Assessment of Quality Indicators for Acute Myocardial Infarction Management in 28 Countries and Use of Composite Quality Indicators for Benchmarking

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Abstract

Background. The European Society of Cardiology (ESC) established a set of quality indicators (QIs) for the management of acute myocardial infarction (AMI). Our aim was to evaluate their degree of attainment, prognostic value and potential use for centre benchmarking in a large international cohort.

Methods. QIs were extracted from the long-tErm follow-uP of antithrombotic management patterns In acute CORonary syndrome patients (EPICOR) (555 hospitals, 20 countries in Europe and Latin America, 2010–2011) and EPICOR Asia (218 hospitals, 8 countries, 2011–2012) registries, including non-ST-segment elevation AMI (n=6,558) and ST-segment elevation AMI (n=11,559) hospital survivors. The association between implementation rates for each QI and 2-year adjusted mortality was evaluated using adjusted Cox models. Composite QIs (cQIs) were categorized for benchmarking assessment at different levels.

Results. The degree of attainment of the 17 evaluated QIs ranged from 13% to 100%. Attainment of most individual QIs was associated with 2-year survival. A higher compliance with cQIs was associated with lower mortality at centre-, country- and region-level. Moreover, the higher the risk for 2-year mortality, the lower the compliance with cQIs.

Conclusions. When EPICOR and EPICOR Asia were conducted, the ESC QIs would have been attained to a limited extent, suggesting wide room for improvement in the management of AMI patients. After adjustment for confounding, most QIs were associated with reduced 2-year mortality and their prognostic value should receive further attention. The two cQIs can be used as a tool for benchmarking either at centre-, country- or world region-level.

Keywords

Acute myocardial infarction; quality indicators; prognosis; benchmarking

Introduction

Acute myocardial infarction (AMI) is a leading cause of morbidity and mortality worldwide[1,2]. Interventions adopted in recent decades have led to widespread improvement in prognosis[3–7]. International guidelines recommend standard, evidence-based management. However, substantial variation in AMI management and clinical outcomes reported across countries[8,9] suggests poor implementation. Notably, measuring and reporting healthcare performance has been associated with good clinical outcomes[10]. Quality indicators (QIs) allow measuring the process of care in AMI patients and identifying the main gaps needing improvement at different healthcare levels.

The European Society of Cardiology (ESC) Acute Cardiovascular Care Association (ACCA) developed QIs for evaluating different domains of AMI care[11] and guiding future quality improvement interventions for worldwide implementation. Although quality assessment through these QIs would ideally require specific surveys, existing registries are suitable for a "reality checkpoint". QI evaluations at a national level [12,13] or comparing two countries[14] have been conducted, but there has not been a thorough assessment in an international registry including patients from different continents.

Using the long-tErm follow-uP of antithrombotic management patterns In acute CORonary syndrome patients (EPICOR) and EPICOR Asia cohorts[15,16] we aimed to assess: 1) the rate of implementation of the ACCA QIs and regional variations; 2) the prognostic value of QIs in terms of 2-year mortality; 3) the use of the composite QIs (cQIs) to benchmark at centre-, country- and world region-level.

Methods

Study design and Study population

EPICOR (NCT01171404) and EPICOR Asia (NCT01361386) are prospective, international, observational, real-world practice cohort studies comprising consecutive patients hospitalized for an acute coronary syndrome (ACS) who survived to hospital discharge[15,16].

The protocol and case record form were almost identical for both studies, and their rationale and designs were previously described[15,16]. Patient informed consent was obtained. The study protocol conforms to ethical guidelines of the 1975 Declaration of Helsinki. The inclusion criteria were: age ≥18 years, hospitalization within 24h (48h for Asia) of index event symptom onset and diagnosis of ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation ACS (NSTE-ACS) at discharge. Exclusion criteria were: 'secondary' ACS (precipitated by, or occurring as, a complication of surgery, trauma, gastrointestinal bleeding or percutaneous coronary intervention [PCI], or occurring during hospitalization for other reasons); any condition/circumstance limiting follow up completion; any serious/severe comorbidities limiting life expectancy to < 6 months; or previous enrolment in EPICOR or another clinical trial.

In total, 23,490 ACS patients were enrolled between September 2010 and March 2011 from 555 hospitals in 20 countries across Europe and Latin America (LA) (EPICOR, n=10,568), and between June 2011 and May 2012 from 219 hospitals across 8 countries in Asia (EPICOR Asia, n=12,922). Only patients with STEMI or NSTEMI were included in this study, hence excluding 5,373 patients with unstable angina (22.9%).

Follow-up and event definition

Patients were followed up by centralized telephone interviews by trained native speakers of each patient's language, supervised by a Direct Patient Contact Manager. Patients were interviewed 6 weeks after index event and every 3 months until censoring at 24 months. Events were recorded through specific questionnaires collecting hospitalizations or emergency

department visits. Medical information was obtained from the patient, hospital physicians or GPs and, whenever necessary, the primary study investigator was contacted to confirm or clarify the identified event. The primary outcome was all-cause mortality over 2-years.

Assessment of quality indicators and adjustment for predicted risk

The European Society of Cardiology (ESC) Acute Cardiovascular Care Association (ACCA) quality indicators (QIs) for AMI include 12 main and 8 secondary QIs[11], selected for their feasibility and reliability of assessment, and aligned with contemporary ESC guidelines.[17,18] These are organized in 3 areas with 7 domains: structure (centre organization), performance (reperfusion-invasive strategy, in-hospital risk assessment, antithrombotic treatment during hospitalization, secondary prevention discharge treatments), and patient satisfaction, with additional composite QIs (cQI)[11].

We evaluated each QI at individual-level, and cQIs at centre-, country- and world region-levels as described previously[19]. The denominators were the number of patients or proportion within hospitals where a QI was applicable. The numerator was the number or proportion of patients or hospitals satisfying the QI among those applicable. Three QIs could not be evaluated from EPICOR data: documentation of GRACE risk score (QI3.1), CRUSADE score (QI3.2) and patient-reported experience (QI6.1). Patients with missing data were excluded from the corresponding QIs. Denominators were calculated separately for each QI as appropriate.

QI domain 7 uses composite scores including one opportunity-based and one all-or-none score. The opportunity-based score was calculated by dividing the number of QIs achieved by the number of QIs the patient was eligible for or the hospital able to provide. We included nine measures available within EPICOR: 1) centre is part of a network organisation, 2) proportion of STEMI patients with first medical contact within 12h of symptom onset receiving reperfusion therapy; 3) coronary angiography in STEMI and NSTEMI without contraindications; 4) assessment of left ventricular (LV) ejection fraction before discharge; prescription of: 5) low-dose aspirin (unless high bleeding risk or oral anticoagulation); 6) $P2Y_{12}$

inhibitors; 7) angiotensin converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB) in patients with clinical evidence of heart failure (HF) or moderate/severe LV systolic dysfunction (LVSD); 8) beta-blockers (unless contraindicated) in patients with clinical evidence of HF or LVSD; and 9) statins. The all-or-none composite score (0 if any intervention is not provided, 1 if all QIs are provided) was calculated as follows: a) for those with LVEF>40% and no evidence of HF, the measures included treatment with low-dose aspirin, $P2Y_{12}$ inhibition, and high-dose statin; b) for those with LVSD or clinical evidence of HF, measures also included receiving beta-blockers and ACEi/ARB.

