SUPPLEMENTAL MATERIAL

Table S1. Incidence rate of recognized and unrecognized MI in the total Lifelines population, in men and women and in different age categories.

	MEN Persons years	No. of cases	Incidence rate per 1000 person years (95% CI)	WOMEN Persons years	No. of cases	Incidence rate per 1000 person years (95% CI)
RECOGNIZED MI						
All participants	154,309	305	1.98 [1.76, 2.21]*	221,295	139	0.63 [0.53,0.74]*
Age (years)						
18-29	16,361	1	0.06 [<0.001, 0.34]	27,010	1	0.04 [<0.001, 0.21]
30-39	31,845	6	0.19 [0.07,0.41]	44,788	6	0.13 [0.05,0.29]
40-49	55,054	85	1.54 [1.23,1.91]	80,162	27	0.34 [0.22,0.49]
50-59	27,488	68	2.47 [1.92,3.14]	40,135	31	0.77 [0.52,1.10]
60-69	18,544	96	5.18 [4.19,6.32]	23,256	46	1.98 [1.45,2.64]
70-79	4,643	45	9.69 [7.07,12.97]	5,546	23	4.15 [2.63,6.22]
80+	375	4	10.67 [2.87,27.31]	398	5	12.56 [4.05,29.32]
UNRECOGNIZED MI						
All participants	153,324	60	0.39 [0.30 – 0.50]*	220,979	59	0.27 [0.20 – 0.34]*
Age (years)						
18-29	16,360	1	0.06 [<0.001,0.34]	27,007	0	-
30-39	31,845	6	0.18 [0.07,0.41]	44,773	4	0.009 [0.002,0.02]
40-49	54,740	17	0.31 [0.18,0.50]	80,131	20	0.25 [0.15,0.39]
50-59	27,243	8	0.29 [0.13,0.58]	40,069	13	0.32 [0.17,0.55]
60-69	18,255	17	0.93 [0.54,1.49]	23,146	16	0.69 [0.39,1.12]
70-79	4,508	9	2.00 [0.91,3.79]	5,470	5	0.91 [0.29,2.13]
80+	372	2	5.38 [0.60,19.41]	384	1	2.60 [0.03,14.49]

MI = myocardial infarction, *Incidence rate in de Lifelines population. Standardized incidence rates for the general Dutch population are 2.67 [1.86, 3.95] per 1000 person years in men and 1.69 [0.84, 3.19] in women for recognized myocardial infarction and 0.63 [0.24, 1.52] per 1000 person years in men and 0.23 [0.14, 1.45] in women for unrecognized myocardial infarction.

Table S2. Baseline characteristics of individuals with unrecognized myocardial infarction and recognized myocardial infarction.

