

## Online supplement

### Long-term outcomes of chronic coronary syndrome worldwide. Insights from the international CLARIFY registry

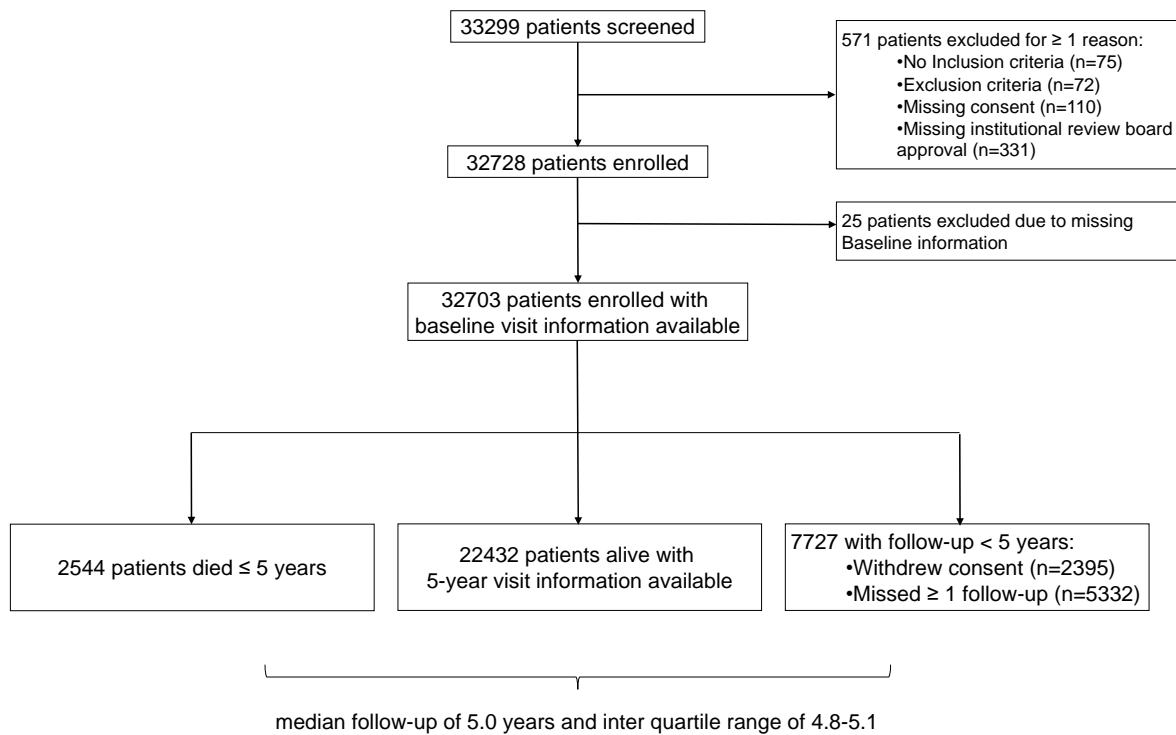
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#### Content:

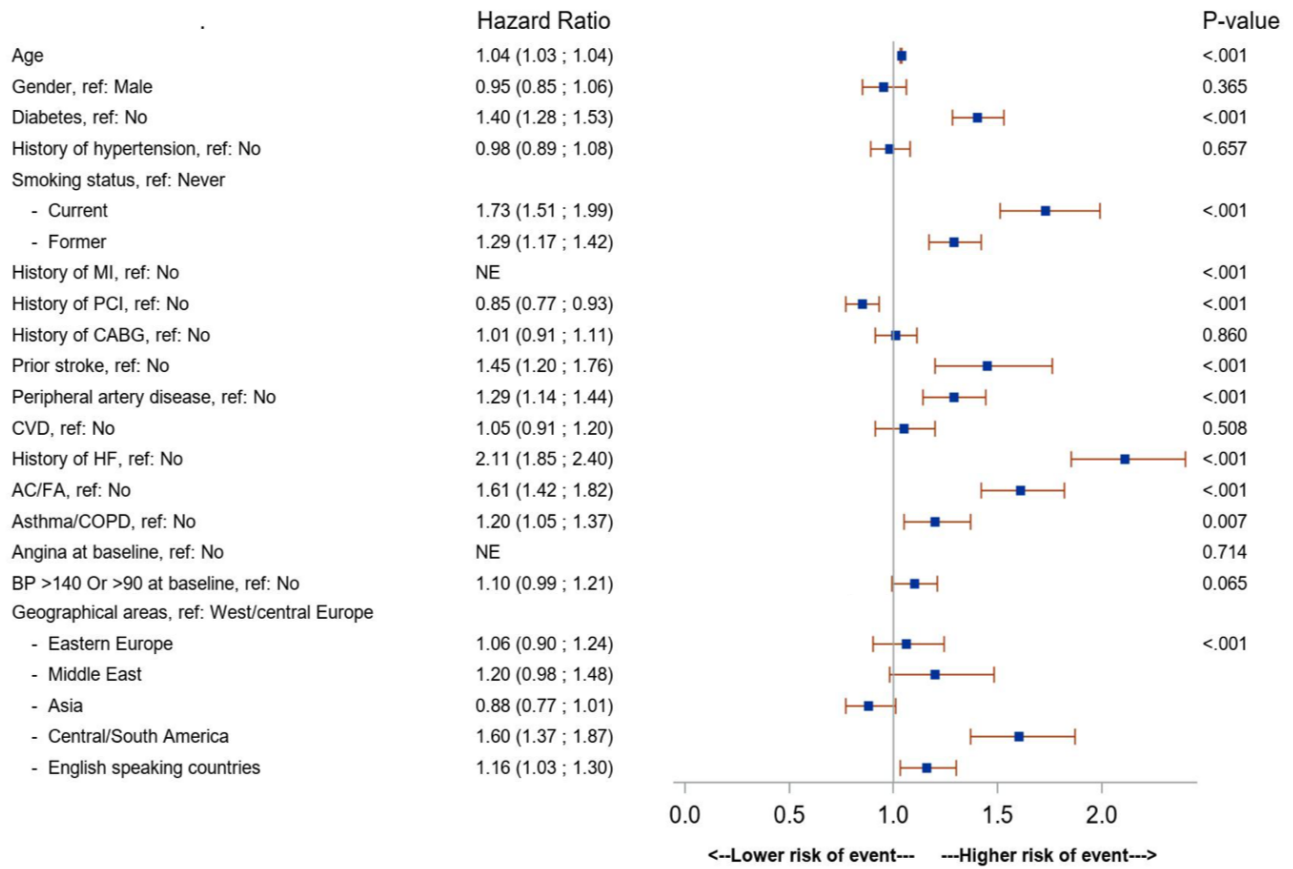
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\* Sorbets E, Greenlaw N, Ferrari R, Ford I, Fox KM, Tardif J-C, Tendera M, Steg PG, CLARIFY Investigators. Rationale, design, and baseline characteristics of the CLARIFY registry of outpatients with stable coronary artery disease. *Clin Cardiol* 2017;**40**:797–806.

