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**Article:**

Alabas, OA, Jernberg, T, Pujades-Rodriguez, M et al. (2020) Statistics on mortality following acute myocardial infarction in 842 897 Europeans. *Cardiovascular Research*, 116 (1). pp. 149-157. ISSN: 0008-6363

<https://doi.org/10.1093/cvr/cvz197>

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1 **Statistics on mortality following acute myocardial infarction in 842 897 Europeans**

2

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24 **Keywords**

25 Mortality, acute myocardial infarction, SWEDHEART, MINAP, Sweden, UK

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31 **Abstract**

32 **Aims**

33 To compare ST-segment elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI)  
34 mortality between Sweden and the UK, adjusting for background population rates of expected death,  
35 case mix and treatments.

36 **Methods and results**

37 National data were collected from hospitals in Sweden (n=73 hospitals, 180,368 patients, Swedish  
38 Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated  
39 According to Recommended Therapies [SWEDEHEART]) and the UK (n=247, 662,529 patients,  
40 Myocardial Ischaemia National Audit Project [MINAP]) between 2003 and 2013. There were lower  
41 rates of revascularisation [STEMI (43.8% vs. 74.9%); NSTEMI (27.5% vs 43.6%)] and  
42 pharmacotherapies at time of hospital discharge including [aspirin (82.9% vs. 90.2%) and (79.9% vs.  
43 88.0%),  $\beta$ -blockers (73.4% vs. 86.4%) and (65.3% vs. 85.1%)] in the UK compared with Sweden,  
44 respectively. Standardised net probability of death (NPD) between admission and 1 month was higher  
45 in the UK for STEMI (8.0 [95% confidence interval 7.4-8.5] vs. 6.7 [6.5-6.9]) and NSTEMI (6.8 [6.4-  
46 7.2] vs. 4.9 [4.7-5.0]). Between 6 months and 1 year and more than 1 year, NPD remained higher in  
47 the UK for NSTEMI (2.9 [2.5-3.3] vs. 2.3 [2.2-2.5]) and (21.4 [20.0-22.8] vs. 18.3 [17.6-19.0]), but  
48 was similar for STEMI (0.7 [0.4-1.0] vs. 0.9 [0.7-1.0]) and (8.4 [6.7-10.1] vs. 8.3 [7.5-9.1]).

49 **Conclusion**

50 Short-term mortality following STEMI and NSTEMI was higher in the UK compared with Sweden.  
51 Mid- and longer-term mortality remained higher in the UK for NSTEMI, but was similar for STEMI.  
52 Differences in mortality may be due to differential use of guideline-indicated treatments.

53

54

55

56

57 **Introduction**

58 Outcomes of acute myocardial infarction (AMI) vary between and within countries,  
59 suggesting that the potential to reduce the burden of cardiovascular disease has not been realised.<sup>1-3</sup>  
60 International research may identify potentially modifiable factors associated with geographic variation  
61 in outcomes of patients with cardiovascular (and other) diseases through access to nationwide  
62 registries, shared resources and specialised expertise.<sup>4</sup> Moreover, the study of clinical outcomes from  
63 countries which have similar population life expectancies, healthcare system access and disease  
64 registration processes enables variation attributable to the delivery of cardiovascular healthcare to be  
65 identified and characterised.

66

67 International comparison studies using population-based registries are rare and, to date,  
68 investigations of AMI outcomes have only considered short-term survival.<sup>1-6</sup> Nowadays, when  
69 survival from AMI is at its highest, it is essential that international comparisons investigate longer-  
70 term outcomes and that these are analysed in light of the high and potentially different proportion of  
71 patients who die from non-cardiovascular causes.<sup>7</sup> That is, deaths attributable to AMI may differ  
72 between countries, but this difference may not be identified when all-cause mortality is assessed.<sup>8</sup>

73

74 To date, no international comparative studies of mortality following ST-segment elevation  
75 myocardial infarction (STEMI) and non-STEMI (NSTEMI), have accounted for background  
76 population rates of expected death. Relative survival is a technique that enables country-specific  
77 correction for deaths with those of the disease of interest, and models time-dependent effects to  
78 express differences in mortality between groups over long follow-up periods.<sup>9,10</sup> Thus, it is particularly  
79 useful for international comparison studies of care and outcomes.<sup>8-14</sup> Given historical evidence of  
80 differing AMI mortality rates between Sweden and the UK, and taking advantage of their unique  
81 nationwide registry-based cohorts of AMI, we investigated the net probability of short- and long-term  
82 death by correcting for deaths from other causes and controlling for differences in demographics,  
83 comorbidities and treatments across the two countries.

