AHRQ's mission is to improve the quality, safety, efficiency, and effectiveness of health care by:

- Using evidence to improve health care.
- Improving health care outcomes through research.
- Transforming research into practice.

**Background**

The mission of the Centers for Education and Research on Therapeutics (CERTs) is to conduct research and provide education that will advance the best use of therapeutics (drugs, medical devices, and biological products). The CERTs seek to increase awareness of the benefits and risks of new, existing, and combined uses of therapeutics, thereby improving the effectiveness and safety of their use.

The program is administered as a cooperative agreement by the Agency for Healthcare Research and Quality (AHRQ), in consultation with the U.S. Food and Drug Administration (FDA). The CERTs receive funds from both public and private sources, with AHRQ providing core financial support. The CERTs network currently comprises 11 research centers (see box, next page), a Coordinating Center, a Steering Committee, and numerous partnerships with public and private organizations. Collectively, the CERTs have more than 40 unique data sources and serve as a national resource of experienced researchers.

All CERTs seek to advance knowledge; inform health care providers, patients, and policymakers about that knowledge; and improve aspects of the health care system related to therapeutics. Since the inception of the CERTs program in September 1999, the centers have developed a portfolio of over 200 completed and ongoing studies with results that have addressed the safe and effective use of therapeutics. Many projects focus on education. Audiences include patients, providers, and policymakers. The following CERTs projects exemplify these educational efforts.

**Improving Clinician Training in Therapeutics**

**Curriculum in Clinical Pharmacology**

Each year, adverse drug events cause numerous injuries and a significant number of deaths. Educating providers, including medical students and residents, in clinical pharmacology can help prevent adverse events by improving understanding of how drugs work and how they should be used. The University of Arizona center
conducted a survey of internal medicine clerkship and residency programs around the country to assess the amount of time invested in clinical pharmacology curriculum at the schools. Their survey found that while most institutions allotted time for clinical pharmacology training in their curricula, there was a great desire for additional training. Based on this survey, the Arizona center developed a new core curriculum in clinical pharmacology for fourth-year medical students. The course was conducted at Georgetown University. It addressed seven major objectives related to medication prescribing, including evaluation of medications, identification of medications and alternative therapies used by patients, effective pain management, recognition and reporting of adverse drug reactions, and recognition and treatment of substance abuse and poisoning. Two hundred medical students participated in the course each time it was offered. The course’s effect was measured using medical student ratings provided in a medical school graduation questionnaire. According to student ratings, instruction improved in the areas of clinical pharmacology, pain management, and managed care when the course was offered. Currently, there are plans to adapt the curriculum for use in health education interventions.

Curriculum in Women’s Health

There is a lack of information about therapeutics used by women. To address this information gap, the Arizona center developed a curriculum for therapeutics in women’s health. The curriculum was designed for pharmacy students and is available on the American Association of Colleges of Pharmacy Web site, www.aacp.org.

Training Programs

Pharmacoepidemiology fellowship. Pharmacoepidemiology is the study of the effects of drugs in large numbers of people. The University of Pennsylvania center has developed an ongoing training program in clinical pharmacoepidemiology to help health practitioners develop skills in this field. Thus far, 11 fellows have received partial support provided by the CERTs for training in pharmacoepidemiology. Most have earned master of science in clinical epidemiology degrees. Graduates of the fellowship program have continued their work as pharmacoepidemiologists in various academic positions.

