Original Articles

Assessment of statin therapy, LDL-C levels, and cardiovascular events among high-risk patients in the United States

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BACKGROUND: Statins have demonstrated significant benefit in reducing cardiovascular disease (CVD) risk.
OBJECTIVE: To evaluate statin treatment patterns by intensity, elevated low-density lipoprotein cholesterol (LDL-C) levels, and cardiovascular (CV) events in high-risk CVD patients.
METHODS: Patients included were aged $\geq$18 years, with a coronary heart disease (CHD; Jan 1, 2007–Dec 31, 2011, index date) or CHD risk equivalent (CHD RE) diagnosis (Jan 1, 2007–Dec 31, 2010, index date), in the Truven MarketScan claims database, continuously enrolled for 2 years pre- and up to 1 (CHD) or 2 (CHD RE) years post-index. Patients with CHD, CHD RE, rhabdomyolysis, or chronic kidney disease any time pre-index were excluded. Statin therapy was assessed at baseline, 30, 90, and 365 days post-index. LDL-C values were captured in patients with available data at 30-day intervals up to 1 year. CV events were evaluated up to 1 year post-index. Descriptive statistics were used to report results.
RESULTS: There were 175,103 CHD and 68,290 CHD RE patients; 3333 CHD RE patients had post-index CV events. At 1 year, 38.7% of CHD patients and 44.3% of CHD RE patients with post-index CV events were not prescribed statins. Most patients who were prescribed statins, received a moderate-intensity statin. The percentage of patients with LDL-C $\geq$ 100 mg/dL reduced over time, but at 1 year, 29.3% of CHD and 30.0% of CHD RE patients with post-index CV events had LDL-C $\geq$ 100 mg/dL. At 1 year post-index, 9.9% CHD and 7.3% CHD RE patients had at least 1 CV event.
CONCLUSION: There is room for better LDL-C management among high-risk CVD patients to reduce their overall CV risk.
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Introduction

Cardiovascular disease (CVD) is the leading cause of mortality in the United States with 235.5 deaths per 100,000 with coronary heart disease (CHD) alone responsible for nearly 1 of every 6 deaths in 2010.[1] A major risk

factor for CVD is elevated low-density lipoprotein cholesterol (LDL-C).[2] Various therapeutic interventions to lower elevated LDL-C such as statins and ezetimibe have shown that decreasing LDL-C levels significantly reduces CVD events.[3–8]

Patients with established CHD and CHD risk equivalent (CHD RE) indications have a high risk of subsequent CV events including myocardial infarction (MI), stroke, and death, and statins have been recommended as the first choice of treatment in these patients to reduce CVD events.[9]

However, statins also have their challenges with several studies indicating suboptimal use in high-risk patients,[10–14] elevated LDL-C levels in spite of statin use,[15] and the issue of residual CVD risk in patients even with high-intensity statin treatment.[16–19]

The National Cholesterol Education Program Adult Treatment Panel III (ATP III) guidelines considered patients with CHD or a CHD RE diagnosis to be high-risk patients and recommended an LDL-C goal of <100 mg/dL.[20] This LDL-C treatment goal was also supported by the 2015 National Lipid Association (NLA) treatment recommendations for patient-centered management of dyslipidemia among patients with low, moderate, or high atherosclerotic CVD (ASCVD) risk.[21] The 2013 American College of Cardiology (ACC)/American Heart Association (AHA) cholesterol guidelines advocated the use of risk appropriate statin intensity (and adjuvant lipid-modifying therapy as indicated) to optimally reduce risk for CV events.[22]

The objective of our study was to evaluate real-world statin treatment patterns using the 2013 ACC/AHA definitions for statin intensity, NLA 2015/ATP III recommended goal attainment of LDL-C < 100 mg/dL, and CV events among high-risk CHD and CHD RE patients.

Materials and methods

Study design

This retrospective cohort study used Truven Health "MarketScan" Research Database. This widely published commercial database[23,24] contains combined medical and pharmacy claims from approximately 40 employers, and a number of health plans representing over 35 million covered lives in 2008. The study period was from January 1, 2005 through December 31, 2012. Please refer to the Supplementary Data section for more information regarding Truven Health *MarketScan* Research Database.

Study population

The study sample (Fig. 1) included patients aged 18 years and older with a diagnosis of hyperlipidemia as per "International Classification of Diseases, 9th Revision" (ICD-9) diagnosis codes 272.0-272.4 and/or a claim for a statin and were categorized into two cohorts. Patients with ICD-

