

Should All Patients Be Treated with Ace-inh /ARB after STEMI with Preserved LV Function?

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Disclosure slide

- No disclosures related to this presentation



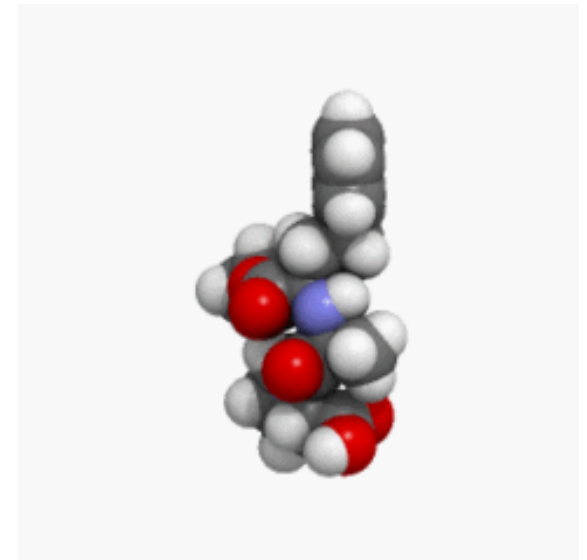
Objectives

- Be familiar with the Guidelines
- There is a knowledge gap



Facts

- ACE-inhibitors/ARBs reduce cardiovascular mortality and morbidity in patients with HF or LV systolic dysfunction



ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation- 2012



| Recommendations | References | | |
|---|------------|---|----------------|
| ACE inhibitors are indicated starting within the first 24 h of STEMI in patients with evidence of heart failure, LV systolic dysfunction, diabetes or an anterior infarct. | I | A | 279 |
| An ARB, preferably valsartan, is an alternative to ACE inhibitors in patients with heart failure or LV systolic dysfunction, particularly those who are intolerant to ACE inhibitors. | I | B | 280, 281 |
| ACE inhibitors should be considered in all patients in the absence of contraindications. | IIa | A | 289,290 |

References 289,290.....

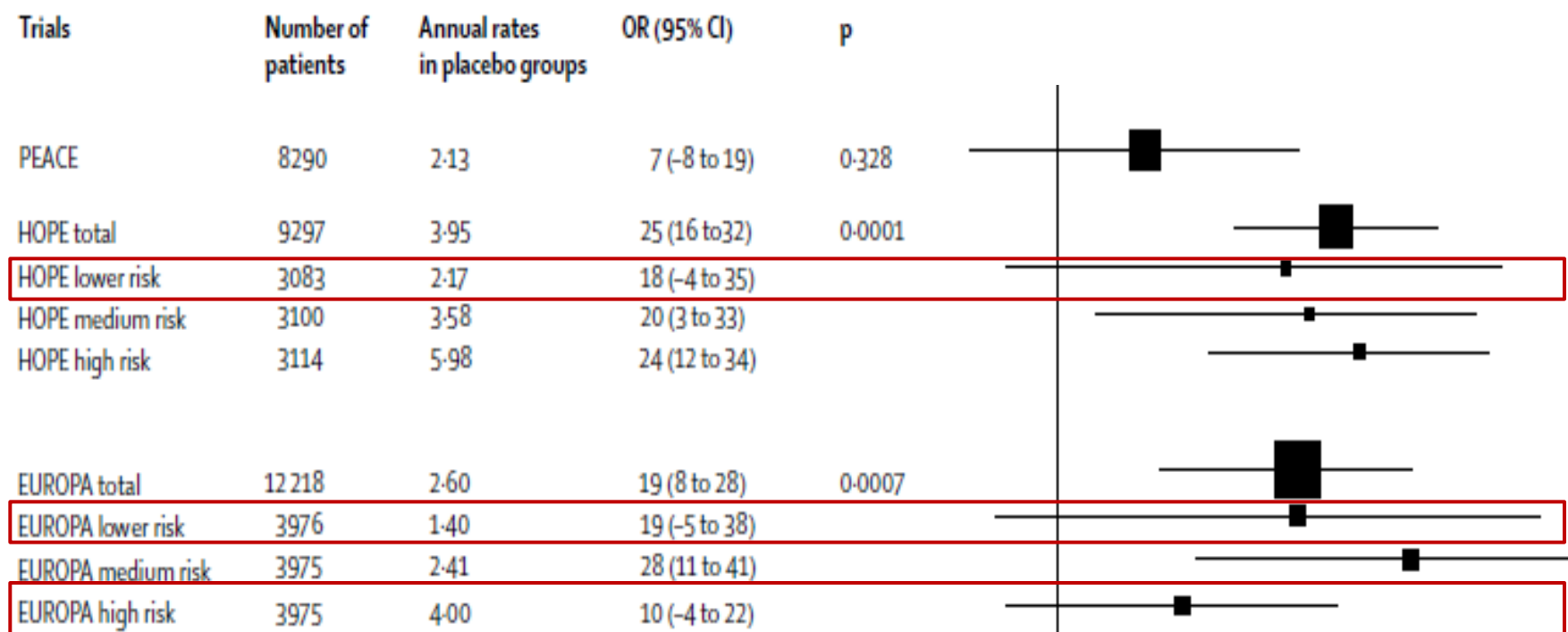
- 289- Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomised, double-blind, placebo-controlled, multicentre trial (**EUROPA** trial). Lancet 2003
- 290- Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation (**HOPE** trial) Investigators. N Engl J Med 2000
- Don't forget trandolapril (**PEACE** trial)

HOPE, EUROPA, PEACE- Not STEMI patients!!

