

Using Comparative Effectiveness Research

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**National
Business
Group on
Health**

Adding ACEIs and/or ARBs to Standard Therapy for Stable Coronary Artery Disease

This guide provides actions suggested by the National Business Group on Health for employers who want to use comparative effectiveness research (CER) findings about medications for stable coronary artery disease in their health plans. It is based on research funded by the Agency for Healthcare Research and Quality (AHRQ). For more information about heart disease or heart disease treatments and medication, see the “Resources” section at the back of this guide.

Impact on Employers

Coronary artery disease (CAD) is the most common type of heart disease; it is also the most costly to manage.¹ CAD accounted for \$156.4 billion in total costs in 2008, more than twice the cost of hypertension and stroke.¹ Prescription drug costs alone totaled \$9.7 billion, and costs associated with lost productivity totaled \$58.6 billion.¹

What is Stable Coronary Artery Disease?

Coronary artery disease (CAD) occurs when heart arteries become hardened and narrowed, restricting the amount of blood and oxygen that reaches the heart. These blockages are most commonly caused by cholesterol deposits, or plaques. A common symptom of coronary artery disease is ischemia, or pain referred to as angina, which occurs when the heart is deprived of oxygen.³

Patients with **stable** coronary artery disease, or “stable angina,” can typically relieve ischemia in less than 10 minutes with medication such as nitrates or with rest.³ These patients are also at risk for heart attack, heart failure and stroke.

Coronary artery disease prevalence increases with age (see chart on page 3). Employers with an older or aging workforce may experience higher spending over time in their medical and pharmacy plans, in addition to productivity consequences. CAD is also directly related to obesity and associated conditions such as diabetes, further emphasizing the importance of prevention and effective disease management.

Studies have demonstrated that the use of angiotensin-converting enzyme inhibitors (ACEIs) or ACE Inhibitors, or angiotensin II receptor blockers (ARBs), in addition to standard treatment, is effective in reducing mortality, nonfatal heart attack, hospitalization and revascularization. However, these medications differ in clinical effectiveness and price. They also have poor adherence rates, especially when added to already complex or expensive treatment regimens.² Employers have an opportunity to address these issues of treatment effectiveness, medication adherence and heart disease prevention through employee education and pharmacy plan management.

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Agency for Healthcare Research & Quality

Comparative Effectiveness Research Findings

In 2009, the AHRQ Effective Health Care Program funded a systematic review of research literature examining the effectiveness of adding an ACEI, ARB, or a combination of these two medications to standard treatment for stable coronary artery disease. The following findings are based on the review, entitled *Comparative Effectiveness of Angiotensin II Receptor Blockers Added to Standard Medical Therapy for Treating Stable Ischemic Heart Disease*. They were the basis for the publication of consumer and clinician guides in May 2010.

What are ACEIs and ARBs?

ACEIs also referred to as “angiotensin-converting enzyme inhibitors” or “ACE Inhibitors” and ARBs or “angiotensin II receptor blockers” are two common prescription medications that lower blood pressure and have been used to treat heart failure. Doctors know more about the benefits and side effects of ACEIs, and so the addition of an ACEI is typically the first choice. People who take ACEIs usually experience only minor side effects. An ARB may be prescribed for those people who experience more serious or bothersome side effects with an ACEI.

Main research findings:

Research demonstrated conclusive evidence that adding an ACEI to standard treatment for stable coronary artery disease reduces total mortality, nonfatal heart attack, heart failure-related hospitalization, and the need for revascularization (surgery to open blocked blood vessels in the heart). In addition, for those patients who have difficulties with ACEIs, adding an ARB to standard therapy reduces the chances of mortality, nonfatal heart attack and stroke.

The study also conclusively demonstrated that adding an ACEI or ARB close to a revascularization procedure, such as balloon angioplasty or coronary artery bypass graft (CABG), increases the risk of needing additional revascularizations.

Finding:

Benefits and risks of adding an ACEI to standard treatment

Possible Benefits

Evidence conclusively demonstrates that adding an ACEI to standard treatment reduces mortality, nonfatal heart attack, heart failure-related hospitalization and the need for revascularization.

Possible Harm

Some studies suggest that the addition of an ACEI can increase the risk for fainting, cough, and hyperkalemia (high blood potassium level which can cause heart arrhythmias), but this evidence is inconclusive. ACEIs may also cause serious birth defects and may not be appropriate for women who are pregnant or may become pregnant.

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Finding:

Benefits and risks of adding an ARB to standard treatment

Possible Benefits

For patients who experience side effects with ACEIs, adding an ARB to standard treatment can reduce the risk of mortality, nonfatal heart attack and stroke.

Possible Harm

There is a low level of evidence that supports an increased risk for hyperkalemia with the addition of an ARB.