9 or "Current Procedural Terminology" codes (Table 1 in Supplementary Data) for CHD (MI, unstable or stable angina, coronary artery bypass graft, or percutaneous coronary intervention) between January 1, 2007 and December 31, 2011 were categorized as the CHD cohort. Patients with ICD-9 codes (Table 1 in Supplementary Data) for CHD RE diagnosis (type 2 diabetes, peripheral vascular disease, stroke, abdominal aortic aneurysm, or transient ischemic attack) between January 1, 2007 and December 31, 2010 were categorized as the CHD RE cohort. The definitions for CHD and CHD RE diagnoses were primarily based on the ATP III guidelines.[20] The date of hospital admission due to CHD and date of CHD RE diagnosis were designated as the index date for the CHD and CHD RE cohorts, respectively. In patients with multiple CHD-associated hospital admissions or multiple CHD RE diagnoses, the date of the first admission or diagnosis was designated as the index date. Patients needed to be continuously enrolled during 2 years before the index date and up to 1 year (CHD cohort) or up to 2 years (CHD RE cohort) after the index date to be included in the study. The follow-up period was longer for the CHD RE cohort to provide adequate time for evaluation of CV events (Table 2 in Supplementary Data), which was one of the study outcomes. However, in this study, we have reported CV events occurring within 1 year in the CHD RE cohort to be consistent with CV outcomes in the CHD cohort. Patients were excluded if they had a CHD (CHD cohort), CHD or CHD RE diagnosis (CHD RE cohort), rhabdomyolysis (ICD-9 code 728.88), or chronic kidney disease (ICD-9 codes 585.x or 403.x or 404.x) any time before index date. As such, the CHD cohort may consist of patients with CHD RE conditions; the CHD RE cohort consisted of newly diagnosed CHD RE patients without prior CHD.

Study measures

Outcomes evaluated included statin treatment patterns, LDL-C values, and post-index CV events.

Assessment of outcomes in the CHD cohort

Statin therapy was categorized as low-, moderate-, high-intensity and fixed-dose combination statins. The categorization by intensity was as per the 2013 ACC/AHA definition for statins (see Table 3 in Supplementary Data), and the fixed-dose combinations included simvastatin with ezetimibe, simvastatin with niacin, and lovastatin with niacin. Statin therapy was evaluated at baseline and at 30, 90, and 365 days after the index date. Baseline statin therapy was defined as the index hospitalization period because all CV events and revascularization procedures for defining CHD would have occurred during hospitalization. A pharmacy claim for a statin during hospitalization was included as baseline statin therapy. In patients with multiple statin claims, the one closest to the hospital discharge date was considered as baseline statin therapy. Post-index statin therapy pattern was evaluated
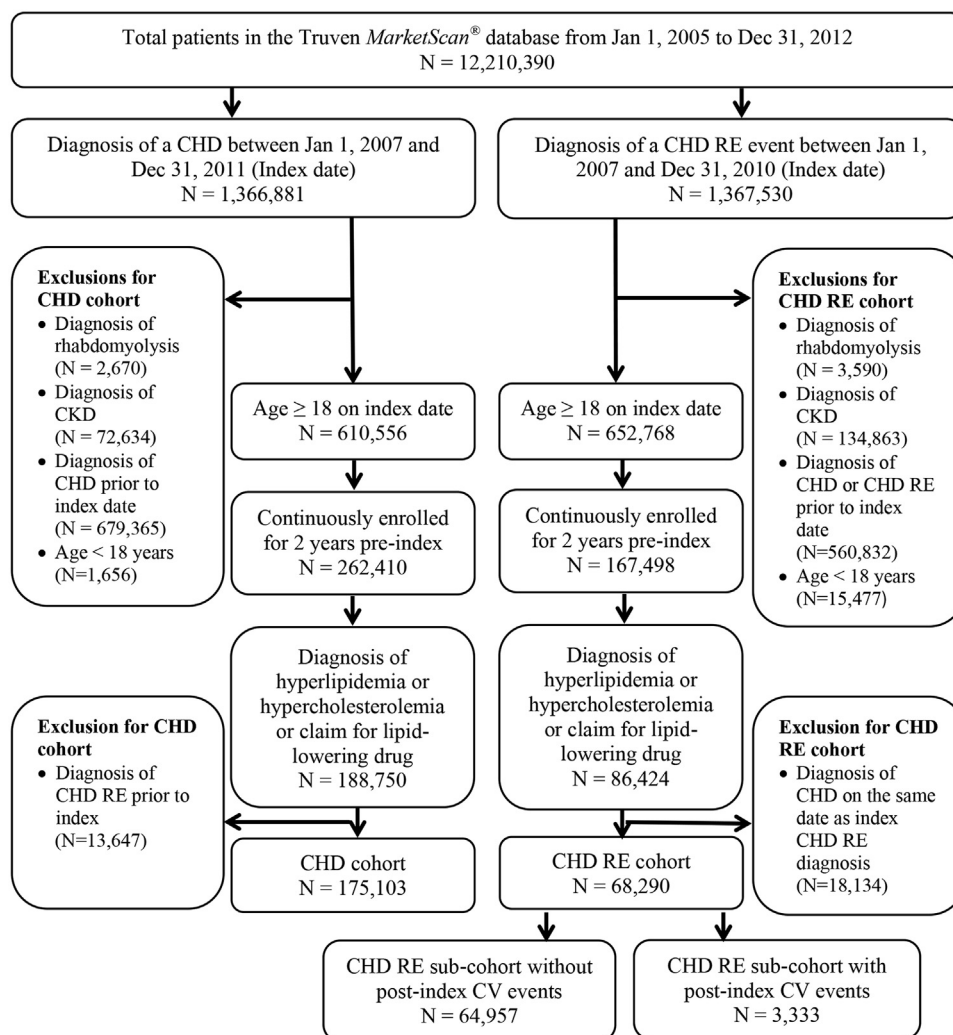
Figure 1   Patient selection flowchart. CHD, coronary heart disease; CHD RE, coronary heart disease risk equivalent; CKD, chronic kidney disease; CV, cardiovascular.

