Clinical Investigations

PREVENTION

Burden of First and Recurrent Cardiovascular Events Among Patients With Hyperlipidemia

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ABSTRACT

Background: Acute cardiovascular (CV) events have been evaluated in patients with specific comorbidities but have not focused on patients with hyperlipidemia or on the their long-term costs.

Objectives: To evaluate incidence of CV events, costs, and resource utilization among patients with hyperlipidemia and baseline risk of CV disease (CVD).

Methods: Patients (age 18 to 64 years) diagnosed with hyperlipidemia or using lipid-modifying medications were identified from administrative claims. Patients were categorized into 3 cohorts based on pre-index clinical characteristics — secondary prevention (SP; history of CV event, n = 15 613); high risk (HR; CVD, n = 47 600); and primary prevention (PP; no CV event history or CVD, n = 60 637) — and followed up to 2 years after the CV event.

Results: During follow-up, ≥1 new CV event occurred in 43.0% of the SP cohort, 33.9% of HR, and 20.9% of PP; and ≥3 new events occurred in 19.8% of the SP cohort, 12.9% of HR, and 5.5% of PP. Incremental total costs were $19 320 for SP, $20 003 for HR, and $17 650 for PP. Compared with patients with only 1 CV event, the mean 2-year cost was 30% higher in patients with 2 CV events and 48% higher in patients with 3 CV events. Only 50% of HR patients (with or without CV events) received statins.

Conclusions: Patients with recurrent CV events had higher total health care costs during 24-month follow-up for each type of CV event. Total health care costs among patients with a CV event were higher for the initial as well as subsequent events. Statins and lipid-modifying medications were significantly underutilized in all cohorts, despite the presence of CVD.

Introduction

As many as 84 million Americans have cardiovascular disease (CVD). Even among those without CVD at age 50 years, the lifetime risk of developing CVD exceeds 50% in men and 39% in women.[1] Patients with a history of coronary heart disease (CHD) or CHD risk equivalents (eg, diabetes mellitus [DM], peripheral arterial disease, symptomatic carotid artery disease, 10-year Framingham risk >20%) are considered at high risk for CV events.[2]

Current information concerning the long-term costs of CV events in commercially insured patients with varying risk is limited.[3,4] Previous studies evaluated acute-CV-event costs in patients with hypertension, acute coronary syndrome, DM, or atherosclerosis, but not among patients with hyperlipidemia.[4–7] Although short-term costs have been examined,[3–9] the extent to which costs and resource utilization vary among subgroups of patients at risk for CVD has not been studied, nor have long-term (up to 2 years post-CV event) costs or resource utilization associated with recurrent CV events been explored. Existing studies estimating costs over a 24-month period are now outdated.[6] To fill this research gap, the current study used administrative claims data from a large US commercial health plan to analyze subsequent CV events, resource utilization, and

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long-term costs among patients with hyperlipidemia and CVD or CHD risk equivalents.

Methods

Data Source and Patient Identification

This retrospective observational cohort study used administrative claims from the HealthCore Integrated Research Database (HIRD). The HIRD contains longitudinal medical and pharmacy claims data for approximately 33 million members from 14 commercial health plans across the United States. All claims data were from a limited dataset with de-identified patient information. No patients were directly involved in the study; therefore, this study was exempt from an institutional review board review.

The study sample included adults age 18 to 64 years with a diagnosis of hyperlipidemia or use of lipid-modifying medications (LMT; statins, ezetimibe, bile acid sequestrants, fibric acid derivatives, nicotinic acid derivatives, and other lipid-modifying agents) from January 1, 2007, to December 31, 2008 (intake period). The index date was defined as the first occurrence of a hyperlipidemia diagnosis or use of any LMT during the intake period. The baseline period was 12 months prior to the index date, and patients were followed until the end of the study period, end of the eligibility period, or death, whichever occurred first. The follow-up period for the occurrence of a new CV event (CV event date) was set from the index date to the end of study follow-up. The follow-up period for health care resource utilization and costs ran from the CV event date until the end of the study follow-up period. Patients were followed for 2 years for the assessment of new CV events, health care resource utilization, and costs.

Patients were categorized into the following 3 cohorts based on CV risk level during the baseline period: (1) secondary CVD prevention (SP; patients with a history of a CV event, including myocardial infarction [MI], stroke, unstable angina [UA], coronary artery bypass graft [CABG], or percutaneous coronary intervention [PCI]); (2) high risk (HR; patients not in the secondary CVD prevention cohort but who had CVD or risk-equivalent conditions, including chronic ischemic heart disease, stable angina, peripheral arterial disease, abdominal aortic aneurysm, transient ischemic attack [TIA], or type 2 DM); and (3) primary prevention (PP; patients with no CV event history or CHD risk equivalents).

