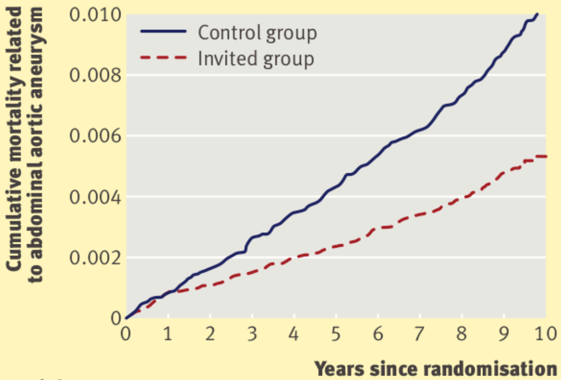
Rate Reductions: time-pattern

NOT SAME as if using . . . to ↓ (risk of) . . .

- ADULT CIRCUMCISION: (HIV).
  VACCINATION: (MEASLES, POLIO, ..),
  Ultrasound SCREENING: (AAA rupture)

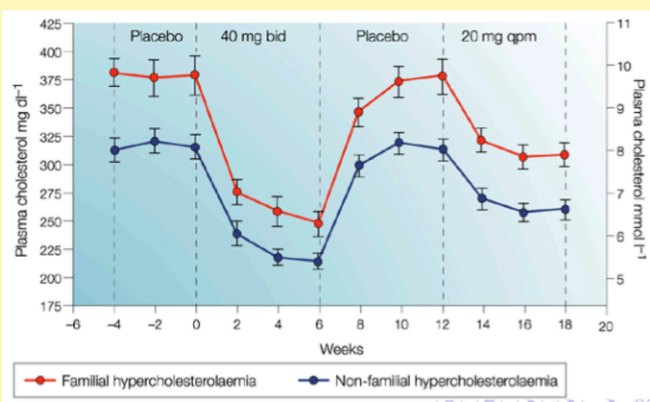


Men at risk

Control group	33 887	32 103	29 992	27 664	25 000	13 242
Invited group	33 883	32076	30 101	27 860	25 388	13 385

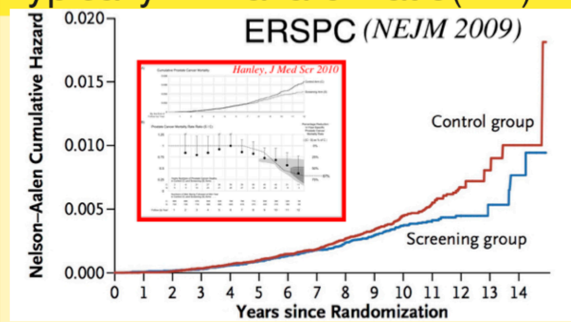
↓ **virtually <u>immediate</u>, and <u>sustained</u>**

- BLOOD THINNERS: (STROKE/MI)
  STATINS: LDL CHOLESTEROL

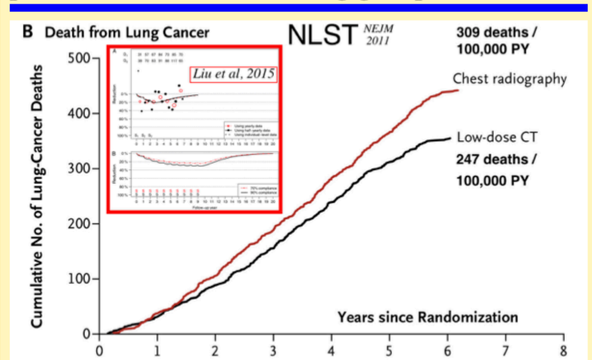


↓ **<u>disappears</u> when <u>agent removed</u>**

Typically: 1 Hazard Ratio(HR)



"Average f.-up: <u>8.8y</u>. **<u>Rate ratio</u>** for death from prostate cancer in screening group: **<u>0.80</u>**."



With **sustained** screening, the steady-state mortality reduction would be more than the 20% observed after just the 3 trial rounds.

Some time **after screening ceases, mortality rates revert** to those in unscreened, e.g., as in the 30 y. FOBT trial [next column]. Baker calls this dilution "post screening noise." Nor should there be mortality deficits in the 21st year if lung cancer screening lasted just 6 years.

