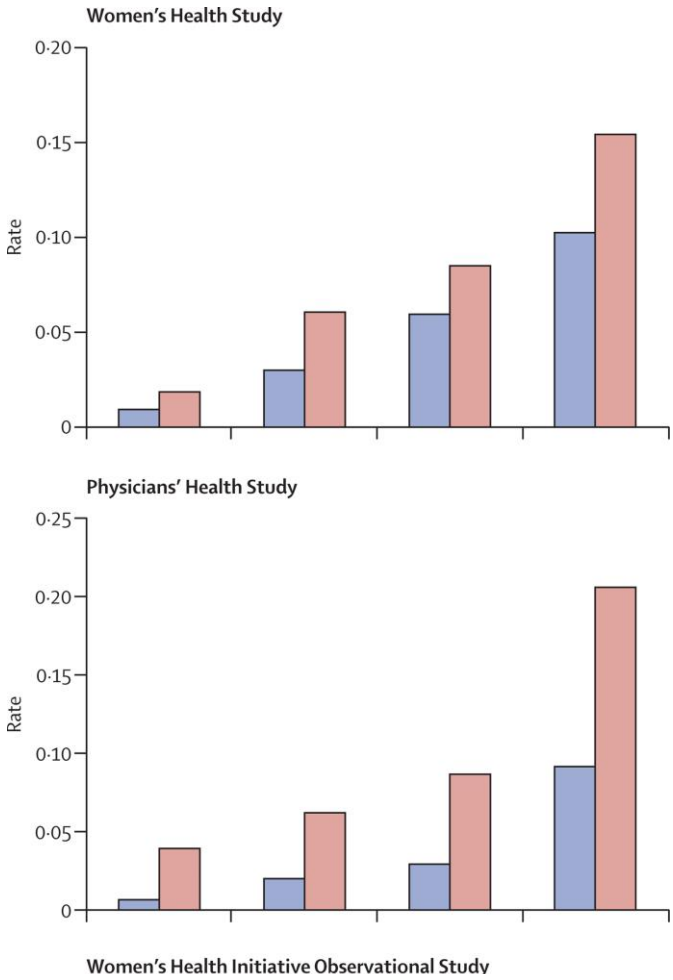
6.4.A Pooled Cohort Equations for estimating risk of cardiovascular events

For many preventive interventions, the balance of benefits and harms depends on the absolute risk of the event(s) to be prevented. Thus, guidelines for statin and aspirin treatment to prevent cardiovascular disease are based on the 10-year risk of heart disease or stroke, estimated using an online calculator (available at http://www.cvriskcalculator.com/).

However, Ridker and Cook(Ridker and Cook 2013, Cook and Ridker 2016, Ridker and Cook 2016) have found that the risk estimated from the pooled cohort equations is substantially higher than that observed in more recent cohorts. (Three examples are shown in Figure 1, from (Ridker and Cook 2013)).



A. Is this a problem with discrimination or calibration? Explain.

Figure: Comparison of observed event rates with event rates predicted by new ACC/AHA risk prediction algorithm in three external validation primary prevention cohorts: the Women's Health Study, the Physicians' Health Study, and the Women's Health Initiative Observational Study. Reprinted with permission. Reprinted from the Lancet, Vol. 382 Paul Ridker And Nancy Cook: Statins: new American guidelines for prevention of cardiovascular disease. Pages 1762-5, Copyright 2013 with permission from Elsevier.

B. The guidelines recommend estimating each subject's risk using a calcualtor, then managing based on whether the predicted 10-year risk is <5%, 5-7.4%, 7.5-9.9%, or ≥ 10%. Based on the description above, do the risk groupings in the figure represent quartiles of risk?

