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Supplementary appendix

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Supplementary Appendix:

Comparative effectiveness of acute myocardial infarction care delivered in Sweden and the United Kingdom using national outcome registries

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Comparability of data in two national outcome registries

The comparability of MINAP and RIKS-HIA data is examined first by the variable definition and response categories between the two registries (Table S1). The list of variables incorporates measures for demographics, clinical presentation, treatment and complications. The comparability of diagnosis between the two registries is showed by the distribution of diagnostic markers during the study period for all MI patients, STEMI and NSTEMI patients (Table S2).

Table S1. Definition of variables in MINAP and RIKS-HIA

Name	MINAP variables	RIKS-HIA variables	Variable in analysis	Assessment of Comparability
Demographics				
Mean age	Mean age as derived by date of birth and date of admission.		**Mean age**	Comparable
Female	Female patients	Female patients	**Female**	Comparable
Risk factors				
Smoking	Current smoking at admission (0) Never smoked: Patient has never smoked. (1) Ex smoker: An ex smoker is one who has given up smoking more than one month previously. (2) Current smoker: A current smoker is a patient regularly smoking an average of 1 or more cigarettes per day, or equivalent. Any cigarettes smoked in the last month classify the patient as a current smoker. (3) Non smoker—smoking history unknown. Currently a non-smoker but past history unknown. (9) Unknown: Smoking status unknown.	Non-smoker: Patient has never smoked. Ex-smoker: Patient has stopped smoking >1 month ago. - There is no upper time limit for ex-smoker. If the patient stopped smoking 40 years ago he/she is still registered as an ex-smoker. - Tobacco chewers are considered ex-smokers - Occasional smokers are considered ex-smokers Smoker: Patient is currently smoking or has quitted <1 month prior to arrival. Unknown: To be used when information is not obtainable as in the case of dementia, stroke or if patient is deceased.	**Current smoker** For example: in MINAP, for patients with non-missing smoking data then current smoker will be 1 if the answer to smoking equals 2, 0 otherwise.	Comparable (recoded binary variable for current smoker)
Systolic blood pressure	The first systolic blood pressure recorded after admission to hospital. The patient should be in a stable cardiac rhythm, i.e. sinus or chronic AF. Where the presenting rhythm is a treatable tachyarrhythmia, the first stable SBP after treatment should be used. Measured in mmHg	Enter patient's blood pressure. It should be the first blood pressure that has been registered by medical personnel, including general practitioner, ambulance personnel or ER medical staff.	**Systolic blood pressure**	Comparable
Heart rate	The heart rate recorded from the first ECG after admission to hospital, whilst in a stable cardiac rhythm i.e. sinus rhythm, or chronic AF. In complete heart block record ventricular rate. Where the presenting rhythm is a treatable tachyarrhythmia, the first stable heart rate after treatment should be used.	Enter patient's heart rate (beats per minute). It should be the first heart rate that has been registered by medical personnel.	**Heart rate**	Comparable
Troponin/ troponin value	Troponin assay used. (1) Troponin I (2) Troponin T (3) High sensitivity Troponin T (9) Unknown	Cardiac marker 0) Not analysed 1) Troponin-T 2) Troponin-I 3) CKMB 4) Myoglobin 5) Unknown The most specific marker should be specified. Hence, the marker that best	**Dummy variable for troponin quartiles.** First create separate ordinal variables for troponin T	Comparable (recoded troponin quartiles)

		verifies the diagnosis of myocardial infarction is to be entered. In most cases troponin.	and troponin I. Then create dummy variables for troponin quartiles. For example, dummy variable for first troponin quartile is 1 for patients with troponin T measure which belongs to the first quartile or troponin I measure which belongs to the first quartile, 0 otherwise.	
	Peak Troponin It is recognised that troponin may be reported as < (less than) or > (greater than) a certain value. Please follow the following conventions: If the reported value indicates that there is no (analysable) elevation of troponin enter zero, 0. If the reported value is greater than the upper limit of the assay range, enter the value at the upper limit: i.e. >50ng/ml, enter 50. If on near patient testing a range is given, enter the value at the upper limit: i.e. between 0.05 and 0.5 ng/ml, enter 0.5.	Maximum value of marker Maximum value to be indicated, hence not the first pathological value. If analysis is only made up to a certain maximum value, this maximum value should be specified.		
Clinical history				
History of heart failure	History of heart failure (1) YES if a previously validated diagnosis of heart failure on any therapeutic regime.	Specify 1=Yes if - the patient has documented heart failure in medical chart, or - the patient has received diagnosis of heart failure by a physician	**History of heart failure** For patients with non-missing data, the variable will be 1 for those answered 'Yes', 0 otherwise.	Comparable
Previous AMI	Previous AMI (1) YES if any previously validated episode of acute myocardial infarction.	Indicate if the patient has had at least one documented myocardial infarction prior to arrival. No: Patient has not had a previous myocardial infarction. Yes: Patient has had a previous myocardial infarction, which is documented in the patient's medical chart, or the patient himself/herself states that he/she has had a previous myocardial infarction. Specify yes even if previous myocardial infarction has been silent, that is even if the patient himself/herself is not aware of it, but ECG or echocardiography findings indicate previous myocardial infarction.	**Previous AMI** For patients with non-missing data, the variable will be 1 for those answered 'Yes', 0 otherwise.	Comparable

		Unknown: It is unknown whether patient has previously had a myocardial infarction prior to arrival.		
History of Diabetes	Patients with a previous diagnosis of diabetes (1) Diabetes (dietary control) (2) Diabetes (oral medicine) (3) Diabetes (insulin) (4) Newly diagnosed diabetes (5) Insulin plus oral medication	Indicate whether patient has a history of diabetes, independent of treatment given, even if only treated with diet. Yes applies here if the patient is aware of the diagnosis.	**History of Diabetes** For patients with non-missing data, the variable will be 1 for those answered 'Yes', 0 otherwise.	Comparable
Hypertension	Patients receive treatment (drug, dietary or lifestyle) for hypertension or with recorded BP > 140/90 on at least two occasions prior to admission.	On-going or previous pharmacological treatment for hypertension.	**Hypertension** For patients with non-missing data, the variable will be 1 for those answered 'Yes', 0 otherwise.	Comparable
Cerebrovascular disease (CVD)	Patients with a history of cerebrovascular ischaemia. To include transient cerebral ischaemic episodes as well as events with deficit lasting >24 hours (Definition in MINAP)	Indicate if patient had previous stroke (Does not include transient ischemic attack [TIA])	**Cerebrovascular disease recorded** For patients with non-missing data, the variable will be 1 for those answered 'Yes', 0 otherwise.	Minor difference
Previous PCI	A percutaneous coronary intervention at any time prior to this admission	Indicate if patient has previously undergone PCI.	**Previous PCI** For patients with non-missing data, the variable will be 1 for those answered 'Yes', 0 otherwise.	Comparable
Previous CABG	Coronary artery bypass grafting at any time prior to this admission	Indicate if patient has undergone heart surgery prior to this admission. 0 = No 1 = CABG 2 = Other heart surgery 9 = Unknown	**Previous CABG** For patients with non-missing data, the variable will be 1 for those	Comparable