In each cohort, patients with CV-event-related hospitalizations for MI, UA, CABG, PCI, ischemic stroke, TIA, or heart failure (HF) after the index dates were included in the case group; those with no CV-event-related hospitalization were in the control group. Cases and controls were matched within each cohort for age, sex, geographic region, comorbidities, baseline health care resource utilization, and length of continuous health plan eligibility during follow-up using propensity score matching. Patients in each cohort were required to have $\geq$24 months of continuous follow-up after the CV event date for evaluation of long-term costs.

Outcome Measures

A CV event during follow-up was defined as hospitalization for MI, ischemic stroke, CABG, PCI, UA, TIA, or HF. If a patient was hospitalized for MI or UA and also had a CABG or PCI on the same date, the CV event was identified as MI or UA. Patient characteristics were captured during baseline. All health care resource utilization, including LMT use, and total health care costs were assessed during baseline and follow-up. Resource utilization included inpatient hospitalizations (including length of stay), emergency department (ED) visits, office visits, outpatient facility visits, and pharmacy prescription fills. Utilization of LMT included the number of patients with prescription fills for each drug in that group. For statins, patients were also stratified by each specific statin and by statin intensity levels (based on dosages and as defined in the 2013 American College of Cardiology/American Heart Association [ACC/AHA] guideline).[10] Total costs included both medical (inpatient services, ED, office visit, and outpatient services) and pharmacy costs. Costs were defined as the sum of the amount paid by the health plan and the patient out-of-pocket. Costs were adjusted to 2013 dollars based on the Consumer Price Index.[11] Total medical costs were further categorized by patients with 1, 2, or 3 CV events during follow-up for each type of CV event. The incremental cost of a new CV event was calculated as the total cost of care for the case group compared with the control group within each CV risk cohort. The burden of subsequent CV events during follow-up included the number of patients with 1, 2, or 3 subsequent CV events and mean time to subsequent CV events. Study outcomes were assessed for each type of CV event and for a composite endpoint of any CV event.

Statistical Analysis

Baseline demographic and clinical characteristics, resource utilization and cost, and medication use were described for all patients in each cohort; burden of subsequent CV events was described only for cases in each cohort. Descriptive analyses included means and standard deviation and relative frequencies for continuous and categorical variables, respectively. Continuous outcomes were compared using independent t tests and categorical outcomes were compared using χ^2 tests. Propensity score matching using a 1:1 greedy algorithm was used to balance the differences in baseline demographic and clinical characteristics, resource utilization and cost, and medication use between cases and controls within each CV risk cohort.[12] Balance after matching was assessed using standardized differences.[13] A standardized difference of 10% indicated negligible correlation between the cases and controls.[14]

Results

Patient Characteristics

A total of 123 850 patients were included: 15 613 (12.6%) in the SP cohort, 47 600 (38.4%) in the HR cohort, and 60 637 (49.0%) in the PP cohort (Table 1). The cases and controls within each cohort were well matched with standardized differences well below 10% for all propensity score matching variables. The mean age at baseline was 55.9 years, with the PP cohort 1.7 years younger than the SP cohort. Approximately two-thirds of the overall population was male (65.4%).

A similar proportion of patients in the SP and HR cohorts (64.1%, both cohorts) received LMT at baseline. Slightly

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Table 1. Baseline Demographics and Clinical Characteristics[a]

