Underestimation of Mortality Reductions in Cancer Screening Studies:

Prostate, Breast, Colon and [???] Lung

James A. Hanley

Department of Epidemiology, Biostatistics & Occupational Health, McGill University

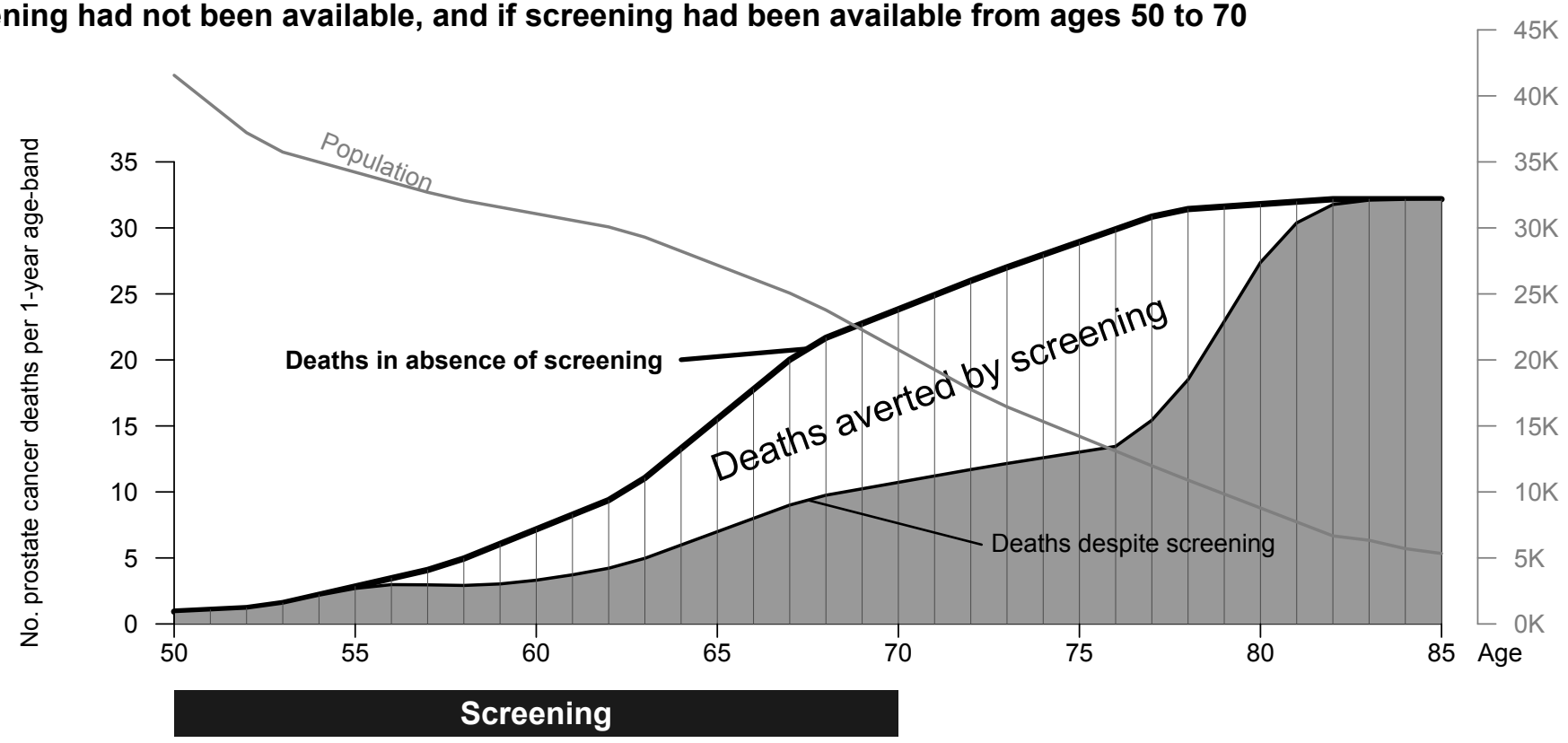
February, 2011

Outline

- The mortality reductions produced by a screening regimen: what payers want to know
- European Randomized Study of Screening for Prostate Cancer
- Data-analysis practice: studies of screening for breast, colon & lung ca.
- How to stop a screening RCT at a 20% mortality reduction? [Theorem]
- The way ahead

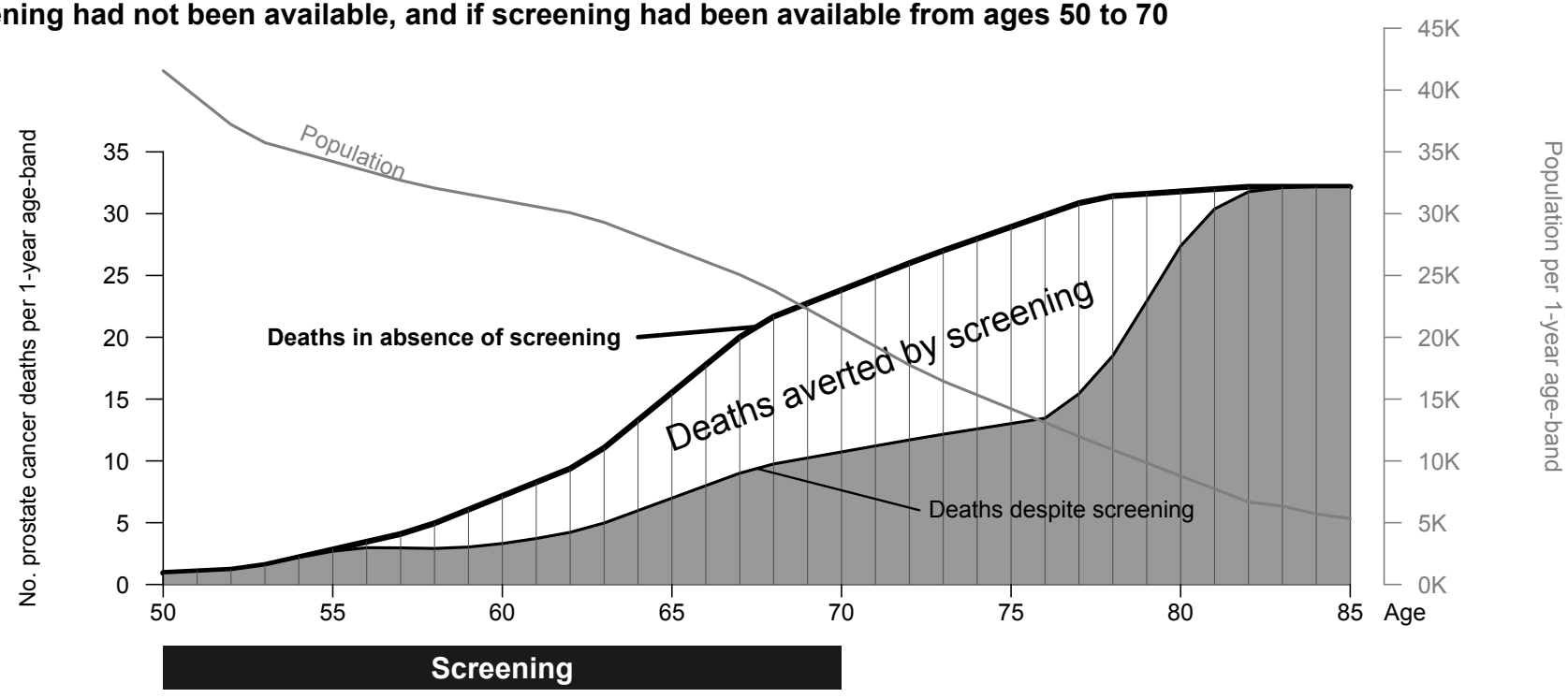
What payers would like to know...

(a) Age-specific numbers of prostate cancer deaths in a steady state population with a given age-structure, if screening had not been available, and if screening had been available from ages 50 to 70

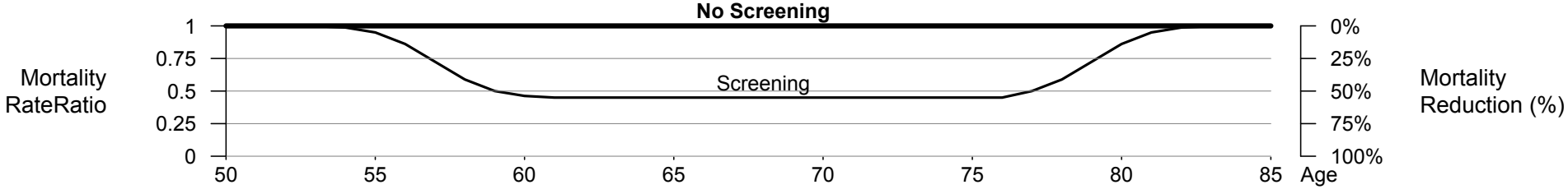


They could arrive at these numbers if they had...

(a) Age-specific numbers of prostate cancer deaths in a steady state population with a given age-structure, if screening had not been available, and if screening had been available from ages 50 to 70



(b) The corresponding age-specific prostate cancer mortality rate ratios



Can they obtain them from published reports?

- 1995 CETS (Québec) Report*: uncertain benefit / certain harms
- 2004 Amer. Coll. Physicians Report: likewise; 'overdiagnosis'
- 2005 RCT: Radical prostatectomy $>$ but $\not>$ watchful waiting in early Pr Ca
- 2009: European Randomized Study of Screening for Pr Ca (ERSPC)

* An Evaluation of benefits, unwanted health effect and costs. http://www.aetmis.gouv.qc.ca/site/home.phtml.

In all, 5 RCTs of Screening for Prostate Cancer

Trial: / Author:	Québec Labrie	Sweden[1] Sandbloma	Sweden[2] Kjellman	USA Andriole	Europe[†] Schröder
Began	1988	1987	1988	1993	1991
Last report	2004	2004	2009	2009	2009
No. men $\frac{\textit{Screening arm}}{\textit{Control arm}}$	$\frac{31{,}000}{15{,}000}$	$\frac{1{,}500}{7{,}500}$	$\frac{2{,}400}{24{,}000}$	$\frac{38{,}000}{38{,}000}$	$\frac{73{,}000}{89{,}000}$
Frequency of testing	?1y	3y	once	1y $\times$ 6	4y*
Duration of follow-up (y)	11	15	15	10	9
Screened $\geq$ once	$\frac{24\%}{7\%}$	$\frac{78\%}{?}$	$\frac{74\%}{?}$	$\frac{85\%}{52\%}$	$\frac{82\%}{??}$
No. Pr Ca deaths	$\frac{153}{75}$	$\frac{20}{97}$	$\frac{53}{506}$	$\frac{92}{82}$	$\frac{214}{326}$

[1] Norrköping [2] Stockholm

† Party-overlapping Göteborg experience, biennial screens, longer follow-up, published separately [Hugosson2010].

