

Perioperative Medicine: Beta-blockers

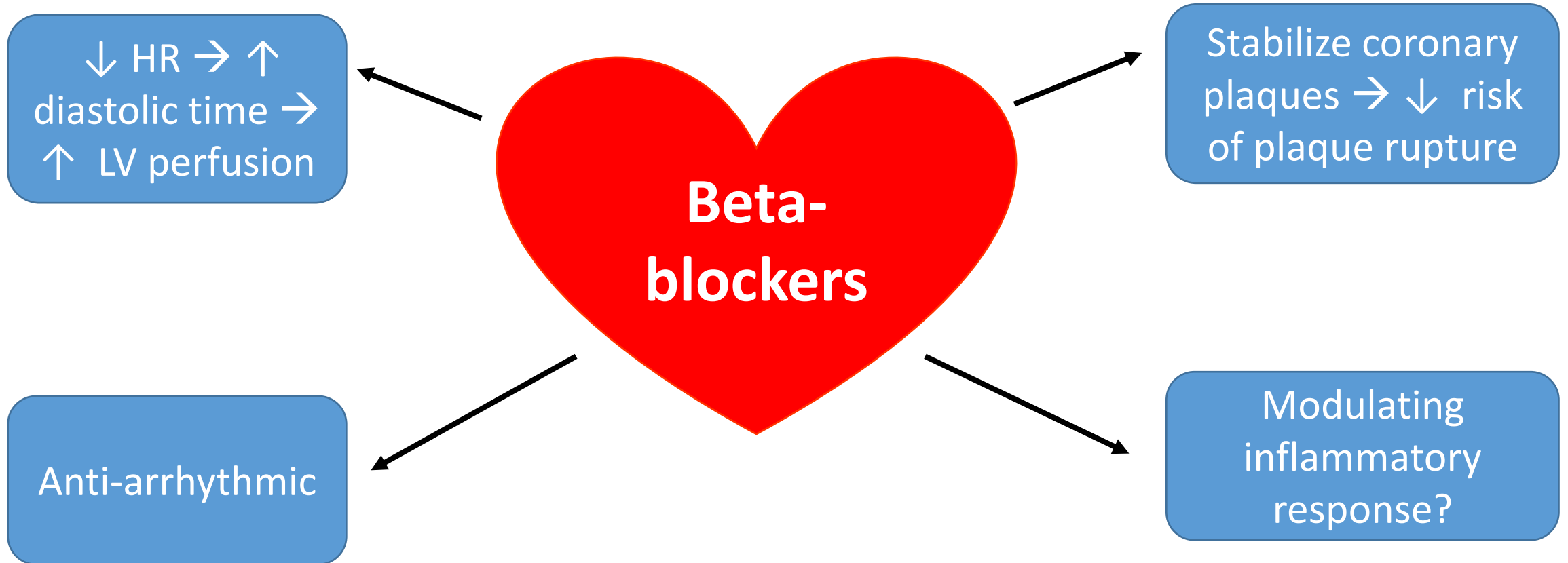
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Benefits of beta-blockers in non-cardiac surgery