84 **Methods**

85

86 **Study Design and Participants**

87 We included all national healthcare hospitals in Sweden (n=73) and in England and Wales  
88 (n=247), which provided care for patients with AMI. Eligible patients were aged between 18 and 100  
89 years, and had been hospitalised following STEMI or NSTEMI between 1<sup>st</sup> January, 2003 and 30<sup>th</sup>  
90 June, 2013. For multiple patient admissions, we used the first recorded episode. Patient-level data  
91 concerning demographics, co-morbidities, cardiovascular risk factors and guideline-indicated  
92 treatments were extracted from the Swedish Web-system for Enhancement and Development of  
93 Evidence-based care in Heart disease Evaluated According to Recommended Therapies  
94 (SWEDEHEART), and the Myocardial Ischaemia National Audit Project (MINAP). SWEDEHEART  
95 and MINAP are population-based registries gathering outcome information from patients hospitalised  
96 for acute coronary syndrome in Sweden and the UK, respectively. Details of these two registries and  
97 data validation have been described previously.<sup>15,16</sup> AMI was classified by the attending Consultant as  
98 STEMI and NSTEMI according to the European Society of Cardiology (ESC), American College of  
99 Cardiology (ACC) and American Heart Association (AHA) guidelines.<sup>17</sup> Patients with unstable angina  
100 or missing subtype of AMI were excluded (Figure 1).

101

102 **Case mix covariates**

103 To account for case mix and cardiovascular risk, we adjusted for patient-specific information  
104 concerning age, sex, year of hospitalisation, risk factors (diabetes mellitus, hypertension, smoking),  
105 prior cardiovascular diseases (myocardial infarction, heart failure, percutaneous coronary intervention  
106 [PCI], coronary artery bypass graft [CABG] surgery, cerebrovascular disease, peripheral vascular  
107 disease [PVD]), other comorbidities (chronic renal failure, chronic obstructive pulmonary disease  
108 [COPD]), presenting clinical characteristics at hospitalisation (systolic blood pressure, heart rate, ST-  
109 segment deviation), in-hospital course (cardiac arrest, use of loop diuretic) and guideline-indicated  
110 cardiovascular treatments. Class 1 guideline recommended treatments included, i) prior to  
111 hospitalisation (aspirin,  $\beta$  blockers, angiotensin converting enzyme inhibitors [ACEi] / angiotensin

112 receptor blockers [ARB], and HMG Co-A reductase inhibitors [statins]); ii) during hospitalisation  
113 (reperfusion treatment [primary PCI, fibrinolysis] and revascularisation [primary PCI or CABG]  
114 surgery for patients with STEMI and [PCI or CABG surgery] for patients with NSTEMI)<sup>18,19</sup> and iii)  
115 at the time of discharge from hospital (Aspirin,  $\beta$  blockers, statins, ACEi /ARB and P2Y<sub>12</sub> inhibitors).  
116 Findings from data quality assessment and validation through regular chart review of randomly  
117 selected patients, including data on demographics, risk factors and medical history, have shown  
118 96.1% agreement in SWEDEHEART<sup>15</sup> and 89.5 in MINAP.<sup>1</sup>

119

## 120 **Outcomes**

121 The primary outcome was the standardised net probability of death (NPD) due to AMI  
122 estimated using relative survival, calculated as 1-mean relative survival. Relative survival was defined  
123 as the ratio of observed survival (all-cause survival) for STEMI or NSTEMI to (all-cause) survival  
124 that would be expected in the absence of AMI in the general population of Sweden and the UK,  
125 matched by age, sex and year of hospitalisation for each country.