**Figure S1: Flow diagram of study population**



**Figure S2: Forest plot for multivariable analysis to determine the main predictors of CV death or non-fatal MI with the interaction term MI x Angina in addition in the entire CLARIFY population.**



The *P* value for interaction= 0.002

BP: blood pressure; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; CV: cardiovascular; HF: heart failure; MI: myocardial infarction; NE Not estimable; PCI: percutaneous coronary intervention

**Table S1. Definitions of the six geographical areas**

West/central Europe	Austria Belgium/Luxembourg Bulgaria Czech Republic Denmark France Germany Greece Hungary Ireland Italy Latvia Lithuania Netherlands Poland Portugal Romania Slovakia Slovenia Spain Switzerland
Eastern Europe	Russia Ukraine
Middle East	Bahrain Kuwait Oman Qatar Saudi Asia United Arab Emirates
Asia	Brunei China India Korea Malaysia Singapore Thailand Vietnam
Central/South America	Argentina Brazil Canada Mexico West Indies
Commonwealth countries	Australia Canada South Africa The United Kingdom

**Table S2. Baseline characteristics of the entire Clarify cohort (adapted from Clinical Cardiology Journal\*)**

	<b>All CLARIFY N=32,703</b>	
<b>Risk factors and lifestyle</b>		
Age (years)	64.2 ± 10.5	(32688)
Female	22.4 %	(25365/32692)
Treated hypertension	71.0 %	(23210/32693)
Diabetes	29.1 %	(9502/32694)
Dyslipidaemia	74.9 %	(24504/32695)
Smoking status : current	12.5 %	(4077/32699)
former	46.2 %	(15109/32699)
never	41.3 %	(13513/32699)
Family history of premature coronary disease	28.5 %	(9326/32693)
No physical activity	16.2 %	(5287/32688)
<b>Medical History†</b>		
Myocardial infarction	59.9 %	(19595/32695)
PCI	58.6 %	(19162/32695)
CABG	23.6 %	(7703/32694)
Cerebrovascular disease		
Stroke	4.0 %	(1314/32698)
Transient ischemic attack	3.1 %	(1001/32697)
Carotid disease	7.6 %	(2474/32699)
Peripheral Arterial Disease		
Lower extremity artery disease	9.9 %	(3239/32695)
Aortic abdominal aneurysm	1.5 %	(504/32695)
Hospitalisation for HF	4.7 %	(1531/32698)
Atrial Fibrillation / Flutter	7.1 %	(2313/32698)
Asthma / COPD	7.4 %	(2419/32698)
<b>Clinical examination</b>		
Angina symptoms	22.1 %	(7212/32691)
HF symptoms	15.1 %	(4925/32691)
HF symptoms and LVEF ≥ 50% ¶	10.2 %	(2256/22513)
Systolic BP (mmHg)	131.0 ±16.7	(32675)
Diastolic BP (mmHg)	77.3 ±10.0	(32675)
Pulse (bpm)	68.2 ±10.6	(32673)
Body mass index (kg/m <sup>2</sup> )	27.9 ± 4.6	(32659)
<b>Paraclinical parameters</b>		
LVEF (%)	56.1 ±11.1	(22519)
Coronary arteries involved††		

Left main	8.7 %	(2848/32687)
LAD	58.3 %	(19062/32687)
Cx	36.1 %	(11793/32687)
RCA	43.5 %	(14233/32687)
Bypass graft	8.0 %	(2630/32687)
No significant stenosis	3.2 %	(1057/32687)
Angiography not done <12 months	14.6%	(4763/32687)
<b>Baseline medications</b>		
Aspirin	87.8 %	(28687/32689)
Single antiplatelet therapy	95.2 %	(31108/32692)
Dual antiplatelet therapy	28.0 %	(9145/32692)
Oral anticoagulants	8.2 %	(2670/32667)
Lipid lowering agents	92.3 %	(30191/32692)
Statins	82.9%	(27099/32692)
Betablockers	75.3 %	(24611/32692)
Calcium antagonists	27.3 %	(8909/32688)
Ivabradine	9.8 %	(3218/32690)
Nitrates or other antianginal drugs†††	30.4 %	(9922/32681)
ACE-inhibitors or ARB	76.3 %	(24925/32684)
Diuretics	29.3 %	(9585/32687)
NSAID	4.9 %	(1614/32682)
Amiodarone/Dronedarone	2.9 %	(962/32682)
Insulin in diabetics	21.6%	(2048/9501)
Oral diabetic drugs in diabetics	69.2%	(6578/9501)

Data are expressed in mean  $\pm$ SD for continuous variables or % for categorical variables. For categorical data, the number of concerned patients/number of available data are indicated in brackets. For continuous data, the number of available data are indicated in brackets.

¶ The prevalence of HF symptoms with LVEF  $\geq$ 50% was higher in female (13.8%) than in male (9.0%),  $P < 0.001$ .

† 5% (1641/32703) of patients had for inclusion criteria: chest pain and proven ischaemia only (no prior MI, no prior revascularization and no previous coronary angiography showing at least one coronary stenosis of more than 50%.

†† with stenosis > 50% at coronary angiography or having required revascularization in the past.

