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ORIGINAL RESEARCH

A Retrospective Study to Examine Healthcare Costs Related to Cardiovascular Events in Individuals with Hyperlipidemia

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ABSTRACT

Introduction: Few studies have demonstrated the cost burden of cardiovascular events (CVEs) among patients with hyperlipidemia. The primary objective of this study was to determine the mean costs associated with CVEs among patients with hyperlipidemia by follow-up time period. Secondary objectives of this study included characterizing costs by CVE type and coronary heart disease (CHD) risk.

Methods: This retrospective cohort study used longitudinal claims to calculate payer costs according to CHD risk level and type of CVE, during several follow-up periods (acute and short-term, comprising year 1; plus years 2 and 3).

Results: There were 193,385 patients with hyperlipidemia with a CVE. Costs in the acute (30-day) period were highest ($22,404) driven by inpatient care (77%). Costs remained high ($15,133 in year 3) with ambulatory care (from 14% in acute to 37% in year 3) and pharmaceutical costs (from 2% in acute to 24% in year 3) representing a greater proportion. After second and third CVEs, acute costs were lower than for the first CVE. But in the post-acute periods, costs were higher after second and third CVEs than after first CVEs. Acute costs varied considerably by type of CVE ($9149 for transient ischemic attack to $54,251 for coronary artery bypass graft; $P < 0.001$), but post-acute costs were more similar across types. Costs differed by baseline CHD risk for all follow-up periods ($P < 0.001$), but less than by CVE type. As expected, patients without CVEs had significantly lower costs.

Conclusion: Among patients with hyperlipidemia, the economic burden of CVEs is substantial up to 3 years after a CVE. Costs remain high after subsequent CVEs and actually increase for non-inpatient utilization.

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INTRODUCTION

The treatment and prevention of hyperlipidemia (elevated low-density lipoprotein-C [LDL-C] levels) have been a significant public health focus for many years. Elevated LDL-C is associated with increased risk of developing coronary heart disease (CHD), the most common cause of death in the United States (US) [1, 2]. Meta-analysis of 26 clinical trials demonstrated that risk of any cardiovascular event (CVE) was reduced by 20% and mortality was reduced by 10%, for every 38.7 mg/dL reduction of LDL-C [2]. Another more recent meta-analysis demonstrated among 40 trials of lipid-modifying drugs that LDL-C, but not high-density lipoprotein, levels were predictive of both primary and secondary CVEs [3]. The newest American College of Cardiology/American Heart Association Task Force on Practice Guidelines defined the characteristics of patients who would most benefit from statin therapy to treat hyperlipidemia and prevent CVEs, including atherosclerotic cardiovascular disease (ASCVD), elevated LDL-C, diabetes, and high estimated 10-year ASCVD risk [4]. Yet, even though high LDL-C affects 71 million (33.5%) US adults, <50% of affected individuals receive treatment [1].

Cardiovascular disease (CVD) and stroke are major contributors of disease burden in the US [5], and globally [6]. In the US, the annual direct cost of CVD and stroke was estimated at $192.1 billion in 2009: Approximately $86.1 billion for inpatient stays, $46.7 billion for outpatient or office-based visits, and $31.8 billion for prescription drugs [7]. Costs related to CVEs include acute treatment, secondary prevention measures, recurrent CVEs, and rehabilitation [7–14]. Age, hyperlipidemia, impaired renal function, depression, and concurrent CVEs have been shown to impact costs [8, 15–19].

Previous research has been valuable in demonstrating the great cost burden of CVEs [8, 16, 20–22], yet only one report specifically assessed cohorts of patients with hyperlipidemia. Given that adequate hyperlipidemia treatment lowers the risks associated with CVEs, it is important to obtain current cost estimates associated with CVEs. The primary objective of this study was to determine the mean costs associated with CVEs among patients with hyperlipidemia by follow-up time period. Secondary objectives of this study included characterizing costs by CVE type and CHD risk; as a reference, we provide cost estimates for a sample of non-CVE patients from the same population.

