

Appendix

Section 1: Life table

Life table of the United Kingdom population mortality estimates was used to calculate expected survival. The latest published life table data available was for 2012; therefore 2012 population data was matched to 2013 and 2014 patient data without extrapolation (Table 1a).

Table1a: Years of procedure and years of follow-up included in the calculations of 5-year relative survival of UPLMS patients for the years 2005-2014. The numbers within the cells indicate the years following procedure.

Year of procedure	Year of follow-up									
	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
2005	1	1/2	2/3	3/4	4/5	5/6	6/7	7/8	8/9	9/10
2006		1	1/2	2/3	3/4	4/5	5/6	6/7	7/8	8/9
2007			1	1/2	2/3	3/4	4/5	5/6	6/7	7/8
2008				1	1/2	2/3	3/4	4/5	5/6	6/7
2009					1	1/2	2/3	3/4	4/5	5/6
2010						1	1/2	2/3	3/4	4/5
2011							1	1/2	2/3	3/4
2012								1	1/2	2/3
2013									1	1/2
2014										1

Section 2: Multiple imputation

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. Excess mortality estimates were averaged over the imputed data. Covariates with 50% or more missing data were excluded from the modelling, as was the case for LVEF function in the STEMI stratum. For each clinical phenotype separate imputed datasets were created. Multiple imputation of missing data made only small changes to point estimates generated from the models though, in general, improved their precision. Though, highlighting the possibility of bias in interpreting data from complete-case analyses (Table 2a).

Table 2a: Excess mortality rate ratios with 95% Cis using complete case analysis

Variable added to baseline	CSA (n=3799)	NSTEACS (n=5114)	STEMI-CS (n=1020)	STEMI+CS (n=749)
	EMRR	EMRR	EMRR	EMRR
Baseline model + Previous AMI	2.88 (1.79-4.61)*	1.57 (1.34-1.82)*	1.57 (1.34-1.83)*	0.99 (0.77-1.28)
Baseline model + Diabetes	2.71 (1.67-4.41)*	1.68 (1.45-1.97)*	1.63 (1.11-2.39)*	1.35 (1.06-1.71)*
Baseline model + LV function				
Good	1.00	1.00	‡	‡
Moderate LVSD	2.99 (1.61-5.56)*	2.47 (1.94-3.15)*		
Severe LVSD	5.45 (2.92-10.18)*	4.07 (3.20-5.19)*		
Baseline model + Renal Failure	7.03 (4.12-12.02)*	7.04 (4.11-12.02)*	2.21 (1.17-4.18)*	1.70 (1.08-2.66)*
Baseline model + Pre-procedure flow in IRA				
TIMI 3 (Normal flow) (reference)	^	^	1.00	1.00
TIMI 0 (No flow)			1.66 (0.99-2.78)	2.66 (1.82-3.88)*
TIMI 1 (Partial flow)			2.00 (1.01-3.94)*	2.18 (1.40-3.39)*
TIMI 2 (Slow flow)			1.34 (0.72-2.52)	1.91 (1.23-2.97)*
Baseline model + Vessels attempted				
One vessel	1.00	1.00	1.00	1.00
Multi vessel PCI	1.65 (0.89-3.07)	0.88 (0.75-1.03)	0.86 (0.61-1.21)	0.74 (0.61-0.90)*
Baseline model + Number of stents				
No stent	1.00	1.00	1.00	1.00
One stent	1.11 (0.37-3.45)	0.91 (0.65-1.26)	0.31 (0.18-0.54)*	0.47 (0.34-0.65)*
More than one stent	2.03 (0.74-5.52)	0.91 (0.66-1.24)	0.32 (0.20-0.53)*	0.43 (0.32-0.59)*
Other interventions				
Baseline model + Pre procedural ventilation	^	6.47 (5.30-7.90)*	6.47 (5.30-7.90)*	2.08 (1.70-2.54)*
Baseline model+LMS stenosis pre-procedure	1.83 (0.99 - 3.35)	2.15 (1.68-2.75)*	2.15 (1.68-2.75)*	1.04 (0.76-1.43)
Baseline model + GPIIb/IIa inhibitors	0.95 (0.55-1.64)	0.95 (0.55-1.64)	0.41 (0.29-0.58)*	0.83 (0.68-1.01)
Baseline model + Diagnostic device (IVUS use)	0.48 (0.28-0.82)*	0.47 (0.39-0.57)*	0.41 (0.24-0.71)*	0.28 (0.17-0.46)*
Baseline model + Diagnostic device (Pressure FFR use)	0.25 (0.05-1.23)	0.45 (0.26-0.77)*	^	^

Abbreviation: *, significance at 5% level; ‡, level of missingness detected >50%; MI, acute myocardial infarction; cardiovascular disease; LVSD, Left ventricular systolic function; IRA, infarct-related artery; TIMI, thrombolysis in myocardial infarction; PCI, percutaneous coronary; LMS, Left main stem; IVUS, intravascular ultrasound; ^, small number of cases; FFR, fractional flow reserve.