Admission heart rate and systolic blood pressure were not available to calculate the 30-day mortality GRACE score for QI7.3.[11,20]Instead, we used the EPICOR risk score to estimate the adjusted 2-year mortality risk, previously derived from the EPICOR and EPICOR Asia cohorts and, therefore, better fitted for risk prediction in this cohort[21]. This risk model contains 18 predictors of 2-year mortality available at discharge[21]: age, LVSD at discharge, lack of coronary revascularization or thrombolysis, elevated serum creatinine at admission, poor EuroQol-5 dimensions score (EQ-5D), low haemoglobin level, previous cardiac disease, previous chronic obstructive pulmonary disease, elevated blood glucose on admission, on diuretics at discharge, male sex, lower educational level, on aldosterone inhibitor at discharge, low body mass index, cardiac complications during index hospitalization, diagnosis of STEMI, Killip class and region. This score has already been used for mortality adjustment in previous studies[8,9,19,22].

Statistical analysis

Baseline categorical data are presented as number (percentage), whereas continuous data are presented as mean±SD or medians (interquartile range, IQR) for normally distributed or highly skewed data, respectively. The level of attainment of QIs is summarized at individual and regional-level, either as a percentage, mean and SD or median and IQR, as appropriate.

To estimate the predicted probabilities of 2-year mortality, we used a Cox regression model adjusted for the 18 EPICOR risk score predictors[21]. Predicted probabilities were used to

categorize the sample by risk deciles and evaluate their association with the percentage of compliance using a test for trends across ordered groups. A multivariable Cox proportional hazard regression model including all EPICOR risk score variables was developed to evaluate the strength of the association between QIs and 2-year mortality risk. "No coronary revascularization or thrombolysis" was excluded given its strong association with all other QIs from domain 2. Unadjusted and adjusted associations between QIs and mortality are presented as hazard ratios (HR) with 95% confidence intervals (CI).

The opportunity-based cQI was categorized as <80%, 80-99% and 100%. Kaplan–Meier survival curves were produced and compared across the three opportunity-based cQI categories using the log-rank test for equality of survivor functions. Cumulative mortality curves were obtained for the two all-or-none cQI categories.

To estimate the association between compliance with cQIs and 2-year mortality, we categorized the sample by terciles of attainment at both centre- and country-level. Comparisons of mortality across terciles were performed using tests for trends. Further, we split centres by the median of cQIs attainment within each country and evaluated their association with 2-year mortality with Cox regression analysis.

All *p* values were 2-sided and values <0.05 were considered as significant. All statistical analyses were performed using STATA software, version 13.1 (Stata Corp, College Station, TX, USA).

Results

Patient characteristics

Overall, 18,117 patients were enrolled from 770 hospitals in 28 countries across Europe and Latin America and Asia; 11,559 had STEMI and 6,558 NSTEMI. Centres included a median of 16 patients (IQR, 7-32). **Table** 1 shows baseline characteristics, clinical status on admission and in-hospital patient management.

QI assessment

Sixteen out of 20 QIs were assessed. **Table 2** shows the degree of completeness and compliance with QIs at an individual-level.

Domain 1: Centre Organization

Overall, 88.2% eligible patients had pre-hospital interpretation of an ECG (**QI1.1**). Time to reperfusion was available in 90.0% STEMI patients (**QI1.2**). All centres participated in a regular registry (EPICOR or EPICOR Asia), indicating 100% compliance with **QI1.3**, but limiting the evaluation of the association between the QI and mortality.

Domain 2: Reperfusion/Invasive strategy

The reperfusion rate within 12h of symptom onset (**QI2.1**) was 56.9%. Among STEMI patients admitted to PCI-capable centres, timely reperfusion occurred in 26.3% (**QI2.2**). Only patients were assessed because door-in-door-out times for transferred patients were unavailable. Time from first medical contact to arterial access (time to balloon was used as a proxy) (**QI2.4**) was available in 17.4% patients: median 2.8h (IQR: 1.4-13.2). Among NSTEMI patients, 67.5% underwent invasive strategy within 72h of presentation (**QI2.3**) (data available in 98.4%).

Domain 3: In-hospital risk assessment

GRACE and CRUSADE scores and some key predictors were not prospectively recorded in our cohorts. LVEF (**QI3.3**) was reported in 74.24% patients.

Domain 4: Antithrombotic treatment during hospitalization

The indication and use of $P2Y_{12}$ inhibitors (clopidogrel, prasugrel and ticagrelor) have changed over time. Use of prasugrel and ticagrelor was barely used in this cohort. Hence, we considered the use of any $P2Y_{12}$ inhibitor as adequate $P2Y_{12}$ inhibition at discharge (**QI4.1**). Overall, 94.0% patients received any $P2Y_{12}$ inhibitor (data available in 99.9%). Only 13.3%

NSTEMI patients received at least one fondaparinux injection (**QI4.2**), while 65.2% received either fondaparinux or low molecular weight heparin (LMWH). Among all STEMI and NSTEMI patients, 89.8% were discharged on DAPT (**QI4.3**).

Domain 5: Secondary prevention

Prescription of statins, beta-blockers and ACEis/ARBs was recorded, but not the type, dose and potential contraindications or intolerance. Statins (**QI5.1**) were prescribed in 91.3% of patients. LVEF≤40% or HF was reported in 2,844 patients (15.7%). Among them, 74.3% and 77.2% received ACEi/ARBs (**QI5.2**) and beta-blockers (**QI5.3**) at discharge, respectively. Data was available for >99% of this subset of patients.

Domain 6: Patient satisfaction

Full information regarding patient satisfaction information was not recorded (**QI6.1**). Nevertheless, we have data about pain control, which is one out of three points defining the patient satisfaction QI. Using the EuroQol-5 dimensions score (EQ-5D) questionnaire at discharge, pain control was recorded in 18,117 patients (98.9%). Among them, 13,883 (77.5%) had no pain, 3,781 (21.1%) had moderate pain and 251 (1.4%) patients had extrema pain. Further information can be found in Supplemental material (see section "Domain 6: Patient satisfaction".

Domain 7: cQI and adjusted mortality

The opportunity-based cQI (calculated using 9 of the original 12 items) was available for 85.3% patients. The mean was 83.1% (**QI7.1**). The all-or-none CQI was available for 99.5% patients and was attained in 92.6% (**QI7.2**). The EPICOR 2-year risk score was used to adjust mortality for confounding factors (**QI7.3**).

Association between risk categories and cQIs

Lower compliance in **QI7.1 and QI7.2** was associated with increasing 2-year mortality risk according to the deciles of EPICOR risk score ($p<0.001$ for the trend test for both comparisons) (**Figure 1**).

