CERTs Annual Report

Year 3

Centers for Education & Research on Therapeutics™

U.S. Department of Health and Human Services

AHRQ Agency for Healthcare Research and Quality

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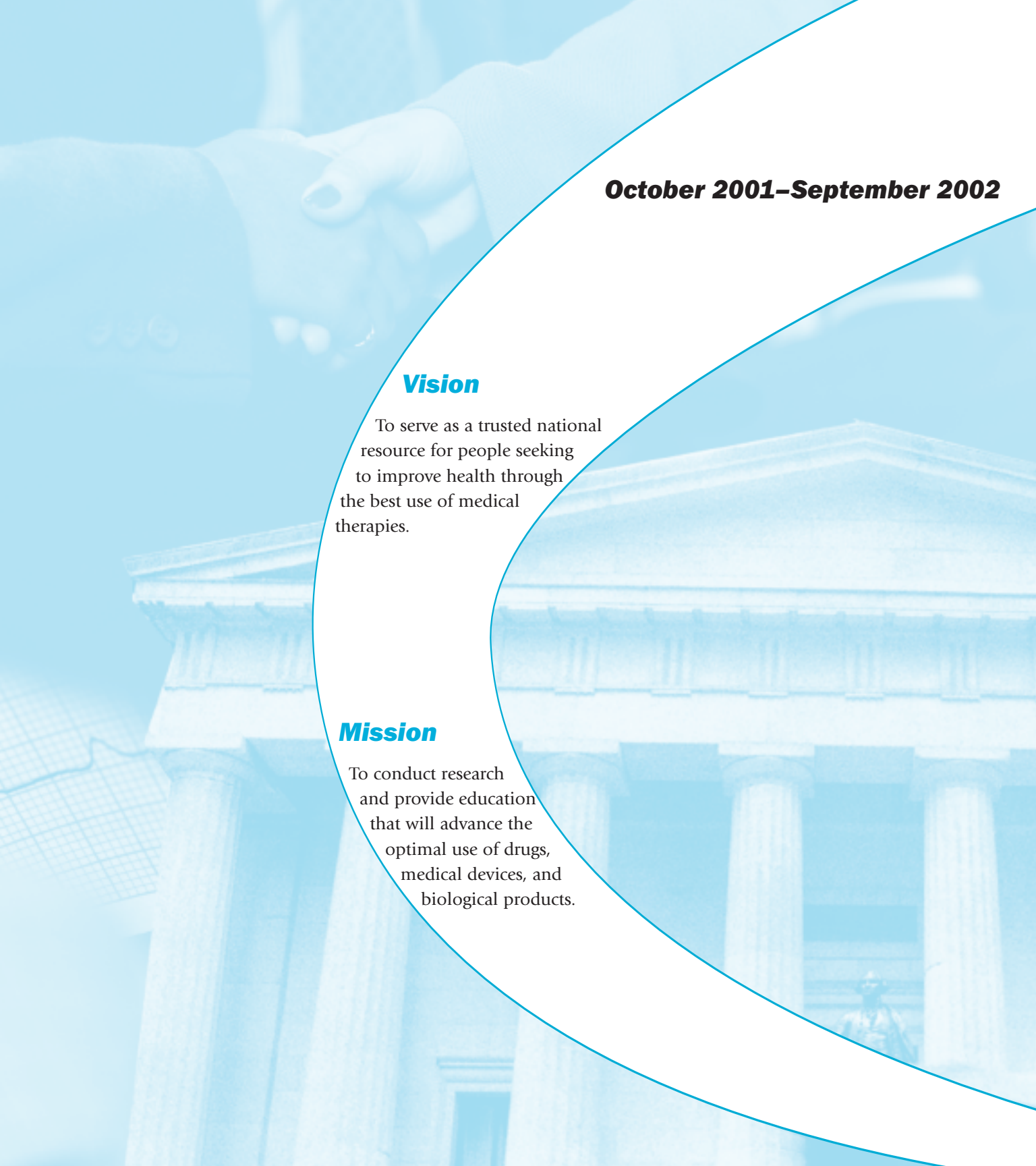

October 2001–September 2002

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.

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Letter from the Agency for Healthcare Research and Quality

Dear Colleague:

The Centers for Education & Research on Therapeutics (CERTs) program was established in 1999 under the sponsorship of the Agency for Healthcare Research and Quality (AHRQ). The CERTs is a national program whose goal is to improve the effectiveness and safety of the use of therapeutics by conducting research and educational programs that examine the benefits and risks of new, existing, or combined uses of therapeutics. A key activity is to develop collaborative relationships with other organizations, both public and private, to further the goals of the program.

This report documents progress in the third year of the program and beyond, and clearly shows the advances being made. With over 130 projects underway in the seven research centers, many being done through partnerships, the CERTs are adding to our knowledge base on how therapeutics work and can work more safely. In the first two years, the CERTs have clearly identified the questions that drive the research, and initiated or completed work on an impressive number of projects. Each of these furthers our understanding of therapeutics.

In a major collaborative effort between public and private organizations interested in pharmaceuticals, the CERTs kicked off a series of workshops designed to inform the process and outcomes associated with risk communication, assessment, and management. This key program from Year 2, the Risk Series, was continued and expanded in Year 3.

Carolyn M. Clancy, MD

In addition, the third year heralds the development of a number of tools that can be used to educate clinicians and researchers, particularly in the area of reducing adverse events caused by medication errors or drug interactions. Research is especially focused on those errors that most affect women and children, as well as tools to help advance the optimal use of cardiovascular drugs and other pharmaceuticals.

We are very pleased to provide you with this report on the work of the CERTs. As they continue to work to build partnerships and to develop new and innovative ways to disseminate and educate, we hope that the CERTs can look forward to another year of landmark accomplishments.

—Carolyn M. Clancy, MD
Director, AHRQ

Letter from the Steering Committee

Dear Fellow Citizens:

The progress of the CERTs is a great source of pride. CERTs projects now number over 130 and the results are already making a difference in the lives of patients every day.

From the very beginning, we wanted CERTs to be a national resource for research and education on therapeutics. Our unique public-private collaborations give us the broad scope and the flexibility we need to identify the most pressing therapeutics issues and tackle them head-on. They also allow us to respond to national needs.

As public and medical concerns shift to national preparedness, access to medicines, and the safety of those using these therapies, so does our attention focus on these matters as well.

Our third year has reminded us that collaboration is the key to responding quickly and judiciously to emerging research needs. We have expanded our partnerships a great deal and, along with them, our ability to address the intricacies of optimizing the use of therapeutics.

We are also learning to fine-tune how the CERTs centers work together, combining our expertise and resources so that the sum is even greater than its already substantial parts.

The program achieved some exciting results in 2001–2002, only a fraction of which can be highlighted in the space of this report. But with each achievement, a new challenge becomes apparent and we are equally excited to address these as well.

As always, we welcome your suggestions to help us become even more productive.

—Hugh 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; Judith M. Kramer, MD, MS; Richard Platt, MD, MSc; Wayne A. Ray, PhD; Kenneth G. Saag, MD, MSc; Marcel E. Salive, MD, MPH; Brian L. Strom, MD, MPH; Karen Williams; Raymond L. Woosley, MD, PhD

Hugh Tilson, MD, DrPH

Introduction

The Centers for Education & Research on Therapeutics (CERTs), administered by the federal Agency for Healthcare Research and Quality (AHRQ), is a unique network of seven centers focused on improving the use of medical therapies. The CERTs harness the power of collaboration across all sectors, public and private, industry and government, academia and business, to find the best possible use of existing medicines and medical devices and then spread the word of these improvements to those who can put them to use.

