

One example of such work would be studying not only the effectiveness of an investigational agent, but also its cost to the patient and whether that cost can impede treatment. Such was the case with bevacizumab, a monoclonal antibody used in breast cancer treatment, among others. The agent demonstrated effectiveness in its ability to treat breast cancer, but was met with criticism in terms of its use due to its high cost.

Still, medical care often involves choices in the treatment selection available for a given diagnosis. Factors such as drug availability, cost, and the preferences and biases of the physician can determine which to use to treat the patient. Some of these factors can be subjective in nature, offering little clear evidence if one treatment is superior to another, even if both are approved for marketing.

Comparative effectiveness research is thus designed to try and answer such questions. Rather than test an investigational agent against a placebo or the standard of care for a diagnosis, it compares two (or more) approved treatments against each other. Such studies may use a superiority model, equivalency, or non-inferiority.

The purpose of using a superiority design is obvious. Equivalency and non-inferiority studies, however, may focus only on demonstrating that both treatments are equally effective. The advantage is seen when crossed with health services research, in that one treatment, though equal in efficacy to the other, may still be of greater benefit due to its lower cost.

At a more complex level of research, "adaptive design" refers to a model that allows adaptations or modifications to a clinical trial, often from a statistics standpoint.[7] This differs from simply amending in that, in the traditional clinical trial, aspects such as the endpoint and its associated endpoints are predetermined during study construction.[8]

Such predetermination introduces uncertainty into the study design. The use of adaptive design can help to address this uncertainty by allowing one to review collected data and make changes to the fundamental aspects of the trial. One change of particular significance involves the ability to reduce the sample size while the study is active. Other aspects that can be modified during the progress of the study include study duration, treatment group allocation, the number of treatment arms and associated dosing, and endpoints. Permitting such changes allows for greater efficiency and reduced subject exposure.

However, as Kairalla et al.[8] indicate, the adaptive design needs to be used cautiously, as it can also easily introduce investigator bias. Further, any such changes cannot be made for the sake of convenience; rather they are carefully controlled. That said, the use of adaptive design allows engagement in research that can respond to the unpredictable variables of healthcare.

Ramifications Down the Road

Much of what has been discussed in this paper focuses on the design of the study. A variety of models and approaches can provide benefit in terms of being better able to focus on the question at hand. However, the changes in research extend beyond study design.

One change is the increasing use of Big Data, an aspect that has gained notoriety in the press. This notoriety stems, in part, from media representation that personal data are being sold or otherwise used for profit. However, Big Data also represent a rich source of information for medical research.

Big Data represent the cumulative total of a population; to that end, the data present opportunities to investigate research questions by using large sample sizes in relatively short periods of time. The limitations come only from the type of data contained in a database, the quality of the data, and the design of algorithms by researchers to explore those data.

The advent of electronic medical records in the healthcare arena only adds to the value of such datasets. This value can extend beyond research into the day-to-day operations of healthcare. In fact, the increased emphasis on productivity, quality, and numerous other metrics makes research incorporating Big Data perhaps the most valuable trend in the industry.

Indeed, the use of research techniques and data by healthcare organizations presents a myriad of opportunities and challenges. The approach many are familiar with is the incorporation of clinical trials into the healthcare environment. In this, providers may engage in clinical research in addition to their task of seeing patients. Research staff may also be present, depending on the extent of the clinical trials being conducted.

The healthcare industry has also extended into fields where research knowledge can prove useful, with many of these fields having a financial impact on the organization. Some prominent factors are quality measures, productivity, community impact, patient satisfaction, prevention of errors, and healthcare economics.

In addition, individual disciplines, such as oncology, may have certain standards and guidelines to meet in order to achieve recognition as an accredited site. The opportunity this presents to the research investigators and personnel of an organization comes through their sharing of knowledge and expertise in research techniques to be used in addressing these parameters. In turn, it demonstrates to an organization's leadership the additional value of research.

Consider the Challenges

The approaches described earlier present a small section of what can be provided to help an organization improve patient satisfaction, decrease the incidence of errors, improve quality, and demonstrate impact on the community, among others. Leveraging Big Data is one approach that has been increasingly used to these ends, as have comparative effectiveness and translational research.

As with most opportunities, however, challenges also exist. The use of research techniques as a business solution may introduce the caveat of conflicting, though worthwhile and necessary goals. The researcher may seek to add to generalizable knowledge, whereas the administration's goal is to improve financial performance, particularly if operating in the realm of single-digit margin many healthcare systems find themselves in.

In the end, however, both are focused on service to the patient. Education and communication are essential for each side to understand the nuances of the other. As an example, research may require considerable time to achieve results. A retrospective study using databases to compare standard-of-care treatment efficacy and costs may take a longer period of time than what leadership typically would be accustomed to.

This represents the use of three research approaches, namely Big Data, comparative effectiveness, and health services research, to arrive at a conclusion. Leadership would value a study of this sort due to its potential to improve quality of care and decrease costs, while indirectly improving patient satisfaction and community outreach via publicity. This value may also translate into a desire to have results in a short period of time, both for more immediate application, as well as the potential for positive marketing. However, such desire must be balanced against the risk of circumventing the careful analysis of results.

Table 2 provides some general examples of the application of research design in the healthcare system.

TABLE 2: Examples of Applications of Research Designs in Healthcare

Study Design Type	Examples of Possible Utilization
Patient-Centered Outcomes Research	Understand the patient experience in healthcare
Translational	Apply real-world results to the next round of discovery
Health Services	Healthcare operations other than treatment
Comparative Effectiveness	Treatment cost as one measure of effectiveness
Adaptive Design	Respond to changes in the healthcare environment
Big Data	Quality metrics, productivity analysis, market assessment

Conclusion

Clinical trial design incorporates a vast array of approaches. The approaches of the Phase I, Phase II, and Phase III type studies are still present and of great importance, but have expanded beyond the traditional study of an investigational agent. The ability to more readily provide the discoveries of basic science to the patient, investigate existing approved treatments for a diagnosis, use economic data as a component of efficacy, and include the patient's input into the study design are only a few examples.

The research approach has expanded to be more inclusive of the healthcare industry. This expansion has been due to the increased metrics of healthcare and the need to provide more complex care to the patient at reduced cost and with greater efficiency.

Research methods can be used in providing the information health systems need. However, these needs extend beyond the abilities of the traditional clinical trial. The expertise of researchers is needed, further demonstrating the value research provides to the healthcare industry.

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Steven Ziemba, PhD, MBA, CRCP, CIP, FACHE, CCRC, (steven.ziemba@gmail.com) is associate director of Marshfield Clinic Research Foundation, Marshfield, Wis., and a member of the ACRP Board of Trustees and Editorial Advisory Board.

Beth D. Harper, MBA

An Interview with Jamie Meseke, MSM, CCRA

From earning a degree in Russian language and international studies to working as a clinical team manager for PPD, Jamie Meseke's unusual career path shows the myriad possibilities available once you are bitten by the clinical research bug.

Q: How did you first became interested in clinical research, and can you describe the path you took to get involved in this field?

A: Right before I graduated from college, I worked as an editorial assistant for an investigative research journal. I had originally planned to move to Moscow and work as a technical editor for the Russian Academy of Sciences. I changed my mind, and instead took a ground-level position with a startup site management organization (SMO). That was my introduction to the world of clinical research.

Q: Can you tell us more about where you started and the different roles you've held?

A: My responsibilities at the SMO included acting as a liaison between investigative sites and study sponsors, which involved a variety of activities. Eventually I left the SMO and went to the University of Wisconsin, where I started as an in-house monitor, working on biostatistics projects within the clinical trials program at the university's Comprehensive Cancer Center. This position really helped me understand the role biostatisticians and data managers play in the development and analysis of research protocols. A few years later, I segued into a clinical research coordinator role and worked my way up to become program manager for clinical trials in hematology.

Subsequently I was fortunate to have several other roles, including director of research for a small urology consortium, a research contract coordinator, and research contracts compliance administrator for the Schools of Nursing and Biomedical Sciences at the University of Central Florida.

Although I really enjoyed working on the finance and legal side of things, I missed being directly involved in clinical trials. So, when opportunity presented itself, I took a senior clinical research associate (CRA) position with a medical device company.

Later, when I was ready to return to the corporate world after enjoying a brief stint as a stay-at-home-mom, I hit the road as a traveling senior CRA with PPD. Four years later, and after having a fourth child, I am now a home-based clinical team manager for PPD, and absolutely love the position.

Q: When did you first get involved in ACRP, and what type of benefits have you reaped from being a member?

A: I first became involved with ACRP in the late 1990s while working for the SMO. I found the organization to be the best venue for reaching sites and sponsors. I loved attending the Global Conferences and working our vendor booth. I also pursued clinical research coordinator certification through ACRP while I was working at the university, and after moving into a monitoring career, I secured CRA certification.

