



# Impact of Optimal Medical Therapy at Discharge on One-year Direct Medical Costs in Patients with Acute Coronary Syndromes: A Retrospective, Observational Database Analysis in China

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## ABSTRACT

**Purpose:** This study was conducted to examine the use of optimal medical therapy (OMT), consisting of an antiplatelet, a  $\beta$ -blocker, an angiotensin-converting enzyme inhibitor/angiotensin receptor blocker (ACEI/ARB), and a statin combined, after hospital discharge and its relationship with direct medical costs in patients with acute coronary syndromes (ACS) in Tianjin, China.

**Methods:** Data were obtained from the Tianjin Urban Employee Basic Medical Insurance database (2011–2015). Data from adult patients with  $\geq 1$  hospitalization for ACS between January 2012 and December 2014 were included. Medications including antiplatelets,  $\beta$ -blockers, ACEIs/ARBs, and statins at discharge were recorded, with OMT defined as the use of all 4 indicated medications. Propensity-score matching was conducted to form matched OMT and non-OMT cohorts based on baseline differences. All-cause and ACS-related health care resource utilization and direct medical costs during a 12-month follow-up period were assessed and compared between cohorts. Generalized linear modeling was conducted to assess the association between OMT at discharge and direct medical costs.

**Findings:** A total of 22,041 patients were identified (mean age, 64.7 [10.7] years; 45.6% female), of whom 15.1% (3336) received OMT at discharge. The OMT cohort had fewer patients hospitalized for any cause during follow-up compared with the matched non-OMT cohort (38.1% vs 43.2%;  $P < 0.001$ ), which was further associated with fewer hospitalizations (1.55 vs 1.64;  $P = 0.019$ ) and shorter annualized length of stay (15.9 vs 17.2 d;  $P = 0.041$ ). Despite

higher costs of outpatient services (9958 vs 10,060 Chinese yuan [CNY] [ $P = 0.006$ ]; adjusted difference, +456 CNY [ $P = 0.004$ ]) (year-2014 1 USD = 6.20 CNY), the OMT cohort had significantly lower all-cause total costs (20,771 vs 22,877 CNY [ $P = 0.174$ ]; adjusted difference, –2089 CNY [ $P = 0.006$ ]), driven by lower costs of inpatient services (10,813 vs 12,817 CNY [ $P < 0.001$ ]; adjusted difference, –2184 CNY [ $P = 0.001$ ]). The difference in ACS-related total costs between the 2 cohorts was not statistically significant (8535 vs 9304 CNY [ $P = 0.128$ ]; adjusted difference, –558 CNY [ $P = 0.214$ ]).

**Implications:** Receiving OMT at discharge was associated with fewer hospitalizations and lower all-cause direct medical costs in these patients with ACS in China. Strategies are needed to improve OMT prescribing rates at discharge, which would lead to better clinical prognosis and total cost-savings among patients with ACS in China. (*Clin Ther.* 2019;41:456–465) © 2019 Elsevier Inc. All rights reserved.

**Key words:** acute coronary syndromes, China, costs, health care resource utilization, medication.

## INTRODUCTION

Ischemic heart disease is a major cause of morbidity and mortality in both developed and developing countries, including China. The potentially life-

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threatening disorders within ischemic heart disease are a spectrum of clinical conditions known as *acute coronary syndromes* (ACS), which include unstable angina, ST-elevation myocardial infarction, and non-ST-elevation myocardial infarction.<sup>1,2</sup> Clinical guidelines issued by the American College of Cardiology/American Heart Association, the European Society of Cardiology, and the Chinese Society of Cardiology all recommend antiplatelets, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEI/ARBs),  $\beta$ -blockers, and statins for the long-term management of patients after an acute coronary event, referred as *secondary prevention* treatment.<sup>1,3–7</sup> When combined together, these 4 medications are demonstrated to be more effective in reducing the risks for cardiovascular events and mortality and thus are called *optimal medical therapy* (OMT).<sup>8–11</sup> Moreover, studies have shown that receiving OMT at discharge is crucial and may have long-term clinical and economic impact among patients with ACS.<sup>12,13</sup> Unfortunately, there is evidence showing that OMT is underused among patients with ACS across countries including the United States, Canada,<sup>12</sup> Korea,<sup>14</sup> India,<sup>15</sup> and China,<sup>13</sup> which may have negative clinical and economic impact.

Among studies of the prevalence, predictors, and clinical impact of OMT at discharge among patients with ACS, very few have explored the relationship between OMT at discharge and the long-term economic impact in clinical practice. As far as we know, only 1 study has compared the total costs between OMT and non-OMT cohorts during a 12-month follow-up period, based on prospective observation in 14 European countries, with similar results between the 2 cohorts, suggesting that the higher medication costs of preventive OMT could be offset by reduced hospitalization costs.<sup>16</sup> Since the evidence of the economic impact of OMT at discharge in Asian countries, including China, is limited, the present study was designed to explore the association between OMT at discharge and 12-month direct medical costs in patients with ACS in the clinical practice setting in China.

