



Annual Report 2013-2014

Centers for Education and Research on Therapeutics (CERTs) Annual Report

September 1, 2013 – August 31, 2014

Introduction

In October 2011, six research centers and a scientific coordinating center were funded through cooperative agreements with the Agency for Healthcare Research and Quality (AHRQ), extending the Centers for Education and Research on Therapeutics (CERTs) Program for 5 years. This report summarizes the work of the CERTs Program from September 2013 through August 2014. In addition, this report provides background information about the purpose and components of the ongoing CERTs Program.

CERTs Program Purpose

The CERTs Program is a national initiative established in 1999 to conduct research and provide education that advances the optimal use of drugs, medical devices, and biological products, collectively described as “therapeutics.” The CERTs Program has three major aims, as established by Congress:

1. **To increase awareness** of the uses and risks of new drugs and drug combinations, biological products, and devices, as well as of mechanisms to improve their safe and effective use.
2. **To provide objective clinical information** to patients and consumers; health care providers; pharmacists, pharmacy benefit managers, and purchasers; health maintenance organizations (HMOs) and health care delivery systems; insurers; and government agencies.
3. **To improve quality while reducing the cost of care** by increasing the appropriate use of drugs, biological products, and devices and by preventing their adverse effects and consequences of these effects (such as unnecessary hospitalizations).

The CERTs are also authorized to conduct research on the comparative effectiveness, cost-effectiveness, and safety of therapeutics.

CERTs Program Components

In addition to the AHRQ-funded research centers and a scientific coordinating center (the **Scientific Forum**), the CERTs network includes a national steering committee and numerous partnerships with public and private organizations dedicated to improving the quality and safety of therapeutics. The **Steering Committee** offers guidance to [the Scientific Forum \(described below\)](#) and research centers, and includes representatives from the drug and device centers of the U.S. Food and Drug Administration (FDA), each research center's principal investigator, an at-large representative of Federal health agencies, and leaders in health care, private industry, and consumer and patient advocacy. The diversity of committee member perspectives ensures that the CERTs remain well-informed and on the cutting edge of significant and emerging health care issues.

CERTs Steering Committee, 2013–2014

Chair

David Ballard, M.D.

Chair, CERTs Steering Committee, Baylor Health Care System

CERTs Principal Investigators

David Bates, M.D., M.Sc.

Principal Investigator, Brigham and Women's Hospital CERT

Carole Lannon, M.D., M.P.H.

Principal Investigator, Cincinnati Children's Hospital Medical Center CERT

Stephen Crystal, Ph.D.

Principal Investigator, Rutgers, The State University of New Jersey CERT

Eric Peterson, M.D., M.P.H.

Principal Investigator, Duke University Medical Center CERT

Stephen Fortmann, M.D.

Principal Investigator, CERTs Scientific Forum

Kenneth Saag, M.D., M.Sc.

Principal Investigator, University of Alabama at Birmingham CERT

Bruce Lambert, Ph.D.

Principal Investigator, Northwestern University CERT

AHRQ, FDA, and At-Large Government Members

Tom Gross, M.D., M.P.H.

Director, Office of Surveillance and Biometrics, Center for Devices and Radiologic Health, Food and Drug Administration

Scott Smith, Ph.D.

Director, Pharmaceutical Outcomes Research, Center for Outcomes and Evidence, Agency for Healthcare Research and Quality

Michael Lauer, M.D. (Government At-Large Member)

Director, Division of Cardiovascular Sciences, National Heart, Lung, and Blood Institute, National Institutes of Health

Wendy Nilsen, Ph.D. (Government At-Large Member)

Health Scientist Administrator, Office of Behavioral and Social Sciences Research (OBSSR), National Institutes of Health

Anne Trontell, M.D., M.P.H.

Program Director, Centers for Education and Research on Therapeutics, Agency for Healthcare Research and Quality

Gwen Zornberg, M.D., Sc.D.

Team Leader, Regulatory Science, Office of Surveillance and Epidemiology, Center for Drug Evaluation and Research, Food and Drug Administration

Healthcare Sector, Consumer, and Industry At-Large Members

George Bo-Linn, M.D., M.H.A.

Chief Program Officer, Gordon and Betty Moore Foundation

Trent Haywood, M.D., J.D.

Chief Medical Officer, Blue Cross Blue Shield Association

Arthur Levin, M.P.H.

Director, Center for Medical Consumers

Gilbert L'Italien, Sc.D.

Executive Director, Global Health Outcomes & Epidemiology, Bristol-Myers Squibb

Robert Reynolds, D.Sc., M.Sc., FISPE

Vice President & Global Head, Epidemiology, World Safety Strategy, Pfizer, Inc.

Amye Leong, M.B.A. (Patient Advocate/ Representative)

President/CEO of Healthy Motivation

The CERTs Scientific Forum is the scientific coordinating center for the CERTs Program and in 2013–14 was led by principal investigator Stephen P. Fortmann, M.D. The Scientific Forum (SF) catalyzes and supports collaborative research and translational activities in therapeutics, supports the CERTs Steering Committee, and serves as the program's communications and translation hub. The SF also cultivates partnerships with public and private entities to help the research centers leverage their funded research into additional projects and to extend their impact. All public-private partnerships are reviewed for potential conflicts of interest using established CERTs principles and practices.

Each **CERTs research center** organizes its research and educational activities within a defined thematic area of therapeutics, which may represent a vulnerable population, a group of related medical conditions, or a specific methodological approach, such as health information technology. The six research centers are listed in Table 1, with their thematic focus and principal investigator.

Table 1. CERTs Program, Research Centers 2013–2014

CERTs	Thematic Focus	Principal Investigator
Brigham and Women’s Hospital (BWH)	Health Information Technology	David Bates, M.D., M.Sc.
Cincinnati Children’s Hospital Medical Center (CCHMC)	Pediatrics	Carole Lannon, M.D., M.P.H.
Duke University Medical Center (Duke)	Cardiovascular Diseases	Eric Peterson, M.D., M.P.H.
Northwestern University	Tools for Optimizing Medication Safety	Bruce Lambert, Ph.D.
Rutgers, The State University of New Jersey (Rutgers)	Mental Health	Stephen Crystal, Ph.D.
University of Alabama at Birmingham (UAB)	Musculoskeletal Disorders	Kenneth Saag, M.D., M.Sc.

