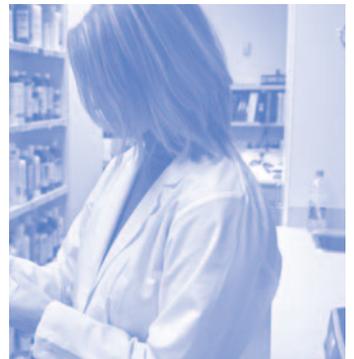


BEST BUY DRUGS™

Using ACE Inhibitors to treat:
**High Blood Pressure and
Heart Disease**

Comparing Effectiveness, Safety, and Price

ConsumerReportsHealth.org/BestBuyDrugs



Our Recommendations

ACE inhibitors (ACEIs) are used by tens of millions of Americans to treat high blood pressure and heart failure, to prevent repeat heart attacks, to reverse thickening of the heart due to high blood pressure, and to prevent the decline of kidney function in people with high blood pressure and/or diabetes.

The monthly cost for ACEIs varies from less than \$10 to more than \$100. This report gives you information that could save you hundreds of dollars a year or more if you are currently taking a brand-name ACEI.

ACEIs are effective, life-saving medicines with more than 20 years of widespread safe use. They help lower the risk of both fatal and non-fatal heart attacks and strokes, and kidney failure. And they improve quality of life. This report compares the effectiveness, safety, and cost of the 10 ACEIs.

We have selected the following five ACEIs as *Consumer Reports Health Best Buy Drugs* based primarily on the evidence for their effectiveness, but also on dosing convenience and cost in treating the following conditions:

- For high blood pressure: *benazepril*, *enalapril*, and *lisinopril*
- For heart failure: *captopril*, and *enalapril*
- After a heart attack: *lisinopril*
- For diabetics: *ramipril*
- For people with kidney disease: *benazepril*, and *ramipril*

All of these medicines are low-cost or moderately-priced generics. All have been proven to be just as effective or superior to other ACEIs in treating the general population. Studies have proven ramipril particularly effective in treating people who have diabetes and other heart disease risk factors, and in the prevention of kidney function decline in diabetics.

Note: The ACEIs can lower blood pressure, but we recommend starting with a diuretic medication as the initial “first-step” treatment for most people with high blood pressure who do not have heart disease, diabetes, or kidney disease because there is stronger evidence for diuretics that they prevent premature death, heart disease, stroke and other cardiovascular problems. If you are unable to tolerate a diuretic or it does not lower your blood pressure enough, then it may be time to consider an ACE inhibitor.

Published in March 2011.

Welcome

This report on a class of drugs called ACE inhibitors (ACEIs) is part of a Consumers Union and *Consumer Reports* project to help you find safe, effective medicines that give you the most value for your health-care dollar. To learn more about the project and other drugs we've evaluated, go to ConsumerReportsHealth.org/BestBuyDrugs.

ACEIs are used by millions of people everyday. (ACE stands for angiotensin-converting enzyme.) ACEIs were the fourth most widely prescribed class of medicines in the U.S. in 2009 (the latest year for which data is available), with almost 163 million prescriptions filled, according to figures from IMS Health. They are used primarily to treat people who have high blood pressure and/or heart failure (also called congestive heart failure). Heart failure occurs when the heart muscle weakens, limiting the heart's ability to pump blood. The condition is usually a chronic disease that can worsen over time. It occurs as a result of untreated or inadequately-controlled high blood pressure, a heart attack, or a number of diseases that attack the heart muscle. (See Table 1 on page 6.)

The ACEIs are also widely used to treat people after a heart attack (in the absence of heart failure) and people with diabetes with and without kidney disease.

Ten ACEIs are currently approved for use in the U.S. (listed on next page). All are now available as generic drugs. Some of the generic ACEIs are very inexpensive, costing less than \$10 a month in some cases. (See Table 4 beginning on page 11.) Certain generic ACEIs cost as little as \$4 for a month's supply through generic drug programs run by major chain stores, such as Kroger, Sam's Club, Target, and Walmart. For an even better bargain, you can obtain a three-month supply for \$10 through these programs. We note in the price chart starting on page 11 which generic ACEIs are available through these programs. Some stores, such as CVS and Walgreens, require a membership fee to participate and might charge higher prices. There might be other restrictions too, so check the details carefully to make sure your drug and dose are covered.

ACEIs are just one class of prescription medicines used to treat high blood pressure, heart failure, and other heart-related ailments. Several other classes are also commonly used to treat high blood pressure. These include diuretics, angiotensin-receptor blockers, beta-blockers and calcium-channel blockers. Those drugs plus the ACEIs are often used in combination, two or more at a time. Indeed, many people with high blood pressure will require two or more drugs to bring their blood pressure down to a normal level. ACEIs and other drugs are also used to treat heart failure.

| Generic Name | Brand Name(s) |
|------------------|-------------------|
| 1. Benazepril | Lotensin |
| 2. Captopril | Capoten |
| 3. Enalapril | Vasotec |
| 4. Fosinopril | Monopril |
| 5. Lisinopril | Prinivil, Zestril |
| 6. Moexipril | Univasc |
| 7. Perindopril | Aceon |
| 8. Quinapril | Accupril |
| 9. Ramipril | Altace |
| 10. Trandolapril | Mavik |

Talk with your doctor about the right mix of blood pressure medicines for you. The discussion should also include lifestyle changes – such as eating a healthy diet, losing weight if needed, exercise, limiting alcohol use, and quitting smoking. These lifestyle changes are an important part of treatment and can reduce the need for drugs.

You should know that high blood pressure is a leading cause of death. The condition is often called a “silent killer” because its symptoms can go undetected until damage to the body has occurred. Because of this, it is one of the most significantly under-diagnosed and under-treated medical conditions in the U.S. If left uncontrolled, it can raise your risk of dementia, heart attack, heart failure, kidney failure, stroke, and vision loss.

High blood pressure is usually a lifelong condition. About 74 million Americans – including a third of adults 20 and older – have high blood pressure, also known as hypertension, according to the Centers for Disease Control and Prevention. In addition, an additional 25 percent, or 1 in 4 of American adults have “prehypertension,” or borderline high blood pressure, which raises the risk of developing high blood pressure. Yet studies show that:

- 20% of people with high blood pressure are unaware of their condition.
- 27% of those with high blood pressure are aware of their condition but are not taking medicine to control it.
- 30% of those with high blood pressure are getting treatment but their high blood pressure is not under control.

Overall, about half of people—50 percent—with high blood pressure do not have their condition under control, according to recent data from the Centers for Disease Control and Prevention and the National Health and Nutrition Examination Survey (NHANES). This increases their risk for developing the complications listed above. In

Note to Readers: This is one of four reports on prescription medicines to treat high blood pressure and other heart conditions. The other three reports focus on treating high blood pressure in general, plus two other classes of drugs: beta-blockers and calcium channel blockers.

