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Longitudinal persistence with secondary prevention therapies relative to patient risk after myocardial infarction

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Abstract

Background—Prior studies have demonstrated that high-risk AMI patients are less likely to receive guideline-directed medications during hospitalization. It is unknown if this paradox persists following discharge. We aimed to assess if persistence with guideline-directed medications post-discharge varies by patients' risk following acute myocardial infarction (AMI).

Methods—Data were analyzed from two prospective, multicenter U.S. AMI registries. The primary outcome was persistence with all prescribed guideline-directed medications (aspirin, beta-blockers, statins, angiotensin-antagonists) at 1, 6, and 12-months post-discharge. The association between risk and medication persistence post-discharge was assessed using multivariable mixed-effect models.

Results—Among 6434 AMI patients discharged home, 2824 were considered low-risk, 2014 intermediate-risk and 1596 high-risk for death based upon their GRACE 6-month risk score. High-risk was associated with a lower likelihood of receiving all appropriate therapies at discharge

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compared with low-risk patients (RR 0.90; 95% CI 0.87–0.94). At 12-months, the rate of persistence with all prescribed therapies was 61.5%, 57.9% and 45.9% among low-, intermediate- and high-risk patients respectively. After multivariable adjustment, high-risk was associated with lower persistence with all prescribed medications (RR 0.87; 95% CI 0.82–0.92) over follow-up. Similar associations were seen for individual medications. Over the 5 years of the study, persistence with prescribed therapies post-discharge improved modestly among high-risk patients (RR 1.05; 95% CI 1.03–1.08 per year).

Conclusion—High-risk AMI patients have a lower likelihood of persistently taking prescribed medications post-discharge as compared with low-risk patients. Continued efforts are needed to improve the use of guideline-directed medications in high-risk patients.

Keywords

myocardial infarction; medication persistence; secondary prevention therapy

Introduction

Among patients with acute myocardial infarction (AMI), guidelines and performance measures aim to improve quality of care delivered by encouraging provision of evidence-based medications in all eligible patients.[1] Prior studies have demonstrated that high-risk AMI patients often do not receive guideline-directed medications during hospitalization, a phenomenon that has been referred to as the “risk-treatment paradox”.[2, 3] However, little is known about whether such paradox exists for use of prescribed medications following hospital discharge.

Both provision of appropriate medications and continued use of these medications are necessary to realize their potential to reduce the risk of mortality and recurrent AMI. While it is known that physicians are less likely to optimally manage high-risk AMI patients at the time of discharge [2, 3], it is unknown whether long-term use of these guideline-directed medications differs by patients’ risk after discharge or whether use of guideline-directed medical therapy post-discharge has improved over time. Identifying such treatment gaps can enable targeted interventions to improve the use and persistence with cardiac medications.

The objective of this study was to assess persistence with guideline-directed therapies during longitudinal follow-up in two large, prospective, multi-centered registries of AMI patients. We assessed prescription of aspirin, statins, beta-blockers and angiotensin converting enzyme inhibitors/angiotensin receptor blockers (ACEI/ARBs) to AMI patients at low, intermediate and high risk for all-cause mortality based on the Global Registry of Acute Coronary Event (GRACE) risk score at hospital discharge. We then sought to describe persistence with these medications in the year following hospital discharge, as well as assess temporal trends in persistence with these cardiac medications across risk strata over the course of this study.

Methods

Data Source

The analytic cohort for this study was derived from the Prospective Registry Evaluating Myocardial Infarction: Events and Recovery (PREMIER) and Translating Research Investigating Underlying Disparities in AMI Patients Health Status (TRIUMPH) registries. Both are prospective, multi-center, observational registries of AMI patients. PREMIER enrolling 2,498 patients from 19 U.S medical centers between January 1, 2003 and June 28, 2004 and TRIUMPH enrolling 4,340 patients from 24 U.S medical centers between April 11, 2005 and December 31, 2008 (31 sites in total; 12 sites participated in both registries). Both registries had identical inclusion and exclusion criteria and employed the same standards in data collection and follow-up. Their study designs have been previously described and further details have been provided in the supplementary appendix.[4, 5]

Study design and cohort

This study was performed as a retrospective analysis of prospectively collected data. We included all patients enrolled in PREMIER and TRIUMPH who were discharged home and had data available on discharge medications (Figure 1). We excluded patients with documented contraindications including active bleeding on arrival or concomitant warfarin use at discharge for aspirin; heart rate <50bpm, 2nd/3rd degree heart block, systolic blood pressure<100 mmHg for beta-blockers; moderate/severe aortic valve stenosis or systolic blood pressure<90 mmHg for ACEI/ARBs, or documented allergies or patient refusal. Contraindications were prospectively abstracted from medical records. For ACEI/ARBs we included only patients with left ventricular systolic dysfunction (ejection fraction<40%) at the time of AMI.[6]

Risk Assessment

Risk was assessed among included patients using GRACE discharge risk-score. This model predicts all-cause mortality in both ST-segment elevation myocardial infarction (STEMI) and non-ST segment elevation myocardial infarction (NSTEMI) patients at various time points post-discharge, ranging from 6-months to 4-years (c-statistic>0.75).[7, 8] Components of GRACE score include age, presenting heart rate, presenting systolic blood pressure, initial serum creatinine, elevated cardiac biomarkers, ST segment depression, in-hospital percutaneous coronary intervention (PCI), in-hospital coronary artery bypass grafting (CABG), history of congestive heart failure and history of myocardial infarction. We calculated GRACE scores separately based on presenting diagnosis (STEMI/NSTEMI) and stratified the cohort into 3 risk categories (low, intermediate, high) based on established and validated criteria. (Supplemental Table 1:[9])

Outcomes

At hospital discharge, we assessed whether eligible patients were appropriately prescribed aspirin, statin, beta-blockers and ACEI/ARBs. A composite measure was calculated as prescription of all guideline-directed medications for which the patient was eligible. Hence, a patient eligible for 2 medications prescribed both medications was classified as receiving

all guideline-directed care, but a patient eligible for 4 medications prescribed only 3 or less was classified as not receiving all guideline-directed care.

