Measuring the mortality reductions produced by organized cancer screening: a principled approach

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Biostatistics Branch Seminar Series
Division of Cancer Epidemiology & Genetics
US-NCI

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Dedication

HARVARDgazette

Campus & Community > Obituaries

HSPH's Marvin Zelen dies at 87

Was considered a 'tremendous force' in biostatistics

November 19, 2014 | Editor's Pick

Photo by Shaina Andelman

Harvard Professor Marvin Zelen was noted for developing the statistical methods and study designs that are used in clinical cancer trials, in which experimental drugs are tested for toxicity, effectiveness, and proper dosage.

HSPH Communications

Professor Marvin Zelen of the Department of Biostatistics at the Harvard T.H. Chan School of Public Health (HSPH) died on Nov. 15 after a battle with cancer. He was 87.

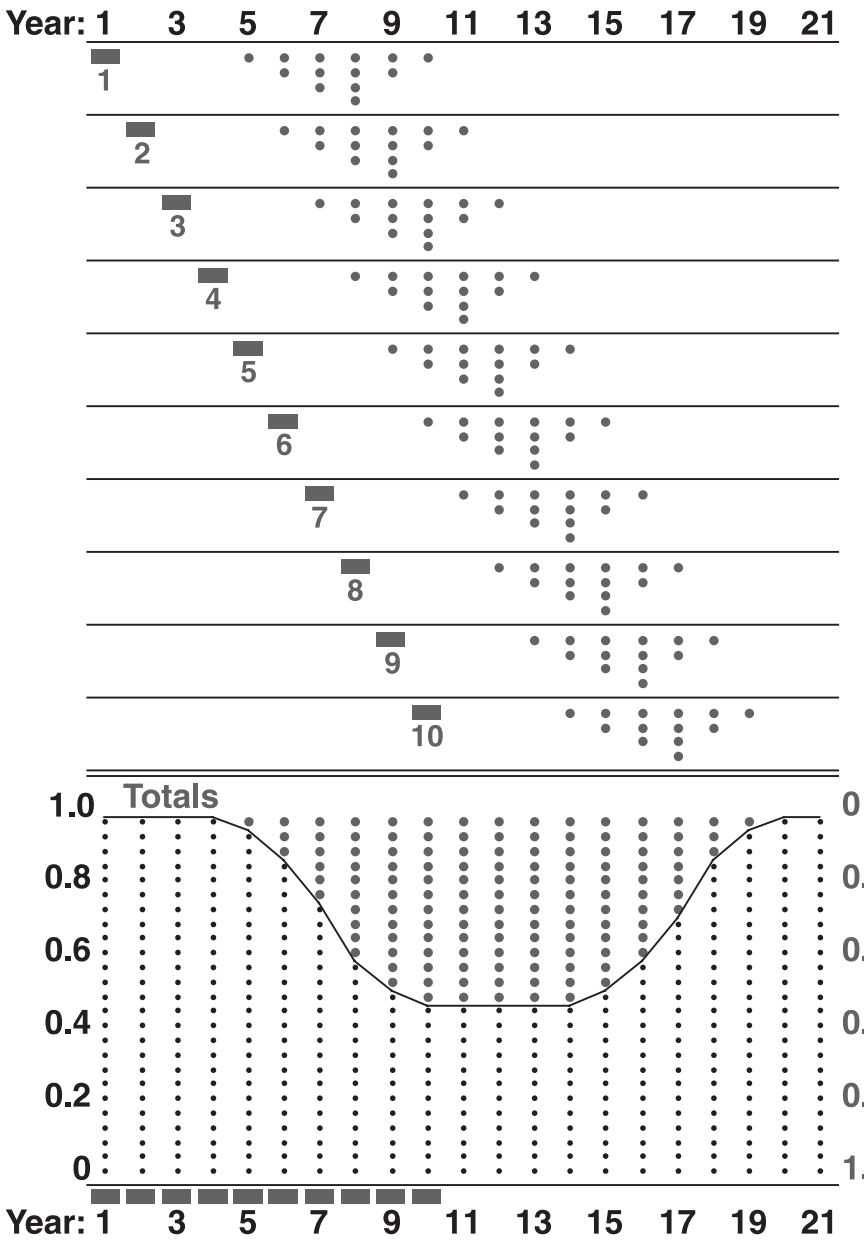
Outline

- Screening is different from prevention/treatment
- Bathtub-shaped Hazard Ratio function
- Trial (experimental) data: prostate (PSA) and colon (FOBT)
- Breast Cancer Screening with Mammography:
  21st century (non-experimental) population-based studies
- Avoiding underestimates: examples from Norway & Ireland
- **It's all about TIMING – and the Lexis diagram helps !!**
- **Technical details on our model**

Ways in which cancer screening differs from prevention/treatment

- Prevention aims to stop cancer from ever developing
- Treatment combats it once it becomes apparent
- Screening: pursuit of earlier diagnosis
  - disease not necessarily present at 1st screen.. must repeat
  - benefits not immediate, but delayed, & time-limited
  - in screening: no screening comparisons, if screening works as intended, mortality hazard rates are non-proportional

Bathtub-shaped Hazard Ratio function



<— deaths averted by screen 1

<— deaths averted by screen 2

...

<— deaths averted by screen 10

Figure (after Miettinen et al. 2002.) is from Hanley JA. Analysis of Mortality Data From Cancer Screening Studies: Looking in the Right Window. *Epidemiology, Vol 16, 2005*, pp 786-790.

See also. Liu Z at al. J Med Screening. 2013.

'*% Reduction function*' (bathtub shape)

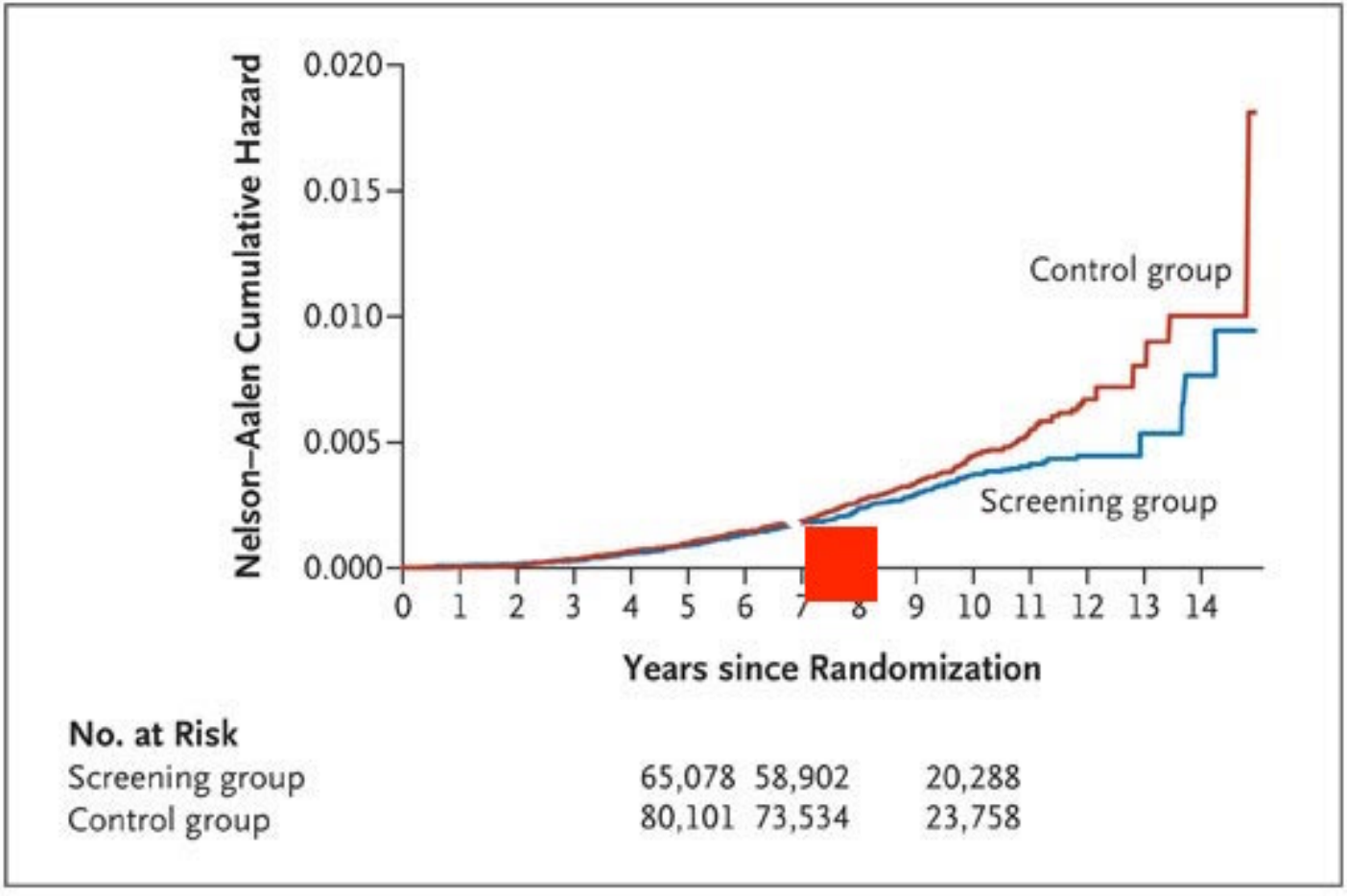
- The asymptote is the ultimate estimand
- It is determined by ...
  - number and spacing of rounds, and
  - the contribution of each round of screening
- From published trials, can one ..
  - estimate the '% Reduction function' ?
  - estimate contribution of each round ?
    (?? function shape if different schedule or if a program)

PROSTATE CANCER

Screening & Prostate-Ca Mortality in Randomized European Study '92-'08 ("ERSPC" nejm2009.04)

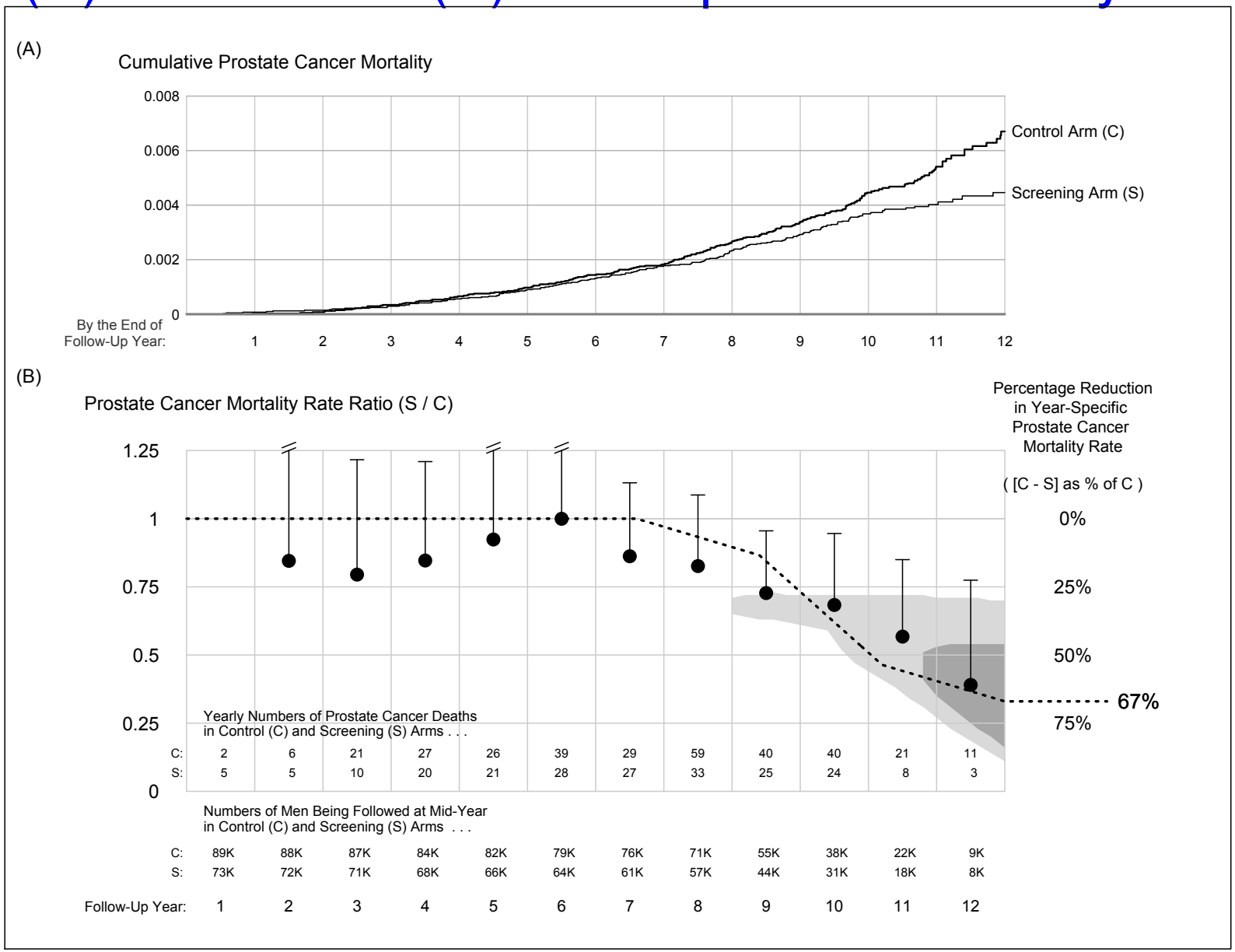
As of December 31, 2006, with an average follow-up time of 8.8 years, there were 214 prostate-cancer deaths in the screening group and 326 in the control group. (...) The adjusted **rate ratio** for death from prostate cancer in the screening group was **0.80** (95% CI, 0.65 to 0.98; P=0.04).