Clinical research fellowship. The Duke University center conducts a fellowship training program in cardiovascular medicine. In conjunction with the Duke Clinical Research Institute (DCRI), the cardiovascular fellowship program provides a well-rounded program for fellows interested in clinical research. Fellows are recruited on an annual basis. Between July 2004 and July 2005, nine cardiovascular fellows received clinical research training at the DCRI. For additional formal training, these fellows can enroll in the Duke University master of science in clinical research program. This training provides cardiovascular fellows with the necessary education to undertake careers in clinical research related to diseases including heart failure, stroke, heart attack, atherosclerosis, and other serious heart- and blood-vessel-related illnesses.
Courses on Antimicrobial-Resistant Pathogens and Emerging Infectious Diseases

Antibiotic-resistant bacterial infections and emerging infectious diseases are two complex issues in modern health care. As bacteria become resistant to antibiotics, previously treatable infections can become life threatening and death from antimicrobial-resistant infections may result. Additionally, emerging diseases can cause serious illness. They are poorly understood and no standard treatments exist to combat them.

In order to train clinicians and public health professionals in the management of these serious health threats, the University of Pennsylvania center, in conjunction with the Department of Health of the Commonwealth of Pennsylvania, taught courses on antimicrobial-resistant pathogens and emerging infectious diseases. Eight courses were presented in 2005 at the semiannual Pennsylvania Public Health Institute. The University of Pennsylvania center also posted the curriculum materials to a secure Web-based management learning system maintained by the Pennsylvania Department of Health so that they can be used in training additional clinicians and public health officials.

Community-associated methicillin-resistant Staphylococcus Aureus.

Methicillin-resistant Staphylococcus Aureus (M RSA), a form of antibiotic-resistant bacteria, can cause serious infections, typically in hospitals. Recently, a nonhospital community-associated M RSA (CA-M RSA) emerged that can cause serious skin infections. Community-based prevention and treatment of CA-M RSA have become widespread public health concerns.

To educate those who may encounter people with CA-M RSA infections, the University of Pennsylvania center taught two courses in 2005 that were attended by 120 professionals, including sports medicine physicians, pediatricians, school nurses, public health officials, college and high school athletic directors, coaches, and correctional officers. The courses discussed both sporadic cases and outbreaks of CA-M RSA among prison inmates, previously healthy children, and competitive sports participants. They also covered the treatment of M RSA infections of the skin and soft tissue. The Fall 2005 course received coverage by the television and print media in Pennsylvania.

Emerging infectious diseases. Both understanding how various infections arise and staying abreast of emerging diseases are critical to managing emerging diseases and antimicrobial-resistant infections. The University of Pennsylvania center, in conjunction with the Department of Health of the Commonwealth of Pennsylvania, conducted a course, “Modern Plagues,” at the Pennsylvania Public Health Institute. Fifty professionals, including physicians, community health nurses, and laboratorians, attended. The course covered factors associated with the emergence of infectious diseases, antimicrobial resistance of food-borne pathogens of animal origin, and hospital-associated antimicrobial-resistant infections. It also introduced factors that can lead to the emergence of a new disease and discussed the emergence of health-care-associated antibiotic-resistant pathogens, especially those resistant to the fluoroquinolone class of antibiotics.
Web-based course on antibiotic resistance. The University of North Carolina center is developing a Web-based course about antibiotic resistance for residents, house staff, and primary care physicians. The course provides information about community-acquired antibiotic resistance and antibiotic-resistant infections. It emphasizes community-acquired antibiotic resistance in children.

Modifying Provider Behavior To Improve Patient Care

Decision Support for Physician Prescribing

Poor prescribing practices are often a cause of adverse drug events. Patients may receive prescriptions for products that interact with each other or that are not appropriate because of risk factors such as age. The HMO Research Network center took advantage of a natural experiment and also designed decision-support modules to test whether custom, computerized electronic medical record (EMR) alerts reduced inappropriate use.

Diminished kidney function and other physiologic changes that come with age may cause older people to respond differently to medications. The lessening of kidney function slows the metabolism of some drugs, leading to possibly harmful blood levels. To reduce potentially harmful prescribing, a health plan created a drug-specific computerized alert for two drugs—tricyclic antidepressants and long-acting benzodiazepines—which was implemented in 15 physician practices. The analysis of this natural experiment showed that alerts to prevent prescribing of the two drugs in the elderly were quite effective, resulting in an immediate 22-percent reduction in the rate of use of the medications.

