Hypertension Epidemiology and Economic Burden: Refining Risk Assessment To Lower Costs

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INTRODUCTION

Although hypertension affects 29.3 percent of the adult population in the United States, less than 40 percent of people with hypertension have their blood pressure controlled to recommended levels (Ong 2007). Accordingly, over 60 percent of the hypertensive population remains at heightened risk of heart attack, stroke, heart failure, and renal disease. As a result, in 2009, the direct and indirect costs for hypertension in the United States are projected to be $73.4 billion (Lloyd-Jones 2009).

The primary reason to treat high blood pressure is to reduce the risk of serious cardiovascular (CV) and renal events. Elevated blood pressure is an independent risk factor for CV disease (CVD), stroke, congestive heart failure, and chronic renal disease and is associated with increased mortality. Moreover, elevated blood pressure frequently occurs in conjunction with obesity, dyslipidemia, and diabetes, all factors that synergistically increase the risk of serious CV and renal events (Erhardt 2007, Yusuf 2004).

Reducing the economic burden of hypertension will require refining CV risk assessment and tailoring treatment to improve the percentage of patients who achieve recommended blood pressure goals. There is no question that existing antihypertensive medications are effective in lowering blood pressure and in reducing the incidence of major CV events. In large clinical trials, antihypertensive treatment has been found to decrease the incidence of heart attack by 20 percent to 25 percent, of stroke 30 percent to 35 percent, and heart failure by at least 50 percent (Chobanian 2003, Neal 2000, Staessen 2000).

As we enter the era of personalized medicine, improvements in the identification of individuals who are at the highest risk of serious events may allow health care resources to be more efficiently utilized and increase the overall impact of antihypertensive therapy. An approach that is theoretically desirable but has been difficult to implement is to adjust prevention strategies to specific patient risk profiles. This review examines a promising approach to this puzzle in the form of expanding the use of established surrogate markers for target organ damage such as echocardiograms and proteinuria levels to improve standard risk assessment. In addition, emerging markers such as coronary artery calcification scores, B-type natriuretic peptide (BNP), and high-sensitivity C-reactive protein (CRP) are also reviewed.

ABSTRACT

Background: Hypertension (HTN) continues to be a serious public health problem in the United States and is a major risk factor for stroke, heart failure, myocardial infarction, and other serious cardiovascular and renal diseases. Because HTN can be asymptomatic, its detection and control continues to be a challenge. The total economic burden of HTN is estimated at $73.4 billion in 2009.

Objective: To examine the potential prognostic utility of biomarkers to assess hypertension-related cardiovascular risk and their potential impact on treatment in the context of current epidemiology and demographics of HTN.

Summary and conclusions: Although blood pressure control rates among people treated for HTN have increased from 51.3 percent to 63.9 percent over the past five years, there remains a vast unmet need for improved efficiency and effectiveness in diagnosis and treatment. Biomarkers provide a promising approach to improve detection and management of disease progression while optimizing health care expenditures.

Keywords: Hypertension, epidemiology, cardiovascular, renal, economic burden, biomarker, risk assessment

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Several demographic factors are changing the environment in which managed care organizations (MCOs) will be considering best practices for diagnosis and treatment of hypertension. The National Health and Nutrition Examination Survey (NHANES) found that in 2003–2004, approximately 1 in 3 U.S. adults had blood pressure 140/90 mmHg or were taking antihypertensive medications (Chobanian 2003). However, the prevalence of hypertension in subgroups defined by age, sex, race/ethnicity, or body mass index did not increase significantly across the 5-year period 1999 to 2004 (Ong 2007).

The effects of race and ethnicity on hypertension are complex and not well understood. However, there are data showing that certain demographic groups are disproportionately affected by hypertension in the United States. The prevalence of hypertension among non-Hispanic blacks (39.1 percent, age adjusted) is higher than non-Hispanic whites (28.5 percent). Awareness of their diagnoses as well as treatment and control rates also has improved among blacks, although blood pressure control of all non-Hispanic black patients with hypertension (28.9 percent) continues to fall short of that in non-Hispanic whites (35.4 percent) (Ong 2007). The overall proportion of people with hypertension is slightly lower among Mexican Americans (27.8 percent) than among other ethnic and racial groups and has remained fairly stable over the last 20 years (Ong 2007). However, even though the rates of treatment (47 percent) and control (24 percent) have improved in Mexican Americans over the same period, these rates are the lowest of the racial or ethnic groups reported (Cutler 2008).

