Costs of the Metabolic Syndrome in Elderly Individuals

Findings from the Cardiovascular Health Study*

Lesley H. Curtis, phd[1,2]
Bradley G. Hammill, ms[1]
M. Angelyn Bethel, md[2]
Kevin J. Anstrom, phd[3,4]
John S. Gottdiener, md[5]
Kevin A. Schulman, md[1,2]

OBJECTIVE — The cardiovascular consequences of the metabolic syndrome and its component risk factors have been documented in elderly individuals. Little is known about how the metabolic syndrome and its individual components translate into long-term medical costs.

RESEARCH DESIGN AND METHODS — We used log-linear regression models to assess the independent contributions of the metabolic syndrome and its individual components to 10-year medical costs among 3,789 individuals aged ≥65 years in the Cardiovascular Health Study.

RESULTS — As defined by the National Cholesterol Education Program Third Adult Treatment Panel report, the metabolic syndrome was present in 47% of the sample. Total costs to Medicare were 20% higher among participants with the metabolic syndrome ($40,873 vs. $33,010; $P < 0.001$). Controlling for age, sex, race/ethnicity, and other covariates, we found that abdominal obesity, low HDL cholesterol, and elevated blood pressure were associated with 15% (95% CI 4.3–26.7), 16% (1.7–31.8), and 20% (10.1–31.7) higher costs, respectively. When added to the model, the metabolic syndrome composite variable did not contribute significantly ($P = 0.32$).

CONCLUSIONS — Abdominal obesity, low HDL cholesterol, and hypertension but not the metabolic syndrome per se are important predictors of long-term costs in the Medicare population.

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The metabolic syndrome is characterized by a group of risk factors including abdominal obesity, dyslipidemia, elevated blood pressure, and impaired glucose tolerance (1). Although the original World Health Organization definition emphasized insulin resistance (2), more recent definitions from the National Cholesterol Education Program Adult Treatment Panel III (ATP III) (3) and the International Diabetes Federation (IDF) (4) have treated the individual components equally. Approximately 47 million U.S. residents or ~25% of the population have the metabolic syndrome (using either the World Health Organization or the ATP III definition) (5). A recent analysis from the San Antonio Heart Study reported age-adjusted prevalence estimates of nearly 36% for Mexican-American women, 33% for Mexican-American men, 30% for non-Hispanic white men, and 25% for non-Hispanic white women (using the ATP III criteria) (6).

Clinical consequences of the metabolic syndrome and its component risk factors have been documented previously. In the Atherosclerosis Risk in Communities Study, middle-aged men and women with the metabolic syndrome were 1.5–2 times more likely than control subjects to develop coronary heart disease (7). An analysis of the Framingham Offspring Study cohort yielded similar results (8). More recently, the relationship between the metabolic syndrome and cardiovascular disease has been examined in the elderly population. Analyses of the Cardiovascular Health Study (CHS) cohort suggest that the risk of a cardiovascular event increases by 20–30% in the presence of the metabolic syndrome (9).

The relationship between the metabolic syndrome, its component risk factors, and long-term medical costs is not well understood. First, it is unclear whether the metabolic syndrome confers risk above and beyond the risk conferred by the component risk factors (10). Second, although there is evidence that individuals with the metabolic syndrome are more likely to develop cardiovascular disease, that risk may not translate into markedly shorter life expectancy. Some evidence suggests that life expectancy among obese elderly individuals is only marginally shorter than that among normal-weight elderly individuals (11). To the extent that the component risk factors of the metabolic syndrome contribute to cardiovascular disease but do not hasten death, the financial impact on the Medicare program may be substantial. Using a population-based, longitudinal study of elderly Americans, we examined the relationship between the metabolic syn-

From the [1]Center for Clinical and Genetic Economics, Duke Clinical Research Institute, Durham, North Carolina; the [2]Department of Medicine, Duke University School of Medicine, Durham, North Carolina; the [3]Outcomes Research and Assessment Group, Duke Clinical Research Institute, Durham, North Carolina; the [4]Department of Biostatistics and Bioinformatics, Duke University School of Medicine, Durham, North Carolina; and [5]Division of Cardiology, University of Maryland School of Medicine, Baltimore, Maryland.

Address correspondence and reprint requests to Lesley H. Curtis, PhD, Center for Clinical and Genetic Economics, Duke Clinical Research Institute, P.O. Box 17969, Durham, NC 27715. E-mail: lesley.curtis@duke.edu.

