



# RESEARCH IN ACTION

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## Prescription Drug Therapies: Reducing Costs and Improving Outcomes

### Introduction

Americans spent over \$553 billion for health care in 1997.<sup>1</sup> Over \$200 billion was spent for hospitalizations, \$180 billion for ambulatory care, and \$72 billion for prescription medicine.<sup>1</sup> Since 1991, prescription drug costs have soared, increasing faster than the inflation rate.<sup>2</sup> The issue of prescription drug costs has captured the attention of legislators and policymakers, insurers, health care providers, and consumers asking the question: Which medicines work best at the lowest cost?

The Agency for Healthcare Research and Quality (AHRQ) has funded research that helps to answer questions about prescription medicine. AHRQ research has:

- Identified conditions for which drug therapy is not necessary.
- Discovered low-cost drug therapies that provide patients with the same quality of care as more expensive drugs.
- Revealed that sometimes the newest, most expensive drug therapy reduces costs overall because it keeps patients healthier and less likely to use other health care services.
- Investigated the cost effectiveness and safety of outpatient vs. inpatient services and the impact of preventive drug therapy.

### Background

Prescription drug spending doubled from \$60.8 billion in 1995 to \$121.8 billion in 2000 and is expected to reach \$160.9 billion in 2002.<sup>3</sup> These increases can be attributed to the research and development of new drugs, as well as the availability of new, more expensive drugs that either replace older drugs or provide treatment for a condition that previously was not treatable.<sup>3,4</sup> Consumers are also purchasing more prescription drugs.<sup>3</sup> In 1993, 7 prescriptions were dispensed per person; by 2000, this number had increased to 10 prescriptions per person.<sup>3</sup>

AHRQ research projects have been funded to determine where the costs for treatment can be reduced without

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reducing the quality of care. The objective is to determine when older, less expensive drugs or no drug treatment can work just as well as newer, more expensive drugs.<sup>5-10</sup> AHRQ has also funded research to determine whether limiting the use of certain drugs, such as antibiotics, can help to reduce the risk of developing antibiotic-resistant bacteria,<sup>11,12</sup> thus decreasing costs related to hospitalization.

Although newer drugs are usually more expensive than older drugs, they are sometimes more effective than their older counterparts in reducing illness, hospitalization, or death,<sup>13</sup> and the improvements in health care outcomes can justify the increased costs.<sup>14</sup> Unfortunately, little information is available to doctors to determine which therapy works best,<sup>5</sup> and very few studies have measured the cost benefits of new drugs.<sup>13</sup>

When better health outcomes involve increased costs, the burden of paying for treatment can have negative consequences. For example, because of cost issues, some patients may resort to drug mismanagement (not filling their prescriptions, taking less than the recommended dose, saving medications for future use, or taking a medicine belonging to another person).<sup>15,16</sup> Increased prescription drug costs translate into higher costs for both insurers and patients and, ultimately, higher health insurance premiums for all consumers. Reimbursement strategies designed to save money may be detrimental to patients and may actually result in higher overall health care costs.<sup>17</sup> For example, limiting reimbursements for drugs can reduce pharmaceutical costs but increase other costs, such as those for hospitalization.<sup>17</sup>

## Impact of AHRQ Research

### Expensive antibiotics do not always have better outcomes

AHRQ research has found that antibiotics are not always necessary or effective and that less expensive antibiotics often work just as well as more expensive antibiotics. The cost of antibiotics varies widely.<sup>8,9</sup> For example, antibiotics to treat middle ear inflammation in children or sinus infections and community-acquired pneumonia in adults cost anywhere from \$2.00 to \$113.00,<sup>6,8,10</sup> resulting in expenses that exceed \$4 billion annually.<sup>7,9</sup> AHRQ research shows that several strategies work to reduce antibiotic expenses.