## MATERIALS AND METHODS

### Data Source

Claims data from the Urban Employee Basic Medical Insurance (UEBMI) database (2011–2015)

of the municipality of Tianjin, China, were used, through a formal request to Tianjin Municipal Human Resources and Social Security Bureau for research purposes. The Tianjin UEBMI system covers all employed workers and retirees from both public and private sectors in Tianjin, representing about 5.2 million enrollees in 2015.<sup>17</sup> The analytical sample in this study was a random sample of 30% of all enrollees. Data provided included demographic characteristics, pharmacy claims (quantity, strength, date of prescription), medical claims of inpatient and outpatient services, and related medical and medication costs. The Tolerability and Ethics Committee at the School of Pharmaceutical Science and Technology, Tianjin University, waived the requirement of ethics approval for the current study.

### Study Population

Adult patients who were discharged after the first hospitalization for ACS (*International Statistical Classification of Diseases and Related Health Problems, 10th Edition* [ICD-10] codes I20.0, I21, and I22, supplemented by Chinese descriptions) from January 1, 2012, to December 31, 2014, were identified, with the first qualifying hospitalization defined as the *index hospitalization*. The 12-month period before the admission date of the index hospitalization was defined as the *baseline period*, and the 12-month period after the discharge date of the index hospitalization was defined as the *follow-up period*. Patients who were not continuously enrolled in UEBMI for both the baseline and follow-up periods, and patients who had a history of malignancy and metastatic cancer during the baseline period, were further excluded. Pharmacy claims for antiplatelets, ACEIs/ARBs,  $\beta$ -blockers, and statins were identified at discharge of the index hospitalization. Patients were classified as OMT or non-OMT according to whether they received prescriptions of all 4 indicated medications concurrently at discharge.

### Outcomes Measures

The demographic characteristics, including age, sex, and employment status, of the included patients are described. Baseline clinical characteristics including Charlson comorbidity index score,<sup>21</sup> comorbidities and complications (hypertension, hyperlipidemia, diabetes mellitus, etc.), baseline use of medication

(antiplatelets, ACEIs/ARBs,  $\beta$ -blockers, statins), and medical resources (use of inpatient and outpatient services, total direct medical costs) were also recorded and are reported. The procedures that patients received (percutaneous coronary intervention [PCI]; coronary artery bypass grafting) and length of stay during the index hospitalization are also described.

Both all-cause and ACS-related health care resource utilization during the 12-month follow-up period in all patients and in the OMT and non-OMT cohorts was assessed. Medical claims under the primary diagnosis of ACS (ICD-10 codes I20.0, I21, and I22, supplemented by Chinese description) were identified as *ACS-related* claims. The percentages of patients who utilized inpatient services were calculated as the number of inpatients divided by the number of total patients, and the numbers of hospitalizations and annualized length of stay (ALOS) among the inpatients were further calculated. Similarly, the percentages of patients who utilized outpatient services were calculated as the number of outpatients divided by the number of total patients, and the numbers of outpatient visits among the outpatients were further calculated.

All-cause and ACS-related direct medical costs were further calculated from the health care system perspective, including the payments by insurance and patients. The *total costs* were composed of costs of inpatient and outpatient services, which included costs of medications, examinations, nonmedication treatments, medical consumables, and other medical services utilized, through inpatient or outpatient claims.

### Statistical Analysis

Descriptive analyses were performed to estimate the baseline characteristics and outcomes measures in all patients and in the OMT and non-OMT cohorts. For subgroup comparisons, the *t* test and nonparametric Wilcoxon rank sum test were utilized for continuous variables, while the  $\chi^2$  test was used for categorical variables.

A one-to-one matching algorithm without replacement was employed to form matched pairs of OMT and non-OMT patients, which would balance baseline demographic and clinical characteristics. Generalized linear modeling (GLM) with a log-link function and a  $\gamma$  distribution were performed to

assess the relationship between OMT and direct medical costs, and the adjusted cost differences between OMT and non-OMT cohorts in GLM models were obtained using the method of recycled predictions. Potential confounding covariates included in the propensity score calculation and GLM models were demographic characteristics (age, sex, employment status), Charlson comorbidity index score, comorbidities and complications (hypertension, hyperlipidemia, diabetes mellitus, etc.), baseline medication utilization (antiplatelets, ACEIs/ARBs,  $\beta$ -blockers, statins), baseline health care resource utilization and total direct medical costs, procedures received (PCI, coronary artery bypass grafting) and length of stay during the index hospitalization.

A 2-sided *P* value of <0.05 was considered statistically significant. All statistical analyses were conducted using Stata version 12.1 (StataCorp, College Station, Texas).

