Centers for Education & Research on Therapeutics ™

Annual Report

Year 1

October 2000

Agency for Healthcare Research and Quality

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Contents

Letter from the Steering Committee

Dear Fellow Citizens:

Neither patients nor their caregivers should have to guess which therapies are the best, or live in fear that a mistake was made in treatment. This is the basis of the CERTs program.

The U.S. system of developing and marketing medical products has produced great benefits. This system requires that adequate, well-controlled studies show that products are safe and effective for their intended use.

The system has some drawbacks, however. For example, to meet the requirements for marketing approval, clinical studies of a new therapy may have a very narrow focus—testing it, say, only in male adults. Information often is lacking about how it may work in other groups.

Further, studies may not test medical products in combination with other therapies often used by the same patients, with occasionally fatal results.

Once approved, drugs and devices often are used for purposes other than those for which they were approved. Sometimes these uses are supported by studies, but not always. It is hard for caregivers and patients to find information about such uses, except through personal experience, which can be risky.

Finally, some side effects of medical products emerge only after they have been approved for sale, when large numbers of people begin to use them. The systems used to capture these events may not be as effective as they could be.

No wonder caregivers and patients in the real world are left with doubts about therapies.

The CERTs program fills several gaps. It aims to answer important questions that have not been addressed. It provides its results, positive or negative, for all to see. It sets out to develop a learning curriculum for current and future caregivers. Finally, it represents a major step toward giving people the information they need to make the best choices possible.

The participants in CERTs—government agencies, academic organizations, managed-care organizations, drug and device companies, practitioners, commercial research groups, and consumer groups, among others—have voluntarily committed to seeking answers together, putting society's interests first.

People of all ages deserve the benefits of the CERTs program. We are committed to establishing a national network of centers that will investigate and educate. We hope that this collaboration will improve health for us all.

—Hugh Tilson, MD, DrPH (chair); Lynn Bosco, MD, MPH; Robert M. Califf, MD; William H. Campbell, PhD; Lisa Egbuonu-Davis, MD; Linda Golodner; Peter Honig, MD, MPH; Judith M. Kramer, MD, MS; Richard Platt, MD, MSc; Wayne A. Ray, PhD; Kenneth G. Saag, MD, MSc; Marcel Salive, MD, MPH; Brian L. Strom, MD, MPH; Karen Williams; Raymond L. Woosley, MD, PhD

Introduction

People need objective, complete, accessible information about the best ways to use medical products, so that they can take action to improve health.

The Centers for Education & Research on Therapeutics (CERTs), administered by the Agency for Healthcare Research and Quality (AHRQ), aim to provide just such information.

> "The great aim of education is not knowledge but action."
>
> —*Herbert Spencer*

Although drugs, medical devices, and biological products improve health for thousands of people, side effects, misuse, and overuse of products seriously impair the health of many others. In addition, many who could benefit from a therapy do not receive it, through lack of information, oversight, or in the mistaken belief that it will do them harm.

We need more guidance about to how to choose and use products most appropriately, how to prevent errors and adverse effects, and how to use products in a cost-effective way.

Drug and device companies, medical education programs, professional groups, and medical journals provide some information, but it may have a narrow focus, may be slanted, and may not consider the risks and benefits of interactions with other therapies. Even when valuable information is available, it often does not get into the hands of the people who need it most.

We are conducting research and educating people about the best uses for drugs, medical devices, and biological products, in the public interest. Armed with knowledge from CERTs, people can take action to improve health.

This Annual Report for Year 1 both introduces the CERTs program and reviews its accomplishments to date. We have made much progress so far but recognize the tremendous challenges and opportunities still before us.

The CERTs Program

Origins

Since 1992, AHRQ, formerly the Agency for Health Care Policy and Research, has studied outcomes associated with prescribed drugs. Their Pharmaceutical Outcomes Program has addressed many important questions about the use of therapies, but critical issues remain.

To address these issues, Congress authorized a CERTs demonstration program in the Food and Drug Administration (FDA) Modernization Act of 1997 (Public Law 105-115). AHRQ, with its expertise, was chosen to administer the program.