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



RE-ANALYSIS OF ERSPC DATA
using
year-specific prostate cancer mortality ratios

(A) Overall vs. (B) Year-specific mortality ratios



Hanley, *J Medical Screening*, 2010.

Screening and prostate cancer mortality: results of the European Randomised Study of Screening for Prostate Cancer (ERSPC) at 13 years of follow-up

*Fritz H Schröder, Jonas Hugosson, Monique J Roobol, Teuvo L J Tammela, Marco Zappa, Vera Nelen, Maciej Kwiatkowski, Marcos Lujan, Liisa Määttänen, Hans Lilja, Louis J Denis, Franz Recker, Alvaro Paez, Chris H Bangma, Sigrid Carlsson, Donella Puliti, Arnauld Villers, Xavier Rebillard, Matti Hakama, Ulf-Hakan Stenman, Paula Kujala, Kimmo Taari, Gunnar Aus, Andreas Huber, Theo H van der Kwast, Ron H N van Schaik, Harry J de Koning, Sue M Moss, Anssi Auvinen, for the ERSPC Investigators**

Summary

Background The European Randomised study of Screening for Prostate Cancer (ERSPC) has shown significant reductions in prostate cancer mortality after 9 years and 11 years of follow-up, but screening is controversial because of adverse events such as overdiagnosis. We provide updated results of mortality from prostate cancer with follow-up to 2010, with analyses truncated at 9, 11, and 13 years.

Methods ERSPC is a multicentre, randomised trial with a predefined centralised database, analysis plan, and core age group (55–69 years), which assesses prostate-specific antigen (PSA) testing in eight European countries. Eligible men aged 50–74 years were identified from population registries and randomly assigned by computer generated random numbers to screening or no intervention (control). Investigators were masked to group allocation. The primary outcome was prostate cancer mortality in the core age group. Analysis was by intention to treat. We did a secondary analysis that corrected for selection bias due to non-participation. Only incidence and no mortality data at 9 years' follow-up are reported for the French centres. This study is registered with Current Controlled Trials, number ISRCTN49127736.

Findings With data truncated at 13 years of follow-up, 7408 prostate cancer cases were diagnosed in the intervention group and 6107 cases in the control group. The rate ratio of prostate cancer incidence between the intervention and control groups was 1·91 (95% CI 1·83–1·99) after 9 years (1·64 [1·58–1·69] including France), 1·66 (1·60–1·73) after 11 years, and 1·57 (1·51–1·62) after 13 years. The rate ratio of prostate cancer mortality was 0·85 (0·70–1·03) after 9 years, 0·78 (0·66–0·91) after 11 years, and 0·79 (0·69–0·91) at 13 years. The absolute risk reduction of death from prostate cancer at 13 years was 0·11 per 1000 person-years or 1·28 per 1000 men randomised, which is equivalent to one prostate cancer death averted per 781 (95% CI 490–1929) men invited for screening or one per 27 (17–66) additional prostate cancer detected. After adjustment for non-participation, the rate ratio of prostate cancer mortality in men screened was 0·73 (95% CI 0·61–0·88).

Interpretation In this update the ERSPC confirms a substantial reduction in prostate cancer mortality attributable to testing of PSA, with a substantially increased absolute effect at 13 years compared with findings after 9 and 11 years. Despite our findings, further quantification of harms and their reduction are still considered a prerequisite for the introduction of populated-based screening.

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See Online/Comment
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*For the full study group see appendix

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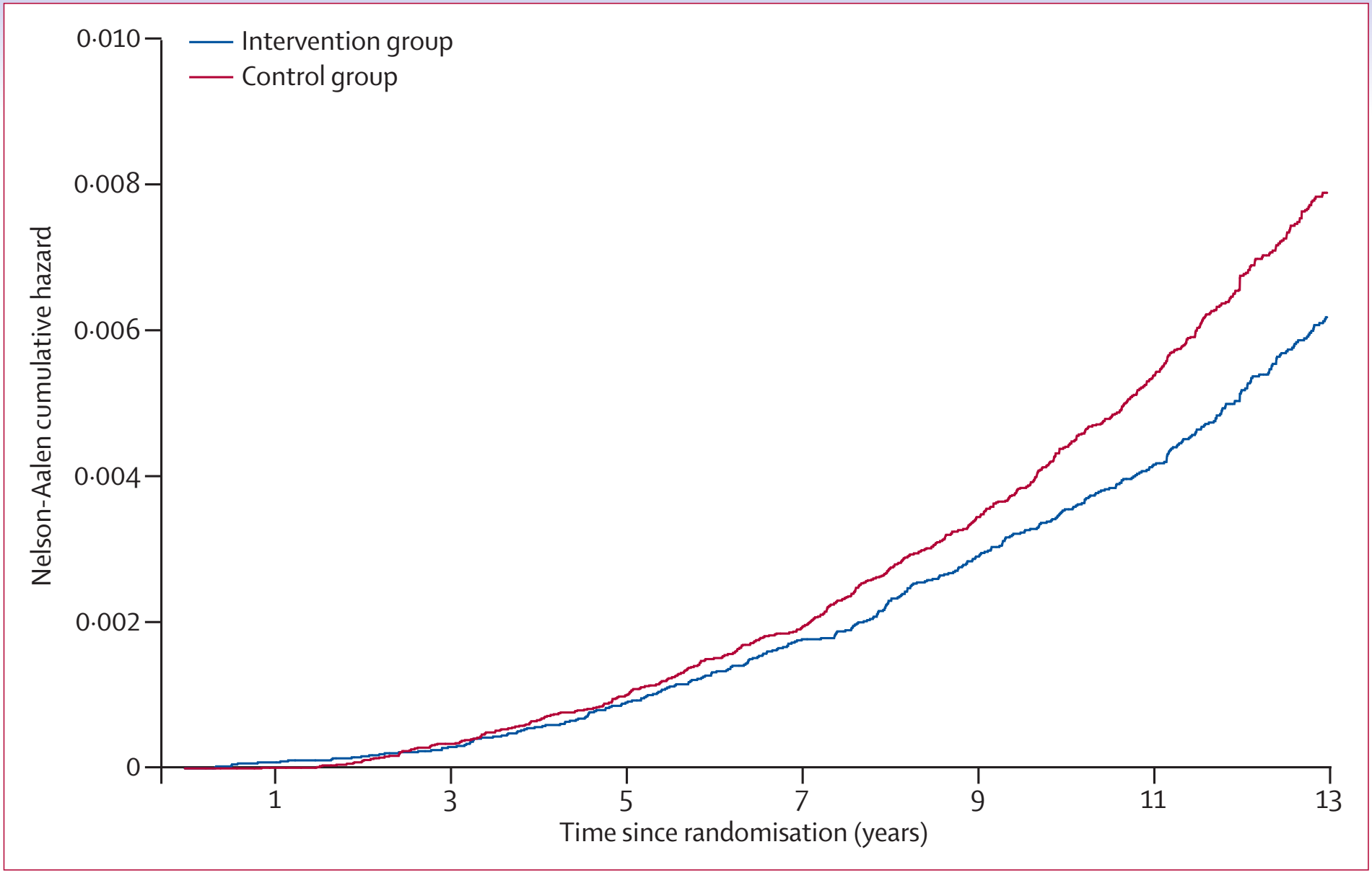


Figure 2: **Nelson–Aalen estimates of cumulative prostate cancer mortality (all centres, excluding France)**

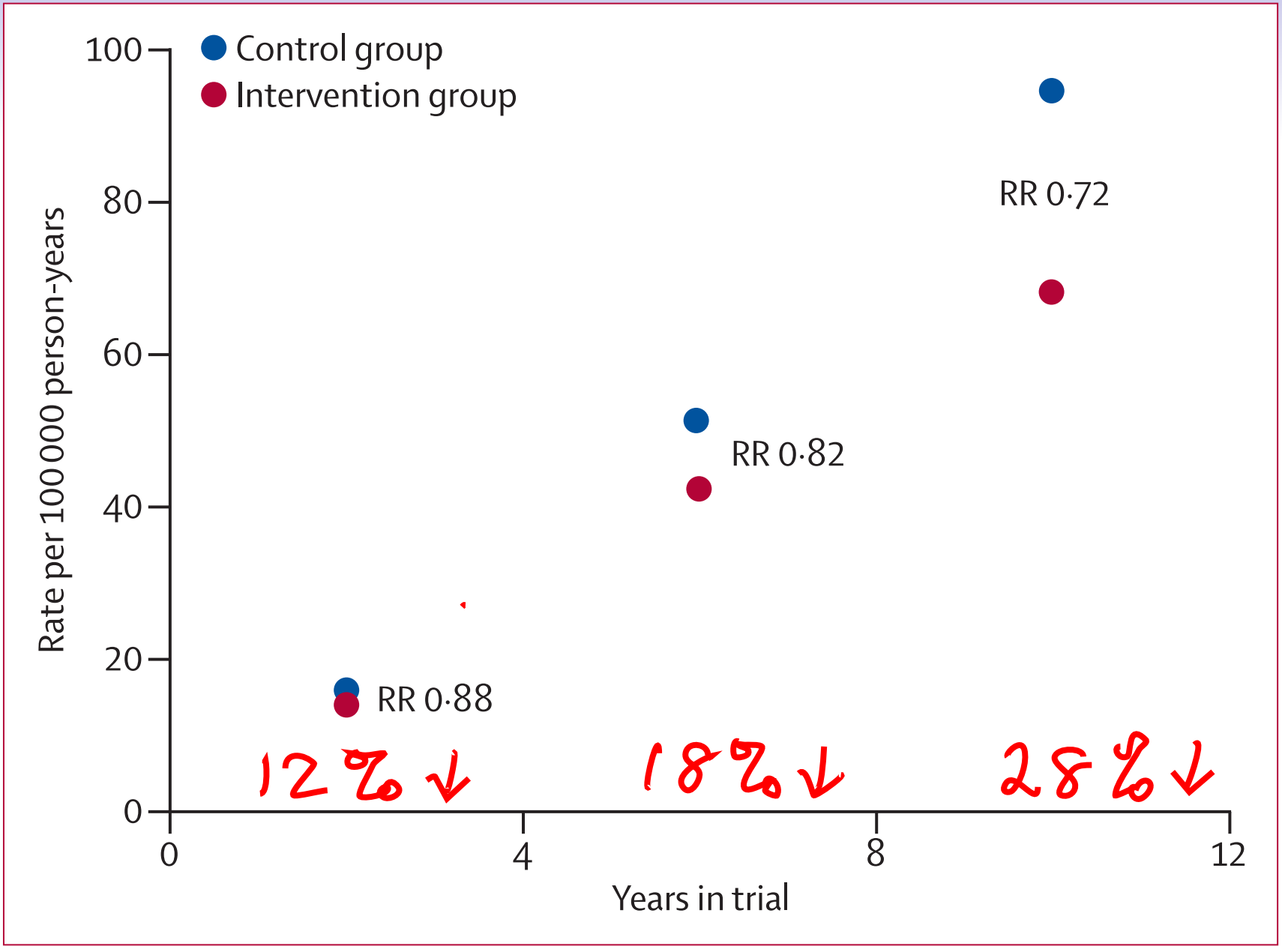


Figure 3: **Nelson-Aalen estimates of cumulative prostate cancer in both groups by 4-year periods (all centres, excluding France)**

COLON CANCER

FOBT screening for colon cancer – Minnesota Trial 1976-2008

Long-Term Mortality after Screening for Colorectal Cancer

Aasma Shaukat, M.D., M.P.H., Steven J. Mongin, M.S., Mindy S. Geisser, M.S., Frank A. Lederle, M.D., John H. Bond, M.D., Jack S. Mandel, Ph.D., M.P.H., and Timothy R. Church, Ph.D.

ABSTRACT

BACKGROUND

In randomized trials, fecal occult-blood testing reduces mortality from colorectal cancer. However, the duration of the benefit is unknown, as are the effects specific to age and sex.

METHODS

In the Minnesota Colon Cancer Control Study, 46,551 participants, 50 to 80 years of age, were randomly assigned to usual care (control) or to annual or biennial screening with fecal occult-blood testing. Screening was performed from 1976 through 1982 and from 1986 through 1992. We used the National Death Index to obtain updated information on the vital status of participants and to determine causes of death through 2008.

From the Divisions of Gastroenterology (A.S., J.H.B.) and Internal Medicine (F.A.L.), Minneapolis Veterans Affairs Health Care System, and the Department of Medicine, School of Medicine (A.S., F.A.L., J.H.B.), and the Division of Environmental Health Sciences, School of Public Health (S.J.M., M.S.G., T.R.C.), University of Minnesota — both in Minneapolis; and Exponent, Menlo Park, CA (J.S.M.). Address reprint requests to Dr. Shaukat at 1 Veterans Dr., 111-D, Minneapolis, MN 55417.

