CERTs Annual Report

Year 4

Centers for Education & Research on Therapeutics

AHRQ Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

U.S. Department of Health and Human Services

This report was developed under the auspices of the Agency for Healthcare Research and Quality (AHRQ) through grant HS13474, although its contents are the sole responsibility of the Centers for Education & Research on Therapeutics (CERTs).

October 2002–September 2003

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. For our results to apply to the "real world," the research must reflect a collaboration of groups with different perspectives and resources: patients, health care providers, government, academia, delivery systems, payers, purchasers, and manufacturers of medical products.

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 Centers for Education & Research on Therapeutics 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 scientific evidence upon which to base policies.

Accountability. Americans should expect the CERTs to be a trusted resource when they need answers to questions about therapies.

Contents

Letter From the Agency for Healthcare Research and Quality **4**

Letter From the Steering Committee **6**

Introduction **8**

CERTs Progress **10**

Advancing Knowledge 10

Informing Providers and Patients 15

Improving the System 18

Referenced Projects 22

CERTs Program Resources **24**

CERTs Partnerships and Collaborations **26**

John M. Eisenberg, MD, Memorial Lectureship on Therapeutics Research 26

Risk Series 27

Government Day 30

Partnerships to Advance THerapeutics (PATHs) 31

Conclusion **33**

The CERTs Organization **34**

Principles of CERTs Public–Private Partnerships **37**

CERTs Project Partners **38**

Peer-Reviewed Publications: October 1, 2002–September 30, 2003 ..... **40**

Referenced Publications 40

Additional Publications 42

Letter From the Agency for Healthcare Research and Quality

Dear Colleague:

The Agency for Healthcare Research and Quality (AHRQ) has sponsored the Centers for Education & Research on Therapeutics (CERTs) since its inception in 1999. The CERTs improve the health of Americans by conducting research on the safety and effectiveness of medical therapeutics—drugs, biological products, and medical devices. In this, their fourth year, the CERTs have increasingly expanded their research into ways that information technology can make the use of therapeutics safer.

We know that the value of research comes when it is actually used in everyday life. Therefore, the CERTs are searching to find out about the obstacles to moving from research to implementation and action. What barriers—technical, organizational, or habitual—keep some health care providers from using beneficial technology such as computerized provider order entry? What are the concerns of health care providers when they balance their use of newer antibiotics against the danger of antibiotic-resistant strains of bacteria? What actions can health care organizations and programs take to increase efficiency while maintaining or enhancing care for their clients?

Carolyn M. Clancy, MD

To answer these questions, the CERTs are opening up new lines of dialogue with the health care community. In CERTs-sponsored workshops, experts from all areas of health care—including consumer groups and the medical products industry as well as providers—analyze the state of knowledge in the field and propose research questions. The John M. Eisenberg, MD, Memorial Lectureship takes the CERTs mission and dialogue about therapeutics research into academic medical centers nationwide. And the list of CERTs public–private partnerships grows each year.

We are pleased to present this report documenting CERTs activities in the fourth year of the program and look forward to more progress in the year ahead.

—Carolyn M. Clancy, MD
Director

Letter From the Steering Committee

Dear Fellow Citizens:

We are pleased to report the results of this year's work to answer questions about and provide strategies to foster better use of drugs and other therapies to improve the nation's health. Since our last report, more than 100 additional projects have been launched that will further inform consumers, health care providers, and other decision makers about therapies and how to use them effectively and safely and that will build the systems in which these practices can function even better.

Our health care system produces great benefits to people every day. But we know it can be improved. There is still much to learn about drug interactions for patients who need treatment for multiple conditions. We need to understand how to best use technology to help health care providers ensure that patients receive the right drug at the right dose at the right time. Through our CERTs research and education, we have the ability to narrow the gap between what we know and what we do to provide better care.

Finding answers is only a first step. Making sure that health care providers, policymakers, and patients are aware of the results is equally important. The CERTs, in collaboration with many agencies and organizations, seek to address both parts of this equation.

This is a long-term commitment that will take considerable time and resources. Still, even in the short time we have been working on these tasks, we have made tangible progress. We still conduct research to improve treatments for specific diseases and work to assure that research findings are translated into clinical practice. In addition, we undertake projects to address the evolving needs of the health care system, such as evaluating the use of electronic prescription systems and other technology to reduce medical errors and save time.

This past year, as you will see in the pages that follow, we have built on our tradition of successful collaboration. Many individuals in universities, government agencies, managed-care organizations, drug and device companies, as well as practitioners and others, have been critical to our progress. Such collaborations allow us to respond quickly and judiciously to emerging health care needs. We thank them here for their strong support, partnership, and considerable contributions.

While the CERTs and our partners have together made significant progress, many challenges remain. We are committed to meeting those challenges in the years ahead and look forward to working with many of you to help ensure that Americans will benefit.

—Hugh H. Tilson, MD, DrPH
Chair, on behalf of the CERTs Steering Committee:
Lynn A. Bosco, MD, MPH; M. Miles Braun, MD, MPH; Robert M. Califf, MD; William H. Campbell, PhD; Lisa C. Egbuonu-Davis, MD; Linda F. Golodner; James G. Kotsanos, MD, MS; Judith M. Kramer, MD, MS; Richard Platt, MD, MS; Wayne A. Ray, PhD; Kenneth G. Saag, MD, MSc; Marcel E. Salive, MD, MPH; Alan D. Stiles, MD; Brian L. Strom, MD, MPH; Karen Williams; Raymond L. Woosley, MD, PhD

Hugh H. Tilson, MD, DrPH

Introduction

The Centers for Education & Research on Therapeutics (CERTs) were mandated by Congress to benefit the American people. Whether you are a consumer, health care provider, or policymaker, you need information about the benefits and risks of medical therapies. The CERTs are working to uncover this information and make it widely known. Medical therapies are commonly referred to as "therapeutics," and they include drugs, medical devices, and biological products.

The CERTs were established in 1999 by the Agency for Healthcare Research and Quality (AHRQ) in consultation with the U.S. Food and Drug Administration (FDA). The program is administered as a cooperative agreement and receives funds from both public and private sources, with AHRQ providing core financial support.

The CERTs consist of a network of seven research centers and a coordinating center dedicated to improving the quality and safety of therapeutics. Projects are aimed at advancing knowledge; informing health care providers, patients, and policymakers about that knowledge; and improving aspects of the health care system related to therapeutics.

Our projects are diverse. They range from learning which drugs cause irregular heart rhythms to evaluating changes in Medicaid policy to identifying better ways for health care providers to write prescriptions.

As we move into our fifth year, more and more of the CERTs projects focus on technology. We live in an era of unprecedented scientific achievement and demand for the best technology available. We are committed to studying how technology is being used in the health care setting and how it can be improved. A number of our projects focus on improving computerized prescribing systems used by health care providers. These advances are likely to have wide-reaching results that could ultimately improve the quality and reduce the cost of health care.

In this report, we highlight many CERTs research and educational projects completed during the past year. We also highlight some of the research projects that are planned or in progress. These projects show a glimpse of the tremendous challenges and opportunities that lie ahead.