	SP Cohort		HR Cohort		PP Cohort	
	Control Group, n = 7814	Case Group, n = 7799	Control Group, n = 23 776	Case Group, n = 23 824	Control Group, n = 30 388	Case Group, n = 30 249
Age (on index date), y, mean (SD)	55.3 (6.6)	54.9 (6.6)	55.3 (6.3)	54.9 (6.5)	53.6 (7.1)	53.2 (7.2)
Age category, n (%)						
18–39 y	201 (2.6)	199 (2.6)	499 (2.1)	628 (2.6)	1337 (4.4)	1504 (5.0)
40–64 y	7613 (97.4)	7600 (97.5)	23 277 (97.9)	23 196 (97.4)	29 051 (95.6)	28 745 (95.0)
Female sex, n (%)	2629 (33.6)	2519 (32.3)	8113 (34.1)	7848 (32.9)	11 530 (37.9)	11 148 (36.9)
Geographic region, n (%)						
Northeast	1628 (20.8)	1653 (21.2)	4905 (20.6)	5139 (21.6)	5641 (18.6)	5858 (19.4)
Midwest	1960 (25.1)	1993 (25.6)	5937 (25.0)	6035 (25.3)	7229 (23.8)	7206 (23.8)
South	2388 (30.6)	2372 (30.4)	7283 (30.6)	7278 (30.6)	9422 (31.0)	9317 (30.8)
West	1285 (16.4)	1228 (15.8)	3962 (16.7)	3872 (30.6)	6258 (20.6)	6204 (20.5)
Unknown/missing	553 (7.1)	553 (7.1)	1689 (7.1)	1500 (6.3)	1838 (6.1)	1664 (5.5)
Type of health plan, n (%)						
HMO	2328 (29.8)	2492 (32.0)	7036 (29.6)	7403 (31.1)	7658 (25.2)	7791 (25.8)
PPO	5411 (69.3)	5235 (67.1)	16 588 (69.8)	16 264 (68.3)	22 402 (73.7)	22 122 (73.1)
CDHP	75 (1.0)	72 (0.9)	152 (0.6)	157 (0.7)	328 (1.1)	336 (1.1)
Medicare Advantage	354 (4.5)	432 (5.5)	1129 (4.8)	1251 (5.3)	816 (2.7)	912 (3.0)
Comorbidities, n (%)						
Hypertension	6108 (78.2)	6088 (78.1)	17 209 (72.4)	17 228 (72.3)	13 468 (44.3)	13 302 (44.0)
Metabolic syndrome	137 (1.8)	135 (1.7)	394 (1.7)	405 (1.7)	215 (0.7)	214 (0.7)
Liver disease	435 (5.6)	454 (5.8)	1165 (4.9)	1217 (5.1)	858 (2.8)	847 (2.8)
Renal disease	502 (6.4)	542 (7.0)	1478 (6.2)	1507 (6.3)	478 (1.6)	528 (1.8)
Quan-Charlson comorbidity index, mean (SD)[§]	2.5 (1.9)	2.5 (1.9)	1.7 (1.6)	1.7 (1.6)	0.4 (1.0)	0.4 (1.1)
Any dyslipidemic medications,[b] n (%)	5013 (64.2)	4992 (64.0)	15 293 (64.3)	15 199 (63.8)	11 247 (37.0)	11 014 (36.4)
Statins[b]	4377 (56.0)	4347 (55.7)	12 645 (53.2)	12 578 (52.8)	9188 (30.2)	9019 (29.8)
Bile acid sequestrants[b]	104 (1.3)	96 (1.2)	250 (1.1)	277 (1.2)	236 (0.8)	229 (0.8)
Fibric acid derivatives[b]	630 (8.0)	657 (8.4)	2546 (10.7)	2490 (10.5)	1305 (4.3)	1288 (4.3)
Ezetimibe[b]	1294 (16.6)	1293 (16.6)	3737 (15.7)	3738 (15.7)	1894 (6.2)	1854 (6.1)
Nicotinic acid derivatives[b]	416 (5.3)	434 (5.6)	968 (4.1)	999 (4.2)	400 (1.3)	377 (1.3)
Other antihyperlipidemics[b]	126 (1.6)	128 (1.6)	326 (1.4)	317 (1.3)	160 (0.5)	154 (0.5)
Inpatient hospitalizations, n (%)	4594 (58.8)	4623 (59.3)	4321 (18.2)	4537 (19.0)	2363 (7.8)	2433 (8.0)
No. of hospitalizations, mean (SD)	0.9 (1.1)	0.9 (1.1)	0.3 (0.9)	0.3 (0.8)	0.1 (0.7)	0.1 (0.5)
Length of stay, d, mean (SD)	4.0 (9.1)	4.4 (9.8)	1.1 (5.3)	1.4 (6.1)	0.3 (2.3)	0.4 (2.9)
Total costs, mean (SD)	$35 255 ($58 631)	$35 300 ($51 281)	$15 814 ($30 368)	$16 038 ($29 048)	$7542 ($16 637)	$7707 ($17 393)

Abbreviations: CDHP, consumer-driven health plan; HMO, health maintenance organization; HR, high risk; PP, primary prevention; PPO, preferred provider organization; SD, standard deviation; SP, secondary prevention.

[a] After matching.

[b] Patients with ≥1 fill, n (%).

[§] Quan H, Sundararajan V, Halfon P, et al.: Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care*. 2005; 43:1130–1139.