The perioperative beta-blocker controversy

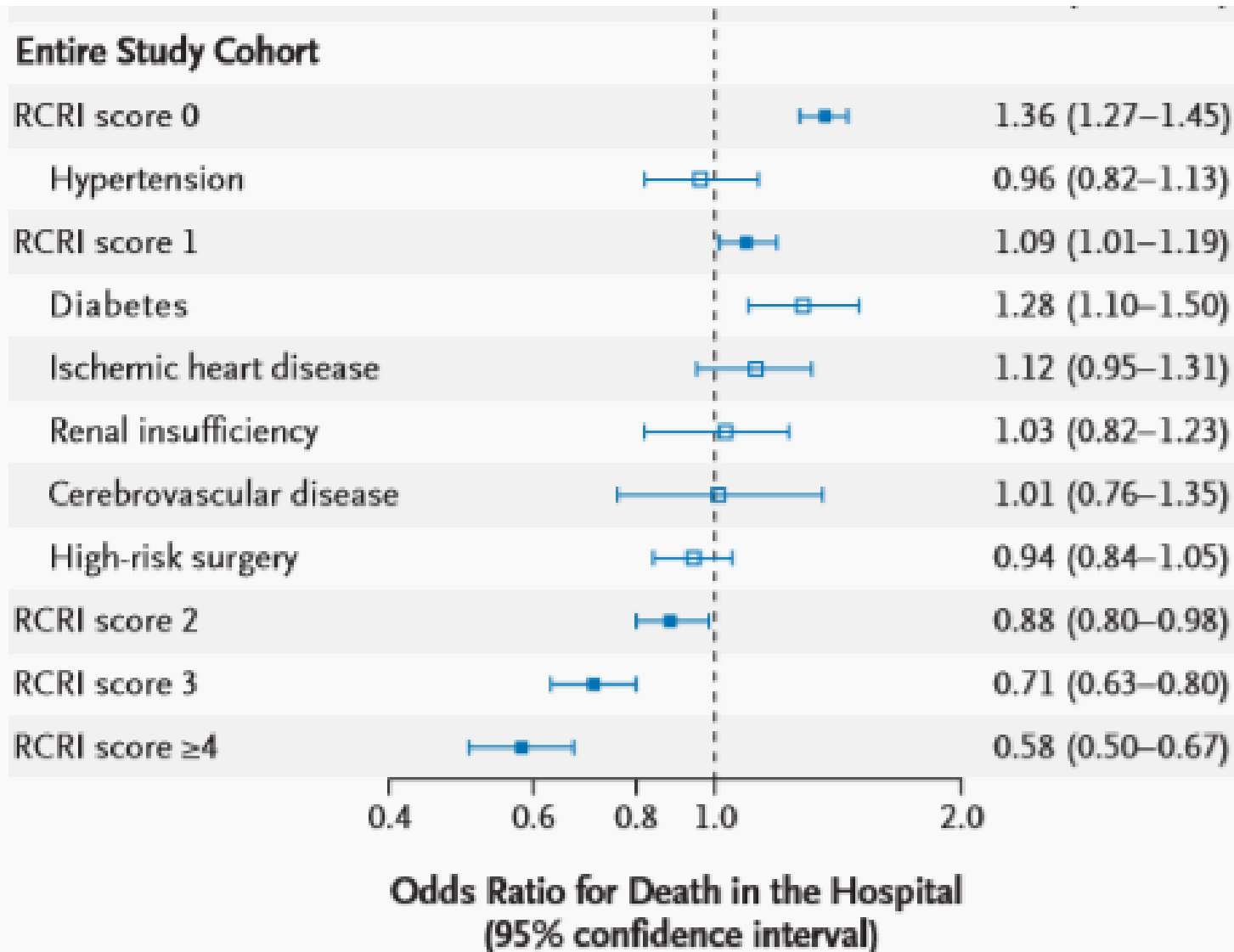
- In the 1990s, two RCTs (n=312) suggested that perioperative beta-blockers reduced perioperative MI and CV mortality^{1,2}
 - Studies were criticized for methodological flaws
 - Mangano study did not follow intention to treat principles¹
 - DECREASE I trial stopped early due to “large” benefit²

1. Mangano DT, et al. *N Engl J Med.* 1996 Dec 5;335(23):1713-20.
2. Poldermans D, et al. *N Engl J Med.* 1999 Dec 9;341(24):1789-94.

Lindenauer, et al (2005)

- Retrospective cohort study at hospitals across U.S.
- Assessed the use of perioperative beta-blockers and association with in-hospital mortality in routine clinical practice