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Abbreviations: ATP III, Adult Treatment Panel III; CHS, Cardiovascular Health Study; IDF, International Diabetes Federation.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Baseline characteristics of the CHS population overall and by metabolic syndrome status*

	Overall	Metabolic syndrome*		
		No	Yes	*P*
n	3,789	2,023	1,766	
Age (years)	75.2 ± 5.2	75.4 ± 5.4	74.9 ± 5.0	0.02
Male sex	1,606 (42.4)	960 (47.5)	646 (36.6)	<0.001
Race				0.93
Black	541 (14.3)	293 (14.5)	248 (14.0)	
White	3,235 (85.4)	1,723 (85.2)	1,512 (85.6)	
Other	13 (0.3)	7 (0.3)	6 (0.3)	
Geographic region				<0.001
California	713 (18.8)	425 (21.0)	288 (16.3)	
Maryland	942 (24.9)	418 (20.7)	524 (29.7)	
North Carolina	1,054 (27.8)	565 (27.9)	489 (27.7)	
Pennsylvania	1,080 (28.5)	615 (30.4)	465 (26.3)	
Hypertension	1,561 (41.6)	604 (30.4)	957 (54.5)	<0.001
Coronary heart disease	831 (21.9)	362 (17.9)	469 (26.6)	<0.001
Prior myocardial infarction	400 (10.6)	168 (8.3)	232 (13.1)	<0.001
Current smoker	358 (9.6)	205 (10.3)	153 (8.8)	0.11
Current use of lipid-lowering agent	290 (7.7)	127 (6.3)	163 (9.2)	<0.001
Prior stroke or transient ischemic attack	280 (7.4)	134 (6.6)	146 (8.3)	0.05
Congestive heart failure	221 (5.8)	96 (4.7)	125 (7.1)	0.002
BMI (kg/m^2)	26.8 ± 4.7	24.9 ± 4.0	28.9 ± 4.6	<0.001
Waist circumference (cm)	97.5 ± 13.2	91.9 ± 11.6	103.9 ± 12.1	<0.001
Triglycerides (mg/dl)	144.2 ± 83.8	107.4 ± 44.2	186.5 ± 97.3	<0.001
HDL cholesterol (mg/dl)	53.0 ± 14.4	58.2 ± 14.2	46.9 ± 12.0	<0.001
LDL cholesterol (mg/dl)	127.1 ± 33.5	124.5 ± 31.8	130.2 ± 35.1	<0.001
Systolic blood pressure (mmHg)	136.0 ± 21.6	133.2 ± 21.7	139.1 ± 21.1	<0.001
Diastolic blood pressure (mmHg)	71.1 ± 11.1	70.7 ± 11.1	71.5 ± 11.0	0.03
Fasting glucose (mg/dl)	108.1 ± 34.4	97.7 ± 20.8	120.1 ± 42.2	<0.001
Fasting insulin (IU/ml)	13.9 ± 21.1	10.0 ± 12.3	18.2 ± 27.3	<0.001
Serum creatinine (mg/dl)	1.1 ± 0.4	1.1 ± 0.3	1.1 ± 0.4	0.86
ATP III criteria				
Waist circumference >102 cm in men and >88 cm in women	2,068 (54.6)	619 (30.6)	1,449 (82.0)	<0.001
Serum triglycerides ≥150 mg/dl	1,331 (35.1)	228 (11.3)	1,103 (62.5)	<0.001
HDL cholesterol <40 mg/dl in men and <50 mg/dl in women	1,172 (30.9)	180 (8.9)	992 (56.2)	<0.001
Blood pressure ≥130/85 mmHg or current use of antihypertensive medication	2,905 (76.7)	1,281 (63.3)	1,624 (92.0)	<0.001
Serum glucose ≥100 mg/dl or current use of medication for diabetes	1,794 (47.3)	478 (23.6)	1,316 (74.5)	<0.001

Data are means ± SD or *n* (%). Percentages may not sum to 100% because of rounding and/or missing data. *Defined by the National Cholesterol Education Program ATP III.

drome, its component risk factors, and long-term medical costs and resource use.