METHODS

Study Design

This was a retrospective cohort study using longitudinal administrative healthcare claims data. Healthcare costs were calculated by baseline level of CHD risk and type of CVE during several follow-up periods: Acute (days 0–30), short-term (days 31–365), first year (days 0–365), second year (days 366–730), and third year (days 731–1095). Costs of first and subsequent CVEs were also obtained. Costs were compared to patients not experiencing a CVE but with similar baseline characteristics.

Data Sources

Data were obtained from the Optum Research Database (ORD), which contains de-identified medical and pharmacy claims data annually for approximately 14 million individuals who are enrolled in a commercial (fully insured or self-insured employer line of business) or Medicare Advantage plan. This paper reports results among commercial health plan enrollees only. The population contained within ORD is geographically diverse and fairly representative across the US, with a concentration of patients in the South. The ORD does not contain protected health information and is fully compliant with federal guidance on human subjects research, thus IRB review and approval was not required [23].

Study Sample

Subjects included members ≥18 years old with hyperlipidemia identified by a claim for a hyperlipidemia drug (see Table S1 in the online supplementary material) or an International Classification of Diseases Clinical Modification 9 (ICD-9-CM) [24] code for hyperlipidemia (272.0, 272.1, 272.2, 272.4, and 272.9) between January 1, 2006 and July 31, 2012 (identification period). The earliest date of a qualifying claim was the hyperlipidemia date.

Multiple types of CVEs [myocardial infarction (MI), ischemic stroke (IS), transient ischemic attack (TIA), heart failure (HF), unstable angina (UA), percutaneous coronary intervention (PCI), and coronary artery bypass graft (CABG)] were studied. The CVEs were identified by the presence of ICD-9-CM or healthcare common procedure coding system (HCPCS) [25] codes: ≥1 ICD-9-CM facility claims for hospitalizations for MI, IS, TIA, HF, or UA, or ≥1 ICD-9-CM or HCPCS procedure claims for PCI or CABG (see Table S2 in the online supplementary material). For patients experiencing a CVE, their index date was the date of the first CVE following their hyperlipidemia date. The baseline period included the 12-month period prior to the index date. Follow-up was a period of variable length 30 days to 3 years, following (and including) the index date until the earlier of disenrollment, August 31, 2012, or 36 months after the index date. Continuous enrollment was required from 12 months prior to the index date.

As a reference, individuals were identified who did not have a CVE, but had similar baseline characteristics, including age, gender, health plan region, health plan type, history of chronic comorbid conditions based on ICD-9-CM diagnoses [hemorrhagic stroke, carotid artery disease, chronic renal failure, chronic obstructive pulmonary disease (COPD), asthma, mental disorders, and osteoarthritis]; number of inpatient hospitalizations in baseline period; and time between hyperlipidemia date and index date. Due to the number of variables, propensity scores (PS) were estimated for each patient using a logistic regression model. Non-CVE patients having similar PS as those experiencing a CVE were then selected. For these non-CVE patients, the index date was defined as their hyperlipidemia date plus a randomly generated number of days (to represent time between hyperlipidemia diagnosis and event 'index' date), based upon a gamma distribution. A gamma distribution was chosen because it best represented the distribution of days between hyperlipidemia date and first CVE among patients who had a CVE.

Study Measures

Demographic and Clinical Characteristics

Patient demographics examined at the index date for all patients included age, gender, and US Census geographic region (Northeast, Midwest, South, West) [26]. Clinical characteristics examined during the baseline period included index CVE type and CHD risk level, as defined by the Adult Treatment Panel (ATP) III [27]; evidence of hemorrhagic stroke, carotid artery disease, chronic renal failure, COPD, asthma, mental disorders, or osteoarthritis; and number of all-cause inpatient hospitalizations, and emergency room and ambulatory visits (see Table S3 in the online supplementary material). The ATP III risk levels are defined as follows: high risk—any CHD or CHD risk equivalent; moderate risk—2 CHD risk factors; or low risk—0 to 1 CHD risk factors.

For individuals with more than one CVE type, the index date was assigned based on the CVE coded in the principal or first-listed position. Second and third CVEs within 30 days following a CVE of the same type did not qualify as a new CVE. The second or third CVE date was the earliest date of the second and third qualifying CVE(s).