With over 130 projects under the CERTs umbrella to date, our research and education efforts range from relatively straightforward questions of "Who is at the highest risk for arthritis?" to randomized trials of new, multifaceted educational interventions in congestive heart failure. CERTs efforts run the gamut from clinical studies to testing teaching methods to policy-changing outcomes research.

Central to the CERTs goal of being a national resource is responsiveness to national needs. The mix of public and private partnerships and the combined expertise of seven centers with both academic and business leaders give CERTs the flexibility to adapt their research to the most pressing healthcare matters as they emerge.

Concerns about patient safety, especially regarding the use of new medicines, have occupied the media spotlight in the past year. The complexities of prescribing, dosing, administering, and monitoring medications are daunting and create a great potential for inadvertent misuse. From the beginning, improving the safe use of therapies has been central to the goals of CERTs.

Reducing risk to patients is integral to the CERTs mission, and the centers have responded. More than 70 projects focused on ensuring the safe use of therapeutics have been completed by the CERTs or are still ongoing. Several more will begin in the near future. The vast majority of these focus on the safe administration and monitoring of medications.

In this report, you'll find some highlights of the centers' successes in therapeutic safety. From tracking prescribing patterns of some of the most commonly used antibiotics to protecting the most vulnerable of patient populations, the CERTs have taken great strides in ensuring the safety of patients while retaining the benefits of today's most effective medicines.

All of this research is useless without the effective dissemination of results, however. Our education efforts seek to target information to the most appropriate audience, tailoring it for the speediest and most effective teaching. Whether they are sweeping national endeavors or more tightly focused seminars and online learning modules for particular therapeutic areas, the CERTs education programs can be customized to fit any need.

Pictured left to right: Richard Platt, MD, MSc; Brian L. Strom, MD, MPH; Kenneth G. Saag, MD, MSc; Wayne A. Ray, PhD; William H. Campbell, PhD; Raymond L. Woosley, MD, PhD; Robert M. Califf, MD; Hugh Tilson, MD, DrPH; Judith M. Kramer, MD, MS

CERTs Progress

University of Arizona Health Sciences Center— Drug Safety Begins in School

Key projects:

- Identifying gaps in education on therapeutics for women and developing responsive curricula
- Establishing and maintaining an international registry of cases of torsades de pointes
- Developing an online educational model on drug interactions, especially in women

A 1999 Institute of Medicine report estimated that as many as 98,000 Americans die each year from medical mistakes. Other studies have put the number at 44,000, but even with this more conservative estimate, medical errors would be one of the 10 worst killers in the United States, ahead of motor vehicle accidents, breast cancer, or AIDS.

One of the chief contributors to medical errors is adverse drug reactions (ADRs), resulting in more than 770,000 injuries or deaths each year. ADRs are responsible for $136 billion in additional healthcare costs each year, more than the total costs for cardiovascular disease or diabetes. With approximately 2.8 billion outpatient prescriptions filled each year, an amount equal to 10 prescriptions for every person in the nation, the potential for ADRs is high.

The focus of the Arizona CERTs is to improve therapeutic outcomes and reduce adverse events caused by drug interactions, especially those affecting women. The CERTs is also focused on identifying and understanding mechanisms for drug-induced arrhythmias. These goals are accomplished by basic and clinical research programs and a variety of educational efforts.

"Your list has been an invaluable resource…a real life saver! Thanks so much for your work in this area. I check your updated list every time my 14-year old son's meds are changed, along with checking with his electrophysiologist/cardiologist."

—Maggie H., mother of a child with long QT syndrome.

Despite recent innovations in healthcare organization, including electronic prescription entry and bar-coding of drugs, adverse drug reactions remain prevalent. Physicians cannot rely on technology alone to prevent them.

Dr. Raymond Woosley, director of the University of Arizona CERTs, and his colleagues are homing in on the root causes of these potentially disastrous interactions.

The major finding from the Arizona CERTs in the last year was the result of the Web-based International Registry for Drug-Induced Arrhythmia. A medication prescribed for over 45 years was discovered as a potential cause of a lethal arrhythmia. Arizona CERTs investigators performed basic laboratory research to prove that methadone, long used to treat narcotic addiction, could block potassium channels in the heart in ways similar to the prescription antihistamine terfenadine (Seldane®), a drug removed from the market for this very complication.

Arizona CERTs investigators then began a series of collaborative clinical research projects with government agencies and addiction treatment specialists to further define the nature of methadone's cardiac risk to women. They not only discovered the avenue by which methadone increases a woman's chance for arrhythmia, but also found that a component of a common methadone solution contributed as well.

These results stimulated a group of clinicians prescribing methadone to review their experience with the drug. As a result, they identified 17 cases, 10 of which were in women, and published their findings in the *Annals of Internal Medicine.*

The Arizona CERTs has recently begun a series of clinical research projects designed to identify risk factors for the development of life-threatening arrhythmias in patients treated with methadone. As with Seldane and other drugs that induce this form of arrhythmia, the available data from spontaneous cases reported to the U.S. Food and Drug Administration and the Arizona CERTs suggest that women are at higher risk than would be expected.

The Arizona CERTs clinical projects will examine gender in relationship to drug interactions and also evaluate the potential importance of drug interactions, heart rate, electrolytes and other factors that could predispose a patient to this form of lethal toxicity. While the whole story is being worked out through more research, drug treatment centers are now actively monitoring patients on methadone to assure its safety as a result of this new finding. The research has also guided the revision of treatment guidelines from the Substance Abuse and Mental Health Services Administration.

Like all CERTs, the Arizona CERTs knows its research findings, no matter how insightful, help no one if they are not properly disseminated. Their educational efforts on ADRs include a significant look at the fundamental medical education on this understudied topic, as well as a pioneering use of the Internet to spread their groundbreaking results.

In 2001, Dr. Woosley and his team surveyed medical schools and training programs across the country, including every director of a third-year internal medicine clerkship. The results were revealing.

Only 16% of internal medicine clerkships had formal lectures on adverse drug reactions/interactions. This medical specialty training was particularly important to the survey and the most telling on the state of education about adverse drug reactions.

"We chose internal medicine clerkship programs because, based on national averages, medical students spend an average of 12 weeks in this rotation, the most of any required clinical experience," notes Dr. Woosley. "Also, the discipline of internal medicine trains future physicians to care for patients with complex medical problems that frequently require multiple medications, which may place patients at an increased risk of experiencing an adverse drug reaction."

The results were published in the September 5, 2001 issue of the *Journal of the American Medical Association*. Clerkship and residency directors overwhelmingly agreed that a significant educational gap existed. In an era of increasingly complicated and time-consuming medical school curricula, how could this be addressed most efficiently?

Demonstrating the synergy across sectors that makes CERTs such a dynamic network, the Arizona CERTs and the Center for Drug Evaluation and Research at the FDA collaborated on a multimedia educational module. The program consists of a computer presentation, accompanying note set, and a pocket reference card. Every third-year clerkship director and residency training director in the U.S. received one.

The module covers the gamut of ADR topics, from the latest incidence and impact figures to the pharmacology behind drug interactions. In addition to the clinical nuts and bolts, the program also teaches young doctors how to develop a systematic approach to and a "tool box" for predicting and preventing adverse drug interactions.

Knowing that information is useless if it is not accessible, the Arizona CERTs and the FDA provide the educational module for download on their respective Websites.

This openness and interactivity are mainstays of the success of CERTs. The Arizona Center is already responsible for two Web sites devoted to gathering information on drug-induced arrhythmias: www.qtdrugs.org and www.torsades.org.