## RESULTS

### Baseline Characteristics and Medication Use at Discharge

A total of 25,397 adult patients discharged from hospitalization for ACS between 2012 and 2014 were identified, among whom 22,041 eligible patients were included as the total study cohort (see [Supplemental Figure 1](https://doi.org/10.1016/j.clinthera.2019.01.005) in the online version at <https://doi.org/10.1016/j.clinthera.2019.01.005>). The mean (SD) age of the total cohort was 64.7 (10.7) years, with 45.6% women and 80.6% retired. Hypertension was the most common comorbidity (75.0%), followed by hyperlipidemia (46.6%) and diabetes mellitus (37.6%). Of the total cohort, 31.1% of patients had all-cause hospitalizations during baseline period, and 22.5% of patients received PCI during the index hospitalization ([Table I](#)).

A total of 3336 patients (15.1%) received all 4 indicated drugs at discharge of the index hospitalization, while the numbers of patients receiving only 1 drug, a 2-drug combination, or a 3-drug combination at discharge were 1939 (8.8%), 3986 (18.1%), and 5100 (23.1%), respectively. As many as 7680 patients (34.8%) were discharged with no prescription for the indicated drugs. The rates of prescription for statins, antiplatelets, ACEI/ARBs,  $\beta$ -blockers at discharge were 53.3%, 51.9%, 35.0%, 34.6%, respectively (see [Supplemental Figure 2](#) in the

Table 1. Baseline characteristics of patients with ACS. Data are given as % of patients unless otherwise noted.

Characteristic	All patients (N = 22,041)	OMT (n = 3336)	Non-OMT Before matching (n = 18,705)		Non-OMT After matching (n = 3336)	
			Value	P	Value	P
<b>Sociodemographic</b>						
Age						
Mean (SD)	64.7 (10.7)	63.8 (10.2)	64.8 (10.8)	<0.001	63.9 (10.4)	0.812
Group				<0.001		0.242
<55 y	16.6	16.9	16.6		17.3	
55–64 y	35.7	37.5	35.4		38.3	
65–74 y	26.8	28.7	26.4		26.2	
≥75 y	20.9	16.9	21.7		18.2	
Female	45.6	37.6	47.1	<0.001	38.7	0.378
Retired	80.6	77.3	81.2	<0.001	77.4	0.509
<b>Clinical</b>						
CCI, mean (SD)	1.7 (1.6)	1.7 (1.6)	1.7 (1.6)	0.812	1.8 (1.6)	0.512
Risk factors						
Current						
Hypertension	75.0	78.4	74.4	<0.001	78.2	0.812
Hyperlipidemia	46.6	48.7	46.2	0.006	49.1	0.788
Diabetes mellitus	37.6	39.9	37.1	0.002	40.5	0.653
History						
Stroke	26.2	25.6	26.4	0.363	24.4	0.270
Angina	24.9	24.3	25.0	0.360	23.5	0.473
MI	15.2	15.3	15.2	0.943	14.8	0.607
PCI	6.6	8.5	6.2	<0.001	8.1	0.564
CABG	0.6	0.8	0.5	0.092	0.8	0.785
Medication history						
Antiplatelet	55.3	59.7	54.5	<0.001	59.8	0.920
β-blockers	40.8	48.8	39.4	<0.001	49.3	0.732
ACEIs/ARBs	53.4	61.7	51.9	<0.001	61.3	0.725
Statins	43.4	45.5	43.1	0.009	46.1	0.606
<b>Baseline resource utilization and costs</b>						
Any hospitalizations	31.1	27.0	31.8	<0.001	26.1	0.421
No. of outpatient visits, mean (SD)	30.5 (31.7)	32.0 (31.9)	30.2 (31.7)	<0.001	39.6 (35.0)	0.168
Total costs, mean (SD)	12,857 (19,236)	12,633 (18,900)	12,897 (19,296)	0.031	12,321 (18,189)	0.994
<b>Index hospitalization</b>						
Any PCI	22.5	45.9	18.3	<0.001	46.2	0.825
Any CABG	1.0	0.4	1.1	<0.001	0.3	0.531
ALOS, mean (SD), d	9.5 (5.6)	9.5 (5.6)	9.6 (5.7)	<0.001	9.6 (5.7)	0.489

ACEI/ARB = angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; ACS = acute coronary syndromes; CABG = coronary artery bypass grafting; CCI = Charlson comorbidity index; COPD = congestive obstructive pulmonary disease; LOS = length of stay; MI = myocardial infarction; OMT = optimal medical therapy (an antiplatelet, a b-blocker, an ACEI/ARB, and a statin combined); PCI = percutaneous coronary intervention.

CCI is a weighted index calculated by the presence of 17 Charlson comorbidities including myocardial infarction, congestive heart failure, dementia, chronic pulmonary disease, etc., with different weights of 1, 2, 3, or 6. The total score equals the index for each patient, and the higher the index is, the more and severe comorbidities the patient has.

online version at <https://doi.org/10.1016/j.clinthera.2019.01.005>).