††† other antianginal drugs: molsidomine, nicorandil, ranolazine, trimetazidine.

ACE: angiotensin converting enzyme; ARB: angiotensin receptor blockers; BP: blood pressure; CABG: coronary artery bypass graft ; HF: heart failure; COPD: chronic obstructive coronary disease; LAD: left anterior descending; LVEF: left ventricular ejection fraction; NSAID: nonsteroidal anti-inflammatory drugs; PCI: percutaneous coronary intervention; RCA: right coronary artery; SD: standard deviation;

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**Table S3. Baseline characteristics according to combined history of angina / prior MI status**

	Prior MI* N=19595			P value	No Prior MI** N=13100			P value
	Angina N=4507	No Angina N=15084	Angina N=2704		No angina N=10394			
<b>Risk factors and lifestyle</b>								
Age (years)	62.1 ± 10.4 (4505)	63.4 ± 10.8 (15078)	<0.001	64.6 ± 9.9 (2702)	66.1 ± 9.80 (10389)	<0.001		
Male	76.1 % (3431/4507)	82.2 % (12392/15079)	<0.001	63.7 % (1722/2702)	75.2 % (7811/10392)	<0.001		
Treated hypertension	78.3 % (3531/4507)	66.3 % (10006/15083)	<0.001	78.6 % (2126/2704)	72.6 % (7542/10393)	<0.001		
Diabetes	28.2 % (1269/4507)	28.7 % (4330/15080)	0.467	29.3 % (792/2704)	29.9 % (3102/10393)	0.572		
Dyslipidaemia	79.6 % (3589/4507)	74.8 % (11286/15082)	<0.001	77.4 % (2093/2704)	72.4 % (7528/10393)	<0.001		
Smoking status : current	17.2 % (776/4507)	13.5 % (2029/15084)	<0.001	11.2 % (302/2704)	9.3 % (970/10394)	0.004		
former	43.5 % (1959/4507)	50.9 % (7680/15084)	<0.001	37.8 % (1022/2704)	42.7 % (4440/10394)	<0.001		
never	39.3 % (1772/4507)	35.6 % (5375/15084)	<0.001	51.0 % (1380/2704)	48.0 % (4984/10394)	0.004		
Family history of premature coronary disease	36.2 % (1631/4507)	27.0 % (4073/15082)	<0.001	34.1 % (921/2704)	26.0 % (2700/10393)	<0.001		
No physical activity	13.5 % (610/4507)	16.1 % (2430/15080)	<0.001	16.5 % (446/2703)	17.3 % (1800/10391)	0.312		
<b>Medical History</b>								
Myocardial infarction	100.0 % (4507/4507)	100.0 % (15084/15084)	NA	0.0 % (0/2704)	0.0 % (0/10394)	NA		
PCI	43.0 % (1940/4507)	65.4 % (9869/15083)	<0.001	39.9 % (1078/2704)	60.3 % (6270/10393)	..<0.001		
CABG	20.3 % (914/4507)	21.9 % (3303/15081)	0.020	17.7 % (478/2703)	28.9 % (3005/10394)	..<0.001		
Cerebrovascular disease								
Stroke	5.3 % (239/4507)	3.7 % (562/15082)	<0.001	5.3 % (144/2704)	3.6 % (369/10394)	<0.001		
Transient ischemic attack	3.9 % (177/4507)	2.4 % (364/15081)	<0.001	6.2 % (168/2704)	2.8 % (292/10394)	<0.001		
Carotid disease	8.5 % (385/4507)	6.1 % (926/15083)	<0.001	11.4 % (309/2704)	8.2 % (853/10394)	<0.001		
Peripheral Arterial Disease								
Lower extremity artery disease	13.3 % (601/4507)	8.6 % (1299/15081)	<0.001	12.4 % (336/2704)	9.6 % (1002/10393)	<0.001		
Aortic abdominal aneurysm	1.4 % (63/4507)	1.6 % (248/15081)	<0.001	1.0 % (26/2704)	1.6 % (167/10393)	0.013		
Hospitalisation for HF	9.2 % (415/4507)	4.4 % (670/15082)	<0.001	4.5 % (122/2704)	3.1 % (323/10394)	<0.001		
Atrial Fibrillation / Flutter	7.4 % (332/4507)	6.1 % (922/15082)	0.003	7.4 % (199/2704)	8.3 % (858/10394)	<0.001		
Asthma / COPD	8.1 % (363/4507)	7.1 % (1074/15082)	0.035	10.8 % (291/2704)	6.7 % (691/10394)	0.128		
<b>Clinical examination</b>								
Angina symptoms	100.0 % (4507/4507)	0.0 % (0/15804)	NA	100.0 % (2704/2704)	0.0 % (0/10394)	NA		
HF symptoms	48.9 % (2203/4507)	9.5 % (1425/15083)	<0.001	26.2 % (708/2703)	5.7 % (588/10394)	<0.001		
HF symptoms and LVEF ≥ 50%	31.9 % (1120/3514)	4.1 % (427/10445)	<0.001	22.5 % (429/1908)	4.2 % (280/6645)	<0.001		
Systolic BP (mmHg)	133.0 ± 17.5 (4507)	129.2 ± 16.2 (15066)	<0.001	134.4 ± 17.4 (2703)	132.0 ± 16.4 (10389)	<0.001		
Diastolic BP (mmHg)	79.7 ± 10.8 (4507)	76.5 ± 9.7 (15066)	<0.001	79.1 ± 10.6 (2703)	76.8 ± 9.5 (10389)	<0.001		
Pulse (bpm)	69.9 ± 10.6 (4507)	67.8 ± 10.4 (15067)	<0.001	69.8 ± 11.3 (2704)	67.7 ± 10.6 (10385)	<0.001		
Body mass index (kg/m <sup>2</sup> )	28.8 ± 4.7 (4502)	27.8 ± 4.6 (15068)	<0.001	28.2 ± 4.8 (2699)	27.5 ± 4.4 (10380)	<0.001		
<b>Paraclinical parameters</b>								
LVEF (%), Coronary arteries involved†	53.2 ± 10.5 (3514)	53.8 ± 11.4 (10446)		59.4 ± 8.9 (1908)	60.2 ± 9.8 (6645)	<0.001		