Association of QIs compliance and completeness with 2-year mortality

At patient-level, multivariable regressions showed an association between the attainment of most QIs and adjusted 2-year mortality risk (**Figure 2**). The association between QI 1.3 could not be evaluated given both the nature of the QI and the study design. Kaplan–Meier curves showed significant differences across levels of compliance with the opportunity-based and the all-or-none cQIs (**Figure 3**). There was a lower adjusted risk of death with increasing compliance for the opportunity-based cQI: (HR 0.68, (95% CI, 0.56-0.81) for 80-99% versus <80%; and 0.70 (0.59-0.82) for 100% versus <80% (p-value<0.001, likelihood ratio test). Similarly, there were significant differences between "non-fully compliant" and the "full compliant" groups in the all-or-none cQI (HR 0.81, 95%CI, 0.71-0.94; p=0.004). Notably, not only the degree of compliance, but also the degree of QI7.1 completeness was associated with the outcome in both the unadjusted ($p<0.001$) and adjusted ($p=0.040$) assessments (**Figure S1**).

Use of cQIs for benchmarking across centres, countries and world regions

Figure 4 shows the degree of attainment of all QIs across regions. Gaps in QI adherence can be identified reading by columns.

Poor compliance with cQIs was significantly associated with 2-year adjusted mortality risk at hospital level ($p<0.001$ for both comparisons using terciles of attainment) (**Figure 5**). This trend was consistent at country-level for QI7.1 (**Figure 5**), with a stronger association for STEMI than for NSTEMI patients (**Figure S2**).

We also evaluated compliance with QI7.1 and QI7.2 for each centre and assessed their distribution within countries (**Figure S3** and **Figure S4**). Moreover, we split the subset of

centres within each country by the median of attainment of the relevant cQIs (**Figure S5**). In most countries, patients admitted to hospitals below the median showed poorer post-discharge prognosis compared with those admitted to centres with QI compliance above the median ($p<0.001$ for both comparisons).

Discussion

Our study shows the strong relationship between compliance with QIs evaluating different domains of AMI care and 2-year adjusted post-discharge mortality risk both at the patient level and a system level, and how this compliance is suboptimal and heterogeneous globally across all examined levels.

Clinical trials demonstrate efficacy and safety of interventions in well-defined selected patient groups. QIs are measures often based on the results found in clinical trials. Proper evaluation of clinical healthcare quality requires the assessment of structures, and evaluating care processes and outcomes in large unselected populations in routine clinical practice[4]. Although the ESC-ACCA QIs have been evaluated in a number of national registries in France[12], UK[13,23], and Israel[14], no international evaluation to assess trans-national differences in patterns and quality of care has been performed. Our study included >18,000 patients from 28 countries and 3 continents, reflecting a variety of clinical practices from different economies, cultures and healthcare systems. Few QIs showed a rate of measurement >90%, indicating a first basic need. Some QIs such as "LV function recorded", which determines indication for evidence-based treatment with beta-blockers, ACEi/ARBs and mineralocorticoid receptor antagonists,[3,6,24] were surprisingly low. However, it is likely that the problem refers more to recording rather than measuring LV function. Similarly, recording the time to reperfusion was not associated with poor prognosis, despite there is plenty of evidence showing that the shorter the time, the better the survival[25]. Two main differences between our cohort and previous reports assessing QIs[12],[13] are evident: the very low proportion of patients with timely reperfusion —attributable to the international nature of our registry, including countries where

STEMI networks may not be as well developed as in France or UK—[8,9] and the high degree of compliance with cQIs. Most QIs were associated with reduced mortality internationally. This is not surprising, as missing ≥1 guideline-indicated intervention in eligible patients has been associated with excess mortality in AMI patients[26]. Interestingly, we found that not only compliance, but also completeness of the opportunity-based cQI was associated with prognosis. Notably, measuring quality performance in healthcare processes is essential in quality management.[10,27] Our results suggest that it may reflect a higher quality standard itself.

Registries are more prone to selection bias —the effect estimate in an observational study is different from the estimate obtainable from the target population[28]. It has been shown that the important proportion of patients missing from inclusion in prospective registries receive fewer guideline-recommended therapies and had a much higher mortality than those initially enrolled[28]. Thus, selection bias may result in an overestimation of actual quality and an underestimation of baseline risk and mortality rate. Likewise, our registry might have also missed some high-risk patients but, in that case, the observed declining compliance across increasing risk categories could in fact indicate an overestimation of QI compliance and underestimation of opportunities for improvement. Importantly, others have shown that optimal use of guideline-indicated care for AMI patients is associated with greater survival gains in patients with higher GRACE risk score values, although its use decreased with increasing GRACE risk[29]. This further emphasises the potential impact of QIs attainment on clinical outcomes.

Assessment of quality in healthcare delivery plays an increasingly relevant role in contemporary clinical practice. Governmental agencies, scientific societies, accreditation organizations and major insurers encourage the setting of performance measures and QIs to be applied by relevant healthcare institutions[27]. The relevance of ESC-ACCA QIs is based on the assumption that higher attainment by hospitals will translate into better clinical outcomes[27]. Our study provides evidence for the application of cQIs to compare health care processes across centres in a country and across countries and world regions. Importantly, cQIs are associated

with survival and can be helpful to classify centres according to quality. Benchmarking with this tool may identify opportunities for quality improvement and potentially improve clinical outcomes for AMI[30].

Our findings may have an impact at different levels. They could help in QIs definition updates and influence the design of future registries to capture this information. Future revisions of the QI set should consider the feasibility of assessing QIs in already available data sets (QIs like 3.1 and 3.2 are consistently not recorded in most reports[12–14]) and update some QIs to remain aligned with current guidelines (i.e. QI 2.1 refers to reperfusion rate within 12h symptom onset, whereas the 2017 STEMI guidelines[24] refers to the percentage of patients arriving in the first 12h who are reperfused). Moreover, it has to be decided whether keeping QIs with already high compliance (i.e. aspirin, statins) is worth, as they leave little room for improvement, whilst there are still vast differences in management and outcomes across countries[8,9]. The need for additional QIs should also be considered, particularly those affecting few patients (i.e. those related with LVSD and/or HF). Notably, our findings might also have a real impact on clinical practice, cQIs can be used for benchmarking and are associated with mortality at patient-, hospital-, country- and region-level. There is still much to improve within each country. Therefore, efforts by relevant stakeholders to improve QIs and hence clinical outcomes in the future are warranted.

