

# Prescription Rates of Guideline-Directed Medications Are Associated With In-Hospital Mortality Among Japanese Patients With Acute Myocardial Infarction: A Report From JROAD-DPC Study

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**Background**—The JROAD-DPC (Japanese Registry of All Cardiac and Vascular Diseases Diagnosis Procedure Combination) is a nationwide claims database comprised of the Japanese DPC/Per Diem Payment System. This study aimed to investigate the relationship between prescription rates of guideline-directed medications in each hospital and in-hospital mortality among patients with acute myocardial infarction.

**Methods and Results**—A total of 61 838 Japanese patients from 741 hospitals with acute myocardial infarction between 2012 and 2013 were enrolled. The relationship between prescription rates of 4 guideline-directed medications for acute myocardial infarction and in-hospital mortality was analyzed. There were variations in the prescription ratio of  $\beta$ -blockers on admission (median prescription rate 23% [interquartile range 11% to 38%]) and at discharge (51% [36% to 63%]), and of angiotensin converting enzyme/receptor blocker (60% [47% to 70%]). The highest prescription rate quartile of each medication was associated with a significantly lower mortality compared with the lowest prescription rate quartile (aspirin on admission, incidence rate ratio 0.67 [95% CI 0.61-0.74],  $P<0.001$ ; aspirin at discharge, incidence rate ratio 0.50 [95% CI 0.46-0.55],  $P<0.001$ ;  $\beta$ -blocker on admission, 0.83 [0.76-0.92],  $P<0.001$ ;  $\beta$ -blocker at discharge, 0.78 [0.71-0.85],  $P<0.001$ ; angiotensin converting enzyme/receptor blocker, 0.68 [0.62-0.75],  $P<0.001$ ; statin, 0.63 [0.57-0.70],  $P<0.001$ ). The composite prescription score was inversely associated with in-hospital mortality ( $\beta$  coefficient= $-0.48$ ,  $P<0.001$ ) and was closer to the plateau in the high-score range (median mortality for composite prescription scores of 6, 15, and 24 were 10.6%, 6.8%, and 4.6%, respectively).

**Conclusions**—The prescription rates of guideline-directed medications for treatment of Japanese acute myocardial infarction patients were inversely associated with in-hospital mortality. (*J Am Heart Assoc.* 2019;8:e009692. DOI: 10.1161/JAHA.118.009692.)

**Key Words:** acute myocardial infarction • medication • quality indicators

Despite the implementation of aggressive medical management and early reperfusion, acute myocardial infarction (AMI) remains the leading cause of death in the world and in Japan.<sup>1-3</sup> Studies have demonstrated that outcomes of AMI can be improved with appropriate treatments that have been summarized into guidelines and performance standards as quality indicators.<sup>4-9</sup> However, it is known that the prognosis

for AMI varies greatly among regions and hospitals. Under these circumstances, assessments of the process of care play an important role in management of AMI and are targets of hospital quality improvement initiatives (eg, the American Heart Association's GWTG [Get With The Guidelines] program).<sup>8-10</sup> The GWTG program has improved the quality of AMI care with important implications in the United States and the

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Accompanying Tables S1 through S9 and Figure S1 are available at <https://www.ahajournals.org/doi/suppl/10.1161/JAHA.118.009692>

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## Clinical Perspective

### What Is New?

- Prescription rates of guideline-recommended medications during hospitalization are related to in-hospital prognosis during the course of care for Japanese patients with acute myocardial infarction.
- Composite prescription scores inversely correlated with in-hospital mortality rates; as the composite prescription score increases, it appears to be closer to the plateau in the high-score area.

### What Are the Clinical Implications?

- Quality indicators related to the prescription rates of guideline-recommended drugs for acute myocardial infarction may be useful even in countries with performance rates of percutaneous coronary intervention as high as in Japan.
- Our result suggests that improvement of prescription rates for guideline-directed medications may improve the prognosis with acute myocardial infarction patients, especially in hospitals with low prescription rates.

United Kingdom.<sup>11</sup> However, different healthcare expenditures could influence the compliance with GWTG standards in countries other than the United States.

The JROAD-DPC (Japanese Registry of All Cardiac and Vascular Diseases Diagnosis Procedure Combination), launched by the Japanese Circulation Society, is a nationwide claim database using data from the Japanese DPC/Per Diem Payment System.<sup>12,13</sup> Data from DPC/Per Diem Payment System list the lump sum medical expenses evaluated based on diagnostic and procedural costs beginning in 2002. In this study we investigated whether there are relationships between the prescription rate of guideline-directed medication in each hospital and in-hospital mortality among patients with AMI, especially with regard to aspirin,  $\beta$ -blockers, angiotensin-converting enzyme inhibitor/angiotensin receptor blockers (ACEI/ARB), and statins using data from 2012 to 2013 in the nationwide JROAD-DPC database. Association of a composite prescription score (CPS) and in-hospital mortality was also investigated.

## Methods

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

The JROAD-DPC database was created by combining JROAD data derived from a Japanese Circulation Society national survey to assess the clinical activity of each Japanese institution with cardiovascular beds and to provide adequate

feedback to teaching hospitals for improving the patient-care database<sup>14</sup> and the DPC, which is a mixed-case patient classification system launched in 2002 by the Ministry of Health, Labor, and Welfare of Japan.<sup>15</sup> The DPC database contains patient demographics and several disease-specific data for each patient. An attending physician is responsible for clinical data entry for each patient. Drugs and procedures are recorded based on receipt data of medical care.<sup>16</sup>

The JROAD-DPC database includes 1 422 703 health records from 794 certificated hospitals that were collected in 2012 and 2013. These data include 61 838 patients with AMI (from 710 hospitals). We examined the prescription ratio of guideline-directed drugs for each hospital. Guideline-directed medications for AMI include aspirin on admission and discharge,  $\beta$ -blocker on admission and discharge, ACEI/ARB at discharge, and statin at discharge. Prescription on admission was defined as prescription by the end of the second hospital day. We categorized hospitals into quartiles based on the prescription rate of each drug (first quartile [Q1], second quartile [Q2], third quartile [Q3], and fourth quartile [Q4]) and investigated the relationships between the quartiles of the prescription rates and mortality rates. For each of the 4 guideline-directed medications for AMI, a CPS was created by giving points ranging from 1 to 4 from the lower quartile of the prescription rates, with the scores ranging from 6 to 24 points. We investigated the association between CPS and mortality at each hospital and the relationship of CPS with hospital-level variation.

## Ethics Statement

This research plan was designed by the authors and approved by the Institutional Review Board of the National Cerebral and Cardiovascular Center, which waived the requirement for individual informed consent by the “opt-out” principle. Each hospital anonymized each patient’s identification using code change equations made by each hospital in the original DPC data, which were sent to the Ministry of Health, Labor, and Welfare. Patients were notified through the hospital homepage and by posters in each hospital that their information was collected for this study. Patients could opt out from having their information included in the database.

## Statistical Analyses

Continuous variables are presented as mean $\pm$ SD for normally distributed variables; they were compared using the t test. Nonnormally distributed variables are presented as medians (interquartile range [IQR]). They were compared using the Mann-Whitney U test. Categorical baseline variables were compared using the Fisher exact test or the  $\chi^2$  test as appropriate. Analysis of variance was used to compare means

across multiple groups. Trends among multiple groups were analyzed by the Cochran-Armitage test. We used the Poisson model to determine the association between each quartile group and in-hospital mortality. For the adjustment of institutional background variation, we also developed mixed Poisson regression models with each institute being considered a random intercept. We also adjusted for the number of cardiologists, number of hospital beds, and number of patients with AMI in each institute added to the last model. The association between CPS and mortality was analyzed using linear regression. All  $P < 0.05$  were considered statistically significant. The analyses were performed using SAS 9.4 (SAS Institute, Cary, NC) and STATA 15 (Stata Corp, College Station, TX).

## Results

### Baseline Characteristics of AMI Patients

Among 73 436 patients with AMI hospitalized in 827 hospitals between 2012 and 2013, we excluded subjects under the age of 18 years ( $n=17$ ), those who had died within 24 hours after admission ( $n=2848$ ), and those without Killip class or prescription information ( $n=8408$ ). We also excluded hospitals with  $<5$  AMI hospitalizations annually. This resulted in a total of 61 838 patients in 710 hospitals who were included in the present analysis (Figure S1).