Highlights

In 2013–2014, the six CERT research centers worked to improve the safety and effectiveness of therapeutics. This year, CERT researchers—

- Examined the safety and efficiency of electronic prescribing systems.
- Gave families a voice in recognizing a child’s clinical deterioration and activating emergency care teams.
- Examined what leads to poor long-term outcomes after treatment for Acute Coronary Syndrome.
- Produced a new textbook to provide researchers with the methods necessary for carrying out research on drug safety.
- Investigated why use of an effective drug for schizophrenia varies widely from State to State.
- Tested new technologies to enroll a greater variety of patients into research studies.

Improving Medication Safety. Electronic health record (EHR) systems use automated alerts to tell physicians when they may be making an error during prescribing. But alert fatigue can result when providers see too many alerts, possibly leading them to ignore important alerts. Brigham and Women’s Hospital (BWH) CERT researchers set out to reevaluate the many alerts that interrupt providers’ workflow and eliminate those that are unnecessary. The team first identified

low-priority alerts—those that occur frequently, yet are nearly always overridden. They then engaged an expert panel to identify changes that could reduce the number of alerts a provider receives by one-third.

Family Activated Medical Emergency Teams Hold Promise. Medical Emergency Teams (METs) are designed to respond quickly to a patient's deteriorating condition. Family members can offer unique expertise in these situations because they may notice significant changes in a patient before clinicians. Recognizing this, the Cincinnati Children's Hospital Medical Center (CCHMC) hospital began allowing families to activate the MET process for their child. CCHMC CERT researchers found that the program led to an increase in calls to activate METs, but the calls were not an undue burden on the health care system, suggesting family-activated METs hold promise for improving care.

Long-Term Outcomes After Treatment for Acute Coronary Syndrome. Many of the treatments for Acute Coronary Syndrome (ACS) are associated with thrombocytopenia—a low blood platelet count. Acquired thrombocytopenia after ACS is associated with increased mortality and bleeding events. Using data from more than 7,000 patients, Duke CERT researchers found that patients with severe thrombocytopenia were less likely to be discharged from the hospital on guideline-recommended antiplatelet therapy, which may contribute to their higher rates of mortality.

Textbook Offers Tools for Drug Safety Research. Robert Gibbons, Ph.D., a Northwestern University CERT researcher, co-authored a new textbook called *Statistical Methods for Drug Safety*. The book provides a detailed overview of statistical tools to identify and analyze adverse drug events (ADEs) in large populations.

Wide Variation in Treatment for Schizophrenia. Clozapine is the only antipsychotic medication known to be effective in adults with treatment-resistant schizophrenia. However, clozapine accounts for only about 5 percent of the antipsychotic medications started in this group. Researchers at the Rutgers CERT found wide State-to-State variation in the use of clozapine among Medicaid-enrolled adults with schizophrenia, possibly due to differences in local practice or to State policy factors.

iPad Enrollment Tool May Enable More Practices to Participate in Research. Before joining a study, participants must understand the risks and benefits they can expect if they participate and sign a consent form. University of Alabama at Birmingham (UAB) CERT researchers developed an interactive iPad informed consent process and recruited community-based medical practices to assess patient and provider comprehension of and satisfaction with the iPad tool as compared to a standard pencil and paper consent form. Use of a patient-administered iPad informed consent process may make it possible for more primary care and community practices to take part in research studies.

CERTs Collaborations

In 2013–2014, the CERTs collaborated with one another and with a diverse range of public and private entities to advance research, advise Federal and State policymakers, and provide evidence-based, objective information to educate patients, doctors, pharmacists, and others about therapeutics.

Identifying Patient-Centered Approaches to Medication Use. Medication use is a central component in the treatment of chronic diseases. However, in spite of the known benefits of medications, 20 to 30 percent of prescriptions are never filled and of those prescriptions that are filled, roughly one-half are not taken as prescribed.¹ Barriers to medication taking can be simple, such as a patient needing a reminder, or they can be more complex, including concerns about costs, side effects, and quality of life. Efforts to more fully involve and hear from patients may hold promise for improving medication use. To explore these possibilities, the CERTs held an October 2012 workshop to examine the scientific evidence on medication adherence interventions from the patient-centered perspective. Published findings from this workshop cited the potential benefits of patient-centered medication management but also identified challenges to implementation that require additional research and innovation.²

In 2013–2014, the CERTs program built on these efforts by planning and hosting a 2-day meeting of 63 diverse stakeholders to share promising collaborative patient-centered strategies that promote appropriate medication use. Attendees of the March 2014 meeting included representatives from national organizations such as the Office of the Surgeon General, the National Council on Patient Information and Education (NCPPIE), and the National Consumers League (NCL), along with key stakeholders including patients, caregivers, providers, researchers, and representatives from industry, healthcare systems, insurance providers, and government.

The meeting sought to foster a patient-centered perspective on medication use; share perspectives on needed innovations in policy, intervention, research, and available resources; and identify key priorities for future action. The opening presentation described the public health impact of medication non-adherence and emphasized the need to recognize suboptimal medication prescribing and use as a public health priority. Meeting presenters then spoke about possible areas of focus to improve medication management, including communication and shared decisionmaking; the use of technology, education and health literacy; and systems-level interventions. Attendees agreed that several patient-centered domains are critical to address in order to substantially improve appropriate medication prescribing and use, including emphasis on patient and physician engagement and communication; incorporating the role of patients and their community outside of the doctor's office into medication management; implementing tools and technology to aid patients in their medication use; focusing attention on patient-relevant concerns and outcomes; and finally, developing new quality improvement efforts to improve the delivery of medical care as well as and leveraging existing quality improvement efforts. A [brief summary of the meeting](#) can be found at CHAINOnline.org. In addition, an editorial piece

authored by CERTs-affiliated researchers and attendees of the stakeholder meeting is planned for publication in a scientific journal.