Torsades.org is a list of drugs that produce a prolongation of the QT interval on an electrocardiogram (ECG). This can result in a dangerous arrhythmia called torsades de pointes. QTdrugs.org is a registry of cases of torsades de pointes. Physicians from across the country can access the registry and submit data on patients suffering from this arrhythmia. The doctors send in ECG readings, as well as a mouth swab or blood sample for genetic information.

From this wealth of data, Arizona CERTs seeks to identify not only the drugs responsible for these QT-interval abnormalities, but also the associated genetic risk factors. Armed with this information, the researchers hope to develop a test to identify those patients most at risk.

Further demonstrating their commitment to education and patient safety, Dr. Woosley and his group have lectured on ADRs at a number of grand rounds this year and Dr. Woosley presented their findings at the Arizona Health Sciences Center's 27th Annual Primary Care Update.

Duke University Medical Center—Adherence and Survival: Taking the Long View on Saving Lives

Key projects:

- Multi-tiered quality improvement intervention to increase the appropriate use of beta blockers in patients with heart failure
- Post-market surveillance of recently FDA-approved transmyocardial revascularization procedure
- Development of educational module on QT-prolonging medications

Much of the focus in patient safety is on the prevention of medication errors. One important, yet often overlooked, type of medication error is an error of omission. Indeed, for epidemic problems such as atherosclerosis, errors of omission may dwarf errors of commission as a cause of death and disability. Simply stated, patients frequently do not receive medicines that have been proven to save lives.

The CERTs mission at Duke is to conduct research and provide education that will advance the optimal use of cardiovascular drugs, medical devices, and biological products. Duke has focused on the gap between research evidence and clinical practice, looking both at errors of omission (failure to prescribe drugs known to improve survival) and errors of commission (failure to heed labeled contraindications, warnings, or drug interactions for high-risk medications or devices).

Improving the use of medications for the nation's leading cause of death, coronary artery disease, is a daunting task. While many national efforts are emphasizing the hospital phase of care, the Duke CERTs is focusing on the long-term, outpatient phase. Numerous studies over the last two decades have shown significant survival advantages from aspirin, beta-blockers, and cholesterol-lowering agents in patients who have obstructed coronary arteries. In the last decade, angiotensin-converting enzyme (ACE) inhibitors and beta-blockers have also been found to improve substantially the survival of patients with heart failure.

"Information from the Duke CERTs Research program was instrumental in helping the Council for Affordable Quality Healthcare [CAQH] select the subject of our national cardiac quality improvement initiative. Duke had found, in their databank of patients with coronary heart disease that consistent use of beta-blockers was only around 35%. This was in stark contrast to estimates collected by health plans indicating that use of beta-blockers at hospital discharge after heart attack is closer to 90%. Thus, CAQH's cardiac initiative will focus on long-term adherence to beta-blocker therapy in patients who have suffered a heart attack."

—Robin Thomashauer, CAQH Executive Director

With this strong evidence, one would expect that almost all patients without a contraindication who have blocked coronary arteries or who have heart failure would be taking these critical medications. Surprisingly, many studies, including those performed at Duke, show this is not the case.

Numerous quality improvement initiatives across the country are trying to change this by working with doctors and hospitals to improve the number of patients who receive these medications appropriately, both in the hospital and upon discharge. These initiatives include programs by the Joint Commission on Accreditation of Healthcare Organizations, the Centers for Medicare & Medicaid Services, the National Committee for Quality Assurance, the American Heart Association, and the American College of Cardiology.

One program, administered by the Duke Clinical Research Institute (DCRI), and endorsed by the American Heart Association, has already demonstrated improved use of beneficial therapies in over 200 hospitals caring for patients with acute coronary syndromes.

A second program with the Society of Thoracic Surgeons and the DCRI, funded by a grant from AHRQ, has recently reported a significant improvement in the use of beta blockers and internal thoracic artery grafting in patients undergoing coronary artery bypass grafting. This program is particularly important because it provides a model for a partnership, including a professional society, a major government agency, and an academic coordinating center, to inform practice nationally.

While hospital discharge is a critical time to get patients started on these medications, the Duke CERTs is also concerned about what happens after the patients go home. These life-saving therapies will only be life-saving if patients continue to take them. Compared with prescribing in the hospital environment, this issue of long-term use of life-saving medications has received relatively little public attention or resources directed at either measurement or solutions.

The Duke CERTs has approached this issue with the valuable asset of long-term, patient-reported follow-up in patients with underlying coronary heart disease (CHD). These data are captured in the Duke Databank for Cardiovascular Diseases. In a series of projects evaluating long-term use of life-saving medications for CHD and heart failure (HF), Duke researchers have detected a consistent pattern. Not only is the proportion of patients who annually report outpatient use of each life-saving drug lower than nationally reported rates at hospital discharge, but also the percentage of individual patients who consistently take a given life-saving medication over a period of years is considerably lower.

Of over 20,000 CHD patients with follow-up information in the year 2000, 46% reported taking beta-blockers. The percentage of individual patients who consistently reported using beta-blockers over the period 1995–2000 was only 37%.

Even more disappointing are the data on combination use of life-saving therapies for CHD. In the year 2000, only 41% of patients with CHD reported taking both aspirin and beta-blockers. For the follow-up period from 1995 to 2000, only 30% of patients consistently reported use of both aspirin and beta-blockers. A mere 16% of patients consistently reported use of the three-drug regimen of aspirin, beta-blocker, and a cholesterol-lowering drug. Chronic treatment of heart failure was even worse, with only 31% of over 7300 HF patients consistently reporting use of a beta-blocker; 33% consistently reporting use of an ACE inhibitor, and only 13% using both regularly.

One of the main goals of the Duke CERTs is to keep patients on all the necessary life-saving therapies over the long term. Critical to attaining this goal is addressing the impediments to consistent use for the individual patient and developing workable solutions for these obstacles. The Duke CERTs is evaluating whether busy physicians could be assisted by other healthcare practitioners, such as community pharmacists, in assessing and overcoming barriers to long-term medication use for individual patients.

In the coming year, the Duke CERTs will be pulling together community and hospital pharmacists along with physicians in both settings to work on increasing adherence to long-term medication regimens for CHD and HF. Central to this process will be effective communication among all members of a patient's treatment "team," combined with empowering the patients themselves through improved education and feedback about their care. In the near future, the Duke CERTs hopes to demonstrate the same progress in preventing cardiac events in the outpatient setting that it has shown in the hospital setting.

University of North Carolina at Chapel Hill—"Small" Errors: Improving Drug Safety for Children

Key projects:

- Development of evidence-based tools to assess pain in pediatric patients for earlier and more effective therapeutic intervention
- Assessment of the skeletal effects of vitamin D and calcium supplementation in children with cystic fibrosis
- Design and testing of toolkits for the more accurate diagnosis and more effective treatment of attention deficit hyperactivity disorder (ADHD)

The University of North Carolina CERTs is targeting safer drug use in a particularly vulnerable population—children. In keeping with its mission of improving the use of therapeutics in the pediatric population, UNC CERTs is tackling the prevalence of medication errors while treating children, a poorly understood problem.

Inpatient adverse drug events among pediatric patients have not been adequately assessed. Children present unique challenges when ordering, dispensing, and monitoring medications. Potential adverse drug event (ADE) rates for children can be three times higher than for adult patients.

Because so few clinical trials involve pediatric subjects, dosing for children has largely been done through calculations based on weight, as much by tradition as by empirical evidence. The more calculations required to prescribe and administer a medicine, the greater the potential for error. Medicines often must be diluted by pharmacists for use by pediatric patients, presenting another opportunity for mistakes.