Table 1 and Tables S1 through S6 summarize patients' characteristics on the basis of individual and hospital data. In terms of individual data, mean age was 68.8 years, and 26.2% of patients were women. A total of 64.0% of patients had hypertension, 29.6% had diabetes mellitus, and 2.8% were on hemodialysis. Overall, 11.4% of patients had a Killip classification of 4. Following hospitalization, 85.7% of patients received percutaneous coronary intervention (PCI), 2.6% had coronary arterial bypass grafting, and 0.9% had fibrinolysis treatment; 52.2% participated in cardiac rehabilitation during hospitalization. Importantly, 39 17 patients (6.3%) reached the primary end point. According to hospital characteristics, the participation rate for cardiac rehabilitation was widely distributed (IQR 12.5% to 80.6%) (Table 1).

### Prescription Rate of Guideline-Directed Medications

The prescription rate of aspirin was 87% (IQR 82% to 92%) at admission and 80% (IQR 75% to 85%) at discharge, with a small amount of hospital-level variation (Figure 1A and 1C). In contrast, there were wide variations in the prescription rates of  $\beta$ -blockers at admission (23%, IQR 11% to 38%) and at discharge (51%, IQR 36% to 63%) (Figure 1B and 1D). The prescription rate of ACEI/ARBs was 52.0% (IQR 40.3% to

**Table 1.** Patient Characteristics

	Patient Base ( $n=61\ 838$ )	Hospital Variation Mean (SD) or Median (IQR) ( $n=741$ )
Age, y, mean (SD)	68.84 (13.03)	69.50 (3.29)
Female	16 197 (26.19)	26.47 (22.33-31.03)
Body mass index, kg/m <sup>2</sup> , mean (SD)	23.10 (3.92)	23.62 (0.91)
Hypertension	39 625 (64.08)	62.50 (50.51-71.55)
Diabetes mellitus	18 307 (29.60)	28.75 (21.88-34.94)
Smoker (current and ex-smoker)	36 684 (59.32)	57.50 (47.22-66.67)
Hemodialysis	1759 (2.84)	1.90 (0-3.88)
Charlson Score, mean (SD)	2.09 (1.07)	2.09 (0.34)
Killip Class		
I	30 593 (49.47)	50.00 (33.33-62.50)
II	18 701 (30.24)	30.00 (19.74-41.38)
III	5524 (8.93)	7.45 (4.08-12.11)
IV	7020 (11.35)	9.88 (5.43-14.89)
CAG	57 870 (93.58)	94.44 (89.36-96.98)
PCI	52 996 (85.70)	85.94 (78.57-90.74)
CABG	1634 (2.64)	0 (0-3.09)
IABP	9532 (15.41)	11.76 (6.58-18.92)
PCPS	1163 (1.88)	0.66 (0-2.38)
Fibrinolysis	523 (0.85)	0 (0-0.52)
Cardiac rehabilitation	32 305 (52.24)	48.57 (12.5-80.58)

Values presented are given as numbers (percentage) unless stated. CABG indicates coronary arterial bypass grafting; CAG, coronary angiography; IABP, intra-aortic balloon pump; IQR, interquartile range; PCI, percutaneous coronary intervention; PCPS, percutaneous cardiopulmonary support.

62.3%) at discharge (Figure 1E), and that of statins was 80% (IQR 75% to 85%) at discharge (Figure 1F).

### Correlation of Prescription Rate of Guideline-Directed Drugs

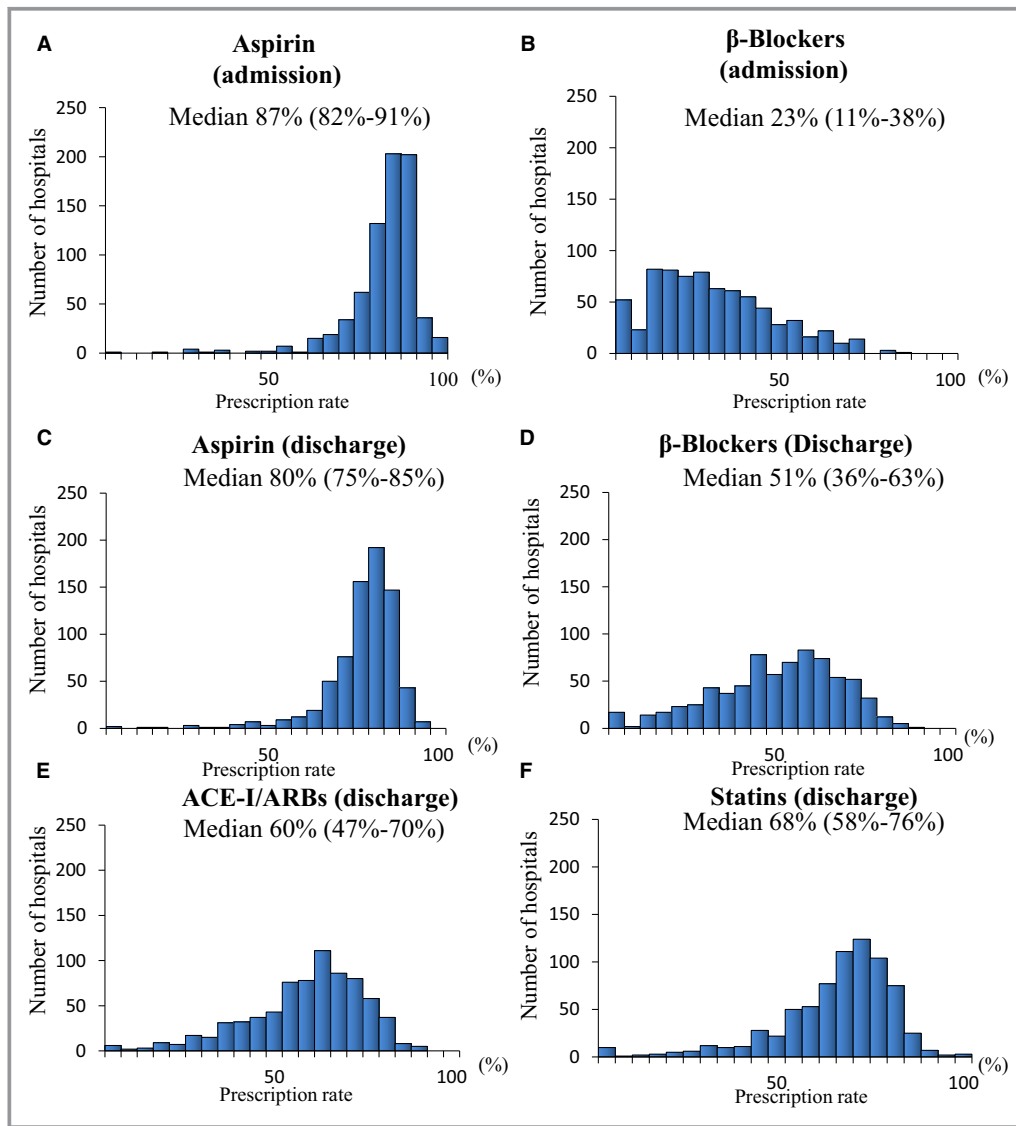
Table S7 shows the correlation of each medication in 15 patterns overall; 7 of 15 combinations showed a weak correlation (Spearman correlation coefficient  $<0.3$ ), and 6 were a combination of admission and discharge medications. Eight showed a moderate correlation (0.3-0.7), and 6 were combinations of medications at discharge.

### Relationships of Prescription Rates of Guideline-Directed Medications and In-Hospital Mortality

We categorized hospitals into quartiles according to the prescription rate of guideline-directed medications for the

following 4 regimens: aspirin at admission and discharge,  $\beta$ -blockers at admission and discharge, ACEI/ARBs, and statins at discharge. Figure 2 shows that the in-hospital mortality decreased from the lower to upper quartiles. The regression analysis indicated an inverse trend for the risk of death across quartiles (Table 2; all  $P$ -values for the trend of in-hospital mortality  $<0.001$ ). The highest prescription rate quartile for each medication was associated with a significantly lower mortality than the lowest prescription rate quartile. For example, aspirin on admission and those at discharge were associated with 33% and 50% decrease of mortality (aspirin on admission, incidence rate ratio 0.67 [95%

CI 0.61-0.74],  $P<0.001$ ; aspirin at discharge, incidence rate ratio 0.50 [95% CI 0.46-0.55],  $P<0.001$ ;  $\beta$ -blocker on admission 0.83 [0.76-0.92],  $P<0.001$ ;  $\beta$ -blocker at discharge 0.78 [0.71-0.85],  $P<0.001$ ; ACE/ARB 0.68 [0.62-0.75],  $P<0.001$ ; statin 0.63 [0.57-0.70],  $P<0.001$ ). After adjustment for age, sex, Charlson score, and Killip class and comparison with the Q1 group as a reference, a higher quantile was associated with a lower mortality rate. Further, to adjust for the differences among hospitals, we have examined using a Poisson mixed model and other hospital characteristics (hospital bed number, number of patients with AMI, and number of cardiologists) (Table S8).