1. Peterson AM, Takiya L, Finley R. Meta-analysis of trials of interventions to improve medication adherence. *Am J Health Syst Pharm* 2003 Apr 1;60(7):657-65.

2. McMullen CK, Safford MM, Bosworth HB, et al. Patient-centered priorities for improving medication management and adherence. *Patient Educ Couns* 2015 Jan; 98(1):102-10.

Collaborating to Improve Meaningful Use Requirements. In 2009, the Health Information Technology for Economic and Clinical Health (HITECH) Act became law, offering substantial government payments to health care providers who use certified EHRs in accordance with Federal “meaningful use” (MU) requirements. In 2014, under the leadership of the BWH CERT, the entire CERTs program critically examined the impact of the Federal Government’s requirements for MU—and specifically, policies relating to medications and devices—based on health systems’ experiences with implementing the requirements in practice. Researchers from the BWH CERT collaborated with a diverse group of health care system stakeholders to gather perspectives on implementing MU requirements in practice and recommended the following changes:

- MU objectives should acknowledge the diversity of systems. For example, integrated delivery systems are more likely to achieve the goal of information sharing because of their integrated structure, greater functionality, and improved interoperability.
- Definitions of transitions in care should enable and support shared patient record systems. Better tools and interoperability with external data are needed for effective and efficient medication reconciliation. However, measures should not drive unnecessary or unreliable data transmission.
- Future MU certification rules and requirements should consider EHR functionalities needed for the accurate prescribing of medications in children.
- A common terminology model is needed to facilitate documentation and encoding of data elements such as patient allergies.
- Future MU requirements should put more emphasis on flexibly understanding, incorporating, and supporting local health IT configuration that addresses population health needs.

Slight SP, Berner EB, Galanter W, et al. Meaningful Use: Experiences from the Field and Future Opportunities. *JMIR Med Inform*. Forthcoming 2015.

Collaborating to Adapt Research Tools. Researchers at the Duke CERT worked with the UAB CERT on potential changes in informed consent tools to accommodate the changing needs of research. The traditional way of enrolling patients in studies involves giving potential participants lengthy paper consent forms that must be filled out by hand and returned. The

process is time consuming and often inconvenient. Recently, researchers have begun piloting new ways of presenting consent forms to potential study participants that make use of tablets and mobile phones, in hopes of including a wider variety of health care settings and patients in research. Duke CERT researchers piloted an iPad-based informed consent tool with patients in the inpatient setting, for a study that evaluated a personalized patient education and health tool in improving adherence to guideline-recommended therapies after a heart attack. Duke CERT researchers collected qualitative input on the tool and shared their experience on how it was received—both in terms of feasibility for the clinic, and in terms of ease of use for patients—with all CERTS. The informed consent application has been mobilized for participant recruitment in an outpatient lipid registry at Duke University, shared with stakeholders at other academic research institutions, and will be rolled out to 175 new outpatient practices.

Collaborating to Raise Awareness About Pediatric Quality Improvement Networks. The CCHMC CERT is partnering with the American Board of Pediatrics (ABP) to raise awareness about successful initiatives for improving the quality and safety of care for children, and to support increased dissemination and spread of these strategies. Through this partnership, the CCHMC CERT and the ABP continue their work to build capacity and capability for quality improvement in pediatrics and to highlight and sustain the multisite networks that are essential to translating evidence into practice, building the scientific foundation for discovery and improving child health.

As part of this collaboration, David G. Nichols, M.D., M.B.A., President and CEO of the ABP, wrote an entry on the Official Blog of the ABP entitled “Parents, Sick Children, and the Network,” (<http://abpedsblog.org/2013/10/30/parents-sick-children-and-the-network/>) in which he discussed the importance of quality improvement networks for children and included references and links to the ImproveCareNow network for Pediatric Inflammatory Bowel Disease and the National Pediatric Cardiology Quality Improvement Collaborative, both networks supported by CERTs. The blog, posted October 30, 2013, described the key benefits of these networks—they allow care teams to share their patients’ data and experiences anonymously so that other care teams and patients in the network can benefit from shared knowledge of best practices. The blog featured two illustrations that showed readers the difference between the usual “tunnel of care”—the relationship between one provider and one patient, in which the patient only receives the benefit of one person’s education and experience—and the collaborative care network’s “funnel of care,” in which one patient benefits from the education and experiences of many providers and many other patients.

Collaborating With the PSO Advisory to Prevent Medication Errors. For more than 3 years, the Northwestern University CERT has enjoyed a productive collaboration with [The PSO Advisory](#), an AHRQ-listed patient safety organization that provides pharmacies and hospitals with expert guidance regarding the Patient Safety and Quality Improvement Act (PSQIA). That law, passed in 2005, created PSOs to enable the confidential reporting of adverse events, near misses, and dangerous conditions.

The Northwestern CERT focuses on building and testing tools to optimize medication safety. The head of the PSO advisory, William P. Smith, R.Ph., contacted Dr. Bruce Lambert, the Northwestern CERT PI, after reading about the CERT's work on predicting and preventing drug name confusion errors on the National Patient Safety Foundation's [Web site](#). Smith also had a keen interest in preventing drug name confusion errors because many of the PSO Advisory's clients face this problem.

The two organizations developed a collaboration to prevent drug name confusion in which the PSO Advisory provided Northwestern CERT researchers with de-identified data about real-world medication errors. Dr. Lambert and his CERT colleagues had been developing a standard battery of memory and perception tests to evaluate potential drug names that may cause confusion before those names are approved by Federal regulatory agencies. These perception and memory tests proved useful in the laboratory setting but had never been validated against real-world data. By providing real-world data on drug name confusions, the PSO Advisory allowed the Northwestern CERT to validate their methods against real-world data for the first time.

Preliminary data show that experimental error rates from a combination of visual perception, auditory perception, and short-term memory tests on drug names do indeed predict real-world error rates. This finding validates the usefulness of preapproval tests for evaluating proposed new drug names and suggests that these tests could be used to reduce future drug name confusion and medication errors.

