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Assessing the Impact of Medication Adherence on Long-Term Cardiovascular Outcomes

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ABSTRACT

BACKGROUND Although guideline-recommended therapies reduce major adverse cardiovascular events (MACE) in patients after myocardial infarction (MI) or those with atherosclerotic disease (ATH), adherence is poor.

OBJECTIVES The goal of this study was to determine the association between medication adherence levels and long-term MACE in these patients.

METHODS We queried the claims database of a large health insurer for patients hospitalized for MI or with ATH. The primary outcome measure was a composite of all-cause death, MI, stroke, or coronary revascularization. Using proportion of days covered for statins and angiotensin-converting enzyme inhibitors, patients were stratified as fully adherent (≥80%), partially adherent (≥40% to ≤79%), or nonadherent (<40%). Per-patient annual direct medical (ADM) costs were estimated by using unit costs from 2 national files.

RESULTS Data were analyzed for 4,015 post-MI patients and 12,976 patients with ATH. In the post-MI cohort, the fully adherent group had a significantly lower rate of MACE than the nonadherent (18.9% vs. 26.3%; hazard ratio [HR]: 0.73; $p = 0.0004$) and partially adherent (18.9% vs. 24.7%; HR: 0.81; $p = 0.02$) groups at 2 years. The fully adherent group had reduced per-patient ADM costs for MI hospitalizations of $369 and $440 compared with the partially adherent and nonadherent groups, respectively. In the ATH cohort, the fully adherent group had a significantly lower rate of MACE than the nonadherent (8.42% vs. 17.17%; HR: 0.56; $p < 0.0001$) and the partially adherent (8.42% vs. 12.18%; HR: 0.76; $p < 0.0001$) groups at 2 years. The fully adherent group had reduced per-patient ADM costs for MI hospitalizations of $371 and $907 compared with the partially adherent and nonadherent groups.

CONCLUSIONS Full adherence to guideline-recommended therapies was associated with a lower rate of MACE and cost savings, with a threshold effect at >80% adherence in the post-MI population; at least a 40% level of long-term adherence needs to be maintained to continue to accrue benefit. Novel approaches to improve adherence may significantly reduce cardiovascular events. (J Am Coll Cardiol 2016;68:789–801) © 2016 by the American College of Cardiology Foundation.

It is estimated that there are 83.6 million patients in the United States with established atherosclerotic (coronary, cerebrovascular, and peripheral artery) disease (1). Furthermore, approximately 735,000 Americans experience a myocardial infarction (MI) every year, and 210,000 have a recurrent event (2). The use of evidence-based and guideline-recommended medications for the secondary prevention of cardiovascular (CV) disease was estimated to be responsible for one-half of the overall 50% reduction in mortality from CV disease observed over the past 2 decades (3). Amazingly, this substantial

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ABBREVIATIONS AND ACRONYMS

ACE = angiotensin-converting enzyme

CI = confidence interval

CV = cardiovascular

HR = hazard ratio

ICD = International Classification of Diseases

MACE = major adverse cardiovascular events

MI = myocardial infarction

PDC = proportion of days covered

reduction in mortality has been achieved despite patients not receiving proven medical therapies to the fullest extent, with nearly one-half of the patients being nonadherent with their prescribed regimen 2 years after experiencing a CV event (4). In the longer term, for patients with documented atherosclerosis, medication adherence is <50% (5). The potential for further improvement in CV outcomes through improved medication adherence is therefore a tantalizing prospect. Improved outcomes will also have a direct impact on the immense financial burden associated with CV disease.

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Although nonadherence with evidence-based secondary prevention medications is common in patients with established atherosclerotic disease, studies on long-term outcomes are limited. The goal of the present paper was to study the association between levels of medication adherence and long-term major adverse cardiovascular events (MACE), resource utilization, and cost differences in an acute post-MI cohort and in a complementary chronic atherosclerosis cohort using a large U.S.-based health insurance database.

MATERIALS AND METHODS

DATA SOURCE. This non-concurrent cohort study was conducted by using 2010 to 2013 medical and pharmaceutical claims obtained from Aetna Commercial and Medicare Advantage population databases. These databases consist of enrollment records from a large, geographically diverse, insured population. These records were linked, allowing for comprehensive tracking of patients' use of health care resources and clinical outcomes over time and across providers. Enrollment files contain individualized demographic and health insurance plan characteristics, such as age, sex, geographic region, type of health insurance plan, and enrollment status. Medical claims included detailed information about inpatient and outpatient care, including date and place of service diagnosis codes according to the International Classification of Diseases (ICD)-Ninth Revision-Clinical Modification, and procedure codes, such as those from Current Procedural Terminology, Fourth Edition. Pharmacy claims files included information on National Drug Code, dispense date, quantity dispensed and supplied, and copayment amounts. In addition, Symmetry episode risk group scores (Ingenix, Inc., Eden Prairie, Minnesota; 2008 proprietary risk prediction algorithm), publicly available data from the U.S. Census 2010 file, and self-reported multisource race/ethnicity data were included in the analysis. For the cost data, 2 separate, federally funded and nationally representative cost databases were analyzed: the Healthcare Cost and Utilization Project and the Medicare files (Medicare Physician Fee Schedule and Medicare Outpatient Prospective Payment System). We also performed a sensitivity analysis of the results by using simple average unit costs for stroke, MI, atherosclerosis or angina, revascularization procedures, and CV test categories.

STUDY POPULATION. The post-MI cohort included adults who initiated both statin and angiotensin-converting enzyme (ACE) inhibitor medications after a hospitalization discharge for MI according to ICD codes 410.x (excluding codes when the fifth digit was 2) and 411.1 with a length of stay of >2 days, between January 1, 2010, and February 28, 2013. Patients were included in the cohort if they had continuous eligibility for both medical and prescription drug benefits from Aetna during 6 months before and after the MI. The discharge date of the MI hospitalization was identified as the index date.

The atherosclerosis cohort included adults who initiated both statin and ACE inhibitor medications and also had 2 coronary, cerebrovascular, or peripheral artery disease ICD codes (claims) within 1 category or a revascularization code between January 1, 2010, and December 31, 2010. Patients were included in the cohort if they had continuous eligibility for both medical and prescription drug benefits from Aetna from January 1, 2010, to December 31, 2011. The first statin and ACE inhibitor refill during 2010 was identified as the index date. For both cohorts, an "out-of-hospital" first medication fill during the period of interest was considered as an inclusion requirement.

Members were excluded from both cohorts if they met any of the following criteria: pregnancy; patients with diagnosis codes indicating psychoses, dementia, bipolar disorder, major depressive disorder (severe with psychotic behaviors), or alcohol/substance abuse; and patients living in a nursing home, hospice, or respite care. Patients who had a refill for angiotensin-receptor blocker (ARB) medication in 2010 were also excluded (to avoid a potential inclusion bias with patients who could have potentially switched to an ARB due to ACE inhibitor intolerance).

Follow-up was through December 31, 2013, and was truncated at the following: 1) disenrollment from the "health care benefits plan" (equivalent to lost to follow-up); 2) death; or 3) end of the follow-up period.

INDEPENDENT VARIABLES. We used clinical judgment to identify the initial set of candidate variables.