Sign up for an e-mail alert at ConsumerReportsHealth.org/BestBuyDrugs if you'd like us to tell you when these reports are updated or to learn about other reports posted on this Web site.

addition, high blood pressure's dangers are thought to extend to an additional 45 to 60 million Americans who have "prehypertension," or borderline high blood pressure. (See Table 2 on page 8.)

You should have your blood pressure checked frequently – at least once a year, more often if you are over age 50, and every time you visit a doctor no matter what your age.

High blood pressure can occur at any age but is far more common in people 35 and over. It is particularly prevalent in African-Americans, those with a family history of high blood pressure, people who are overweight or obese, people with diabetes, and heavy drinkers. Women taking birth control pills are also at high risk, as are people who take nonsteroidal anti-inflammatory drugs – such as ibuprofen, naproxen, and the COX-2 drug celecoxib (Celebrex) – over long periods.

Heart failure is also under-diagnosed and under-treated, especially in its early stages. People often assume its symptoms are a sign of normal aging or that they are not serious. And doctors can sometimes misdiagnose these symptoms, which include shortness of breath on exertion, unexplained coughing or wheezing, and ankle swelling. (See Table 1 on page 6 for a list of symptoms.)

This report is based on a comprehensive expert analysis of the medical evidence. There's more information on page 17 and at ConsumerReportsHealth.org/BestBuyDrugs about how we conducted our evaluation.

This report was updated in March 2011.



What Are ACEIs and Who Needs Them?

ACEIs work by blocking an enzyme that leads to the release of a substance called angiotensin, an active hormone, which causes blood vessels to constrict. Thus, ACEIs relax blood vessels throughout the body, thereby lowering blood pressure and reducing the workload on the heart.

If you only have high blood pressure and do not have diabetes or other heart problems, inexpensive, generic diuretics are a good first choice. The evidence is stronger that thiazide diuretics prevent premature death, heart disease, strokes and other cardiovascular problems due to high blood pressure. There have been fewer studies with ACEIs, although the available evidence indicates they are likely just as effective as thiazide diuretics.

However, some people who are already taking a diuretic and are not getting adequate blood pressure control can benefit from adding an ACEI to their regimen. If you fall in that category, your doctor will weigh the relative merits of giving you an ACEI, a beta-blocker, or another type of drug, based on your individual medical circumstances.

ACEIs are often a first choice, however, if you have one or more of the following conditions, with or without high blood pressure:

- Heart failure
- Heart attack (myocardial infarction) or stroke in the past
- Diabetes
- Diabetic kidney disease

Table 1. Heart Failure – Types, Symptoms, and Tests

| Two Types | Symptoms and Tests |
|--|---|
| <p>Systolic heart failure occurs when the heart cannot contract forcefully enough to push enough blood into circulation.</p> <p>Diastolic heart failure occurs when the heart's pumping chambers become stiff, preventing them from filling with enough blood before the heart contracts to push the blood into circulation.</p> <p>In both types, blood coming into the left chamber from the lungs can "back up," causing fluid to leak into the lungs. This condition is called pulmonary edema and is a medical emergency. Heart failure can also cause fluid build up elsewhere in the body. Doctors refer to this as edema.</p> <p>Heart failure (both types) occurs over time, with the heart losing its pumping capacity little by little over years. Thus, it is a chronic disease. The heart compensates at first – by enlarging or pumping faster, for example. This can mask the condition. But over time, the heart loses its capacity to compensate, and symptoms develop.</p> | <ul style="list-style-type: none"> - Fatigue - Shortness of breath on exertion - Difficulty breathing - Wheezing - Frequent coughing (especially at night) - Swollen ankles - Unexplained weight gain - Bulging neck veins <p>Ask your doctor to check for heart failure if you have any of these symptoms and they can not be explained by other causes.</p> <p>A test called an echocardiogram measures the pumping capacity of the heart and can detect thickening of the wall of the heart and heart failure.</p> |

Sources: *Guide to a Healthy Heart*, Consumer Reports on Health, Consumers Union, (2007); American Heart Association

The Basics on High Blood Pressure

Americans' health could be markedly improved if they were more alert to the dangers of high blood pressure and the need to have their blood pressure checked regularly.

Blood pressure is the force exerted upon the wall of the arteries when blood is pumped out of the heart. It's measured in millimeters of mercury (abbreviated as mm Hg) and the measurement consists of two numbers. One number, usually given first, is the pressure when the heart contracts. That's called the systolic pressure. The second number is the pressure when the heart is at rest. That's called the diastolic pressure. Your doctor may say or present them, for example, as "120 over 80" or 120/80 mm Hg.

Both the systolic and diastolic pressure are important. High blood pressure – the causes of which are not well understood – is defined, for adults, as a systolic pressure of 140 mm Hg or greater and/or a diastolic pressure of 90 mm Hg or greater. Normal blood pressure is defined as a systolic reading of less than 120 mm Hg and a diastolic reading of less than 80 mm Hg.

That leaves a gap between "normal" and "high." If your blood pressure rates fall into that gap, the condition is called "prehypertension," and based on recent studies, you are at risk of developing high blood pressure and you already have some elevated risk of heart disease and stroke. So, it's important for your health to lower your blood pressure. Table 2, on page 8, presents these levels of blood pressure and general treatment guidance. If your blood pressure levels are prehypertensive and you have heart disease, kidney disease, or diabetes, you may need drug treatment to lower your blood pressure.

Note: Both numbers – systolic and diastolic – don't have to be high at the same time, and often are not. Even if only one is elevated, you are considered to have high blood pressure. Indeed, in people aged 50 and over, a high systolic reading appears to be much more strongly linked to a higher risk of heart disease and heart attack than a high diastolic blood pressure reading.

High blood pressure's relationship to stress, anxiety, nervousness, or feeling tense is often misunderstood. Feeling excited, anxious, or fearful can indeed raise blood pressure, but usually only temporarily – due to the surge of adrenaline that often accompanies these feelings. But those are not symptoms of high blood pressure. You can be a calm, relaxed person who never gets anxious or fearful and still have high blood pressure. And you will probably not have any indications that anything is wrong. Most of the time, people don't have any noticeable symptoms that their blood pressure is high, so the only reliable way to detect the condition is to have your blood pressure checked regularly using a blood pressure arm cuff (go to [ConsumerReportsHealth.org](https://www.ConsumerReportsHealth.org) for more information and Ratings of blood pressure monitors).

In particular, ACEIs have become a cornerstone of treatment for heart failure. They effectively – sometimes dramatically – slow the progression of the condition. Selected ACEIs are also now commonly used in people whose kidneys are failing due to diabetes. Indeed, evidence is emerging that ACEIs may prevent the decline of kidney function in people with diabetes and are being routinely prescribed for most diabetics.