Healthcare Costs

Costs were reported for the follow-up periods and represented the sum of all health plan- and patient-paid amounts for all medical (ambulatory [office and outpatient hospitalization] visits, emergency room visits, inpatient hospitalization, and other services) and retail pharmacy services during the time of enrollment in the health plan. Costs prior to 2012 were adjusted to 2012 costs using the medical care component of the Consumer Price Index [28]; those incurred by other payers or managed through coordination of benefits (e.g., Medicare part A/B) were excluded.

Statistical Analysis

To estimate the health care cost and resource utilization of patients, in the same insured population, with hyperlipidemia but not experiencing a CVE we used a sample with similar baseline characteristics as patients who did experience a CVE. Given the number of baseline characteristics, we selected patients with hyperlipidemia not experiencing a CVE who had a similar propensity of having a CVE as the CVE cohort. The propensity calculation included hyperlipidemia date, index date, age, gender, health plan region, health plan type, chronic comorbid conditions (see Table S3 in the online supplementary material), number of inpatient hospitalizations in baseline period, and time to CVE. Because patients experiencing a CVE often have higher risk levels, costs within the non-CV cohorts are presented by risk level strata.

Analyses were conducted using SAS version 9.2 (SAS Institute, Inc., Cary, NC, USA) or Stata SE version 11 (StataCorp LP, College Station, TX, USA). The conventional significance level $\alpha = 0.05$ was used.

RESULTS

Sample Description

The sample included 193,385 commercial enrollees with hyperlipidemia and a CVE who met study criteria. Their average [± standard deviation (SD)] age was 62.0 (±12.1) years, with the majority of patients being male (62.5%), at least 55 years of age, and having high baseline CHD risk (Table 1). During the 12 months prior to their CVE, nearly 34% had been hospitalized

Table 1 Baseline characteristics

Characteristic	Total ($N = 193,385$)
Age (years), mean (SD)	62.0 (12.1)
Age category (years)	
18–24	179 (0.09)
25–34	1573 (0.81)
35–44	10,598 (5.48)
45–54	39,424 (20.39)
55–64	72,784 (37.64)
65–74	33,942 (17.55)
75–84	28,124 (14.54)
≥85	6761 (3.50)
Gender	
Male	120,790 (62.46)
Female	72,595 (37.54)
Geographic region	
Northeast	19,530 (10.10)
Midwest	48,983 (25.33)
South	100,032 (51.73)
West	24,797 (12.82)
Other	43 (0.02)
Baseline clinical conditions	
Hemorrhagic stroke	2505 (1.30)
Carotid artery disease	16,202 (8.38)
Chronic renal failure	21,141 (10.93)
Chronic obstructive pulmonary disease	14,212 (7.35)
Asthma	17,076 (8.83)
Mental disorders	62,524 (32.33)
Osteoarthritis	45,594 (23.58)
Baseline CHD risk	
Low risk: 0–1 CHD risk factors	31,307 (16.19)
Moderate risk: 2 CHD risk factors	33,512 (17.33)
High risk: any CHD or CHD risk equivalent	128,566 (66.48)
Hospitalized in baseline period (any cause)	65,440 (33.84)
Emergency room visit in baseline period (any cause)	96,448 (49.87)
Number of ambulatory visits in baseline period (any cause), mean (SD)	21.67 (20.69)

Values are presented as *n* (%) unless otherwise stated
CHD coronary heart disease, *SD* standard deviation

and mean baseline total costs were $25,250 (±64,970). A relatively low proportion of patients had evidence of stroke, carotid artery disease, or COPD. However, mental disorders and osteoarthritis were common. The average length of follow-up after a CVE was 530 days (median = 456) with 94% ($n = 182,416$) being enrolled during the short-term period, 57% ($n = 109,950$) during the second year, and 33% ($n = 63,869$) during the third year.

