PRM124

Modelling Likely Cardiovascular Disease Mortality With PCSK9 Inhibitors Using a Synthetic Population

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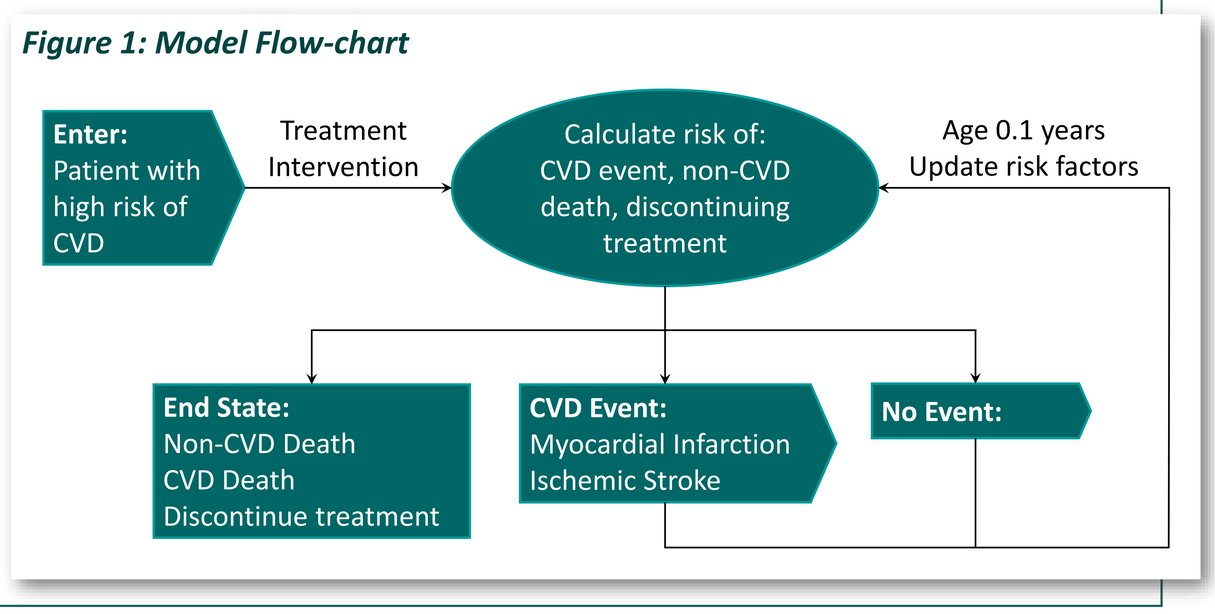
Objectives:

- A Cochrane review concluded that PCSK9 inhibitors reduce cholesterol levels and cardiovascular events but do not decrease mortality, however the largest study (FOURIER) included participants with low baseline LDL-cholesterol.
- To generate a synthetic population to **model the likely impact of PCSK9 inhibitors in a high risk population with LDL-C levels typical of the 4S study.**

Methods:

- Population characteristics were taken from the 4S study placebo group.
- **A synthetic population of 2,222 people** was generated that matched the placebo group characteristics on:
  - binary variables (gender, smoking status, diabetes);
  - continuous factors (age, BMI, systolic BP, total cholesterol: HDL cholesterol ratio, cigarettes and alcohol consumption).
- **A stochastic Markov model** was created in R using the Framingham points-based system for CVD events and calibrated to match the event outcomes in the 4S placebo group.
- Reduction in cholesterol with the PCSK9i evolocumab was taken from the FOURIER study, in which patients were already being treated with simvastatin.
  - Reduction in LDL for PCSK9 and statins was 61% and 25% respectively.
- We modelled 1,000 simulations for three treatment arms over 5.4 years:
  - **Simvastatin 20-40 mg daily;**
  - **Evolocumab 420 mg every 4 weeks;**
  - **Placebo.**
- At each cycle individuals could experience no change, CVD events or related death, non-CVD death, or treatment discontinuation.

Figure 1: Model Flow-chart



Results:

- Myocardial infarctions (MI), ischaemic strokes (IS) and CVD deaths were all lower in the PCSK9i group compared with the statin and placebo groups.
  - Differences were significant for IS events and CVD deaths, but not for MI events.