In November 1998, AHRQ asked the community to nominate research topics. AHRQ then selected topics on the basis of several criteria:

1. High incidence overall or in subgroups such as minorities, women, or children
2. Significance to Federal health programs such as Medicare and Medicaid
3. High associated costs
4. Uncertain effectiveness of current therapies
5. Potential to improve decision making
6. Potential to reduce major variations in management, use, or outcomes of treatment
7. Available scientific data to support study of the topic
8. Potential for rapid implementation

The demonstration program began in September 1999, when AHRQ awarded $7.7 million over three years to support four research centers and a coordinating center. Congress authorized the permanent CERTs program in December in the Healthcare Research and Quality Act of 1999 (Public Law 106-129). A fifth center was added in July 2000, and two more in September 2000.

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, caregivers, government, academia, delivery systems, payers, purchasers, and manufacturers of medical products.

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

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

Education: Education of current and future caregivers, policy makers, and patients is critical to improving health.

Public Policy: Policy makers must be provided with the best available scientific evidence upon which to base policies.

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

Vision

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

THE SEVEN CENTERS

Duke University
Principal Investigator: Elizabeth R. DeLong, PhD; Therapies for disorders of the heart and blood vessels

Georgetown University
Principal Investigator: Raymond L. Woosley, MD, PhD; Drug interactions, particularly in women

HMO Research Network
Principal Investigator: Richard Platt, MD, MSc; Usefulness of HMOs for studying drug use, safety, and effectiveness

University of Alabama at Birmingham
Principal Investigator: Kenneth G. Saag, MD, MSc; Therapies for disorders of the joints and bones

University of North Carolina at Chapel Hill
Principal Investigator: William H. Campbell, PhD; Therapies for children

University of Pennsylvania
Principal Investigator: Brian L. Strom, MD, MPH; Therapies for infection

Vanderbilt University
Principal Investigator: Wayne A. Ray, PhD; Prescription drug use in a Medicaid population

Carrying Out the Mission

We achieve our mission through activities that:

…*develop knowledge* about therapies and how best to use them;

…*manage risk* by improving the ability to measure both beneficial and harmful effects of therapies as used in practice;

…*improve practice* by advancing strategies to ensure that therapies are used always and only when they should be; and

…*inform policies* by describing the state of clinical science and effects of current and proposed policies.

Structure and Administration

Within the U.S. Department of Health and Human Services, AHRQ is the lead agency supporting research into how to make health care better, more cost-effective, and more accessible. It sponsors and conducts research about outcomes, quality, cost, use, and accessibility of health care.

AHRQ's Center for Outcomes and Effectiveness Research, consulting with the FDA, oversees the CERTs program and provides technical assistance and research support to the centers.

There is a Steering Committee composed of a chairperson; the CERTs principal investigators; representatives from AHRQ, the FDA, and the National Institutes of Health (NIH); and three at-large members.

Representatives from all centers have formed work groups to address broader issues related to the CERTs effort, such as quality of care and the use of databases in research.

Duke University coordinates CERTs activities among the seven centers, each of which focuses on therapies for one group or disease area (see sidebar).

Year 1 Progress

We have organized our efforts around four themes, which guide the interactions of the entire program.

Developing Knowledge

We are developing knowledge about therapies and how best to use them. Our research examines both basic mechanisms (through clinical pharmacology and genomics research) and medical outcomes.

CHILDREN AND ADOLESCENTS

More than 80% of the prescription drugs given to children have not been tested in children and are not labeled for pediatric use. But children are not "small adults." They have different metabolic rates, their bodies are changing rapidly, and their ability to understand and express information varies widely. For these reasons, assessment of therapeutics in children is critical.

We have two projects assessing how drugs move and work in the bodies of children and adolescents, one examining children with **cystic fibrosis**, and another assessing the levels of drugs called protease inhibitors in the blood of children with human immunodeficiency virus (**HIV**) infection. The goal is to identify how children's bodies handle drugs differently from adults', which may result in more tailored (and thus more effective) treatment.

Drugs to treat attention deficit/hyperactivity disorder (**ADHD**) and **depression** in children have been used more and more in recent years, despite a lack of supporting evidence for their safety and long-term effectiveness. During Year 1, we assessed how the use of these drugs has changed among doctors and patients, in preparation for more detailed future studies.

The incidence of **Type 2 diabetes** in adolescents may be increasing because of lifestyle changes. We are gathering the data needed to determine whether this is true. The earlier this disease is diagnosed, the sooner treatment can begin.