from baseline to 30 days, 31 to 90 days, and 91 to 365 days. The statin claim closest to 30th, 90th, or 365th day was included as post-index statin therapy. The study did not assess statin initiation or discontinuation rates, rather a snapshot of statin claims during the various post-index intervals was evaluated for the CHD and CHD RE cohorts. The proportion of patients with LDL-C $\geq$ 100 mg/dL was evaluated at 30 days before the index date and at 30-day intervals up to 1 year after the index date. Patients were not longitudinally followed over time, but a cross section of patients with available LDL-C values was evaluated at each 30-day intervals. For assessing baseline LDL-C status, a 13-month LDL-C value capture window (365 days before index date through 30 days after index date) was used, and the value closest to index date was included. CV events (MI, stroke, unstable angina, heart failure, revascularizations procedures [coronary artery bypass graft and percutaneous coronary intervention], and transient ischemic attack) were evaluated over a 1-year period after index date.

Assessment of outcomes in the CHD RE cohort

Statin treatment and lipid values were evaluated separately for a sub-cohort of patients who experienced post-index CV events vs those who did not experience a post-index CV event to observe for differences in these respective outcomes between the cohorts. For assessment of statin therapy, baseline was the time period from 90 days pre-index date to index diagnosis date. In patients with multiple statin pharmacy claims, the one closest to the index date was considered as the baseline statin. The definitions for post-index periods were same as those used for defining the CHD cohort. Assessment of patients with LDL-C $\geq$ 100 mg/dL and post-index CV events was the same as that for the CHD cohort.

Statistical analysis

The analysis included means and standard deviations for continuous variables and counts and percentages for categorical variables. Baseline demographic variables included

Table 1 Baseline demographic and clinical characteristics

Variable	CHD cohort (N = 175,103)	CHD RE sub-cohort without post-index CV events (N = 64,957)	CHD RE sub-cohort with post-index CV events (N = 3333)
Age, mean (SD)	62.6 (13.0)	61.3 (14.6)	64.9 (13.8)
Age < 65 (n, %)	112,694 (64.4)	42,916 (66.1)	1885 (56.6)
Male (n, %)	105,499 (60.2)	31,038 (47.8)	1832 (55.0)
Payer type (n, %)			
Preferred provider organizations	87,378 (49.9)	34,532 (53.2)	1697 (50.9)
Health maintenance organizations	23,925 (13.7)	9722 (15.0)	518 (15.5)
Comprehensive insurance	38,341 (21.9)	12,435 (19.1)	771 (23.1)
Other/unknown[*]	25,459 (14.5)	8268 (12.7)	347 (10.5)
Geographic distribution (n, %)			
Northeast	23,734 (13.6)	7460 (11.5)	473 (14.2)
North Central	53,021 (30.3)	18,894 (29.1)	1144 (34.3)
South	64,996 (37.1)	27,388 (42.2)	1223 (36.7)
West	24,661 (14.1)	11,025 (17.0)	481 (14.4)
Unknown	8691 (5.0)	190 (0.3)	12 (0.4)
Patients with available baseline LDL-C values (n, %)[†]	5329 (3.0)	2017 (3.1)	74 (2.2)
LDL-C, mean (SD)	104.9 (43.5)	109.2 (42.2)	108.8 (48.4)
LDL-C ≥ 100 mg/dL (n, %)	2816 (52.8)	1205 (59.7)	44 (59.5)
Comorbidities			
Type 2 diabetes (n, %)	49,628 (28.3)	0[‡]	0[‡]
Hypertension (n, %)	100,004 (57.1)	31,890 (49.1)	1673 (50.2)
Charlson Comorbidity Index score			
Mean (SD)	2.3 (2.3)	1.5 (1.8)	1.7 (1.8)
0 (n, %)	44,477 (25.4)	23,952 (36.87)	1010 (30.30)
1 (n, %)	37,870 (21.6)	15,301 (23.56)	728 (21.84)
2 (n, %)	27,393 (15.6)	9930 (15.29)	588 (17.64)
≥3 (n, %)	65,363 (37.3)	15,774 (24.28)	1007 (30.21)

CHD, coronary heart disease; CHD RE, coronary heart disease risk equivalent; CV, cardiovascular; LDL-C, low-density lipoprotein cholesterol; SD, standard deviation.

*Other payer types include exclusive provider organization, non-capitated, partially capitated, and capitated point of service, consumer-directed health plan, and high-deductible health plan. Unknown also includes missing.

†Due to limited availability of LDL-C values, a 13-month window (365 days before index date through 30 days after index date) was used to capture the LDL-C values, and the one closest to index date was included as baseline LDL-C value.

‡Comorbidities were evaluated over a 1-year time period before index date. As part of CHD RE cohort inclusion criteria, patients have no prior/baseline type 2 diabetes.

age, categorical age (<65 and ≥65), gender, geographic region, and payer type. Clinical variables included LDL-C values, diabetes status, hypertension status, and Charlson Comorbidity Index score. The proportion of patients receiving statins by intensity (low, moderate, and high) and as fixed-dose combinations and proportion of patients with LDL-C ≥ 100 mg/dL were assessed. The figures for displaying the proportion of patients also included error bars to estimate the 95% confidence intervals. Post-index CV events were evaluated as cumulative incidence rates using the Kaplan–Meier estimator. All statistical analyses were performed using SAS 9.2 (SAS institute, Cary, NC).