I can attest that ACRP certification credentials have definitely increased my value as an employee, and I am now a member of the Editorial Advisory Board for *Clinical Researcher* and co-edit the CRA Central column.

I can attest that ACRP certification credentials have definitely increased my value as an employee.

Q: Since your career has spanned many years, what is the most significant change (or top changes) you have seen? How has this affected the industry, either positively or negatively?

A: In my opinion, cost increases across the board have had the greatest effect on the industry. It has always been expensive to run clinical trials, but the cost has escalated dramatically over the past 20 years. There are many contributing factors, such as more regulations and increasing protocol complexity.[1,2] The technology used by sites to calculate their costs has also become more sophisticated. Budget considerations are now made on a micro level—sometimes down to the number of bandages required.

Q: What advice do you have for clinical research professionals concerning how to advance their career?

A: The best advice I can give is to think in broader, more general terms about your career trajectory and skillset. Too often, research staff are blinded by their current role and don't understand how it could be possible for them to jump into another position. I tell them to capitalize on their past experience and think about how they can apply their knowledge and skills to a new position.

I majored in Russian language and international studies as an undergraduate, and my masters and PhD work are in business management, which shows that well-rounded education and experience allow one to wear many hats.

It's also important to keep a keen eye out for opportunity and network with people all across the industry.

Q: As you think about the future generation of clinical research professionals, what three "lessons learned" would you like to share?

A: Foremost, I would stress the importance of listening and trying to understand all of the factors that go into developing, managing, and analyzing clinical research projects. I owe most of my successes to translating communications across stakeholders. Having held so many roles in the industry, I am prepared and able to explain the rationale behind various decisions.

Second, I would have to point out the importance of going above and beyond what is written in your job description. In today's tight job market, a person is much more likely to advance to the next career level if he or she can demonstrate already having the experience and understanding the responsibilities entailed in the higher position. So my advice is to proactively ask for new responsibilities, and to offer superiors help whenever possible.

Third, I have learned not to be afraid to ask for help or clarifications. Colleagues are much more likely to respect people who confirm and demonstrate correct understanding, rather than those who make erroneous assumptions.

Q: Do you have any closing thoughts you would like to share?

A: Because there are so many career options in the clinical research industry, regardless of your background, I would recommend taking inventory of the skills and knowledge you've acquired to date. Study the research job postings and become familiar with the expectations of the new position. Then, consider how your past experience and training could translate into the expectations and responsibilities of the new position.

Thank you for sharing your story and insights with us. It is amazing all of the ways people come to the world of clinical research. There are so many transferable skills that relate to our industry, which, when combined with passion and open-mindedness, can lead to a rewarding career.

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Beth D. Harper, MBA, (bharper@clinicalperformancepartners.com) is the president of Clinical Performance Partners, Inc., and a former member of the ACRP Editorial Advisory Board.

Health Policy to Promote Colorectal Cancer Screening: *Improving Access and Aligning Federal and State Incentives*

PEER REVIEWED | Gloria D. Coronado, PhD | Amanda F. Petrik, MS
Sarah E. Bartelmann, MPH| Lori A. Coyner, MA | Jennifer Coury, MA
[DOI: 10.14524/CR-14-0044]

A major goal of the U.S. Affordable Care Act (ACA) is to expand access to healthcare coverage for individuals. Since October 1, 2013, more than 7 million individuals have gained coverage through government programs, including Medicaid and the Children's Health Insurance Program. Nationwide, as of July 2014, more than 67 million individuals were covered on Medicaid.[1]

The ACA created a national minimum eligibility standard that extends coverage to individuals and families earning up to 133% of the federal poverty level, up from 100% of the federal poverty level in prior years.[1] However, even with federal subsidies being offered, to date only 26 U.S. states have opted to expand their Medicaid programs.

States that expanded Medicaid have seen enrollment surge up to 20%, while those that have not expanded registered only a 5% increase.[1] Oregon

boasts one of the highest percentage increases in Medicaid enrollment since the Medicaid expansion program took effect; data from the Centers for Medicare and Medicaid Services (CMS) from July 2014 show that upward of 357,000 individuals have been newly enrolled in the state, for an increase of 57%.[1]

Meanwhile, Medicaid has historically provided coverage mainly for women and children; in 2010, 47% of Medicaid enrollees were children and 58% were female.[2] However, recent enrollment is anticipated to expand coverage for adult males.[3]

The ACA also expands coverage for specific preventive health services, including colorectal cancer screening. As part of its Preventive Health Mandate, implemented in 2011, the ACA requires all new private health plans to provide coverage, with no patient out-of-pocket costs, for colorectal cancer screening tests having a U.S. Preventive Services Task Force rating of "A" or "B": high-sensitivity fecal testing annually, sigmoidoscopy every five years, or colonoscopy every 10 years for average-risk adults age 50–75.[4]

Federal incentive programs that aim to improve healthcare quality recently have begun to include colorectal cancer screening, for which screening quality reporting is required for the CMS Star Incentives.[5] To earn a four-star rating by the 2014 Medicare Star Incentives program, a provider must have a screening rate of at least 58% of targeted patients screened, and five stars are earned if 65% or more are screened. Also, as of February 2013, the Health Resources and Services Administration's (HRSA's) Bureau of Primary Health Care requires federally qualified health centers and look-alike organizations receiving federal subsidies to report colorectal cancer screening rates using specific measures.[6]

The remainder of this paper describes Oregon's experience in including colorectal cancer screening as an incentivized measure for the state's Medicaid program.

Background

As part of a larger effort to implement health system transformation in the state, in 2012, Oregon successfully obtained authorization from CMS to launch a coordinated care model for the state's Medicaid managed care program. Under this model, the Medicaid program is managed by coordinated care organizations (CCOs), which are local health entities that deliver healthcare and coverage for individuals eligible for Medicaid.

The CCO model focuses on patient-centered primary care homes, improved coordination of care, and aligned incentives that reward providers and beneficiaries for achieving good outcomes. The state provides CCOs a flat fee, based on monthly enrollment, to provide services to the Medicaid population. CCOs also receive annual incentives in the amount of up to 3% of their Medicaid budgets in 2014, based on performance on quality metrics.

CCOs focus on prevention, primary care, and the needs of particular communities. They have community-driven, rather than provider-led, governance and are supported through a global budget that increases at a fixed rate. CCOs are required to adopt alternative payment methodologies, and the state publicly reports performance on metrics. State legislation also mandated the formation of a nine-member external stakeholder group (the Metrics and Scoring Committee) and charged its members with identifying measures for the new pay-for-performance program.

In 2012, the Metrics and Scoring Committee approved 17 measures tied to incentive payments for CCOs and established performance targets (i.e., reaching a benchmark) and/or improvement targets (i.e., improving a certain percentage beyond the previous year) for each. The colorectal cancer screening rate was one of these measures.

Meeting the Measures?

Given the rapid growth of Oregon's Medicaid population, expanded access to preventive health services under the ACA, and the inclusion of colorectal cancer screening as a reported and incentivized measure for CCOs, we characterize changes in screening rates in the context of the alignment of national and state quality-improvement measures.

We focused our analyses on colorectal cancer screening for two reasons:

- First, such screening has only recently become a reportable measure at the national level.
- Second, changes to the demographic characteristics of Medicaid enrollees (e.g., serving more individuals 50 and older) mean that such "adult" measures will become more relevant as states expand their Medicaid programs.

Federal incentive programs that aim to improve healthcare quality recently have begun to include colorectal cancer screening, for which screening quality reporting is required for the CMS Star Incentives.

Methods

The CCO Metrics and Scoring Committee met regularly to discuss quality metrics, and CCOs were incentivized for meeting performance or improvement targets. As mentioned earlier, 17 metrics were adopted for the first year of the program:

- adolescent well-care visits
- screening for alcohol and drug misuse
- outpatient and emergency department use
- Consumer Assessment of Healthcare Providers and Systems (CAHPS) access-to-care composite score
- CAHPS patient experience composite score
- colorectal cancer screening
- controlling hypertension
- depression screening and follow-up
- developmental screening
- HbA1c control
- early elective delivery
- electronic health record adoption
- follow-up after mental illness–related hospitalization
- follow-up care for children prescribed attention deficit hyperactivity disorder medications
- completion of mental and physical health assessments for children in foster care
- patient-centered primary care home enrollment
- timeliness of prenatal care

Data Collection

Medicaid member enrollment data were provided by the Office of Health Analytics of the Oregon Health Authority, which maintains an active database of Medicaid enrollees. Member demographic data are gathered during enrollment and entered into the electronic database.

In May 2013, Oregon began regularly reporting incentivized metrics, including colorectal cancer screening, for each CCO. The reports relied on claims for any colorectal cancer screening test recommended by the U.S. Preventive Services Task Force. We report CCO-specific rates of colorectal cancer screening, in both 2011 and 2013. The Healthcare Effectiveness Data Information Set (HEDIS) measure of colorectal cancer screening was modified by the Oregon office, given the desire of the Metrics and Scoring Committee to reduce the burden that requiring medical record reviews would have placed on CCOs.

