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REVIEW

Comparative overview of ST-elevation myocardial infarction epidemiology, demographics, management, and outcomes in five Asia-Pacific countries: a meta-analysis

Paul Jie Wen Tern [1†], Aaron Kwun Hang Ho[2†], Rehena Sultana[3], Youngkeun Ahn[4], Wael Almahmeed[5], David Brieger[6], Derek P. Chew[7], Alan Yean Yip Fong[8], Jinyong Hwang[9], Yongcheol Kim[10], Issei Komuro[11], Koji Maemura[12], Rosli Mohd-Ali[13], David Kwang Leng Quek[14], Christopher Reid[15], Jack Wei Chieh Tan[16], Wan Azman Wan-Ahmad[17], Satoshi Yasuda[18], and Khung Keong Yeo[16]*

[1]Department of Medicine, Singapore General Hospital, Outram Rd, Singapore 169608; [2]School of Medicine, Gaol Walk, University College Cork, Cork, T12 YN60, Republic of Ireland; [3]Graduate Medical School, Duke-National University of Singapore, 8 College Rd, Singapore 169857; [4]Division of Cardiology, Department of Internal Medicine, Chonnam National University Hospital, 42 Jebong-ro, Dong-gu, Gwangju 61469, Korea; [5]Heart and Vascular Institute, Cleveland Clinic Abu Dhabi, Zayed The First St - Jazeerat Al Maryah Sowwah Square, Abu Dhabi, United Arab Emirates; [6]Department of Cardiology, Concord Hospital, University of Sydney, Sydney, Hospital Rd, Concord NSW 2139, Australia; [7]College of Medicine and Public Health, Flinders University of South Australia, Adelaide, Level 5, Room 5E209 Flinders Medical Centre, Bedford Park SA 5042, Australia; [8]Department of Cardiology, Clinical Research Center, Sarawak General Hospital, Jalan Hospital, 93586 Kuching, Sarawak, Malaysia; [9]Division of Cardiology, Department of Internal Medicine, Gyeongsang National University Hospital, Gyeongsangnam-do, Korea; [10]Division of Cardiology, Department of Internal Medicine, Yonsei University College of Medicine and Cardiovascular Center, Yongin Severance Hospital, Yongin, Republic of Korea, 50-1 Yonsei-ro, Sinchon-dong, Seodaemun-gu, Seoul, South Korea; [11]Department of Cardiovascular Medicine, The University of Tokyo Hospital, 7 Chome-3-1 Hongo, Bunkyo City, Tokyo 113-8655, Japan; [12]Department of Cardiovascular Medicine, Graduate School of Biomedical Sciences, Nagasaki University, 1-14 Bunkyomachi, Nagasaki, 852-8521, Japan; [13]Department of Cardiology, National Heart Institute, IJN, 145, Jalan Tun Razak, 50400 Kuala Lumpur, Malaysia; [14]Department of Cardiology, Pantai Hospital Kuala Lumpur, 8, Jalan Bukit Pantai, Bangsar, 59100 Kuala Lumpur, Wilayah Persekutuan Kuala Lumpur, Malaysia; [15]School of Epidemiology and Preventive Medicine, Monash University, 553 St Kilda Road, Melbourne VIC 3004, Australia; [16]Department of Cardiology, National Heart Centre Singapore, 5 Hospital Dr, Singapore 169609; [17]Faculty of Medicine, University Malaya Medical Center, Jalan Universiti, 59100 Kuala Lumpur, Selangor, Malaysia; and [18]Department of Cardiovascular Medicine, National Cerebral and Cardiovascular Center, 6-1 Kishibeshinmachi, Suita, Osaka 564-8565, Japan

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The aim of this study is to gain insight into the differences in demographics of ST-elevation myocardial infarction (STEMI) patients in Asia-Pacific, as well as inter-country variation in treatment and mortality outcomes. Systematic review of published studies and reports from known registries in Australia, Japan, Korea, Singapore, and Malaysia that began data collection after the year 2000. Supplementary self-report survey questionnaire on public health data answered by representative cardiologists working in these countries. Twenty studies comprising of 158 420 patients were included in the meta-analysis. The mean age was 61.6 years. Chronic kidney disease prevalence was higher in Japan, while dyslipidaemia was low in Korea. Use of aspirin, $P2Y_{12}$ inhibitors, and statins were high throughout, but ACEi/ARB and β-blocker prescriptions were lower in Japan and Malaysia. Reperfusion strategies varied greatly, with high rates of primary percutaneous coronary intervention (pPCI) in Korea (91.6%), whilst Malaysia relies far more on fibrinolysis (72.6%) than pPCI (9.6%). Similarly, mortality differed, with 1-year mortality from STEMI was considerably greater in Malaysia (17.9%) and Singapore (11.2%) than in Korea (8.1%), Australia (7.8%), and Japan (6.2%). The countries were broadly similar in development and public health indices. Singapore has the highest gross national income and total healthcare expenditure per capita, whilst Malaysia has the lowest. Primary PCI is available in all countries 24/7/365. Despite broadly comparable public health systems, differences exist in patient profile, in-hospital treatment, and mortality outcomes in these five countries. Our study reveals areas for improvements. The authors advocate further registry-based multi-country comparative studies focused on the Asia-Pacific region.

Keywords STEMI • Systematic review • Demographics • Treatment • Mortality • Asia-Pacific

* Corresponding author. Tel: +65 670 48963, Email: yeo.khung.keong@singhealth.com.sg
†These authors are joint first authors.

Highlights

- Mean age of ST-elevation myocardial infarction (STEMI) patients is highest in Japan (67.1 years); chronic kidney disease prevalence is highest in Japan (36.6%); dyslipidaemia prevalence is considerably lower in Korea (10.1%).
- Similar prevalence in risk factors of medical history of hypertension, cerebrovascular disease, previous myocardial infarction, previous percutaneous coronary intervention (PCI), and previous Coronary Artery Bypass Graft (CABG).
- Use of aspirin, statin and $P2Y_{12}$ inhibitors are high in all countries; lower use of β-blockers and Angiotensin Converting Enzyme Inhibitors/Angiotensin Receptor Blockers (ACE-i/ARB) in Japan and Malaysia.
- High rates of primary PCI use in Korea (91.6%); far lower rates of PCI use in Malaysia (9.6%). Primary PCI use in Australia (65.0%), Japan (77.5%), and Singapore (63.8%) in line with international rates.
- One-year mortality from STEMI was greatest in Malaysia (17.9%) and Singapore (11.2%) than in Korea (8.1%), Australia (7.8%), and Japan (6.2%).