N Engl J Med 2013;369:1106-14.
DOI: 10.1056/NEJMoa1300720

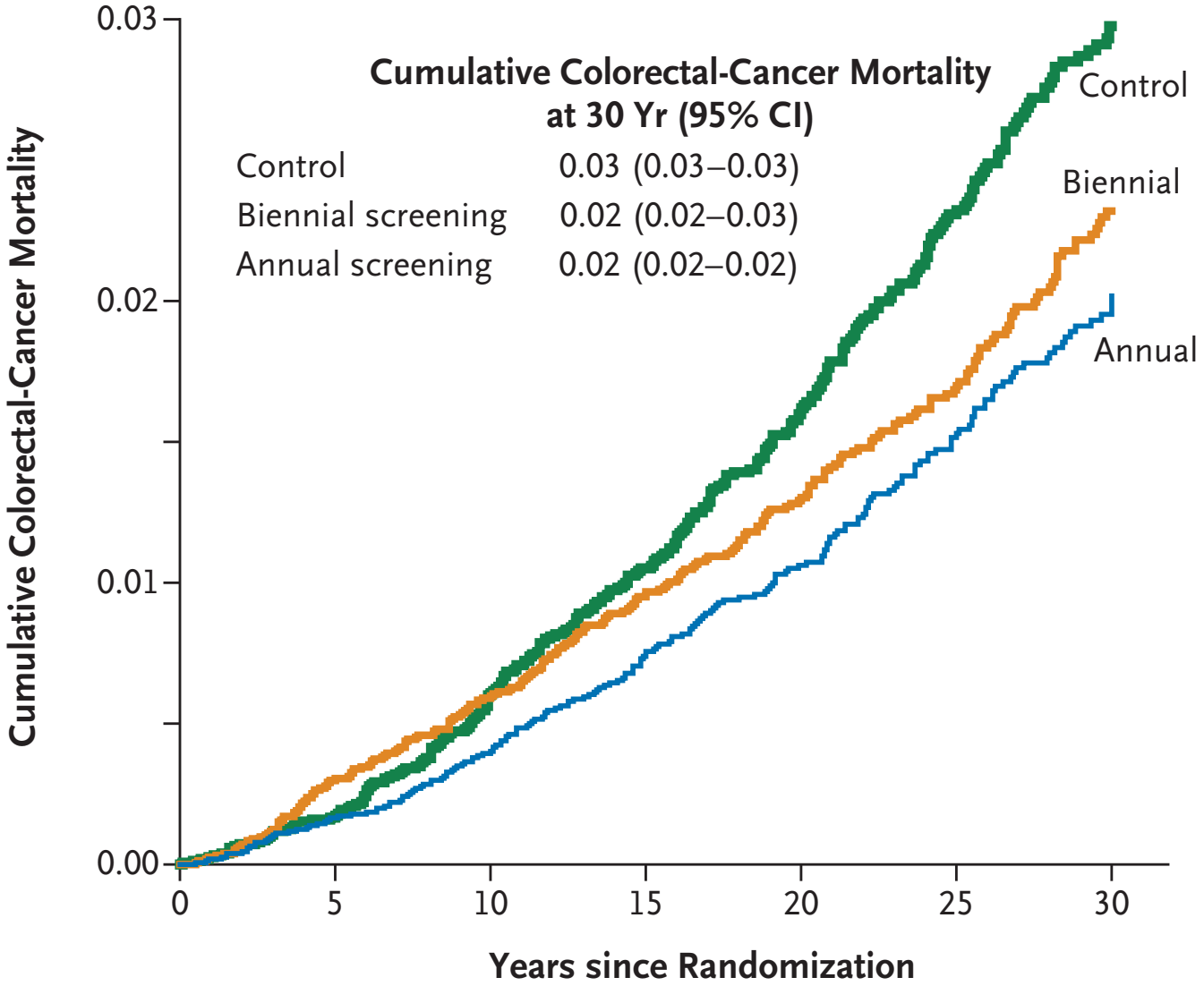
FOBT screening for colon cancer – Minnesota Trial 1976-2008

RESULTS

Through 30 years of follow-up, 33,020 participants (70.9%) died. A total of 732 deaths were attributed to colorectal cancer: 200 of the 11,072 deaths (1.8%) in the annual-screening group, 237 of the 11,004 deaths (2.2%) in the biennial-screening group, and 295 of the 10,944 deaths (2.7%) in the control group. Screening reduced colorectal-cancer mortality (relative risk with annual screening, 0.68; 32% onfidence interval [CI], 0.56 to 0.82; relative risk with biennial screening, 0.78; 22% , 0.65 to 0.93) through 30 years of follow-up. No reduction was observed in all-cause mortality (relative risk with annual screening, 1.00; 95% CI, 0.99 to 1.01; relative risk with biennial screening, 0.99; 95% CI, 0.98 to 1.01). The reduction in colorectal-cancer mortality was larger for men than for women in the biennial-screening group (P=0.04 for interaction).

CONCLUSIONS

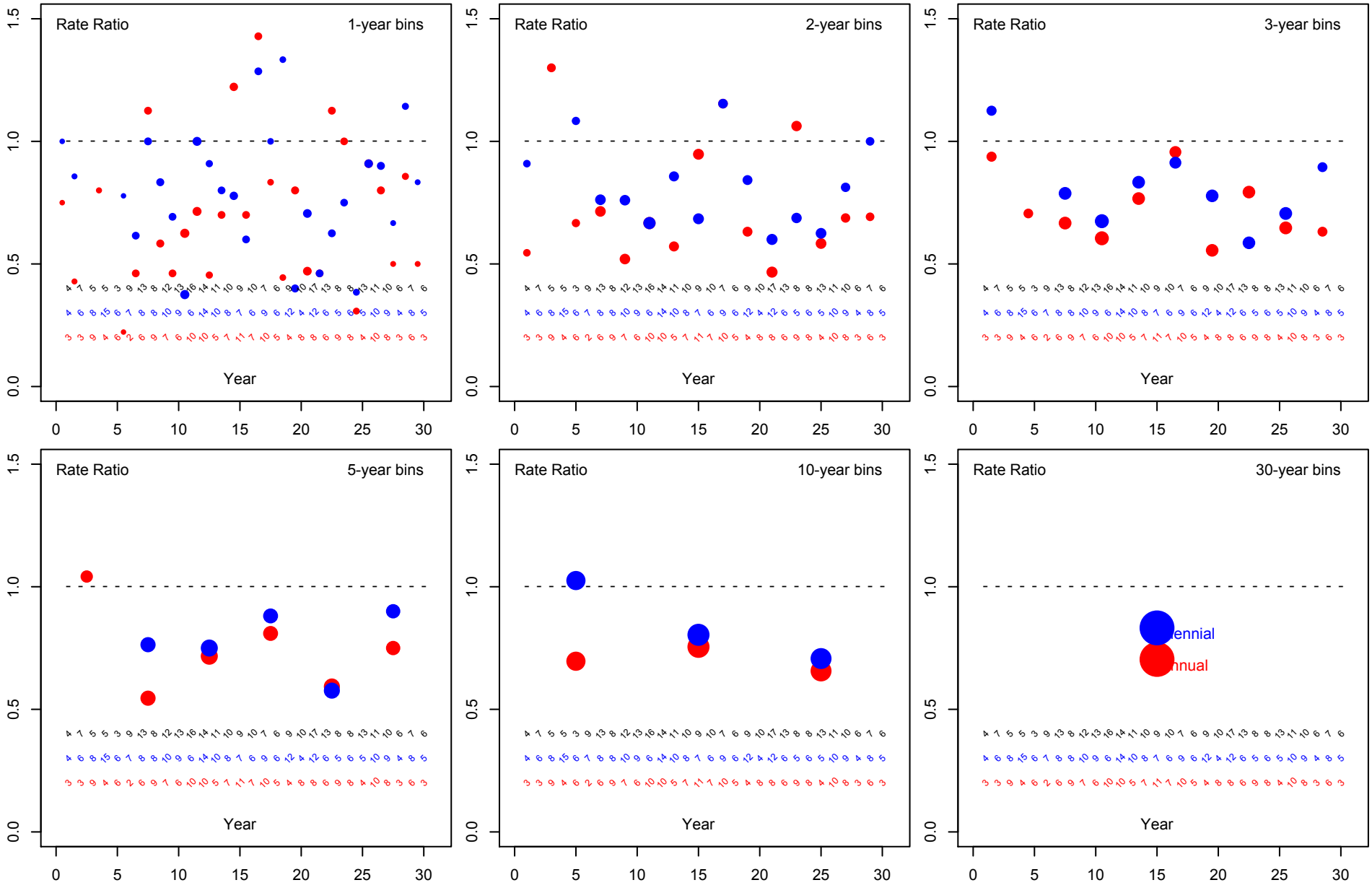
The effect of screening with fecal occult-blood testing on colorectal-cancer mortality persists after 30 years but does not influence all-cause mortality. The sustained reduction in colorectal-cancer mortality supports the effect of polypectomy. (Funded by the Veterans Affairs Merit Review Award Program and others.)