			answered 'Yes' in MINAP and 'CABG' in RIKS-HIA, 0 otherwise.	
Cardiac arrest prior to admission	Date and time of FIRST verified arrest only to be reported. Excludes syncope or profound vagally-mediated bradycardia. Enter date and time of death if resuscitation not attempted. Location of cardiac arrest. (1) No arrest, (2) Before ambulance arrival: Implies arrest did not take place in presence of a trained medic/paramedic (specifically called to the scene) and including trained first responders deployed by the ambulance services. (3) After ambulance arrival: Implies arrest in the presence of a medic/paramedic, (4) A&E, (5) CCU, (6) Medical ward, (7) Elsewhere in hospital: Refers to OPD, X-ray, etc, (8) Catheter lab	Pre-hospital CPR: Specify whether patient suffered cardiac arrest and if CPR was carried out prior to hospital arrival. (0) No, (1) Yes (9) Unknown	**Cardiac arrest prior to admission** For MINAP to match up with RIKS-HIA, if patients with non-missing arrest time or location of arrest data, arrest before admission is defined as arrest time prior to hospital admission or arrest site documented as 2 or 3.	Comparable
Treatment				
Median hospitalization	Median hospitalization days as derived by date of discharge and date of admission.		**Hospitalization days**	Comparable
Aspirin/ other antiplatelet inhibitors prior to admission	Where was aspirin/other antiplatelet given? (1) Already on aspirin / antiplatelet drug: Regular use of aspirin/antiplatelet before this episode. Ignore the administration of additional doses by paramedics.), (2) Aspirin / antiplatelet drug given out of hospital: Aspirin or other antiplatelet drug started for this episode before admission. Patient not previously taking any antiplatelet drug, (3) Aspirin / antiplatelet drug given after arrival in hospital, (4) Aspirin / antiplatelet contraindicated, (8) Not given, (9) Unknown.	Indicate if patient has regularly been taking Aspirin prior to this hospital admission (e.g. chronic use) Note that other platelet inhibitors (clopidogrel/ticlopidine and others) are listed separately. (0) No, (1) Yes (9) Unknown	**Categorical variable for antiplatelet therapy prior to admission: 0) no antiplatelet therapy, 1) single antiplatelet therapy (either aspirin or thienopyridine inhibitor) or, 2) combined antiplatelet therapy (both aspirin and thienopyridine inhibitor)**	Comparable (recoded categorical variable)
Clopidogrel use prior to admission	Use of any thienopyridine inhibitor (includes Clopidogrel and Prasugrel) prior to this admission.	Indicate if patient has regularly been taking Clopidigrel, Ticlopidine or Other platelet inhibitor drugs prior to this hospital admission (e.g. chronic use). (0) No, (1) Clopidogrel, (2) Ticlopidine,		

		(3) Other, (9) Unknown.		
Unfractionated heparin/LMW heparin or Fondaparinux during hospitalization	Unfractionated heparin use during hospitalization. Low molecular weight heparin use during hospitalization. Fondaparinux used while in hospital.	(0) No (1) intravenous unfractionated heparin (2) subcutaneous low molecular weight heparin (3) subcutaneous Fondaparinux Note that use of anticoagulation during angiography or angioplasty should not be registered here.	**Heparin use** For MINAP to match up with RIKS-HIA, for patient with non-missing data for either one of the three variables for heparin, if the answer is yes to one of them then heparin use equals to 1.	Comparable
Intravenous IIB/IIIA Agent use during hospitalization	Intravenous IIB/IIIA Agent use during hospitalization.	(0) No (1) abciximab (2) Tirofiban (3) Eptifibatide	**Intravenous IIB/IIIA Agent use during hospitalization** For patients with non-missing data, assing 1 for MINAP answer 'Yes', and RIKS-HIA answer 1, 2, or 3.	Comparable
Aspirin at discharge	Discharged from hospital taking aspirin. (0) No, (1) Yes, (2) Contraindicated, (3) Patient declined treatment, (4) Not applicable For patients who die or are transferred to another hospital. (8) Not indicated, (9) Unknown	Indicate if patient has been prescribed Aspirin at discharge. (0) No, (1) Yes (9) Unknown	**Categorical variable for antiplatelet therapy at discharge:** 0) no antiplatelet therapy, 1) single antiplatelet therapy (either aspirin or thienopyridine inhibitor) or, 2) combined antiplatelet therapy (both aspirin and thienopyridine inhibitor) For the definition of denominator	Comparable (recoded categorical variable)
Clopidogrel at discharge	Discharged from hospital taking Clopidogrel (0) No, (1) Yes, (2) Contraindicated, (3) Patient declined treatment, (4) Not applicable For patients who die or are transferred to another hospital. (8) Not indicated, (9) Unknown	Indicate if patient has been prescribed other platelet inhibitors at discharge. (0) No, (1) Clopidogrel, (2) Ticlopidine, (3) Other, (9) Unknown.		

			to be equal, in MINAP, patients who answered 0, 1, 2, 3, or 8 will be included in the denominator.	
Beta-blocker at Discharge	Discharged from hospital taking beta-blocker. (0) No, (1) Yes, (2) Contraindicated, (3) Patient declined treatment, (4) Not applicable For patients who die or are transferred to another hospital. (8) Not indicated, (9) Unknown	Indicate if patient has been prescribed Beta-blockers at discharge. (0) No, (1) Yes (9) Unknown	**Beta-blocker at discharge** For the definition of denominator to be equal, in MINAP, patients who answered 0, 1, 2, 3, or 8 will be included in the denominator.	Comparable
Statin at discharge	Discharged from hospital on a statin. (0) No, (1) Yes, (2) Contraindicated, (3) Patient declined treatment, (4) Not applicable For patients who die or are transferred to another hospital. (8) Not indicated, (9) Unknown	Indicate if patient has been prescribed statin at discharge. (0) No, (1) Yes (9) Unknown	**Statin at discharge** For the definition of denominator to be equal, in MINAP, patients who answered 0, 1, 2, 3, or 8 will be included in the denominator.	Comparable
ACEI or ARB at discharge	Discharged from hospital on angiotensin converting enzyme inhibitor or angiotensin receptor blocker. (0) No, (1) Yes, (2) Contraindicated, (3) Patient declined treatment, (4) Not applicable For patients who die or are transferred to another hospital. (8) Not indicated, (9) Unknown	Indicate if patient has been prescribed ACE-inhibitors at discharge. (0) No, (1) Yes (9) Unknown Indicate if patient has been prescribed A2-receptor antagonists at discharge. (0) No, (1) Yes (9) Unknown	**ACEI or ARB at discharge** For the definition of denominator to be equal, in MINAP, patients who answered 0, 1, 2, 3, or 8 will be included in the denominator. In RIKS-HIA, For patient with non-missing	Comparable

			data for either ACE-inhibitors or A2-receptor antagonists variables, if he or she replied yes to one of them then ACEI or ARB at discharge equals to 1.	
Pre-hospital fibrinolytic therapy	Location of initial reperfusion treatment. (0) No reperfusion attempted, (1) Before admission to hospital: Treatment before reaching hospital regardless of who initiated treatment. (2) In A&E: Regardless of who initiated treatment there. (3) In CCU (direct admission): A patient who enters CCU directly from an ambulance without assessment by hospital clinical staff before arrival. (4) In CCU (slow-track): Implies admission via A&E or other assessment unit where a diagnosis of definite infarction was made, followed by transfer to CCU where thrombolytic treatment was initiated. (5) Elsewhere in hospital: Includes acute admission units, general medical wards and catheter laboratories. (6) Cath lab. (9) Unknown	Pre-hospital thrombolysis (0) No (1) Yes Start of reperfusion treatment: specify date and time for start of reperfusion therapy (thrombolysis/PCI/CABG)	**Pre-hospital fibrinolytic therapy** In MIANP, for patients with non-missing data on reperfusion time or location of initial reperfusion treatment, pre-hospital reperfusion equals 1 if reperfusion time prior to admission time or if the answer is 1 for location of initial reperfusion treatment.	Comparable
Reperfusion treatment given in hospital.	Reperfusion treatment given in hospital. (0) None, (1) Thrombolytic treatment, (2) pPCI in house, Primary PCI for STE MI. Includes patients presenting with a clear history of AMI and LBBB. (3) Referred for consideration for pPCI elsewhere, Intended primary PCI for STEMI/LBBB. At the time of referral (or data entry) the reperfusion treatment actually performed may not be known. These cases will subsequently be linked with the interventional hospital record. (9) Unknown	Reperfusion treatment, specify type of initial reperfusion treatment. (0) None: No initial reperfusion treatment given. (1) Thrombolysis: one thrombolytic agent has been administered. (2) Primary PCI: Emergency PCI for acute STEMI, no thrombolysis given. Includes patients presenting with a clear history of AMI and LBBB. (3) Facilitated PCI: PCI performed in the acute setting as soon as possible after thrombolysis for acute STEMI (or new LBBB) with a clear history of AMI, provided as a routine treatment in addition to thrombolysis. (4) Acute CABG: CABG for acute STEMI, either no thrombolysis given or no Primary PCI performed. Includes patients presenting with a clear history of AMI and LBBB.	**Dummy variable for primary reperfusion therapy: primary PCI, pre-reperfusion therapy, inhospital reperfusion therapy.** Primary PCI > pre-reperfusion therapy > inhospital reperfusion therapy.	Comparable (recoded dummy variable)