Costs Following a CVE

The largest total cost occurred in the first year, and most notably in the first 30 days following a CVE (acute period), driven primarily by inpatient costs at $22,404 (comprising 77% of first year costs) while 68% of patients were hospitalized in the first 30 days (average length of stay 4.8 days). However, over time inpatient rates decreased to approximately 19% (average length of stay 2.4–3.3 days) in the second and third years. Though costs remained high ($15,133 in year 3) over time, with inpatient

costs accounted for a lower proportion of costs and ambulatory care (from 14% in acute to 37% in year 3) and pharmaceutical costs rose (from 2% in acute to 24% in year 3) (Table 2). This pattern continued for those experiencing a second ($n = 84,386$) and third CVE ($n = 52,977$), but in contrast, costs were greater in the short-term versus acute period (Fig. 1). These patterns were similar across CVE type.

Costs by CVE Risk Level

The costs for each of the follow-up periods, by risk level, are shown in Table 3 and Fig. 2. Interestingly, mean costs differed by baseline CHD risk for all time periods (overall $P < 0.001$), but without a consistent pattern in the acute period for the CVE cohort. However, short-term, second-year, and third-year patterns were more similar (Fig. 2) between years and among risk levels, with third-year costs lower than second-year costs.

Costs by Type of CVE

Table 3 and Fig. 2 also show costs for the different event types studied. Acute costs varied considerably by type of CVE, ranging from $9149 for TIA to $54,251 for CABG (overall $P < 0.001$). Although remaining significantly different (overall $P < 0.001$) by types, costs beyond the first 30 days (short-term, second year, third year) varied less by index CVE type. In the second and third years, HF was the costliest type, while CABG was the least costly.

Costs Among Patients with no CVE

A total of 154,354 patients with hyperlipidemia but not experiencing a CVE were selected among those with a similar PS to patients experiencing a CVE. Characteristics used in the PS model were similar except a few distinctions (e.g., age and risk level) which can be attributed to the fact that patients with CVEs are typically older and at higher risk due to the inherent nature of the disease. As expected, patients without a CVE were found to have much lower costs in each of the time periods overall and within each CHD risk level (Fig. 2). Acute period costs for those with no CVE were very low compared to those with a CVE, but costs over the follow-up time periods in both groups were substantial and remained relatively steady across risk level. However, follow-up costs were double for those experiencing a CVE than those not experiencing a CVE.

DISCUSSION

The importance of this study was the focus upon the costs incurred by commercial payers following a CVE within a population of patients with hyperlipidemia, to further understand the economic burden associated with CVD among this high-risk population.

Prior claims-based studies have demonstrated recurrent hospitalizations and follow-up care are major contributors to CVE-related costs, although direct comparison between studies is hindered by differing costs captured. Roberts et al. [30] reported acute stroke-related hospitalization costs of $16,889, plus $2203 for additional cardiovascular-related medical services, similar to our all-cause costs for patients having stroke events. Engel-Nitz et al. [20] demonstrated patients with recurrent IS had higher hospitalization costs following subsequent stroke ($17,121) compared to their first stroke ($15,634). Among all CVE types combined in the current study, first year inpatient costs were also higher

Table 2 Healthcare costs ($USD) following initial cardiovascular event

Costs	First year									Second year			Third year		
	Total *N* = 193,385 (100%)			Acute *N* = 193,385 (100%)			Short term *N* = 182,416 (94%)			Total *N* = 109,950 (57%)			Total *N* = 63,869 (33%)		
	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median
Total costs	41,937	72,513	20,675	22,404	41,622	9432	20,621	54,159	6817	16,786	48,132	5794	15,133	41,503	5433
Medical costs	38,249	71,466	16,960	21,945	41,593	8979	17,230	53,007	3395	13,168	46,860	2386	11,489	40,199	2085
Inpatient costs	24,993	57,793	5902	17,333	39,745	2647	8098	39,122	0	5727	34,482	0	4764	27,754	0
Emergency room costs	586	1862	74	253	883	0	352	1586	0	313	1298	0	290	1404	0
Ambulatory costs	10,232	26,001	3370	3218	7995	526	7413	23,765	2016	6165	22,397	1504	5541	19,658	1298
Office visit costs	2237	6537	1008	331	984	120	2012	6273	851	1740	5198	731	1594	4786	646
Outpatient visit costs	7995	24,298	1707	2887	7889	199	5401	22,104	637	4425	21,079	315	3947	18,282	248
Other medical costs	2438	13,130	234	1140	8715	11	1367	9261	85	962	7872	61	894	7790	55
Pharmaceutical costs	3689	5657	2358	459	744	293	3391	5326	2135	3619	5962	2122	3645	5967	2083