An AHRQ-funded study that evaluated randomized clinical trials conducted from 1968 through 1994 found that about 80 percent of children recover from middle ear inflammation without the use of antibiotics.<sup>12</sup> More appropriate use of antibiotics would not only lower costs, but reduce the growing problem of antibiotic resistance.

A clinical trial funded by AHRQ showed that amoxicillin performed no differently than a placebo in preventing middle ear inflammation in children. The proportion of children who remained free of inflammation after receiving amoxicillin twice a day (61 percent) was no different from the proportion for children who received amoxicillin once a day and a placebo once a day (64 percent) or children who received a placebo twice a day (63 percent).<sup>7</sup>

Researchers funded by AHRQ also found that more expensive antibiotics were not associated with better outcomes than less expensive antibiotics for treating middle ear inflammation in children ages 30 months to 13 years (Table 1). This retrospective study of children enrolled in Colorado's Medicaid program showed that the average rate at which a second dose was prescribed because the infection did not respond to the first dose of antibiotics was 11.6 percent for less expensive antibiotics and 13.2 percent for more expensive antibiotics.<sup>8</sup>

AHRQ-funded researchers more recently found that older antibiotics such as amoxicillin provide better treatment outcomes than newer antibiotics for children with middle ear inflammation. Researchers for the Center for Education and Research on Therapeutics (CERTs) at the University of North Carolina discovered that children covered by Medicaid in North Carolina who received older drugs had fewer return visits to their physicians than children who received newer, more expensive drugs. The average cost of drug therapy for older drugs such as amoxicillin was \$12.00, while the newer drugs cost an average of \$42.00.<sup>18</sup>

AHRQ funded an evaluation of randomized trials that showed 69 percent of patients with an uncomplicated sinus infection recovered without any antibiotic treatment at all. Researchers reviewed randomized clinical trials conducted from 1970 through 1998 that compared the use of older antibiotics (amoxicillin and folate inhibitors) with placebos and antibiotics that were newer and more expensive at the time of the studies (such as azithromycin, clarithromycin, and cefixime). Their analysis showed that two-thirds of the patients using placebos got well without any treatment, and

**Table 1. Percent of children ages 30 months to 13 years with unresponsive acute otitis media by type and cost of oral antibiotics**

Antibiotic	Cost range (10-day course)	Percent of children prescribed a second course of antibiotics	
		Within 10 days	Within 24 days
Amoxicillin	\$2.94-\$5.88	2.8	11.6
Amoxicillin/clavulanate	\$48.70-\$97.44	3.1	13.3
Cefaclor	\$41.83-\$86.16	2.2	10.7
Cefixime	\$44.33-\$86.16	2.1	12.9
Erythromycin with sulfa	\$24.99-\$48.36	3.3	12.3
Trimethoprim with sulfa	\$1.35-\$6.92	1.8	13.4

Source: Berman S, Byrns PJ, Bondy J, et al. Otitis media-related antibiotic prescribing patterns, outcomes, and expenditures in a pediatric Medicaid population. *Pediatrics* 1997; 100(4):585-92.

the older antibiotics worked just as well as the newer antibiotics.<sup>5</sup>

The AHRQ Patient Outcomes Research Team (PORT) on pneumonia found that there were no differences in outcomes between outpatients with community-acquired pneumonia who were treated with less expensive antibiotics and those treated with more expensive antibiotics.<sup>9</sup> In an observational study, patients who received treatment with antibiotics whose average daily costs were relatively inexpensive (ranging from 36¢ to \$4.04) had outcomes similar to those of patients who were given more expensive antibiotics (ranging from \$5.10 to \$7.52 per day).<sup>9,10</sup>

A second observational study conducted by the AHRQ pneumonia PORT examined antibiotic costs and outcomes among outpatients with community-acquired pneumonia at five different medical institutions. The treatment site with the lowest antibiotic cost also had the lowest rates of subsequent hospital admissions, while the facility with the highest costs had the highest rate (Table 2).<sup>10</sup>