Next, we ascertained patients' persistence with prescribed guideline-directed medications post-discharge (i.e., among those patients discharged on the corresponding medication). Medication usage at follow-up was based on patients' self-report assessed via in-person or telephone interviews at 1, 6 and 12-months post-index AMI. At each of these interviews, patients were asked to collect all their current medications and read each medicine to the interviewer. Since we evaluated only self-reported use of medications (yes/no), we used the term "persistence" as opposed to adherence, which quantifies intensity of medication use. [10, 11, 12, 13] Persistence was assessed for the composite endpoint (i.e., all prescribed guideline-directed medications as defined above) as well as for use of aspirin, statins, beta-blockers and ACEI/ARBs individually.

Previous studies examining validity of self-reported medication use have found it to be comparable to other direct measures of persistence such as blood drug levels.[13, 14, 15, 16] Additionally, in real-world clinical practice, medication use among patients is predominantly assessed by self-report.

Other covariates included in our model are detailed in supplementary appendix.

Statistical Analysis

Baseline characteristics were compared between low-, intermediate- and high-risk patients using chi-square or Fisher's exact tests for categorical variables and one-way analysis of variance for continuous variables. Relative risk regression was used to assess association between risk-category and prescription of all eligible guideline-directed therapies at discharge, adjusting for enrolling site and other covariates (provided in supplement). Since prescribing medications was not a "rare event," we used a modified Poisson regression model to estimate relative risks directly, as opposed to odds ratios obtained by logistic regression, which overestimate relative risks in such situations. Because Poisson model misspecifies the distribution of outcome, robust variance estimation was used to provide correct standard errors.[17]

Next, association between risk and post-discharge persistence with prescribed medications was assessed, both for composite of all prescribed medications and for each prescribed medication individually. Effect of risk on persistence was assessed with generalized linear mixed models, using the modified Poisson framework described above but including random effects to accommodate within-patient correlations among repeated assessments at 1, 6 and 12-months. The model included fixed effects for risk-category, enrolling site, all covariates, follow-up month and patient-level random intercepts for each of the three follow-up time points. An unstructured covariance matrix for the random intercepts was used to accommodate within-patient correlation between follow-up assessments. Interaction between risk and time was also assessed; however, no interaction achieved the 0.05 significance level for any outcome (p-values ranged from 0.09 to 0.55), so only main effects are presented here. Sensitivity analyses were performed using logistic regression instead of

Poisson models to evaluate robustness of our findings; results were consistent and so are not reported.

Finally, we assessed temporal trends in use of guideline-directed therapies at and post-discharge across risk-strata. Observed rates of medication use were calculated within 6-month intervals across the study duration (2003–2008), stratified by patient-risk. Temporal trends, adjusting for patient factors, were statistically assessed by augmenting the above regression models with a linear term for year and a year-by-risk group interaction.

Details regarding missing data analyses are provided in supplementary appendix. All analyses were conducted using SAS v9.4 (SAS Institute Inc., Cary, NC) and R version 3.1.1. [18] Our models were fitted with SAS PROC GLIMMIX. All statistical tests were evaluated at a two-sided significance level of 0.05.

Results

Patient Population

Between January-1-2003 and December-31-2008 a total of 6,838 AMI patients were enrolled in PREMIER and TRIUMPH registries. We excluded patients who died prior to discharge (n=41), patients discharged to hospice or nursing homes (n=146) and patients on whom data regarding discharge medications was lacking (e.g., those transferred to another acute or non-acute care facility, patients who signed out against medical advice or were lacking data on final disposition, n=217; Figure 1). The final analytic cohort comprised of 6434 patients of which 2824 (43.9%) patients were low-risk, 2014 (31.3%) intermediate-risk and 1596 (24.8%) high-risk by GRACE risk-score. Overall, follow-up data was available on 5,684 (88.3%) patients.

Baseline comparison

Table 1 summarizes the baseline characteristics of the study cohort stratified by risk. Compared with patients in low- and intermediate-risk strata, high-risk patients were older, more likely to be women, less likely to be Caucasian and had a greater burden of all co-morbidities. High-risk patients were more likely to be insured and less likely to report avoiding medications due to cost, compared with low- and moderate-risk patients. Furthermore, high-risk patients were less likely to undergo diagnostic coronary angiography and coronary revascularization (PCI/CABG) during index AMI.

Therapy use at discharge

Table 2 shows rates of medication use at discharge among eligible patients in the study population stratified by risk. Overall, 1136 (71.2%) high-risk patients received all guideline-directed therapies at discharge as compared with 1,583 (78.6%) intermediate-risk patients and 2,385 (84.5%) low-risk patients (p<0.001). Following multivariable adjustment, high-risk was associated with a lower rate of receipt of all eligible therapies at discharge compared with low-risk patients (RR 0.90; 95% CI 0.87–0.94). Similarly, intermediate-risk was also associated with lower rate of receipt of all eligible therapies at discharge (RR 0.95; 95% CI 0.92–0.98) as compared with low-risk patients.