126

## 127 **Observed survival**

128 Data for all-cause survival were obtained through linkage to the National Population Registry  
129 (in Sweden) and the Office for National Statistics (in the UK) using each patient's unique identifier  
130 number. Patients were followed-up for their vital status after their hospitalisation, with censoring at  
131 the end of follow-up on 30<sup>th</sup> of June 2013 (Supplementary Table 1). Survival time was the duration  
132 between the date of hospitalisation and the date of death or censored at the end of the study period, as  
133 appropriate.

134

## 135 **Expected survival**

136 Expected survival was derived from death data for the general population of Sweden and  
137 England and Wales matched by age, sex and year of hospitalisation to that of the observed survival  
138 from the SWEDEHEART and MINAP patients, respectively. This was calculated using life tables

139 produced by the Human Mortality Database of Sweden (<http://www.mortality.org>) and the Office for  
140 National Statistics in the UK (<https://www.ons.gov.uk>).

141

## 142 **Statistical Analyses**

143 We used percentages to describe categorical variables and means and standard deviations  
144 (SD) for continuous variables (all continuous variables were normally distributed). Differences in  
145 means for continuous variables and proportions for categorical variables were tested using t tests and  
146 two-sample tests.

147

148 We used flexible parametric survival models to calculate standardised NPD estimates. This  
149 approach uses restricted cubic spline functions to estimate the baseline cumulative hazard function.  
150 This enables cumulative hazards to be modelled by incorporating more than one time-dependent  
151 factor in the same model.<sup>9</sup> The base model (model 1) was adjusted for age bands ( $\leq 55$  years, 56 to  
152  $\leq 65$  years, 66 to  $\leq 75$  years [reference], 76 to  $\leq 85$  years and  $> 85$  years), sex and year of  
153 hospitalisation (categories 2003-05 [reference], 2006-08, 2009-11 and 2012-13). We incrementally  
154 fitted case mix factors which included prior cardiovascular diseases and other comorbidities (model  
155 2), cardiovascular risk factors, presenting and in-hospital clinical characteristics (model 3),  
156 reperfusion and revascularisation for STEMI and revascularisation for NSTEMI (model 4), and the  
157 use of guideline-indicated pharmacotherapies for AMI prior to admission and at discharge (model 5).  
158 Given that differences in survival may be due to differences in patient characteristics and management  
159 between the two countries, we also calculated standardised NPD by applying the Swedish model  
160 parameters to the UK population.

161

162 To examine differences in short and longer term NPD between the countries, we performed a  
163 landmark survival analysis.<sup>20</sup> Four landmarks were selected: i) admission to 1 month post-discharge;  
164 ii) 1 month to 6 months; iii) 6 months to 1 year; and iv) 1 year to date of censorship (see  
165 supplementaterial). The adjusted relative survival for each landmark can be interpreted as the  
166 proportion of patients alive after a given time of follow-up compared with the general population,

167 whereby a ratio of 100% indicates that survival was equivalent to that of the general population  
168 during that landmark. For the admission to 1 month landmark analyses, pharmacotherapies at  
169 discharge were excluded from model 5.

170 The proportional excess hazards assumption was assessed by including interaction terms  
171 between three baseline variables (age, sex, calendar year) and follow-up time and tested using the  
172 likelihood ratio test. All tests were two-tailed, the level of statistical significance pre-specified at 5%  
173 ( $p < 0.05$ ) and estimates derived with 95% confidence intervals (CI). P values were calculated from Z  
174 values obtained from the difference between the main effect and 95% confidence intervals at each  
175 time point between the two countries (see supplementary material). Missing covariates were imputed  
176 using the approach suggested for MINAP, imputing unrecorded as 'absent' or 'no'<sup>21</sup>.

177

178 A series of sensitivity analysis were included: i) calculating non-standardised NPDs; ii) using  
179 non-imputed covariate data; iii) estimating all-cause mortality; iv) calculating NPDs in subset samples  
180 including: 1. patients who received invasive treatment [(STEMI, reperfusion or revascularisation and  
181 (NSTEMI, revascularisation)]; and 2. the latest cohort (2010-2013). All statistical analyses were  
182 performed using Stata version 15.1 (StataCorp).