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Table 2. CV-Related Event Risk

	SP Cohort, n = 8218	HR Cohort, n = 23 959	PP Cohort, n = 30 250
Any CV event (composite endpoint), n (%)			
≥1 events	3532 (43.0)	8123 (33.9)	6320 (20.9)
Only 1 event	1152 (14.0)	3040 (12.7)	2952 (9.8)
Only 2 events	756 (9.2)	1984 (8.3)	1695 (5.6)
≥3 events	1624 (19.8)	3099 (12.9)	1673 (5.5)
Events per patient for all patients, mean (SD)	1.56 (3.3)	1.00 (2.3)	0.46 (1.2)
Events per patient for patients with ≥1 events, mean (SD)	3.64 (4.1)	2.94 (3.0)	2.19 (1.9)
Time to first event from index date, d, mean (SD)	870 (562)	1009 (565)	1007 (555)
Time between first and second events, d, mean (SD)	299 (339)	274 (324)	272 (345)
Time between second and third events, d, mean (SD)	225 (266)	205 (258)	213 (290)

Abbreviations: CV, cardiovascular; HR, high-risk; PP, primary prevention; SD, standard deviation; SP, secondary prevention.

more than half of patients in the SP (55.9%) and HR (53.2%) cohorts received a statin at baseline. A sizeable proportion of patients in the SP (43.6%) and HR cohorts (42.7%) were using nonstatin LMT (eg, ezetimibe, bile acid sequestrants, fibric acid derivatives, nicotinic acid derivatives, omega-3 fatty acids). In the PP cohort, 36.7% received lipid-lowering medication at baseline, with 30.0% using statins and 16.7% using nonstatin LMT. At baseline, 7.2% in the SP cohort, 6.4% in the HR cohort, and 2.7% in the PP cohort received combination therapy. Patterns of statin use were similar across all 3 cohorts, with atorvastatin used most commonly (SP cohort, 33.6%; HR cohort, 31.2%; PP cohort, 17.9%). In the SP and HR cohorts, 8.2% and 5.6% of patients received high-intensity statins, respectively, and 2.8% from the PP cohort received low-intensity statins (Table 1).

Burden of Cardiovascular Events

In the SP cohort, 43.0% of cases had ≥1 new CV event, with 19.8% having ≥3 new events over 2 years of follow-up (Table 2). In the HR cohort, 33.9% of cases had ≥1 new CV event, with 12.9% having ≥3 new events. In the PP cohort, 20.9% of cases had ≥1 CV event, with 5.5% having ≥3 events.

In the SP cohort, among 3532 patients who had ≥1 CV event, 52.6% had ≥1 HF event, followed by UA (36.9%), ischemic stroke (33.5%), and PCI (26.0%). Among 8123 patients with ≥1 CV event in the HR cohort, 59.3% had ≥1 HF event, followed by UA (28.1%), ischemic stroke (24.5%), and PCI (21.5%). Lastly, among 6230 patients with ≥1 CV event in the PP cohort, 43.9% had ≥1 HF event, followed by UA (26.5%), ischemic stroke (26.2%), and MI (21.7%).

The mean time to the first new CV event was shortest for the SP cohort (870 days) compared with the HR (1009 days) and PP (1007 days) cohorts (Table 2). The time between the first and second CV event was 299 days in the SP cohort, 274 days in the HR cohort, and 272 days in the PP cohort. The time between the second and third CV event was 225 days in the SP cohort, compared with 205 days in the HR cohort and 213 days in the PP cohort.

Long-Term Health Care Resource Utilization and Costs

Health care resource utilization at 24 months of follow-up was higher among cases than controls in each of the CV risk cohorts (Table 3). Differences between cases and controls were significant in each cohort for inpatient hospitalizations, ED visits, and outpatient services. In the HR cohort, controls had significantly higher utilization than cases for office visits and prescriptions. Although the proportion of patients with office visits and prescriptions was not significantly different between cases and controls in the SP and PP cohorts, the mean number of office visits and prescriptions was significantly higher among cases compared with controls.

Total health care costs were higher among cases compared with controls in all 3 cohorts, and costs remained higher throughout the follow-up period for each type of CV event. The incremental total costs over 2 years of follow-up were highest for the HR cohort ($20 003) compared with the SP ($19 320) and PP ($17 650) cohorts (Table 4). Mean 2-year total costs among patients with only 1 CV event ranged from $46 133 to $76 239 in the SP cohort and from $54 011 to $79 442 in the HR cohort. Across all cohorts, CABG was associated with the highest incremental costs (SP cohort, $76 958; HR cohort, $73 318; PP cohort, $70 416); TIA was associated with the lowest incremental costs (SP cohort, $37 478; HR cohort, $36 186; PP cohort, $26 723). Forty-three percent of first-year costs associated with TIA events occurred during the first 30 days post-CV event among cases in the SP cohort; 48% occurred during the first 30 days in the HR cohort. Across all cohorts, 63% to 73% of first-year costs associated with CABG occurred during the first 30 days post-CV event (SP cohort, 63%; HR cohort, 69%; PP cohort, 73%).