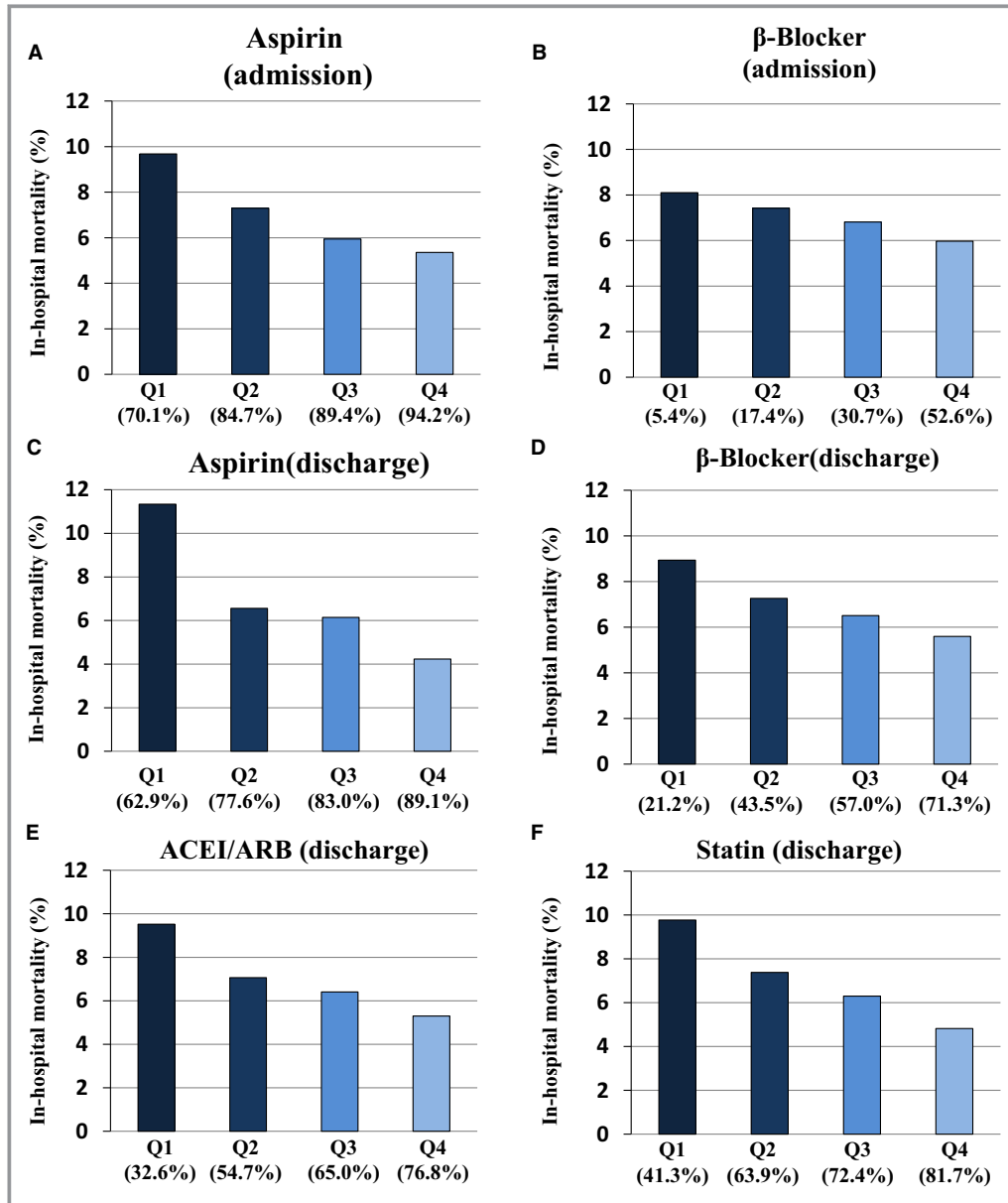
**Figure 1.** Distribution of prescription rates for aspirin (A) and  $\beta$ -blockers (B) on admission, and aspirin (C),  $\beta$ -blockers (D), ACEI/ARBs (E), and statins (F) at discharge among 741 hospitals in patients with AMI. ACEI indicates angiotensin-converting enzyme inhibitor; AMI, acute myocardial infarction; ARB, angiotensin receptor blocker.

### Relationship of CPS and Outcome

The CPS for the 710 hospitals was widely distributed with a median score of 15, and CPS was inversely associated with in-hospital mortality (Figure 3). The mortality rate declined as the score increased in the low-score range. However, the score increased gradually and approached a plateau in the high-score area (median mortality for CPS scores of 6, 15, and 24 were 10.6%, 6.8%, and 4.6%, respectively).

### CPS and Hospital Characteristics

We examined the relationship between the highest CPS quartile and the factors representing hospital characteristics (Table 3 and Table S9). The number of hospital beds and the AMI case volume were positively correlated with CPS, as was the presence of a cardiac surgery division. However, the number of cardiologists per number of AMIs was not significantly correlated with CPS.



**Figure 2.** Relationship between in-hospital mortality and prescription rates (quartiles) for aspirin (A) and β-blockers (B) on admission, and aspirin (C), β-blockers (D), ACEI/ARBs (E), and statins (F) at discharge among 741 hospitals in patients with AMI. ACEI indicates angiotensin-converting enzyme inhibitor; AMI, acute myocardial infarction; ARB, angiotensin receptor blocker; Q1-Q4, quartiles based on prescription rates.

**Table 2.** Incidence Rate Ratio for In-Hospital Mortality According to the Quartile of Each Guideline-Directed Medication

	Q1	Q2	P Value	Q3	P Value	Q4	P Value	P for Trend
	IRR	IRR (95% CI)		IRR (95% CI)		IRR (95% CI)		
<b>Univariate analysis</b>								
Aspirin (admission)	1.00	0.83 (0.75-0.91)	<0.001	0.70 (0.64-0.77)	<0.001	0.67 (0.61-0.74)	<0.001	<0.001
β-Blocker (admission)	1.00	0.98 (0.90-1.08)	0.699	0.90 (0.82-0.99)	0.035	0.83 (0.76-0.92)	<0.001	<0.001
Aspirin (discharge)	1.00	0.73 (0.67-0.80)	<0.001	0.66 (0.61-0.72)	<0.001	0.50 (0.46-0.55)	<0.001	<0.001
β-Blocker (discharge)	1.00	0.88 (0.80-0.97)	0.009	0.79 (0.72-0.87)	<0.001	0.78 (0.71-0.85)	<0.001	<0.001
ACEI/ARB (discharge)	1.00	0.86 (0.78, 0.94)	0.001	0.78 (0.71-0.86)	<0.001	0.68 (0.62-0.75)	<0.001	<0.001
Statin (discharge)	1.00	0.83 (0.76-0.92)	<0.001	0.73 (0.66-0.80)	<0.001	0.63 (0.57-0.70)	<0.001	<0.001
<b>Multivariate analysis*</b>								
Aspirin (admission)	1.00	0.88 (0.80-0.97)	0.008	0.76 (0.69-0.84)	<0.001	0.74 (0.67-0.82)	<0.001	<0.001
β-Blocker (admission)	1.00	1.00 (0.92-1.10)	0.960	0.93 (0.85-1.02)	0.139	0.86 (0.78-0.95)	0.002	<0.001
Aspirin (discharge)	1.00	0.77 (0.70-0.84)	<0.001	0.71 (0.65-0.78)	<0.001	0.54 (0.49-0.60)	<0.001	<0.001
β-Blocker (discharge)	1.00	0.89 (0.81-0.97)	0.011	0.82 (0.75-0.90)	<0.001	0.82 (0.74-0.90)	<0.001	<0.001
ACEI/ARB (discharge)	1.00	0.89 (0.80-0.98)	0.014	0.82 (0.74-0.91)	<0.001	0.74 (0.67-0.81)	<0.001	<0.001
Statin (discharge)	1.00	0.88 (0.80-0.96)	0.007	0.79 (0.72-0.87)	<0.001	0.68 (0.62-0.76)	<0.001	<0.001

P<0.05 is statistically significant. ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; IRR, incidence rate ratio; Q1-Q4, quartiles based on prescription rates.