Introduction

Ischaemic heart disease represents a major source of morbidity and mortality in the Asia-Pacific region.[1–4] In particular, ST-elevation myocardial infarction (STEMI) mortality remains high and continues to demonstrate significant geographical variation.[3–8] Despite a relative decrease in the proportion of myocardial infarction (MI) due to STEMI over the years,[1,9] it still accounts for ~40% of all presentations with acute myocardial infarction (AMI).[1,3]

STEMI is a well-defined clinical entity, with established guidelines[10,11] around diagnosis and optimal management supported by a large body of high-quality evidence. These guidelines recommend a defined and standardized pathway of early reperfusion, involving the co-ordination of many aspects of the healthcare system ranging from emergency services to catheter laboratories. Hence, such explicit algorithms are useful for broadly comparing public health systems based on whether they are able to meet these yardsticks, as well as by comparing downstream outcomes such as mortality. Furthermore, STEMI mortality can be seen as a useful indicator of healthcare system maturity, and these outcome measures can be used to stimulate change and measure progress.

The Asia-Pacific countries are at different stages of economic development and have different treatment pathways, but the extent of the differences between these countries is not clear. In order to drive improvement, it is imperative that an understanding of the 'lay-of-the land' be available. This process of capturing the current epidemiological picture and benchmarking individual countries' performances is facilitated by international registries. Yet, with the exception of the GRACE[12] and EPICOR-Asia cohorts,[13] there has been a notable lack of representation of the Asia-Pacific region.

In the absence of a current prospective observational Asia-Pacific registry, we sought to achieve a similar analysis by a retrospective meta-analysis of published data from multiple country-wide registries. We began by focusing on the demographics, comorbidity profile, presentation characteristics, treatments, and outcomes of STEMI patients in five Asia-Pacific countries, which were selected for the availability of data as well as their similarity in terms of development indices to other Western nations in the aforementioned registries.

Methods

This review was registered with PROSPERO (CRD42018104470). A systematic search of MEDLINE, Embase, and Cochrane databases was carried out on 22 May 2020. The articles published between 1 January 2000 and the date of the search were identified. In addition to these articles, we hand-searched known country-specific registries for their reports, which may not have been indexed by these databases. A data request was also submitted to Singapore's National Registry of Diseases Offices for supplementary data that had been collected but not featured in their 2018 report.[14] Articles were restricted to those published in English. The search strategy is provided in Supplementary material online, *Table S3*.

Study selection

Figure 1 shows the screening process of articles. Inclusion criteria were patients presenting with STEMI in the countries Australia, Japan, Korea, Malaysia, and Singapore. Standard ECG definitions of STEMI were adopted.[15] Studies were limited to those that commenced data collection after the year 2000 and recruited at least 500 participants. Studies with data pertaining to non-STEMI (NSTEMI) or mixed STEMI/NSTEMI populations (e.g. JAMIR) were excluded.

Care was taken to ensure that shortlisted articles had patient populations that were representative of STEMI all-comers in the respective countries. As such, study populations that were deemed too specific (e.g. specific age groups and uni-modality of treatment) were excluded from the final analysis due to having a scope that was too narrow. By the same token, we did not include percutaneous coronary intervention (PCI)-based registries, despite these registries offering rich datasets. We judged that omission of patients who were not treated with PCI would not be an accurate reflection of the country's overall STEMI population as this selection would omit a sizeable proportion of patients who would also be substantially different in demographics and outcomes. P.T. and A.H. independently screened all the records and discussed all conflicting assessments until consensus was achieved.

Additionally, to avoid duplication of data, if multiple articles from the same data source were shortlisted, then only the article with the most 'complete' dataset was selected for data extraction. Completeness of dataset was judged by (i) longest duration of patient recruitment and (ii) largest size (*n*).

The final shortlist of articles is found in Supplementary material online, *Table S1*. Definitions of extracted variables, where available, are compared in Supplementary material online, *Table S2*. Risk of bias was

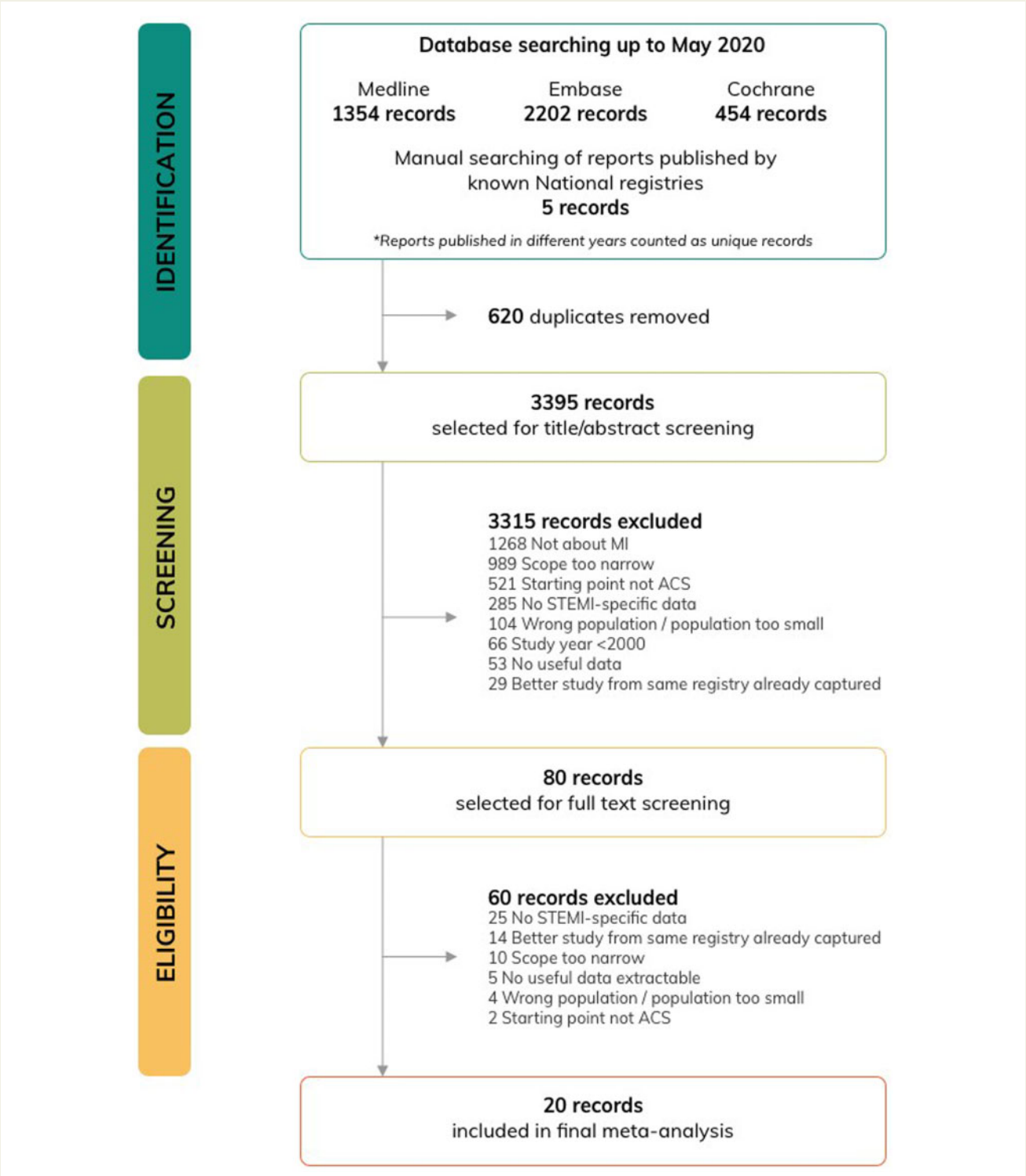

Figure 1 PRISMA diagram of study selection.

assessed using the Risk of Bias in Non-randomised studies of Exposures (ROBINS-E) tool (version July 2017), which assess seven domains of bias: confounding, selection of participants, classification of exposures, departure from intended exposures, missing data, measurement of outcomes, and selection of the reported result. The judgement of bias of the articles is found in Supplementary material online, *Table S4*.