ADULTS

Heart disease has been the number-one killer of adults in the U.S. for all but one of the last 100 years. Although **aspirin** can save lives in people who have coronary artery disease (CAD), a very common form of heart disease, only about half of them take aspirin regularly. We have examined the use of aspirin in this group, tapping into the resources of a 30-year-old database for cardiovascular disease. We have found that 87% of the people in the database have been taking aspirin. This is better than average but still shows room for improvement, especially among women.

We have used similar methods to examine the use of **beta-blocking** drugs in people who have congestive heart failure (CHF). Compared with aspirin, beta-blockers cost more; they also require a prescription and, until recently, were thought to be harmful to people with CHF. Before beta-blockers can be widely used, then, educational efforts must overcome resistance based on outdated information. Only about 45% of the people with CHF in the database have been taking beta-blockers, and the rates of use for the individual drugs known to save lives have been extremely low.

More than 2 billion prescriptions are written in the U.S. every year, and two thirds of all visits to doctors result in at least one new prescription. Thus people likely are taking more than one drug at a time. **Interactions** between these drugs can be fatal. In fact, several drugs have been removed from the market because of fatal interactions in recent years. Further, most drugs used by adults have been studied only in men. How women process drugs taken alone or with other drugs is largely unknown.

Our initial efforts in addressing the issue of drug interactions includes studying drug usage and interaction patterns, to identify targets for further testing. This effort involves the use of large databases and collaborations with the FDA.

People over the age of 65 are the fastest-growing segment of the U.S. population, and the older a person gets, the greater the risk of having a heart attack. Several drugs can reduce the risk of death after a heart attack, chief among them **aspirin**, **beta-blockers**, and drugs to reduce **cholesterol**. These drugs might be greatly underused in men and women covered by managed-care plans such as Medicaid, which includes substantial numbers of elderly people.

We are studying the rates of use for these three types of drugs in a large Medicaid population, by physician and hospital, with the goal of identifying targets for future education, including policy makers.

Managing Risk

People must have an accurate picture of the benefits and risks associated with therapies as used in practice. Our focus is on improving the ability to detect beneficial and harmful effects of therapies, then maximizing the benefits and minimizing the risks. The systems that we are developing will provide the information needed to stimulate basic research into mechanisms of disease and the effects of therapies.

CHILDREN AND ADOLESCENTS

We know much more about the safety of drugs for adults than we do for children. We have begun a pilot study of a new reporting system for **adverse drug events in children**. For the larger issue of how many drug errors occur in children, we are studying another **reporting system, MedMARx**.

More than 20,000 children and teens in this country may be infected with **HIV**. How they respond to given doses of anti-HIV drugs such as protease inhibitors may differ from how adults respond. We are assessing the relation between the dose of protease inhibitors, the amount of drug in the bloodstream, measures of drug safety and effectiveness, and what may cause variations in the response to treatment.

Few **tools** exist to measure a child's health status and quality of life, which are an important part of the assessment of therapeutic effects. Existing tools typically are variations of those used in adults. We are grading and evaluating these tools, to tailor them to the needs of children. We also have proposed establishing a **common definition** or set of definitions for adverse medical events, to allow them to be measured consistently across studies.

ADULTS

Many drugs used to correct an irregular heartbeat carry an increased risk of death, especially many of the older drugs, but they continue to be prescribed in large numbers despite this risk. A newer agent for

> "To believe with certainty we must begin by doubting."
>
> —*King Stanislas I of Poland*

treatment of atrial fibrillation or flutter, **dofetilide**, appears not to increase mortality, but its use can carry an increased risk of other abnormal heart rhythms. The FDA therefore requires that doctors complete a risk-management program before using the drug.

Many prescribers may be unaware of the evidence or how to monitor therapy properly. We are now tracking the use of dofetilide at one center, before examining compliance with the FDA's rigorous requirements for education and monitoring with dofetilide use.

For our **drug-interactions** project, we will be testing potential interactions in the laboratory. When this is complete, we will begin verifying their relevance with studies in humans.

We are harnessing the power of the Internet to aid in our efforts to manage risk. For example, we have been working with MedWatch scientists at the FDA to analyze cases of a potentially fatal, irregular heart rhythm (**torsades de pointes**). People can develop torsades de pointes because of an inherited gene, but they also can develop it after taking certain drugs, and women are more susceptible than men.

We have created a Web-based registry (www.qtdrugs.org) for physicians to report cases of torsades de pointes that are caused by drugs. The program will help identify individual drugs, drug interactions, and genetic mutations associated with this disorder.