* Varied somewhat by country. ? Information not reported.

?? ERSPC-wide estimate not available; by 2006 in Rotterdam portion, 24% had had PSA tested at least once [Kerkhof, 2010]

ORIGINAL ARTICLE

Screening and Prostate-Cancer Mortality in a Randomized European Study

Fritz H. Schröder, M.D., Jonas Hugosson, M.D., Monique J. Roobol, Ph.D., Teuvo L.J. Tammela, M.D., Stefano Ciatto, M.D., Vera Nelen, M.D., Maciej Kwiatkowski, M.D., Marcos Lujan, M.D., Hans Lilja, M.D., Marco Zappa, Ph.D., Louis J. Denis, M.D., Franz Recker, M.D., Antonio Berenguer, M.D., Liisa Määttänen, Ph.D., Chris H. Bangma, M.D., Gunnar Aus, M.D., Arnauld Villers, M.D., Xavier Rebillard, M.D., Theodorus van der Kwast, M.D., Bert G. Blijenberg, Ph.D., Sue M. Moss, Ph.D., Harry J. de Koning, M.D., and Anssi Auvinen, M.D., for the ERSPC Investigators*

ABSTRACT

BACKGROUND

The European Randomized Study of Screening for Prostate Cancer was initiated in the early 1990s to evaluate the effect of screening with prostate-specific–antigen (PSA) testing on death rates from prostate cancer.

METHODS

We identified 182,000 men between the ages of 50 and 74 years through registries in seven European countries for inclusion in our study. The men were randomly assigned to a group that was offered PSA screening at an average of once every 4 years or to a control group that did not receive such screening. The predefined core age group for this study included 162,243 men between the ages of 55 and 69 years. The primary outcome was the rate of death from prostate cancer. Mortality follow-up was identical for the two study groups and ended on December 31, 2006.

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Schröder at the Erasmus Medical Center, P.O. Box 2040, Rotterdam 3000 CA, the Netherlands, or at secr.schroder@erasmusmc.nl.

*Members of the European Randomized Study of Screening for Prostate Cancer (ERSPC) are listed in the Appendix.

This article (10.1056/NEJMoa0810084) was published at NEJM.org on March 18, 2009.

N Engl J Med 2009;360:1320-8.

ERSPC Results and "Conclusions"

"During a median follow-up of 9 years, the prostate cancer mortality rate ratio in the screening group, as compared with the control group, was 0.80 (95% confidence interval [CI], 0.65 to 0.98; adjusted P=0.04). The absolute risk difference was 0.71 death per 1000 men."

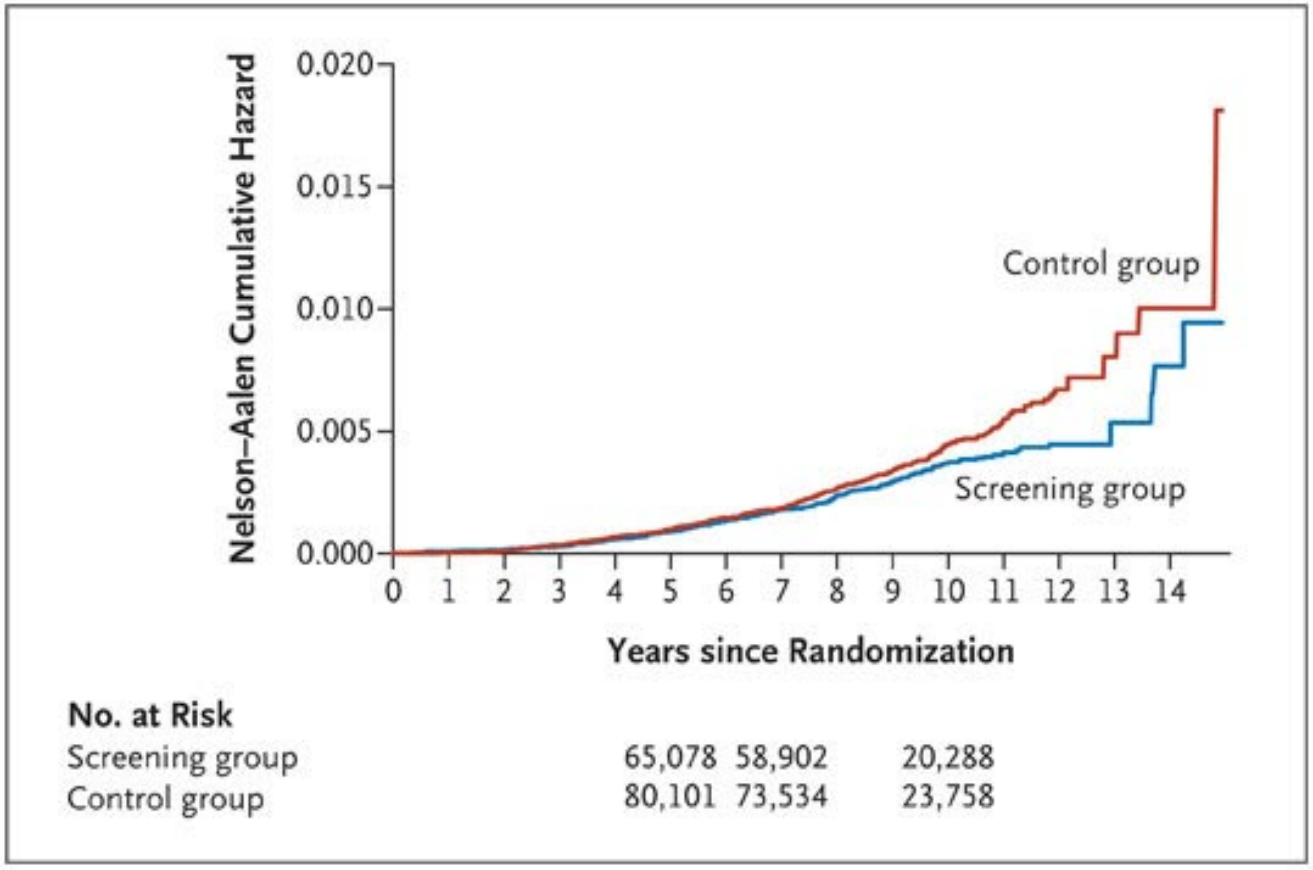
Number Needed... to Screen: 1410; to Treat: 48

"The analysis of men who were actually screened during the first round (excluding subjects with noncompliance) provided a rate ratio of 0.73 (95% CI, 0.56 to 0.90)."

CONCLUSIONS

"PSA-based screening reduced the rate of death from prostate cancer by 20%."

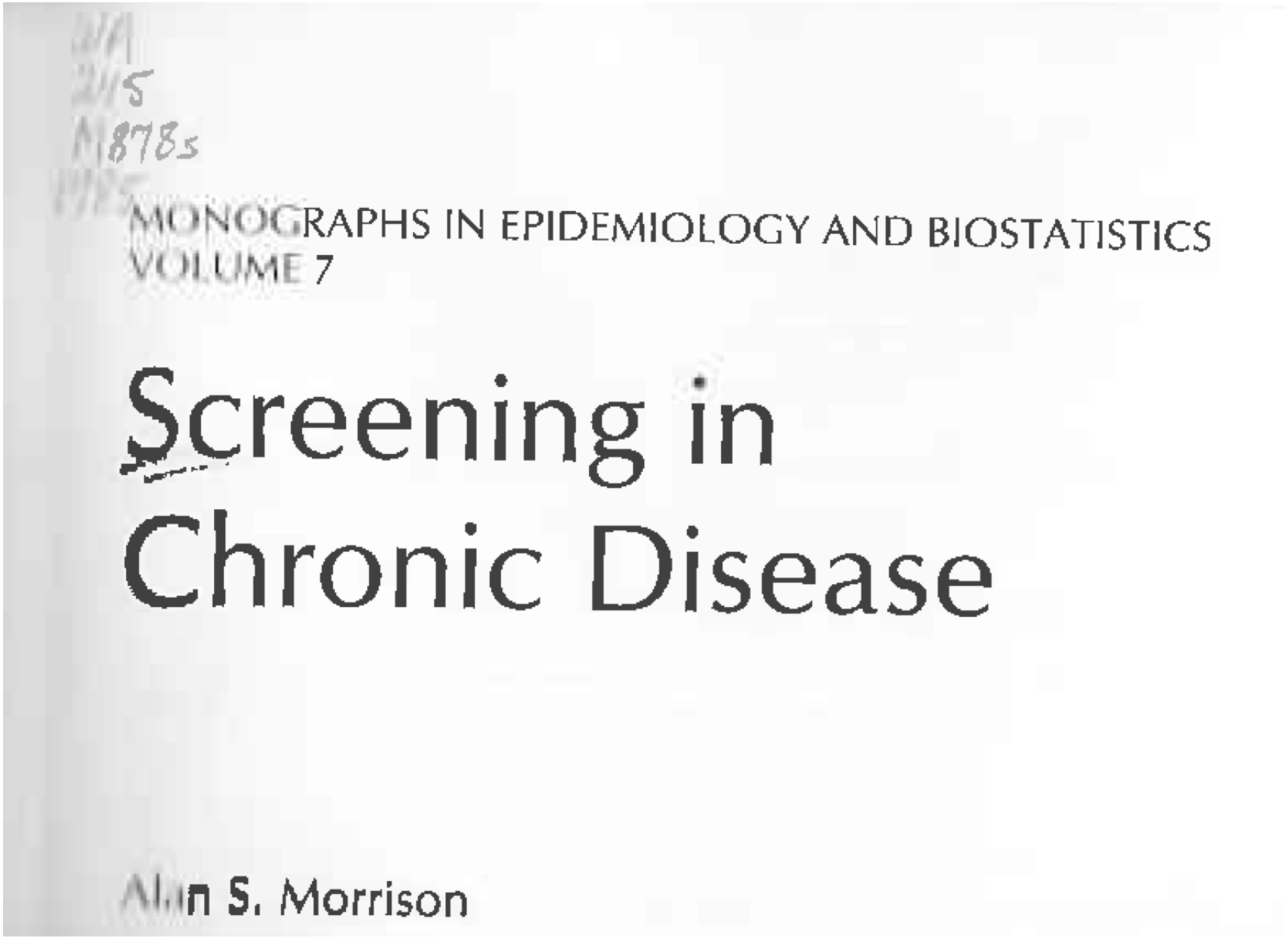
Cumulative Risk of Death from Prostate Cancer.



As of December 31, 2006, with an average follow-up time of 8.8 years, there were 214 prostate-cancer deaths in the screening group and 326 in the control group. Deaths that were associated with interventions were categorized as being due to prostate cancer. The **adjusted rate ratio** for death from prostate cancer in the screening group was **0.80** (95% CI, 0.65 to 0.98; P=0.04). The Nelson-Aalen method was used for the calculation of cumulative hazard.

NEJM, March 2009.