RESEARCH DESIGN AND METHODS

— We used data from the CHS, a prospective study of 5,888 individuals aged ≥65 years in four communities (Sacramento County, California; Washington County, Maryland; Forsyth County, North Carolina; and Pittsburgh, Pennsylvania) (12,13). In 1989, investigators recruited a random sample of 5,201 Medicare beneficiaries and other elderly household members. From 1992 to 1993, they recruited an additional cohort of African Americans (n = 687). At baseline and at the 1992–1993 interview, investigators collected data on anthropometric characteristics, current medication use, blood pressure, and blood chemistry (12). The study followed participants annually via clinic visits through 2002. Study personnel telephoned participants in the interim 6 months to establish vital status and to screen for primary events and hospitalizations.

The 1992–1993 interview was the baseline for our analyses, since matching Medicare claims data were available beginning with 1992. Of the 5,888 participants, 5,264 were alive and completed the 1992–1993 interview. Of these, 610 participants were missing data on at least one component of the metabolic syndrome and were excluded. We matched 4,413 of the remaining 4,654 (95%) participants to Medicare records. We limited the cohort to the 3,789 participants with Medicare fee-for-service coverage at the time of the 1992–1993 CHS visit. We followed patients for 10 years from their 1992–1993 CHS visit date.

Table 2—*Ten-year resource use and medical costs overall and by metabolic syndrome status

	Overall	Metabolic syndrome*		
		No	Yes	*P*
n	3,789	2,023	1,766	
Inpatient stays per patient	2.8 ± 2.3	2.6 ± 2.2	3.2 ± 2.4	<0.001
Outpatient visits per patient	24.8 ± 10.4	24.1 ± 10.3	25.5 ± 10.4	<0.001
Evaluation and management visits per patient	62.5 ± 14.4	60.8 ± 14.5	64.4 ± 14.4	<0.001
Primary care visits†	26.1 ± 8.2	24.4 ± 8.1	28.0 ± 8.3	<0.001
Specialist visits†	30.8 ± 10.2	30.7 ± 10.3	30.9 ± 10.2	0.47
Total costs to Medicare per patient ($)	36,663 ± 29,832	33,010 ± 26,530	40,873 ± 33,138	<0.001
Medicare Part A (inpatient)	21,319 ± 25,801	18,806 ± 22,756	24,214 ± 28,834	<0.001
Medicare Part B (physician)	11,485 ± 5,142	10,779 ± 4,810	12,299 ± 5,487	<0.001
Medicare Part B (institutional)	3,859 ± 3,508	3,425 ± 3,151	4,359 ± 3,867	<0.001

Data are means ± SD. *Defined by the National Cholesterol Education Program ATP III. †Approximately 8% of evaluation and management visits could not be identified as primary care visits or specialty visits.

We defined the metabolic syndrome using the most recent ATP III criteria (14). Specifically, we deemed participants who met at least three of the following criteria to have the metabolic syndrome: *1*) waist circumference >102 cm for men and >88 cm for women, *2*) serum triglycerides ≥150 mg/dl, *3*) blood pressure ≥130/85 mmHg or current use of antihypertensive medication, *4*) HDL cholesterol <40 mg/dl for men and <50 mg/dl for women, and *5*) serum glucose ≥100 mg/dl or current use of medication for diabetes. To test the robustness of our findings to alternative definitions of the metabolic syndrome, we repeated all analyses using the IDF definition (4), which requires a waist circumference ≥94 cm for men and ≥80 cm for women and two of the following: *1*) serum triglycerides ≥1.7 mmol/l or treatment for this lipid abnormality; *2*) HDL cholesterol <1.03 mmol/l for men and <1.29 mmol/l for women or treatment for this lipid abnormality; *3*) systolic blood pressure ≥130 mmHg, diastolic blood pressure ≥85 mmHg, or treatment of previously diagnosed hypertension; or *4*) fasting plasma glucose ≥100 mmol/l or previously diagnosed type 2 diabetes.