Data recorded

Data were collected in five main areas—patient demographics (e.g. age, sex, and smoking status), past medical history, condition at presentation (i.e. Killip class), treatments/medications received in-hospital, and outcomes (e.g. in-hospital, 30-day, and 1-year mortality).

Our final analysis included data from approximately the same time frame for all five countries, hence, it was assumed that these datasets could be reasonably compared within those time frames.

Statistical analysis

Our primary outcomes were in-hospital mortality, 30-day mortality, and 1-year mortality. These outcomes were treated as binary data. All extracted outcomes were pooled using DerSimonian–Laird inverse-variance weighted random-effects model. Outcomes were reported as pooled mortality rate with 95% confidence interval (95% CI). All STEMI-associated risk factors, e.g. demographic and presentation symptoms were also considered for analysis to find pooled effects. Categorical risk factors were pooled using inverse-variance and reported as pooled event rate with 95% CI, whilst continuous risk factors were pooled using mean with 95% CI. All the meta-analyses were stratified by country status and we also calculated pooled estimates at the overall level. We used I^2 statistics to quantify heterogeneity across studies, and I^2 statistic of 90% or more was considered to indicate considerable heterogeneity. However, owing to the broad review question resulting in an inherently heterogeneous population among included studies, we accepted I^2 statistics up to 95% for inclusion in a meta-analysis. To account for substantial level of heterogeneity in the pooling, we used random effects model.[16]

Public health data

To complement the systematic review and provide context on the countries compared, data on the countries and their systems of care were gathered. Data were collected by self-report from surveys sent out to one representative senior cardiologist for each country who was working in that country, held a position of leadership amongst cardiologists in that country, and was affiliated to the Asia Pacific Society of Cardiology. This was supplemented with publicly available data published by World Health Organisation (WHO).

Results

STEMI variables

Twenty datasets were included in the final meta-analysis. There were 15 8420 patients included—22 929 from Australia, 7367 from Japan, 55 369 from Korea, 23 824 from Malaysia, and 48 931 from Singapore. Pooled estimates of STEMI demographics and treatments rendered are summarized in *Table 1*. Forest plots for each of the pooled estimates are found in Supplementary material online. Overall, the STEMI population had a mean BMI of 24.9 kg/m^2 (minimum 23.6 kg/m^2 in Korea and maximum 28.4 kg/m^2 in Japan) and comprised predominantly of males (pooled proportion of 78.7% with minimum 75.4% in Korea and 85.9% in Malaysia) and smokers (pooled proportion of 53.0%, range: 32.8–68.1%). There was a wide spread of mean age of presentation, with the youngest STEMI population in Malaysia (pooled mean of 56.0 years) and the oldest in Japan (pooled mean of 67.1 years).

There was a highest degree of family history of MI in Australia (32.8%) and lowest in Korea (7.5%) with overall estimate of MI of 14.9%. Overall proportion of chronic kidney disease (CKD) amongst STEMI patients was 7.5% with highest and lowest proportion of CKD in Japan (36.6%) and Korea (3.6%).

Use of aspirin was consistently high in all countries (pooled proportion of 97.2%, range: 92.1% in Australia to 98.6% in Singapore) and use of $P2Y_{12}$ inhibitors were similarly high though less uniformly (pooled proportion of 93.0%, range: 87.6% in Australia to 97.3% in Singapore). Statins were also frequently prescribed (pooled proportion of 90.2%, min: 75.0% in Japan max: 96.2% in Australia). Overall estimate of ACEi/ARB use was 80.1% with lowest use in Malaysia with 54.1% and highest use in Singapore with 94.5%. Use of in-hospital β-blockers was highest in Singapore (98.1%), followed by Australia (87.5%), Korea (80.1%), and lowest in Japan (48.1%).

Overall, 61.4% patients received primary percutaneous coronary intervention (pPCI) and this was unequally distributed with the highest rates of pPCI in Korea (91.6%) and the lowest rates in Malaysia (9.6%). On average 15.5% patients received fibrinolysis—highest in Malaysia (72.6%) and lowest in Singapore (1.1%). The use of pPCI in Australia (65.0%), Japan (77.5%), and Singapore (63.8%) was broadly comparable with the 59% pPCI rate reported in Europe.[17]

A more detailed analysis of the underlying data in Malaysia (drawn from the NCVD-ACS registry) did show a year-on-year increasing trend of patients treated with pPCI, with pPCI rates of 13.7% in the year 2014–15 compared with 6.75% for data from 2006 to 2010. However, although treatment with fibrinolysis was highest in Malaysia, only 29.3% of patients received PCI post-STEMI, implying that even with the reliance on fibrinolysis as the immediate reperfusion strategy of choice, not many patients go on to have follow-up intervention or stenting.

Table 2 and *Figure 2* summarize the pooled estimates of in-hospital, 30-day, and 1-year post-STEMI all-cause mortality. In-hospital mortality was similar in Australia (5.6%; 95% CI 4.8–6.5%), Japan (5.7%; 95% CI 4.7–6.9%), and Korea (5.6%; 95% CI 4.6–6.9%) but far higher in Singapore (10.3%; 95% CI 9.4–11.3%) and Malaysia (10.3%; 95% CI 8.8–12.1%). A similar pattern was observed in 30-day mortality. One-year STEMI mortality was higher in Malaysia (17.9%; 95% CI 13.1–23.8%) and Singapore (11.2%; 95% CI 10.1–12.3%) than in Korea (8.1%; 95% CI 6.4–10.3%), Australia (7.8%; 95% CI 5.1–11.7%), and Japan (6.2%; 95% CI 4.3–9.0%). *Figure 3* provides a time series comparison of in-hospital mortality rates as recorded by the various study registries. Similar time series registries were generated for 30-day and 1-year mortality rates and is found in Supplementary material online.