Table I shows the baseline characteristics of the patients in the OMT and non-OMT cohorts. Compared with non-OMT cohort, the OMT cohort at discharge was relatively younger (OMT vs non-OMT before matching, 63.8 vs 64.8;  $P < 0.001$ ); comprised fewer women (37.6% vs 47.1%;  $P < 0.001$ ); had greater prevalences of hypertension (78.4% vs 74.4%;  $P < 0.001$ ), hyperlipidemia (48.7% vs 46.2%;  $P = 0.006$ ), and diabetes (39.9% vs 37.1%;  $P = 0.002$ ); and had a higher rate of PCI during the index hospitalization (45.9% vs. 18.3%;  $P < 0.001$ ). Propensity score matching selected 3336 patients in the non-OMT cohort who had propensity score values most similar to their counterparts in the OMT cohort. After matching, the OMT and non-OMT cohorts were comparable regarding all baseline characteristics (Table I).

### Health Care Resource Utilization

Of the total patients, 43.7% had  $\geq 1$  all-cause hospitalization during the 12-month follow-up period, with a mean (SD) number of 1.7 (1.2) hospitalizations and an annualized length of stay of 19.8 (27.1) days among hospitalized patients. A total of 96.9% of patients utilized outpatient services during the follow-up period, with a mean number of 37.5 (32.3) visits. When considering ACS-related health care resource utilization, 18.6% of patients had  $\geq 1$  ACS-related hospitalization, with 1.3 (0.7) hospitalizations on average, and 88.7% of patients had ACS-related outpatient visits with 12.7 (9.9) visits during the 12-month follow-period (Table II).

Compared with the non-OMT cohort after matching, the OMT cohort had fewer patients hospitalized for any cause during the follow-up period (38.1% vs 43.2%;  $P < 0.001$ ), with fewer hospitalizations (1.55 vs 1.64;  $P = 0.019$ ) and a

Table 2. Health care resource utilization during 12-month follow-up period in patients with ACS.

Resource	All patients	OMT	Non-OMT Before matching (n = 18,705)		Non-OMT After matching (n = 3336)	
	N = 22,041	n = 3336	Value	P	Value	P
<b>All-cause</b>						
<b>Inpatient service</b>						
Any hospitalizations, %	43.7	38.1	44.7	<0.001	43.2	<0.001
No. of admissions, mean (SD)	1.7 (1.2)	1.55 (1.0)	1.7 (1.2)	<0.001	1.64 (1.0)	0.019
ALOS, mean (SD), d	19.8 (27.1)	15.9 (16.1)	20.4 (28.3)	<0.001	17.2 (19.2)	0.041
<b>Outpatient service</b>						
Any outpatient visits, %	96.9	99.2	96.5	<0.001	98.3	0.001
No. of visits, mean (SD)	37.5 (32.3)	40.3 (32.5)	37.0 (32.3)	<0.001	40.3 (34.9)	0.976
<b>ACS-related</b>						
<b>Inpatient service</b>						
Any hospitalizations, %	18.6	16.6	18.9	0.001	20.2	<0.001
No. of admissions, mean (SD)	1.3 (0.7)	1.3 (0.6)	1.3 (0.7)	0.054	1.2 (0.6)	0.675
ALOS, mean (SD), d	13.6 (14.9)	11.8 (9.3)	13.9 (15.6)	<0.001	11.4 (9.4)	0.208
<b>Outpatient service</b>						
Any outpatient visits, %	88.7	95.6	87.5	<0.001	92.6	<0.001
No. of visits, mean (SD)	12.7 (9.9)	14.9 (9.9)	12.4 (9.8)	<0.001	14.7 (10.7)	0.464

ACS = acute coronary syndromes; ALOS = annualized length of stay; CABG = coronary artery bypass grafting; LOS = length of stay; OMT = optimal medical therapy (an antiplatelet, a b-blocker, an ACEI/ARB, and a statin combined); PCI = percutaneous coronary intervention.

shorter annualized length of stay (15.9 vs 17.2 d;  $P = 0.041$ ) in hospitalized patients. Conversely, patients in the OMT cohort were more likely to have an all-cause outpatient visit (99.2% vs 98.3%;  $P = 0.001$ ), with a similar number of visits (40.3 vs 40.3;  $P = 0.976$ ), compared with the matched non-OMT cohort. For ACS-related resource utilization, the OMT cohort had fewer patients who utilized inpatient services (16.6% vs 20.2%;  $P < 0.001$ ) and more patients who utilized outpatient services (95.6% vs 92.6%;  $P < 0.001$ ) in comparison with the non-OMT cohort, with a similar number of hospitalizations/visits and annualized length of stay in medical resource users (Table II).