The majority (70%) of respondents supported maintaining colorectal cancer screening as an incentivized metric in 2015, and the remaining 30% wanted to drop or modify the measure, citing concerns that the measurement approach was difficult or problematic.

The 2011 and 2013 rates are reported as the number of colorectal cancer screenings that occurred in the 12-month measurement period, reported per 1,000 member months for enrollees ages 50–75. CCOs would be paid if they showed an improvement in colorectal cancer screening rates in 2013 as compared to 2011. For 2014, the Metrics and Scoring Committee adopted the HEDIS reporting specifications and set a performance target of 47%. Because the measure specifications had changed between 2013 and 2014, an improvement target was not set.

Oregon Office of Health Analytics staff developed a survey that sought feedback on the existing 17 CCO incentive measures, and provided an opportunity for respondents to propose new measures for 2015. A link to an online survey was distributed to multiple listservs run by the office as outreach to representatives of various healthcare sectors; the number of individuals who were e-mailed the link to the online survey is unknown.

The survey asked respondents to self-identify as belonging to one or more stakeholder group, including healthcare provider, community partner, CCO leader, Oregon Health Authority staff, consumer advocate, member of the Metrics and Scoring Committee or of the Technical Advisory Workgroup, and others. Surveys were completed between April 29, 2014 and June 12, 2014.

Data Analysis

We present frequencies of individuals who are enrolled in Medicaid at two time points: December 2013 (before Medicaid expansion was launched in Oregon) and June 2014 (after Medicaid expansion was launched). We calculate percentage changes in enrollment by age group and race/ethnicity for the total population, females, and males.

Our analysis of colorectal cancer screening rates is based on claims data only. The CCO Metrics and Scoring Committee opted to set a 3% improvement target for CCOs to hit by 2013; that is, they did not set a target percent of colorectal cancer–screened patients. Thus, CCOs could fulfill the metric and receive an incentive payment by increasing, by 3%, the number of colorectal cancer screenings that occurred in a 12-month period versus the rate in 2011.

We report frequencies of respondents who supported keeping the colorectal cancer screening as an incentivized measure for 2015, and the frequency that supported dropping or modifying it. For presentation here, data from open-ended questions were coded and organized into themes, and representative quotes were identified.

Results

In December 2013, a total of 659,114 individuals were enrolled in Oregon's Medicaid program; by June 2014, that number rose to more than 971,095, for a 47% increase (see Table 1). The highest percentage increases were observed for the age groups 22–35, 36–50, and 51–64, which showed increases of 114%, 110%, and 117%, respectively.

In the same time frame, the size of the population that was age-eligible for colorectal cancer screening grew from 104,920 to 163,078, for a 55% increase. Increases in enrollment varied slightly by race and ethnicity, with the lowest proportionate increase observed for blacks (28%), and the highest observed for non-Hispanic whites (43%). Notably, there were 57,000 individuals with missing race information in June 2014 (data not shown).

When we examined changes in enrollment by gender, we found a greater relative increase among males compared to females. In December 2013, 365,808 females were enrolled in Medicaid; this rose to 516,918 in June 2014, for a 41% increase. Fewer males were enrolled at both time points (293,318 in December 2013 and 454,177 in June 2014); however, the proportionate increase was greater (55%).

Rates of colorectal cancer screening (based solely on claims data for individuals aged 50–75) ranged from 4.5 to 12.5 per 1,000 member-months of coverage in 2011 (see Figure 1). Rates for 2013 ranged from 7.2 to 15.7 per 1,000 member-months of coverage. Comparing data from 2013 and 2011, six of the 15 CCOs improved their rates by 3% or more (and met the improvement target).

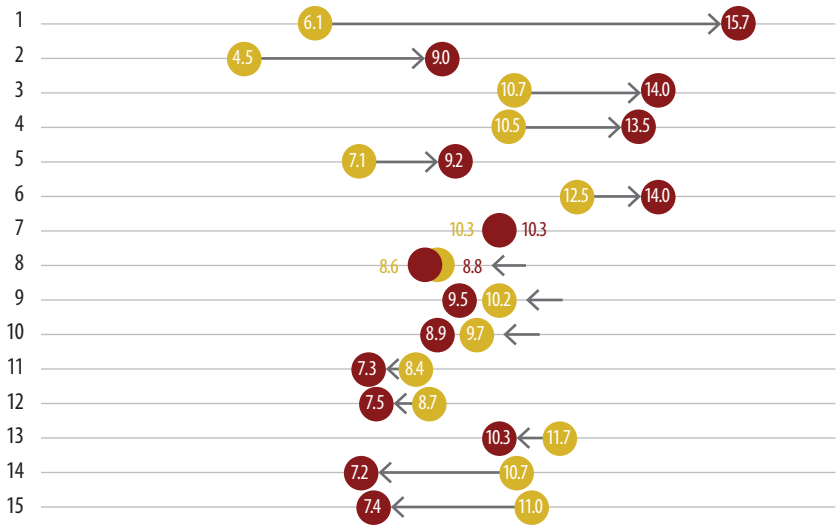
The CCO model focuses on patient-centered primary care homes, improved coordination of care, and aligned incentives that reward providers and beneficiaries for achieving good outcomes.

TABLE 1: Demographic characteristics of Oregon Medicaid Enrollees, December 2013 and June 2014

	Total			Females			Males		
	Before Medicaid Expansion	After Medicaid Expansion		Before Medicaid Expansion	After Medicaid Expansion		Before Medicaid Expansion	After Medicaid Expansion	
	December 2013	June 2014		December 2013	June 2014		December 2013	June 2014	
	N = 659,114	N = 971,095		N = 365,796	N = 516,918		N = 293,318	N = 454,177	
	N	N	% change	N	N	% change	N	N	% change
AGE									
All ages	659,114	971,095	47.3%	365,796	516,918	41.3%	293,318	454,177	54.8%
<19	372,639	426,130	14.4%	182,129	208,281	14.4%	190,510	217,849	14.4%
19-21	20,996	41,625	98.3%	13,145	23,246	76.8%	7,851	18,379	134.1%
22-35	90,356	193,078	113.7%	64,110	113,244	76.6%	26,246	79,834	204.2%
36-50	70,203	147,184	109.7%	42,654	79,709	86.9%	27,549	67,475	144.9%
51-64	57,295	124,418	117.2%	32,098	66,615	107.5%	25,197	57,803	129.4%
65 +	47,625	38,660	-18.8%	31,660	25,823	-18.4%	15,965	12,837	-19.6%
RACE/ETHNICITY									
Black or African-American	26,063	33,276	27.7%	14,198	17,100	20.4%	11,865	16,176	36.3%
American Indian or Alaska Native	11,927	15,736	31.9%	6,782	8,724	28.6%	5,145	7,012	36.3%
Asian, Native Hawaiian/ Pacific Islander	23,430	30,549	30.4%	13,308	16,903	27.0%	10,122	13,646	34.8%
Non-Hispanic White	405,897	581,103	43.2%	227,834	315,132	38.3%	178,063	265,971	49.4%
Hispanic or Latino	146,442	192,173	31.2%	78,727	99,282	26.1%	67,715	92,891	37.2%
Other/Unknown/Missing	45,355	118,258	160.7%	24,947	59,777	139.6%	20,408	58,481	186.6%

[1] *Data Source: Oregon Health Authority, Office of Health Analytics: DSSURS warehouse; 150M database.*

FIGURE 1: Changes in Colorectal Cancer Screening Rate by Coordinated Care Organization, Comparing 2011 to 2013



Source: Oregon Health Authority Office of Health Analytics

Survey Data

A total of 207 surveys were completed (see Table 2) by healthcare providers (58; 28.6%), community partners (51; 25.1%), CCO leaders (41; 20.2%), Oregon Health Authority staff (31; 15.3%), consumer advocates (18; 8.9%), members of the Metrics and Scoring Committee or of the Technical Advisory Workgroup (18; 8.9%), and other stakeholders (82; 40.4%) (respondents could select more than one stakeholder category).

The majority (70%) of respondents supported maintaining colorectal cancer screening as an incentivized metric in 2015, and the remaining 30% wanted to drop or modify the measure, citing concerns that the measurement approach was difficult or problematic. Among those who supported dropping or modifying the measure, most preferred to align the reporting requirements with national reporting standards (i.e., HEDIS).

Other concerns were that the measure would result in an under-reporting of colorectal cancer screening, either because successful colonoscopy screening requires a 10-year historical reporting period or because of inconsistent coding of fecal testing in the medical record. One respondent expressed the belief that colonoscopy rates were unlikely to change substantially and that providers held a bias favoring the use of colonoscopy over other tests. Another respondent noted that colorectal cancer screening was a lower priority than other health conditions, and another believed that the measure was more appropriate for individuals covered on Medicare.

