

Medical Care Costs Among Patients With Established Cardiovascular Disease

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Objective: To estimate direct medical costs among patients with established cardiovascular disease (CVD).

Study Design: Observational longitudinal cohort study.

Methods: We identified 12,278 patients who were added to the Kaiser Permanente Northwest CVD registry from 2000 to 2005. We observed patients until they died or left the health plan or until June 30, 2008. Total direct medical costs were calculated over an individual’s entire follow-up and were then annualized by dividing by the months of follow-up. We also calculated and compared age- and sex-adjusted incidence rates per 1000 person-years of secondary CVD hospitalization and all-cause mortality and a composite outcome of both.

Results: The total mean (SD) annual direct medical costs for the entire sample were \$18,953 (\$39,036). With approximately 22 million US residents having prevalent CVD or stroke, this extrapolates to direct costs of more than \$400 billion. Inpatient costs accounted for 42.8% of total costs (mean [SD], \$8114 [\$25,410]). The greatest differences in costs were found when comparing patients who did versus did not experience a secondary CVD hospitalization (\$62,755 vs \$13,509, $P < .001$). Other large differences were found in comparisons of patients with versus without diabetes (\$27,258 vs \$17,210), an estimated glomerular filtration rate of less than 60 mL/min/1.73 m² (\$29,498 vs \$16,326), depression (\$26,681 vs \$17,303), and death (\$28,689 vs \$17,779) ($P < .001$ for all).

Conclusions: The economic burden of providing care to patients with CVD may be substantially greater than current American Heart Association estimates. Although several comorbid conditions undoubtedly contribute to these costs, avoidance of secondary CVD hospitalization may be the key to substantially reducing healthcare consumption.

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For author information and disclosures, see end of text.

An estimated 1 in 3 American adults has 1 or more types of cardiovascular disease (CVD), and CVD remains the leading cause of death in the United States.¹ Not surprisingly, CVD is the most costly of all diseases, accounting for an estimated \$448.5 billion in 2008, of which two-thirds was attributed to direct patient care.² Given the improving survival of patients following CVD events, the aging population, the obesity epidemic, the rising incidence of diabetes and cardiometabolic syndrome, and the less-than-optimal control of risk factors, the economic burden of CVD can be expected to increase.³

Individually, patients with CVD incur more than twice the medical costs of age- and sex-matched patients without CVD⁴ largely because of the increased likelihood of subsequent hospitalizations. However, specific estimates of medical costs among patients with established CVD are scant. A recent study⁵ based on the US subset of the Reduction of Atherothrombosis for Continued Health Registry found that 1-year medical costs ranged from \$3949 to \$11,482, but the study did not include outpatient or non-CVD hospitalization costs. Two other recent studies^{6,7} found costs of approximately \$18,000 to \$27,000 in the year after discharge for acute coronary syndromes, but Medicare patients were not included in either analysis. To our knowledge, no study has fully described the medical care costs for the full range of patients with existing CVD. Therefore, we sought to estimate the annual direct medical costs incurred over follow-up of up to 7 years following entry into the CVD registry of a health maintenance organization (HMO) with complete capture of medical utilization and cost data. In addition, we sought to identify high-cost subgroups of patients with CVD to describe the demographic and clinical characteristics that are associated with excess medical costs. We also report the incidence of secondary CVD events among these high-cost groups.

METHODS

The study population was Kaiser Permanente Northwest (KPNW), a 480,000-member group-model HMO that uses clinical practice guidelines to assist clinicians with patient management. Members enroll through employer-sponsored or individual insurance plans, and KPNW also participates in Med-

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icaid and Medicare contracts. We used an observational study design that capitalizes on the comprehensive medical utilization data maintained by KPNW, including an electronic medical record (EMR) of all inpatient and outpatient encounters, laboratory results that are analyzed by a single regional laboratory using standardized methods, and dispensation from pharmacies located in all clinics. The institutional review board of the Kaiser Permanente Center for Health Research reviewed and approved the study.