Across all cohorts, the mean total cost among cases with only 1 CV event was lower than that for those who had 2 or 3 CV events, except for TIA. Compared with patients with only 1 CV event, the mean 2-year cost was 30% higher in patients with 2 CV events and 48% higher in patients with 3 CV events.

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Table 3. Overall All-Cause Resource Utilization and Costs

	SP Cohort				HR Cohort				PP Cohort			
	Control Group, n = 6903	Case Group, n = 7024	p-value[a]	Incremental Costs[b]	Control Group, n = 20 516	Case Group, n = 26 640	p-value[a]	Incremental Costs[b]	Control Group, n = 26 567	Case Group, n = 26 337	p-value[a]	Incremental Costs[b]
Inpatient hospitalizations, n (%)	883 (12.8)	5550 (79.0)	<0.0001		1928 (9.4)	15198 (73.6)	<0.0001		1513 (5.7)	18590 (70.6)	<0.0001	
Mean no. of hospitalizations per patient (SD)	0.2 (0.58)	1.4 (1.4)	<0.0001		0.1 (0.5)	1.3 (1.4)	<0.0001		0.1 (0.5)	1.07 (1.1)	<0.0001	
Mean length of stay, d, (SD)	0.7 (4.0)	5.8 (12.8)	<0.0001		0.6 (4.0)	6.1 (14.0)	<0.0001		0.3 (2.4)	4.4 (10.7)	<0.0001	
Mean cost, $ (SD)	3298 (19 556)	31 320 (60 027)	<0.0001	15 077	2062 (13 917)	31 252 (64 632)	<0.0001	15 245	1200 (8397)	27 816 (59 213)	<0.0001	13 599
ED visits, n (%)	1108 (16.1)	1850 (26.3)	<0.0001		2756 (13.4)	4773 (23.1)	<0.0001		2606 (9.8)	5107 (19.4)	<0.0001	
Mean visits per patient (SD)	0.2 (1.0)	0.5 (1.4)	<0.0001		0.2 (1.0)	0.4 (1.0)	<0.0001		0.1 (0.9)	0.3 (0.9)0	<0.0001	
Mean cost, $ (SD)	393 (1812)	757 (2349)	<0.0001	359	282 (1941)	600 (2036)	<0.0001	286	201 (1485)	526 (2069)	<0.0001	251
Office visits, n (%)	5836 (84.5)	(85.7)	0.0568		17 139 (83.5)	16 788 (81.3)	<0.0001		21 117 (79.5)	20 951 (79.6)	0.8556	
Mean visits per patient (SD)	7.8 (8.5)	11.0 (10.1)	<0.0001		7.3 (8.2)	10.7 (10.3)	<0.0001		5.4 (7.4)	9.0 (9.2)	<0.0001	
Mean cost, $ (SD)	1128 (2554)	1592 (3365)	<0.0001	498	1107 (4349)	1591 (3674)	<0.0001	527	783 (2121)	1439 (4008)	<0.0001	516
Outpatient office visits, n (%)	5690 (82.4)	5949 (84.7)	0.0003		16 805 (81.9)	16 639 (80.6)	0.0008		20 390 (76.8)	20 640 (78.4)	<0.0001	
Mean visits per patient (SD)	9.0 (13.5)	16.4 (23.3)	<0.0001		9.0 (14.4)	17.1 (24.6)	<0.0001		6.3 (10.6)	13.7 (19.4)	<0.0001	
Mean cost, $ (SD)	4066 (10 253)	7641 (19 180)	<0.0001	3063	3680 (10 522)	8090 (21 604)	<0.0001	3408	2472 (8971)	6378 (18 161)	<0.0001	2726
Prescriptions, n (%)	5819 (84.3)	5976 (85.1)	0.1994		17 038 (83.1)	16 600 (80.4)	<0.0001		20 864 (78.5)	20 736 (78.7)	0.575	
Mean no. of prescriptions per patient (SD)	40.8 (36.9)	52.2 (41.4)	<0.0001		39.9 (36.5)	52.0 (43.4)	<0.0001		22.3 (25.9)	37.1 (34.0)	<0.0001	
Mean cost, $ (SD)	4209 (6838)	5246 (6860)	<0.0001	1673	4259 (7127)	5205 (6889)	<0.0001	1643	2157 (4926)	3514 (6465)	<0.0001	1284
Total medical costs, $, mean (SD)	8884 (24 188)	41 309 (67 779)	<0.0001	18 117	7131 (20 994)	41 534 (73 203)	<0.0001	18 824	4655 (14 334)	36 159 (66 368)	<0.0001	16 638
Total costs,[c] $, mean (SD)	13 094 (26 050)	46 555 (69 423)	<0.0001	19 320	11 389 (23 403)	46 739 (74 939)	<0.0001	20 003	6813 (16 004)	39 673 (68 039)	<0.0001	17 650

Abbreviations: ED, emergency department; HR, high risk; PP, primary prevention; SD, standard deviation; SP, secondary prevention.