- **Three main large trials of ACE inhibitors in patients with atherosclerosis, but without heart failure or LVSD.**
 - HOPE- LVEF>40% (not truly normal...)
 - EUROPA- No evidence of heart failure But... LVEF?
 - PEACE- LVEF>40% (not truly normal...)

- **MI before enrolment was documented in only 65%, 55%, and 53% of the EUROPA, PEACE, and HOPE patients, respectively.**
 - HOPE- cardiovascular disease or diabetes; 43% PCI/CABG
 - EUROPA- if MI.... At least 3 months before enrolment; 58-60% PCI/CABG
 - PEACE- if MI.... At least 3 months before enrolment; 72% PCI/CABG

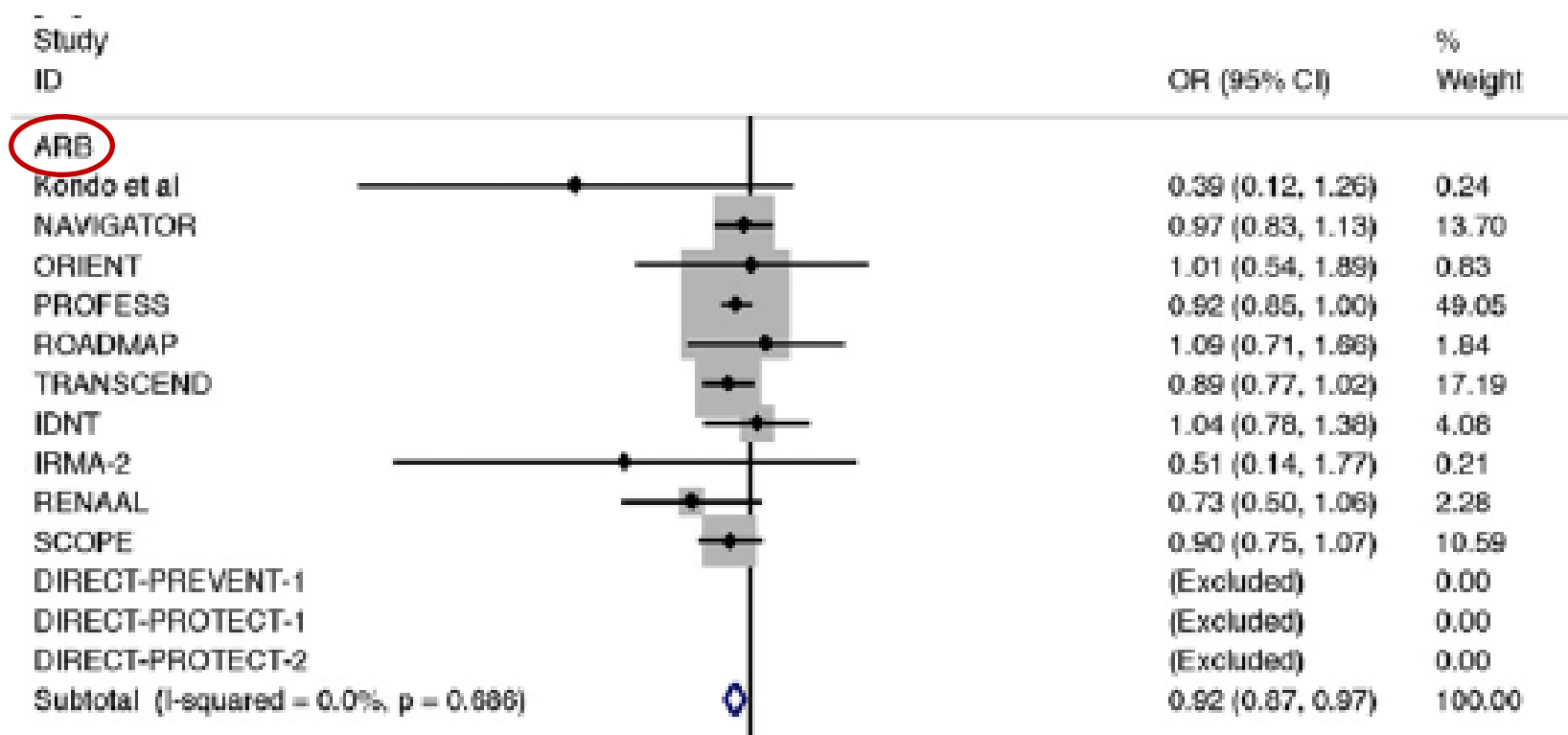
Percentage reduction in odds of cardiovascular death, non-fatal myocardial infarction, or stroke for PEACE, HOPE, and EUROPA



A Meta-Analysis Reporting Effects of Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers in Patients Without Heart Failure

Not STEMI patients!!

