Chronic coronary syndromes:
Final 5-year results from the CLARIFY registry

E. Sorbets*, K.M. Fox, Y. Elbez, N. Danchin, P. Dorian, R. Ferrari, I. Ford, N. Greenlaw, P.R. Kalra, Z. Parma, S. Shalnova, J.C. Tardif, M. Tendera, J.L. Zamorano, E. Vidal-Petiot, and P.G. Steg, for the CLARIFY investigators

Assistance Publique - Hôpitaux de Paris, France

DISCLOSURES

September 3rd, 2019

E. Sorbets reports fees and non-financial support with Astra-Zeneca, Bayer, BMS, MSD, Novartis, Servier

CLARIFY was sponsored and supported by **Servier**

The database was housed at the **Robertson Centre for Biostatistics** in UK
All analyses were performed by **academic statisticians**

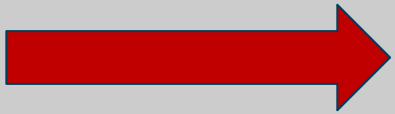
Stable coronary artery disease: a changing entity

Previously

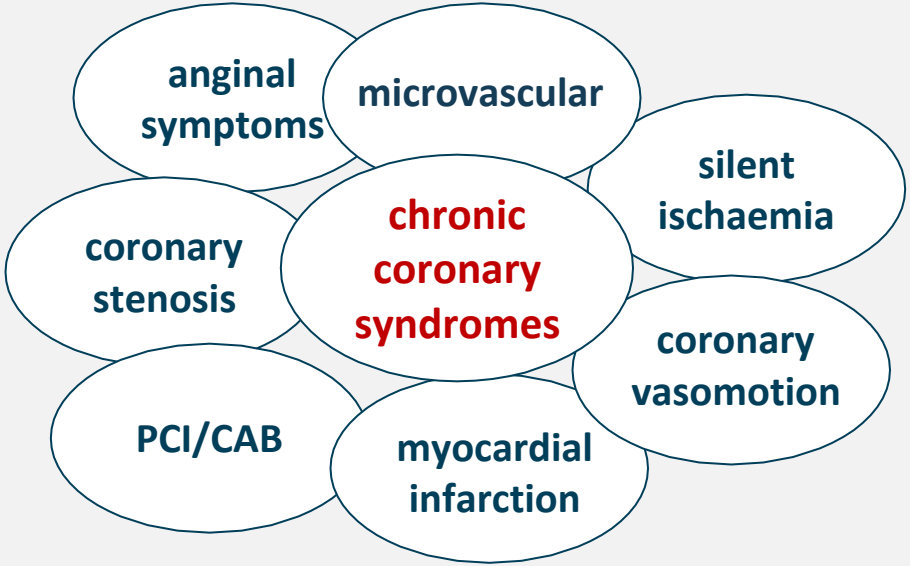
stable angina

Improved management

Secondary prevention
New therapies
Revascularisation



Nowadays



CLARIFY a prospective observational Longitudinal Registry of patients with stable coronary artery disease

32,703 patients
45 countries

2898 physicians
to consecutively enrol 10-15 patients

Enrolment: 2009 - 2010
Database locked: 2016

Yearly visit
Median follow-up: 5.0 years

Medical care at the discretion of each physician

Inclusion criteria for chronic coronary syndromes, non-mutually exclusive:

- **prior myocardial infarction >3 months**
- **prior revascularisation >3 months**
- **proven symptomatic myocardial ischaemia**
- **angiographic coronary stenosis >50%**

Exclusion criteria:

- conditions interfering with life expectancy
- advanced heart failure

E. Sorbets et al, Clinical Cardiology 2017;40:797

Aims:

1. to describe demographics, clinical characteristics, and management of patients with chronic coronary syndromes

2. to assess the rates and determinants of outcomes in patients with chronic coronary syndromes

Baseline characteristics

Demographics	**Age, years ±SD**	**64.2 ± 10.5**
	Gender, male	**77.6 %**
CV risk factors	**Treated hypertension**	**71.0 %**
	Diabetes	**29.1 %**
	Current smoking	**12.5 %**
	Dyslipidaemia	74.9 %
	Family history of premature CAD	28.5 %
Past medical history	**Prior MI**	**59.9 %**
	Prior PCI	**58.6 %**
	Prior CABG	**23.6 %**
	Peripheral artery disease	9.9 %
	Atrial fibrillation/flutter	7.1 %
	Hospitalisation for heart failure	4.7 %
	Asthma/COPD	7.4 %