### The Impact of Comorbidities

Hypertension rarely occurs in isolation from other diseases or risk factors. It is considered one of the traditional “independent” CV risk factors shown in Table 1. However, many individuals with hypertension have comorbid conditions that are also independent risk factors for CVD. In the 2003–2004 NHANES population, 78.6 percent of patients with diabetes and 51.8 percent of those with dyslipidemia also had hypertension (Wong 2007). An analysis of the 1999–2004 NHANES data found that among people with hypertension, central obesity, elevated total cholesterol, and low high-density lipoprotein cholesterol were common comorbidities and were significantly more common in women (Table 2). Women with diagnosed hypertension were significantly more likely than men to have 3 of these risk factors regardless of age or race (Ong 2008).

Figure 1 illustrates the relationship among multiple risk factors in increasing CV risk. The likelihood of a patient with 4 CV risk factors having a heart attack (odds ratio=42), for example, is more than 3 times that of a patient who has 3 CV risk factors (odds ratio=13) (Yusuf 2004).

### Diabetes

The prevalent comorbidity of hypertension and diabetes is particularly significant to note as the economics associated with prevention of CV and renal events are high. The prevalence of diabetes in the United States is estimated at 7.8 percent of the total population and is growing (CDC 2007). In 2003–2004, 75 percent of adults with diabetes also had hypertension or were taking antihypertensive medicine. Patients with diabetes are at high risk for heart disease and stroke as well as blindness and chronic kidney disease (Grundy 1999).

### Metabolic syndrome

Hypertension is one of the hallmarks of the metabolic syndrome, which is defined as including at least 3 of 5 CV risk factors (Table 3) (NCEP 2002). Recent analyses suggest that 10 percent to 30 percent of the adult population in most industrialized countries have metabolic syndrome and that this condition effectively predicts the development of type 2 diabetes and CVD (Ismail 2007).

### Renal disease

Hypertension and type 2 diabetes are major causes of chronic kidney disease (CKD). The cost of CKD and end stage renal disease now approaches 6.4 percent of the entire Medicare expenditure (Lalibert 2009). In diabetic and hypertensive individuals, even low levels of

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**TABLE 1**

Traditional cardiovascular risk factors

<table>
<thead>
<tr>
<th>Modifiable</th>
<th>Nonmodifiable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension (140/90 mmHg or taking antihypertensive medication)</td>
<td>Older age</td>
</tr>
<tr>
<td>Low-density lipoprotein cholesterol 130 mg/dL</td>
<td>Male sex</td>
</tr>
<tr>
<td>High-density lipoprotein cholesterol &lt;40 mg/dL</td>
<td>Family history of premature coronary artery disease in a first-degree relative</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td></td>
</tr>
<tr>
<td>Physical inactivity</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Grundy (1999) and Grundy (2004)
urinary protein excretion (microalbuminuria) can be predictive of kidney damage and poor cardiovascular outcomes. Decreased creatinine clearance, although unrelated to protein excretion, is also predictive of poor renal and CV outcomes. In a study of 459 nondiabetic untreated hypertensive patients (64 percent men; mean age, 47.3 years), the prevalence of renal damage, microalbuminuria, and reduced creatinine clearance was 24 percent, 12 percent, and 13 percent, respectively (Leoncini 2008). There was no correlation between albuminuria and estimated creatinine clearance, and only 0.9 percent of patients showed both microalbuminuria and reduced creatinine clearance. Renal damage was associated with a 3-fold higher risk of CV abnormalities, and 58 percent of study patients were classified as being at high or very high risk for CVD.