J Am Coll Cardiol 2013;61:131-42



- ACE-Inhibitors- class effect or not?
- What are the actual evidence in STEMI patients (ARB's, ACE-I)?
- Is there a benefit in the current era of treatment?
- Adherence to post-AMI treatment



ACE-Inhibitors- A class effect??

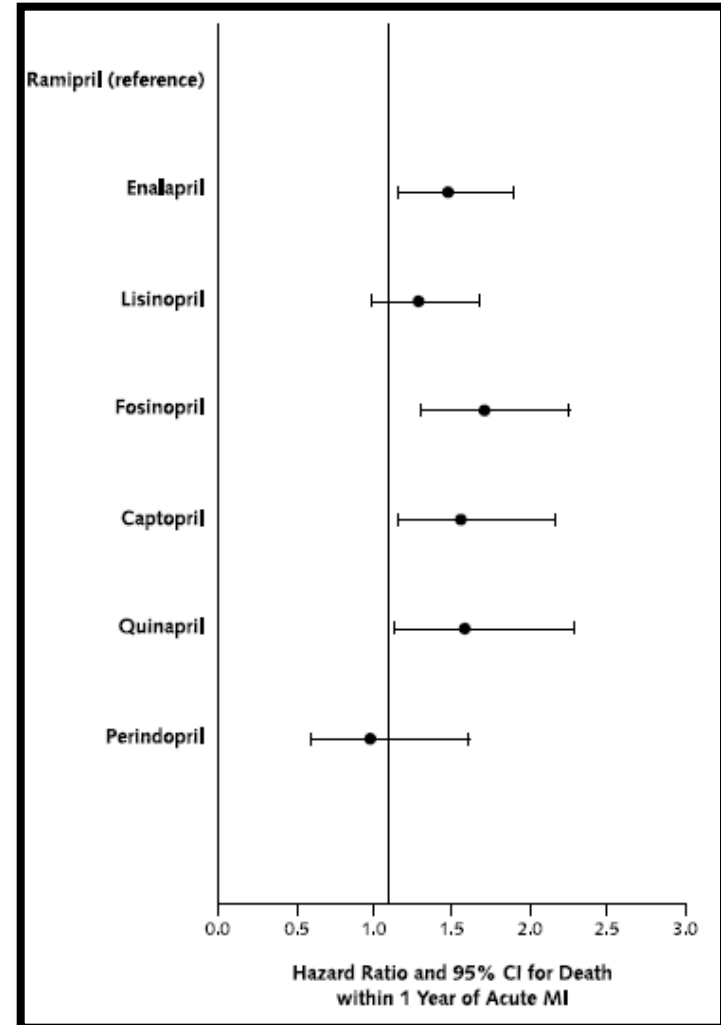
Mortality rates in elderly patients who take different angiotensin-converting enzyme inhibitors after acute myocardial infarction: a class effect?

Ann Intern Med. 2004 Pilote L. et al.

- Administrative database
- 109 hospitals in Quebec (N=7512)
- To evaluate whether all ACE inhibitors are associated with similar mortality

Survival benefits in the first year after acute MI differ according to the specific ACE inhibitor prescribed.

Ramipril was associated with lower mortality than most other ACE inhibitors.



Use of ACE-I in MI patients

| Early intervention trials (<24-36hr) | Late intervention trials (>48hr) |
|--|--|
| Largely unselected patients | Largely selected high-risk patients |
| ISIS-4 | SAVE |
| GISSI-3 | TRACE |
| CCS-1 | AIRE |
| CONSENSUS-2 | |
| SMILE | |

Use of ACE-I in MI patients

- Overall, in the trials most patients were treated with either fibrinolytic therapy or no reperfusion!!



ISIS-4 captopril vs. placebo

- 58,000 patients; 8 hr after MI
- ~70% treated with fibrinolysis
- Mortality benefit in 5 weeks – 7.2% vs. 7.7%
- No benefit was observed when the location of the infarct was other than anterior
- Rates of reinfarction, post infarction angina, cardiogenic shock and stroke were similar in both groups

CCS-1 captopril vs. placebo

- Over 13,000 patients
- 650 Chinese hospitals
- All cause mortality RR 0.93 , [95% CI 0.84-1.03]
- No mortality benefit in 35 days (9.1% vs 9.6; ns)