Results

The final study sample consisted of 175,103 patients in the CHD cohort and 68,290 patients in the CHD RE cohort (Fig. 1). Of the 68,290 CHD RE patients, 3333 patients had a CV event during the post-index period, and 64,957 patients did not have a post-index CV event. Table 1 summarizes the baseline demographic and clinical characteristics of the CHD and CHD RE sub-cohorts. Mean age was highest in the CHD RE sub-cohort with post-index CV events (64.9 ± 13.8 years); CHD cohort had a higher proportion of patients aged ≥65 years (64.4%) and more male patients (60.2%) vs other cohorts. Throughout the study period, 4.1% to 4.5% of the patients had at least 1 LDL-C value recorded. Mean baseline LDL-C ranged from 108.8 ± 48.4 mg/dL (CHD RE sub-cohort with post-index CV events) to 104.9 ± 43.2 mg/dL (CHD cohort). LDL-C ≥ 100 mg/dL at baseline was observed in more than 52% of patients with available LDL-C measures at baseline. Mean Charlson Comorbidity Index was highest for CHD cohort vs the CHD RE sub-cohorts (2.3 vs 1.5 and 1.7).
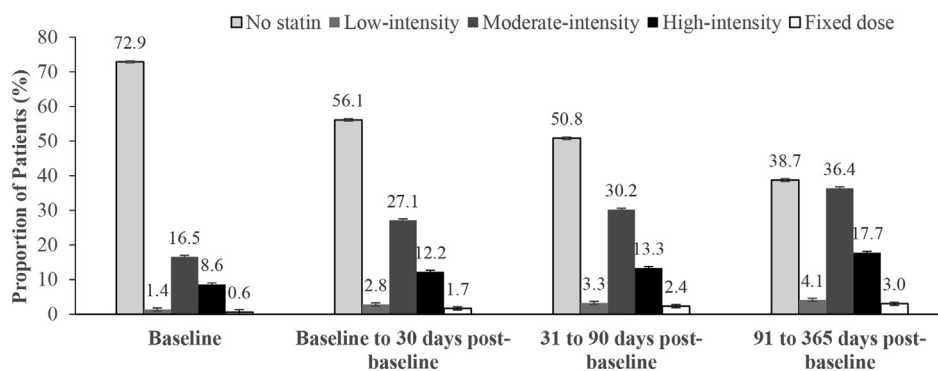
Statin therapy patterns

Of those patients who were prescribed statins, most had a pharmacy claim for a moderate-intensity statin followed by high-intensity statin at the measured time points (Fig. 2). There was an increase in the proportion of patients prescribed statins at each time period from baseline up to 365 days across all cohorts. Comparatively, a greater proportion of patients in the CHD cohort were prescribed statins during all measured time points. At the end of 1 year, approximately 39% of patients in the CHD cohort and 44%

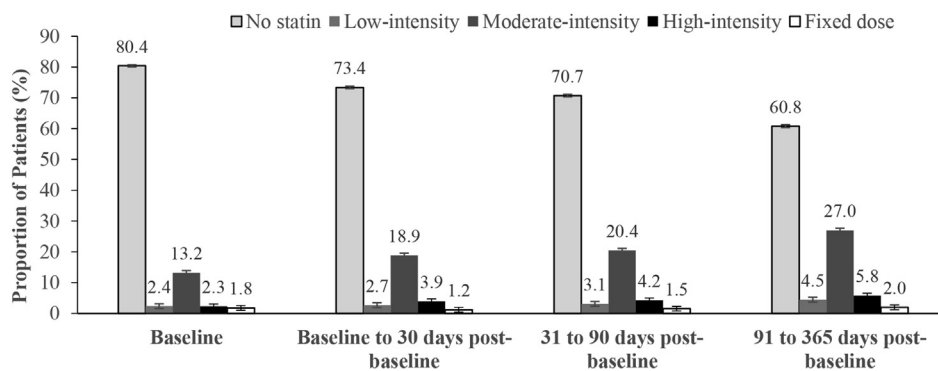patients in the CHD RE sub-cohort with post-index CV events were not prescribed statins.