Collaborating to Develop Standard Quality Measurement Tools. Antipsychotic medications are one of the fastest growing classes of medications prescribed for children with mental disorders. In fact, antipsychotic prescriptions for children in the U.S. increased from 8.6 per 1,000 children to 39.4 per 1,000 children from 1996 to 2002. Although evidence supports use of antipsychotics for certain conditions in children, the majority of children on antipsychotics today do not have one of these conditions. Of further concern, these medications come with significant safety concerns, including weight gain, hyperprolactinemia, and metabolic disturbance.

In response to concerns over the rising use of these medications and the safety risks they pose to children, the Rutgers CERTs collaborated with State and Federal stakeholders to develop standard quality measurement tools for antipsychotic medication use among children and adolescents. These antipsychotic safety and effectiveness metrics were adapted into national Medicaid and National Committee for Quality Assurance (NCQA) HEDIS metrics for children, through the AHRQ-funded, NCQA-led Children's Health Insurance Program Reauthorization Act (CHIPRA) National Collaborative for Innovation in Quality Measurement (NCINQ) Center of Excellence. The Rutgers CERT also supported this effort by providing analytical services and direct links to stakeholder communities.

The potential of the use of these metrics as national measures was significantly improved after partner States used the metrics. In 2013, a proposed suite of quality measures for antipsychotic use among children covered through Medicaid and Children's Health Insurance Program (CHIP)

was released by NCQA. In 2014, NCQA released a modified version of these metrics for public comment as part of proposed new HEDIS measures for 2015. The measures are intended for children enrolled in Medicaid, commercial health plans, and for children in the foster care system. This collaborative effort represents an important national step forward toward a more systematic approach to monitoring and improving care for children and youth who face mental health challenges and receive antipsychotic treatment each year.

Measures: Safe and Judicious Antipsychotic Use in Children and Adolescents:

http://www.ahrq.gov/sites/default/files/wysiwyg/policymakers/chipra/factsheets/chipra_1415-p011-1-ef.pdf

Collaborating to Make Research Results Accessible to Patients. In addition to producing research results, the UAB CERT also communicates these results widely in collaboration with Baylor College of Medicine (BCM) and the Clinician-Consumer Health Advisory Information Network—CHAINOnline (www.chainonline.org). Researchers at the UAB CERT have worked with communication specialists at BCM to create accessible articles for the general public about their studies as well as continuing education courses for physicians and other health care providers. Most recently, CHAINOnline featured a UAB study that tested an iPad-based informed consent process for study participants.

Involving Primary Care Patients and Their Physicians in Pragmatic Clinical Trials: High-Tech Interactive Tools Aid Study Recruitment: <http://www.chainonline.org/research-tools/pragmatic-clinical-trials-high-tech-study-recruitment/>

Researchers at the UAB CERT examined the co-occurring conditions associated with poor pain outcomes after total knee replacement, the results of which have been made accessible to the general public on CHAINOnline. Using data from the Mayo Clinic Total Joint Registry, the research team found that anxiety was a significant predictor of poor pain outcomes at 2 years post-total knee replacement surgery, while anxiety, depression, and heart disease were significant predictors of poor pain outcomes 5 years after surgery. Additionally, depression was a significant predictor of poor pain outcomes 2 years after a surgery to correct a total knee replacement. The findings point to conditions that predict poor outcomes can influence clinical practice. Close, careful management of co-occurring medical and psychological conditions before and after the surgery might improve pain outcomes. Future research might examine whether better management of these conditions might improve pain outcomes after total knee replacement surgery.

Comorbidities as Predictors of Pain Outcomes after Primary and Revision Total Knee Arthroplasty: <http://chainonline.org/research-tools/knee-arthroplasty-pain/>

UAB researchers also collaborated with the CERTs Scientific Forum team at the BCM Center for Collaborative and Interactive Technologies to create an online Continuing Medical Education (CME) course, “Bone Health, Race/Ethnicity, and Emerging Technologies for Predicting Risk of Fracture and Limitations in Use with Specified Subpopulations.” The CME is designed for

clinicians who treat patients with osteoporosis, including those in primary care, internal medicine, and obstetrics and gynecology. The course summarizes the role of race/ethnicity as a factor in the development of osteoporosis and fracture risk to foster appropriate risk assessment and management. It provides clinicians with up-to-date information about osteoporosis and fracture risk in different subpopulations, promoting awareness of the Fracture Risk Assessment (FRAX[®]) tool and its limitations.

Bone Health, Race/Ethnicity, and Emerging Technologies for Predicting Risk of Fracture and Limitations in Use With Specified Subpopulations: <http://www.chainonline.org/cme-ce/bone-health/>

Program Activities 2013–2014

The six research centers covered a broad range of pressing issues in health care, from evaluating health information technology systems to investigating medication practices for some of the Nation's most vulnerable patients—including elderly nursing home residents and children in foster care.

The following sections present a selection of the research and educational projects completed between September 2013 and August 2014, the third year of the current CERTs 5-year funding period. The content is organized by center and each project description is followed by a published paper citation, or, in some cases, a link to another type of product. In addition, we provide a full list of CERTs publications for the year at the end of this report.

Brigham and Women's Hospital CERT

The Brigham and Women's Hospital (BWH) CERT continued its focus on health information technology (IT). As the U.S. Government, health care systems, and providers make substantial investments in technologies, such as EHRs, systems that enable doctors to enter their orders into computers (computerized provider order entry or CPOE), and systems designed to help physicians and other health professionals make better informed decisions (clinical decision support or CDS), there is a pressing need to evaluate whether these systems improve patient care as well as ways these systems could be more safely designed. Researchers at the BWH CERT worked to ensure that health IT interventions (1) improve safety and avoid the inadvertent introduction of harm for patients and (2) are monitored for adverse effects of medications, whether they are outpatients, inpatients, or transitioning out of the hospital.

Modifying Alerts to Decrease Fatigue

CDS systems in EHRs use automated alerts to tell physicians when they may be making an error during prescribing. Alerts are designed to keep patients safe, but they can be too numerous, disruptive, or irrelevant, causing physicians to override or ignore them. Alert fatigue results when too many overall alerts cause providers to ignore alerts that may be important or

clinically significant. Studies have cited alert override rates ranging from 49 to 96 percent, with a 90-percent override rate specifically for drug-drug interaction (DDI) alerts.