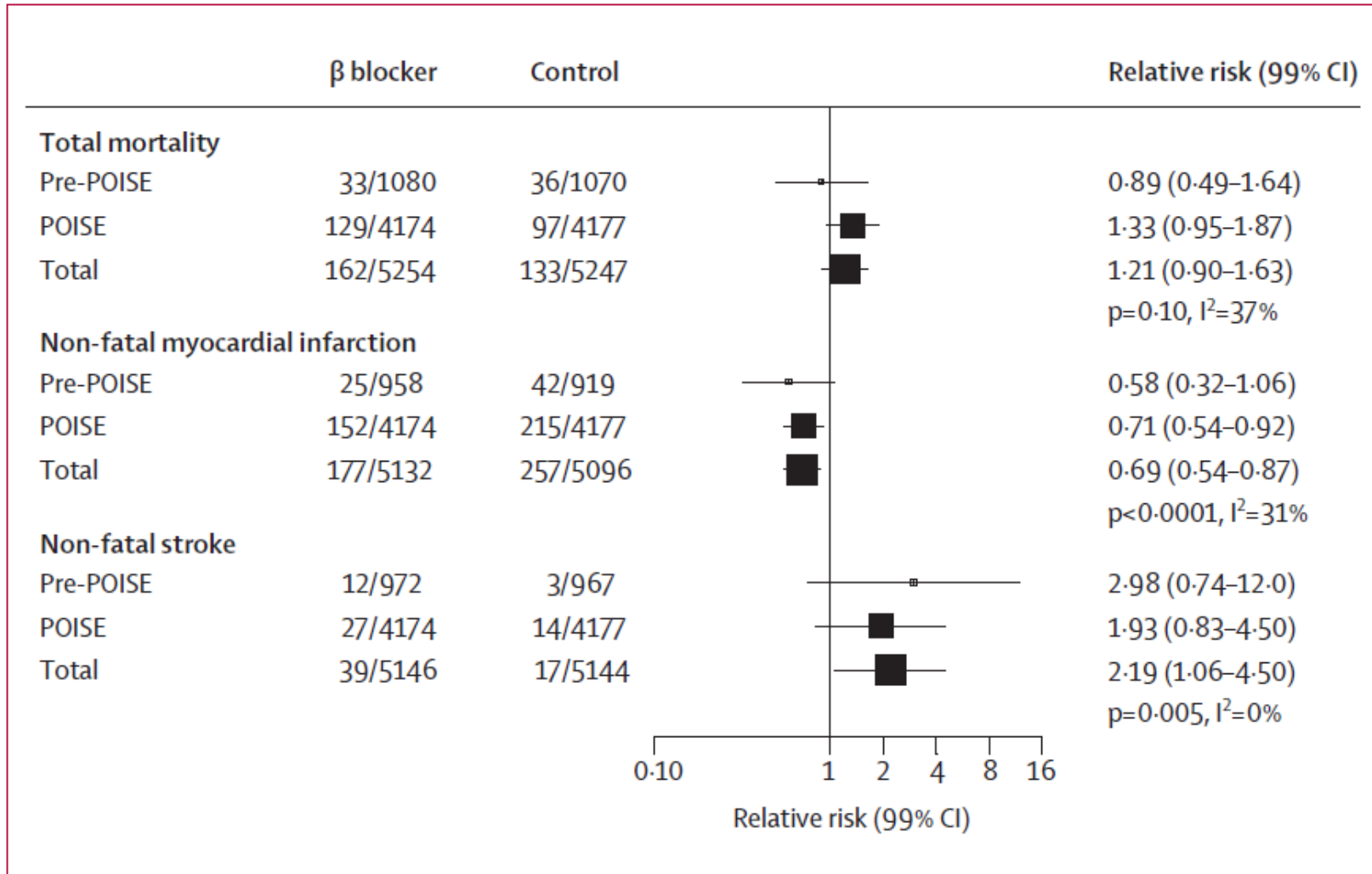
Beta-blockers and in-hospital mortality



POISE Trial (2008)

- Patients: 8351 patients at risk for perioperative cardiac events in 190 hospitals in 23 countries
- Intervention: Metoprolol 100 mg 2-4 hours pre-op, then metoprolol XL 200mg/day post-operatively
- Primary outcome: Composite of CV death, non-fatal MI, non-fatal cardiac arrest within 30 days

POISE Trial Results



POISE Trial Results

Compared to placebo, perioperative beta-blocker was associated with:

- ↓↓ in primary endpoint (HR 0.84; 95%CI 0.70-0.99)
- ↓↓ in MI (HR 0.73; 95%CI 0.60-0.89).
- ↑↑ in stroke (HR 2.17; 95%CI 1.26-3.74)
- ↑↑ in periop mortality (HR 1.33; 95%CI 1.03-1.74)

DECREASE IV trial (2009)