Medical Therapies

CATEGORY	EXAMPLES
Drugs	Prescriptions; over-the-counter medicines
Medical devices	Blood glucose monitors; cardiac laser devices
Biological products	Vaccines; blood products

The Centers

CENTER	EMPHASIS
Duke University Medical Center	Therapies for disorders of the heart and blood vessels
HMO Research Network	Drug use; safety and effectiveness studies in health maintenance organization populations
University of Alabama at Birmingham	Therapies for musculoskeletal disorders
University of Arizona Health Sciences Center	Reduction of drug interactions that result in harm to women
University of North Carolina at Chapel Hill	Therapies for children
University of Pennsylvania School of Medicine	Therapies for infection; reduction in antibiotic drug resistance
Vanderbilt University Medical Center	Prescription drug use in a Medicaid population

CERTs Progress

Advancing Knowledge

Medical therapies are created with the goal of improving health. However, the use of medical therapies involves risk. We focus on uncovering such risks because people need an accurate picture of both the benefits and risks of the medical therapies they use. The CERTs work to improve our ability to detect both the beneficial and harmful effects of medical therapies so that the benefits can be maximized and the risks minimized.

UNDERSTANDING MEDICINES THAT CAN CAUSE SERIOUS HEART RHYTHM DISTURBANCES AND DEATH[1,2,3]

Many different types of drugs, including some antihistamines, antibiotics, and antipsychotics, have been shown to cause serious heart rhythm disturbances. The CERTs help to identify individual drugs, drug interactions, and genetic mutations that are associated with torsades de pointes, a potentially fatal irregular heart rhythm. Torsades de pointes can develop because of an inherited gene or as the result of taking certain drugs. Women are more susceptible than men, and we have identified the basis for this increased sensitivity to these drugs.

As a result of reports received by CERTs investigators, we suspect that methadone, which is used for pain and to treat heroin addiction, might cause torsades de pointes. Normal electrical impulses that coordinate heartbeat require potassium. Drugs known to cause torsades de pointes actually block the channels that allow potassium to move out of heart cells. Therefore, we examined the effects of methadone on these channels in single heart cells. This past year we reported that methadone does block these potassium channels. Chlorobutanol, a preservative found in intravenous methadone, also blocks potassium channels. With further clinical studies, we found that intravenous methadone causes heart rhythm disturbances that often precede torsades de pointes. Because of this work, there is a much better appreciation of the risk factors for this condition.

Unfortunately, not all drugs have been characterized as to their ability to cause heart rhythm disturbances. To gather more information on the risks associated with various drugs, we developed the Web site www.qtdrugs.org. This is an Internet-based registry that physicians can use to report cases of torsades de pointes caused by drugs.

We know that using two or more drugs that interfere with potassium channels can further increase the risk of torsades de pointes, but it was not known how often people are prescribed two or more such drugs at once. Using data from an insurance claims database, we reviewed the prescriptions of nearly 5 million people. We identified overlapping prescriptions among drugs that can either interfere with potassium channels or slow the breakdown of such drugs. We found that 9.4% of people filled overlapping prescriptions for two or more of these drugs. More studies are needed to determine the exact risks for these patients and how the risks weigh against the benefits of taking the drugs. With that information, we hope it will be possible to prevent these irregular heart rhythms before they harm patients.

EXAMINING THE SAFETY OF TRANSMYOCARDIAL REVASCULARIZATION[4]

Transmyocardial revascularization (TMR) is a procedure developed to relieve severe chest pain in patients who cannot undergo angioplasty or traditional bypass surgery known as coronary artery bypass grafting (CABG). In the procedure, a surgeon uses a laser to make a series of small holes in the heart to deliver more blood to the heart muscle. TMR is also used with CABG, but this combination has not been widely studied and is not approved by the FDA.

To learn more about the use of TMR and its associated risks, we collaborated with the Society of Thoracic Surgeons and the FDA. We reviewed the use of the procedure between 1998 and 2002 in more than 400 hospitals that contribute to the Society of Thoracic Surgeons National Cardiac Database.

We found that nationwide the use of TMR is on the rise. However, in two-thirds of cases, it was used in combination with CABG. Thus, there is a crucial need to determine whether the combined procedure is safe and effective. We also found that patients who underwent TMR after having a recent heart attack or having a diagnosis of unstable angina had higher risks of dying during the procedure or having major complications. These findings are consistent with FDA guidance to avoid using TMR in patients with unstable angina or recent heart attack.

This study underscores the value of collaboration between professional societies, universities, and the FDA to study how therapies are used once they are approved by the FDA.

STUDYING THE SAFETY OF TREATMENTS FOR RHEUMATOID ARTHRITIS

Tumor necrosis factor (TNF) is a molecule that helps the body fight diseases caused by invading bacteria and viruses. However, excess TNF may have adverse consequences in autoimmune disorders. In the case of rheumatoid arthritis, which is one type of autoimmune disorder, the molecule participates in the inflammation response and can contribute to joint swelling and pain.

Three FDA-approved drugs—infliximab, etanercept, and adalimumab—block the activity of TNF. This may help relieve some of the pain and swelling in people with rheumatoid arthritis. Despite the potential benefit, there is concern that certain people who take these agents may be more vulnerable to infections such as tuberculosis, to some types of cancer, and to worsening heart failure.

Our studies evaluate whether infliximab and etanercept increase the risk of serious infections. We are examining enrollment, physician, and pharmacy claims data in the UnitedHealthcare Research Database, which includes more than 2,000 people taking these prescription medications. We are comparing the frequency of serious infections in rheumatoid arthritis patients who have received these medications with those who have not. We are also evaluating the frequency of heart failure in these two groups from the UnitedHealthcare Research Database.

We also study the effectiveness of efforts by the Federal government and the pharmaceutical industry to communicate the risk of infections. Patients who have latent tuberculosis and then take infliximab are at an increased risk for becoming sick with tuberculosis. Therefore, the manufacturers of these products and the FDA now recommend that patients undergo a skin test for tuberculosis before taking infliximab. In a study of 1,396 infliximab users, we found that rates of tuberculosis skin testing increased following efforts to convey information about the need for such tests. In fact, the number of people who received the test doubled during a two-year time frame. We are currently trying to learn which methods of communication worked best.

EXAMINING BETTER WAYS TO MONITOR BLOOD GLUCOSE IN CHILDREN WITH DIABETES

Controlling blood glucose levels closely can prevent or delay the serious complications of type 1 diabetes (low insulin production) in children, adolescents, and adults. Yet controlling glucose too closely can lead to episodes of hypoglycemia (low blood glucose) severe enough to cause unconsciousness. It is harder in developing children than in adults to maintain close glucose control without causing hypoglycemia. Also, compared with adults, young children are less able to recognize and respond to early symptoms of hypoglycemia.

Continuous glucose monitors may help doctors control glucose ranges in children. The systems have a small sensor that is inserted under a patient's skin and connects to a pager-sized monitor. The device measures glucose every few minutes and stores the records for up to three days. Then the records are transferred to a computer in a manner similar to downloading pictures from a digital camera.