183

## 184 **Results**

185 There were 180,368 Swedish (33.7% STEMI) and 662,529 English and Welsh patients  
186 (39.7% STEMI). In Sweden compared with the UK, patients with STEMI were older (mean age 68.9  
187 [SD 12.6] vs. 65.8 [SD 13.6] years). Swedish patients more frequently had diabetes mellitus (15.6%  
188 vs. 12.2%), heart failure (4.6% vs. 1.8%), previous CABG surgery (3.4% vs. 2.1%) and  
189 cerebrovascular disease (7.5% vs. 4.7%). Swedish patients less frequently had COPD (5.0% vs. 9.8%)  
190 and were smokers (58.4% vs. 66.0%), but had more hypertension (40.2% vs. 36.3%). Patients with  
191 STEMI in Sweden more frequently had aspirin (90.2% vs. 82.9%),  $\beta$ -blockers (86.4% vs. 73.4%),  
192 P2Y<sub>12</sub> inhibitors (77.6% vs. 56.2%) at discharge from hospital and revascularisation (74.9% vs.  
193 43.8%). However, statins (81.6% vs. 82.7%), ACEi or ARB (75.2% vs. 79.1%) at discharge from

194 hospital and receipt of reperfusion during hospitalisation (75.7% vs. 78.9%) were higher in the UK  
195 (Table 1).

196

197 Patients with NSTEMI in Sweden, compared with the UK, less frequently had chronic renal  
198 failure (3.8% vs. 5.7%), COPD (7.8% vs. 14.6%) and cardiac arrest during hospitalisation (2.4% vs.  
199 4.7%). However, they more frequently had heart failure (12.2% vs. 6.5%), cerebrovascular disease  
200 (11.3% vs. 8.9%) and peripheral vascular disease (PVD) (6.8% vs. 4.7%). Patients with NSTEMI in  
201 Sweden more frequently received aspirin (88.0% vs. 79.9%),  $\beta$ -blockers (85.1% vs. 65.3%), P2Y<sub>12</sub>  
202 inhibitors (63.7% vs. 50.7%) at discharge, and revascularisation during hospitalisation (43.6% vs.  
203 27.5%), and had lower rates of prescription of statins (75.1% vs. 79.0%) and ACEi/ARBs (67.9% vs.  
204 69.9%) at discharge (Table 1). See supplementary Table 2 for information about missing data.

205

206 During the 8.5 years of study follow-up, amongst patients with STEMI there were 18,465  
207 (30.4%) deaths after a median of 1.5 years post-AMI (25%-75% IQR, 0.04 to 4.6) in Sweden, and  
208 58,171 (22.1%) deaths after a median of 0.1 years (25%-75% IQR, 0.008 to 1.7) in the UK. Amongst  
209 patients with NSTEMI, there were 48,482 (40.5%) deaths after a median of 1.7 years post-AMI (25%-  
210 75% IQR, 0.3 to 4.3) in Sweden, and 128,723 (32.2%) deaths after a median of 0.5 years post-AMI  
211 (IQR 25%-75%, 0.07 to 1.9) in the UK. The proportion of in-hospital deaths was higher in the UK  
212 than Sweden for NSTEMI (8.1% vs. 4.8%, p=0.001), but similar for STEMI (9.3% vs. 7.6%, p=0.26).

213

#### 214 **Adjusted standardised net probability of death**

215 For STEMI, after controlling for demographics, previous medical history and cardiovascular  
216 risk factors (model 3) there was no significant difference in NPDs between Sweden and the UK  
217 (NPDs at all landmarks; between admission to 1 month (NPD [95% CI] 6.9 [6.7-7.1] vs. 6.7 [6.6-7.4]),  
218 1 to 6 months (1.7 [1.6-1.9] vs. 1.7 [1.4-2.0]), 6 months to 1 year 0.8 [0.7-0.9] vs. 1.0 [0.7-1.3]) and >1  
219 year (7.7 [7.0-8.5] vs. 8.2 [7.1-9.3]). However, after adjustment for reperfusion and revascularisation  
220 (model 4), NPDs were higher in the UK compared with Sweden at all landmarks; between admission  
221 to 1 month (8.6 [8.1-9.1] vs. 6.9 [6.7-7.1]), between 1 to 6 months (2.4 [1.9-2.8] vs. 1.8 [1.6-1.9]), 6