Subsequent work by the HMO Research Network center created custom alerts that were patient specific to reduce clinician “alert burden.” Although the number of alerts was reduced by about 75 percent, the desired lower level of prescribing was maintained.

Another EMR alert intervention addressed the coprescribing of the blood-thinning drug warfarin with any of five classes of medications known to interact with it. Before the intervention, almost one-third of patients on warfarin had a drug interaction event each month. Twelve months after implementation of the computerized alerts, these drug interactions had decreased by 14.9 percent. Computerized decision support may prove to be a useful tool for physicians.

The intervention improved little with the addition of face-to-face group sessions (group detailing) with prescribers.

Vitamin D Supplementation

Vitamin D is crucial for childhood development. A deficiency of vitamin D causes rickets, a serious condition that can cause skeletal abnormalities and failure to thrive. Vitamin D supplementation prevents rickets. Breastfed infants may require supplementation, as breast milk can contain an inadequate amount of vitamin D. In recent years, rickets caused by vitamin D deficiency has been on the rise in infants and toddlers in the United States. Despite this increase, a study conducted by the University of North Carolina (UNC) center found that 44.5 percent of physicians did not recommend vitamins for any infants. Using the UNC center’s work as well as other research, the American Academy of Pediatrics (AAP)
developed new guidelines for physicians in 2003 recommending vitamin D supplementation for all breastfed infants. To assess the effect of these guidelines on physician behavior, researchers at the UNC center sent a survey to a nationwide sample of members of the AAP and the American Academy of Family Physicians, with half of the sample receiving an information sheet outlining the new recommendations. Forty-two percent of the recipients responded to the survey. The UNC team found that pediatricians and, to a lesser extent, family practitioners who received information about the new guidelines were more likely to begin recommending vitamin D supplementation for all breastfed infants. The UNC center concluded that clear, useful, and targeted information can change provider behavior.

**Use of Antibiotics**

Antibiotics should be chosen with caution. These drugs kill or damage bacteria but are ineffective against other infective agents, such as viruses. In addition, each antibiotic will kill only certain kinds of bacteria. If not used properly, antibiotics may cause persistent or progressive infection, emerging resistance to treatment, and increased medical costs. In order to improve the appropriate use of antibiotics by physicians, the University of Pennsylvania center designed a program to restrict the use of certain antibiotics. The restrictions were enacted to encourage physicians to use antibiotics that killed only the type of bacteria causing the infection, were less expensive, and had the least number of side effects. The program compared the effectiveness of two groups in making recommendations for effective antibiotic treatment regimens. One group, the Antimicrobial Management Team (AMT), consisted of a clinical pharmacist and an infectious diseases (ID) physician; the other group consisted of fellows currently being trained in ID medicine. To compare the performance of the two groups, researchers measured the appropriateness of recommendations, cure rate, number of treatment failures, and cost of care. The AMT showed superior performance to the ID fellows in the measures of recommendation appropriateness (87 percent vs. 47 percent), cure rate (64 percent vs. 42 percent), and number of treatment failures (15 percent vs. 28 percent).

**Quality Measures at Discharge for Heart Patients**

The Vanderbilt center designed a computerized provider order entry (CPOE) intervention tool to determine if the prescription of medications and dissemination of instructions for patients with the common conditions heart failure (HF) and heart attack (or acute myocardial infarction, AMI) could be improved. During patient discharge, physicians received computerized alerts that provided information about drug prescribing and patient counseling for HF and AMI patients. Various outcomes were measured, including the use of appropriate drugs, the provision of smoking cessation counseling for patients who smoked, and the provision of written discharge instructions for HF patients. After implementation of the CPOE intervention, the percentage of patients receiving smoking cessation counseling significantly increased for both AMI patients (from 21 percent to 62 percent) and HF patients (from 1 percent to 43 percent). The number of HF patients who received written...
instructions also increased significantly, from 3 percent before CPOE to 56 percent after the intervention. The study found that CPOE did not significantly change the already high rates of heart medication prescriptions.