Patients with LDL-C ≥ 100 mg/dL

There were respectively 7,162, 2,924, and 137 patients in the CHD cohort and CHD RE sub-cohorts without and with post-index CV events that had at least 1 LDL-C value at 30 days pre-index date through 1-year post-index date. The number of patients with LDL-C ≥ 100 mg/dL showed no clear trend across the measured time periods for all
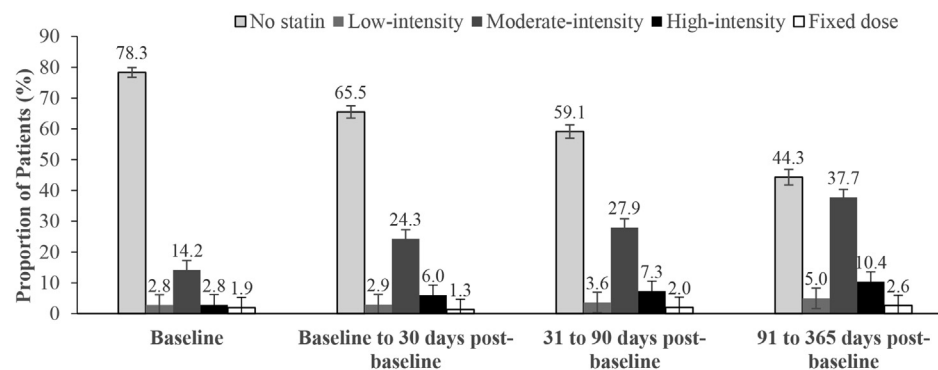
CHD Cohort (N=175,103)

CHD RE Sub-Cohort without Post-Index CV Events (N=64,957)

CHD RE Sub-Cohort with Post-Index CV Events (N=3,333)

Note: The error bars denote 95% confidence intervals

Figure 2   Statin therapy patterns. CHD, coronary heart disease; CHD RE, coronary heart disease risk equivalent; CV, cardiovascular.

cohorts. At the end of 1 year, approximately 30% patients in the CHD cohort and CHD RE sub-cohort with post-index CV events and approximately 46% patients in the CHD RE sub-cohort without post-index CV events continued to have an elevated LDL-C value (Fig. 3).

Post-index CV events

The most common CV events within 1 year post-index were MI (4.3%) and heart failure (2.8%) in the CHD cohort and stroke (6.1%) and heart failure (1.3%) in the CHD RE cohort (Table 4 in Supplementary Data). There were 9.9% patients in the CHD cohort and 7.3% patients in the CHD RE cohort with at least 1 CV event within 1 year post-index date (Fig 4).

Discussion

The results of this contemporary study aid in the understanding of statin therapy patterns, LDL-C status, and CV events in a commercially insured, large national sample of the US population with high-risk CHD and CHD RE diagnosis. A key finding in this study was the lack of statin therapy among 39% of CHD and 61% of CHD RE patients 91 to 365 days after baseline. This is concerning as it indicates substantial gaps in statin therapy among high-risk patients in spite of the overarching support of ATP III guidelines for statin therapy in these patients. Statin use was relatively lower from baseline to 90 days post-baseline vs 91 to 365 days post-baseline. This may be due to patients receiving a 3-month prescription fill of statins at baseline. Among patients who were prescribed statins, most of them
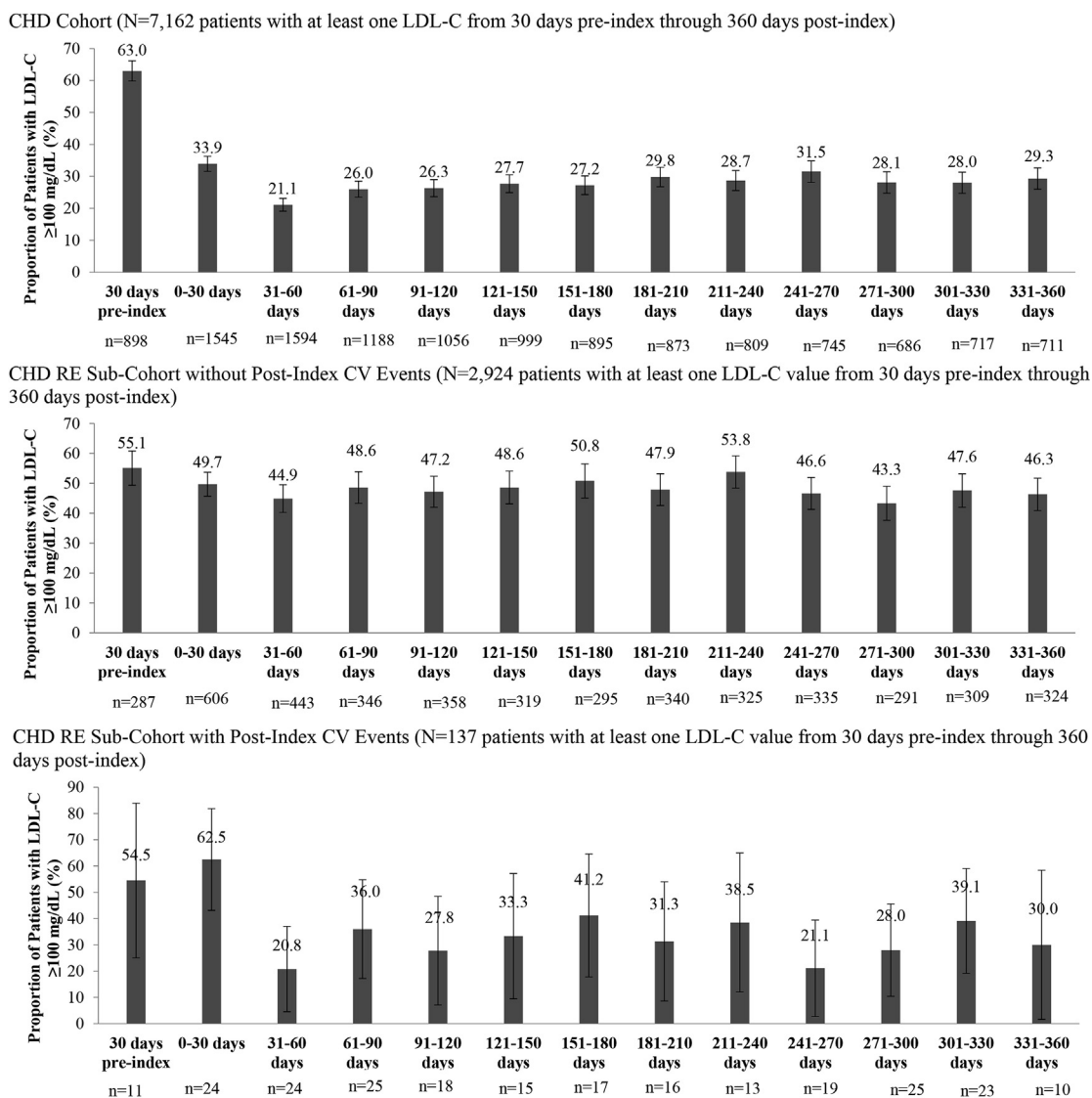
Notes: The error bars denote 95% confidence intervals. Patients were not followed longitudinally over time but a cross section of patients with available LDL-C values at the measured time points were included in the analysis.

