

# CERTs YEAR 7 ANNUAL REPORT



Agency for Healthcare Research and Quality  
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## Vision

To serve as a trusted national resource for people seeking to improve health through the best use of medical therapies.

## Mission

To conduct research and provide education that will advance the optimal use of drugs, medical devices, and biological products.



## Values

**Public Interest.** Research must be conducted to answer important questions that otherwise may not be addressed, with higher priority given to projects that offer better opportunities to achieve our mission and vision.

**Public-Private Partnership.** Collaboration of groups with different perspectives and resources—patients, health care providers, government, academia, delivery systems, payers, purchasers, and manufacturers of medical products—is a cost effective way to achieve results of mutual benefit and with greater responsiveness to the needs and interests of more sectors in society.

**Multidisciplinary Alliances.** The best research harnesses the collective expertise of medical practitioners, biostatisticians, clinical pharmacologists, health services researchers, clinical epidemiologists, pharmacists, clinical researchers, and others involved in health care.

**Communication.** The information from the CERTs must be made readily available to all relevant audiences.

**Education.** Education of current and future health care providers, policymakers, and patients is critical to improving health.

**Public Policy.** Policymakers must be provided with the best available evidence upon which to base policies.

**Accountability.** Americans should expect the CERTs to be a trusted resource of scientific evidence regarding therapeutics when they need answers to questions about therapies.

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## Letter from the Agency for Healthcare Research and Quality



Dear Colleague:

This report from the Agency for Healthcare Research and Quality (AHRQ) outlines the work of the Centers for Education & Research on Therapeutics (CERTs) in their seventh year. We are pleased to present this summary of CERTs contributions to the

optimal use of medical therapeutics.

Optimal use of medicines and devices involves many components dealing with safe and effective prescribing or use by clinicians and patients. The CERTs research summarized in this report illustrates multiple CERTs efforts, in consultation with the Food and Drug Administration (FDA), to identify risks and/or the most effective use of medications and devices. Relative to devices, a preliminary CERTs study suggested children with diabetes who use continuous glucose monitoring systems could improve their hemoglobin A1c without increased risk of hypoglycemia. The CERTs also convened a multidisciplinary expert workshop on the evaluation of diagnostic imaging technologies and therapeutics devices and published the key issues that were identified.

From a medication safety standpoint, the CERTs studied the consequences of using ACE inhibitors early in pregnancy. Adverse events of antidepressants and steroids were examined for children and adolescents as well. Other CERTs

research aimed to determine how often dosing errors occur when medicines are prescribed (for pediatric medicines or for treating gout). Research on safe prescribing dealt with computerized alert systems, including those on PDAs (personal digital assistants) and in drug alert systems in pharmacies. In addition, CERTs research addressed optimal prescribing in situations where pretesting of patients is needed to avoid adverse consequences, such as TB testing in association with prescribing infliximab, a medication for rheumatoid arthritis and Crohn's disease. Pretesting can determine whether patients are harboring latent TB infection that could be activated by use of the medicine.

As always, AHRQ is focused on the needs of consumers. One CERTs study evaluated the quality of online consumer drug information and provided a list of recommended sites providing free information. And, while it is important that medicines be prescribed appropriately, it is also important that patients take their prescribed medicines as directed, a subject examined this year in relation to medicines for myocardial infarction, heart failure, and osteoporosis. Likewise, the CERTs examined methods of patient education to increase adherence to statins (which help prevent heart attacks and strokes.)

With the addition of four new CERTs research centers in 2006, we look forward to even greater productivity and impact of the CERTs Program.

Carolyn M. Clancy, M.D.  
Director

## Letter from the Steering Committee



Dear Fellow Citizens:

On behalf of the Steering Committee for the Centers for Education & Research on Therapeutics (CERTs) I am pleased to present the CERTs Year 7 Annual Report.

We made unprecedented progress this year in our mission to provide the public with a trusted national resource. We conducted research and provided education in therapeutics, and brought researchers with related agendas together to work on a broad range of projects to further our vision of improved public health through the safe and effective use of drugs, medical devices, and biological products.

This year we are particularly excited to welcome four new centers to the CERTs program: the University of Texas MD Anderson Cancer Center and Baylor College of Medicine; Rutgers, The State University of New Jersey; the University of Iowa; and the Weill Medical College of Cornell University. With the addition of these new centers, our areas of research cover an even broader array of critical areas in therapeutics research, including consumer and patient education, mental health, aging and the elderly, and medical devices.

This report highlights the ongoing work of the CERTs, summarizes but a few of the projects completed this year, and introduces the efforts from the new centers. These projects range from the

study of herbal supplement use to an examination of health care spending and comparative costs of particular therapeutics. An important focus is development of methodology to better ensure drug safety and to fulfill the academic components of the national strategy to implement the recommendations of the landmark 2006 Institute of Medicine report on the future of drug safety.

As we complete our seventh year, we remain committed to generating and providing independent, unbiased, and useful information about the benefits and risks of important therapeutic products. We thank our extensive list of public and private partners in this enterprise. Working together, we can move toward our shared vision: to better inform health care providers, patients, policymakers, and others about the drugs, devices, and biological products that play such an important role in our daily lives.

Sincerely,



Hugh H. Tilson, MD, DrPH  
Chair, on behalf of the CERTs Steering Committee

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## Introduction

The Centers for Education & Research on Therapeutics (CERTs) program serves the American people by providing valuable information to health care providers, patients, and policymakers about the safety and effectiveness of therapeutics—drugs, medical devices, and biological products such as vaccines. The CERTs conduct state-of-the-art research about the safe use, risks and benefits, and cost-effectiveness of therapeutics.

The CERTs program currently consists of a network of 11 research centers, public and private partners, a coordinating center, and a national steering committee — all dedicated to making improvements to the quality and safety of therapeutics. This year four new research centers joined the CERTs program to build on and enhance the work of the existing centers.

Since the inception of the CERTs program in 1999, the centers have developed a portfolio of nearly 400 projects. Subjects range from therapies for mental health to therapies for older adults and the effects of aging. As we complete our seventh year of work, we remain involved in research related to some of the most challenging medical issues of the day. In addition to research, the centers take a leading role in providing objective information to educate patients, doctors, pharmacists, health plan providers, and others about the drugs, devices, and biological products that play such an important role in our daily lives.

This report highlights the various CERTs research and educational projects completed over the past year, as well as several projects in progress.

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The CERTs program is funded and managed as a cooperative agreement by the Agency for Healthcare Research and Quality (AHRQ) in consultation with the U.S. Food and Drug Administration (FDA). The CERTs receive funds from both public and private sources, with AHRQ providing core financial support.

## Examples of Medical Therapies

Therapy	Examples
Drugs:	Prescription medications; over-the-counter medicines
Medical devices:	Coronary stents; blood glucose monitors
Biological products:	Vaccines; blood products

## Centers and Their Emphases

Arizona CERT at The Critical Path Institute (C-Path): Detection and prevention of adverse drug interactions

Duke University Medical Center: Therapies for disorders of the heart and blood vessels

HMO Research Network: Use, safety, and effectiveness studies of therapeutics, using health plans for defined populations

\*Rutgers, The State University of New Jersey: Therapies for mental health

University of Alabama at Birmingham: Therapies for musculoskeletal disorders

\*University of Iowa: Therapies for older adults and the effects of aging

University of North Carolina at Chapel Hill: Therapies for children

University of Pennsylvania School of Medicine: Therapies for infection; reduction in antibiotic resistance

\*University of Texas MD Anderson Cancer Center and Baylor College of Medicine: Risk and health communication; patient, consumer, and professional education; health decisionmaking and decision support; therapeutic adherence

Vanderbilt University Medical Center: Prescription drug use in Medicaid and veteran populations

\*Weill Medical College of Cornell University: Therapeutic medical devices

\*New center as of April 2006.

## CERTs Progress

### Herbal Supplement Use and Interactions in Diabetes

Treating and controlling diabetes usually includes diet, exercise, blood glucose testing, and in many cases, using oral or injected medications such as insulin to control hyperglycemia. However, herbal remedies are used by many Mexican Americans in the Southwestern United States, where there is a long history of using plants to treat a variety of ailments. Because of this practice, it is important for physicians to understand the possible adverse effects and potential drug interactions that may occur in persons with diabetes who use herbal remedies.