Sample Selection

Kaiser Permanente Northwest maintains a registry of patients with known CVD, which is generated by automated processes that access EMR data. The criteria for registry entry include the following: an inpatient diagnosis of myocardial infarction (MI) (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] code 410.xx), coronary occlusion without MI (code 411.81), other acute ischemic heart disease (code 411.89), unstable angina (code 411.1), angina pectoris (code 413.x), cerebrovascular disease (codes 433.x, 434.x, 437.x, and 438.x), a revascularization procedure (codes 35.96, 36.01, 36.02, 36.05, 36.09, 36.1x, 36.29, V45.81, and V45.82), or an outpatient diagnosis or entry on the patient's problem list of old MI (code 412.x), chronic ischemic heart disease (code 414.x), atherosclerosis (code 440.x), or aortic aneurysm (code 441.x). We selected all 14,705 patients who were added to the CVD registry from 2000 to 2005 and defined the registry entry date as the index date. To obtain stable estimates of individuals' costs, we required that patients survive and remain eligible for at least 6 months following their index date. This resulted in the exclusion of 2427 patients, for a final analysis sample of 12,278.

CVD Outcomes and Covariates

We observed patients until they died or left the health plan for other reasons or until June 30, 2008, whichever came first. Deaths were ascertained from KPNW membership records, but cause of death was unavailable. Cardiovascular disease hospitalizations were defined as an overnight stay with a primary discharge diagnosis of CVD (ICD-9-CM codes 410.x-429.x, 430.x, 431.x, 432.x, 434.x, 435.x, 436.x, 437.1, and 402.91) or for a revascularization procedure (codes 35.96, 36.01, 36.02, 36.05, 36.09, 36.1x, 36.29, V45.81, and V45.82). We considered a composite outcome of secondary CVD hospitalization or all-cause mortality and also analyzed these independently. To identify characteristics that contrib-

Take-Away Points

The total mean direct medical care costs for patients with established cardiovascular disease (CVD) were \$18,953 per patient per year. Cost estimates varied widely, however, depending on the presence or absence of other health conditions.

- Patients who experienced a secondary CVD hospitalization incurred annual costs that were 4.5 times higher compared with those who avoided inpatient stays.
- Costs for persons who were not hospitalized for CVD during follow-up were about 30% lower than the mean, suggesting that successful prevention efforts could substantially reduce the economic burden of CVD.
- Costs were also substantially elevated for those with specific comorbid conditions, including diabetes, chronic kidney disease, and depression.

ute to high costs, we used the date of entry into the CVD registry as the index date and categorized individuals using baseline values assessed as of that date. Age at index date and sex were extracted from KPNW membership records. Body mass index was calculated from height and weight data in the EMR. Blood pressure, presence of type 1 or type 2 diabetes mellitus (ICD-9-CM code 250.xx), and history of depression (codes 296.2x, 296.3x, 300.4, 309.1, and 311.x) were also collected from the EMR. We extracted baseline lipid values from those recorded in the laboratory database in the year preceding registry entry and used serum creatinine values to obtain the estimated glomerular filtration rate (eGFR) using the Modification Diet in Renal Disease formula.⁸ Pharmaceutical use was defined as 1 or more dispenses of a specific drug class or product.

Costing Methods

Total and component direct medical costs were calculated for an individual's entire follow-up, but did not include the primary event that qualified him or her for the CVD registry. We based our costing method on procedures developed and validated by the Kaiser Permanente Center for Health Research.^{9,10} For outpatient costs, this method creates standard costs for office visits by specialty or department and by type of clinician (medical doctor vs physician assistant or nurse practitioner). The number of visits per department per clinician type is then multiplied by the appropriate unit cost. Pharmaceutical costs are based on retail prices within the service area. Hospitalizations were assigned to diagnosis-related groups (DRGs) based on the primary reason for hospitalization. The mean daily rate per DRG was then multiplied by the length of stay. Costs for medical services incurred at facilities not owned by KPNW were derived from an automated claims system and were based on the amount paid by KPNW to nonplan providers. Therefore, although the costs reported herein may be specific to KPNW, they approximate the charges a nonmember would be billed if these services were purchased from KPNW. All costs were adjusted to 2008 US dollars using the medical care component of the Consumer

