Supplemental appendix

Improved outcomes in patients with ST-elevation myocardial infarction during the last 20 years are related to implementation of evidence based treatments – experiences from the SWEDEHEART registry 1995 to 2014.

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Figure 1s. Flow chart of included patients

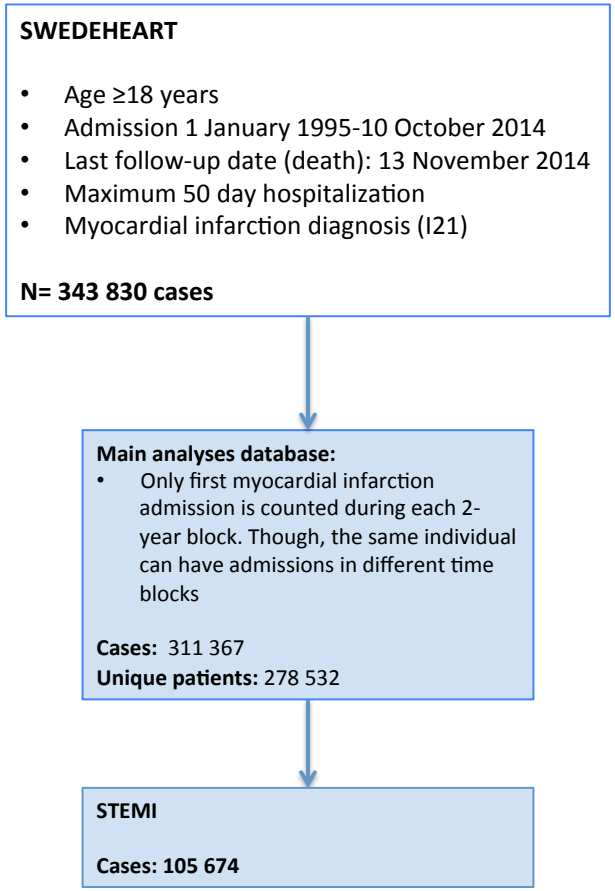

Figure 2s. Kaplan-Meier curves for long-term outcomes in STEMI cases included from 1995-96 (dark red) to 2013-14 (dark green). For death. the coloured dashed lines represent the corresponding age-gender and calender-year mateched background population.