SD standard deviation

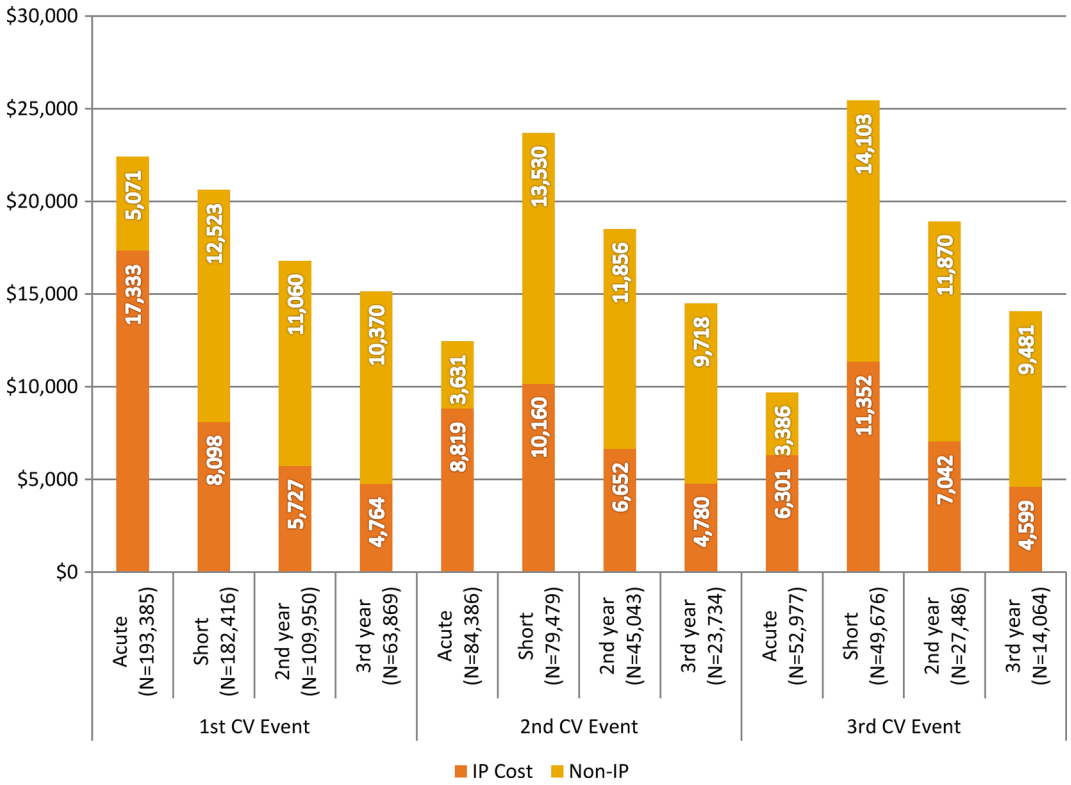


Fig. 1 Total costs (in $USD) following first, second, and third CVE. *CVE* cardiovascular event, *IP* inpatient

for subsequent CVEs, but non-inpatient costs accounted for greater proportions. Other studies evaluated CVE costs with respect to hypertension (Duh et al. [18]) and diabetes (Straka et al. [16]) comparing costs between patients with and without CVEs. Similar to the current study, these authors found CVEs imparted significantly greater inpatient, outpatient, and prescription costs, and high continuing costs during up to three follow-up years [16]. Chapman et al. [8] conducted an observational study on costs of CVEs using dyslipidemia as one of the potential confounders in a multivariable analysis. In their study, mean total costs were at $33,563 for the first year, compared to $41,937 in the current study [8]. Higher estimates in the current study may be attributed to Chapman et al.'s inclusion of non-commercial insurance plans (Medicaid, Medicare, etc.), or attributing $0 costs to disenrolling patients, as well as different patient populations/sample selection, and inflation.