Unfortunately, patient awareness of chronic kidney disease remains low (Coresh 2007, Bakris 2009) as does physician awareness of some risk factors for chronic kidney disease (Bakris 2009, Pantinga 2008). Because chronic kidney disease is largely asymptomatic until the later stages, early detection and aggressive treatment of comorbidities such as hypertension and diabetes may delay the progression to later and more costly stages of the disease, including dialysis or transplantation (Laliberte 2009, Bakris 2009).

REDUCING THE ECONOMIC BURDEN OF HYPERTENSION

Costs associated with hypertensive illness are not limited to hospitalizations for major CV events or for renal disease. Hypertension is the most common primary diagnosis reported for ambulatory care visits. Management of hypertension accounts for 30 percent of office visits for people aged 45 to 64 years, and for more than 40 percent of visits among individuals aged 60 to 74 years and >75 years. For people of working age (45–64 years), this translates to 1,021 visits per 1,000 individuals (Cherry 2008).

Kahn (2008) used a computer simulation model and data from NHANES to estimate the clinical and economic effects of 11 current prevention activities focused on controlling high blood pressure, elevated cholesterol, hemoglobin A1c, and fasting plasma glucose (FPG) levels, weight reduction, smoking cessation, and/or aspirin therapy for patients with history of myocardial infarction on CVD morbidity, mortality and costs on the U.S. population. In the case when the simulation model assumed that having 70 percent of patients reach their treatment goals was the maximum feasible level of performance, current hypertension treatments would result in approximately 2.1 million fewer heart attacks and 3.4 million fewer strokes over the next 30 years. Their calculations also projected the somewhat surprising result that this reduction in serious CV event would not pay for itself in reduced medical costs. This model found that reducing blood pressure to goal would come at a cost of $52,983/quality-adjusted life-year (QALY) for patients without diabetes, and less ($25,317/QALY) for those with diabetes. Over 30 years, overall costs without medical intervention would be $9.5 trillion, yet the total medical costs associated with reducing to goal would increase by 14 percent (Kahn 2008). Achieving blood pressure goals was not the only prevention strategy that did not achieve the intended economic outcome. Of the 11 CV risk factors considered in the model, only smoking cessation was cost-effective in the long term. However, if the cost of prevention activities could be reduced, the full and
aggressive implementation of recommended prevention goals could prevent two-thirds of the myocardial infarctions and one third of strokes in the United States (Kahn 2008).

Because of the high cost of diabetes (the CDC estimated total direct and indirect costs of diabetes in the United States for the year 2007 to be $174 billion), a number of key studies have evaluated the cost effectiveness of blood pressure control in this specific population. For example, a study in the United Kingdom of patients with type 2 diabetes found that tight blood pressure control (<150/85 mmHg) reduced the cost of complications from diabetes, increased survival and had a cost effectiveness ratio comparable with many other accepted health care programs in that country (UKPDS 1998). An early study in the United States evaluated medical resource cost data to clinical trial results comparing captopril to placebo. The model was designed to extend the results of this trial to cost data on end stage renal disease, and to apply these results to patients with diabetes. The study reported an overall lifetime savings in direct medical costs of $32,550 in young patients with type 1 diabetes and renal im-