People who have one or more of the conditions listed on page 6 may also benefit from taking a beta-blocker in addition to an ACEI. Both classes of drugs have been proven to be protective to the heart, and they can act together to lower your risk of a heart attack, stroke, or death. Our beta-blocker report can be obtained at ConsumerReportsHealth.org/BestBuyDrugs.

Table 2. Blood Pressure Levels and Treatment Guidance

| Blood Pressure Classification | Systolic Measure (mm Hg) | Diastolic Measure (mm Hg) | General Treatment Guidance |
|-------------------------------|--------------------------|---------------------------|--|
| Normal | Below 120 | Below 80 | <ul style="list-style-type: none"> ■ No treatment needed ■ Healthy lifestyle encouraged to maintain normal blood pressure |
| Prehypertension | 120-139 | 80-89 | <ul style="list-style-type: none"> ■ Lifestyle changes needed: weight loss, quitting smoking, low-salt and low-fat diet, curb excessive alcohol use, and increased exercise ■ Drug treatment <i>not</i> needed except if you have diabetes, kidney, or heart disease |
| Stage 1 High Blood Pressure | 140-159 | 90-99 | <ul style="list-style-type: none"> ■ Lifestyle changes needed, same as above ■ Drug treatment needed. Doctor may start with one medicine (usually a diuretic) to see if it works. |
| Stage 2 High Blood Pressure | 160 or above | 100 or above | <ul style="list-style-type: none"> ■ Contact your doctor immediately ■ Drug treatment needed. Two or more medicines usually required to bring blood pressure down ■ Lifestyle changes, as described above, are a critical component of your treatment |

Source: Chobanian AV, Bakris GL, Black HR, et al., "The seventh report of the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure," *Journal of the American Medical Association*, 2003; 289(19):2560-2572

Choosing an ACEI – Our *Best Buy* Picks

Choosing an ACEI depends on what it is being used to treat. Studies show that some ACEIs are more effective and safer than others for certain conditions. If you have two or more of the medical conditions we discuss below, or others, your doctor will make a judgment about which ACEI and dose is best for you.

The information in this report will help you talk to your doctor about which ACEI is right for you, and which may cost you the least money out-of-pocket.

People respond to the various ACEIs differently, meaning that one may be more effective than another for you. So you may have to try more than one if your doctor determines that the one you were initially prescribed is not working well. In addition, ACEIs can have side effects and you may tolerate one drug better than another. Side effects include dizziness, fatigue, weakness, a persistent dry cough, and a condition called angioedema. Angioedema – facial, lip, or throat swelling that can close off the wind pipe – is rare but can be life-threatening. It is more common in African-Americans. ACEIs can also increase your blood potassium levels, so your doctor should monitor this, especially if you are taking other medicines that can increase potassium (certain diuretics, lithium, nonsteroidal anti-inflammatory drugs, and potassium supplements).

Starting with as low a dose of an ACEI as possible can reduce the risk of side effects. That can be an important factor for people with heart failure, who often are prescribed higher doses of ACEIs. If the side effects persist, you may want to talk with your doctor about trying a different ACEI.

You and your doctor should choose an ACEI based primarily on its record in reducing heart attacks, strokes, and preventing the progression of heart disease and failure, coronary artery disease, and kidney disease. Where the evidence is equivocal, cost may be a deciding factor, especially if you do not have drug coverage under a health insurance plan. The monthly cost of ACEIs varies from \$10 or less to about \$50 for most generics to more than \$100 for some brand-name versions.

For many people, the convenience of once-a-day dosing also may be important. An advantage in using a drug proven to prevent serious events—such as heart attacks, strokes, and death from one of these causes—is that your doctor will (or should) know what dosage of the drug has been shown to save lives.

Ramipril (Altace) and captopril (Capoten) have the strongest evidence across various medical conditions in that regard. But several other ACEIs have been proven to preserve health and reduce deaths in at least one condition. (See Table 3 on page 10). Evidence is more limited for fosinopril (Monopril), moexipril (Univasc), perindopril (Aceon), and quinapril (Accupril).

Taking effectiveness, safety, dosing convenience, and cost into account, we have selected the following ACEIs (at all doses listed) as *Consumer Reports Health Best Buy Drugs* for these medical conditions:

- *For high blood pressure:* benazepril, enalapril, and lisinopril
- *For heart failure:* captopril, and enalapril
- *After a heart attack:* lisinopril
- *For diabetics:* ramipril
- *For people with kidney disease:* benazepril, and ramipril

All of these medicines are low-cost or moderately-priced generics. All have been proven to be just as effective or *superior* to other ACEIs. There is no reason to take the brand-name versions of these medicines.

Treating high blood pressure. All 10 ACEIs are approved by the FDA to treat high blood pressure. All are effective for this purpose; studies do not indicate that any one ACEI is better than any other in lowering blood pressure.

As mentioned earlier, thiazide diuretics are generally a better first choice than ACEIs for people with high blood pressure alone. However, ACEIs are prescribed frequently as a second drug for people who have high-

ly elevated blood pressure or whose blood pressure has failed to be lowered by a single drug. But no studies indicate that any ACEI is better for that than any other.

Thus, if you have high blood pressure but no other heart condition, any ACEI can help when used in combination with another class of high blood pressure drugs (such as a diuretic).

Our choice of three *Best Buy* ACEIs for high blood pressure – **benazepril**, **enalapril**, and **lisinopril** – is based on cost and dosing convenience. All are relatively low-cost generics and need to be taken just once a day. There is no reason to take the more expensive brand-name version of any of these medicines, other brand-name ACEIs, or their somewhat more expensive generic drugs.

Treating heart failure. Evidence supports seven ACEIs in the treatment of heart failure, with the strongest evidence for four – captopril, enalapril, ramipril, and trandolapril (See Table 3, below.) No studies indicate a clear advantage for any one of

these four over the others in slowing the progression of heart failure or improving the quality of life. On the basis of cost and dosing convenience, we have chosen generic **enalapril** as the *Best Buy* drug for people with early or mild heart failure. This drug costs \$8 to \$15 a month for once a day dosing.

As indicated above, people with heart failure, especially as it worsens, may require higher doses or multiple daily doses of an ACEI. Enalapril is frequently prescribed at higher doses and is still a good value at twice daily dosing. But captopril has an advantage for some people with heart failure. It has a quick onset and short duration of action; this benefits frail patients with more severe heart failure. It's also why captopril needs to be taken three times a day. The \$19 to \$54 per month cost for three daily doses is a good value for such patients. For that reason we have chosen **captopril** as a *Best Buy* for people who need more frequent dosing.