Continuous glucose monitors have been used in adults for nearly two decades. However, experience in children is very limited. We are conducting a study among children and adolescents with type 1 diabetes to determine whether continuous glucose monitoring devices are better than current techniques in helping doctors control glucose and reduce hypoglycemia. This study should assist doctors in deciding whether continuous glucose monitoring is feasible, well tolerated, and beneficial in children and adolescents with type 1 diabetes.

TESTING WHETHER CHOLESTEROL-LOWERING MEDICINES CAN PREVENT FRACTURES[5]

Fractures caused by osteoporosis can harm a person's health and well-being. Therefore, medicines that lower the risk of fractures are of great benefit. Recent reports suggest that people who take statins, the most commonly used cholesterol-lowering drugs, have fewer osteoporotic fractures than people who do not. But factors other than the use of statins may explain the difference. For example, patients who take cholesterol-lowering drugs are likely to weigh more than people who do not, and extra weight protects against hip and other fractures.

We compared rates of hip fracture between people taking statins and people taking other cholesterol-lowering drugs. There was no difference between the two groups. This study shows that currently there is no reason to use statins for preventing fractures caused by osteoporosis. This study highlights the importance of studying therapies used in ways not approved by the FDA.

Informing Providers and Patients

Understanding the risks and benefits of medical therapies is a critical step to improving the safety and effectiveness of their use. Also critical is ensuring that medical therapies are used appropriately.

To address these situations, we are studying physician prescribing habits. As part of these studies, we aim to uncover any biases in prescribing patterns. We are also studying why some physicians are prescribing certain drugs more frequently than others. The CERTs are committed to informing both health care providers and patients about the results of our research in these important areas.

PREVENTING ANTIBIOTIC RESISTANCE[6,7,8]

Throughout our four-year history, the CERTs have been concerned about the problem of antibiotic-resistant bacteria. In the 1940s, antibiotics became available to treat human diseases caused by bacteria. Unfortunately, the more antibiotics are used, the more opportunity bacteria have to become resistant to them. We are attempting to lower inappropriate antibiotic use by learning about the types of situations in which antibiotics are needlessly prescribed.

Antibiotics called fluoroquinolones treat a wide range of bacterial infections that include diarrhea, pneumonia, urinary tract infections, and bone infections. Fluoroquinolones also treat infections caused by the bioterrorism agent anthrax. With the increased use of fluoroquinolones, bacterial resistance to them has also increased. To learn more about whether fluoroquinolones are being used inappropriately, we studied their use in emergency departments at two hospitals. Of 100 patients who received fluoroquinolones, 81 received them outside of established guidelines. Of these 81 cases, 53% should have received a different antibiotic, 33% had no evidence of infection, and 14% were not fully evaluated before receiving treatment. Future studies should test ways to educate health care providers in emergency departments about using fluoroquinolone antibiotics less often.

New antibiotics have been created to fight resistant bacteria, but as use of these newer antibiotics increases, the same problems of resistance will arise. From a societal perspective, it would be best to use the newest antibiotics only when they are truly needed. However, this leaves health care providers with the dilemma of deciding when to prescribe newer antibiotics or when not to prescribe them to preserve their effectiveness. Many doctors believe they must choose between an individual patient's needs and the needs of the population.

We studied whether physicians are willing to use established antibiotics in the face of drug resistance to preserve newer antibiotics for future use. We found that in hypothetical situations, the decision to prescribe newer antibiotics is based on how sick a patient is. The sicker the patient, the more likely it is that a doctor will prescribe a newer antibiotic. This attitude is more prevalent among generalist physicians than infectious disease specialists. As physicians are being asked to follow guidelines that encourage reduced use of newer, broad antibiotics, the conflicts they face need to be considered. Unfortunately, most physician education programs do not address these issues. Because generalists and infectious disease specialists have different attitudes, educational programs should be tailored accordingly.

Our work has most often uncovered areas where antibiotics are prescribed too often. But antibiotic use has recently dropped in one area. Between 1996 and 2000, there was a significant drop in the number of antibiotics prescribed to children aged three months to 17 years. In previous years, from 1977 through the early 1990s, antibiotic use in children had increased. This increase coincided with more children being placed in group child care and more reports of ear infections, which are the most common cause of prescribing antibiotics to children.

In 1998, the Centers for Disease Control and Prevention, working with other national and state organizations, began to actively promote more judicious prescribing for children. Their efforts appear to have paid off. The drop in antibiotic prescriptions for children is encouraging and suggests that it is possible to effectively educate both health care providers and patients about the dangers of overusing antibiotics.

FINDING GAPS IN OSTEOPOROSIS TREATMENT[9,10]

Approximately 10 million Americans have osteoporosis, a condition that leads to low bone mass and bone fragility. Bone fragility can cause fractures, disability, pain, deformity, and even death.

Fortunately, there are medicines that lower the risk of having a fracture. Unfortunately, people who need treatment do not always get it.

People with both osteoporosis and a fracture are 20 times more likely to have a future fracture than those who have neither osteoporosis nor a history of fracture. At least 80% to 90% of bone fractures in women past menopause are associated with osteoporosis. For these patients, getting treatment for osteoporosis is especially important. Yet recent studies suggest that physicians are missing opportunities to deliver treatment.

To explore this issue, we used databases from seven health maintenance organizations to examine how often physicians recommended treatment to women 60 years and older to prevent a second fracture. We found that the vast majority of these women did not receive treatment for osteoporosis in the year after they suffered a fracture.

This is not the only gap in osteoporosis care that we found. We surveyed 8,909 black and white women about the care they received for osteoporosis. The women were at least 50 years old and were participants in a health maintenance organization. Compared with white women, black women reported having fewer bone density tests and receiving less osteoporosis therapy. The difference was not fully explained by lifestyle or other health factors. Even black women who had fractures in the past received less care than white women.

Our study suggests that physicians are not taking needed steps to prevent and treat osteoporosis as readily in black women. This may be because black women are less likely than white women to have osteoporosis. But when black women do have fractures, they have more disability, longer hospital stays, and greater risk of death than white women do. Work is needed to find ways of making osteoporosis treatment available to all who need it.

Improving the System

The CERTs' most broad-reaching efforts are those aimed at improving aspects of the health care system related to therapeutics. We conduct research that evaluates the policies that govern health care delivery. We also evaluate computer technology to improve the efficiency of health care, make therapies safer, and give health care providers better access to current treatment information.

EFFECTS OF CHANGING DELIVERY OF MENTAL HEALTH CARE[11]

People with mental illnesses such as schizophrenia need long-term treatment to prevent psychotic episodes and hospitalization. Many patients with mental illnesses receive care through state Medicaid programs. To save money, some states are turning over care of these patients to specialty behavioral health organizations. This often means that patients have to see new health care providers, a disruption that can cause them to stop their treatment. Once patients stop treatment, they may not start again, which puts them at risk for serious decline.

We studied the effects of changes in Tennessee's mental health services from a Medicaid program to a specialty behavioral health organization, TennCare Partners. After the change, patients were more likely to miss therapy for more than 60 days. Patients who had been hospitalized for psychosis were among those most likely to miss therapy. These results suggest that organizational changes may put patients at risk and that such risks should be minimized by keeping patient care constant or by incorporating special safeguards.

