Une ordonnance sans β-bloquants ni IEC: est ce possible ?

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Ph Gabriel Steg - Liens d'intérêt

- **Bourses de recherche:** Bayer, Merck, Sanofi, Servier

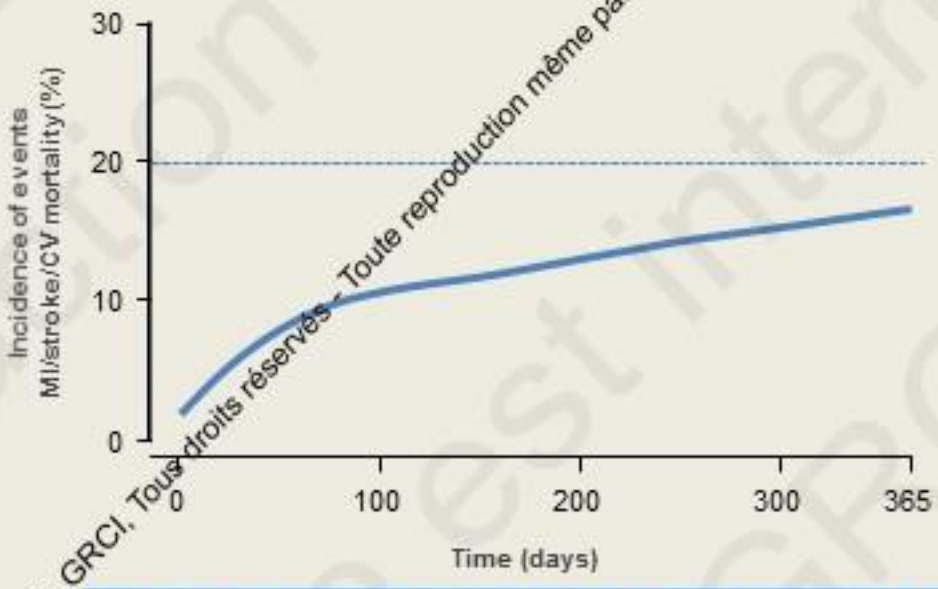
- **Honoraires (orateur ou consultant):** Amarin, Amgen, AstraZeneca, Bayer, Boehringer-Ingelheim, Bristol-Myers-Squibb, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Sanofi, Servier

Une ordonnance sans β-bloquants ni IEC: est ce possible ?

- **Le pronostic du post infarctus a été transformé**

CV event rates are high in the 1st year post-MI...

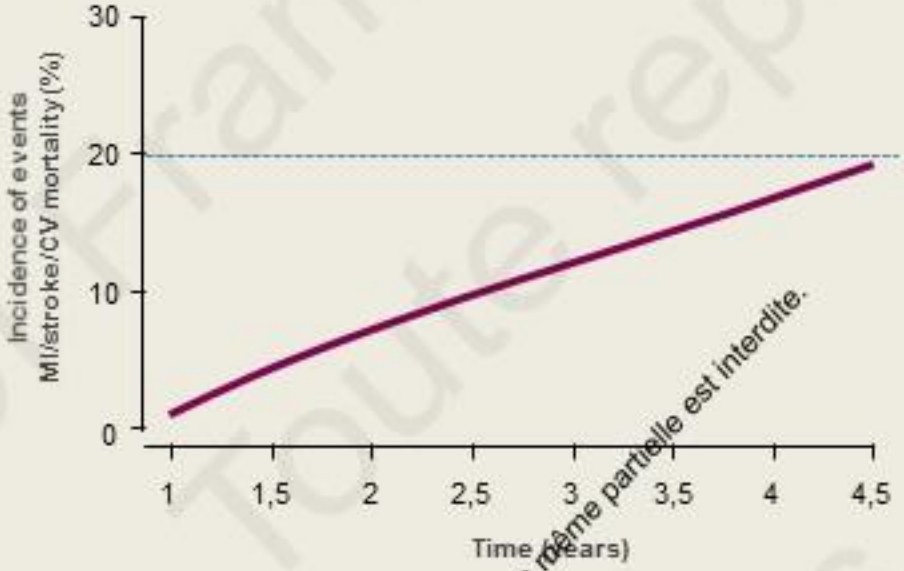
CV events during the first 365 days



97 254 patients admitted with 1st MI between July 2006 and June 2011

...and remain high in the following 3.5 years

CV events between 1 and 4.5 years

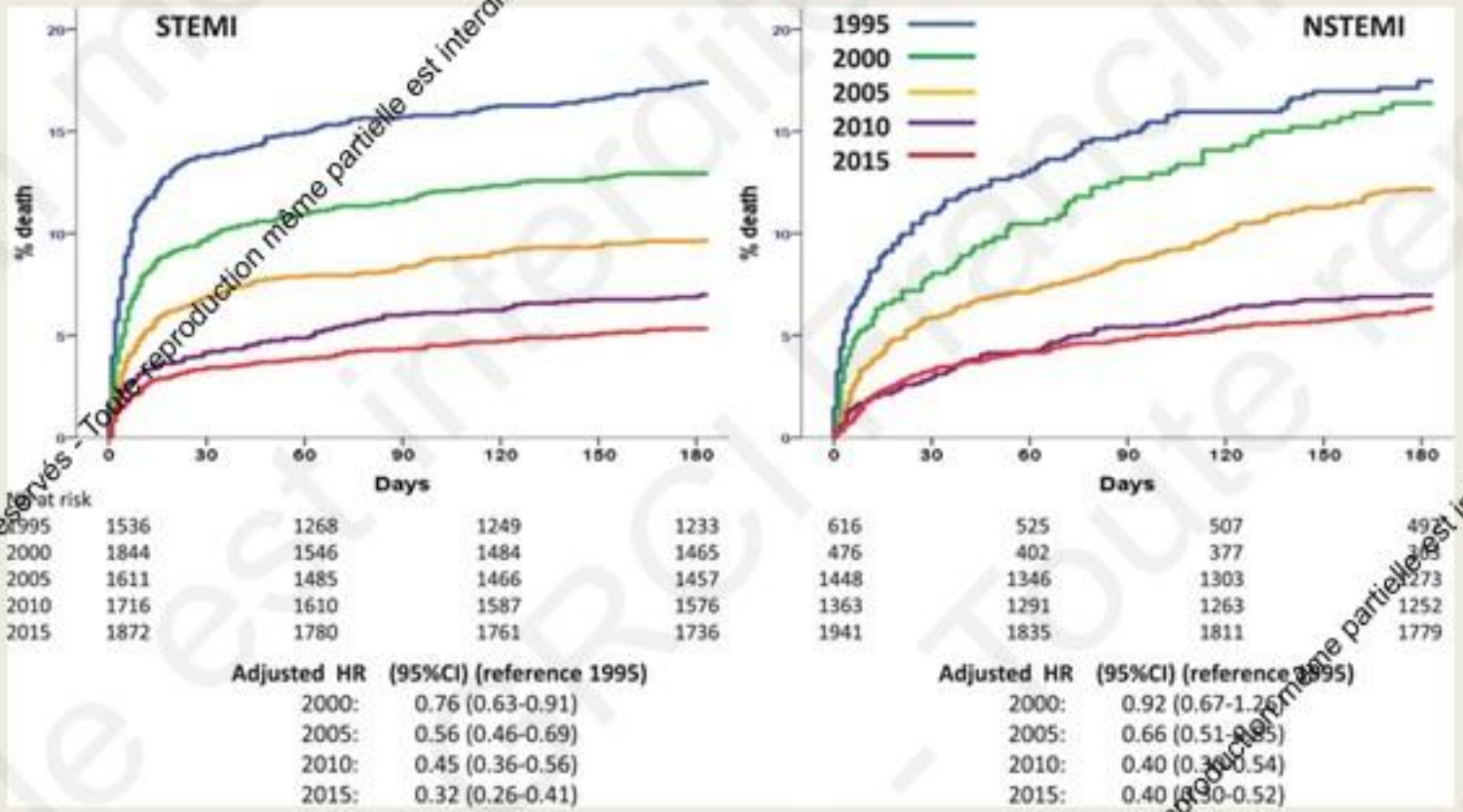


76 687 patients surviving during 365 days after MI with recurrent MI or stroke

Jernberg T, et al. ***Eur Heart J*** 2015;**36**:1163–1170

CV, cardiovascular; MI, myocardial infarction

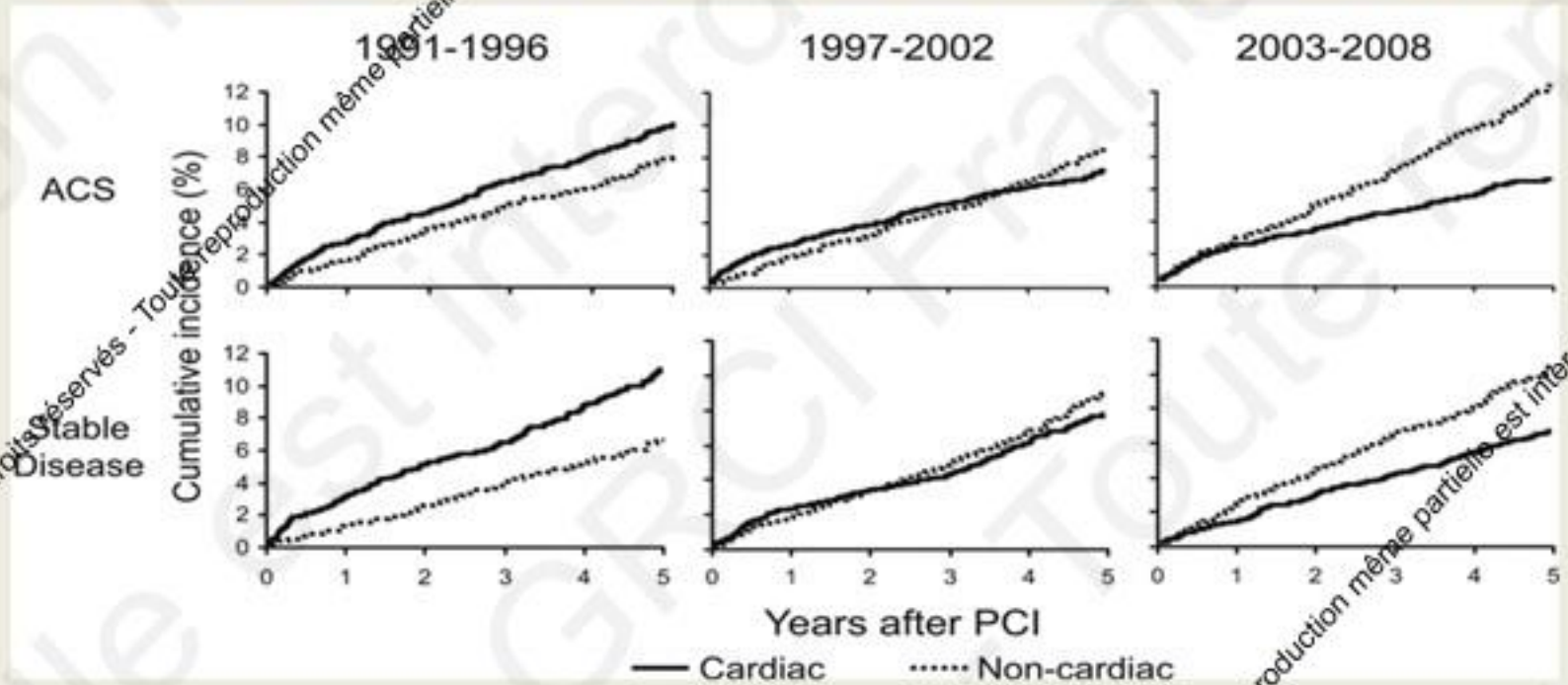
Continued improvement in mortality at 6-month after MI in France



Puymirat et al. ***Circulation*** 2017

The most frequent causes of death in ACS survivors are now noncardiac

Temporal trends in incidence of cause-specific mortality after PCI for ACS



Spoon D B et al. ***Circulation***. 2014;129:1286-1294

The Fab Four

Antiplatelet agents

Beta-blockers

ACE-I/ARBs

Statins

Une ordonnance sans β-bloquants ni IEC: est ce possible ?