Expected 'Response function': Guidance from 1985 textbook



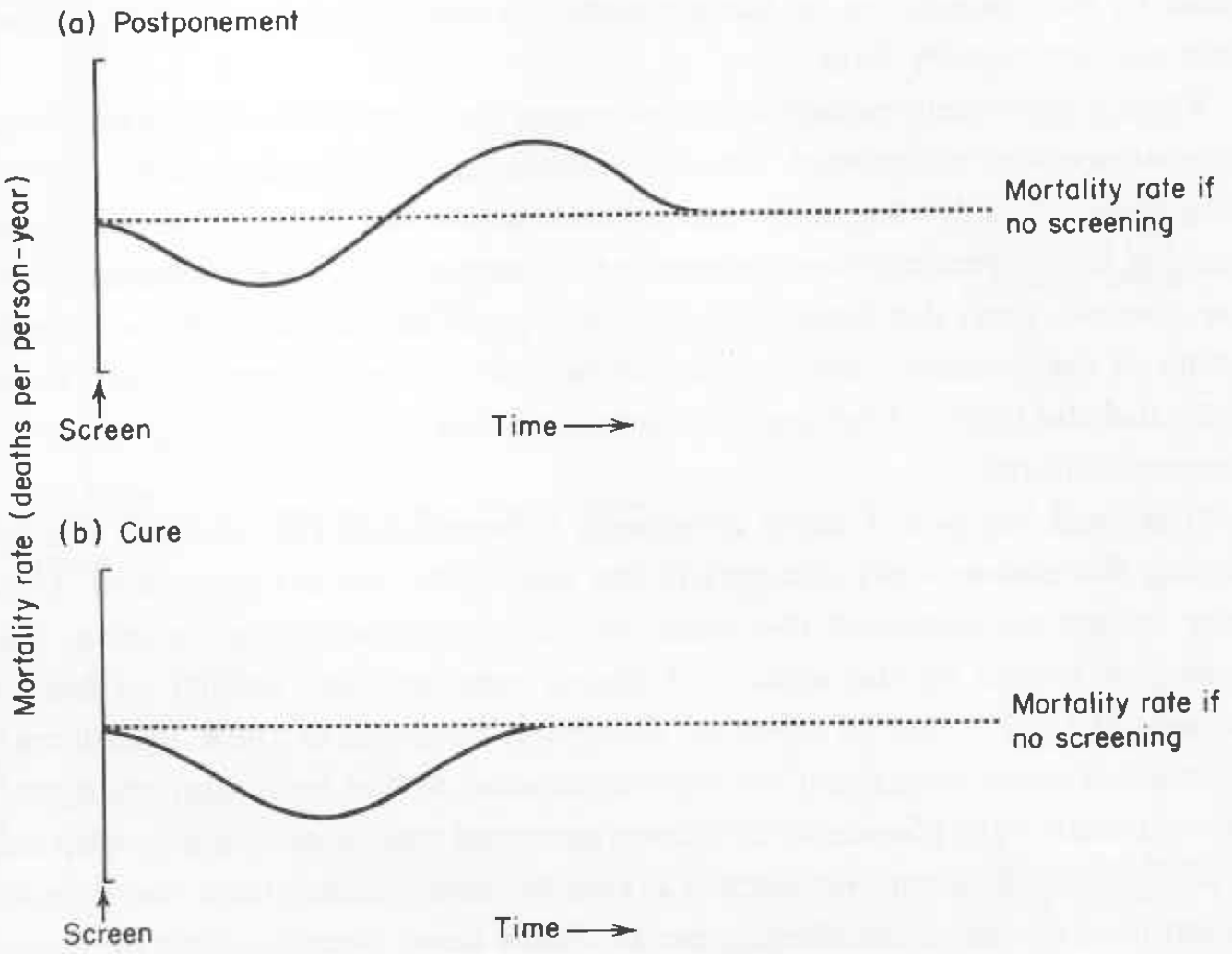


Figure 2-5. Changes in the disease-specific mortality rate brought about by postponement of death and by "cure" of screen-detected cases.

Cumulative and Year-specific Mortality...

in 100,000 men

(average age at entry: 62 years)

if screened using PSA test

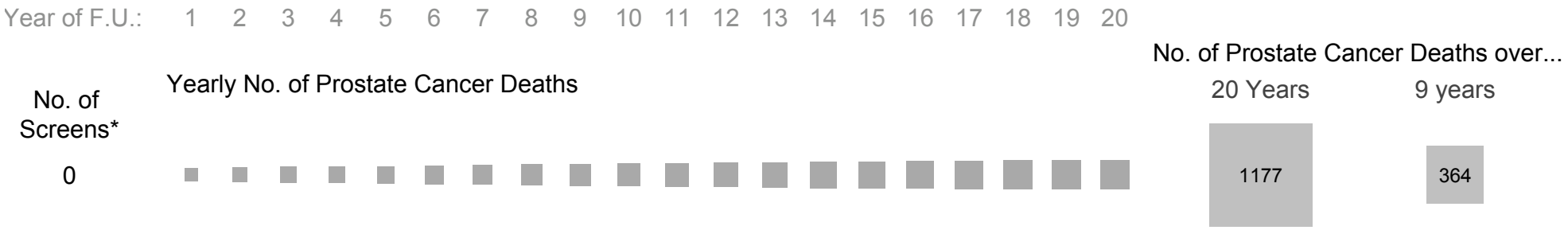
0, 1, 2, 3, or 4 times,

tests 4 years apart

and followed for (9) 20 years

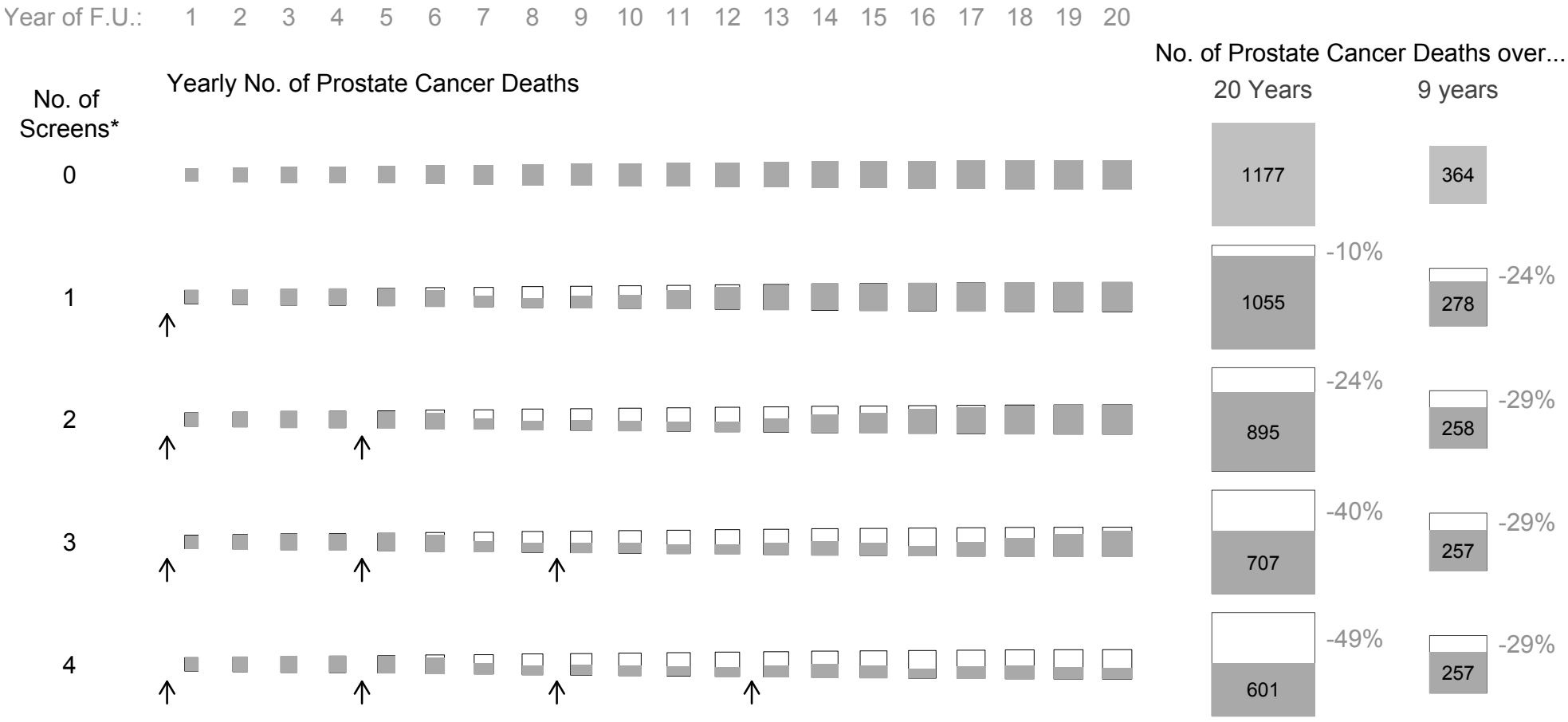
HYPOTHETICAL DATA

Cumulative & Year-specific results, if screen 0 times [HYPOTHETICAL]



[over these 20 years, approx. 65,000 men would die of other causes]

Cumulative & Year-specific results, if screen 0,1,...,4 times, q 4y [HYPOTHETICAL]



* Each arrow indicates the timing of a screen for prostate cancer.