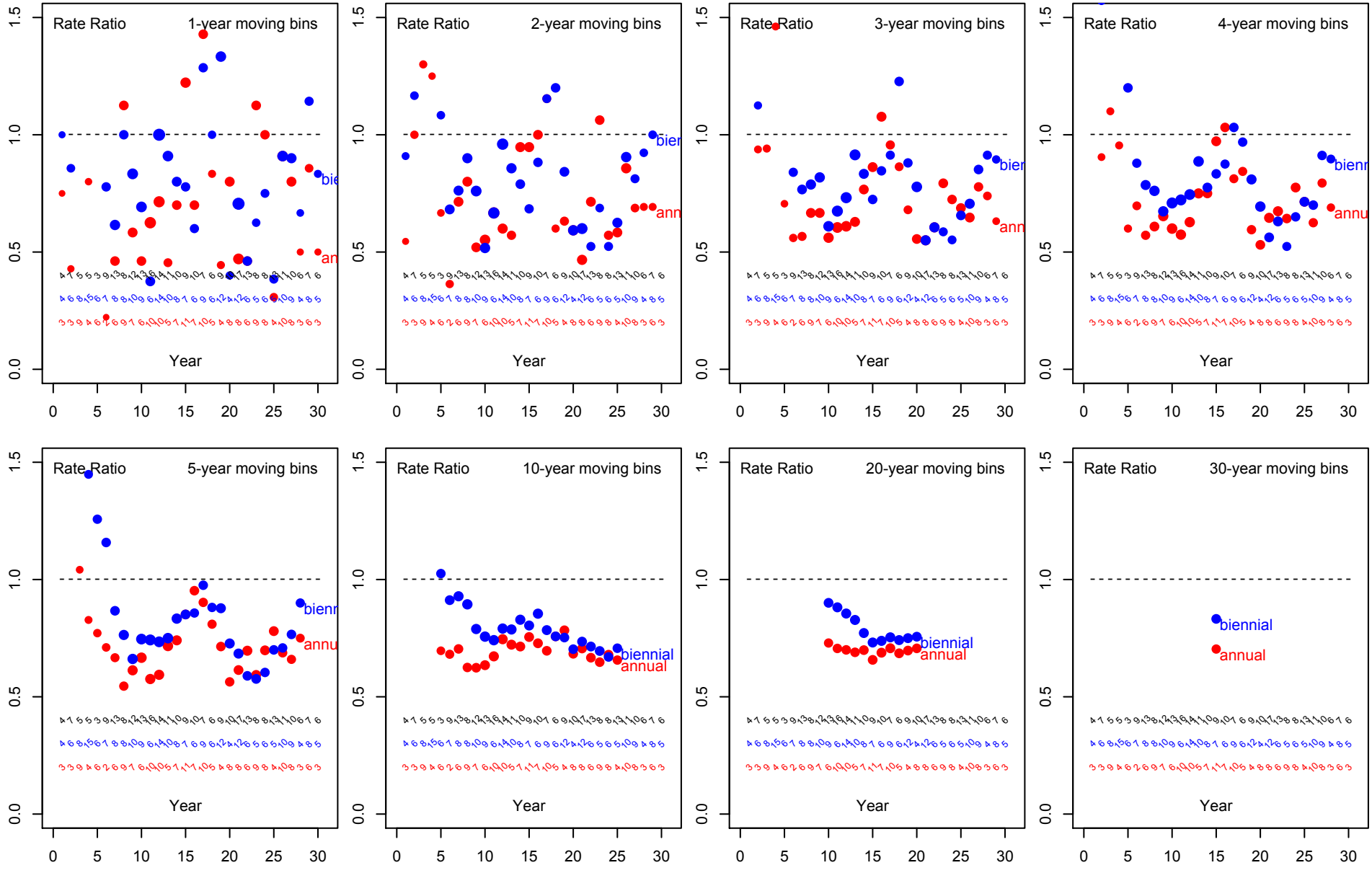
No. at Risk

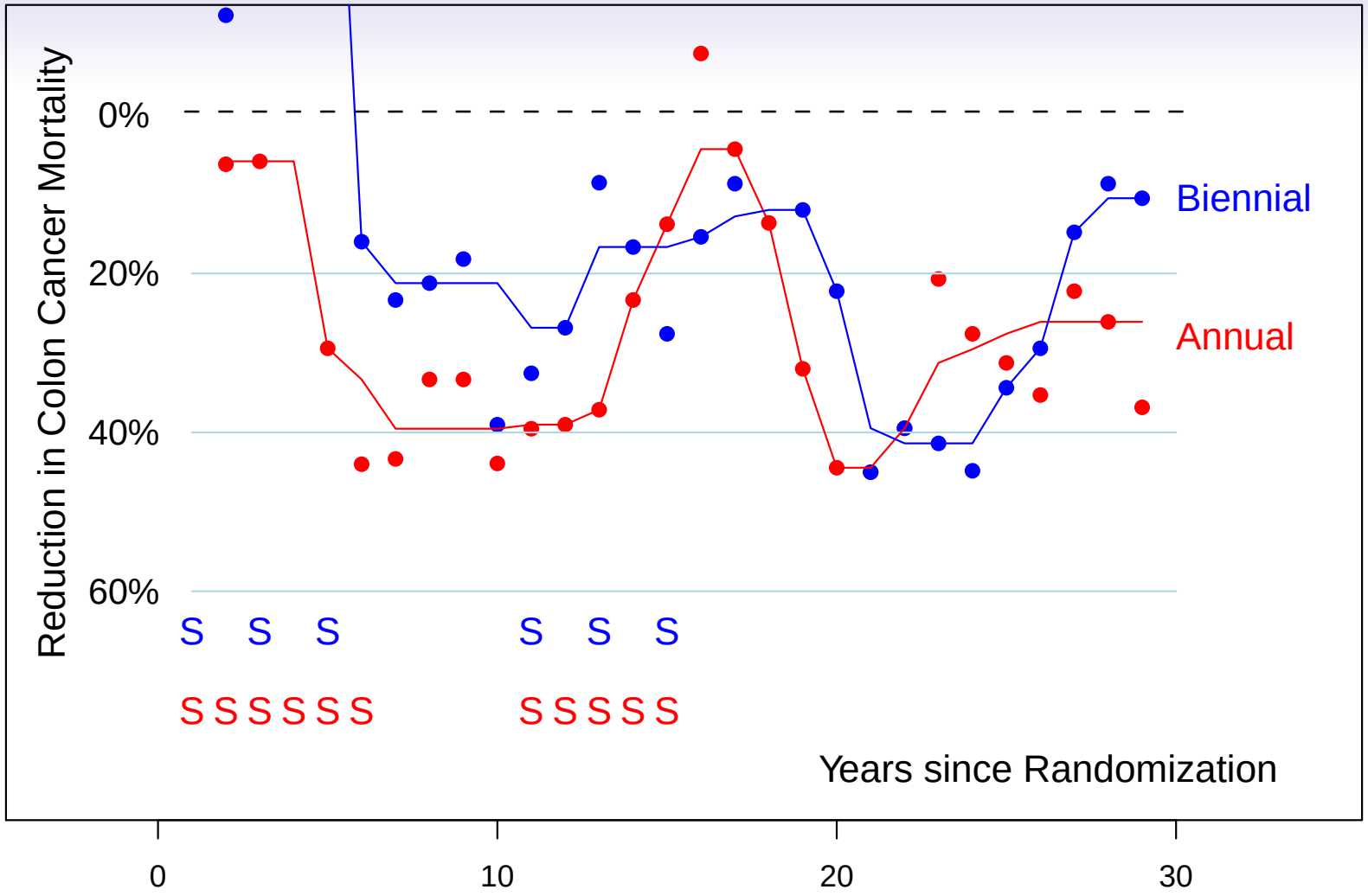
Control	14,497	13,103	11,320	9157	6741	4450
Biennial screening	14,635	13,243	11,445	9323	6802	4583
Annual screening	14,658	13,294	11,437	9219	6802	4498

Time-**split** versus time-**lumped** Rate Ratios



Time-**split** versus time-**lumped** Rate Ratios

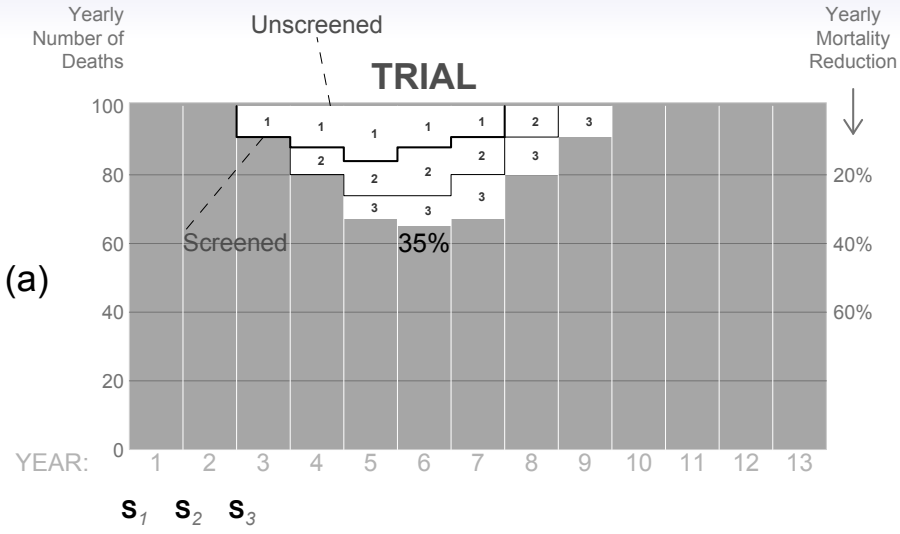




Yearly reductions in colon cancer mortality in two screening arms. Each dot is based on number of deaths in a three year moving window; smooth curves were fitted though them. Because the hiatus was in calendar-time rather than follow-up time, and entries were staggered, the timing of the screens (each denoted by an ‘S’) is only approximate.

From **Trial** to **Program**

STATISTICAL MODEL



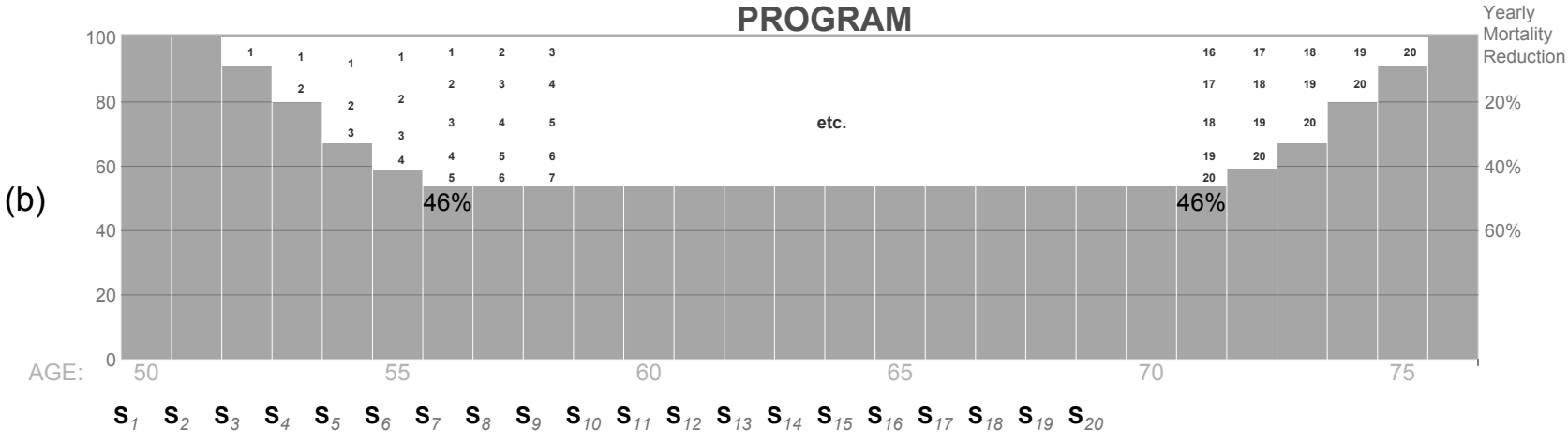
Remarks

If one round of screening reduces mortality in each of 5 future years, then in a trial, 3 rounds of screening -- S1, S2 and S3 -- would produce 3 'waves' of mortality reductions ('1', '2', '3'), each 5 years wide, over 7 years (Y3-Y9).

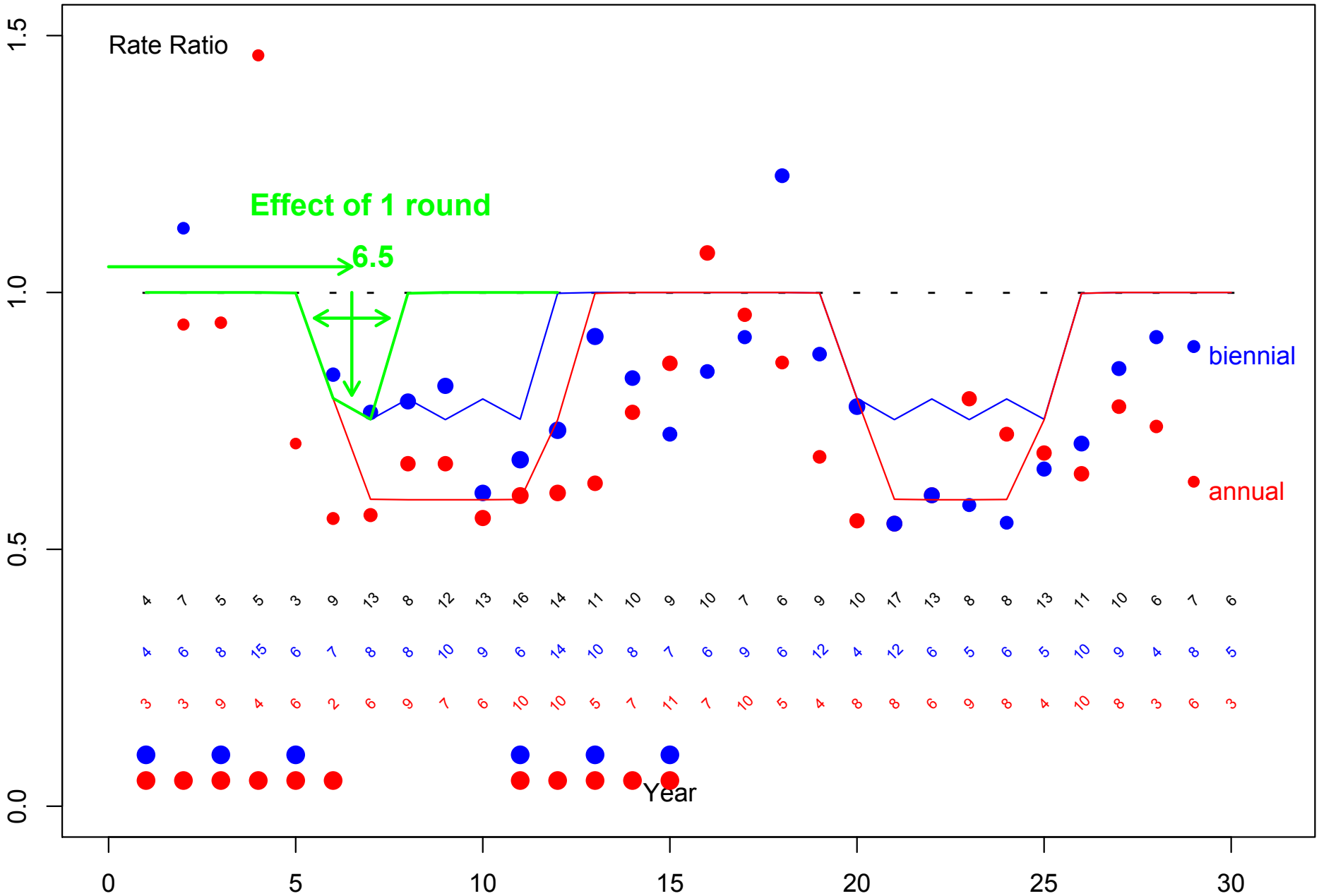
In such a trial, the maximal reduction (35%, year 6) would be smaller than the sustained (46%) reductions produced by a 20-year screening program.

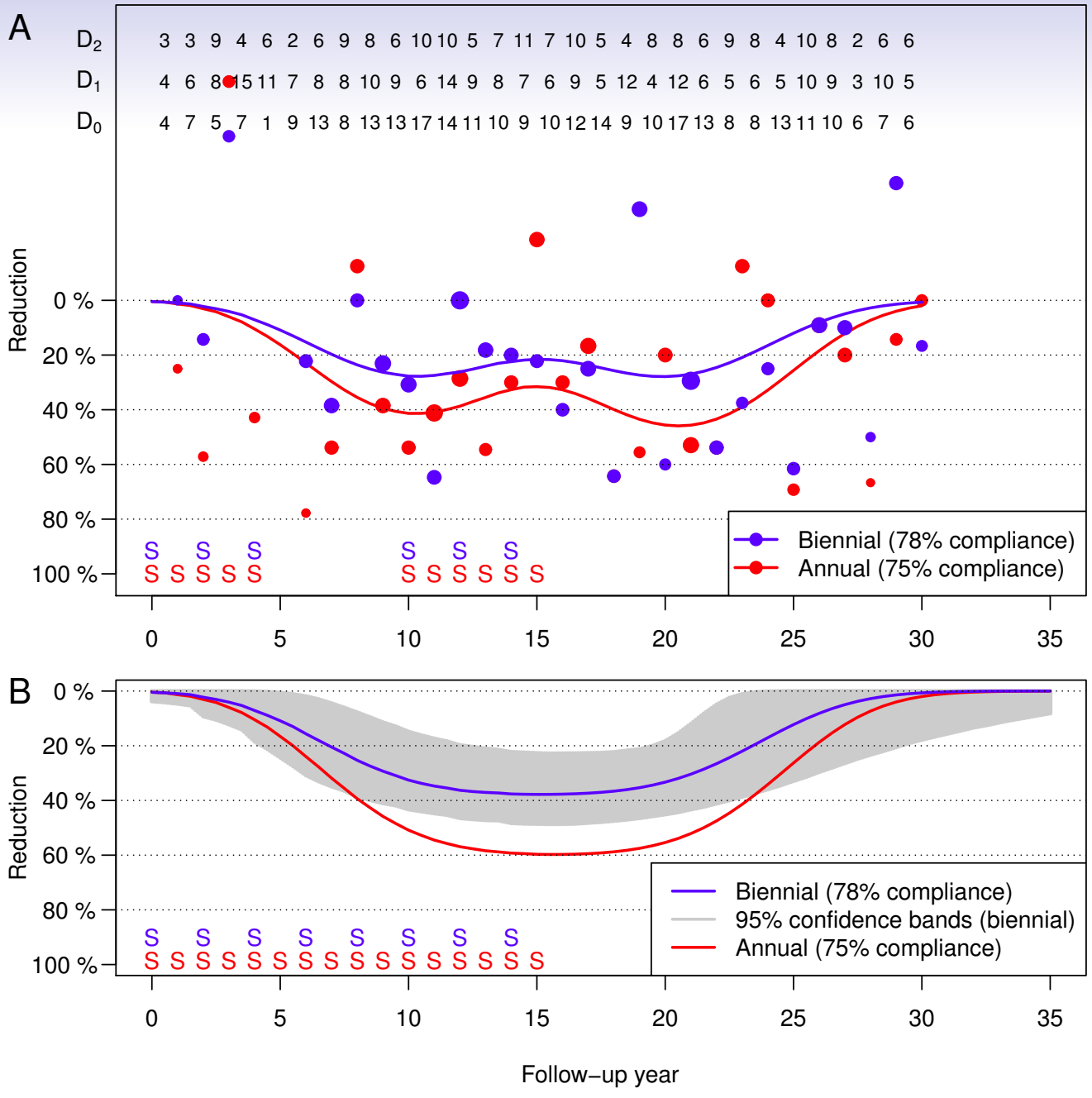
The average reduction, computed over 13 years of follow-up in such a trial would be an even more serious underestimate of the impact of a 20-year program.