CERTs investigators examined the use of herbal remedies by Hispanic women with type II diabetes in two community health centers in the southwestern United States.<sup>1</sup> A total of 91 percent of the participants interviewed reported using one or more herbal remedies, and 6.7 percent used herbal remedies intended specifically for diabetes.

Researchers found that most of the 77 herbal remedies identified were included as part of commercial preparations and were used by patients to supplement standard medical therapies for diabetes. Although herbal supplements may have adverse effects or interactions with other medications, those found in use in this study were unlikely to have a significant effect on outcomes in diabetes.

### Categorizing Antibiotic Use To Understand Antibiotic Resistance

Antibiotic resistance is an important concern. Many studies have sought to identify risk factors for resistant infections. While many of these studies explore the association between antibiotic use and resistance, little attention has been paid to the methods by which prior antibiotic use is defined (e.g., by agent, class, and/or the spectrum of activity against different organisms). To best identify targets for intervention, it is critical to establish whether a resistant pathogen is associated with use of a specific class of antibiotics or whether the specific agents used are associated with certain spectra of activity.

The objective of this project<sup>2</sup> was to explore the variability and possible impact of methods of categorizing antibiotic use on the association between prior antibiotic use and resistant infection. Using infections due to extended-spectrum beta-lactamase-producing *Escherichia coli* and *Klebsiella* species (ESBL-EK) as a model, researchers conducted a systematic review of the existing literature and reanalysis of the database from a previous study of risk factors for ESBL-EK infection.

The literature revealed tremendous variability across studies in the categorization of prior antibiotic use, with no study justifying its method for categorization. The reanalysis of a past data set also showed great variability across bivariate and



multivariate analyses, depending on which antimicrobial use categorization (i.e., class of agent vs. spectrum of activity) was employed.

Identifying modifiable risk factors is paramount in efforts to curb the further emergence of antibiotic resistance. This study is the first to investigate the impact of different methods of antibiotic use categorization on the epidemiological study of resistance.

Future studies assessing risk factors for antibiotic resistance should describe which antibiotics were assessed and how they were categorized. Such information is essential to inform antibiotic use interventions and to facilitate comparison of results across studies.

### Patient Adherence to Preventive Cardiovascular Medications

**Beta-blockers**—Although beta-blockers have been shown to improve survival after myocardial infarction (MI) and reduce the frequency of recurrent MI, little attention has been paid to the need to sustain beta-blocker therapy long term.

In collaboration with the Council for Affordable Quality Healthcare (CAQH), a not-for-profit organization of health plans that promotes collaborative initiatives for administrative simplification and quality, CERTs investigators examined the long-term use of beta-blockers over the first year after MI in patients with commercial health insurance and prescription drug benefits.<sup>3</sup> The investigators also looked at adherence in relation to

time from discharge, type of health plan, age, sex, and region. In this study, patients were considered adherent if they had prescription claims for beta-blockers for 75 percent or more of the days during the first year after MI.

Over the first year after discharge, only 45 percent of the 17,000 patients adhered to beta-blocker therapy. Lower adherence occurred in patients with Medicare-Plus-Choice plans, patients in the Southeast, and young females in commercial health plans. The study suggests that factors in addition to cost affect long-term adherence.

Beyond targeting physicians who prescribe beta-blockers, educational efforts need to target patients and their families to encourage continued use of beta-blocker therapy during long-term outpatient care. Since this study showed that compliance fell off the most between 30 and 90 days after discharge, interventions to improve adherence need to be initiated early after discharge.

Quality measures that focus on long-term persistence of beta-blocker therapy can help move practice in the right direction. The first example of such a tool is the new 2005 HEDIS® (Healthcare Effectiveness Data and Information Set) measure from the National Committee for Quality Assurance (NCQA), derived by the same methods used in the CAQH study. This HEDIS measure looks at persistence of beta-blocker therapy over the first 6 months after MI. Certainly, the interests of all parties (physicians, patients, health plans, pharmaceutical companies, pharmacists, and nurses) should be well

aligned to promote patients' long-term adherence to this life-saving medication.

**Secondary prevention therapies**—A great deal of research is directed toward understanding and improving in-hospital and discharge prescription practices of doctors, but less goes toward determining long-term adherence to these medications by patients. To address this issue, CERTs researchers analyzed data from the Duke Databank for Cardiovascular Disease from 1995 to 2002 in order to determine adherence to several secondary preventive medications, including beta-blockers, aspirin, angiotensin-converting enzyme (ACE) inhibitors, and lipid-lowering therapies.<sup>4</sup>

Starting in 1995, a routine followup questionnaire was sent to patients who had undergone a cardiovascular procedure at 6 and 12 months after their procedure and yearly thereafter. Patients were prompted to report all medications they were using. Based on these surveys, patterns of long-term medication use were described. Consistent use was defined as use reported on two or more consecutive surveys up to an endpoint of death, withdrawal, or the end of the study.

From one perspective, the results of this analysis were encouraging, showing that patient-reported use of medications after discharge has increased steadily since the beginning of the study. In 2002, use of aspirin was 83 percent; beta-blockers, 61 percent; and lipid-lowering agents, 63 percent. However, these overall rates of medication use are still suboptimal. In addition, many patients do not use these medications consistently. Aspirin is the

oldest and least expensive drug used in secondary prevention and the one with the fewest absolute contraindications and least controversy over its indication for secondary prevention, but only 71 percent of these patients used it consistently. Only 46 percent of patients consistently used prescribed beta-blockers, 44 percent used prescribed lipid-lowering agents, and only 21 percent consistently used a prescribed combination of aspirin, beta-blockers, and lipid-lowering agents. Further, consistent use was lowest among patients who had the greatest potential for benefit from these agents, including the elderly, patients with diabetes, and patients with heart failure. Although quality improvement initiatives have shown modest success in encouraging adherence to medications, much more research is needed to determine the most effective means of bolstering long-term medication adherence.

### Physician Oversight of NSAIDs Use

Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most common medications prescribed to older Americans, and they often are prescribed inappropriately. Adverse events associated with long-term NSAID use are common and often result in substantial illness and death. Physician adherence to guidelines recommending NSAID safety monitoring practices is low.

Researchers conducted a randomized trial to determine whether providing audit/feedback and educational materials to prescribing physicians would improve adherence to three



recommendations: laboratory monitoring for blood counts, laboratory monitoring for kidney function, and use of cytoprotective agents (medications to prevent stomach problems).<sup>5</sup>

There were no significant differences in performance between intervention and control physicians before or after the intervention for any of the three recommendations. However, results suggested a trend toward higher performance among physicians who reported receipt of the intervention materials and participated in the continuing medical education activities. Provider and patient factors and health services use were more strongly associated with adherence to NSAID safety-monitoring guidelines than were the educational materials tested.

The results highlight the challenges of interventions designed to improve adherence to NSAID safety-monitoring guidelines. No single intervention or set of interventions has proven effective in altering physician practice patterns in all settings. Although multimodal interventions have been effective for changing practice in other chronic diseases, no significant difference in NSAID safety-monitoring practices was found in this study.

The clinical and methodological insights gained from this work may lead future studies to greater success in improving physician adherence to evidence-based practice guidelines.

### **ACE Inhibitor Use and Risks in Early Pregnancy**

Use of angiotensin-converting enzyme (ACE) inhibitors during the second and third trimesters of pregnancy has been associated with an increased

risk of fetal abnormalities. In contrast, until now, based on several small, uncontrolled studies and unpublished reports, first-trimester use of ACE inhibitors had not been linked to adverse fetal outcomes. However, because angiotensin II receptors are widely expressed in fetal tissue and could play an important role in fetal development, it was postulated that first-trimester exposure to ACE inhibitors could increase the risk of congenital malformations.

Using a large Medicaid database, investigators assessed the association between exposure to ACE inhibitors during the first trimester of pregnancy and the risk of congenital malformations.<sup>6</sup>

Infants with exposure to ACE inhibitors solely in the first trimester had an increased risk of major congenital malformations compared with infants who had no exposure to antihypertensive medications. Use of other antihypertensive medications did not confer an increased risk. Infants exposed to ACE inhibitors were at increased risk of malformations of the cardiovascular system and the central nervous system.