Finally, a clinical trial funded by AHRQ at Brigham and Women’s Hospital, in Boston, found that costs could be reduced by decreasing prescription orders for the antibiotic vancomycin. Vancomycin was at one time the only antibiotic physicians could use to treat bacteria that had

become resistant to all other antibiotics. It is prescribed primarily for patients who have a serious infection that is resistant to other antibiotics, who are allergic to other antibiotics, or who may have sepsis, and to prevent infection in patients who are about to undergo surgery. Overuse of vancomycin in the past 10 years, however, has resulted in the emergence of at least one strain of bacteria that is showing vancomycin resistance. Controlling the use of vancomycin would help to control development of new strains of antibiotic-resistant bacteria.<sup>11</sup>

All of the physicians studied used computerized order entry. The intervention group received computerized guidelines for ordering intravenous vancomycin; the control group of physicians did not. When compared to the control group of physicians, intervention physicians:

- Ordered 29 percent less initial courses of vancomycin.
- Wrote 36 percent less renewal orders.
- Had 32 percent less total orders for vancomycin.
- Prescribed vancomycin for 28 percent less patients.
- Prescribed vancomycin for 36 percent less days.<sup>11</sup>

The number of patients who received vancomycin during their hospitalization decreased by 15 percent (from 2,715 to

**Table 2. Costs and subsequent admission rates for outpatients with community-acquired pneumonia at five medical institutions**

Item	Study site <sup>a</sup>				
	UPMC	SFMC	MGH	HCHP	VGH
Median cost	\$6.10	\$54.90	\$7.70	\$5.40	\$7.50
Subsequent hospital admission	13.0%	22.2%	7.9%	2.2%	4.7%

<sup>a</sup>UPMC—University of Pittsburgh Medical Center; SFMC—St. Francis Medical Center; MGH— Massachusetts General Hospital; HCHP—Harvard Community Health Plan, Kenmore Center; VGH—Victoria General Hospital.

**Source:** Gilbert K, Gleason PP, Singer DE, et al. Variations in antimicrobial use and cost in more than 2,000 patients with community-acquired pneumonia. *Am J Med* 1998; 104:17-27.

2,341) compared to 9 months prior to the study. This might have led to a cost savings of \$90,000 per year. However, because many patients still required treatment for infection or to prevent infection, another antibiotic would have been prescribed instead of vancomycin. For example, physicians may have substituted cefazolin, which cost \$9.00 per day compared to \$12.00 per day for vancomycin. The hospital still saved \$22,500 a year. Because of the impact the computerized guidelines had on physician ordering practices, at the study's conclusion these guidelines were made available to all users of the computerized order entry system.<sup>11</sup>

### New expensive drugs can reduce overall costs

In some instances newer, more expensive drugs can lead to cost benefits. For example, new drugs could provide treatment for conditions such as HIV for which very few treatments had previously existed. In addition, newer drugs may be more effective, have fewer side effects, and represent better quality of care than older drugs. They also may lower costs overall by lessening the need for other health care services.<sup>4</sup>

An AHRQ-funded observational study done soon after the approval of the first protease inhibitors (drugs that keep HIV from reproducing) in the mid and late 1990s showed that HIV-infected patients taking protease inhibitors had lower hospital inpatient costs, community care costs, and costs associated with the treatment of opportunistic illness. Researchers found that the average monthly Medicaid payments for pharmacy costs were higher for patients

taking protease inhibitors. However, Medicaid patients who took protease inhibitors, when compared to Medicaid patients who did not, had:

- Significantly lower average monthly total payments for the sickest patients (those with low CD4<sup>a</sup> cell counts) in 1997 (Table 3).
- Significantly lower payments when hospitalized with an opportunistic illness both in 1996 and 1997 (Figure 1).<sup>19</sup>

### Outpatient drug treatment can be effective and reduce costs

AHRQ research has demonstrated that some drug treatments offered on an outpatient basis have the same outcomes as those given on an inpatient basis at lower cost. For example, treating women with pelvic inflammatory disease (PID) as outpatients rather than inpatients could save as much as \$500 million a year.<sup>20</sup>