Persistence with therapy after discharge

Among patients discharged on guideline-directed therapies, increasing risk was associated with lower persistence with all prescribed medications at 1-month (low- vs. intermediate- vs. high-risk patients: 70.4% vs. 63.8% vs. 51.0%), 6-months (63.9% vs. 59.3% vs. 45.8%) and 12-months after index AMI (61.5% vs. 57.9% vs. 45.9%; Figure 2). After multivariable adjustment, high-risk was significantly associated with lower persistence with all guideline-directed therapies across follow-up compared with low-risk patients (RR 0.87; 95% CI 0.82–0.92), although intermediate-risk was not (RR 0.98; 95% CI 0.94–1.01; Table 3). Other variables associated with lower persistence with all guideline-directed therapies post-discharge are shown in Supplemental Figure 1. This included socio-economic factors such as non-white race, lack of high school education and insurance, other chronic medical conditions (e.g., diabetes, congestive heart failure, chronic kidney disease), depression and higher anginal burden assessed by the Seattle Angina Questionnaire.

Individual observed persistence rates for aspirin, statins, beta-blockers and ACEI/ARBs post-discharge were also lowest among high-risk patients, but tended to be comparable between low- and intermediate-risk patients (Figure 3). Following multivariable adjustment, high-risk was associated with lower persistence, but in general intermediate-risk was not (Table 3).

Temporal trends in medication utilization at and after discharge

Figure 4 shows medication use at and post-discharge over the study duration from 2003–2008 (no data was available between July-2004 and July-2005, the period between end of PREMIER enrollment and start of TRIUMPH enrollment). From 2003–2008, we observed a modest increase in receipt of all guideline-directed therapies at discharge for all risk-groups. Although the increase was greatest among high-risk patients, interaction by risk-group did not quite achieve statistical significance ($p=0.06$). Similarly, persistence with all prescribed therapies post-discharge increased modestly and significantly over time for all risk-groups; and again although the increase was greatest among high-risk patients, the interaction by risk-group was not significant ($p=0.06$; Table 4).

Discussion

Our objective was to determine the receipt of cardiac medications at discharge and persistence with their use during longitudinal follow-up in a large, prospective cohort of AMI patients stratified by their mortality risk. We found an association between high-risk and a lower receipt of indicated cardiac medications at hospital discharge. Furthermore, among patients discharged on appropriate therapies, high-risk patients had lower persistence with medications over the year following AMI. Largest drop in medication persistence occurred in the first-month post-discharge. Less than half of high-risk patients persisted with all guideline-directed therapies at 12-months post-discharge. Additionally, examination of temporal trends in discharge prescription rates and persistence with these therapies in high-risk patients revealed a trivial increase over time. To our knowledge, this is one of the first studies addressing the concept of “risk-persistence paradox” among guideline-directed medical therapies in a prospective cohort of AMI patients post-discharge.

Annually over 715,000 Americans have an AMI. With dramatic improvements in acute care, majority of AMI patients survive index hospitalization.[19] Thus, long-term use of optimal secondary prevention therapies is a major focus of care. To date, efforts to improve use of evidence-based medications among AMI patients have focused primarily on administration of appropriate medications during hospitalization and at discharge. Prior studies describe lower rates of medication use among high-risk AMI patients during hospitalization and at discharge.[2, 3] Our study extends findings of prior reports and evaluates persistence in the year following AMI to all guideline-directed therapies prescribed at discharge among patients stratified by risk. While we observed high rates of prescription of guideline-directed therapies at discharge, even among high-risk patients, persistence with these therapies post-discharge was suboptimal and lowest among high-risk patients who would potentially benefit most. For example, after adjusting for a wide range of clinical characteristics that influence medication persistence, among 10 high-risk patients 2 were not taking aspirin, 2 were not taking beta-blocker, 3 were not taking statin and 3 were not taking ACEI/ARB by 1-month post-discharge. These rates continued to decline over the observation time period of 1-year. While persistence rates were also dismal in low and intermediate-risk groups, these groups showed better persistence with medications compared to high-risk population. Our findings highlight the need to emphasize on persistence with therapy post-discharge among all AMI patients and particularly for high-risk AMI patients.

Non-persistence is known to be a marker of adverse cardiovascular outcomes irrespective of baseline-risk and other co-morbidities.[13] Hence, efforts to bolster persistence with therapy are important potential opportunities to improve patient outcomes and lack of natural improvements in persistence is demonstrated by the marginal increase in persistence rates we observed over the entire study duration in all risk-categories. Our findings suggest that educational and persistence intervention programs should target all patients, but particularly those at higher risk. Interestingly, for all medications, the largest drop in persistence was observed over the first-month after discharge. This likely represents primary medication non-adherence; i.e. failure in filling prescriptions issued at discharge. An alternative explanation may include early onset medication side-effects leading to their discontinuation. However, the high rates of discontinuation observed are unlikely to be explained entirely by side-effects.