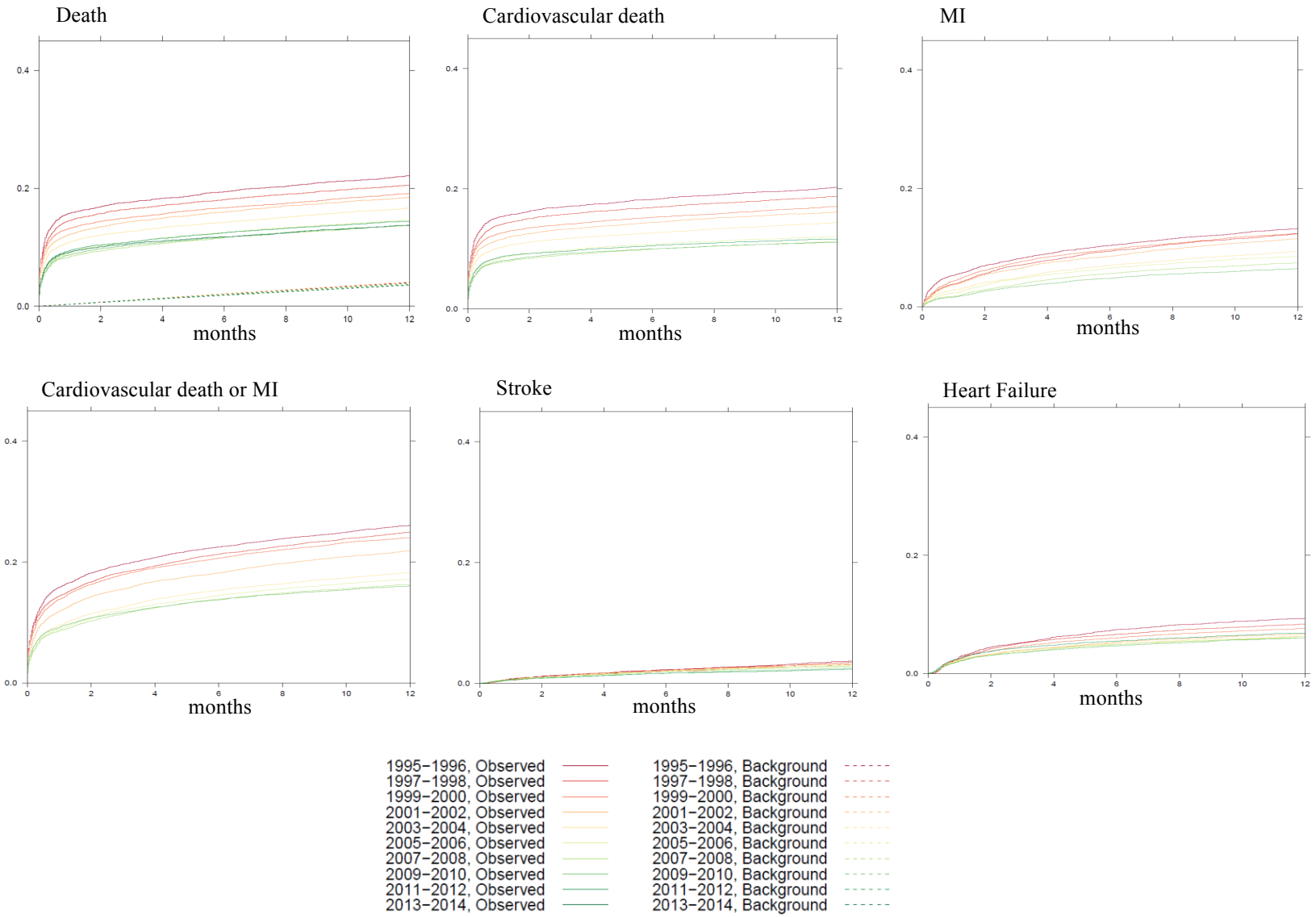

Table S1. Endpoint definition and data source

Event	Event timing	Source	ICD-codes or definition
Re-infarction	In-hospital	SWEDEHEART (collected prospectively as part of the protocol)	I21-diagnosis registered in the SWEDEHEART registry
Re-infarction	30-day	New SWEDEHEART myocardial infarction registration (occurring >2 days and ≤30 days after discharge)	I21-diagnosis registered in the SWEDEHEART registry
Re-infarction	1-year	SWEDEHEART for MI ≤30 days after discharge date & Patient-registry for MI >30 days after discharge	ICD-10:I21–I22. ICD-9: 410. 412
Stroke	In-hospital, 30-day and 1-year events	Patient-registry	Ischemic stroke: ICD-10: I63.0–I63.6. ICD-9: 433–436
Heart failure hospitalization	In-hospital, 30-day and 1-year events	National Patient registry; heart failure as main diagnosis only	ICD-10: I50. I110. K761 ICD 9: 428
Death	In-hospital, 30-day and 1-year events	Population registry	-
Cardiovascular death	In-hospital, 30-day and 1-year events	National Cause of Death registry	ICD-9: 390-459 ICD-10: I