Left main	8.8 %	(396/4506)	7.7 %	(1159/15076)	0.017	8.4 %	(228/2704)	10.3 %	(1065/10392)	0.005
LAD	42.6 %	(1918/4506)	59.9 %	(9027/15076)	<0.001	47.8 %	(1293/2704)	65.6 %	(6820/10392)	<0.001
Cx	28.3 %	(1277/4506)	36.9 %	(5555/15076)	<0.001	31.5 %	(851/2704)	39.5 %	(4108/10392)	<0.001
RCA	37.8 %	(1702/4506)	46.5 %	(7007/15076)	<0.001	35.2 %	(953/2704)	44.0 %	(4567/10392)	<0.001
Bypass graft	7.9 %	(357/4506)	7.70 %	(1153/15076)	0.544	6.9 %	(186/2704)	9.0 %	(934/10392)	<0.001
No significant stenosis	2.9 %	(132/4506)	3.2 %	(476/15076)	0.439	5.6 %	(152/2704)	2.9 %	(297/10392)	<0.001
Angiography not done <12 months	34.3 %	(1546/4506)	11.1 %	(1677/15076)	<0.001	27.2 %	(736/2704)	7.7 %	(804/10392)	<0.001
<b>Baseline medications</b>										
Aspirin	90.0 %	(4057/4507)	88.8 %	(13386/15077)	0.020	87.5 %	(2365/2704)	85.4 %	(8871/10393)	0.005
Single antiplatelet therapy	95.3 %	(4294/4507)	95.9 %	(14464/15080)	0.061	94.6 %	(2559/2704)	94.1 %	(9783/10393)	0.314
Dual antiplatelet therapy	23.9 %	(1077/4507)	30.3 %	(4568/15080)	<0.001	23.6 %	(639/2704)	27.5 %	(2857/10393)	<0.001
Oral anticoagulants	8.4 %	(379/4505)	8.0 %	(1211/15065)	0.420	7.0 %	(189/2702)	8.6 %	(889/10387)	0.008
Lipid lowering agents	92.8 %	(4182/4507)	93.8 %	(14148/15080)	0.013	88.1 %	(2401/2704)	91.0 %	(9452/10393)	<0.001
Statins	85.3 %	(3845/4507)	84.5 %	(12735/15080)	0.159	78.9 %	(2133/2704)	80.6 %	(8379/10393)	0.043
Betablockers	83.2 %	(3751/4507)	77.7 %	(11717/15081)	<0.001	71.4 %	(1930/2704)	69.3 %	(7206/10392)	0.040
Calcium antagonists	28.0 %	(1261/4507)	21.5 %	(3243/15078)	<0.001	38.3 %	(1035/2704)	32.4 %	(3370/10391)	<0.001
Ivabradine	21.8 %	(980/4506)	6.9 %	(1035/15079)	<0.001	20.5 %	(553/2704)	6.3 %	(650/10393)	<0.001
Nitrates or other antianginal drugs††	57.0 %	(2568/4505)	22.7 %	(3419/15073)	<0.001	54.1 %	(1462/2703)	23.8 %	(2468/10393)	<0.001
ACE-inhibitors or ARB	84.0 %	(3786/4507)	78.3 %	(11800/15074)	<0.001	74.2 %	(2007/2704)	70.5 %	(7326/10391)	<0.001
Diuretics	39.4 %	(1776/4507)	27.8 %	(4186/15075)	<0.001	30.8 %	(833/2704)	26.8 %	(2788/10393)	<0.001
NSAID	6.1 %	(274/4506)	4.4 %	(655/15072)	<0.001	6.8 %	(184/2704)	4.8 %	(500/10393)	<0.001
Amiodarone/Dronedaron	4.3 %	(195/4506)	2.8 %	(428/15072)	<0.001	2.6 %	(70/2704)	2.6 %	(268/10392)	0.977
Insulin in diabetics	23.1 %	(293/1269)	21.2 %	(916/4329)	0.142	23.7 %	(188/792)	21.0 %	(650/3102)	0.089
Oral diabetic drugs in diabetics	67.7 %	(859/1269)	68.7 %	(2975/4329)	0.487	68.7 %	(544/792)	70.9 %	(2198/3102)	0.232

Data are expressed in mean  $\pm$ SD for continuous variables or % for categorical variables. For categorical data, the number of concerned patients/number of available data are indicated in brackets. For continuous data, the number of available data are indicated in brackets

\*Among the subset with prior MI, angina status was missing for 4 patients.

\*\*Among the subset without prior MI, angina status was missing for 2 patients.

†with stenosis > 50% at coronary angiography or having required revascularization in the past.

†† other antianginal drugs: molsidomine, nicorandil, ranolazine, trimetazidine.

Categorical and continuous variables were compared across groups by Chi square and Student test respectively.

ACE: angiotensin converting enzyme; ARB: angiotensin receptor blockers; BP: blood pressure; CABG: coronary artery bypass graft ; HF: heart failure; COPD: chronic obstructive coronary disease; LAD: left anterior descending; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NA: not applicable; NSAID: nonsteroidal anti-inflammatory drugs; PCI: percutaneous coronary intervention; RCA: right coronary artery; SD: standard deviation;