	WOMEN			MEN			Sex
	Unrecognized MI N = 59	Recognized MI N = 139	P-value	Unrecognized MI N = 60	Recognized MI N = 305	P-value	Interaction P-value
Age (mean +/- SD)	54.6 (11.1)	59.2 (11.9)	0.012	56.4 (13.3)	57.7 (11.0)	0.39	0.21
Anthropometry (mean +/- SD)							
BMI (kg/m2)	27.1 (4.4)	27.2 (4.5)	0.92	27.1 (4.3)	27.5 (3.4)	0.70	0.82
Heart rate (BPM)	69 (11)	70 (3)	0.33	66 (13)	67 (12)	0.46	0.81
Risk factor % (n)							
Hypertension	39.0 (23)	56.1 (78)	0.027	65.0 (39)	62.0 (189)	0.66	0.06
Hypercholesterolemia	20.3 (12)	48.9 (68)	<0.001	28.3 (17)	37.7 (115)	0.17	0.06
Diabetes Mellitus	6.8 (4)	9.4 (13)	0.55	10.0 (6)	9.5 (29)	0.91	0.59
Active or former smoker	64.4 (38)	60.4 (84)	0.56	73.3 (44)	75.1 (229)	0.78	0.57
Family Health – CVD	8.5 (5)	13.0 (18)	0.37	6.7 (4)	12.1 (37)	0.22	0.81
Framingham risk – 10 year risk (median – 25th and 75th percentiles)	4 (12 - 30)	10 (20 – 30)	0.013	6 (10 - 18)	12 (6 – 16)	0.32	0.47
Blood biomarkers							
Triglycerides (mmol/L)	1.0 (0.7 – 1.9)	1.2 (0.9 – 1.6)	0.12	1.4 (1.0 – 1.9)	1.3 (1.0 – 1.9)	0.40	0.37
Cholesterol (mmol/L)	5.2 (0.9)	5.7 (1.3)	0.016	5.5 (1.1)	5.4 (1.1)	0.51	0.026
HDL (mmol/L)	1.6 (0.4)	1.5 (0.4)	0.60	1.2 (0.3)	1.2 (0.3)	0.75	0.56
LDL (mmol/L)	3.2 (0.9)	3.7 (1.1)	0.004	3.6 (1.0)	3.6 (1.0)	0.94	0.028
Glucose (mmol/L)t	5.3 (1.8)	5.2 (0.9)	0.80	5.7 (1.5)	5.5 (1.1)	0.38	0.78
HbA1c (%)	5.7 (0.6)	5.8 (0.4)	0.35	5.8 (0.7)	5.8 (0.6)	0.86	0.51
Pharmacotherapy % (n)							
Blood pressure lowering	36.1 (13)	60.2 (59)	0.013	52.8 (19)	58.9 (109)	0.50	0.18
Cholesterol lowering	8.5 (5)	26.6 (37)	0.004	15.0 (9)	23.3 (71)	0.16	0.08
Platelet inhibitors	3.4 (2)	17.3 (24)	0.008	11.7 (7)	14.8 (45)	0.53	0.20
Self-reported symptoms at baseline or follow-up % (n)							
Dizziness	51.7 (30)	60.3 (82)	0.27	35.6 (21)	48.3 (146)	0.07	0.68
Chest Pain	32.8 (19)	53.3 (73)	0.009	18.6 (11)	54.8 (166)	<0.001	0.09
Nausea	43.1 (25)	52.9 (72)	0.21	37.3 (22)	34.1 (103)	0.64	0.22
Dyspnea	24.1 (14)	48.2 (65)	0.002	23.7 (14)	40.2 (121)	0.017	0.53
Physically weak	24.1 (13)	28.3 (34)	0.56	25.5 (12)	29.6 (84)	0.57	0.97

BMI = body mass index, BPM = beats per minute, CVD = cardiovascular disease, HbA1c = Hemoglobin A1c, HDL = high density lipoprotein, LDL = low density lipoprotein, SD = standard deviation

Table S3. Univariate and multiple logistic regression analysis for predictors of unrecognized myocardial infarction versus recognized myocardial infarction.

	Univariate logistic regression			Multiple logistic regression		
	P-value	Odds ratio	95% CI	P-value	Odds ratio	95% CI
Age group						
18-39 years (*reference*)						
40-49 years	0.05					
50-59 years	0.005	0.27	0.11 – 0.68	0.028	0.34	0.13 – 0.89
60-69 years	0.006	0.30	0.12 – 0.71			
70+ years	0.009	0.28	0.11 – 0.73			
Anthropometry						
BMI	0.61					
Heart rate	0.49					
Risk factor						
Hypertension	0.12					
Hypercholesterolemia	0.001	0.46	0.29 – 0.73			
Hypercholeserolemia * Sex[#]	0.06					
Diabetes Mellitus	0.72					
Active or former smoker	0.74					
Family Health – CVD	0.15					
Blood biomarkers						
Triglycerides	0.63					
Cholesterol	0.32					
HDL	0.10					
LDL	0.044	0.81	0.67 – 0.99			
LDL* Sex[#]	0.028	0.62	0.40 – 0.95			
Glucose	0.74					
HbA1c	0.35					

BMI = body mass index, CI = confidence interval, CVD = cardiovascular disease, HbA1c = Hemoglobin A1c, HDL = high density lipoprotein, LDL = low density lipoprotein [#]Interaction term with sex. Values are given for women.