Table S2. In hospital investigations, procedures and medical treatments

Variable	1995-1996	1997-1998	1999-2000	2001-2002	2003-2004	2005-2006	2007-2008	2009-2010	2011-2012	2013-2014	P-value*
N	5567	9450	11473	11657	11483	11259	11628	11663	11745	9749	
Reperfusion therapies											
Coronary angiography	114 (2.0%)	516 (5.5%)	1453 (12.7%)	3285 (28.2%)	6259 (54.5%)	8711 (77.4%)	9768 (84.0%)	10173 (87.2%)	10521 (89.6%)	8968 (92.0%)	<0.001
Reperfusion for STEMI	3677 (66.2%)	6339 (67.2%)	7706 (67.3%)	7779 (67.3%)	7599 (66.8%)	8143 (72.3%)	8807 (75.7%)	9181 (78.7%)	9379 (79.9%)	7961 (81.7%)	<0.001
PCI in hospital	380 (6.8%)	795 (8.4%)	1735 (15.1%)	3133 (26.9%)	5572 (48.5%)	7868 (69.9%)	8860 (76.2%)	9403 (80.6%)	9917 (84.4%)	8536 (87.6%)	<0.001
CABG in hospital	49 (0.9%)	86 (0.9%)	129 (1.1%)	178 (1.5%)	239 (2.1%)	245 (2.2%)	206 (1.8%)	251 (2.2%)	295 (2.5%)	204 (2.1%)	<0.001
Findings on angiography											
Left main/3-vessel disease**	357 (49.5%)	761 (44.5%)	981 (41.6%)	1082 (39.6%)	1075 (37.8%)	860 (35.2%)	775 (33.9%)	686 (33.3%)	528 (32.4%)	304 (32.2%)	<0.001
In-hospital treatment											
Intravenous inotrope	521 (9.6%)	843 (9.2%)	790 (7.1%)	700 (6.2%)	650 (5.8%)	621 (5.6%)	640 (5.5%)	653 (5.6%)	714 (6.1%)	620 (6.4%)	<0.001
Intravenous diuretic	2373 (43.7%)	3526 (38.2%)	4067 (36.3%)	3597 (31.6%)	3168 (28.1%)	2824 (25.3%)	2633 (22.7%)	2425 (20.8%)	2376 (20.2%)	1971 (20.3%)	<0.001
Medication at discharge											
Aspirin	3831 (81.7%)	7055 (87.2%)	8770 (87.0%)	9011 (86.9%)	9305 (89.7%)	9717 (93.4%)	10217 (94.5%)	10322 (95.5%)	10374 (96.6%)	8420 (94.3%)	<0.001
Dual antiplatelet	0 (0.0%)	106 (1.3%)	935 (9.3%)	2461 (23.7%)	5423 (52.3%)	7976 (76.7%)	9029 (83.5%)	9463 (87.6%)	9691 (90.3%)	7993 (89.6%)	<0.001
Warfarin	842 (18.1%)	1044 (13.1%)	1003 (10.0%)	834 (8.1%)	667 (6.5%)	498 (4.8%)	568 (5.3%)	605 (5.6%)	651 (6.0%)	723 (8.0%)	<0.001
Betablocker	3659 (78.2%)	6587 (81.7%)	8621 (85.6%)	9099 (87.9%)	9235 (89.1%)	9353 (89.9%)	9824 (90.9%)	9914 (91.7%)	9911 (91.6%)	8176 (91.0%)	<0.001
Calcium antagonist	550 (11.9%)	756 (9.5%)	956 (9.6%)	954 (9.4%)	843 (8.2%)	859 (8.3%)	948 (8.8%)	1072 (9.9%)	1100 (10.2%)	1011 (11.3%)	0.056
Digoxin	445 (9.6%)	645 (8.1%)	669 (6.7%)	521 (5.1%)	421 (4.1%)	319 (3.1%)	268 (2.5%)	222 (2.1%)	184 (1.7%)	120 (1.3%)	<0.001
ACEi/ARB	1907 (40.8%)	3276 (40.9%)	4477 (44.7%)	5315 (51.7%)	5975 (57.8%)	7017 (67.4%)	8193 (75.8%)	8883 (82.2%)	9240 (85.4%)	7656 (85.2%)	<0.001
Diuretic	1834 (39.4%)	2993 (37.4%)	3534 (35.3%)	3553 (34.7%)	3233 (31.3%)	3093 (29.7%)	2881 (26.7%)	2700 (25.0%)	2590 (23.9%)	1936 (21.5%)	<0.001
Statin	657 (14.2%)	2447 (30.6%)	4653 (46.4%)	6339 (61.7%)	7588 (73.4%)	8644 (83.1%)	9548 (88.3%)	9893 (91.6%)	10017 (92.6%)	8413 (93.6%)	<0.001