We calculated costs by summing Medicare payments for each participant, and we discounted costs at 3% annually (15). Costs are given in year 2000 U.S. dollars. In addition to total costs, we summarized Medicare Part A (inpatient) costs, Medicare Part B (physician/provider) costs, and Medicare Part B (institutional outpatient) costs. We calculated costs beginning with the 1992–1993 visit for 10 years or until death, enrollment in Medicare managed care, or loss of Medicare Part B coverage. We calculated the number of inpatient stays per participant by counting unique discharge dates (excluding transfers) in the Medicare Part A file. We calculated outpatient visits as the number of distinct visits in the Medicare Part B institutional outpatient file, and we calculated physician visits as the number of distinct evaluation and management claims in the Medicare Part B physician/provider file. We used the Centers for Medicare and Medicaid Services unique physician identification number directory to distinguish primary care physicians from specialists. For this analysis, primary care providers included general practitioners, family practitioners, internists, geriatricians, obstetrician/gynecologists, and physicians trained in preventive medicine. We considered all other physicians to be specialists.

Statistical analysis

We describe the study cohort using numbers and frequencies for categorical variables and means ± SD for continuous variables. We used χ^2 tests and Wilcoxon's rank-sum tests to assess differences between groups. To calculate mean costs and resource use per participant for a 10-year period, we used semiparametric weighted estimators (16,17). This method inversely weights observations by their probability of not being censored. Censoring may occur when participants switch from fee-for-service to managed care or when the study ends. We used a

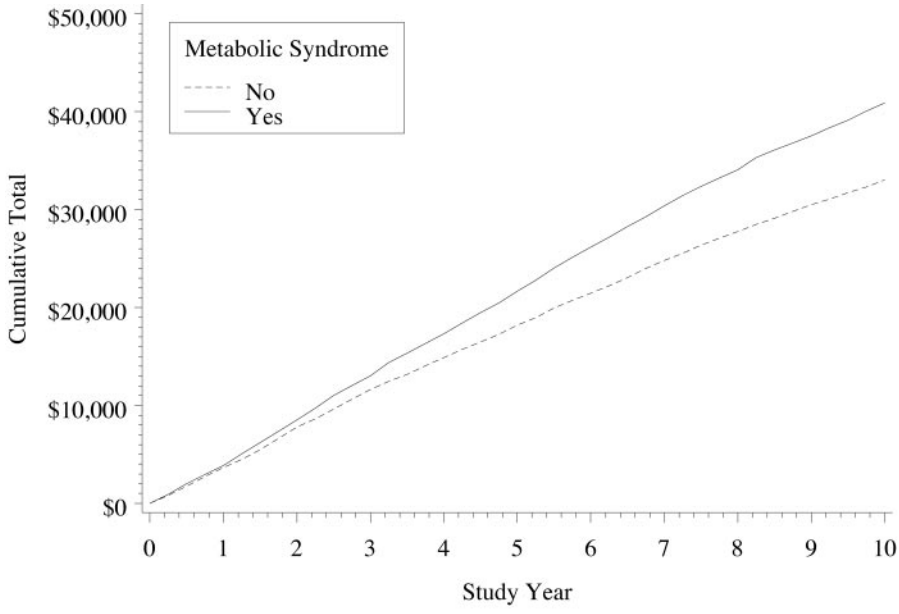

Figure 1—*Cumulative 10-year costs to Medicare per patient with and without the metabolic syndrome.*

Table 3—*Effect of the metabolic syndrome and its component risk factors on total costs*

Variable	Univariate model	Multivariable model 1*	Multivariable model 2†	Multivariable model 3‡
Metabolic syndrome	23.7 (14.4 to 33.8)§		29.6 (18.8 to 41.5)§	7.6 (−6.8 to 24.3)
Waist circumference >102 cm in men and >88 cm in women	8.7 (0.5 to 17.5)‖	14.9 (4.3 to 26.7)¶		12.1 (0.3 to 25.2)‖
Serum triglycerides ≥1.7 mmol/l	14.9 (6.1 to 24.4)§	8.2 (−3.6 to 21.4)		5.8 (−6.7 to 19.9)
HDL cholesterol <1.0 mmol/l in men and <1.3 mmol/l in women	20.2 (9.9 to 31.6)§	15.8 (1.7 to 31.8)‖		13.3 (−0.5 to 29.1)
Blood pressure ≥130/85 mmHg	21.5 (11.6 to 32.4)§	20.4 (10.1 to 31.7)§		18.2 (7.2 to 30.5)§
Serum glucose ≥6.1 mmol/l	15.7 (6.9 to 25.1)§	1.2 (−7.1 to 10.2)		–1.1 (−9.9 to 8.5)

Data are estimated percent changes in costs (95% CI). *Multivariable model 1 controls for age, sex, race/ethnicity, geographic region, current smoking status, and LDL cholesterol level, but does not include the composite metabolic syndrome variable. †Multivariable model 2 includes the composite metabolic syndrome variable and controls for age, sex, race/ethnicity, geographic region, current smoking status, and LDL cholesterol level. ‡Multivariable model 3 includes the composite metabolic syndrome variable and its component risk factors, and controls for age, sex, race/ethnicity, geographic region, current smoking status, and LDL cholesterol level. §$P < 0.001$. ‖$P < 0.05$. ¶$P < 0.01$.