Table 1. Characteristics of Patients Entering the CVD Registry

Characteristic	Men (n = 7276)	Women (n = 5002)	Total (N = 12,278)
Age, mean (SD), y ^a	64.1 (11.8)	69.0 (13.0)	66.1 (12.5)
BMI, mean (SD)	30.2 (5.4)	30.1 (7.3)	30.2 (6.2)
Blood pressure, mean (SD), mm Hg^a			
Systolic	133.7 (17.0)	137.3 (17.3)	135.2 (17.3)
Diastolic	77.5 (10.0)	75.6 (9.8)	76.7 (10.0)
LDL-C level, mean (SD), mg/dL ^a	105.5 (32.7)	111.5 (36.2)	107.6 (34.2)
eGFR, mean (SD), mL/min/1.73 m ^{2a}	80.2 (26.6)	72.6 (24.9)	76.8 (26.0)
Age ≥65 y, % ^a	47.0	63.1	53.5
Nonwhite race/ethnicity, %	93.3	93.4	93.4
BMI ≥30, %	45.1	44.3	44.8
Uncontrolled blood pressure, % ^{a,b}	42.0	48.3	44.6
LDL-C level ≥100 mg/dL, % ^a	52.7	59.8	55.5
Low HDL-C level, % ^c	51.8	51.4	51.6
eGFR <60 mL/min/1.73 m ² , % ^a	16.6	30.4	22.2
Diabetes, %	18.8	20.4	19.4
Depression, % ^a	6.9	11.4	8.7
Ever smoked, % ^a	63.2	44.9	55.8
Source of identification, %^a			
Inpatient diagnosis	13.4	13.8	13.6
Revascularization procedure	16.2	8.1	12.9
Outpatient diagnosis	70.4	78.2	73.5
Type of entry diagnosis, %^a			
CVD	89.7	79.8	85.7
Cerebrovascular disease	10.3	20.2	14.3

BMI indicates body mass index (calculated as weight in kilograms divided by height in meters squared); CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol. SI conversion factor: To convert cholesterol level to millimoles per liter, multiply by 0.0259.

^aP < .001.

^bAt least 130/80 mm Hg for patients with diabetes and at least 140/90 mm Hg for all other patients.

^cLess than 40 mg/dL for men and less than 50 mg/dL for women.

Price Index and were then annualized on an individual basis by summing them over each individual's entire follow-up, dividing by individual months of observation, and multiplying by 12. These costs represent the payer's perspective; therefore, out-of-pocket costs are not included.

Statistical Analysis

All analyses were performed using SAS version 8.2 (SAS Institute, Cary, NC). We calculated and compared age- and sex-adjusted incidence rates of each outcome per 1000 person-years using regression for incidence densities based on the first occurrence of the outcome.¹¹ Annualized costs were adjusted for age and sex using SAS Proc GLM, and bivariate comparisons were made with the LSMEANS statement. Although cost data are typically nonnormal, we did not trans-

form the data before analysis to allow for straightforward interpretation of the parameter estimates. Normalizing the data via log transformation did not change the direction or statistical significance of the results.

RESULTS

Data describing the 12,278 study subjects are given in **Table 1**. The mean (SD) age at registry entry was 66.1 (12.5) years, and 59.3% were men. Most (85.7%) entered the registry because of CVD (as opposed to cerebrovascular disease) diagnoses, most of which were recorded during an outpatient visit. Diabetes (19.4%) and chronic kidney disease as defined by an eGFR of less than 60 mL/min/1.73 m² (22.2%) were common comorbidities.

Table 2. Healthcare Utilization During Follow-Up

Variable	Men	Women	Total	P
Follow-up, mean (SD), mo	47.2 (23.1)	43.8 (22.3)	45.8 (22.8)	<.001
Patients with hospitalization, %	55.5	49.4	53.5	<.001
Annual outpatient visits, mean (SD)	23.0 (41.3)	31.6 (52.4)	26.5 (46.3)	<.001
Dispenses, mean (SD)	45.6 (70.5)	60.4 (87.5)	51.6 (78.2)	<.001
Aspirin or antiplatelet use, %	76.2	70.4	73.8	<.001
ACE inhibitor or ARB use, %	45.0	41.4	43.6	<.001
Statin use, %	69.9	58.3	65.2	<.001
β-Blocker use, %	68.0	69.4	68.6	.10

ACE indicates angiotensin-converting enzyme; ARB, angiotensin II receptor blocker.