As the approved uses for ACE inhibitors have expanded, their use among women of childbearing age has increased. This increase in use is likely to result in an increase in first-trimester fetal exposures. These data suggest that such exposures cannot be considered safe and should be avoided.

### **Continuous Glucose Monitoring Devices and Their Effectiveness in Children**

Controlling blood glucose levels delays the long-term complications from type 1 diabetes mellitus but

increases the risk for hypoglycemia. The continuous glucose-monitoring system (CGMS) gives blood glucose readings every 5 minutes and is very accurate and reliable in adults. However, there is not much information available about how effective this system is in children.

CERTs researchers conducted a study to determine whether the CGMS would improve blood glucose control in 27 children with type 1 diabetes mellitus.<sup>7</sup> Children were assigned to one of two groups. Both groups wore the CGMS for 72-hour periods. Therapy was adjusted for the intervention group based on the CGMS and self-monitoring data. Therapy for the control group was based only on self-monitoring data. Hemoglobin A1c levels were determined and the change from 0 to 6 months for the two groups was compared. At the beginning of the study, hemoglobin A1c levels were similar for the two groups, but by the end of the study, they were significantly lower for the intervention group. The decrease in the intervention group was statistically significant, but the decrease in the control group was not.

The CGMS may improve blood glucose control in children with type 1 diabetes mellitus without increasing the risk for hypoglycemia. However, the long-term benefits of the CGMS on metabolic control remain to be determined.

### **Vaccine Coverage – Unexpected Benefits and Challenges**

**Reduced pneumococcal bacteremia in adults when children in the home are vaccinated—A**

new pneumococcal conjugate vaccine containing seven serotypes was released in February 2000 for use in infants and children. In the following years, several observations were published linking the vaccine to a reduced rate of invasive pneumococcal disease among adults. CERTs investigators sought to determine if pediatric vaccination lowers the risk of pneumococcal bacteremia in adults living in the same home.<sup>8</sup>

The study had two parts: a 2-year prospective population-based surveillance for pneumococcal bacteremia in adults and a case-control study of risk factors for the disease. The study was carried out in a five-county region of Pennsylvania. The surveillance tracked all cases of pneumococcal bacteremia, while the case-control study involved contacting and interviewing both adults with the disease and a healthy control population.

Although the overall rate of pneumococcal bacteremia for the adults in the study decreased by a statistically insignificant 9 percent from 2002 to 2004, there was a significant 22-percent decrease in the cases that involved serotypes included in the new vaccine. The results of this study showed that vaccination of the youngest child in the home corresponded to an 80-percent reduction in the odds of the disease among adults in the same home.

**Examining surgeons' attitudes about hepatitis B vaccination—**In the 1990s, prior to the Occupational Safety and Health Administration (OSHA) mandate to offer hepatitis B vaccination to all health care workers, studies showed that many



surgeons were not adequately vaccinated. It is unknown if vaccination rates have improved since the OSHA mandate. Inadequately vaccinated surgeons may be a risk to their patients.

CERTs investigators sought to identify the proportion of U.S. transplant surgeons adequately vaccinated against the hepatitis B virus, identify characteristics associated with inadequate vaccination, and assess the proportion that had been evaluated for immunization after potential exposures to the hepatitis B virus.<sup>9</sup>

Of the 619 eligible surgeons, 347 (56.1 percent) returned completed questionnaires. A total of 23 percent had received fewer than the recommended three injections. Some factors associated with inadequate vaccination were increasing length of time a surgeon was in clinical practice, an increased fear of infection from patients, and a lack of recent testing for the hepatitis C virus. Of the 94 surgeons (27.3 percent) reporting at least one needle-stick exposure while operating on a patient with the hepatitis B virus, 14 (14.9 percent) were inadequately vaccinated; of these 14, only 5 (35.7 percent) sought appropriate testing and counseling for active immunization. Surgeons underestimated both the risk of exposure while operating and the risk of becoming infected if exposed.

Despite the mandate from OSHA that all health care workers be offered hepatitis B virus vaccination, some transplant surgeons are inadequately vaccinated and do not seek appropriate post-exposure evaluation. This increases risks to both the surgeons and their patients.

Determining the reasons for inadequate vaccination may help target interventions that promote vaccination and a change in behavior. Because inadequately vaccinated surgeons underestimate their risk of exposure, although they also express fear of acquiring hepatitis B, education regarding true transmission risks may increase the number willing to be vaccinated.

## Interventions to Change Physician Behavior

**Changing prescribing for heart failure**—Despite the incorporation of beta-blocker use into clinical practice guidelines for the treatment of heart failure, use of this proven therapy remains low. This may result from previously held beliefs that beta-blockers are harmful in heart failure and from the typically slow translation of evidence into practice.

A study was conducted to develop and test a multifaceted intervention using Internet-based academic detailing, physician feedback, and patient education to improve outpatient use of beta-blockers in patients with heart failure.<sup>10</sup>

Practices receiving intervention did not have a significantly higher use of beta-blockers than a control group of medical practices given written educational materials. However, a trend toward greater use of beta-blockers in the intervention group, coupled with results of prespecified secondary analyses demonstrating significantly more patients starting a beta-blocker than stopping a beta-blocker in intervention practices, put the findings in a more encouraging light.



The survival benefit associated with beta-blockers in patients with heart failure is large. Therefore, interventions with even modest increases in beta-blocker use could result in substantial benefits.

Investigators should continue to explore new types of interventions, physician incentives, and technological advances to stimulate adherence to guidelines for recommended therapies for heart failure.

**Testing for tuberculosis before starting infliximab**—After infliximab was approved by the Food and Drug Administration (FDA) to treat Crohn's disease (1998) and rheumatoid arthritis (1999), tuberculosis was reported in the FDA's spontaneous reports as one potential infliximab-related adverse event.

Researchers conducted a study to examine the impact of Federal, industry, and academic efforts to communicate this risk to users of infliximab.<sup>11</sup> The effectiveness was evaluated by the proportion of patients getting tuberculin skin tests, which assess whether patients are harboring latent tuberculin infection before or soon after taking infliximab. The investigators also wanted to determine if there was a difference in tuberculin skin testing rates among the various medical specialists who treated patients requiring infliximab.

Tuberculin skin testing rates doubled over a 30-month period as the risk communication efforts continued. Rheumatologists were the only specialists who showed a significantly higher than average rate of tuberculin skin testing among their patients.

The study showed that risk-communication efforts can increase physician compliance in tuberculosis testing of their patients, and, in this case, might decrease the risk of activating latent tuberculosis infection potentially associated with infliximab.

The findings of this study suggest opportunities for further research to determine what types of communications elicit the greatest compliance, whether multiple communications are more effective, and whether repetition of messages further increases compliance, thus optimizing public health.

### Patient Self-Reporting of Medication Use

**NSAIDs use**—Each year an estimated 16,000 people die from NSAID-induced gastrointestinal complications. Patients frequently fail to report to their doctors that they are taking over-the-counter NSAIDs, and serious problems may occur when nonprescription NSAIDs are used alone or in combination with other medications.

CERTs investigators sought to determine if self-reported use of nonprescription and prescription NSAIDs matched the information in the patient's medical records, and to determine which of two survey formats aided patients' recognition and recall of medication use.<sup>12</sup>

Patients in a rheumatology clinic completed 361 surveys: 182 in list format and 179 in open-ended format. Medical records review confirmed 26.1 percent of patient-reported nonprescription NSAID use and 59.1 percent of patient-reported

prescription NSAID use. For patients using both prescription and nonprescription NSAIDs, both medications were confirmed in only 2.3 percent of the medical records. Fewer patients reported nonprescription NSAID use with the open-ended format survey (24.0 percent) than with a checklist format (41.8 percent).

Agreement between self-reported NSAID use and medical record documentation is especially poor for nonprescription NSAIDs. This lack of communication and understanding about concomitant prescription and nonprescription medication use may lead to serious adverse reactions, including death.

Although this study did not test an intervention, it suggests that using a checklist for obtaining history of medication use might increase patient-physician communication regarding NSAID use. Addressing NSAID use at the point of purchase (pharmacies) using a list-type survey may offer a unique opportunity to decrease risky concomitant prescription and nonprescription NSAID use.