Time from symptom onset to fibrinolytic therapy (minutes) for fibrinolytic therapy	Median time from symptom onset to fibrinolytic therapy (if administered prior to or after hospital admission) in MI patients with ST-segment elevation		**Symptom to fibrinolysis time**	Comparable
Median time from hospital admission to primary PCI (minutes)	Median time from hospital arrival to primary PCI in MI patients with ST-segment elevation.		**Symptom to primary PCI time**	Comparable
Coronary intervention (other than primary PCI)	Coronary intervention during this episode performed either in your hospital or by referral to another hospital. Do not use for primary PCI or rescue PCI. (1) Percutaneous coronary intervention, (2) CABG, (4) PCI planned after discharge, (5) CABG planned after discharge, (6) Not applicable: For use when there is advanced malignancy, dementia, progressive neurological disease or other conditions having an immediate impact on prognosis. Includes other clinical reasons identified by the clinician, (7) Patient refused, (8) Not performed or arranged, (9) Unknown, (1) Angioplasty	Indicate if a PCI (other than primary) was performed during this admission (0) No, (1) Yes, (2) Planned after discharge, (9) Unknown. Indicate if a CABG was performed during this admission (0) No, (1) Yes, acute CABG, (2) Yes, during hospitalization, (3) Planned after discharge, (9) Unknown.	**Coronary intervention (other than primary PCI)** For patients with non-missing data, coronary intervention (other than primary PCI) equals to 1, if response equals to 1 or 2 in MINAP; and for patient with replied (1) Yes to either one of the variables in RIKS-HIA.	Comparable (recoded categorical variable)

Table S2. Distribution of diagnostic markers for defining MI in all MI patients, STEMI and NSTEMI patients

Diagnostic markers among all MI patients

Year	N		Maximum troponin T (µg/L)				Maximum troponin I (µg/L)			
	Sweden	UK	Sweden		UK		Sweden		UK	
			%	Median (Q1, Q3)	%	Median (Q1, Q3)	%	Median (Q1, Q3)	%	Median (Q1, Q3)
2004	18440	55467	49.3	0.87 (0.26, 2.66)	3.4	0.91 (0.31, 2.56)	38.0	7.4 (1.7, 30.18)	3.6	11.3 (2.4, 45)
2005	17403	54440	49.6	0.76 (0.22, 2.4)	33.8	0.71 (0.23, 2.2)	41.6	5.7 (1.33, 22.9)	27.4	6.9 (1.43, 28.18)
2006	17007	52791	50.3	0.68 (0.2, 2.2)	43.1	0.67 (0.22, 2.18)	43.7	4 (0.89, 16)	41.3	5.8 (1.25, 23.99)
2007	17764	53287	45.3	0.60 (0.18, 2.07)	40.6	0.65 (0.206, 2.15)	50.1	3.8 (0.74, 15.9)	48.4	4.8 (0.93, 21.38)
2008	16845	55865	39.8	0.64 (0.2, 2.14)	36.5	0.58 (0.18, 2)	55.7	3.40 (0.63, 15.58)	55.0	4.1 (0.7, 21.09)
2009	15939	58496	38.9	0.68 (0.2, 2.39)	34.6	0.54 (0.16, 1.98)	56.5	3.43 (0.62, 15.4)	58.1	3.7 (0.59, 19.82)
2010	16388	60731	44.4	0.65 (0.19, 2.4)	37.1	0.7 (0.17, 3.69)	46.1	3.2 (0.6, 17)	54.9	3.2 (0.48, 17.81)
2004-2010	119786	391077	45.5	0.7 (0.2, 2.3)	32.7	0.65 (0.20, 2.26)	47.2	4.15 (0.83, 18.01)	41.6	4.4 (0.77, 21.68)

*During 2004-2010, among all patients, the % of patients that did not have information on biomarkers is 6.9% in Sweden and 4.1% in the UK; the % of patients with missing troponin values was 7.3% in Sweden and 10.7% in the UK.

Diagnostic markers among all STEMI patients

Year	N		Maximum troponin T (µg/L)				Maximum troponin I (µg/L)			
	Sweden	UK	Sweden		UK		Sweden		UK	
			%	Median (Q1, Q3)	%	Median (Q1, Q3)	%	Median (Q1, Q3)	%	Median (Q1, Q3)
2004	5951	20311	49.1	2.12 (0.68, 6.23)	3.5	2.55 (0.88, 5.91)	34.4	25.91 (5.8, 66.8)	3.7	45 (12, 50)
2005	5709	22197	52.2	2 (0.49, 5.2)	31.5	2.19 (0.76, 5.7)	34.2	20.85 (4.4, 50)	24.9	26.3 (7.16, 50)
2006	5482	22447	53.0	1.9 (0.46, 4.9)	39.9	2.13 (0.65, 5.33)	37.0	14.67 (3.11,47.43)	36.8	23.8 (6.02, 50)
2007	5542	22767	48.7	1.7 (0.415, 5)	39.9	2 (0.56, 5.32)	44.3	17 (3.53, 50)	41.7	21.7 (5.1, 50)
2008	5343	22787	44.3	1.74 (0.48, 4.7)	36.6	1.9 (0.54, 5.03)	49.4	16.97 (3.13, 50)	48.3	22.87 (4.7, 50)
2009	5148	23365	43.0	2.1 (0.56, 5.23)	37.2	1.82 (0.51, 4.54)	50.7	16.5 (3.47, 50)	50.8	23.315 (4.51, 50)
2010	5257	23544	48.1	2.20 (0.69, 5.43)	39.1	2.61 (0.7, 8.355)	42.1	18.6 (3.1, 50)	48.0	22.58 (3.9, 50)
2004-2010	38432	157418	48.5	2 (0.53, 5.24)	33.0	2.08 (0.62, 5.51)	41.5	18.03 (3.7, 50)	37.0	23.36 (5.02, 50)

*In all STEMI patients during 2004-2010, the % of patients that did not have information on biomarkers is 9.6% in Sweden and 8% in the UK; the % of patients with missing troponin values was 10% in Sweden and 20.4% in the UK.

Diagnostic markers among all NSTEMI patients

Year	N		Maximum troponin T (µg/L)				Maximum troponin I (µg/L)			
	Sweden	UK	Sweden		UK		Sweden		UK	
			%	Median (Q1, Q3)	%	Median (Q1, Q3)	%	Median (Q1, Q3)	%	Median (Q1, Q3)
2004	12489	35156	49.4	0.58 (0.2, 1.66)	3.3	0.56 (0.22, 1.39)	39.7	4.7 (1.3, 16.34)	3.5	5.62 (1.4, 19.1)
2005	11694	32243	48.4	0.5 (0.18, 1.52)	35.4	0.41 (0.17, 1.1)	45.3	4 (1.1, 13.2)	29.2	3.49 (0.86, 12.2)
2006	11525	30344	48.9	0.44 (0.17, 1.37)	45.5	0.39 (0.17, 1)	46.9	2.6 (0.69, 9.29)	44.6	2.9 (0.76, 9.93)
2007	12222	30520	43.8	0.4 (0.15, 1.1)	41.1	0.37 (0.15, 0.93)	52.7	2.31 (0.56, 8.6)	53.4	2.43 (0.55, 8.65)
2008	11502	33078	37.7	0.41 (0.15, 1.2)	36.4	0.33 (0.13, 0.86)	58.7	2 (0.48, 8)	59.6	2.01 (0.43, 8.04)
2009	10791	35131	37.0	0.41 (0.15, 1.2)	33.0	0.29 (0.12, 0.75)	59.3	2 (0.47, 7.5)	63.0	1.78 (0.37, 7.3)
2010	11131	37187	42.6	0.378 (0.14, 1.1)	35.8	0.33 (0.12, 1.19)	48.0	1.9 (0.45, 7.65)	59.2	1.55 (0.31, 6.67)
2004-2010	81354	233659	44.1	0.45 (0.17, 1.3)	32.5	0.36 (0.14, 0.96)	49.9	2.6 (0.63, 9.69)	44.6	2.18 (0.46, 8.36)

*In all NSTEMI patients during 2004-2010, the % of patients that did not have information on biomarkers is 5.6% in Sweden and 1.4% in the UK; the % of patients with missing troponin values was 6% in Sweden and 4.2% in the UK.

Propensity analyses

There are two propensity analyses used in the study, with different aims.