\*Adjusted for age, sex, Charlson comorbidity index, and Killip class.

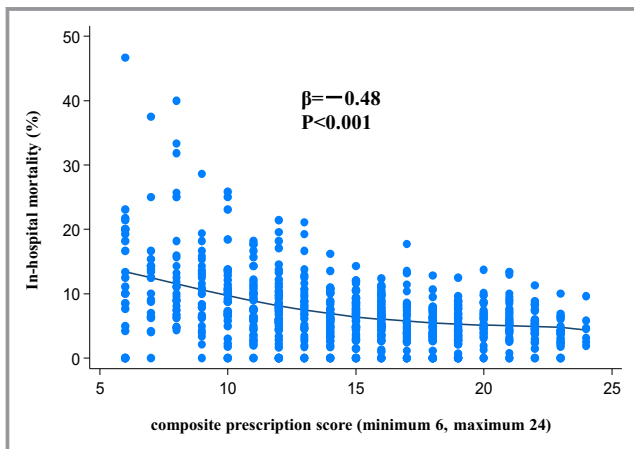
## Discussion

The major findings of the present study using a nationwide claim database containing more than 60 000 cases and over 700 hospitals between 2012 and 2013 are as follows: (1) there were wide variations in the prescription rates of guideline-directed medications, (2) the prescription rates of these medications were inversely associated with in-hospital mortality even after adjustment for variables, (3) the relationship between CPS and mortality appears to be closer to the

plateau in the high-score area, and (4) a high CPS score was associated with hospital performance (eg, the number of hospital beds, the AMI case volume, or involvement of a certified cardiologist).

### Comparison of Guideline-Directed Medication Prescription Rate With Studies in Other Countries

Among the guideline-directed drugs, the prescription rate for aspirin on admission and discharge was high (87% and 80%, respectively). In contrast, the prescription rates for β-blockers at admission and discharge and for ACEI/ARBs at discharge were low. Compared with the US study of the National Registry of Myocardial Infarction, the prescription rate for aspirin at admission was comparable between Japan (87%) and the United States (86%), whereas the prescription rate for β-blockers at admission was lower in Japan than in the United States (23% versus 78%).<sup>17</sup> The prescription rate for aspirin at discharge was comparable across different countries: United States 80%, the United Kingdom 98.1%, and Sweden (any antiplatelet therapy) 94.6%.<sup>17-19</sup> However, the prescription rate of β-blockers at discharge was lower in our study (51%) compared with the United States (75.8%), the United Kingdom (95.6%), and Sweden (88.7%).<sup>17-19</sup> It was comparable to that in other Japanese registries (PACIFIC 49.5%, Credo Kyoto 43.7%, and Tokyo CCU 38.8%).<sup>20-22</sup> In Japan the prescription rate for β-blockers was relatively low in both PCI-capable high-



**Figure 3.** Association of composite prescription score of guideline-directed medications and in-hospital mortality in patients with AMI. AMI indicates acute myocardial infarction.

**Table 3.** Relationship of the Highest Quartile of CPS and Hospital Characteristics

Hospital Variables	OR	95% CI	P Value
Hospital bed number per 10 beds	1.02	1.01 to 1.03	<0.001
Number of patients with AMI per 10	1.12	1.10 to 1.15	<0.001
Cardiac surgery division	1.64	1.23 to 2.17	<0.001
Number of cardiologists per number of AMIs			
First quartile	Ref	Ref	
Second quartile	1.10	0.77 to 1.57	0.6
Third quartile	0.91	0.63 to 1.32	0.62
Fourth quartile	0.71	0.48 to 1.04	0.075

$P < 0.05$  is statistically significant. AMI indicates acute myocardial infarction; CPS, composite prescription score; OR, odds ratio.

quality hospitals and in the nationwide claims database. The prescription rate for ACEI/ARBs at discharge was also low in our population (52%) compared with that in other countries (United States 70.7%, the United Kingdom 93.9%, and Sweden, 56.2%).<sup>17-19</sup> The prescription rate for statins was as follows: Japan 80%, the United Kingdom 96.5%, and Sweden 79.7%.<sup>18,19</sup> These findings indicate that the overall prescription rate for guideline-recommended drugs, except for aspirin, was relatively low in Japan. It should be noted that the rate of PCI in Japan (85.7%) was higher than that of other nations: the United Kingdom 65.6% (2012-2013) and the United States 64% (1994-2006). The high rate of PCI may affect the medication strategy. In the 2013 ST-elevation MI guidelines of the Japanese Circulation Society, the recommendation for  $\beta$ -blocker use for low-risk AMI (successful reperfusion, no left ventricular dysfunction, no severe arrhythmia) has been changed from Class 1 to Class 2A. Further investigation is needed for causes of relatively low prescription rate and secular change of the rate.

Previous studies in other countries have revealed that there is often little or no correlation between each component of the quality indicators or PMs (performance measures).<sup>17,18,23</sup> In our study all 15 prescription combinations demonstrate significant correlations. However, the relationship remained weak, especially between drugs prescribed on admission and at discharge. These data support the concept that a broad range of process metrics is needed to fully characterize hospital-level care practices.<sup>17,18,23,24</sup>

### Prescription Rate and Short-Term Mortality

To date, several reports have been published addressing whether prescription rates of guideline-recommended medications are related to prognosis.<sup>17,18,23</sup> A report from the United States revealed that quality indicators or PMs

(performance measures), including prescription rates of guideline-recommended drugs, are associated with short-term mortality rates in patients with AMI and acute coronary syndrome.<sup>17,23,25</sup> A recent study from the United Kingdom also showed that quality indicators, including prescription rates, are associated with mortality rates.<sup>18</sup> In the present study we showed that the prescription rate of 4 medications and the CPS were associated negatively with in-hospital mortality in patients with AMI. These findings show that even in a country in which the performance rate of PCI is as high as it is in Japan, the prescription rate of guideline-recommended drugs during hospitalization is related to short-term prognosis. A comparison study between Sweden and the United Kingdom<sup>26</sup> showed that the potential for death prevention by optimal medical therapy was similar to or greater than that by reperfusion therapy. Especially in Japan, a relatively low prescription rate and large interhospital variation showed that there is much potential for improvement in short-term mortality by increasing the rate of guideline-directed medication prescriptions. Furthermore, according to the relationship of CPS and mortality rate, as the CPS increases, it appears to be closer to the plateau in the high-score area. This result suggests that if prescription rates for guideline-directed medications rise in hospitals with low prescription rates, the prognosis for patients with AMI may improve. To improve guideline-directed medications in low-CPS hospitals, intervention using a simple toolkit such as the ACS QUIK (Acute Coronary Syndrome Quality Improvement in Kerala) in India may be useful.<sup>27</sup>

### Association of Guideline Adherence With Hospital Features

It has been revealed that hospital features are related to the guideline adherence of each hospital.<sup>17,23</sup> In the present analysis the highest quartile CPS was associated with the hospital case volume of AMIs, the number of hospital beds, and the parallel establishment of cardiovascular surgery. In contrast, there was no significant relationship between the prescription rates and the number of cardiovascular physicians per number of AMIs. These results suggest that factors of hospital performance are also related in part to prescription rates. Indeed, a previous study investigated multiple factors that included hospital structure and other factors contributing to the variation in mortality rates among hospitals beyond variations in hospital treatment.<sup>25,28-32</sup> Another study showed that hospitals with high performance were characterized by well-organized features to improve AMI care across all departments.<sup>33</sup> It is also possible that the low prescription rate not only contributes to the prognosis but also represents the difficulty in implementing high-quality care for AMI. Because the severity of the patient's condition and

comorbidities, difference in hospital levels, and regional factors including prehospital care may be involved, these factors that create a variation in prescription rates need to be improved.

## Limitations

Our study has limitations. First, although DPC data must be confirmed by a doctor and are highly reliable, some of the data are based on medical claims. Therefore, there is a possibility that these data may contain certain errors, and some data may be underestimated (such as comorbidities) because they are not captured in claims. Second, although this research was conducted using nationwide databases and very closely represents the current situation in Japan, there is a possibility that actual conditions in nonspecialized facilities and small clinics are not reflected. Third, because this database does not contain data from before arrival at the hospital, there is a possibility that patients who die before hospital arrival may be missing. For the same reason, factors affecting the prognosis, such as time from onset to hospital arrival, cannot be included in the analysis. Fourth, missing data or unknown confounding factors may affect the analysis results. Fifth, although we have demonstrated that the prescription rate was inversely associated with in-hospital mortality (Figure 2 and Table 2) and may reflect general activity in each hospital, further evaluation of quality as an indicator and variance of quality across institutes and settings is needed.