A DDI alert warns prescribers that the medication they are ordering for a patient is known to interact with another drug the patient is taking. DDI alerts use data from patients' active medication lists and from a database of known drug reactions and interactions, and they appear as providers enter medication orders into CPOE systems.

In previous work, BWH CERT researchers identified a list of high-priority DDI alerts that should *always* be included in medication-related knowledge databases. In the current study, the team sought to identify low-priority alerts—alerts for DDIs that occur frequently, yet are nearly always overridden, suggesting these alerts can be made non-interruptive. Non-interruptive alerts are alerts that do not interrupt providers' workflow because they do not require a response when generated.

To accomplish this, researchers at the BWH CERT convened an 11-member panel with expertise in medicine, pharmacy, and clinical informatics, and who represented academic institutions, electronic health records systems, and the Food and Drug Administration (FDA). The panel's goal was to decide whether some alerts could safely be made non-interruptive.

The panel began with a list of 49 DDIs that occurred most often and were frequently overridden. In fact, these alerts accounted for half of the alerts that were shown to providers and they had an average override rate of between 95 and 99 percent. Each panelist was given a list of DDIs as well as detailed information about what type of interaction between medications could be expected and what consequences could result. While the group decided that 16 of the DDI alerts should remain interruptive, they created a list of 33 low-priority DDI alerts that could safely be made non-interruptive. The team concluded that if those changes were made, providers' overall alert volume could be reduced by one-third.

Phansalkar S, van der Sijs H, Tucker AD, et al. Drug-drug interactions that should be non-interruptive in order to reduce alert fatigue in electronic health records. *J Am Med Inform Assoc* 2013 May; 20(3):489-93. Select to access the [abstract](#).

Cincinnati Children's Hospital Medical Center CERT

The Cincinnati Children's Hospital Medical Center (CCHMC) CERT focused on the safe and effective use of medications in children. Under that broad umbrella, two specific themes were patient safety and improving outcomes through multisite clinical specialty networks. Since 2007, the CCHMC CERT has supported a collaborative project to improve care for children with Inflammatory Bowel Disease (IBD). This network of collaborating clinical practices, called ImproveCareNow, is helping children with pediatric IBD feel better and move into remission. Building on the lessons learned from this work, the CCHMC CERT also supported research and quality improvement networks for infants with complex congenital heart disease and for children

with juvenile idiopathic arthritis. Many of the networks have already shown improvements in care delivery and outcomes for children.

Evaluating Family Activated Medical Emergency Teams

Medical Emergency Teams (METs) are rapid response teams that are designed to recognize a patient's deteriorating condition and respond quickly, preventing acute respiratory and cardiopulmonary arrests. The CCHMC hospital, a nearly 600-bed academic children's hospital in Cincinnati, Ohio, began a clinician-initiated MET process in 2005 and, in 2007, began to allow families to activate the MET process. While family-activated METs have the potential to reduce preventable adverse events, concerns that they would overload resources have kept them from being widely implemented. In response to these concerns, the CCHMC research team developed a process for implementing family-activated METs and then evaluated its effect.

This evaluation found that family members may recognize significant changes in a patient before experienced clinicians. Thus, the family-activated MET calling program was based on the idea that families offer a unique expertise in identifying their own child's deterioration. The MET, as established at CCHMC, allowed families to activate a team consisting of five members—a nurse, a respiratory therapist, a resident physician, a nurse manager, and a critical-care fellow (a physician with pediatric and critical care training).

The researchers found that while the family-activated MET program resulted in an overall increase in calls, the additional family calls were not a burden on responders. Over a 6-year study period, the research team counted 83 family-activated MET calls, representing 2.9 percent of all MET calls. The study compared MET calls from families with a set of age-matched and nursing-unit-matched clinician activated-MET calls, and compared the reasons why families initiated METs and the reasons clinicians initiated METs. They found that family members and clinicians generally called METs for similar reasons, the most common being a child's clinical deterioration. However, families also cited lack of response from clinicians and dismissive interaction between care team and family as reasons for initiating an MET. The team concluded that family-activated METs should be tested and implemented in other hospitals that care for children.

Brady PW, Zix J, Brill R, et al. Developing and evaluating the success of a family activated medical emergency team: a quality improvement report. *BMJ Qual Saf* 2015 Mar;24(3):203-11. Select to access the [abstract](#).

Duke University Medical Center CERT

The Duke CERT focuses on cardiovascular (CV) disease, the leading cause of illness and death in the United States. Duke's CERT team identifies gaps in CV care and their consequences, generates evidence on the safety and effectiveness of treatments, and translates knowledge into practice through work with providers around the country.

Thrombocytopenia During Acute Coronary Syndrome

Acute Coronary Syndrome (ACS) refers to any condition brought on by sudden reduced blood flow to the heart. The umbrella term includes heart attack, unstable angina, and other conditions. Many of the treatments for ACS, including anti-thrombotic medications and procedures, are associated with thrombocytopenia—a low blood platelet count; platelets are the cells that help blood clot. Previous research had found that acquired thrombocytopenia after ACS was associated with increased in-hospital mortality and bleeding events, but long-term outcomes for patients with acquired thrombocytopenia were unclear.

Duke CERT researchers examined the association between thrombocytopenia and patients' long-term outcomes. Using data from 7,435 patients enrolled in the SYNERGY trial, a randomized trial testing two blood-thinning medications for patients with ACS who have had a mild heart attack, they examined in-hospital bleeding events and mortality at 1-year post hospitalization. They found that 675 patients (9.1 percent) developed mild thrombocytopenia and 139 patients (1.9 percent) developed severe thrombocytopenia. In-hospital bleeding risk was higher among patients with mild or severe thrombocytopenia (7.7 and 28.2 percent, respectively) than in patients without the condition (5.2 percent).