### TABLE 2
Blood pressure control and cardiovascular risk factors in individuals with diagnosed hypertension

<table>
<thead>
<tr>
<th>Outcome Measures</th>
<th>1999–2004</th>
<th>Change: 2000–2004*</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>1,617</td>
<td>1,858</td>
<td>NA</td>
</tr>
<tr>
<td>Mean (SE) systolic, mmHg</td>
<td>136.0 (0.7)</td>
<td>140.1 (0.7)‡</td>
<td>-2.7 (-6.2 to 0.7)</td>
</tr>
<tr>
<td>Mean (SE) diastolic, mmHg</td>
<td>75.6 (0.5)</td>
<td>72.1 (0.4)‡</td>
<td>-3.1 (-5.3 to -0.9)</td>
</tr>
<tr>
<td>Uncontrolled blood pressure, percent (SE)*</td>
<td>50.8 (2.1)</td>
<td>55.9 (1.5)</td>
<td>-3.3 (-14.0 to 7.4)</td>
</tr>
<tr>
<td>Waist circumference</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>1,542</td>
<td>1,768</td>
<td>NA</td>
</tr>
<tr>
<td>Mean (SE), cm</td>
<td>107.9 (0.5)</td>
<td>101.3 (0.5)‖</td>
<td>1.7 (-0.6 to 4.0)</td>
</tr>
<tr>
<td>Central obesity, percent (SE)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCEP-ATPⅢ定义</td>
<td>63.9 (1.6)</td>
<td>79.0 (1.0)‖</td>
<td>8.8 (0.8 to 16.8)</td>
</tr>
<tr>
<td>IDF definition</td>
<td>86.2 (1.0)</td>
<td>92.8 (0.7)‖</td>
<td>-1.4 (-5.2 to 2.5)</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>1,544</td>
<td>1,726</td>
<td>NA</td>
</tr>
<tr>
<td>Mean (SE), mg/dL</td>
<td>201.8 (1.6)</td>
<td>212.9 (1.4)‖</td>
<td>-6.7 (-13.2 to -0.2)</td>
</tr>
<tr>
<td>200 mg/dL, percent (SE)</td>
<td>48.1 (1.8)</td>
<td>61.3 (1.6)‖</td>
<td>-9.9 (-18.5 to -1.3)</td>
</tr>
<tr>
<td>HDL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>1,544</td>
<td>1,727</td>
<td>NA</td>
</tr>
<tr>
<td>Mean (SE), mg/dL</td>
<td>46.0 (0.4)</td>
<td>56.5 (0.4)‖</td>
<td>2.1 (-0.1 to 4.4)</td>
</tr>
<tr>
<td>40 mg/dL in men or</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50 mg/dL in women, percent (SE)</td>
<td>35.6 (1.7)</td>
<td>39.7 (1.6)*</td>
<td>-13.2 (-21.4 to -5.0)‖</td>
</tr>
<tr>
<td>HbA1c</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>1,559</td>
<td>1,777</td>
<td>NA</td>
</tr>
<tr>
<td>Mean (SE), percent</td>
<td>5.89 (0.04)</td>
<td>5.83 (0.03)</td>
<td>0.05 (-0.14 to 0.23)</td>
</tr>
<tr>
<td>7.0 percent, percent (SE)</td>
<td>11.1 (0.9)</td>
<td>9.8 (0.9)</td>
<td>-2.9 (-6.3 to 0.5)</td>
</tr>
<tr>
<td>Current smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>1,615</td>
<td>1,858</td>
<td>NA</td>
</tr>
<tr>
<td>percent (SE)</td>
<td>18.7 (1.3)</td>
<td>15.1 (1.1)</td>
<td>4.5 (-2.1 to 11.0)</td>
</tr>
</tbody>
</table>

HbA1c = glycosylated hemoglobin; HDL = high-density lipoprotein; IDF = International Diabetes Federation; JNC7 = 7th Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; NA = not available; NCEP-ATPⅢ = National Cholesterol Education Program-Adult Treatment Panel III; NHANES = National Health and Nutrition Examination Survey.

*P<0.05, †P<0.01, and ‡P<0.001 for sex difference; §P<0.05 and ‖P<0.01 for time trend after adjusting for age and race/ethnicity; ■Blood pressure 140/90 mmHg in nondiabetic patients and ≥130/90 mmHg in diabetic patients according to JNC7 guidelines. Data are age-adjusted by direct standardization to the NHANES 1999–2004 population with diagnosed hypertension. Reprinted with permission from Ong (2008).
pairment treated with captopril versus placebo (Rodby 1996). More recent studies have shown that the greatest cost savings in type 2 diabetes are achieved by preventing cardiovascular events (Brown 1999) and lowering blood pressure to 130/85 mmHg (Elliott 2000). Finally, a study compared the cost effectiveness of blood pressure control compared to glycemic control or cholesterol reduction in patients with type 2 diabetes (CDC Diabetes Cost-effectiveness Group 2002). Of the 3 interventions, only blood pressure control reduced costs by -$1,959/QALY) and improved health outcomes.