TESTING WHETHER PRESCRIPTION REVIEW PROGRAMS REDUCE ERRORS[12]

All state Medicaid programs are required to conduct a retrospective drug utilization review, which is intended to decrease errors in drug prescriptions. In the review, a computer sorts through a patient's prescribed medicines and reports certain errors, such as harmful interactions or incorrect dosage. A drug use review board reviews the computer reports and recommends appropriate educational programs to improve drug therapy. The Medicaid program conducts the educational programs specified by the drug use review board, which can include contacting the prescriber to suggest changes in prescribing practices.

We studied the effectiveness of retrospective drug reviews in six Medicaid programs. Based on an examination and evaluation of six drug utilization programs, the study's authors concluded that such programs do not reduce the frequency of medication-use problems or of medication-related admissions. Given the lack of evidence for effectiveness and suggestions from previous research of possible harm, policymakers may wish to evaluate the use of such programs.

USING TECHNOLOGY TO REDUCE MEDICAL ERRORS AND INCREASE EFFICIENCY

Computerized provider order entry programs allow physicians to enter prescriptions into a computer rather than write them out by hand. Programs are designed to reduce medical errors by providing health care providers with relevant information about their patients, such as a patient's allergies, and general reference information about treatment guidelines, warnings, and drug interactions. There are anecdotes and some research findings that these systems improve prescribing by reducing the number of errors. However, much of this research has involved only small numbers of patients in an institutional setting.

Some providers believe that the programs are difficult to use and take more time than writing a prescription. Others find that the alert messages for drug allergies and interactions are annoying and inaccurate.

Computerized provider order entry programs have been slow to catch on in private practice. But they are common in government medical centers, such as Veterans Affairs and Department of Defense medical centers. We are currently studying the programs at 10 Veterans Affairs medical centers to learn how well they work and how they could be improved. This study has three parts: (1) evaluating the order entry process at each medical center; (2) asking doctors how satisfied they are with the process; and (3) studying whether the process decreased harmful drug interactions and improved patients' health outcomes.

Pharmacies have been on the forefront in using technology to improve drug safety and save time. Unfortunately, current systems are not perfect. Patients still sometimes receive combinations of medicines that have harmful interactions despite computerized warnings to the pharmacist. No one knows for certain why pharmacists do not always act on these alerts. It could be because of overwork, a training issue, or the sheer volume or type of alerts.

We are also studying ways to improve pharmacy systems and prevent harmful drug interactions to patients. We are surveying community pharmacies to learn more about where systems work well and where they do not. This should help pharmacies and software developers design better ways to identify harmful drug interactions.

FDA's new requirement for bar coding of prescription drugs is another area that has the potential to reduce medical errors.

USING SURVEILLANCE SYSTEMS TO IMPROVE SAFETY

When we access information about medical therapies, the information available should be as accurate and complete as possible. Several CERTs projects focus on gathering information about the safety of therapeutics so that health care providers can be confident in the treatments they prescribe.

One study aims to learn more about the safety of prescription drug use by pregnant women. We will record drug use before and during pregnancy for 150,000 women in eight different health systems and geographic regions. Our goal is to assess how often unborn babies are exposed to drugs that may cause them harm. This is the first such study in the United States.

We worked with the United States Pharmacopeia to develop recommendations for safe prescribing for children. Together we studied more than 5,600 medication errors reported by more than 500 hospitals to the United States Pharmacopeia's anonymous Web-based reporting system, MEDMARX℠. We considered the error reports and the best published evidence on the causes of and solutions to pediatric medication errors. Based on this information, we made five sets of recommendations about all phases of medication use. These topics ranged from packaging and storing, to prescribing and administering medications to pediatric patients. In April 2003, the United States Pharmacopeia published the recommendations on its Web site: www.usp.org/patientSafety/tools/pedRecommnds 2003-01-22.html. The recommendations can be used by all health care providers who treat children.

Referenced Projects

CENTER	PROJECT	PAGE
University of Arizona Health Sciences Center	Data mining for drug interactions	10
University of Arizona Health Sciences Center	International registry for drug-induced arrhythmias	11
Duke University Medical Center	Evaluation of the prescribing of concomitant QT-prolonging medications	11
Duke University Medical Center	Postmarket surveillance of transmyocardial revascularization	11–12
University of Alabama at Birmingham	Risk assessment for biological agents in rheumatoid arthritis	12–13
University of North Carolina at Chapel Hill	Safety and efficacy of continuous subcutaneous blood glucose monitoring systems in the management of type 1 diabetes mellitus in children	13–14
Vanderbilt University Medical Center	Cholesterol-lowering drugs and hip fracture	14
University of Pennsylvania School of Medicine	Investigation of inappropriate use of fluoroquinolone antibiotics	15
University of Pennsylvania School of Medicine	Prescribing patterns for newer antibiotics	16
HMO Research Network	Antibiotic use in children	16–17
HMO Research Network	Under treatment of osteoporosis in postmenopausal women following a fracture	17
University of Alabama at Birmingham	Racial variations in osteoporosis management	18
Vanderbilt University Medical Center	Effects of changing mental health care for people with schizophrenia	18–19
University of Pennsylvania School of Medicine	Efficacy of prescription drug reviews	19

CENTER	PROJECT	PAGE
University of Arizona Health Sciences Center and HMO Research Network	Evaluating computer prescription entry systems	20
University of Arizona Health Sciences Center	Evaluating computer alert systems in pharmacies	20–21
HMO Research Network	Prescription drug use in pregnant women	21
University of North Carolina at Chapel Hill	Recommendations for safe prescribing in children	21

CERTs Program Resources

ADHD Online Toolkit for Providers, Patients, and Families: Web Tool
nichq.org/resources/toolkit

Arthritis Outcomes Initiative Resource for Patients and Families: Web Resource
www.engalitcheff.uab.edu

Arthritis Self-Help for Patients: Web Site
www-cme.erep.uab.edu/arthritispatient/welcome.html

Beta-Blocker Fact Sheet
dukecerts.dcri.duke.edu

Cases Reflecting Emerging Topics in Adult Medicine: Online Continuing Medical Education Course
www.test1.cme.uab.edu/giop/welcome.html

Drug Interaction Card: Reference Guide
www.drug-interactions.com

Drugs that Prolong the QT Interval and/or Induce Torsades de Pointes
www.qtdrugs.org

Head and Chest Colds: Patient Education Brochure
www.penncert.org

Preventable Adverse Drug Interactions—A Focus on Drug Interactions: Education Module
www.arizonacert.org/medical-pros/education/module01.htm

Safer Use of Nonsteroidal Anti-Inflammatory Drugs: Online Continuing Medical Education Course
www-cme.erep.uab.edu/nsaids/nsaids.html

Saving Lives with Beta-Blockers: Duke CERTs Cybersession
dukecerts.dcri.duke.edu

Secondary Prevention of Osteoporosis and Fractures in Nursing Homes: Online Continuing Medical Education Course
www.test1.cme.uab.edu/spof/welcome.html

Tools and Techniques of Improved Medication Use for Health Care Professionals: Web Resource
www.aahp.org/redirect/improvedmedicationuse.htm

Treating Congestive Heart Failure with Beta-Blockers: What You Can Do To Help Yourself Feel Better: Patient Education Brochure
dukecerts.dcri.duke.edu

Treating Congestive Heart Failure with Beta-Blockers: Patient Education Videotape
dukecerts.dcri.duke.edu

Understanding the QT Interval—A Duke CERTs Educational Program: Internet-Based Module
qtmodule.mc.duke.edu

NOTE: For additional information about CERTs program resources, please e-mail the CERTs Coordinating Center at certs@onyx.dcri.duke.edu.