- Le pronostic du post infarctus a été transformé
- **Les β-bloquants en post infarctus**

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Les β-bloquants dans le post infarctus

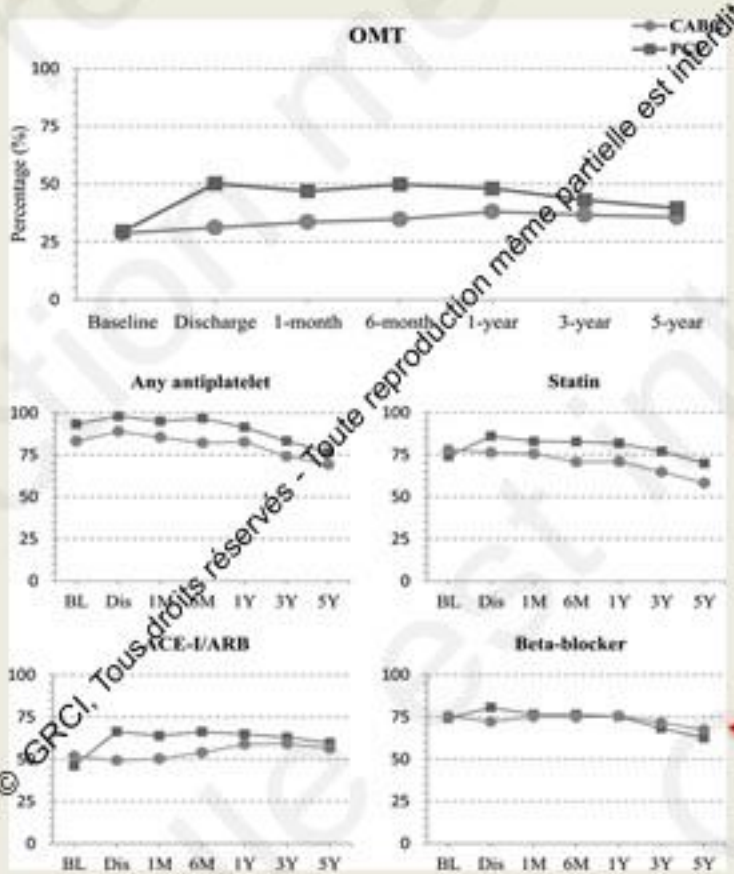
Bénéfices

- Réduisent les symptômes angineux
- Améliorent le pronostic des pts avec insuffisance cardiaque ou dysfonction VG
- Réduisent les troubles du rythme ventriculaires
- Améliorent le pronostic du post infarctus sans dysfonction VG ni insuffisance cardiaque ?

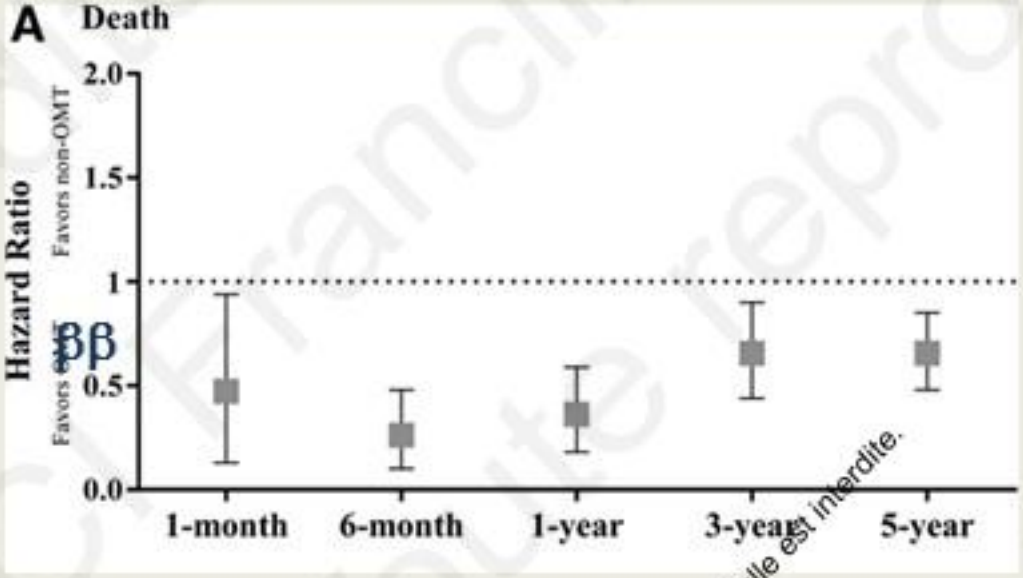
Inconvénients

- Fatigue
- Bradycardie/troubles conductifs
- Hypotension
- Raynaud
- Claudication
- Exacerbation asthme/BPCO
- Dépression/Troubles du sommeil
- Dysfonction érectile
- Troubles métaboliques

Use of cardiac medication in the PCI and CABG arms of the SYNTAX trial



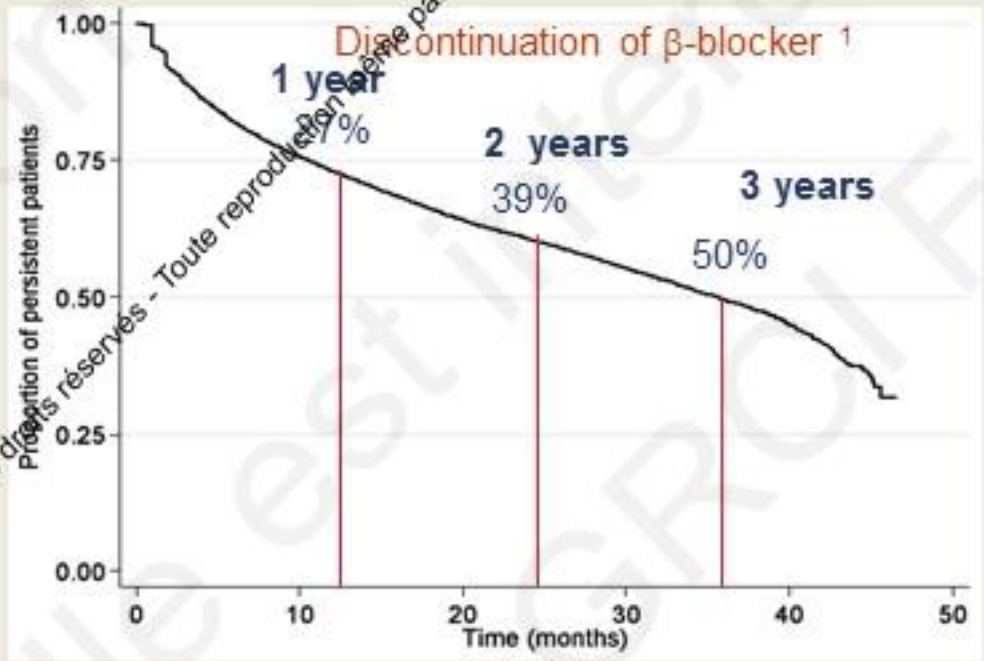
Mortality as a function of adherence to Optimal Medical Therapy (OMT)



Iqbal et al. **Circulation**. 2015;131:1269-1277

Persistence with β-blockers over time in CAD patients in primary care

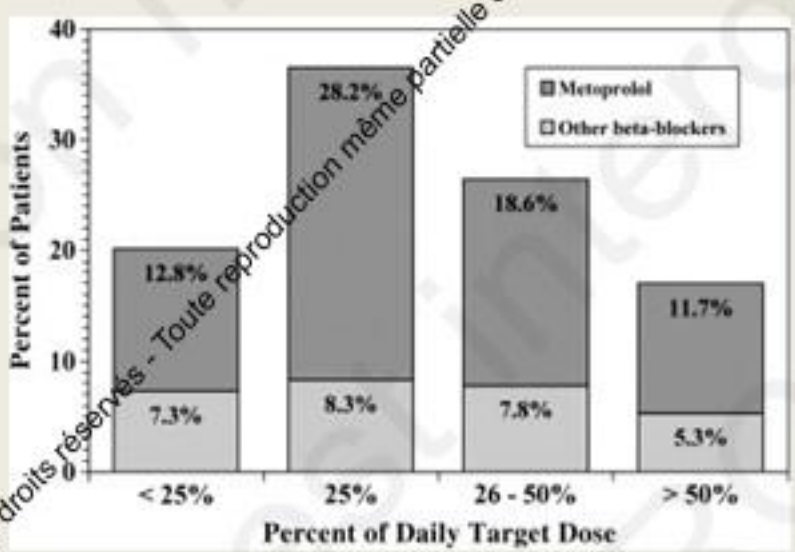
430 UK primary care practices, 12 493 patients with first ever diagnosis of CAD (angina, or previous MI) or HF and first prescription of a β-blocker initiated



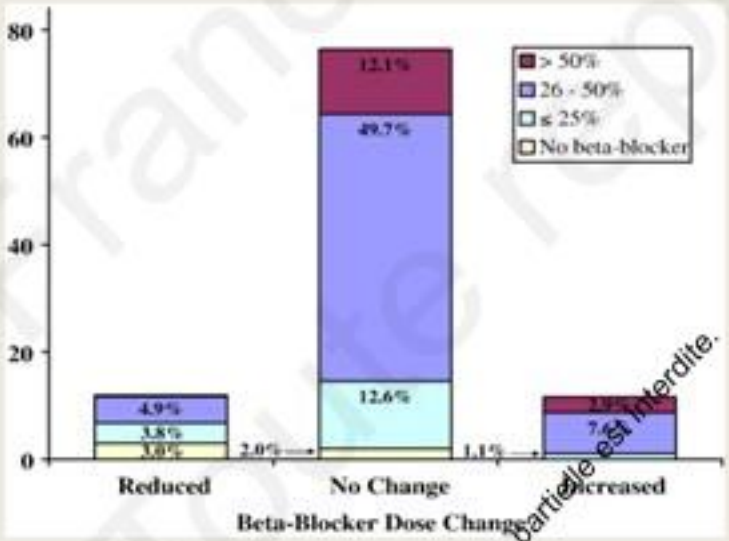
- The majority of CAD patients treated in UK primary care receive suboptimal doses of β-blockers (58.8% with doses <50% of recommended)[2]
- Discontinuation of β-blocker therapy was most associated with bronchospasm (13.9%), sleep disturbance (13.2%), and fatigue (11.5%)[3]

1- Setakis E. Euro Heart J. 2009; 30 (Abstr Suppl), 303; 2- Setakis E. Euro Heart J. 2009; 30 (Abstr Suppl), 511;
3- Setakis E. Euro Heart J. 2009; 30 (Abstr Suppl), 974.

Underdosing of Beta-Blockers Following MI



Percent of Daily Target Dose



Beta-Blocker Dose Change

Goldberger JJ et al. ***Am Heart*** J 2010;160:435-42

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- **Les β-bloquants en post infarctus**
  - **Les essais randomisés**

Méta-analyse de Freemantle

83 essais avec des **patients en post-IDM** sous bêta bloquant
51 essais évaluant leur effet à court terme (n=29 260)
et 32 essais évaluant leur effet à plus long terme (n=24 974)

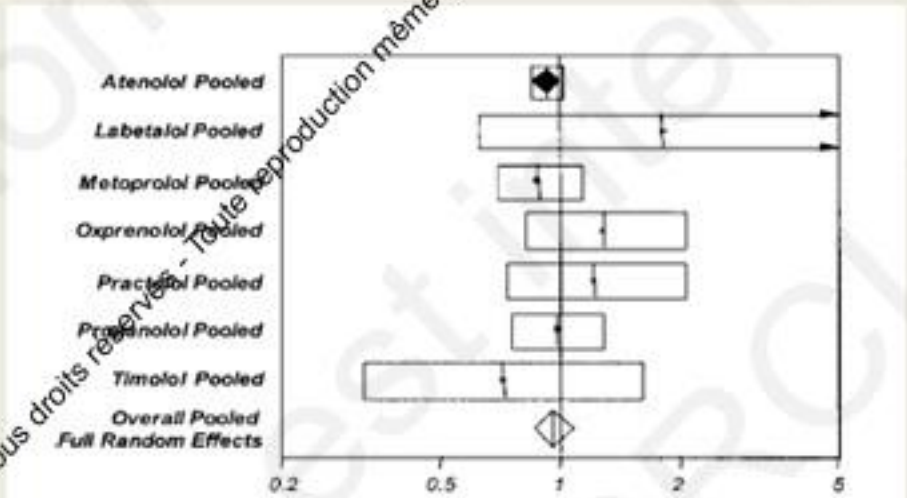


Fig. 1. Short-term effect of β-blockers on all-cause mortality: odds ratios and 95% confidence intervals.