C. Explain briefly, step by step, how the numbers needed produce figures like the bar graphs above would be obtained.

D. In which cohort was the calculator most poorly calibrated? Explain your answer including any assumptions you had to make given your answer to (b) above.

e) As already mentioned, treatment recommendations are based on a patient's risk group as determined by the calculator. If we assume that, in fact, the risk calculator is overestimating risk, what more do we need to know about the recommended treatment thresholds to conclude that these overestimated risks will lead to excessive treatment? Explain.

f. Ridker and Cook(Ridker and Cook 2016) have pointed out that American Heart Association/American College of Cardiology (AHA/ACC) risk calculator was based on pooled cohort equations derived from cohorts that enrolled subjects from 1968 to 1990, whereas the contemporary external validation cohorts in which risk was found to be overestimated enrolled subjects 20-30 years later. During that time, death rates from cardiovascular disease (CVD) and coronary heart disease (CHD) were declining (figure).

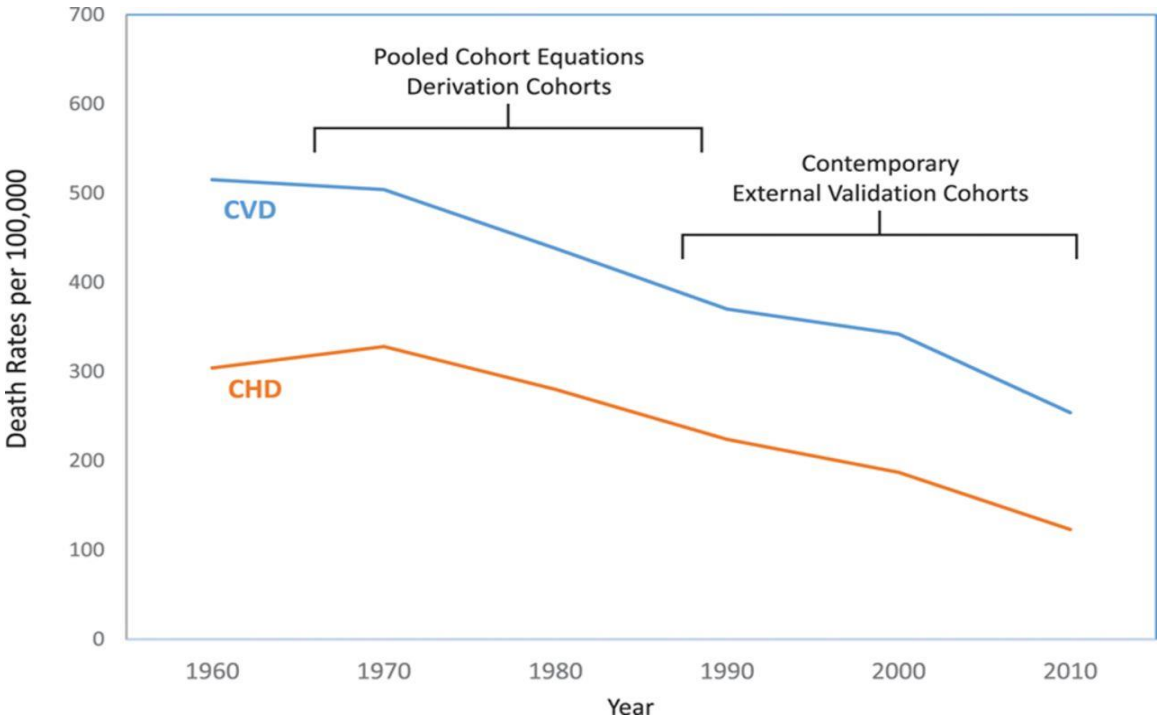


Figure. US death rates per 100 000 from cardiovascular disease (CVD) and coronary heart disease (CHD). From Ridker and Cook(Ridker and Cook 2016). (Open access article; figure reprinted with permission from the author.)

They wrote that data from these older cohorts "do not reflect the lower current rates of cardiovascular disease that largely result from secular shifts in smoking, diet, exercise, and blood pressure control." The calculator's inputs include current

smoking (yes or no), and levels of total cholesterol, HDL-cholesterol and systolic and diastolic blood pressure.

f) If secular shifts in cardiovascular risk factors are responsible for poor calibration, which of the above risk factors do you think are the most likely to be responsible?

g.) The secular decrease in CHD-death rates shown in the figure could also be partly due to widespread use of statins in later years. If you wish to use the calculator to help decide whether to start taking a statin, all else being equal, would it be better to have it be well calibrated for cohorts not taking statins, or cohorts in which statin use was common?