Public health data

Table 3 compares the public health indices among the five countries. The five countries compared were roughly similar in terms of broad development and public health indices, with the exception of Malaysia, which ranked slightly lower in terms of Human Development Index and had comparatively lower expenditure on health per capita. All countries had round-the-clock pPCI and fibrinolysis services available. Local cardiologists' estimates of the number of hospitals with pPCI services, round-the-clock pPCI services, and number of cardiac catheterisation laboratories provided perspective in the differences of provision of reperfusion services relative to their respective population sizes. All countries apart from Australia had national MI registries, but only Singapore's was compulsory.

Data availablity

The data that support the findings of this study are available from the corresponding author, YKK, upon reasonable request.

Table 1 **Pooled estimates of STEMI patients for different variables**

Characteristics	Australia	I^2	Japan	I^2	Korea	I^2	Malaysia	I^2	Singapore	I^2	Overall	I^2
Baseline												
Age (years), mean (95% CI)	62.0 (61.1–62.9)	86.2	67.1 (66.2–68.1)	94.0	62.8 (60.2–65.4)	0.0	56.1 (54.0–58.2)	0.0	59.8 (58.0–61.7)	0.0	61.6 (57.9–65.3)	99.2
Male, proportion (95% CI)	75.7 (73.7–77.5)	58.5	76.5 (74.4–78.4)	96.4	75.4 (72.6–78.1)	90.3	85.9 (84.3–87.3)	56.8	78.6 (77.2–79.9)	83.1	78.7 (74.6–82.3)	97.1
Smoker, proportion (95% CI)	50.0 (41.4–58.6)	99.6	43.1 (36.4–50.1)	99.4	45.6 (37.3–54.0)	95.0	67.1 (60.7–72.9)	73.1	57.4 (53.2–61.6)	91.2	53.0 (44.1–61.7)	99.5
BMI (kg/m^2), mean (95% CI)	–	–	24.9 (24.3–25.5)	98.8	23.8 (23.3–24.4)	98.6	25.9 (25.5–26.3)	96.0	–	–	24.9 (23.6–26.2)	99.8
Family history of MI, proportion (95% CI)	32.8 (29.1–36.8)	0.0	–	–	7.5 (6.8–8.3)	0.0	12.0 (11.4–12.7)	60.0	–	–	14.9 (7.7–26.9)	0.0
Past medical history												
CABG, proportion (95% CI)	3.8 (2.6–5.6)	72.0	1.1 (0.7–1.8)	82.7	0.4 (0.2–0.9)	0.0	–	–	1.4 (0.7–3.0)	0.0	1.3 (0.5–3.3)	94.7
Chronic kidney disease, proportion (95% CI)	5.0 (3.7–6.8)	44.4	36.6 (29.7–44.2)	98.0	3.6 (2.3–5.5)	0.0	3.5 (2.7–4.6)	57.6	–	–	7.5 (2.0–23.7)	99.8
Cerebrovascular disease, proportion (95% CI)	5.3 (4.3–6.5)	51.6	–	–	4.8 (3.8–6.1)	0.0	2.9 (2.5–3.4)	67.8	–	–	4.2 (2.7–6.3)	0.0
Diabetes mellitus, proportion (95% CI)	20.3 (18.6–22.1)	25.8	31.9 (30.2–33.6)	89.5	24.8 (23.1–26.7)	0.0	38.2 (36.3–40.0)	85.7	39.8 (38.6–41.1)	59.6	30.5 (23.9–37.9)	98.8
Dyslipidaemia, proportion (95% CI)	43.9 (36.7–51.2)	24.2	50.2 (43.1–57.3)	98.9	10.1 (7.0–14.4)	72.7	25.9 (20.1–32.7)	95.3	66.7 (62.0–71.0)	98.6	36.7 (18.9–59)	99.9
Hypertension, proportion (95% CI)	49.6 (45.5–53.8)	0.0	60.4 (56.7–63.9)	98.4	46.8 (41.7–52)	0.0	52.1 (47.8–56.3)	96.9	58.6 (56.0–61.2)	74.3	53.7 (48.5–58.9)	98.2
Myocardial infarction, proportion (95% CI)	13.7 (11.3–16.6)	95.5	7.5 (5.8–9.6)	0.0	8.5 (6.3–11.4)	99.4	11.3 (8.9–14.3)	57.8	12.9 (11.2–14.9)	72.4	10.7 (8.4–13.5)	95.7
PCI, proportion (95% CI)	8.9 (6.7–11.7)	62.3	9.1 (6.8–12.1)	94.9	8.3 (5.0–13.4)	0.0	–	–	9.5 (5.8–15.2)	0.0	9.0 (7.5–10.6)	85.9
Presentation												
Killip Class I, proportion (95% CI)	84.8 (80.8–88.2)	95.2	76.0 (71.7–79.9)	95.6	70.2 (60.3–78.5)	0.0	57.9 (51.6–63.9)	98.7	81.5 (73.9–87.3)	0.0	75.1 (63.8–83.7)	99.6
TIMI ≥8, proportion (95% CI)	–	–	–	–	–	–	7.9 (7.1–8.8)	83.0	–	–	7.9 (7.1–8.8)	83.0
Treatment variables												
Fibrinolysis, proportion (95% CI)	30.0 (15.7–49.7)	69.3	–	–	8.3 (1.7–32.1)	99.6	72.6 (50.5–87.4)	97.1	1.1 (0.6–1.9)	99.6	15.5 (1.1–74.8)	99.9
Primary PCI, proportion (95% CI)	65.0 (51.6–76.5)	99.4	77.5 (58.9–89.2)	99.9	91.6 (76.0–97.4)	0.0	9.6 (4.9–17.8)	99.1	63.8 (55.5–71.3)	99.4	61.4 (32.2–84.2)	99.9
PCI, proportion (95% CI)	67.1 (53.9–78.0)	99.6	94.7 (90.5–97.2)	98.7	94.8 (89.3–97.5)	99.3	29.3 (18.1–43.8)	99.8	75.0 (68.3–80.7)	98.7	79.1 (53.5–92.6)	99.9
CABG, proportion (95% CI)	4.8 (3.2–7.2)	90.6	2.2 (1.3–3.8)	97.5	2.7 (1.3–5.4)	0.0	0.8 (0.5–1.2)	87.5	2.1 (1.7–2.6)	86.8	2.1 (1.2–3.8)	97.0
Median door-to-balloon time (min), mean (95% CI)	113.9 (9.1–218.7)	0.0	57.4 (19.2–95.7)	0.0	–	–	–	–	63.0 (31.3–94.6)	0.0	63.5 (39.7–87.2)	0.0
In-hospital aspirin, proportion (95% CI)	92.1 (80.3–97.1)	0.0	98.8 (97.5–99.5)	99.0	–	–	94.6 (90.5–97.0)	96.3	98.6 (97.9–99.1)	96.1	97.2 (93.1–98.9)	98.2
In-hospital clopidogrel/other P2Y12 inhibitor, proportion (95% CI)	87.6 (58.6–97.2)	0.0	91.2 (77.0–97.0)	98.8	–	–	89.3 (76.7–95.5)	99.8	97.3 (95.0–98.5)	98.7	93.0 (83.4–97.3)	99.7
In-hospital statin, proportion (95% CI)	96.2 (88.9–98.8)	0.0	75.0 (57.1–87.1)	98.9	84.4 (70.6–92.4)	99.8	90.5 (83.0–94.8)	98.3	94.7 (92.0–96.5)	98.7	90.2 (81.0–95.2)	99.6
In-hospital ACEi/ARB, proportion (95% CI)	80.7 (64.8–90.4)	0.0	73.6 (61.0–83.3)	99.6	81.3 (71.0–88.6)	99.3	54.1 (42.5–65.4)	99.0	94.5 (92.6–95.9)	98.6	80.1 (56.4–92.6)	99.8
In-hospital β-blocker, proportion (95% CI)	87.5 (80.3–92.3)	0.0	48.1 (38.9–57.5)	98.8	80.1 (73.5–85.4)	98.8	58.9 (51.4–66.0)	95.3	98.1 (97.6–98.5)	97.4	82.0 (45.3–96.2)	99.8