222 months to 1 year (1.4 [0.9-1.8] vs. 0.8 [0.7-1.0]) and >1 year (10.7 [9.2-12.3] vs. 8.1 [7.3-8.9]). NPDs  
223 remained higher in the UK compared with Sweden after adjustment for pharmacotherapies (model 5)  
224 between admission to 1 month (8.0 [7.4-8.5] vs. 6.7 [6.5-6.9]), but were similar between 6 months to 1  
225 year (0.7 [0.4-1.0] vs. 0.9 [0.7-1.0]) and >1 year (8.4 [6.7-10.1] vs. 8.3 [7.5-9.1]). Only between 1 and  
226 6 months was NPD higher in Sweden compared with the UK (1.8 [1.7-2.0] vs. 1.4 [1.1-1.7]) (Figures  
227 2, 4 and Supplementary Table 3).

228

229 For NSTEMI, NPDs were higher in the UK compared with Sweden at all landmarks for  
230 model 3 between admission to 1 month (NPD [95% CI] 6.6 [6.3-6.8] vs. 4.9 [4.8-5.1]), 1 to 6 months  
231 (4.3 [4.0-4.7] vs. 3.7 [3.5-3.8]), 6 months to 1 year (2.8 [2.5-3.2] vs. 2.2 [2.1-2.3]) and >1 year (21.0  
232 [19.6-22.4] vs. 17.2 [16.5-17.9]). NPDs remained higher in the UK after further adjustment for  
233 revascularisation (model 4) between admission to 1 month (7.9 [7.5-8.3] vs. 4.9 [4.8-5.1]), 6 months  
234 to 1 year (3.8 [3.3-4.2] vs. 2.3 [2.2-2.4]) and >1 year (25.8 [24.2-27.4] vs. 17.8 [17.1-18.5]) and  
235 pharmacotherapies (model 5) between admission to 1 month (6.8 [6.4-7.2] vs. 4.9 [4.7-5.0]), 6 months  
236 to 1 year (2.9 [2.5-3.3] vs. 2.3 [2.2-2.5]) and >1 year (21.4 [20.0-22.8] vs. 18.3 [17.6-19.0]), but were  
237 similar between 1 and 6 months (3.8 [3.3-4.2] vs. 3.8 [3.7-3.9]) and (3.6 [3.3-4.0] vs. 3.8 [3.7-4.0]) for  
238 model 4 and 5 respectively (Figures 3, 5 and Supplementary Table 3).

239

#### 240 **Sensitivity analysis**

241 Non-standardised NPDs were higher for STEMI and NSTEMI in the UK compared with  
242 Sweden at all landmarks and for all models (Figures 2-5 and Supplementary Table 3). Results from  
243 all-cause mortality analyses are presented in Supplementary Table 4 and Supplementary Figures 3-7.  
244 Results from the non-default imputed data were similar to the main analysis (Supplementary Figures  
245 8&9, Supplementary Tables 5&6). NPDs for those who received invasive treatments are presented in  
246 (Supplementary Tables 7&8). NPDs for model 5 using only the latest cohort (2010-2013) were similar  
247 to findings from the main analysis (Supplementary Figures 10&11).

248

249 **Discussion**

250 We used registry-based nationwide cohorts within a relative survival framework to study  
251 international differences in care and short-, mid- and longer-term outcomes for 842,897 patients  
252 hospitalized with AMI. This approach enabled the comparison of deaths in Sweden and the UK that  
253 were attributable to STEMI and NSTEMI (rather than using all-cause mortality that, nowadays, is  
254 driven predominantly by non-cardiovascular deaths, and which may vary between countries). We  
255 found that after adjusting for demographics, co-morbidities and treatments received to our final  
256 models, standardised short-term mortality was significantly higher in the UK compared with Sweden  
257 for STEMI and NSTEMI. While mid- and long-term mortality remained higher in the UK for  
258 NSTEMI, it was similar in each country for STEMI.