After a heart attack. Evidence supports four ACEIs in the treatment of people after a heart attack –

Table 3. Summary of Evidence on the Effectiveness of the ACEIs

| Drug (Generic Name) | People With Heart Failure | | People Who Have Had a Heart Attack | People Who Have Diabetes and Other Heart Risk Factors | | People With Kidney Disease | |
|---------------------------|------------------------------|-------------------------------|--|---|------------------|--|---|
| | Reduce Deaths | Improve Quality of Life | Reduce Deaths | Reduce Risk of Heart Attack or Stroke | Reduce Deaths | Reduce Risk of Heart Attack or Stroke | Prevent Decline in Kidney Function, Kidney Failure, and/or Reduce Deaths |
| Benazepril | + | | | | | | ++ |
| Captopril | ++ | ++ | ++ | ++ | | | ++ |
| Enalapril | ++ | ++ | | + | | ++ | |
| Fosinopril | | ++ | | | | | |
| Lisinopril | + | ++ | ++ | ++ | | | |
| Moexipril | | | | | | | |
| Perindopril | | | 0 | ++ | 0 | | |
| Quinapril | | | | | 0 | | ++ |
| Ramipril | ++ | ++ | ++ | ++ | ++ | ++ | ++ |
| Trandolapril | ++ | ++ | ++ | ++ | | | |

++ good evidence for effectiveness + probably effective 0 probably not effective

captopril, lisinopril, ramipril, and trandolapril. All help lower the risk of a repeat heart attack, heart failure, and death. Based on the studies to date, none of these four seems to have a clear advantage over the others in either effectiveness or safety.

Taking cost and dosing convenience into account, we have chosen generic **lisinopril** as the *Best Buy* drug for most people who need an ACEI after a heart attack.

For people with diabetes. Studies show that five ACEIs are effective at substantially lowering the risk of heart attacks and strokes in people with diabetes. (See Table 3, page 10.) Most studies have been done in people who also have other risk factors for heart disease as well as diabetes – such as elevated cholesterol, being a smoker, or being overweight.

But only one ACEI – **ramipril**– has been shown so far to reduce premature deaths among people with

diabetes who have other heart disease risk factors. Despite its higher cost (\$36 to \$39 a month) relative to some of the other generic ACEIs, we have chosen it as a *Best Buy* drug for diabetics because of this superior effectiveness.

Treating kidney disease. Studies show that five ACEIs are effective at preventing a decline in kidney function or lowering the risk of heart disease or stroke, or both. All are acceptable choices. The strongest evidence is for benazepril, captopril, and ramipril, however.

On this basis, and taking dosing convenience and cost into consideration, we have chosen generic **benazepril** as the *Best Buy* drug for people with declining kidney function who do not have diabetes. **Ramipril** is the preferred drug and *Best Buy* for people with diabetes who have declining kidney function, as indicated above.

Table 4. ACEI Cost Comparison and *Best Buy* Indication

Note: If the price box contains a , that indicates the dose of that drug is available for a low monthly cost through programs offered by large chain stores. For example, Kroger, Sam's Club, Target, and Walmart offer a month's supply of selected generic drugs for \$4 or a three-month supply for \$10. Other chain stores, such as Costco, CVS, Kmart, and Walgreens, offer similar programs. Some programs have restrictions or membership fees, so check the details carefully for restrictions and to make sure your drug is covered.

| | Generic name, dosage strength and form | Brand Name ^A | Frequency of Use (per day) ^B | Total daily dose | Average Monthly Cost ^C | <i>Best Buy</i> Indication |
|---|--|-------------------------|---|------------------|--|---|
| | Benazepril 10 mg tablet | Lotensin | One | 10 mg | \$76 | |
|  | Benazepril 10 mg tablet | Generic | One | 10 mg | \$8  | High blood pressure, for people with kidney disease |
| | Benazepril 20 mg tablet | Lotensin | One | 20 mg | \$69 | |
|  | Benazepril 20 mg tablet | Generic | One | 20 mg | \$8  | High blood pressure, for people with kidney disease |
| | Benazepril 40 mg tablet | Lotensin | One | 40 mg | \$69 | |
|  | Benazepril 40 mg tablet | Generic | One | 40 mg | \$7  | High blood pressure, for people with kidney disease |
|  | Captopril 12.5 mg tablet | Generic | Three | 37.5 mg | \$21  | Heart failure |
|  | Captopril 25 mg tablet | Generic | | 75 mg | \$19  | Heart failure |
|  | Captopril 50 mg tablet | Generic | Three | 150 mg | \$57  | Heart failure |
|  | Captopril 100 mg tablet | Generic | Three | 300 mg | \$54  | Heart failure |
| | Enalapril 5 mg tablet | Vasotec | One | 5 mg | \$91 | |

Table 4. ACEI Cost Comparison and Best Buy Indication (Continued)

| | Generic name, dosage strength and form | Brand Name ^A | Frequency of Use (per day) ^B | Total daily dose | Average Monthly Cost ^C | Best Buy Indication |
|--------------------|--|-------------------------|---|------------------|-----------------------------------|------------------------------------|
| CR BEST BUY | Enalapril 5 mg tablet | Generic | One | 5 mg | \$8 | High blood pressure, heart failure |
| | Enalapril 10 mg tablet | Vasotec | One | 10 mg | \$96 | |
| CR BEST BUY | Enalapril 10 mg tablet | Generic | One | 10 mg | \$8 | High blood pressure, heart failure |
| | Enalapril 20 mg tablet | Vasotec | One | 20 mg | \$134 | |
| CR BEST BUY | Enalapril 20 mg tablet | Generic | One | 20 mg | \$15 | High blood pressure, heart failure |
| | Fosinopril 10 mg tablet | Generic | One | 10 mg | \$29 | |
| | Fosinopril 20 mg tablet | Generic | One | 20 mg | \$26 | |
| | Fosinopril 40 mg tablet | Generic | One | 40 mg | \$29 | |
| | Lisinopril 5 mg tablet | Prinivil | One | 5 mg | \$41 | |
| | Lisinopril 5 mg tablet | Zestril | One | 5 mg | \$53 | |
| CR BEST BUY | Lisinopril 5 mg tablet | Generic | One | 5 mg | \$7 | Heart attack, high blood pressure |
| | Lisinopril 10 mg tablet | Prinivil | One | 10 mg | \$46 | |
| | Lisinopril 10 mg tablet | Zestril | One | 10 mg | \$57 | |
| CR BEST BUY | Lisinopril 10 mg tablet | Generic | One | 10 mg | \$6 | Heart attack, high blood pressure |
| | Lisinopril 20 mg tablet | Prinivil | One | 20 mg | \$48 | |
| | Lisinopril 20 mg tablet | Zestril | One | 20 mg | \$57 | |
| CR BEST BUY | Lisinopril 20 mg tablet | Generic | One | 20 mg | \$7 | Heart attack, high blood pressure |
| CR BEST BUY | Lisinopril 30 mg tablet | Generic | One | 30 mg | \$18 | Heart attack, high blood pressure |
| | Lisinopril 40 mg tablet | Zestril | One | 40 mg | \$85 | |
| CR BEST BUY | Lisinopril 40 mg tablet | Generic | One | 40 mg | \$17 | Heart attack, high blood pressure |
| | Moexipril 7.5 mg tablet | Univasc | One | 7.5 mg | \$74 | |
| | Moexipril 7.5 mg tablet | Generic | One | 7.5 mg | \$32 | |
| | Moexipril 15 mg tablet | Univasc | One | 15 mg | \$89 | |
| | Moexipril 15 mg tablet | Generic | One | 15 mg | \$32 | |
| | Perindopril 2 mg tablet | Aceon | One | 2 mg | \$92 | |
| | Perindopril 2 mg tablet | Generic | One | 2 mg | \$51 | |
| | Perindopril 4 mg tablet | Aceon | One | 4 mg | \$99 | |
| | Perindopril 4 mg tablet | Generic | One | 2 mg | \$54 | |