PID, an infection and inflammation of organs in the pelvis, affects about 1.2 million women in the United States each year, resulting in infertility, chronic pelvic pain, and ectopic pregnancies. AHRQ funded the PID Evaluation and Clinical Health (PEACH) Study, which conducted a clinical trial to compare the effectiveness of inpatient and outpatient treatment. After 30 days, there were no significant differences in adverse outcomes between the outpatient and

<sup>a</sup>CD4 cells are a type of white blood cell that helps the body fight off infections. HIV invades CD4 cells. Eventually, the body loses its ability to produce CD4 cells and therefore loses its ability to fight infection.

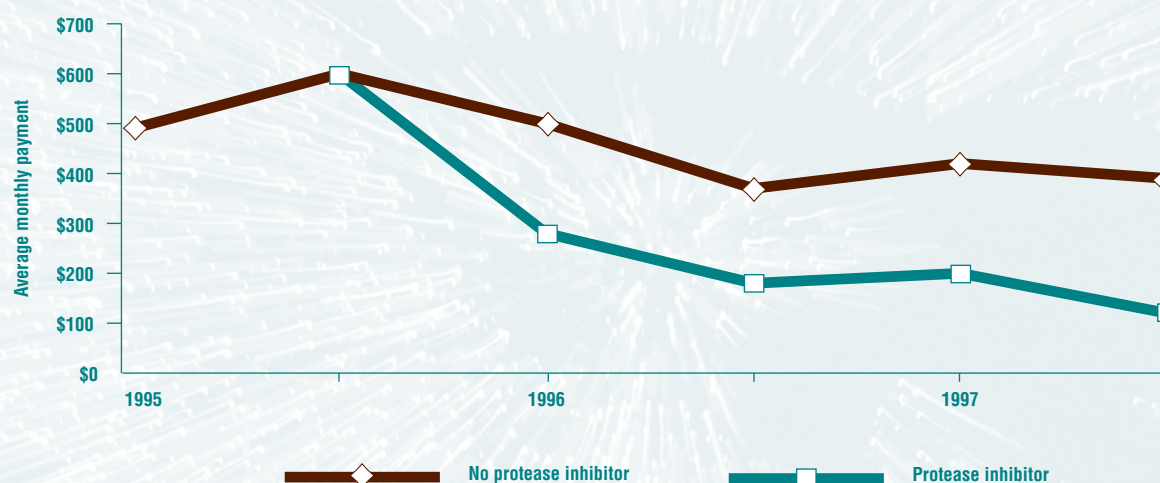
**Table 3. Average monthly Medicaid payments for HIV patients by protease inhibitor use**

CD4 cell count and cost	1996		1997	
	No protease inhibitor use	Protease inhibitor use	No protease inhibitor use	Protease inhibitor use
<b>CD4 cell count less than 50 x 10<sup>6</sup></b>				
Pharmacy cost	\$487	\$852	\$508	\$745
Total average cost	\$2,047	\$1,704	\$2,805	\$1,814
<b>CD4 cell count 50-200 x 10<sup>6</sup></b>				
Pharmacy cost	\$390	\$663	\$398	\$763
Total average cost	\$1,515	\$1,123	\$1,495	\$1,623
<b>CD4 cell count 200-500 x 10<sup>6</sup></b>				
Pharmacy cost	\$267	\$455	\$299	\$652
Total average cost	\$1,036	\$780	\$1,395	\$1,031