E. Sorbets et al, Clinical Cardiology 2017;40:797

Baseline characteristics

Clinical examination	Systolic blood pressure (mmHg), mean ±SD	131.0 ± 16.7
	Diastolic blood pressure (mmHg), mean ±SD	77.3 ± 10.0
	Resting heart rate (bpm), mean ±SD	68.2 ± 10.6
Anginal symptoms	**Current angina**	**22.1 %**
	CCS 1	6.3 %
	CCS 2	11.7 %
	CCS 3	3.8 %
	CCS 4	0.2 %
Heart failure symptoms	**Current heart failure**	**15.1 %**
	NHYA 2	12.6 %
	NHYA 3	2.5 %
LVEF*	**Percentage**, mean ±SD	**56.1** ± 11.1

* n= 22,519, measured by TTE, MRI or scintigraphy

E. Sorbets et al, Clinical Cardiology 2017;40:797

Baseline medication: a high rate of evidence-based therapies

Antiplatelets/Antithrombotics	**Any antiplatelet**	**95.2 %**
	Aspirin	87.8 %
	Thienopyridines	27.2 %
	Dual antiplatelet	28.0 %
	Oral anticoagulant	8.2 %
	Antiplatelet + oral anticoagulant	5.2 %
Lipid lowering therapies	Lipid lowering therapy	92.3 %
	Statins	**82.9 %**
Antianginal/Antihypertensive therapies	**β-blockers**	**75.3 %**
	ACEi or ARBs	**76.3 %**
	Calcium antagonists	27.3 %
	Long-acting nitrates	21.9 %
	Ivabradine	9.8 %
	Diuretics	29.3 %

E. Sorbets et al, Clinical Cardiology 2017;40:797

Baseline levels of BP and LDL-cholesterol

Conventional recommended targets at enrolment	
BP <140/90mmHg[1]	64.8 %
LDL-cholesterol <100mg/dl[2]	60.9 %
BP <140/90mmHg and LDL-cholesterol <100mg/dl	42.1 %
Most stringent and recent recommended targets	
BP <130/80mmHg[3,4]	29.0 %
LDL-cholesterol <70mg/dl[4]	20.9 %
BP <130/80mmHg and LDL-cholesterol <70mg/dl	7.4 %

1- 2007 ESC Guidelines on cardiovascular disease prevention, Graham I. et al. *Eur Heart J* 2007;39:3021
2- 2003 ESC Guidelines on cardiovascular disease prevention, De Backer G. et al. *Eur Heart J* 2003;24:1601
3- 2018 ESC Guidelines on the management of hypertension, *Eur Heart J* 2018;39:3021
4- 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. Knuuti J. et al, *Eur Heart J 2019* doi:10.1093/eurheartj/ehz425

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Primary and secondary outcomes

	5-year Kaplan Meier estimates, % (95% CI)	Incident event rates per 100 patient-years
Primary outcome		
CV death or non-fatal MI	**8.0 (7.7 - 8.3)**	**1.7 (1.6 - 1.7)**
Secondary outcomes		
CV death	**5.5 (5.3 - 5.8)**	**1.1 (1.1 - 1.2)**
All-cause death	**8.5 (8.2 - 8.9)**	**1.8 (1.7 - 1.8)**
CV death, non-fatal MI or non-fatal stroke	9.5 (9.2 - 9.9)	2.0 (1.9 - 2.1)
Non-fatal MI	2.8 (2.6 - 3.0)	0.6 (0.5 - 0.6)
Non-fatal stroke	1.9 (1.7 - 2.0)	0.4 (0.3 - 0.4)
Hospitalisation for heart failure	5.4 (5.2 - 5.7)	1.2 (1.1 - 1.2)
PCI	7.5 (7.2 - 7.8)	1.6 (1.5 - 1.6)
CABG	1.5 (1.4 - 1.7)	0.3 (0.3 - 0.3)