Figure 3 Proportion of patients with low-density lipoprotein cholesterol ≥ 100 mg/dL pre- and post-index date in the 3 cohorts. CHD, coronary heart disease; CHD RE, coronary heart disease risk equivalent; CV, cardiovascular; LDL-C, low-density lipoprotein cholesterol.
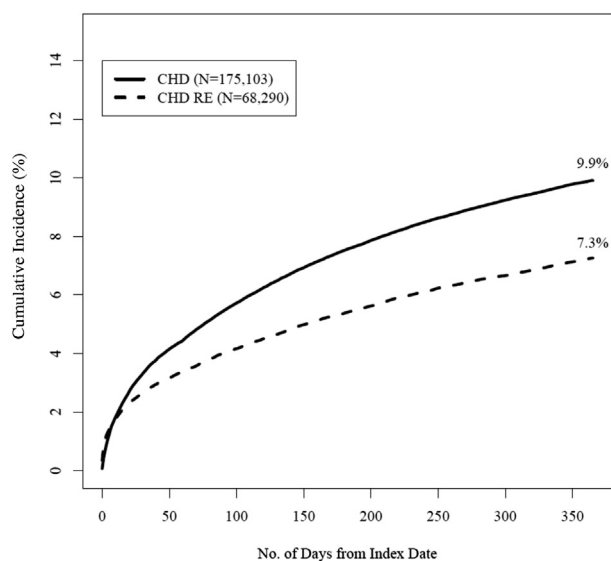
Note: Post-index CV events included myocardial infarction, stroke, unstable angina, revascularization procedures (CABG and PCI), heart failure and transient ischemic attack. At the end of one year, there were 17,349 (9.9%) patients in the CHD cohort and 4,965 (7.3%) patients in the CHD RE cohort with at least one CV event.

Figure 4 Cumulative incidence rate of post-index CV events for CHD and CHD RE cohorts. CABG, coronary artery bypass graft; CHD, coronary heart disease; CHD RE, coronary heart disease risk equivalent; CV, cardiovascular; PCI, percutaneous coronary intervention.

(13%–17% across all study cohorts) received a moderate-intensity statin at baseline, and this outcome is similar to that reported by Simpson et al[25] who evaluated statin treatment patterns in high-risk patients with CHD, atherosclerotic vascular disease, and diabetes in a payer-specific population. However, unlike the study by Simpson et al, more patients in this non-payer-specific database study were prescribed a high-intensity statin (8.6% vs 2.0%), and fewer patients were prescribed a low-intensity statin (1.4% vs 17.0%) at baseline. This may be due to differences in the identification of the study sample and definition of statin intensity (Simpson et al study did not use the ACC/AHA guidelines definition).

An encouraging upward trend was observed for overall use of moderate- and high-intensity statins from baseline to end of follow-up. Nevertheless, the use of high-intensity statins at 1-year follow-up in the CHD cohort was considerably lower than moderate-intensity statins (17.7% vs 36.4%) indicating underutilization of high-intensity statins in most of the high-risk patients. Similar findings were reported by Rosenson et al[26] who evaluated statin use by intensity using the ACC/AHA guidelines among Medicare beneficiaries after CHD events and Rodriguez et al[19] who examined use of high-potency statins in ASCVD patients in a managed care database. A more recent study by Nguyen et al[27] reported that 42% of ASCVD patients received guideline-recommended high-intensity statins. However, Nguyen's study was conducted in a single academic medical center from January 1, 2013 through November 11, 2013 vs our study, which evaluated statin therapy over a 5-year period in a nationally representative

database. Thus, our results are consistent with existing studies, which demonstrated the low use of high-intensity statins among high-risk CVD patients. Although the reasons associated with the gaps in high-intensity statin utilization and lack of statin use were not assessed, studies have implicated low rates of patient compliance with statins[25,28] and statin intolerance being reported in 7% to 29% of patients[29–31] as potential reasons.

