Appendix

Section 1: Life tables

Life tables of England and Wales containing population mortality estimates were used to calculate expected survival. The latest life table data was available up to 2012; therefore 2012 population data was matched to 2013 patient data without extrapolation. Years of diagnosis and years of follow-up included in the calculations of long term relative survival of AMI patients for the years 2003-2013 were shown in Table 1a. The numbers within the cells indicate the years following procedure.

Table 1a: Years of diagnosis and years of follow-up

Year of diagnosis	**Year of follow-up**										
	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
2003	1	1/2	2/3	3/4	4/5	5/6	6/7	7/8	8/9	9/10	10/11
2004		1	1/2	2/3	3/4	4/5	5/6	6/7	7/8	8/9	9/10
2005			1	1/2	2/3	3/4	4/5	5/6	6/7	7/8	8/9
2006				1	1/2	2/3	3/4	4/5	5/6	6/7	7/8
2007					1	1/2	2/3	3/4	4/5	5/6	6/7
2008						1	1/2	2/3	3/4	4/5	5/6
2009							1	1/2	2/3	3/4	4/5
2010								1	1/2	2/3	3/4
2011									1	1/2	2/3
2012										1	1/2
2013											1

Section 2: Model selection

Choice of scale (hazards, odds, probit or Aranda-Ordaz) and baseline complexity (number of knots) shown in Table 2a and Table 2b.

Table 2a: Choice of scale and baseline complexity for the full model, STEMI cohort

d.f.	**PH**		**PO**		**Probit**		**AO**	
	AIC	BIC	AIC	BIC	AIC	BIC	AIC	BIC
1	22262.80	22461.81	22163.27	22362.27	22266.68	22465.69	22162.28	22367.14
2	22261.18	22466.04	22158.37	22363.24	22240.79	22445.65	22156.46	22367.18
3	22123.78	22334.50	22011.25	22221.97	22070.57	22281.29	22005.91	22222.48
4	22099.81	22316.38	21986.94	22203.51	22044.89	22261.46	21981.40	22203.82
5	**22077.86**	**22300.28**	**21965.42**	**22187.84**	22021.22	22243.65	**21959.76**	**22188.04**
6	22072.15	22300.43	21960.24	22188.52	**22015.12**	**22243.40**	21954.63	22188.76
7	22070.81	22304.94	21959.38	22193.51	22013.37	22247.50	21953.82	22193.80
8	22072.68	22312.66	21961.30	22201.28	22014.97	22254.96	21955.73	22201.57
9	22073.45	22319.28	21961.93	22207.77	22015.48	22261.32	21956.32	22208.01
10	22074.06	22325.75	21962.45	22214.14	22016.06	22267.75	21956.79	22214.33

Abbreviations: d.f., degree of freedom; PH: proportional hazard, PO: proportional odds, AO: Aranda-Ordaz

Table 2b: Choice of scale and baseline complexity for the full model, NSTEMI cohort

d.f.	**PH**		**PO**		**Probit**		**AO**	
	AIC	BIC	AIC	BIC	AIC	BIC	AIC	BIC
1	32147.91	32366.00	32023.93	32242.02	32246.41	32464.49	32025.81	32250.30
2	32147.61	32372.11	32022.73	32247.23	32199.72	32424.22	32024.70	32255.61
3	32076.93	32307.84	31941.26	32172.17	**32121.38**	**32352.30**	31942.91	32180.24
4	**32069.60**	**32306.93**	**31934.51**	**32171.84**	32116.93	32354.25	**31936.19**	**32179.93**
5	32069.05	32312.79	31934.28	32178.03	32117.40	32361.14	31935.98	32186.13
6	32069.58	32319.74	31934.83	32184.98	32118.26	32368.41	31936.52	32193.09
7	32069.94	32326.51	31935.17	32191.74	32118.71	32375.28	31936.87	32199.85
8	32070.93	32333.92	31936.14	32199.13	32119.67	32382.65	31937.84	32207.24
9	32071.82	32341.22	31937.04	32206.44	32120.41	32389.81	31938.74	32214.55
10	32071.81	32347.63	31937.02	32212.84	32120.07	32395.89	31938.72	32220.95

Abbreviations: d.f., degree of freedom; PH: proportional hazard, PO: proportional odds, AO: Aranda-Ordaz

Section 3: Multiple imputation

Multiple imputation by chained equations was performed to account for missing data. Ten imputed datasets were generated using a model with all variables included in the analysis plus all variables predictive of the missing values and values averaged to obtain the final estimates. To avoid underestimation of the covariate-outcome association, the survival outcome was included in the imputation model in the form of the Nelson-Aalen estimate of the hazard function in addition to including the censoring indicator. [1,2] Excess mortality estimates were averaged over the imputed data according to Rubin's Rules. Level of missingness for each variable was shown in Table 3a. Estimates from complete case analyses were similar to those derived from the imputed data (Table 3b, Table 3c).