Devices used in the treatment of heart disease generally undergo even less study than drugs, especially after the devices have been approved for use. We are working with the FDA, device manufacturers, and professional societies to develop models for learning more about cardiovascular devices. One model is to use existing databases.

We are working on a program to monitor outcomes of transmyocardial laser revascularization (**TMR**), a new device used to bring more blood to the heart muscle. In this case, the Society for Thoracic Surgeons (STS) holds the database. This project is partly funded by the Women's Health Initiative and includes partners from the FDA's Center for Devices and Radiological Health (CDRH) and the STS.

The elderly take an average of 16 prescription drugs each year and three to four of them at any given time. The likelihood that one is a

drug that combats an inflammatory condition, such as arthritis, is high. Traditional anti-inflammatory drugs (but not steroids) carry increased risks of bleeding and ulcers in the gut, especially in older people. Newer agents, such as the cyclo-oxygenase **(COX)-2 inhibitors**, are presumed to cause less bleeding and fewer ulcers than the older drugs while being just as effective, but they also are much more expensive than over-the-counter drugs such as ibuprofen.

We are comparing the rates of ulcers among elderly men and women taking these new agents, those taking another anti-inflammatory drug, and people taking no such drug. We also are measuring the costs associated with disorders of the gut in these same three groups.

Improving Practice

We aim to improve practice by educating people about the best ways to use therapies and aiding them in their efforts to translate such knowledge into action. Through research and demonstration projects, we are learning the best ways to achieve these aims.

CHILDREN AND ADOLESCENTS

The prevalence of **asthma** increased by 38% from 1982 to 1996 in those under age 18, and even more among black children and teens. With several partners, we aim to bring to local physicians and their patients the tools they need for the best management of asthma.

We are offering a **Summer Institute**, *Using the Evidence on Therapeutics to Enhance Quality of Care*, that introduces pediatric caregivers to the process of evaluating the quality of evidence in the literature and provides practical ways to use evidence and decision-making tools in their practices. Our Web site also provides information for patients and caregivers.

ADULTS

About 1 million Americans at any given time are taking drugs called **glucocorticoids**. These drugs treat inflammatory conditions such as rheumatoid arthritis, asthma, and certain bowel disorders. Although helpful, glucocorticoids also can cause bone loss leading to osteoporosis. In fact, glucocorticoid use is the second-commonest cause of osteoporosis, after menopause.

Osteoporosis caused by glucocorticoid drugs is being underrecognized and undertreated among adults taking these drugs. We are planning an intervention to aid in prevention and treatment of this disorder.

A Web site (georgetowncert.org) is providing information for patients, pharmacists, and physicians about **drug interactions** and prescription-drug use. Other sites offer tools to aid in prescribing. We also will be developing comprehensive educational programs for patients and caregivers about known interactions.

We have conducted a **national survey** of physicians in training, to identify the needs of such training programs in educating future caregivers on the prevention of drug errors. We already have identified an educational target: how to prevent adverse drug effects.

Informing Policies

We aim to provide policy makers with the information needed to make informed choices, by describing the scientific underpinnings for possible policies designed to improve the use of therapies. For example, Investigator Dr. Lucy Savitz testified about the CERTs program in September at the National Summit on Medical Errors and Patient Safety Research, organized by AHRQ.

CHILDREN AND ADOLESCENTS

Unlike drugs, devices, and biological products, the clinical effects of policy changes typically don't undergo prospective evaluation. Our project in a **Medicaid** population will assess the effects of losing insurance coverage on clinical outcomes in children with asthma.

We have published a preliminary CERTs study that shows a link between a lack of vitamin D supplementation and the development of **rickets** in breast-fed children, especially among black infants. As a result of this study, the North Carolina Department of Health and Human Services has begun making vitamin D available free to breast-feeding women throughout the state.

ADULTS

We are examining the effects of **two policy changes** on clinical outcomes in a large Medicaid population:

- Changing quickly to a different third-party administrator for mental-health coverage
- Differences in the drugs approved for use among managed-care organizations

Program-wide Activities

To carry out our activities as a cohesive entity, CERTs has developed working groups to enhance communication and scientific efficiency:

- The *Public-Private Partnership Work Group* reviews potential partnerships for compliance with CERTs' principles for collaboration (see page 23).
- The *Database Work Group* provides a forum for sharing knowledge about databases and for discussing joint database research efforts.
- The *Publications Work Group* provides a forum for collaborative review of all CERTs-related publications.
- The *Quality Work Group* provides a forum for identifying methods for best practice and dissemination activities.