**Osteoporosis medications**—Pharmacy and linked claims databases are used to determine whether patients receive medications as a quality-of-care measure. However, these databases have not been compared with self-reported data for patients receiving medications used to treat glucocorticoid-induced osteoporosis.

CERTs researchers examined agreement between filled prescriptions in a pharmacy database and self-reported current use of several osteoporosis medications among chronic glucocorticoid users

enrolled in a large U.S. managed care plan.<sup>13</sup> Chronic glucocorticoid use was defined as 60 or more days of filled outpatient oral glucocorticoid prescriptions from July 2001 to December 2002.

Agreement between the pharmacy data and the self-reported data was high, and underreporting of current osteoporosis medication was uncommon among chronic glucocorticoid users enrolled in managed care. Both sources of information seem to be appropriate in assessing exposure to osteoporosis medications.

CERTs investigators found that use of pharmacy data alone is unlikely to lead to an underestimate of osteoporosis treatment, but there is a need for a longer assessment period in studies that rely only on pharmacy data.

## Assessing Risks of Medication Errors and Adverse Events

**Pediatric dosing errors**—Prescription dosing errors are common in children. Their smaller size makes them more vulnerable to dosing errors and less able to communicate signs and symptoms that indicate a problem. CERTs investigators analyzed the prevalence of potential outpatient prescription errors in the dosages of 22 medications commonly prescribed to children.<sup>14</sup>

A total of 15 percent of the 22 most commonly prescribed medications for children appeared to have dosing errors, 8 percent of which involved overdosing and 7 percent of which involved underdosing. The most frequently potentially



overdosed drugs were the four analgesics examined—acetaminophen with codeine, ibuprofen, naproxen, and oxycodone. The most frequently underdosed drugs were antiepileptics. Medications prescribed “as needed” were the most likely to be overdosed when the projected total daily dose was calculated as the amount a child would possibly receive if given the upper range of the dose at the most frequent dosing interval. The formulation of the drug did not affect the number of dosing errors. The number of errors also was not affected by one site’s use of computerized prescription order entry (CPOE) that contained decision support for some medications, but no child-specific decision support, calculation of doses, or error checking.

Particularly disturbing was the high rate of overdosing of analgesics, since these drugs can have serious or fatal adverse events. Also, the youngest children and children with complex health conditions appeared to be the most vulnerable to potential dosing errors.

Only one medication, trimethoprim-sulfamethoxazole, was dosed within the recommended weight-based dosing range for all doses dispensed. This medication had only a few outpatient formulations and a simple standard weight-based dosing range for most uses. If such simplicity in formulation and dosing helps correct dosing, then standardization of medication dosing regimens for children may be an important strategy for preventing dosing errors.

All parties, health care providers and parents, need to be vigilant with drug prescriptions for children. In addition, computerized prescription systems need to

take into account the complexities of medication dosing for children’s weight. Standardization and simplification of medication dosing regimens merit further consideration as a means to lower the risk of medication dosing errors.

**Measuring EKG changes related to arrhythmias**—Over 25 drugs on the market can have an effect on the electrocardiogram to prolong the QT intervals. This effect is associated with the development of life-threatening ventricular arrhythmias called torsades de pointes. FDA guidelines recommend that the QT interval of people taking these medicines be monitored for the excessive prolongation that increases the risk of torsades de pointes. Because the QT interval changes when the heart rate changes, guidelines recommend that the interval be corrected for any differences in heart rate. Over 15 different rate correction formulas have been recommended, of which the Bazett and Fridericia formulas are most commonly used. The formulas have not been thoroughly evaluated to determine if they can be applied when monitoring the effects of drugs that can prolong the QT interval.

CERTs investigators developed a standardized clinical exercise protocol that accurately defined the QT interval over a wide range of heart rates.<sup>15</sup> They then administered an intravenous infusion of ibutilide, an antiarrhythmic drug chosen for use because it prolongs the QT interval. A total of 18 male and female volunteers were enrolled and performed the exercise protocol before and during the ibutilide infusion. Four heart rate correction formulas were



applied to the data and compared with the results obtained during exercise (uncorrected). The most commonly used formulas, the Bazett and Fridericia formulas, overestimated the change in QT interval. However, the Framingham and Hodges formulas did not change the accuracy of the assessment of QT interval change. This study found that the standard Bazett and Fridericia formulas can introduce significant errors in the assessment of drug effects on the QT interval. If the results of this study are verified using additional drugs, then practicing cardiologists and the manufacturers of electrocardiogram machines may require changes to the rate correction formulas that they use.

**Errors with the use of allopurinol and colchicines**—Gout-specific medication dosing errors are common, often having harmful or even fatal consequences. CERTs researchers examined gout-specific medication errors using an Internet-accessible error-reporting system, MEDMARX®.<sup>16</sup>

Of the medication errors reported in MEDMARX over a 5-year period, 0.15 percent occurred with gout-specific medicines: primarily allopurinol, followed by

colchicine, probenecid, and sulfipyrazone. Errors involving allopurinol and colchicine were more likely than other medication errors to result from prescribing errors rather than drug-administration errors. Physicians were the health care providers most responsible for these errors. This study explores the reasons for gout-related medication errors by looking at personnel involved, contributing factors, harm rates, and error type and origin.

Quality improvement measures need to be initiated in gout management, focusing on physician practice and prescribing behaviors.

**Adverse events associated with glucocorticoids**—The prevalence and severity of adverse events associated with glucocorticoid use are unknown, and concern for the possible occurrence of such events often limits use of these drugs. Potential adverse events may range from mild (acne, weight gain, sleep disturbances) to severe (osteoporosis, fractures, cataracts).

CERTs investigators sought to determine the prevalence of glucocorticoid-associated adverse



events in a large U.S. managed care population.<sup>17</sup> In the survey of 2,446 managed care enrollees, glucocorticoid users reported weight gain (80 percent) as the most common adverse event, followed by skin bruising/thinning and sleep disturbances. Cataracts and fractures were reported less frequently. Strong dose-response relationships were observed between glucocorticoids and most adverse events, and such events were reported relatively frequently, even at lower doses. A high prevalence of self-reported adverse events is associated with glucocorticoid use among individuals treated long term for a variety of conditions.

Physicians should closely monitor patients for glucocorticoid-related adverse events and should provide counseling about possible risks before beginning glucocorticoid therapy.

### Using Health Information Technology To Reduce Medication Interactions and Errors

**Warfarin medication interactions**—The use of computerized systems to help clinicians avoid making medication errors through a system of automatic alerts and reminders has been shown to be effective in hospitals and clinics. It is not known how effective such systems are at preventing outpatient medication errors, or how effective they are at preventing problems that occur due to the interaction of two or more medications.

The objective of this study was to assess the effectiveness of computerized alerts in electronic medical records in preventing prescriptions of medications that interact with warfarin, a commonly prescribed drug known to have many potential drug interactions with possibly serious consequences.<sup>18</sup>

Almost one-third of the patients included were found to have a prescription that interacted with warfarin. The use of computerized alert systems in the electronic medical record resulted in a relative reduction of 15 percent in the observed rate of interacting prescriptions at 12 months. The reduction was immediate, with a progressive monthly reduction for interacting prescriptions over the followup period. Special training for groups of clinicians, sometimes called “academic detailing,” did not appear to have an additional effect in reducing prescriptions of interacting medications.

This study supports using computer assistance to prevent potential medication errors in the outpatient care setting, but effects on patient outcomes (e.g., bleeding) were not part of the study design.

Further studies should focus on finding the best strategies for incorporating academic detailing efforts in the context of electronic alerts, as well as estimating effects on patient outcomes.

**Computerized drug-drug interaction alerts in community pharmacy**—Community pharmacies play a vital role in the safe use of medications and in helping to prevent potentially harmful drug-drug interactions (DDIs). CERTs researchers sought to examine community pharmacists’ attitudes about the

usefulness of computerized DDI alerts and to determine what factors are associated with favorable perceptions of these alerts.<sup>19</sup>

The researchers found that pharmacy managers did not think that DDI alerts are a waste of their time, but there was some concern that their computer systems might not be providing them with potential DDI (PDDI) alerts. The majority of pharmacists were confident in their ability to identify and discuss PDDIs with physicians. More favorable perceptions of PDDI alerts were found in pharmacies with software that provided detailed DDI information and allowed pharmacists to customize PDDI alerts.