Strengths and limitations

There are several limitations. Three QIs could not be fully evaluated (use of GRACE and CRUSADE risk scores and patient satisfaction), although this is the first time that an aspect of quality of care (i.e. pain control) is measured alongside other QIs defined by the ESC-ACCA and associated with clinical outcome, which is a key argument in favour of maintaining and developing patient-reported outcomes in quality assessment programmes. Some QIs related to antiplatelet therapy might not reflect reality given that antithrombotic therapy was particularly well recorded in EPICOR because it was the goal of this registry. Nevertheless prasugrel and ticagrelor were not available in the majority of countries while the study was conducted, thus

limiting the generalisability of QI 4.1. Despite these figures are not representative of clinical practice nowadays, there were appropriate at the time the study was conducted – the 2008 STEMI guidelines in use when patients were recruited recommend only clopidogrel, whereas the NSTEMI changed their recommendations in 2011, at the end of our study. Rates of prasugrel and ticagrelor prescription have increased over time in ACS[31] and, unlike when this registry was conducted, now most patients should have access to them. Time from first medical contact to arterial access was available only in 17.4% patients, with a median time of 2.8 hours - despite these figures (lack of reporting and long time) are representative of real-world clinical practice across 3 continents, they may have had an impact on prognosis[32]. Regarding survival analysis, most patients were censored during the last follow-up interview (24 months ±2 weeks). Selection of site investigators was not random and some degree of selection bias cannot be discarded, particularly if we take into account that a high proportion of highly motivated centers might overestimate QIs adherence [28]. Other sources of selection bias include lack of in-hospital quality assessment and as well as the inclusion of patients with an hospitalization within 24h (48h for Asia) of index event symptom onset. Central adjudication of outcomes was not used in EPICOR, though all-cause death is an unambiguous outcome. Some comparisons in mortality across terciles of QI compliance at country-level and between centres above or below their country median might be underpowered and hence some true associations may have been undetected. A major strength of our study is the comprehensive set of patients distributed in 28 countries assessed, and the evaluation of cQIs role for benchmarking at different levels. Our findings can be generalized as they derive from a large international database that includes subjects from different health systems treated in various hospital settings.

Conclusions

Our findings provide a picture of the variability in care quality for AMI patients in Europe, Latin America and Asia, identify domains of care where improvement is most needed, and confirm the association of most ESC-ACCA QIs with reduced adjusted post-discharge

mortality risk. The data support the use of cQIs as a useful tool for assessing quality of care at patient-, centre-, country- and world region-level.

Funding

The EPICOR and EPICOR Asia studies were funded by AstraZeneca.

Acknowledgements

CNIC is partially supported by a competitive grant from the Carlos III Institute of Health–Fondo de Investigacion Sanitaria and the European Regional Development Fund (ERDF/FEDER) (PI13/01979), the Spanish Ministry of Science, Innovation and Universities (MICINN) and the Pro-CNIC Foundation and is a Severo Ochoa Centre of Excellence (MINECO award SEV-2015-0505). X.R. received support from the SEC-CNIC CARDIOJOVEN fellowship program.

Declaration of conflicting interests

X Rossello has nothing to disclose. J Medina is an employee of AstraZeneca. S Pocock has received research funding from AstraZeneca. F Van de Werf has received consulting fees and research grants from Boehringer Ingelheim, Merck and Sanofi, and consulting and speaking fees from Boehringer Ingelheim, Roche, Sanofi, AstraZeneca, and The Medicines Company. CT Chin has received consulting or speaking fees from AstraZeneca, Merck, Servier, and Medtronic. N Danchin has received consulting or speaking fees from Amgen, AstraZeneca, Bayer, BMS, Boehringer-Ingelheim, MSD, NovoNordisk, Pfizer, Sanofi-Aventis, and Servier. SW-L Lee has nothing to disclose. Y Huo has nothing to disclose. H Bueno receives research funding from the Instituto de Salud Carlos III, Spain (PIE16/00021 & PI17/01799), AstraZeneca, BMS, Jansen and Novartis, has received consulting fees from AstraZeneca, Bayer, BMS-Pfizer, Novartis, and speaking fees or support for attending scientific meetings from AstraZeneca, Bayer, BMS-Pfizer, Ferrer, Novartis, and MEDSCAPE-the heart.org.

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Figure legends

Figure 1. Composite quality indicator attainment by predicted mortality risk deciles

Panel A represents the mean percentage of cQI7.1 attainment by mortality risk deciles Panel B stands for cQI7.2. The definition of the composite quality indicators are detailed in Table S1.

cQI, composite quality indicator; D1, decile 1; D2, decile 2…; D10, decile 10

Figure 2. Associations between quality indicators and 2-year mortality risk

Association of quality indicators with 2-year mortality by Cox proportional hazards regressions. Hazard ratios are adjusted for 17 risk factors: age, ejection fraction at admission, serum creatinine at admission, EuroQol-5Dscore, hemoglobin, previous cardiac disease, previous chronic obstructive pulmonary disease, blood glucose at admission, on diuretics at discharge, male sex, educational level, on aldosterone inhibitor at discharge, body mass index, in hospital cardiac complications, diagnosis of STEMI, Killip class and region.

ACEI/ARB, angiotensin converting enzyme inhibitors/angiotensin II receptor blockers; BB, beta-blocker; cQI, composite quality indicator;DAPT, dual antiplatelet therapy; HR, hazard ratio; LV, left ventricular; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction

Figure 3. Kaplan-Meier survival curves for 2-year mortality by composite quality indicators

Cumulative time-to-first-event curves and p-value for the log-rank test for patients according to the degree of compliance of the opportunity-based composite quality indicator (A) and categories of the "all or none" composite quality indicator (B). On the right, unadjusted and adjusted hazard ratios with their 95% confidence intervals (HR, 95% CI) are shown. The adjusted model contains all 18 factors of the EPICOR 2-year risk score. The definition of the composite quality indicators are detailed in Table S1.

cQI, composite Quality Indicator

Figure 4. **Degree of attainment of quality indicators by region**

Definition of regions: Southern Europe (France, Greece, Italy and Spain), Northern Europe (Belgium, Denmark, Finland, Germany, Luxembourg, The Netherlands, Norway, and United Kingdom), Eastern Europe (Poland, Romania, Slovenia and Turkey), Latin America (Argentina, Brazil, Mexico and Venezuela), China, India, South-East Asia (Malaysia, Vietnam and Thailand) and South Korea-Singapore-Hong Kong. The definition of the composite quality indicators are detailed in Table S1.