Numbers are n(%) or median (interquartile range. IQR) as appropriate.
MI: myocardial infarction; PCI: Percutaneous coronary intervention; CABG: Coronary artery by-pass grafting; LVEF: Left ventricular ejection fraction; ACEi/ARB: Angiotensin-converting-enzyme inhibtor/angiotensin receptor blocker. * p-values were tested with Jonckheere-Terpstra trend test for categorical variables and with linear-by-linear trend test for continuous data. ** This data contains a large proportion of missing >20%.

Table S3. In-hospital, 30-day and 1-year outcomes

	1995-1996	1997-1998	1999-2000	2001-2002	2003-2004	2005-2006	2007-2008	2009-2010	2011-2012	2013-2014	P for trend
N	5567	9450	11473	11657	11483	11259	11628	11663	11745		
In-hospital outcome											
In-hospital death	13.60%	11.90%	11.10%	10.00%	8.90%	7.40%	6.90%	7.20%	7.90%	756/9749 (7.8%)	<0.001
In-hospital CV death	13.20%	11.50%	10.50%	9.50%	8.40%	6.90%	6.40%	6.60%	7.20%		<0.001
In-hospital MI		2.90%	1.60%	1.70%	1.70%	1.40%	1.10%	1.00%	0.90%		<0.001
In-hospital MI or death		13.90%	12.20%	11.20%	10.20%	8.40%	7.50%	7.90%	8.50%		<0.001
In-hospital MI or CV death		13.50%	11.70%	10.80%	9.60%	7.90%	7.00%	7.30%	7.90%		<0.001
30-day outcome											
Death	15.80%	14.60%	13.20%	12.20%	10.90%	9.10%	8.40%	8.70%	9.40%	894/9749 (9.2%)	<0.001
CV death	15.20%	13.90%	12.50%	11.50%	10.10%	8.30%	7.70%	7.90%	8.50%		<0.001
MI		4.90%	3.50%	4.00%	3.40%	2.70%	2.20%	1.70%	1.50%		<0.001
MI or death		18.20%	16.10%	15.60%	13.80%	11.20%	10.10%	10.10%	10.70%		<0.001
MI or CV death		17.70%	15.40%	14.90%	13.10%	10.50%	9.40%	9.30%	9.80%		<0.001
Stroke	0.60%	0.60%	0.50%	0.60%	0.60%	0.50%	0.60%	0.60%	0.50%		0.86
Stroke or death	16.30%	15.00%	13.60%	12.70%	11.40%	9.50%	9.00%	9.20%	9.90%		<0.001
Heart failure	2.40%	2.30%	2.20%	2.00%	2.00%	2.10%	2.00%	2.00%	2.40%		0.56
Heart failure or death	18.00%	16.60%	15.30%	14.00%	12.80%	11.00%	10.30%	10.50%	11.50%		<0.001
1-year outcomes		9450	11473	11657	11483	11259	11628	11663	11745		
Death	22.1%	20.5%	19.1%	18.4%	16.7%	14.6%	13.8%	13.7%	14.4%	688/4884 (14.1%)	<0.001
CV death	20.1%	18.6%	16.9%	16.0%	14.3%	12.0%	11.2%	11.0%	11.6%		<0.001
MI		11.5%	10.7%	10.9%	10.2%	8.5%	7.8%	6.7%	5.8%		<0.001
MI or death		29.2%	27.6%	26.9%	24.8%	21.1%	19.7%	19.1%	19.1%		<0.001
Stroke	3.00%	2.9%	2.7%	2.8%	2.7%	2.6%	2.6%	2.3%	2.1%		<0.001
Stroke or death	24.5%	22.7%	21.0%	20.5%	18.7%	16.5%	15.9%	15.5%	16.0%		<0.001

Heart failure	7.8%	7.1%	6.6%	5.8%	5.6%	5.7%	5.5%	5.5%	6.2%		<0.001
Heart failure or death	27.9%	25.8%	24.1%	22.8%	21.0%	18.9%	18.0%	18.0%	19.0%		<0.001

MI: Myocardial infarction: CV: Cardiovascular.