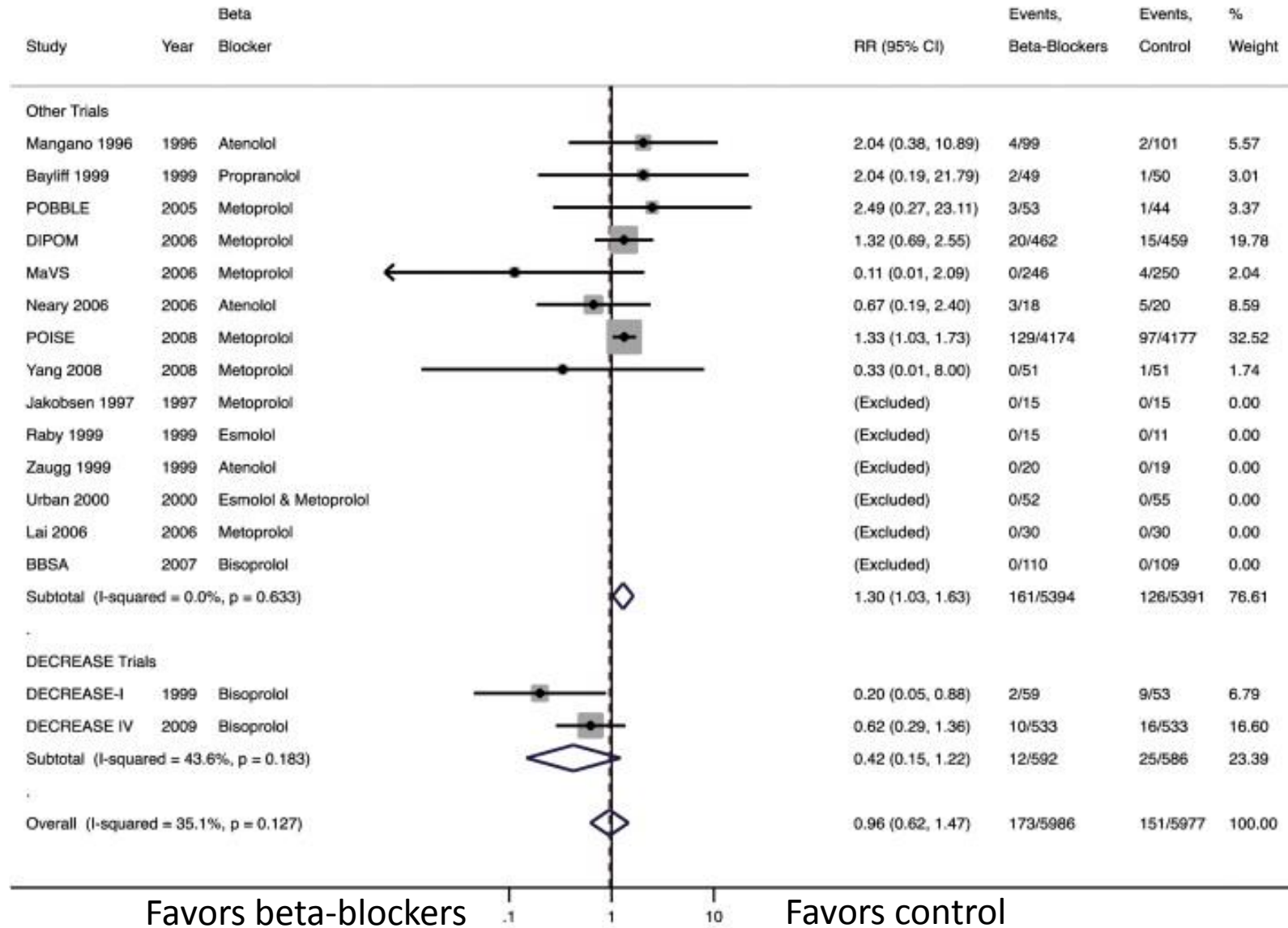
- DECREASE IV trial demonstrated a benefit of perioperative bisoprolol in reduction of cardiac death and non-fatal MI
- However, Dr. Polderman's research and results in the DECREASE trials have been questioned due to scientific misconduct

ACC/AHA systematic review (2014)

Perioperative Beta Blockade in Noncardiac Surgery: A Systematic Review for the 2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery

A Report of the American College of Cardiology/American Heart Association
Task Force on Practice Guidelines

ACC/AHA: beta-blockers and mortality



ACC/AHA systematic review (2014)

- “In summary, this systematic review found that perioperative beta blockade started within 1 day or less before noncardiac surgery helps prevent nonfatal MI but at the cost of increased risks of stroke, death, hypotension, and bradycardia.”