During a mean (SD) follow-up of 45.8 (22.8) months, 53.5% of patients were hospitalized (Table 2). Patients averaged more than 2 outpatient visits per month and filled more than 4 prescriptions per month. Women averaged more annual visits than men (31.6 vs 23.0) and had more annual dispenses (60.4 vs 45.6) ($P < .001$ for both). Use of medications for secondary prevention of CVD was high among both sexes.

Table 3 compares the age- and sex-adjusted incidence rates per 1000 person-years of secondary CVD hospitalization, all-cause mortality, and the composite outcome for 13 risk factors dichotomized by baseline characteristics. For example, patients 65 years or older experienced the composite outcome at a sex-adjusted rate of 88.0 per 1000 person-years (95% confidence interval [CI], 84.3-91.8) compared with 36.0 per 1000 person-years (95% CI, 33.6-38.5) among patients younger than 65 years. Diabetes, entry into the registry because of prior hospitalization, and an eGFR of less than 60 mL/min/1.73 m² were the strongest risk factors for secondary CVD hospitalization; age 65 years or older and an eGFR of less than 60 mL/min/1.73 m² were the strongest risk factors for mortality. History of depression was strongly predictive of all 3 outcomes.

The total mean (SD) annual direct medical costs for the entire sample were \$18,953 (\$39,036), of which 42.8% (\$8114 [\$25,410]) were attributable to inpatient costs, 39.3% (\$7451 [\$13,461]) were incurred in outpatient settings, and the remaining 17.9% (\$3388 [\$6954]) were for pharmaceuticals (Table 4). Costs were highly skewed; the median costs were substantially lower than the means. Almost all patients incurred at least some outpatient and pharmaceutical costs, but 46.5% had no inpatient costs.

Annualized age- and sex-adjusted costs, in total and for inpatient, outpatient, and pharmaceutical resources, are compared in Table 5 across 15 dichotomies. The greatest differences in total costs were found when comparing patients who

did versus did not experience a secondary CVD hospitalization (\$62,755 vs \$13,509, $P < .001$). Other large differences included comparisons of patients with vs without diabetes (\$27,258 vs \$17,210), entry into the registry because of prior hospitalization (\$28,800 vs \$16,895), an eGFR of less than 60 mL/min/1.73 m² (\$29,498 vs \$16,326), depression (\$26,681 vs \$17,303), and death (\$28,689 vs \$17,779) ($P < .001$ for all). Although inpatient costs accounted for most of the observed differences, outpatient and pharmaceutical costs were also significantly different among these dichotomies.

DISCUSSION

In this observational longitudinal cohort study of 12,278 patients with established CVD observed for up to 7 years, the mean total direct medical care costs were \$18,953 per patient per year. Our cost estimates varied widely, however, depending on the presence or absence of other health conditions. In particular, patients who experienced a secondary CVD hospitalization incurred annual costs that were 4.5 times higher compared with those who avoided inpatient stays. With a mean annual cost differential of almost \$50,000, the value of preventing hospitalizations in patients with established CVD cannot be understated. Furthermore, because costs for persons who were not hospitalized for CVD during follow-up were about 30% lower than the mean, successful prevention efforts could substantially reduce the economic burden of CVD.