Cox proportional hazards model for the censoring distribution.

We developed covariate-adjusted log-linear regression models to estimate the relationship between the metabolic syndrome, its component risk factors, and 10-year medical costs. The parameters, when exponentiated, estimate the proportional increase in costs due to the presence of the risk factor. In addition to the mean cost models, we modeled costs conditional on survival. In other words, a participant's costs for a given time period were included only if the participant survived to the end of the time period.

First, we estimated the univariate association between total costs and the metabolic syndrome and its components. Next, we fit three multivariable models for each definition of the metabolic syndrome. Model 1 included the individual components of the metabolic syndrome and controlled for demographic and clinical covariates including age, sex, race/ethnicity, current smoking status, and LDL cholesterol level (9,18). This model estimated the independent effects of the components, controlling for confounders. Model 2 included an indicator variable for the metabolic syndrome to assess whether the metabolic syndrome itself was an independent predictor of total costs. Model 3 included the indicator variable and the components of the metabolic syndrome to assess whether the metabolic syndrome was independently related to total costs after controlling for its component parts. As a sensitivity analysis, we replicated the analysis after excluding participants with a history of cardiovascular disease or stroke at baseline.

We used SAS (version 9.1.3; SAS Institute, Cary, NC) for all analyses. The institutional review board of the Duke University Health System approved the study.

RESULTS — Table 1 shows the characteristics of the participants. Over the 10-year period, 1,315 participants (34.7%) died. Forty-six percent met the ATP III criteria for the metabolic syndrome, and 53% met the IDF definition. Women were disproportionately represented among participants with the metabolic syndrome, and about 8% of participants with the metabolic syndrome had a prior stroke or transient ischemic attack. As expected, there were marked differences in waist circumference and triglyceride levels between participants with the metabolic syndrome and those without it. Similarly, mean fasting glucose and insulin measures were higher among participants with the metabolic syndrome. More than three-fourths of the participants and >90% of those with the metabolic syndrome had blood pressure ≥130/85 mmHg. More than half of the participants and ~80% of those with the metabolic syndrome had abdominal obesity.

Resource use and costs were higher among participants with the metabolic syndrome than among those without (Table 2). On average, participants with the metabolic syndrome had more inpatient stays and primary care visits. The differences translated into 20% higher total costs to Medicare among participants with the metabolic syndrome compared with those without it. Cumulative costs for participants with the metabolic syndrome began to exceed costs for participants without the metabolic syndrome in years 2 and 3, and the trend persisted until the end of the study (Fig. 1).

Table 3 shows the results of the univariate and multivariable models. In univariate analyses, the metabolic syndrome and its component risk factors were significantly associated with total costs. The metabolic syndrome was associated with 25% higher costs. Low HDL cholesterol and high blood pressure were associated with 20% higher costs.

In the multivariable models, abdominal obesity, low HDL cholesterol, high blood pressure (Model 1), and the metabolic syndrome (Model 2) were significant predictors of total costs after controlling for age, sex, race/ethnicity, geographic region, current smoking status, and LDL cholesterol. However, when added to the model that included the individual components of the metabolic syndrome, the composite metabolic syndrome variable was not a significant predictor of total costs ($P = 0.32$). The results were similar when we used the IDF definition of the metabolic syndrome. Low HDL cholesterol, high blood pressure, and the metabolic syndrome were significant independent predictors of total costs, controlling for other covariates. Again, when added to the model, the composite metabolic syndrome variable did not contribute significantly ($P = 0.72$).

Results from an analysis of survivors only were similar. Independent predictors of total costs among survivors were abdominal obesity (estimated change in costs, 11.1% [95% CI 1.2–22.1]), high triglycerides (10.4% [0.3–21.5]), low HDL cholesterol (14.6% [4.0–26.3]), high blood pressure (20.8% [9.2–33.6]), and the metabolic syndrome (30.4%

[20.1–41.7]). When included in a model with the individual components of the metabolic syndrome, the composite metabolic syndrome variable was not a significant predictor of total costs ($P = 0.36$).