### Direct Medical Costs

The total all-cause direct medical costs during the 12-month period were 21,346 CNY in the total cohort (year-2014 1 USD = 6.20 CNY), of which 12,370 CNY (57.9%) were costs of inpatient services and 8976 CNY (42.1%) were costs of outpatient services (Figure, part A). Correspondingly, the ACS-related total costs were 8531 CNY, of which 5074 CNY (59.5%) was attributable to inpatient services and 3457 CNY (40.5%) was attributable to outpatient services (Figure, part B).

OMT was associated with significantly lower all-cause total costs (20,771 vs 22,877 CNY [ $P = 0.174$ ]; adjusted difference, -2089 CNY

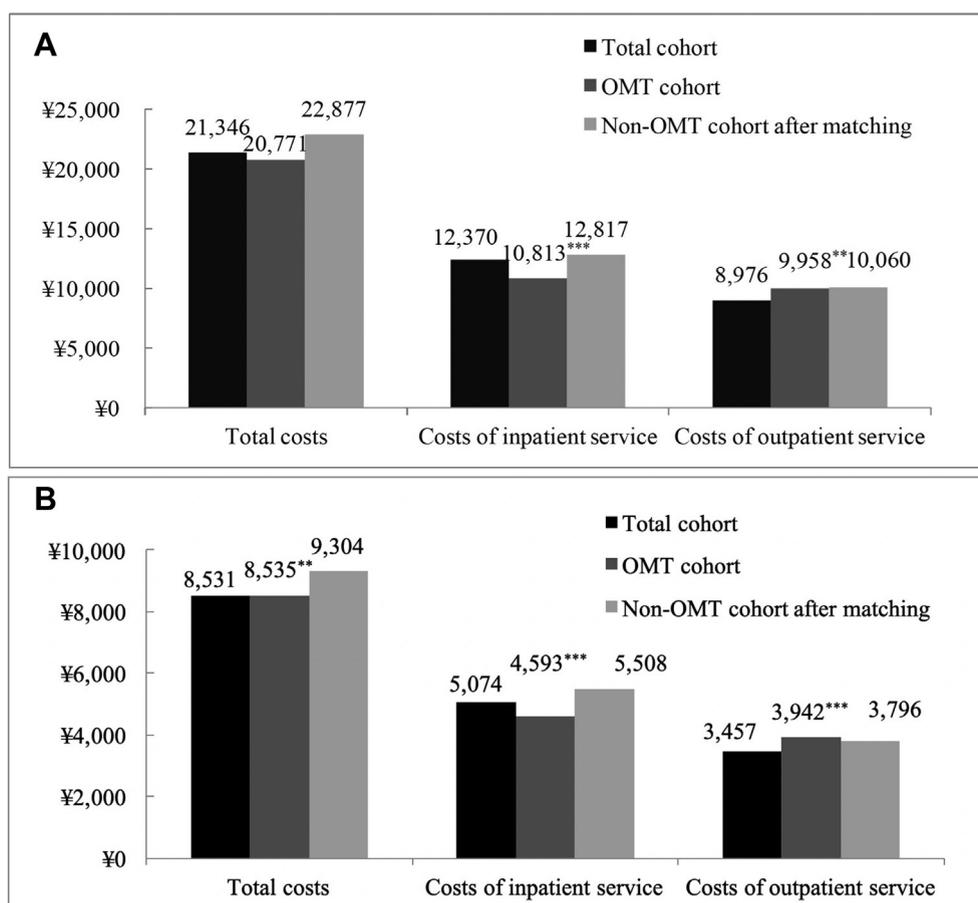


Figure. All-cause (A) and acute coronary syndrome (ACS)-related costs during the 12-month follow-up period after discharge from hospitalization in patients with ACS. \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ . OMT = optimal medical therapy (an antiplatelet, a  $\beta$ -blocker, an angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, and a statin combined).

[ $P = 0.006$ ]), driven by lower costs of inpatient services (10,813 vs 12,817 CNY [ $P < 0.001$ ]; adjusted difference,  $-2184$  CNY [ $P = 0.001$ ]), as shown by the unadjusted and adjusted analyses (Figure and Table III, respectively). For the ACS-related estimates, both total costs (8535 vs 9304 CNY;  $P = 0.128$ ) and costs of inpatient services (4593 vs 5508 CNY;  $P < 0.001$ ) were lower in the OMT cohort relative to the matched non-OMT cohort, as shown by the unadjusted analyses, while these differences were not statistically significant in the adjusted results (total costs: adjusted difference,  $-558$  CNY [ $P = 0.214$ ]; costs of inpatient services: adjusted difference,  $-950$  CNY [ $P = 0.025$ ]). The costs of outpatient services were consistently higher in the OMT cohort in the adjusted analyses, with regard to both all-cause costs (9958 vs 10,060 CNY [ $P = 0.006$ ]; adjusted difference,  $+¥456$  [ $P = 0.004$ ]) and ACS-related costs (3942 vs 3796 CNY [ $P < 0.001$ ]; adjusted difference,  $+363$  CNY [ $P < 0.001$ ]).