CERTs Partnerships and Collaborations

Public–private partnership is one of the core values of the CERTs. Collaboration among groups sharing different perspectives and resources is essential in carrying out the mission of the CERTs. In addition to the many partnerships that enable the CERTs research centers to study important therapeutics issues, the CERTs have established several program-wide initiatives in collaboration with other public and private organizations.

John M. Eisenberg, MD, Memorial Lectureship on Therapeutics Research

In 2003, the CERTs established the John M. Eisenberg, MD, Memorial Lectureship on Therapeutics Research. The lectureship was named to honor the life and work of the late Dr. Eisenberg, who was committed to reducing medical errors and improving patient safety. Dr. Eisenberg's work as a clinician and leader in health services research spanned more than 30 years and included serving as director of the AHRQ when the CERTs program began in 1999.

This unique lectureship program was designed to extend the reach of the CERTs network over a broad array of academic medical centers nationwide. The goals of the lectureship include educating future leaders about the discipline of therapeutics research; increasing awareness about the risks and benefits of new, existing, or combined uses of therapeutics; and emphasizing the importance of applying CERTs research in clinical practice.

In the fall of 2003, CERTs investigators conducted lectureships at the following institutions: Baylor College of Medicine, Houston, Texas; Creighton University Medical Center, Omaha, Nebraska; Medical University of South Carolina, Charleston, South Carolina; Morehouse School of Medicine, Atlanta, Georgia; Regenstrief Institute at Indiana University, Indianapolis, Indiana; University of California, San Francisco, California; and the University of Colorado Health Sciences Center, Denver, Colorado. The John M. Eisenberg, MD, Memorial Lectureship on Therapeutics Research was made possible by a gift from Pfizer Inc.

Risk Series

A critical goal of CERTs research is to increase awareness of therapeutic benefits and risks. Equally important is that people understand how to apply that knowledge to ensure that the benefit patients receive from therapeutics outweighs any harm they experience. In 2001 the CERTs began the Risk Series to identify priority research issues that could improve the nation's ability to assess, communicate, and manage therapeutic risk.

Risk management is important because medical therapies are not 100% safe. Much of the impetus for risk management comes from sensational cases, such as when drugs are taken off the market or when a major medical mistake occurs. But the important issues in risk management relate to decisions made every day by patients, health care providers, and other health care decision makers about which therapeutics will be used.

To make decisions, both patients and health care providers need objective, complete, and accessible information about the benefits and risks of medical therapies. Although there is no one source or vehicle that could possibly develop and disseminate all of the information needed, the CERTs, working in partnership with others, can address some aspects of this issue. During the past two years, experts from the government, consumer groups, the medical products industry, the media, health care, and academia convened for a series of workshops called "Think Tanks" to review how the risk associated with different medical products is assessed, communicated, and managed. Results of the first two workshops are published in *Pharmacoepidemiology and Drug Safety*.

The five workshops covered risk communication, risk assessment, benefit assessment, risk communication and the media, and risk management. Based upon an in-depth analysis of the current status of knowledge in the field, more than 150 participants were asked to propose the top research questions and other unresolved issues pertaining to their individual workshop topic. Each workshop resulted in a list of ideas—research questions to be answered and issues to be resolved. The CERTs Steering Committee subsequently discussed and ranked the findings from the workshops (see CERTs Risk Series: Research Issues, pages 29 and 30) and presented them for the first time at the *Benefit the Patient; Manage the Risk: CERTs Risk Series Strategic Symposium* held in March 2003. Discussion of the issues and questions raised at the symposium provides a context for future research.

The CERTs Risk Series Strategic Symposium was held in conjunction with two annual CERTs meetings—Government Day and Partnerships to Advance THerapeutics (PATHs).

CERTs Risk Series: Research Issues

Identifying Risk. What are the best practices for finding and quantifying therapeutics risk from existing systems (for example, the FDA's Adverse Event Reporting System)? How should dissimilar findings, extreme values, and unique cases be taken into account?

Interpreting Signals. What are the conflicts between results from analyses of structured studies, spontaneous reports, and large, structured databases? How should they be reconciled? Can such studies substitute for large clinical trials? What are the characteristics of database analyses and clinical trials that provide the best information about the balance of risk and benefit?

Acceptable Risk. What factors influence the level of risk that is acceptable to health care providers and patients? What factors influence the way health care providers and patients interpret benefit and risk probabilities?

Knowledge Base. How knowledgeable are health care providers about the balance of benefit and risk of the therapeutics that they administer, distribute, monitor, and prescribe to patients? How knowledgeable are patients about the risk associated with their medication? How knowledgeable are patients about their roles and the roles of others in the risk communication process?

Information Sharing. What are the most effective methods of informing health care practitioners about the balance of benefit and risk of therapeutics? What are the most effective methods of informing patients about the risk of therapeutics in the context of known benefits? What are the most effective methods of informing administrative health system decision makers about the balance of risk and benefit of therapeutics?

Effective Communications. What are the effects of the media, professional organizations, and other information sources in prescribing decisions and patients' use of medications? How can the media and professional organizations more effectively communicate to health care practitioners and patients?

Impact of Current Methods. What positive and negative effects have current methods of communicating risk information (for example, product labeling and continuing medical education) had on health care practitioners?

CERTs Risk Series: Research Issues *(continued)*

Decision Factors. What factors (for example, technology, practice setting) increase the likelihood that health care providers will take into account benefit and risk information when prescribing medications and following patients? What factors (for example, level of education) increase the likelihood that patients will take into account benefit and risk information when making decisions about their medical care?

Program Criteria. What are the characteristics of a risk-management program that should be in place for all therapeutics? What are the criteria for requiring or strongly encouraging a risk-management program that goes beyond the basal level?

Multidisciplinary Approaches. How can multidisciplinary approaches to risk communication be developed and tested, particularly those involving nurses, other non-physician providers, and pharmacists?

Measuring Effectiveness. What is the effectiveness of each individual element of a risk-management program? Which risk-management tools work best in which situations? What are the parameters of a successful risk-management program, and what indicators of success should be used?

Privacy Concerns. What is the impact of privacy legislation on the ability to conduct risk-management programs? How do different implementation strategies in response to privacy legislation affect the ability to improve prescribing and adherence in alignment with the balance of benefit and risk?

Government Day

Government Day is an opportunity for the CERTs to present information about the program to participants from a number of government agencies and discuss opportunities for collaboration. At the 2003 meeting, following the presentation of the Risk Series results, leaders from AHRQ, the FDA, the National Institutes of Health, the medical products industry, and the Institute of Medicine's Clinical Research Roundtable presented their perspectives related to risk management. The meeting concluded with a roundtable discussion of the roles and responsibilities of government agencies in risk-management programs.