Discussion

Over the past five years, changes in federal healthcare policy have influenced who has access to healthcare coverage, what healthcare quality measures are reported to the federal government, and how health systems and plans are incentivized to provide quality care. Several national organizations, such as HRSA and CMS, have emphasized colorectal cancer screening by either incentivizing systems that meet specified screening targets or

TABLE 2: Themes and Illustrative Quotes from Respondents Who Supported Modifying or Dropping the Colorectal Cancer Screening Measure

Theme/Subtheme	Illustrative Quote
Need to align reporting format to a national standard	*This is a very difficult measure to track and should be in line with national reporting standards.*
10-year look back for colonoscopy receipt is problematic	*The number of years necessary for an appropriate look-back for this metric (according to HEDIS) makes data difficult to accurately obtain in this population.*
May result in over-screening due to lack of colonoscopy data	*This measure . . . promotes over-screening. This measure should be modified to better account for members with a full colonoscopy that do not need a test each year.*
Fecal tests are not consistently coded/billed and likely under-reported	*. . . numerous folks get screened by FOBT [fecal occult blood test] and are probably improperly billed and coded to count.*
Bias toward colonoscopy; rates of colonoscopy screening are difficult to change	*From a resource utilization standpoint, we ought to [focus] on increasing FIT as the screening of choice and to [reserve] colonoscopy for those who fail screening. Unfortunately, we will not be able to convince the medical industry to change its highly profitable focus on colonoscopy, and, therefore we will be unlikely to change this measure.*
Age range overlaps with Medicare; more appropriate for more stable Medicare population	*A plan with more fluctuating population [such as Medicaid] would have less opportunity to provide colorectal cancer screening to its beneficiaries, even though the total member month(s) could be relatively big. And the age range overlaps with Medicare, so it is hard to say this is about Medicaid.*
Colorectal cancer screening is a lower priority than other health conditions	*Testing the feces of every patient who shows up for any health issue is a waste of resources. Most people have a much higher risk of having cardiac disease, hypertension, or diabetes than they do colon cancer.*

requiring that it be reported. This emphasis is driven by the fact that colorectal cancer screening rates are lower than they are for other screen-preventable cancers, and that screening is shown to substantially reduce mortality from the disease.

This paper describes Oregon's experience in including colorectal cancer screening as an incentivized measure since 2012, with incentive payments provided to CCOs that demonstrated at least a 3% improvement in screening rates between 2011 and 2013.

Nationally and in the state of Oregon, the Medicaid program has seen a shift in demographics. We observed a 55% increase in the number of Medicaid-enrolled individuals in Oregon who are age-eligible for colorectal cancer screening—104,920 in December 2013 to 163,078 in June 2014—suggesting that such measures may increasingly become relevant for Medicaid programs.

Six of the 15 CCOs met the improvement target for colorectal cancer screening in 2013, and performance was mixed for the others. These findings might be related to the fact that Oregon used a nonstandard method of calculating rates of colorectal cancer screening in 2013, relying only on documented claims for screening that occurred that year. As a result, colonoscopies done in prior years (resulting in a patient being up-to-date) would not be counted. The conversion of the metric to the HEDIS hybrid measure specifications for 2014 will likely ameliorate this issue.

Findings from surveys conducted with stakeholders revealed overwhelming support for keeping colorectal cancer screening as an incentivized measure. A minority who advocated for dropping or modifying it suggested aligning it with national reporting standards (such as HEDIS), confirming the Metrics and Scoring Committee's decision to do so. Some respondents noted a reliance on colonoscopy screening and concerns that colonoscopy rates are slow to change.

The perception that colonoscopy is the "best test" or "community standard" is consistent with data from Zapka et al., who surveyed 1,266 providers in the U.S. and reported that 86% strongly agreed that colonoscopy was the best of the available colorectal cancer screening tests; yet only 69% thought it was readily available for their patients.[8] Such bias persists in spite of documented reductions in late-stage cancer detection with programs that promote fecal testing for first-line screening.[9]

Other respondents perceived that colorectal cancer screening was a lower priority than other health conditions, and thought the 10-year period for capturing historical colonoscopy would lead to under-reporting.

Oregon is the only state known to us that has included colorectal cancer screening as an incentivized quality metric for the state's Medicaid program. This action, combined with changes in federal reporting requirements for achieving benchmarks for colorectal cancer screening and dramatic increases in insured populations, represents the external context that can push health systems to document that screening is occurring and to deliver more screening to more eligible individuals.

Such is the environment in which the Strategies and Opportunities to Stop Colon Cancer in Priority Populations (STOP Colorectal Cancer) study is being tested. STOP is a large-scale pragmatic study focused on raising rates of colorectal cancer screening in federally qualified health centers. The project's primary evaluation involved 26 clinics in Oregon and Northern California.[7]

Conclusion

With increasing proportions of adults enrolling in Medicaid programs nationwide, inclusion of colorectal cancer screening as a quality metric may present a unique opportunity to raise rates in a historically underserved segment of our population.

Acknowledgments

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Gloria D. Coronado, PhD, is an investigator at the Center for Health Research, Kaiser Permanente Northwest, Portland, Ore.

Amanda F. Petrik, MS, (amanda.f.petrik@kpchr.org) is a research associate III at the Center for Health Research, Kaiser Permanente Northwest, Portland, Ore.

Sarah E. Bartelmann, MPH, is a policy analyst for the Oregon Health Authority, Salem, Ore.

Lori A. Coyner, MA, is director of the Office of Health Analytics at the Oregon Health Authority, Salem, Ore.

Jennifer Coury, MA, is a research associate II at the Center for Health Research, Kaiser Permanente Northwest, Portland, Ore.

Jeff Kingsley, DO, MBA, MS, CPI, FAAFP

One Word and One World of Difference

Extra! Extra! Read all about it... "Certified **Physician** Investigator" becomes "Certified **Principal** Investigator"!

If you have not heard yet, ACRP's affiliate body for certification programs, the Academy of Clinical Research Professionals, has announced a dramatic change in the CPI® qualifications. Those initials, which formerly stood for Certified Physician Investigator, now stand for Certified Principal Investigator. The significance of this change is that one no longer must be a physician to apply for CPI certification. I've run into a decent number of physicians who feel slighted by that.

Sitting for the CPI exam is now an opportunity open to all principal investigators (PIs), as opposed to only physician investigators.

The CPI certification issued by the Academy will continue to be an accredited certification in the U.S., and will continue to require several years of prior experience in clinical research. It also will continue to be a rigorous, competency-based exam, which then requires continuing education for maintenance of certification.

What has changed, however, is that sitting for the CPI exam is now an opportunity open to all principal investigators (PIs), as opposed to only physician investigators. This reflects the fact that an immense amount of medical and clinical research going on in the world is conducted by doctors who are not physicians, such as PhDs, PharmDs, DMDs, DPMs, and AuDs. Additionally, the questions within the CPI exam were never structured to be answerable only by a physician.

I'm personal friends with numerous doctoral-level individuals actively conducting research, but who are not physicians. Despite having impressive CVs and taking on all of the responsibilities mandated by the Food and Drug Administration Form 1572, they have been excluded from attaining any research certification as an investigator.

What is curious about some physicians' concern about "letting others in" is that many doctoral-level designations mandate research as part of their doctoral degrees. Earning your PhD, for example, requires that you design, conduct, analyze, present, and defend novel research. That's not the case for physicians. Most physicians practice a brand of medicine best characterized by linear algorithmic thinking ("If this, then that"); when they veer from a guideline algorithm, it's to insert some anecdotal medicine with no scientific underpinning.

So I don't feel slighted by the new inclusiveness that the Academy and ACRP have adopted. I feel proud to be a member of an exclusive club—not a club of physicians, but a club of scientists—a club of principal investigators whose members must think scientifically about the patient in front of them and all the various treatment options, both in the standard of care and in the realm of research.

For medical PIs, this includes understanding class effects from the chemical class the investigational product is in, and considering a patient's own medical conditions to determine probabilities of causality in assessing adverse events (AEs). For audiology and dental PIs, considerations are often the same as those experienced in medical device trials, where a deep understanding is needed of what devices are available, how they work, and where the treatment gaps exist. For behavioral science PIs, data considerations include understanding how treatment modalities affect behavioral change, and considering how a patient's comorbid conditions affect treatment results and AE causalities.

You see? Principal investigators are cool; cooler than ordinary physicians and practitioners. So I'm proud to be a CPI—a Certified Principal Investigator. (I also happen to be a physician.)

Jeff Kingsley, DO, MBA, MS, CPI, FAAFP, (jeffkingsley@serrg.com) is chief executive officer of the Southeast Regional Research Group in Savannah, Ga., and is treasurer of the ACRP Board of Trustees.