Annual mortality reductions produced by once-a-year screening that begins when women reach 50, and ends when they reach 69



Fitted Model (each round) & Resulting Fits for 6 and 11 Rounds (JH)

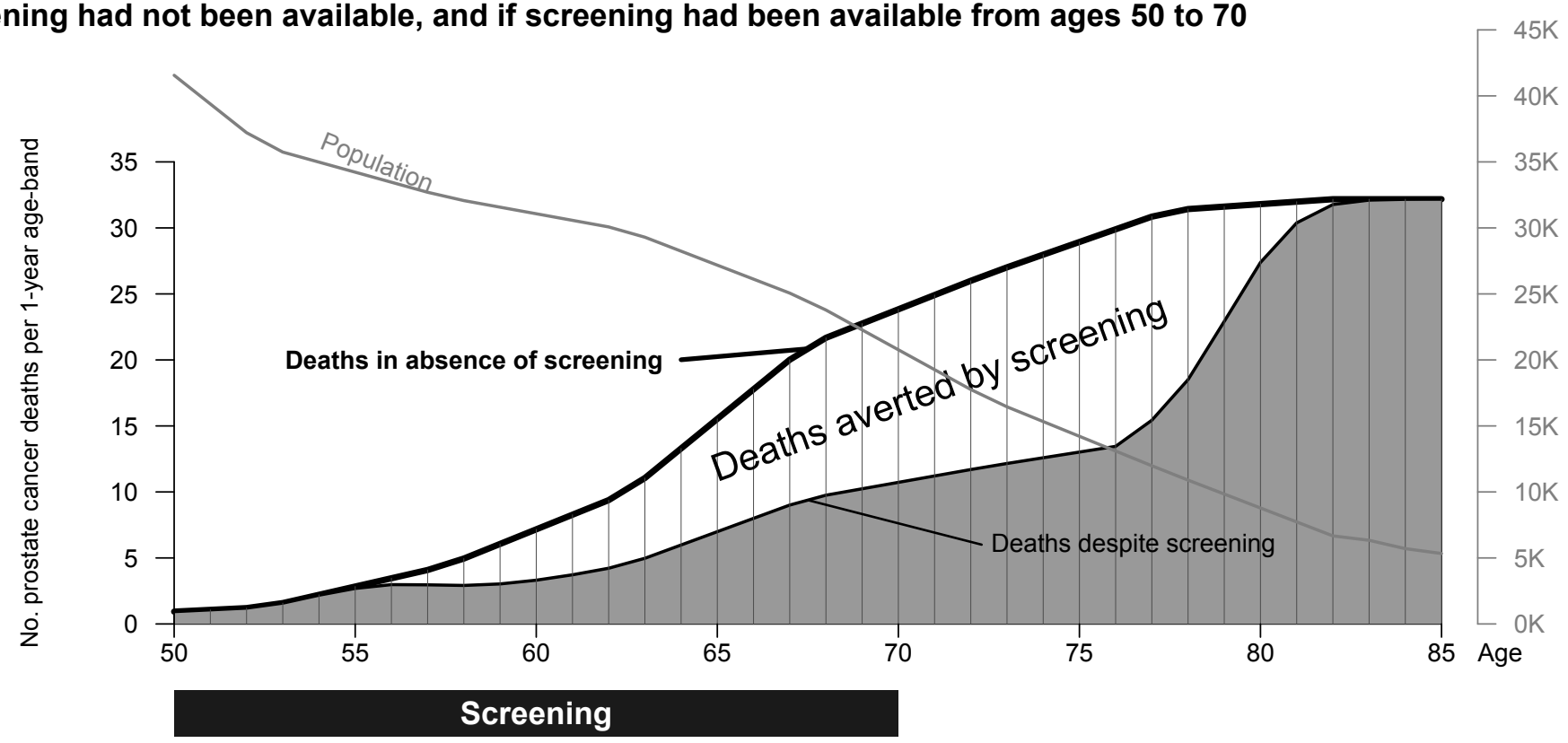




Liu, PhD Biostatistics, McGill 2014; International Statistical Review 2015.

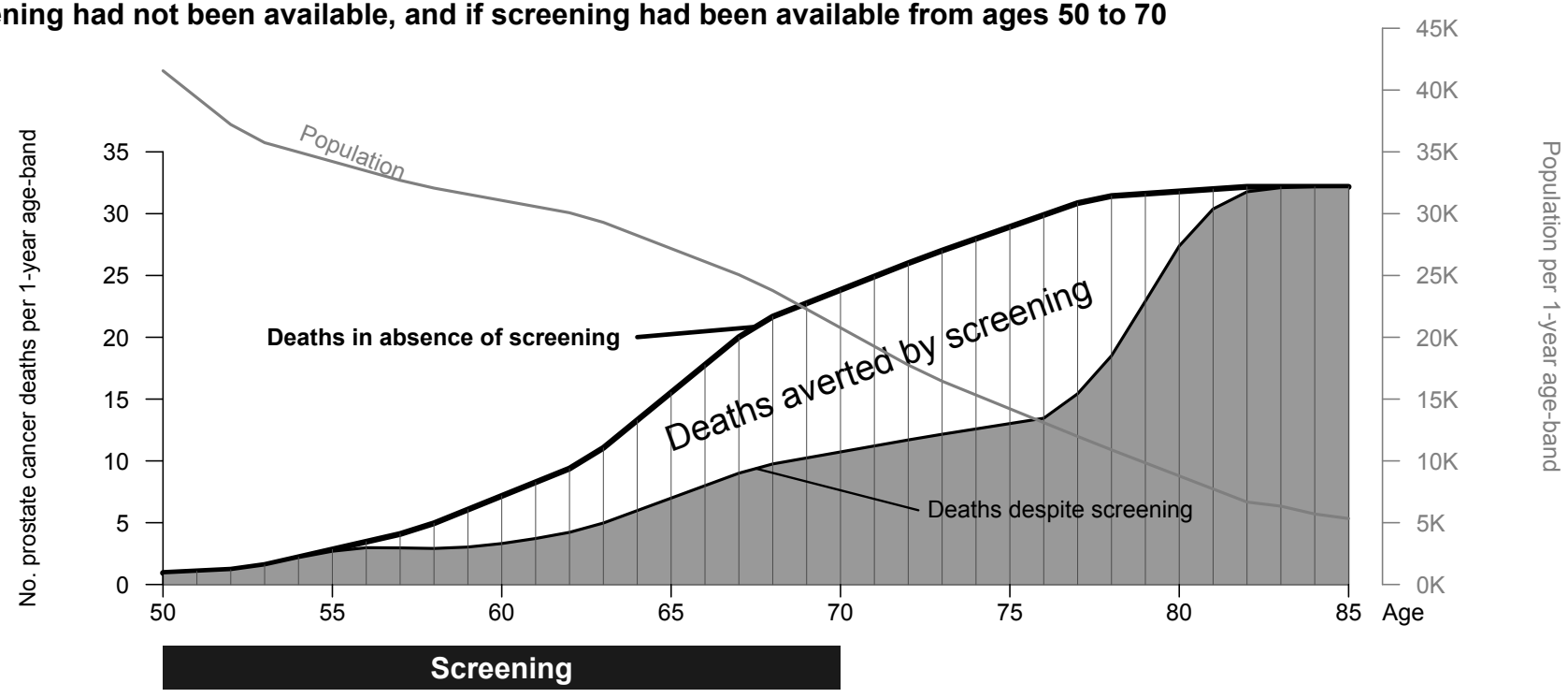
What payers would like to know about a PROGRAM

(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

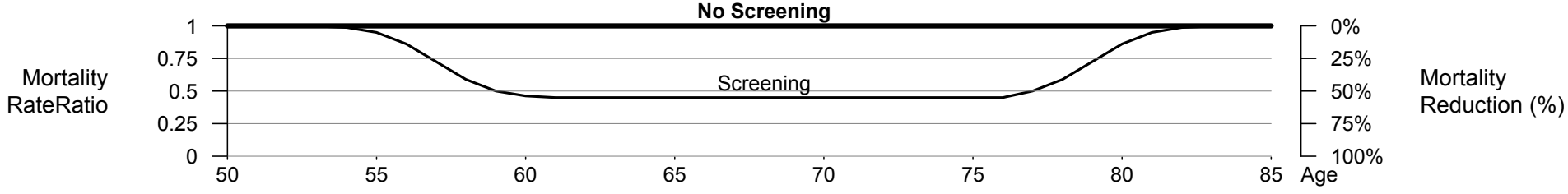


or (b) the Rate Ratio (or %Reduction) **Function** ...

(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



BREAST CANCER

???

Magnitude of reductions being achieved with contemporary mammography

Estimates from (non-experimental) population-based studies

HOW NOT TO conduct population-based studies

BMJ

BMJ 2011;343:d4411 doi: 10.1136/bmj.d4411

RESEARCH

Breast cancer mortality in neighbouring European countries with different levels of screening but similar access to treatment: trend analysis of WHO mortality database

Philippe Autier *research director*[1], Mathieu Boniol *senior statistician*[1], Anna Gavin *director*[2], Lars J Vatten *professor*[3]

[1]International Prevention Research Institute, 95 Cours Lafayette, 69006 Lyon, France; [2]Northern Ireland Cancer Registry, Belfast, Northern Ireland, UK; [3]Department of Public Health, Norwegian University of Science and Technology, Trondheim, Norway

Abstract

Objective To compare trends in breast cancer mortality within three pairs of neighbouring European countries in relation to implementation of screening.

Design Retrospective trend analysis.

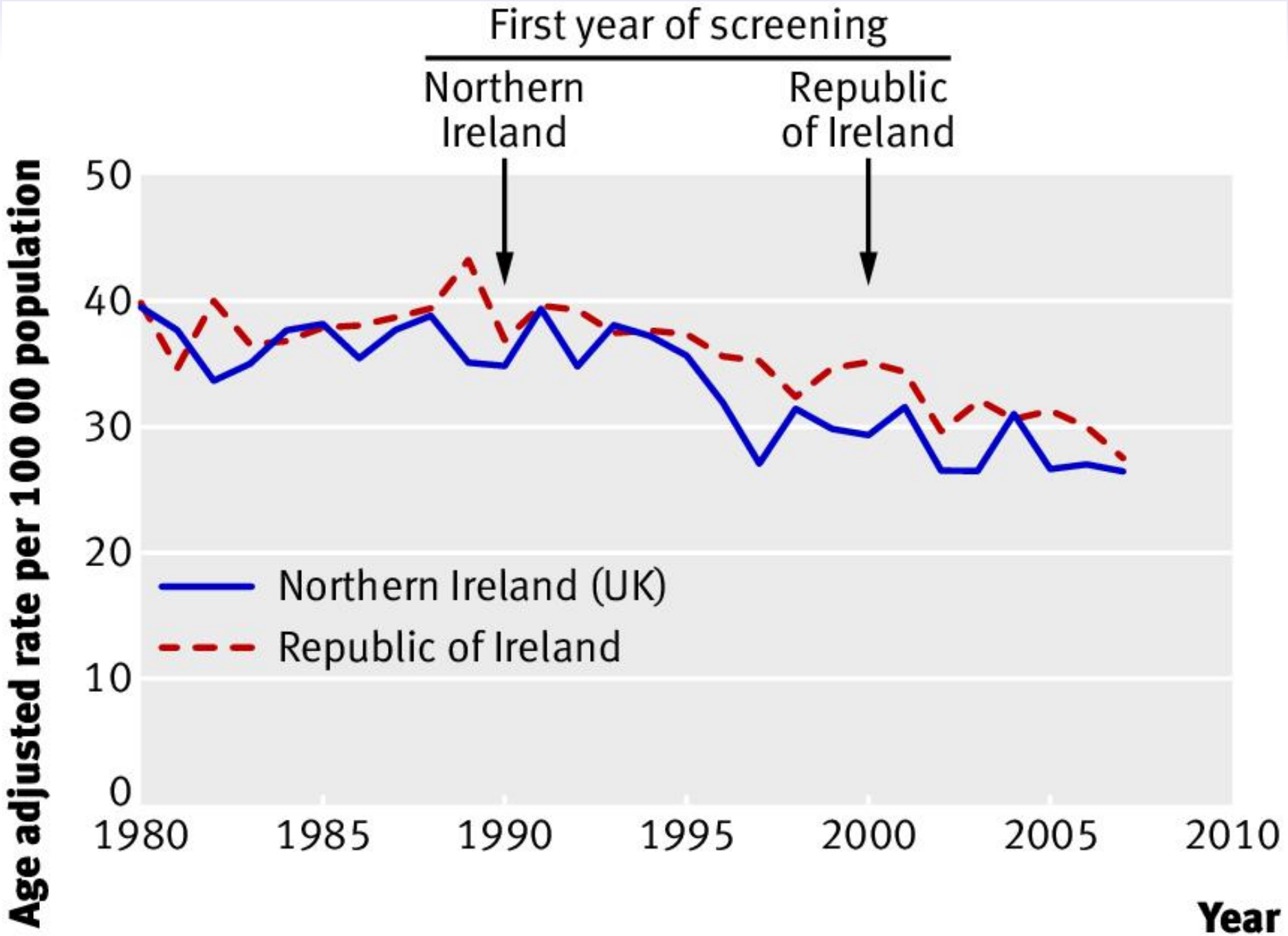
Setting Three country pairs (Northern Ireland (United Kingdom) *v* Republic of Ireland, the Netherlands *v* Belgium and Flanders (Belgian region south of the Netherlands), and Sweden *v* Norway).