**Pharmacy technicians and computerized alerts**—Community pharmacies are important in identifying and preventing serious DDIs. Technicians in community pharmacies are often the first to become aware of alerts about potential DDIs.

CERTs researchers examined the role of pharmacy technicians in managing PDDI alerts in community pharmacies and the possible relationship to the pharmacy manager's attitude about PDDI alerts.<sup>20</sup> Pharmacy managers in 3,000 community pharmacies across the United States were surveyed, and data were collected about demographics, workload issues, handling of DDIs, and pharmacists' attitudes toward computerized DDI alerts.

It was found that technicians were often allowed to override the less significant PDDI alerts without having to consult the pharmacist. In some pharmacies (2.1 percent), technicians were allowed to override interactions with the highest potential

clinical significance. In pharmacies with the highest use of technology, technicians were less likely to be allowed to override insignificant interactions. The pharmacies that allowed technicians to override clinically significant interactions were more likely to feel that the alerts are a waste of time and that the volume of alerts makes it difficult to determine which are important and which are not.

The education and role of pharmacy technicians continue to evolve and the quality of decision support provided with alerts is improving. Since pharmacy technicians are likely to play an increasingly important role in managing PDDI alerts, further study of this evolution and how it impacts patient care and pharmacy efficiency is needed.

**Drug-drug interaction software for personal digital assistants**—Medication errors, including DDIs, have been estimated to cause 106,000 deaths annually in hospitalized patients. Personal digital assistants (PDAs) allow health care professionals to check for potential DDIs at the point of care, thereby reducing the time needed to consult traditional references, which are often out of date. PDAs, however, can only be as effective as the software programs they use.

CERTs investigators in this study<sup>21</sup> examined the capacity of drug-drug interaction software programs manufactured for Palm OS-compatible PDAs in detecting important DDIs. A prospective evaluation of the ability of eight software programs for PDAs to detect important DDIs was conducted. Sensitivity (the ability to correctly indicate that an interaction exists) and specificity (the ability to indicate correctly

that no interaction exists) were measured for each of the software programs. Five of the programs had a perfect score on sensitivity; only one program had a perfect score on specificity.

To provide high-quality health care, all health care providers who prescribe and/or dispense medications need to catch prescribing errors before patients receive the medication. As more drugs appear on the market, the potential for DDIs increases, making the value of timely information even more important. It is critical that software correctly identify important interactions. Because evaluation of any program is a point-in-time determination and manufacturers are constantly striving to update and improve their products, programs should be periodically evaluated and compared.

### Web-Based Provider and Patient Education

**Online education on drug interactions**—Six of the last 19 drugs removed from the market were found to cause a potentially lethal heart rhythm abnormality, torsades de pointes, especially when there was an interaction with other drugs that caused the drug levels to increase. Over 25 drugs with this potential remain on the market, making it important for health care providers to understand this particular form of cardiac toxicity, its relation to prolongation of the QT interval on the electrocardiogram, and the important role of drug interactions. In an analysis of drugs prescribed to over five million people, CERTs investigators found a high frequency of coprescribing of drugs that each



prolong the QT interval, thereby putting these patients at risk of torsades de pointes.

To address the need to make better information available for prescribers, CERTs investigators maintain an educational Web site, [www.QTdrugs.org](http://www.QTdrugs.org). Based on an ongoing evidence-based process to monitor and assess drugs for their potential to prolong the QT interval and cause torsades de pointes, drugs are classified into lists according to risk. In 2006, there were 344,689 visitors to the site and the QT Drug Lists received 41 percent of all page views. In addition, CERTs investigators provide a free online version of an educational module titled Preventable Adverse Drug Reactions: A Focus on Drug Interactions. Created in collaboration with the

FDA, the module contains teaching slides, sample questions, references, and a pocket reference tool showing how to predict and prevent the major metabolic drug interactions. The educational module has been downloaded from [www.QTdrugs.org](http://www.QTdrugs.org) 28,000 times in the last 3 years and more than 12,000 times in the last year.

**Online consumer drug information**—The Internet has become an increasingly important source for consumers searching for drug information. Over 25 percent of Americans have used the Internet to search for prescription drug information. However, seeking health information online can be a formidable task. The abundance and technical complexity of such information are overwhelming, and consumers often lack the knowledge to efficiently search the Internet for dependable drug information or how to distinguish high-quality from poor-quality drug information.

With this dilemma in mind, CERTs investigators conducted a systematic search of prescription drug information Web sites and evaluated them for information quality and utility for consumers.<sup>22</sup> CERTs pharmacists and health communication specialists created a Webliography, or annotated list of recommended Web sites providing free prescription drug information, and made it available online along with a printable brochure and patient information sheet (available at [www.azcert.org](http://www.azcert.org)).

## Health Care Spending and Costs

**Spending on post-approval drug safety**—Recent withdrawals of high-profile drugs have focused

attention on post-approval safety surveillance by pharmaceutical manufacturers and the FDA. The public relies on such surveillance to detect rare and unexpected reactions to new medications that go undetected before they are approved. Currently, the primary post-approval method for tracking adverse drug reactions relies on spontaneous reporting—i.e., patients or clinicians report adverse events (AEs) directly to the FDA or to the manufacturer (who must report them to the FDA within a specific timeframe). Depending on the number and severity of AEs reported, a manufacturer may be required to take action, which may include new research, revised labeling, or removal of the drug from the marketplace.

To gauge the amount of funding devoted to post-approval surveillance efforts, CERTs researchers surveyed 25 large pharmaceutical companies, 11 of which responded.<sup>23</sup> Those 11 companies' sales accounted for 71 percent of sales by the top 20 pharmaceutical manufacturers in 2003. Using the safety spending data provided by these respondents, the researchers estimated that the top 20 companies spent \$800 million (or 0.3 percent of their total sales) on post-approval safety in 2003. In the same year, drug companies spent 15.6 percent of sales on research and development. The study also reported that the U.S. government budgeted \$22.1 million for the FDA's Office of Drug Safety in 2003, less than the average spending on post-approval safety by any one drug company surveyed.

The United States is where most new and innovative drugs are launched, so the need for effective and



well-financed post-approval safety surveillance is great. The CERTs survey, the first of its kind, will help to inform ongoing discussions about proposed changes to the system.

**Impact of cost-sharing on use of oral hypoglycemics**—Increased cost-sharing (copayments) for chronic-disease medications may lead to their reduced use, which over time could lead to increased medical complications.

Segmented time-series regression models were used to estimate the effects of small (\$1-\$6), moderate (\$7-\$10), and large (more than \$10) increases in cost-sharing for a 30-day supply of an average daily dose of oral hypoglycemics among adults with type 2 diabetes in five managed care organizations.<sup>24</sup> Large copayment increases were associated with an immediate and continued decrease in the average daily dose of oral hypoglycemics. Other studies have shown that adults with diabetes mellitus who report cost-related medication underuse also report poorer glycemic control and worse health status than patients who do not report cost-related medication underuse.

Collectively, studies of the impact of cost-sharing on medication use suggest that drug-benefit plans should be designed in a way that lessens the potential adverse effects of large cost-sharing increases among patients requiring essential chronic-disease medications.

**Health care costs of undertreated heart failure**—In a study of managed care heart failure patients, it was found that fewer than 14 percent adhere to pharmacotherapeutic or drug regimens to treat their disease, resulting in significantly higher rates of hospitalization and health care costs.

A team of CERTs investigators sought to evaluate the effect of regular use of four heart failure agents (angiotensin-converting enzyme inhibitors, beta-blockers, loop diuretics, and digoxin) on rates of hospitalization and total health care costs in patients enrolled in managed care organizations.<sup>25</sup>

Patients who received none of the four heart failure agents were at 2.5 times greater risk of hospitalization and had 43.6 percent higher health care costs compared with all other heart failure patients. Patients who consistently used the agents had 80 percent fewer hospitalizations and incurred 70 percent less health care costs than the patients receiving no therapy.

Physicians treating patients with heart failure may need to monitor their patients' drug therapies, identify patients not being treated according to guideline recommendations, and prescribe the appropriate regimens for these patients.