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- ✓ Employ trial-specific analytical techniques to handle missing data
- ✓ Explore best practices for increasing participant retention and compliance

A successful clinical trial greatly depends on high-quality, accurate data. However, incomplete data points do occur. This can significantly compromise all areas of the research, from key inferences made to regulatory compliance. When clinical trials increase in complexity and scope, this problem becomes magnified. Recent studies have shown that data reanalysis changes roughly 35% of trial conclusions, which can have a negative effect on drug approval.

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Ronald S. Waife

HONESTY is the Only Policy

When was the last time you told someone the whole truth? When was the last time you thought someone was telling you the whole truth? Have you told that underperforming monitor he is, in fact, underperforming? Did you tell your sponsor about the problems you had with that investigative site? Did you tell your customer about the true delivery date for the next software release? Did you tell your staff how big a bonus you earned from their long hours or work?

These are all examples of how, every day, we treat each other dishonestly. You can argue that these "white lies" make work easier, but I would argue they strongly contribute to the highly inefficient state of clinical research. Honesty isn't the best policy; it's the only policy.

Mistrust and passivity can be the direct byproducts of a failure of honesty.

The Ubiquitous White Lie

Let me emphasize from the start that when I discuss "dishonesty" in this column I am not talking about criminal behaviors—dishonest handling of trial data, noncompliance with regulations, cutting corners in analytical rigor, insider trading, and so on. I've never seen them, and they are not my point. I'm talking about "process dishonesty"—dishonesty in the way we treat each other every day.

There are so many examples of dishonesty in everyday research life that any reader can quickly provide his or her own list. Here are just a few:

- Sponsors lie to contract research organizations (CROs) about when the trial will start.
- CROs lie to sponsors about the qualifications of who will work on their trial.
- Clinicians lie when they say, "This is the final protocol."
- Quality assurance staff are often lying when they say, "The Food and Drug Administration requires this."
- Every department lies to its fellow departments when setting deadlines, knowing the deadlines will be missed and leaving room to maneuver.
- Sponsors lie to their own staff about plans for job elimination or outsourcing.
- Consultants lie when they tell clients what they want to hear, instead of what they found.
- Sponsors lie when they tell consultants they want help with "x," when they actually want justification for "y."
- Upper management lies when they tell their direct reports how much money is in the budget for next year, and their direct reports lie about how much money they need.

So, okay, this is hardly unique to clinical research; it's universal and as old as time. It has survived as standard business practice for so long because it doesn't seem to matter. However, I suggest it does matter—a lot—not just on ethical grounds, but to sponsors who are trying to change their approach to research and make the development of new therapies a faster and less costly process.

Inefficient Dishonesty

How does all this hurt clinical development, if it is such a standard business practice? Dishonesty and efficiency don't mix:

- If you put somebody on a team because you have to, instead of because he or she is qualified, that leads to inefficiency.
- If you can't tell someone he or she is not good enough at the job, you're employing inefficiency.
- If you avoid the opportunity to provide constructive criticism, that's permitting inefficiency.
- If requestor and bidder play a game of "chicken" when negotiating a budget, resulting in weeks of delay in the name of "best practice contracting" or Sarbanes-Oxley, the only best practice being done is expert time-wasting.
- We all know the truism that it takes three times, or 10 times, more resources to fix a problem downstream rather than when it happens, but because being honest upfront is not safe, we'd rather "kick the can down the road," wasting more time.
- You will not have a chance to really know if your in-house staff has the ideas, skills, and flexibility to perform better if you don't tell them that their performance issues are so dire that you've already decided to outsource their jobs.

White lies are so ingrained, they are second nature. We congratulate ourselves for avoiding confrontation, which usually means we avoided the truth. The financial, personal, and professional pressures to bypass hard truths are all too real and way too strong. Our slippery sidesteps are all too understandable; yet if we start to believe our own white lies, no one can save us from ourselves.

Mistrust and Passivity as Symptoms

Our problem with honesty in the research process creates deeper and more subtle negative effects. Mistrust and passivity can be the direct byproducts of a failure of honesty; indeed, they contribute to dishonesty in a nasty feedback loop.

We mistrust our CROs, and they mistrust their customers because disinformation has become the mode of communication. Our staff mistrust our managers when outsourcing or acquisitions are announced out of the blue. Further, nobody believes the software vendor's delivery date, or the first specifications of a protocol, because it is not acceptable for us to acknowledge unpredictability or unreasonable deadlines.

Passivity is a cousin of mistrust and dishonesty. If I don't trust you, and I've learned to speak in white lies, my best course of action is to lay low, do only as I'm told, and otherwise stay passive. No wonder research executives today decry the rampant lack of urgency and energy in their organizations!

Getting to Honest

Diogenes is described as searching with his lamp high and low in ancient Athens, in vain, for an honest man. Diogenes was also a philosopher of Cynicism, whose modern meaning may be too harsh and excessively pessimistic for this topic. The good news is that, not only can we find honest people, we can make them.

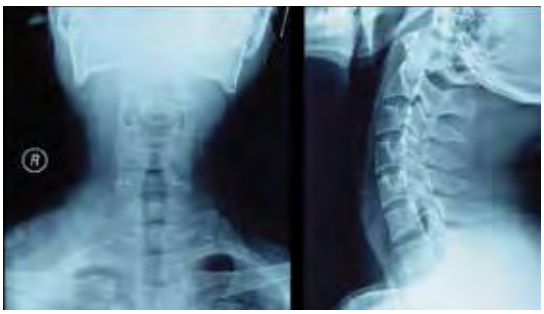
How do we get more honest in our treatment of each other?

- **Make it safe** to be honest. Few of us think we can be honest with our bosses, staff, providers, or customers without negative consequences. We need to make honesty permissible and desirable.
- **Make it a cultural imperative.** We should not only make it safe to be honest; we need to recognize it as a necessity for our organizations' efficiency, productivity, and respect.
- **Educate each other** about our jobs or "walk a mile in their shoes." The more we understand the work, motivations, potential, and limitations of the work of others, the more we will understand and accept honestly delivered information, and the more honest we can be in our own communication.
- **Demonstrate and model** honesty in our own behaviors. We've described how this can be risky: Who's going to go first? I don't think we can wait for the other guy to blink. Instead, we need the courage to trust and respect other enough to treat one another with honesty and bear the consequences. In time, we can start a safe and productive feedback loop.

I think I hear the Golden Rule echoing nearby.

The good news is that, not only can we find honest people, we can make them.

Ronald S. Waife (ronwaife@waife.com) is president of Waife & Associates, Inc. (www.waife.com).



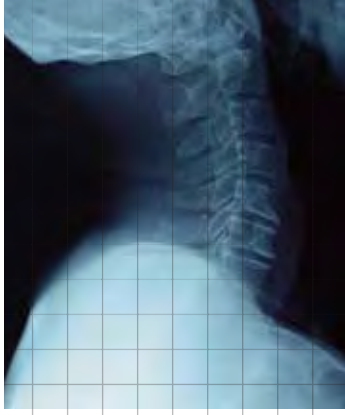
QUALITY Measures and Efforts in Head and Neck Cancer Care

PEER REVIEWED
Farhan S. Huq, MD, MS
Christine C. Johnson, MPH, PhD
Steven S. Chang, MD
[DOI: 10.14524/CR-14-0049]

An often cited and influential Institute of Medicine report entitled "Crossing the Quality Chasm" succinctly describes quality, patient-centric care as having six key attributes:[1]

- **Safe** care implies avoidance of patient injury;
- **Effective** care is two-pronged: services should be based on scientific knowledge and administered to those it may benefit, and withheld from those not likely to benefit;
- **Patient-centered** care is driven by patient values in all clinical decision making, leading to care tailored to patient preferences, needs, and values;
- **Timely** care means minimizing delays for both patients and providers;
- **Efficient** care curtails waste of time, equipment, supplies, money, ideas, and energy; and
- **Equitable** care assures quality is not altered by any personal characteristic, including age, gender, sexual orientation, socioeconomic status, ethnicity, and geographic location.

Some efforts already under way focus on streamlining healthcare infrastructure, which encompasses attention paid to physician coverage and institution of preoperative optimization clinics and patient support groups.



The U.S. Agency for Healthcare Research and Quality (AHRQ) summarizes this tersely, by noting that quality care involves "doing the right thing, at the right time, in the right way, for the right person—and having the best possible results."[2]

Quality in head and neck cancer care is assessed using both qualitative and quantitative measures. Traditionally, overall survival and disease-free survival have been assessed for several decades in head and neck cancer patients as the only measures of quality. However, in the early 1990s, a movement to include quality of life as a measure of quality treatment began. Newer treatments were effecting little improvement in survival, but significant gains were made in quality of life after treatment. For instance, the concept of "laryngectomy free survival" was established after chemoradiation of laryngeal cancers was shown to be equivalent to surgical treatment of laryngeal cancer in patient survival[3]; yet, with the nonsurgical approach, the larynx was preserved.