Our results suggest that the societal burden of CVD may be much greater than previously believed. The American Heart Association (AHA)¹ estimated that direct medical costs for approximately 21.8 million Americans with prevalent CVD or stroke totaled \$131.3 billion in 2008, or about \$6000 per person. In our sample, we found medical care costs to be 3 times greater than that, which extrapolates to US-wide direct costs of more than \$400 billion. In addition, the AHA¹ estimates that patients with CVD or stroke incur another \$222

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■ **Table 3.** Age- and Sex-Adjusted Incidence Rates per 1000 Person-Years for Outcomes by Selected Strata

Variable	Value (95% Confidence Interval)		
	Secondary CVD Hospitalization	Death	Secondary CVD Hospitalization or Death
Age ≥65 y	32.8 (30.5-35.1)	51.3 (48.6-54.1)	88.0 (84.3-91.8)
Age <65 y	23.8 (21.9-25.9)	11.3 (10.0-12.7)	36.0 (33.6-38.5)
<i>P</i> value	<.001	<.001	<.001
Men	28.1 (26.3-30.1)	22.7 (21.1-24.5)	54.7 (52.1-57.6)
Women	27.6 (25.3-30.1)	26.1 (24.0-28.5)	58.5 (55.2-62.1)
<i>P</i> value	.73	.006	.07
Diabetes	40.4 (36.5-44.8)	26.9 (24.0-30.1)	72.3 (67.0-77.9)
No diabetes	24.9 (23.4-26.6)	23.7 (22.1-25.5)	53.0 (50.6-55.4)
<i>P</i> value	<.001	.04	<.001
eGFR <60 mL/min/1.73 m ²	42.5 (38.4-47.1)	34.6 (31.4-38.2)	84.4 (78.8-90.4)
eGFR ≥60 mL/min/1.73 m ²	24.5 (22.9-26.1)	20.7 (19.2-22.3)	48.8 (46.5-51.2)
<i>P</i> value	<.001	<.001	<.001
Depression	36.9 (33.2-41.1)	30.2 (27.1-33.6)	73.0 (67.8-78.7)
No depression	25.6 (23.9-27.3)	22.8 (21.3-24.5)	52.4 (50.1-54.9)
<i>P</i> value	<.001	<.001	<.001
LDL-C level ≥100 mg/dL	27.3 (25.3-29.4)	17.5 (15.9-19.1)	47.6 (45.0-50.4)
LDL-C level <100 mg/dL	29.0 (26.7-31.6)	20.9 (19.0-23.0)	53.4 (50.2-56.8)
<i>P</i> value	.27	.003	.005
Low HDL-C level ^a	33.9 (31.5-36.3)	19.8 (18.1-21.6)	56.8 (53.8-60.0)
Normal HDL-C level	24.9 (22.9-27.0)	19.1 (17.4-21.0)	47.0 (44.3-50.0)
<i>P</i> value	<.001	.57	<.001
Uncontrolled blood pressure ^b	33.3 (31.0-39.3)	23.5 (21.6-25.5)	60.9 (57.7-64.3)
Controlled blood pressure	23.3 (21.4-25.2)	25.2 (23.3-27.2)	53.0 (50.2-55.9)
<i>P</i> value	<.001	.16	.001
BMI ≥30	27.6 (25.4-30.0)	17.7 (16.0-19.6)	48.1 (45.1-51.2)
BMI <30	24.4 (22.4-26.4)	25.2 (23.2-27.3)	53.8 (50.9-56.9)
<i>P</i> value	.04	<.001	.007
Ever smoked	29.1 (27.0-31.2)	25.1 (23.3-27.1)	58.8 (55.9-61.9)
Never smoked	26.3 (24.2-28.7)	23.4 (21.4-25.5)	53.8 (50.7-57.1)
<i>P</i> value	.08	.16	.02
Prior hospitalization ^c	45.0 (41.2-49.3)	24.7 (22.2-27.5)	74.9 (69.9-80.2)
No prior hospitalization	22.9 (21.4-24.6)	24.3 (22.6-26.0)	51.4 (49.0-53.8)
<i>P</i> value	<.001	.75	<.001
CVD diagnosis	29.9 (28.2-31.6)	22.9 (21.4-24.5)	56.6 (54.2-59.0)
Cerebrovascular disease diagnosis	13.7 (11.0-17.1)	35.6 (31.5-40.2)	56.9 (51.4-63.0)
<i>P</i> value	<.001	<.001	.93
Revascularization procedure	33.5 (29.4-38.3)	18.5 (16.0-21.6)	55.0 (49.8-60.8)
No revascularization procedure	27.0 (25.4-28.7)	25.3 (23.7-27.0)	56.9 (54.5-59.4)
<i>P</i> value	.003	<.001	.53

BMI indicates body mass index (calculated as weight in kilograms divided by height in meters squared); CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

SI conversion factor: To convert cholesterol level to millimoles per liter, multiply by 0.0259.