## CERTs Research Centers Added in 2006

In April 2006, four new research centers were added to the CERTs program: the University of Texas MD Anderson Cancer Center and Baylor College of Medicine; Rutgers, The State University of New Jersey; Weill Medical College of Cornell University; and the University of Iowa. Investigators at these new centers are working on a wide range of topics, including consumer and patient education and adherence, mental health therapeutics, medical devices, aging, and the elderly.

### Consumer and Patient Education and Adherence

#### **Improving outcomes for multiple morbidities—**

Despite the demonstrated efficacy and cost-effectiveness of treatment and prevention strategies for many chronic conditions, many older persons, especially those with comorbid conditions, continue to suffer from uncontrolled hypertension, hyperglycemia, and other predictors of poor health outcomes. To address this gap in the implementation of effective and efficient medical care, CERTs researchers will develop and test a model of collaborative group clinics that seeks to empower older patients to adopt goal-setting behaviors and communicate with their health care provider to improve diabetes-related outcomes.

#### **Informed decisionmaking about statins—**

Studies have consistently shown that statins reduce the risk of heart attack and stroke by 30-40 percent. Despite this, many patients reject or stop taking statins because of concerns about potential side effects and other problems. A patient education

intervention that improves statin compliance would likely prevent many heart attacks and strokes. Researchers are working to develop and evaluate the potential efficacy of a new statin decision aid in Spanish and English for low-literacy primary care patients.

### Mental Health Therapeutics

**Pharmaceutical care for mental illness under Medicare Part D—**Pharmaceutical care provided through the Medicare Part D program is critical for elderly and disabled persons with mental illnesses. A particular concern involves persons dually eligible for Medicare and Medicaid, a population that includes many with severe chronic mental illness. To address this problem, CERTs researchers are examining the provision, quality, and outcomes of pharmaceutical care for beneficiaries with mental illness under the Medicare Part D program.

**Psychotropic therapy among children and adolescents—**Rates and use of psychotropic medications among children and adolescents have increased sharply in recent years, raising a number of concerns related to safety, quality, appropriateness, and management of these regimens. Since there is considerable variation in treatment patterns, studies are needed to examine patterns across multiple States, especially for economically disadvantaged children and adolescents. CERTs researchers are examining treatment patterns, predictors, and trends in the use of psychotropic medications among child and adolescent Medicaid patients.



**SSRI use and suicidality in depressed children and adolescents**—Scientific uncertainty and controversy continue over the possible impact and magnitude of selective serotonin reuptake inhibitors (SSRIs) on suicidality, particularly among depressed youths. Recent analyses raise significant safety concerns about such effects. Analyses of large administrative databases such as Medicaid can support informed treatment decisionmaking by physicians, patients, families, and others. Investigators are examining the rates of suicide and suicide attempts in high-risk youths who received treatment for depression with SSRIs.

## Medical Devices

**Impact of regionalization**—Regionalization of complex surgical procedures involves moving patients from low-volume sites and moving surgeons to high-volume sites. This may lead to better short- and long-term outcomes, but the impact on patient populations, including rural and minority populations, has not been assessed. CERTs researchers are evaluating whether the regionalization of total joint replacement procedures would lead to a reduction of in-hospital adverse events.

**Volume-outcome relationships**—Automatic implantable cardioverter defibrillators (AICDs) are being used more frequently across a wide population of patients with cardiovascular disease. It is not clear whether physician and hospital experience is associated with improved short-term outcomes. CERTs investigators are conducting research to determine whether there is a relation

between physician volume of AICD implantation and short-term complication rates.

**Prospective registry**—Predictors of short- and long-term outcomes from total joint replacement, variations in outcomes across different models of joint prostheses, and cost-effectiveness of joint prosthetic devices are important areas of concern in light of the growing use of these procedures in the aging population. CERTs researchers are working to determine the clinical, demographic, patient, and device characteristics associated with improved outcomes for patients undergoing total joint replacement procedures.

## Aging and the Elderly

**Guideline implementation**—Numerous studies have documented that practitioners are not providing care in a manner that conforms to clinical practice guidelines. Blood pressure is controlled in only 34 percent of patients with hypertension, despite six sets of guidelines over the last 30 years. Most cases of uncontrolled hypertension occur in patients who are over 65 years of age with access to health care and relatively frequent contact with physicians. It is possible that physicians' decisions and behavior, rather than limited access to care, may be factors contributing to poor blood pressure control. Improving adherence to hypertension guidelines is critical, but little information is available about underlying factors that contribute to poor adherence rates. Investigators are evaluating blood pressure control and guideline adherence among elderly patients. In addition, they are identifying



barriers to achieving and sustaining blood pressure control and developing strategies for improvements in blood pressure management.

**Medical decisionmaking for persons with lymphoma**—Older adulthood is a time of complex decisionmaking regarding medical issues. A significant proportion of healthy older adults have impaired cognitive decisionmaking abilities. Cognitive studies have suggested age-related declines in the amount of information used and in the thoroughness of the information search process undertaken by older adults engaged in various decisionmaking tasks. Treatment decisionmaking is particularly complex for the low-grade non-Hodgkin's lymphomas. A popular treatment choice (anthracycline-based combinations of chemotherapy) has the potential for significant morbidity, with uncertain impact on long-term disease control. Therefore, such patients must make difficult treatment decisions (e.g., short-term cost vs. long-term benefit). Older patients may be at increased risk for disadvantageous decisionmaking.

Investigators are evaluating which patient-related variables predict both strong and poor decisionmaking capacity. They are creating abbreviated and extended “menus” of medical treatment options that are appropriate for poor and strong medical decisionmakers.

**Botanical dietary supplements**—There is growing use of dietary supplements in the United States, with sales for 2004 estimated at \$19 billion. At least 15 million American adults are at potential risk for interactions between botanical dietary supplements and medications. Most physicians are not aware of their patients' use of botanical dietary supplements and are not able to advise their patients because they do not have sufficient knowledge about the safety and effectiveness of these supplements. As data become available, it is critical that they be widely disseminated to consumers and health care professionals. Investigators are developing new venues for disseminating information about the safety and efficacy of botanical dietary supplements for the elderly.

## CERTs Program Resources

ADHD Online Toolkit for Providers, Patients, and Families: Web Tool

[nichq.org/resources/toolkit](http://nichq.org/resources/toolkit)

Arthritis Outcomes Initiative Resource for Patients and Families: Web Resource

[www.Engalitcheff.uab.edu](http://www.Engalitcheff.uab.edu)

Arthritis Self-Help for Patients: Web Site

[www.arthritispatient.cme.uab.edu/](http://www.arthritispatient.cme.uab.edu/)

Beta-Blocker Fact Sheet for Providers

[dukecerts.dcri.duke.edu](http://dukecerts.dcri.duke.edu)

Challenging Cases in Musculoskeletal Medicine: Online Education Course for Providers

[www.giop.certs.cme.uab.edu/](http://www.giop.certs.cme.uab.edu/)

Doubly Robust SAS Macro: Data Analysis Tool

[HarryGuess.unc.edu](http://HarryGuess.unc.edu)

Drug Interaction Card: Reference Guide for Providers and Patients

[www.drug-interactions.com](http://www.drug-interactions.com)

Drugs That Prolong the QT Interval and/or Induce Torsades de Pointes: List for Providers and Patients

[www.qtdrugs.org](http://www.qtdrugs.org)

Harry Guess Virtual Research Community: Web-Based Repository of Pediatric Therapeutics Tools

[HarryGuess.unc.edu](http://HarryGuess.unc.edu)

Head and Chest Colds: Brochure for Patients

<http://www.cceb.upenn.edu/cert/consumers.html>

Medications That Interact with Methadone: Wallet Card for Patients and Providers

[www.arizonacert.org/methadone-card.pdf](http://www.arizonacert.org/methadone-card.pdf)

Osteoporosis Management: Online Case-Based Disease Education Program for Providers

[www2.edserv.musc.edu/osteo/index.lasso](http://www2.edserv.musc.edu/osteo/index.lasso)

Over-the-Counter Medicine “Interaction” Cabinet: Web Tool for Patients

[www.arizonacert.org/consumers/MCSurvey/router.asp](http://www.arizonacert.org/consumers/MCSurvey/router.asp)

Preventable Adverse Drug Reactions—A Focus on Drug Interactions: Education Course for Providers

[www.arizonacert.org/medical-pros/education/module01.cfm](http://www.arizonacert.org/medical-pros/education/module01.cfm)