The UNC CERTs is devoted to improving the use of therapeutics in the pediatric population (neonates, infants, toddlers, children and adolescents). Thus, the UNC CERTs couples broad attention to practical improvements with a targeted emphasis on mainstream problems in therapeutics. The UNC CERTs distills these focal points into strategies for improving outcomes from the use of drugs and devices in the pediatric population.

"My office set up a structured system for evaluating ADHD patients, using the tools in the UNC CERTs toolkit. This helped us standardize the way ADHD is approached and diagnosed. It's just a better way to practice medicine."

—New York pediatrician

Dr. William Campbell, co-principal investigator of the UNC CERTS, along with Dr. Brian Strom, principal investigator for the University of Pennsylvania CERTs, were named to a new subcommittee of the FDA in December 2001. The Drug Safety and Risk Management Subcommittee will advise the FDA on safety issues in the evaluation of new therapies and new uses for existing therapies.

"A goal of the CERTs is to optimize the balance of the risks and benefits of medical products," says Dr. Rob Califf, director of the CERTs Coordinating Center. "Having CERTs Steering Committee members on this subcommittee is a logical extension of this mission. As the FDA moves more vigorously to implement programs of risk management, I expect that this committee will play an important role in giving both general and specific advice to the FDA."

As age decreases, vulnerability increases. Very young children are not able to warn care providers about potential mistakes with medication. Infants, especially newborns, are particularly subject to injury from even the smallest dosing error with particular drugs. But many differences between adults and children in susceptibility to ADEs are not as clearly understood.

To get a better picture of the rates and character of adverse drug events in young patients, UNC illustrated one of the chief strengths of the CERTs program, its partnerships with a diverse array of institutions. Enlisting the aid of the United States Pharmacopeial (USP) Convention Inc., UNC set out to get a detailed picture of medication errors in relation to the continuum of pediatric care (where medication errors are most likely to occur, where interventions will be most effective) as well as which therapies are most susceptible to misuse.

USP is a not-for-profit organization that has promoted public health by establishing standards of quality for medicines and other therapies. These standards are published in the federally recognized *United States Pharmacopeia and National Formulary (USP-NF)*.

USP offered an innovative and powerful way for UNC to track medication errors in its pediatric patients. MedMARx™ is a Web-based system for entering and tracking mistakes made when prescribing, documenting, and administering medications. Participants can enter anonymous patient information, including age, and a host of relevant details on the particular medication error. These include the level of injury done to the patient, if any, and the stage at which the error occurred, allowing healthcare providers to pinpoint where quality improvement should be aimed.

Because MedMARx is anonymous, anyone using the system can access it to find drug errors similar to ones happening at his or her institution. A flexible and powerful search function helps find only those instances that pertain to a physician's or hospital's particular interests.

This potent feature was the key to a revealing and dramatic UNC CERTs success. Co-principal investigators Drs. William H. Campbell and William L. Roper and their team analyzed over 2000 pediatric inpatient records among the more than 70,000 currently in the MedMARx database.

Their findings revealed good news and bad. The majority of errors were cases in which the misused medication reached the patient but did not cause harm. Most of the mistakes, about 52%, occurred at the administration phase, where errors of omission or an improper dose or quantity were the most commonly reported types.

Most commonly misused, according to the UNC team, were:

- IV fluids, e.g. dextrose/sodium chloride solution
- Gentamicin, a common antibiotic used against group B streptococci and E. coli
- Total parenteral nutrition, i.e., nutrient fluids delivered intravenously or subcutaneously, which is primarily a concern in premature infants
- Cefotaxime, another common antibiotic

Overall, the analysis supported previous studies that suggested pediatric populations are more vulnerable to adverse drug events. The results have led to the drafting of an addition to the USP recommendations, *Error Avoidance Recommendations for Pediatric and Neonatal Medicine Use*. This is currently under review and should be published soon.

UNC CERTs efforts to protect children from ADEs continue. Adding to the wealth of information from the MedMARx system, UNC researchers are also analyzing errors in pediatric patients submitted to the USP Medical Error Reporting Program. The aggregate data from both of these systems will be compared with data on adult patients to further refine the big picture of adverse drug events in children.

The Penn CERTs hopes to optimize drug prescribing and improve the risk/benefit balance from drugs, particularly for anti-infectives. The Penn CERTs accomplishes this research and dissemination effort by linking the pharmacoepidemiology skills of the Center for Clinical Epidemiology and Biostatistics with the pharmacoeconomics skills of the Leonard Davis Institute of Health Economics, the experience in patient-oriented research of the General Clinical Research Center, basic science laboratories interested in evaluating the molecular mechanisms of drug effects, and the social science skills of non-biomedical researchers at Penn.

University of Pennsylvania— The Patient or the Community: Balancing Tensions Created by Antibiotic Resistance

Key projects:

- Development of computer simulations of various data analysis approaches to improve the methods and reporting of results from multi-center or multi-site analyses
- Evaluation of risk factors for antibiotic-resistant infection in liver transplant patients
- Development and management of a fellowship training program in pharmacoepidemiology, in keeping with the mission of educating professionals

The University of Pennsylvania is working to preserve drug safety and efficacy for future generations of patients. Their focus on the best use of anti-infectives has led to great insights on prescribing patterns and the tensions exerted on caregivers when weighing the threat of growing bacterial resistance to antibiotics and the immediate need of their patients for the most effective treatment. This knowledge is being applied at the Penn CERTs and around the country to safeguard the efficacy of antibiotics for all patients.

Increasingly, research is showing that the misuse and overuse of antibiotics is leading to the development of more resistant strains of bacteria. Treating infections caused by bacteria resistant to more than one antibiotic becomes difficult.

At first, most of the attention on drug resistance was directed towards hospitals. With very ill patients in such close proximity to one another and antibiotic use so heavy, many drug-resistant strains emerged in this setting.

One means of ensuring proper antibiotic use is a hospital-based antimicrobial management program developed by the Penn CERTs faculty. Selected antibiotics are available to patients in the hospital, but only to those who fit certain criteria. The goal of this program is protection against the development of resistance. Penn CERTs faculty have demonstrated this project to be effective in improving patient outcomes and in reducing hospital costs, and it is now being copied by hospitals around the country. Follow-up studies are underway to determine how to improve its function even further, such as by reducing miscommunication between the house staff treating the patients and those staffing the program.

"The Penn CERTs is addressing a problem of extreme public health importance. Too many interventions have consisted of simply distributing new guidelines. It is time we realize that this will not in and of itself change behavior."

—Rich Besser, Centers for Disease Control and Prevention

But problems outside the hospital setting persist. Researchers are realizing that bacterial infections acquired in the community are showing resistance and putting otherwise healthy people at risk. Common infections such as pneumonia and ear infections are increasingly hard to treat with standard antibiotics.

With studies identifying misuse and overuse of antibiotics for predominately non-bacterial respiratory infections as the likely culprit, physicians are under pressure to withhold antibiotic prescriptions, particularly for new agents, in order to preserve their effectiveness for future patients. But when faced with the needs of their sick patient, doctors are reluctant to do so.

The tensions created between the danger to the community (resistant bacteria created by antibiotic misuse) and the danger to the individual patient (the need for the most effective medicines) can force a difficult choice on a physician.

To explore this conundrum, Dr. Joshua Metlay and colleagues from the Penn CERTs surveyed both generalist physicians and infectious disease specialists to gauge their attitudes towards antibiotic prescribing for patients with community-acquired (vs. in-hospital) pneumonia.