## Conclusions

There were wide variations in the prescription rates of guideline-directed medications for the treatment of Japanese AMI patients, and these rates were inversely associated with in-hospital mortality. Therefore, there may be a necessity for interventions to improve short-term mortality in hospitals with low prescription rates.

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## Disclosures

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# **SUPPLEMENTAL MATERIAL**

**Table S1. Baseline hospital characteristics per quantiles by prescription rate of aspirin on admission.**

	Q1 (189 Hospitals)	Q2 (182 Hospitals)	Q3 (186 Hospitals)	Q4 (186 Hospitals)	<b>P</b>
Age in years, mean (SD)	71.26 (4.51)	69.19 (2.62)	68.68 (2.45)	68.82 (2.36)	<0.001
Female	28.57 (24.14, 37.93)	26.87 (23.08, 30.77)	25.00 (21.21, 29.33)	25.35 (22.08, 28.89)	<0.001
Body mass index, mean (SD), kg/m <sup>2</sup>	23.34 (1.32)	23.71 (0.76)	23.73 (0.61)	23.73 (0.71)	<0.001
Hypertension	54.55 (41.67, 65.71)	62.07 (53.95, 69.01)	64.71 (53.13, 74.40)	66.67 (56.10, 75.00)	<0.001
Diabetes	27.86 (19.51, 35.56)	28.22 (21.74, 35.21)	28.85 (21.88, 33.33)	30.17 (25.00, 36.26)	0.047
Smoker (current and ex- smoker)	53.33 (38.46, 63.64)	58.26 (50.00, 66.67)	59.09 (50.00, 66.97)	58.76 (50.00, 67.05)	<0.001
Hemodialysis	0.00 (0.00, 4.44)	2.60 (0.00, 4.55)	1.65 (0.00, 3.14)	1.76 (0.00, 3.13)	0.002
Charlson Score, mean (SD)	2.16 (0.33)	2.11 (0.32)	2.05 (0.35)	2.05 (0.35)	0.002

Killip Class I	41.94 (22.22, 57.14)	51.59 (33.33, 62.50)	52.78 (38.26, 62.92)	52.76 (36.46, 67.79)	<0.001
II	32.35 (21.21, 44.00)	30.97 (17.65, 39.71)	29.44 (20.67, 39.66)	26.72 (18.42, 41.51)	0.24
III	9.09 (5.00, 16.67)	7.32 (3.97, 11.16)	7.25 (3.90, 11.11)	6.67 (3.37, 10.00)	0.001
IV	12.20 (5.88, 19.35)	9.17 (5.56, 14.44)	9.43 (5.00, 14.89)	9.40 (5.43, 13.19)	0.031
CAG	87.50 (75.00, 94.44)	94.12 (90.00, 96.15)	95.24 (92.50, 97.39)	96.34 (93.88, 97.98)	<0.001
PCI	75.00 (62.50, 84.38)	85.05 (79.45, 89.13)	87.69 (82.93, 91.96)	90.54 (85.71, 93.63)	<0.001
CABG	0.00 (0.00, 3.13)	0.00 (0.00, 4.35)	1.18 (0.00, 3.23)	0.00 (0.00, 2.11)	0.005
IABP	8.00 (0.00, 16.46)	11.94 (6.78, 20.00)	13.04 (9.33, 19.13)	12.85 (7.69, 18.92)	<0.001
PCPS	0.00 (0.00, 1.67)	1.00 (0.00, 2.80)	1.12 (0.00, 2.47)	1.01 (0.00, 2.38)	<0.001
Fibrinolysis	0.00 (0.00, 0.00)	0.00 (0.00, 0.43)	0.00 (0.00, 0.00)	0.00 (0.00, 1.01)	0.023
Cardiac Rehabilitation	71.26 (4.51)	69.19 (2.62)	68.68 (2.45)	68.82 (2.36)	<0.001

Values presented are given as number (percentage) unless stated.

SD = standard deviation, IQR = interquartile range, CAG = coronary angiography, PCI = percutaneous coronary intervention, CABG = coronary arterial bypass grafting, IABP = intra-aortic balloon pump, PCPS = Percutaneous Cardio Pulmonary Support.

**Table S2. Baseline hospital characteristics per quantiles by prescription rate of  $\beta$ -Blocker on admission.**

	Q1 (186 Hospitals)	Q2 (185 Hospitals)	Q3 (186 Hospitals)	Q4 (187 Hospitals)	P
Age in years, mean (SD)	70.49 (4.06)	69.45 (3.33)	69.20 (2.75)	68.85 (2.63)	<0.001
Female	27.98 (22.22, 32.50)	26.47 (22.36, 31.25)	25.71 (22.50, 30.23)	25.54 (22.22, 29.98)	0.063
Body mass index, mean (SD), kg/m <sup>2</sup>	23.48 (1.18)	23.63 (0.92)	23.67 (0.78)	23.72 (0.69)	0.074
Hypertension	59.94 (45.45, 69.19)	61.11 (50.78, 68.75)	62.55 (51.61, 70.97)	66.67 (54.06, 76.24)	0.002
Diabetes	28.88 (20.00, 35.56)	28.75 (20.69, 34.78)	29.23 (24.00, 35.90)	28.57 (22.30, 33.14)	0.33
Smoker (current and ex- smoker)	55.34 (45.68, 65.71)	58.54 (49.21, 68.18)	57.94 (47.22, 68.09)	57.14 (48.98, 65.36)	0.099
Hemodialysis	0.93 (0.00, 3.33)	2.38 (0.00, 4.88)	2.32 (0.00, 4.00)	1.94 (0.00, 3.31)	<0.001
Charlson Score, mean (SD)	2.05 (0.34)	2.09 (0.33)	2.11 (0.36)	2.11 (0.33)	0.32

Killip Class I	46.77 (30.00, 61.90)	51.52 (34.69, 62.92)	50.13 (33.94, 62.86)	50.00 (34.29, 61.80)	0.61
II	30.93 (20.00, 43.48)	28.57 (18.03, 38.69)	29.01 (19.05, 39.02)	31.54 (20.71, 43.16)	0.48
III	7.60 (3.94, 14.67)	8.04 (4.35, 12.50)	6.95 (3.90, 11.11)	7.49 (4.17, 10.70)	0.72
IV	9.54 (5.00, 15.56)	10.00 (5.67, 15.33)	10.53 (6.25, 14.95)	9.76 (4.94, 14.29)	0.40
CAG	93.65 (86.05, 97.37)	93.75 (88.95, 96.89)	95.03 (91.03, 96.97)	94.94 (91.58, 97.07)	0.036
PCI	85.09 (75.00, 90.85)	85.37 (78.26, 90.16)	87.10 (80.56, 91.18)	86.42 (79.89, 90.96)	0.11
CABG	0.00 (0.00, 1.18)	0.33 (0.00, 4.08)	0.00 (0.00, 3.66)	0.00 (0.00, 3.86)	<0.001
IABP	8.63 (3.37, 16.67)	11.49 (6.45, 18.97)	11.99 (7.81, 19.86)	13.31 (8.46, 20.09)	<0.001
PCPS	0.00 (0.00, 1.39)	0.86 (0.00, 2.80)	1.09 (0.00, 2.56)	1.35 (0.00, 2.58)	<0.001
Fibrinolysis	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 1.31)	0.007
Cardiac Rehabilitation	33.33 (10.00, 78.57)	56.86 (12.68, 80.97)	48.68 (13.56, 80.41)	60.77 (14.06, 84.15)	0.089

Values presented are given as number (percentage) unless stated.



SD = standard deviation, IQR = interquartile range, CAG = coronary angiography, PCI = percutaneous coronary intervention, CABG = coronary arterial bypass grafting, IABP = intra-aortic balloon pump, PCPS = Percutaneous Cardio Pulmonary Support.