Primary non-adherence to cardiovascular medications has been previously described in literature as well. In particular, this holds true for medications for chronic conditions such as coronary artery disease, hypertension and diabetes.[20, 21] Furthermore patients not filling medications have a higher 1-year mortality.[20] These findings are comparable to our results as we also found similar rates of medication non-persistence at 1-month post-discharge and higher risk patients at greater risk of mortality were least likely to be taking appropriate medications at 1-month post-discharge. Hence, interventions addressing persistence should target patients early post-discharge. Addition of new multiple medications, as is commonly seen after hospitalizations,[22] may be accompanied by inadequate patient education,[23] follow-up and continuity of care. Accordingly, improved efforts to facilitate transition in care from hospital into the community are needed. Discharge medication counseling, involvement of pharmacists and ancillary staff with education and post-discharge follow-up may provide reliable solution to this issue.

Another factor that may contribute to low persistence rates could be lack of continued emphasis on importance of medications by physicians. Physician support for use of a drug is an important factor to patients in their long-term medication use.[24] Prior literature has suggested an underestimation of patient-risk by treating physicians.[25] Other studies have suggested under-use due to concerns of higher risk of side-effects in high-risk patients compounded by risks of poly-pharmacy.[26] While such concerns may be well founded, benefits of therapy are more likely to outweigh risks in such patients who have the greatest potential to benefit from therapy.[27, 28] Incorporation of validated risk-score models, such as the GRACE score, in clinical practice to identify high-risk patients can assist physicians in decision-making.

Limitations

Our findings should be interpreted in the light of several potential limitations. First, our finding of lower persistence with therapies among high-risk patients could be secondary to the development of side-effects or contra-indications to specific therapies (e.g., a new gastrointestinal bleed, hypotension). However, we limited our analysis to eligible patients at discharge and also adjusted for a number of possible contraindications to therapy such as kidney disease (ACEI/ARB) and lung disease (beta-blockers). Second, persistence with medication was determined through patient self-report and could introduce recall bias. However, patients were asked to read the labels of all their medications in an attempt to minimize recall bias in ascertaining medication persistence. Nonetheless, self-report is used routinely in clinical practice to assess medication persistence and has been validated in other studies against direct persistence measures such as blood drug levels and pill counts.[15, 16] Additionally, self-report would bias our findings towards null suggesting that real-world persistence is likely to be lower than we report. Third, we did not have follow-up data on roughly 10% of patients. While our use of imputation and likelihood-based estimation ameliorates any missing-data biases associated with observed factors, it is possible that non-ignorable biases may remain (e.g., medication persistence may be lower among patients missing medication use data).[29] However, as noted in the methods we did evaluate the potential impact of this bias by imputing a value of “not persistent” for patients with incomplete data, and the results did not change appreciably, so we believe the impact of non-ignorable missing data is small. Fourth, residual confounding in determining the association between risk and treatment persistence cannot be eliminated. Finally, compared to a retrospective description of AMI patients enrolled in a large, national cohort, patient characteristics were comparable suggesting that our results are generalizable to a wide range of patients seen in clinical characteristics.[30]

Conclusions

The results of our study show that high-risk AMI patients have lower persistence rates to guideline-directed therapy in the year following discharge. While trends in the use of therapy at discharge are improving, there have been marginal changes in use after discharge. Further research is necessary to understand reasons for low persistence with therapy after discharge. Additionally, targeted efforts toward improving the use of outpatient therapy are necessary.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key Messages

What is already known about this subject?

- Acute myocardial infarction patients at high risk for mortality are less likely to be discharged on optimal medical therapy compared to intermediate- and low-risk patients.

What does this study add?

- Among patients discharged on optimal therapy, overall persistence with medications is low at 1 year post-discharge.
- Persistence rates are lowest among high-risk patients, with only 45% of high-risk patients taking all prescribed therapies at 1 year post-discharge.
- Improvement in medication persistence over a 5-year observation period was minimal.

How might this impact clinical practice?

- Efforts to improved medication persistence after AMI hospitalization are needed.