(B) Year-specific Rate Ratios & Percent Reductions [HYPOTHETICAL]

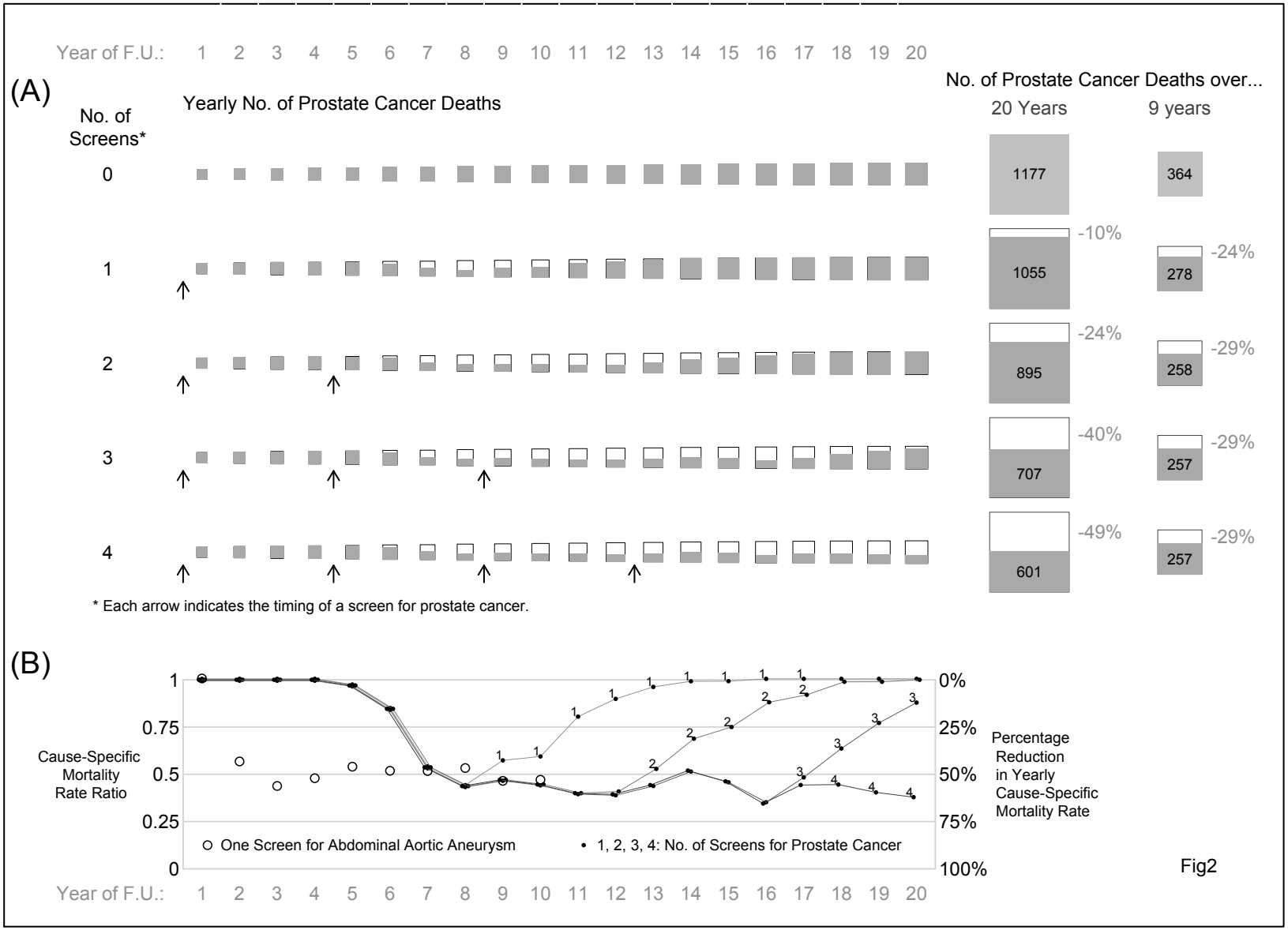


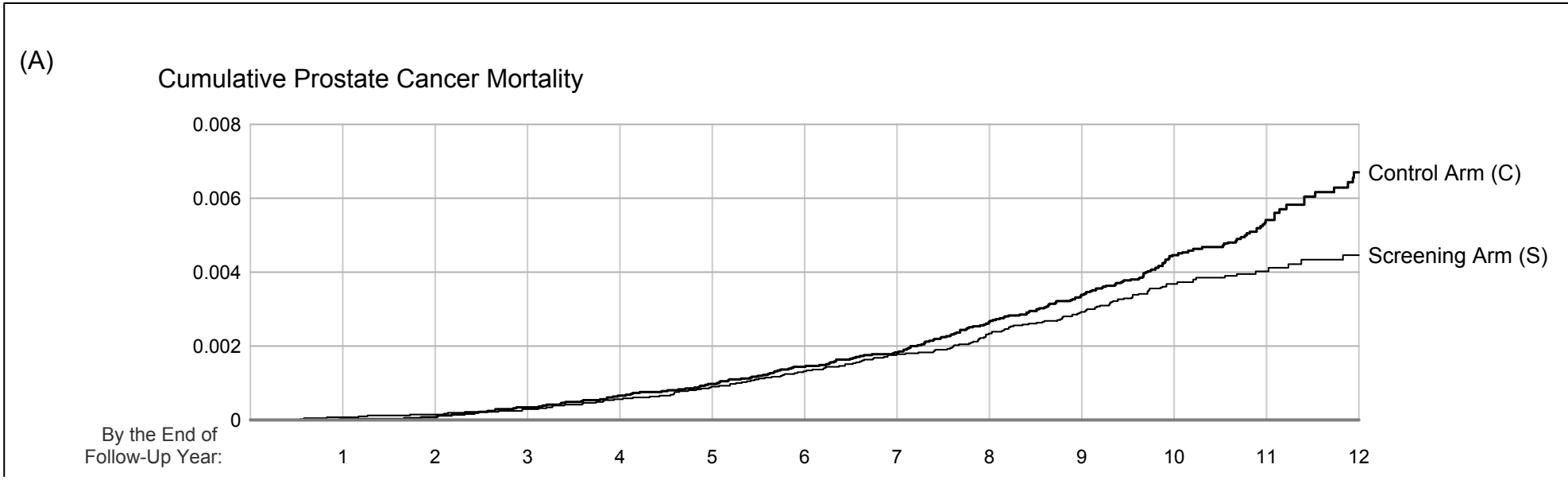
Fig2

RE-ANALYSIS OF ERSPC DATA

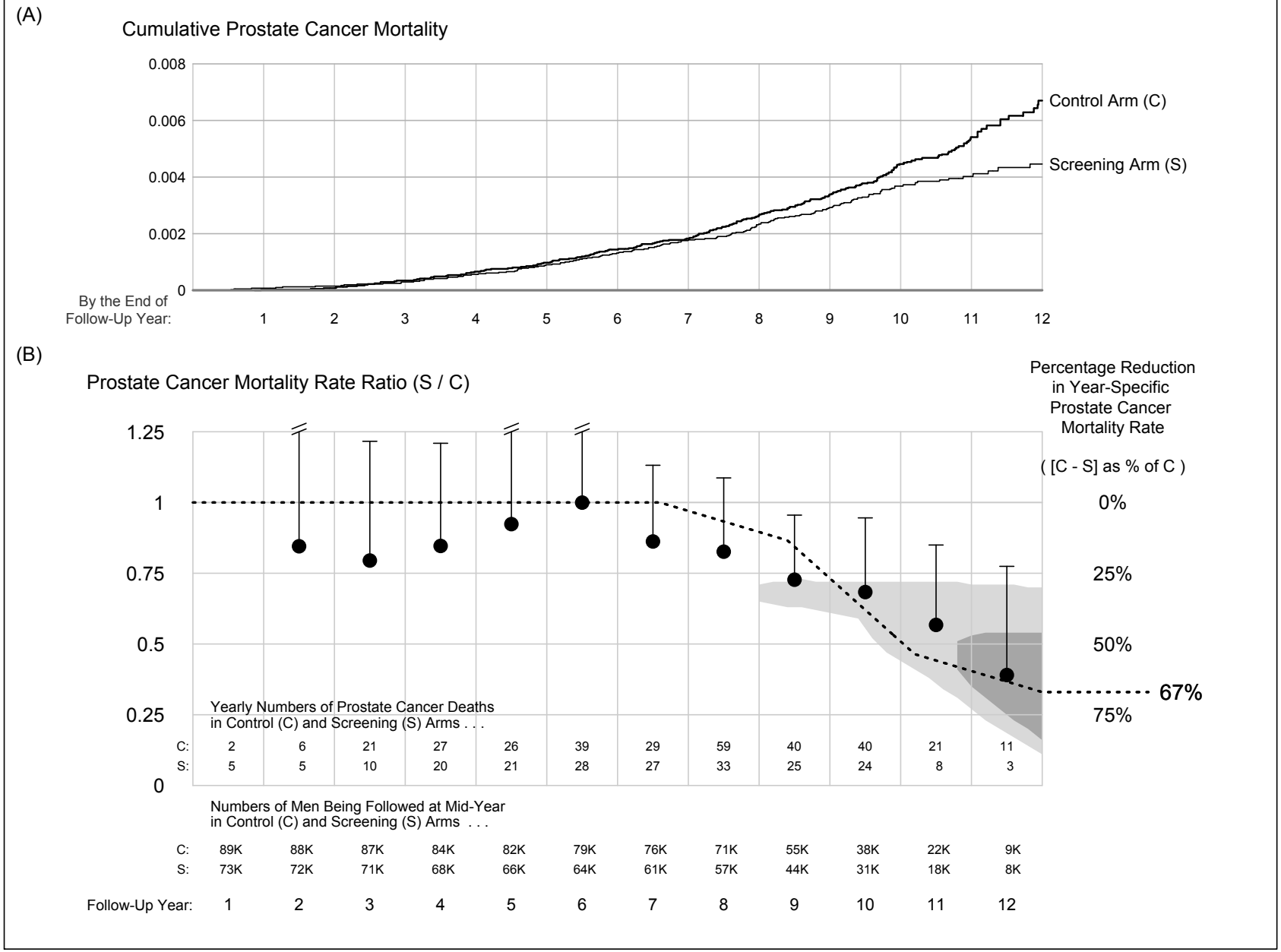
emphasis on time-specificity

- Year-by-year mortality rate ratios
  - pdf file containing Fig 2 $\rightarrow$ encapsulated postscript (eps) file format;
  - eps file $\rightarrow$ exact information (co-ordinates of line segments and dots) that statistical program, Stata, had used to draw two Nelson- Aalen cumulative hazard curves. eps file contained exact co-ordinates of each of 89,308 and 72,837 line segments or dots, one per man.
  - horizontal/vertical co-ordinates of each segment/dot $\rightarrow$ exact numbers of men being followed at each point in follow-up time, and thus at exact times of the vertical steps in curves (pr ca deaths).
  - size of step $\times$ number being followed $\rightarrow$ number of prostate cancer deaths at each time point
  - Numbers aggregated by year (each of 1st 12) and study arm $\rightarrow$ counts listed in new Figure.
- Moving averages to reduce the statistical noise (deaths in moving 3-year intervals)
- Smooth curve for rate ratio function (data bins 0.2 y wide).

Year-specific prostate cancer mortality ratios



Year-specific prostate cancer mortality ratios



Interpretation

- After an expected delay (data indicate $\approx$ 7 years), the prostate cancer mortality reductions that become evident in years 9 and beyond are statistically significant and considerably greater than the reported 20% reduction in the rate of prostate cancer deaths.
- The best (ML) estimate is that, although the rate ratio became non-null starting at $\approx$ 7 years, the steady state reduction has not yet been reached: the point estimate so far is a sustained 67% reduction (80%CI 30% to 89%) beginning at year 12.
- Numbers of deaths are not sufficient to establish its timing and magnitude more precisely. (Data cutoff: Dec 2006)

Implications - substantive

- '**Downsides**' of PSA-based prostate cancer screening: well documented and long since agreed upon.
- Even if screening could achieve a sustained reduction of 67%, (or even 77 or 87%!) the very low prostate mortality rates in the control group means that the **small absolute reductions** would be achieved at what some people would consider to be an unacceptable cost. (So far, only 326 or 0.36% of the 89,353 men in control group have died of prostate cancer; the number will approximately triple by follow-up year 20.)
- 'Upsides': 5 RCTs; 23 years; 321,000 men; 10 countries average f.-u. ranging from 7-15 years.
  - 4 have virtually no resolving power.
  - **ERSPC**: much larger Δ in screening activity b/w 2 arms $\rightarrow$ considerably greater **resolving power**.
  - Must measure signal in f.-u. window where probably strongest $\rightarrow$ collect **additional data**.
- Casual reader of ERSPC report **should not conclude** that best we can expect from PSA screening is a reduction in prostate cancer mortality of **20%**.
- Re-analysis: if screening is carried out for several years, and **if f.-u. pursued into window where reduction in mortality becomes manifest**, reduction to be seen there will be **50-60%**.
- ERSPC report published March 2009, but **f.-u. ended in Dec 2006**, just when pattern had begun to emerge. **Not possible to put precise statistical bounds** on this reduction.
- Prostate cancer deaths from **2007 onwards crucial to more precisely measure** the reduction achieved.