[a] *P* values are from *t* test for mean values.

[b] Incremental cost equals all-cause cost for the case – all-cause cost for the matched control.

[c] Sum of medical and pharmacy costs.

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Table 4. Overall Follow-up Total All-Cause Costs[a]

	SP Cohort					HR Cohort					PP Cohort				
	n	Control Group,Mean (SD)	Case Group, Mean (SD)	p-value[b]	Incremental Costs[c]	n	Control Group, Mean (SD)	Case Group, Mean (SD)	p-value[b]	Incremental Costs[c]	n	Control Group, Mean (SD)	Case Group, Mean (SD)	p-value[b]	Incremental Costs[c]
MI total cost, $	1830	12 535 (25 112)	58 720 (78 345)	<0.0001	49 504	4868	9890 (18 410)	61 303 (97 892)	<0.0001	54 082	6651	5975 (12 968)	51 058 (80 138)	<0.0001	46 626
For patients with only 1 event	580	13 443 (23 276)	66 633 (71 796)	<0.0001	55 734	1220	10 559 (19 041)	75 310 (88 360)	<0.0001	66 979	1092	6893 (14 050)	76 100 (95 386)	<0.0001	70 614
For patients with only 2 events	103	17 369 (48 136)	96 642 (106 992)	<0.0001	84 548	218	12 305 (21 487)	104 709 (242 503)	<0.0001	95 543	143	6453 (8528)	98 554 (207 302)	<0.0001	92 865
For patients with only 3 events	45	10 525 (11 855)	128 938 (174 925)	<0.0001	118 751	69	16 865 (27 083)	124 552 (144 163)	<0.0001	109 650	19	13 297 (29 805)	133 705 (173 904)	<0.0001	127 380
UA total cost, $	2785	12 234 (23 548)	47 520 (61 901)	<0.0001	38 672	7247	10 223 (20 486)	46 945 (71 085)	<0.0001	39 580	8252	6207 (14 531)	39 863 (57 284)	<0.0001	35 364
For patients with only 1 event	768	13 441 (25 749)	56 039 (58 364)	<0.0001	46 133	1698	11 213 (27 483)	64 409 (103 689)	<0.0001	55 880	1266	6681 (16 328)	62 855 (93 300)	<0.0001	57 398
For patients with only 2 events	240	13 982 (30 035)	66 558 (53 590)	<0.0001	54 665	295	11 091 (17 725)	68 901 (63 113)	<0.0001	59 594	225	8334 (15 966)	72 224 (60 022)	<0.0001	65 068
For patients with only 3 events	65	22 586 (42 403)	68 917 (61 004)	<0.0001	53 766	76	9520 (13 110)	86 962 (78 016)	<0.0001	78 217	56	6960 (9552)	81 153 (51 829)	<0.0001	74 210
Ischemic stroke total cost, $	2330	11 794 (20 477)	50 658 (76 577)	<0.0001	42 128	5033	9592 (17 909)	53 983 (103 521)	<0.0001	47 247	6964	6345 (14 622)	43 456 (87 001)	<0.0001	39 381
For patients with only 1 event	711	12 619 (23 036)	63 076 (85 956)	<0.0001	53 046	1342	10 759 (20 846)	74 773 (136 656)	<0.0001	66 293	1203	7008 (14 285)	70 270 (119 946)	<0.0001	64 984
For patients with only 2 events	186	12 711 (15 929)	85 678 (114 452)	<0.0001	74 749	311	10 367 (15 360)	89 122 (128 049)	<0.0001	80 429	207	6960 (14 021)	92 298 (127 481)	<0.0001	86 613
For patients with only 3 events	60	11 421 (11 363) 7887	85 728 (80 322) 58 700	<0.0001	75 833	93	7941 (10 104)	106 255 (128 189)	<0.0001	99 059	59	5845 (6082)	119 760 (174 762)	<0.0001	114 968
CABG total cost, $	693	13 270 (27 939)	87 348 (107 744)	<0.0001	76 958	2602	9814 (17 394)	81 448 (91 101)	<0.0001	73 318	2726	6965 (14 280)	76 035 (78 195)	<0.0001	70 416
For patients with only 1 event	229	14 028 (35 727)	86 943 (94 871)	<0.0001	76 329	668	9839 (19 626)	87 406 (94 244)	<0.0001	79 442	495	7537 (15 386)	90 895 (96 337)	<0.0001	84 911
For patients with only 2 events	4	17 853 (27 237)	174 856 (92 124)	<0.0001	157 002	8	12 133 (17 811)	174 647 (174 419)	<0.0001	164 666	5	13 038 (18 438)	201 245 (129 253)	<0.0001	188 207
For patients with only 3 events	0					0					0				