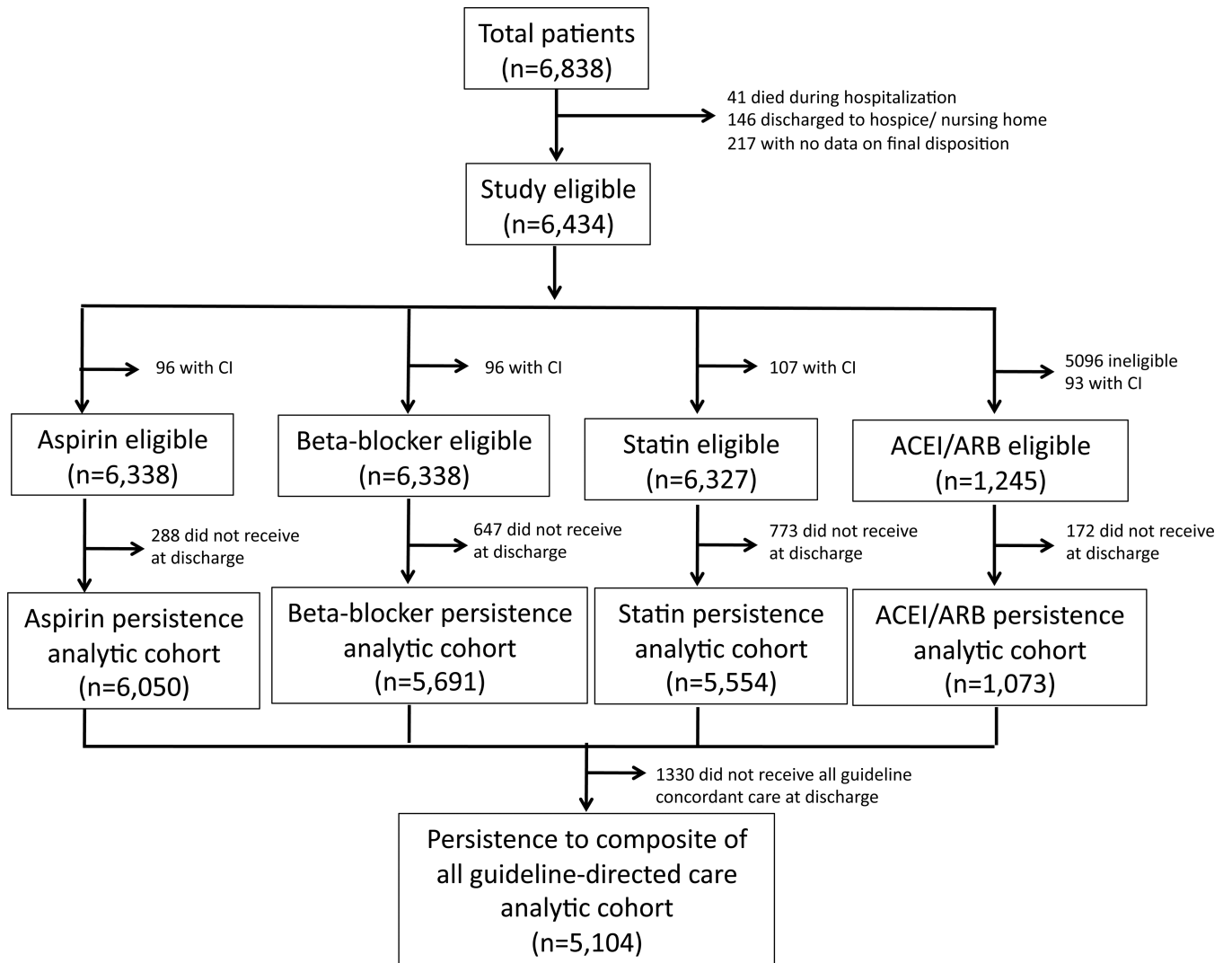
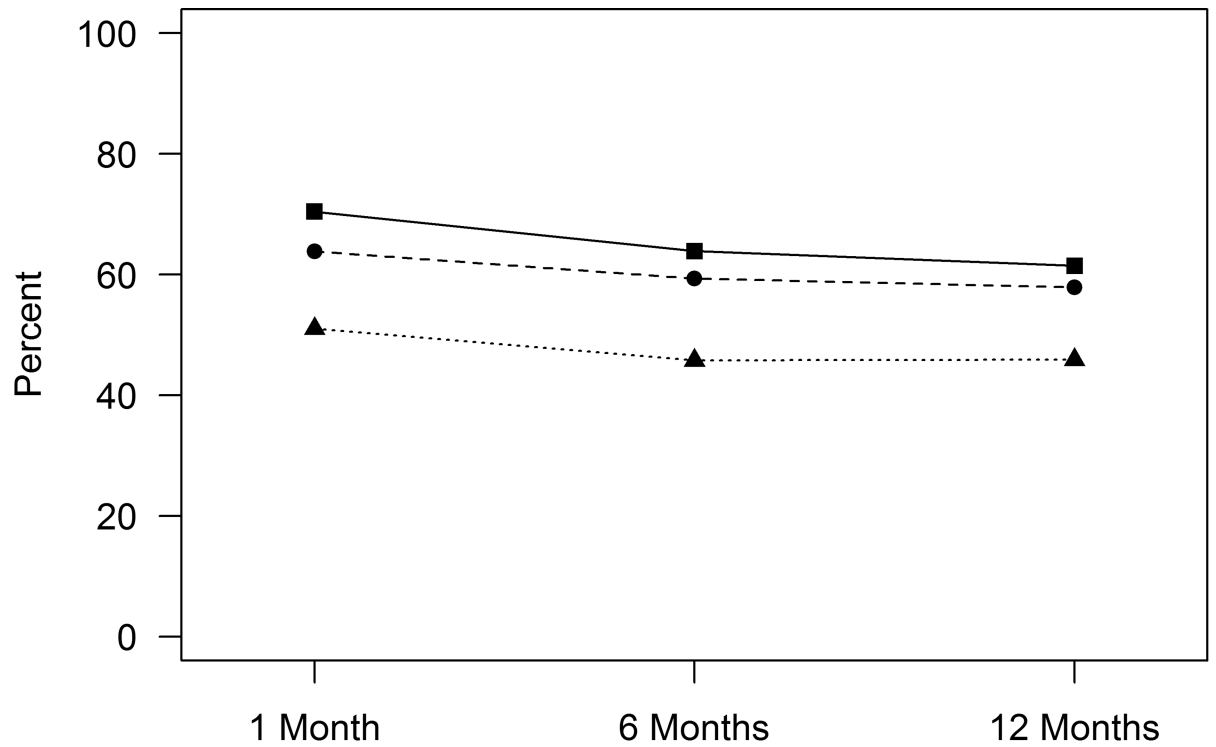