Implications - Methodologic

Time-specificity...

- Avoids dilution caused by averaging
  - 7 years of (expected) non-reductions with
  - 5 years of progressively larger reductions
- With current data, imprecise estimates: fixable.
- Follows intention to treat principle
- With objective curve-fitting...
  - avoid need to "pre-specify" **when** reduction reaches steady state
  - data themselves inform us about two critical parameters that determine 'response curve' (i.e., **timing** & **extent** of prostate cancer mortality reduction caused by screening).

Data-analysis using proportional hazards (ph) model: no place in cancer screening programs!

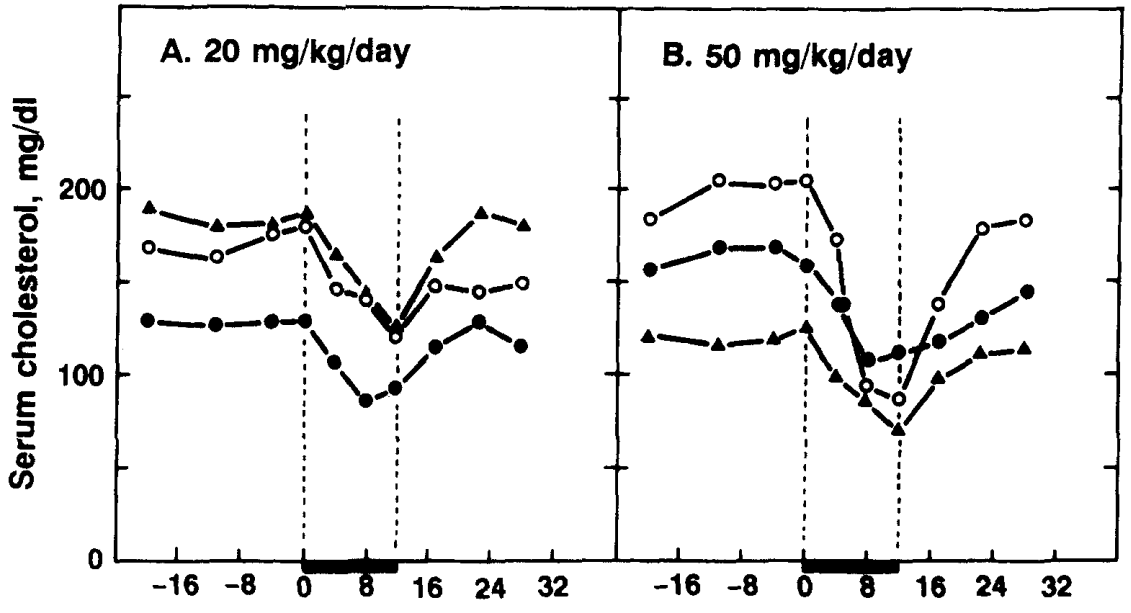
- Time-specific analysis (non-proportional hazards model) necessary to accommodate delayed mortality reductions (unless screening program doesn't reduce mortality at all)
- **Screening for abdominal aneurysms**: immediate and sustained reduction in mortality from ruptured aneurysms; difference in cumulative, or average mortality (ph model) captures full benefit of screening.
- Need to distinguish between interventions with immediate and delayed effects.
- Data from all trials of cancers screening need to be re-analyzed.

IMPLICATIONS: data-analysis, meta-analyses, public health

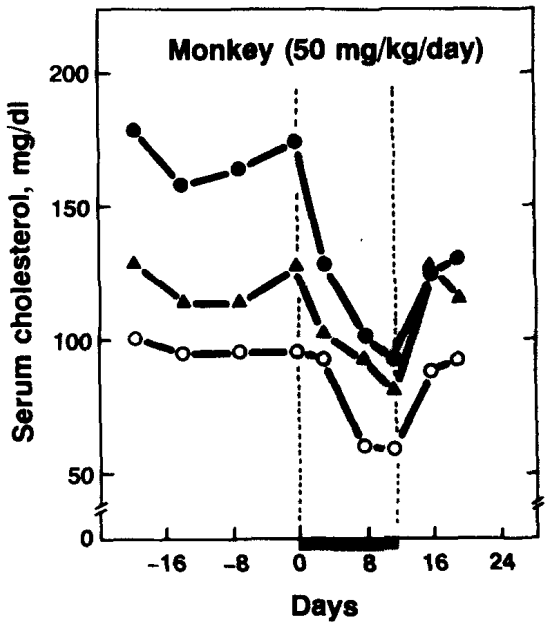
- 'Response Curve' in any one RCT is a function of the number and timing of screens [& compliance]
- Time-specificity in data-analysis is paramount
- No common parameter (response curve) to meta-analyze: trials not uniform w.r.t. number and timing of screens
- REAL Q: reduction with SUSTAINED SCREENING ?
- METRIC: nadir or (ideally) asymptote of response curve