### DISCUSSION

The use of medications including statins, antiplatelets, ACEI/ARBs,  $\beta$ -blockers have been demonstrated to be associated with significantly improved clinical outcomes among patients discharged from hospitalization for ACS through numerous

studies.<sup>8–13</sup> The present study evaluated the use of 4-drug combined OMT after hospital discharge in patients with ACS, and explored its impact on health care resource utilization and direct medical costs from the payers' perspective in China. Despite universal guideline recommendations,<sup>1,3–7</sup> we found that more than one third of patients with ACS did not receive a prescription for any of the 4 indicated medications at discharge. The prescription rates were 53.3% with statins and 34.6% with  $\beta$ -blockers, while only 15.1% of total patients received OMT at discharge as recommended.<sup>1,6–7</sup> Compared with patients who did not receive OMT at discharge, the OMT cohort had significantly fewer hospitalizations, with a shorter annualized length of stay. Receiving OMT at discharge was associated with lower all-cause total costs, and similarly ACS-related total costs, in comparison with the non-OMT cohort.

Although the suboptimal use of secondary prevention treatment has been reported by numerous studies worldwide, our estimates were much lower than the reported ranges.<sup>12–15,18</sup> We found that only 15.1% of the study cohort were prescribed OMT at the time of discharge, which was much lower than the percentage reported by Bi et al<sup>13</sup> in 2009 (48%) based on a multicenter prospective study in China, and also lower than the percentages

Table III. Impact of OMT on direct medical costs at discharge in patients with ACS (generalized linear model;  $n = 6672$ ).

Variable	Adjusted Coef. (95% CI)	Adjusted diff., CNY	<i>P</i>
All causes			
Inpatient services	-0.094 (-0.160 to 0.027)	-2089	0.006
Outpatient services	-0.185 (-0.293 to -0.076)	-2184	0.001
Total*	+0.036 (0.012–0.061)	+456	0.004
ACS related			
Inpatient services	-0.062 (-0.160 to 0.036)	-558	0.214
Outpatient services	-0.188 (-0.352 to 0.024)	-950	0.025
Total	+0.091 (0.052–0.129)	+363	<0.001

ACS = acute coronary syndromes; CNY = Chinese yuan (year-2014 1 USD = 6.20 CNY); OMT = optimal medical therapy (an antiplatelet, a  $\beta$ -blocker, an ACEI/ARB, and a statin combined).

The dependent variables in the generalized linear model were all-cause and ACS-related charges, respectively. Covariates including optimal medical therapy at discharge, age group, sex, Charlson comorbidity index score, medical history, number of any all-cause inpatient/outpatient visits, all-cause costs during baseline and characteristics during the index event.

\*Mean (SD) total costs at baseline (CNY): all patients, 12,857 (19,236); OMT, 12,633 (18,900); non-OMT before matching, 12,897 (19,296) ( $P = 0.031$ ); non-OMT after matching, 12,321 (18,189) ( $P = 0.994$ ).

from other countries (28.9%–51.8% in Canada,<sup>12</sup> 49% in Middle Eastern countries,<sup>18</sup> 50.4% in Korea,<sup>14</sup> 71.0% in Australia and New Zealand<sup>19</sup>). The prescription rates of each individual indicated medication presented in this study were also much lower than the estimates reported by Bi et al.<sup>13</sup> Regardless of the variations in the reported OMT percentages, a significant gap exists between clinical guideline and practice, which may be mostly attributable to the low prescription rates from physicians.<sup>9</sup> First, physicians may have been reluctant to prescribe aggressive medication therapies to avoid adverse effects; this practice is supported by the findings that patients' high-risk characteristics may have an important impact on discharge medication decision making.<sup>13,14</sup> Second, physicians may be unfamiliar with treatment recommendations and/or unaware of the importance of preventive treatment. As Bi et al.<sup>13</sup> suggested, "not indicated" by the physician was recorded as the most common reason for not prescribing medications, which means that the medication was not prescribed because of a perceived lack of indication rather than the presence of a contraindication or intolerance.<sup>13</sup>

As stated above, the clinical guideline–practice gap varies across different nations, regions, hospitals, physicians, as well as patients. Increased age and a high prevalence of comorbidities including hypertension, hyperlipidemia, and diabetes may partly explain the extreme underuse of preventive treatments in this study.<sup>15,19,20</sup> These patients may be reluctant to take additional preventive medication as they may have already received a number of medications during hospitalization. Adverse reactions, intolerance, and contraindications are also likely to influence medication use, which may not have been captured in this study. In addition, treatment cost is a major barrier of medication use in patients. Despite the universal health insurance coverage in China, patients still need to pay quite a proportion of total medical costs (ie, out-of-pocket costs), which may further limit the use of preventive OMT.