Data sources WHO mortality database on cause of death and data sources on mammography screening, cancer treatment, and risk factors for breast cancer mortality.

Main outcome measures Changes in breast cancer mortality calculated from linear regressions of log transformed, age adjusted death rates. Joinpoint analysis was used to identify the year when trends in mortality for all ages began to change.

Results From 1989 to 2006, deaths from breast cancer decreased by 29% in Northern Ireland and by 26% in the Republic of Ireland; by 25% in the Netherlands and by 20% in Belgium and 25% in Flanders; and by 16% in Sweden and by 24% in Norway. The time trend and year of downward inflexion were similar between Northern Ireland and the Republic of Ireland and between the Netherlands and Flanders. In Sweden, mortality rates have steadily decreased since 1972, with no downward inflexion until 2006. Countries of each pair had similar healthcare services and prevalence of risk factors for breast cancer mortality but differing implementation of mammography screening, with a gap of about 10-15 years.

Conclusions The contrast between the time differences in implementation of mammography screening and the similarity in reductions in mortality between the country pairs suggest that screening did not play a direct part in the reductions in breast cancer mortality.


First year of screening
Northern Ireland
Republic of Ireland
Age adjusted rate per 100 00 population
50
40
30
20
10
0
1980
1985
1990
1995
2000
2005
2010
Year
Northern Ireland (UK)
Republic of Ireland

Why this big-data approach DILUTES the impact

Most of the breast cancer deaths in Northern Ireland in the early 1990s involved cancers that had been DIAGNOSED BEFORE the screening was introduced.

These women could not have been helped by the program.

Screening pursues not-yet-diagnosed cancers (so as to treat them earlier)

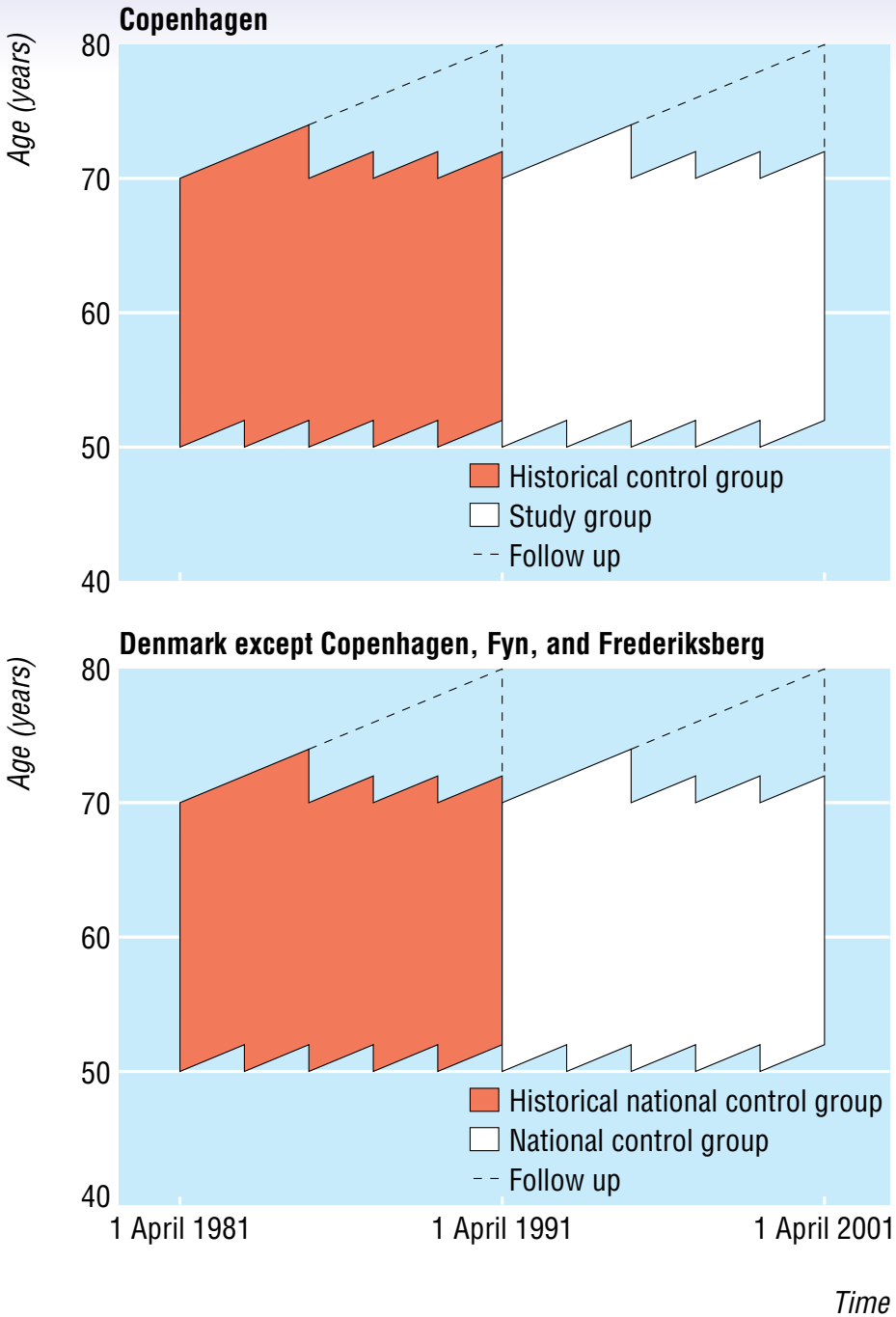
HOW TO conduct population-based studies

Cite this article as: BMJ, doi:10.1136/bmj.38313.639236.82 (published 13 January 2005)

Papers

Breast cancer mortality in Copenhagen after introduction of mammography screening: cohort study

Anne Helene Olsen, Sisse H Njor, Ilse Vejborg, Walter Schwartz, Peter Dalgaard, Maj-Britt Jensen, Ulla Brix Tange, Mogens Blichert-Toft, Fritz Rank, Henning Mouridsen, Elsebeth Lynge



Authors excluded women with prevalent breast cancer on their invitation date or pseudo-invitation date.

i.e., they focused on women who were eligible for the program, or would have been, had it been available in that region or at that time.

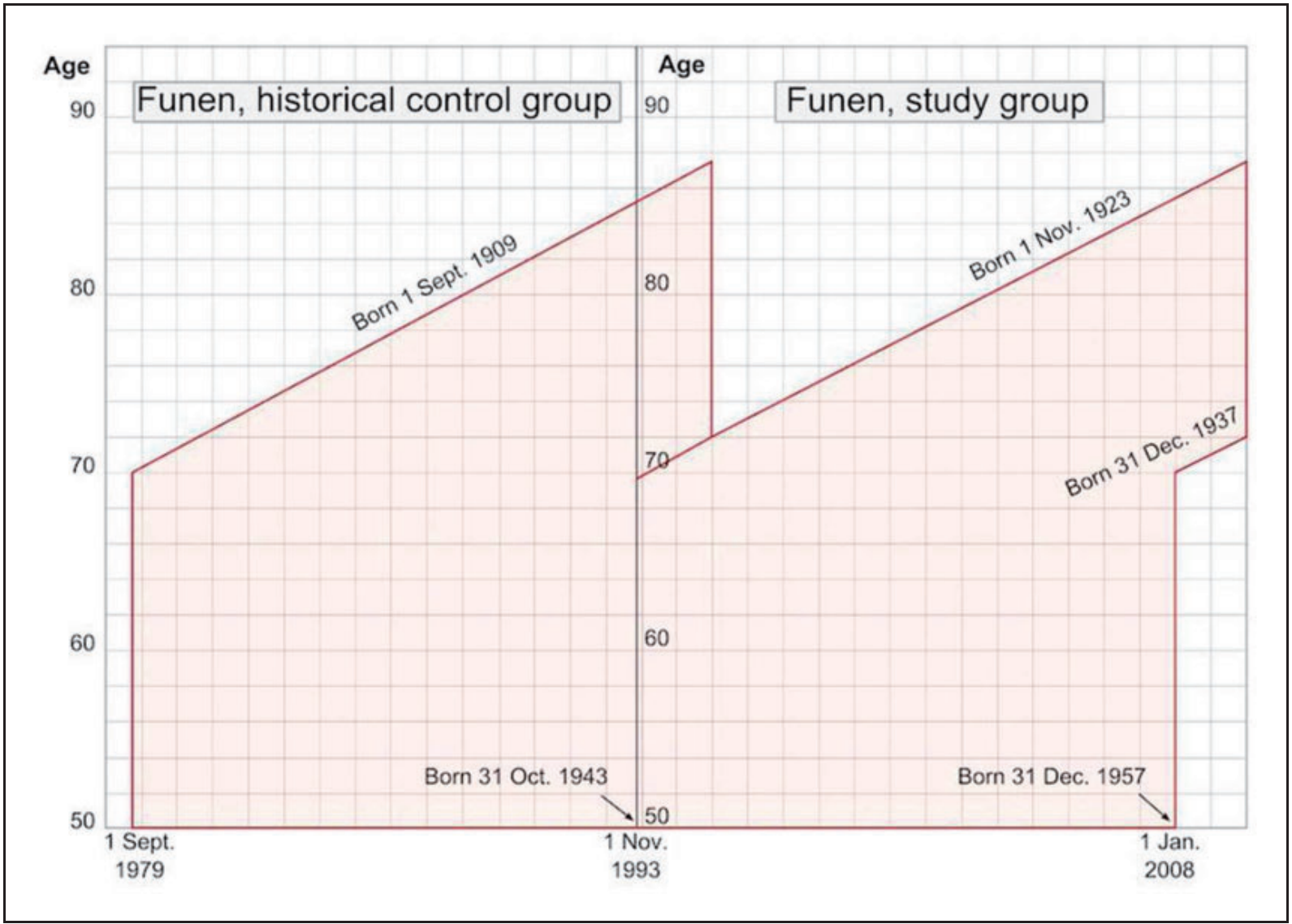
in FUNEN

Decline in breast cancer mortality: How much is attributable to screening?

J Med Screen
2015, Vol. 22(1) 20–27

DOI: 10.1177/0969141314563632
msc.sagepub.com
SAGE

Sisse Helle Njor[1], Walter Schwartz[2], Mogens Blichert-Toft[3] and Elsebeth Lynge[1]



Breast cancer mortality in mammographic screening in Europe: a review of incidence-based mortality studies

Sisse Njor, Lennarth Nyström, Sue Moss, Eugenio Paci, Mireille Broeders, Nereo Segnan, Elsebeth Lynge and The Euroscreen Working Group (members listed at the end of the paper)

J Med Screen 2012;**19 Suppl 1**:33–41
DOI: 10.1258/jms.2012.012080

Objectives To estimate the impact of service mammography screening on breast cancer mortality using European incidence-based mortality (IBM) studies (or refined mortality studies). IBM studies include only breast cancer deaths occurring in women with breast cancer diagnosed after their first invitation to screening.

Methods We conducted a literature review and identified 20 publications based on IBM studies. They were classified according to the method used for estimating the expected breast cancer mortality in the absence of screening: (1) women not yet invited; (2) historical data from the same region as well as from historical and current data from a region without screening; and (3) historical comparison group combined with data for non-participants.

Results The estimated effect of mammography screening on breast cancer mortality varied across studies. The relative risks were 0.76–0.81 in group 1; 0.75–0.90 in group 2; and 0.52–0.89 in group 3. Study databases overlapped in both Swedish and Finnish studies, adjustment for lead time was not optimal in all studies, and some studies had other methodological limitations. There was less variability in the relative risks after allowing for the methodological shortcomings.

Conclusions Based on evidence from the most methodologically sound IBM studies, the most likely impact of European service mammography screening programmes was a breast cancer mortality reduction of 26% (95% confidence interval 13–36%) among women invited for screening and followed up for 6–11 years.

See end of article for authors' affiliations

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Accepted for publication 20 June 2012

Norway

Diluted estimate of impact

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 23, 2010 VOL. 363 NO. 13

Effect of Screening Mammography on Breast-Cancer Mortality in Norway

Mette Kalager, M.D., Marvin Zelen, Ph.D., Frøydis Langmark, M.D., and Hans-Olov Adami, M.D., Ph.D.

Screening program was started in one region in 1996 and expanded to all 6 regions during subsequent 9 years.

Women between the ages of 50 and 69 years were offered screening mammography every 2 years.