**Note:** Total average cost includes inpatient, outpatient, pharmacy, community care, and emergency room costs.

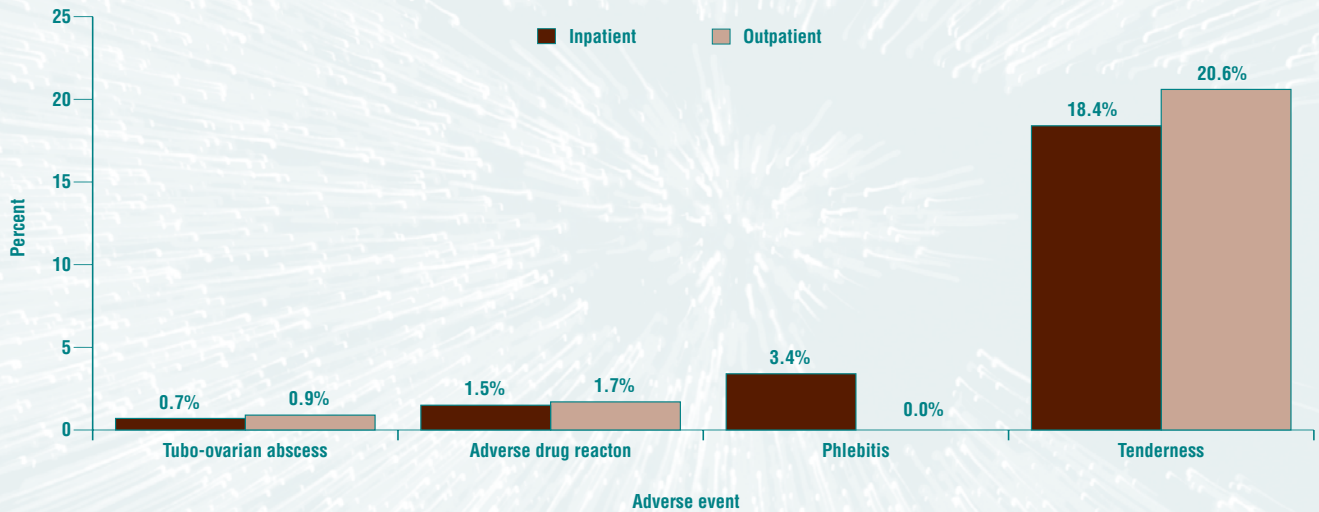
**Source:** Gebo KA, Chaisson RE, Folkemer JG, et al. Costs of HIV medical care in the era of highly active antiretroviral therapy. AIDS 1999; 13(8):963-9.

**Figure 1. Average inpatient Medicaid payment per month for hospitalization associated with a principal discharge diagnosis of opportunistic illness for HIV patients**



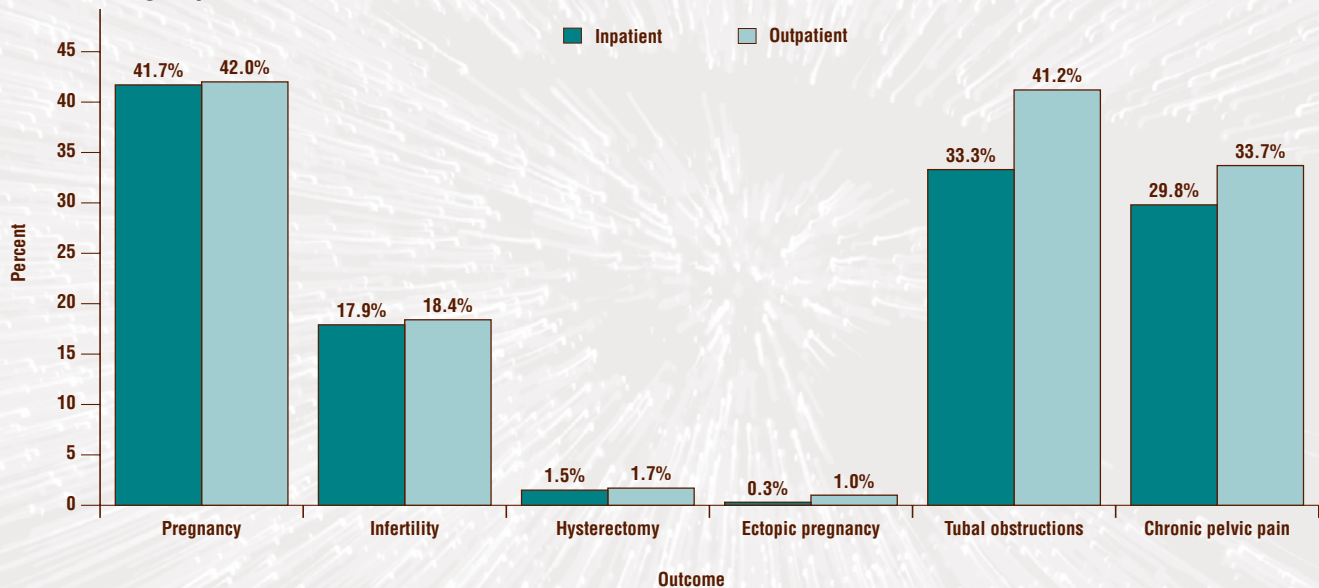
**Source:** Gebo KA, Chaisson RE, Folkemer JG, et al. Costs of HIV medical care in the era of highly active antiretroviral therapy. AIDS 1999; 13(8):963-9.