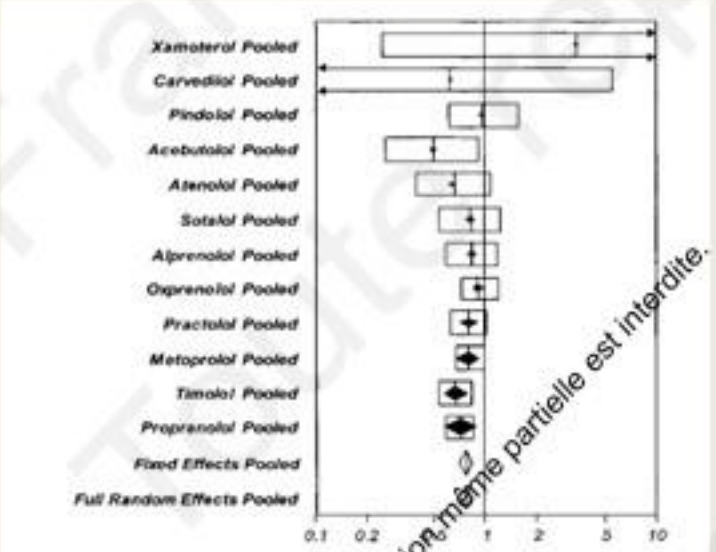
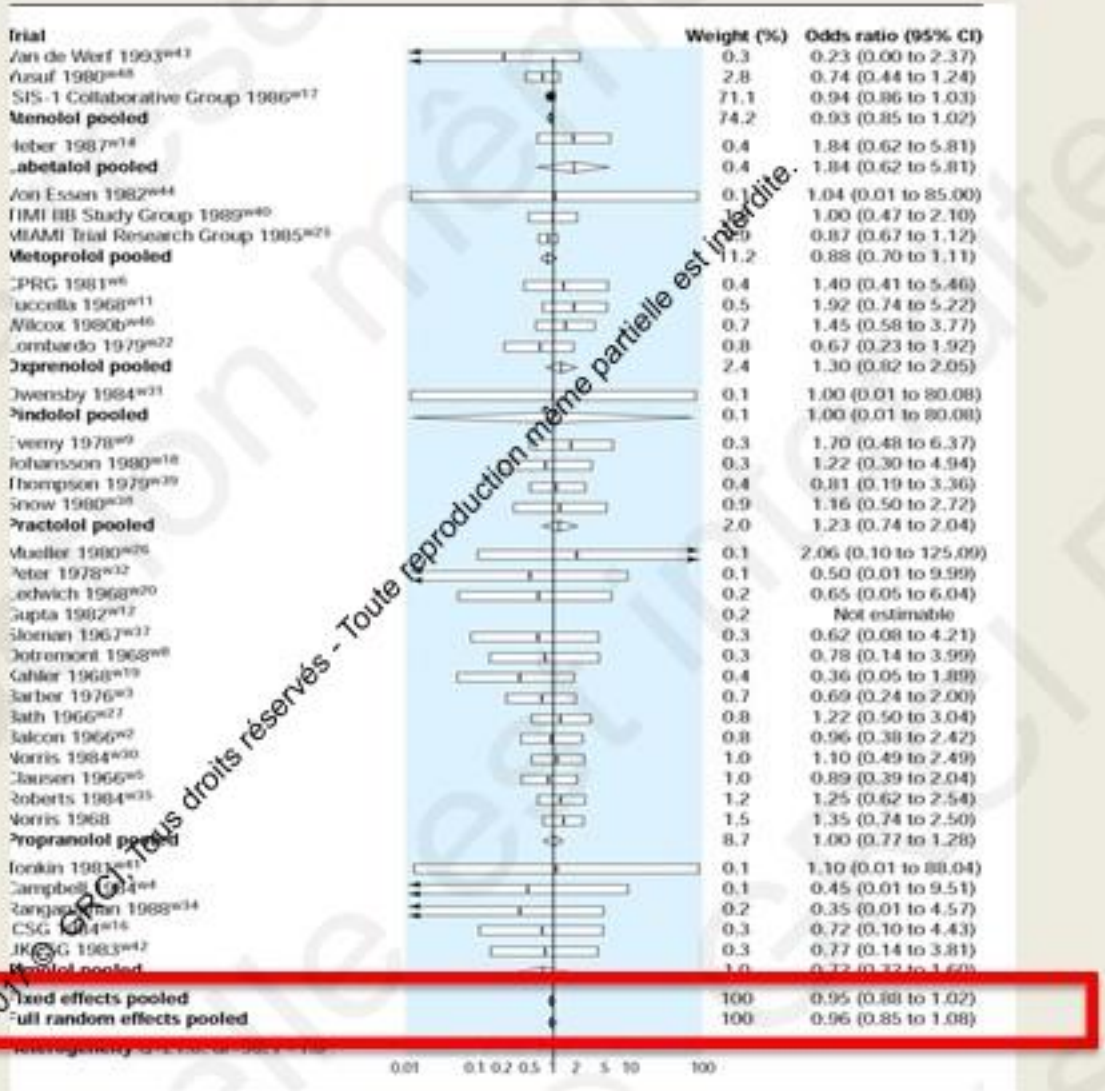


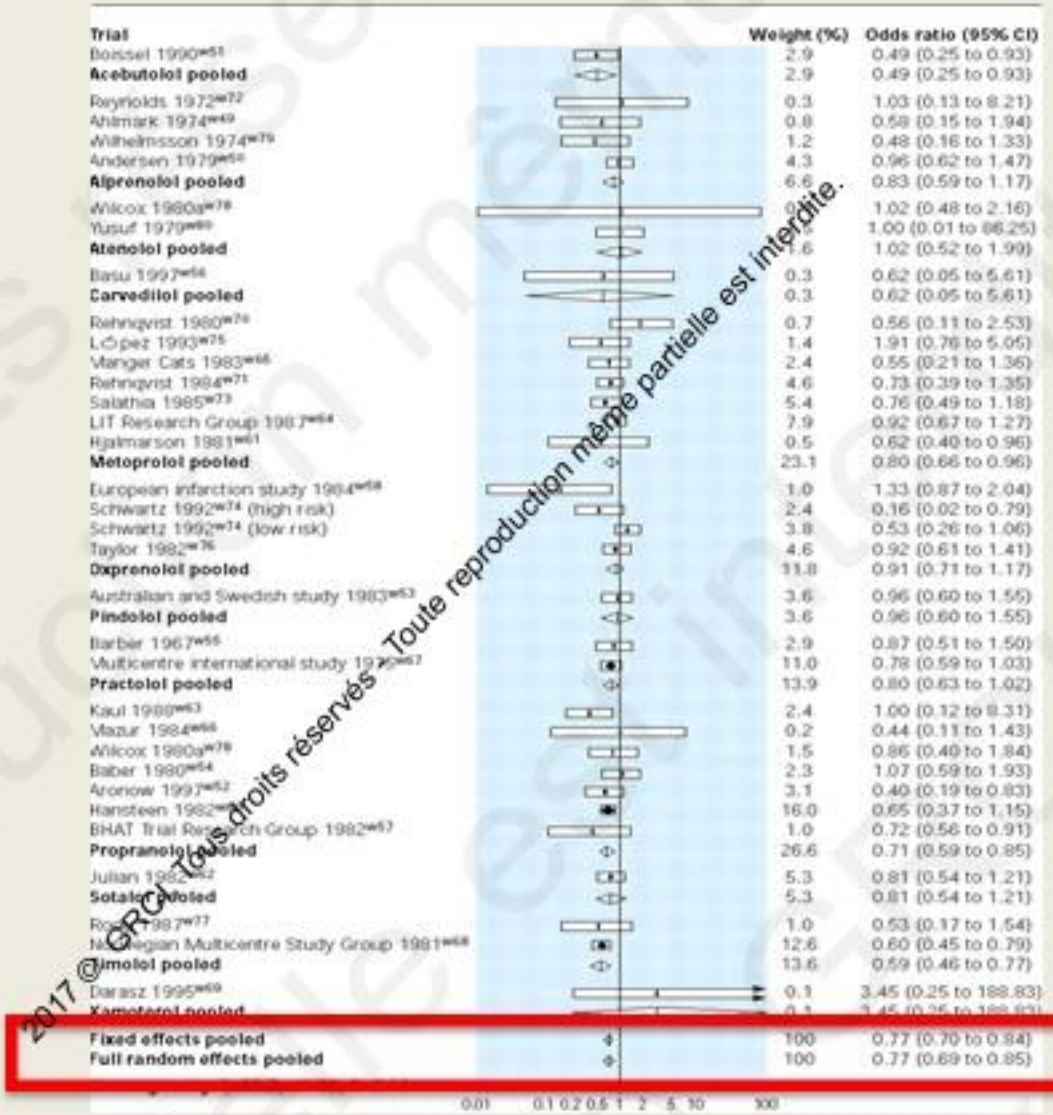
Fig. 2. Long-term effect of β-blockers on all-cause mortality: odds ratios and 95% confidence intervals.