^aLess than 40 mg/dL for men and less than 50 mg/dL for women.

^bAt least 130/80 mm Hg for patients with diabetes and at least 140/90 mm Hg for all other patients.

^cEntered registry because of prior hospitalization.

Costs Among Patients With Established Cardiovascular Disease

Table 4. Descriptive Statistics of Annualized Costs by Resource Component

Variable	Inpatient	Outpatient	Pharmaceuticals	Total
Annualized costs per patient per year, \$				
Mean (SD)	8114 (25,410)	7451 (13,461)	3388 (6954)	18,953 (39,036)
Median (IQR)	678 (6205)	4006 (5352)	1727 (2600)	7763 (13,926)
Patients with zero costs, No. (%)	5712 (46.5)	8 (0.07)	65 (0.5)	2 (0.02)

IQR indicates interquartile range.

billion in indirect costs from lost productivity because of morbidity and premature death. If that estimate is also low, the total annual costs for these conditions may approach \$1 trillion.

Managed care plans are likely already aware that most of their costs are driven by CVD and related conditions such as diabetes and chronic kidney disease. Our results clearly indicate that substantial cost reduction is possible by the avoidance of high-cost CVD events. Preventive medicine also can be expensive: it has been estimated that fully applied prevention activities would increase healthcare costs by approximately \$1700 per person per year.¹² Nevertheless, this is substantially less than the enormous expense of the secondary hospitalizations we report. Therefore, health plan managers and policy analysts searching for ways to reduce costs, while improving quality, may recognize that much greater prevention efforts seem to be a bargain.

Our findings are consistent with recent studies^{6,7} that reported costs of \$18,000 to \$27,000 for patients with acute coronary syndromes; however, those studies did not include patients with other forms of CVD such as MI or stroke. Therefore, to our knowledge, these are the first estimates of per-person medical costs for a heterogeneous population of patients with the full array of CVDs. Although our distribution of costs across inpatient, outpatient, and pharmacy resources was almost identical to that by Menzin et al,⁶ our cost estimates may be low by comparison. The cited studies included much lower proportions of patients 65 years or older, who are likely to incur higher costs. We also excluded patients who did not survive for at least 6 months following entry into the registry. Given that we found significantly greater costs among patients who subsequently died, the excluded patients were likely to have incurred higher than average costs. Therefore, inclusion of those patients would have increased the mean. Furthermore, 12.9% of our study sample qualified for inclusion by having undergone revascularization procedures. Because these high-cost procedures occurred before follow-up, they were not included in subsequent cost calculations. Indeed, all costs associated with an event that qualified a patient for the CVD registry are excluded. Last,

the organizational structure of our study setting is unique. The closed group model that emphasizes low-cost preventive medicine and investment in highly computerized processes that help clinicians coordinate cost-effective care may have led to lower costs than can be achieved in other settings. For all of these reasons, we believe that our cost estimates are conservative. Conversely, annualizing costs could result in overestimation, especially among patients who die. However, sensitivity analyses that excluded various subgroups, including those who died, did not produce different results.

Our findings were also remarkably similar to the results of other studies that have estimated the relative costs of CVD in the presence of other comorbidities. For example, we found that costs were 54% higher among patients with a history of depression relative to those without such a history. Previous studies reported costs that were 47% to 51% higher among older patients with depression¹³ and 15% to 53% higher among women with versus without depression who had suspected myocardial ischemia.¹⁴ We also found that chronic kidney disease, as defined by an eGFR of less than 60 mL/min/1.73 m², was associated with 81% higher costs, similar to the 76% greater costs seen among patients with stage 3 disease in a previous study¹⁵ in this setting. In the present study, diabetes was associated with 58% higher costs, almost identical to the 59% difference found in the same setting using data that were 10 years older⁴ and similar to a more recent study¹⁶ in another setting of managed care patients with and without diabetes and macrovascular disease. Because of the independent contribution of these conditions to cardiovascular risk, secondary prevention of CVD and associated cost reductions may be difficult to achieve. On the other hand, such patients may be more motivated to comply with currently recommended treatment regimens that may provide substantial risk reduction.^{12,17}