With reference to the placebo group outcomes we found:

- 28% reduction in MI mortality in the statin group, and 49% reduction in MI mortality in the PCSK9i group.
- 45% reduction in IS mortality in the statin group, and 70% reduction in IS mortality in the PCSK9i group.
- No differences in non-CVD-related deaths.

Figure 2: CVD events
Relative risk with reference to the control group

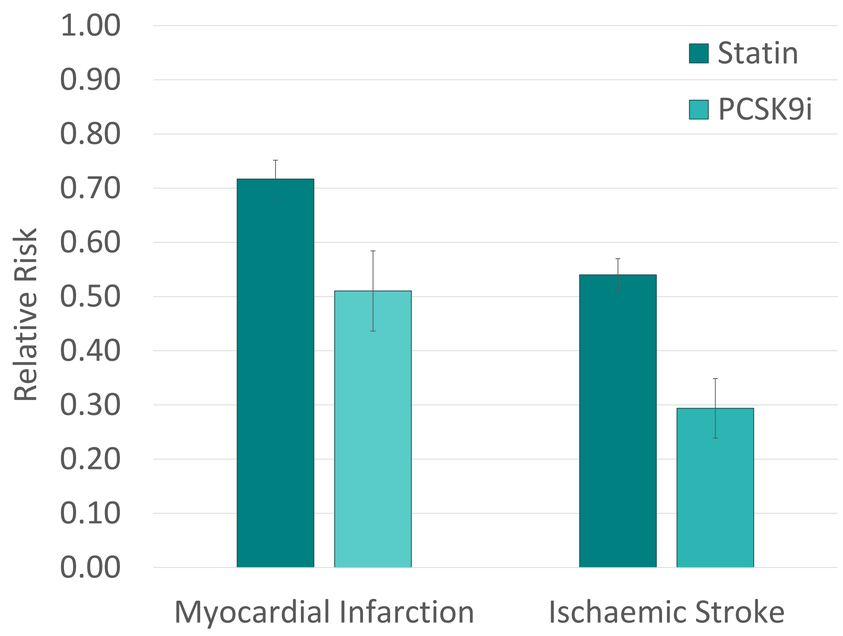
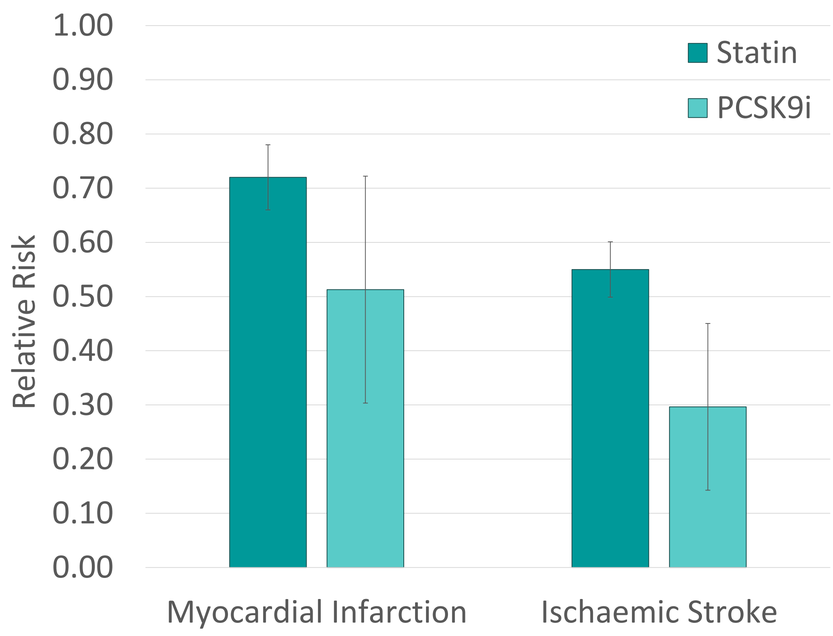


Figure 3: CVD related mortality
Relative risk with reference to the control group



Conclusions:

- Our model suggests that adding PCSK9is to statins in a higher-risk population could reduce CVD mortality compared with statins alone.
- The simulated sample is a rapid and low-cost approach to estimating treatment effects compared to a clinical trial.

Scan for supplementary data:

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