



Care of Patients With Ischemic Heart Disease

## Adherence to evidence-based secondary prevention pharmacotherapy in patients after an acute coronary syndrome: A systematic review



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### ABSTRACT

**Objective:** To synthesize current evidence on medication adherence rates and associated risk factors in patients after an acute coronary syndrome (ACS).

**Methods:** A systematic review was conducted. Five electronic databases and article bibliographies were searched for publications from 1990 to 2013 which assessed adherence to secondary prevention pharmacotherapy in adults after hospital discharge for an ACS. Identified studies were screened using pre-defined criteria for eligibility. A standardized form was used for data abstraction. Methodological quality was assessed using modified criteria for quantitative studies.

**Results:** Sixteen studies met our inclusion criteria. Post-discharge medication adherence rates at 1-year ranged between 54% and 86%. There were no consistent predictors of non-adherence across all cardiac medication classes examined.

**Conclusions:** Adherence to secondary prevention pharmacotherapy was suboptimal in patients after hospital discharge for an ACS. Risk factors associated with non-adherence were examined in a limited number of studies, and the associations varied between these investigations.

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### Introduction

Cardiovascular disease remains the leading cause of morbidity and mortality in the United States.<sup>1</sup> The acute coronary syndromes (ACS), including unstable angina and acute myocardial infarction (AMI) with or without ST-segment elevation, are the major forms of acute coronary heart disease (CHD) and affect more than 1.1 million adults in the U.S. in 2010.<sup>1</sup>

Patients surviving an ACS are at increased risk for developing a wide range of complications, highlighting the importance of secondary prevention efforts.<sup>2</sup> The American College of Cardiology/American Heart Association guidelines currently recommend that all patients recovering from an ACS, unless a relevant

contraindication exists, be initiated on angiotensin-converting-enzyme inhibitors (ACEI) or angiotensin II receptor blockers (ARBs), antiplatelet therapy, beta-blockers, and statins for long-term treatment.<sup>3</sup> Numerous large-scale randomized clinical trials have demonstrated the efficacy of these guideline recommended treatments in reducing the risk of recurrent ischemic events and mortality in patients after an ACS.<sup>4–9</sup> Current evidence, however, has shown less than optimal patient adherence to evidence-based therapies<sup>10,11</sup>; non-adherence is associated with an increased risk of cardiovascular hospitalizations and mortality, coronary revascularization procedures, and increased costs.<sup>12–14</sup>

Although medication adherence is an important concern in managing patients after an ACS, it has been a challenge to assess medication adherence on a long-term basis in routine clinical practice due to time and resource constraints. A better understanding of the barriers to more optimal adherence, and changes in adherence over time, to effective cardiac medications in patients discharged from the hospital after an ACS would help to identify patients at increased risk for poor adherence and in designing targeted intervention strategies for both patients and their health care providers.

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To our knowledge, there have been no prior systematic reviews assessing medication adherence in patients discharged from the hospital after an ACS. The purpose of this systematic review was to synthesize current evidence on medication adherence in patients after an ACS. Following the definition proposed by The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Medication Compliance and Persistence Work Group,<sup>15</sup> “medication adherence” was defined as “the extent to which a patient acts in accordance with the prescribed interval and dose of a dosing regimen.”<sup>15</sup> Our primary objective was to examine adherence to evidence-based cardiac medications at different follow-up points in patients discharged from the hospital after an ACS. Our secondary objective was to examine risk factors associated with non-adherence to evidence-based medications after hospital discharge in these patients.

## Methods

### Search strategy

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.<sup>16</sup> Searches to identify relevant articles were performed in PubMed, PsycINFO, CINAHL, Health and Psychosocial Instruments, and ISI Web of Science from January 1, 1990 to September 30, 2013. We began our search from January 1, 1990, since the first ACC/AHA Guidelines for the Management of Patients with Acute Myocardial Infarction, which was published in 1990.<sup>17</sup> Two research librarians at the University of Massachusetts Medical School helped to develop a search algorithm. For the PubMed search, we derived 3 comprehensive search themes of “acute coronary syndrome,” “adherence,” and “medication” that were combined with the Boolean operator “and.” Our search terms, including specific key words and a medical subject heading (MeSH) term, were listed in Table 1. The search was limited to articles published during the specified time period and in English language. We used a similar strategy to perform article search in PsycINFO, CINAHL, Health and Psychosocial Instruments, and ISI Web of Science. All articles obtained from the 5 databases would be compared and duplicates would then be removed. The bibliographies of eligible articles were searched for additional references.