As expected, the present study found that patients who received OMT at discharge from the index hospitalization were less likely to be hospitalized during the follow-up period and more likely to have a lower frequency of hospitalizations and a shorter length of stay. These findings support the better

prognosis among patients who did receive OMT at discharge compared with those who did not, as suggested in previous studies.<sup>12,13</sup> Van der Elst et al.<sup>8</sup> reported that multiple drug treatment was associated with a lower number of admissions for recurrent myocardial infarction in patients with a history of myocardial infarction, and that the magnitude of the risk reduction increased as the number of drugs concurrently increased.<sup>8</sup> A study conducted by Zeymer et al.<sup>16</sup> also suggested more outpatient visits after discharge from hospitalization for ACS and a shorter length of stay for the initial admission among patients who did receive OMT at discharge compared to those who did not.

As a result of less use of inpatient services and more use of outpatient services, OMT was associated with lower hospitalization costs, higher costs of outpatient services, and lower total direct medical costs. In other words, the higher costs of outpatient services driven by more use of medications were offset by the reduced costs of inpatient services, which was consistent with the findings reported by Zeymer et al.<sup>16</sup> based on the prospective, observational APTOR (Antiplatelet Treatment Observational Registries) study from 14 European countries in 2013. The higher medication costs and greater frequency of outpatient visits among the OMT cohort also suggest that receiving OMT at discharge may correlate with optimal medication adherence during the follow-up period, which highlights the importance of OMT at discharge as a key step toward improving quality of care in ACS. In addition, we found that compared with the non-OMT cohort, the OMT cohort had lower all-cause total costs after adjustment for confounders, and similar ACS-related total costs. The primary reason for these findings may be that the positive effect of OMT is not limited to ACS-related prognosis. It may also improve the overall health status of patients and reduce all-cause costs. Another plausible reason may be that the medication costs of 4 indicated medications contributed to a higher percentage of ACS-related costs compared with its percentage in all-cause costs. Therefore, the higher medication costs in the OMT cohort would be more evident in the ACS-related cost analyses.

There were several potential limitations of our study. First, the present study was based on data from an insured population under employment and

those who had retired in Tianjin, and may not be representative of other people in China. Second, the UEBMI claims database did not have available detailed clinical information such as adverse reactions, medication intolerance, and contraindications, which might justify some cases of nonuse or underuse of studied medications. In addition, some patients who received prescriptions of studied medications prior to their index hospitalization may have had enough medication supply to cover a short period after discharge. Consequently, we might have underestimated the prescription rates for OMT. Third, we were unable to control for unmeasured factors such as socioeconomic factors, living habits, and disease severity, which may have influenced medication use at discharge and direct medical costs in this observational study. Last, the present study focused on the impact of OMT only on economic outcomes and did not explore the impact on clinical outcomes directly, given the limited clinical information in the UEBMI claims database. Further studies that explore both the clinical and economic outcomes of OMT in patients with ACS based on data from clinical practice are warranted.

## CONCLUSIONS

The rates of prescribing recommended preventive OMT—consisting of a statin, an antiplatelet, an ACEI/ARB, and a  $\beta$ -blocker—in patients discharged with ACS are suboptimal in China, and this guideline—practice gap represents an opportunity for improvement. Receiving OMT at discharge of the index hospitalization was associated with less use of inpatient services and more use of outpatient services, possibly as a result of better clinical prognosis and lower all-cause total costs. Strategies such as physician education and higher reimbursement ratios are needed to improve OMT prescribing rates at discharge, which would lead to total cost-savings among patients with ACS in China.

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X. He provided study design, writing of the original draft, project administration, and validation. Y. Wang provided literature search, methodology,

investigation, formal analysis, figure creation, and review and editing of the manuscript. H. Cong and C. Lu provided data interpretation, review and editing of the manuscript. J. Wu provided conceptualization, funding acquisition, investigation, supervision, data interpretation, and review and editing of the manuscript.

## CONFLICTS OF INTEREST

The study was funded by Sanofi China. The authors have indicated that they have no other conflicts of interest with regard to the content of this article.

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## APPENDIX A. SUPPLEMENTARY DATA