259 Our data show that patients who received revascularisation/reperfusion had a lower mortality  
260 than those who did not received treatment, in both Sweden and the UK (Supplementary Tables 7&8).  
261 Whilst the rates of reperfusion for STEMI were similar between the countries, there were higher rates  
262 of revascularisation in Sweden. It is possible that, in addition to higher rates of use of  
263 pharmacotherapies, during the study period the more frequent use of primary PCI in Sweden  
264 explained some of the difference in mortality between the countries for STEMI. The higher NPDs  
265 found in model 4 (after adjusting for revascularisation and reperfusion) in the UK, but not Sweden  
266 primarily for STEMI patients could be, in part explained by differences in treatment provision  
267 between Sweden and the UK. For example, if in the UK patients who received invasive treatment  
268 were primarily those with a more severe presentation of AMI or those considered high-risk patients  
269 (who would therefore have also a higher risk of death regardless of the treatment administered) and in  
270 Sweden all patients were equally likely to receive the treatment regardless of presentation (so low-risk  
271 patients or with less severe AMI would also benefit from the treatment), then the estimates of  
272 mortality would increase after adjustment for invasive treatment in the UK (because of the higher risk  
273 of death among patients who received an invasive treatment) and not in Sweden. This explanation is  
274 also supported by the finding of a stronger increase in mortality following adjustment for invasive  
275 treatment for STEMI than for NSTEMI (given all NSTEMI were also likely to have a 'more severe

276 AMI' and therefore differences in treatment provision between both countries would be smaller). A  
277 similar argument may be presented for NSTEMI, whereby earlier research found that delays to the  
278 uptake of guideline-indicated care for NSTEMI in the UK were associated with potentially avoidable  
279 deaths.<sup>22</sup>

280 Our results are consistent with, and extend findings from previous international comparisons  
281 of mortality.<sup>1-3</sup> For our investigation, however, we study much longer-term outcomes and present  
282 unbiased estimates of standardised NPD by applying the Swedish model parameters to the UK  
283 population variables - forcing the distribution of the case mix covariates to be similar across the two  
284 countries and, thus, reducing the likelihood of bias in comparison. In addition, the use of a relative  
285 survival framework is relevant to, and recommended for, international comparisons studies<sup>22</sup> because  
286 it corrects estimates for expected mortality rates in the general population, thereby permitting a direct  
287 comparison of deaths due to AMI.

288 This study has important implications. We have found that for both STEMI and NSTEMI the  
289 higher mortality in the UK compared with Sweden was associated with differences in the delivery  
290 and/or uptake of invasive and guideline-indicated pharmacotherapies. The higher late mortality rates  
291 among NSTEMI in the UK compared with Sweden may also be influenced by differences in ongoing  
292 treatments in each country. However, nationwide data concerning the persistence of  
293 pharmacotherapies would be required to study this. This shows that even in high performing, high  
294 income countries there are opportunities to improve care and therefore outcomes. Equally, such high  
295 resolution interrogation of national health system performance was possible because Sweden and the  
296 UK each have registry-based nationwide cohorts which continuously collect data for clinically  
297 derived variables. This form of analysis would be challenging with administrative and/or  
298 geographically and temporally constrained cohorts.

299 Nevertheless, we acknowledge the study limitations. Relative survival relies on the  
300 assumption that the survival probability of the study group is similar to that of the reference  
301 (population) group. The main driver of the extent of the impact of this assumption will depend on the

