Development and Validation of a Coronary Risk Prediction Model for Older U.S. and European Persons in the Cardiovascular Health Study and the Rotterdam Study

I Background
- 10-year risk prediction of coronary heart disease is recommended
- Models include Framingham Heart Study, Women's Health Study, PROCAM, and SCORE project
- Elderly persons are under-represented or neglected in these models
- Competed causes of death may preclude CHD death

II Hypothesis of the study
- Develop and evaluate a population-based algorithm to predict coronary risk in elderly persons (CORE model) on the basis of traditional risk factors
- Add newer risk markers to improve algorithm

III Methods review
- TYPE: Prospective, cohort, population-based study from collaboration of 2 CV disease studies: Cardiovascular Health Study (CHS) in the US, and Rotterdam Study (RS) in Netherlands
  - CHS: ≥ 65 yo sampled from Medicare eligibility lists in 4 US communities
  - RS: ≥ 55 yo in suburb of Rotterdam, Netherlands
- POPULATION:
  - ≥ 65 yo
  - Free of definite CHD or cerebrovascular disease at baseline
  - 4946 CHS, 4303 RS patients
- ENDPOINT:
  - Time to first CHD
- STATISTICAL ANALYSIS
  - PRIMARY VARIABLES: Sex, systolic BP (treated or untreated), presence of DM, total/HDL cholesterol, smoking status
  - ADDITIONAL VARIABLES: BMI, CRP levels, ABI, carotid intima-media thickness, LVH on EKG
  - Competing-risk method used, based on Fine and Gray model
- EVALUATION OF MODELS
  - Evaluated the pooled model on each cohort individually
  - Models were fit to one cohort and evaluated in the other
  - Quantified discriminative ability up to 10 years of follow-up
  - Compared 10-year risk predictions between Framingham and CORE model via c-statistic
  - Also focused on high and low risk categorizations via net reclassification improvement [NRI]
  - Performed sensitivity analysis on those aged 65-79 comparing FPS
IV Results

- Median followup = 16.5 years
- 10-year cumulative incidences of CHD events:
  - Male: 19.9% & 15.8% in CHS & RS, respectively
  - Female: 11.5% & 10.4% in CHS & RS, respectively
- Non-coronary deaths exceeded CHD deaths (2000 & 2244 vs. 387 & 376) and increased more rapidly with age than CHD
- CHD prediction:
  - Risk factors generally associated with CHD equally between men and women (except total cholesterol predictive in European but not US women)
  - Systolic BP in men treated for HTN was not statistically significant
  - Smoking was only borderline statistically significant
  - c-statistic was moderate and lower in men then in women
    - (c-statistic, 0.63 in both U.S. and European men and 0.68 and 0.67 in U.S. and European women, respectively)
- Comparison between CORE and FPS:
  - c-statistic of FPS was 0.02 to 0.03 units lower than that of the CORE in both cohorts
  - In US:
    - CORE classified many more into high-risk group than FPS (47.7% vs. 22.5%)
    - In women, CORE model classified fewer events and nonevents as low-risk than the FPS (differences of 20.7% and 19.0%, respectively)
  - In Europeans:
    - In men, the CORE model classified fewer nonevents as high-risk (a difference of 14.2%) but at the expense of a 10.5% increase in events misclassified in lower risk strata
- Additional Risk Markers
  - Only EKG-LVH and low ABI were associated with CHD in both sexes (NRI of 2-4%)

V Authors conclusions

- Our model had moderate discrimination, its accuracy was not substantially better than the FPS, and adding newer coronary risk markers did not substantially improve risk prediction
- In contrast to risk scores based on models that ignore or censor competing events, our model provides real-life and therefore more meaningful estimates of CHD risk for elderly patients and physicians.
- The 10-year risk for CHD did not exceed ~20% in men or 15% in women, and the occurrence of noncoronary death dominated the occurrence of CHD. This observation refutes the perception that all elderly men are at high risk for CHD
- Because of the availability of effective treatment for CHD prevention with limited side effects, the increase in the true-positive rate (those who would correctly qualify for treatment) in U.S. men with the CORE model may outweigh the increase in the false-positive rate (those who would receive unnecessary preventive treatment). At the same time, very few U.S. women were classified as high-risk in both models, and therefore only a few women with future CHD events would have received preventive treatment.
• Excluding participants >80 yo did not lead to meaningful changes in our results. This is consistent with the observation that absolute risk for CHD stabilizes after age 80 years
• LIMITATIONS:
  o Cohorts differed ethnically, particularly in AA.
  o Differences in end-point ascertainment may have led to unknown difference in CHD incidence
  o CORE model was developed and compared in the same population
  o Re-classification evaluation did not discriminate between non-CHD events and non-events

VI Reviewers Critique
• Study labeled as prospective cohort study, yet the CORE model is designed retrospectively.
• Another source of error is Medical data which is possibly flawed.
• As authors mentioned, CORE model was developed and compared in same population. A proper cohort study would use the CORE model and test it on a third population and compare such records with FPS predictions.
• Regardless, as authors stated, CORE is not significantly better than the Framingham, which, although may be a Type II error, suggests that FPS is a good model.