An anonymous survey to 400 general internists and family medicine doctors and 429 infectious disease specialists turned up a consensus from both groups. Both were more likely to prescribe newer, more broadly acting antibiotics than older medicines still recommended by national guidelines.

The older medicines were more susceptible to bacterial resistance, but using them prevented the overuse of these new, more powerful agents and thus delayed resistance to the newer drugs. The doctors overwhelmingly considered the individual health concern over the public health issue of future drug resistance.

The risk of contributing to antibiotic resistance ranked last among seven factors influencing the physicians' treatment choice. The efficacy of the chosen drug was far and away the most important among both groups of physicians.

The tension and confusion created by emerging antibiotic resistance showed in the doctors' other responses to the survey.

About 82% of generalists and 94% of infectious disease specialists believe that bacterial drug resistance is a growing and major public health problem. But just over half said they would consider the potential benefit for their patient against the potential harm to the community before prescribing an antibiotic.

While the vast majority of the polled physicians agreed that patient demand was a significant factor in over-prescribing of new antibiotics, only 36% of generalists and 22% of the specialists believed they prescribed antibiotics more than they should.

The overall message from the study was clear. Physicians' concern for their individual patients' health trumped any worries over public health issues in the arena of antibiotic resistance, despite guidelines to the contrary from such influential bodies as the Infectious Diseases Society of America and the American Thoracic Society.

Dr. Metlay and his team concluded that because of this ingrained attitude, educational programs and the issuance of guidelines would not be enough. The matter is further muddled by the presence of multiple, and often conflicting, guidelines.

Insights from these types of results have contributed to the development of several intervention programs that aim to improve the quality of antibiotic use in hospital and community-based settings. A central feature of the Penn CERTs programs to improve antibiotic use is the reliance on multidimensional interventions that incorporate patient, provider, and organizational components.

For example, a Penn CERTs study showed that outpatient use of academic detailing directed at physicians is effective in reducing the prescribing of antibiotics unnecessarily for upper respiratory infections. A follow-up study has added efforts to educate patients who had received antibiotics after the first intervention that such antibiotics are not necessary in the future. An evaluation of that program is underway.

The Penn CERTs continues not only to provide insight on the mechanics of antibiotic use, but also its implications on public health, policy, and economics. This multifaceted approach to improving a single but far-reaching therapy is fast becoming a hallmark of CERTs research. The Penn CERTs program to improve antibiotic prescribing reflects the core belief that maximizing the benefit and minimizing the risk of drugs requires educational efforts that involve not only physicians, but patients as well.

University of Alabama at Birmingham—The Long-Term Safety of NSAIDs and Coxibs: A Burning Question

Key projects:

- Pharmacoepidemiology and risk communication in biological therapeutics
- Quality indicators in both the management of gout and the use of analgesics for musculoskeletal disorders
- Impact of a multi-modal, provider-based intervention on the prevention and treatment of glucocorticoid-induced osteoporosis

Assessing drug safety often must start at the very beginning of the care process. The University of Alabama at Birmingham (UAB) CERTs is probing the patterns of drug prescription for musculoskeletal disorders, tracking some of the most common chronic diseases and the most frequently prescribed medications in the nation. The researchers hope to identify the best use of alternative drugs for these debilitating conditions, particularly arthritis, gout, and osteoporosis, and to find the perfect balance between benefit and risk.

For example, non-steroidal anti-inflammatory drugs (NSAIDs) are among the most commonly prescribed medications in the world. They are used for pain and inflammation relief in a host of disorders, most commonly arthritis and back pain. Despite their popularity, they can have serious side effects, especially when not managed properly.

Chronic use of traditional NSAIDs has been linked to a variety of gastrointestinal (GI) problems, ranging from small ulcers to life-threatening perforations of the stomach wall. These GI complications result in over 100,000 hospitalizations and 16,500 deaths each year with annual healthcare costs in excess of $500 million. The GI effects can be suppressed, but this requires an additional prescription.

The mission of the University of Alabama at Birmingham (UAB) CERTs is both to evaluate the effectiveness, safety, and impact on health-related quality of life (HRQOL) of musculoskeletal disorder therapeutics, and to guide and evaluate changes in the practice community based on new therapeutic knowledge.

In order to accomplish this, the UAB CERTS is working in collaboration with the UAB Center for Outcomes Effectiveness Research and Education, Center for Metabolic Bone Disease, Arthritis and Musculoskeletal Center, and the General Clinical Research Center to investigate innovative methods for effecting meaningful changes in provider behavior and patient-level outcomes.

A new class of anti-inflammatory drugs called COX-2 enzyme inhibitors, or coxibs, has emerged to help solve this problem. The most well known of these are celecoxib (Celebrex™) and rofecoxib (Vioxx™), which are among the 10 most frequently prescribed drugs in the world. Research shows these drugs offer pain relief equal to traditional NSAIDs, but with fewer GI side effects.

The long-term safety of coxibs versus traditional NSAIDs, or NSAIDs plus Prilosec™, however, remains unknown. Using the collaborative power of CERTs, Dr. Saag and his colleagues are working on this problem with a regional managed care organization, United Healthcare of Alabama, Inc. (UHC), with the Veterans Administration and the Alabama Medicare Quality Improvement Organization (QIO). These studies are expected to lead to improved prescribing for millions of arthritis sufferers.

In addition, Dr. Saag and colleagues have recently completed a study of physicians' NSAID safety practices in comparison to published guidelines. The purpose of this study is to test an intervention that will lead to improved adherence to guidelines for NSAID toxicity monitoring and better patient outcomes. According to Dr. Sandra Nichols, senior medical director for United Healthcare of North Carolina, Inc., "the UAB CERTs method of translating current evidence-based guidelines into clinical practice may help managed care organizations to minimize practice-pattern variations."

The practices will be improved by better monitoring of complications, avoiding use of unsafe combinations of drugs (both over-the-counter and prescribed), and by proper use of other medications to prevent complications.

As the cornerstone of this project, UAB investigators use their own innovative analytical method called Achievable Benchmarks of Care (ABCs). ABCs not only provide physicians feedback on their performance in relation to established guidelines, but also as compared with the best of their peers. Novel approaches such as ABCs allow CERTs research not only to improve clinical practice, but also refine policy and professional communication.

This past year, the UAB team worked with RAND and the National Committee for Quality Assurance (NCQA) to develop quality-of-care indicators for the management of patients with osteoporosis. Through NCQA, this work will be used nationwide by employer-based health plans to assure the quality of care for their beneficiaries with osteoporosis.

Related work in collaboration with the Arizona Medicare QIO and colleagues at the Duke CERTs will improve the care of nursing home residents who suffer from osteoporosis. This experimental intervention will ensure that nursing home residents receive state of the art care for this condition, which is common and associated with severe morbidity.

These projects demonstrate the impact on standard care that the CERTs can achieve. Not only are patients made less susceptible to unnecessary risks, but the very definition of "quality care" is changed by this evidence-based approach. The UAB CERTs melds research and education into a seamless quality-improvement mission.

Vanderbilt University Medical Center—Prescribing NSAIDs for Cardioprotection: A Red Herring?

Key projects:

- Retrospective study to assess outcomes of medical vs. surgical treatment of gastroesophageal reflux disease
- Evaluation and documentation of effectiveness of risk-awareness campaigns on coxib use in various communities and clinical settings
- Measurement of the comparative safety and efficacy for two major classes of non-aspirin, non-steroidal anti-inflammatory drugs in patients with heart disease

The safe use of anti-inflammatory drugs is a central concern of the Vanderbilt University CERTs as well. Principal investigator Dr. Wayne Ray and his colleagues concentrate on observational studies of existing medications and apply the results to changing the clinical use of these drugs and the policies surrounding them. This year they turned to the use of non-aspirin, non-steroidal anti-inflammatory drugs (NANSAIDs) and their effects on heart disease.