Further, severe thrombocytopenia was significantly associated with increased mortality. The research found that patients with severe thrombocytopenia were less likely to be discharged from the hospital on guideline-recommended antiplatelet therapy, which may contribute to their higher rates of mortality over the long term. The researchers suggest that this mortality risk may be mitigated by following these patients more closely after hospital discharge to monitor their platelet counts, so that, once their thrombocytopenia has resolved, patients can be safely restarted on guideline-recommended therapies.

Vora AN, Chenier M, Schulte PJ, et al. Long-term outcomes associated with hospital acquired thrombocytopenia among patients with non-ST-segment elevation acute coronary syndrome. *Am Heart J* 2014 Aug;168(2):189-96. Select to access the [abstract](#).

Northwestern University CERT

The Northwestern University CERT works to improve patient safety by developing and refining tools for safer medication use by patients and clinicians. The Northwestern CERT researches and develops targeted tools that optimize the efficacy, safety, and cost-effectiveness of drug therapy.

New Textbook Offers Tools for Analyzing Adverse Drug Events

Pharmacoepidemiology is the study of the uses and effects of drugs in large populations. In 2014, Robert Gibbons, Ph.D., who leads the Northwestern CERT's statistical core and is a Professor in the University of Illinois Chicago's Departments of Medicine and Public Health Sciences, completed a new textbook, with co-author Anup Amatya, an Assistant Professor at

New Mexico State University, called *Statistical Methods for Drug Safety*. The book presents a wide variety of statistical approaches for analyzing pharmacoepidemiologic data, providing statisticians with a detailed overview of tools available to identify and analyze adverse drug events (ADEs). ADEs are injuries resulting from medication use, including physical harm, mental harm, or loss of function; analyzing data on ADEs and potential ADEs is necessary for much research on drug safety.

Statistical Methods for Drug Safety covers commonly used techniques, such as proportional reporting ratios for analyzing spontaneous adverse event reports, and newer approaches, such as methods to control selection bias in the analysis of large-scale longitudinal data, medical claims databases, EHRs, and observational data. The book presents many examples from the real world of health care to illustrate how to use these methods, and encourages readers to develop new statistical methods of their own.

Gibbons RD, Amatya A. *Statistical Methods for Drug Safety*. Chapman and Hall/CRC 2015. Available at: <http://www.amazon.com/Statistical-Methods-Safety-Chapman-Biostatistics/dp/146656184X>

Rutgers, The State University of New Jersey CERT

The Rutgers Mental Health CERT serves as a national resource for improving the safety and effectiveness of treatments for mental health problems. In 2011–2012, the Mental Health CERT partnered with the American Psychiatric Association and Columbia University to assemble an extensive database that allows researchers to study a range of mental health issues, including the safe and effective use of psychotropic drugs and antidepressants, especially among young people and the elderly. This CERT's educational initiative has included quality-improvement collaborations with State mental health and Medicaid officials and development of national treatment guidelines.

Wide Variation in States' Use of Clozapine for Treatment-resistant Schizophrenia

Clozapine is the only antipsychotic medication known to be effective in adults with treatment-resistant schizophrenia. However, although 20 to 30 percent of people with schizophrenia have treatment-resistant schizophrenia, clozapine accounts for only about 5 percent of the antipsychotic medications started in this group. Researchers at the Rutgers CERT examined patterns and trends in clozapine use from 2006–2009 among Medicaid-enrolled adults with schizophrenia in 46 States. The researchers found that clozapine accounted for 2.4 percent of new antipsychotic medications started. The highest percentage of new starts occurred in South Dakota (8.9 percent) and Colorado (5.7 percent); the lowest in Mississippi (0.8 percent) and Alabama (0.9 percent). When researchers examined only people with treatment-resistant schizophrenia, the overall percentage of new clozapine starts was 6.1 percent, with the highest percentages in Illinois (13.8 percent) and Vermont (12.5 percent) and the lowest in Mississippi (1.9 percent) and Kentucky (2.7 percent). The wide variations in States' use of clozapine for schizophrenia may be due to differences in local practice, or to State policy factors, including

whether States offer optional Medicaid mental health services and services that may encourage Medicaid-financed clozapine use.

Stroup TS, Gerhard T, Crystal S, et al. Geographic and clinical variation in clozapine use in the US. *Psychiatric Serv* 2014 Feb; 65(2):186-92. Select to access the [abstract](#).

University of Alabama at Birmingham CERT

The University of Alabama at Birmingham (UAB) Deep South Arthritis and Musculoskeletal CERT seeks to improve the safety and effectiveness of musculoskeletal therapeutics; educate health care practitioners, insurers, and policymakers; and broaden the impact that musculoskeletal research has on public health. This focus is both important and timely, given the rising burden of musculoskeletal diseases in an aging society.

Since 1999, the UAB CERT has successfully conducted more than 50 projects, creating new knowledge and products, disseminating research and education, and improving public health. The UAB CERT invests substantial resources for infrastructure research as well as specific research projects. Research includes the use of large administrative databases to examine serious adverse events associated with biologic therapies, methods development in pragmatic clinical trials, and efforts to promote adherence to therapies and reduce disparities in risk assessment and communication.

Using Technology to Make Informed Consent Processes More Efficient

In recent years, pragmatic clinical trials (PCTs), which compare treatments in real-world settings, have become more common. Because PCTs have broader inclusion criteria and allow recruitment of a larger, more diverse population, findings from pragmatic trials are potentially more applicable to the general population than those of randomized clinical trials (RCTs).

PCTs that compare different therapeutic options require a variety of research sites for sufficient sample size and generalizability. The need to conduct informed consent as part of the enrollment process for these studies can be a major barrier to conducting PCTs in primary care, family care, and rural clinics where clinicians often have limited time and research experience.

Researchers at the UAB CERT recognized a need to improve the efficiency of the informed consent process. They hypothesized that a patient-administered iPad informed consent tool would lead to better patient comprehension and satisfaction than traditional paper-based informed consent processes and forms. They set out to test the feasibility of such an approach for use in a future osteoporosis PCT of bisphosphonate discontinuation vs. continuation.