302 proportion of cardiovascular deaths to overall deaths in the population. We accounted for differentials  
303 in mortality for other causes in the countries by incorporating this information. This assumption could  
304 be called into question for older age groups who are more likely to have multiple comorbidities<sup>23</sup> and  
305 might have a higher proportion of deaths due to cardiovascular disease. This could explain the  
306 observed difference in long-term survival between the two countries for NSTEMI. Yet, our estimates  
307 were adjusted for comorbidities to minimise this bias and the analyses were performed separately for  
308 STEMI and non-STEMI, which, to an extent, also limits the potential impact of this bias. We did not  
309 correct for the prevalence of AMI in the general population and this may have overestimated the  
310 survival rates.<sup>10,24</sup> Moreover, given that cardiovascular and non-cardiovascular diseases are  
311 independent competing causes of death and that the prevalence of prior AMI in Sweden and England  
312 and Wales is small (9% and 6%, respectively; Supplementary Figures 1&2), further adjustment to  
313 address this would unlikely affect the results. Despite the fact that national hospital coverage is 100%  
314 for Sweden and the UK not all patients are captured. According to SWEDEHEART annual report  
315 2017, 90% of patients with Acute Coronary syndrome are included in the registry.<sup>25</sup> In England and  
316 Wales, the majority of STEMI are likely to be captured but fewer NSTEMI are recorded due to  
317 complexity of diagnosis.<sup>2</sup> We adjusted the estimates for patient-specific information, risk factors,  
318 prior cardiovascular diseases and guideline-indicated cardiovascular treatments administered pre-,  
319 intra- and at discharge from hospital, but information on treatments provided during follow-up were  
320 not available in the dataset. Finally, the completeness and accuracy across the two registries are  
321 different although high.<sup>2</sup> However, our sensitivity analysis using default imputed covariate data  
322 showed that neither the direction nor the significance of the results changed compared to the findings  
323 from primary analysis (see Supplementary Figures 8&9 and Supplementary Tables 5&6).

324

## 325 **Conclusion**

326 The observed differences in the delivery of guideline-indicated care between Sweden and the  
327 UK, coupled with a robust statistical technique for international comparisons of outcomes, suggests

328 that disparities in the delivery of invasive coronary treatments and guideline-indicated  
329 pharmacotherapies is a contributing factor to differentials in AMI mortality between countries.

330 **Author Contributions:** CPG and TJ conceived the study. OAA performed the data cleaning, analyses  
331 and wrote the initial draft with support from MJR and MPR. All authors contributed to critical  
332 revision of the manuscript and approved the final version. The corresponding author attests that all  
333 listed authors meet authorship criteria and that no others meeting the criteria have been omitted. TJ  
334 and CPG are the guarantors.

335 **Conflict of Interest Disclosures:** All authors have completed and submitted the ICMJ form for  
336 Potential Conflicts of Interest at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf). Prof Fox reports receipt of  
337 grants and/or personal fees from Bayer/Janssen, AstraZeneca, Sanofi/Regeneron and Verseon. Prof  
338 Gale reports receipt of personal fees and/or nonfinancial support from AstraZeneca, Novartis, Bristol  
339 Myers Squibb, Bayer and Vifor Pharma. No support from any organisations that might have an  
340 interest in the submitted work and no other relationships or activities that could appear to have  
341 influenced the submitted work were reported.

342

343 **Funding/Support:** This work was supported by grants from the Swedish Heart and Lung Foundation  
344 and the regional agreement on medical training and clinical research (ALF) between Stockholm  
345 County Council and Karolinska Institute. The Myocardial Ischaemia National Audit Project (MINAP)  
346 is commissioned by the Health Quality Improvement Partnership (HQIP) as part of the National  
347 Clinical Audit and Patient Outcomes Programme (NCAPOP).

348

### 349 **Figure Legends**

350 Figure 1: STROBE diagram of exclusion of cases from the SWEDHEART and MINAP datasets, to  
351 derive the analytical cohort.

352 Figure 2: Adjusted standardised net cumulative probability of death for STEMI for: A) admission to 1  
353 month post-AMI discharge; B) 1 month to 6 months; C) 6 months to 1 year; and D) over 1 year post-  
354 AMI.

355 Figure 3: Adjusted standardised net cumulative probability of death for NSTEMI for: A) admission to  
356 1 month post-AMI discharge; B) 1 month to 6 months; C) 6 months to 1 year; and D) over 1 year  
357 post-AMI.

358 Figure 4: Adjusted net probability of death estimates with and without standardisation for STEMI, in  
359 Sweden (A) and in the UK (B).