Table 3a: Baseline and clinical characteristics for the 2003-2013 AMI cohort with missing levels

	STEMI N=281,259	**NSTEMI** N=422,661	**Missing (%)** N=703,209
Age	0	0	0
Male (%)	1,104 (0.4%)	1,013 (0.2%)	2,117 (0.3%)
2003-05	0	0	0
2006-08	0	0	0
2009-11	0	0	0
2012-13	0	0	0
Co-morbidities			
Myocardial infarction	38,471 (13.7%)	35,957 (8.5%)	74,428 (10.6%)
Heart failure	45,418 (16.2%)	46,290 (11.0%)	91,708 (13.0%)
PCI	44,640 (15.9%)	44,811 (10.6%)	89,451 (12.7%)
CABG	44,138 (15.7%)	43,324 (10.3%)	87,462 (12.4%)
Cerebrovascular disease	46,344 (16.5%)	46,967 (11.1%)	93,311 (13.3%)
Peripheral vascular disease	48,074 (17.1%)	50,750 (12.0%)	98,824 (14.0%)
Diabetes	34,149 (12.1%)	32,396 (7.7%)	66,545 (9.5%)
Chronic renal failure	46,504 (16.5%)	46,797 (11.0%)	93,301 (13.3%)
Hypertension	39,653 (14.1%)	37,154 (8.0%)	76,807 (10.9%)
COPD	48,282 (17.2%)	51,074 (12.1%)	99,356 (14.1%)
Family history of CHD	105,979 (37.7%)	161,740 (38.3%)	267,719 (38.0%)
Risk factors			
Systolic BP	64,888 (23.1%)	74,973 (17.7%)	139,861 (19.9%)
Heart rate	63,813 (22.7%)	73,494 (17.4%)	137,307 (19.5%)
Current/ex-smoker	30,848 (11.0%)	35,077 (8.3%)	65,925 (9.4%)
ST-segment deviation	10,468 (3.7%)	39,414 (9.3%)	49,882 (7.1%)
Cardiac arrest	22,167 (7.9%)	24,737 (5.9%)	46,904 (6.7%)
Elevated Enzyme	30,363 (10.8%)	11,980 (2.8%)	42,343 (6.0%)
Use of a loop diuretic	69,693 (24.8%)	75,898 (18.0%)	145,591 (20.7%)
Treatments at discharge			
Aspirin	27,865 (9.9%)	39,538 (9.4%)	67,403 (9.6%)
β –blockers	29,732 (10.6%)	42,839 (10.1%)	72,571 (10.3%)
Statin	29,077 (10.3%)	42,175 (10.0%)	71,252 (10.1%)
ACEi or ARB	31,411 (11.2%)	46,890 (11.1%)	78,301 (11.1%)
Thienopyridine	111,518 (39.7%)	166,300 (39.4%)	277,818 (39.5%)
Cardiac rehabilitation	15,986 (5.7%)	13,684 (3.2%)	29,670 (4.2%)
Coronary angiography	---	39,478 (9.3%)	---
Reperfusion	21,547 (7.7%)	---	---
Care by a cardiology	107,915 (38.4%)	167,039 (39.5%)	274,954 (39.1%)
Admission ward	7,993 (2.8%)	5,185 (1.2%)	13,178 (1.9%)

Abbreviations: PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; COPD, chronic obstructive pulmonary disease; ARB, angiotensin receptor blocker; ACE, angiotensin converting enzyme; CABG, coronary artery bypass graft; BP, blood pressure; -: the procedure was not performed.

Table 3b: Excess mortality rate ratios stratified by age, sex, calendar year and country with 95% CIs using complete case analysis