A few other limitations warrant discussion. We assessed clinical characteristics at baseline and then observed patients for several years without reassessing those characteristics. Therefore, the extent to which the cost differences we report account for improvements in risk factors cannot be determined. We also required patients to remain enrolled for at

■ **Table 5.** Age- and Sex-Adjusted Mean Annualized Costs by Selected Strata

Variable	Mean Cost, \$			
	Inpatient	Outpatient	Pharmaceuticals	Total
Age ≥65 y	8920	7805	3256	19,981
Age <65 y	7186	7042	3540	17,768
<i>P</i> value	<.001	.002	.03	.002
Men	7421	6952	3190	17,563
Women	8971	8109	3701	20,781
<i>P</i> value	.001	<.001	<.001	<.001
Diabetes	12,528	9983	4747	27,258
No diabetes	7145	6935	3130	17,210
<i>P</i> value	<.001	<.001	<.001	<.001
eGFR <60 mL/min/1.73 m ²	13,944	11,067	4487	29,498
eGFR ≥60 mL/min/1.73 m ²	6537	6594	3195	16,326
<i>P</i> value	<.001	<.001	<.001	<.001
Depression	11,534	10,103	5044	26,681
No depression	7365	6890	3048	17,303
<i>P</i> value	<.001	<.001	<.001	<.001
LDL-C level ≥100 mg/dL	7165	7275	3284	17,724
LDL-C level <100 mg/dL	8593	7959	3759	20,311
<i>P</i> value	.001	.008	<.001	<.001
Low HDL-C level ^a	8735	8577	3796	21,108
Normal HDL-C level	6240	6912	3134	16,286
<i>P</i> value	<.001	<.001	<.001	<.001
Uncontrolled blood pressure ^b	9633	8213	3759	21,605
Controlled blood pressure	7032	6978	3192	17,202
<i>P</i> value	<.001	<.001	<.001	<.001
BMI ≥30	8111	7871	3725	19,707
BMI <30	7200	7069	3189	17,458
<i>P</i> value	.05	.002	<.001	.002
Ever smoked	9051	8097	3741	20,889
Never smoked	7173	6852	3092	17,117
<i>P</i> value	<.001	<.001	<.001	<.001
Prior hospitalization ^c	13,309	10,741	4750	28,800
No prior hospitalization	6987	6771	3137	16,895
<i>P</i> value	<.001	<.001	<.001	<.001
CVD diagnosis	8645	7856	3582	20,083
Cerebrovascular disease diagnosis	5626	5668	2665	13,959
<i>P</i> value	<.001	<.001	<.001	<.001
Revascularization procedure	9021	8518	4014	21,553
No revascularization procedure	8082	7395	3367	18,844
<i>P</i> value	.17	.002	<.001	.01
Died	15,085	9469	4135	28,689
Survived	7187	7247	3345	17,779
<i>P</i> value	<.001	<.001	<.001	<.001
Secondary CVD hospitalization	31,595	21,692	9468	62,755
No secondary CVD hospitalization	5156	5690	2663	13,509
<i>P</i> value	<.001	<.001	<.001	<.001

BMI indicates body mass index (calculated as weight in kilograms divided by height in meters squared); CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

SI conversion factor: To convert cholesterol level to millimoles per liter, multiply by 0.0259.

^aLess than 40 mg/dL for men and less than 50 mg/dL for women.

^bAt least 130/80 mm Hg for patients with diabetes and at least 140/90 mm Hg for all other patients.

^cEntered registry because of prior hospitalization.

least 6 months following registry entry. This requirement generates survival bias that could have affected our results. Finally, as already indicated, the unique structure of KPNW may limit the generalizability of our findings. Kaiser Permanente Northwest has long emphasized preventive medicine and uses various tools, including electronic assists, nonphysician personnel, and physician payment incentives, to maximize quality of care in a cost-containment environment. Nevertheless, the consistency of our results with other published findings is reassuring, suggesting that our data will translate well to other settings.