**Beta-Blockers for Patients With Heart Failure**

The use of beta-blocker drugs by heart failure patients improves survival and reduces hospitalization. However, they are often not prescribed. The Duke center designed an educational intervention targeting both physicians and patients to increase beta-blocker use. All medical practices participating in the study received brochures to provide to their HF patients. All providers received an information sheet about the evidence for beta-blocker use in heart failure. A subset of the practices received both brochures and video tapes for their HF patients. The physicians in this group were also invited to participate in a live Webcast presentation led by cardiology experts about HF management and beta-blocker use. Additionally, these physicians received information on which of their HF patients were or were not taking beta-blockers. The study found that beta-blocker use increased in both groups. The practices that received the more intensive intervention had a greater proportion of patients taking beta-blockers, although the difference was not statistically significant.

**Using the Internet as an Educational Medium**

**Continuing Medical Education**

The University of Alabama at Birmingham (UAB) center conducted a survey of physicians to understand how they use the Internet for professional and educational purposes. UAB faxed the survey to a random sample of office-based physicians in all specialties nationwide and received 2,200 responses. Survey results indicated that physician Internet use is widespread. Eighty percent of respondents said they use the Internet to find medical information. Additionally, physicians indicated they believe that the Internet is of professional value to them. The factors cited by physicians as being most important when seeking information on the Internet include credibility of the information source, quick and immediate access to information, and ease of searching. Slightly less than one-third of survey participants reported that they used the Internet several times a year or more for accessing continuing medical education (CME) activities. Factors deemed important to the physicians when using an online CME course include accessibility, relevance, credibility, and ease of use. Eighty-four percent of respondents anticipated increased Internet use over the next year.

These results informed development of an Internet-based educational resource to prevent adverse effects associated with glucocorticoids. Glucocorticoids, including the drug prednisone, suppress the immune system in diseases such as asthma, where the immune system may be overactive. However, they may cause glucocorticoid-induced osteoporosis (GIOP), which can lead to fractures.

The UAB center conducted a study that showed the utilization of preventive treatment for GIOP was less than optimal, with only 42 percent of at-risk patients receiving proper care. A three-module Internet-based intervention called Challenging Cases in Musculoskeletal Medicine was designed
to help physicians improve GIOP management. It included personalized practice-based feedback, case-based CME, and a quality improvement toolbox with information about osteoporosis risk assessment, diagnosis, and treatment. Physicians were recruited to use the intervention with mailings of three color brochures, six faxes, and four e-mails. Of the 153 participants, 81 percent finished at least one computer module and 45 percent visited the Web site repeatedly and completed more than one module. The information from the modules can be applied by physicians in their practices to better prevent and treat GIOP.

Harry Guess Research Community
Harry Guess, M.D., Ph.D., was the Principal Investigator of the University of North Carolina center from 2003 until his death in January 2006. He was a pediatrician, a leader in the field of pharmacoepidemiology, and an outstanding mentor, enthusiastically imparting knowledge to everyone from graduate students to senior scientists and colleagues. The University of North Carolina center has created the Web site HarryGuess.unc.edu—the Harry Guess Research Community—as a tribute to his dedication to the ideals of learning. HarryGuess.unc.edu serves as a repository for educational materials about pharmacoepidemiology, pediatric therapeutics, and patient-reported outcomes. The Web site accepts continuous additions of new tools and resources. All who share the vision of Harry Guess are welcome to offer educational and research tools for free dissemination through the Web site.

Drug-Induced Arrhythmia
The QT interval is a measurement of the electrical activity of the heart that can be quantified using an electrocardiogram. Various drugs can lengthen the QT interval. This can lead to a dangerous and potentially fatal heart rhythm called torsades de pointes. To prevent this adverse event, physicians should measure the QT interval before and during the use of any medication that can prolong it.