**Table S4: Baseline characteristics according to the six geographical areas**

	Western/Central Europe N=15301		Eastern Europe N=3025		Middle East N=1511		Asia N=5688		Central/South America N=2230		Commonwealth countries N=4948		P value
<b>Risk factors and lifestyle</b>													
Age (years)	65.9 ±10.2	(15296)	58.9 ±9.0	(3025)	61.6 ±11.4	(1510)	62.5 ±10.5	(5688)	64.5 ±10.7	(2227)	66.6 ±10.0	(4942)	<0.001
Male	79.0 %	(12089/15295)	75.0 %	(2268/3025)	78.3 %	(1510/1183)	76.8 %	(4367/5688)	74.5 %	(1660/2228)	76.8 %	(3798/4946)	<0.001
Treated hypertension	72.5 %	(11094/15299)	79.2 %	(2397/3025)	74.1 %	(1504/1114)	67.6 %	(3846/5688)	71.2 %	(1586/2229)	64.1 %	(3173/4948)	<0.001
Diabetes	28.1 %	(4292/15297)	17.1 %	(517/3025)	59.8 %	(150/8902)	31.1 %	(1768/5688)	36.4 %	(811/2229)	24.5 %	(1212/4947)	<0.001
Dyslipidaemia	81.2 %	(12422/15299)	77.4 %	(2342/3025)	74.9 %	(1128/1507)	58.5 %	(3329/5688)	72.0 %	(1604/2229)	74.4 %	(3679/4947)	<0.001
Smoking status : current	11.4 %	(1738/15300)	19.1 %	(577/3025)	10.9 %	(165/1508)	14.9 %	(849/5688)	6.1 %	(136/2230)	12.4 %	(612/4948)	<0.001
former	50.3 %	(7695/15300)	36.1 %	(1092/3025)	23.8 %	(360/1508)	38.2 %	(2175/5688)	47.8 %	(1066/2230)	55.0 %	(2721/4948)	
never	38.4 %	(5867/15300)	44.8 %	(1356/3025)	65.2 %	(983/1508)	46.8 %	(2664/5688)	46.1 %	(1028/2230)	32.6 %	(1615/4948)	
Family history of premature coronary disease	28.4 %	(4350/15299)	38.4 %	(1160/3025)	12.7 %	(191/1505)	16.2 %	(922/5688)	28.2 %	(629/2229)	41.9 %	(2074/4947)	<0.001
No physical activity	16.6 %	(2536/15296)	5.1 %	(154/3025)	34.2 %	(514/1505)	15.4 %	(875/5688)	30.2 %	(673/2229)	10.8 %	(535/4945)	<0.001
<b>Medical History</b>													
Myocardial infarction	58.1 %	(8882/15298)	78.9 %	(2387/3025)	63.8 %	(962/1507)	50.9 %	(2895/5688)	62.2 %	(1388/2230)	62.3 %	(3081/4947)	<0.001
PCI	64.5 %	(9864/15299)	26.4 %	(798/3025)	59.2 %	(893/1508)	71.2 %	(4051/5688)	59.6 %	(1328/2228)	45.0 %	(2228/4947)	<0.001
CABG	26.1 %	(3991/15299)	20.0 %	(606/3025)	29.6 %	(446/1508)	9.6 %	(543/5688)	24.8 %	(553/2229)	31.6 %	(1564/4945)	<0.001
Cerebrovascular disease													
Stroke	3.8 %	(570/15298)	4.5 %	(137/3025)	3.1 %	(46/1510)	5.5 %	(315/5688)	3.0 %	(66/2230)	3.6 %	(180/4947)	<0.001
Transient ischemic attack	3.4 %	(524/15297)	2.7 %	(83/3025)	1.2 %	(16/1510)	2.5 %	(142/5688)	2.0 %	(46/2230)	3.8 %	(190/4947)	<0.001
Carotid disease	10.7 %	(1640/15299)	9.8 %	(297/3025)	1.9 %	(29/1510)	3.9 %	(219/5688)	3.2 %	(72/2230)	4.4 %	(217/4947)	<0.001
Peripheral Arterial Disease													
Lower extremity artery disease	12.8 %	(1962/15298)	12.7 %	(385/3025)	3.1 %	(47/1508)	4.4 %	(251/5688)	6.5 %	(144/2229)	9.1 %	(450/4947)	<0.001
Aortic abdominal aneurysm	2.4 %	(361/15297)	0.2 %	(7/3025)	0.3 %	(5/1509)	0.2 %	(13/5688)	0.9 %	(21/2229)	2.0 %	(97/4947)	<0.001
Hospitalisation for HF	4.6 %	(710/15299)	7.6 %	(230/3025)	4.5 %	(68/1510)	3.7 %	(213/5688)	4.1 %	(91/2230)	4.4 %	(219/4946)	<0.001
Atrial Fibrillation / Flutter	8.4 %	(1281/15299)	9.2 %	(278/3025)	2.2 %	(33/1510)	3.1 %	(175/5688)	3.6 %	(80/2230)	9.4 %	(466/4946)	<0.001
Asthma / COPD	8.4 %	(1291/15299)	5.9 %	(177/3025)	5.7 %	(86/1510)	3.2 %	(181/5688)	4.4 %	(97/2230)	11.9 %	(587/4946)	<0.001
<b>Clinical examination</b>													
Angina symptoms	16.7 %	(2557/15298)	78.1 %	(2362/3025)	10.3 %	(154/1503)	16.5 %	(940/5688)	9.6 %	(215/2230)	19.9 %	(984/4947)	<0.001
HF symptoms	10.2 %	(1564/15299)	77.5 %	(2343/3025)	5.3 %	(80/1504)	7.7 %	(440/5688)	6.5 %	(145/2230)	7.1 %	(353/4945)	<0.001
HF symptoms and LVEF ≥ 50%	4.0 %	(494/12509)	55.7 %	(1485/2666)	1.7 %	(22/1268)	4.6 %	(130/2804)	2.8 %	(36/1303)	4.5 %	(89/1963)	<0.001
Systolic BP (mmHg)	131.9 ±16.1	(15277)	134.3 ±17.2	(3025)	131.7 ±18.1	(1510)	128.5 ±16.6	(5688)	126.8 ±16.9	(2229)	131.1 ±17.0	(4946)	<0.001
Diastolic BP (mmHg)	77.6 ±9.4	(15277)	83.1 ±9.9	(3025)	74.4 ±10.6	(1510)	76.6 ±10.0	(5688)	76.2 ±9.9	(2229)	74.8 ±10.1	(4946)	<0.001
Pulse (bpm)	66.7 ±10.5	(15274)	70.2 ±10.2	(3025)	71.1 ±11.4	(1510)	71.3 ±10.3	(5688)	68.8 ±9.8	(2228)	67.1 ±10.7	(4948)	<0.001