At baseline, more than half of the CHD and CHD RE patients with available LDL-C measures had LDL-C levels ≥ 100 mg/dL. This number dropped considerably during follow-up and at the end of 1 year, approximately 29% to 46% patients had elevated LDL-C. These results are similar to those by Jones et al[32] who reported 23% to 33% of CHD and CHD RE patients across 3 data sources with LDL-C ≥ 100 mg/dL after receiving statin therapy for at least 90 days. LDL-C goal attainment has been found to be especially challenging as reported by Boekholdt et al[33] in a meta-analysis of statin trials where more than 40% of the trial participants receiving high-dose statins did not achieve LDL-C goal. This indicates the significant interpatient variability in LDL-C reduction with a fixed statin dose. As per the NLA 2015 recommendations for patient-centered management of dyslipidemia, LDL-C goal attainment is important for CV risk management. Our study indicates that even among high-risk patients, there are many who do not reach LDL-C goal. Further investigation to understand the underlying reasons associated with the lack of LDL-C goal attainment is warranted.

The cumulative CV incidence rate was higher among CHD patients, which was expected given the high risk for subsequent CV events in this patient population.[34,35] At the end of 1 year, at least 9.2% of all patients experienced at least 1 CV event. Although we did not assess statin therapy status or LDL-C levels of patients who had CV events during follow-up, studies have demonstrated that residual CV risk remains in high-risk patients despite LDL-C reduction.[18] Therefore, these patients with CV events would likely benefit from more intensive LDL-C treatment and monitoring.

Evidence from the large-scale statin meta-analysis studies[5,33] and the recently concluded IMPROVE-IT trial[8] has demonstrated a CV outcomes benefit with reductions in LDL-C. These studies further support that additional LDL-C lowering is beneficial, and a floor LDL-C value has not been determined. CHD and CHD RE patients may require more robust treatment, and our study highlights the need for better LDL-C management among these patients.

Limitations of the study include its observational nature using a retrospective claims data source. ICD-9 codes used to identify and categorize the CHD and CHD RE patients may have been subjected to errors associated with miscoding of relevant diagnoses. There was no information on dietary or exercise habits of these patients that might have been used in addition to statin therapy to control LDL-C levels. Also, the higher proportion of patients not receiving statins (39%–61%) and the relatively lower prevalence of

patients with LDL-C ≥ 100 mg/dL (21%–54%) ≥ 91 days after baseline may be attributed to patients paying for their statins out-of-pocket without going through their insurance provider and hence not captured in the study database. In addition, LDL-C values were available in 4.1% to 4.5% of patients throughout the study period. For patients with LDL-C values, they were not available longitudinally across the different time periods. LDL-C value-related limitations are not unique to our study.[36,37] Nevertheless, this limitation highlights the need for more frequent monitoring of LDL-C among high-risk patients. The lack of detailed clinical information or notes precluded us from analyzing reasons behind treatment decisions, and we were unable to ascertain if patients took the prescribed medication. Additional research should use contemporary data to further understand the effects of the introduction of current guidelines and 2015 NLA LDL-C goal of <70 mg/dL among very high-risk patients.

Conclusions

Although statin treatment was observed for most of the patients at high risk for CVD, 39% to 44% patients had no statin therapy at the end of 1 year. More than 9.2% of patients had at least 1 CV event during follow-up. Elevated LDL-C was observed in 29% to 46% of patients at the end of 1 year. The high proportion of patients with elevated LDL-C indicates that there is room for better LDL-C management among high-risk patients.

Financial disclosures

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Description of Truven MarketScan database

The Truven Health MarketScan Research Database integrate individual-level health (medical, drug), laboratory results and hospital discharge, and death data into de-identified data sets. The data are submitted by large employers, managed care organizations, hospitals, and Medicare and Medicaid programs.

The Truven MarketScan database offer the largest convenience sample available in proprietary databases, with more than 200 million unique patients since 1995 and are large enough to allow creation of a nationally representative data sample of Americans with employer-provided health insurance.

The Truven MarketScan Database consists of 3 core claims databases, the MarketScan Commercial Claims and Encounters Database, the MarketScan Medicare Supplemental and Coordination of Benefits database, and the MarketScan Medicaid Multi-State database. These databases are described in more detail in the following list.

1. The MarketScan Commercial Claims and Encounters Database (commercial database) consists of medical and drug data from employers and health plans for several million individuals annually, encompassing employees, their spouses, and dependents who are covered by employer-sponsored private health insurance. Healthcare for these individuals is provided under a variety of fee-for-service, fully capitated, and partially capitated health plans including PPOs and exclusive provider organizations, point of service (POS) plans, indemnity plans, health maintenance organization (HMO), and consumer-directed health plans. Medical claims are linked to outpatient prescription drug claims and person-level enrollment information. The database is constructed by combining, standardizing, and enhancing the databases Truven Health builds on behalf of large employers and health plans nationwide.