360 Figure 5: Adjusted net probability of death estimates with and without standardisation for NSTEMI,  
361 in Sweden (A) and in the UK (B).

## 362 **Supplementary material**

### 363 **Tables**

364 Supplementary Table 1: Years of diagnosis and years of follow-up.

365 Supplementary Table 2: Number (%) of demographic and clinical characteristics of the 2003-2013  
366 AMI cohorts with missing information, stratified by country.

367 Supplementary Table 3: Estimated adjusted standardised net probability of death for Models 1 to 5 at  
368 individual landmark time.

369 Supplementary Table 4: Non-adjusted all-cause probability of death

370 Supplementary Table 5: Patient characteristics and treatments for STEMI and NSTEMI, by country  
371 using non-default imputed covariate data.

372 Supplementary Table 6: Estimated adjusted standardised net probability of death for Models 1 to 5 at  
373 individual landmark time using non-default imputed covariate data.

374 Supplementary Table 7: NPDs and 95% CIs for those who received/did not receive either reperfusion  
375 or revascularisation in STEMI and revascularisation in NSTEMI using the Swedish parameters.

376 Supplementary Table 8: NPDs and 95% CIs for those who received/did not receive either reperfusion  
377 or revascularisation in STEMI and revascularisation in NSTEMI using the UK parameters.

378 **Figures**

379 Supplementary Figure 1: Trends in age-specific rates of death for males from 2003 to 2013 in the  
380 general population of Sweden (A) and the UK (B).

381 Supplementary Figure 2: Trends in age-specific rates of death for females from 2003 to 2013 in the  
382 general population of Sweden (A) and the UK (B).

383 Supplementary Figure 3: Non-adjusted all-cause probability of death (1-mean survival) for STEMI  
384 for: A) admission to 1 month post-AMI discharge; B) 1 month to 6 months; C) 6 months to 1 year;  
385 and D) over 1 year post-AMI.

386 Supplementary Figure 4: Non-adjusted all-cause probability of death (1-mean survival) for NSTEMI  
387 for: A) admission to 1 month post-AMI discharge; B) 1 month to 6 months; C) 6 months to 1 year;  
388 and D) over 1 year post-AMI.

389 Supplementary Figure 5: Non-adjusted all-cause probability of death (1-mean survival) for STEMI  
390 (A) and NSTEMI (B) for the whole follow-up.

391 Supplementary Figure 6: Adjusted standardised all-cause probability of death (1-mean survival) for  
392 STEMI for: A) admission to 1 month post-AMI discharge; B) 1 month to 6 months; C) 6 months to 1  
393 year; and D) over 1 year post-AMI using default imputed covariate data.

394 Supplementary Figure 7: Adjusted standardised all-cause probability of death (1-mean survival) for  
395 NSTEMI for: A) admission to 1 month post-AMI discharge; B) 1 month to 6 months; C) 6 months to  
396 1 year; and D) over 1 year post-AMI using default imputed covariate data.

397 Supplementary Figure 8: Adjusted standardised net cumulative probability of death (1-mean relative  
398 survival) for STEMI for: A) admission to 1 month post-AMI discharge; B) 1 month to 6 months; C) 6  
399 months to 1 year; and D) over 1 year post-AMI using non-default imputed covariate data.

400 Supplementary Figure 9: Adjusted standardised net cumulative probability of death (1-mean relative  
401 survival) for NSTEMI for: A) admission to 1 month post-AMI discharge; B) 1 month to 6 months; C)  
402 6 months to 1 year; and D) over 1 year post-AMI using non-default imputed covariate data.

403 Supplementary Figure 10: Adjusted standardised net cumulative probability of death for STEMI for:  
404 A) admission to 1 month post-AMI discharge; B) 1 month to 6 months; C) 6 months to 1 year; and D)  
405 over 1 year post-AMI for the 2010-2013 AMI cohorts.

406 Supplementary Figure 11: Adjusted standardised net cumulative probability of death for NSTEMI for:  
407 A) admission to 1 month post-AMI discharge; B) 1 month to 6 months; C) 6 months to 1 year; and D)  
408 over 1 year post-AMI for the 2010-2013 AMI cohorts.

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