ACC/AHA systematic review (2014)

- With the exclusion of the DECREASE trials:
- “There are insufficient robust data on the efficacy and safety of perioperative beta-blocker regimens that use agents aside from metoprolol or initiate treatment 2 to 45 days prior to surgery”

ACC/AHA perioperative guidelines (2014)

- Beta blockers should be continued in patients undergoing surgery who have been on beta blockers chronically (*Class I, LOE B*)

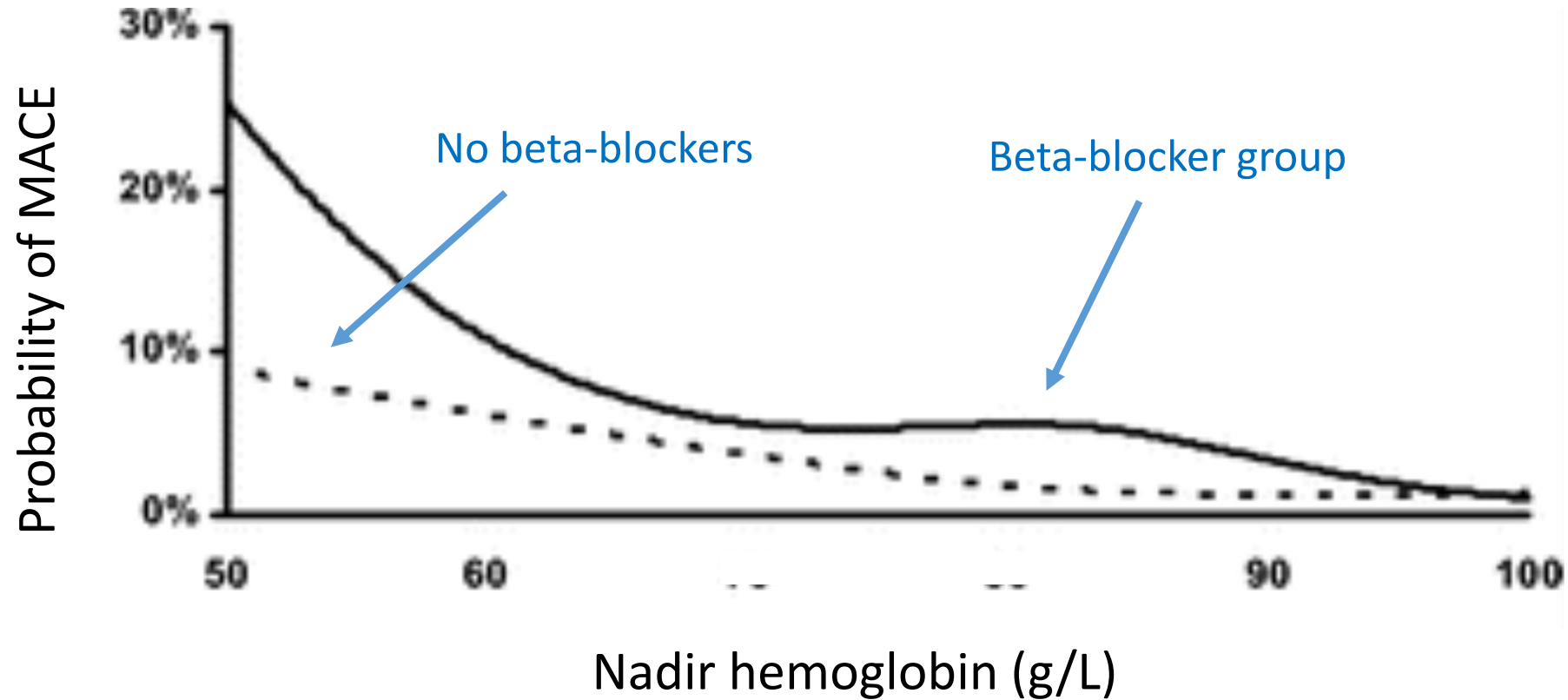
ACC/AHA perioperative guidelines (2014)

- In patients with intermediate- or high-risk myocardial ischemia noted in preoperative risk stratification tests, it may be reasonable to begin perioperative beta blockers (*Class IIb, LOE C*)
- In patients with RCRI ≥ 3 , it may be reasonable to begin beta blockers before surgery (*Class IIb, LOE B*)