* the estimates related to QI2.4 in red should be taken with caution as only 2,012 (17.4%) patients had available data

ACE/ARB, angiotensin converting enzyme inhibitor/angiotensin II receptor blocker; BB, beta blocker; cQI, composite Quality Indicator; LVEF, left ventricular ejection fraction; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction

Figure 5. **Association between terciles (T1, T2, T3) of compliance with composite quality indicators at hospital- and country-level and 2-year mortality rates**

The definition of the composite quality indicators are detailed in Table S1.

cQI, composite quality indicator

Table 1. *Baseline characteristics and patient management by type of event*

	Overall population	NSTEMI	STEMI
Number of hospitals	770	716	737
Number of patients (% of patients)	18,117	6,558 (36.2%)	11,559 (63.8%)
Baseline characteristics			
Age (years), mean (SD)	60.5 (12.2)	63.3 (12.3)	58.9 (11.9)
Age>75 y, n (%)	2,642 (14.6%)	1,382 (21.1%)	1,260 (10.9%)
Male, n (%)	14,170 (78.2%)	4,800 (73.2%)	9,370 (81.1%)
Hypertension, n (%)	9,454 (52.8%)	4,023 (62.0%)	5,431 (47.5%)
Hypercholesterolemia, n (%)	5,392 (31.0%)	2,543 (40.2%)	2,849 (25.7%)
Diabetes mellitus, n (%)	4,160 (23.3%)	1,828 (28.2%)	2,332 (20.5%)
Currently smoking, n (%)	5,930 (35.0%)	2,332 (38.0%)	3,598 (33.3%)
Prior CVD, n (%)	4,678 (26.2%)	2,484 (38.4%)	2,194 (19.3%)
Clinical data collected during hospitalization, n (%)			
LVEF <40%, n (%)	1,771 (10.5%)	578 (9.6%)	1,193 (11.1%)
Creatinine ≥1.2 mg/dl, n (%)	4,130 (26.0%)	1,400 (24.4%)	2,730 (27.0%)
Glucose >160 g/dl, n (%)	4,239 (24.6%)	1,770 (28.1%)	2,469 (22.5%)
Hemoglobin ≤13 mg/dl, n (%)	4,720 (27.5%)	1,924 (30.8%)	2,796 (25.6%)
Patient management, n (%)			
Coronary intervention, n (%)	12,856 (71.7%)	4,034 (62.0%)	8,822 (77.2%)
PCI, n (%)	12,584 (70.1%)	3,838 (58.9%)	8,746 (76.5%)
CABG, n (%)	294 (1.6%)	204 (3.1%)	90 (0.8%)
Aspirin at discharge, n (%)	17,392 (96.1%)	6,258 (95.5%)	11,134 (96.5%)
BB at discharge, n (%)	14,201 (78.6%)	5,307 (81.2%)	8,894 (77.1%)
ACEI/ARB at discharge, n (%)	12,926 (71.6%)	4,687 (71.7%)	8239 (71.5%)
MRA at discharge, n (%)	1,658 (9.2%)	474 (7.3%)	1,184 (10.3%)
Observed 2-year mortality, n (%)	1,046 (5.8%)	472 (7.2%)	574 (5.0%)

ACE/ARB, angiotensin converting enzyme inhibitor/angiotensin II receptor blocker; BB, beta blocker; CABG, coronary artery bypass graft; CVD, cardiovascular disease; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction

Table 2

Table 2. *Quality indicators assessment in the EPICOR and EPICOR Asia registries*

Domain	Quality indicator (QI)	Type of QI	Eligible patients	No. of patients with available data (%)	QI attainment at individual-level
1: Centre organization	1.1 Centre organization: part of network	Main	18,117	15,971 (88.2%)	88.2%
	1.2: Routine assessment of times to reperfusion in STEMI patients	Secondary	11,559	11,559 (100%)	90.0%
	1.3: Participate in regular registry	Secondary	18,117	11,559 (100%)	100%
2: Reperfusion/invasive strategy	2.1: Reperfusion within 12 h of presentation (STEMI)	Main	11,559	11,225 (97.1%)	56.9%
	2.2 Timely reperfusion (STEMI)	Main	11,559	11,225 (97.1%)	26.3%
	2.3: Coronary angiography received within 72 h (NSTEMI patients only)	Main	6,558	6,455 (98.4%)	67.5%
	2.4: Time from diagnosis to wire passage (STEMI), minutes (median, IQR)	Secondary	11,559	2,012 (17.4%)	2.8 (1.4 - 13.2)
3: In Hospital risk assessment	3.1: GRACE risk score recorded in notes	Main	NR	NR	NR
	3.2: CRUSADE risk score recorded in notes	Main	NR	NR	NR
	3.3: LV function recorded in notes	Main	18,117	16,885 (93.2%)	74.2%
4: Anti thrombotics during hospital	4.1: Adequate P2Y12 inhibition on discharge	Main	18,117	18,101 (99.9%)	94.0%
	4.2: Fondaparinux received (NSTEMI patients only) Main	Main	6,558	6,558 (100%)	13.3%
	Fondaparinux or LMWH received (NSTEMI patients only)		6,558	6,558 (100%)	65.2%
	4.3: DAPT received on discharge	Secondary	18,117	18,027 (99.5%)	89.8%
5: Secondary prevention	5.1: High intensity statins on discharge	Main	18,117	18,034 (99.5%)	91.3%
	5.2: ACEi/ARB on discharge for those with HF or LVEF ≤40	Secondary	2,844	2,833 (99.6%)	74.3%
	5.3: Beta-blocker on discharge for those with HF or LVEF ≤40	Secondary	2,844	2,835 (99.7%)	77.2%
6: Patient satisfaction		Main	NR	NR	NR
7: Composite QI	7.1 Composite QI (opportunity-based) , mean (SD)	Main	18,117	15,451 (85.3%)	84.0 (15.8)
	7.2 Composite QI (all-or-none, overall score), mean (SD)	Secondary	18,117	18,024 (99.5%)	92.8 (15.8)
	7.3 Mortality rate adjusted for GRACE risk*	Secondary	18,117	18,117 (100%)	N/A

NR, not recorded

*To adjust mortality for potential confounding factors, we used the 2-year EPICOR risk score rather than the GRACE risk score