Section 3: Sensitivity analysis

Limited general populace information concerning comorbidities may have introduced bias to the estimates because we could only match cases by age, sex, year of procedure and country. However, we addressed this by i) running a baseline model which included covariates available both in the cohort and general population groups (Table 3a) and ii) performing a Poisson regression which found no substantial difference in estimates between all-cause mortality (MRR) (Table 3b) and excess mortality using the relative survival approach.

Table 3a: Excess mortality rate ratios, with 95% CIs using imputed data, baseline model

Baseline Model	CSA (n=3799)	NSTEACS (n=5114)	STEMI-CS (n=1020)	STEMI+CS (n=749)
	EMRR	EMRR	EMRR	EMRR
Age (years)				
< 55 (reference)	1.00	1.00	1.00	1.00
55-65	1.11 (0.56-2.20)	1.58 (1.11-2.25)*	1.85 (0.99-3.48)*	1.77 (1.28-2.45)*
65-75	1.64 (0.87-3.12)	2.46 (1.78-3.38)*	2.68 (1.48-4.85)*	1.66 (1.23-2.24)*
>75	1.26 (0.59-2.69)	2.61 (1.91-3.57)*	3.49 (1.99-6.10)*	1.73 (1.29-2.33)*
Sex				
Female (reference)	1.00	1.00	1.00	1.00
Male	1.20 (0.72-1.99)	0.98 (0.85-1.14)	0.81 (0.59-1.13)	1.04 (0.84-1.30)
Calendar year				
2005-06 (reference)	1.00	1.00	1.00	1.00
2007-08	0.97 (0.51-1.84)	1.06 (0.81-1.40)	0.88 (0.36- 2.18)	1.16 (0.69-1.96)
2009-10	0.47 (0.23-0.99)	1.01 (0.78-1.31)	1.09 (0.48-2.50)	0.63 (0.38-1.03)
2011-12	0.73 (0.39-1.36)	0.91 (0.71-1.19)	0.77 (0.33-1.76)	0.54 (0.33-0.91)*
2013-14	0.53 (0.20-1.41)	0.94 (0.70-1.27)	0.91 (0.39-2.16)	0.55 (0.33-0.91)*

Abbreviations: *, significance at 5% level .

Table 3b: Factors associated with Mortality Rate Ratios (MRR) for cases of UPLMS PCI by CSA, NSTEMACS, STEMI-CS and STEMI+CS. Results are pooled estimates over 20 imputations.

Variable added to baseline	CSA (n=3799)	NSTEMACS (n=5114)	STEMI-CS (n=1020)	STEMI+CS (n=749)
	MRR	MRR	MRR	MRR
Baseline model + Previous AMI	1.68 (1.40 - 2.01)*	1.39 (1.25 - 1.54)*	1.34 (0.99 - 1.82)	0.98 (0.76 - 1.25)
Baseline model + Diabetes	1.48 (1.20 - 1.82)*	1.45 (1.29 - 1.62)*	1.69 (1.24 - 2.30)*	1.32 (1.03 - 1.68)*
Baseline model + LV function				
Good	1.00	1.00	‡	‡
Moderate LVSD	1.66 (1.31 - 2.11)*	1.70 (1.47 - 1.96)*		
Severe LVSD	1.98 (1.49 - 2.64)*	2.21 (1.92 - 2.54)*		
Baseline model + Renal Failure	2.39 (1.78 - 3.21)*	2.46 (2.15 - 2.81)*	2.24 (1.31 - 3.80)*	1.69 (1.10 - 2.61)*
Baseline model + Pre-procedure flow in IRA				
TIMI 3 (Normal flow) (reference)	^	^	1.00	1.00
TIMI 0 (No flow)			1.23 (0.74 - 1.79)	2.37 (1.67 - 3.34)*
TIMI 1 (Partial flow)			1.48 (0.88 - 2.48)	2.02 (1.35 - 3.01)*
TIMI 2 (Slow flow)			1.19 (0.76 - 1.86)	1.72 (1.14 - 2.59)*
Baseline model + Vessels attempted				
One vessel	1.00	1.00	1.00	1.00
Multi vessel PCI	0.98 (0.81 - 1.19)	0.88 (0.79 - 0.98)*	0.86 (0.66 - 1.14)	0.75 (0.62 - 0.90)*
Baseline model + Number of stents				
No stent	1.00	1.00	1.00	1.00
One stent	1.08 (0.75 - 1.54)	1.00 (0.78 - 1.28)	0.39 (0.24 - 0.63)*	0.46 (0.33 - 0.63)*
More than one stent	1.21 (0.87 - 1.70)	0.94 (0.74 - 1.19)	0.38 (0.24 - 0.58)*	0.44 (0.32 - 0.60)*
Other interventions				
Baseline model + Pre procedural ventilation	^	4.37 (3.59 - 5.32)*	5.16 (3.25 - 8.19)*	1.94 (1.59 - 2.36)*
Baseline model + LMS stenosis pre-procedure	1.35 (1.08 - 1.68)*	1.71 (1.46 - 2.00)*	1.33 (0.96 - 1.84)	1.02 (0.74 - 1.41)
Baseline model + GPIIb/IIIa inhibitors	0.89 (0.71 - 1.12)	0.91 (0.80 - 1.02)	0.46 (0.35 - 0.61)*	0.84 (0.68 - 1.02)
Baseline model + Diagnostic device (IVUS)	0.72 (0.59 - 0.87)*	0.60 (0.53 - 0.68)*	0.53 (0.36 - 0.78)*	0.33 (0.21 - 0.51)*
Baseline model + Diagnostic device (Pressure and FFR)	0.74 (0.54 - 1.01)	0.61 (0.44-0.84)*	0.98 (0.31-3.07)	^

