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Longitudinal treatment patterns among US patients with atherosclerotic cardiovascular disease or familial hypercholesterolemia initiating lipid-lowering pharmacotherapy

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BACKGROUND: The most recent American College of Cardiology–American Heart Association guidelines recommend high-dose statin therapy for most patients with confirmed atherosclerotic cardiovascular disease (ASCVD) and patients with high cardiovascular risk. There is limited information regarding long-term treatment patterns among these patients.

OBJECTIVE: To examine longitudinal treatment modifications in patients with ASCVD or familial hypercholesterolemia (FH).

METHODS: This retrospective analysis of administrative claims data identified patients initiating statin or ezetimibe therapy between January 1, 2007, and December 31, 2012, who had evidence of ASCVD or FH. Patients were followed for up to 3 years and up to 4 treatment episodes. After initial treatment, subsequent treatment episodes began on the date of a treatment modification, which included discontinuation, statin dose change, switching, and augmentation.

RESULTS: A total of 92,621 patients (mean age 64.7 years, 57.3% male) were identified; 91,740 had ASCVD, 937 had FH (56 had both). Most ASCVD (89.6%) and FH (85.8%) patients initiated on statin monotherapy. The most common treatment modification in the first treatment episode was discontinuation (ASCVD: 42.0%; FH: 58.4%); among patients who discontinued, most reinitiated therapy (70.5% of ASCVD, 76.8% of FH). Most ASCVD (68.2%) and FH (71.1%) patients initiated on moderate-dose statins; statin dose increase occurred in 10.3% of ASCVD and 18.5% of FH patients in the first episode.

CONCLUSION: Among patients with high cardiovascular risk, most initiated on moderate-dose statins with infrequent uptitration. In light of the recent American College of Cardiology–American Heart Association guidelines, statin initiation practices will need to change to ensure appropriate therapy for high-risk patients.

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Introduction

Cardiovascular disease (CVD) affects more than 85 million Americans and accounts for about 1 out of every 3 deaths–more than cancer and chronic respiratory disease combined.[1] In 2011, the direct and indirect costs of CVD were estimated to total $320 billion annually,[1] with projected costs nearing $700 billion by 2020 and exceeding $1 trillion by 2030.[2]

Elevated low-density lipoprotein cholesterol (LDL-C) levels are a known risk factor for CVD and statin therapy is widely recommended to lower LDL-C and reduce CVD risk.[3–7] Although previous guidelines focused on LDL-C goal attainment, the 2013 American College of Cardiology–American Heart Association (ACC–AHA) guidelines instead target patients according to CVD risk[7] and recommend high-intensity statin therapy for patients with confirmed atherosclerotic CVD (ASCVD) who are aged 75 years and younger and patients with LDL-C ≥190 mg/dL. Familial hypercholesterolemia (FH) is a genetic disorder that causes elevated LDL-C levels from birth.[8] Patients with FH may have difficulty lowering LDL-C below recommended certain levels even with statin therapy and lifestyle modifications and can often develop premature atherosclerosis and ASCVD; for these reasons, the National Lipid Association considers patients with FH at high risk for a CVD event.[9]

Although more than one-quarter of US adults aged 40 or older use statins[10] and an additional 14 million adults may be eligible for statin therapy under the newest guidelines,[11] discontinuation of statin therapy is common[12–15] and statins are often initiated at a suboptimal dose without subsequent dose increases or the addition of other medications.[16] Long-term treatment patterns among patients at high risk for cardiovascular events are not well known: studies of statin treatment have frequently examined treatment in the first year of therapy only.[16–18] There is a need to examine treatment patterns over longer intervals within this population. The objective of this study was to examine treatment modifications over time among patients initiating statin or ezetimibe therapy with either ASCVD or elevated LDL-C indicative of FH.

Methods

Study design and data source

The study was a retrospective analysis of administrative claims from the Optum Research Database from January 1, 2006, to December 31, 2013. The Optum Research Database is a proprietary research database with medical and pharmacy claims linked to enrollment information from a large US health plan. The medical claims capture diagnoses and procedures from *International Classification of Diseases, Ninth Revision, Clinical Modification* codes, Healthcare Common Procedure Coding System procedure codes, and Current Procedural Technology procedure codes. Pharmacy claims are submitted at the time of a prescription fill and include National Drug Code, quantity dispensed, drug strength, and days supply. Patient and prescriber identifiers allow for longitudinal tracking of refill patterns and changes in medications. No identifiable protected health information was extracted or accessed during the course of the study. Pursuant to the Health Insurance Portability and Accountability Act, the use of deidentified data does not require Institutional Review Board approval or waiver of authorization.

Patient selection

Health plan members aged ≥18 years with either commercial or Medicare Advantage with Part D prescription drug coverage were identified. To be eligible for study inclusion, patients were required to have ≥ 2 outpatient pharmacy claims for a statin or ≥ 2 outpatient pharmacy claims for ezetimibe within 6 months of each other, where the date of the first claim (the index date) occurred between January 1, 2007, and December 31, 2012. Patients were also required to have at least 12 months of continuous medical and pharmacy coverage before (baseline) and after the index date and were followed for a minimum of 1 year and up to 3 years ending at the earliest of: death, the end of health plan enrollment, or the end of the study period (December 31, 2013). Patients with claims for either a statin or ezetimibe during the baseline period or evidence of pregnancy at any time during the baseline or follow-up periods were excluded.

Study cohorts

Among patients who met eligibility criteria, patients retained for analysis were those with evidence of either ASCVD or FH. Although ASCVD and FH were identified separately, there was modest overlap among the ASCVD and FH cohorts. Patients were identified as having ASCVD if they had at least one medical claim during the baseline period with a diagnosis code in any position for a cardiovascular event: acute myocardial infarction, coronary revascularization (coronary artery bypass graft or percutaneous coronary intervention), ischemic stroke or transient ischemic attack, peripheral arterial disease or unstable angina (see Appendix 1 for codes). Patients were defined as having FH if their baseline LDL-C measurement closest to the index date exceeded an age-specific threshold. Patients aged 30 years or older with LDL-C ≥ 250 mg/dL, aged 20 to 29 with LDL-C ≥ 220 mg/dL, and younger than 20 years with LDL-C ≥ 190 mg/dL were identified as having FH.[19]

Measures

The primary outcome of interest was the occurrence of and time to a treatment modification, defined as one of several mutually exclusive events: discontinuation,