Partnerships to Advance THerapeutics (PATHs)

The PATHs program was created to cultivate partnerships between organizations interested in advancing the best use of therapeutics. Each spring, the CERTs host a meeting of leaders from public and private organizations concerned about the quality and safety of health care. Partners and participants include organizations representing patients, health care providers, government, academia, delivery systems, payers, purchasers, and manufacturers of medical products.

In March 2003, the PATHs meeting was held in conjunction with the *Benefit the Patient; Manage the Risk: CERTs Risk Series Strategic Symposium*. Participants discussed the findings and recommendations from the Risk Series "Think Tanks" and how to proceed based on the research issues identified in the process. Major goals of the meeting included the following:

- To discuss the Risk Series research agenda, establish priorities, and delineate next steps
- To share and receive information from agencies and organizations about their programs affecting the management of therapeutic risk
- To refine the research agenda and expand commitments to adopt specific research areas
- To launch the research and education agenda from the five Risk Series workshops

Partners presented different perspectives to facilitate the discussion. The perspectives included those of patients, clinicians, public health, managed care, the medical products industry, and government.

The PATHs meeting is a visible example of the CERTs commitment to creating a wide collaborative environment to improve public health through therapeutics. A registry of educational and research projects of PATHs organizations is published and can be accessed through the CERTs Web site at www.certs.hhs.gov/partners/paths/regis/.

PATHs Partners

We would like to thank the following organizations for participating in the *Benefit the Patient; Manage the Risk: CERTs Risk Series Strategic Symposium:*

Academy of Managed Care Pharmacy

AcademyHealth

Agency for Healthcare Research and Quality

American Academy of Pharmaceutical Physicians

American Association of Colleges of Pharmacy

American Association of Health Plans

American College of Cardiology

American College of Clinical Pharmacy

American College of Preventive Medicine

American Medical Association

American Nurses Association

American Organization of Nurse Executives

American Pharmacists Association

American Public Health Association

American Society for Clinical Pharmacology and Therapeutics

American Society of Consultant Pharmacists Research and Education Foundation

American Society of Health-System Pharmacists

Arnold & Porter

Arthritis Foundation

Association of American Medical Colleges

AstraZeneca

Aventis

Bristol-Myers Squibb Company Worldwide

Center for Studying Health System Change

Centers for Medicare & Medicaid Services

Council for Affordable Quality Healthcare

Eli Lilly and Company

GlaxoSmithKline

Hoffmann-La Roche Inc.

International Society for Pharmacoepidemiology

Merck & Co., Inc.

National Committee for Quality Assurance

National Consumers League

National Council on Patient Information and Education

National Health Council

National Hispanic Medical Association

National Patient Safety Foundation

Novartis

Pharmaceutical Research and Manufacturers of America

RTI Health Solutions

Society for Women's Health Research

UMWA Health and Retirement Funds

United States Pharmacopeial Convention, Inc.

U.S. Food and Drug Administration

Wyeth

Conclusion

As noted in our first annual report, no one should have doubts about the medical products he or she prescribes or uses. The goal of our research and education activities is to understand more about the benefits and risks of certain therapies so that we can remove some of those doubts. This goal is ambitious, especially since both health care and the field of therapeutics are constantly changing. As new medical therapies are brought to the market, they raise new questions that need to be studied.

Therefore, there are many challenges ahead. The annual report is one opportunity to report some of our key accomplishments in the past year. Because there are so many projects—and they are so diverse—we only described a fraction of them. A renewed focus is on efforts that could benefit the entire health care system, such as studies of retrospective drug utilization review and changes in mental health care delivery and ongoing studies to improve prescribing technology.

For the past four years, partnership has been the cornerstone of the CERTs. As our projects become broader in scope, the importance of these partnerships will only increase. We are grateful to all those who have been our partners in improving therapeutics. We look forward to collaborating with new partners as well.

We also look forward to expanding our efforts to develop knowledge, manage risk, improve practice, and inform decision makers about the latest research evidence in the field of therapeutics.

The CERTs Organization

Administration

Agency for Healthcare Research and Quality, Rockville, MD
Contact: Lynn A. Bosco, MD, MPH
Program Officer
Fax: 301-427-1520
E-mail: lbosco@ahrq.gov
Web: www.ahrq.gov

Coordinating Center

Duke University Medical Center, Durham, NC
Principal Investigator: Robert M. Califf, MD
Contact: Leanne K. Madre, MHA, JD
Fax: 919-668-7166
E-mail: madre005@mc.duke.edu
Web: www.certs.hhs.gov

Centers

Duke University Medical Center, Durham, NC
Principal Investigator: Judith M. Kramer, MD, MS
Contact: Nancy M. Allen LaPointe, PharmD
Fax: 919-668-7166
E-mail: allen003@mc.duke.edu
Web: dukecerts.dcri.duke.edu

HMO Research Network, Boston, MA
Principal Investigator: Richard Platt, MD, MS
Contact: Kimberly Lane, MPH
Fax: 617-509-9851
E-mail: kimberly.lane@channing.harvard.edu
Web: www.certs.hhs.gov/centers/hmo.html

University of Alabama at Birmingham, Birmingham, AL
Principal Investigator: Kenneth G. Saag, MD, MSc
Contact: Angela Becker, MPH
Fax: 205-975-6859
E-mail: angela.becker@ccc.uab.edu
Web: www.uab.edu/certs

University of Arizona Health Sciences Center, Tucson, AZ
Principal Investigator: Raymond L. Woosley, MD, PhD
Contact: Tina Pearson, BSN, MPH
Fax: 520-626-7382
E-mail: pearsone@email.arizona.edu
Web: www.arizonacert.org

University of North Carolina at Chapel Hill, Chapel Hill, NC
Principal Investigator: William H. Campbell, PhD
Contact: Sue Tolleson-Rinehart, PhD
Fax: 919-843-9477
E-mail: stolleso@email.unc.edu
Web: www.sph.unc.edu/certs/index.htm

University of Pennsylvania School of Medicine, Philadelphia, PA
Principal Investigator: Brian L. Strom, MD, MPH
Contact: Judith L. Kinman, MA
Fax: 215-573-5315
E-mail: jkinman@cceb.med.upenn.edu
Web: www.penncert.org

Vanderbilt University Medical Center, Nashville, TN
Principal Investigator: Wayne A. Ray, PhD
Contact: Marie R. Griffin, MD, MPH
Fax: 615-343-8722
E-mail: marie.griffin@mcmail.vanderbilt.edu
Web: www.certs.hhs.gov/centers/vanderbilt.html

Steering Committee

Hugh H. Tilson, MD, DrPH
(Chair)

Lynn A. Bosco, MD, MPH
CERTs Program Officer
Agency for Healthcare Research and Quality

M. Miles Braun, MD, MPH
Director
Division of Epidemiology
Center for Biologics Evaluation and Research
U.S. Food and Drug Administration

Robert M. Califf, MD
Principal Investigator
Coordinating Center

William H. Campbell, PhD
Principal Investigator
University of North Carolina at Chapel Hill
(October–June)