The results of the sensitivity analysis were similar. When we excluded participants with a history of cardiovascular disease or stroke at baseline, abdominal obesity (15.4% [95% CI 1.9–30.7]), high blood pressure (14.9% [3.6–27.5]), and the metabolic syndrome (33.6% [19.0–49.9]) were significant independent predictors of total costs. The composite metabolic syndrome variable was not a significant predictor of total costs when included in a model with the individual components of the metabolic syndrome.

CONCLUSIONS — To our knowledge, this is the first study to examine the relationship between the metabolic syndrome, its component risk factors, and long-term costs among elderly individuals. The results suggest that abdominal obesity, low HDL cholesterol, and high blood pressure are important predictors of long-term costs in the Medicare population. Combined, these risk factors are independently associated with a 50% increase in 10-year medical costs. When added to a model that includes the component risk factors, the metabolic syndrome is not an independent predictor of total costs, which suggests that cardiovascular risk accumulates in an additive rather than a multiplicative fashion.

The results are consistent with prior studies examining the impact of the metabolic syndrome and its component risk factors on cardiovascular disease and mortality. In the Kuopio Ischemic Heart Disease Risk Factor Study, the metabolic syndrome was associated with 2.6 times greater cardiovascular disease mortality and 2 times greater all-cause mortality (19). Data from the Framingham Offspring Study suggested that the metabolic syndrome nearly triples the relative risk of coronary heart disease (20). In that cohort, blood pressure and HDL cholesterol were the strongest predictors of cardiovascular outcomes. Similar findings were reported in the Atherosclerosis Risk in Communities Study (7).

Our findings complement prior analyses from the CHS. With 4 years of follow-up, Scuteri et al. (18) found that the metabolic syndrome was associated with a 38% greater risk of coronary or cerebrovascular events (hazard ratio [HR] 1.4 [95% CI 1.1–1.8]). The composite metabolic syndrome variable remained significant even after controlling for the individual components. In a more recent analysis of the same cohort over 11 years, the metabolic syndrome was associated with a 30% greater risk of incident coronary heart disease among women (1.3 [1.1–1.6]) and a 35% greater risk among men (1.4 [1.1–1.7]) (9). In analyses adjusted for age and race/ethnicity and using each component of the metabolic syndrome separately, high blood pressure, low HDL cholesterol, and fasting glucose were significantly associated with a greater risk of incident coronary heart disease. The composite metabolic syndrome variable was not a significant predictor when added to the model. Our findings are similar. Specifically, low HDL cholesterol, elevated blood pressure, and abdominal obesity, but not the metabolic syndrome as a composite variable, were significantly associated with total costs over a comparable time frame. Thus, the metabolic syndrome may not be a useful predictor of costs in the elderly population above and beyond the contribution of its individual components (10).

Our findings are also consistent with previously reported relationships between cardiac risk factors and medical costs. Sturm (21) found that obese individuals incur medical expenditures nearly 40% higher than those of normal-weight individuals. Notably, Finkelstein et al. (22) found that the per capita increase in spending attributable to obesity is greatest for Medicare beneficiaries. More recently, Fitch (23) estimated that the per-member per-month cost for working-age individuals with the metabolic syndrome is $259 higher than for those without it.

The prevalence of obesity and associated cardiac risk factors in the elderly population is increasing (24). Coupled with that trend, our findings suggest that the total financial impact of the metabolic syndrome and its component risk factors on the Medicare program may be substantial. Future research should examine how prevention or treatment of obesity and associated risk factors affects medical costs. Until then, the net financial impact of preventing or treating these conditions is unclear.

This study was strengthened by the availability of baseline risk factors and long-term costs in a population-based sample, but it had some limitations. The CHS cohort is elderly and relatively healthy, so the results may not generalize to younger individuals or those who are very ill. Second, we relied on Medicare claims data, which are available only for patients with fee-for-service coverage. To account for patients with periods of managed care coverage, we applied increased weight to individuals with complete data. Finally, medication costs and other costs not covered by Medicare are not included in our estimates.

In summary, we found that the individual components of the metabolic syndrome but not the metabolic syndrome per se are important independent predictors of long-term medical costs among elderly individuals.

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