Timing of cholesterol reductions produced by statins

3 dogs at 20 mg/kg/day; 3 at 50 mg/kg/day

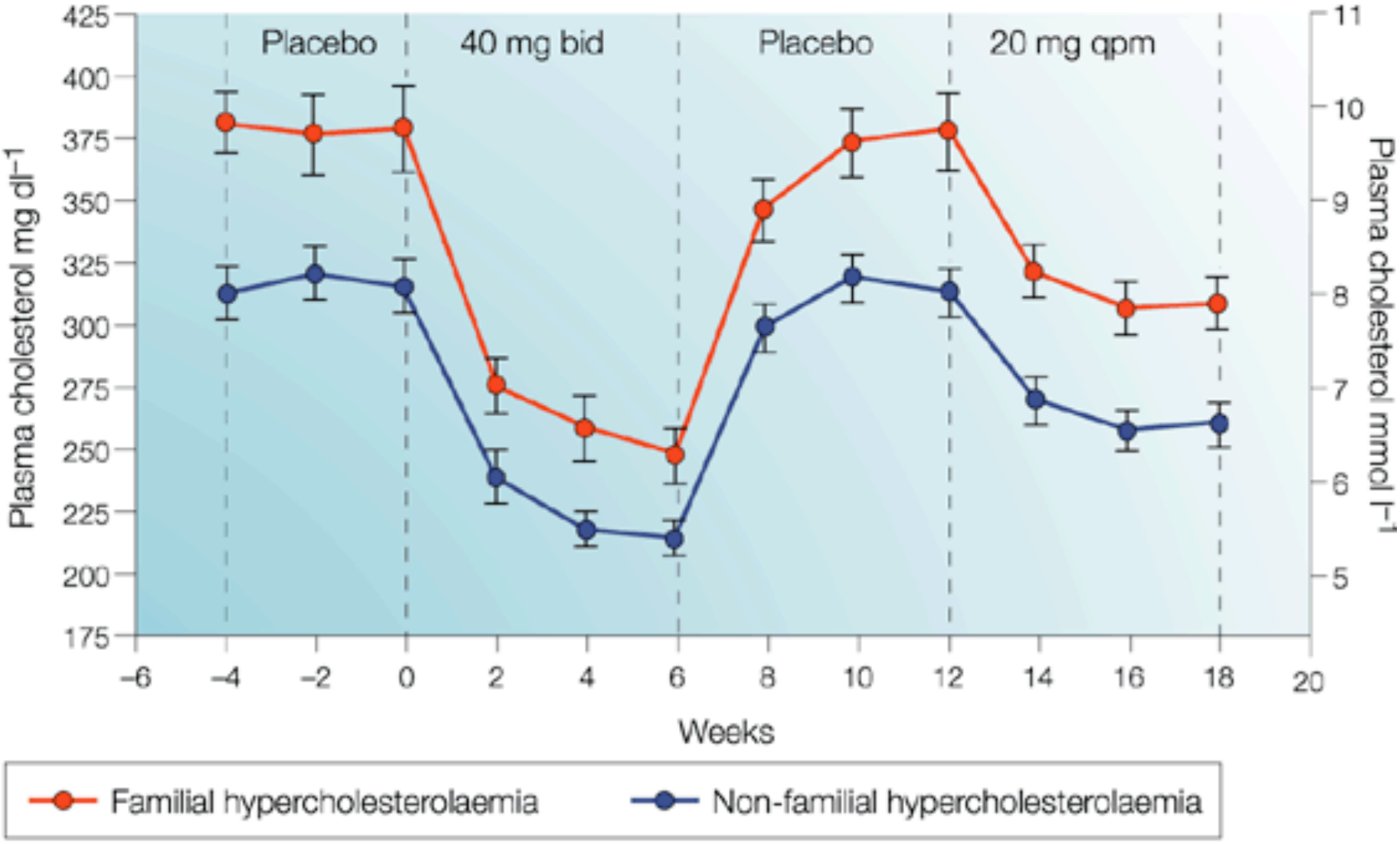


3 monkeys at 50

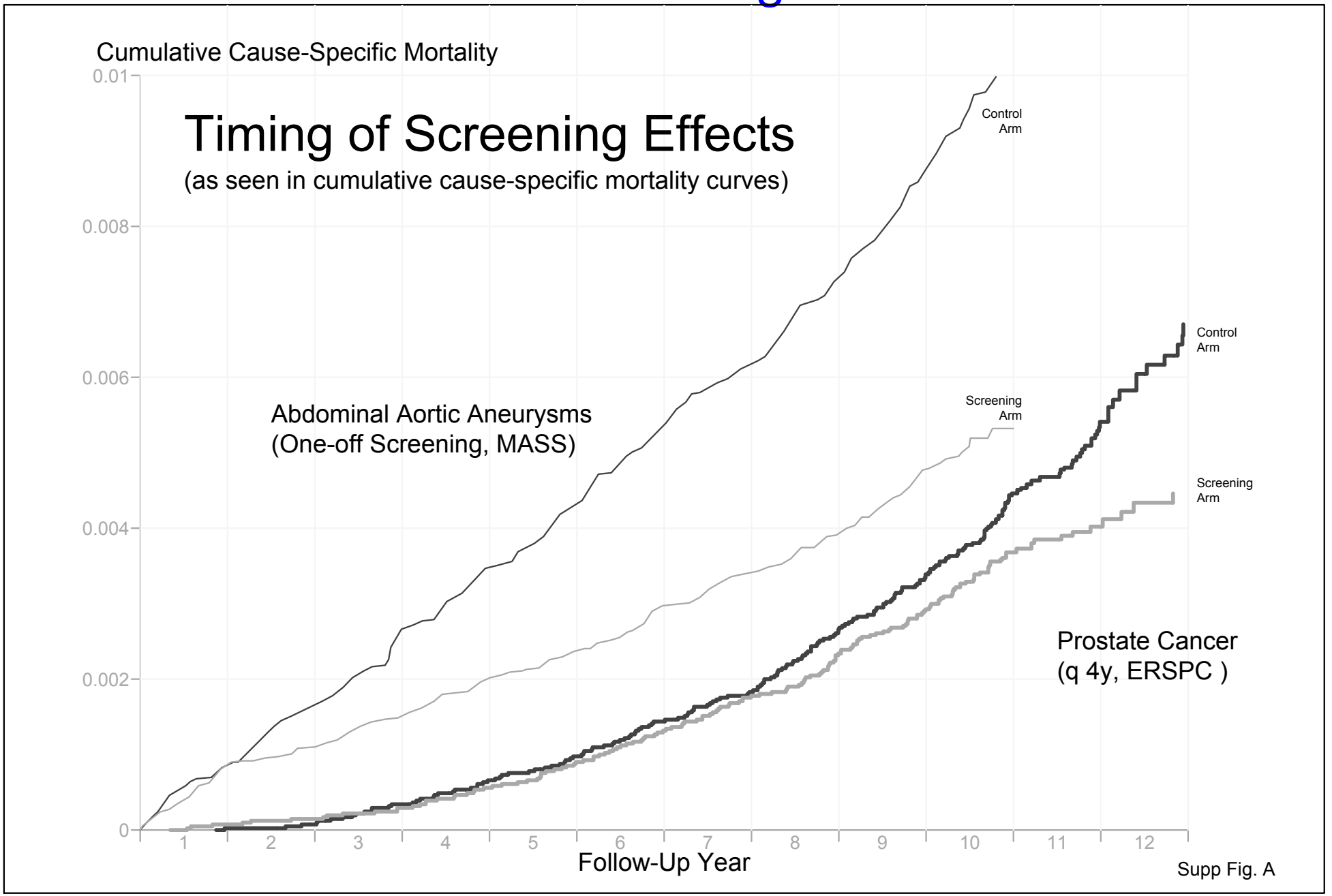


Timing of cholesterol reductions produced by statins

Humans



The loneliness of the long-distance trialist



Supp Fig. A

BREAST CANCER

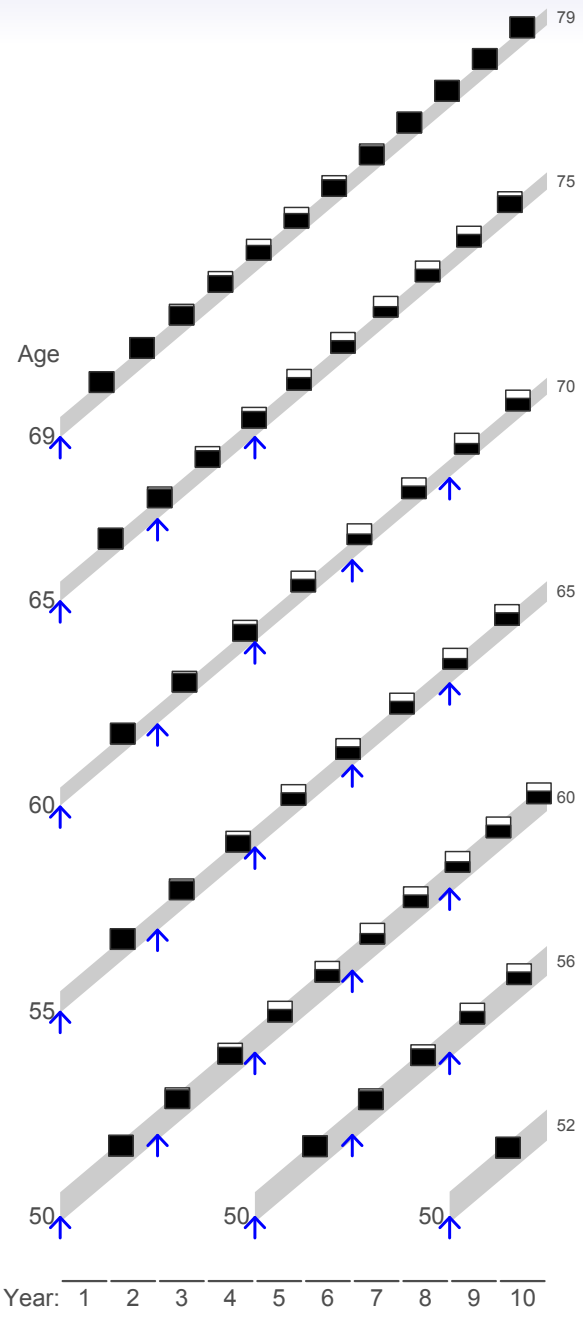
Data-analysis: 1977-2010

- 1977/85(HIP study): Shapiro/Morrison sensitive to time since start/end of screening
- 1985(year 7 of Swedish 2-County Trial): “significant 30% reduction in mortality ; control group invited to screening”
- 2000(Meta-analysis): Gøtzsche et al. ignored time (and intensity/duration of screening)
- 2002(Malmö data): Miettinen et al. : time-specific data bring out true signal
- Organized Population-based Screening Programs
  - Copenhagen, England, Norway, Sweden 40-49
  - Insensitive to timing (calendar, age) of mortality reductions
- IN EVERY INSTANCE: REDUCTION UNDER-ESTIMATED

Paraphrase of (refused) letter to NEJM re 2010 analysis of data from Norway

Will appear in:

Epidemiologic Reviews, 2011



WebFigure 6:

[Illustrative] Reductions in breast-cancer mortality as functions of the duration of screening and the time elapsed since it was begun, in the 10-year period 1996-2005 in Norway.

Reductions only occur several years after screening commences; the more rounds of screenings there are, the greate the attained reduction is; at some point after the last screening the rates return to what they would have been in the absence of screening.

An average that includes – and is dominated by - the (early) years in which mortality is not affected by screening and excludes (later) years in which it is, provides a diluted measure of a cancer screening program's impact on mortality from the disease.

COLON CANCER:

excerpts from JH's 2005 and 2011 reviews

Fecal Occult Blood testing: U.S. RCT

Biennial screening:

- Re-analyses, which focused on Year-specific data: had biennial screening not been interrupted, there would be:
  - $\approx$ 40% sustained reduction in *new cancers* and
  - $\approx$ 40% in cancer mortality
- Original report:
  - based on cumulative data
  - ignored 5-year hiatus and 2 waves of delayed reductions
  - 18% reduction in *new cancers*
  - 21% reduction in *cancer mortality*

American Journal of Gastroenterology

Published by Blackwell Publishing

ISSN 0002-9270
doi: 10.1111/j.1572-0241.2008.01875.x

CLINICAL REVIEWS

Cochrane Systematic Review of Colorectal Cancer Screening Using the Fecal Occult Blood Test (Hemoccult): An Update

Paul Hewitson, B.A. (Hons), M.MSc,[1] Paul Glasziou, M.B.B.S., Ph.D., F.A.F.P.H.M., F.R.A.C.G.P.,[2] Eila Watson, B.Sc., Ph.D.,[3] Bernie Towler, M.B.B.S. M.PH.,[4] and Les Irwig, M.B.B.Ch., Ph.D., F.F.P.H.M.[5]

[1]*Department of Primary Health Care,* [2]*Centre for Evidence Based Medicine, Department of Primary Health Care, University of Oxford, Oxford, United Kingdom;* [3]*School of Health and Social Care, Oxford Brookes University, Oxford, United Kingdom;* [4]*Department of Health and Aging Services, Macarthur, Australia; and* [5]*Screening and Test Evaluation Program, School of Public Health, University of Sydney, Sydney, Australia*

BACKGROUND: AND AIMS: Reducing mortality from colorectal cancer (CRC) may be achieved by the introduction of population-based screening programs. The aim of the systematic review was to update previous research to determine whether screening for CRC using the fecal occult blood test (FOBT) reduces CRC mortality and to consider the benefits, harms, and potential consequences of screening.

METHODS: We searched eight electronic databases (Cochrane Library, MEDLINE, EMBASE, CINAHL, PsychINFO, AMED, SIGLE, and HMIC). We identified nine articles describing four randomized controlled trials (RCTs) involving over 320,000 participants with follow-up ranging from 8 to 18 yr. The primary analyses used intention to screen and a secondary analysis adjusted for nonattendance. We calculated the relative risks and risk differences for each trial, and then overall, using fixed and random effects models.

RESULTS: Combined results from the four eligible RCTs indicated that screening had a 16% reduction in the relative risk (RR) of CRC mortality (RR 0.84, 95% confidence interval [CI] 0.78–0.90). There was a 15% RR reduction (RR 0.85, 95% CI 0.78–0.92) in CRC mortality for studies that used biennial screening. When adjusted for screening attendance in the individual studies, there was a 25% RR reduction (RR 0.75, 95% CI 0.66–0.84) for those attending at least one round of screening using the FOBT. There was no difference in all-cause mortality (RR 1.00, 95% CI 0.99–1.02) or all-cause mortality excluding CRC (RR 1.01, 95% CI 1.00–1.03).

CONCLUSIONS: The present review includes seven new publications and unpublished data concerning CRC screening using FOBT. This review confirms previous research demonstrating that FOBT screening reduces the risk of CRC mortality. The results also indicate that there is no difference in all-cause mortality between the screened and nonscreened populations.

This Cochrane review of 4 RCTs...