Body mass index (kg/m <sup>2</sup> )	28.1 ±4.2	(15283)	29.2 ±4.3	(3025)	29.4 ±5.3	(1510)	25.1 ±3.6	(5683)	27.7 ±4.4	(2225)	29.1 ±5.3	(4933)	<0.001
<b>Paraclinical parameters</b>													
LVEF (%)	56.6 ±10.7	(12509)	56.1 ±9.0	(2666)	50.0 ±10.8	(1273)	57.9 ±12.1	(2804)	54.0 ±12.8	(1303)	55.5 ±11.9	(1964)	<0.001
Coronary arteries involved†													
Left main	11.2 %	(1708/15289)	8.8 %	(267/3025)	6.6 %	(100/1510)	5.3 %	(302/5688)	5.7 %	(128/2230)	6.9 %	(343/4945)	<0.001
LAD	61.6 %	(9417/15289)	26.1 %	(789/3025)	74.8 %	(1129/1510)	65.2 %	(3708/5688)	66.4 %	(1480/2230)	51.3 %	(2539/4945)	<0.001
Cx	41.0 %	(6270/15289)	19.9 %	(602/3025)	44.8 %	(677/1510)	34.1 %	(1942/5688)	37.4 %	(834/2230)	29.7 %	(1468/4945)	<0.001
RCA	48.4 %	(7403/15289)	28.3 %	(856/3025)	50.8 %	(767/1510)	39.6 %	(2251/5688)	45.5 %	(1014/2230)	39.3 %	(1942/4945)	<0.001
Bypass graft	9.0 %	(1368/15289)	6.6 %	(198/3025)	9.2 %	(139/1510)	3.0 %	(173/5688)	6.2 %	(138/2230)	12.4 %	(614/4945)	<0.001
No significant stenosis	3.0 %	(468/15289)	2.4 %	(71/3025)	1.4 %	(21/1510)	2.0 %	(114/5688)	4.4 %	(98/2230)	5.8 %	(285/4945)	<0.001
Angiography not done <12months	7.2 %	(1091/15289)	50.6 %	(1532/3025)	6.5 %	(98/1510)	13.6 %	(771/5688)	12.5 %	(278/2230)	20.1 %	(993/4945)	<0.001
<b>Baseline medications</b>													
Aspirin	85.6 %	(13087/15293)	90.7 %	(2743/3025)	95.7 %	(1443/1508)	88.2 %	(5017/5688)	92.2 %	(2053/2228)	87.8 %	(4344/4947)	<0.001
Single antiplatelet therapy	95.1 %	(14547/15295)	94.6 %	(2863/3025)	99.3 %	(1497/1508)	96.2 %	(5469/5688)	96.0 %	(2140/2229)	92.8 %	(4592/4947)	<0.001
Dual antiplatelet therapy	25.3 %	(3875/15295)	14.9 %	(451/3025)	33.8 %	(510/1508)	47.7 %	(2715/5688)	41.0 %	(914/2229)	13.8 %	(680/4947)	<0.001
Oral anticoagulants	10.0 %	(1525/15293)	5.6 %	(170/3025)	4.2 %	(63/1507)	6.4 %	(361/5688)	6.9 %	(154/2229)	8.1 %	(397/4925)	<0.001
Lipid lowering agents	93.1 %	(14242/15294)	90.1 %	(2724/3025)	96.6 %	(1457/1508)	88.5 %	(5033/5688)	90.5 %	(2018/2230)	95.4 %	(4717/4947)	<0.001
Statins	82.5 %	(12624/15294)	85.1 %	(2573/3025)	88.8 %	(1339/1508)	77.6 %	(4411/5688)	84.3 %	(1879/2230)	86.4 %	(4273/4947)	<0.001
Betablockers	77.0 %	(11781/15294)	86.9 %	(2630/3025)	87.5 %	(1319/1508)	70.9 %	(4035/5688)	69.9 %	(1558/2230)	66.5 %	(3288/4947)	<0.001
Calcium antagonists	26.2 %	(4005/15291)	26.8 %	(810/3025)	23.9 %	(361/1508)	32.7 %	(1858/5688)	26.8 %	(598/2229)	25.8 %	(1277/4947)	<0.001
Ivabradine	13.8 %	(2108/15293)	25.4 %	(769/3025)	5.2 %	(78/1508)	2.5 %	(141/5688)	4.1 %	(91/2229)	0.6 %	(31/4947)	<0.001
Nitrates or other antianginal drugs††	25.2 %	(3851/15286)	52.1 %	(1375/3025)	32.8 %	(494/1508)	45.2 %	(2571/5688)	21.1 %	(471/2229)	19.4 %	(960/4945)	<0.001
ACE-inhibitors or ARB	77.7 %	(11880/15293)	87.5 %	(2248/3025)	73.5 %	(1109/1508)	69.5 %	(3953/5688)	68.7 %	(1530/2228)	76.9 %	(3805/4947)	<0.001
Diuretics	33.3 %	(5086/15291)	36.9 %	(1116/3025)	30.1 %	(454/1508)	16.4 %	(930/5688)	29.4 %	(656/2230)	27.2 %	(1343/4945)	<0.001
NSAID	4.9 %	(747/15287)	3.9 %	(119/3025)	4.5 %	(67/1508)	1.7 %	(100/5688)	8.6 %	(191/2229)	7.9 %	(390/4945)	<0.001
Amiodarone/Dronedrone	3.3 %	(499/15286)	5.5 %	(165/3025)	1.3 %	(20/1508)	1.6 %	(91/5688)	4.9 %	(109/2229)	1.6 %	(78/4946)	<0.001
Insulin in diabetics	23.9 %	(1027/4291)	13.5 %	(70/517)	27.7 %	(249/899)	16.1 %	(285/1768)	17.4 %	(141/811)	22.8 %	(276/1211)	0.932
Oral diabetic drugs in diabetics	67.4 %	(2895/4291)	66.9 %	(346/517)	65.7 %	(591/899)	71.4 %	(1263/1768)	75.8 %	(615/811)	71.7 %	(868/1211)	0.044

Data are expressed in mean ±SD for continuous variables or % for categorical variables. For categorical data, the number of concerned patients/number of available data are indicated in brackets. For continuous data, the number of available data are indicated in brackets.