Baseline model	STEMI	NSTEMI
	EMRR (95% CI) N=263,159	**EMRR (95% CI) N= 399,370**
Age		
66-75 years (reference)	1.00	1.00
6 month/ <55 years	0.31 (0.27-0.36)*	0.19 (0.17-0.21)*
1 year/ <55 years	0.32 (0.27-0.37)*	0.22 (0.20-0.24)*
5 year/ <55 years	0.31 (0.28-0.35)*	0.29 (0.25-0.33)*
6 month/ 55-65 years	0.49 (0.43-0.55)*	0.43 (0.40-0.47)*
1 year/ 55-65 years	0.49 (0.42-0.56)*	0.47 (0.43-0.50)*
5 year/55-65 years	0.51 (0.46-0.56)*	0.54 (0.49-0.59)*
6 month/76-85 years	2.16 (1.98-2.36)*	2.14 (2.05-2.23)*
1 year/76-85 years	2.16 (1.97-2.38)*	2.05 (1.96-2.15)*
5 year /76-85 years	1.94 (1.82-2.07)*	1.84 (1.73-1.95)*
6 month/Above 85 years	4.43 (4.04-4.86)*	3.85 (3.68-4.03)*
1 year/Above 85 years	4.48 (4.05-4.95)*	3.49 (3.32-3.68)*
5 year/ Above 85 years	3.39 (3.15-3.65)*	2.75 (2.57-2.94)*
Sex		
Female (reference)	1.00	1.00
6 month*Male	0.73 (0.68-0.79)*	0.91 (0.88-0.94)*
1 year *Male	0.73 (0.67-0.79)*	0.88 (0.84-0.91)*
5 year *Male	0.77 (0.73-0.81)*	0.83 (0.79-0.88)*
Calendar year		
2003-05 (reference)	1.00	1.00
2006-08	0.86 (0.82-0.89)*	0.76 (0.73-0.78)*
2009-11	0.68 (0.65-0.71)*	0.62 (0.60-0.64)*
2012-13	0.64 (0.61-0.68)*	0.55 (0.52-0.59)*
6month/2006-08	---	0.84 (0.81-0.88)*
1 year/2006-08	---	0.81 (0.78-0.85)*
5 year/2006-08	---	0.80 (0.75-0.85)*
6month/2009-11	---	0.73 (0.70-0.76)*
1 year/2009-11	---	0.75 (0.72-0.79)*
5 year/2009-11	---	0.82 (0.77-0.88)*
6month/2012-13	---	0.62 (0.58-0.68)*
1 year/2012-13	---	0.66 (0.60-0.73)*
5 year/2012-13	---	0.74 (0.65-0.85)*

Abbreviations:*, Significance level <0.05; ---, no time dependent effect by calendar year was found for STEMI; Baseline model, adjusted for age, sex and year.

Table 3c: Excess mortality rate ratios stratified by all variables with 95% CIs using complete case analysis

	STEMI	NSTEMI
	EMRR (95% CI) N=263,159	**EMRR (95% CI) N= 399,370**
Model 1=Baseline model + diabetes		
Diabetes	1.72 (1.66-1.79)*	1.66 (1.62-1.70)*
Model 2=Baseline model + diabetes + comorbidities		
Diabetes	1.51 (1.45-1.57)*	1.45 (1.41-1.48)
Model 3=Baseline model + diabetes + comorbidities + risk factors		
Diabetes	1.57 (1.50-1.65)*	1.34 (1.30-1.38)*
Model 4=Baseline model+ diabetes + comorbidities + risk factors + treatment		
Diabetes	1.58 (1.49-1.69)*	1.39 (1.34-1.44)*
Comorbidities		
Previous MI	1.26 (1.17-1.35)*	1.27 (1.23-1.32)*
Heart failure	1.38 (1.24-1.53)*	1.40 (1.34-1.46)*
Previous PCI	0.85 (0.74-0.97)*	0.84 (0.79-0.90)*
Previous CABG	1.21 (1.04-1.40)*	0.97 (0.92-1.03)
Cerebrovascular disease	1.40 (1.30-1.52)*	1.29 (1.23-1.34)*
PVD	1.47 (1.31-1.65)*	1.40 (1.32-1.48)*
Chronic renal failure	1.39 (1.25-1.54)*	1.40 (1.34-1.46)*
Astma or COPD	1.22 (1.14-1.31)*	1.24 (1.20-1.29)*
Family history of CHD	0.70 (0.64-0.76)*	0.70 (1.20-1.29)*
Risk Factors		
SBP>90mmHg (reference)	1.00	1.00
SBP<=90mmHg	2.33 (2.15-2.52)*	1.84 (1.73-1.96)*
Current/Ex-smoker*	0.94 (0.89-1.00)*	1.07 (1.04- 1.11)*
Heart rate <=110bpm (reference)	1.00	1.00
Heart rate >110bpm	1.04 (1.01-1.14)*	1.28 (1.23-1.32)*
St Deviation	0.93 (0.86-1.00)	1.31 (1.27-1.36)*
Cardiac arrest	5.26 (4.92-5.60)*	6.73 (6.42-7.10)*
Elevated cardiac troponin	0.96 (0.85-1.08)	3.40 (3.11-3.72)*
Use of loop diuretic	1.50 (1.41-1.58)*	1.81 (1.75-1.87)*
Treatment at hospital discharge		
Aspirin	0.49 (0.43-0.54)*	0.49 (0.47-0.51)*
β –blockers	0.53 (0.48-0.59)*	0.57 (0.551-0.60)*
Statin	0.39 (0.35-0.44)*	0.45 (0.43-0.46)*
ACEi or ARB	0.45 (0.40-0.50)*	0.60 (0.56-0.60)*
Thienopyridine	0.91 (0.80-1.03)	0.86 (0.81-0.90)*
Cardiac rehabilitation	0.24 (0.22-0.26)*	0.49 (0.47-0.50)*
Angiography	---	0.13 (0.13-0.14)*
Reperfusion	0.79 (0.74-0.84)*	---