Figure 1

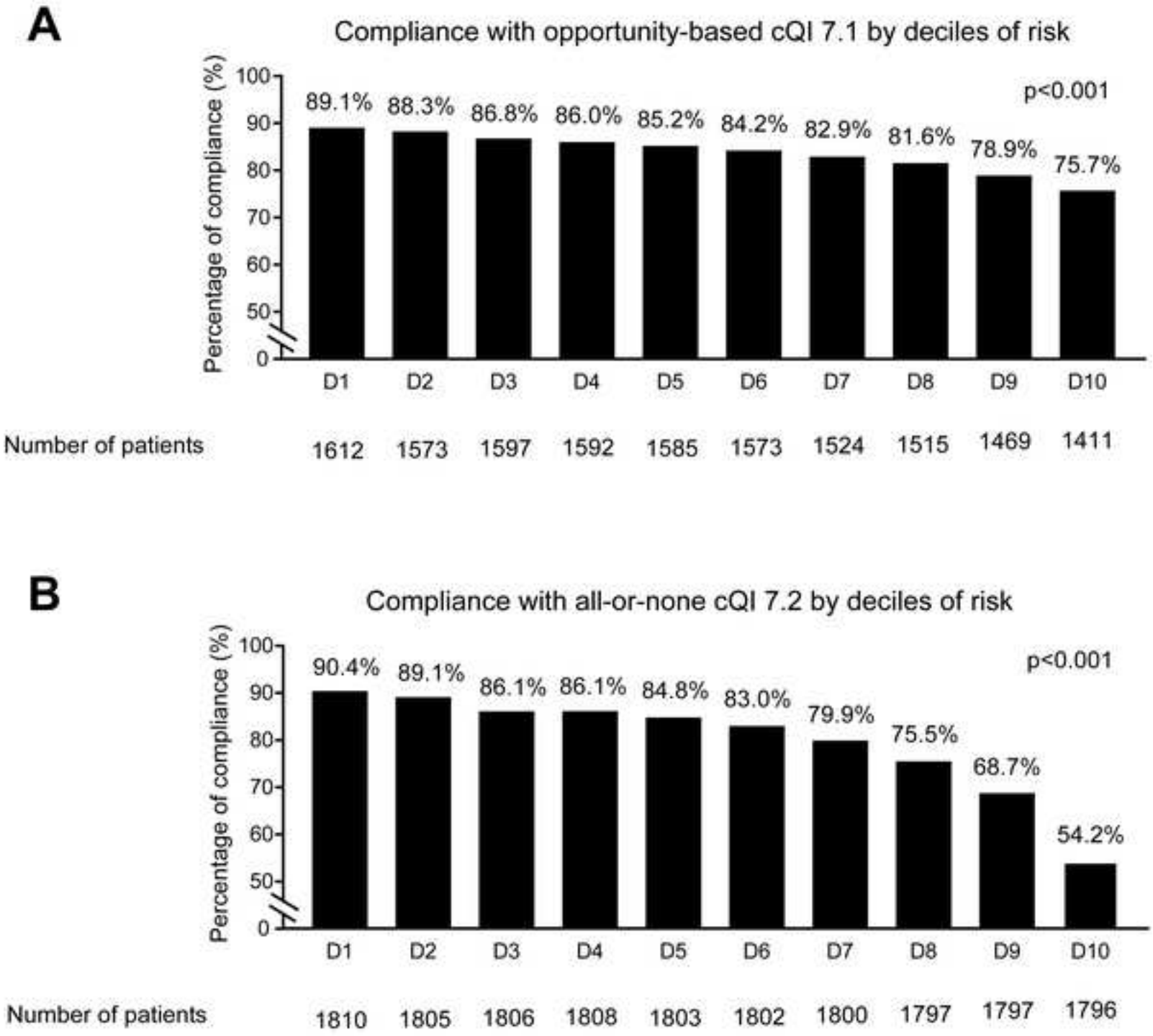

A
Compliance with opportunity-based cQI 7.1 by deciles of risk
Percentage of compliance (%)
100
90
80
70
60
50
0
p<0.001
89.1%
88.3%
86.8%
86.0%
85.2%
84.2%
82.9%
81.6%
78.9%
75.7%
D1
D2
D3
D4
D5
D6
D7
D8
D9
D10
Number of patients
1612
1573
1597
1592
1585
1573
1524
1515
1469
1411
B
Compliance with all-or-none cQI 7.2 by deciles of risk
Percentage of compliance (%)
100
90
80
70
60
50
0
p<0.001
90.4%
89.1%
86.1%
86.1%
84.8%
83.0%
79.9%
75.5%
68.7%
54.2%
D1
D2
D3
D4
D5
D6
D7
D8
D9
D10
Number of patients
1810
1805
1806
1808
1803
1802
1800
1797
1797
1796