2. The MarketScan Medicare Supplemental and Coordination of Benefits Database (Medicare Supplemental Database) is the first in the United States to profile the health-care experience of retirees with Medicare supplemental insurance paid by employers. The database includes the Medicare-covered portion of payment (represented as Coordination of Benefits Amount), the employer-paid portion, and any out-of-pocket patient expenses. The Medicare Supplemental Database provides detailed cost, use, and outcomes data for health-care services performed in both inpatient and outpatient settings. For most of the population, the medical claims are linked to outpatient prescription drug claims and person-level enrollment data through the use of unique patient or enrollee identifiers.

3. The MarketScan Medicaid Multi-State Database contains the medical, surgical, and prescription drug experience of more than 36.6 million Medicaid enrollees from multiple states. It includes records of inpatient services, inpatient admissions, outpatient services, and prescription drug claims, and information about long-term care and other medical care. Data on eligibility (by month), service, and provider type are also included. In addition to standard demographic variables, such as patient age and gender, the database includes variables of particular value to researchers investigating Medicaid populations, such as aid category (eg, blind or disabled, Medicare eligible) and race.

Note: Information on Truven MarketScan database was based on a white article titled "Health research data for the real world: the MarketScan databases" published by Truven Health Analytics in January 2015.

Table 1   ICD-9/CPT codes for identifying CHD and CHD RE cohorts

CHD indication	ICD-9/CPT code(s)
Myocardial infarction (MI)	410.xx, 411.0, 412
Unstable angina	411.1
Stable angina	413.xx
Other chronic ischemic heart disease	414.xx
Coronary artery bypass graft (CABG)	ICD-9: 36.1x, 3610-3619 CPT: 33510-33536, 33572
Percutaneous coronary intervention (PCI)	ICD-9: 066, 3601-3607 CPT: 92973, 92980-92982, 92984, 92995, 92996
CHD RE indication	ICD-9/CPT code(s)
Type 2 diabetes (in patients aged ≥40 y)	250.x0, 250.x2
Peripheral vascular disease	440.xx, 443.9, 443.81
Stroke	430.xx, 431.xx, 432.xx, 433.x1, 434.x1, 997.02, 436
Abdominal aortic aneurism	441.3, 441.6, 441.4, 441.7
Transient ischemic attack	435.xx

CHD, coronary heart disease; CHD RE, coronary heart disease risk equivalent; CPT, Current Procedural Terminology; ICD-9, International Classification of Diseases, 9th Revision.

Table 2   ICD-9 codes/CPT codes for identifying CV events/procedures in the post-index period

CV event	ICD-9/CPT code(s)
Myocardial infarction (MI)[*]	410.xx
Stroke	430.xx, 431.xx, 432.xx, 433.x1, 434.x1, 997.02, 436
Unstable angina hospitalization[†]	411.1
Coronary artery bypass graft (CABG)	ICD-9: 36.1x, 3610-3619
	CPT: 33510-33536, 33572
Percutaneous coronary intervention (PCI)	ICD-9: 066, 3601-3607
	CPT: 92973, 92980-92982, 92984, 92995, 92996
Heart failure hospitalization[†]	428.xx

CPT, Current Procedural Terminology; CV, cardiovascular; ICD-9, International Classification of Diseases, 9th Revision.
*Only new MI diagnosis.
†To confirm that hospitalization was associated with heart failure or unstable angina, we looked for "in-patient status" in the database for a primary diagnosis of heart failure or unstable angina.

Table 3   Categorization of statins according to 2013 ACC/AHA guidelines[22]

Low-intensity Statin	Moderate-intensity statin	High-intensity statin
Fluvastatin 20–40 mg	Fluvastatin 40 mg twice daily	Atorvastatin 40–80 mg
Lovastatin 20 mg	Fluvastatin XL 80 mg	Rosuvastatin 20 mg and 40 mg
Pravastatin 10–20 mg	Lovastatin 40 mg	Simvastatin 80 mg
Simvastatin 10 mg	Pravastatin 40 mg and 80 mg	
Pitavastatin 1 mg	Simvastatin 20–40 mg	
	Atorvastatin 10 mg and 20 mg	
	Rosuvastatin 5 mg and 10 mg	
	Pitavastatin 2–4 mg	

ACC/AHA, American College of Cardiology/American Heart Association.
Note: Simvastatin 80 mg was not included in this categorization by the guidelines because initiation with this strength or titration to this strength is not recommended by the Food and Drug Administration due to the increased risk of myopathy, including rhabdomyolysis. However, in this study, we have categorized simvastatin 80 mg as a high-intensity statin.

Table 4   Patients with post-index CV events within 1 year in the CHD and CHD RE cohorts

| | Post-index events | | | |
| | CHD cohort (N = 175,103) | | CHD RE cohort (N = 68,290) | |
Type of CV event	Number of patients	%	Number of patients	%
Myocardial infarction	7505	4.3	486	0.7
Stroke	2055	1.2	4135	6.1
Unstable angina	3535	2.0	168	0.2
Revascularization (CABG and PCI)	3344	1.9	282	0.4
Heart failure	4983	2.8	872	1.3
Transient ischemic attack	440	0.3	619	0.9
Patients with at least 1 CV event	17,349	9.9	4965	7.3

CABG, coronary artery bypass graft; CHD, coronary heart disease; CHD RE, coronary heart disease risk equivalent; CV, cardiovascular; PCI, percutaneous coronary intervention.