Consensus-II enalapril vs. placebo

- 6,090 patients
- Within 24hr of the onset of Acute MI

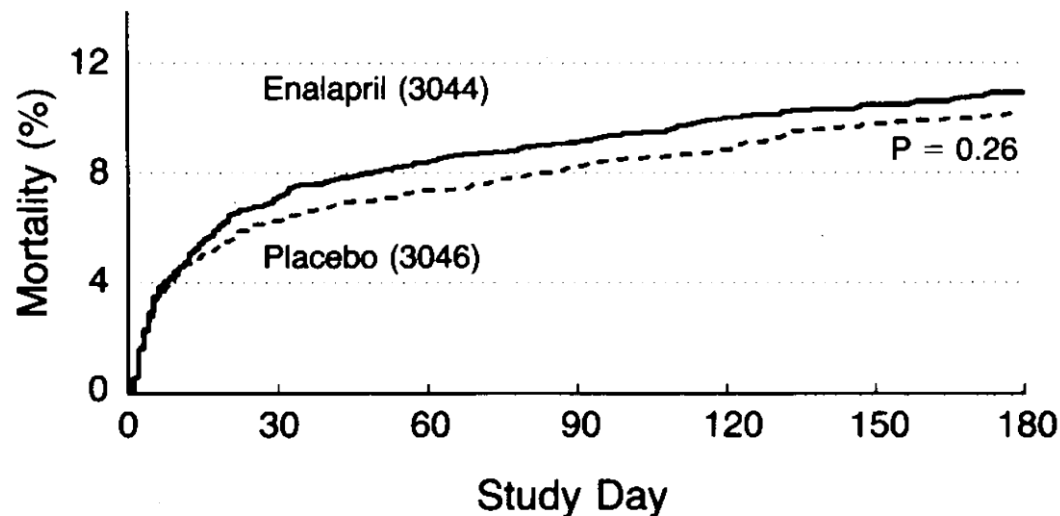
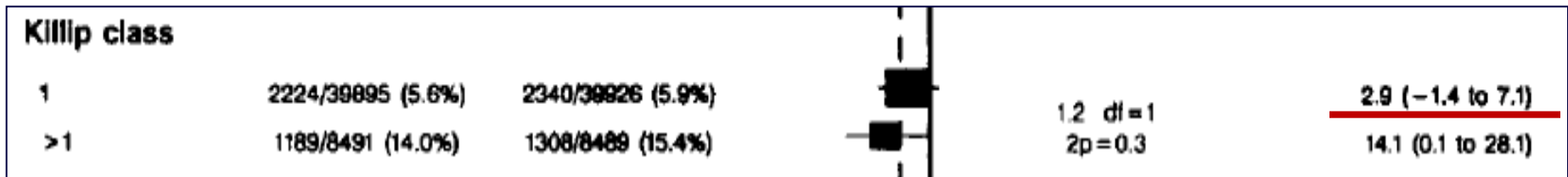
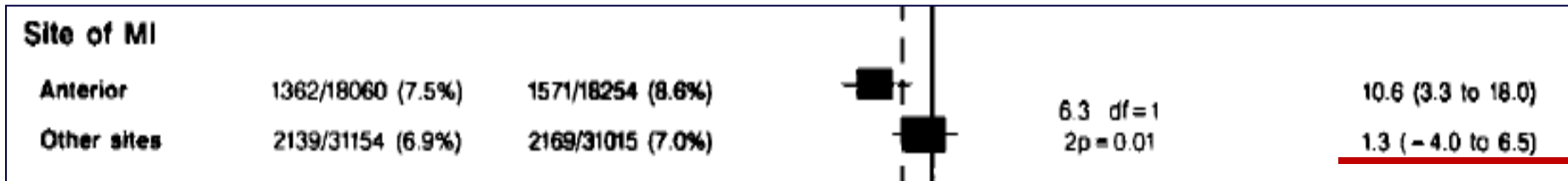


Figure 1. Kaplan-Meier Life-Table Mortality Curves for the Placebo and Enalapril Groups.

Indications for ACE Inhibitors in the Early Treatment of Acute Myocardial:
 Systematic Overview of Individual Data From 100 000 Patients in Randomized
 Infarction Trials. *Circulation*. 1998;97:2202-2212