**Table S3. Baseline hospital characteristics per quantiles by prescription rate of aspirin on admission.**

	Q1 (186 Hospitals)	Q2 (185 Hospitals)	Q3 (187 Hospitals)	Q4 (183 Hospitals)	P
Age in years, mean (SD)	71.44 (4.26)	69.21 (2.64)	68.80 (2.21)	68.54 (2.86)	<0.001
Female	29.40 (24.39, 37.93)	26.87 (22.86, 30.00)	25.00 (21.88, 29.17)	24.83 (21.05, 29.55)	<0.001
Body mass index, mean (SD), kg/m <sup>2</sup>	23.21 (1.18)	23.81 (0.80)	23.71 (0.67)	23.76 (0.80)	<0.001
Hypertension	54.86 (40.00, 65.06)	64.57 (54.29, 70.71)	64.84 (55.00, 74.03)	64.54 (53.13, 76.44)	<0.001
Diabetes	27.27 (19.10, 34.21)	29.29 (22.58, 35.81)	28.75 (22.37, 33.54)	29.29 (23.81, 35.80)	0.038
Smoker (current and ex- smoker)	53.87 (40.74, 63.16)	56.25 (47.83, 65.90)	60.61 (50.00, 67.95)	58.33 (50.94, 67.74)	<0.001
Hemodialysis	2.11 (0.00, 5.56)	2.13 (0.00, 4.05)	1.92 (0.00, 3.25)	1.32 (0.00, 3.08)	0.083
Charlson Score, mean (SD)	2.17 (0.35)	2.11 (0.31)	2.06 (0.32)	2.03 (0.36)	<0.001

Killip Class I	41.18 (25.81, 57.14)	54.29 (37.17, 65.00)	51.72 (36.96, 62.50)	49.32 (32.14, 65.06)	<0.001
II	30.22 (20.00, 42.86)	25.71 (19.64, 38.71)	30.41 (18.31, 40.00)	32.35 (20.67, 46.59)	0.067
III	9.09 (5.21, 16.67)	6.78 (3.08, 11.43)	6.80 (4.17, 10.17)	7.14 (3.90, 11.11)	0.002
IV	12.86 (6.25, 20.37)	10.00 (5.83, 14.29)	9.52 (6.31, 14.91)	8.11 (4.32, 13.24)	<0.001
CAG	90.62 (78.67, 94.48)	94.68 (90.00, 96.83)	94.90 (92.19, 97.28)	96.12 (93.44, 97.80)	<0.001
PCI	78.50 (63.64, 85.71)	85.51 (79.41, 89.74)	87.72 (82.14, 91.67)	89.19 (84.62, 92.86)	<0.001
CABG	0.00 (0.00, 2.17)	0.00 (0.00, 3.33)	0.74 (0.00, 3.60)	0.00 (0.00, 2.63)	0.006
IABP	9.86 (2.50, 19.51)	11.76 (7.32, 19.75)	13.39 (8.00, 18.45)	11.11 (6.58, 18.18)	0.021
PCPS	0.00 (0.00, 2.56)	1.06 (0.00, 3.28)	1.19 (0.00, 2.13)	0.00 (0.00, 1.94)	0.014
Fibrinolysis	0.00 (0.00, 0.00)	0.00 (0.00, 0.83)	0.00 (0.00, 0.73)	0.00 (0.00, 0.52)	0.16
Cardiac Rehabilitation	30.66 (10.96, 67.77)	56.51 (16.67, 79.10)	56.86 (11.02, 82.22)	57.55 (12.00, 87.84)	<0.001

Values presented are given as number (percentage) unless stated.

SD = standard deviation, IQR = interquartile range, CAG = coronary angiography, PCI = percutaneous coronary intervention, CABG = coronary arterial bypass grafting, IABP = intra-aortic balloon pump, PCPS = Percutaneous Cardio Pulmonary Support.

**Table S4. Baseline hospital characteristics per quantiles by prescription rate of  $\beta$ -Blocker on discharge.**

	Q1 (186 Hospitals)	Q2 (185 Hospitals)	Q3 (185 Hospitals)	Q4 (185 Hospitals)	P
Age in years, mean (SD)	70.89 (4.43)	69.73 (2.90)	68.75 (2.41)	68.62 (2.51)	<0.001
Female	28.03 (23.44, 34.62)	27.45 (22.73, 31.25)	25.26 (22.12, 28.87)	25 (21.66, 30.00)	<0.001
Body mass index, mean (SD), kg/m <sup>2</sup>	23.44 (1.24)	23.54 (0.81)	23.80 (0.67)	23.72 (0.79)	<0.001
Hypertension	55.04 (40.00 , 64.52)	62.07 (51.03, 70.73)	65.73 (54.37, 75.00)	67.48 (56.63, 76.44)	<0.001
Diabetes	28.03 (19.64, 35.35)	28.57 (22.22, 34.00)	29.29 (23.53, 35.56)	29.03 (22.86, 34.78)	0.46
Smoker (current and ex- smoker)	54.93 (42.31, 65.22)	56.90 (46.30, 65.71)	61.11 (52.11, 68.42)	57.14 (48.04, 65.20)	<0.001
Hemodialysis	0 (0, 3.33)	2.30 (0, 4.13)	2.24 (0, 4.26)	1.96 (0, 3.33)	0.002
Charlson Score, mean (SD)	2.07 (0.39)	2.09 (0.32)	2.11 (0.36)	2.09 (0.29)	0.72

Killip Class I	47.06 (30.77, 60.98)	50 (32.08, 62.50)	52.94 (35.16, 64.71)	48.94 (33.33, 61.40)	0.24
II	30.93 (20.00, 42.37)	28.57 (19.10, 39.47)	29.46 (19.00, 41.03)	30.65 (20.39, 44.44)	0.53
III	8.52 (4.17, 15.38)	7.69 (3.95, 11.48)	6.90 (3.41, 10.37)	7.45 (4.42, 10.87)	0.19
IV	10.00 (4.76, 15.11)	10.23 (6.25, 14.71)	9.09 (5.56, 15.19)	10 (5.06, 14.48)	0.68
CAG	92.27 (82.76, 96.77)	94.12 (89.02, 96.88)	94.55 (91.07, 96.72)	95.24 (92.68, 97.22)	<0.001
PCI	84.67 (69.17, 90.24)	85.04 (78.05, 89.66)	86.54 (81.25, 91.01)	87.69 (81.78, 91.67)	<0.001
CABG	0 (0, 0.08)	0 (0, 3.13)	1 (0, 4.08)	1.22 (0, 3.97)	<0.001
IABP	7.00 (0, 14.44)	11.48 (6.78, 18.92)	12.31 (8.04, 21.36)	15.38 (9.68, 20.51)	<0.001
PCPS	0 (0, 1.19)	0 (0, 2.36)	1.35 (0, 2.74)	1.37 (0, 2.87)	<0.001
Fibrinolysis	0 (0, 0)	0 (0, .68)	0 (0, 0.75)	0 (0, 0.66)	0.26
Cardiac Rehabilitation	25.25 (6.67, 68.57)	48.78 (13.41, 78.95)	48.57 (13.38, 81.00)	68.18 (20.00, 86.90)	<0.001

Values presented are given as number (percentage) unless stated.

SD = standard deviation, IQR = interquartile range, CAG = coronary angiography, PCI = percutaneous coronary intervention, CABG = coronary arterial bypass grafting, IABP = intra-aortic balloon pump, PCPS = Percutaneous Cardio Pulmonary Support.

**Table S5. Baseline hospital characteristics per quantiles by prescription rate of ACEI/ARB on discharge.**

	Q1 (187 Hospitals)	Q2 (184 Hospitals)	Q3 (186 Hospitals)	Q4 (184 Hospitals)	<b>P</b>
Age in years, mean (SD)	71.15 (4.28)	69.49 (3.00)	68.83 (2.65)	68.49 (2.22)	<0.001
Female	28.57 (22.73, 36.00)	26.54 (22.22, 30.87)	26.67 (22.63, 30.37)	25.00 (22.06, 28.57)	<0.001
Body mass index, mean (SD), kg/m <sup>2</sup>	23.35 (1.19)	23.61 (0.87)	23.69 (0.72)	23.86 (0.70)	<0.001
Hypertension	51.61 (40.00, 63.16)	61.14 (51.88, 68.61)	65.17 (55.17, 73.68)	69.14 (59.03, 78.21)	<0.001
Diabetes	27.27 (19.64, 33.54)	30.74 (22.80, 37.19)	28.85 (21.88, 34.48)	28.41 (23.29, 33.34)	0.026
Smoker (current and ex- smoker)	54.17 (40.00, 63.89)	57.03 (46.39, 65.52)	59.94 (50.00, 68.00)	59.30 (51.93, 67.81)	<0.001
Hemodialysis	0.00 (0.00, 4.26)	2.15 (0.00, 4.24)	2.35 (0.67, 3.70)	1.64 (0.00, 3.51)	0.032
Charlson Score, mean (SD)	2.11 (0.38)	2.09 (0.36)	2.12 (0.33)	2.05 (0.29)	0.13