Finding:

Benefits and risks of adding both an ACEI and an ARB to standard treatment

Possible Benefits

Adding both ACEI and ARB provides no additional benefit compared to only ACEI added to standard treatment.

Possible Harm

Combining ACEIs and ARBs increases the risk of hypotension (low blood pressure), sudden fainting and kidney failure.

Finding:

Benefits and risks of adding an ACEI or ARB close to a revascularization procedure

Possible Benefits

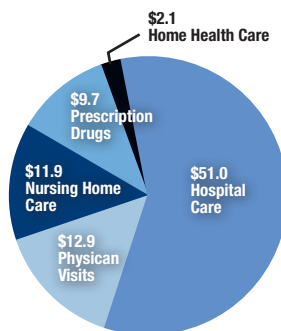
Adding an ACEI or ARB close to a revascularization procedure provides no additional benefit over standard therapy.

Possible Harm

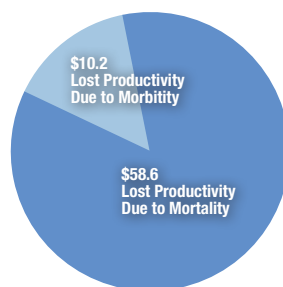
Evidence conclusively states that adding an ACEI or ARB close to a revascularization procedure increases the risk for needing future procedures. This can also increase the risk for hypotension.

Cost of CAD in 2008 = \$156.4 Billion

Direct costs = \$87.6 billion
(in billions)

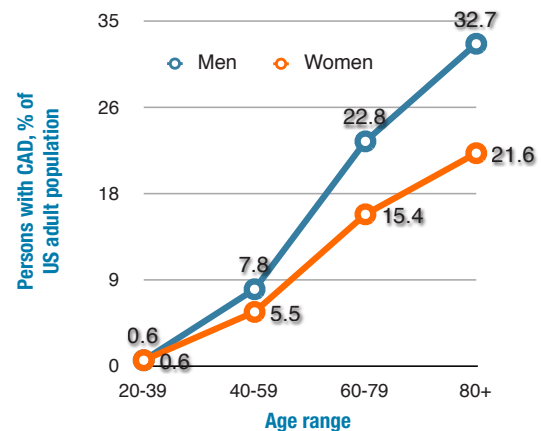


Indirect costs = \$68.8 billion
(in billions)



Source: American Heart Association. Heart Disease and Stroke Statistics—2008 Update.

CAD Prevalence Increases With Age



Source: American Heart Association. Heart Disease and Stroke Statistics—2008 Update.

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Standard treatment for stable coronary artery disease can include aspirin, statins, beta-blockers, dual anti-platelet therapy or combinations of these agents. Doctors may also recommend nitrates and calcium channel blockers as ways to manage symptoms.

Still Unknown

Recent studies have begun to examine the potentially different effects that ACEIs and ARBs may have on different demographic populations.⁴ However, additional research is needed to assess the actual benefits, harm and disparities of these medications on the basis of age, gender, race and ethnicity. Additional research is also warranted in specific racial groups such as African-Americans and Latinos. Studies also are needed that examine comorbidities such as hypertension and diabetes, use of additional medications such as antiplatelet therapies (a medication such as aspirin that interferes with the process that forms blood clots), and the presence of a single or multivessel disease.

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Coronary artery disease can be a very costly condition for employers. However, employers can help reduce the costs and health risks associated with the disease by doing the following:

- Educating employees on heart disease prevention and how to work with their doctor to effectively manage the disease;
- Working with pharmacy benefit managers to examine and address medication adherence; and
- Encouraging cost-effective choices such as generics and delivery of medications by mail.

Heart Disease Prevention

Encourage employees to maintain a healthy weight and active lifestyle. Consider providing healthy lifestyle incentives such as gym reimbursements; include healthy options in the cafeteria; and start team-based fitness or weight-loss competitions. Studies have demonstrated a direct relationship between obesity and coronary artery disease. Encourage employees to keep active and maintain a diet low in fat and sodium.

Institute a tobacco-free workplace and offer tobacco cessation programs. Smoking heightens the development of plaque in the arteries which can lead to coronary artery disease.⁵ Smoking also increases the amount of carbon monoxide in the bloodstream, which decreases the amount of oxygen available to the heart and increases the likelihood of angina.⁵

Consider providing screenings at the workplace. It is relatively easy and inexpensive to provide blood pressure, diabetes and blood lipid screening in the workplace, all of which can indicate a person's risk for heart disease. Employers may want to consider providing incentives for participation in screening and making screening available to dependents.

Treatment Adherence

Work with your pharmacy benefit managers (PBMs) to monitor adherence rates for ACEIs and ARBs. Studies have shown that adherence rates for ACEIs and ARBs are traditionally low. Ask your PBM to institute targeted solutions to improve medication adherence if rates are suboptimal.