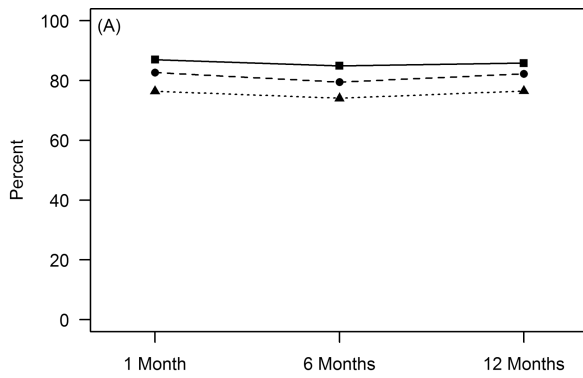
Figure 1.
 Cohort creation
 CI – contraindication, ACEI – angiotensin converting enzyme inhibitor, ARB – angiotensin receptor blocker



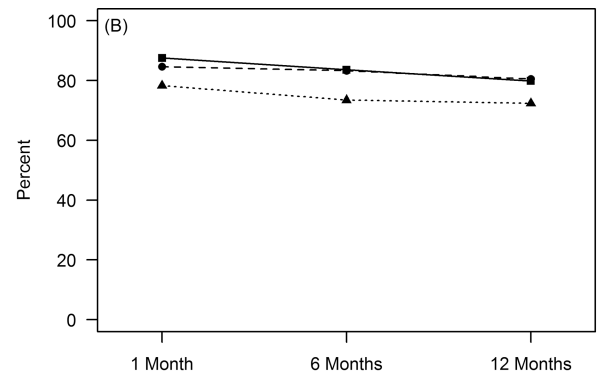
Risk

■ Low	70.4% (1417/2012)	63.9% (1179/1846)	61.5% (1102/1793)
● Intermediate	63.8% (914/1432)	59.3% (837/1411)	57.9% (773/1335)
▲ High	51.0% (550/1078)	45.8% (475/1038)	45.9% (428/933)

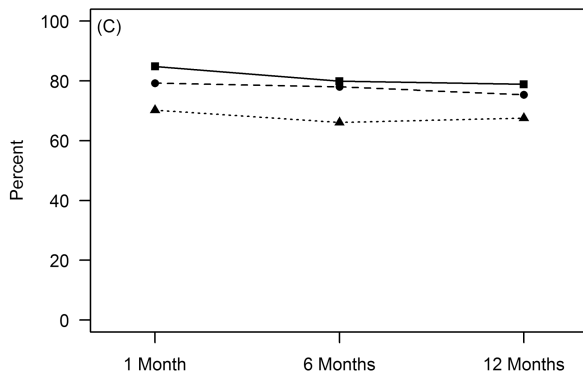
Figure 2. Unadjusted rates of post-discharge persistence with composite of all prescribed medical therapies among acute myocardial infarction, patients stratified by risk



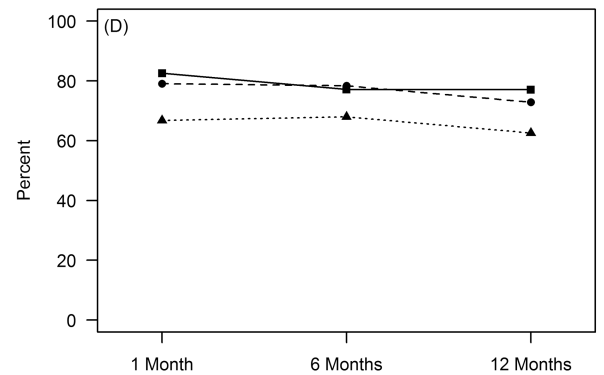
Risk	1 Month	6 Months	12 Months
■ Low	87.0% (1734/1993)	84.9% (1554/1830)	85.8% (1527/1779)
● Intermediate	82.7% (1164/1408)	79.5% (1106/1391)	82.3% (1082/1315)
▲ High	76.4% (800/1047)	74.0% (747/1009)	76.5% (692/905)



Risk	1 Month	6 Months	12 Months
■ Low	87.6% (1703/1945)	83.6% (1492/1785)	79.8% (1383/1732)
● Intermediate	84.6% (1168/1380)	83.3% (1138/1366)	80.5% (1039/1291)
▲ High	78.3% (803/1026)	73.4% (727/990)	72.4% (647/894)



Risk	1 Month	6 Months	12 Months
■ Low	84.9% (1681/1981)	79.9% (1449/1814)	78.9% (1391/1764)
● Intermediate	79.2% (1114/1406)	78.0% (1081/1386)	75.4% (989/1312)
▲ High	70.2% (739/1053)	66.1% (672/1017)	67.5% (618/915)



Risk	1 Month	6 Months	12 Months
■ Low	82.6% (237/287)	77.2% (206/267)	77.0% (198/257)
● Intermediate	79.1% (208/263)	78.4% (203/259)	72.9% (172/236)
▲ High	66.8% (199/298)	68.0% (193/284)	62.5% (157/251)

Figure 3. Unadjusted rates of post-discharge persistence with each medication among acute myocardial infarction patients, stratified by risk: aspirin (A), beta blockers (B); statins (C); ACEI/ARBs (D)
ACEI – angiotensin converting enzyme inhibitor, ARB – angiotensin receptor blocker