Killip Class I	46.67 (30.00, 60.00)	48.96 (33.70, 61.72)	51.04 (33.94, 63.31)	51.91 (35.26, 64.85)	0.14
II	32.11 (20.00, 42.31)	29.41 (19.48, 39.74)	27.59 (20.41, 40.63)	29.66 (19.42, 42.89)	0.78
III	8.22 (3.66, 14.67)	7.54 (4.32, 13.45)	7.16 (3.85, 10.34)	7.43 (4.06, 10.62)	0.33
IV	10.00 (4.88, 16.22)	10.65 (5.92, 15.89)	10.26 (5.56, 15.20)	8.70 (5.32, 13.43)	0.16
CAG	91.43 (76.92, 96.08)	94.86 (90.08, 97.01)	93.98 (90.16, 96.55)	95.68 (93.19, 97.33)	<0.001
PCI	81.71 (62.50, 87.80)	86.52 (80.15, 90.88)	85.71 (79.79, 90.00)	88.81 (82.31, 92.59)	<0.001
CABG	0.00 (0.00, 0.00)	0.00 (0.00, 3.43)	0.84 (0.00, 3.45)	1.22 (0.00, 3.92)	<0.001
IABP	6.78 (0.00, 15.00)	12.67 (8.00, 21.21)	12.50 (8.54, 19.35)	13.75 (8.02, 19.66)	<0.001
PCPS	0.00 (0.00, 1.27)	1.03 (0.00, 3.10)	1.38 (0.00, 2.56)	1.06 (0.00, 2.17)	<0.001
Fibrinolysis	0.00 (0.00, 0.00)	0.00 (0.00, 0.68)	0.00 (0.00, 0.52)	0.00 (0.00, 0.70)	0.40
Cardiac Rehabilitation	35.05 (10.96, 70.83)	59.95 (14.15, 81.77)	41.41 (12.43, 80.77)	60.75 (12.59, 85.63)	0.020

Values presented are given as number (percentage) unless stated.

SD = standard deviation, IQR = interquartile range, CAG = coronary angiography, PCI = percutaneous coronary intervention, CABG = coronary arterial bypass grafting, IABP = intra-aortic balloon pump, PCPS = Percutaneous Cardio Pulmonary Support.

**Table S6. Baseline hospital characteristics per quantiles by prescription rate of statin on discharge.**

	Q1 (188 Hospitals)	Q2 (183 Hospitals)	Q3 (185 Hospitals)	Q4 (185 Hospitals)	P
Age in years, mean (SD)	71.45 (4.39)	69.50 (2.51)	69.00 (2.34)	68.01 (2.44)	<0.001
Female	28.57 (24.39, 36.60)	27.30 (22.73, 30.77)	25.68 (22.05, 30.19)	24.52 (21.03, 28.44)	<0.001
Body mass index, mean (SD), kg/m <sup>2</sup>	23.26 (1.20)	23.67 (0.71)	23.72 (0.74)	23.86 (0.79)	<0.001
Hypertension	53.85 (40.00, 63.97)	62.80 (51.61, 71.26)	64.84 (56.82, 71.43)	67.97 (54.55, 77.78)	<0.001
Diabetes	27.27 (19.84, 35.34)	29.55 (22.22, 35.21)	29.29 (23.33, 35.71)	28.52 (22.60, 33.79)	0.40
Smoker (current and ex- smoker)	53.84 (41.62, 63.76)	57.14 (47.33, 65.79)	59.34 (50.53, 66.67)	60.00 (50.00, 67.95)	0.002
Hemodialysis	1.33 (0.00, 5.32)	2.27 (0.00, 4.04)	1.67 (0.00, 3.33)	1.95 (0.00, 3.08)	0.60
Charlson Score, mean (SD)	2.13 (0.38)	2.12 (0.32)	2.06 (0.31)	2.06 (0.34)	0.086

Killip Class I	42.86 (27.27, 57.79)	50.00 (34.15, 62.30)	50.68 (36.76, 63.36)	52.94 (35.38, 66.67)	<0.001
II	32.42 (21.40, 44.22)	28.89 (17.78, 40.00)	29.13 (20.41, 40.38)	29.44 (18.99, 40.00)	0.18
III	8.99 (4.35, 16.11)	8.06 (4.26, 12.23)	7.14 (3.23, 10.75)	6.58 (4.29, 9.72)	0.009
IV	10.60 (5.04, 17.52)	10.31 (6.41, 14.71)	10.00 (6.03, 14.29)	8.75 (4.79, 13.85)	0.091
CAG	90.91 (78.29, 96.43)	93.83 (88.71, 96.55)	94.74 (92.11, 97.06)	95.83 (92.89, 97.44)	<0.001
PCI	80.51 (63.64, 87.66)	85.94 (78.26, 90.14)	87.25 (81.71, 91.78)	87.72 (83.94, 92.31)	<0.001
CABG	0.00 (0.00, 1.36)	0.00 (0.00, 2.94)	1.05 (0.00, 4.11)	0.66 (0.00, 3.36)	<0.001
IABP	8.65 (0.00, 16.29)	12.41 (7.84, 20.41)	12.46 (7.76, 20.41)	12.40 (7.89, 18.25)	<0.001
PCPS	0.00 (0.00, 1.80)	1.04 (0.00, 2.90)	1.22 (0.00, 2.74)	0.53 (0.00, 2.00)	<0.001
Fibrinolysis	0.00 (0.00, 0.00)	0.00 (0.00, 0.26)	0.00 (0.00, 0.83)	0.00 (0.00, 0.69)	0.035
Cardiac Rehabilitation	30.22 (10.54, 71.13)	48.57 (13.38, 76.92)	66.67 (16.87, 85.37)	50.00 (10.77, 85.19)	<0.001

Values presented are given as number (percentage) unless stated.

SD = standard deviation, IQR = interquartile range, CAG = coronary angiography, PCI = percutaneous coronary intervention, CABG = coronary arterial bypass grafting, IABP = intra-aortic balloon pump, PCPS = Percutaneous Cardio Pulmonary Support.

**Table S7. Correlation of hospital prescription rate of guideline-directed medications.**

	<b>Aspirin (admission)</b>	<b>β-blocker (admission)</b>	<b>Aspirin (discharge)</b>	<b>β-blocker (discharge)</b>	<b>ACE-I/ARB (discharge)</b>	<b>Statin (discharge)</b>
<b>Aspirin (admission)</b>	1.00					
<b>β-blocker(admission)</b>	0.15*	1.00				
<b>Aspirin (discharge)</b>	0.37*	0.09*	1.00			
<b>β-blocker (discharge)</b>	0.13*	0.43*	0.34*	1.00		
<b>ACE-I/ARB (discharge)</b>	0.2*	0.14*	0.43*	0.33*	1.00	
<b>Statin (discharge)</b>	0.26*	0.13*	0.54*	0.31*	0.40*	1.00

\* Indicates p<0.05

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker

**Table S8. Incidence Rate Ratio for In-hospital Mortality According to the Quantile of Each Guideline-directed Medication by mixed Poisson regression model.**

	Q1	Q2		Q3		Q4		P for
	IRR	IRR (95% CI)	P	IRR (95% CI)	P	IRR (95% CI)	P	trend
<b>Multivariate analysis model 1</b> (Adjusted for age, sex, Charlson's comorbidity index and Killip class)								
<b>Aspirin (admission)</b>	1.00	0.89 (0.80-0.99)	0.039	0.77 (0.68-0.86)	<0.001	0.74 (0.66-0.83)	<0.001	<0.001
<b>β-blocker(admission)</b>	1.00	1.00 (0.90-1.11)	0.999	0.92 (0.83-1.03)	0.156	0.86 (0.77-0.97)	<0.001	0.003
<b>Aspirin (discharge)</b>	1.00	0.76 (0.68-0.84)	<0.001	0.70 (0.63-0.77)	<0.001	0.53 (0.47-0.59)	<0.001	<0.001
<b>β-blocker (discharge)</b>	1.00	0.87 (0.78-0.97)	0.011	0.81 (0.73-0.91)	<0.001	0.80 (0.72-0.90)	<0.001	<0.001
<b>ACE-I/ARB (discharge)</b>	1.00	0.89 (0.80,1.00)	0.042	0.82 (0.73-0.92)	0.001	0.74 (0.66-0.83)	<0.001	<0.001
<b>Statin (discharge)</b>	1.00	0.88 (0.79-0.98)	0.020	0.79 (0.71-0.88)	<0.001	0.68 (0.60-0.76)	<0.001	<0.001