ACC/AHA perioperative guidelines (2014)

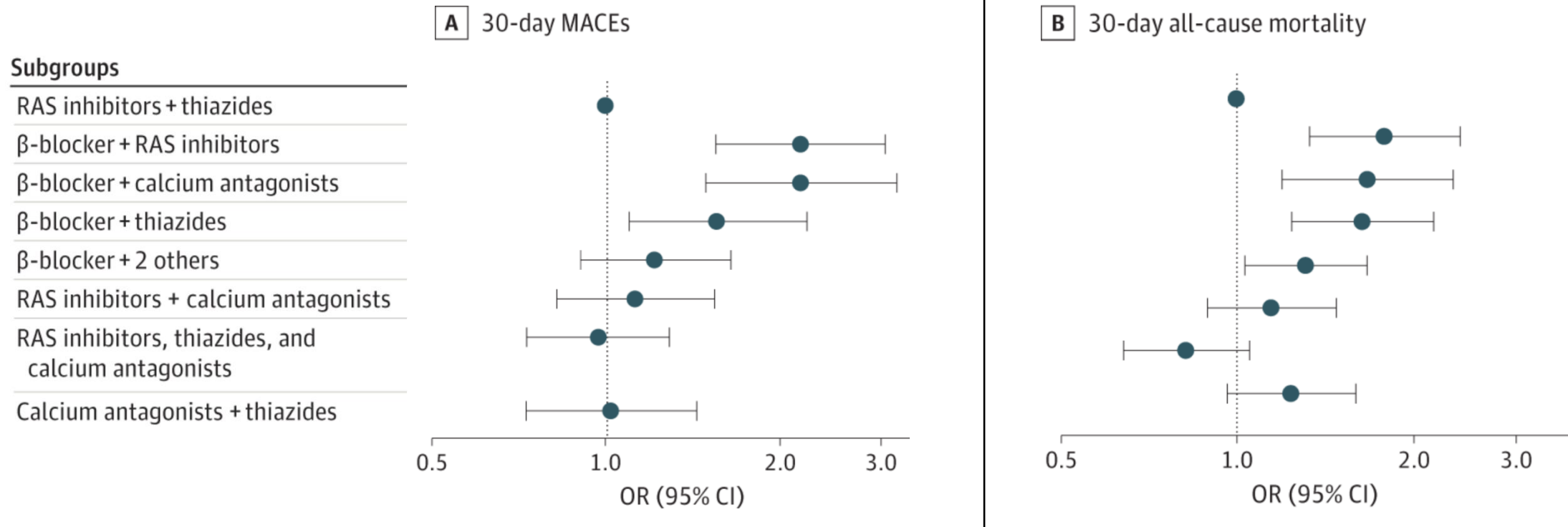
- In patients in whom beta-blocker therapy is initiated, it may be reasonable to begin perioperative beta blockers long enough in advance to assess safety and tolerability, preferably more than 1 day before surgery (*Class IIb, LOE B*)

Beta-blockers and acute anemia



MACE = Major Adverse Cardiovascular Event

Beta-blockers and uncomplicated HTN (2015)



Antihypertensive therapy with beta-blockers associated with \uparrow risk of perioperative MACE and all-cause mortality in patients with uncomplicated HTN.

Recommendations for perioperative beta-blockers

- Do not initiate on the day of surgery
- Continue chronic therapy if tolerated (even if for HTN)
- Do not initiate for uncomplicated HTN
- Consider pre-operative initiation if
 - Long-term indication (CAD, CHF, arrhythmia)
 - RCRI score > 3?
 - Able to start ≥ 1 week before surgery to ensure tolerance
- May be continued postoperatively if clinically safe (SBP > 100, HR > 55, no acute anemia)

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10. Fleisher LA, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130(24):2215-45
11. Beattie WS, et al. Acute Surgical Anemia Influences the Cardioprotective Effects of β -Blockade: A Single-center, Propensity-matched Cohort Study. *Anesthesiology*. 2010;112(1):25-33
12. Jørgensen ME, et al. β -blocker–associated risks in patients with uncomplicated hypertension undergoing noncardiac surgery. *JAMA Intern Med*. 2015;175(12)