In conclusion, we found that the total direct medical costs of patients with established CVD were approximately 3 times greater than AHA estimates. The economic burden of providing care to these patients is staggering. Although several comorbid conditions undoubtedly contribute to this burden, avoidance of secondary CVD hospitalization, which in turn drives outpatient and pharmaceutical costs, could substantially reduce healthcare consumption.

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REFERENCES

1. Rosamond W, Flegal K, Furie K, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics: 2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2008;117(4):e25-e146.
2. National Heart, Lung, and Blood Institute. NHLBI Factbook: HTML/ Web version. 2008. <http://www.nhlbi.nih.gov/about/factbook/toc.htm>. Accessed January 5, 2010.
3. Mensah GA, Brown DW. An overview of cardiovascular disease burden in the United States. *Health Aff (Millwood)*. 2007;26(1):38-48.
4. Nichols GA, Brown JB. The impact of cardiovascular disease on medical care costs in subjects with and without type 2 diabetes. *Diabetes Care*. 2002;25(3):482-486.
5. Mahoney EM, Wang K, Cohen DJ, et al; REACH Registry Investigators. One-year costs in patients with a history of or at risk for atherothrombosis in the United States. *Circ Cardiovasc Qual Outcomes*. 2008;1(1):38-45.
6. Menzin J, Wygant G, Hauch O, Jackel J, Friedman M. One-year costs of ischemic heart disease among patients with acute coronary syndromes: findings from a multi-employer claims database. *Curr Med Res Opin*. 2008;24(2):461-468.
7. Etemad LR, McCollam PL. Total first-year costs of acute coronary syndrome in a managed care setting. *J Manag Care Pharm*. 2005;11(4):300-306.
8. Manjunath G, Sarnak MJ, Levey AS. Prediction equations to estimate glomerular filtration rate: an update. *Curr Opin Nephrol Hypertens*. 2001;10(6):785-792.
9. Hornbrook MC, Goodman MJ. Adjusting health benefit contributions to reflect risk. In: Hornbrook MC, ed. *Advances in Health Economics and Health Services Research*. Greenwich, CT: JAI Press Inc; 1991:41-76.
10. Hornbrook MC, Goodman MJ, Fishman PA, Meenan RT, O'Keefe-Rosetti M, Bachman DJ. Building health plan databases to risk adjust outcomes and payments. *Int J Qual Health Care*. 1998;10(6):531-538.
11. Stokes ME, Davis CS, Koch GG. Categorical Data Analysis Using the SAS System. Cary, NC: SAS Institute; 2000.
12. Kahn R, Robertson RM, Smith R, Eddy D. The impact of prevention on reducing the burden of cardiovascular disease. *Circulation*. 2008;118(5):576-585.
13. Katon WJ, Lin E, Russo J, Unutzer J. Increased medical costs of a population-based sample of depressed elderly patients. *Arch Gen Psychiatry*. 2003;60(9):897-903.
14. Rutledge T, Vaccarino V, Johnson BD, et al. Depression and cardiovascular health care costs among women with suspected myocardial ischemia: prospective results from the WISE (Women's Ischemia Syndrome Evaluation) study. *J Am Coll Cardiol*. 2009;53(2):176-183.
15. Smith DH, Gullion CM, Nichols G, Keith DS, Brown JB. Cost of medical care for chronic kidney disease and comorbidity among enrollees in a large HMO population. *J Am Soc Nephrol*. 2004;15(5):1300-1306.
16. Gandra SR, Lawrence LW, Parasuraman BM, Darin RM, Sherman JJ, Wall JL. Total and component health care costs in a non-Medicare HMO population of patients with and without type 2 diabetes and with and without macrovascular disease. *J Manag Care Pharm*. 2006;12(7):546-554.
17. Robinson JG, Maheshwari N. A "poly-portfolio" for secondary prevention: a strategy to reduce subsequent events by up to 97% over five years. *Am J Cardiol*. 2005;95(3):373-378. ■