Prog Cardiovasc Dis 2002;44:243-250

Effects of BB on mortality after MI Short-term trials



Freemantle et al. ***BMJ*** 1999

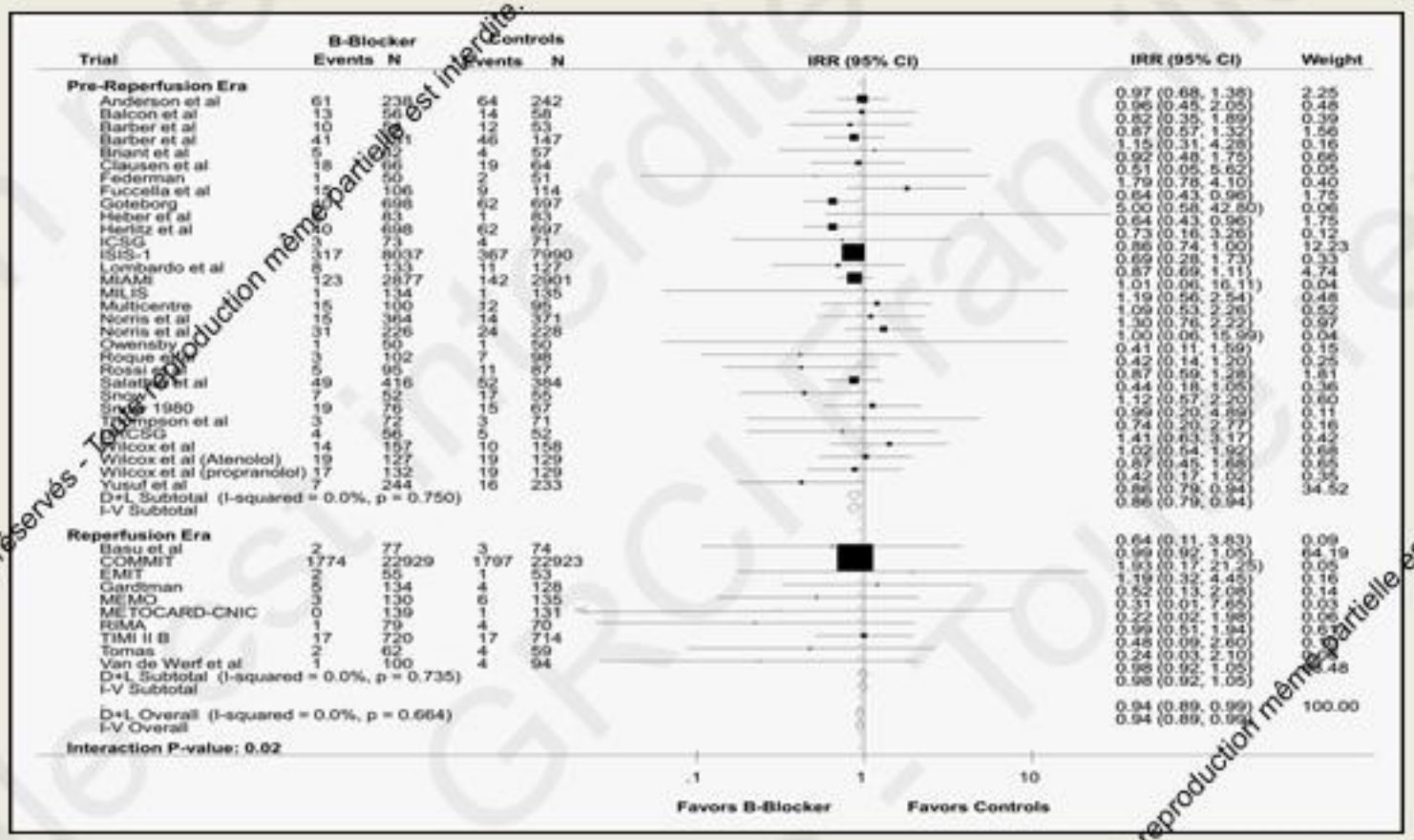


Effects of BB on mortality after MI Long-term trials

Freemantle et al. ***BMJ*** 1999

Meta-analysis of AMI RCTs : All-cause mortality

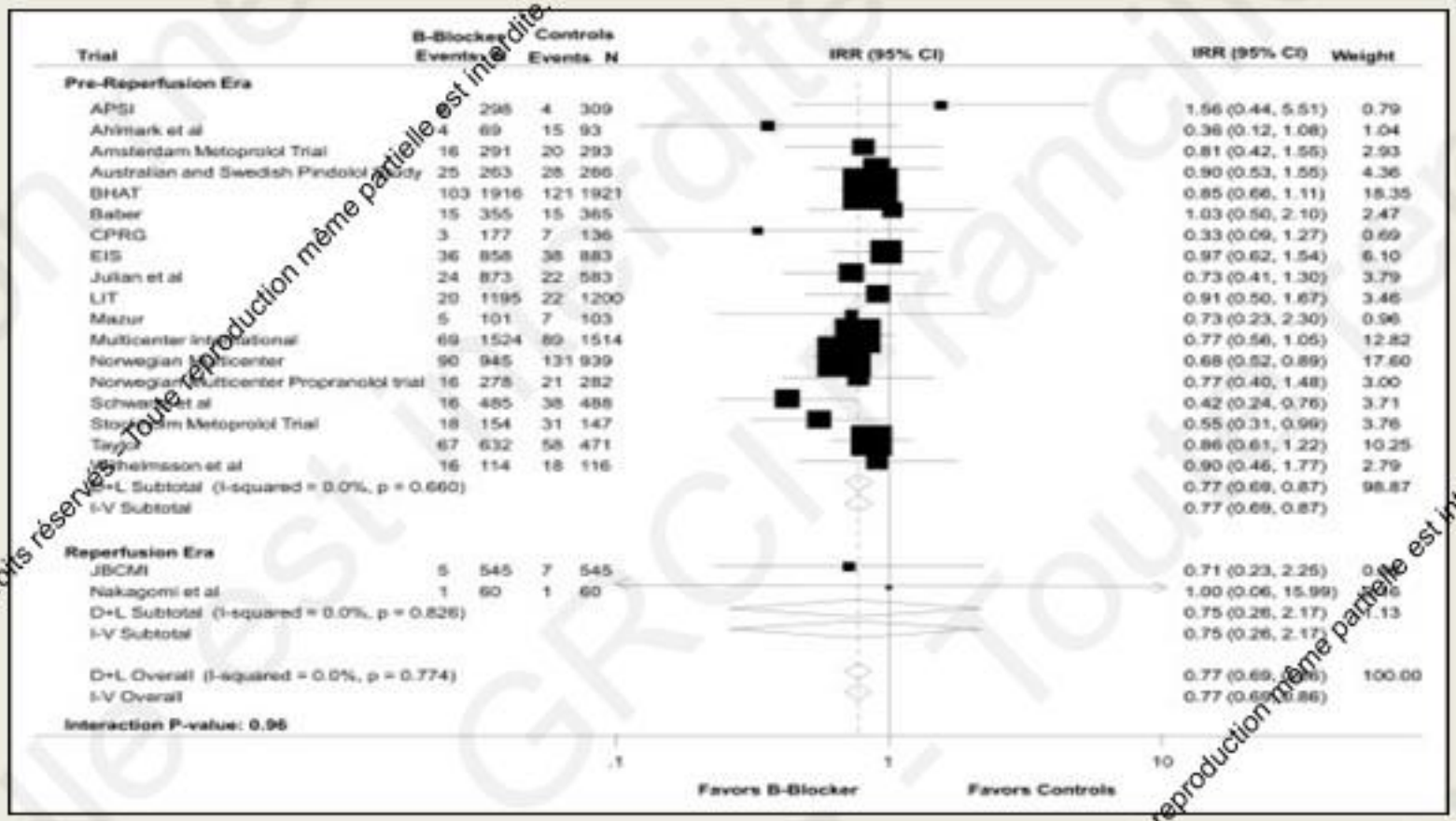
Analysis stratified by reperfusion status.



Bangalore S et al. ***Am J Med*** 2014;127::939-53

Meta-analysis of AMI RCTs : Myocardial Infarction

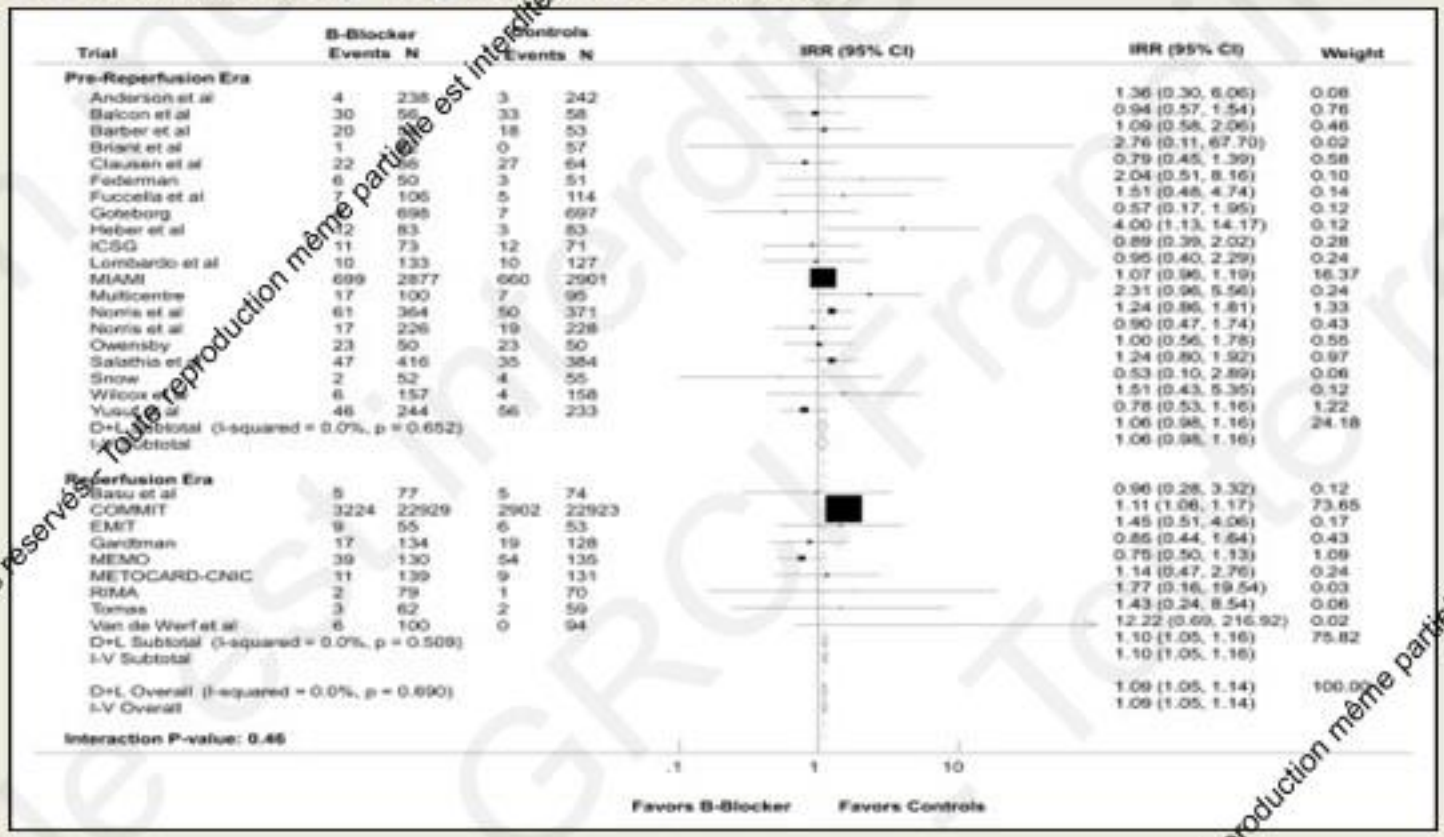
Analysis stratified by reperfusion status.



Bangalore S et al. ***Am J Med*** 2014;127::939-53

Meta-analysis of AMI RCTs : heart failure

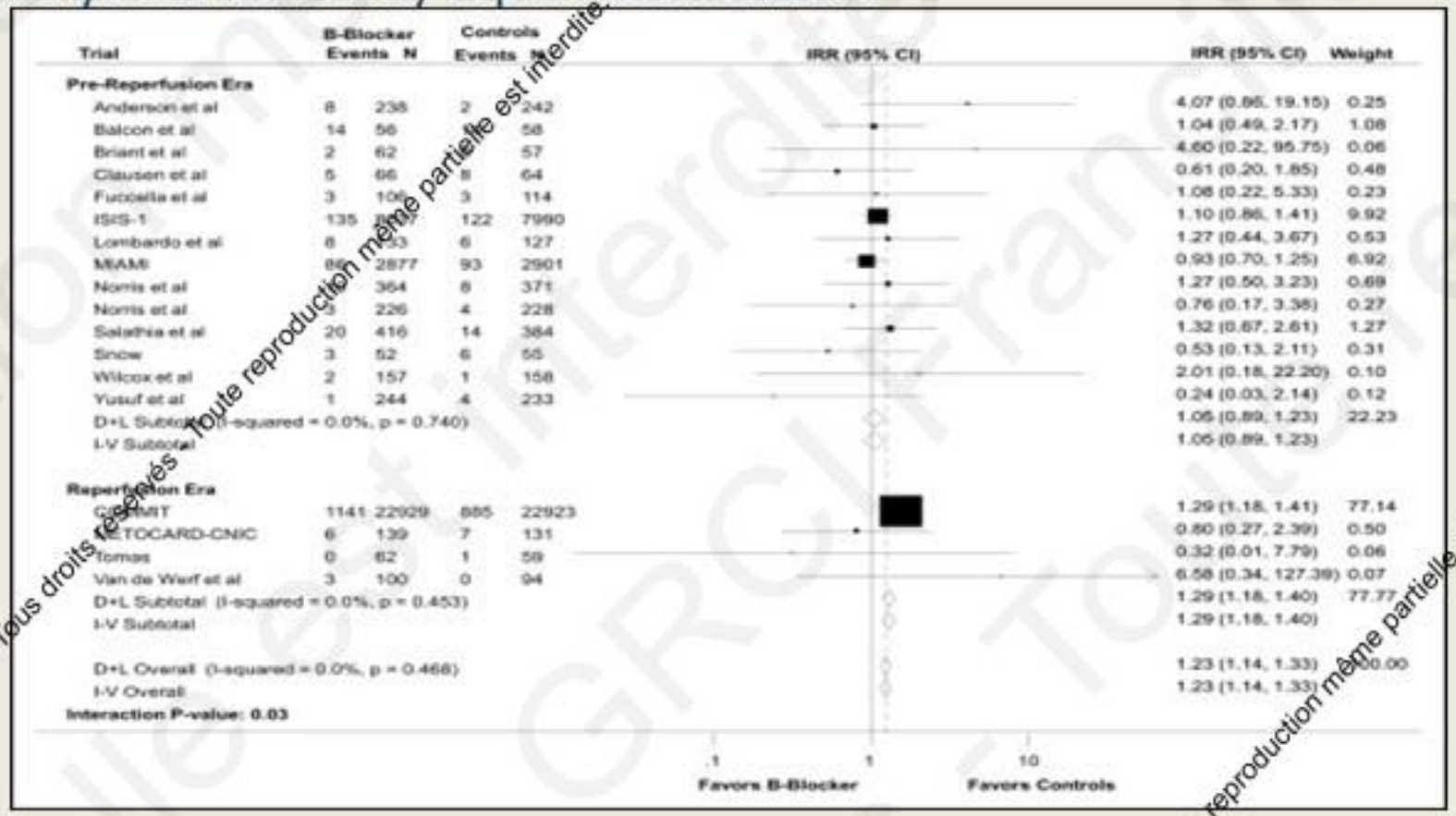
Analysis stratified by reperfusion status.



Bangalore S et al. ***Am J Med*** 2014;127::939-53

Meta-analysis of AMI RCTs : cardiogenic shock

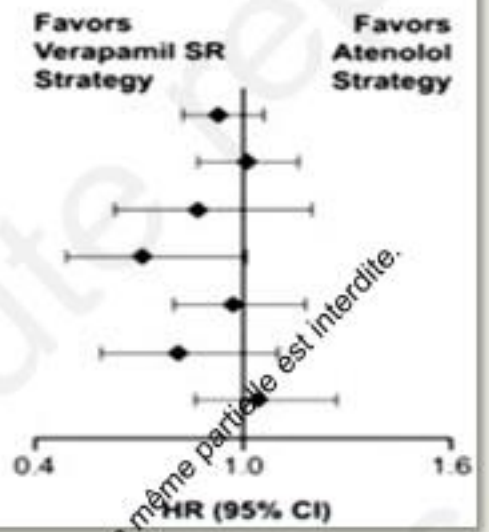
Analysis stratified by reperfusion status.



Bangalore S et al. ***Am J Med*** 2014;127::939-53

Verapamil–based treatment strategy is equivalent to atenolol-based strategy at reducing CV events in patients with prior MI: An INVEST substudy

	Strategy		
	Verapamil SR n = 3622 No. (%)	Atenolol n = 3596 No. (%)	HR (95% CI)
Primary Outcome	495 (13.7)	517 (14.4)	0.94 (0.83–1.06)
Death	396 (10.9)	388 (10.8)	1.01 (0.87–1.16)
Nonfatal MI	70 (1.9)	79 (2.2)	0.87 (0.63–1.20)
Nonfatal stroke	51 (1.4)	71 (2.0)	0.71 (0.49–1.01)
Fatal and nonfatal MI	203 (5.6)	206 (5.7)	0.97 (0.80–1.18)
Fatal and nonfatal stroke	73 (2.0)	89 (2.5)	0.81 (0.59–1.10)
CV death	200 (5.5)	189 (5.3)	1.04 (0.86–1.27)



Bangalore S et al. ***Am Heart J*** 2008;156: 241-7

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- Le pronostic du post infarctus a été transformé
- **Les β-bloquants en post infarctus**
  - Les essais randomisés
  - **Les études observationnelles**

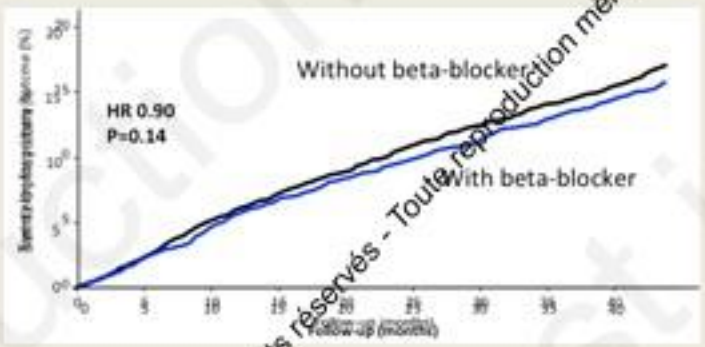
Risk of primary outcome by beta-blocker use according to patient profile

Matched cohorts from REACH registry, 44 months of FU.