Lisa C. Egbuonu-Davis, MD
Vice President of Global Outcomes Research and Medical
Director of Outcomes Research
Pfizer Pharmaceuticals Group
Pfizer Inc
(October–January)

Linda F. Golodner
President
National Consumers League

James G. Kotsanos, MD, MS
Director
Global Product Safety
Eli Lilly and Company
(January–September)

Judith M. Kramer, MD, MS
Principal Investigator
Duke University Medical Center

Richard Platt, MD, MS
Principal Investigator
HMO Research Network

Wayne A. Ray, PhD
Principal Investigator
Vanderbilt University Medical Center

Kenneth G. Saag, MD, MSc
Principal Investigator
University of Alabama at Birmingham

Marcel E. Salive, MD, MPH
Director
Division of Medical & Surgical Services
Centers for Medicare & Medicaid Services

Alan D. Stiles, MD
Interim Principal Investigator
University of North Carolina at Chapel Hill
(July–September)

Brian L. Strom, MD, MPH
Principal Investigator
University of Pennsylvania School of Medicine

Karen Williams
President
National Pharmaceutical Council

Raymond L. Woosley, MD, PhD
Principal Investigator
University of Arizona Health Sciences Center

Principles of CERTs Public–Private Partnerships

Issues of Public Interest. The CERTs program is a major initiative to improve the rational use of therapeutics through research and education activities that are in the public interest but would not otherwise be done.

Public–Private Partnership. The CERTs program is a public–private partnership. Therefore, centers should seek useful, appropriate interactions with private organizations to support and enhance education, research, and demonstration projects. AHRQ will work with the centers to establish appropriate agreements to optimize use and sharing of resources.

Conflicts of Interest. Potential conflicts of interest are likely to exist in any public–private partnership. These potential conflicts cannot be completely avoided or eliminated. The obligation is to disclose fully and manage potential conflicts in a manner that minimizes the risk of those conflicts and at the same time maximizes progress to achieve CERTs' goals.

Academic Integrity. As academic researchers, individuals conducting projects under the CERTs umbrella will maintain final decision making about study design, analysis, conclusions, and publication and will 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.

AdvaMed

AdvancePCS

Aetna US Healthcare

Agency for Healthcare Research and Quality

Agouron Pharmaceuticals, Inc.

Alabama Department of Public Health

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 Pharmacists Association

American Pharmacists Association Foundation

Amgen

Arthritis Foundation

Arthritis Foundation, Alabama Chapter

Arthritis Foundation, Maryland Chapter

AstraZeneca

Aventis

Berlex Inc

Bowman Gray School of Medicine

Brigham and Women's Hospital

Bristol-Myers Squibb Company Worldwide

Center for Health Care Policy and Evaluation

Centers for Disease Control and Prevention

Centers for Disease Control Foundation

Centers for Medicare & Medicaid Services

Children's National Medical Center

Cincinnati Children's Hospital Medical Center

Columbus Children's Hospital

Conceptis Technologies Inc.

Council for Affordable Quality Healthcare

Crohn's & Colitis Foundation of America

Department of Veterans Affairs

Duke Clinical Research Institute

Duke Heart Center

Fallon Community Health Plan

Genentech

General Practice Research Database/EPIC

Georgetown University

GlaxoSmithKline

Group Health Cooperative of Puget Sound

Harvard Pilgrim Health Care

Harvard School of Medicine

Harvard School of Public Health

Health Resources and Services Administration

HealthPartners

Henry Ford Health System

Infectious Diseases Society of America

Institute for Healthcare Improvement

Institute of Medicine

Janssen Pharmaceutica

John A. Hartford Foundation

Kaiser Permanente Colorado

Kaiser Permanente Georgia

Kaiser Permanente Northern California

Kaiser Permanente Northwest

La Frontera Hope Center

Massachusetts Department of Public Health

Massachusetts Division of Medical Assistance

Ortho-McNeil Pharmaceuticals, Inc.

Medco & Co., Inc.

Medtronic, Inc.

Merck & Co., Inc.

Nanogen Inc.

National Initiative for Children's Healthcare Quality

National Institutes of Health

National Institutes of Health/National Cancer Institute

National Institutes of Health/National Institute of 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 and Digestive and Kidney Diseases

National Institutes of Health/National Institute of General Medical Sciences

National Institutes of Health/National Institute of Mental Health

National Institutes of 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

North Carolina Association of Pharmacists

North Carolina Department of Health and Human Services

North Carolina Medicaid

North Carolina State Children's Health Insurance Program

North Carolina Women, Infants & Children

Office of Women's Health

Parke-Davis Pharmaceutical

Pennsylvania Department of Health

Pennsylvania Pharmaceutical Assistance Contract for the Elderly

Pfizer Inc

Pharmaceutical Research and Manufacturers of America

Pharmacia & Upjohn Company

Public Health Service

QED Solutions, Inc.

Robert Wood Johnson Foundation

Roche Laboratories Inc.

RTI Health Solutions

Society for Healthcare Epidemiology of America

Society for Women's Health Research

Society of Thoracic Surgeons

TAP Pharmaceuticals

TennCare Medicaid

UCLA/Rand Center for Adolescent Health Promotion

United States Pharmacopeial Convention, Inc.

UnitedHealth Group

UnitedHealthcare

UnitedHealthcare of Alabama

University of Illinois at Chicago

University of Massachusetts Medical School

University of Pennsylvania Health System

U.S. Food and Drug Administration

Wake Forest Baptist Medical Center

Wyeth

Peer-Reviewed Publications:

OCTOBER 1, 2002–SEPTEMBER 30, 2003

Referenced Publications

1 Katchman AN, McGroary KA, Kilborn MJ, Kornick CA, Manfredi PL, Woosley RL, Ebert SN. Influence of opioid agonists on cardiac human ether-a-go-go-related gene K+ currents. *J Pharmacol Exp Ther*. 2002;303:688–694.

2 Kornick CA, Kilborn MJ, Santiago-Palma J, Schulman G, Thaler HT, Keefe DL, Katchman AN, Pezzullo JC, Ebert SN, Woosley RL, Payne R, Manfredi PL. QTc interval prolongation associated with intravenous methadone. *Pain*. 2003;105:499–506.

3 Curtis LH, Ostbye T, Sendersky V, Hutchison S, Allen LaPointe NM, Al-Khatib SM, Yasuda SU, Dans P, Wright A, Califf RM, Woosley RL, Schulman KA. Prescription of QT-prolonging drugs in a cohort of about 5 million outpatients. *Am J Med*. 2003;114:135–141.

4 Peterson ED, Kaul P, Kaczmarek RG, Hammill BG, Armstrong PW, Bridges CR, Ferguson TB Jr, for the Society of Thoracic Surgeons. From controlled trials to clinical practice: monitoring transmyocardial revascularization use and outcomes. *J Am Coll Cardiol*. 2003;42:1611–1616.

5 Ray WA, Daugherty JR, Griffin MR. Lipid-lowering agents and the risk of hip fracture in a Medicaid population. *Inj Prev*. 2002;8:276–279.