Controversial findings from a previous study suggested that the NANSAID naproxen, a commonly prescribed and popular over-the-counter pain reliever, could protect against heart attack and other cardiovascular complications. But the data were far from conclusive and physicians were unsure if naproxen could be given to their patients most at risk for heart disease to prevent heart attacks.

One of the actions of NANSAIDs is platelet inhibition. NANSAIDs help keep platelets, the blood cells that produce clotting, from binding together and so potentially blocking blood vessels. Specifically, they can block the production of an enzyme called thromboxane, which helps make platelets "sticky."

The Vanderbilt CERTs focuses on observational studies of medication effects, evaluation of the effects of policy changes, and improving medication use.

Of course, the primary function of NANSAIDs is to reduce inflammation. As recent study findings highlighted in the news have shown, inflammation may be a prime culprit in the development of coronary artery disease and other cardiovascular ills, perhaps even more important than cholesterol. The anti-inflammatory effect of naproxen could hold the potential to reduce the damage done to arteries and decrease the likelihood of a heart attack.

However, NANSAIDs are complex medicines. They have a wide range of effects on the body that vary greatly depending on dosage. At high doses, NANSAIDs inhibit the production of a compound called prostacyclin. Prostacyclin is one of the body's natural platelet blockers and so the clot-preventing effects of NANSAIDs may be reversed at sufficient doses. At these high doses, NANSAIDs may also contribute to high blood pressure, another risk factor for heart disease.

The intricacies of NANSAIDs' physiological effects leave doctors and patients at an impasse. Do NANSAIDs protect against heart disease and should they be prescribed just for this effect? If a patient needs a NANSAID for arthritis pain, is there a need to prescribe aspirin also? As a new class of pain relievers called coxibs increases in popularity and NANSAIDs perhaps become less commonly prescribed, this is an issue much on physicians' minds.

While few doctors were prescribing NANSAIDS for prevention of heart disease, consideration of discontinuing aspirin if a NANSAID was required for arthritis pain was an issue for millions of Americans.

Answering this kind of question on the best and safest use of a medication is the heart of the CERTs mission. Dr. Ray and his team set out to do so with a challenging and far-reaching study of 11 years' worth of records from the Tennessee Medicaid program.

The investigators combed the records of over 180,000 new NANSAIDs users and an equal number of non-users as a control group, all over the age of 50 and at risk for heart disease. They looked for hospitalizations for heart attack or death from heart disease. The records were from 1987 to 1998, before coxibs came to market, so these latest anti-inflammatories were not included in the study.

Dr. Ray's team performed several complex analyses to adjust for various baseline risk factors for heart disease. One excluded those patients who had existing heart failure, a condition that some research suggests is worsened by NANSAIDs. Another analysis focused on those patients most likely to benefit from any cardioprotective effect of NANSAIDs, including those taking the drugs at doses sufficient to reach the anti-platelet effect.

No matter how the data were approached and filtered, no protective benefit from NANSAIDs was found. The two groups of patients suffered heart attacks at roughly equal rates. Without randomized trials providing evidence to the contrary, Dr. Ray concluded that naproxen and other NANSAIDs should not be prescribed to protect against heart disease. Most importantly, we can now tell doctors that patients who must be treated with NANSAIDS must also be treated with aspirin if they meet the usual criteria for primary or secondary prevention of vascular disease with aspirin.

Dr. Ray's study demonstrates an important function of CERTs. Not only can CERTs research identify how existing medications are being used, as in the UAB CERTs coxib study, it can also penetrate the clouds of conflicting data and insufficient study to answer important questions about common therapies and provide sound evidence on their safe use.

Dr. Ray and his team published their findings in the January 12, 2002 issue of *The Lancet*.

The HMO Research Network CERTs comprises the investigators, information resources, delivery systems, and members of 10 HMOs across the country committed to public domain research. The center emphasizes studies of the use and outcomes of therapeutics in large, defined populations, and of methods for changing provider and patient behavior regarding prescribing and adherence to therapy. The research typically involves multiple HMOs to achieve a large, diverse population and range of delivery systems that result in easily applicable findings.

HMO Research Network—Collaboration and the Big Picture of Prescribing Safety

Key projects:

- A study to assess and ultimately reduce misuse of antibiotics in children
- Assessment of the incidence of Churg-Strauss syndrome, a rare form of inflammation of blood vessels, to determine if the use of certain asthma medications is more common among these patients
- Evaluation of patient preferences for communicating medication errors

The HMO Research Network CERTs presents a unique array of resources. Made up of 10 HMOs across the country, each with experienced investigators committed to public domain research, the center has access to a large, diverse, and well-defined patient population, as well as the clinicians who care for them and the supporting information systems. The HMOs have over 16,000 care providers, who treat 7 million patients. Their research benefits from a "real world" clinical setting plus the statistical power of large study populations.

The HMO CERTs is leading an ambitious drug safety program that includes all seven of the CERTs centers. Until now, most work on drug safety has focused on the inpatient setting. However, far more prescribing is done for outpatients, and it is into this vast and relatively uncharted territory that the HMO Network can lead the way. Identifying the most important errors in this largely unexamined setting in order to develop methods for preventing them is a necessary first step. These two aims, identification and prevention, are the subjects of the largest federal patient safety grant awarded in the past year—the CERTs Prescribing Safety Program, awarded to the HMO Research Network CERTs.

"These HMOs are an ideal environment in which to learn how to improve care, both for their own members and for others as well," said Dr. Richard Platt of Harvard Medical School and Harvard Pilgrim Healthcare, principal investigator of the HMO Research Network CERTs and of the CERTs Prescribing Safety Program.

The project will characterize the frequency and severity of medication errors, focusing on the most commonly misused drugs, those with especially strong warnings against misuse, and on medication errors in vulnerable populations, such as children and the elderly.

"Nothing has the potential to improve the health of our nation more than evidence-based medicine. Our collaboration with the CERTs is one of the most productive ways to promote an evidence-based system. Programs like the safety initiative being conducted in the health plans of the HMO Research Network CERTs demonstrate the leadership of the health plan community to improve America's health care system."

—Karen Ignagni, President and CEO, American Association of Health Plans

Analyzing the HMOs' data, the researchers will evaluate how often medicines are prescribed outside FDA "black box" warnings, extremely strong cautions added to prescribing information when a serious potential adverse effect is noted in a medicine's use. Other commonly accepted safety guidelines and input from the expert advisory committee will be used as benchmarks as well.

Once the investigators have determined the frequency and severity of these medication errors, they will implement three educational interventions and measure their impact by reviewing the records again afterwards.

Two of the interventions based on this project's research are experiments with electronic prescription order entry, which will give physicians informed assistance in making medication choices and help reduce errors in dosing. These also include ongoing outreach to the physician users to further refine the power of these systems. The third intervention will use a randomized trial design to assess the effects of group physician education.

This is the first independently funded project that involves all of the CERTs, with each of the seven centers represented on the advisory committee. This not only ensures expert opinion from a variety of sources, but also provides timely access to investigators whose expertise may be perfectly suited to further studies arising from these research findings.

Other centers are leading parts of the research. The Duke CERTs, with its experience in cardiology, will pay particular attention to drugs that prolong the QT-interval and may create dangerous heart arrhythmias.

The UNC CERTs, true to its mission of improving therapeutics for children, is playing a leading role in defining the problems specific to prescribing medicines to young patients.