Primary outcome: composite of CV death, nonfatal MI, or nonfatal stroke

Stable CAD & Prior MI

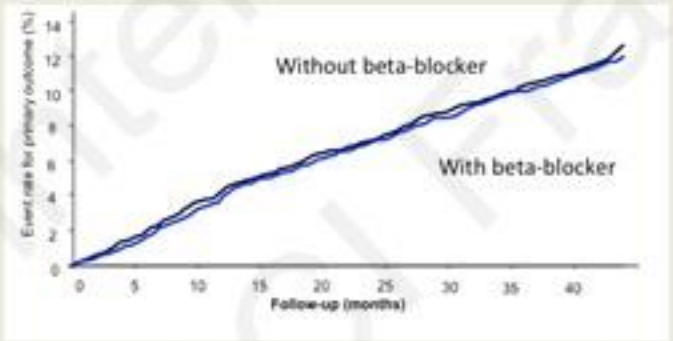
6758 pts



HR 0.90
P=0.14

Stable CAD – No MI

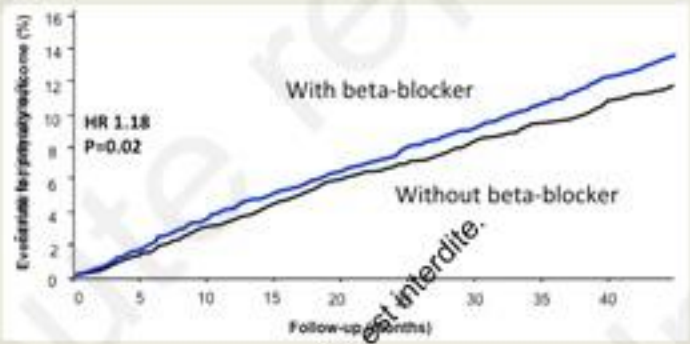
6854 pts



HR 0.92
P=0.31

RF only

7904 pts

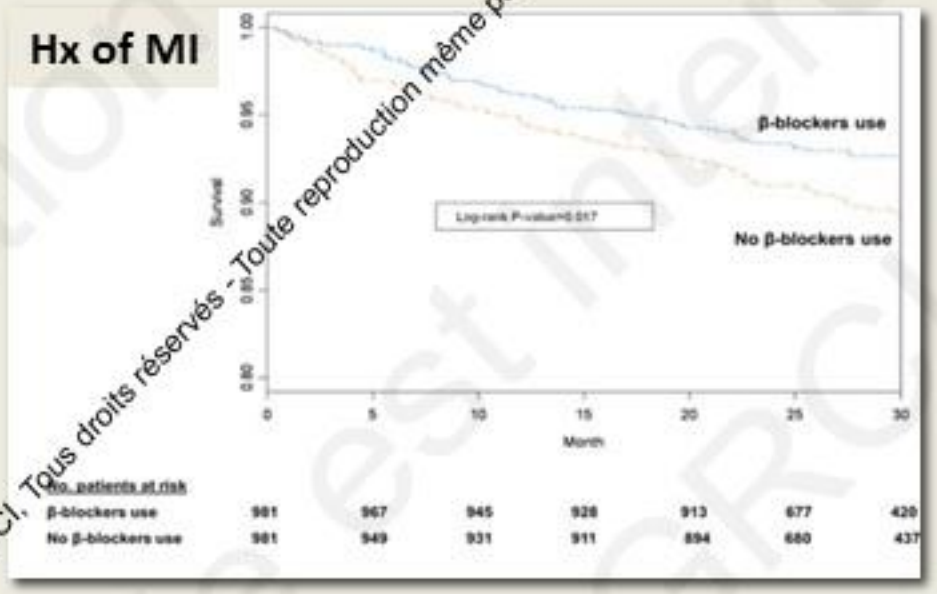


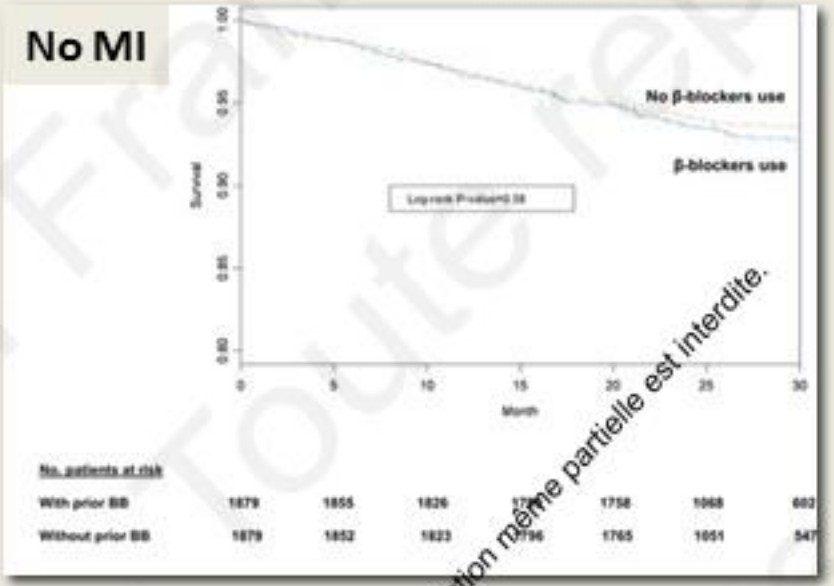
HR 1.18
P=0.02

Bangalore S et al. *JAMA*. 2012;308(13):1340-1349

CHARISMA: β-blockers are associated with improved outcomes in pts with prior MI but not in pts without MI

Outcomes in propensity-matched patients on and not on β-blockers in the prior MI cohort (P values from Cox proportional hazards model).

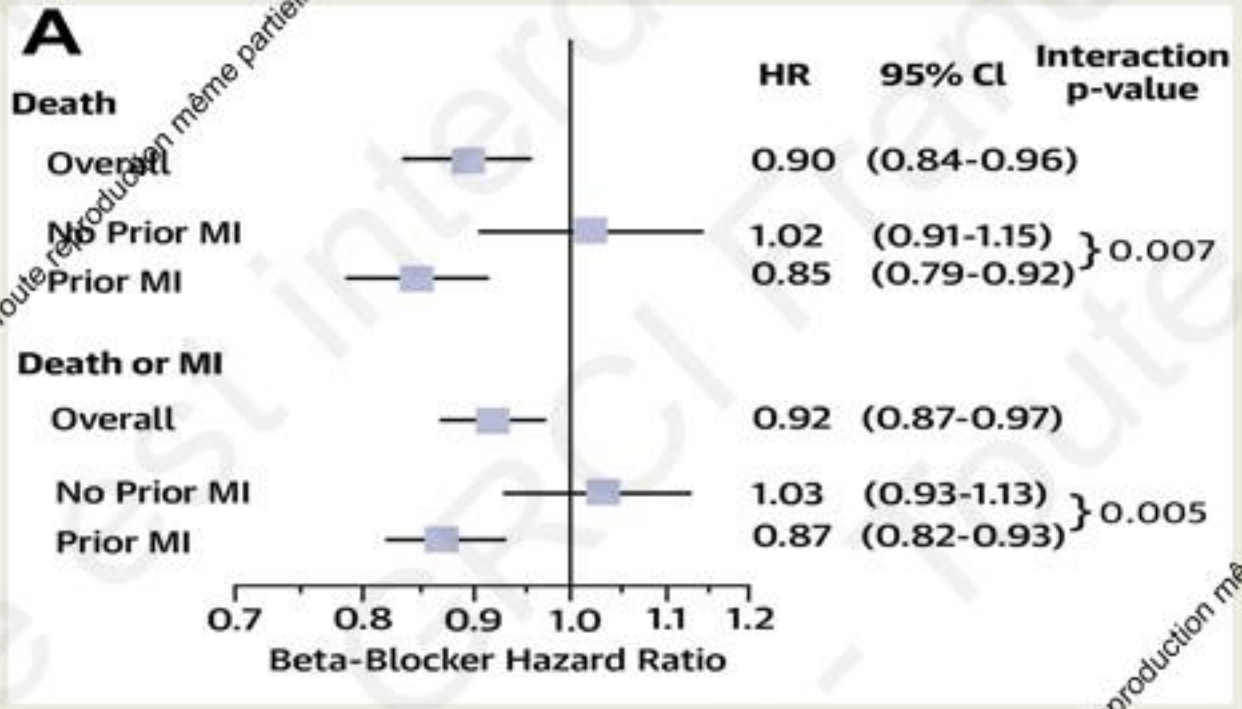




Bangalore et al. ***Circ Cardiovasc Qual Outcomes.*** 2014;7:872-881

Beta-Blockers are associated with improved outcomes only in pts with prior MI

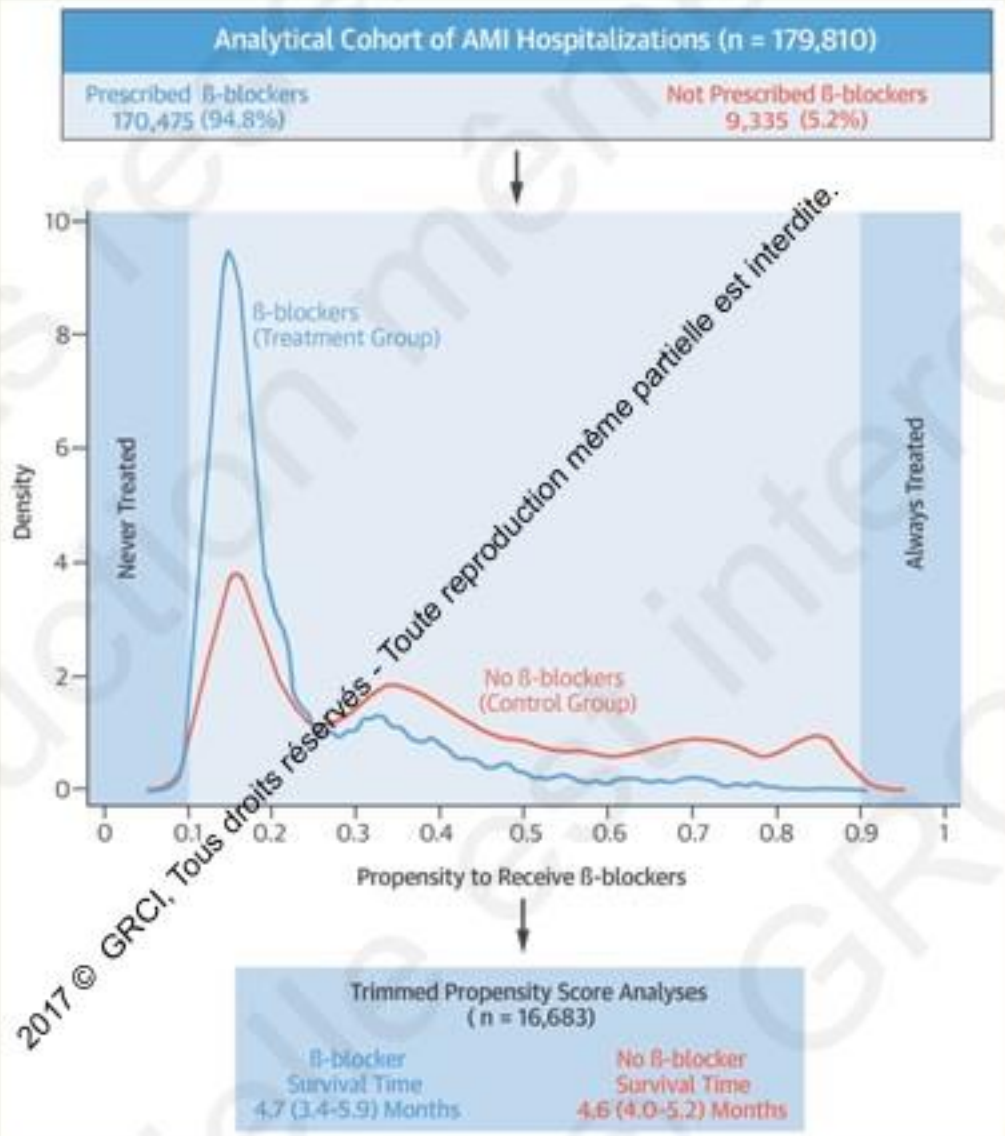
The Kaiser Permanente study



Andersson et al; *J Am Coll Cardiol.* 2014;64:247-52.