Table 4. ACEI Cost Comparison and Best Buy Indication (Continued)

| Generic name, dosage strength and form | Brand Name ^A | Frequency of Use (per day) ^B | Total daily dose | Average Monthly Cost ^C | Best Buy Indication |
|--|-------------------------|---|------------------|--|--|
| Perindopril 8 mg tablet | Aceon | One | 8 mg | \$111 | |
| Perindopril 8 mg tablet | Generic | One | 2 mg | \$63 | |
| Quinapril 10 mg tablet | Accupril | One | 10 mg | \$70 | |
| Quinapril 10 mg tablet | Generic | One | 10 mg | \$24  | |
| Quinapril 20 mg tablet | Accupril | One | 20 mg | \$69 | |
| Quinapril 20 mg tablet | Generic | One | 20 mg | \$23  | |
| Quinapril 40 mg tablet | Accupril | One | 40 mg | \$70 | |
| Quinapril 40 mg tablet | Generic | One | 40 mg | \$24  | |
|  Ramipril 1.25 mg capsule | Generic | One | 1.25 mg | \$36 | For people with diabetes or kidney disease |
| Ramipril 2.5 mg capsule | Altace | One | 2.5 mg | \$87 | |
|  Ramipril 2.5 mg capsule | Generic | One | 2.5 mg | \$36 | For people with diabetes or kidney disease |
| Ramipril 5 mg capsule | Altace | One | 5 mg | \$90 | |
|  Ramipril 5 mg capsule | Generic | One | 5 mg | \$36 | For people with diabetes or kidney disease |
| Ramipril 10 mg capsule | Altace | One | 10 mg | \$101 | |
|  Ramipril 10 mg capsule | Generic | One | 10 mg | \$39 | For people with diabetes or kidney disease |
| Trandolapril 1 mg tablet | Mavik | One | 1 mg | \$53 | |
| Trandolapril 1 mg tablet | Generic | One | 1 mg | \$35 | |
| Trandolapril 2 mg tablet | Mavik | One | 2 mg | \$52 | |
| Trandolapril 2 mg tablet | Generic | One | 2 mg | \$35  | |
| Trandolapril 4 mg tablet | Mavik | One | 4 mg | \$58 | |
| Trandolapril 4 mg tablet | Generic | One | 4 mg | \$32  | |

- A. "Generic" indicates that this drug is sold under its generic name. For example, in this table, the first drug listed is available as both generic benazepril and as brand-name Lotensin. Both have the same active ingredient. When column 2 says "generic," the price listed is for the generic version at the specified dose.
- B. Depending on your health conditions, symptoms and response to the medicine, your doctor may adjust your dose to be either higher or lower than what we've stated in this price chart.
- C. Prices reflect nationwide retail average for January 2011, rounded to the nearest dollar. Information derived by *Consumer Reports Health Best Buy Drugs* from data provided by Wolters Kluwer Pharma Solutions, which is not involved in our analysis or recommendations.

The Evidence

This section presents more information on the effectiveness and safety of ACEIs.

This report is based on an analysis of the scientific evidence on ACEIs. More than 6,000 studies either published in the peer-reviewed medical literature (worldwide) or submitted by pharmaceutical companies were identified and screened. From these studies, the analysis focused on 144 meeting a set of strict criteria. Most of these were controlled clinical trials or “meta-analyses” of multiple clinical trials. A meta-analysis study combines the results of previous individual studies and tries to draw conclusions based on all of them.

How Effective Are ACEIs?

ACEIs are highly effective medicines. A substantial body of evidence indicates that they improve quality of life and prevent both non-fatal and fatal heart attacks and strokes in a fairly wide range of patients with high blood pressure, heart disease, diabetes, and kidney disease.

Unfortunately, no large-scale studies have been specifically designed to compare the ACEIs to each other in term of either effectiveness or safety. However, many studies evaluating various treatment regimens and combinations for high blood pressure, heart disease, and diabetes have included one or more ACEIs.

Overall, such studies have yielded mixed results for ACEIs compared to other medicines. Some show ACEIs to be superior and other studies have found no advantage for ACEIs. Notably, a study published in 2003 (known as the Second Australian National Blood Pressure Study) indicated that ACEIs were superior to diuretics in preventing heart attacks, strokes, and deaths among older men with high blood pressure. Another, more recent study found that an ACEI (perindopril) combined with a drug called amlodipine (a calcium channel blocker) was superior to a regimen of a beta-blocker and a diuretic in preventing heart attacks and strokes in people with high blood pressure. But several other well-done studies have found diuretics to be better in people of all ages, either alone or combined with a beta-blocker, ACEI,

or calcium channel blocker. A 2009 Cochrane Review of first-line high blood pressure medications that included 24 trials found that there was stronger evidence for the benefit of diuretics but that ACEIs were likely just as effective.

A heated debate in the medical community over these divergent results has been underway for several years, and is expected to continue. Your doctor will likely be aware of that debate and he or she may well have an opinion about the studies.

If you have significantly elevated blood pressure and one or more other heart conditions, this debate may be of interest to you. You should talk with your doctor about the best combination of drugs for you. *Using the right drugs at the right doses can be an issue of life and death for you.* Unfortunately, it is not possible yet to say with certainty what the best combination of heart drugs is for many people who have several heart ailments.

Some of the strongest evidence for the benefit of ACEIs is from studies in people with heart failure, or of ACEI use to slow the progression of heart failure. Most studies show a clear case for the drug versus placebo. And about a dozen trials have compared one ACEI to another in the treatment of heart failure. The majority of these studies do not find a superiority of one ACEI over another. However, the evidence is stronger for some ACEIs than others, as addressed earlier in the *Best Buy Picks* section.