First propensity score

The purpose of *first propensity score* is to examine the selection bias from differences in making the MI diagnosis, and the results are used only to support credibility regarding (absence of) selection bias for MI diagnosis. To reassure the reviewer there were non-MI cases used in this score.

In practise, the probability of diagnosis with AMI was derived from propensity model constructed in the UK among all ACS patients (including non-MI diagnoses, N=482,684). The model included 17 casemix variables, with discrimination as indicated by a c-statistic of 0.81. The same model was applied both to the UK and Sweden population, then compare the propensity of AMI diagnosis between UK AMI patients and Sweden AMI patients.

Findings

The propensity scores for AMI diagnosis were very similar with a median (interquartile range, 1st and 3rd quartiles) of 0.97 (0.82, 0.98) in Swedish patients and 0.96 (0.79, 0.98) in UK patients. The similar propensity suggests low selection bias for AMI diagnosis between the two countries.

Second propensity score

The purpose of the *second propensity score* matching was to identify a subgroup of UK AMI patients that were comparable to Sweden patients, to study if the treatment and mortality differ.

As UK AMI patient population was greater than Sweden, we thus identify the best comparable UK patients to Swedish patients using propensity matching, and the matching was stratified by STEMI and NSTEMI. For matching among STEMI patients, the propensity of being a STEMI patient in Sweden was calculated from a propensity model based on all AMI patients in Sweden. The logistic regression model discrimination as indicated by the c-statistic was 0.76. The model was applied to the UK to calculate the propensity of being a STEMI patient among all AMI patients in the UK. Same method was applied for NSTEMI matching, and the matching patients were combined as one matching AMI patients in the UK to Sweden AMI patients. The Greedy matching technique was applied for the matching, in which the initial matching was performed with a precision of 4 digits after decimal point of the propensity score.(1) For those who were not matched at 4-digit level, the matched were performed with a precision of 3 digits after decimal point, again for those who were unmatched; the match was performed at 2-digit precision level, then 1-digit precision level.(1) The analyses were based on multiple imputed data.

Findings

119,714 UK patients were matched to 119,786 Sweden patients, a matching completeness of 99.9%. The distributions of most casemix variables were balanced between UK matching patients and Sweden patients. For few variables with different distribution between the two countries (smoking, history of hypertension, heart failure, cardiac arrest, and prior PCI), the magnitude of difference decreased markedly as compared to the entire UK AMI population (Table 1 of the manuscript).

Between Sweden AMI patients and the matching UK patients, differences in AMI treatment and outcome resembled the differences observed between all AMI patients (unmatched) in Sweden and the UK, where percentage of primary PCI among STEMI patients was significantly higher in Sweden and percentage of fibrinolysis was higher in the UK. Sweden had higher percentage of coronary intervention other than primary PCI and intravenous glycoprotein IIb/IIIa receptor inhibitors use than the UK. (Table S3) The 30-day mortality was 7.7% (95% CI: 7.6%, 7.9%) in Sweden and 11.0% (95% CI: 10.8%, 11.2%) in the UK matching patients. The 30-day mortality difference between Sweden and the matching UK patients decreased over time, especially in the later years. In 2004, the 30-day AMI mortality was 14.8%, 95% CI: (14.2%, 15.3%) in the UK matching patients, and 9.9% (9.4%,10.3%) in Sweden; in 2009 was 8.7% (8.2%, 9.1%) in the UK matching group and 6.4% (6%,6.8%) in Sweden; in 2010 was 8.6% (8.1%, 9.0%) in the UK and 6.5% (6.1%,6.9%) in Sweden, corresponding to a reduction of relative risk from 1.50 (95% CI: (1.41,1.58)) in 2004 to 1.31 (1.22,1.42) in 2010, comparing the mortality in the UK matching patients to Sweden patients (p for time effect: 0.04, Figure S1). Results of propensity matching analyses were in agreement with results from standardised mortality in the manuscript.

Table S3. Casemix and treatment for patients with acute MI in Sweden (n=119,786) and the matching UK patients (n=119,714), % (95% confidence interval) if not indicated

	Sweden (n=119,786)	UK matching group (n=119,714)
Casemix		
STEMI	32.1 (31.8, 32.3)	32.1 (31.8, 32.3)
Age, year, mean, SD	71.2, 12.3	70.9, 13.5
Female	36.3 (36.1, 36.6)	35.9 (35.6, 36.2)
MI severity, median (1st and 3rd quartiles)		
Systolic blood pressure, mmHg	145 (125, 165)	140 (120, 160)
Heart rate, beat per minute	78 (65, 93)	80 (68, 97)
Troponin I, µg/L	4.2 (0.8, 18.0)	3.04 (0.59, 16.44)
Troponin T, µg/L	0.7 (0.2, 2.3)	0.47 (0.16, 1.76)
Risk factor, clinical history, treatment prior to admission		
Current smoking	23.3 (23.0,23.5)	26.1 (25.9, 26.4)
History of diabetes	22.7 (22.4,22.9)	19.9 (19.6, 20.1)
History of hypertension	45.2 (44.9,45.5)	49.9 (49.6, 50.2)
Heart Failure	9.7 (9.5,9.8)	8.8 (8.6, 8.9)
Cardiac arrest prior to admission	1.3 (1.3,1.4)	2 (1.9, 2.1)
Cerebrovascular disease	10.1 (9.9,10.3)	9.9 (9.7, 10.1)
Myocardial infarction	22.4 (22.1,22.6)	22.5 (22.3, 22.8)
Antiplatelet mono-therapy	36.6 (36.3,36.9)	30.8 (30.5, 31.1)
Antiplatelet dual therapy	4 (3.9,4.1)	4.2 (4, 4.3)
Prior PCI	8.0 (7.8,8.2)	6 (5.9, 6.2)
Prior CABG	7.7 (7.6,7.9)	7.2 (7.1, 7.4)
Hospital treatment		
STEMI patients		
Pre-hospital fibrinolysis	4.1 (3.9, 4.4)	8.7 (8.4, 9)
Primary PCI	59.3 (58.8, 59.8)	21.5 (21.1, 21.9)
In-hospital fibrinolysis	11.8 (11.5,12.1)	51.7 (51.2, 52.2)
Delay time, minutes, median (interquartile range)		
From symptom onset to fibrinolysis	177 (108,322)	152 (95, 290)
From symptom onset to primary PCI	198 (129,365)	201 (139,331)
STEMI and NSTEMI patients		
Coronary intervention other than primary PCI	28.6 (28.4, 28.9)	17.1 (16.9, 17.3)
Intravenous glycoprotein IIb/IIIa receptor inhibitors	21.0 (20.8, 21.2)	7.7 (7.6, 7.9)
Anticoagulants	73.2 (73.0, 73.5)	83.6 (83.4, 83.8)
Hospitalization, days, median (interquartile range)	5 (3,7)	6 (4, 11)
30-day mortality	7.7 (7.6,7.9)	11.0 (10.8,11.2)