Table 2 Pooled estimates of mortality outcomes among STEMI patients

Outcomes	Australia		Japan		Korea		Malaysia		Singapore		Overall	
	Event rate (95% CI)	I^2 (%)	Event rate (95% CI)	I^2 (%)	Event rate (95% CI)	I^2 (%)	Event rate (95% CI)	I^2 (%)	Event rate (95% CI)	I^2 (%)	Event rate (95% CI)	I^2 (%)
In-hospital mortality (proportion)	5.6 (4.7–6.7)	58.5	5.7 (4.7–7)	96.4	5.6 (4.5–7)	90.3	10.3 (8.7–12.2)	56.8	10.3 (9.4–11.3)	83.1	7.3 (5.3–9.9)	97.1
30-Day mortality (proportion)	6.3 (4.9–7.9)	80.9	—	—	5.9 (5.0–7.0)	92.4	12.6 (11.1–14.3)	86.8	10.4 (9.7–11.1)	84.3	8.5 (6.1–11.6)	97.5
1-Year mortality (proportion)	7.8 (5.1–11.7)	0.00	6.2 (4.3–9.0)	0.00	8.1 (6.4–10.3)	14.2	17.9 (13.1–23.8)	0.00	11.2 (10.1–12.3)	91.2	9.7 (7.1–13.1)	98.0

Discussion

Patient characteristics

Although we have only reported descriptive statistics with no comparison of means, it is clear that there is heterogeneity in patient characteristics in the five Asia-Pacific countries, with differing prevalence of the various risk factors for STEMI. The fact that prevalence of risk-factors varies geographically to such a large extent is not new; similar observations have been reported in the Long-tErm follow-uP of Antithrombotic Management Patterns In Acute CORonary Syndrome Patients (EPICOR) and EPICOR-Asia studies.[13]

Japan has the oldest STEMI population, which likely corresponds to the wider trend of an aging population in Japan when compared with the other countries.[18] Meanwhile, Australia's greater degree of family history of cardiovascular disease almost approach the levels observed in Europe. This could be due to differences in ethnic composition in the countries; other ethnicity-based studies have reported a higher prevalence of family history of cardiovascular disease (and premature disease) amongst White Caucasians and conversely the lowest prevalence amongst Chinese.[19]

Interesting differences also exist in the prevalence of CKD and dyslipidaemia across the five countries. The higher proportion of CKD in Japan's STEMI cohort probably correlates to a significantly greater prevalence of CKD amongst the general Japanese population.[20,21] Dyslipidaemia was low amongst Korean patients. Comparatively low rates of dyslipidaemia in AMI patients in Korea have been noted before in the Korea Acute Myocardial Infarction Registry (KAMIR)-based reports,[22] whilst international STEMI registries have previously recorded wide-ranging rates of dyslipidaemia across different geographical regions.[13] Prevalence of diabetes was lower in Australia but otherwise comparable across the other four countries.

Treatment

Despite clear guidance from the European Society of Cardiology (ESC) and American Heart Association (AHA) on use of aspirin, $P2Y_{12}$ inhibitors, high intensity statins, ACE-i/ARBs, and β-blockers post–STEMI,[10,11] differences in the use of these medications in actual clinical practice persist.[6,23] Our data similarly show inter-country differences in in-hospital prescription of these medications. There was much more variation in use of ACEi/ARB and β-blockers, with in-hospital use high in Singapore and Korea but far lower in Japan and Malaysia. Further studies examining why the use of these medications is so low in these countries are warranted.

More striking differences were seen in the reperfusion strategies employed. Whilst Korea was highly PCI-centric, Malaysia was at the other end of the spectrum. It is not surprising that such differences in reperfusion strategy exists between countries, despite strong evidence for the use of emergency pPCI in STEMI patients.[24] Similarly, in the EUROHOBOP study,[25] there was a vast spread of pPCI rates with Greece lowest at 18.4% and Germany highest at 84.7%. As outlined in the ESC guidelines,[10] an effective nationwide pPCI service requires a hub-and-spoke healthcare model sub-served by a robust ambulance service that can appropriately triage patients and divert them to tertiary centres for pPCI if necessary. Such a system is not easily engineered, and the differences in pPCI use probably reflect the differences between countries in their progress in developing such