Figure 2

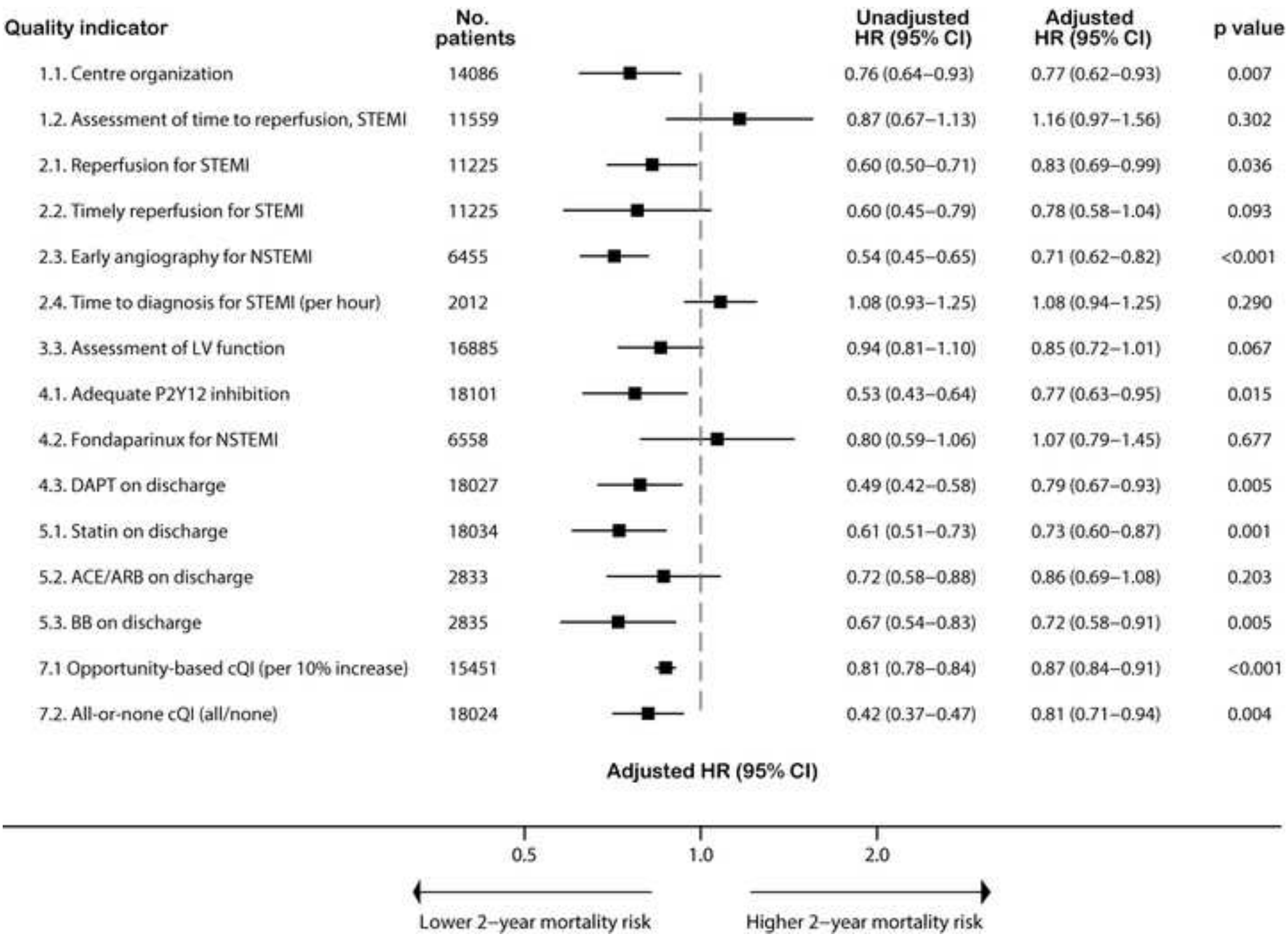

Quality indicator
No. patients
Unadjusted HR (95% CI)
Adjusted HR (95% CI)
p value
1.1. Centre organization
14086
0.76 (0.64–0.93)
0.77 (0.62–0.93)
0.007
1.2. Assessment of time to reperfusion, STEMI
11559
0.87 (0.67–1.13)
1.16 (0.97–1.56)
0.302
2.1. Reperfusion for STEMI
11225
0.60 (0.50–0.71)
0.83 (0.69–0.99)
0.036
2.2. Timely reperfusion for STEMI
11225
0.60 (0.45–0.79)
0.78 (0.58–1.04)
0.093
2.3. Early angiography for NSTEMI
6455
0.54 (0.45–0.65)
0.71 (0.62–0.82)
<0.001
2.4. Time to diagnosis for STEMI (per hour)
2012
1.08 (0.93–1.25)
1.08 (0.94–1.25)
0.290
3.3. Assessment of LV function
16885
0.94 (0.81–1.10)
0.85 (0.72–1.01)
0.067
4.1. Adequate P2Y12 inhibition
18101
0.53 (0.43–0.64)
0.77 (0.63–0.95)
0.015
4.2. Fondaparinux for NSTEMI
6558
0.80 (0.59–1.06)
1.07 (0.79–1.45)
0.677
4.3. DAPT on discharge
18027
0.49 (0.42–0.58)
0.79 (0.67–0.93)
0.005
5.1. Statin on discharge
18034
0.61 (0.51–0.73)
0.73 (0.60–0.87)
0.001
5.2. ACE/ARB on discharge
2833
0.72 (0.58–0.88)
0.86 (0.69–1.08)
0.203
5.3. BB on discharge
2835
0.67 (0.54–0.83)
0.72 (0.58–0.91)
0.005
7.1 Opportunity-based cQI (per 10% increase)
15451
0.81 (0.78–0.84)
0.87 (0.84–0.91)
<0.001
7.2. All-or-none cQI (all/none)
18024
0.42 (0.37–0.47)
0.81 (0.71–0.94)
0.004
Adjusted HR (95% CI)
0.5
1.0
2.0
Lower 2–year mortality risk
Higher 2–year mortality risk

Figure 3

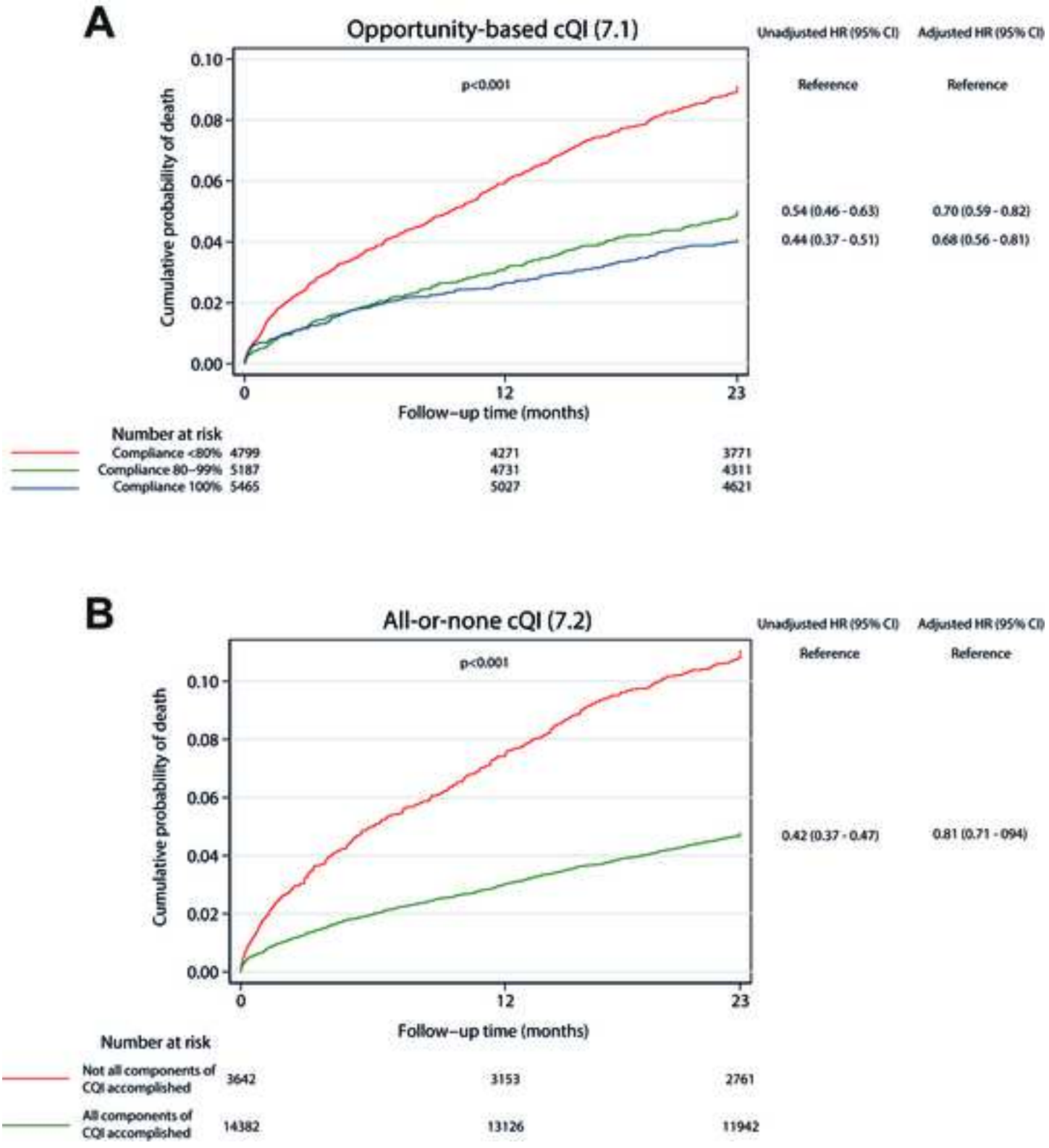

A
Opportunity-based cQI (7.1)
Unadjusted HR (95% CI)
Adjusted HR (95% CI)
p<0.001
Reference
Reference
0.54 (0.46 - 0.63)
0.70 (0.59 - 0.82)
0.44 (0.37 - 0.51)
0.68 (0.56 - 0.81)
Cumulative probability of death
0.10
0.08
0.06
0.04
0.02
0.00
0
12
23
Follow-up time (months)
Number at risk
Compliance <80% 4799 4271 3771
Compliance 80–99% 5187 4731 4311
Compliance 100% 5465 5027 4621
B
All-or-none cQI (7.2)
Unadjusted HR (95% CI)
Adjusted HR (95% CI)
p<0.001
Reference
Reference
0.42 (0.37 - 0.47)
0.81 (0.71 - 094)
Cumulative probability of death
0.10
0.08
0.06
0.04
0.02
0.00
0
12
23
Follow-up time (months)
Number at risk
Not all components of CQI accomplished 3642 3153 2761
All components of CQI accomplished 14382 13126 11942

