

# PROGRAM BRIEF

## CERTs Research: Women's Health

### Agency for Healthcare Research and Quality

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 & Research on Therapeutics (CERTs) program is to conduct research and provide education that will advance the best use of therapeutics (drugs, medical devices, and biological products). The program seeks 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 comprise seven centers (see box), 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 and educators.

### CERTs Program Centers

Each center focuses its educational and research efforts on therapies in a particular population or therapeutic area:

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



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## CERTs and Women's Health

The overarching goals of CERTs projects are 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 more than 200 completed and ongoing studies whose results have addressed important issues regarding the best use of therapies. Several of these projects address women's health issues.

According to the U.S. Bureau of the Census, in 2000 females represented 51 percent of the total U.S. population, 59 percent of the population age 65 and over, and 71 percent of Americans age 85 and over, which is the fastest growing segment of the population. But until recently, women were underrepresented in research studies. As a result, most women receive diagnoses and treatment based on what has worked for men.

However, medical research is beginning to yield insights into conditions that predominantly affect women, and also how women respond to individual medications and to treatment regimens. The following CERTs projects are examples of such efforts.

### Advancing Knowledge

The CERTs study the beneficial and potentially harmful effects of medical therapies in women so that patients, providers, and policymakers can make informed decisions about treatments.

**Cholesterol-lowering drugs and hip fractures.<sup>1</sup>** Osteoporosis is a condition that leads to low bone mass and bone fragility. Bone fragility can cause fractures, disability, pain, deformity, and

even death. Of the approximately 10 million Americans who have osteoporosis, 8 million are women.

Fractures caused by osteoporosis can severely harm an individual's health and well-being; thus medicines that lower the risk of fractures are of great benefit. Some studies suggest that people who take statins, the most commonly used cholesterol-lowering drugs, have fewer osteoporotic fractures than people who do not. However, factors other than the use of statins may explain this difference. It has been suggested that patients who take cholesterol-lowering drugs are likely to weigh more than people who do not, and extra weight protects against hip and other fractures.

In one study, the Vanderbilt center compared rates of hip fracture between people taking statins and those taking other cholesterol-lowering drugs. They observed no difference in fracture rates between the two groups. Results also show that using statins alone is not effective for preventing fractures caused by osteoporosis. This study highlights the importance of studying off-label use of therapies, or therapies used in ways that are not approved by the FDA.

**Irregular heart rhythms and the menstrual cycle.<sup>2</sup>** Many different types of drugs, including some antihistamines, antibiotics, and antipsychotics, may cause serious heart rhythm disturbances. Women are more susceptible than men, suggesting that sex hormones affect the impact that drugs have on heart rhythms, such as QT prolongation.

During the menstrual cycle there is a dynamic change in levels of estrogen and progesterone. The Arizona center studied whether drugs that can cause QT prolongation have different effects during the different stages of the menstrual cycle.

The researchers gave small doses of ibutilide, a drug commonly prescribed for atrial fibrillation that can cause QT prolongation, to healthy women during different stages of the menstrual cycle and to men. They found that the women in general had longer QT prolongations than men, and the greatest increase was during the first half of the menstrual cycle.

These differences provide prescribing physicians with information that can help determine whether the benefits of such drugs outweigh the risks, especially in women. It also calls attention to the need to examine drug response in women very carefully.

**Antibiotic resistance and urinary tract infections.** Women are more prone to bacterial urinary tract infections than men are. About 20 percent of women develop a urinary tract infection sometime during their life.

Urinary tract infections are the most common type of infections in hospitalized patients. These infections increase morbidity and the cost of hospitalizations. Infections have been treatable with antimicrobial drugs. However, recently physicians have found that some types of the infection-causing bacteria are antibiotic resistant.

Researchers at the University of Pennsylvania center have been studying determinants of resistance to a class of antibiotics called fluoroquinolones. Such information will help determine appropriate treatments. The researchers have measured the outcomes and impact of fluoroquinolone resistance. The research should improve prescribing and reduce antibiotic resistance.

## Informing Patients and Providers

Understanding the risks and benefits of medical therapies is critical to improving the safety and effectiveness of their use. It is also critical to ensure that practitioners and patients have the knowledge needed to use medical therapies appropriately.

**Finding gaps in osteoporosis treatment.**<sup>3-6</sup> Even though there are medicines that lower the risk of fracture for people with osteoporosis, many of those who need treatment do not always receive it or know it is available.