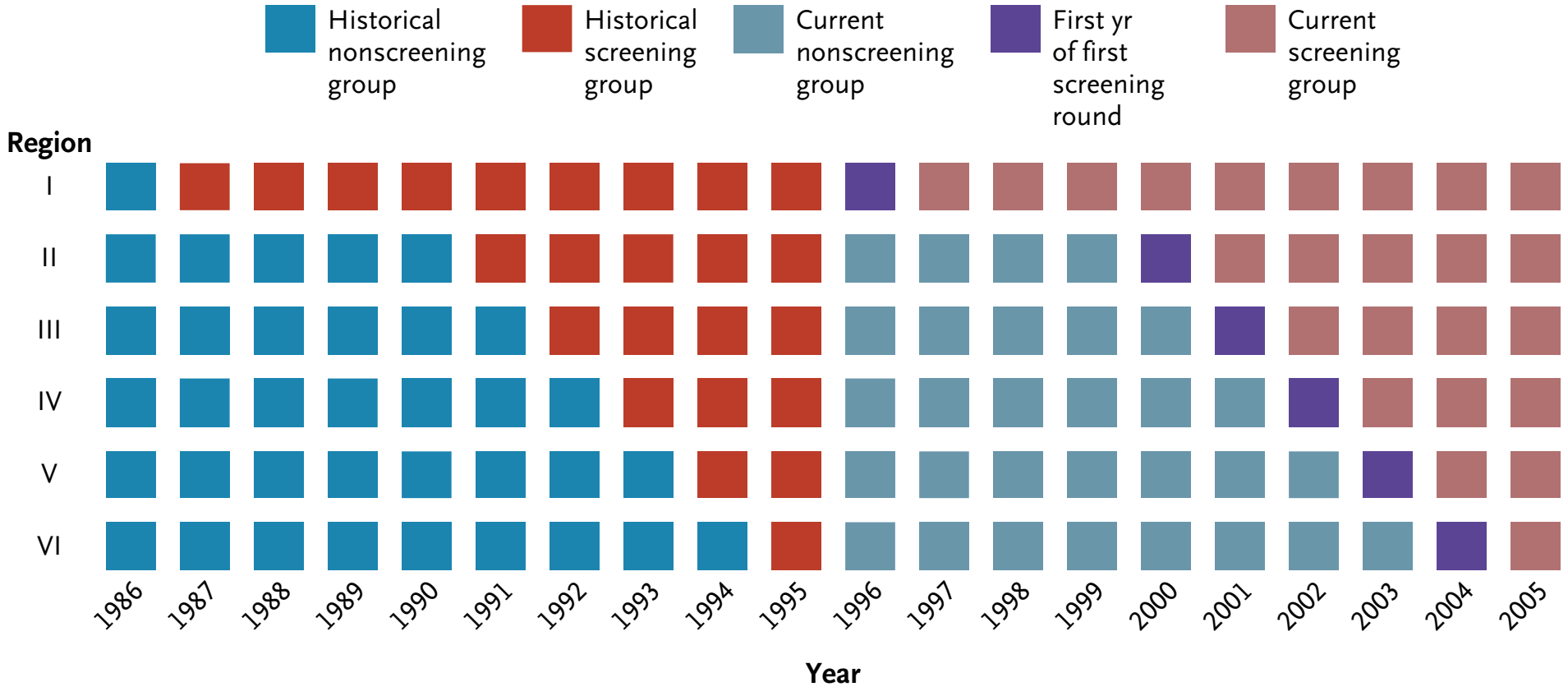


Figure 1. The Four Study Groups, According to Region and Year.

The 19 counties were grouped into six regions according to the date of introduction of the screening program, which was implemented throughout the country in a staggered fashion, starting in 1996. The screening group consisted of women who received a diagnosis of breast cancer after the introduction of the screening program. The nonscreening group consisted of women living in regions where screening was not offered in the same calendar period that screening was offered in other regions. The historical study groups consisted of women residing in the 19 counties in the 10-year period before screening was offered. A screening round lasted for 2 years, and the first year of the first round was included in both the screening and nonscreening groups (purple).

Double-difference: adjust for concomitant improvements in treatment

Table 1. Rates of Death from Breast Cancer, According to Study Group and Age.*

Age Group and Mortality Data	Nonscreening Groups		Screening Groups		Difference		
	Historical Group	Current Group	Historical Group	Current Group	Nonscreening Groups†	Screening Groups‡	Nonscreening Groups vs. Screening Groups§
50–69 Yr							
No. of deaths	494	396	555	423			
No. of person-yr	1,898,989	1,866,741	2,197,469	2,337,323			
No. of deaths/100,000 person-yr	26.0	21.2	25.3	18.1	4.8	7.2	2.4±4.1
Rate ratio for death (95% CI)					0.82 (0.71–0.93)	0.72 (0.63–0.81)	0.10
20–49 Yr							
No. of deaths	238	183	332	267			
No. of person-yr	3,842,740	4,030,443	5,134,212	5,357,163			
No. of deaths/100,000 person-yr	6.2	4.5	6.5	5.0	1.7	1.5	–0.2±4.4
Rate ratio for death (95% CI)					0.73 (0.63–0.92)	0.77 (0.65–0.90)	–0.04
70–84 Yr							
No. of deaths	429	386	623	465			
No. of person-yr	1,101,019	1,173,624	1,349,967	1,318,004			
No. of deaths/100,000 person-yr	39.0	32.9	46.1	35.3	6.1	10.8	4.7±6.9
Rate ratio for death (95% CI)					0.84 (0.74–0.97)	0.76 (0.68–0.86)	0.08

* Only women between the ages of 50 and 69 years were invited to participate in screening mammography. All women in this group were also eligible for treatment by the multidisciplinary teams that are part of the screening program.

† For the nonscreening groups, the value shown is the difference between the rate of death in the historical group and that in the current group. This difference represents changes in mortality over time as a result of increased breast-cancer awareness, improved therapy, and more sensitive diagnostic tools.

Results & Conclusions

The rate of death was reduced by 7.2 deaths per 100,000 person-years in the screening group as compared with the historical screening group (rate ratio, 0.72; and by 4.8 deaths per 100,000 person-years in the nonscreening group as compared with the historical nonscreening group (rate ratio, 0.82; for a relative reduction in mortality of 10% in the screening group. Thus, the difference in the reduction in mortality between the current and historical groups that could be attributed to screening alone was 2.4 deaths per 100,000 person-years, or a third of the total reduction of 7.2 deaths.

The availability of screening mammography was associated with a reduction in the rate of death from breast cancer, but the screening itself accounted for only about a third of the total reduction.

Time-insensitivity DILUTES estimated impact.

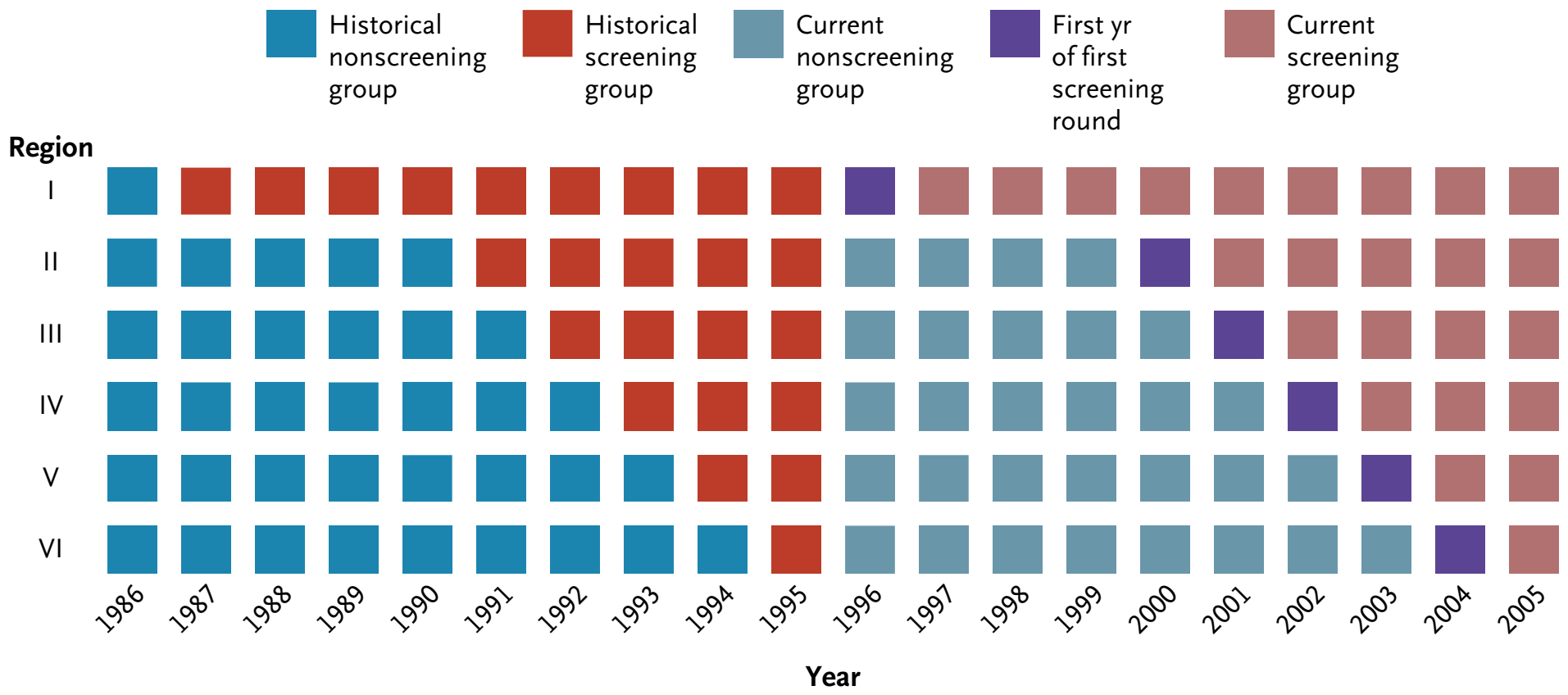
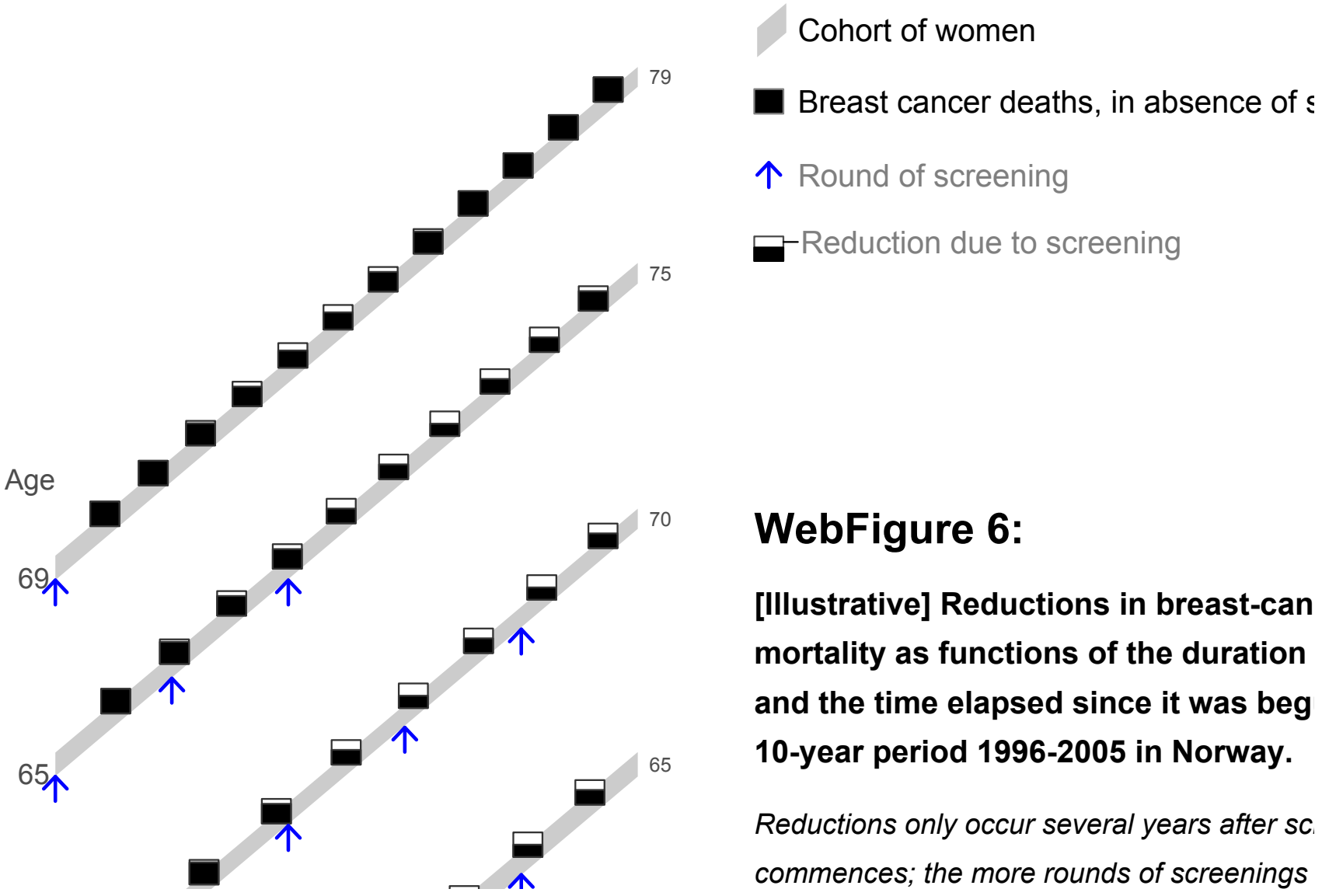


Figure 1. The Four Study Groups, According to Region and Year.