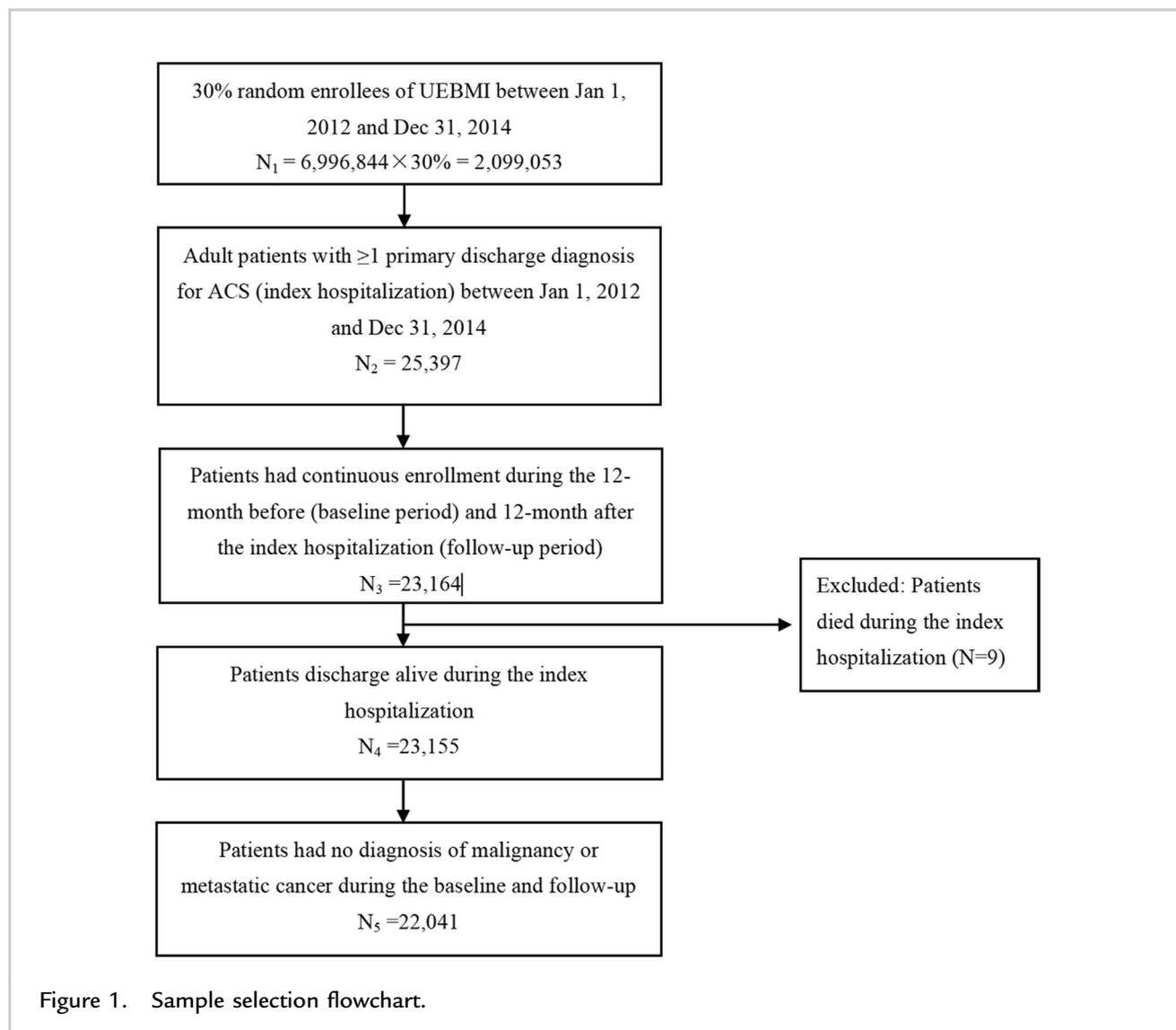


Figure 1. Sample selection flowchart.

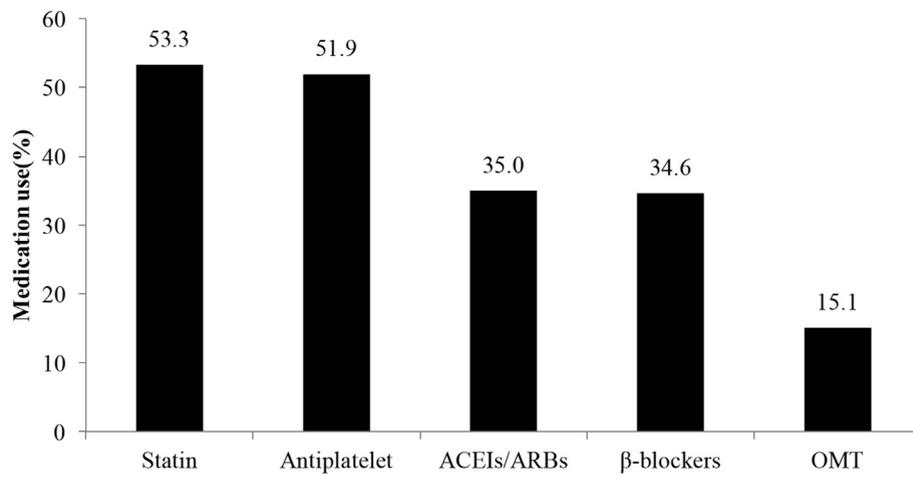


Figure 2. Use of the medications at discharge among total cohort (N = 22,041).