Considering Quality of Life

Quality of life is essential in the treatment of head and neck cancers because of the importance of the five senses affected, as well as the cosmetic and structural sequelae of treatment.

Precise quantification and validation in quality of life, which may be separated into physiologic, functional, and psychosocial, are now incorporated into all major clinical trials. Physiologic quality of life refers to the ability to breathe, speak, chew, salivate, and swallow, as well as use the senses, including sense of taste, smell, and hearing. Functional and performance quality of life refers to the impact on activities of daily living and work. Psychosocial quality of life integrates the impact of appearance, mental well-being, and social environment. Whether directly or indirectly, treatment algorithms all incorporate these factors. Although more nuanced than classical measures, monitoring, studying, and improving upon these are vital.

Quality-of-life indicators may be clinically assessed by the practitioner or derived from patient-reported data. The National Comprehensive Cancer Network (NCCN) guidelines state that the three validated and accepted measures for head and neck cancer issues are the University of Washington Quality of Life scale (UW-QOL), the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-HN35), and the Functional Assessment of Cancer Therapy Head and Neck module (FACT-H&N).[4]

Other Sources of Input

The Performance Status Scale is a clinician-rated performance scale widely used for patients with head and neck cancers.[4] Utility of patient-reported outcomes is limited by patient effort and capacity. In addition, patients require an investment of more up-front counseling to use the tools correctly.

Administration of questionnaires adds a burden to clinical resources. Inherently, patient-reported outcomes based on the Likert scale are more subjective, as opposed to practitioner-derived metrics. Despite their drawbacks, patient-reported outcomes allow patients to be more proactive in their care. Both physician- and patient-reported outcomes are tremendously useful and can serve as adjuncts in monitoring quality of care.

Meanwhile, third-party hospital ranking systems have become increasingly used by patients for healthcare decisions. The annual *U.S. News & World Report* rankings are a source of well-known, publicly accessible, hospital- and specialty-specific rankings.[5] Hospitals are scored in reputation, with 200 randomly selected specialists (weighted as 27.5% of the score), patient survival within 30 days of inpatient admission (32.5% of the score), and patient safety (10%).

The remaining factors, including patient volume, nursing intensity (number), nursing magnet recognition, advanced technologies (such as stereotactic radiosurgery), patient services (including programs such as genetic testing and counseling and patient-controlled analgesia), trauma center availability, and having an intensivist on staff, together comprise 30% of the score. All variables are combined into a composite score out of 100 and then are compared to other hospitals.

One of the major criticisms of the *U.S. News & World Report* rankings has been the reliance on reputation, implying that the scores are not sufficiently indicative of the remaining objective measures of quality. Although subjective, reputation alone coincides with the top-ranked hospital in each adult specialty 100% of the time.[6]

The Spearman correlation coefficients from specialty-specific multilinear regression of rankings with objective measures range from less than 0.01 to 0.43.[6] The scores also correlate with academic research productivity,[7] which is expected, given the close interplay of national recognition, reputation, and research standing. The ranking scheme could be made more useful if quality and outcomes were more strongly linked to higher hospital scores and rankings.

Quality of life is essential in the treatment of head and neck cancers because of the importance of the five senses affected, as well as the cosmetic and structural sequelae of treatment.

Is a Satisfied Patient a Quality Recipient?

Patient satisfaction is a major component of the quality discourse. One tool for its measurement is the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS), a standardized survey jointly developed by the Centers for Medicare & Medicaid Services (CMS) and the AHRQ.

HCAHPS is composed of 27 questions addressing such issues as communication with doctors and nurses, responsiveness of hospital staff, cleanliness and quietness of the hospital environment, details of pain management, communication about medicines, discharge information, overall rating of hospital, and recommendation of hospital. Pay-for-performance measures, part of the Physician Quality Reporting System (PQRS) from the Affordable Care Act (ACA), dictate that 30% of the score be derived from patient satisfaction and 25% from mortality rates, underscoring the significance of patient satisfaction.[8]

PQRS had been an optional part of the process since 2007, but will be mandated in 2015 as part of ACA. Under the PQRS, physicians who fail to report quality measures can be penalized 1.5% to 2.0% of their total estimated Medicare Part B Physician Fee Schedule.[8,9] Thus, they must be not only ethically and morally responsible to heed HCAHPS, but also prudent financially.

Patient satisfaction, however, is not infallible. Despite higher patient satisfaction correlating with better therapy compliance,[10] patient satisfaction may be tied to overuse of healthcare resources and increased healthcare spending, and correlation with improved clinical outcome is not guaranteed.[10,11]

Clinicians report their own scores fluctuating widely from one extreme to another over a matter of days, possibly weighted by outliers of patients with overwhelmingly positive or negative experiences. Satisfaction scores must be carefully culled and thoroughly analyzed to construct productive information.

Some patients are better at providing feedback than others. Perhaps, as opposed to a random (or biased) selection of reported scores, advisory councils of several patients can allow for constructive feedback. This would validate certain patient concerns, allay others, and pool voices to a unified consensus upon which a practitioner would have more of a foundation to act.

Patient advisory councils are groups of patients, family members, caregivers, and facilitators meeting regularly to improve care. Together, they might provide valuable feedback on issues ranging from clinic flow and parking to research design. Historically, these advisory councils were borne from a desire to make increasingly patient-centric care in children's hospitals.

Several benefits and drawbacks exist for these councils. Given the nonrandom selection process council members undergo, selection bias is possible; diverse perspectives must be sought to represent the populations served.

In our practice, oversight of the advisory council is separate from the clinical practice, to maintain independence. Disseminating and implementing change from these councils usually falls to hospital leadership.

Since a healthy volunteer base is necessary to implement and sustain an advisory council, appreciation of member work is paramount. Widely sharing successes resulting from council efforts can go a long way in fostering passion and motivation. Work remains in fine-tuning and validating emerging advisory council outcomes.

Follow the Evidence

Evidence-based medicine is instrumental in quality care. It results in better survival,[12–16] wound healing,[17,18] infection control,[15,19,20] respiration,[12,21,22] tobacco-cessation rates,[23] pain control, sleep, mental health,[18,24–26] and fewer disease recurrences and exacerbations,[21] postoperative complications,[16,27] repeat visits,[21] and shorter hospital and intensive care unit (ICU) stays.[15,16,20,28] As an example, after implementing evidence-based guidelines, 85 ICUs eliminated central line infections.[29,30]

In oncology, to deliver on the ideal of safe and effective care, the NCCN, representing aggregate effort from medical oncology, surgical oncology, and radiation oncology, critically examined, appraised, and synthesized evidence-based guidelines from more than 400 studies.[4,10] These guidelines are uniquely important to the care of the head and neck cancer patient.

Contemporary head and neck oncological care is complex. Significant coordination of cancer care and rehabilitation is required for optimal outcomes for patients. Although early-stage disease typically requires single-modality treatment in 30–40% of care, combined modality therapy is indicated for the remaining 60–70% of patients presenting with locally or regionally advanced disease.[4] For advanced-stage disease, participation in clinical trials is often preferred or recommended.

High-quality head and neck cancer care includes rehabilitation and preventive care. This includes counseling on tobacco cessation and excessive alcohol consumption, adequate nutritional support, and distress screening for depression.[4]

Strict adherence to guidelines has been shown to both increase effectiveness and reduce costs. Multiple studies evaluating clinical "pathways" adhering to evidence-based guidelines—in which timing and coordination of essential interventions

Addressing noncompliance reflects a marked potential for improvement in quality of cancer care, being mindful of the substantial cost and increased morbidity and mortality that these patients experience.

by multiple care disciplines aimed to minimize delays, omissions, and duplications—found cost reductions, reduction in patients' length of stay, and trends suggesting decreased postoperative complications such as pneumonia, DVT, pressure ulcers, malnutrition, and readmission rates.[31] This may cause higher patient satisfaction.[31]

In a prospective evaluation of a clinical pathway in patients undergoing microvascular reconstruction for head and neck oncologic surgery, initiating the clinical pathway reduced mean costs from $22,733 to $16,564 per patient.[31] Foreseeably, this principle of streamlining utilization and automation of electronic medical records more broadly will pay dividends in cost-effectiveness.

All About Adherence

Studies on adherence to NCCN guidelines are limited. Repeated assessment of adherence is necessary because the guidelines serve as a foundation for physician practice quality measures and medical economics.