<b>Multivariate analysis model 2</b> (Adjusted for age, sex, Charlson's comorbidity index, Killip class, hospital bed number, number of patients of AMI and number of cardiologists)								
<b>Aspirin (admission)</b>	1.00	0.91 (0.82-1.02)	0.115	0.79 (0.71-0.89)	<0.001	0.77 (0.69-0.87)	<0.001	<0.001
<b>β-blocker(admission)</b>	1.00	1.03 (0.93-1.14)	0.595	0.92 (0.82-1.02)	0.128	0.88 (0.78-0.98)	0.020	0.002
<b>Aspirin (discharge)</b>	1.00	0.79 (0.71-0.87)	<0.001	0.71 (0.64-0.78)	<0.001	0.54 (0.49-0.61)	<0.001	<0.001
<b>β-blocker (discharge)</b>	1.00	0.85 (0.76-0.95)	0.003	0.82 (0.73-0.91)	<0.001	0.80 (0.72-0.89)	<0.001	<0.001
<b>ACE-I/ARB (discharge)</b>	1.00	0.88 (0.79-0.98)	0.023	0.82 (0.74-0.92)	0.001	0.73 (0.65-0.82)	<0.001	<0.001
<b>Statin (discharge)</b>	1.00	0.88 (0.79-0.98)	0.021	0.80 (0.72-0.90)	<0.001	0.67 (0.62-0.76)	<0.001	<0.001

IRR = incidence rate ratio.

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; AMI, acute myocardial infarction



**Table S9. Hospital characteristics according to composite prescription score (CPS).**

	CPS 6-10 (188 Hospitals)	CPS 12-15 (195 Hospitals)	CPS 16-19 (217 Hospitals)	CPS 20-24 (141 Hospitals)	<b>P</b>
Age in years, mean (SD)	71.54 (4.32)	69.30 (2.69)	68.79 (2.47)	68.15 (2.15)	<0.001
Female	29.29 (24.32, 36.60)	26.83 (22.73, 31.03)	25.84 (22.08, 29.63)	24.53 (21.21, 27.01)	<0.001
Body mass index, mean (SD), kg/m <sup>2</sup>	23.27 (1.22)	23.73 (0.79)	23.72 (0.80)	23.81 (0.55)	<0.001
Hypertension	53.14 (40.00, 63.82)	61.54 (53.33, 67.78)	65.38 (54.90, 73.91)	69.62 (58.97, 78.64)	<0.001
Diabetes	27.68 (19.60, 34.81)	28.57 (21.26, 36.17)	29.58 (22.64, 34.72)	28.57 (23.53, 33.33)	0.45
Smoker (current and ex- smoker)	52.92 (40.00, 61.32)	58.52 (48.55, 67.05)	60.19 (51.18, 68.64)	57.92 (49.32, 65.90)	<0.001
Hemodialysis	0.31 (0.00, 4.52)	2.44 (0.00, 4.48)	1.96 (0.00, 3.39)	1.65 (0.00, 3.03)	0.029

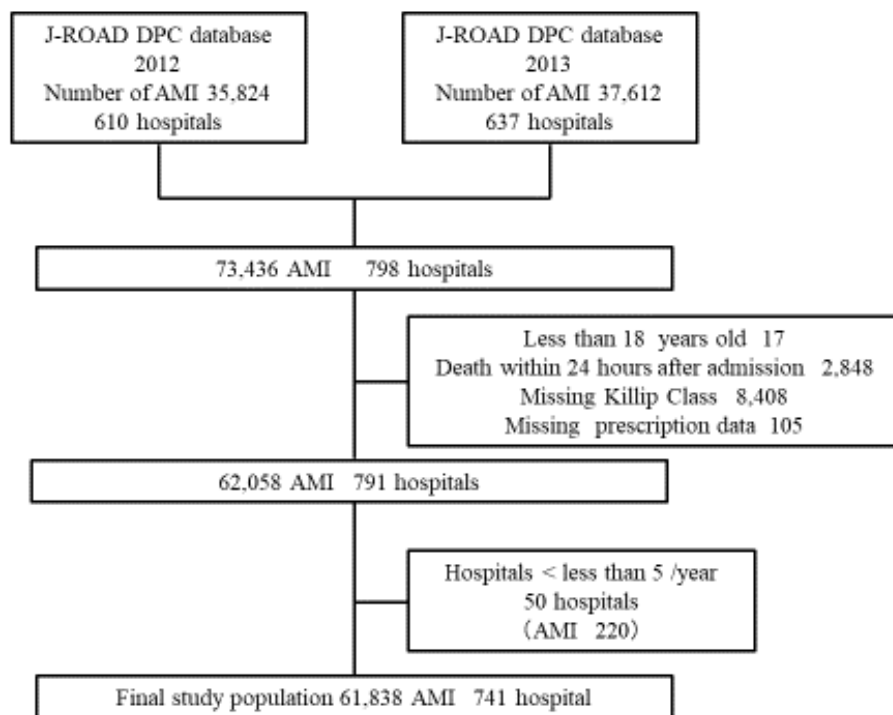
Charlson Score, mean (SD)	2.14 (0.35)	2.08 (0.34)	2.09 (0.36)	2.05 (0.30)	0.13
Killip Class I	43.66 (28.39, 60.00)	48.78 (34.48, 60.98)	53.13 (34.07, 65.00)	52.13 (37.87, 65.32)	0.011
II	30.66 (20.00, 42.62)	29.51 (19.32, 39.71)	30.34 (19.74, 44.44)	28.00 (20.00, 36.84)	0.70
III	8.75 (4.61, 15.87)	8.16 (4.30, 13.33)	6.51 (3.16, 10.23)	7.25 (4.42, 10.00)	0.003
IV	11.00 (5.56, 16.67)	11.02 (6.52, 17.07)	8.74 (5.00, 12.37)	9.52 (5.00, 13.95)	0.003
CAG	90.16 (77.00, 95.49)	93.67 (88.46, 96.67)	95.24 (92.59, 97.44)	96.10 (93.99, 97.40)	<0.001
PCI	78.20 (62.41, 87.37)	85.37 (79.19, 90.52)	87.40 (82.14, 91.72)	89.23 (85.71, 92.81)	<0.001
CABG	0.00 (0.00, 0.80)	0.00 (0.00, 3.23)	0.52 (0.00, 4.11)	1.22 (0.00, 2.78)	<0.001
IABP	6.67 (0.00, 14.50)	12.41 (7.69, 21.36)	11.90 (8.00, 19.35)	14.44 (9.52, 19.15)	<0.001
PCPS	0.00 (0.00, 1.67)	1.00 (0.00, 2.90)	1.10 (0.00, 2.47)	1.30 (0.00, 2.27)	<0.001
Fibrinolysis	0.00 (0.00, 0.00)	0.00 (0.00, 0.66)	0.00 (0.00, 0.77)	0.00 (0.00, 0.78)	0.056
Cardiac Rehabilitation	32.58 (11.75, 69.45)	45.00 (11.02, 80.00)	60.56 (15.33, 83.12)	65.91 (13.13, 87.18)	<0.001

Aspirin (admission)	77.95 (69.74, 84.57)	86.21 (81.82, 89.47)	88.89 (85.37, 91.84)	92.31 (89.94, 94.17)	<0.001
β-blocker(admission)	10.34 (5.04, 20.00)	18.54 (10.08, 29.63)	29.01 (18.67, 40.24)	45.68 (32.56, 58.14)	<0.001
Aspirin (discharge)	71.08 (62.87, 76.23)	79.17 (75.00, 83.33)	82.44 (78.57, 86.21)	85.90 (82.26, 88.89)	<0.001
β-blocker (discharge)	27.72 (16.52, 40.56)	44.22 (34.48, 55.24)	58.33 (50.00, 64.56)	68.99 (61.54, 75.13)	<0.001
ACE-I/ARB (discharge)	39.23 (27.27, 49.83)	58.21 (50.62, 64.29)	66.13 (59.09, 71.62)	74.15 (66.67, 79.25)	<0.001
Statin (discharge)	50.00 (39.24, 60.62)	65.31 (58.02, 71.00)	73.23 (67.95, 77.78)	79.08 (74.77, 82.72)	<0.001

Values presented are given as number (percentage) unless stated.

SD = standard deviation, IQR = interquartile range, CAG = coronary angiography, PCI = percutaneous coronary intervention, CABG = coronary arterial bypass grafting, IABP = intra-aortic balloon pump, PCPS = Percutaneous Cardio Pulmonary Support.

**Figure S1. Study Flow Chart.**



JROAD, Japanese Registry of All Cardiac and Vascular Diseases; DPC, Diagnostic Procedure Combination.