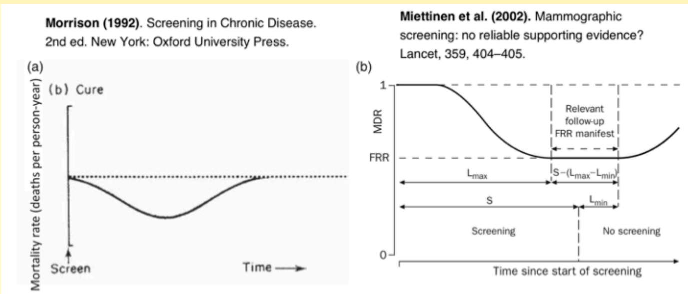
Bottom Line (1)

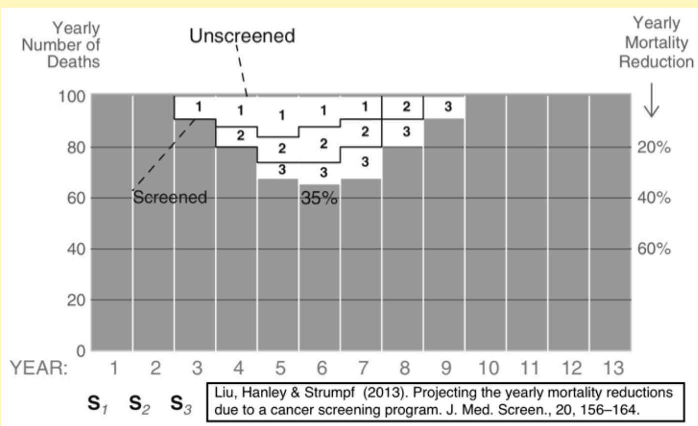
The unprincipled 1-number hazard-ratio (HR) measure ignores **1. how many** screens, **2. when** the **last screen** was, **3. when follow-up ended** or **4. when mortality deficits are expected to manifest.**

First Principles

Screening: pursuit of **earlier Dx** (& earlier Tx). Because of the **Detectability : Curability trade-off**, the course of many cancers, 'otherwise' fatal at $T = t$, is not altered by screen at $T = 0$. They are too early/late to be detected/cured. **Mortality deficits manifest after some delay, and disappear at some point after last screen.**

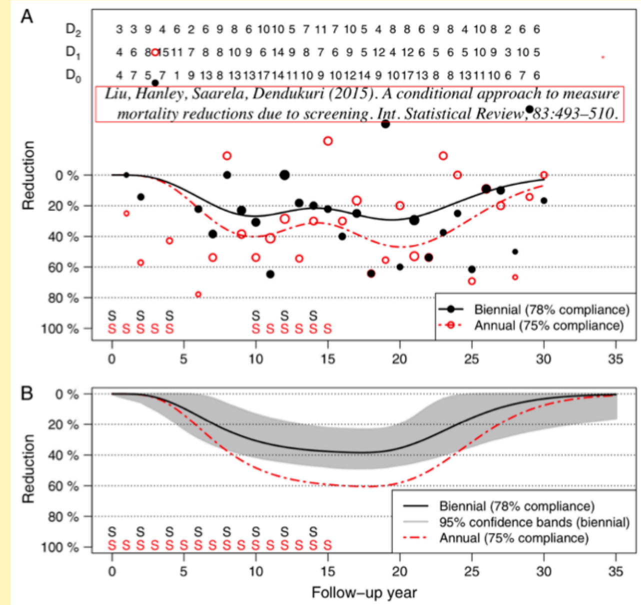
Principles → HR **function**



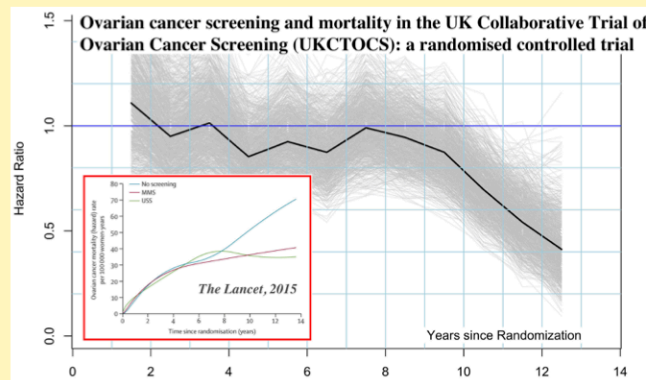


The **depth** & **duration** of the mortality deficits produced by **3** screenings. In women screened from 50-69, deficits would reach their max. at ≈ age 56 & maintain this level for many age-bins.