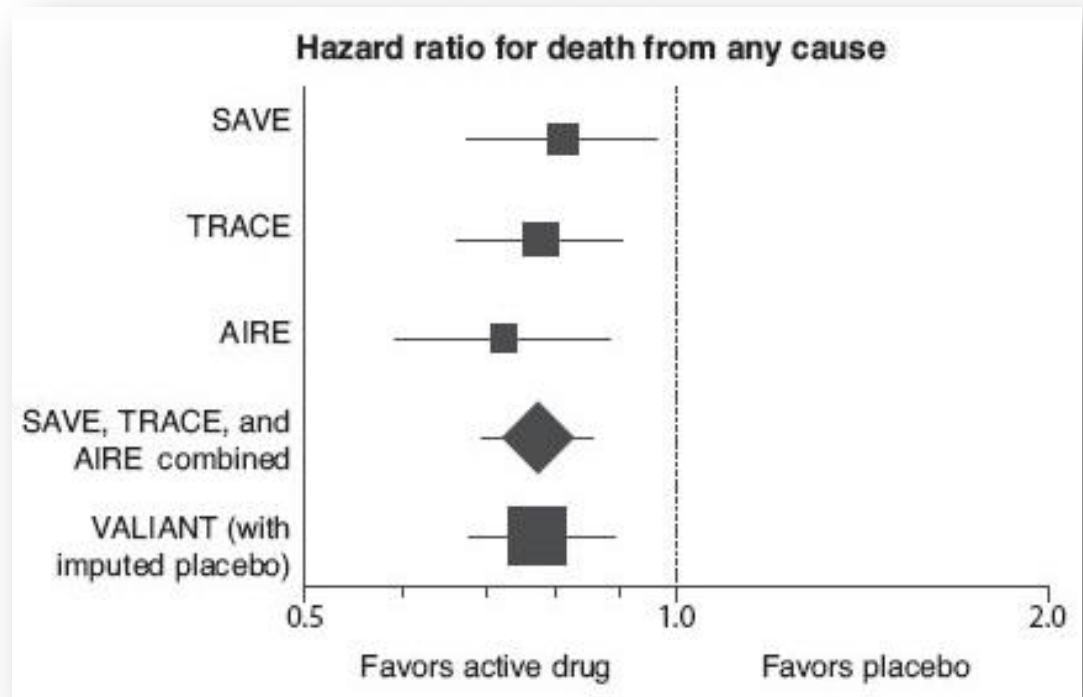
No clear benefit in lower risk groups

SAVE, TRACE trials

- Inclusion criteria- evidence of LV systolic dysfunction

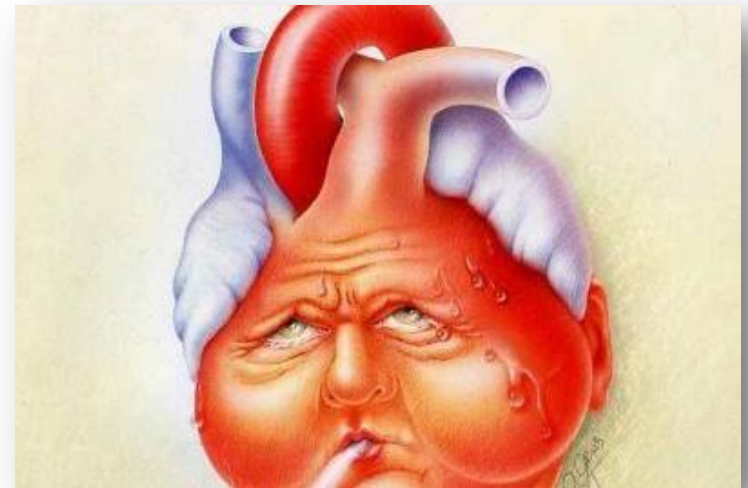
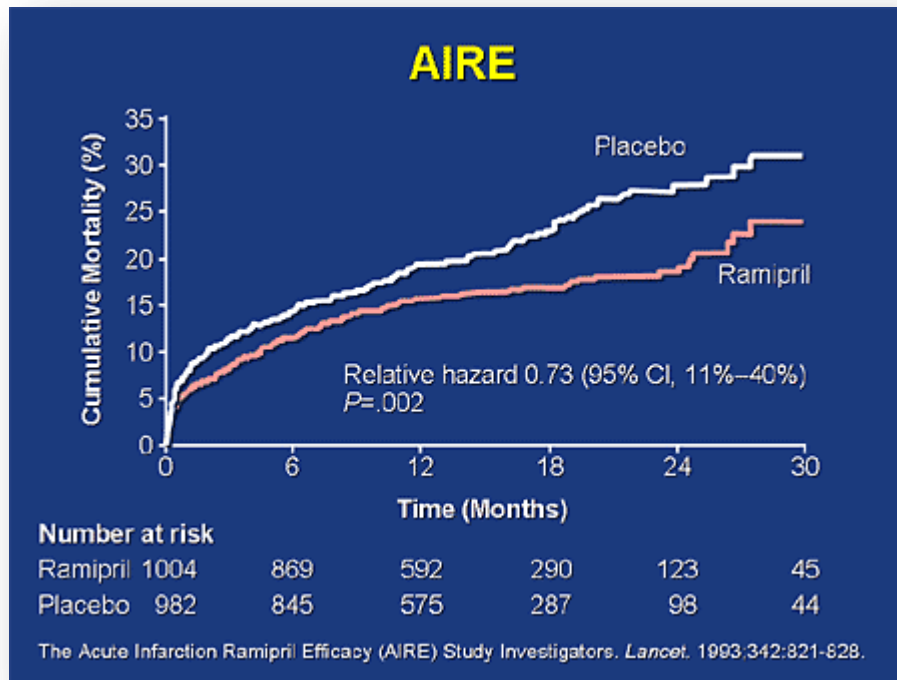
- SAVE- <40%

- TRACE- <35%



AIRE- Ramipril vs. placebo

- Inclusion criteria- clinical signs of heart failure



ARB's- OPTIMAAL 2002, VALIANT 2003

- Losartan, Valsartan
- Inclusion criteria – LVEF <35-40%
- No randomized trial for ARB's in STEMI patients with preserved LV function