Provide employees with information to help them talk with their doctors about the benefits and risks of adding an ACEI or ARB to their heart disease treatment regimen. The information should state that research shows that adding an ACEI or an ARB may be beneficial, however; adding an ACEI and an ARB not only provides no additional benefit, but it also may increase the risk for low blood pressure, sudden fainting and renal problems. See the Resources section of this paper for a free consumer guide with questions for doctors.

Encourage employees to use generic medications to keep their costs low. When the out-of-pocket copayment is \$50 or more, patients are almost four times more likely to abandon medication use.⁶ With ACEIs

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specifically, a \$10 increase in copayment was associated with a 2.6% decrease in adherence, which in turn increased the risk of heart failure-related hospitalization by over 6%.⁷

Encourage employees to use home delivery for maintenance medications. Beneficiaries with heart disease typically have complex drug regimens involving multiple medications and frequent pharmacy visits. A recent study demonstrated that ACE inhibitor users typically have multiple refills in several different pharmacies, resulting in adherence of about 66%.⁸ Mail-order pharmacy is an effective way to consolidate these refills and make it easier for employees to receive their medications, thus making it more likely that they will continue taking them. In a separate study, refill consolidation (coordination of multiple refills on the same pharmacy visit) boosted adherence by 13% for both ACEIs and ARBs.²

Conclusion

Adding ACEIs or ARBs to standard therapy for stable CAD has been shown to reduce poor health outcomes including non-fatal heart attack, heart failure-related hospitalization and the need for revascularization procedures. However, both medications have potentially serious side effects. Employers can provide employees with information to help them understand the benefits and risks of these medications and work with their doctors to make treatment decisions. Employers can also work with their PBMs to encourage generics, mail order use, and patient adherence to these medications when prescribed.

Resources

Adding ACEIs and/or ARBs to Standard Therapy for Stable Ischemic Heart Disease: Benefits and Harms: Clinician Guide
Agency for Healthcare Research and Quality,
May 2010

“ACE Inhibitors” and “ARBs” To Protect Your Heart? A Guide for Patients Being Treated for Stable Coronary Heart Disease
Agency for Healthcare Research and Quality,
May 2010

Questions are the Answer

Agency for Healthcare Research and Quality
This is an easy-to-use consumer website that helps patients take an active role in their health care by asking questions so that they understand their condition and options.
<http://www.ahrq.gov/questionsaretheanswer/>

American Heart Association

The AHA's mission is to build healthier lives free of cardiovascular diseases and stroke. The AHA

is a comprehensive source of information on treatment, prevention and research on cardiovascular health.
<http://www.heart.org/HEARTORG/>

National Heart, Lung, and Blood Institute

The NHLBI provides research, training and education to promote the prevention and treatment of heart, lung and blood diseases and enhance the health of all individuals.
<http://www.nhlbi.nih.gov/>

Best Buy Drugs

This series of reports from Consumer Reports provides information on cost and effectiveness of several different drugs and medications, organizing information by drug, drug category and medical condition.
<http://www.consumerreports.org/health/best-buy-drugs/index.htm>

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For Free Print Copies of the Consumer and Clinician Guides

AHRQ Publications Clearinghouse – 800.358.9295

“ACE Inhibitors” and “ARBs” To Protect Your Heart? A Guide for Patients Being Treated for Stable Coronary Heart Disease, AHRQ Pub. No. 10-EHC002-A

Adding ACEIs and/or ARBs to Standard Therapy for Stable Ischemic Heart Disease: Benefits and Harms: Clinician Guide, AHRQ Pub. No. 10-EHC002-3

Comparative Effectiveness of Angiotensin Converting Enzyme Inhibitors or Angiotensin II Receptor Blockers Added to Standard Medical Therapy for Treating Stable Ischemic Heart Disease: Executive Summary, AHRQ Pub. No. 10-EHC002-1

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Written by:

Demian T. Kendall

Program Assistant, National Business Group on Health

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About the National Business Group on Health

The Business Group is the only non-profit organization devoted exclusively to representing large employers' perspectives on national health issues and providing solutions to its members' most important health care and health benefits challenges. The Business Group fosters the development of a safe health care delivery system and treatments based on scientific evidence. Members share strategies for controlling costs, improving patient safety and quality of care, increasing productivity and supporting healthy lifestyles.

National Business Group on Health

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20 F Street, N.W., Suite 200 • Washington, D.C. 20001

Phone (202) 558-3000 • Fax (202) 628-9244 • www.businessgrouphealth.org

Helen Darling, President, National Business Group on Health

National Committee on Evidence-Based Benefit Design

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