Abbreviations:*, Significance level <0.05; ---, no time dependent effect by calendar year was found for STEMI; Baseline model, adjusted for age, sex and year

Section 4: Sensitivity analyses

Excess mortality rates associated with diabetes type of treatment; 1. no treatment, 2. dietary control, 3. oral medications, 4. insulin, and 5. insulin and medications combined. The EMRR are presented in Table 4a with those without diabetes as the reference group for STEMI and NSTEMI .

Table 4a: Excess mortality rate ratios stratified by all variables using imputed data, diabetes type treatment

	STEMI	NSTEMI
	EMRR (95% CI) N= 263,159	EMRR (95% CI) N= 399,370
Model 4 = Baseline model + diabetes + co-morbidities + risk factors + treatments		
Diabetes		
Non-diabetic (reference)	1.00	1.00
No treatment received (newly diagnosed)	1.32 (0.97-1.81)	1.04 (0.83-1.30)
Dietary control	1.33 (1.21-1.46)*	1.17 (1.11-1.24)*
Oral medications	1.51 (1.42-1.60)*	1.28 (1.24-1.33)*
Insulin	1.88 (1.74-2.04)*	1.82 (1.75-1.90)*
Insulin and medications combined	1.95 (1.49-2.55)*	1.48 (1.30-1.68)*
Co-morbidities		
Previous AMI	1.25 (1.19-1.32)*	1.28 (1.24-1.32)*
Heart failure	1.31 (1.22-1.42)*	1.38 (1.32-1.44)*
Previous PCI	0.98 (0.89-1.08)	0.85 (0.79-0.91)*
Previous CABG	1.19 (1.07-1.32)*	0.96 (0.90-1.02)
Cerebrovascular disease	1.45 (1.37-1.53)*	1.29 (1.24-1.34)*
PVD	1.43 (1.32-1.56)*	1.38 (1.30-1.45)*
Chronic renal failure	1.47 (1.35-1.59)*	1.36 (1.30-1.45)*
Asthma or COPD	1.11 (1.05-1.17)*	1.25 (1.21-1.30)*
Family history of CHD	0.76 (0.72-0.81)*	0.70 (0.69-0.74)*
Risk Factors		
Systolic BP>90mmHg (reference)	1.00	1.00
Systolic BP≤90mmHg	2.23 (2.11- 2.36)*	1.82 (1.71-1.94)*
Current/ex-smoker	1.05 (1.01-1.09)*	1.09 (1.05-1.12)
Heart rate ≤110bpm (reference)	1.00	1.00
Heart rate >110bpm	1.73 (1.64-1.82)*	1.28 (1.24-1.33)*
ST-segment deviation	1.00 (0.94-1.05)	1.32 (1.28-1.37)*
Cardiac arrest	5.48 (5.27-5.70)*	6.73 (6.41-7.06)*
Elevated cardiac enzyme	1.16 (1.06-1.27)*	3.33 (2.96-3.51)*
Use of a loop diuretic	1.34 (1.29-1.40)*	1.79 (1.74-1.85)*
Treatments		
Aspirin	0.55 (0.51-0.59)*	0.49 (0.47-0.51)*
β–blockers	0.51 (0.48-0.54)*	0.58 (0.55-0.60)*
Statin	0.42 (0.39-0.45)*	0.45 (0.43-0.46)*
ACEI or ARB	0.50 (0.46-0.53)*	0.58 (0.56-0.61)*
Thienopyridine	0.89 (0.81-0.99)*	0.86 (0.82-0.91)*
Cardiac rehabilitation	0.23 (0.22-0.25)*	0.49 (0.48-0.51)*
Coronary angiography	-	0.13 (0.13-0.14)*
Reperfusion	0.83 (0.80- 0.87)*	-

Abbreviations: PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; COPD, chronic obstructive pulmonary disease; CHD, coronary heart disease; ARB, angiotensin receptor blocker; ACE, angiotensin converting enzyme; CABG, coronary artery bypass graft; CAD, coronary artery disease; BP, blood pressure; * Significance level <0.05; -, the procedure was not performed, Baseline model adjusted for age, sex and year.

References

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