Table 4. Continued

	SP Cohort					HR Cohort					PP Cohort				
	n	Control Group,Mean (SD)	Case Group, Mean (SD)	p-value[b]	Incremental Costs[c]	n	Control Group, Mean (SD)	Case Group, Mean (SD)	p-value[b]	Incremental Costs[c]	n	Control Group, Mean (SD)	Case Group, Mean (SD)	p-value[b]	Incremental Costs[c]
PCI total cost, $	2185	12 084 (23 226)	49 624 (55 336)	<0.0001	40 438	5670	9900 (20 679)	49 841 (62 458)	<0.0001	42 337	6475	6281 (13 847)	46 045 (60 895)	<0.0001	41 158
For patients with only 1 event	601	13 260 (29 009)	58 943 (68 049)	<0.0001	48 474	1319	9633 (13 715)	62 240 (77 698)	<0.0001	54 011	1017	6308 (11 524)	66 936 (83 694)	<0.0001	61 421
For patients with only 2 events	144	16 030 (32 957)	69 829 (53 671)	<0.0001	58 581	224	11 175 (19 678)	83 760 (75 464)	<0.0001	74 519	144	7515 (13 331)	74 917 (59 475)	<0.0001	68 583
For patients with only 3 events	43	11 883 (13 806)	73 371 (63 880)	<0.0001	62 713	62	12 213 (21 914)	116 029 (105 987)	<0.0001	106 109	27	7662 (12 432)	91 527 (66 572)	<0.0001	83 899
TIA total cost, $	996	12 134 (22 654)	46 183 (64 114)	<0.0001	37 478	2508	9312 (17 766)	42 897 (99 019)	<0.0001	36 186	4138	6016 (14 100)	30 525 (68 767)	<0.0001	26 723
For patients with only 1 event	326	13 327 (28 721)	65 131 (83 869)	<0.0001	54 677	652	10 961 (23 197)	74 284 (172 482)	<0.0001	65 818	602	6948 (14 187)	63 335 (105 228)	<0.0001	58 256
For patients with only 2 events	66	13 398 (19 164)	61 893 (71 100)	<0.0001	51 141	74	13 482 (30 615)	76 061 (104 643)	<0.0001	66 248	66	8295 (15 051)	55 348 (67 532)	<0.0001	48 486
For patients with only 3 events	16	13 886 (17 644)	72 647 (72 967)	<0.0001	63 748	16	6502 (5042)	75 826 (45 384)	<0.0001	69 746	11	2954 (6159)	123 247 (155 736)	<0.0001	120 521
HF total cost, $	2627	12 335 (21 780)	65 357 (97 613)	<0.0001	56 078	8769	10 402 (18 690)	60 539 (100 804)	<0.0001	53 247	7893	6757 (15 465)	54 205 (97 553)	<0.0001	49 637
For patients with only 1 event	739	12 844 (25 296)	66 087 (78 464)	<0.0001	55 996	2126	10 926 (19 511)	63 390 (85 300)	<0.0001	55 451	1541	7705 (18 000)	69 771 (103 004)	<0.0001	64 167
For patients with only 2 events	285	13 078 (17 770)	76 136 (99 449)	<0.0001	65 473	848	10 526 (20 368)	85 251 (114 790)	<0.0001	76 976	515	7532 (15 733)	96 620 (153 105)	<0.0001	90 921
For patients with only 3 events	174	13 821 (19 010)	92 482 (92 496)	<0.0001	80 646	453	11 650 (19 353)	101 438 (162 312)	<0.0001	92 392	204	7983 (15 475)	95 393 (95 319)	<0.0001	89 004

Abbreviations: CABG, coronary artery bypass graft; HF, heart failure; HR, high risk; MI, myocardial infarction; PCI, percutaneous coronary intervention; PP, primary prevention; SP, secondary prevention; TIA, transient ischemic attack; UA, unstable angina.

[a]All-cause total costs includes both medical and pharmacy costs for all medical events during the follow-up period.

[b]*P* values are from *t* test for mean values.

[c]Incremental cost equals all-cause cost for the case – all-cause cost for the matched control.