Table S4. Standardized incidence rate ratio (SIR)

The SIR of 1year total mortality for cases with ST-elevation myocardial infarction versus the general population was calculated based on the mortality rates of an age, sex and calendar (2-year block) matched general population from Statistics Sweden (www.scb.se).

	1995-1996	1997-1998	1999-2000	2001-2002	2003-2004	2005-2006	2007-2008	2009-2010	2011-2012	2013-2014	P for trend
Number of deaths	5567	9450	11473	11657	11483	11259	11628	11663	11745	4884	
Observed number of deaths	1231	1937	2191	2149	1916	1646	1600	1598	1692	688	
Expected number of deaths	222	365	462	478	446	434	431	424	450	184	
Standardized incidence ratio (95% CI)	5.54 (5.24-5.86)	5.30 (5.07-5.54)	4.74 (4.55-4.94)	4.49 (4.31-4.69)	4.29 (4.10-4.49)	3.79 (3.61-3.98)	3.71 (3.53-3.90)	3.77 (3.59-3.96)	3.76 (3.58-3.94)	3.74 (3.47-4.03)	<0.001

Table S5. Standardized 1-year risk of death, myocardial infarction, and death or myocardial infarction.
Adjusted model for age, gender, and baseline characteristics and reperfusion strategies (see details below table)*. For details on modeling and interpretation, see below**.

	Death		MI		Death or MI	
Years	**Observed**	**Standardized**	**Observed**	**Standardized**	**Observed**	**Standardized**
1995-1996	22.1	16.4	-	-	-	-
1997-1998	20.5	15.9	11.5	9.6	29.2	23.5
1999-2000	19.1	14.7	10.7	9.0	27.6	22.1
2001-2002	18.4	14.2	10.9	9.1	26.9	21.6
2003-2004	16.7	13.6	10.2	9.0	24.8	21.1
2005-2006	14.6	13.1	8.5	8.1	21.1	19.6
2007-2008	13.8	13.3	7.8	7.8	19.7	19.5
2009-2010	13.7	13.5	6.7	6.7	19.1	19.2
2011-2012	14.4	14.2	5.8	5.8	19.1	19.1
2013-2014	14.1	14.1	-	-	-	-

*Adjustments were made as follows: Age (3 knots. restricted cubic spline) and gender, baseline characteristics (diabetes, hypertension, previous myocardial infarction, previous peripheral vascular disease, previous stroke, any previous stroke, previous congestive heart failure, previous chronic obstructive pulmonary disease, cancer within 3 years, presence of any pulmonary rales on admission, atrial fibrillation on admission, medication on admission (antiplatelet therapy, beta-blocker, angiotensin-converting-enzyme inhibitor/angiotensin-receptor-blocker.,statin) and in-hospital intervention for STEMI: reperfusion therapy and primary percutaneous coronary intervention.
** As an example of how the standardized mortality was obtained. the myocardial infarction cases admitted during the last 2-year period (2013-2014) were extracted from the main dataset. Admission year for these cases was changed to an earlier time-period (e.g. 1996-1997). The predicted probabilities of one-year mortality were computed per case. The average of these probabilities was computed. which was the standardized mortality for this imputation. The above-described steps were repeated for each imputation and the standardized mortality averaged over 5 imputations. The standardized mortality can be interpreted as the mortality that we would expect to see in the 2013-2014 cohort. had they been admitted in a different time-period.