No association between prescription of β-blockers and survival in AMI survivors without HF or LVSD

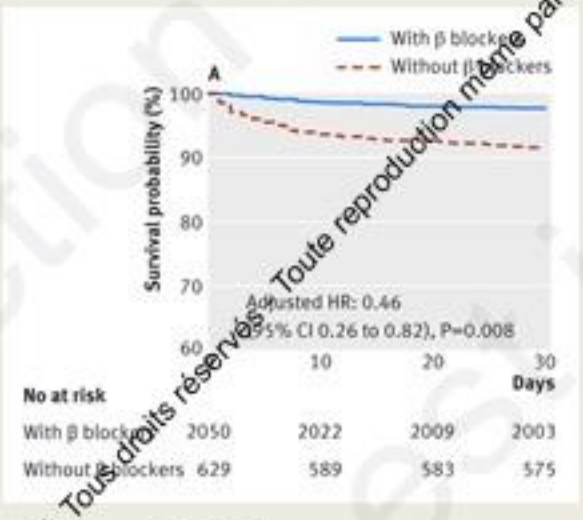
A MINAP analysis of 179,810 survivors of hospitalization with AMI without HF or LVSD, between January 1, 2007, and June 30, 2013



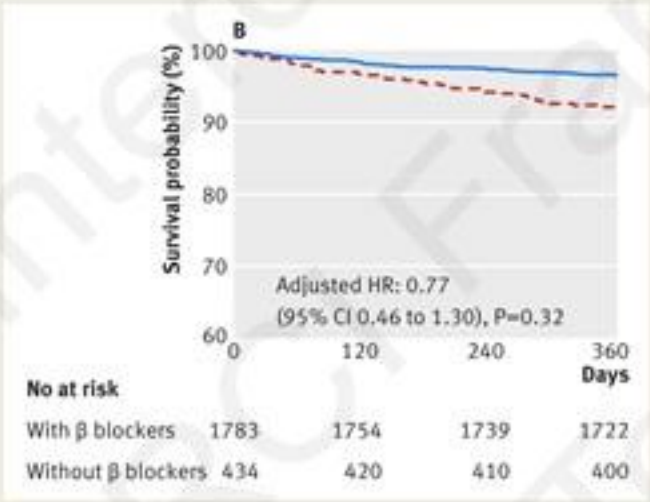
Dondo TB et al. **J Am Coll Cardiol** 2017;69:2710-20

β blockers and mortality after myocardial infarction in patients without heart failure: multicentre prospective cohort study

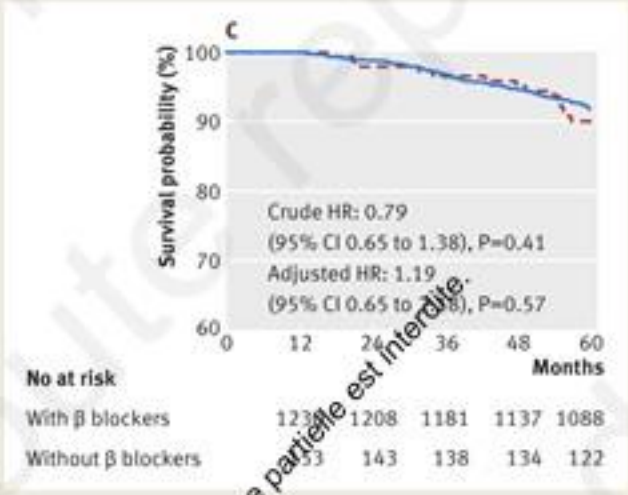
A FAST MI analysis



30 days



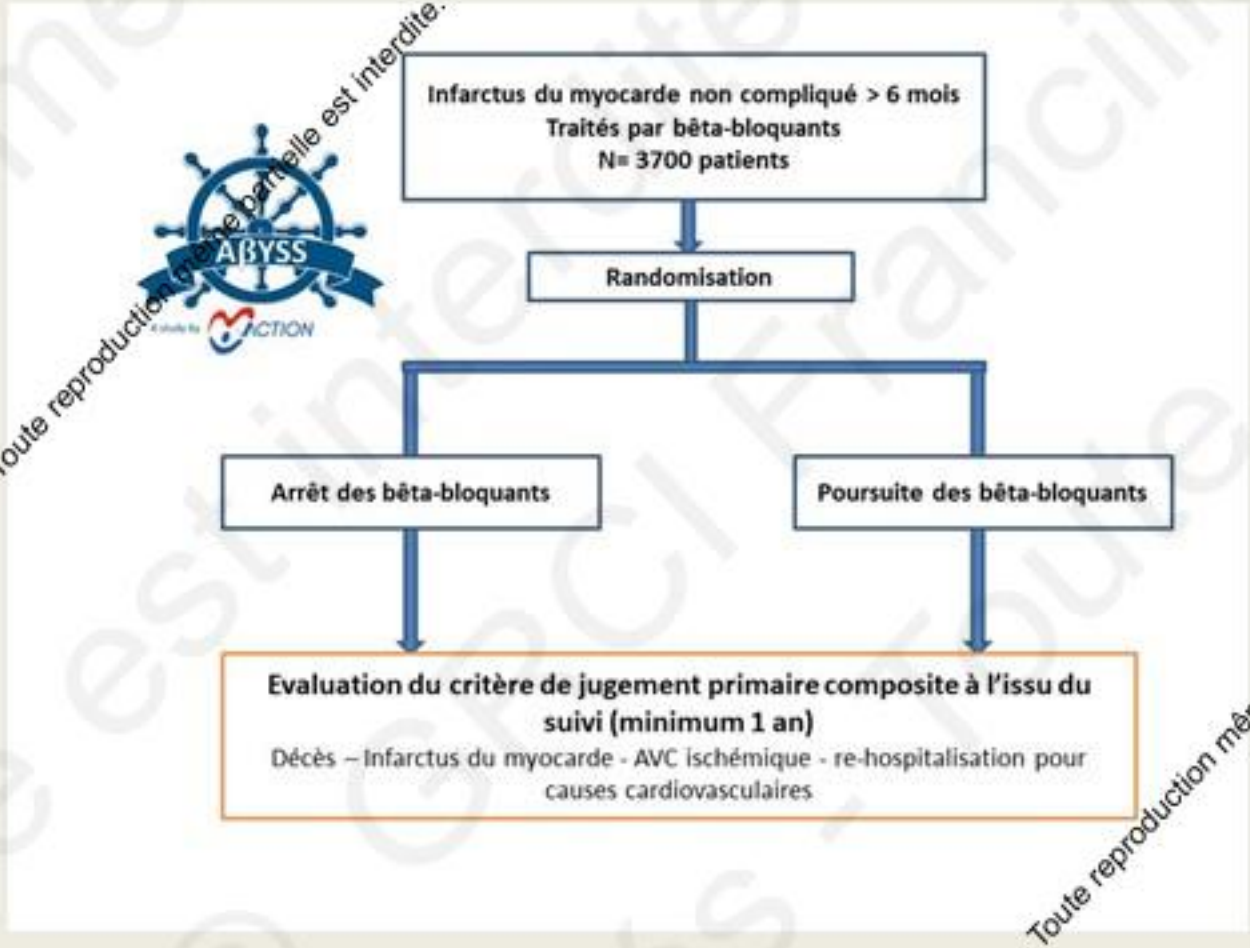
1 year



5 years

Roubymirat E et al. **BMJ** 2016;354:i4801

The ABYSS trial: stopping or continuing beta blockers > 6 months post MI



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- Le pronostic du post infarctus a été transformé
- Les β-bloquants en post infarctus
  - Les essais randomisés
  - Les études observationnelles
- **Les IEC en post infarctus**
  - **Les essais randomisés**

ACE inhibitors in post AMI patients with ventricular dysfunction

12 763 patients from SAVE, AIRE, TRACE and SOLVD

Mortality Reduction: 20 %
HR: 0.80: 0.74-0.87
p < 0.0001

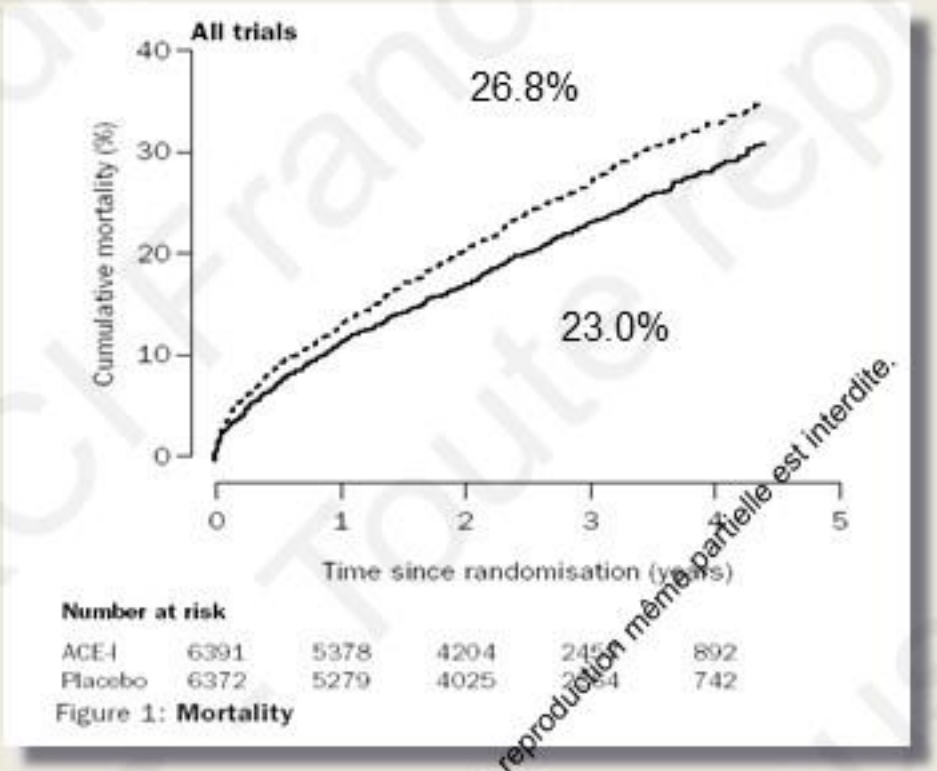
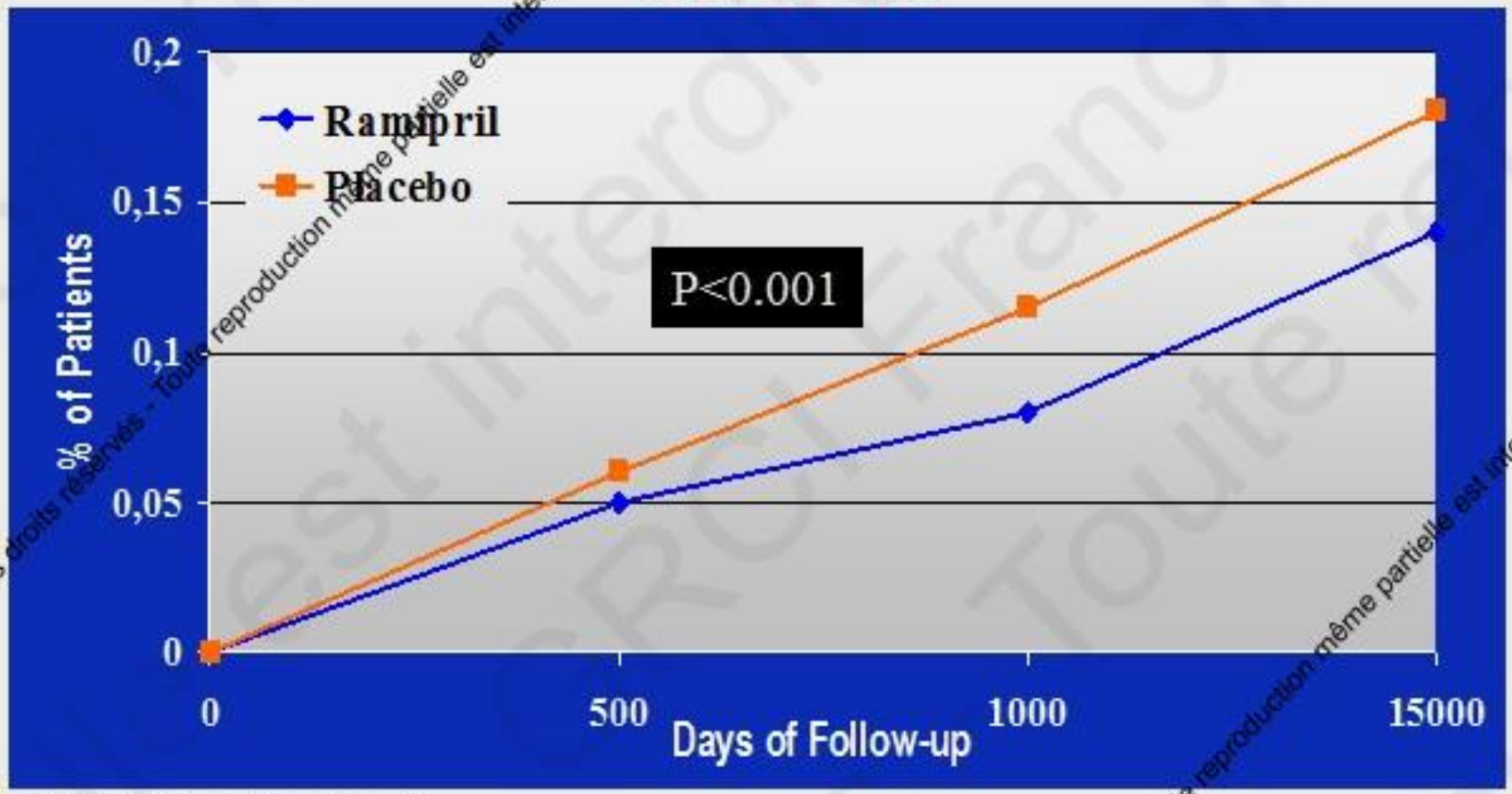