We are linked to the public through a Web site (www.certs.hhs.gov), hosted by AHRQ and maintained by the CERTs Coordinating Center to provide information about our mission and progress.

We have detailed our common vision and integrated approach in a manuscript, "A Call To Arms," submitted to a peer-reviewed medical journal.

Year 2 and Beyond

In Year 2, we will capitalize on the groundwork laid in Year 1 to continue our work around the program's themes.

Developing Knowledge

We will improve knowledge by completing the demonstration projects at individual research centers and developing synergy among centers.

CHILDREN AND ADOLESCENTS

We will continue our effort to understand the relation between **rickets** and breast-feeding, by monitoring how many breast-feeding women are getting vitamin D, tracking new cases of rickets, and repeating our survey of doctors' recommendations about vitamin use to their patients.

Another project will assess the usefulness of a large health-maintenance organization (HMO) database for studying the safety of and reasons for **antibiotic** use in children. This will allow us to identify targets to improve prescribing, to ensure that children receive antibiotics when needed but avoid the unnecessary prescribing that gives rise to antibiotic resistance.

ADULTS

Although the 87% rate of **aspirin** use in people with heart disease is encouraging, we intend to survey the remaining men and women to find out why they were not taking aspirin. Depending upon the results, we will design an intervention to increase the use of aspirin or similar drugs whenever possible.

A similar survey in the **beta-blocker** project is identifying the specific drugs and doses being used, if any, or the reasons for not taking these drugs. We will determine physician awareness, understanding, agreement, and adoption of the beta-blocker recommendations. We also will try to identify barriers to the use of beta-blockers in medical practice, and develop an intervention to improve the rate of use.

We will continue our work to identify drugs that prolong the QT interval and cause **torsades de pointes**, and to identify related risk factors for this complication.

For the **dofetilide** project, we will examine nationwide prescribing patterns for all antiarrhythmic drugs, including dofetilide. We hope to identify trends in use by practitioner characteristics. We also will evaluate compliance with the FDA-required risk-management program for dofetilide use.

> "First weigh the considerations, then take the risks."
>
> —*Helmuth von Moltke*

We will survey caregivers and administrators to assess their perceptions, understanding, and acceptance of the risk-management program. We will obtain a time-cost estimate to implement this program. We also will evaluate inpatient-prescribing patterns of all antiarrhythmic drugs at one hospital.

The last component of the dofetilide project will be a nationwide survey of physicians and nurses, to assess their understanding about the risks of using drugs, including dofetilide, that prolong the QT interval on the electrocardiogram. With all of this information, we hope to develop a nationwide continuing medical education program to improve understanding and minimize the risk with the use of these agents. A manuscript also is planned on the differences in the approval and marketing of two antiarrhythmic drugs for atrial fibrillation.

Almost 16 million people in the U.S. have **diabetes**, and the costs of treatment range up to $98 billion each year. Most people with diabetes do not require insulin injections but rather take drugs by mouth to control their disease. We will assess the usefulness of a large HMO database for studying the safety and effectiveness of oral drugs for diabetes.

An estimated 4.6 million Americans have **heart failure**, and this number is increasing each year. The death rate from heart failure at 5 years is 50%, and Medicare paid $3.6 billion in heart failure costs in 1996. We will assess the usefulness of a large HMO database for studying the safety and effectiveness of drugs to treat heart failure.

Managing Risk

We will work to assess the effects, maximize the benefits, and minimize the harm of therapies by working jointly among the research centers, AHRQ, and the FDA. We will evaluate the use of a range of approved medical products, including therapeutic devices, nonsteroidal anti-inflammatory drugs, and systems to report adverse events in children.

CHILDREN AND ADOLESCENTS

We will be analyzing data available from our Year 1 project on a **new reporting system** for adverse drug events and releasing the results as soon as possible.

We will continue our efforts to improve the care of children and teens with **asthma**. A new project in a Medicaid population will test different interventions designed to increase the appropriate use of corticosteroids in asthma.