REACH: REducing Antibiotics for CHildren: Education for Providers, Patients, and Families

[www.reachmass.org/](http://www.reachmass.org/)

Safer Use of Nonsteroidal Anti-Inflammatory Drugs: Online Education Course for Providers

[www-cme.erep.uab.edu/nsaids/nsaids.html](http://www-cme.erep.uab.edu/nsaids/nsaids.html)

Saving Lives with Beta-Blockers: CyberSession for Providers

[dukecerts.dcri.duke.edu](http://dukecerts.dcri.duke.edu)

Tools and Techniques of Improved Medication Use: Web Site for Providers

<http://www.ahip.org/content/default.aspx?bc=38|77|529>

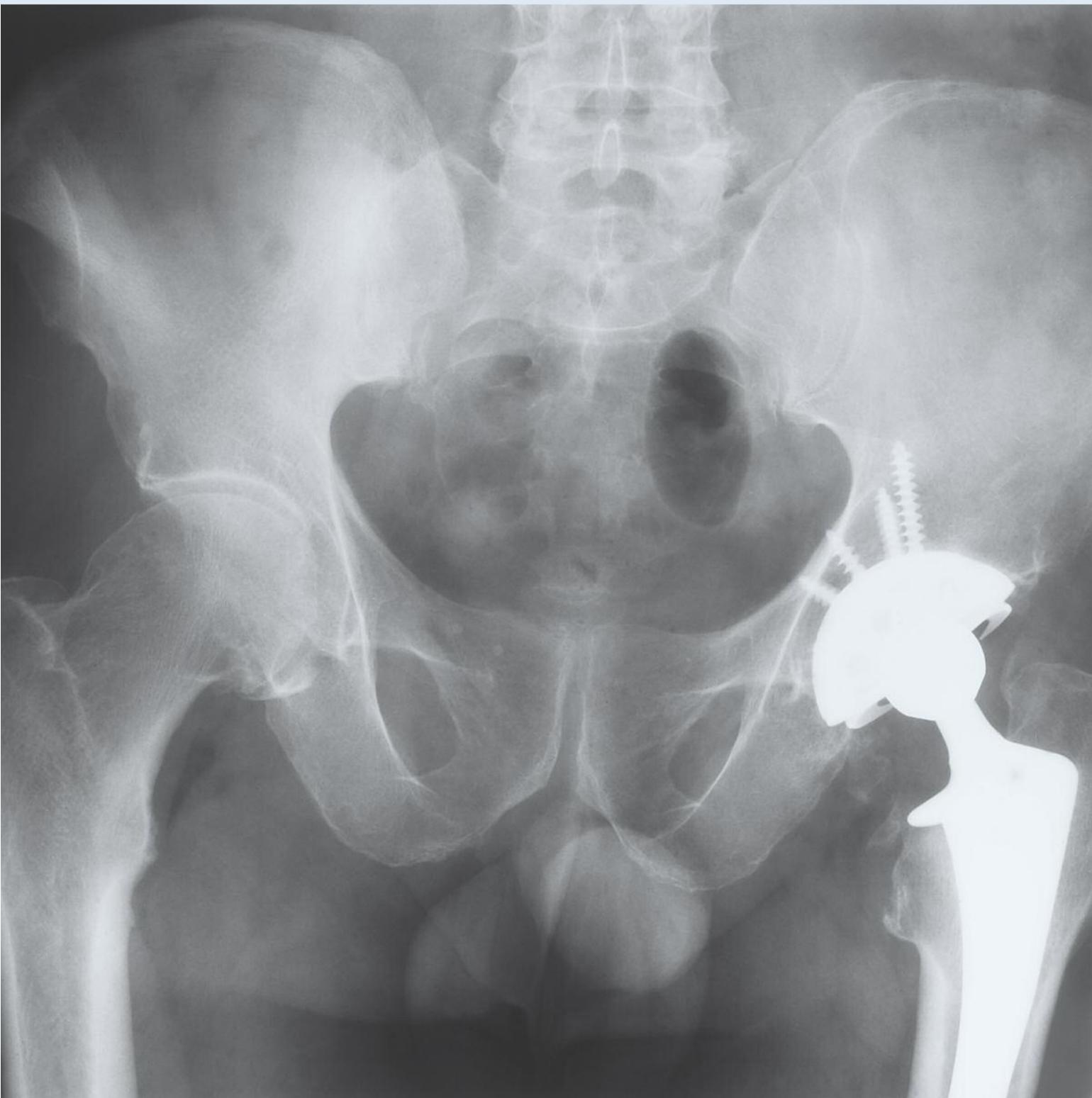
Treating Congestive Heart Failure with Beta-Blockers: Brochure and Videotape for Patients

[dukecerts.dcri.duke.edu](http://dukecerts.dcri.duke.edu)

Understanding the QT Interval—Web-Based Education Module for Providers

[qtmodule.mc.duke.edu](http://qtmodule.mc.duke.edu)

**NOTE:** For additional information about CERTs program resources, please contact the CERTs Coordinating Center at [certs@kpchr.org](mailto:certs@kpchr.org).





## CERTs Partnerships and Collaborations

Public-private partnership is a cornerstone of the CERTs program. Program activities are greatly enhanced by working with partner organizations. Collaboration among organizations with similar missions is essential to accomplishing program objectives. In addition to the many partnerships that enable the CERTs centers to study issues concerning therapeutics, the CERTs also collaborate with other public and private organizations on initiatives to support and enhance other program projects.

### **Partnerships to Advance Therapeutics (PATHs)**

Established by the CERTs in 2001, the PATHs program is a means to cultivate partnerships among national organizations interested in promoting the safe and effective use of therapeutics.

Every year, the CERTs host a meeting for PATHs partners. Participating organizations represent patients, health care providers, government, academia, delivery systems, payers, purchasers, and manufacturers of medical products.

The annual PATHs meeting provides a forum for organizations to plan and implement goals related to the improvement of therapeutics. With the expansion of the program this year (four new centers were added midyear), no annual meeting was held. In lieu of the meeting, program activities focused on the development of internal partnerships through a comprehensive orientation process. As a core value of the program, centers will continue to build upon this strong base of partnership within the program to help attract new external partners.

The PATHs program is an integral part of the CERTs program and exemplifies the value of public-private partnership. See the list of project partners in this report. A registry of PATHs partner projects can be accessed through the CERTs Web site at: [www.certs.hhs.gov/partners/paths/regist/](http://www.certs.hhs.gov/partners/paths/regist/).

## Partnership and CERTs Medical Devices Workshop\*

As published in the July 2006 issue of the *American Heart Journal*, the CERTs convened a group of experts to discuss the key issues affecting the development and use of medical devices in this country. Medical devices include products such as coronary stents, glucose monitoring devices, and joint prosthetic devices.

Although many new medical devices are available in the United States, there are many knowledge gaps concerning benefits and risks. This lack of information impacts patients and physicians, as well as decisionmakers at insurance companies and government agencies. Everyone involved needs sensible, evidence-based information to determine which products offer the best long-term benefits without unnecessary risks. These decisionmakers need cost-benefit information when weighing policy decisions so that they can be good stewards of society's health care dollars.

The United States would benefit from efficient ways to evaluate medical devices. Given our aging population, the number of patients in whom medical devices could be used poses a significant impact to the health care budget. The goal of the workshop was to develop a list of ideas for future research projects to improve our current system.

Representatives from the Centers for Medicare & Medicaid Services, health services researchers, practitioners, device manufacturers, and regulators discussed various perspectives, issues, and hurdles surrounding the limitations in knowledge about medical devices. Funding shortages were identified as a central issue; therefore, the group shared ideas for developing better public-private partnerships to help increase research funding. In addition, the workshop participants discussed ideas for priority setting, ways to improve current research methods, and new approaches to integrate the Federal agencies to address needs.

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\*Califf RM, for the Workshop Participants. Evaluation of diagnostic imaging technologies and therapeutics devices: better information for better decisions: proceedings of a multidisciplinary workshop. *Am Heart J* 2006;152:50-8.



## Conclusion

Although drugs and other therapeutic products have improved the lives of many Americans, our current health care system does not always guarantee that they will be used safely and effectively, nor that all adverse effects will be identified before they are put on the market. Today, with more choices available than ever before, people need independent, unbiased information about the benefits and risks of various therapeutic products. While government, the medical products industry, and others have made progress, vital questions remain unanswered. The CERTs program was created to address this need and continues to conduct research and disseminate information about the benefits and risk of the various therapeutic options available.