6 Lautenbach E, Larosa LA, Kasbekar N, Peng HP, Maniglia RJ, Fishman NO. Fluoroquinolone utilization in the emergency departments of academic medical centers: prevalence of, and risk factors for, inappropriate use. *Arch Intern Med*. 2003;163:601–605.

7 Metlay JP, Shea JA, Asch DA. Antibiotic prescribing decisions of generalists and infectious disease specialists: thresholds for adopting new drug therapies. *Med Decis Making*. 2002;22:498–505.

8 Finkelstein JA, Stille C, Nordin J, Davis R, Raebel MA, Roblin D, Go AS, Smith D, Johnson CC, Kleinman K, Chan KA, Platt R. Reduction in antibiotic use among US children, 1996–2000. *Pediatrics*. 2003;112:620–627.

9 Andrade SE, Majumdar SR, Chan KA, Buist DS, Go AS, Goodman M, Smith DH, Platt R, Gurwitz JH. Low frequency of treatment of osteoporosis among postmenopausal women following a fracture. *Arch Intern Med*. 2003;163:2052–2057.

10 Mudano AS, Casebeer L, Patino F, Allison JJ, Weissman NW, Kiefe CI, Person S, Gilbert D, Saag KG. Racial disparities in osteoporosis prevention in a managed care population. *South Med J*. 2003;96:445–451.

11 Ray WA, Daugherty JR, Meador KG. Effect of a mental health "carve-out" program on the continuity of antipsychotic therapy. *N Engl J Med*. 2003;348:1885–1894.

12 Hennessy S, Bilker WB, Weber A, Zhou L, Brensinger C, Wang Y, Strom BL. Retrospective drug utilization review, prescribing errors, and clinical outcomes. *JAMA*. 2003;290:1494–1499.

Additional Publications

Al-Khatib SM, LaPointe NM, Kramer JM, Califf RM. What clinicians should know about the QT interval. *JAMA*. 2003;289:2120–2127.

Al-Khatib SM, LaPointe NM, Curtis LH, Kramer JM, Swann J, Honig P, Califf RM. Outpatient prescribing of antiarrhythmic drugs from 1995 through 2000. *Am J Cardiol*. 2003;91:91–94.

Butler J, Arbogast PG, BeLue R, Daugherty J, Jain MK, Ray WA, Griffin MR. Outpatient adherence to beta-blocker therapy after acute myocardial infarction. *J Am Coll Cardiol*. 2002;40:1589–1595.

Califf RM, Peterson ED, Gibbons RJ, Garson A Jr, Brindis RG, Beller GA, Smith SC Jr., American College of Cardiology, American Heart Association. Integrating quality into the cycle of therapeutic development. *J Am Coll Cardiol*. 2002;40:1895–1901.

Campbell WH, Califf RM. Improving communication about drug risks to prevent patient injury: proceedings of a workshop. *Pharmacoepidemiol Drug Saf*. 2003;12:183–194.

Chan KA, Truman A, Gurwitz JH, Hurley JS, Martinson B, Platt R, Everhart JE, Moseley RH, Terrault N, Ackerson L, Selby JV. A cohort study of the incidence of serious acute liver injury in diabetic patients treated with hypoglycemic agents. *Arch Intern Med*. 2003;163:728–734.

Everett WW, Coffin SE, Zaoutis T, Halpern SD, Strom BL. Smallpox vaccination: a national survey of emergency health care providers. *Acad Emerg Med*. 2003;10:606–611.

Hagen EA, Lautenbach E, Olthoff K, Blumberg EA. Low prevalence of colonization with vancomycin-resistant enterococcus in patients awaiting liver transplantation. *Am J Transplant*. 2003;3:902–905.

Hennessy S, Bilker WB, Weber A, Strom BL. Descriptive analyses of the integrity of a US Medicaid claims database. *Pharmacoepidemiol Drug Saf*. 2003;12:103–111.

LaPointe NM, Al-Khatib SM, Kramer JM, Califf RM. Knowledge deficits related to the QT interval could affect patient safety. *Ann Noninvasive Electrocardiol*. 2003;8:157–160.

Lautenbach E, Fishman NO, Bilker WB, Castiglioni A, Metlay JP, Edelstein PH, Strom BL. Risk factors for fluoroquinolone resistance in nosocomial Escherichia coli and Klebsiella pneumoniae infections. *Arch Intern Med*. 2002;162:2469–2477.

Lautenbach E, Larosa LA, Marr AM, Nachamkin I, Bilker WB, Fishman NO. Changes in the prevalence of vancomycin-resistant enterococci in response to antimicrobial formulary interventions: impact of progressive restrictions on use of vancomycin and third-generation cephalosporins. *Clin Infect Dis*. 2003;36:440–446.

Levy RM, Huang EY, Roling D, Leyden JJ, Margolis DJ. Effect of antibiotics on the oropharyngeal flora in patients with acne. *Arch Dermatol*. 2003;139:467–471.

Liu X, Katchman A, Whitfield BH, Wan G, Janowski EM, Woosley RL, Ebert SN. In vivo androgen treatment shortens the QT interval and increases the densities of inward and delayed rectifier potassium currents in orchiectomized male rabbits. *Cardiovasc Res*. 2003;57:28–36.

Localio AR, Berlin JA, Ten Have TR. Confounding due to cluster in multicenter studies—causes and cures. *Health Services and Outcomes Research Methodology*. 2002;3:195–210.

Metlay JP, Hardy C, Strom BL. Agreement between patient self-report and a Veterans Affairs national pharmacy database for identifying recent exposures to antibiotics. *Pharmacoepidemiol Drug Saf*. 2003;12:9–15.

Metlay JP, Strom BL, Asch DA. Prior antimicrobial drug exposure: a risk factor for trimethoprim-sulfamethoxazole-resistant urinary tract infections. *J Antimicrob Chemother*. 2003;51:963–970.

M'ikantha NM, Southwell B, Lautenbach E. Automated laboratory reporting of infectious diseases in a climate of bioterrorism. *Emerg Infect Dis*. 2003;9:1053–1057.

Mikuls TR, Saag KG, Criswell LA, Merlino LA, Kaslow RA, Shelton BJ, Cerhan JR. Mortality risk associated with rheumatoid arthritis in a prospective cohort of older women: results from the Iowa Women's Health Study. *Ann Rheum Dis*. 2002;61:994–999.

Patino FG, Allison J, Olivieri J, Mudano A, Juarez L, Person S, Mikuls TR, Moreland L, Kovac SH, Saag KG. The effects of physician specialty and patient comorbidities on the use and discontinuation of coxibs. *Arthritis Rheum*. 2003;49:293–299.

Ray WA, Stein CM, Daugherty JR, Hall K, Arbogast PG, Griffin MR. COX-2 selective non-steroidal anti-inflammatory drugs and risk of serious coronary heart disease. *Lancet*. 2002;360:1071–1073.

Saag KG. Glucocorticoid-induced osteoporosis. *Endocrinol Metab Clin North Am*. 2003;32:135–157.

Stiles RA, So SA. Impact of transaction costs on healthcare outcomes. *Expert Review of Pharmacoeconomics & Outcomes Research*. 2003;3:283–291.

AHRQ Pub. No. 04-0090
September 2004