Abbreviation: *, significance at 5% level; ‡, level of missingness detected >50%; MI, acute myocardial infarction; cardiovascular disease; LVSD, Left ventricular systolic function; IRA, infarct-related artery; TIMI, thrombolysis in myocardial infarction; PCI, percutaneous coronary; LMS, Left main stem; IVUS, intravascular ultrasound; ^, small number of cases; FFR, fractional flow reserve.

Table 4a: Factors associated with excess mortality for cases of UPLMS PCI by CSA, NSTEMACS, STEMI-CS and STEMI+CS after excluding patients with previous PCI using imputed data

Variable added to baseline	CSA (n=2616)	NSTEMACS (n=4143)	STEMI-CS (n=921)	STEMI+CS (n=669)
	EMRR	EMRR	EMRR	EMRR
Baseline model + Previous MI	3.33 (2.07-5.34)*	1.76 (1.49-2.08)*	1.03 (0.57-1.86)*	0.86 (0.59-1.26)
Baseline model + Diabetes	2.48 (1.50-4.08)*	1.59 (1.34-1.88)*	1.80 (1.19-2.74)*	1.31 (0.99-1.72)*
Baseline model + LVSD				
Good	1.00	1.00	^	^
Moderate LVSD	2.82 (1.41-5.66)*	2.25 (1.77-2.86)*		
Severe LVSD	4.28 (2.19-8.36)*	3.47 (2.72-4.42)*		
Baseline model + Renal Failure	4.31 (2.21-8.41)*	3.03 (2.51-3.66)*	2.22 (1.12-4.40)*	1.69 (1.01-2.81)*
Baseline model + Pre-procedure flow in IRA				
TIMI 3 (Normal flow) (reference)	^	^	1.00	1.00
TIMI 0 (No flow)			1.73 (0.98-3.04)	3.22 (2.05-5.03)*
TIMI 1 (Partial flow)			2.32 (1.14-4.70)*	2.78 (1.64-4.69)*
TIMI 2 (Slow flow)			1.34 (0.67-2.70)*	2.08 (1.24-3.49)*
Baseline model + Vessels attempted				
One vessel	1.00	1.00	1.00	1.00
Multivessel PCI	1.65 (0.85-3.18)	0.83 (0.70-0.98)*	0.82 (0.57-1.18)	0.73 (0.59-0.90)*
Baseline model + Number of stents				
No stent	1.00	1.00	1.00	1.00
One stent	0.84 (0.27-2.59)	1.29 (0.81-2.03)	0.27 (0.15-0.49)*	0.43 (0.30-0.61)*
More than one stent	1.56 (0.56-4.30)	1.15 (0.73-1.81)	0.27 (0.16-0.48)*	0.38 (0.27-0.53)*
Other interventions				
Baseline model + Pre procedural ventilation	‡	6.22 (4.95-7.82)*	5.98 (3.59-9.97)*	2.23 (1.80-2.77)*
Baseline model+LMS stenosis pre-procedure	2.07 (1.03-4.15)*	2.25 (1.69-2.99)*	1.69 (1.03-2.75)*	1.03 (0.72-1.48)
Baseline model + GPIIb/IIIa inhibitors	0.96 (0.54-1.72)	0.96 (0.80-1.15)*	0.39 (0.27-0.57)*	0.90 (0.73-1.12)
Baseline model + Diagnostic device (IVUS use)	0.47 (0.27-0.82)*	0.45 (0.36-0.56)*	0.36 (0.19-0.68)*	0.21 (0.12-0.38)*
Baseline model + Diagnostic device (Pressure and FFR use)	0.49 (0.16-1.50)	0.42 (0.22-0.82)*	‡	‡

Abbreviation: *, significance at 5% level; ‡, level of missingness detected >50%; MI, acute myocardial infarction; cardiovascular disease; LVSD, Left ventricular systolic function; IRA, infarct-related artery; TIMI, thrombolysis in myocardial infarction; PCI, percutaneous coronary; LMS, Left main stem; IVUS, intravascular ultrasound; ^, small number of cases; FFR, fractional flow reserve.