How Safe Are ACEIs?

ACEIs are generally safe medicines, with some in widespread use for more than 20 years. They have not been shown to cause any serious long-term or irreversible negative consequences, even after many years of use.

As with most medicines, ACEIs can cause some annoying side effects. The most common of these is an irritating dry cough, which may be quite persistent. It usually occurs within a month of starting an ACEI. If it persists, talk to your doctor about switching to another ACEI or even a medication in another class.

Most of the other side effects occur less commonly. These include dizziness, excessively low blood pressure, fatigue, headache, high blood levels of potassium, loss of taste, nausea, renal failure, and swollen ankles.

Though rare, ACEIs can also cause swelling involving the face, tongue, lips, and larynx. This is called angioedema and is a potentially life-threatening complication if it closes off the larynx. The risk of this side effect appears to be higher in African-Americans.

All ACEIs can also cause birth defects and should not be used by women who are pregnant.

There is no clear evidence that any one ACEI has more or fewer side effects than the others. The risk of all the ACEI-triggered side effects is greater for people who take an ACE inhibitor in addition to another medication for high blood pressure, such as a diuretic. If side effects persist, talk to your doctor about adjusting your dose of one or more medicines.

People who take multiple medicines are more likely to discontinue taking them, too, due to side effects.

You should never stop taking your blood pressure medicines without consulting your doctor, as it can be dangerous.

All people taking ACEIs should have periodic blood tests to make sure they do not have elevated levels of potassium in their blood and that their kidneys are processing the drug effectively. People who take lithium, nonsteroidal anti-inflammatory drugs, potassium supplements, or potassium-sparing diuretics (such as eplerenone, spironolactone, and triamterene) are at higher risk of developing these complications.

Age, Race, and Gender Differences

As cited above, one study has indicated that a specific ACEI may be selectively effective in older people. But it is too premature to say whether all ACEIs as a class of medicine are more effective or safer among older people than other blood pressure and heart medicines.

ACEIs may, however, be somewhat less effective in women than in men, studies indicate. But there is no evidence that any one ACEI has an advantage over any other among women.

ACEIs appear to be as effective in African-Americans as in other population groups. But African-Americans may need to take higher doses of ACEIs than caucasians, or use them in combination with a diuretic, to achieve a similar clinical benefit. Ramipril is one of the few drugs in any class proven to improve long-term outcomes in a trial conducted exclusively in African-Americans. The trial showed that ramipril reduced the risk of end-stage renal disease and death in patients with kidney disease.

Talking With Your Doctor

It's important for you to know that the information we present in this report is not meant to substitute for a doctor's judgment. But we hope it will help your doctor and you arrive at a decision about which ACEI drug and dosage is best for you.

Bear in mind that many people are reluctant to discuss the cost of medicines with their doctors and that studies show doctors do not routinely take price into account when prescribing medicines. Unless you bring it up, your doctors may assume that cost is not a factor for you.

Many people (including many physicians) also believe that newer drugs are always or almost always better. While that's a natural assumption to make, the fact is that it's not true. Studies consistently show that many older medicines are as good as, and in some cases better than, newer medicines. Think of them as "tried and true," particularly when it comes to their safety record. Newer drugs have not yet met the test of time, and unexpected problems can and do crop up once they hit the market.

Of course, some newer prescription drugs are indeed more effective and safer. Talk with your doctor about the pluses and minuses of newer versus older medicines, including generic drugs.

Prescription medicines go "generic" when a company's patents on a drug expires, usually after about 12 to 15 years from when a drug is put on the market. At that point, other companies can make and sell the drug.

Generics are almost always much less expensive than newer brand name medicines, but they are not lesser-quality drugs. Indeed, most generics remain useful medicines even many years after first being marketed. That is why today more than half of all prescriptions in the U.S. are for generics.

Another important issue to talk with your doctor about is keeping a record of the drugs you are taking. There are several reasons for this:

- First, if you see several doctors, they may not always tell each other which drugs have been prescribed for you.
- Second, it is very common for doctors today to prescribe several medicines for you before finding one that works well or best, mostly because people vary in their response to prescription drugs.
- Third, more and more people today take several prescription medications, nonprescription drugs, and dietary supplements all at the same time. Many of these interact in ways that can be very dangerous.
- And fourth, the names of prescription drugs—both generic and brand—are often hard to pronounce and remember.

For all these reasons, it's important to keep a list of the drugs you are taking, both prescription and nonprescription, and include dietary supplements.

Always be sure, too, that you understand the dose of the medicine being prescribed for you and how many pills you are expected to take each day. Your doctor should tell you this information. When you fill a prescription at the pharmacy, or if you get it by mail, you may want to check to see that the dose and the number of pills per day on the pill bottle match the amounts that your doctor told you.

How We Conducted Our Review of the ACEIs

Our evaluation is based in large part on an independent review of the scientific evidence on the effectiveness, safety, and adverse effects of ACEIs. A team of physicians and researchers at Oregon Health & Science University Evidence-based Practice Center conducted the analysis. A consultant to *Consumer Reports Health Best Buy Drugs* is also a member of the Oregon-based research team, which has no financial interest in any pharmaceutical company or product.

The prescription drug costs we cite were obtained from a healthcare information company that tracks the sales of prescription drugs in the U.S. Prices for a drug can vary quite widely, even within a single city or town. All the prices in this report are national averages based on sales of prescription drugs in retail outlets. They

reflect the cash price paid for a month's supply of each drug in January 2011, except where noted otherwise.

Consumers Union and *Consumer Reports* selected the *Best Buy Drugs* using the following criteria. The drug had to:

- Be as effective or more effective than other ACEIs
- Have a safety record equal to or better than other ACEIs
- Cost roughly the same or less than other ACEIs

The *Consumer Reports Health Best Buy Drugs* methodology is described in more detail in the methods section at ConsumerReportsHealth.org/BestBuyDrugs.

About Us

Consumers Union, publisher of *Consumer Reports*[™] magazine, is an independent and non-profit organization whose mission since 1936 has been to provide consumers with unbiased information on goods and services and to create a fair marketplace. Consumers Union's main Web site is ConsumersUnion.org. The magazine's Web site is ConsumerReports.org. Our new health Web site is ConsumerReportsHealth.org.

Consumer Reports Health Best Buy Drugs[™] is a public education project administered by Consumers Union. It is partially grant funded. Principal current outside funding comes from the state Attorney General Consumer and Prescriber Education Grant Program, which is funded by the multi-state settlement of consumer fraud claims regarding the marketing of the prescription drug Neurontin.

The Engelberg Foundation provided a major grant to fund the creation of the project from 2004 to 2007. Additional initial funding came from the National Library of Medicine, part of the National Institutes of Health.