Baseline characteristics according to gender

		Male (25,365)	Female (7327)	P value
Risk factors	Age, years ± SD	63.4 ± 10.5	66.5 ± 9.9	< 0.001
	Treated hypertension	68.9 %	78.5 %	< 0.001
	Diabetes	28.0 %	32.7 %	< 0.001
	Current smoking	14.1 %	7.2 %	< 0.001
Medical history	Prior MI	62.1 %	51.1 %	< 0.001
	Prior PCI	59.5 %	54.8 %	< 0.001
	Prior CABG	25.2 %	17.9 %	< 0.001
Examination	Anginal symptoms	20.3 %	28.1 %	< 0.001
	Heart Failure symptoms	14.3 %	17.9 %	< 0.001
	LVEF*, percentage ± SD	55.6 ± 11.1	57.9 ± 10.7	< 0.001
Medication	Any antiplatelet	95.2 %	95.0 %	0.097
	Dual antiplatelet	28.4 %	26.3 %	< 0.001
	Statins	83.6 %	80.4 %	< 0.001
	Betablockers	75.3 %	75.1 %	0.702
	ACEi or ARBs	76.2 %	76.6 %	0.466

* n= 22,514, measured by TTE, MRI or scintigraphy

adapted from PG Steg et a, European Heart Journal 2012;33,2831

Outcomes according to gender

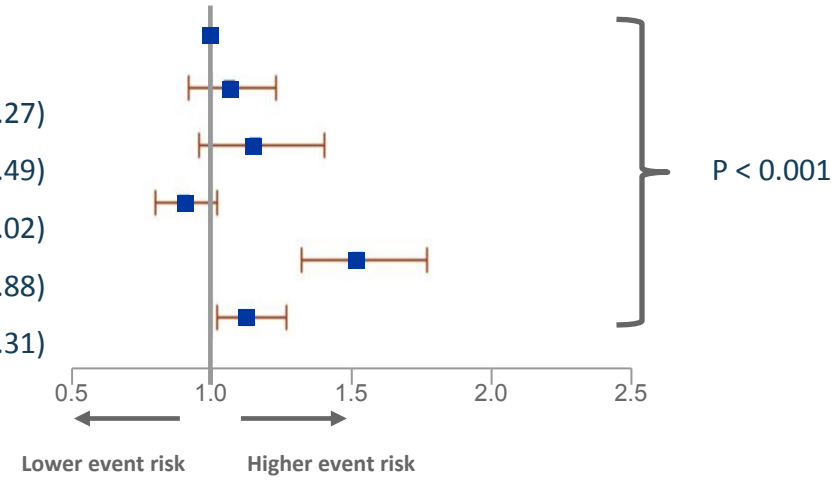
5-year Kaplan Meier estimated event rates	Female % (95% CI)	Male % (95% CI)	P value Log ranks tests
Primary outcome			
CV death or Non-fatal MI	**7.6 (7.0-8.3)**	**8.1 (7.8-8.5)**	**0.257**
Secondary outcomes			
CV death	5.4 (4.9-6.0)	5.6 (5.3-5.9)	0.824
All-cause death	8.1 (7.4-8.8)	8.7 (8.3-9.1)	0.168
CV death, Non-fatal MI or Non-fatal stroke	9.5 (8.8-10.3)	9.5 (9.1-9. 9)	0.969
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
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)**	**< 0.001**

	Adjusted* hazard ratio	CV death or non-fatal MI	P value
Gender, reference: male	**0.95 (0.85-1.06)**	0.5 1.0 1.5 Lower event risk Higher event risk	**0.334**

* Cox proportional hazards model including: age, gender, diabetes, smoking status, history of hypertension, MI, PCI, CABG, hospitalisation for heart failure, asthma, COPD, atrial fibrillation/flutter, prior stroke, cerebrovascular disease, peripheral artery disease, current angina, blood pressure <140/90 mmHg, geographical zones