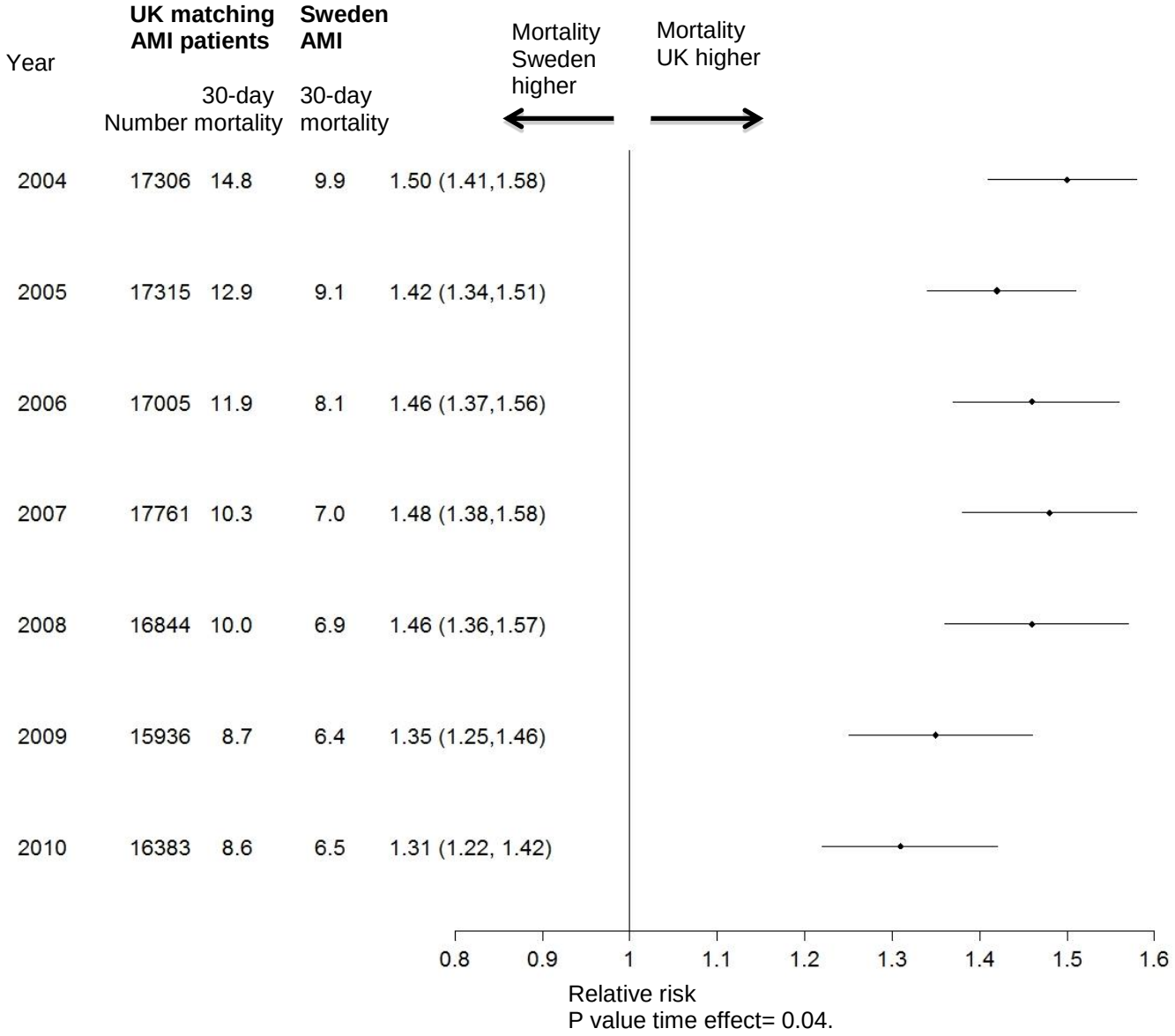


Figure S1. AMI 30-day mortality of Sweden patients and matching UK patients admitted in each study year (2004-2010)

Management of missing values for casemix modelling

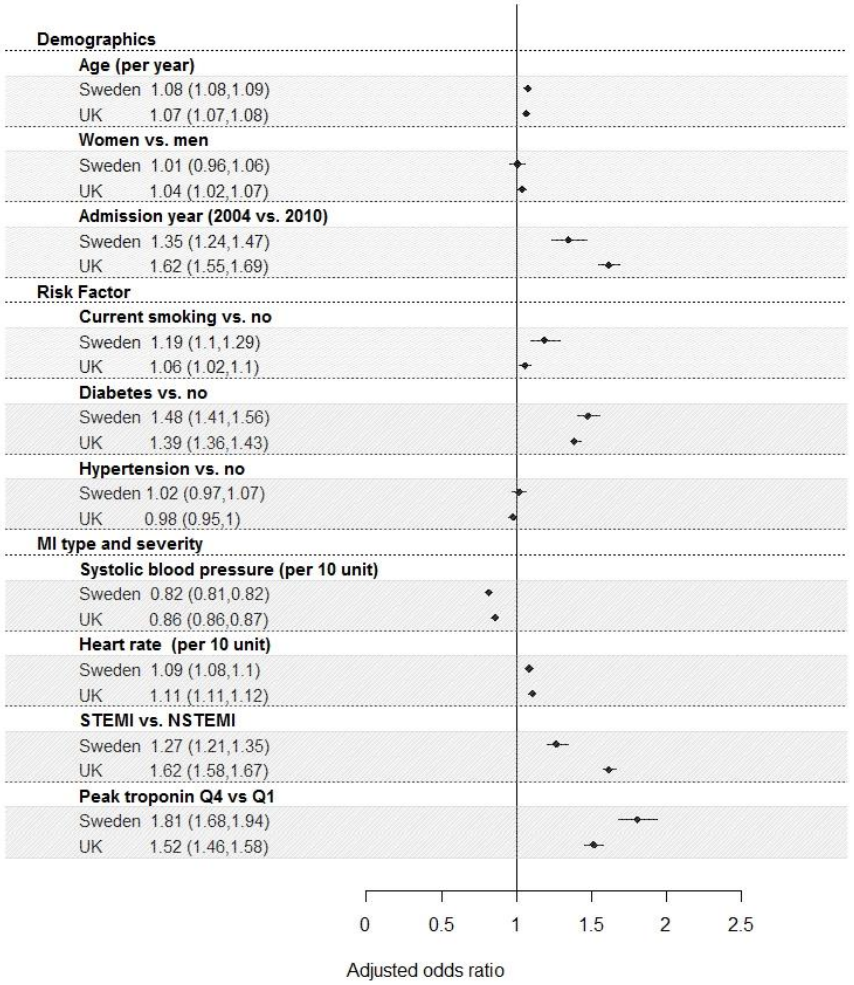
The extent of missing data in RIKS-HIA and MINAP are shown in Table S4. To appropriately utilize all available data, specifically for the casemix model of 30-day mortality in Sweden and the UK, we imputed missing casemix variables using the SAS multiple imputation procedures, replacing each missing value with a set of values which represent a random sample of the missing value.(2) We used the Markov Chain Monte Carlo algorithm for arbitrary missing data patterns.(3) The number of imputations in the study is 35.

In multiple imputation for missing casemix information, we include casemix variables of gender, smoking, history of diabetes and hypertension, troponin, admission systolic blood pressure, admission heart rate, history of cardiovascular disease (heart failure, cardiac arrest prior to admission, cerebrovascular disease, MI), procedure and medication prior to hospital admission (anti-platelet treatment, PCI, CABG), treatment applied for all AMI patients (non-primary PCI, Intravenous glycoprotein IIb/IIIa receptor inhibitors use, heparin use), the follow-up time and vital status of each patient during the entire study period from 2004 to 2010. For analyses based on multiple imputed data, imputed values for categorical variables were not rounded to avoid bias in the estimates.(4;5) Figure S2 summarized the adjusted odds ratios for the association of casemix with 30-day mortality based on multiple imputed data.

For sensitivity analyses to verify the results based on multiple imputed data, we construct identical casemix models for patients with complete data for all casemix variables. The adjusted odds ratios for 30-day mortality (Figure S3) from models based on these patients were similar to results based on imputed data (Figure S2).

Table S4. The extent of missingness (%) of casemix variables for multivariate models of the study

Variables of interest	RIKS-HIA N=119,786	MINAP N=391,077
STEMI	2	0
Age, year	0	0
Female	0	0
MI severity		
Systolic blood pressure, mmHg	12	14
Heart rate, beat per minute	11	14
Troponin categories	7	29
Risk Factor		
Current smoking	10	9
History of diabetes	1	5
History of hypertension	2	6
Cardiovascular Disease History		
Heart Failure	6	9
Cardiac arrest prior to admission	0	5
Cerebrovascular disease	19	9
Myocardial infarction	1	6
Pre-hospital Treatment		
Antiplatelet therapy	1	5
Prior PCI	1	8
Prior CABG	1	8