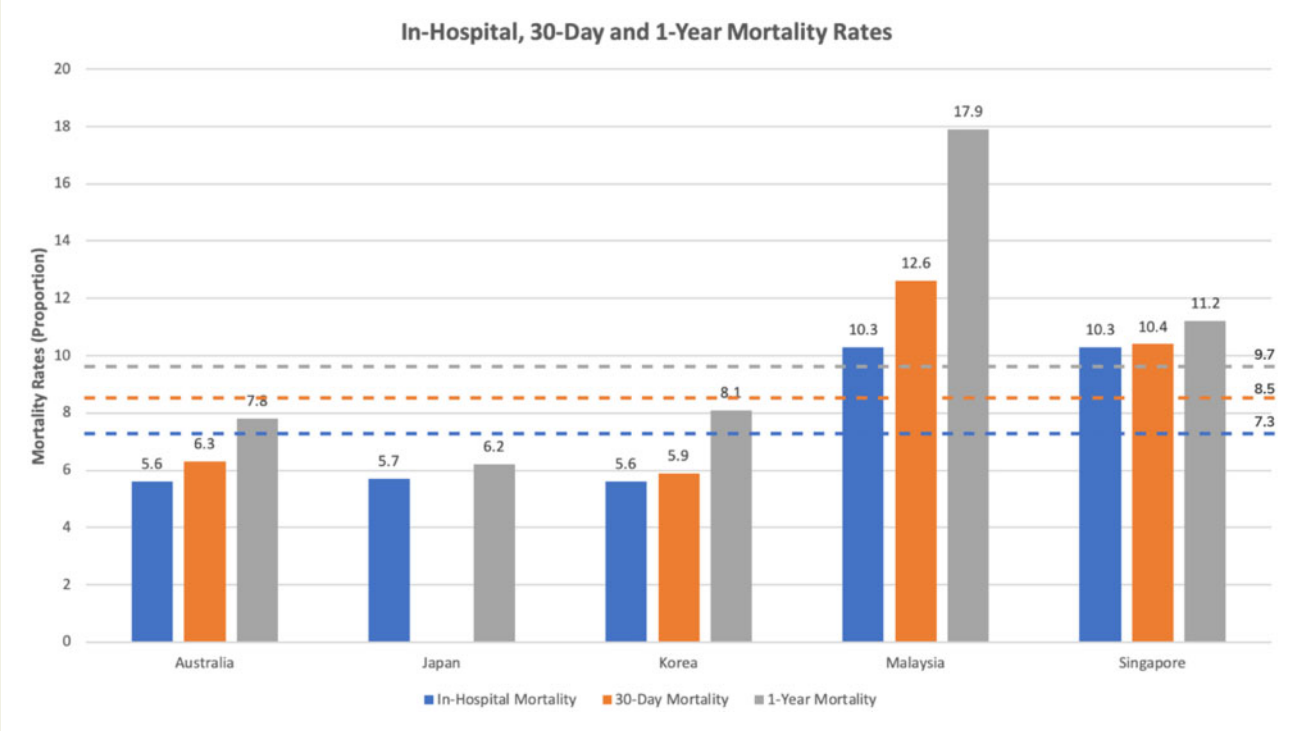

Figure 2 In-hospital, 30-day and 1-year mortality rates. Pooled estimates of in-hospital, 30-day, and 1-year mortality outcomes for each country. Dotted lines represent pooled estimates across all five countries.

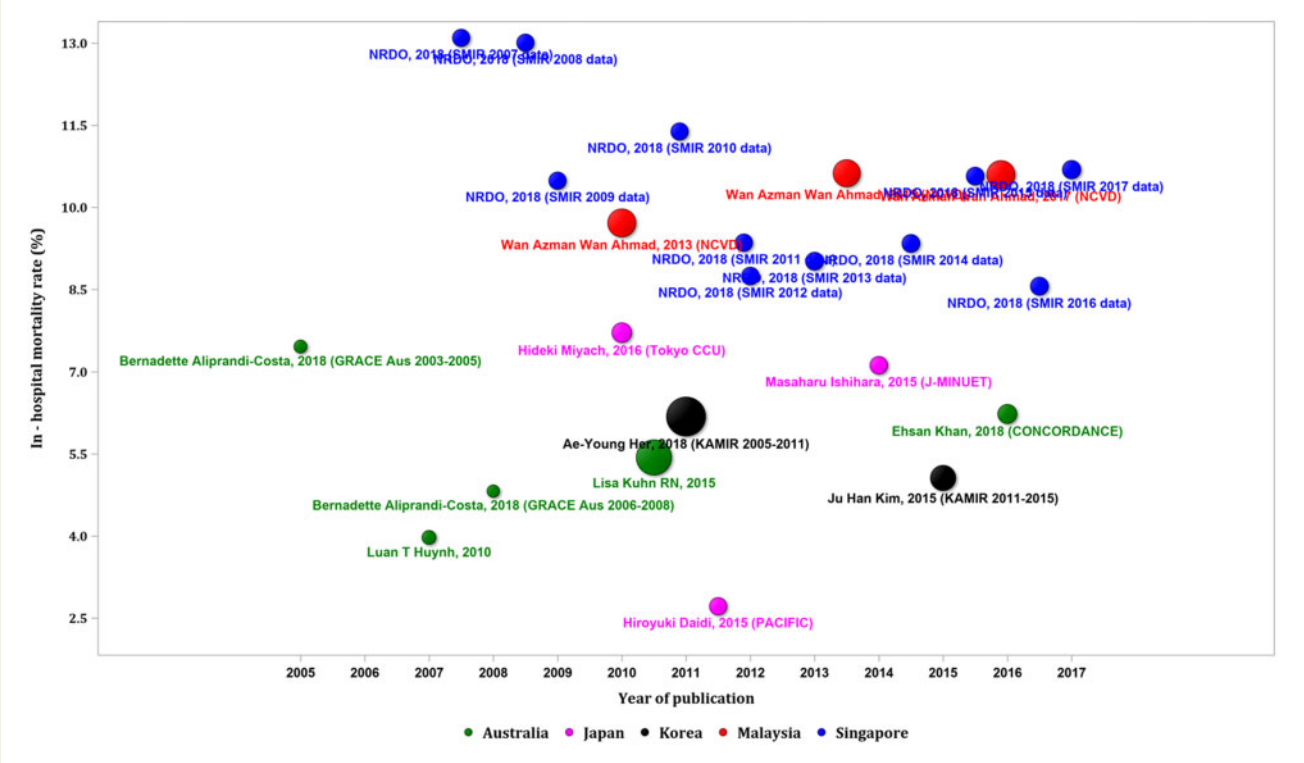

Figure 3 Time series comparison of in-hospital post-STEMI mortality rates. Time-series comparison of in-hospital mortality outcomes. Studies are arranged according to the year in which data collection for that particular study ended. Size of bubble corresponds to number of patients recruited into study. Similar time series comparisons were performed for 30-day and 1-year mortality rates and can be found in Supplementary material online.

Table 3 Public health data

Serial no.	Characteristics	Australia	Japan	Korea	Malaysia	Singapore
1	Population size[a] (*n*, 2018)	24 600 000	126 800 000	51 470 000	31 620 000	5 612 000
2	Human Development Index[b] (World Ranking Position; 2018)	3	19	22	57	9
3	Gross national income per capita[a] (PPP International $; 2013)	42	37	33	22	76
4	Total expenditure on health per capita[a] (International $; 2014)	4357	3727	2531	1040	4047
5	Total expenditure on health[a] (as % of GDP; 2014)	9.4	10.2	7.4	4.2	4.9
6	Life expectancy at birth, m/f[a] (years; 2016)	81/85	81/87	80/86	73/78	81/85
7	Median cost of each STEMI hospitalization[c] (USD; 2018)	18 000	2700	2000	3700 (public)7300–9700 (private)	No information
8	Bloomberg Health Care Efficiency Index[d] (World ranking position; 2018)	8	7	5	29	2
9	Bloomberg Health Care Efficiency Index[d] (efficiency score; 2018)	62.0	64.3	67.4	50.4	85.6
10	National Registry for MI present,[c] Y/N (including name of National Registry)	N	Y, voluntary JAMIR (Japan Acute Myocardial Infarction Registry)	Y, voluntary KAMIR (Korean Acute Myocardial Infarction Registry)	Y, voluntary NCVD (National Cardiovascular Disease Registry)	Y, compulsory SMIR (Singapore Myocardial Infarction Registry)
11	Data of National Registry Audited,[c] Y/N	N/A	N	Y	Y	Y
12	Existence of guidelines for treatment of ACS,[c] Y/N	Y	Y	N	Y	N
13	Public education on chest pain awareness,[c] Y/N	Y National Heart Foundation TV advert. Online resources	N	Y Media such as TlactV and radio, Lecture for public education	N	Y Initiatives from Health Promotion Board Singapore
14	Public ambulance system,[c] Y/N	Y	Y	Y	Y	Y
15	Private ambulance system,[c] Y/N	N	N	Y, but only inter-hospital transfers	Y	Y
16	pPCI available,[c] Y/N	Y	Y	Y	Y	Y
17	Number of hospitals with pPCI available[c] (*n*)	No information	No information	>150 mixed	15 public 58 private	5 public
18	pPCI 24/7/365 available,[c] Y/N	Y	Y	Y	Y	Y
19	Number of hospitals with pPCI 24/7/365 available[c] (*n*)	No information	1353	No information	2 public Estimated 15 private	5 public
20		>110–120	No information	No information	95	No information