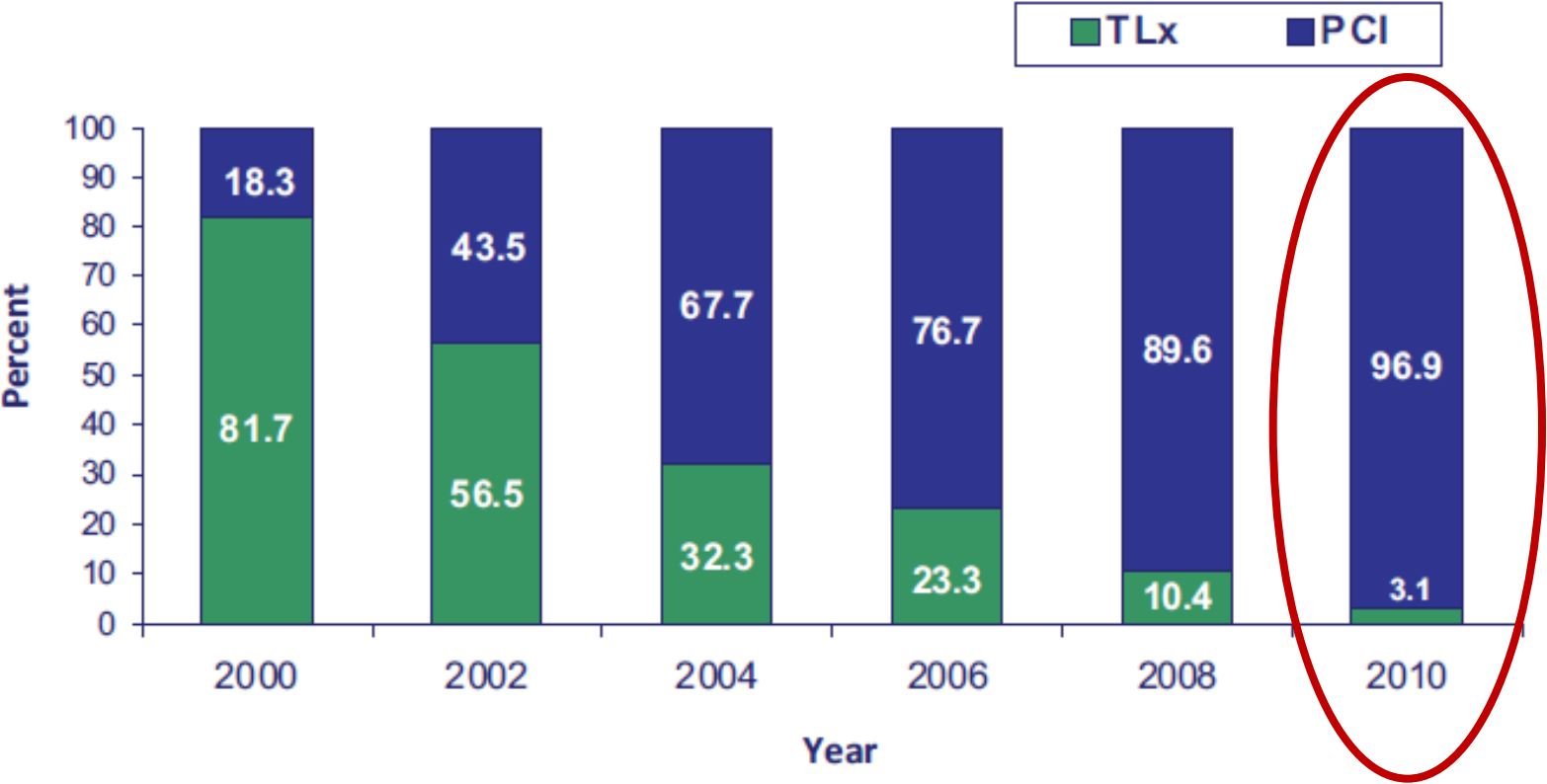
Current era- ACSIS 2000-2010

Table 2.14: Rates of Mortality and MACE by ECG on Admission

| Outcome | 2000 | 2002 | 2004 | 2006 | 2008 | 2010 | p for trend |
|--------------|---------|---------|---------|-------|-------|-------|-------------|
| ST ↑ | N=1,006 | N=1,011 | N=1,025 | N=895 | N=761 | N=776 | |
| Mortality: | | | | | | | |
| on discharge | 7.4 | 4.8 | 4.3 | 4.1 | 3.7 | 2.7 | <.0001 |
| 7-day | 7.3 | 5.0 | 4.3 | 4.3 | 4.1 | 2.7 | <.0001 |
| 30-day | 11.1 | 7.1 | 6.7 | 5.8 | 6.0 | 4.8 | <.0001 |