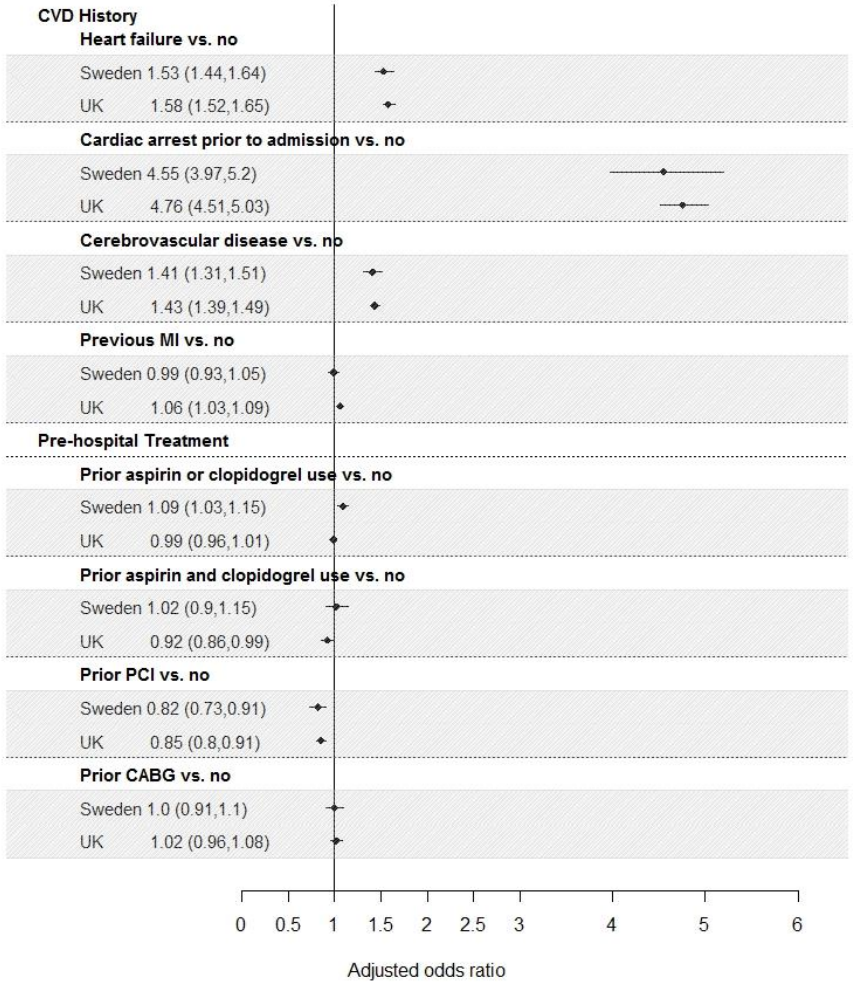


Figure S2. Forest plot of odds ratios with 95% confidence intervals from multivariate models for the association of casemix with 30-day mortality among AMI patients using multiple imputed data in Sweden (n=119,786) and the UK (n=391,077). *Troponin quartiles were defined separately for I and T and separately within each country

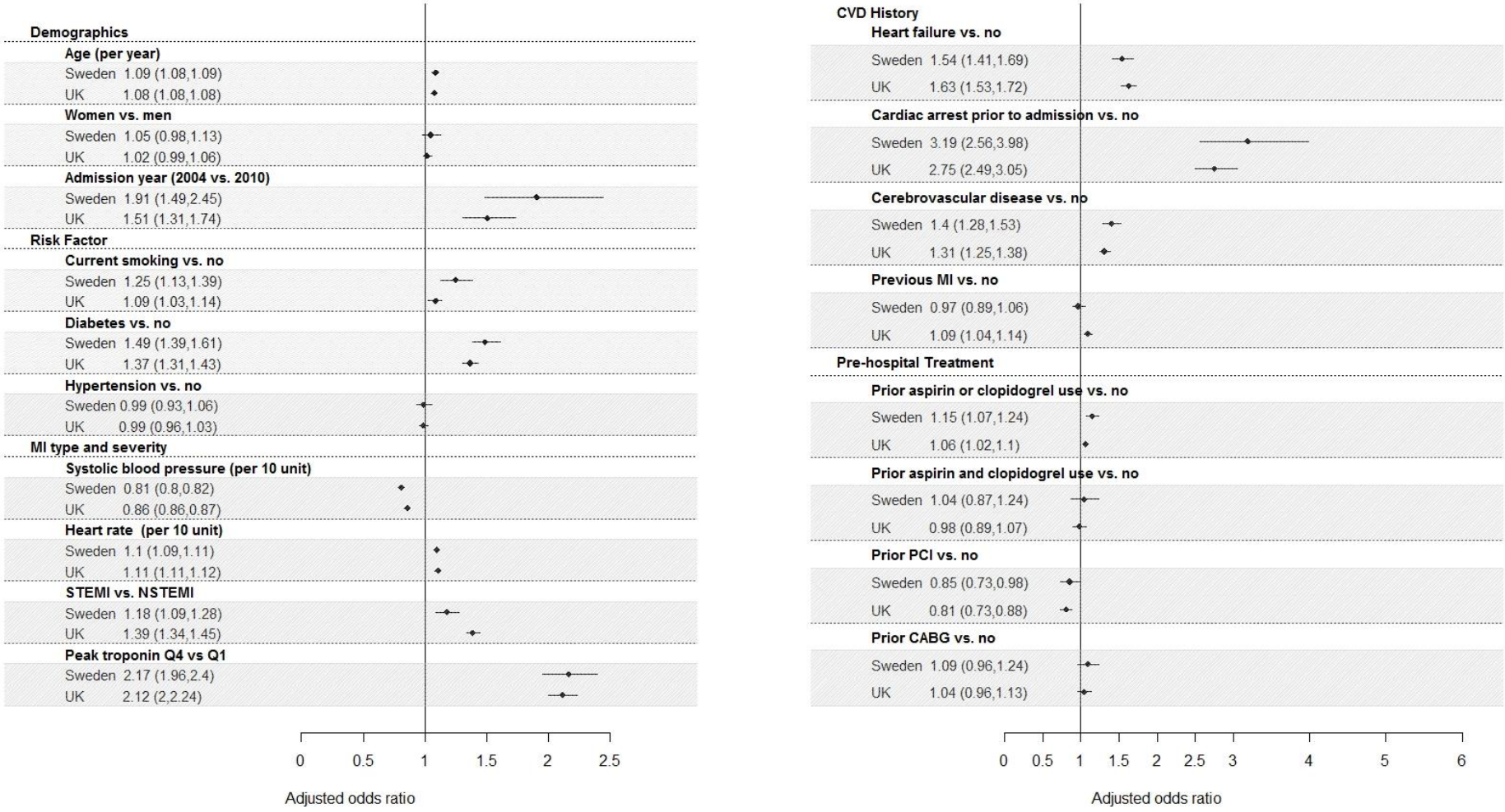


Figure S3. Forest plot of odds ratios with 95% confidence intervals from multivariate models for the association of casemix with 30-day mortality among patients with complete data for casemix variables and 30-day mortality in Sweden (n=73,968) and the UK (n=209,330)

Treatment

Table S5. Use of treatment for AMI by year in Sweden and the UK, %

	Reperfusion among STEMI patients Sweden (n=38,432) and the UK (n=157,418)				Medications at discharge from hospital Sweden (n=112,837) and the UK (n=355,616)									
	Primary PCI		Any fibrinolysis[1]		Any antiplatelet		Dual antiplatelet		Beta-blocker		ACEI/ARB		Statin	
	Sweden	UK	Sweden	UK	Sweden	UK	Sweden	UK	Sweden	UK	Sweden	UK	Sweden	UK
2004	35.5	3.4	29.8	83.5	92.4	93.4	50.9	2.4	87.6	74.4	51.5	80.2	69.7	90.5
2005	49.6	5.0	18.8	73.8	93.6	94.0	59.9	36.8	87.9	75.4	50.8	80.0	73.8	92.1
2006	61.5	10.1	10.0	66.7	94.4	94.8	67.1	64.7	88.0	75.9	52.9	81.5	78.1	93.3
2007	64.9	15.0	6.9	60.1	94.8	95.7	69.4	78.2	89.4	77.8	56.3	82.6	81.6	93.6
2008	67.4	25.5	6.0	48.8	95.5	95.5	73.5	78.7	89.2	79.6	58.7	82.8	83.9	93.3
2009	70.2	39.8	5.6	33.4	96.1	96.1	76.3	81.0	89.0	80.7	60.9	84.0	85.4	93.4
2010	69.7	53.1	5.9	19.9	96.0	96.4	77.8	82.7	89.9	82.5	62.8	84.8	86.4	93.6

. [1] Includes pre-hospital fibrinolysis or in-hospital fibrinolysis

In-hospital mortality

Table S6. In-hospital crude mortality (%) in AMI patients in Sweden (n=119,786) and the UK (n=391,077) in clinically relevant sub-groups