### Inclusion and exclusion criteria

Our review focused on “secondary” non-adherence (i.e., when prescriptions are filled, but the medication is not taken as

**Table 1**  
Search themes and search terms.

Search themes	Search terms
Acute coronary syndrome	Acute coronary syndrome, acute coronary syndromes, myocardial infarction, heart attack, unstable angina
Adherence	Patient compliance (mesh), adherence, compliance, compliant, comply, complying, complies, concordance, nonadherence, noncompliance, noncompliant, noncomply, noncomplying, nonconcordance
Medication	Medication, medications, pharmacotherapy, pharmacotherapies, therapy, therapies, treatment, treatments, drug, drugs, medicine, medicines, secondary prevention, beta-blocker, beta-blockers, angiotensin-converting enzyme inhibitor, angiotensin-converting enzyme inhibitors, ACE inhibitor, ACE inhibitors, angiotensin receptor blocker, angiotensin receptor blockers, ARB, ARBs, statin, statins, lipid-lowering agent, lipid-lowering agents, aspirin, aspirins, antiplatelet, antiplatelets

Mesh, medical subject heading.

prescribed), since our review was designed to examine post hospital discharge medication adherence at several follow-up points. Publications included in this review had to: (1) be published between January 1, 1990 and September 30, 2013; (2) have human subjects aged  $\geq 18$  years old; (3) have subjects hospitalized for an ACS; (4) have subjects prescribed at least one evidence-based medication after hospital discharge: beta-blockers, lipid-lowering agents, antiplatelet agents, and ACEIs/ARBs; (5) include a measure of medication adherence and its method of measurement; (6) be published in English; and (7) be published in a peer-reviewed journal, irrespective of the type of study design used.

Publications were excluded for further review if they: (1) did not specify the type of medication examined; (2) did not report post hospital discharge medication use; (3) did not have a specific follow-up time point for calculating medication adherence; (4) did not calculate medication adherence based on patients with at least one filled prescription for the drug of interest during follow-up; (5) were study summaries without original results; or (6) were subgroup analyses of original study population; (7) were review articles, opinion pieces, letters, commentaries, case reports, or case series; or (8) examined primary medication non-adherence (i.e., a patient does not fill a prescribed medication at the start of therapy) or medication persistence (i.e., the duration of time from initiation to discontinuation of therapy).<sup>15</sup>

### Data collection

An initial review of the titles and abstracts of all articles was performed to exclude any studies that did not meet our pre-defined inclusion criteria. Full review of all remaining studies was undertaken to determine eligibility for inclusion. We used a standardized form to abstract data from all included studies. Information was abstracted for study type, study country and setting, number of participants, patient’s socio-demographic characteristics, study condition, data source, drugs or therapeutic classes studied, medication adherence measure(s), reported medication adherence and cut-point used for assessing good adherence, study inclusion period, follow up time point(s) of adherence assessment, and risk factors examined in relation to medication non-adherence. Two reviewers evaluated the abstraction during weekly discussions of this project.

### Measures of medication adherence

A variety of measures have been used to assess medication adherence, such as patient questionnaires, self-report, pill counts, and electronic medication monitors.<sup>18</sup> Commonly used measures in claims-based research include the medication possession ratio (MPR; defined as “number of days of medication supplied within the refill interval/number of days in refill interval”) and the proportion of days covered (PDC; defined as “total days all drug(s) available/days in follow-up period”).<sup>18</sup> Patients were considered as having “good” medication adherence, if a specified threshold (e.g., 80%) was attained. In this review, the specific cut point used to define good adherence in each study was determined by the authors, which varied among the included studies. For example, a good medication adherence of 74% measured by the PDC with an 80% cut-off meant that 74% of patients achieved good medication adherence as they were covered by the prescribed medication at least 80% of days during the period of assessment.

### Risk factors associated with medication non-adherence

We categorized potential risk factors for medication non-adherence into 5 broad groups, including patient (e.g.,

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