The CERTs model of collaboration and public-private partnership creates an environment conducive to solving problems beyond the reach of any individual center. This approach uses the unique resources of each element of the CERTs to contribute knowledge towards a generalized solution that can be tested in the variety of practice settings represented by the CERTs network.

Putting Our Heads Together: Fostering Collaboration

The Risk Series—"Benefit the Patient, Manage the Risk"

No medical product can be 100% safe or effective. Caregivers, researchers, regulators, and all involved with the administration of healthcare must continually seek a balance between the risks and benefits of therapies as they are developed and used—a concept that has been called "risk management."

But measuring, communicating, and minimizing these risks is an intricate labyrinth. Currently, these daunting tasks are performed piecemeal, using many different methods in the various geographic, scientific, and therapeutic areas. Unfortunately, little of this critical effort is guided by research aimed at defining the best ways of aggregating appropriate data and applying it to individual patients in practice or communicating it to the public. The result is gaps in our knowledge of risk and benefit as they exist in the everyday, clinical setting. Defining a research agenda that can fill in these missing pieces is the focus of the Risk Series.

The CERTs program continues to work towards improving the balance of benefit and risk across all therapeutics. Calling on its eclectic collaborative resources, the CERTs has teamed with the FDA, the Pharmaceutical Research and Manufacturers of America (PhRMA), and the AHRQ to gather academic researchers, leading physicians, government representatives, leaders from the pharmaceutical industry, and safety advocates from a variety of disciplines and sectors, to conduct the Risk Series. These workshops focus on three key areas:

- **Communication:** How are the risks of a therapy best communicated to a particular audience? How do the communication needs of the patient differ from the physician or the media?

- **Assessment:** What are the information gaps in the current system for quantifying a given therapy's risk to the patient? How can the various sectors, i.e. government, academia, business, etc., work together to create a more seamless system?

- **Management:** Once risk is identified, how do we minimize patient exposure to it? How do we tip the balance towards benefit?

In 2001, the first of these workshops took place to discuss communicating risk to caregivers and their patients. Participants concluded that there is no source of a coordinated view of the system of risk communication. Multiple independent parties are doing their best, but they often lack guidance based on evidence about how to proceed and how to coordinate their efforts. While many intermediate steps were identified, the overwhelming consensus of the participants was that a comprehensive approach to information management is needed. The results of the meeting are currently in review for publication.

The following year saw an even more complex matter being tackled. The Risk Series workshop on risk assessment was held in the spring of 2002 and gathered a who's who of regulatory, industry, academic, and scientific experts.

One of the greatest challenges to accurate risk assessment is the way in which drug safety is primarily monitored today. A chief source of information is the Adverse Event Reporting System (AERS), maintained by the FDA's Center for Drug Education and Research (CDER). This system gathers data on adverse drug reactions submitted either directly by caregivers via the FDA's MedWatch service or through the drug's manufacturer, as mandated by law.

Once the AERS receives enough reports of an adverse event related to a particular therapy, an alarm is sounded and regulatory action is taken to minimize risk. But a reporting system is only as good as the data that it receives. If important adverse events are not reported, or even identified as important in the first place, the AERS cannot be an adequate, standalone catch-all.

The Risk Series workshop on assessment identified the obstacles to gathering more accurate risk data and offered several suggestions on which research questions to pursue. Throughout the meeting, the importance of multi-sector collaboration was made clear repeatedly. Risk information without a clear denominator or common nomenclature has important, but ultimately limited, value.

A particular emphasis in the assessment workshop was on the acceptability of risk. For patients with cancer, a much greater amount of risk is acceptable when taking a potentially life-saving medication than for someone with a common upper respiratory infection taking a prescription antibiotic. But how much risk is acceptable when weighed against a therapy's benefit? How is this quantified?

Public acceptability of the risk inherent to medication use is understudied, though the Risk Series will conduct a workshop on communicating risk to the media and how the media then relays that information. This is a key component that shapes the public's attitude towards the issue. More systematic analyses of acceptability of risk are an urgent need.

Advances in technology must also be harnessed. A nationwide, electronic medical records system could improve therapeutic safety, but is such a system feasible? What other technological innovations, existing or yet to be developed, might reduce risk? These and other high-tech questions became one of the top priorities on the meeting's resulting research agenda.

A relatively simple solution offered by the panelists was requiring that a diagnosis be written on every prescription, greatly reducing the risk of an error at the dispensing stage of therapy use. This one step would also provide a wealth of data for future study of risk.

The results of the risk assessment workshop are being prepared for journal publication, offering the group's conclusions and full recommendations on how to proceed.

The third of the five Risk Series workshops took place in the fall of 2002 and focused on assessing benefit. Once risk is assessed and communicated effectively, how do clinicians and regulators weigh it against the potential benefits of a therapy?

The workshop concluded that research aimed at the marketing approval for medical products often does not provide those who must make therapeutic decisions (patients, doctors, health system and payer administrators) with the information they need concerning the comparative medical outcomes and costs of therapeutic strategies.

Major recommendations of the participants included the formation of a "national problem list" outlining the therapeutic questions considered highest priority from the perspective of public health, the funding of significant research on the way in which information can be presented to improve the correspondence between the values of patients and their medical decisions, and a continued focus on large, simple, post-marketing clinical trials.

Many questions exist about the methodology of assessing benefits, including a variety of statistical and clinical issues. How can we be sure that an apparent difference in treatment effect based on a clinical patient characteristic is real or just the play of chance? How do we interpret apparent differences in treatment effect in different countries? How can supposed surrogate endpoints be validated to allow generalization of short-term findings to broad populations over the long term?

Little funding goes into research to understand medical decision-making. The value of assessing benefits and risks could be greatly enhanced by such research because it will reveal the methods of information presentation and professional interaction that led to the best decisions, providing a model for future endeavors.

Those who make decisions about healthcare at the individual level and those who fund healthcare remain concerned that inadequate empirical data exist on the risks and benefits of many routine therapies. By increasing the number of comparative clinical trials focused on answering questions that drive medical decisions, such as the effects on longevity and quality of life, the balance of benefits and risks can be tipped in the patient's favor.

The fourth Risk Series meeting will examine risk communication and the media. The enormous impact of the media on public perceptions and individual decision-making is obvious and the recent national discussions about anthrax and smallpox vaccines have reinforced the importance of this issue. Yet little research is done to develop an understanding of the implications of local and mass media on specific perceptions of risk and benefit.

This meeting will bring together a small, representative group from the media, academic researchers, government agencies, the medical products industry, and consumers. The product of the meeting will be a research agenda that will provide a resource for those interested in communicating broadly about the risks and benefits of proposed therapies and for the press to intensify its efforts at self-examination.

The final Risk Series meeting developed a research agenda concerning the tools available to implement risk management programs. Held in early 2003, the workshop gathered leaders across all sectors to draw the big picture on the state of risk management. The participants brainstormed on a number of key issues:

- The effectiveness of risk management techniques for patients
- The effect of risk management programs on the healthcare system
- The interaction between multiple risk management programs
- The unintended consequences of risk management programs

In March of 2003 the CERTs hosted a "roll out" of the risk management series in which the findings and recommendations of the series were presented to policymakers and the public. At this event, the major concepts of risk management were concisely summarized so that what we already know can be more effectively integrated into policy, regulatory processes, and clinical practice.

Just as importantly, the research agenda emanating from the Risk Series charts the course to a much brighter future in which the best therapy can be offered to each individual person through a well-informed consideration of specific benefits and risks of therapeutic options.