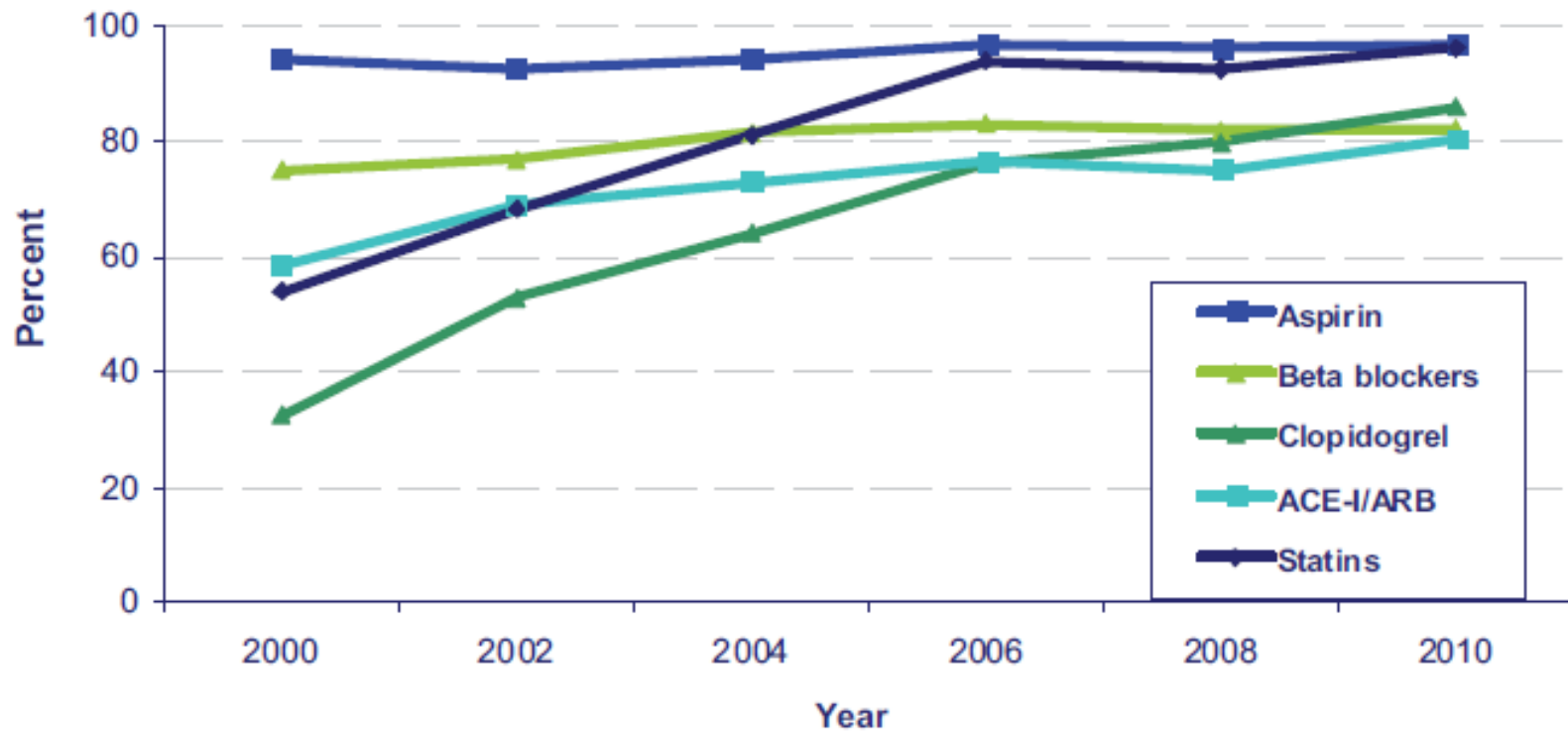
Current era- ACSIS 2000-2010

Type of Primary Reperfusion among Patients with ST Elevation



Current era- ACSIS 2000-2010

Figure 2.5: Medical Treatment on Discharge among Hospital Survivors



Compliance and medications reminders....

The image is a composite graphic. In the center, Uncle Sam, wearing his iconic top hat with a white star and stripes, points directly at the viewer. Below him, the text reads: "I WANT YOU To Take Your Medications". To the left, a thought bubble contains a purple rectangular app interface with the text "Med Time Compliance" at the top. Below the text are five circular icons: a sun, a gear, a crescent moon, and a vertical bar with a horizontal line. To the right, a partial line drawing of a person in a white lab coat is visible, with the text "r device" and "on?" appearing below it.

Pharm
w

r device
on?"