Approximately one-third of healthcare expenditures in head and neck cancers are related to inappropriate initial therapy.[2] Lewis et al. evaluated compliance with NCCN guidelines in 107 patients and found that inadequate surgery was the predominant factor, comprising 43% of noncompliance, followed by misdiagnosis (15.2%), inadequate adjuvant surgery (10.9%), patient refusal of recommended treatment (10.9%), and inadequate radiation therapy (4.4%).[32] Noncompliance was found in 43% of patients referred for persistent or recurrent disease.[32]

Addressing noncompliance reflects a marked potential for improvement in quality of cancer care, being mindful of the substantial cost and increased morbidity and mortality that these patients experience. Underscoring the importance of right treatment at the right time for the right patients, recurrent aerodigestive tract cancers have an average survival rate of 39%.[33] In tongue cancer, Weber et al. studied 116 T1-2 and N0-1 patients and found 90.5% compliance with TNM staging (tumor, nodes, metastasis) for classification of malignant tumors at presentation, 99.1% for documentation of margin status, 98.2% for adequate referral to radiation therapy, and 88.7% for neck dissection based on depth of invasion.[34]

Regarding Risk Factors and Uncertainties

To help deliver more effective, anticipatory care, careful documentation of the comorbidities associated with encounters is important. Recently, Nussenbaum et al. investigated risk factors for unplanned readmission following total laryngectomy, a procedure that has a fivefold higher risk of 30-day readmission

Guidelines for Levels and Categories of Evidence

To avoid ambiguity, areas of uncertainties or disagreements among committees generating practice guidelines can be added in supplemental areas, as footnotes, or color-coded so that they can be readily made available. As of July 2012, the U.S. Preventative Services Task Force (USPSTF) has a grading scheme for guidelines into A, B, C, D, or I classifications, as well as levels of certainty into high, moderate, or low classifications.

Creating guidelines that both embrace uncertainty and avoiding ambiguity to increase adherence is a fine balancing act.

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

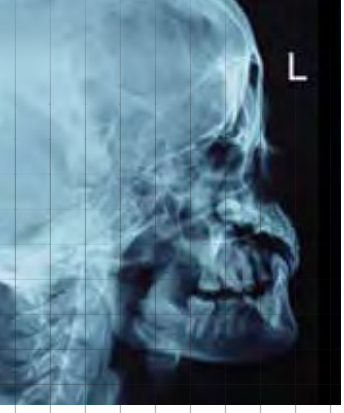
Level of Certainty—The USPSTF defines certainty as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

- **High—**The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
- **Moderate—**The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as:
  - The number, size, or quality of individual studies.
  - Inconsistency of findings across individual studies.
  - Limited generalizability of findings to routine primary care practice.
  - Lack of coherence in the chain of evidence.

  As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
- **Low—**The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of:
  - The limited number or size of studies.
  - Important flaws in study design or methods.
  - Inconsistency of findings across individual studies.
  - Gaps in the chain of evidence.
  - Findings not generalizable to routine primary care practice.
  - Lack of information on important health outcomes.

  More information may allow estimation of effects on health outcomes.

Adapted from U.S. Preventative Services Task Force: Grade Definitions. Accessed December 2014 from www.uspreventiveservicestaskforce.org/Page/Name/gradedefinitions#ast.



compared to general otolaryngology (40% vs. 7.3%).[35] Risk factors included post-operative complications after discharge (OR, 11.50), visit to the emergency department within 30 days after discharge (OR, 5.25), salvage total laryngectomy (OR, 3.52), and chyle fistula during the index hospitalization (OR, 5.25).[35] As time progresses, similar risk profiles by tumor stage, anatomic location, and treatment modality can be constructed and tailored to fit the individual patient.

The scientific process followed to create the guidelines must also be a target for refinement. One venue of change is increasing the transparency in uncertainty. Guideline-authoring committees are known to occasionally have disagreements or uncertainties regarding a decision, but rarely incorporate these into the final guideline document. This gives an illusion that uncertainty or disagreement did not occur.[36,37]

Rather than shying away from uncertainty, it should be acknowledged and embraced, as it can guide future investigation. Guidelines should clearly include the level of evidence and the categories of evidence (see the sidebar on preceding page for an explanation of how this works).

What's Trending

Some efforts already under way focus on streamlining healthcare infrastructure, which encompasses attention paid to physician coverage and institution of preoperative optimization clinics and patient support groups. Reorganization of staff coverage on inpatient duties, such as with dedicated rotating hospitalists, allows caregivers to focus their attention without negatively affecting revenue.[38] Also, patients can convene to offer unified recommendations to their healthcare providers. Head and neck cancer survivorship meetings, for example, are gaining wider adoption, which can fortify the structure of social support, improve psychological outcomes, and help set more realistic expectations.[39]

Enhanced education of practitioners and patients is an excellent, cost-effective mechanism for augmenting quality. One avenue to this ideal would be to take advantage of technological and telecommunication advancements. A cursory website search reveals advancements such as 3D printing, streaming videos, podcasts, smartphone applications, and eBooks, all rare in the average healthcare setting.

However, to an increasingly tech-savvy patient population, the potential is tremendous. Use of telemedicine, such as smartphone videoconferencing or multimedia messaging, adds a dimension of real-time visual communication that can supplement communication between care providers and their patients, a heavily emphasized area of patient satisfaction in HCAHPS. This would also improve patient understanding and compliance.

Simultaneously, for researchers, secure Internet data collection that would centralize information on head and neck cancer patients could greatly facilitate and improve cancer care databases.[10]

Patients without access to technology must not be neglected; they should be offered public health seminars, lectures, and/or expert panels. Pamphlets and brochures with rich infographics and diagrams can serve as adjuncts.

On the other side of the equation, practitioners need education, too. Studies evaluated surgeons' comfort levels with the terms "odds ratio," "number needed to treat/harm," "meta-analysis," and "confidence interval." Less than half of the respondents reported that they understood and could explain these terms to others, except for the term "meta-analysis," which slightly more than half of the respondents understood well.[40]

Helping healthcare providers to build facility with and a deeper understanding of evidence-based medicine is just one area in which quality in healthcare can be fostered.

Conclusion

We have embarked upon a transformative era in research and healthcare. Quality measures and efforts in research and care delivery are complex and evolving fields. We are tasked with doing more and knowing more in the right setting, while using less time, energy, and resources—all under conditions of scrutiny higher than our predecessors.

Change should be undertaken in a systematic, yet thoughtful way; it must be statistically robust and scientifically valid, timely, lucid, convenient, unobtrusive, cost-effective, and actionable.

The recipe for quality in healthcare has many ingredients; improvements in the scientific basis and validity of guidelines, and adherence to those guidelines, are just a few contributors to the final meal. Another layer of complexity lies in disseminating the knowledge in a clear, unobtrusive way, and promoting both acceptance and understanding of evidence-based medicine. Add in the ingredients of optimizing healthcare and educational infrastructure and delivery, better use of technology, and augmented, yet more meaningful patient involvement, and a more responsive, safe, effective, patient-centered, timely, efficient, and equitable healthcare system will result.

Several lofty goals lie ahead, but we owe ourselves and our patients nothing less than to work diligently toward them.

We are tasked with doing more and knowing more in the right setting, while using less time, energy, and resources—all under conditions of scrutiny higher than our predecessors.

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Farhan S. Huq, MD, MS, (fhuq1@hfhs.org) is resident physician in the Department of Otolaryngology—Head and Neck Surgery, Henry Ford Hospital, Detroit, Mich.

Christine C. Johnson, MPH, PhD, is the chair of the Department of Public Health Sciences, Henry Ford Hospital, Detroit, Mich.

Steven S. Chang, MD, is a physician in the Department of Otolaryngology—Head and Neck Surgery, Division of Head and Neck Oncologic Surgery, Henry Ford Hospital, Detroit, Mich.

Margo Michaels, MPH

How Well Can You or Your Staff Answer Difficult Questions During the Consent Process?

Whether just beginning the consent process or being already well down the path, research participants and their families share several common concerns. As research professionals, we may know what the answers to most questions should be, but we don't always know how to respond in concise and clear ways. For example, one of the most memorable training programs I attended was one in which an experienced research nurse became flustered in explaining a clinical trial to a patient during a role play.

Review the nine questions below and the details that follow them for guidance on how you can respond to concerns and confusion, using easy-to-understand language.

Question 1: What is a clinical trial?

- A clinical trial is a research study with people that helps improve knowledge about ways to prevent, find, or treat diseases or conditions.
- There are many kinds of research studies—those for people dealing with a condition/disease, and studies for people that want to prevent a condition/disease.

For people currently needing treatment for a disease or condition	For healthy people or people with a disease or condition in their families
• Treatment	• Prevention
• Genetics	• Screening and Early Detection
• Quality-of-Life/Supportive Care	• Diagnostic
	• Genetics

Question 2: Aren't people who join research studies just "guinea pigs"?