These materials are made possible from the state Attorney General Consumer and Prescriber Education Grant Program, which is funded by the multi-state settlement of consumer fraud claims regarding the marketing of the prescription drug Neurontin. A more detailed explanation of the project is available at ConsumerReportsHealth.org.

Sharing this Report

This report should not be viewed as a substitute for a consultation with a medical or health professional. The information is meant to enhance communication with your doctor, not replace it. Use of our drug reports is also at your own risk. Consumers Union cannot be liable for any loss, injury, or other damages related to your use of this report.

You should not make any changes in your medicines without first consulting a physician.

We followed a rigorous editorial process to ensure that the information in this report and on the *Consumer Reports Health Best Buy Drugs* Web site is accurate and describes generally accepted clinical practices. If we find, or are alerted to, an error, we will correct this as quickly as possible. However, Consumer Reports and its authors, editors, publishers, licensors, and any suppliers cannot be responsible for medical errors or omissions, or any consequences from the use of the information on this site.

Your use of this report is also subject to our User Agreement available at ConsumerReportsHealth.org/BestBuyDrugs. The reports are intended solely for your personal, noncommercial use and may not be used in advertising, promotion, or for any other commercial purpose. You are free to download, copy, and distribute the reports for individual and family use. You may not modify or create derivative works from the text of the reports, however, or remove any copyright or trademark notices. Any organization interested in broader distribution of this or any of our reports in print or on the Internet should contact us at crbestbuydrugs@cu.consumers.org. All quotes from the reports should cite *Consumer Reports Health Best Buy Drugs*[™] as the source. *Consumer Reports Health Best Buy Drugs*[™], Consumers Union[®] and *Consumer Reports*[®] are trademarks of Consumers Union of U.S., Inc.

© 2011 Consumers Union of United States, Inc.

References

1. Adalet K, Nalbantgil I, Kiliccioglu B, Koylan N, Bugra Z, Adalet I, et al. Multicenter double blind comparative trial with benazepril versus captopril in the treatment of mild to moderate hypertension. *Med Bull Istanbul Med Faculty* 1995;28(2):1-9.
2. Anonymous. Effect of ramipril on mortality and morbidity of survivors of acute myocardial infarction with clinical evidence of heart failure. The Acute Infarction Ramipril Efficacy (AIRE) Study Investigators. *Lancet* 1993;342(8875):821-8.
3. Anonymous. ISIS-4: a randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. [see comments]. *Lancet* 1995;345(8951):669-85.
4. Anonymous. Six-month effects of early treatment with lisinopril and transdermal glyceryl trinitrate singly and together withdrawn six weeks after acute myocardial infarction: the GISSI-3 trial. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico. [see comments]. *J Am Coll Cardiol* 1996;27(2):337-44.
5. Anonymous. Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 39. UK Prospective Diabetes Study Group. [see comments]. *British Medical Journal* 1998;317(7160):713-20.
6. Anonymous. Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomised, double-blind, placebo-controlled, multicentre trial (the EUROPA study). *Lancet*. 2003;362(September 6):782-88.
7. Brown NJ, Ray WA, Snowden M, Griffin MR. Black Americans have an increased rate of angiotensin converting enzyme inhibitor-associated angioedema. *Clinical Pharmacology & Therapeutics* 1996;60(1):8-13.
8. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, Jr., et al. The seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *JAMA* 2003;289:2560-2572.
9. Cleland JG, Erhardt L, Murray G, Hall AS, Ball SG. Effect of ramipril on morbidity and mode of death among survivors of acute myocardial infarction with clinical evidence of heart failure. A report from the AIRE Study Investigators. [see comments]. *Eur Heart J* 1997;18(1):41-51.
10. Domanski MJ, Exner DV, Borkowf CB, Geller NL, Rosenberg Y, Pfeiffer MA. Effect of angiotensin converting enzyme inhibition on sudden cardiac death in patients following acute myocardial infarction: A meta-analysis of randomized clinical trials. *J Am Coll Cardiol* 1999;33(3):598-604.
11. Foy SG, Crozier IG, Turner JG, Richards AM, Frampton CM, Nicholls MG, et al. Comparison of enalapril versus captopril on left ventricular function and survival three months after acute myocardial infarction (the "PRACTICAL" study). *Am J Cardiol* 1994;73(16):1180-6.
12. Franzosi MG. Indications for ACE inhibitors in the early treatment of acute myocardial infarction: Systematic overview of individual data from 100 000 patients in randomized trials. *Circulation* 1998;97(22):2202-2212.
13. Furberg CD, Wright Jr JT, Davis BR, Cutler JA, Alderman M, Black H, et al. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT). *JAMA* 2002;288(23):2981-2997.
14. Giles TD, Fisher MB, Rush JE. Lisinopril and captopril in the treatment of heart failure in older patients. Comparison of a long- and short-acting angiotensin-converting enzyme inhibitor. *Am J Med* 1988;85(3B):44-7.
15. Giles TD, Katz R, Sullivan JM, Wolfson P, Haugland M, Kirlin P, et al. Short- and long-acting angiotensin-converting enzyme inhibitors: a randomized trial of lisinopril versus captopril in the treatment of congestive heart failure. The Multicenter Lisinopril-Captopril Congestive Heart Failure Study Group. [see comments]. *J Am Coll Cardiol* 1989;13(6):1240-7.
16. Gomma AH, Fox KM. The EUROPA trial: design, baseline demography and status of the sub-studies. *Cardiovasc Drugs Ther* 2001;15(2):169-79.