Primary outcome across geographical zones

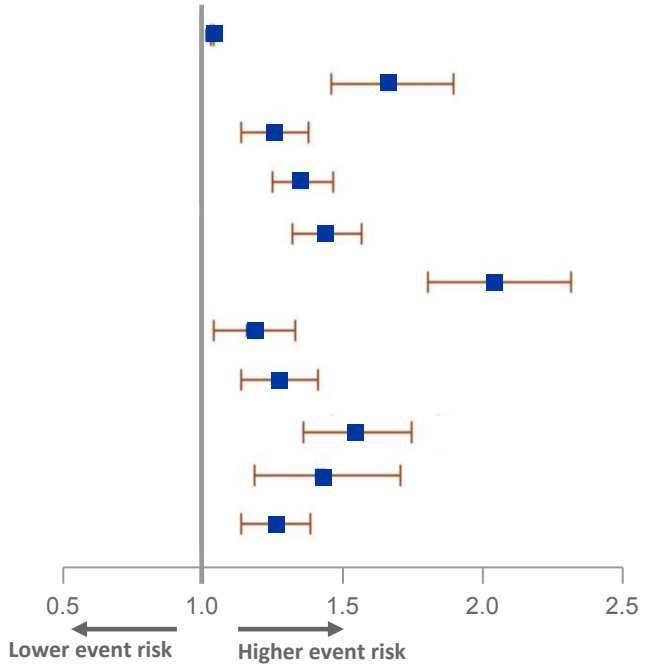
	Adjusted* hazard ratios
Western/Central Europe (reference)	
Eastern Europe	1.09 (0.93 - 1.27)
Middle East	1.21 (0.99 - 1.49)
Asia	0.89 (0.78 - 1.02)
Central/South America	1.61 (1.38 - 1.88)
Australia/Canada/South Africa/United Kingdom	1.16 (1.04 - 1.31)



* Multivariable analysis (Cox proportional hazards model) including: age, gender, diabetes, smoking status, history of hypertension, MI, PCI, CABG, hospitalisation for heart failure, asthma/COPD, atrial fibrillation/flutter, prior stroke, cerebrovascular disease, peripheral artery disease, current angina, blood pressure (BP) <140/90 mm Hg, geographical zones

Positive predictors of the primary outcome

	Adjusted* hazard ratios	P value
Age, per year increase	1.04 (1.03 - 1.04)	< 0.001
Current smoking, reference: never	1.74 (1.51 - 1.99)	< 0.001
Former smoking, reference: never	1.29 (1.17 - 1.42)	< 0.001
Diabetes, reference: no	1.40 (1.28 - 1.53)	< 0.001
History of MI, reference: no	1.50 (1.37 - 1.65)	< 0.001
History of hospitalisation for HF, reference: no	2.13 (1.87 - 2.42)	< 0.001
Asthma/COPD, reference: no	1.19 (1.04 - 1.36)	0.009
Peripheral artery disease, reference: no	1.29 (1.15 - 1.45)	< 0.001
Atrial fibrillation/flutter, reference: no	1.61 (1.42 - 1.82)	< 0.001
History of stroke, reference: no	1.45 (1.20 - 1.76)	< 0.001
Angina at baseline, reference: no	1.30 (1.18 - 1.45)	< 0.001