FOBT Screening. HR function



Ovarian Cancer. HR function



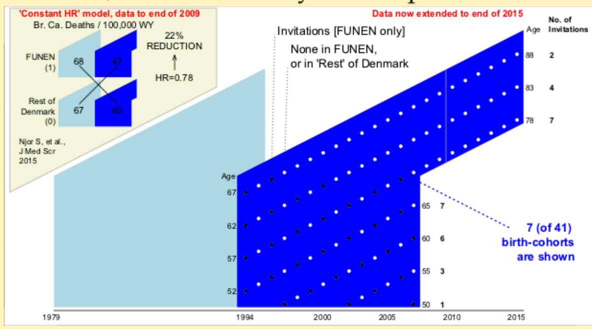
Bottom Line (2)

IT'S ABOUT TIME: to not just recognize the importance of the HR function & its determinants, but to use them in data analysis

Pop'l^n Mammography Programs

- **Norway** (NEJM): Some counties only in 2nd or 6th year, too short for full impact to manifest. (cf. Hanley, Epi Reviews , 2011)

- **Funen, Denmark**: 22 years' experience.



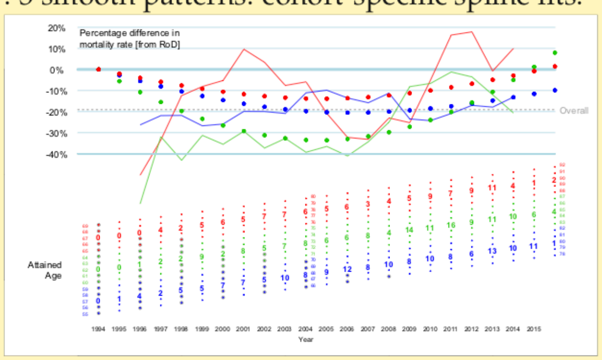
Funen-'RoD' differences in Rates

Average, and followup-year-specific, differences in breast cancer mortality, in 3 birth cohorts, each 5 years wide (color-coded). In modified Lexis diagram in bottom panel, grey circles indicate invitations to those Funen women who attained the indicated ages in the years indicated. Numbers are numbers of deaths from breast cancer in the 3 age-bands. Percentage differences in upper panel:

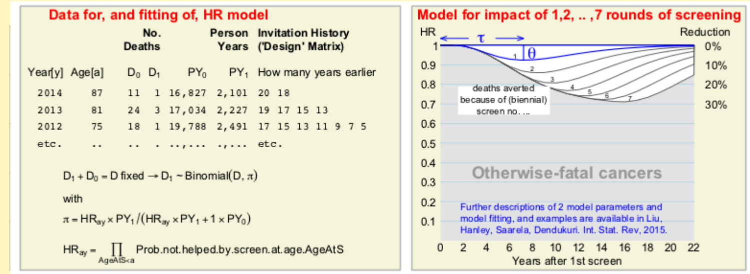
. Dotted line: age-year-matched M-H '**average**'.

. 3 lines: age-matched M-H **year-specific**.

. 3 smooth patterns: cohort-specific spline fits.

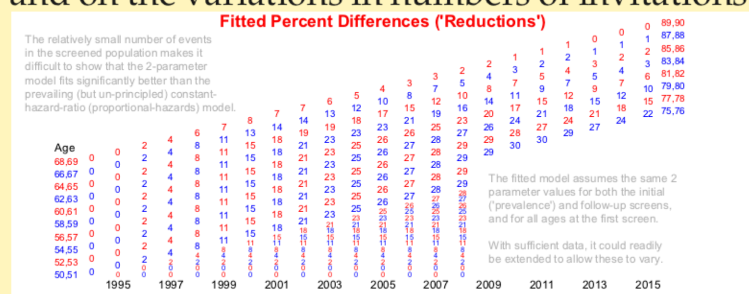


Effects of 1,2,3, ... , 7 screens



Fitted Percentage Reductions

Fitted reductions (%) based on parameters ($\hat{\tau}$, $\hat{\theta}$) of model for effect of 1 round of screening, and on the variations in numbers of invitations.



THE BOTTOM LINE

- This first principles model can use RCT or population data to pursue more realistic measures of mortality reductions, and better inputs for cost effectiveness calculations.
- To more precisely measure reductions due to mammography, we wish to collaborate with those already holding suitable population data.