17. Hansson L, Lindholm LH, Ekblom T, Dahlöf B, Lanke J, Schersten B, et al. Randomised trial of old and new antihypertensive drugs in elderly patients: Cardiovascular mortality and morbidity the Swedish trial in old patients with hypertension-2 study. *Lancet* 1999;354(9192):1751-1756.
18. Hansson L, Lindholm LH, Niskanen L, Lanke J, Hedner T, Niklason A, et al. Effect of angiotensin-converting-enzyme inhibition compared with conventional therapy on cardiovascular morbidity and mortality in hypertension: the Captopril Prevention Project (CAPPP) randomised trial. [see comments]. *Lancet* 1999;353(9153):611-6.
19. Hunt SA, Baker DW, Chin MH, Cinquegrani MP, Feldman AM, Francis GS, et al. ACC/AHA guidelines for the evaluation and management of chronic heart failure in the adult. American College of Cardiology Web site 2001; http://www.acc.org/clinical/guidelines/failure/hf_index.htm.
20. Jafar TH, Schmid CH, Landa M, Giatras I, Toto R, Remuzzi G, et al. Angiotensin-converting enzyme inhibitors and progression of nondiabetic renal disease. A meta-analysis of patient-level data.[comment][erratum appears in *Ann Intern Med* 2002 Aug 20;137(4):299]. *Ann Int Med* 2001;135(2):73-87.
21. Lau CP, Tse HF, Ng W, Chan KK, Li SK, Keung KK, et al. Comparison of perindopril versus captopril for treatment of acute myocardial infarction. *Am J Cardiol* 2002;89(2):150-4.
22. MacMahon S, Sharpe N, Gamble G, Clague A, Mhurchu CN, Clark T, et al. Randomized, placebo-controlled trial of the angiotensin-converting enzyme inhibitor, ramipril, in patients with coronary or other occlusive arterial disease. PART-2 Collaborative Research Group. Prevention of Atherosclerosis with Ramipril. *J Am Coll Cardiol* 2000;36(2):438-43.
23. Mann JF, Gerstein HC, Yi QL, Lonn EM, Hoogwerf BJ, Rashkow A, et al. Development of renal disease in people at high cardiovascular risk: results of the HOPE randomized study. *J Am Soc Nephrol* 2003;14(3):641-7.
24. Marre M, Lievre M, Chatellier G, Mann JF, Passa P, J MA, et al. Effects of low dose ramipril on cardiovascular and renal outcomes in patients with type 2 diabetes and raised excretion of urinary albumin: randomised, double blind, placebo controlled trial (the DIABHY-CAR study). *British Medical Journal* 2004;328(7438):28.
25. Moya LA, Pfeffer MA, Wun CC, Davis BR, Geltman E, Hayes D, et al. Uniformity of captopril benefit in the SAVE Study: subgroup analysis. *Eur Heart J* 1994;15(Suppl B):2-8; discussion 26-30.
26. Neal B, MacMahon S, Chapman N, Cutler J, Fagard R, Whelton P, et al. Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: Results of prospectively designed overviews of randomised trials. *Lancet* 2000;356(9246):1955-1964.
27. Packer M, Lee WH, Yushak M, Medina N. Comparison of captopril and enalapril in patients with severe chronic heart failure. *N Engl J Med* 1986;315(14):847-53.
28. Pfeffer MA, Braunwald E, Moya LA, Basta L, Brown EJ, Jr., Cuddy TE, et al. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction. Results of the survival and ventricular enlargement trial. The SAVE Investigators. *N Engl J Med* 1992;327(10):669-77.
29. Pitt B, O'Neill B, Feldman R, Ferrari R, Schwartz L, Mudra H, et al. The QUinapril Ischemic Event Trial (QUIET): evaluation of chronic ACE inhibitor therapy in patients with ischemic heart disease and preserved left ventricular function. *Am J Cardiol* 2001;87(9):1058-63.
30. Psaty BM, Lumley T, Furberg CD, Schellenbaum G, Pahor M, Alderman MH, et al. Health outcomes associated with various antihypertensive therapies used as first-line agents: a network meta-analysis. *JAMA* 2003;289(19):2534-44.
31. Ravid M, Lang R, Rachmani R, Lishner M. Long-term renoprotective effect of angiotensin-converting enzyme inhibition in non-insulin-dependent diabetes mellitus. A 7-year follow-up study. [see comments]. *Arch Intern Med* 1996;156(3):286-9.
32. Ruggenenti P, Perna A, Mosconi L, Matalone M, Garini G, Salvadori M, et al. Randomised placebo-controlled trial of effect of ramipril on decline in glomerular filtration rate and risk of terminal renal failure in proteinuric, non-diabetic nephropathy. *Lancet* 1997;349(9069):1857-1863.
33. Ryan TJ, Antman EM, Brooks NH, Califf RM, Hillis LD, Hiratzka LF, et al. ACC/AHA Guidelines for the Management of Patients With Acute Myocardial Infarction: Executive Summary and Recommendations. *Circulation* 2001;100(9):1016-1030.
34. Shekelle PG, Rich MW, Morton SC, Atkinson SW, Tu W, Maglione M, et al. Efficacy of angiotensin-converting enzyme inhibitors and beta-blockers in the management of left ventricular systolic dysfunction according to race, gender, and diabetic status. A meta-analysis of major clinical trials. *J Am Coll Cardiol* 2003;41:1529-1538.
35. Smith SC, Jr., Blair SJ, Bonow RO, Brass LM, Cerqueira MD, Dracup K, et al. AHA/ACC guidelines for preventing heart attack and death in patients with atherosclerotic cardiovascular disease: 2001 update. *Circulation* 2001;104:1577-1579.
36. Steiner SS, Friedhoff AJ, Wilson BL, Wecker JR, Santo JP. Antihypertensive therapy and quality of life: a comparison of atenolol, captopril, enalapril and propranolol. *J Hum Hypertens* 1990;4(3):217-25.
37. Testa MA, Anderson RB, Nackley JF, Hollenberg NK. Quality of life and antihypertensive therapy in men. A comparison of captopril with enalapril. The Quality-of-Life Hypertension Study Group. *N Engl J Med* 1993;328(13):907-13.
38. Wing LM, Reid CM, Ryan P, Beilin LJ, Brown MA, Jennings GL, et al. Second Australian National Blood Pressure Study (ANBP2). Australian Comparative Outcome Trial of ACE inhibitor- and diuretic-based treatment of hypertension in the elderly. Management Committee on behalf of the High Blood Pressure Research Council of Australia. *Clinical & Experimental Hypertension* 1997;19(5-6):779-91.
39. Wing LM, Reid CM, Ryan P, Beilin LJ, Brown MA, Jennings GL, et al. A comparison of outcomes with angiotensin-converting enzyme inhibitors and diuretics for hypertension in the elderly.[comment]. *N Eng J Med* 2003;348(7):583-92.
40. Wright JT, Jr., Bakris G, Greene T, Agodoa LY, Appel LJ, Charleston J, et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. *JAMA* 2002;288(19):2421-31.
41. Wright JT, Jr., Agodoa L, Contreras G, Greene T, Douglas JG, Lash J, et al. Successful blood pressure control in the African American Study of Kidney Disease and Hypertension. *Arch Intern Med* 2002;162(14):1636-43.
42. Wright JM, Musini VM. "First-line drugs for hypertension," *Cochrane Database of Systematic Reviews* 2009, Issue 3. Art. No.: CD001841. DOI: 10.1002/14651858.CD001841.pub2.
43. Yasky J, Verho M, Erasmus TP, Luus HG, Angela M, Grandin L, et al. Efficacy of ramipril versus enalapril in patients with mild to moderate essential hypertension. *Br J Clin Pract* 1996;50(6):302-10.
44. Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. *N Engl J Med* 2000;342(3):145-53.
45. Yusuf S, Gerstein H, Hoogwerf B, Pogue J, Bosch J, Wolfenbuttel BH, et al. Ramipril and the development of diabetes. *JAMA* 2001;286(15):1882-5.