- Everyone who participates in research studies has rights protected under the law. As part of informed consent, a person has the right to know everything that is going to happen in a study before agreeing to participate. He/she may leave a study at any time and for any reason.
- If someone is participating in a treatment study, he/she always receives appropriate treatment. (Note: The word "appropriate" is purposefully used here.)
- Placebos, "sugar pills," or fake medicine can be used in certain types of research studies (will be used in this study), but no one is ever given fake medicine instead of appropriate treatment.
- All participants are told if the possibility of being selected randomly to receive a placebo is part of the research design before they decide to join a clinical study.

Question 3: Why should someone join a research study, if studies only benefit people in the future?

- Although the overall purpose of a research study is to answer a research question, people can and do benefit themselves from participating.
  - » Clinical trials provide high quality of care for patients. Many experts believe that therapies offered through clinical trials should be considered the preferred treatment choice for many diseases and conditions.

For more information on topics related to this column, please visit the ACRP Clinical Trials Recruitment Interest Group online at www.acrpnet.org/Interest-Groups/Clinical-Trials-Recruitment-.aspx.

- Clinical trials provide careful medical attention to patients. This extra time allows many patients to learn more about their disease/condition.
- Patients participating in trials can have access to promising new approaches to care that may not be available outside a trial.

- For any research study, many participants feel good about providing information that can help their family or their community in the future.

Question 4: Is participating in a research study a "last resort" for someone who has (xxx)?

- No. Taking part in a research study is not limited to people who have no other care options left. Often, receiving treatment through a clinical trial or research study can be the first treatment people receive for their condition/disease.
- Research studies are also available for healthy volunteers that look at ways to prevent, detect, or better understand the risk of a condition/disease.

Question 5: In some research studies, people are placed into different groups. Why can't people choose which group they get assigned to?

- Research studies are done to learn if a new way of preventing, finding, or treating a condition/disease is safe and more effective than what is used today. If it was known ahead of time which treatment worked best, it would not be necessary to do the study.
- By giving people an equal chance to be assigned to any group in a study, we can ensure that people in all groups are similar and comparable. Each person has a fair and equal chance of receiving the new medicine/approach being studied or receiving commonly accepted care.

Question 6: What happens if someone wants to stop participating in a research study?

- People may always leave a research study at any time and for any reason.

Question 7: Do people have to pay to be part of a research study?

- The short answer is—it depends.
- Some studies are free for participants. Costs are paid for by the group doing the study.
- Some studies may have costs for participants, and sometimes this is paid for by insurance.
- What's important to know is that participating in health research does not guarantee free medical treatment and care, and there may be limitations on what costs are covered.
- Before deciding to participate in a research study, people must understand what their costs will be.

Question 8: Can a person be put in a research study without his or her knowledge?

- No. The law requires that the people in charge of the study explain all information about it, so that people can make an informed decision about participating. This is called informed consent.
- Informed consent is a process by which the research team explains in clear and understandable language the purpose of the study, what will happen during the study, the study's potential risks and benefits, and the fact that participants may leave the study at any time.
- The informed consent process ends with an individual either turning down the opportunity to join a study, or signing a written document stating that he or she entered the study of his or her own free will, without being pressured, and that he or she has full knowledge and understanding of the study risks and possible benefits.

Question 9: Why are there restrictions about who can join each study?

- Research is done using strict guidelines to protect each patient's safety, while allowing researchers to answer the question being studied.
- Some people have other health problems that could be made worse by the treatment offered in a study, and therefore would be excluded from participating.
- Some things that might restrict someone from participating in a research study may be someone's age, gender, exposure to other ongoing or prior treatments, and/or experience with other medical conditions.

For any research study, many participants feel good about providing information that can help their family or their community in the future.

Margo Michaels, MPH, (margomichaels@hc-aa.com) was the founder of the Education Network to Advance Cancer Clinical Trials (ENACCT), and now is a consultant developing patient-centered accrual programs.

RESEARCH COMPLIANCE
Brent Ibata, PhD, JD, MPH, RAC, CCRC, CHRC

Limited Datasets and Data Use Agreements

Under regulations promulgated under the Health Insurance Portability and Accountability Act of 1996 (HIPAA), a covered entity may use and disclose a limited dataset for research,[1] public health, or healthcare operations if it obtains an assurance, in the form of a data use agreement, that the recipient will only use and disclose the protected health information for specific, limited purposes.[2]

The Details of De-Identification

A "limited dataset" is protected health information that excludes 16 of the 18 identifiers that make health information protected.[3] The 16 identifiers that must be removed for protected health information to qualify as a limited dataset are:

(i) Names;
(ii) Postal address information, other than town or city, state, and ZIP code;
(iii) Telephone numbers;
(iv) Fax numbers;
(v) Electronic mail addresses;
(vi) Social security numbers;
(vii) Medical record numbers;
(viii) Health plan beneficiary numbers;
(ix) Account numbers;
(x) Certificate/license numbers;
(xi) Vehicle identifiers and serial numbers, including license plate numbers;
(xii) Device identifiers and serial numbers;
(xiii) Web Universal Resource Locators (URLs);
(xiv) Internet Protocol (IP) address numbers;
(xv) Biometric identifiers, including finger and voice prints; and
(xvi) Full face photographic images and any comparable images.[4]

In a limited dataset, the address may include the entire ZIP code, whereas de-identification requires the removal of all but the first three digits of the ZIP code. A limited dataset may retain the elements of dates (including birth date, admission date, discharge date, date of death, and all ages), and may include unique identifying codes (except for those above that must be excluded).

If you have a research compliance issue you would like covered in this column, please send an e-mail to the author at **ibataba@gmail.com**.

Furthermore…

To satisfy the limited dataset regulations, a covered entity must have a written data use agreement with the recipient that contains the following elements:

> (A) Establish the permitted uses and disclosures of such information by the limited dataset recipient, consistent with paragraph (e)(3) of this section [research, public health, or healthcare operations]. The data use agreement may not authorize the limited dataset recipient to use or further disclose the information in a manner that would violate the requirements of this subpart, if done by the covered entity;
>
> (B) Establish who is permitted to use or receive the limited dataset; and
>
> (C) Provide that the limited dataset recipient will:
>
> (1) Not use or further disclose the information other than as permitted by the data use agreement or as otherwise required by law;
>
> (2) Use appropriate safeguards to prevent use or disclosure of the information other than as provided for by the data use agreement;
>
> (3) Report to the covered entity any use or disclosure of the information not provided for by its data use agreement of which it becomes aware;
>
> (4) Ensure that any agents to whom it provides the limited dataset agree to the same restrictions and conditions that apply to the limited dataset recipient with respect to such information; and
>
> (5) Not identify the information or contact the individuals.[5]

Although limited datasets are excepted from the *Code of Federal Regulations'* accounting requirement at 45 CFR 164.528(a)(1)(viii),[6] they are not excepted from the breach notification requirements at 45 CFR 164.400-414.[7] If a covered entity identifies a pattern of activity or practice of a limited dataset that constitutes a breach or violates the data use agreement, it must try to cure the breach or end the violation. If unsuccessful, it must discontinue the disclosure of protected health information to the recipient and report the incident to the Secretary of Health and Human Services.[8]

Conclusion

Protected health information may be used and disclosed with individual authorization, institutional review board (IRB), or privacy board approval. In limited situations, health information may be also used and disclosed preparatory to research (45 CFR 164.512(i)(1)(ii)), when sought for research on decedents (45 CFR 164.512(i)(1)(iii)), and in the limited dataset with a data use agreement (45 CFR 164.514(e)).

A limited dataset cannot include 16 of the 18 HIPAA identifiers, and must be tethered to a written data use agreement that requires that the recipient use appropriate safeguards to prevent unauthorized use or disclosure.

Researchers should know that local rules may require IRB, privacy board, or institutional approval when intending to use a covered entity's patient data in a limited dataset for research.

References

1. "Research" is defined as the systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge (45 CFR 164.501).
2. 45 CFR 164.514(e).
3. 45 CFR 164.514(b)(2)(i).
4. 45 CFR 164.514(e)(2).
5. 45 CFR 164.514(e)(4)(ii).
6. Office for Civil Rights HIPAA FAQ, available at www.hhs.gov/ocr/privacy/hipaa/faq/limited_data_sets/467.html (accessed November 29, 2014)
7. 74 *Fed. Reg.* 42740 (Aug. 24, 2009) at 42746 (codified at 45 CFR 164.402).
8. 45 CFR 164.514(e)(4)(iii).

Brent Ibata, PhD, JD, MPH, RAC, CCRC, CHRC, (ibataba@gmail.com) is the director of operations at the Sentara Cardiovascular Research Institute, teaches for the online Masters of Clinical Research Administration Program through the University of Liverpool and Master of Science in Regulatory Affairs at Northeastern University, is on the faculty of Eastern Virginia Medical School, and is vice chair of the ACRP Board of Trustees.

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Francisco Moncada, R.N., B.S.N., C.C.R.C., President & Director of Clinical Research
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FXM Research Corp.
Hector Wiltz, M.D., C.C.T.I.
(305) 220-5222 Office
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