Perhaps the most valuable products of these workshops are the collaborations and research that have already sprung from them. Each of these new projects, like the Risk Series itself, will further explore the assessment, communication, and management of risks associated with therapeutics.

Partnerships to Advance Therapeutics

Collaboration across sectors is a key to CERTs success and at the core of the program's values. The early achievements of the CERTs centers underscore this approach and in 2001, CERTs sought new ways to bring research partners together. The Partnerships to Advance Therapeutics (PATHs) was founded.

Each spring, the CERTs host a meeting of leaders from over 35 organizations that span the healthcare gamut. Government agencies, insurers, physicians, professional associations, patient advocacy groups, private industry, and even U.S. Congress are all represented, with a single goal in mind—foster research and education collaborations founded on open communication and a consensus on priorities.

The first of the annual PATHs meetings in 2001 bore immediate fruit, as a registry of educational and research projects, as well as interested collaborators, was created. The registry was published and also posted on the CERTs Website for easy access at www.certs.hhs.gov/partners/paths/regis. Organizations, public and private, interested in participating in research that pursues the optimal use of therapeutics can add their information to the registry.

The second meeting of PATHs was held in March 2002 and the focus quickly turned to the challenges of communicating the latest evidence to physicians and patients alike.

Technology holds a lot of promise in streamlining the sharing of information. Electronic medical records, computer order entry systems for prescriptions, and other innovations can cut down on medication errors and duplications of effort. But a balance with protecting the patient's privacy must always be struck.

PATHs partners look towards government representatives and professional societies to help tackle this issue. Only the array of experts brought together by PATHs can address all sides of the matter. Scientists, policymakers, and care providers from all sectors can identify technological priorities and help set research agendas. The credibility of academic research lends PATHs-inspired projects the power of hard-worn evidence. Legislative leadership helps turn that evidence into policy.

PATHs met again during March 2003 to discuss how to proceed based on the research agenda arising from the Risk Series workshops.

Through the registry and the relationships created via the PATHs meetings, the advancement of rational and optimal therapeutic use is given even greater momentum.

PATHs Partners

We would like to thank the following organizations for participating in the PATHs program:

AcademyHealth

AdvancePCS

Agency for Healthcare Research and Quality

American Academy of Pediatrics

American Academy of Pharmaceutical Physicians

American Association of Health Plans

American College of Cardiology

American College of Clinical Pharmacology

American College of Clinical Pharmacy

American Health Quality Association

American Heart Association

American Medical Association

American Organization of Nurse Executives

American Pharmaceutical Association

American Society for Clinical Pharmacology and Therapeutics

American Society of Consultant Pharmacists Research & Education Foundation

American Society of Health-System Pharmacists

Arthritis Foundation

Association of American Medical Colleges

Centers for Disease Control and Prevention

Centers for Medicare & Medicaid Services

Coalition for Affordable Quality Healthcare

Department of Veterans Affairs

Eli Lilly & Company

Food and Drug Administration

Henry Ford Health System

Johnson & Johnson

Marshfield Medical Research and Education Foundation

Merck-Medco Managed Care

National Committee for Quality Assurance

National Consumers League

National Health Council

National Institutes of Health

National Patient Safety Foundation

National Pharmaceutical Council

National Quality Forum

Pharmaceutical Research and Manufacturers of America

Pfizer, Inc.

Policy Directions, Inc.

Rx Intelligence

Society for Women's Health Research

United States Pharmacopeial Convention, Inc. (USP)

Outreach

Another offshoot of CERTs is taking a more tightly focused approach to building collaborative partnerships.

As an adjunct to the PATHs meeting in March 2002, CERTs held its first "Government Day," a gathering of CERTs leaders and government representatives from a number of healthcare-related agencies.

Serving as a means to introduce the work and potential of CERTs to possible government collaborators, "An Opportunity to Maximize Interagency Collaboration" gave an in-depth look at the individual CERTs centers and their work, as well as how this research and education tie into the big picture of optimizing therapeutics use.

The CERTs showcase was followed by a roundtable in which all participants could brainstorm on potential collaborative projects between their respective agencies and the CERTs, particularly those that could best use the cumulative expertise and far-reaching goals of the program as a whole.

Projects like PATHs and this conference of government leaders highlight the long-term vision and constant focus on forward momentum of CERTs. One of the clearest lessons from the first three years of CERTs is that the power of collaboration is essential to unraveling the complexities of modern therapies.

The CERTs Organization

The CERTs program is administered by the AHRQ, in consultation with the FDA. Two bodies offer unique support to the CERTs on their quest to improve the nation's healthcare—the Coordinating Center and the Steering Committee.

The Coordinating Center at Duke University Medical Center provides overall CERTs support through strategic planning, program development and outreach. The Steering Committee offers scientific and operational guidance to the Coordinating Center and research centers.

The heart of CERTs success is its collaboration with a diverse host of partners. Establishing relationships with agencies and organizations that will provide valuable opportunities for improving the use of medical therapies through CERTs research is one of the most important roles for the Coordinating Center. For example, the wide range of views and expert opinions brought together for the Risk Series workshops demonstrates the ability of the Coordinating Center to concentrate the efforts of many partners on a single, critical mission.

Once research is underway, the Coordinating Center rolls up its sleeves and provides the infrastructure necessary for the most important aspect of any study—dissemination—in collaboration with AHRQ and other partners. Results are meaningless if no one learns of them and the Coordinating Center provides the information management and the communications expertise necessary to see hard-won evidence put into practice.

Simply putting results on the printed page is not enough, however. The Coordinating Center develops and manages outreach programs such as the PATHs. These ensure that not only are CERTs research findings reaching critical ears, but also that future CERTs projects will be responsive to national needs and continue to pursue a focused, effective research agenda.

Steering Committee

Hugh H. Tilson, MD, DrPH
(Chair)

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

M. Miles Braun, MD, MPH
U.S. Food and Drug Administration

Robert M. Califf, MD
Duke University Medical Center

William H. Campbell, PhD
University of North Carolina at Chapel Hill

Lisa C. Egbuonu-Davis, MD
Pfizer Pharmaceuticals Group

Linda F. Golodner
National Consumers League

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

Richard Platt, MD, MSc
HMO Research Network

Wayne A. Ray, PhD
Vanderbilt University Medical Center

Steering Committee *(continued)*

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

Marcel E. Salive, MD, MPH
National Institutes of Health

Brian L. Strom, MD, MPH
University of Pennsylvania

Karen Williams
National Pharmaceutical Council

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

Guiding all of this activity is the Steering Committee. The embodiment of the multi-sector, collaborative CERTs model, the Steering Committee is comprised by each center's principal investigator and by representatives of government agencies, as well as leaders in private industry and consumer advocacy. The blend of academia, government, the public, and business means the intellectual and strategic leadership of the Steering Committee is well rounded and on the cutting edge of emerging healthcare issues.

Together, the Coordinating Center and the Steering Committee both anchor and pilot the CERTs ship.

Administration

Agency for Healthcare Research and Quality, Rockville, MD
www.ahrq.gov

Program Coordination

Duke University Medical Center, Durham, NC www.certs.hhs.gov

Centers

Duke University Medical Center, Durham, NC
dcri.mc.duke.edu/research/fields/certs.html

HMO Research Network, Boston, MA

University of Alabama at Birmingham
www.uab.edu/certs

University of Arizona Health Sciences Center, Tucson
www.arizonacert.org; www.qtdrugs.org; www.drug-interactions.com; www.torsades.org

University of North Carolina at Chapel Hill
www.sph.unc.edu/health-outcomes/certs

University of Pennsylvania, Philadelphia
www.penncert.org

Vanderbilt University Medical Center, Nashville, TN

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