Children with **cystic fibrosis** are susceptible to decreases in bone mass and outright loss of bone tissue. Late in 2001, we will begin to assess the effects on the bones of replacing vitamin D and calcium in children and adolescents with cystic fibrosis.

ADULTS

For the **TMR** project, we hope to develop a surveillance mechanism that manufacturers of cardiovascular devices easily could use to fulfill their regulatory requirements.

We will host a conference with representatives from academia, the FDA, the device industry, and professional societies. The goal is to develop more efficient models for studying approved cardiovascular devices. In conjunction, we will submit a “white paper” that describes current ways to monitor approved devices and proposes a model to address the limitations of these methods.

The increasingly high cost of therapy is a problem for many areas of disease. This is especially true for **rheumatoid arthritis**, where new biological agents have been shown to be very effective but also carry heavy costs. We will compare these newer treatments with traditional drug regimens.

Ever since antibiotics emerged in the 1940s, we have encountered the problem of **resistant germs**. Some bacteria and viruses are sensitive to almost all antimicrobial drugs; others are resistant to several drugs. The latter problem threatens our ability to treat many common community- and hospital-acquired infections.

These observations highlight a unique aspect of antimicrobial drugs—their misuse threatens not only individuals but also society as a whole. How to reduce antibiotic resistance is the subject of five projects that will begin in Year 2.

The first project will examine ways to reduce the use of antibiotics for **acute bronchitis** in outpatients. Another will assess how the drugs **approved for use** at different hospitals may affect the rate of antibiotic resistance for two types of bacteria. A third project will assess the effects of **tetracycline** on patterns of antibiotic resistance in people with acne. Fourth, we will study the use of a large, general-practice database in measuring the patterns of antibiotic use that place people at risk for **pneumonia** caused by drug-resistant bacteria.

The fifth project will explore the greater use of **meta-analysis**, a way to combine the results from different studies, in measuring rare side effects of antibiotics.

Results from different studies often are combined to overcome two possible problems of single studies: smaller populations, which can have a rate of rare events too low to measure accurately; and systematic bias, which can mask the true effect of therapy. The problem is that the most convenient mathematical methods for such analyses can produce results not easily applied to clinical situations.

We will develop statistical approaches to estimate risk that people can readily use to evaluate therapies, for overall populations and for subgroups by sex, age, and race.

Improving Practice

We will collaborate to produce reports on effective methods of changing practice. We will share knowledge gained from demonstration projects aimed at both increasing the use of beneficial therapies and reducing the use of harmful ones.

CHILDREN AND ADOLESCENTS

The **ADHD** project, once the data are complete, will be providing a standard "toolkit" to caregivers. The hope is that use of the materials will improve the diagnosis and treatment of the disorder.

We should have substantial data compiled on the incidence of **Type 2 diabetes** in adolescents during Year 2. If, as we suspect, this disease is more common in this group than has been realized, we can begin to develop better ways to screen for it.

Another project, on **ear infections**, will involve collaboration with a Medicaid organization. We will assess outcomes by choice of drugs prescribed, send personalized information to the physicians, and assess whether this intervention can improve prescribing and reduce costs for this condition.

The NC **Immunization Registry**, set to begin in May 2001, aims to improve the ability of primary-care doctors to monitor children's immunization schedules. We will be working with the state Department of Public Health to achieve this goal.

Because drugs typically have not been tested in children, pediatricians may not be familiar with how to **participate in clinical trials**. We will conduct seminars in pediatric clinical trials, provide pediatric pharmacology fellowships, and perform public outreach.

The results of a collaboration with Research Triangle Institute, on **evidence-based tools** to assess the health status of children, also will be disseminated.

ADULTS

We will release a patient education brochure and video on the use of **beta-blockers in CHF**. Other interventions could include education through an Internet-based technology (Medical CyberSessions™), a training session for nurses to start community-based support groups, and brochures for caregivers on the use of beta-blockers. We will give physicians feedback on their rates of beta-blocker use before and after intervention, and a toll-free Helpline will be available for questions.

The methods used in the **aspirin** and **beta-blocker** projects (using a database to obtain use rates of drugs) may be applied to study of other therapies, such as drugs to lower cholesterol in people with

CAD. After we develop and apply the beta-blocker intervention, we could tailor similar interventions to improve the use of other life-saving drugs. We also may study which components of interventions work best for specific types of therapies, physicians, or medical practices. This would be critical for tailored, cost-effective future interventions.