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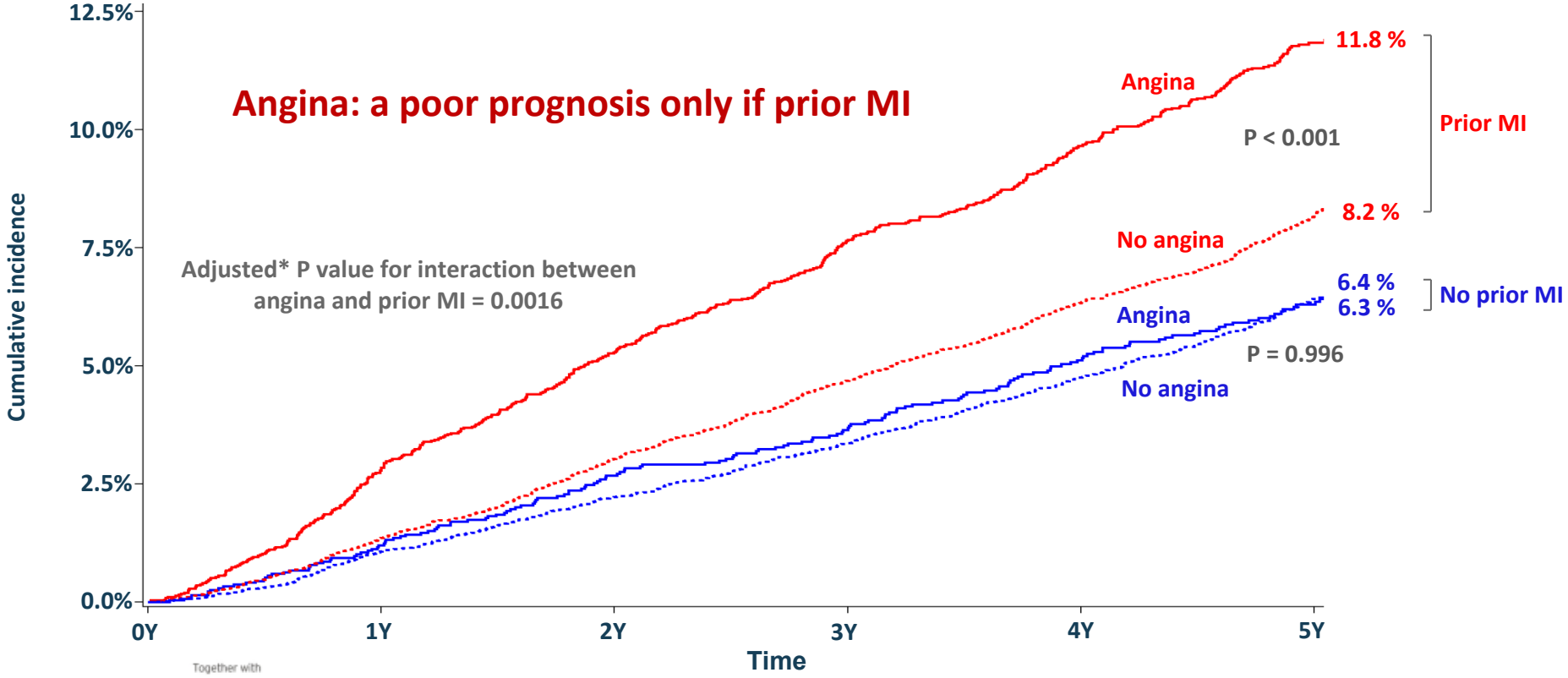
According to angina and prior MI
5-year incidence of CV death or non-fatal MI



* Multivariable analysis (Cox proportional hazards model) including: age, gender, diabetes, smoking status, history of hypertension, MI, PCI, CABG, hospitalisation for heart failure, asthma/COPD, atrial fibrillation/flutter, prior stroke, cerebrovascular disease, peripheral artery disease, current angina, blood pressure <140/90 mm Hg, geographical zones

CONCLUSIONS

In CLARIFY a global cohort of 32,703 patients with chronic coronary syndromes followed-up for 5 years, receiving guideline-recommended therapies:

- Outcome of CV death or non-fatal MI was 1.7 per 100 patient-years
- This outcome rate was similar in males and females, despite differences in baseline characteristics

- Angina was prognostic only in patients with prior MI
- Angina and prior MI were a higher risk subgroup that may warrant more intensive management

Is there more that can be done?

- Can we do even better if we achieve guidelines-recommended targets?
- Consider more intensive management in patients with both angina and prior MI?

European Heart Journal

ESC European Society of Cardiology

European Heart Journal (2019) **00**, 1–10
doi:10.1093/eurheartj/ehz660

FASTTRACK CLINICAL RESEARCH
Coronary artery disease

Long-term outcomes of chronic coronary syndrome worldwide: insights from the international CLARIFY registry

Emmanuel Sorbets [1,2,3,4,5], Kim M. Fox[3,4]*, Yedid Elbez[5], Nicolas Danchin[6,7], Paul Dorian[8], Roberto Ferrari[9], Ian Ford [10], Nicola Greenlaw[10], Paul R. Kalra[11], Zofia Parma[12], Svetlana Shalnova[13], Jean-Claude Tardif[14], Michal Tendera [12], José Luis Zamorano[15], Emmanuelle Vidal-Petiot [6,16], and Philippe Gabriel Steg [3,4,5,6]; on behalf of the CLARIFY investigators

Thanks to the 2898 investigators and colleagues who played a full role in the CLARIFY registry for 5 years!