†with stenosis > 50% at coronary angiography or having required revascularization in the past.

††other antianginal drugs: molsidomine, nicorandil, ranolazine, trimetazidine.

- Categorical variables were compared across groups by Chi square and continuous variables by analyse of variance.

- ACE: angiotensin converting enzyme; ARB: angiotensin receptor blockers; BP: blood pressure; CABG: coronary artery bypass graft; HF: heart failure; COPD: chronic obstructive coronary disease; LAD: left anterior descending; LVEF: left ventricular ejection fraction; NSAID: nonsteroidal anti-inflammatory drugs; PCI: percutaneous coronary intervention; RCA: right coronary artery; SD: standard deviation.

**Table S5: 5-year event rates (95% CI) in the entire cohort and according to gender**

	<b>Female N=7327</b>	<b>Male N=25365</b>	<b>P value</b>
<b>Primary outcome</b>			
CV death or Non-fatal MI	7.6 (7.0 - 8.3)	8.1 (7.8 - 8.5)	0.257
<b>Secondary outcomes</b>			
CV death	5.4 (4.9 - 6.0)	5.6 (5.3 - 5.9)	0.824
Non-CV death	2.8 (2.4 - 3.3)	3.3 (3.1 - 3.6)	0.046
All-cause death	8.1 (7.4 - 8.8)	8.7 (8.3 - 9.1)	0.168
CV death non-fatal MI or non-fatal stroke	9.5 (8.8 - 10.3)	9.5 (9.1 - 9.9)	0.969
Fatal MI	1.1 (0.9 - 1.4)	1.1 (1.0 - 1.3)	0.880
Fatal stroke	0.8 (0.6 - 1.0)	0.6 (0.5 - 0.7)	0.093
Non-fatal MI	2.5 (2.1 - 2.9)	2.9 (2.7 - 3.1)	0.103
Non-fatal stroke	2.2 (1.9 - 2.6)	1.8 (1.6 - 1.9)	0.035
Hospitalization for heart failure	5.6 (5.1 - 6.2)	5.4 (5.1 - 5.7)	0.294
Coronary angiography	14.9 (14.0 - 15.8)	15.0 (14.6 - 15.5)	0.799
PCI	6.6 (6.1 - 7.3)	7.7 (7.4 - 8.1)	0.006
CABG	1.0 (0.8 - 1.2)	1.7 (1.5 - 1.8)	<.001

Groups according to history of prior MI or angina are non-mutually exclusive.

All risks are described as Kaplan Meier estimates with their 95% CI. *P* values for group comparisons were estimated by Log ranks tests.

CABG: coronary artery bypass graft; CI: confidence interval; CV: cardiovascular; MI: myocardial infarction; PCI: percutaneous coronary intervention.

**Table S6. *P* values for interaction between angina and prior MI, angina and prior MI  $\leq 1$  year, angina and prior MI  $> 1$  year.**

	All CLARIFY		Subset with prior MI $\leq 1$ year		Subset with prior MI $> 1$ year	
	<i>P</i> value Univariate model	<i>P</i> value Multivariable model	<i>P</i> value Univariate model	<i>P</i> value Multivariable model	<i>P</i> value Univariate model	<i>P</i> value Multivariable model
<b>Primary outcome</b>						
CV death or non-fatal MI	0.0001	0.0016	0.0001	0.0026	0.0012	0.0072
<b>Main secondary outcomes</b>						
CV death	0.0002	0.0029	0.0003	0.0037	0.0015	0.0102
CV death, non-fatal MI, or non-fatal stroke	0.0010	0.0108	0.0006	0.0101	0.0064	0.0354

CV: cardiovascular; MI: myocardial infarction.

*P* values were assessed using COX model.

In multivariable model, the variables used for adjustment were age, smoking status, history of hypertension and diabetes, history of percutaneous coronary intervention, of coronary artery bypass graft of heart failure, of asthma/chronic obstructive pulmonary disease, of peripheral artery disease, of cerebrovascular disease, or atrial fibrillation/flutter and of stroke, blood pressure  $< 140/90$  mmHg at baseline, aspirin, statins, geographical zones.