The Duke center conducted a series of surveys of physicians in cardiovascular medicine, internal medicine, and psychiatry to assess their understanding of the QT interval and medications that may alter the QT interval. They found that, while most physicians reported the need to measure the QT interval before and during the use of a QT-prolonging drug, only 42 percent of respondents were able to correctly measure the QT interval. In addition, many physicians were unable to correctly identify drugs and combinations of drugs that can lengthen the QT interval.

To educate physicians about the QT interval, the Duke center designed an Internet module about both the QT interval and QT-prolonging drugs. The module contains a didactic session and two case studies designed to improve understanding of the importance of the QT interval and its monitoring. It is accessible through the Duke CERTs Web site and the American Heart Association Web site.

The Arizona center also provides a Web-based educational resource for providers about the QT interval of the electrocardiogram and drug-induced arrhythmias. Drugs that prolong the QT interval have caused serious life-threatening arrhythmias and deaths. The use of these drugs is a major safety concern, and there are more than 30 marketed drugs listed on the Arizona Web site. The Web site also contains articles describing the QT interval, the symptoms that arise from lengthening of the QT interval, and how people taking QT-interval-lengthening drugs
should be monitored. In addition, it contains a comprehensive list of drugs that can lengthen the QT interval and/or cause torsades de pointes along with a printable drug list for patients and health care providers.

**Drug Interactions**

The administration of interacting drugs is a common cause of adverse drug events. In collaboration with the FDA, the Arizona center developed a Web-based educational module that focuses on drug interactions and how they can be prevented. The module includes a PowerPoint presentation, written text to accompany each slide in the presentation, self-assessment questions, and a laminated pocket guide as a quick reference for how to prevent the prescription of drugs capable of causing adverse events due to interactions.

A related project is a virtual medicine cabinet showing various over-the-counter drugs. Visitors can click on various types of over-the-counter drugs to learn how they can interact with prescription drugs. In addition, the Arizona center Web site has a Drug Interaction Advisory that lists links to articles about various topics related to drug interactions.

**Providing and Disseminating Information Resources**

**New Cardiovascular Information**

The Duke center, in conjunction with the American College of Cardiology (ACC) and the FDA, identified a need to provide health professionals with up-to-date information on cardiovascular drugs and devices. To address this need, the ACC’s Cardiosource Web site began including key recalls and alerts on cardiovascular drugs and devices for its members. When necessary, cardiology experts comment on the implications of such alerts. FDA’s Center for Devices and Radiological Health recently made another advance in this arena by launching a new, improved Web site to consolidate and communicate device safety information for health care professionals.

**Issue Briefs**

The University of Pennsylvania center develops Issue Briefs in conjunction with the University of Pennsylvania Leonard Davis Institute of Health Economics. Each four-page brief covers a single issue and provides highlights of academic studies in a simple, easy-to-read format. Some past issues covered by the Issue Briefs include tensions in antibiotic prescribing; adherence to HIV drug therapy; and antibiotics, acne, and upper respiratory tract infections. These briefs concisely summarize public policy and public health issues for a broad audience.

**ADHD Toolkit**

Attention-deficit/hyperactivity disorder (ADHD) can cause severe behavioral problems in children. Although ADHD is not a new phenomenon, it has become increasingly common, or at least is more frequently diagnosed, in recent years. The University of North Carolina center, in conjunction with the American Academy of Pediatrics, has developed a toolkit that helps give providers a thorough understanding of best practices in the diagnosis and management of ADHD. The toolkit, based on AAP guidelines, provides resources for diagnosis and treatment of ADHD. It can be found on the AAP Web site at http://aap.org/healthtopics/adhd.cfm.
Educating Patients

**Beta-Blocker Use After a Heart Attack**

Beta-blockers are often prescribed to patients after a heart attack to reduce the chances of having another heart attack and to improve survival. Although most patients take their medications shortly after leaving the hospital, they may stop taking them once they begin to feel better. This increases the risk of future heart problems.