UAB CERT researchers developed an interactive iPad informed consent tool that uses animation to explain a study and includes intermittent quizzes that test how well the patient understands the study procedures. Researchers recruited community-based practices (n=9) from the Alabama Practice Based Research Network, the South Texas Ambulatory Research

Network, and the American Academy of Family Physicians National Research Network to test the tool. The practices were randomized to either the iPad or paper consent process and aimed to recruit three participants for each informed consent approach. Patient inclusion criteria included ≥ 1 year alendronate use, and willingness to use an iPad for the informed consent process.

Researchers assessed patients' comprehension and satisfaction using surveys and a quiz. Patient satisfaction with, and comprehension of both consent methods was high overall. Health care providers consistently favored the iPad over paper for efficiency and ease of use, despite a slightly longer perceived time to complete it. The researchers concluded that patients and providers trended towards being more satisfied with the iPad-delivered informed consent process than with traditional paper processes. Use of a patient-administered iPad informed consent process may have the potential to improve this necessary study enrollment process for PCTs that involve primary care and community practices.

Warriner AH, Foster PJ, Wright NC, et al. Effectiveness and feasibility of an iPad based patient administered informed consent (IC) vs. paper consent for osteoporosis pragmatic clinical trials (PCT). 2014 Annual Meeting of the American Society for Bone and Mineral Research, Houston, TX, September 12–15, 2014.

CERTs Scientific Forum

The Scientific Forum continued to support the work of the CERTs Program during the third year of the CERTs cooperative agreement. The Scientific Forum convened quarterly Steering Committee meetings; topics explored at the October 2013 and January 2014 Steering Committee meetings included shared decisionmaking and patient engagement in health care and patient activation to improve health care outcomes and reduce costs. Under the guidance of the CERTs Steering Committee, the Scientific Forum also supported collaborative project activities. The primary project for the third year was a stakeholder meeting to share promising collaborative patient-centered strategies that promote appropriate medication use ([go to CERTs Collaborative Activity, above](#)). In addition, the Scientific Forum disseminates research and educational materials developed by the six research centers. Two public Web sites supported by the Scientific Forum are used to actively disseminate the new knowledge and tools generated by the CERTs research centers—the AHRQ CERTs Web site (www.certs.hhs.gov) and the Clinician-Consumer Health Advisory Information Network (CHAIN) Online Web site (www.chainonline.org; see CHAIN Online, below).

CHAIN Online: Disseminating Projects and Findings of the CERTs

The CHAIN Online Web site (www.chainonline.org), developed and hosted by BCM, is a dissemination vehicle for the CERTs Program. CHAIN Online offers information and tools for patients, practitioners, and researchers, including articles on methods, recent CERTs publications, and features on CERTs research. Editors for the Web site also work with the

CERT centers to translate research into handouts for consumers and clinicians and to create CME activities for health care professionals.

A BCM editorial board ensures that CHAIN Online offers a range of materials and topics representing CERTs that will appeal to all visitors. The following items were published between September 1, 2013, and August 31, 2014, and feature the CERTs, their research findings, and tools translated from their work by BCM as resources for researchers, practitioners, and patients and their families:

1. Solving the Problem of Alert Fatigue To Minimize Medication Errors (<http://chainonline.org/research-tools/bwh-cert-alert-fatigue/>)
2. Involving Primary Care Patients and Their Physicians in Pragmatic Clinical Trials: High-Tech Interactive Tools Aid Study Recruitment (<http://chainonline.org/research-tools/pragmatic-clinical-trials-high-tech-study-recruitment/>)
3. CERT Researcher Engages Nurses To Address Low Health Literacy (<http://chainonline.org/research-tools/literacy/>)
4. Optimizing the Use of an Electronic Fall Prevention Toolkit To Prevent Falls in Hospitalized Patients (<http://chainonline.org/research-tools/electronic-fall-prevention-toolkit/>)
5. Bone Health, Race/Ethnicity, and Emerging Technologies for Predicting Risk of Fracture and Limitations in Use With Specified Subpopulations (<http://chainonline.org/cme-ce/bone-health/>)
6. Comorbidities as Predictors of Pain Outcomes After Primary and Revision Total Knee Arthroplasty (<http://chainonline.org/research-tools/knee-arthroplasty-pain/>)
7. The Rutgers CERT Helps Establish Updated Parameters for Psychotropic Medication Use in Texas Foster Children (<http://chainonline.org/practice-tools/foster-children-psychotropic-use/>) and the consumer handout, Mental Health Problems in Foster Care Children (<http://chainonline.org/patient-tools/mental-health-problems-foster-children/>)
8. Medication Nonadherence Is Associated With Increased Healthcare Utilization in Pediatric Patients With Chronic Diseases (<http://chainonline.org/cme-ce/medication-adherence/>) and Clinicians and Their Chronically Ill Pediatric Patients Together Can Improve Medication Adherence and the Use of Health Care Services (<http://chainonline.org/practice-tools/medication-adherence-handout/>)
9. Opportunities for Suicide Prevention in the Emergency Department (<http://chainonline.org/research-tools/suicide-prevention/>)

10. Advancing Safety Efforts To Protect Patients Who Have Implantable Medical Devices
(<http://chainonline.org/news/implantable-medical-devices/>)

CERTs Publications: 2013-2014

2013

A-E

Ayers DC, Zheng H, Franklin PD. Integrating patient-reported outcomes into orthopedic clinical practice: proof of concept from FORCE-TJR. *Clin Orthop Relat Res* 2013 Nov;471(11):3419-25. PMID: PMC3792269. Select to access the [abstract](#).

Curtis JR, Silverman SL. Commentary: the five Ws of a Fracture Liaison Service: why, who, what, where, and how? In osteoporosis, we reap what we sow. *Curr Osteoporos Rep* 2013 Dec;11(4):365-8. PMID: PMC3847905. Select to access the [abstract](#).

Danford CP, Navar-Boggan AM, Stafford J, et al. The feasibility and accuracy of evaluating lipid management performance metrics using an electronic health record. *Am Heart J* 2013 Oct;166(4):701-8. [Epub 2013 Sep 17] PubMed PMID: 24093850. Select to access the [abstract](#).