Discussion

Cardiovascular disease is a major cause of morbidity and mortality in the United States, not only in terms of the immediate acute phase for CV events, but also in subsequent years. This retrospective, real-world analysis demonstrated that utilization and health care costs were higher among patients with a CV event for the initial event as well as for subsequent events during 2 years of follow-up. A higher proportion of patients who had a CV event at baseline (SP cohort) had a recurrent CV event during the study period, compared with patients who had no CV event at baseline (HR and PP cohorts). Secondary prevention cohort patients also had shorter time to the first recurrent CV event compared with other cohorts. A relatively large number of patients in each cohort had secondary or tertiary events during the 2-year follow-up period. Heart failure was the most frequent type of CV event among all cohorts. Acute MI is associated with myocardial necrosis and fibrosis. The incremental loss of myocardial tissue mass from sequential acute coronary syndromes and the progression of atherosclerotic disease increase risk for developing left ventricular systolic dysfunction and ischemic cardiomyopathy, respectively. Both of these clinical sequelae increase risk of the development of HF and can be directly related to dyslipidemia because they correlate with severity of atherosclerotic disease. However, we were unable to ascertain subtypes of HF in this study.

Despite the fact that this study was conducted 5 years after the National Cholesterol Education Program Adult Treatment Panel III guidelines were introduced into clinical care,[15] a surprisingly low percentage of patients with CVD or CHD risk equivalents received statin therapy, leaving these patients at high risk of CV events.

Additionally, across all cohorts, the percentage of patients using high-intensity statin therapy was considerably lower than in other recently published US studies. For example, among Medicare beneficiaries discharged following a CHD event, 27% of first-fill statin prescriptions were for high-intensity statins,[16] whereas among veterans with CVD, 36.5% received high-intensity statins.[17] Both studies acknowledged these rates of high-intensity statin use were low. However, the rates of high-intensity statin use reported in the current study were more closely aligned with those reported in recent European studies. In those studies, high-intensity statin use ranged from 7.4% among unselected patients to 9.4% in high-risk patients with controlled low-density lipoprotein cholesterol (LDL-C) levels.[18,19]

The ACC/AHA blood cholesterol guidelines advocate for use of risk-appropriate statin dose and potency (as well as adjuvant LMY as indicated) to optimally reduce risk for cardiovascular events.[10] There is a clear continued need to encourage clinicians to treat patients at risk more aggressively and with higher doses of statins than is currently observed. It is also important to emphasize that among high-risk patients, if a >50% reduction in LDL-C cannot be achieved, then use of adjuvant LMT is indicated as promulgated by the guideline.

Total health care resource utilization was higher among cases compared with controls in all 3 cohorts, and the cost difference was maintained throughout the follow-up period. The costs incurred beyond the acute phase are significant, because a substantial number of patients had second and third CV events during this 24-month period. Costs increased with the number of subsequent events, with mean 2-year costs nearly 50% higher for a third CV event compared with the first event. Avoidance of subsequent CV events through more effective management of hyperlipidemia could reduce this current cost burden. Incremental costs remained higher for cases than controls throughout the entire follow-up period; costs for the case groups did not fall to the levels observed in the control group at any point, which adds to the economic burden.

The health care costs associated with CVD can be staggering. Although the initial hospitalization for a CV event can range from $7000 to > $56 000, the follow-up costs can be just as burdensome, averaging $16 600 in the first year following the CV event and $34 000 3 years later.[8] The costs in the current study were greater, with the 2-year total ranging from $46 133 to $79 442 for the first CV event.

Study Limitations

The claims database used for this study is large and geographically diverse, with long follow-up data available. However, a limitation of claims analyses is that the data are intended for reimbursement purposes, not research, so the coding for CV events and comorbid conditions may contain undetected errors or omissions. All patients included in the study were members of US commercial health plans; the results may not be generalizable to patients with other types of health insurance or living outside the United States. Lack of clinical and health behavior information (eg, blood pressure, smoking status) limits the determination of specific risk level for the study population. Additionally, because laboratory results were unavailable, the success of statin therapy in lowering LDL-C levels to treatment goals was uncertain.

Conclusion

The results of this retrospective study show a substantial proportion of patients experience subsequent CV events both near term and 2 years after an initial CV event. Patients with recurrent CV events had higher total health care costs for the initial as well as subsequent events, compared with patients who did not have subsequent events. Statins and LMT were significantly underutilized in all cohorts, despite the presence of CVD. Future research is needed to thoroughly examine patient-physician behavior and treatment patterns to improve patient outcome. A better understanding of the reasons for underutilization of current LMT and availability of new therapies to reduce LDL-C may provide clinicians and patients an opportunity to reduce the burden of CV events among a high-CVD-risk population.

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