The HMO Research Network center, in collaboration with the Duke center, designed an education program for patients to improve the long-term adherence to beta-blocker therapy. The center identified a group of heart attack patients from four HMOs and mailed a customized information sheet to the patients explaining the importance of taking a beta-blocker long term following a heart attack; a followup mailing reinforced the messages. The mailing also included a card for patients to take to their physician that outlined important questions to ask about beta-blockers. The study compared beta-blocker use after 1 year in the group that received the information and a group that did not receive an educational mailing. Specific findings of this study will be known soon. It is predicted that providing patients with information about beta-blocker therapy will increase the number of people who continue to take the drug.

**Living With Arthritis**

Arthritis is a common and debilitating condition. The joint pain and swelling that accompany arthritis may limit a person’s activities severely. The UAB center developed a Web-based educational module entitled “Taking Care of Yourself With Arthritis,” which teaches arthritis patients to cope with the illness. The module focuses on six important topics related to arthritis care: getting needed care, communicating with the doctor, taking medication properly, monitoring arthritis symptoms, self-care, and dealing with stress. Patients answer a series of questions on each topic. Based on the answers, they are given a series of tips containing specific advice about dealing with arthritis. By using this module, patients can become better informed and incorporate the knowledge into their daily lives, improving their quality of life.

Looking to the Future

The CERTs will continue to develop methods, tools, and resources dedicated to education about the safety, efficacy, and use of therapeutics. The University of Arizona center is developing a “Webliography”—an annotated list of recommended Web sites that will provide reliable drug information for patients and caregivers. The Webliography provides a table showing features of various Web sites, links to those Web sites, and printable brochures and patient information sheets describing the Web sites in both English and Spanish. The University of Pennsylvania center is designing a computerized game based on “Space Invaders” that will teach children how and when antibiotics should be used. The Vanderbilt University center is implementing a computerized support tool for physicians to improve the gastrointestinal safety of NSAID (nonsteroidal anti-inflammatory drug) prescribing in Veterans Affairs (VA) facilities. Future educational projects from the CERTs will be used to promote the optimal use of therapeutics for the improvement of health.
For More Information

The CERTs welcome input about the types of research and education needed to better address costs, effectiveness, and safety issues related to the use of therapeutics. More information on the CERTs program is available at www.certs.hhs.gov.

References


CERTs Resources

- Curriculum in Women's Health (for providers)
  www.aacp.org/site/page.asp?TRACKID=&VID=1&CID=879&DID=5620

- Challenging Cases in Musculoskeletal Medicine: Online Educational Course for Providers (for providers)
  www.giop.certs.cme.uab.edu/

- Harry Guess Educational Web Site (for providers, patients, public)
  http://HarryGuess.unc.edu/

- Understanding the QT Interval (for providers)
  http://qtmodule.mc.duke.edu/

- Practical Approach to Long QT Syndrome and Torsades de Pointes (for providers)

- Drugs That Prolong the QT Interval and/or Induce Torsades de Pointes Ventricular Arrhythmia (for providers, patients, public)
  www.azcert.org/medical-pros/drug-lists/drug-lists.htm

- Over the Counter Medication Interaction Medicine Cabinet (for patients, public)
  http://www.azcert.org/consumers/MCsurvey/router.asp

- Preventable Adverse Drug Reactions: A Focus on Drug Interactions (for providers)
  http://www.azcert.org/medical-pros/education/module01.htm
Drug Interaction Advisory (for patients, public)
www.azcert.org/consumers/interaction-advisory.htm

ADHD Toolkit (for providers, parents, patients, public)
www.aap.org/pubserv/adhdtoolkit

Beta Blockers For Heart Failure (for providers, patients)
http://dukecerts.dcni.duke.edu/resources/bb/index.html#bb_brochure

Taking Care of Yourself With Arthritis (for patients)
www.arthritispatient.cme.uab.edu/