**Figure 2. Percent of adverse events after 30 days for women treated for pelvic inflammatory disease by treatment group**



**Source:** Ness RB, Soper DE, Holley RL, et al. Effectiveness of inpatient and outpatient treatment strategies for women with pelvic inflammatory disease: results from the Pelvic Inflammatory Disease Evaluation and Clinical Health (PEACH) randomized trial. *Am J Obstet Gynecol* 2002; 186(5):929-37.

**Figure 3. Long-term outcomes (average of 35 months) for women treated for pelvic inflammatory disease by treatment group**



**Source:** Ness RB, Soper DE, Holley RL, et al. Effectiveness of inpatient and outpatient treatment strategies for women with pelvic inflammatory disease: results from the Pelvic Inflammatory Disease Evaluation and Clinical Health (PEACH) randomized trial. *Am J Obstet Gynecol* 2002; 186(5):929-37.

inpatient treatment groups, with the exception of phlebitis (inflammation of a vein) sometimes caused in inpatients by intravenous treatment with the antibiotic doxycycline (Figure 2). After an average followup period of 35 months, there were no differences in outcomes between outpatients and inpatients (Figure 3).<sup>20</sup>

### Preventive drug therapy can be cost effective

AHRQ research has shown that using drugs to prevent opportunistic illnesses such as *Pneumocystis carinii* pneumonia (PCP) in HIV patients can lower costs. Drugs such as trimethoprim-sulfamethoxazole (TMP-SMZ), aerosol pentamidine, or dapsone can help prevent PCP, but many patients do not receive these medications.<sup>21-23</sup>

Researchers funded by AHRQ in the early 1990s examined past charts of HIV patients. They found that, among patients who developed PCP, those who took preventive drugs were less likely to require hospitalization or admission to the intensive care unit than those who did not take preventive drugs (Table 4). Patients who did not take preventive drugs accounted for 800 (85 percent) of 937 hospital days associated with this illness and were also more likely to die.<sup>21</sup> More recent studies conducted by other researchers confirm that preventive drug therapy in HIV patients reduces the risk of PCP as well as other bacterial infections.<sup>22-24</sup> Public Health Service guidelines today recommend that persons with CD4 counts less than 200 take drug therapy to prevent PCP, and treatment with TMP-SMX is covered under all of the Drug Assistance Programs funded by the Ryan White CARE Act.<sup>25</sup>

### Ongoing Research

AHRQ continues to fund studies that investigate the costs and outcomes of pharmaceutical therapies.