Whether the challenge is using technology to reduce medical errors or developing ways to improve communications to help people make more informed decisions, CERTs researchers are undertaking projects on a wide range of topics to improve everyday health care for the American people.

This year the CERTs program expanded, with the addition of four new centers and several new partners. We look forward to increasing the scope of our projects as we continue to advance knowledge of medical therapeutics in ways that will inform health care providers, patients, policymakers, and others, leading to improvements in the safe and effective use of therapeutics.

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(April-September)

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Director, Office of Surveillance and Biometrics  
Center for Devices and Radiological Health  
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(October-January)

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**Alvin I. Mushlin, MD, ScM**

Principal Investigator  
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(April-September)

**Richard Platt, MD, MS**

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**Wayne A. Ray, PhD**

Principal Investigator  
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**Kenneth G. Saag, MD, MSc**

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**Marcel E. Salive, MD, MPH**

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Centers for Medicare & Medicaid Services  
(October-April)

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Executive Vice President  
American Health Quality Association

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**Maria E. Suarez-Almazor, MD, PhD**

Principal Investigator  
University of Texas MD Anderson Cancer Center and  
Baylor College of Medicine  
(April-September)

**Myrl Weinburg, CAE**

President  
National Health Council

**Raymond L. Woosley, MD, PhD**

Principal Investigator  
Arizona CERT at The Critical Path Institute (C-Path)



## Principles of CERTs Public-Private Partnerships

**Issues of Public Interest.** CERTs is a national initiative to foster the optimal use of therapeutics through research and education activities that are in the public interest but would not otherwise be done.

**Public-Private Partnership.** CERTs is a public-private partnership on two levels: (1) between the U.S. Department of Health and Human Services and the CERTs centers and (2) between CERTs centers as representatives of the government-sponsored CERTs program and other research-sponsoring organizations. In the latter relationship, the CERTs centers seek useful, appropriate interactions with private organizations to support and enhance education, research, and demonstration projects. AHRQ works with the centers to establish appropriate agreements to optimize use and sharing of resources.

**Conflicts of Interest.** Public-private partnerships typically present the potential for conflicts of interest. While these potential conflicts of interest cannot be completely avoided or eliminated, a CERTs center has an obligation to disclose fully and

to manage conflicts in a manner that minimizes the risk of those conflicts, while at the same time permitting as much progress as possible to achieve CERTs goals within the constraints of maintaining respected research activity.

**Academic Integrity.** As academic researchers, individuals conducting projects under the CERTs umbrella make the final decision about study design, analysis, conclusions, and publication in any partnership with other organizations and ensure that their work complies with their respective institutions' conflict-of-interest rules.

**Activities.** CERTs activities are defined as projects supported in whole or in part by AHRQ funds under the CERTs demonstration program. Activities such as the review of potential conflicts of interest are subject to processes established for the CERTs program. Individuals affiliated with the centers also conduct education and research activities outside of CERTs that are not subject to CERTs processes.

## CERTs Project Partners

We gratefully acknowledge the following organizations for their expertise and support of CERTs research and education projects:

Academic Medicine and Managed Care Forum

AccessCare, Inc.

Advanced Medical Technology Association

Aetna Inc.

Agency for Healthcare Research and Quality

Agouron Pharmaceuticals, Inc.

Alabama Chapter of the American College of Physicians

Alabama Department of Public Health

Alabama Practice-based Continuing Medical Education and Research Network

Alacare Home Health Care

American Academy of Family Physicians

American Academy of Pediatrics

American Association of Colleges of Pharmacy

American College of Cardiology

American College of Clinical Pharmacy

American College of Rheumatology

American Heart Association

American Pharmaceutical Association Foundation

American Pharmacists Association

America's Health Insurance Plans

Amgen

Arizona Area Health Education Centers

Arthritis Foundation

Arthritis Foundation, Alabama Chapter

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AstraZeneca

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Children's National Medical Center

Cincinnati Children's Hospital Medical Center

Columbus Children's Hospital

Community Cares of North Carolina

Community Health Centers

Computer Sciences Corporation (CSC)/Clinical Data Abstraction Center (CDAC)

Conceptis Technologies

Council for Affordable Quality Healthcare

Critical Path Institute (The)

Crohn's & Colitis Foundation of America

Department of Veterans Affairs

Duke Clinical Research Institute

Duke Educational Media Services

Duke Heart Center

Duke Infection Control Outreach Network

Duke University Department of Psychology

Duke University Health System  
Eli Lilly and Company  
Express Scripts, Inc.  
Fallon Community Health Plan  
Genentech, Inc.  
General Practice Research  
Database/EPIC  
Georgetown University  
GlaxoSmithKline  
Group Health Cooperative of  
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Harvard Pilgrim Health Care  
Harvard School of Medicine  
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Health Resources and Services  
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HealthPartners  
Henry Ford Health System  
IMS Health  
Infectious Diseases Society of  
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Institute for Healthcare  
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Institute of Medicine  
Integrative Pain Center of  
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International Society for  
Pharmacoepidemiology

Iowa Women's Health Study  
Janssen Pharmaceutica  
John A. Hartford Foundation  
Kaiser Permanente Colorado  
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Kaiser Permanente Northern  
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La Frontera Hope Center  
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Research Council Clinical Trials  
Centre, Sydney, Australia  
National Initiative for Children's  
Healthcare Quality

National Institutes of  
Health/National Cancer Institute  
National Institutes of  
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Allergy and Infectious Diseases  
National Institutes of  
Health/National Institute of  
Arthritis and Musculoskeletal  
and Skin Diseases  
National Institutes of  
Health/National Institute of  
Diabetes & Digestive & Kidney  
Diseases  
National Institutes of  
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Health/National Institute of  
Nursing Research  
National Institutes of  
Health/National Institute on  
Aging  
National Institutes of  
Health/Office of Research on  
Women's Health  
National Patient Safety  
Foundation  
North Carolina Access Care  
North Carolina Area Health  
Education Centers

North Carolina Association of Pharmacists  
North Carolina Center for Children's Healthcare Improvement  
North Carolina Department of Health and Human Services  
North Carolina Medicaid  
North Carolina State Children's Health Insurance Program  
North Carolina Women, Infants, and Children Program  
Ortho-McNeil Pharmaceutical, Inc.  
Parke-Davis Pharmaceutical  
Pediatric Research in Office Settings  
Penn Center for AIDS Research  
Pennsylvania Department of Public Health  
Pennsylvania Pharmaceutical Assistance Contract for the Elderly  
Pfizer Inc.  
Pharmaceutical Research and Manufacturers of America  
Pharmacia & Upjohn  
Pharmacogenetics Network  
Premier  
Proctor and Gamble  
ProVantage Health Services, Inc.

QED Solutions, Incorporated  
Reliant Pharmaceuticals, Inc.  
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RTI Health Solutions  
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Society for Healthcare Epidemiology of America  
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Society of Thoracic Surgeons  
South Carolina Office of Research and Statistics  
Southeastern Regional Osteoporosis Board  
TAP Pharmaceutical Products, Inc.  
Tennessee Department of Health  
UCLA/RAND Center for Adolescent Health Promotion  
U.S. Department of Health and Human Services/Office on Women's Health  
U.S. Food and Drug Administration  
U.S. Food and Drug Administration/Office of Women's Health  
U.S. Public Health Service

U.S. Quality Algorithms, Inc.  
United Mine Workers of America Health and Retirement Funds  
United States Pharmacopeial Convention, Inc.  
UnitedHealthcare of Alabama  
University of Arizona  
Department of Communication  
University of Arizona National Center of Excellence in Women's Health  
University of Arizona Poison and Drug Information Center  
University of Illinois at Chicago  
University of Massachusetts Medical School  
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University of Pennsylvania School of Medicine  
University of Texas Health Science Center at San Antonio  
University of Washington  
Wake Forest Baptist Medical Center  
Walgreens Co.  
WellPoint, Inc.  
Whitehall-Robbins Inc.  
Wyeth  
Wyeth-Ayerst Laboratories

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October 1, 2005-September 30, 2006

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