Given the different

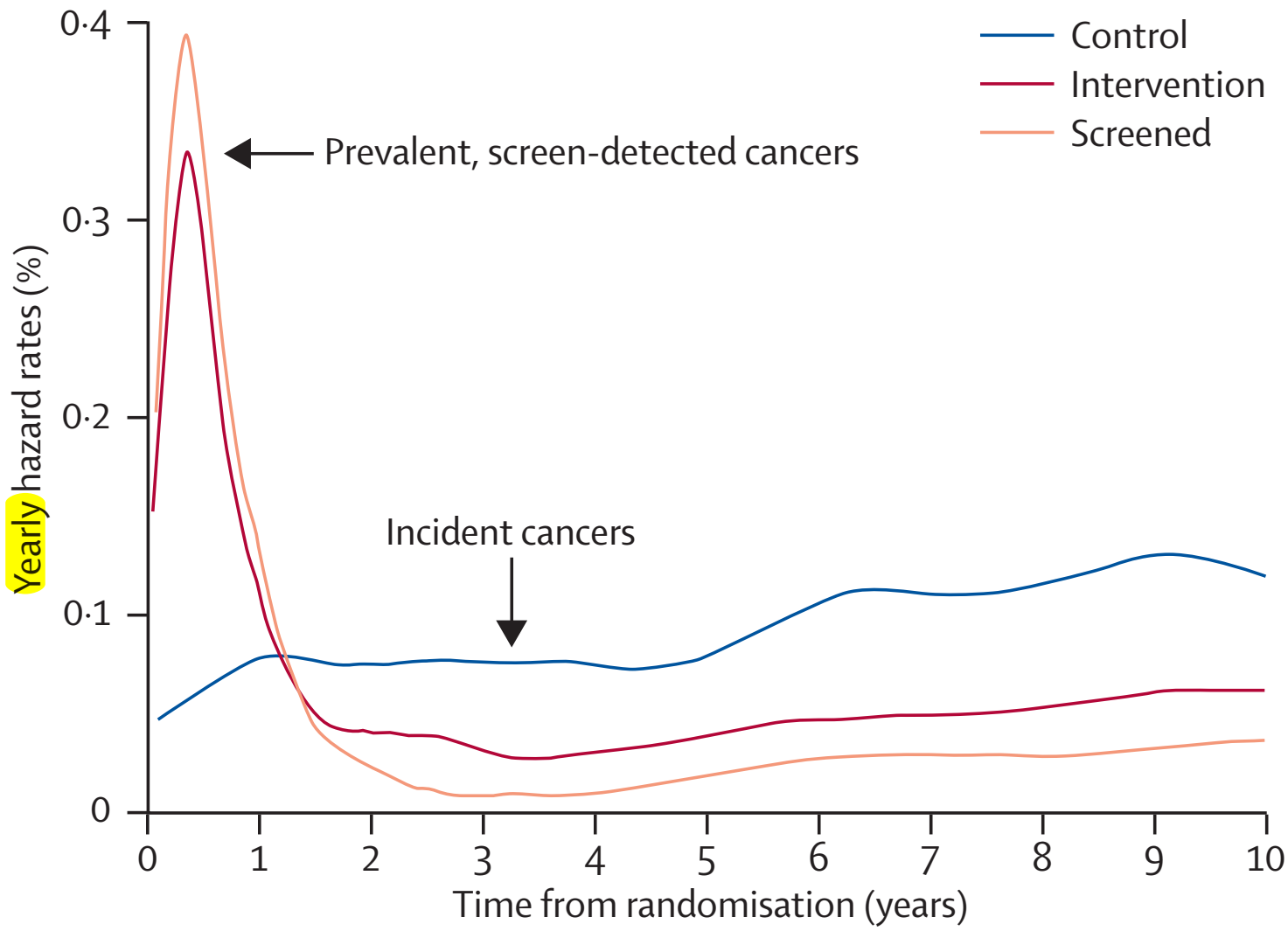
- random allocation methods (volunteers vs. all)
- tests (rehydrated vs. non-rehydrated)
- numbers of rounds of screening (2, 6, 6, 9)
- participation rates (60% - 80%)
- lengths of follow-up (12, 16, 17, 18 years)
- time-specific rate ratios

more meaningful if displayed 4 separate rate ratio time curves .

UK trial: % ↓ in cancer mortality in each of the years 2-15:
5, 17, 15, 23, 17, 23, 23, 16, 15, 6, 4, -2, 1, 2.
13% ↓ in cancer mortality over entire f-up period (median 12y) was given weight of 40% in meta-analysis.

Swedish trial: 16% ↓ over 15.5 years; screens: 0 & 1.7 years.

Once-only flexible sigmoidoscopy (U.K. trial)



Explicitly discussed the non-applicability of proportional hazards model

31% mortality reduction based on cumulative mortality

Cancers of proximal and distal colon were ...

separated for incidence rates

conflated for mortality rates

***Figure 3*: Smoothed yearly hazard rates for distal cancer (rectum and sigmoid**

LUNG CANCER

Mayo Lung Project (chest x-ray & sputum cytology)

- Enrollment: 1971-1976;
  negative on 'prevalence' screen;
  screening every 4 mo. for 6 years (vs., on enrollment, recommendation to receive annual chest x-ray & sputum cytology).
- JNCI 2000: "Lung Cancer Mortality in the Mayo Lung Project: Impact of Extended Follow-up"

  Would 24-year follow up "allow for a reduction in lung cancer mortality to be observed?"

- ALL lung cancer deaths, from those in year...
  - 1, before impact could become evident,
    to
  - 24, 18 years after last screen.

National Lung Screening Trial (NLST)

- Enrollment: August 2002 - March-2004
  3 annual screens: low-dose helical CT (vs. standard chest X-ray).
  Primary scientific goal:

  to determine whether three annual screenings with low-dose helical computerized tomography (LDCT) reduces [sic] mortality from lung cancer

- Press Releases, November 2010:

  Screening of people at high-risk for lung cancer with low dose CT significantly reduces lung cancer death: 20% fewer lung cancer deaths [ACR]

  An interim analysis of the study's primary endpoint, reported to the DSMB on October 20, 2010, revealed a deficit of lung cancer deaths in the LDCT arm, and the deficit exceeded that expected by chance, even allowing for the multiple analyses conducted during the course of the trial. Data presented at previous meetings of the DSMB did not meet the requirements for statistical significance with respect to the primary endpoint. [NCI(US)]

ACR Imaging Network: Press Release

Table 3: Interim Analysis of Primary Endpoint Reported on October 20, 2010

Trial Arm	Person years (py)	Lung cancer deaths	Lung cancer mortality per 100,000 py	Reduction in lung cancer mortality (%)	Value of test statistic	Efficacy boundary
LDCT	144,097.6	354	245.7	20.3	–3.21	–2.02
CXR	143,363.5	442	308.3			

Timing of the ‘deficit’ of (442-354=) 88 deaths

? ? ?

Year:	1	2	3	4	5	6	7	8	ALL
? CXR arm:	10	38	65	75	82	90	60	22	442
?? LDCT arm:	10	36	59	59	56	63	50	21	354
?? deficit (no.):	0	-2	-6	-16	-26	-27	-10	-1	-88
?? deficit (%):	0%	5%	9%	21 %	32%	30%	17%	5%	20%
?? LDCT arm:	8	30	52	60	66	73	48	17	354
?? deficit (no.):	-2	-8	-13	-15	-16	-17	-12	-5	-88
?? deficit (%):	20%	21%	20%	20%	20%	19%	20%	23%	20%
?? LDCT arm:	?	?	?	?	?	?	?	?	354
?? deficit (no.):	-?	-?	-?	-?	-?	-?	-?	-?	-88
?? deficit (%):	? %	? %	? %	? %	? %	? %	? %	? %	20%

20% MORTALITY REDUCTION

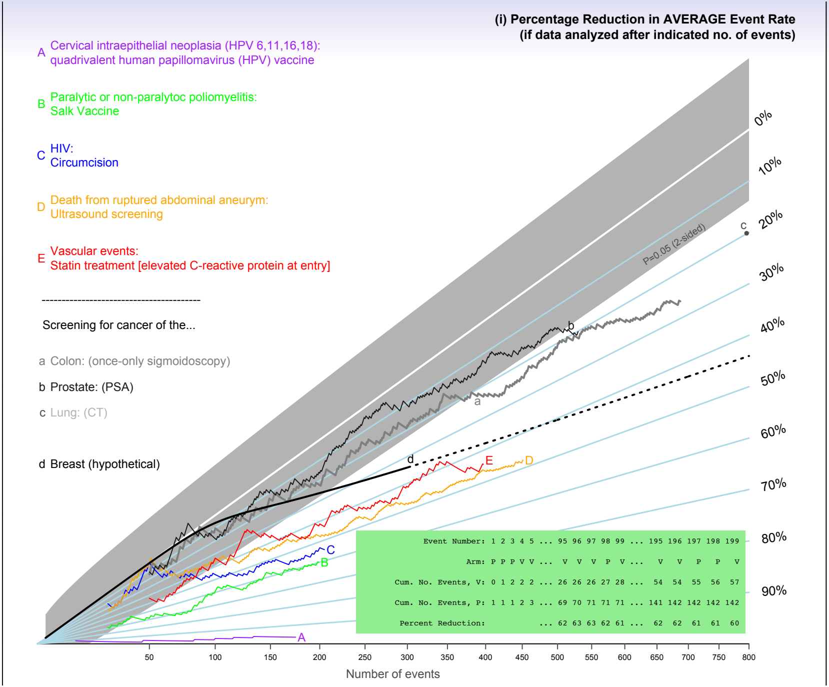
A UNIVERSAL CONSTANT IN SCREENING TRIALS?