Figure S1. Baseline (A) and follow-up (B) ECG of a Lifelines cohort participant who developed an unrecognized MI. Figure (A) shows a normal baseline ECG. Figure (B) shows a QS complex in V2-V3 indicative of a previous anterior myocardial infarction.
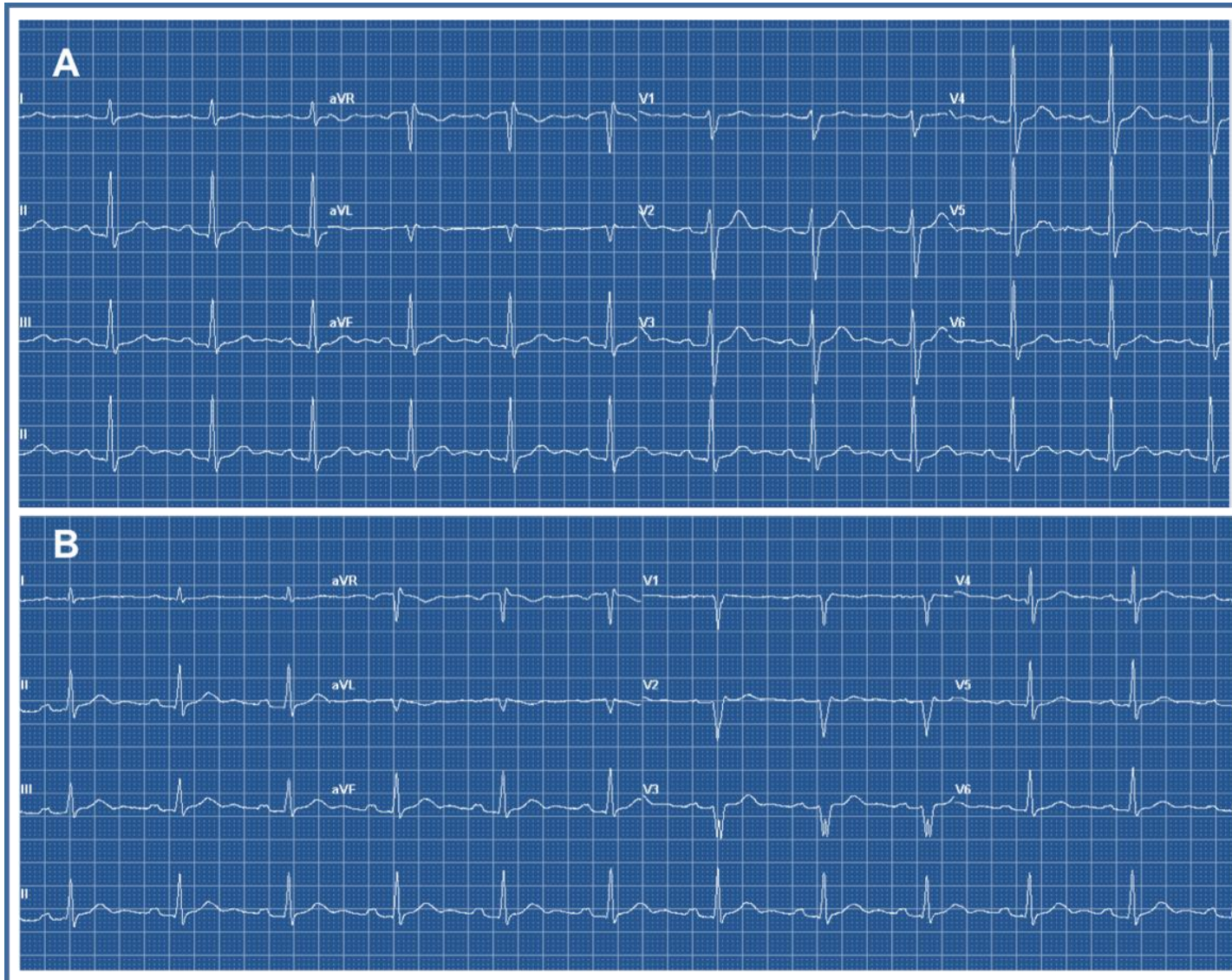
Figure S2. Age distribution of participants with recognized myocardial infarction (green) and unrecognized myocardial infarction (red). MI = myocardial infarction, UMI = unrecognized myocardial infarction.