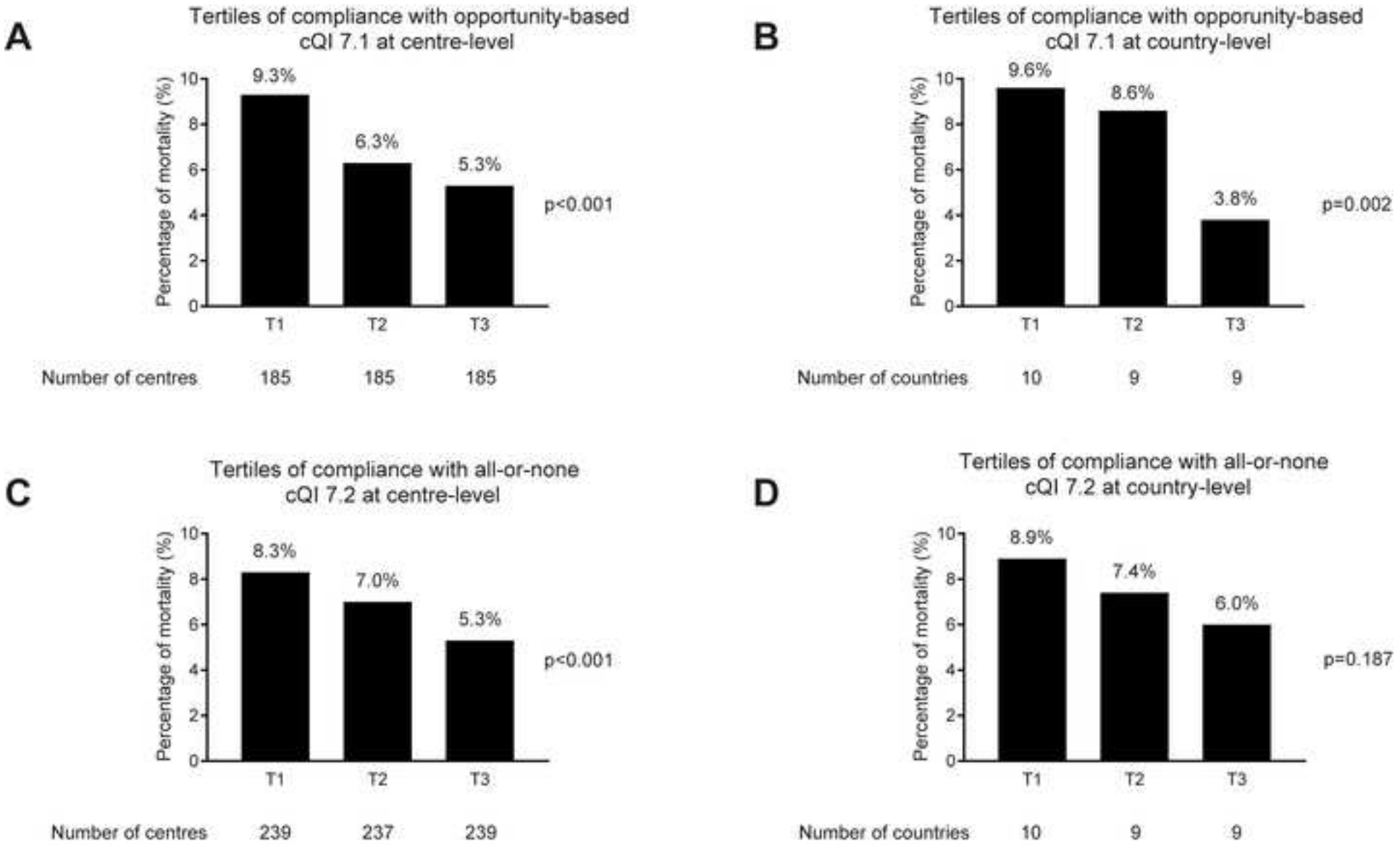
Figure 4

	Southern Europe	Northern Europe	Eastern Europe	Latin America	China	SK, HK & Singapore	India	South-East Asia
N, (%)	2034	3443	1806	1649	5276	745	2044	1121
Quality indicators								
1.1. Centre organization	90%	66%	93%	81%	95%	95%	98%	79%
1.2. Routine assessments of times to reperfusion in STEMI	86%	87%	97%	92%	97%	88%	67%	98%
2.1. STEMI reperfused	70%	74%	72%	49%	47%	72%	38%	65%
2.2. STEMI timely reperfusion	19%	22%	29%	3%	14%	25%	5%	9%
2.3. NSTEMI early angiography	81%	81%	77%	52%	81%	88%	55%	61%
2.4. STEMI: diagn.-wire time(h)*	2.0 (1.1-4.9)	1.7 (1.0-3.4)	2.0 (1.3-3.2)	5.3 (2.7-47.6)	6.6 (2.8-124.9)	1.7 (1.4-3.8)	7.3 (3.7-29.5)	6.2 (2.8-15.2)
3.3. LVEF assessment	93%	78%	88%	73%	81%	84%	60%	81%
4.1. Adequate $P2Y_{12}$ inhibition	93%	91%	94%	89%	97%	96%	93%	95%
4.2. Fondaparinux for NSTEMI	14%	15%	6%	3%	16%	0%	1%	6%
4.3. DAPT on discharge	89%	87%	90%	85%	96%	94%	81%	93%
5.1. Statin on discharge	94%	94%	93%	93%	94%	84%	78%	90%
5.2. ACEI/ARB on discharge	83%	86%	86%	80%	68%	73%	55%	64%
5.3. BB on discharge	85%	91%	94%	81%	71%	78%	58%	57%
7.1 Opportunity-based cQI	90%	84%	90%	78%	85%	89%	74%	83%
7.2. All-or-none cQI	95%	94%	95%	92%	95%	92%	84%	92%

Legend for proportions:

100-90%	89-80%	79-70%	69-60%	59-50%	<50%

Figure 5


A
Tertiles of compliance with opportunity-based cQI 7.1 at centre-level
Percentage of mortality (%)
9.3%
6.3%
5.3%
p<0.001
T1
T2
T3
Number of centres
185
185
185
B
Tertiles of compliance with opporunity-based cQI 7.1 at country-level
Percentage of mortality (%)
9.6%
8.6%
3.8%
p=0.002
T1
T2
T3
Number of countries
10
9
9
C
Tertiles of compliance with all-or-none cQI 7.2 at centre-level
Percentage of mortality (%)
8.3%
7.0%
5.3%
p<0.001
T1
T2
T3
Number of centres
239
237
239
D
Tertiles of compliance with all-or-none cQI 7.2 at country-level
Percentage of mortality (%)
8.9%
7.4%
6.0%
p=0.187
T1
T2
T3
Number of countries
10
9
9