	Distribution (%)		In-hospital mortality (%)	
	Sweden	UK	Sweden	UK
STEMI	32	40	7 (6.7, 7.3)	9.4 (9.3, 9.6)
NSTEMI	68	60	5.2 (5.1, 5.4)	8.3 (8.2, 8.5)
Severity of Myocardial infarction				
Troponin I (µg/L) categories				
<5	53	52	3.4 (3.2, 3.6)	5.9 (5.8, 6.1)
5-9.9	11	11	4.8 (4.3, 5.4)	7.7 (7.4, 8.2)
10-20	11	11	5.5 (5, 6.1)	7.9 (7.5, 8.3)
≥20	24	26	8.1 (7.6, 8.5)	9.4 (9.2, 9.7)
Troponin T (µg/L) categories				
<0.2	24	25	4.3 (3.9, 4.6)	6.1 (5.9, 6.4)
0.2-0.5	19	19	4.1 (3.7, 4.5)	7 (6.7, 7.4)
0.5-1	15	14	5.2 (4.7, 5.7)	7.6 (7.2, 8)
≥1	43	41	8.5 (8.2, 8.9)	9.9 (9.7, 10.2)
Admission Systolic Blood Pressure, mmHg				
<110	9	14	19.5 (18.7, 20.3)	19.1 (18.7, 19.4)
110-140	30	37	6.7 (6.4, 6.9)	8.8 (8.7, 9)
≥140	60	49	3 (2.9, 3.2)	5.5 (5.4, 5.6)
Admission heart rate, beat per minute				
<90	70	68	4.2 (4.1, 4.4)	6.5 (6.4, 6.6)
90-120	23	24	8.5 (8.2, 8.9)	12.7 (12.5, 13)
≥120	7	7	10.4 (9.7, 11)	15.3 (14.8, 15.7)
Demographic characteristics				
Male	64	65	5 (4.8, 5.1)	7.2 (7.1, 7.3)
Female	36	35	7.2 (7, 7.5)	11.8 (11.6, 12)
Age <65 years	30	36	1.5 (1.4, 1.6)	2.4 (2.3, 2.5)
Age 65-75 years	25	24	3.5 (3.3, 3.7)	6.5 (6.3, 6.6)
Age 75-85 years	30	26	7.9 (7.6, 8.1)	13.3 (13.1, 13.5)
Age ≥85 years	14	13	14.5 (14, 15)	21.6 (21.2, 21.9)
Year				
2004	15	14	7.5 (7.1, 7.9)	11.1 (10.8, 11.3)
2005	15	14	6.9 (6.5, 7.3)	10.4 (10.2, 10.7)
2006	14	14	6.2 (5.8, 6.5)	9.4 (9.1, 9.6)
2007	15	14	5.1 (4.8, 5.5)	8.5 (8.3, 8.7)
2008	14	14	5.2 (4.9, 5.5)	8.1 (7.9, 8.3)
2009	13	15	4.6 (4.3, 4.9)	7.4 (7.2, 7.6)
2010	14	15	4.9 (4.6, 5.3)	6.9 (6.7, 7.1)
Risk factors				
Diabetes	23	18	7.4 (7.1, 7.7)	10.6 (10.3, 10.8)
No diabetes	77	82	5.2 (5.1, 5.4)	7.9 (7.9, 8)
Current smoker	23	29	3.3 (3.1, 3.5)	4.3 (4.2, 4.4)
Non smoker	77	71	5.3 (5.2, 5.5)	8.6 (8.5, 8.7)

UK 30-day mortality standardised by Swedish casemix associated mortality

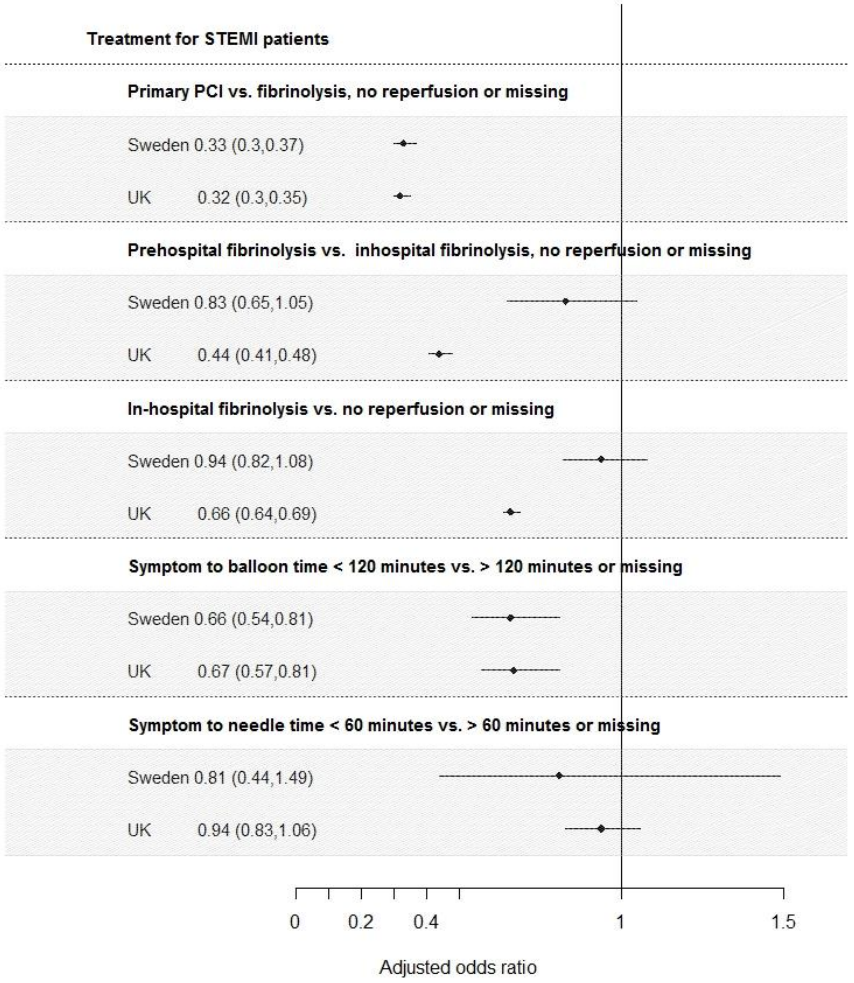
UK 30-day mortality was standardised by applying 10,000 randomly sampled Sweden casemix models to the UK MINAP population (with multiply imputed data). We assumed that for each simulation and for each UK patient, that patient was treated by any given Swedish hospital with a chance proportional to the number of AMI patients treated during 2004-2010 at the hospital.

UK 30-day mortality standardised by Swedish casemix and in-hospital treatment

Using the same approach, this time including in the model in-hospital treatment in addition to casemix variables, we obtained UK standardised mortality. We report the association between hospital treatment and 30-day mortality in Sweden and the UK, adjusted for casemix (Supplementary figure S4). The results needed to be interpreted with caution, as efficacy of these evidence-based treatments has been well established in randomized clinical trials, and discrepancy in treatment effects between the two countries may be due to the observational nature of the study, where estimates represent a combination of treatment effect and factors influencing treatment selection, and such factors may not be readily available in the captured clinical data.

Section 9: UK number of deaths prevented assuming the level of Swedish treatment use

We estimated the number of deaths at 30-day prevented if the use of primary PCI and discharge beta-blockers in the UK was at the same level as in Sweden. The two treatments were selected as their use in the UK was consistently lower than in Sweden. The treatment effect for the estimation is based on literature (6;7) (Table S7). The estimated number of deaths prevented had the UK implemented primary PCI and beta-blocker medication with the same frequency as Sweden during 2004 and 2010 was 1,741, resulting in a reduction of observed UK mortality from 10.61% to 10.17%. Given the Sweden casemix standardized UK mortality of 7.73%, the estimated standardised mortality ratio consequently reduced from 1.37 (1.30, 1.45) to 1.31 (1.30, 1.33).