A recent study by Punekar et al. [22] investigated healthcare resource utilization and costs. Some similarities exist between studies: Those with CVEs had higher healthcare costs than matched controls, and CABG and TIA events were associated with highest and lowest costs, respectively [22]. Punekar et al. [22] found total 2-year costs for their secondary prevention, high risk, and primary prevention cohorts of $46,555, $46,739, and $39,673, respectively. The costs in the current study for high, moderate, and low risk categories were $42,903, $38,194, and $41,978, respectively, for the first year post-CVE, and $18,186, $14,331, $13,645,

Table 3 Average costs ($USD) for CVE group by risk level and type of CVE following the index CVE

	First year			Second year	Third year
	Total	Acute	Short	Total	Total
Risk level					
Low risk: 0–1 CHD risk factors					
N	31,307	31,307	29,909	18,038	10,396
Mean	41,978	24,509	18,264	13,645	11,738
SD	73,773	44,594	52,401	42,773	35,603
Moderate risk: 2 CHD risk factors					
N	33,512	33,512	31,504	18,666	10,677
Mean	38,194	21,122	18,072	14,331	13,043
SD	66,452	39,406	48,145	46,880	37,190
High risk: any CHD or CHD risk equivalent					
N	128,566	128,566	121,003	73,246	42,796
Mean	42,903	22,226	21,867	18,186	16,480
SD	73,676	41,416	55,992	49,610	43,728
Type of CVE					
Myocardial infarction					
N	38,851	38,851	36,285	21,682	12,558
Mean	48,131	30,258	19,083	14,536	12,745
SD	73,948	48,922	48,000	39,139	33,825
Ischemic stroke					
N	24,757	24,757	22,920	12,661	6944
Mean	39,608	20,086	20,996	15,072	13,528
SD	80,497	45,600	59,176	43,219	39,748
Percutaneous coronary intervention					
N	31,455	31,455	30,589	20,203	12,327
Mean	39,720	23,539	16,593	15,228	14,215
SD	46,733	22,335	37,426	34,154	30,601
Coronary artery bypass graft					
N	10,998	10,998	10,664	6962	4213
Mean	69,598	54,251	15,804	11,671	11,003
SD	71,263	55,042	37,180	28,822	34,267
Angina					
N	18,970	18,970	18,349	11,763	7226

Table 3 continued

	First year			Second year	Third year
	Total	Acute	Short	Total	Total
Mean	29,069	14,077	15,465	14,131	13,971
SD	47,035	26,364	35,364	32,062	32,596
Transient ischemic attack					
N	17,694	17,694	16,998	10,429	6038
Mean	23,089	9149	14,416	12,653	11,873
SD	45,322	21,863	36,596	32,618	35,226
Heart failure					
N	50,660	50,660	46,611	26,250	14,563
Mean	45,098	17,644	29,672	24,860	21,859
SD	91,161	44,566	74,990	73,803	59,825

CHD coronary heart disease, *CVE* cardiovascular event, *SD* standard deviation

respectively, for the second year post-CVE. Differences in costs between studies are likely due to differing risk definitions, health plan inclusion, and propensity scoring strategies.