Continued

Table 3 *Continued*

Serial no.	Characteristics	Australia	Japan	Korea	Malaysia	Singapore
	Number of cardiac catheterization laboratories[c] (*n*)					
21	Thrombolytics available,[c] Y/N	Y	Y	Y	Y	Y
22	Number of Interventional Cardiologists[c] (*n*)	Estimated 230–240	1135	350	293	No information
23	National Accreditation for Interventional Cardiologist,[c] Y/N	No information	No information	N	Y	No information

N, no; *n*, number; PPP, purchasing power parity; pPCI, primary percutaneous coronary intervention; Y, yes.
[a]Data from World Health Organisation (WHO): https://www.who.int/countries/en/.
[b]Data accessed from United Nations Development Programme HDI: http://hdr.undp.org/en/2018-update.
[c]All other data obtained by personal communication with representative cardiologists from each country.
[d]Data accessed from Bloomberg: https://www.bloomberg.com/news/articles/2018-09-19/u-s-near-bottom-of-health-index-hong-kong-and-singapore-at-top.

systems alongside the local geographic challenges. Our results show that there is room for improvement; nevertheless, the rising yearly trend of pPCI in Malaysia augurs well.

Outcomes

The pooled in-hospital mortality in Australia, Japan, and Korea compares favourably to multi-national European registries, which report mortality rates of 5.3% in the 2004 Euro Heart Survey,[17] 7.9% in the 2009 Euro Heart Survey Snapshot[23] and 8.4% in the EUROHOBOP registry.[25] In comparison, Malaysia and Singapore had a higher rate of 10.3%.

Thirty-day mortality rates for Australia and Korea were close to rates reported in other studies—5.0% in the ACCESS cohort,[3] 6.4% in the 2004 Euro Survey,[17] and 6.61–6.75% in the TIMI cohort.[26]

One-year mortality from STEMI (*Figure 4*) was considerably greater in Malaysia and Singapore. The mortality rates in Korea, Australia, and Japan were more in line with those reported in other registries. For example, the 1 year STEMI mortality rate was between 10.0 and 10.3% in the TIMI cohort[26] and more recently reported to be 8.4% in the ACCESS registry[3] that recruited from 19 developing countries from the Middle East, Africa, and Latin America.

The higher in-hospital, 30-day, and 1-year mortality rates in Malaysia could be attributed in-part to its lower use of pPCI in emergency reperfusion. Meanwhile, the higher mortality rates seen in Singapore could be attributed to the inclusion of patients who had died in ED or out-of-hospital without admission by the Singapore Myocardial Infarction Registry (SMIR),[14,27] hence increasing mortality figures. These out-of-hospital or ED deaths are often omitted from other studies but were included in SMIR as it is a compulsory registry. Another possible explanation could be the greater ethnic diversities in Singapore and Malaysia than the other countries,[28] with Malay patients found to have the greatest long-term mortality risk after adjustment for baseline clinical features.

In Malaysia, the STEMI registry is predominantly derived from public tertiary PCI centres, after which the surviving post-STEMI patients are referred back to the public sector for primary care follow-up. This follow-up may be anything from 2 to 9 months after the index event. Therefore, there is uncertainty as to the continuity of care or adherence of prescribed post-STEMI/PCI medications. This could result in poorer outcomes. More studies should look into this aspect of possible poorer adherence to standard protocols or guidelines on management.[29]

It must also be noted that mortality outcomes may not tell the full story about STEMI care, as these values could be affected by patient/family choice to treat this condition conservatively. This would also be reflected in reperfusion rates. Again, it would be interesting to look into patient choice of conservative care, and how this might be affected by sociocultural differences.

The importance of registries

Whilst drafting this article, we noticed the value of large-scale national registries. In particular, the Singaporean SMIR registry, the Korean KAMIR registry, and the Malaysian NCVD-ACS registry stood out in the comprehensiveness of their data sets and their multi-year recruitment that effectively allowed year-on-year comparison of the country's progress in lowering mortality or any shifts in AMI demographics. However, we note from *Table 3* that only the SMIR is compulsory, thus giving it the advantage of capturing and tracking all the MI diagnoses in the country in that year.

In addition, there are a number of registries in Asia-Pacific that extend beyond STEMI and focus more generally on AMI or patients undergoing PCI. The JROAD,[30] JAMIR,[31] and MIG-R[32] registries provide examples of registries with large sample sizes. Whilst these registries were excluded from our study for the reasons highlighted in *Figure 1*, it was reassuring to note that our pooled estimates broadly agreed with their reported data.

Despite well-evidenced treatment pathways in STEMI management, geographical variations in actual clinical practice and outcomes continue to persist[5,6,13,33] both within and between countries. Our data reaffirm that this remains the case in Asia-Pacific as well. The goal, then, is to use these studies to shed light on the areas for improvement and to close the gap between the best and the worst