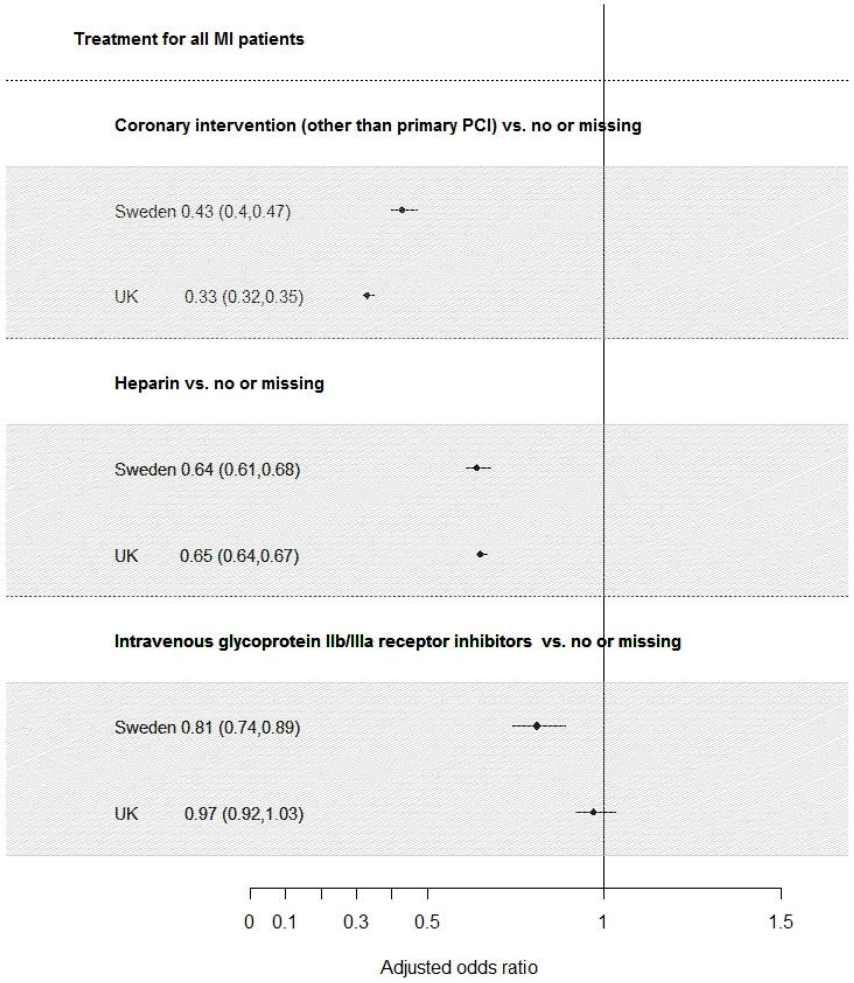


Figure S4. Forest plot of odds ratios with 95% confidence intervals from multivariate models for the association of hospital treatment with 30-day mortality among AMI patients using multiple imputed data in Sweden (n=119,786) and the UK (n=391,077), adjusted for casemix and hospital volume.

Table S7. Estimated number of deaths at 30-day prevented if use of treatment in the UK reached Swedish levels[1,2]

Year	% Primary PCI		N of UK STEMI patients	Estimated number of STEMI patients switched to receive Primary PCI based on Sweden use	Observed 30-day mortality, %	Reduced mortality (%) due to switch. Relative risk of primary PCI versus thrombolytic therapy = 0.75	Estimated number of deaths prevented
	Sweden	UK					
2004	35.5	3.4	20311	6520	12.3	9.2	202 (175,230)
2005	49.6	5	22197	9900	13	9.8	317 (282,351)
2006	61.5	10.1	22447	11538	11.9	8.9	346 (310,382)
2007	64.9	15	22767	11361	11.3	8.5	318 (284,353)
2008	67.4	25.5	22787	9548	10.6	8	248 (218,279)
2009	70.2	39.8	23365	7103	10.1	7.6	178 (152,203)
2010	69.7	53.1	23544	3908	9.7	7.3	94 (75,113)
All years			157418	59878			1703 (1623,1782)

Year	% Beta-blocker		UK AMI patients survived beyond discharge	Estimated number of MI patients switched to receive beta-block based on Sweden use	Observed mortality from discharge to 30-day, %	Reduced mortality (%) due to switch. Relative risk of beta-blocker versus placebo = 0.95	Estimated number of deaths prevented
	Sweden	UK					
2004	87.6	74.4	48987	6466	1.7	1.6	6 (1,11)
2005	87.9	75.4	48495	6062	1.9	1.8	6 (1,11)
2006	88	75.9	47628	5763	1.8	1.7	6 (1,10)
2007	89.4	77.8	48630	5641	1.9	1.8	6 (1,10)
2008	89.2	79.6	51264	4921	1.8	1.7	5 (1,9)
2009	89	80.7	54119	4492	1.6	1.5	4 (0,9)
2010	89.9	82.5	56493	4180	1.6	1.5	4 (0,8)
All years			355616	37525			38 (26,60)

[1] Meta-analysis of 23 trials of primary PCI versus thrombolytic therapy, gives a relative risk reduction of 0.75 (absolute risks 6.97% versus 9.31%) for short term mortality. (Keeley EC et al. Lancet. 2003 Jan 4;361(9351):13-20).

[2] Systematic review of 6 trials of beta-blocker versus placebo on mortality at 28 days, gives a relative risk reduction of 0.95 (absolute risks 12.93% versus 13.50%) (Freemantle N, et al. BMJ. 1999 Jun 26;318(7200):1730-7.)

Table S8. Casemix for STEMI patients and STEMI patients not receiving reperfusion in Sweden and the UK. Values are **%** (95% confidence interval) unless otherwise indicated

Casemix	Sweden		UK	
	All STEMI (n=38,432)	STEMI without reperfusion (n=11,075)	All STEMI (n= 157,418)	STEMI without reperfusion (n=36,395)
Age, year, mean, SD	68.7, 12.6	73.8, 12.6	66.2, 13.5	70.9,14.0
Female	33.6 (33.2, 34.1)	43.5 (42.6, 44.4)	30.1 (29.9, 30.3)	38.5 (38, 39)
MI severity, median (1st and 3rd quartiles)				
Systolic blood pressure, mmHg	140 (120, 160)	140 (120, 160)	136 (117, 155)	134 (115, 154)
Heart rate, beat per minute	75 (63, 90)	80 (67, 98)	76 (64, 90)	81 (68, 98)
Troponin I, µg/L	18.03 (3.7, 50)	8.9 (2.3, 28.3)	23.4 (5.0, 50)	12.05 (3.03, 36.17)
Troponin T, µg/L	2 (0.53, 5.24)	1.18 (0.39,2.92)	2.08 (0.62, 5.51)	1.17 (0.4, 2.805)
Risk factor				
Current smoking	30.1 (29.6, 30.6)	22.7 (21.9, 23.6)	38.4 (38.2, 38.7)	29.4 (28.9, 29.9)
History of diabetes	18.2 (17.9, 18.6)	22.4 (21.6, 23.2)	12.8 (12.7, 13.0)	16.3 (15.9, 16.7)
History of hypertension	39.7 (39.2, 40.2)	43.6 (42.7, 44.5)	41.6 (41.4, 41.9)	45.8 (45.3, 46.3)
Cardiovascular disease history				
Heart Failure	4.1 (3.9, 4.3)	8.9 (8.4, 9.5)	2.1 (2, 2.2)	4.1 (3.8, 4.3)
Cardiac arrest prior to admission	2.3 (2.2, 2.5)	1.5 (1.3, 1.7)	3.8 (3.7, 3.9)	3.6 (3.4, 3.8)
Cerebrovascular disease	7.5 (7.2, 7.8)	12.1 (11.4, 12.8)	5.8 (5.7, 5.9)	10 (9.7, 10.4)
Myocardial infarction	13.6 (13.3, 14)	20.3 (19.5, 21)	11.2 (11, 11.4)	13.7 (13.3, 14.1)
Pre-hospital treatment				
Antiplatelet mono-therapy	25 (24.6, 25.5)	34.8 (33.9, 35.7)	19.3 (19.1, 19.5)	23.4 (22.9, 23.8)
Antiplatelet dual-therapy	2.4 (2.2, 2.5)	3.2 (2.9, 3.5)	1.8 (1.8, 1.9)	2.6 (2.5, 2.8)
PCI	5.5 (5.3, 5.8)	5.2 (4.8, 5.7)	4 (3.9, 4.2)	3.4 (3.2, 3.6)
CABG	3.4 (3.2, 3.5)	5.3 (4.9, 5.7)	2.2 (2.2, 2.3)	2.9 (2.7, 3.1)

Abbreviations: STEMI, ST-elevation myocardial infarction; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft surgery.

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