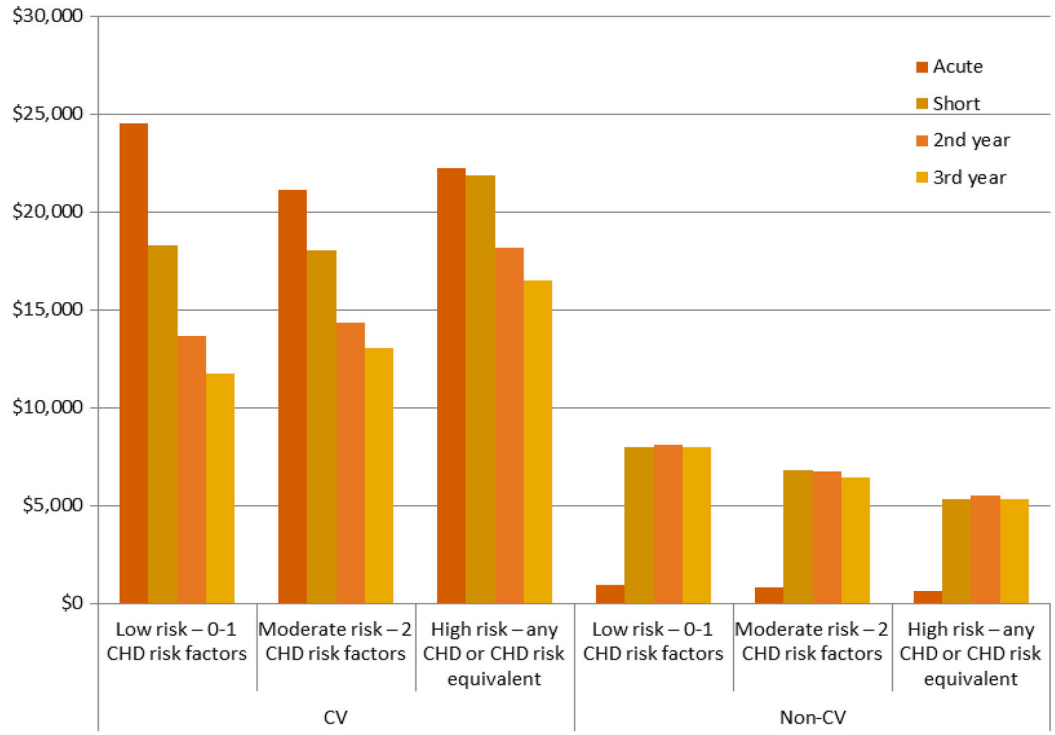
In summary, previous claims studies have shown that patients having CVEs incur substantially greater costs than those with no CVE, even among varying datasets with differing inclusion criteria. These costs were largely driven by inpatient utilization. This study demonstrating continuing economic burden of CVEs over time in patients with hyperlipidemia is supported by previous findings. Furthermore, this research provides a valuable base to support future studies on the impact of lipid-lowering medications and predicting costs projected over longer time periods.

LIMITATIONS

Certain limitations of administrative claims studies should be considered. Misclassification and miscoding are possible and diagnostic codes are not definitive proof of disease. The analytic dataset may be affected by the lack of data not available from claims databases, such as certain lab values, family history and smoking status. Also, retrospective studies are prone to spurious associations attributed to bias by way of confounding variables [29, 31, 32], some of which represent unknown risk factors. However, the propensity scores allowed identification of a sample of patients that was balanced across several demographic and known relevant clinical characteristics. The severity of disease represented by the matching factors may differ for those having and not having a CVE. Finally, the findings in this study are not generalizable to a non-commercially insured population.

CONCLUSIONS

The costs associated with CVEs among patients with hyperlipidemia are high and remain elevated. The CVE costs are largely driven by inpatient hospitalization in the first 30 days,



Acute	24,509 (44,594)	21,122 (39,406)	22,226 (41,416)	957 (4,406)	829 (4,885)	624 (4,938)
Short	18,264 (52,401)	18,072 (48,185)	21,867 (55,992)	7,993 (20,485)	6,810 (17,769)	5,322 (15,794)
2nd year	13,645 (42,773)	14,331 (46,880)	18,186 (49,610)	8,079 (20,878)	6,747 (17,951)	5,522 (14,345)
3rd year	11,738 (35,603)	13.043 (37,190)	16,480 (43,728)	7,975 (24,778)	6,456 (18,069)	5,311 (13,345)

Fig. 2 Mean (standard deviation) costs (in $USD) following index date for patients experiencing a CVE and in the non-CVE group by CHD risk level in baseline period. *CHD* coronary heart disease, *CVE* cardiovascular event

but significant costs persist for several years. After the acute period, outpatient and ambulatory costs represent a larger proportion of costs. The main driver of CVE costs in this study is CHD risk level, with costs varying by index CVE type. To assess the impact of lipid-lowering medications, a similar study including variables on medication use is necessary. Future clinical decision-making and cost-effectiveness studies will benefit from these findings.

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Compliance with ethics guidelines. This article does not contain any studies with human or animal subjects performed by any of the authors.

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