While glycemic control ($41,384/QALY) and cholesterol reduction ($51,889/QALY) improved health outcomes, their cost effectiveness, while similar to other health care interventions, was much lower than that observed with blood pressure control.

**BIOMARKERS AND THE REFINEMENT OF RISK ASSESSMENT**

As the burden and economic impact of hypertension can be high, traditional CV risk factors (Table 1) provide the basis for a number of risk assessment algorithms, such as the Framingham Risk Score (FRS), that are commonly used in clinical practice (Grundy 1999). The FRS estimates the likelihood of developing coronary artery disease or having a serious CV event over 10 years and is calculated using the following components: age, total cholesterol, high density lipoprotein cholesterol, systolic blood pressure, diabetes, and smoker status (Wilson 1998). Combined with clinical judgment, the FRS can provide valuable information to guide preventive treatment. Ideally, improving the sensitivity and specificity of risk assessment will identify a greater percentage of high-risk patients, as well as those patients who are treated more aggressively than necessary based on their current risk assessment. Better risk assessment tools will allow treatment to be targeted to those who can benefit most.

The identification of CV and renal surrogate biomarkers and development of imaging techniques that detect early subclinical disease have shown great promise in individualizing risk assessment. To be useful, a biomarker should provide information on the pathology over and above that obtained by a careful clinical assessment. A clinically useful biomarker should also allow for fast, accurate and repeatable measurements at a reasonable cost, demonstrate sensitivity to disease severity, and aid in clinical decision making (Morrow 2007, Vasan 2006). Because the intensity of preventive therapy is generally driven by the risk stratification, a surrogate endpoint marker is expected to predict the extent of clinical benefit on the basis of epidemiologic, therapeutic, pathophysiologic, or other scientific evidence (Vasan 2006). Use of surrogate biomarkers in clinical studies can facilitate early clinical decision-making as we await results of “hard” endpoints, such as occurrence of heart attack or stroke, from long-term studies. Increasing evidence supports the use of novel biomarkers to evaluate risk in high-risk patients, such as those with heart failure, acute coronary syndromes, hypertension, and kidney disease (Cirillo 2008, Grewal 2008, Wang 2007, Tardif 2006).

Physiologic alterations described in hypertensive individuals include vascular hypertrophy; endothelial dysfunction; phenomena such as renal, neurohormonal, and adrenergic abnormalities; inflammation; reduced fibrinolytic potential; and enhanced oxidative stress (Wang 2007). Vascular hypertrophy is most often presented as left ventricular hypertrophy where left ventricular mass index is a recognized surrogate marker of risk and CVD progression. Urinary albumin to creatinine excretion ratio and estimated glomerular filtration rate are good candidates for hypertension and diabetes-associated renal disease assessment because they provide independent and nonoverlapping data (Cirillo 2008). Baseline urinary albumin-to-creatinine ratios (UACR), sensitive enough to be associated with as much as a 20 percent increase in the odds of any patient developing hypertension (Wang 2007), are also predictive of CV outcomes.

BNP is a cardioprotective peptide.
which, together with the inactive NH₂-terminal part of its prohormone (NT-proBNP), is released in response to different kinds of myocardial stress (Levin 1998). Current evidence suggests that BNP may be the most powerful indicator of outcomes in heart failure patients, with reductions in BNP levels consistently being associated with improved outcomes in heart failure (Daniels 2007). This marker is useful in gauging heart failure but also has other important applications (Grewal 2008, McCullough 2002). For example, the African-American Study of Kidney Disease (Astor 2008) examined the role of NT-proBNP in 994 hypertensive black patients with chronic kidney disease and found that individuals with high NT-proBNP were more likely to have a CV event than participants with undetectable NT-proBNP (Astor 2008).