**Consequences of Drug Cost Sharing in the Elderly;** Brigham and Women’s Hospital, Boston, MA, Grant No. R01 HS10881-01. This study is examining the effects of differential cost sharing for pharmaceutical costs, an increasingly common strategy to discourage use of more expensive medications in many drug benefits plans. Specifically, researchers will assess the impact of differential cost sharing applied to angiotensin-converting enzyme inhibitors and calcium channel blockers on patterns of medication use and health care use in all elderly recipients of these drugs.

**Table 4. Hospitalization, mortality, and resource use over a 1-year period for HIV patients who developed PCP**

Item	Taking preventive drugs	
	Yes	No
<b>Number of patients:</b>		
Hospitalized	11	54
Had an ICU stay	0	10
Died	0	12
<b>Total hospital days</b>	<b>137</b>	<b>800</b>
<b>ICU days</b>	<b>0</b>	<b>202</b>
<b>Total charges</b>	<b>\$95,932</b>	<b>\$753,608</b>

**Note:** ICU—intensive care unit. PCP—*Pneumocystis carinii* pneumonia.

**Source:** Gallant JE, McAvinue SM, Moore RD, et al. The impact of prophylaxis on outcome and resource utilization in *Pneumocystis carinii* pneumonia. *Chest* 1995; 107:1018-23.

**Effect of Medicaid Drug Copayments on Outcomes and Costs;** University of Minnesota, Grant No. R03 HS10791-01. This study is estimating the effect of Medicaid prescription drug copayments on the use of drugs and other types of health care and on total Medicaid expenditures.

**Patient-Centered Care and Health Care Costs;** University of Rochester, Grant No. R01 HS10610-01A1. This research study is examining the relationship between measures of physicians’ patient-centeredness (a process where the physician incorporates the patient’s experience of illness and shares decisionmaking) and patients’ health care costs (total, inpatient, outpatient, testing, and medication), health status, and satisfaction. It will also characterize features of patient-physician communication that contribute to lower health care costs.

**Centers for Education and Research on Therapeutics (CERTs).** The CERTs demonstration program is a national initiative to conduct research and provide education that advances the optimal use of therapeutics (drugs, medical devices, and biological products). The program is administered as a cooperative agreement by AHRQ in consultation with the U.S. Food and Drug Administration. The research conducted by the CERTs program is intended to increase awareness of the uses and risks of new drugs

and drug combinations, biological products, and devices as well as ways to improve their safe and effective use. The CERTs research will improve quality while reducing the cost of care by increasing the appropriate use of drugs, biological products, and devices and by preventing their adverse effects and consequences. The CERTs centers are:

- Duke University (HS10548): Therapies for disorders of the heart and blood vessels.
- HMO Research Network (HS10391): Usefulness of health maintenance organizations for studying drug use, safety, and effectiveness.
- University of Alabama-Birmingham (HS10389): Therapies for disorders of the joints and bones.
- University of Arizona (HS10385): Reduction of adverse drug interactions, especially in women.
- University of North Carolina (HS10397): Therapies for children.
- University of Pennsylvania (HS10399): Therapies for infection and antibiotic drug resistance.
- Vanderbilt University (HS10384): Prescription drug use in a Medicaid population.<sup>26</sup>

## Conclusion

AHRQ-funded research helps identify drug therapies that can lower health care costs while maintaining quality of care. Less expensive drugs such as antibiotics can work just as effectively as more expensive drugs, lowering costs without compromising patients' health. However, some newer, more expensive drugs can also lower costs because they improve patients' health overall and reduce other medical expenses. More research needs to be conducted to identify those new drugs that have an advantage over older, existing drugs. AHRQ research has shown that some drug therapies can be provided on an outpatient basis, thus saving the costs of inpatient treatment. Finally, studies funded by AHRQ have helped lower costs by showing the benefit of providing preventive drug therapies.

## For more information

For more information about AHRQ research on pharmaceuticals, please contact Lynn Bosco, M.D., M.P.H., at 301-594-2416 or [lbosco@ahrq.gov](mailto:lbosco@ahrq.gov).

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\* *AHRQ-funded/sponsored research*



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