Reductions in 'event rates': 5 'prevention' studies

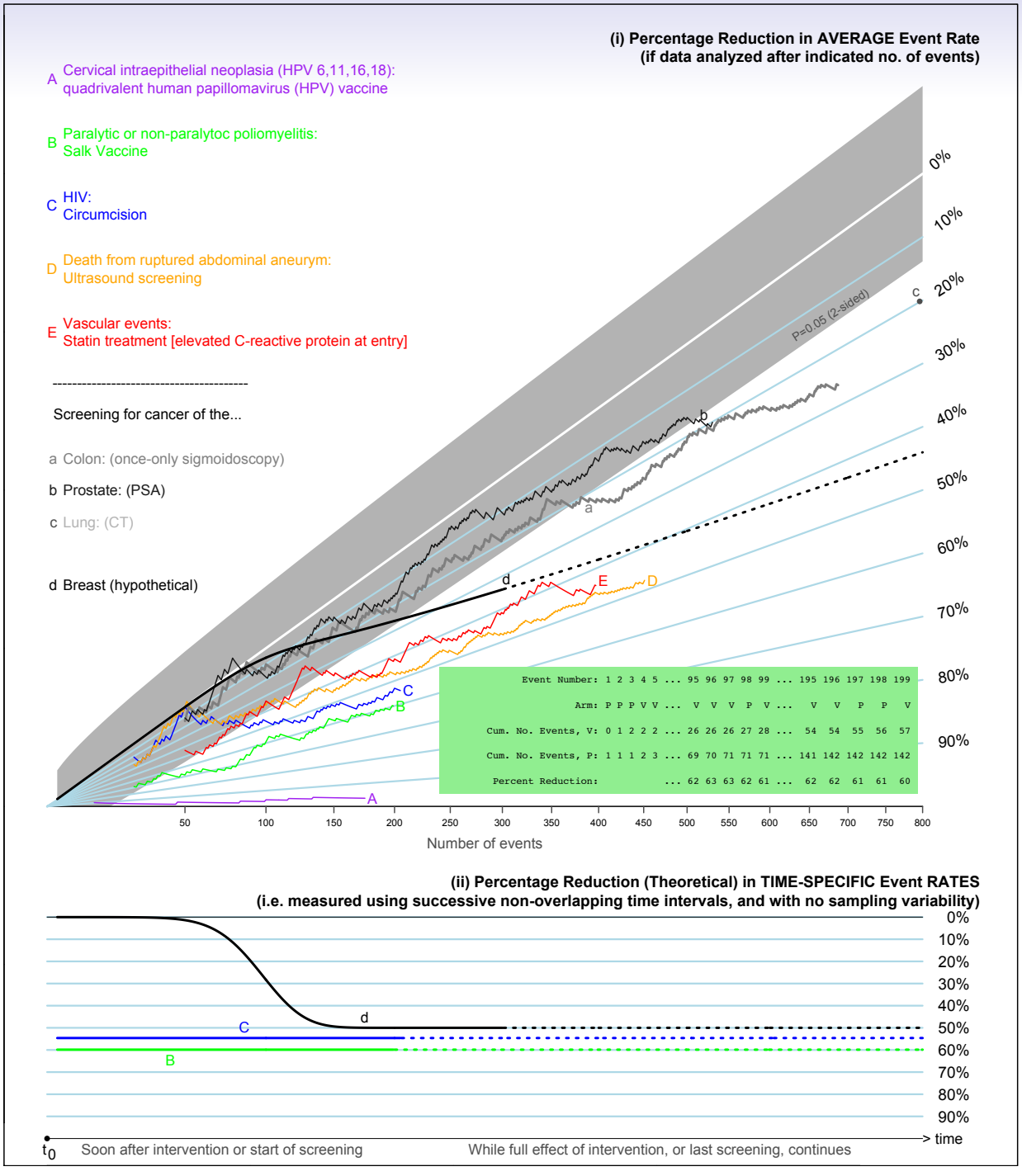
- Cervical intraepithelial neoplasia (HPV 6,11,16,18):
  - Quadrivalent human papillomavirus (HPV) vaccine
- Paralytic or non-paralytic poliomyelitis:
  - Salk Vaccine
- HIV:
  - (Adult) Circumcision
- Death from ruptured abdominal aneurym:
  - Ultrasound screening
- Vascular events:
  - Statin treatment [elevated C-reactive protein at entry]

QUESTION: Shape of $\downarrow(t)$ function, i.e., % Reduction in Rate as function of follow-up time, if rates based on...

- all events up to that point in f-up time? (*1 'average' rate*) ?
- when in f-up time events occurred (*'time-specific'* rates) ?


(i) Percentage Reduction in AVERAGE Event Rate
(if data analyzed after indicated no. of events)
A Cervical intraepithelial neoplasia (HPV 6,11,16,18): quadrivalent human papillomavirus (HPV) vaccine
B Paralytic or non-paralytoc poliomyelitis: Salk Vaccine
C HIV: Circumcision
D Death from ruptured abdominal aneurym: Ultrasound screening
E Vascular events: Statin treatment [elevated C-reactive protein at entry]

Screening for cancer of the...
a Colon: (once-only sigmoidoscopy)
b Prostate: (PSA)
c Lung: (CT)
d Breast (hypothetical)
P=0.05 (2-sided)
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
Event Number: 1 2 3 4 5 ... 95 96 97 98 99 ... 195 196 197 198 199
Arm: P P P V V ... V V V P V ... V V P P V
Cum. No. Events, V: 0 1 2 2 2 ... 26 26 26 27 28 ... 54 54 55 56 57
Cum. No. Events, P: 1 1 1 2 3 ... 69 70 71 71 71 ... 141 142 142 142 142
Percent Reduction: ... 62 63 63 62 61 ... 62 62 61 61 60
50
100
150
200
250
300
350
400
450
500
550
600
650
700
750
800
Number of events



If **intervention continues over time to deflect the same % of events**, an estimate of the % reduction, based on the total number events in more (person)-time will be more precise

Mortality reductions from cancer screening manifest distally. Enrolling and following more people for short length of time yields a more precise UNDERestimate.

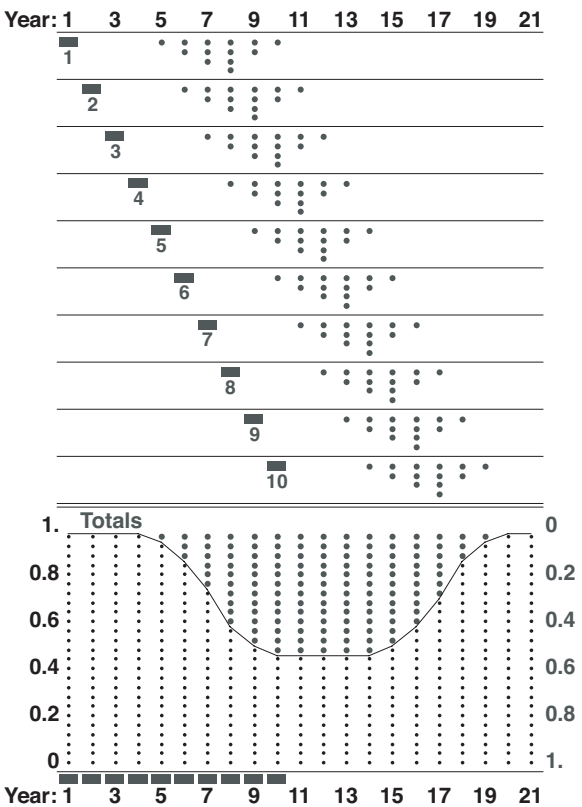
The seemingly-universal 20% reduction is an artifact of prevailing data-analysis methods and stopping rules.

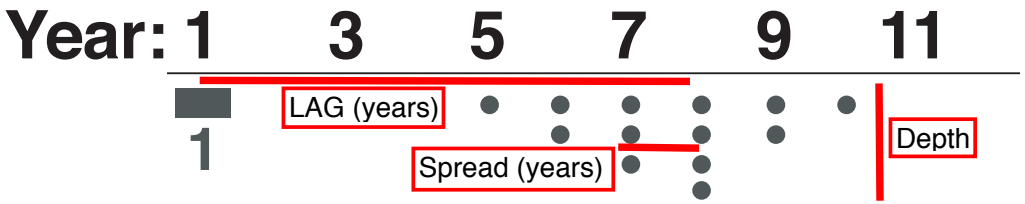
If use all data from time screening commences, the first % reduction which was statistically different from zero does not answer the question of interest to payers.

PLANS

Data and Methods, Parameters, their Use

- **Data**: completed RCTs of screening for prostate, breast, colon and lung ca; population-based screening programs.
- **3 Parameters** (‘*deliverables*’) and how they will be fitted:





y = years since screening commenced

- Rate ratio in Year *y*, Age *a* in Study *s* :

RateRatio(*y, a, s*) =

sum of reductions from all previous rounds of screening in study *s*

- Design matrix: 1 row per y-a-s ‘cell’
- $\frac{\text{No. deaths in screening arm}}{\text{No. deaths in 2 arms combined}}$ in each ‘cell’
- Fit by Max. Likelihood (binomial model)

- **USE**: project mort. reductions due to a screening regimen

Acknowledgments

- A Morrison 1985 textbook on Screening
- O. Miettinen 2002 Lancet article
- J. Caro and M. McGregor

  Screening for breast cancer in women aged 40-49 years. Montreal: CETS Report no. 22, 1993. 91p. Available at: http://www.aetmis.gouv.qc.ca/en/ Accessed July 6, 2005.

- F. Galton, Natural Inheritance, 1889.

Why do statisticians commonly limit their inquiries to Averages?

“It is difficult to understand why statisticians commonly limit their inquiries to Averages, and do not revel in more comprehensive views.

Their souls seem as dull to the charm of variety as that of the native of one of our flat English counties, whose retrospect of Switzerland was that, if its mountains could be thrown into its lakes, two nuisances would be got rid of at once.”

FUNDING, CO-ORDINATES, DOWNLOADS

Natural Sciences and Engineering Research Council of Canada

Le Fonds québécois de la recherche sur la nature et les technologies

James.Hanley@McGill.CA

http://www.biostat.mcgill.ca/hanley

→ **r e p r i n t s / talks**

McGill **Biostatistics**
Biostatistique

http://www.mcgill.ca/epi-biostat-occh/grad/biostatistics/

Some References

1. Hanley JA. Mortality reductions produced by sustained prostate cancer screening have been underestimated. Journal of Medical Screening. Fall 2010. [+ Br & Colon *Epidemiologic Reviews* 2011]
2. Hanley JA. CANNeCTIN Clinical Trials Methodology Seminar Series. Videoconference April 9, 2010. Slides: http://www.cannectin.ca/ . Video: Archived Events, http://webcast.otn.ca/
3. Schröder FH, Hugosson J, Roobol MJ, et al. Screening and prostate-cancer mortality in a randomized European study. N Engl J Med 2009;360:1320-1328
4. Sandbloma G, Varenhorst E, Löfman, Rosell J, Carlsson P. Clinical Consequences of Screening for Prostate Cancer: 15 Years Follow-up of a Randomised Controlled Trial in Sweden. European Urology 46 (2004) 717-724.
5. Kjellman A, Akre O, Norming U, Törnblom M, and Gustafsson O. 15-Year Followup of a Population Based Prostate Cancer Screening Study. The Journal of Urology 2009; 181:1615- 1621.
6. Labrie F, Candas B, Cusan L, Gomez, LL, Bélanger A, Brousseau G, Chevrette E, Lévesque J. Screening decreases prostate cancer mortality: 11-year follow-up of the 1988 Quebec prospective randomized controlled trial. Prostate. 2004 May 15;59(3):311-318.
7. Andriole GL, Grubb RL 3rd, Buys SS,et al.. Mortality Results from a Randomized Prostate- Cancer Screening Trial. N Engl J Med 2009;360:1310-1319.
8. Thompson SG, Ashton HA, Gao L, Scott RAP on behalf of the Multicentre Aneurysm Screening Study Group. Screening men for abdominal aortic aneurysm: 10 year mortality and cost effectiveness results from the randomised Multicentre Aneurysm Screening Study. BMJ 2009;338:b2307 doi:10.1136/bmj.b2307.
9. Hanley JA. Analysis of Mortality Data From Cancer Screening Studies: Looking in the Right Window. Epidemiology 2005; 16: 786-790.
10. Miettinen OS, Henschke CI, Pasmantier MW, et al. Mammographic screening: no reliable supporting evidence? Lancet 2002;359:404-406.
11. Miettinen OS, Henschke CI, Pasmantier MW, et al. Mammographic screening: no reliable supporting evidence? Available at: http://image.thelancet.com/extras/1093web.pdf. Accessed July 6, 2005.
12. Barry MJ. Screening for Prostate Cancer–The controversy that refuses to die. Editorial. N Engl J Med. 2009 Mar 26;360(13):1351-1354.