Eapen ZJ, Hammill BG, Setoguchi S, et al. Who enrolls in the Medicare Part D prescription drug benefit program? Medication use among patients with heart failure. *J Am Heart Assoc* 2013 Sep 11;2(5):e000242. PubMed Central PMID: PMC3835226. Select to access the [abstract](#).

J-N

Lipstein EA, Brinkman WB, Sage J, et al. Understanding treatment decision making in juvenile idiopathic arthritis: a qualitative assessment. *Pediatr Rheumatol Online J* 2013 Sep 30;11(1):34. PubMed Central PMID: PMC3849714. Select to access the [abstract](#).

O-Z

Ringold S, Weiss PF, Beukelman T, et al. 2013 update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: recommendations for the medical therapy of children with systemic juvenile idiopathic arthritis and tuberculosis screening among children receiving biologic medications. *Arthritis Rheum* 2013 Oct;65(10):2499-512. PubMed PMID: 24092554. Select to access the [abstract](#).

Singh JA, Lewallen DG. Patients with osteoarthritis and avascular necrosis have better functional outcomes and those with avascular necrosis worse pain outcomes compared to rheumatoid arthritis after primary hip arthroplasty: a cohort study. *BMC Med* 2013 Sep 24;11:210. PubMed Central PMID: PMC3850929. Select to access the [abstract](#).

Steinberg BA, Hasselblad V, Atwater BD, et al. Dabigatran for periprocedural anticoagulation following radiofrequency ablation for atrial fibrillation: a meta-analysis of observational studies. *J*

Interv Card Electrophysiol 2013 Sep;37(3):213-21. [Epub 2013 Jul 24] PubMed Central PMCID: PMC3878716. Select to access the [abstract](#).

Teng GG, Tan CS, Santosa A, et al. Serum urate levels and consumption of common beverages and alcohol among Chinese in Singapore. *Arthritis Care Res (Hoboken)* 2013 Sep;65(9):1432-40. PubMed Central PMCID: PMC3710722. Select to access the [abstract](#).

Zullig LL, Shaw RJ, Crowley MJ, et al. Association between perceived life chaos and medication adherence in a postmyocardial infarction population. *Circ Cardiovasc Qual Outcomes* 2013 Nov;6(6):619-25. [Epub 2013 Nov 12] PubMed PMID: 24221839. Select to access the [abstract](#).

2014

A-E

Brady PW, Goldenhar LM. A qualitative study examining the influences on situation awareness and the identification, mitigation and escalation of recognized patient risk. *BMJ Qual Saf* 2014 Feb;23(2):153-61. [Epub 2013 Sep 23] PubMed PMID: 24062473. Select to access the [abstract](#).

Brady PW, Wheeler DS, Muething SE, et al. Situation awareness: a new model for predicting and preventing patient deterioration. *Hosp Pediatr* 2014 May;4(3):143-6. PubMed PMID: 24785557. Select to access the [abstract](#).

Compston JE, Flahive J, Hooven FH, et al. Obesity, health-care utilization, and health-related quality of life after fracture in postmenopausal women: Global Longitudinal Study of Osteoporosis in Women (GLOW). *Calcif Tissue Int* 2014 Feb;94(2):223-31. PubMed Central PMCID: PMC3917823. Select to access the [abstract](#).

Díez-Pérez A, Adachi JD, Adami S, et al. Risk factors for treatment failure with antiosteoporosis medication: the global longitudinal study of osteoporosis in women (GLOW). *J Bone Miner Res* 2014 Jan;29(1):260-7. PubMed PMID: 23794198. Select to access the [abstract](#).

Downes KJ, Rao MB, Kahill L, et al. Daily serum creatinine monitoring promotes earlier detection of acute kidney injury in children and adolescents with cystic fibrosis. *J Cyst Fibros* 2014 Jul;13(4):435-41. [Epub 2014 Apr 6] PubMed Central PMCID: PMC4058368. Select to access the [abstract](#).

F-I

Galanter WL, Bryson ML, Falck S, et al. Indication alerts intercept drug name confusion errors during computerized entry of medication orders. *PLoS One* 2014 Jul 15;9(7):e101977. eCollection 2014. PubMed Central PMCID: PMC4098994. Select to access the [abstract](#).

J-N

Nanji KC, Slight SP, Seger DL, et al. Overrides of medication-related clinical decision support alerts in outpatients. *J Am Med Inform Assoc* 2014 May-Jun;21(3):487-91. [Epub 2013 Oct 28]; PubMed Central PMCID: PMC3994856. Select to access the [abstract](#).

Navar-Boggan AM, Fanaroff A, Swaminathan A, et al. The impact of a measurement and feedback intervention on blood pressure control in ambulatory cardiology practice. *Am Heart J* 2014 Apr;167(4):466-71. [Epub 2014 Jan 16. PubMed PMID: 24655694]. Select to access the [abstract](#).

O-Z

Schaffzin JK, Dodd CN, Nguyen H, et al. Administrative data misclassifies and fails to identify nephrotoxin-associated acute kidney injury in hospitalized children. *Hosp Pediatr* 2014 May;4(3):159-66. PubMed PMID: 24785560. Select to access the [abstract](#).

Sherwood MW, Wiviott SD, Peng SA, et al. Early clopidogrel versus prasugrel use among contemporary STEMI and NSTEMI patients in the US: insights from the National Cardiovascular Data Registry. *J Am Heart Assoc* 2014 Apr 14;3(2):e000849. PubMed Central PMCID: PMC4187510. Select to access the [abstract](#).

Solomon DH, Kremer JM, Fisher M, et al. Comparative cancer risk associated with methotrexate, other non-biologic and biologic disease-modifying anti-rheumatic drugs. *Semin Arthritis Rheum* 2014 Feb;43(4):489-97. [Epub 2013 Sep 5] PubMed PMID: 24012043. Select to access the [abstract](#).

Vora AN, Chenier M, Schulte PJ, et al. Long-term outcomes associated with hospital acquired thrombocytopenia among patients with non-ST-segment elevation acute coronary syndrome. *Am Heart J* 2014 Aug;168(2):189-96.e1. [Epub 2014 Apr 24] PubMed PMID: 25066558. Select to access the [abstract](#).

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