What medication adjustments will help my pre-operative patient?: The results of the DECREASE-IV trial

- The DECREASE-IV trial is a prospective, open label, randomized controlled trial designed to assess if the perioperative administration of beta-blockers and/or statins improve cardiovascular related morbidity and mortality in patients with a 1%-6% risk of a perioperative cardiovascular event
  - Population: Patients ≥40 scheduled for elective noncardiovascular surgery with a perioperative risk of cardiovascular event of 1-6%.
  - Intervention: Perioperative Bisoprolol and/or Fluvastatin vs. Control
  - Findings: Bisoprolol was associated with a significant reduction of 30-day cardiac death and nonfatal MI (2.1% vs. 6.0%), while fluvastatin showed trend for improved outcome.
  - Relevance: No widely applicable perioperative cardiovascular risk reduction strategies for intermediate-risk patients have been developed. Intervention with Bisoprolol significantly reduces the incidence of perioperative cardiac death and MI without increasing morbidity or noncardiac mortality.

- Methods
  - Patients: 1066 patients with median age of 64, who were 60% male. Current beta-blocker or statin use precluded from participation. Surgeries included general (39%), urological (19%), orthopedic (16%) and ENT (12%).
  - Intervention/Comparison: Bisoprolol—starting at 2.5 mg and titrated to HR 50-70; Fluvastatin 80 mg daily, combination of Bisoprolol and Fluvastatin and a fourth group that received neither.
  - Outcome: (30 Day Follow-up Postoperatively)
    - Primary Endpoints: Cardiovascular Death, Non-fatal Myocardial Infarction
    - Secondary Endpoints: All-cause mortality, Cardiac Arrhythmias, Acute Heart Failure, Coronary Revascularization
    - Safety Endpoints: Stroke, Symptomatic Bradycardia/Hypotension, Clinically Significant Liver Dysfunction, CK 10>normal, Myopathy, Rhabdomyolysis

- Validity
  - Inclusion and exclusion criteria are appropriate and an attempt to randomize patients enrolled in the study is made. Although when evaluated by subgroups there are some differences it is unclear whether these are enough to be significant.
  - There is a paucity of information related to overall patient pool from which these patients were drawn
  - Basis of risk of perioperative cardiac event is not definitively clear but appears to be based on the Lee cardiac risk index—allowing for standardization with a verified staging protocol.
  - They were not able to obtain the sample size they estimated necessary to be able to detect the desired anticipated risk reduction.
  - Due to smaller sample sizes they were forced to combine groups, i.e. half the members of the bisoprolol group also received fluvastatin.
  - Data collection and analysis appear transparent, but closer analysis reveals some deficits, such as the accounting of the 2 deaths in the thirty day total mortality that actually occurred pre-operatively.

- Results
  - There was a 67% relative reduction in the incidence of cardiac death or MI in patients who received metoprolol.
  - There were no significant differences between the bisoprolol and the bisoprolol control groups in incidence of ischemic stroke or occurrence of beta-blocker related safety endpoints.
  - A reduction in the incidence of cardiac death or MI in patients who received fluvastatin was observed but not significant (note this combined fluvastatin alone and the combination therapy group).
  - There were no significant differences in incidence of stroke or occurrence of clinically significant liver dysfunction between the fluvastatin and control groups

- Application
  - The results of this study are very applicable to our population inasmuch as we have numerous patients who would fall into the Lee cardiac risk index category 1 or 2.
  - However the results of this study, although encouraging, must be weighed against evidence of research such as the POISE trial which show increased risk of stroke and mortality in the beta-blocker group. Also, differences in the designs of each study must be considered.
  - For patients who are Lee cardiac risk index category 1 or 2 with no history of stroke/TIA and adequate blood pressure I would use a beta blocker at least one month pre- and postoperatively.
GATE Frame:

- **Population:**
  - **Source:** 45,000 patients screened, Erasmus Medical Center Rotterdam
  - **Inclusion Criteria:** 6460
    - 78% on beta-blocker or statin
    - 5.5% did not provide informed consent/had previously participated
  - **Participant Population:** 1066