Based on the data gathered from the glucocorticoid project, we will begin to design programs to improve the identification and treatment of **osteoporosis** caused by these drugs. A collaboration of two CERTs centers will look at preventing fractures due to postmenopausal osteoporosis in people at risk.

For our studies of **drug interactions**, the goal for Year 2 is to develop targeted educational programs to reduce interactions in specific groups. We will select groups according to the potential for a drug interaction and by screening a large insurance database. We will expand upon our prototype approach, a Web-based international registry for cases of drug-induced torsades de pointes.

We will address the training needs of future caregivers by developing a **curriculum** for preventing drug errors, which will be made available to training programs. We also will evaluate curricula for therapies in women, a group often neglected in clinical research and medical education.

We should have substantial data by Year 2 on the use of **aspirin**, **beta-blockers**, and drugs to reduce **cholesterol** in a large Medicaid population. With this information, we aim to identify targets for education, including caregivers, patients, insurers, and policy makers.

We also should have data available from the **COX-2** inhibitors project. Once analyzed, we will begin to release the information to the public.

Informing Policies

We will work with governmental agencies to inform policy makers about issues involving the use of therapeutic products as they arise.

Conclusion

In November 1999, just after the CERTs demonstration program began, the Institute of Medicine reported that drug errors alone kill up to 7000 Americans each year—more than are killed by workplace injuries. Thousands more are inconvenienced, harmed, or disabled by errors in therapies, whether drugs or other products. Clearly the time has come for CERTs.

For the first time, the public and private sectors have come together to address critical questions about the way medical products are and should be used in the U.S. By continuing to have a broad pool of collaborators and support, we can persevere in our effort to answer questions so important to society.

Partners in CERTs, whether government agencies, academic groups, practitioners, drug and device companies, commercial research groups, or consumer representatives, are committed to seeking answers together, putting society's interests first. This makes CERTs unique.

Already, the knowledge gained from CERTs has been translated into action that will improve health—the bottom line for us. Hundreds of breast-fed infants in one state now receive free vitamin D supplements, because of a CERTs pilot study. Parents of these infants, and soon perhaps of infants in all states, will have one less thing to lose sleep over: rickets.

We have started to answer important questions, but much work remains. We are excited to be a part of this program and look forward to making a difference in all the years to come.

—The CERTs Group

CERTs

Developing knowledge
Managing risk
Improving practice
Informing policies

The CERTs Organization

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Public-Private Partnerships

PRINCIPLES

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

Public-Private Partnership. CERTs is a public-private partnership. Centers should seek useful, appropriate relations 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 likely exist in any public-private partnership and cannot be completely avoided or eliminated. The obligation is to disclose fully and manage potential conflicts in a way that both minimizes the risk of those conflicts and maximizes progress to achieve CERTs' goals.

Academic Integrity. Persons conducting projects under the CERTs umbrella will make decisions about study design, analysis, conclusions, and publication and will ensure that the work complies with their local institutions' conflict-of-interest rules.

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

PARTNERS
(through August 2000)

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AdvancePCS

Aetna U.S. Healthcare

American Association of Colleges of Pharmacy

American Pharmaceutical Association

American College of Cardiology

AstraZeneca L.P.

Aventis Pharma

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U.S. Quality Algorithms

United States Pharmacopeial Convention, Inc.

UnitedHealth Group

University of Illinois Chicago College of Pharmacy

Wyeth-Ayerst Laboratories

CERTs Projects

Project Description	Year Begun	Status	Center
NC asthma improvement project	1	Complete	UNC
Drug metabolism in children with and without cystic fibrosis	1	Complete	UNC
Tailored implementation strategy for pediatric therapeutic guidelines	1	Complete	UNC
Evidence-based tools to assess pediatric population	1	Ongoing	UNC
Efficacy, safety, and pharmacokinetics of drugs in pediatric HIV	1	Ongoing	UNC
Prevalence of Type 2 diabetes in childhood	1	Ongoing	UNC
Prescribing patterns of psychotropic drugs for adolescents	1	Ongoing	UNC
Fellowships and education programs: pediatric pharmacology, pediatric clinical trials, and public outreach	1	Ongoing	UNC
CERTs Summer Institute: *Using the Evidence on Therapeutics to Enhance Quality of Care*	1	Ongoing	UNC
MedMARx monitoring and surveillance project	1	Ongoing	UNC
Aspirin use and nonuse in cardiovascular disease	1	Ongoing	Duke
Beta-blocker use in heart failure	1	Ongoing	Duke
Dofetilide in atrial fibrillation	1	Ongoing	Duke
Transmyocardial laser revascularization devices	1	Ongoing	Duke
Identification of, testing of, and education about drug interactions, especially in women	1	Ongoing	Georgetown
International registry for drug-induced arrhythmias	1	Ongoing	Georgetown
National medication-errors survey of third-year medical students, internal medicine clerkship, and residency programs	1	Ongoing	Georgetown