Figure 1: **Mortality**

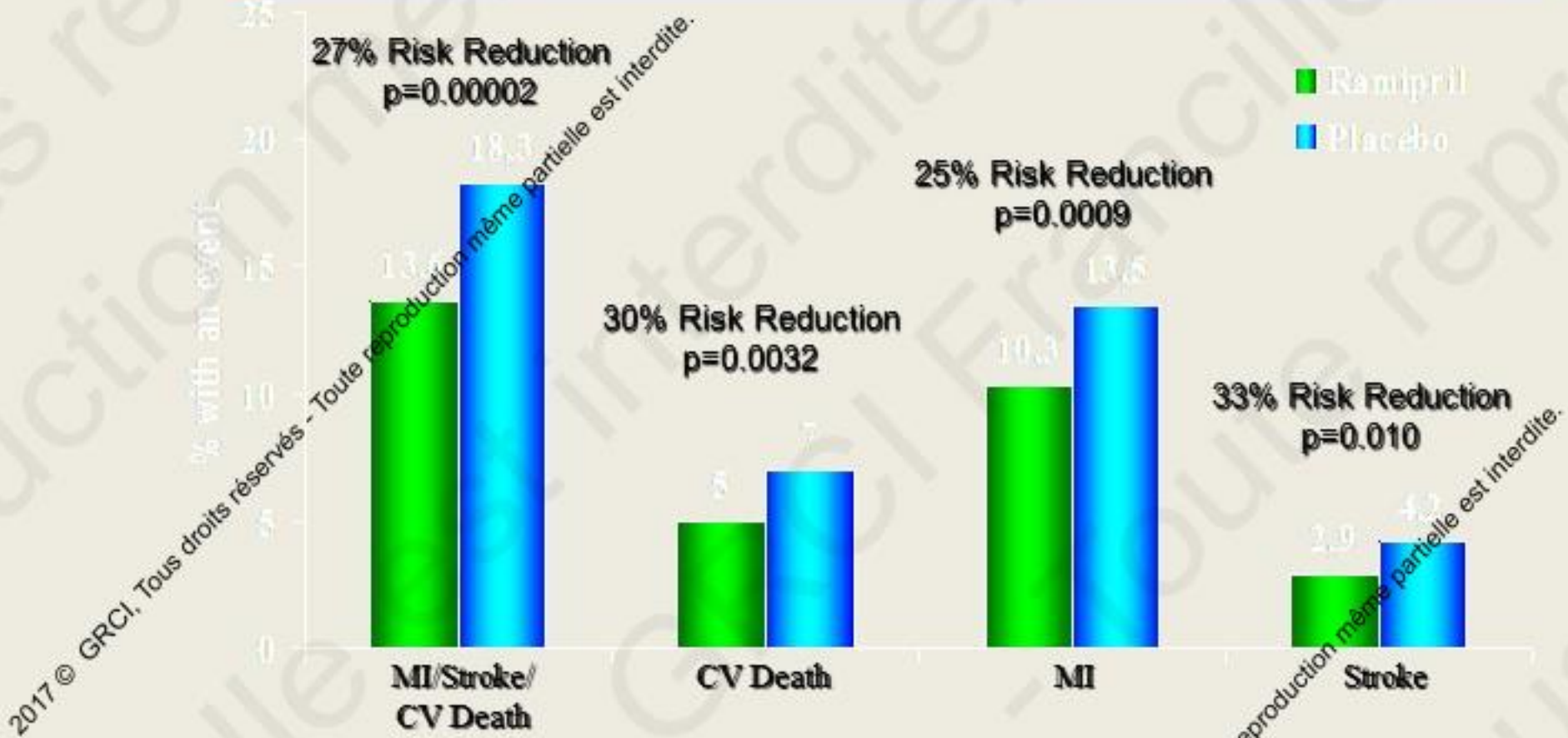
Flather et al. ***Lancet*** 2000;355:1575-81

HOPE - Composite Endpoint of CV Death, MI or Stroke



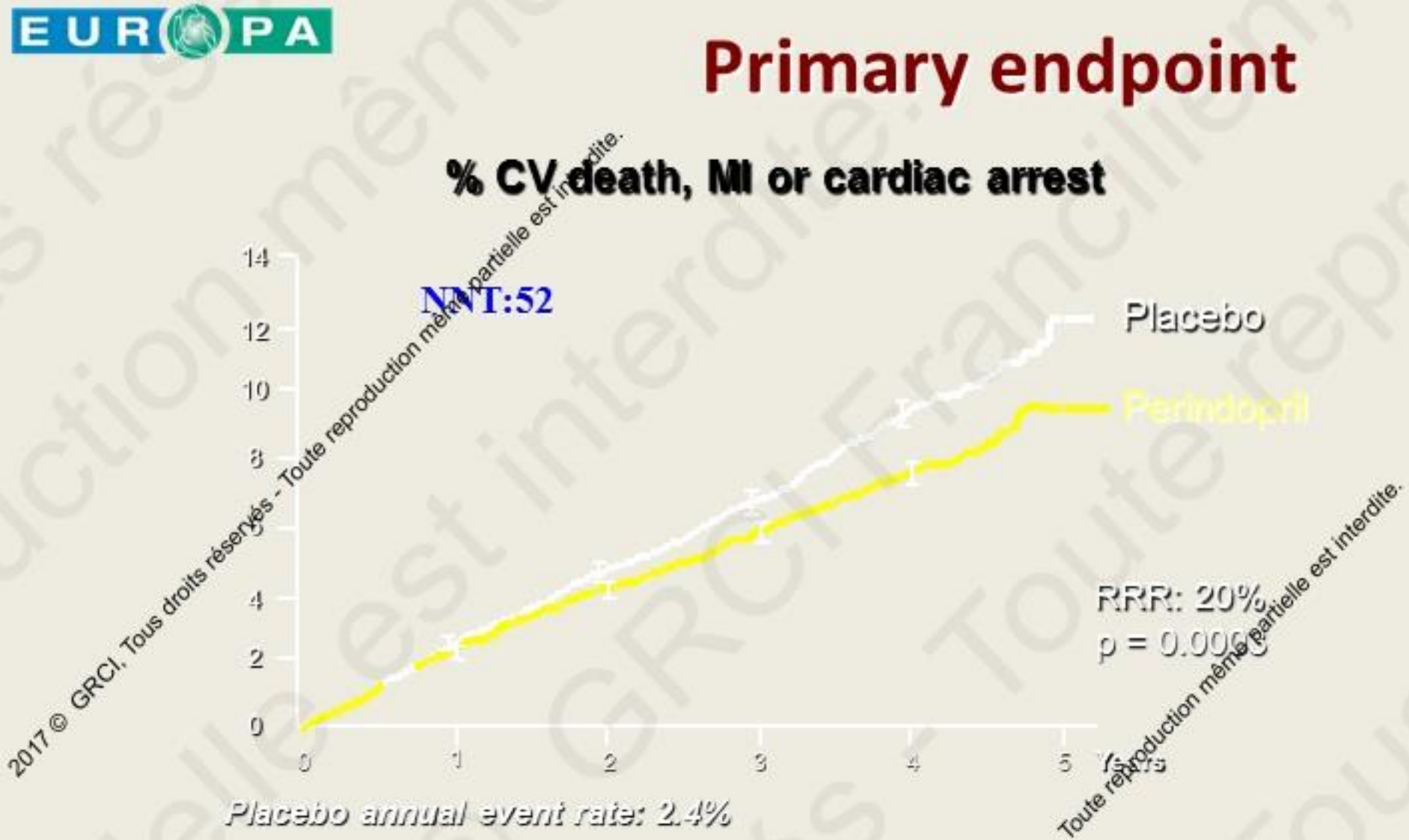
N Engl J Med, January 20, 2000

HOPE - Results in Patients with Normal EF

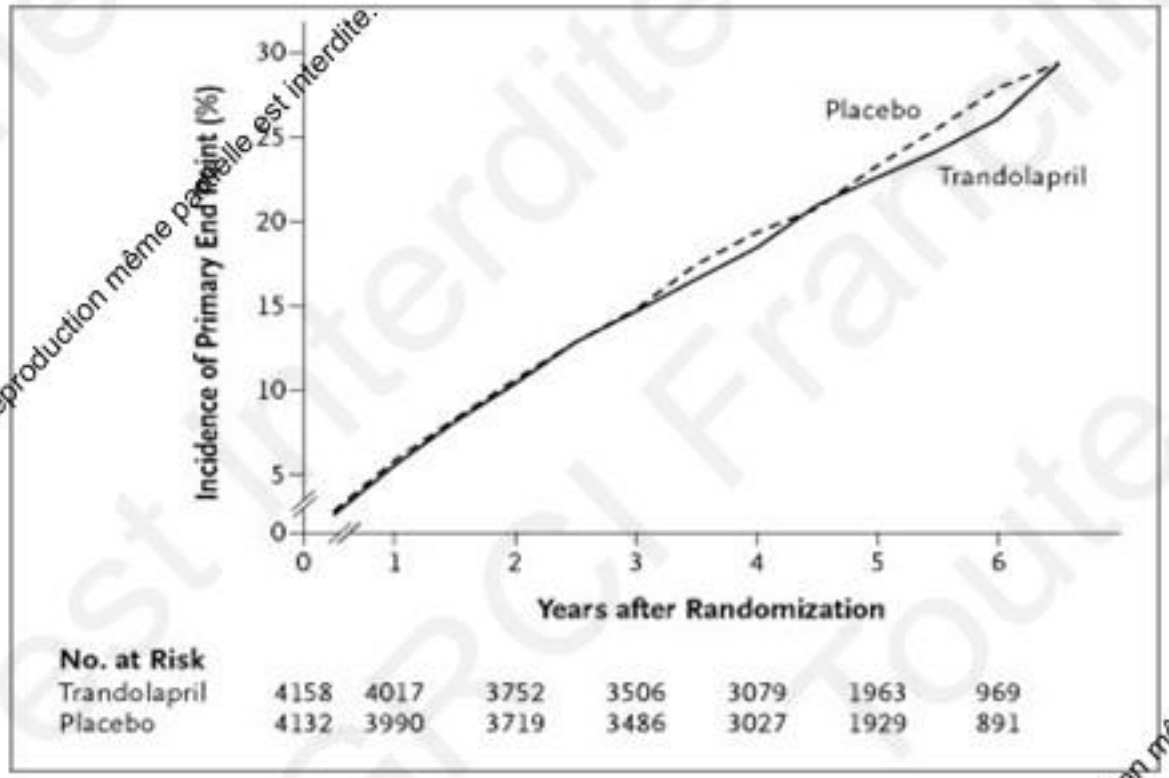


G. Dagenais, ESC 1999

Primary endpoint



PEACE :Cumulative Incidence of the Primary End Point



The NEW ENGLAND JOURNAL of MEDICINE

The PEACE Trial Investigators, *N Engl J Med* 2004;351:2058-2068

Incidence of the Primary End Point and Its Components and of Death from All Causes

Table 3. Incidence of the Primary End Point and Its Components and of Death from All Causes.*

Outcome	Trandolapril (N=4158)	Placebo (N=4132)	Hazard Ratio (95% CI)	P Value
	no. of patients (%)			
Primary (death from cardiovascular causes, nonfatal MI, CABG or PCI)†	909 (21.9)	929 (22.5)	0.96 (0.88–1.06)	0.43
Death from cardiovascular causes	146 (3.5)	152 (3.7)	0.95 (0.76–1.19)	0.67
Nonfatal MI	222 (5.3)	220 (5.3)	1.00 (0.83–1.20)	1.00
CABG	271 (6.5)	294 (7.1)	0.91 (0.77–1.07)	0.24
PCI†	515 (12.4)	497 (12.0)	1.03 (0.91–1.16)	0.65
Death from noncardiovascular or unknown causes	153 (3.7)	182 (4.4)	0.83 (0.67–1.03)	0.09
Death from any cause	299 (7.2)	334 (8.1)	0.89 (0.76–1.04)	0.13

* CI denotes confidence interval, MI myocardial infarction, CABG coronary-artery bypass grafting, and PCI percutaneous coronary intervention.
† PCI included laser revascularization.