In the clinical study, “Justification for the Use of Statins in Primary Prevention: An Intervention Trial Evaluating Rosuvastatin (JUPITER),” levels of the inflammatory biomarker CRP were found to accurately identify patients with normal lipid profiles who could benefit from statin therapy. Treatment of these individuals with rosuvastatin reduced the composite risk of a heart attack, stroke, and CV death by 44 percent compared with placebo (Ridker 2008). In this study, 57 percent of participants were hypertensive and the benefits of statin therapy were similar in hypertensive and non-hypertensive subjects. A recent scientific statement from the American Heart Association and Centers for Disease Control and Prevention (Pearson 2003) supported the use of CRP as an independent predictor of increased coronary risk. The writing group discouraged the use of CRP in high-risk patients and in the adult population at large, but proposed that patients at intermediate risk of CHD may benefit from CRP testing in order to help physicians decide on further evaluation or therapy.

A recent study that looked at the utility of a number of biomarkers to predict the risk of cardiovascular events and death confirmed the utility of BNP, CRP and UACR (Wang 2006). This study measured 10 different biomarkers in 3,209 participants in the Framingham Heart Study. The biomarkers that most strongly predicted the risk of death were (in descending order) BNP, CRP, UACR, homocysteine and renin. Biomarkers that best predicted major cardiovascular events were BNP and UACR.

Another example of the progress being made in refining risk assessment is the coronary artery calcification (CAC) score. CAC is strongly correlated with the extent of atherosclerotic disease in a given patient. The value of CAC score as an independent predictor of myocardial infarction and stroke has been established in recent studies (Arad 2005, Greenland 2004, Kondos 2003, Taylor 2005). Although a 2007 consensus statement from the American College of Cardiology Foundation and the American Heart Association concludes that use of CAC screening is not warranted in lower-risk patients, use in asymptomatic patients at intermediate risk based on the FRS (Wilson 1998) may be justified because the results may alter treatment decisions (Greenland 2007). This recommendation was based on the finding that a high CAC score was significantly associated with CV risk in patients with an FRS 10 percent, but not in those with an FRS <10 percent (Greenland 2004). In recent years, it has become clear that further refining risk assessment using surrogate markers is an effective way of identifying individuals at high risk for CVD and who thereby may be candidates for more intensive treatment.

Cost effectiveness is a key factor when assessing the usefulness of biomarkers, especially as screening tools (Vasan 2006). For example, a study evaluating various tests for microalbuminuria screening in patients with diabetes found that a simple measurement of urinary albumin concentration in a random urine sample provided an accurate screening test at a cost of only $1.74/patient (Incerti 2005). A study in the United Kingdom found that prescreening of patients with suspected heart failure using NT-proBNP could avoid up to 38 percent of echocardiograms and 23 percent of the cost compared with a direct referral for echocardiography (Goode 2008). In an emergency room setting, NT-proBNP testing in patients presenting with acute dyspnea reduced hospital admission and heart failure diagnostic costs of $1,364/patient (Rutten 2008). Finally, a study analyzed the cost effectiveness of CRP screening followed by targeted statin therapy, compared to dietary counseling alone, for CVD prevention in individuals without overt hyperlipidemia. It was found that CRP screening was a cost effective option, especially among 65-year old men ($42,600 per QALY) (Blake 2003).

**SUMMARY**

Analysis of the most recent NHANES data reveals promising changes in the epidemiology of hypertension, as the overall prevalence of hypertension appears to have stabilized, especially among blacks in the United States. These recent data indicate that an increasing percentage of individuals with hypertension are aware of the diagnosis, are being treated, and have their blood pressure controlled. Despite this progress, there is still a great deal of room for improvement as only 33 percent of patients with hypertension have achieved treatment goals. In addition, the rise in prevalence of related cardiometabolic risks in the overall population, especially in those with hypertension, is troubling. Of particular concern is the recognition that cur-
rent prevention strategies are costly to implement and have not effectively reduced the economic burden of hypertension and attendant cardiometabolic risk factors. New methods to assess hypertension-related cardiovascular risk and individualize treatment are needed to improve the value of health care dollars expended and services provided. Imaging techniques that can significantly improve risk assessment in patients who fall in the intermediate-risk category have evolved rapidly over the last several years. A particularly promising area is the rapidly expanding development of biomarkers, such as BNP and CRP, which may improve the sensitivity of risk assessment. Biomarkers have the potential to guide treatment in select high-risk patients and ultimately to help reduce health care costs, at a time when control of health care expenditures is a national priority.

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