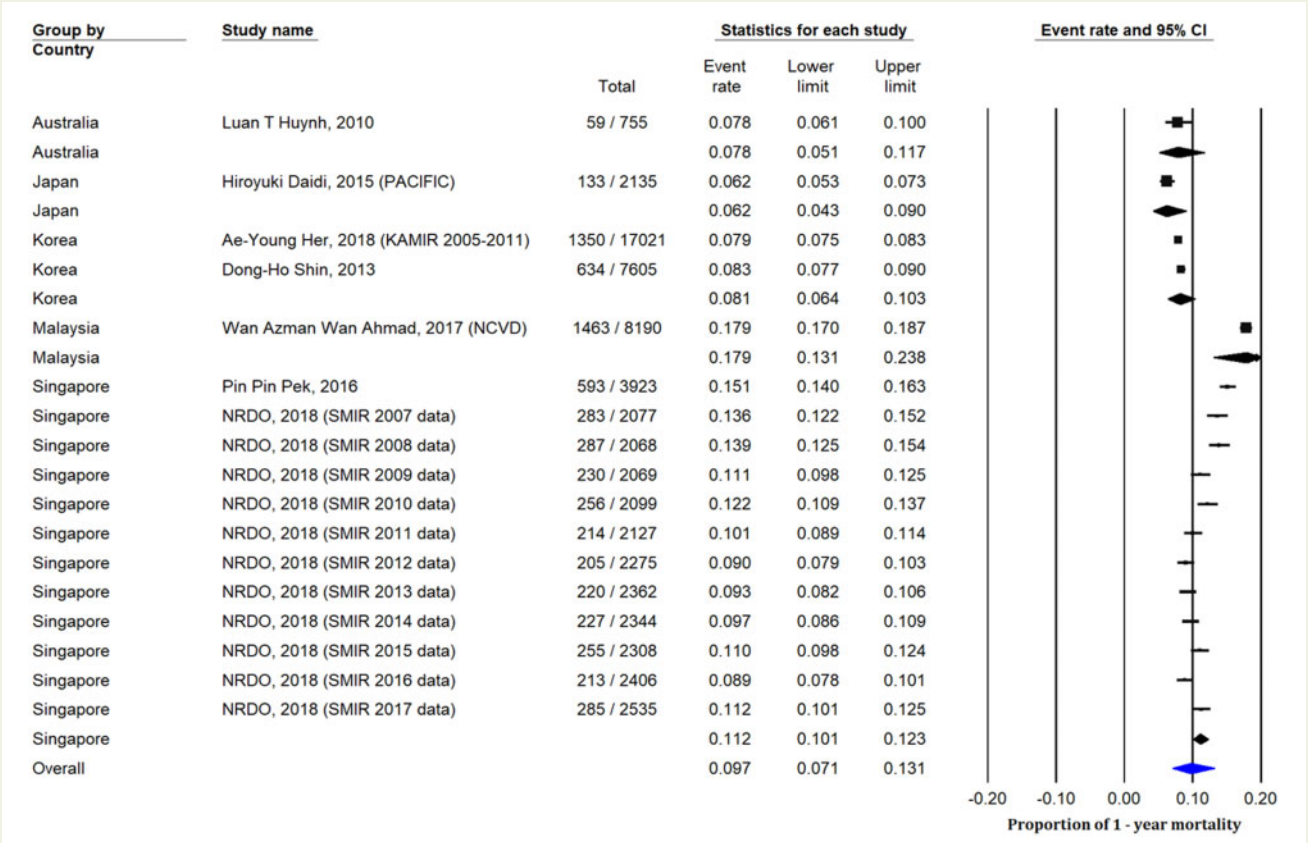

Figure 4 Forest plot of 1-year post-STEMI all-cause mortality.

performers. This is indeed the stated objective of many such registries,[34–36] and it has also been shown on multiple occasions that registries provide a way of assessing adherence to guidelines, which in turn translates into improvement in clinical outcomes.[37–39] In addition, these registries have provided a rich source of data for subpopulation studies comparing patients with different demographics or who had received different treatments.[40]

Given the advantages of registries as laid out above, the authors advocate their use in more Asia-Pacific countries. Particularly, it would be helpful to have multi-centre, international registries, especially given the relative lack of such registries in the Asia-Pacific region as highlighted in our introduction.

Strengths and limitations

This article represents one of the few attempts to chart and examine the patient profile, status of treatment provision, and mortality outcomes associated with STEMI in the Asia-Pacific region, especially given the relative lack of multi-national prospective registries focused on this geographical area. Nevertheless, there are inherent limitations with a meta-analysis. Data were obtained from a combination of studies with variability in methodology, definitions, and recruitment criteria (Supplementary material online, *Tables S1 and S2*). Definitions of variables were not always available from the source articles, but we have nonetheless chosen to analyse and display these data as we judged that it would be useful to readers.

Studies that met our inclusion criteria were all observational registries, which was useful in addressing our research question of taking a census of STEMI patients. Nevertheless, opting to use such registries as data sources rather than randomized controlled trials performed under specific conditions meant that there is risk of confounding bias on mortality outcomes. Furthermore, despite best efforts to choose registries that were most representative of STEMI all-comers in these countries, sampling bias may still exist, especially since all of the registries used in our study (with the exception of the SMIR) were voluntary and hence only recorded a subset of all STEMI patients in that country. On the whole, most of our studies were judged to have a low to moderate overall risk of bias (Supplementary material online, *Table S4*).

As expected, data from different registries within the same country were heterogenous, with I^2 values of up to 98%. Even so, we accepted this high level of heterogeneity when pooling estimates, as our stated objective aimed to pull together disparate registries in each country in order to allow comparison between countries, and we controlled for this heterogeneity using the random-effects method.

In addition, our meta-analysis does not have the ability to track year-on-year improvements in treatment provision or mortality that longitudinal prospective registries would otherwise be able to demonstrate. In order to collect sufficient data for analysis, it was necessary to extend the inclusion criteria to studies recruiting between

years 2000 and 2020. Studies that performed temporal analyses[41,42] report that improvements have been made over this time, but these might be obfuscated by combining results from multiple years. Such an analysis also obscures regional differences which would likely be especially prevalent in larger countries which experience a degree of rural-urban divide. Differences in mortality could arise both from different incidence of cardiac risk factors as well as differences in access to treatment (e.g. in terms of chest pain-to-door or chest pain-to-needle time, as well as access to PCI-equipped hospitals).[43] It would be useful to subdivide countries into regions based on per-capita income (as a gross proxy for urbanization) and compare similar populations across countries. However, all but a few[44–46] registries we found amalgamate information across large and heterogenous geographical areas, meaning that these nuances are lost.

Finally, we limited the scope of our research to five selected countries in the Asia-Pacific region. It is our hope that similar analyses could be expanded to more countries in the future, especially given how diverse the Asia-Pacific countries are in terms of population make-up and healthcare systems.

Conclusion

Although Australia, Japan, Korea, Malaysia, and Singapore have broadly comparable public health systems, we have shown that there is heterogeneity of risk factors in the profile of patients presenting with STEMI in these countries. Use of anti-platelets and statins are high across the five countries. Reperfusion strategies differed greatly, with pPCI use low in Malaysia but extremely high in Korea. Mortality rates in Australia, Japan, and Korea were similar to those reported in other international registries, whereas mortality rates in Singapore and Malaysia were higher. This study reveals areas for improvement, and the authors advocate further registry-based studies focused on the Asia-Pacific region.

Supplementary material

Supplementary material is available at *European Heart Journal – Quality of Care and Clinical Outcomes* online.

A full table of papers included in this meta analysis can be found in the supplementary material—supplementary Table 1: [14,22,27,28,42,45-60].

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