Women with osteoporosis who experience a bone fracture are 20 times more likely to have another fracture in the future than women who do not have the condition. Approximately 80 to 90 percent of bone fractures in postmenopausal women are associated with osteoporosis. For these patients, getting treatment for osteoporosis is especially important. Recent studies, however, suggest that physicians may be missing opportunities to provide treatment.

To explore this issue, the HMO Research Network center used databases from seven health maintenance organizations (HMOs) to determine whether physicians appropriately recommended treatment to women 60 years and older to prevent a second fracture. The researchers found that 76 percent of these women did not receive treatment for osteoporosis in the year after they suffered a fracture.

Researchers at the University of Alabama at Birmingham (UAB) center have ongoing studies of racial disparities in osteoporosis prevention and of osteoporosis induced by use of glucocorticoids (steroids).

To examine racial disparities in a managed care population, UAB surveyed 8,909 women age 50 and over who received care in an HMO. Black women reported fewer bone density tests and less prescription treatment for osteoporosis than white women did. The difference was not fully explained by lifestyle or other health factors. Even black women with a history of fracture received less care than white women.

The study suggests that physicians do not always take the necessary steps to prevent and treat osteoporosis in black women, perhaps because black women are less likely than white women to have osteoporosis. Black women do have fractures, and they tend to have more disability, longer hospital stays, and a greater risk of death from fractures than white women. Future plans include dissemination of information about osteoporosis and education to physicians.

Glucocorticoids are used to treat an estimated one million Americans each year for a variety of conditions. However, the use of glucocorticoids can lead to bone loss and osteoporosis. This is one of the most frequently reported serious adverse outcomes of chronic glucocorticoid use. An estimated 50 percent of long-term users are at risk of fracture.

The UAB center conducted a study to characterize glucocorticoid use and patterns of osteoporosis prevention therapies within a large HMO. Researchers identified 2,378 people receiving chronic glucocorticoid therapy and determined that only 21 percent of them received anti-osteoporotic prescription therapy. For women age 50 and over, the group at greatest risk for fractures, preventive therapies were administered to just over 40 percent. Bone density measurement,

commonly recommended for long-term glucocorticoid users, was obtained in less than 10 percent of the overall group and in just 16 percent of women age 50 and over. The UAB center continues to study glucocorticoid-induced osteoporosis and strategies to improve preventive care.

#### **Arthritis resources for patients.**

Arthritis refers to a group of diseases that cause pain, swelling, stiffness, and loss of motion in the joints. Some people have pain so severe that it limits their daily activities. Fortunately, there are medicines that can help treat arthritis, and many people find that lifestyle changes, such as adding exercise and controlling weight, help relieve symptoms. The following Web sites, which are supported in part through the UAB center, help patients and their families find information about arthritis:

- Arthritis Outcomes Initiative Resource for Patients and Families: <http://www.engalitcheff.uab.edu>
- Arthritis Self-Help for Patients: <http://www-cme.erep.uab.edu/ArthritisPatient/welcome.html>

### **Improving the System**

The CERTs' broadest reaching and potentially most beneficial efforts are those that improve aspects of the health care system. The CERTs projects increase the efficiency of health care, make therapies safer, and give health care providers, patients, and policymakers better access to current treatment information.

**Prescription drug use by pregnant women.**<sup>7,8</sup> The use of medications during pregnancy poses a potential risk to both the mother and the fetus. To assess how often unborn babies are exposed to drugs that may cause them

harm, the HMO Research Network center recorded drug use before and during pregnancy for 152,531 women in eight different health systems and geographic regions. They analyzed prescription drug use according to therapeutic class and categories A, B, C, D, and X of the U.S. FDA's risk classification system. The risk classification system is designed to alert physicians and pharmacists about the possible risks of prescribing medications during pregnancy. The risks of drugs in category C are unknown, drugs in category D have known risks that may be outweighed by their benefits, and those in X have definite risks that outweigh benefits.

Of the women studied, 71,913, or almost half, were prescribed drugs that fall within categories C, D, or X of the risk classification system. These findings suggest that a significant number of pregnant women are prescribed drugs that present unknown or harmful risks.