Project Description	Year Begun	Status	Center
Postmarketing/pharmacoeconomic study of cyclooxygenase (COX)-2 anti-inflammatory drugs in Medicaid population	1	Ongoing	Vanderbilt
Study of policy changes as they relate to quality of pharmacotherapy in Medicaid population: loss of coverage in pediatric asthma, change in third-party mental-health carrier, differences in drug formularies	1	Ongoing	Vanderbilt
Effects of separate mental-health coverage on compliance in schizophrenia	1	Ongoing	Vanderbilt
Use of beta-blocker, aspirin, and lipid-lowering therapy after heart attack	1	Ongoing	Vanderbilt
Long-term safety and toxicity monitoring of nonsteroidal anti-inflammatory drugs	1	Ongoing	UAB
Attention deficit/hyperactivity disorder (ADHD) project	2	Ongoing	UNC
Pediatric adverse drug event and reaction reporting program	2	Ongoing	UNC
Skeletal effects of oral replacement of vitamin D and calcium in adolescents with cystic fibrosis	2	Ongoing	UNC
Prevalence of vitamin D-deficient rickets in minority infants	2	Ongoing	UNC
Optimizing prescribing and treatment for otitis media	2	Planned	UNC
Usefulness of large HMO databases in studying oral drugs for diabetes	2	Planned	HMO Research
Effect of provider profiling on management of glucocorticoid-induced osteoporosis (GIOP)	2	Planned	UAB
Selecting cost-effective treatments for rheumatoid arthritis	2	Planned	UAB
Increasing adherence to drugs to prevent osteoporosis	2	Planned	UAB
Secondary prevention of fractures due to osteoporosis	2	Planned	Duke/UAB
Reducing the use of antibiotics for acute bronchitis in outpatients	2	Planned	Penn
Effect of formulary changes on the resistance patterns of *E. coli* and *Klebsiella*	2	Planned	Penn

Project Description	Year Begun	Status	Center
Use of tetracycline for acne in an outpatient clinic: effects on antibiotic resistance patterns	2	Planned	Penn
Using a large database to study the epidemiology of resistant *Pneumococcus* pneumonia	2	Planned	Penn
Expanding the use of meta-analysis to study rare side effects of antibiotics	2	Planned	Penn
Usefulness of large HMO database for studying the safety and efficacy of antibiotics in children	2	Planned	HMO Research
Usefulness of a large HMO database for studying the safety and efficacy of drugs to prevent heart failure	2	Planned	HMO Research
NC immunization registry	3	Planned	UNC

Peer-reviewed CERTs Publications

Campbell W, Sleath B. Encyclopedia of Clinical Pharmacy. Washington, DC: Agency for Healthcare Research and Quality (in press).

Meredith S, Feldman P, Frey D, Hall K, Arnold K, Brown NJ, Ray WA. Possible medication errors in home health care patients. J Am Geriatr Soc (in press).

Merlino L, Bagchi I, Taylor T, Utrie P, Chrischilles E, Mudano A, Saag K. Preferences for fractures and other glucocorticoid-associated adverse effects among rheumatoid arthritis patients. Med Decis Making (in press).

Mudano A, Casebeer L, Burst N, Carillo A, Gilbert D, Seay K, Saag K. Racial variation in use of hormone replacement therapy (HRT) and osteoporosis prevention in a large managed care population. Arthritis Rheum 2000;43:S282.

Sleath B, Rubin R, Campbell W, Gwyther L, Clark T. Physician-patient communication about OTC medications. Soc Sci Med (in press).

Smalley WS, Shatin D, Wysowski DK, Gurwitz J, Andrade SE, Goodman M, Chan KA, Platt R, Schech SD, Ray WA. Contraindicated use of cisapride: the impact of an FDA regulatory action. JAMA (in press).