The PEACE Trial Investigators, N Engl J Med 2004;351:2058-2068

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Meta-Analysis of Data on Mortality from the HOPE, EUROPA, and PEACE Trials

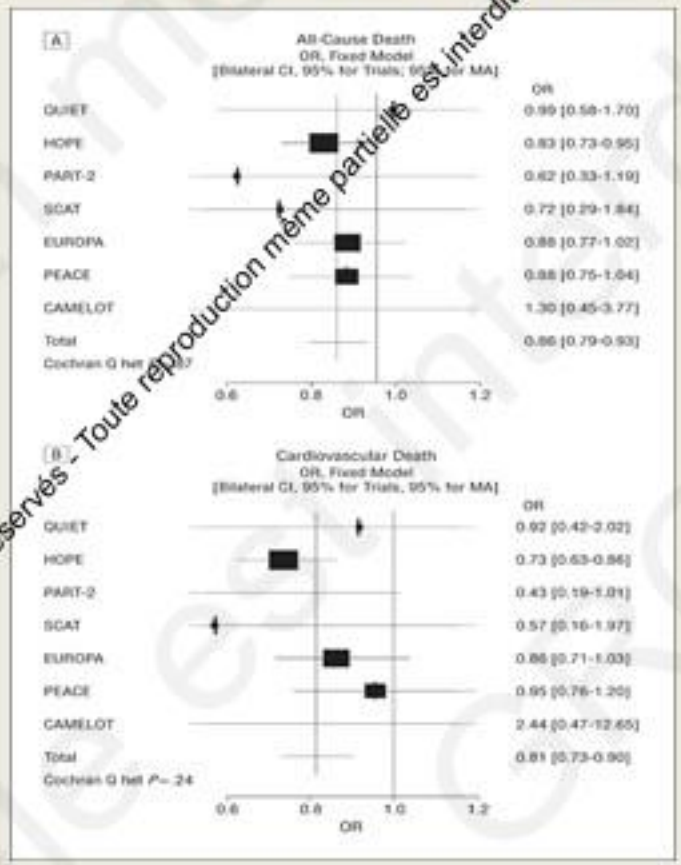
Trial	ACE Inhibitor	Control	Odds Ratio (95% CI)	P Value
	no. of deaths/no. of patients (%)			
HOPE	482/4645 (10.4)	569/4652 (12.2)	0.83 (0.73–0.95)	0.005
EUROPA	375/6110 (6.1)	420/6108 (6.9)	0.89 (0.77–1.02)	0.098
PEACE	299/4158 (7.2)	334/4132 (8.1)	0.88 (0.75–1.04)	0.126
Total	1156/14,913 (7.8)	1323/14,892 (8.9)	0.86 (0.79–0.94)	<0.001

* HOPE denotes the Heart Outcomes Prevention Evaluation Study, EUROPA the European Trial of Reduction of Cardiac Events with Perindopril in Stable Coronary Artery Disease, PEACE the Prevention of Events with Angiotensin Converting Enzyme Inhibition, ACE angiotensin-converting enzyme, and CI confidence interval.

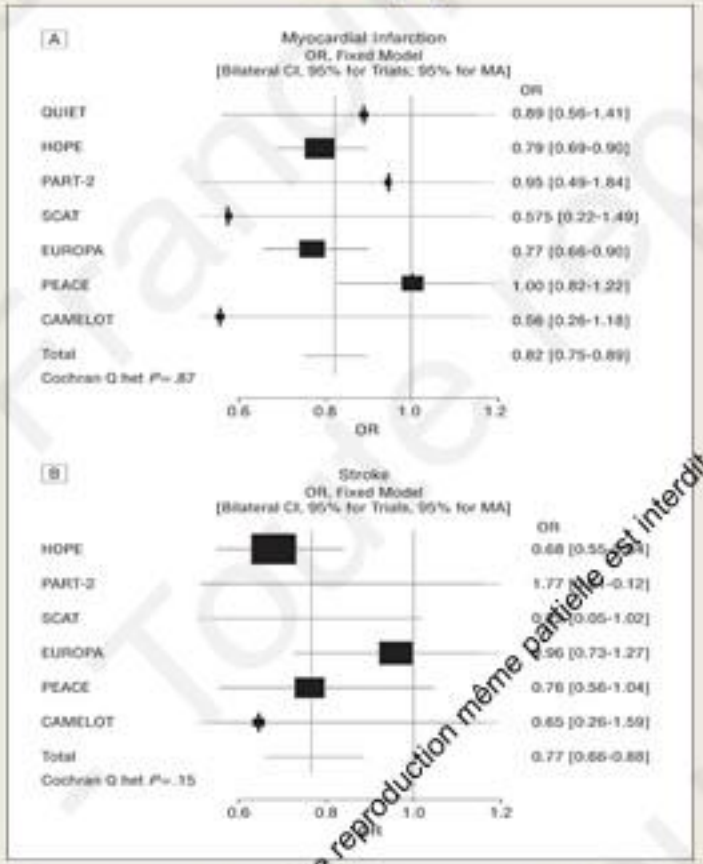
Yusuf S et al ***N Engl J Med*** 2005;352:937-939

Pts with CAD and no LV systolic dysfunction randomized to long-term ACEI or placebo

All-cause mortality (A) and cardiovascular mortality (B) in



Nonfatal myocardial infarction (A) and stroke (B)

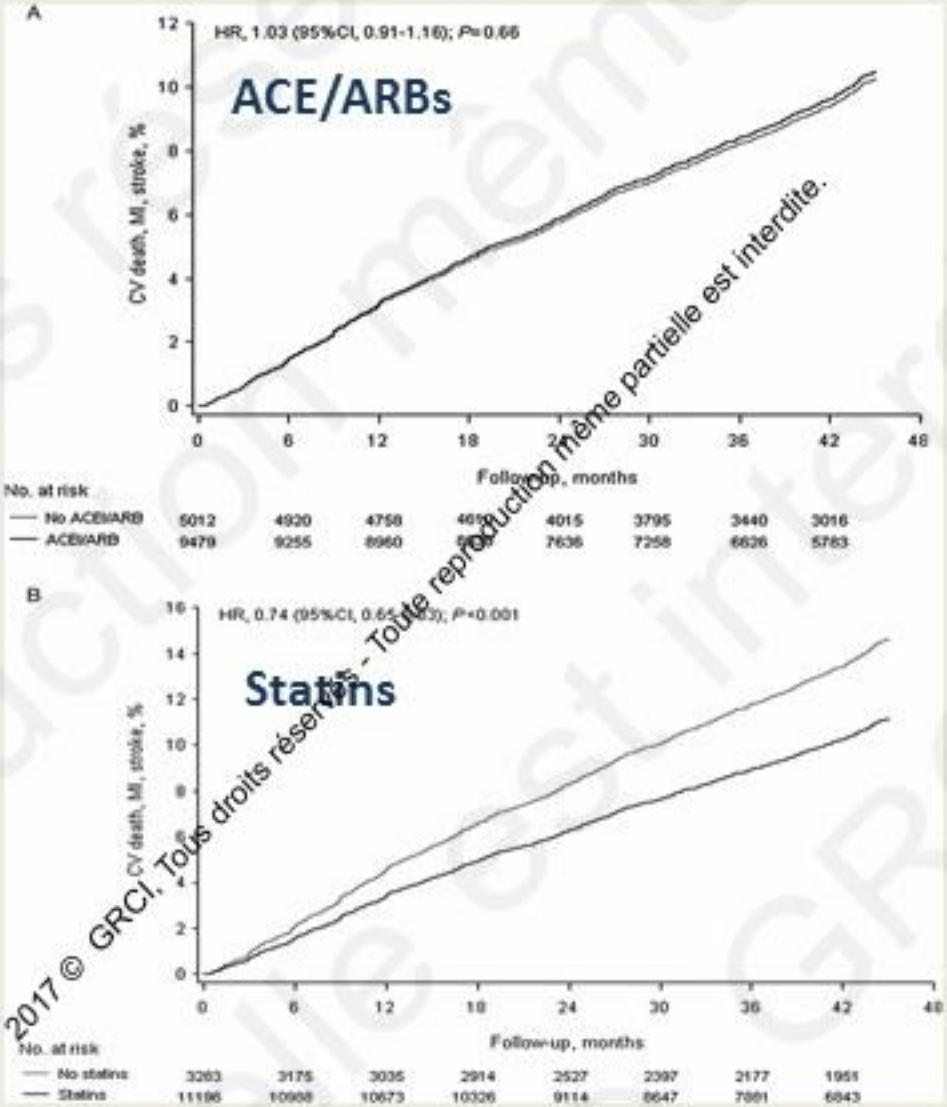


Danchin et al ***Arch Intern Med*** 2006;166:787-796

Une ordonnance sans β-bloquants ni IEC: est ce possible ?

- Le pronostic du post infarctus a été transformé
- Les β-bloquants en post infarctus
  - Les essais randomisés
  - Les études observationnelles
- **Les IEC en post infarctus**
  - **Les essais randomisés**
  - **Les études observationnelles**

Benefit of statins but not ACEI/ARBs in stable CAD without CHF



CV death, MI and Stroke in the REACH registry subset of 20,909 pts with CAD but without CHF

Adjusted event curves after correction for propensity

Sorbets et al. ***Eur Heart J*** 2014

Une ordonnance sans β-bloquants ni IEC: est ce possible ?

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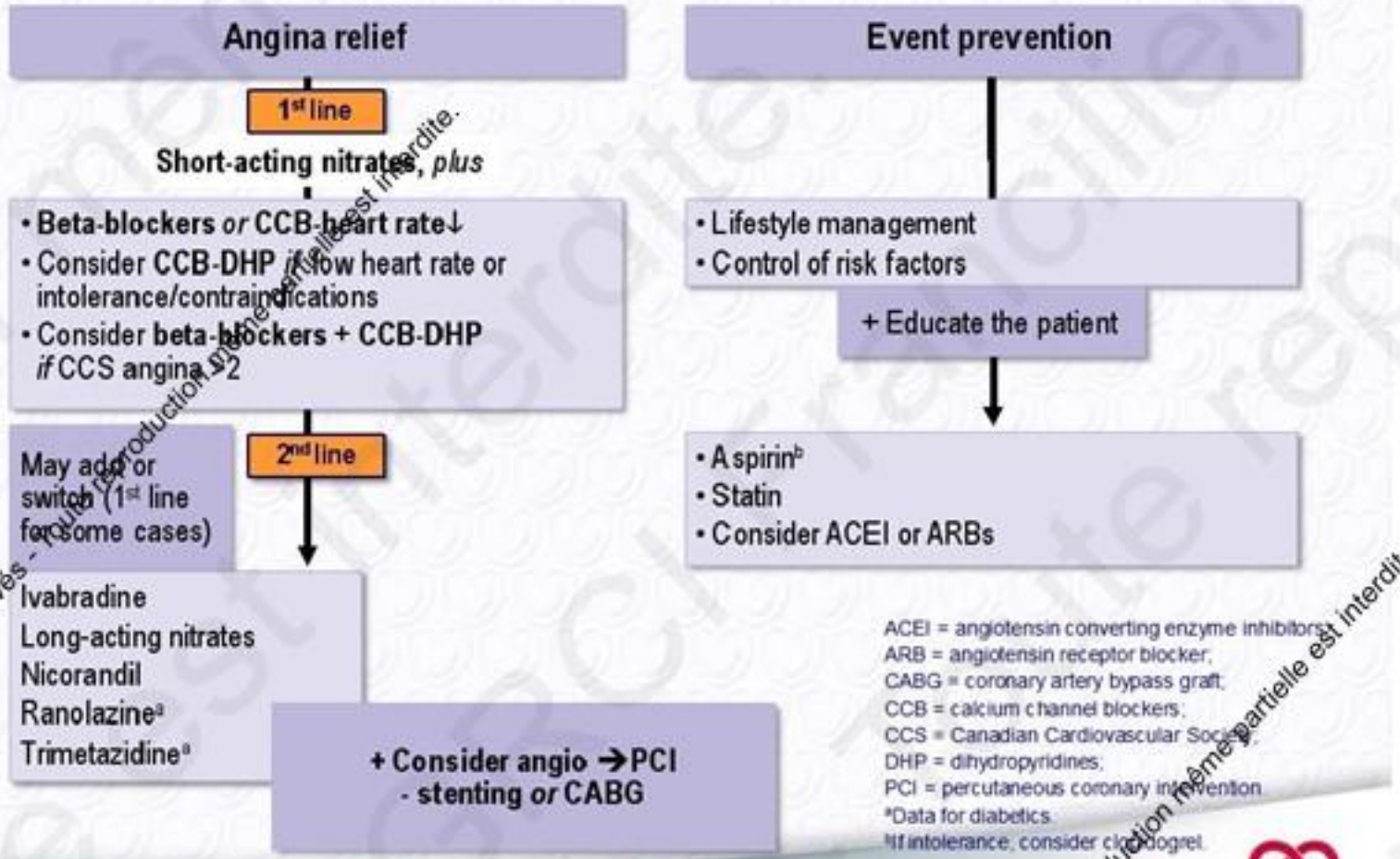
Que disent les recommandations ?

Medical management of patients with SCAD



ACEI = angiotensin converting enzyme inhibitors;
ARB = angiotensin receptor blocker;
CABG = coronary artery bypass graft;
CCB = calcium channel blockers;
CCS = Canadian Cardiovascular Society;
DHP = dihydropyridines;
PCI = percutaneous coronary intervention.
[a]Data for diabetics.
[b]If intolerance, consider clopidogrel.

This slide corresponds to Figure 4 of the full text.

www.escardio.org/guidelines

Eur Heart J 2013;34:2949–3003. doi:10.1093/eurheartj/eht296

En pratique,

les β-bloquants en post infarctus

- restent indiqués formellement pour les patients insuffisants cardiaques ou avec dysfonction VG
- restent indiqués comme traitement symptomatique de première intention de l'angor d'effort

Les IECs en post infarctus

- restent indiqués formellement pour les patients insuffisants cardiaques ou avec dysfonction VG ou diabétiques

Dans les autres cas, ces médicaments ont un bénéfice « incertain », notamment au long cours

Il est raisonnable de les instaurer par principe, mais si un patient développe des effets secondaires ou est peu compliant, on peut envisager leur arrêt.