The Vanderbilt center has also looked at the use of prescription drugs during pregnancy, focusing on drugs in the FDA's category X. The investigators looked at how many of 95,284 pregnant women in Tennessee's Medicare program, TennCare, filled prescriptions for category X medications. Within the group, 391 filled such prescriptions, meaning that about 4 in 1,000 fetuses were exposed to potentially harmful medication. Women over the age of 35 and those enrolled in TennCare because of chronic disabilities were at the greatest risk for filling prescriptions for these drugs. Study results underscore the need to inform both physicians and women so they can consider the risks in taking these medications during pregnancy.





**Use of hormone therapy.** The Women's Health Initiative (WHI), one of the largest prevention studies in the United States to date, was launched in 1991 by the National Institutes of Health to address the most common causes of death, disability, and impaired quality of life in post-menopausal women. Over 160,000 women participated in this 15-year, multi-million dollar study of the effects of hormone therapy on cardiovascular disease, breast and colon cancer, and fractures. Effects of diet modification, and calcium and vitamin D supplementation on post-menopausal women were also studied.

The WHI included studies of two hormone products used by women with different conditions: estrogen-plus-progestin was taken by women with a uterus, and estrogen-alone was taken by women without a uterus. The hormone products are known as conjugated equine estrogen, or CEE.

In July 2002, the estrogen-plus-progestin study was stopped earlier than planned because the women who received the hormone therapy had an increased risk of breast cancer, and also of heart attack and stroke. The estrogen-alone study stopped in 2004 for similar reasons. These findings led experts to conclude that hormone therapy should be used only on a short-term basis in selected women for menopausal symptoms.

In order to study adherence to these recommendations, the HMO Research Network center gathered data on the prevalence of both kinds of estrogen and progestin treatment, and on the discontinuation and initiation rates in the 2 years before the WHI results were published and for the 5 months after their release. They found that immediately after the study results were

published in July 2002, use of estrogen and progestin therapy dropped.

However, a substantial number of women are still using estrogen and progestin therapy, and many are likely to continue using it over the long term.

Future studies will explore why women continue to use estrogen and progestin therapy despite the risk and what additional education directed toward patients and providers is necessary.

## Looking to the Future

The CERTs continue to conduct research and develop educational projects, such as those described above, that study and report on the efficacy, safety, and use of various medical therapies in women. The results of completed and future projects can be used by patients, providers, and policymakers to make sure women receive the highest quality, most cost-effective care possible.

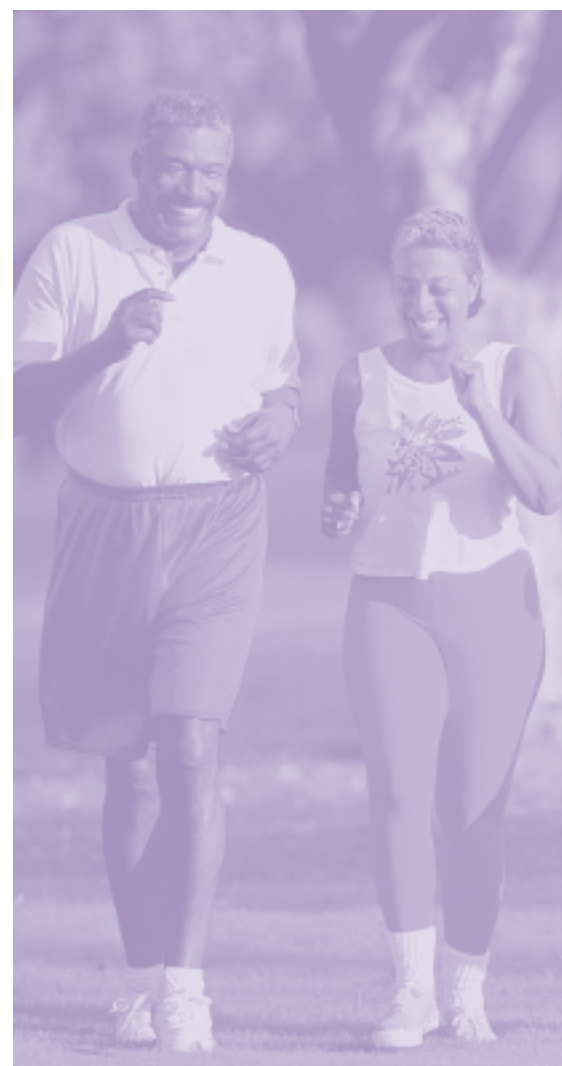
## For More Information

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 from AHRQ's Center for Outcomes and Evidence:

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