**Table S7. 5-year outcomes according to geographical areas**

	<b>Western/Central Europe N=15301</b>	<b>Eastern Europe N=3025</b>	<b>Middle East N=1511</b>	<b>Asia N=5688</b>	<b>Central/South America N=2230</b>	<b>Commonwealth countries N=4948</b>	
	5-year event rates % (95% CI)	5-year event rates % (95% CI)	5-year event rates % (95% CI)	5-year event rates % (95% CI)	5-year event rates % (95% CI)	5-year event rates % (95% CI)	<i>P</i> value
Primary outcome							
CV death, or Non-fatal MI	8.0 (7.5 - 8.5)	8.7 (7.7 - 9.8)	7.7 (6.4 - 9.2)	5.6 (5.0 - 6.2)	10.6 (9.2 - 12.1)	9.7 (8.8 - 10.6)	<0.001
Secondary outcomes							
CV death	5.6 (5.3 - 6.1)	5.2 (4.4 - 6.1)	5.7 (4.6 - 7.1)	3.8 (3.3 - 4.4)	8.5 (7.3 - 9.9)	6.2 (5.6 - 7.0)	<0.001
Non-CV death	3.5 (3.2 - 3.9)	2.6 (2.1 - 3.2)	2.8 (2.1 - 3.9)	2.1 (1.8 - 2.6)	3.2 (2.4 - 4.1)	4.0 (3.5 - 4.7)	<0.001
All-cause death	9.0 (8.5 - 9.5)	7.6 (6.7 - 8.6)	8.4 (7.0 - 10.0)	5.8 (5.2 - 6.5)	11.4 (10.0 - 13.0)	10.0 (9.2 - 11.0)	<0.001
CV death, Non-fatal MI, or Non-fatal stroke	9.4 (8.9 - 10.0)	10.6 (9.5 - 11.8)	8.6 (7.2 - 10.2)	7.3 (6.6 - 8.0)	11.9 (10.5 - 13.5)	11.1 (10.2 - 12.1)	<0.001
Fatal MI	0.7 (0.6 - 0.9)	1.0 (0.7 - 1.5)	1.2 (0.7 - 1.9)	0.9 (0.7 - 1.2)	3.3 (2.6 - 4.3)	1.6 (1.3 - 2.1)	<0.001
Fatal stroke	0.6 (0.5 - 0.8)	1.0 (0.7 - 1.4)	0.3 (0.1 - 0.9)	0.6 (0.4 - 0.8)	0.7 (0.4 - 1.2)	0.5 (0.3 - 0.7)	0.052
Non-fatal MI	2.7 (2.4 - 3.0)	3.8 (3.1 - 4.5)	2.3 (1.6 - 3.3)	1.9 (1.5 - 2.3)	2.4 (1.8 - 3.2)	3.9 (3.4 - 4.6)	<0.001
Non-fatal stroke	1.8 (1.5 - 2.0)	2.4 (1.9 - 3.0)	1.1 (0.6 - 1.9)	2.0 (1.6 - 2.4)	1.9 (1.4 - 2.7)	1.9 (1.5 - 2.3)	0.063
Hospitalisation for heart failure	4.7 (4.4 - 5.1)	16.9 (15.6 - 18.3)	4.4 (3.4 - 5.7)	3.1 (2.7 - 3.6)	4.5 (3.6 - 5.6)	3.3 (2.8 - 3.9)	<0.001
Coronary angiography	17.2 (16.6 - 17.9)	14.9 (13.6 - 16.3)	12.7 (11.0 - 14.6)	13.0 (12.1 - 14.0)	9.5 (8.2 - 10.9)	13.7 (12.7 - 14.8)	<0.001
PCI	8.8 (8.3 - 9.3)	6.4 (5.6 - 7.4)	7.5 (6.2 - 9.1)	6.8 (6.2 - 7.5)	4.8 (3.9 - 6.0)	5.9 (5.2 - 6.7)	<0.001
CABG	1.3 (1.1 - 1.5)	2.5 (2.0 - 3.1)	1.6 (1.0 - 9.1)	0.8 (0.6 - 1.1)	1.4 (0.9 - 2.0)	2.4 (2.0 - 2.9)	<0.001

All risks are described as Kaplan Meier estimates with their 95%CI.

*P* values for group comparisons were estimated by Log rank tests.

CABG: coronary artery bypass graft; CI: confidence interval; CV: cardiovascular; PCI: percutaneous coronary intervention; MI: myocardial infarction.

**Table S8. Univariate and multivariable predictors of CV death or non-fatal MI**

Categories	Hazard ratios (95% CI) Univariate models	<i>P</i> value Univariate models	Hazard ratios (95% CI) Multivariable models	<i>P</i> value Multivariable models
<b>CV risk factors</b>				
Age per 1-year increase	1.04 (1.04 - 1.05)	<0.001	1.04 (1.03 ; 1.04)	<0.001
Gender (reference Male)	0.94 (0.85 - 1.04)	0.257	0.95 (0.85 ; 1.06)	0.334
History of hypertension (reference: No)	1.22 (1.11 - 1.34)	<0.001	0.98 (0.88 ; 1.08)	0.621
Diabetes (reference: No)	1.50 (1.38 - 1.63)	<0.001	1.40 (1.28 ; 1.53)	<0.001
Smoking status (reference: Never)				
- Current	1.36 (1.19 - 1.54)	<0.001	1.74 (1.51 ; 1.99)	<0.001
- Former	1.24 (1.14 - 1.36)		1.29 (1.17 ; 1.42)	
<b>Medical history and comorbidities</b>				
History of PCI (reference: No)	0.71 (0.65 - 0.77)	<0.001	0.85 (0.78 ; 0.93)	<0.001
History of CABG (reference: No)	1.28 (1.16 - 1.40)	<0.001	1.02 (0.92 ; 1.12)	0.709
History of MI (reference: No)	1.45 (1.33 - 1.59)	<0.001	1.50 (1.37 ; 1.65)	<0.001
History of heart failure (reference: No)	3.24 (2.86 - 3.67)	<0.001	2.13 (1.87 ; 2.42)	<0.001
Asthma/COPD (reference: No)	1.70 (1.49 - 1.93)	<0.001	1.19 (1.04 ; 1.36)	0.009
Peripheral artery disease (reference: No)	1.92 (1.73 - 2.14)	<0.001	1.29 (1.15 ; 1.45)	<0.001
Cerebrovascular disease (reference: No)	1.70 (1.54 - 1.89)	<0.001	1.05 (0.91 ; 1.20)	0.536
Atrial fibrillation/flutter (reference: No)	2.45 (2.18 - 2.75)	<0.001	1.61 (1.42 ; 1.82)	<0.001
Prior stroke (reference: No)	2.16 (1.85 - 2.51)	<0.001	1.45 (1.20 ; 1.76)	<0.001
<b>Clinical examination</b>				
Angina at baseline (reference: No)	1.35 (1.24 - 1.48)	<0.001	1.30 (1.18 ; 1.45)	<0.001
BP < 140/90 mmHg at baseline (reference: No)	0.85 (0.78 - 0.92)	<0.001	0.90 (0.83 ; 0.99)	0.023

<b>Geographical areas</b>				
(reference: Western/Central Europe)				
- Eastern Europe	1.12 (0.97 - 1.28)	<0.001	1.09 (0.93 ; 1.27)	<0.001
- Middle East	0.97 (0.80 - 1.19)		1.21 (0.99 ; 1.49)	
- Asia	0.70 (0.61 - 0.80)		0.89 (0.78 ; 1.02)	
- Central/South America	1.37 (1.18 - 1.60)		1.61 (1.38 ; 1.88)	
- Commonwealth countries	1.23 (1.10 - 1.38)		1.16 (1.04 ; 1.31)	

BP: blood pressure; CV: cardiovascular; CABG: coronary artery bypass graft; CI: confidence interval; COPD: chronic obstructive pulmonary disease; PCI: percutaneous coronary intervention; MI: myocardial infarction; Univariate analysis and multivariable analysis were performed from Cox proportional hazard models

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