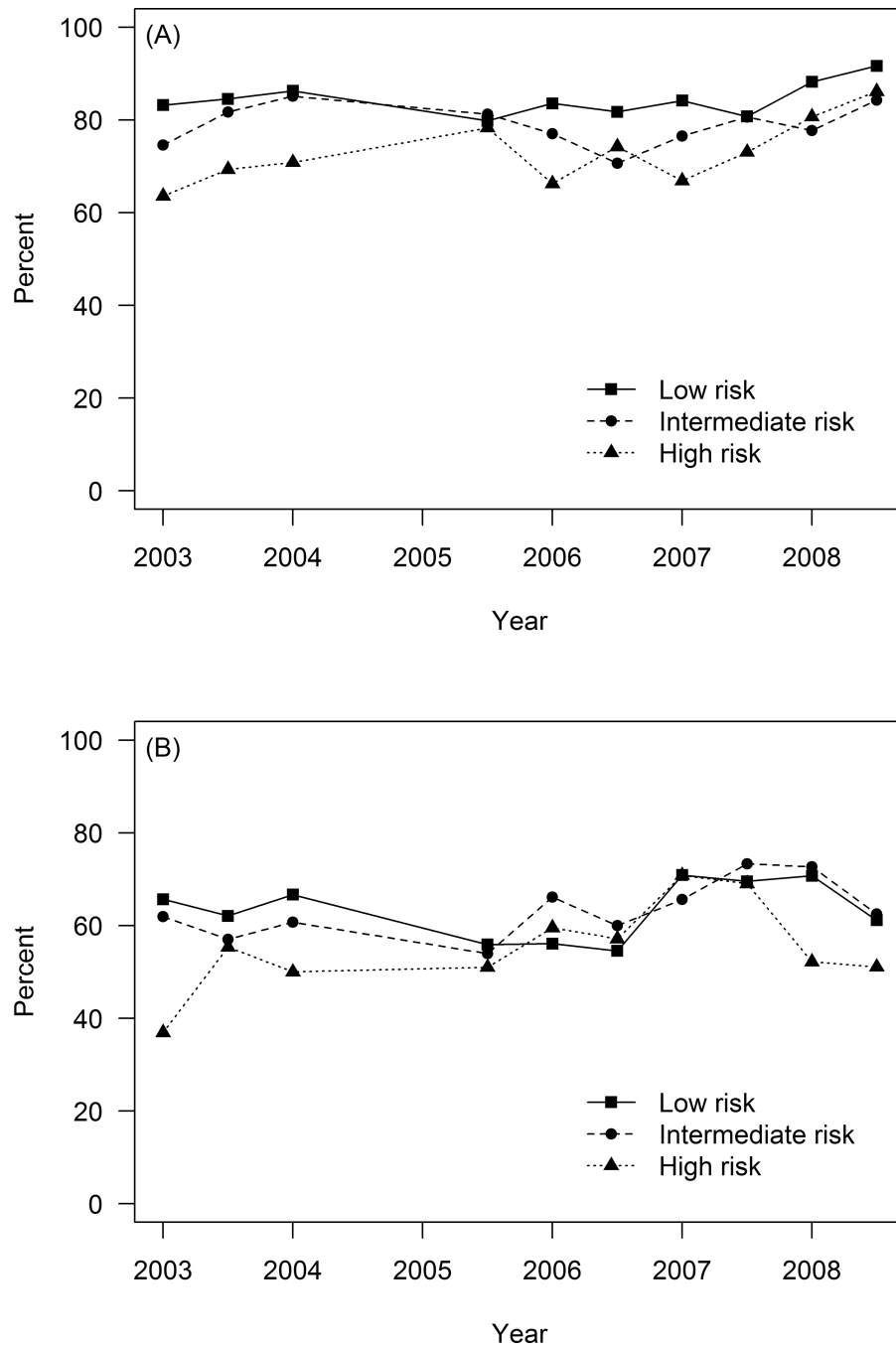


Figure 4. Temporal trends in prescription of indicated medications (A) and persistence at 1 year with prescribed medications (B)
 ACEI – angiotensin converting enzyme inhibitor, ARB – angiotensin receptor blocker