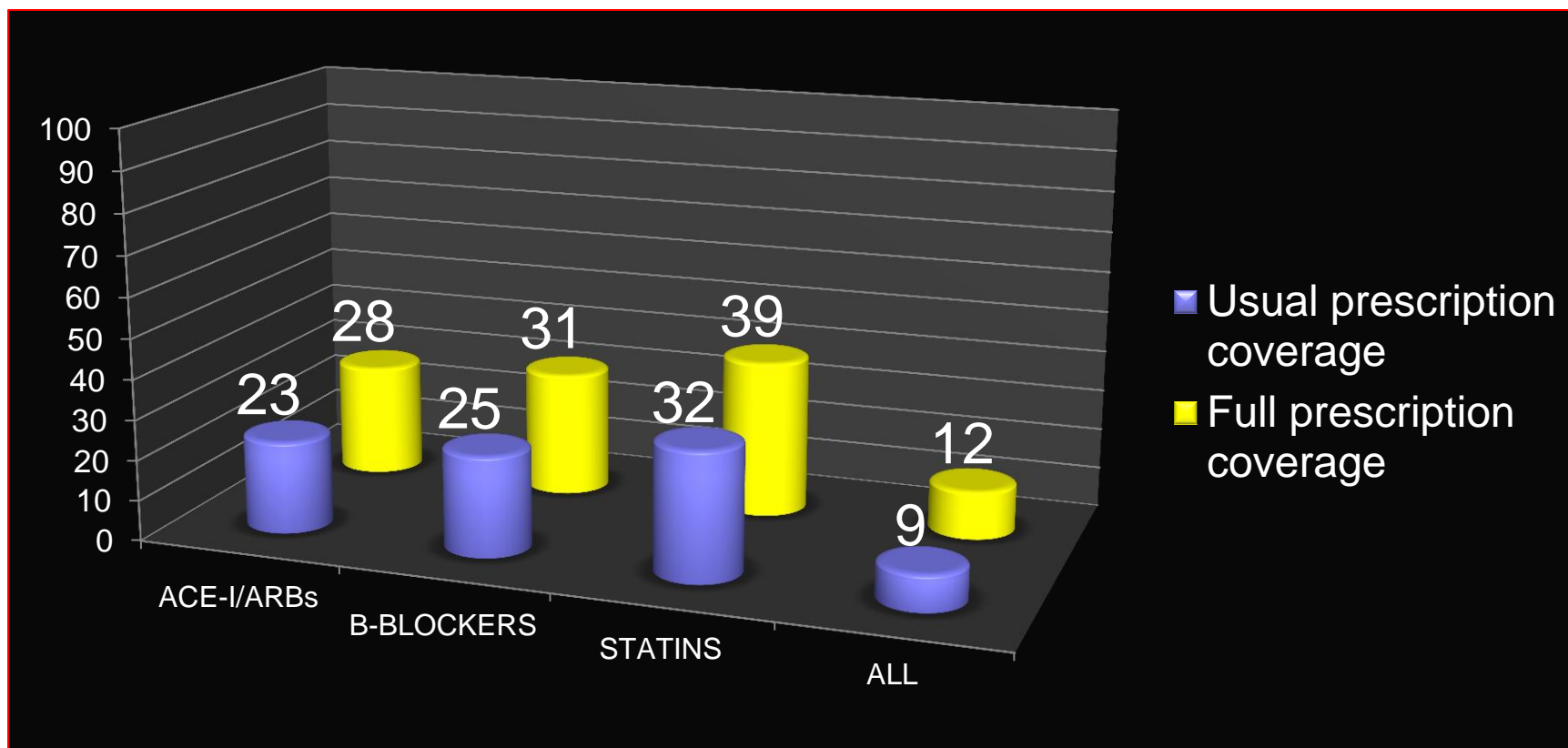
Post MI-FREEE trial (NEJM 2011)

- To evaluate the impact of full coverage for preventive medications after myocardial infarction on recurrent vascular events
- Full prescription coverage (N=2845) vs. usual prescription coverage (N=3010)
- Median duration of follow-up- 394 days



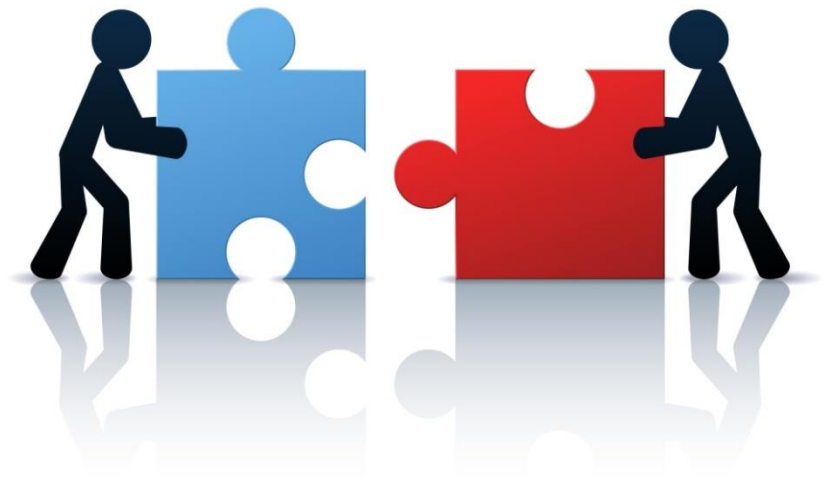
Full adherence- very poor!!!

(defined as a medication possession of $\geq 80\%$) to each and to all three study medication classes throughout follow-up



State-of-the-art treatment in low-risk STEMI patients with preserved LV function????

- ☑ Rapid reperfusion therapy (preferably primary-PCI)
- ☑ Aspirin
- ☑ P2Y12-inhibitors
- ☑ Statins
- ? β -blockers
- ? ACE-inhibitors



Thank you