Table 1

Baseline characteristics of study cohort stratified by risk

Characteristic	Low-risk (n = 2,824)	Moderate-risk (n = 2,014)	High-risk (n = 1,596)	p-value
Demographics	n(%)	n(%)	n(%)	
Age, years (mean ± SD)	50.1 ± 8.2	61.7 ± 8.4	71.8 ± 9.8	<0.001
Sex (Female)	742 (26)	684 (34)	660 (41)	<0.001
Race				<0.001
White/Caucasian	2005 (71)	1399 (69)	1073 (67)	
Black/African-American	602 (21)	495 (25)	444 (28)	
Asian	20 (1)	13 (1)	7 (0)	
American Indian/Alaska Native	46 (2)	23 (1)	13 (1)	
Native Hawaiian/Pacific Islander	5 (0)	2 (0)	0 (0)	
Multiracial	57 (2)	46 (2)	27 (2)	
Other	77 (3)	29 (1)	26 (2)	
Avoiding health-care due to cost	800 (29)	430 (22)	227 (15)	<0.001
Insurance present	1964 (71)	1469 (75)	1213 (77)	<0.001
Less than high-school education	1311 (47)	1005 (51)	89 (57)	<0.001
BMI (kg/m ² , mean ± SD)	30 ± 7	29 ± 6	28 ± 6	<0.001
Clinical covariates				
Current smoker	1495 (53)	650 (33)	280 (18)	<0.001
Hypercholesterolemia	1195 (42)	1051 (52)	902 (57)	<0.001
Hypertension	1511 (54)	1409 (70)	1247 (78)	<0.001
Peripheral Arterial Disease	56 (2)	108 (5)	180 (11)	<0.001
Diabetes Mellitus	592 (21)	629 (31)	651 (41)	<0.001
Prior Myocardial Infarction	275 (10)	437 (22)	632 (40)	<0.001
Prior Angina	283 (10)	328 (16)	395 (25)	<0.001
Prior CABG	106 (4)	242 (12)	414 (26)	<0.001
Prior PCI	352 (13)	439 (22)	439 (28)	<0.001
Prior CVA/TIA	73 (27)	159 (8)	208 (13)	<0.001
Chronic kidney disease	63 (2)	147 (7)	296 (19)	<0.001
Chronic lung disease	129 (5)	170 (8)	260 (16)	<0.001
Congestive heart failure	17 (1)	107 (5)	460 (29)	<0.001
Prior ICD/Pacemaker	19 (1)	25 (1)	105 (7)	<0.001
Self reported depression	575 (21)	350 (18)	267 (18)	0.005
In-hospital characteristics				
Presenting with STEMI	1750 (62)	788 (39)	315 (20)	<0.001
Admission SBP (mmHg, mean ± SD)	145 ± 29	141 ± 30	138 ± 32	<0.001
Final Heart Rate (beats/minute, mean ± SD)	72 ± 12	73 ± 13	74 ± 12	0.004
Diagnostic catheterization	2747 (97)	1867 (93)	1247 (78)	<0.001
Revascularization (PCI/ CABG)	2502 (88)	1482 (74)	771 (48)	<0.001
Laboratory results				
Hemoglobin A1c (% , mean ± SD)	6.5 ± 1.9	6.7 ± 1.8	6.6 ± 1.5	0.022

Characteristic	Low-risk (n = 2,824)	Moderate-risk (n = 2,014)	High-risk (n = 1,596)	p-value
LDL (mmol/L, mean \pm SD)	3.0 \pm 1.1	2.6 \pm 1.0	2.4 \pm 1.0	<0.001
BNP (ng/L, mean \pm SD)	363 \pm 778	792 \pm 1383	1168 \pm 1621	<0.001

SD – standard deviation, BMI – body mass index, CABG – coronary artery bypass grafting, PCI – percutaneous coronary intervention, CVA – cerebrovascular accident, TIA – transient ischemic attack, ICD – implantable cardioverter defibrillation, SBP – systolic blood pressure, LDL – low density lipoprotein, BNP – brain natriuretic peptide

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Table 2

Medication use at discharge among eligible patients, stratified by risk status

Discharge medications	Low risk (n=2,824) n (%)	Intermediate risk (n=2,014) n (%)	High risk (n=1,596) n (%)	p value
Aspirin	2,708 (96.7)	1,883 (94.9)	1,459 (93.9)	<0.001
Beta Blocker	2,589 (94.7)	1,797 (92.4)	1,368 (89.9)	<0.001
Statin	2,516 (90.4)	1,735 (87.6)	1,303 (83.3)	<0.001
ACEI/ARB in patients with LVEF 40%	381 (90.1)	341 (88.6)	351 (80.3)	<0.001
All eligible guideline-directed medications	2,385 (84.5)	1,583 (78.6)	1,136 (71.2)	<0.001

ACEI – angiotensin converting enzyme inhibitors, ARB – angiotensin receptor blocker, LVEF – left ventricular ejection fraction

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Table 3

Adjusted association between risk and therapy persistence after discharge

Medication	Low risk	Intermediate risk RR (95% CI)	High risk RR (95% CI)
All prescribed guideline-directed medications	1.00 (reference)	0.98 (0.94, 1.01)	0.87 (0.82, 0.92)
Aspirin	1.00 (reference)	0.96 (0.95, 0.99)	0.92 (0.89, 0.95)
Beta-blockers	1.00 (reference)	1.00 (0.98, 1.03)	0.93 (0.90, 0.96)
Statins	1.00 (reference)	0.98 (0.96, 1.00)	0.92 (0.89, 0.96)
ACEI/ARBs	1.00 (reference)	1.00 (0.94, 1.08)	0.88 (0.79, 0.97)

ACEI – angiotensin converting enzyme inhibitor, ARB – angiotensin receptor blocker, RR- relative risk, CI – confidence interval.

All reported relative risks with confidence intervals crossing 1 signify statistically non-significant difference compared to reference group. Risks ratios >1 signify higher rate of therapy use post-discharge and risk ratios <1 signify lower rate of therapy use post-discharge compared to reference group of low-risk patients. These results have been adjusted for covariates described above in the methods section.

Table 4

Temporal trends for improvement among each category per year from 2003–2008

Risk Stratum	Composite of all guideline-directed medications at discharge RR (95% CI)	Persistence with composite of all guideline-directed medications after discharge RR (95% CI)
Low risk	1.01 (1.00, 1.02)	1.02 (1.01, 1.04)
Intermediate risk	1.01 (0.99, 1.02)	1.03 (1.01, 1.04)
High risk	1.03 (1.01, 1.05)	1.05 (1.03, 1.08)

RR – relative risk, CI – confidence interval

All risk ratios >1 signify an increase in medication use over the duration of this study and risk ratios crossing 1 signify no statistically significant difference in medication use over the duration of this study.

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