The 19 counties were grouped into six regions according to the date of introduction of the screening program, which was implemented throughout the country in a staggered fashion, starting in 1996. The screening group consisted of women who received a diagnosis of breast cancer after the introduction of the screening program. The nonscreening group consisted of women living in regions where screening was not offered in the same calendar period that screening was offered in other regions. The historical study groups consisted of women residing in the 19 counties in the 10-year period before screening was offered. A screening round lasted for 2 years, and the first year of the

Age-insensitivity DILUTES estimated impact



WebFigure 6:

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

Reductions only occur several years after sc commences; the more rounds of screenings

Hanley JA. *Epidemiologic Reviews*, 2011

Avoiding dilution, & improving precision

BMJ 2014;348:g3701 doi: 10.1136/bmj.g3701 (Published 17 June 2014)

NORWAY

RESEARCH

Modern mammography screening and breast cancer mortality: population study

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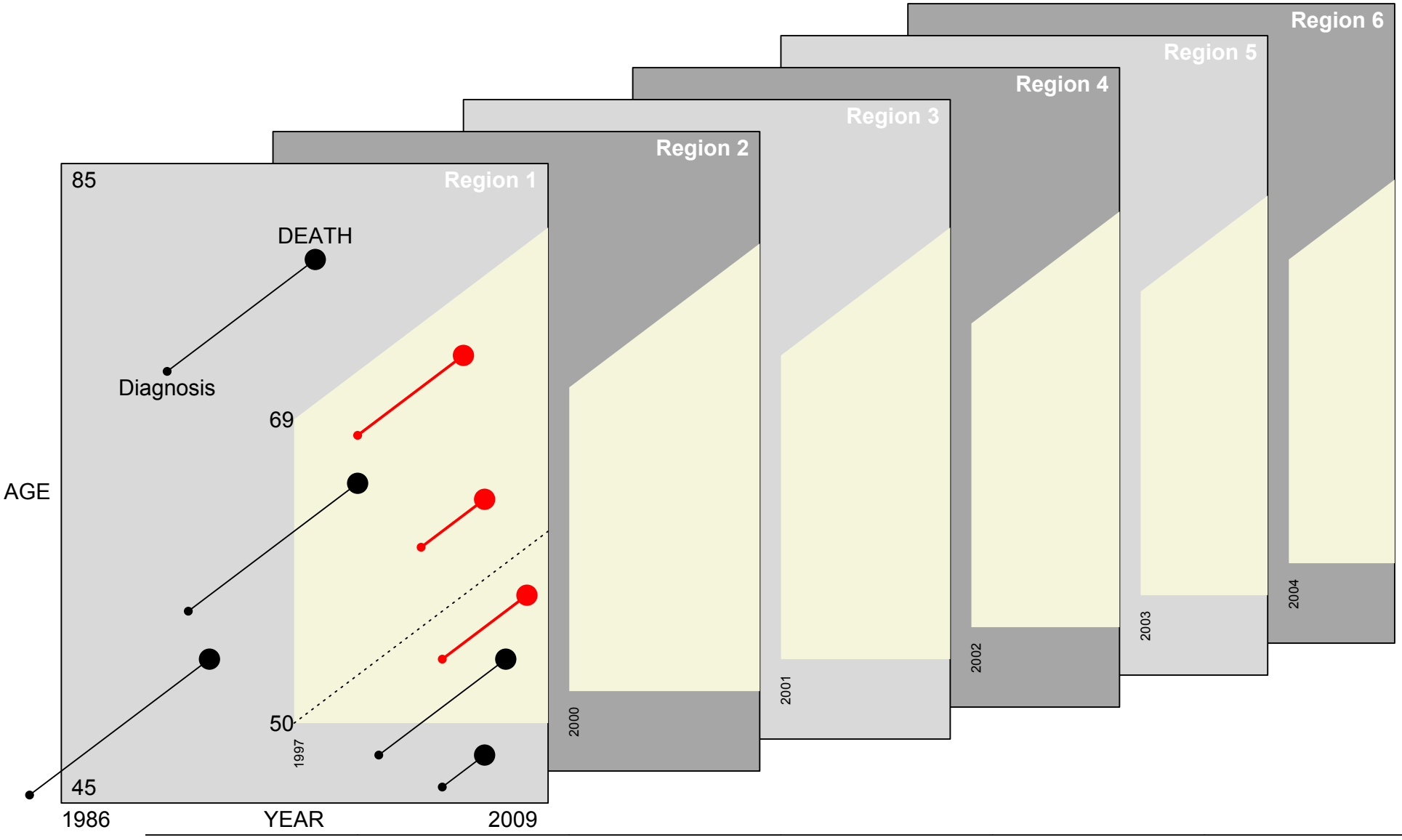
[1]Department of Public Health, Norwegian University of Science and Technology, 7491 Trondheim, Norway; [2]Oslo Center for Biostatistics and Epidemiology, Department of Biostatistics, University of Oslo, Oslo, Norway; [3]Oslo Center for Biostatistics and Epidemiology, Research Support Services, Oslo University Hospital, Oslo, Norway; [4]Harvard School of Public Health, Department of Epidemiology, Boston, MA, USA


Region 6
Region 5
Region 4
Region 3
Region 2
Region 1
85
DEATH
Diagnosis
69
50
45
AGE
1997
2000
2001
2002
2003
2004
1986
YEAR
2009

Breast cancer mortality rates in women who were invited to screening (intention to screen)

vs.

in women who were not invited,

with a clear distinction between cases of breast cancer diagnosed before (without potential for screening effect) and after (with potential for screening effect) the first invitation for screening.

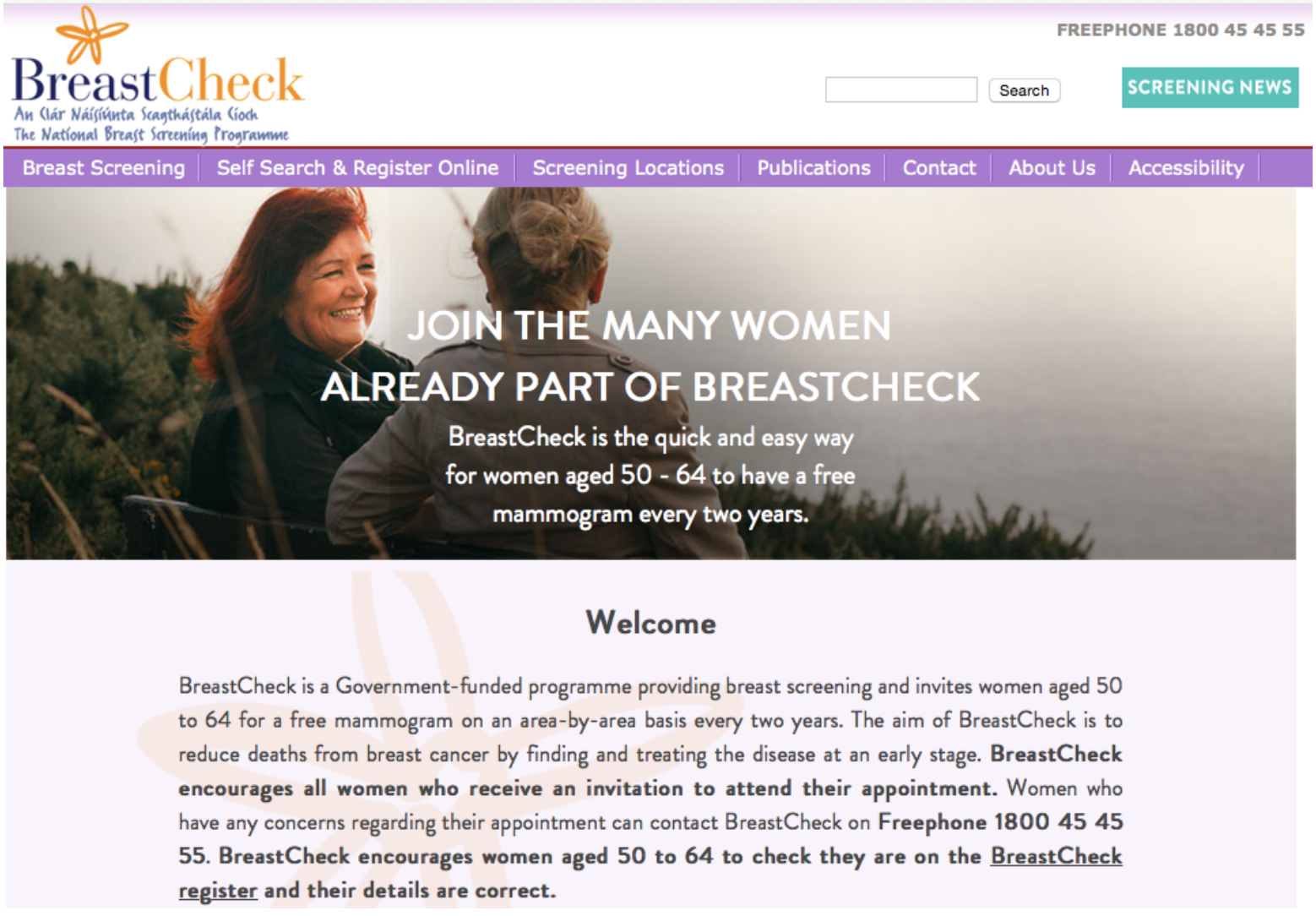
[$\approx$ 35 term] model included county as a factor, and natural splines to allow for non-linear variations in age, period, and cohort effects.

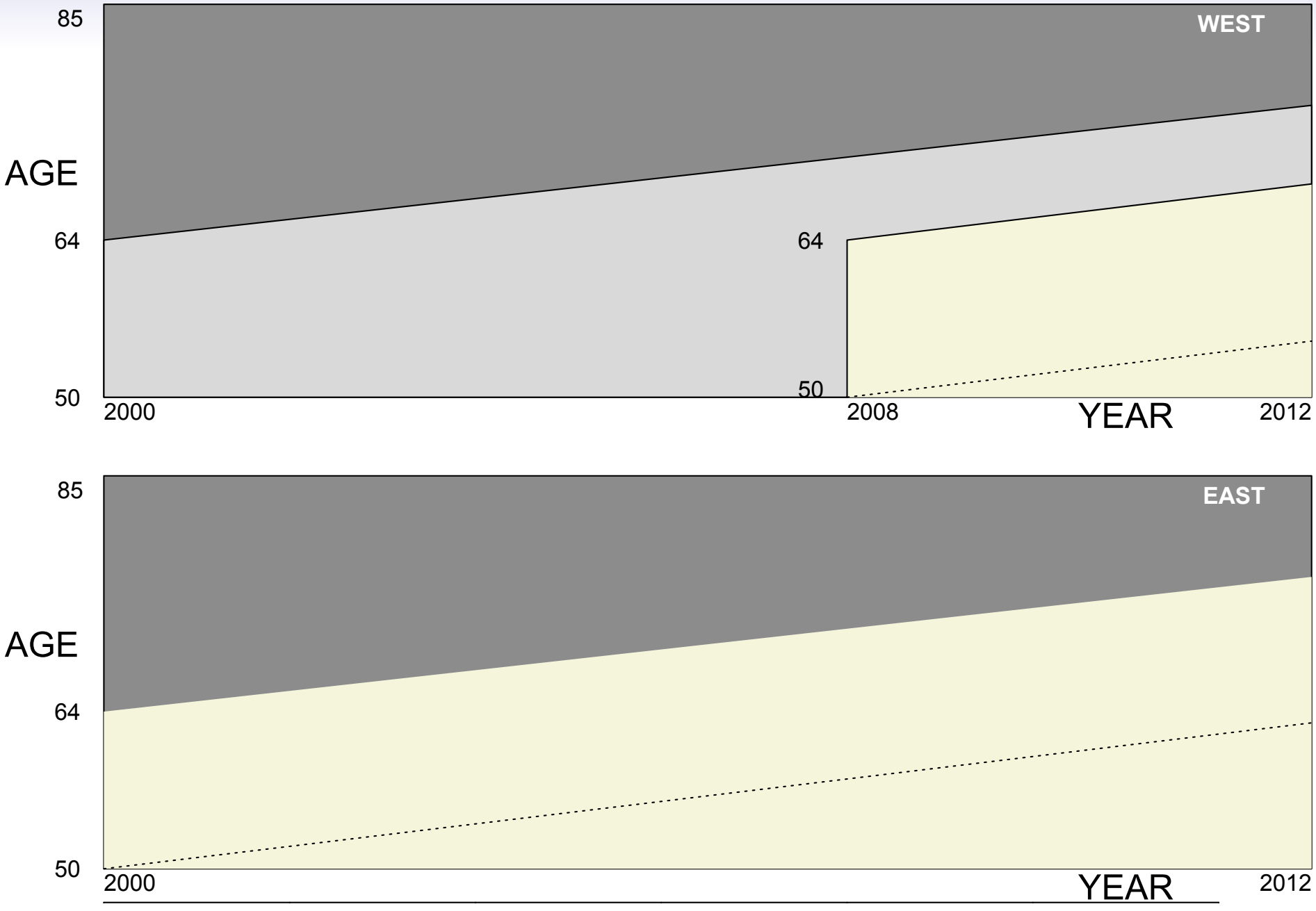
Results During 15 193 034 person years of observation (1986-2009), deaths from breast cancer occurred in 1175 women with a diagnosis after being invited to screening and 8996 women who had not been invited before diagnosis. After adjustment for age, birth cohort, county of residence, and national trends in deaths from breast cancer, the mortality rate ratio associated with being invited to mammography screening was 0.72 (95% confidence interval 0.64 to 0.79). To prevent

28% REDUCTION

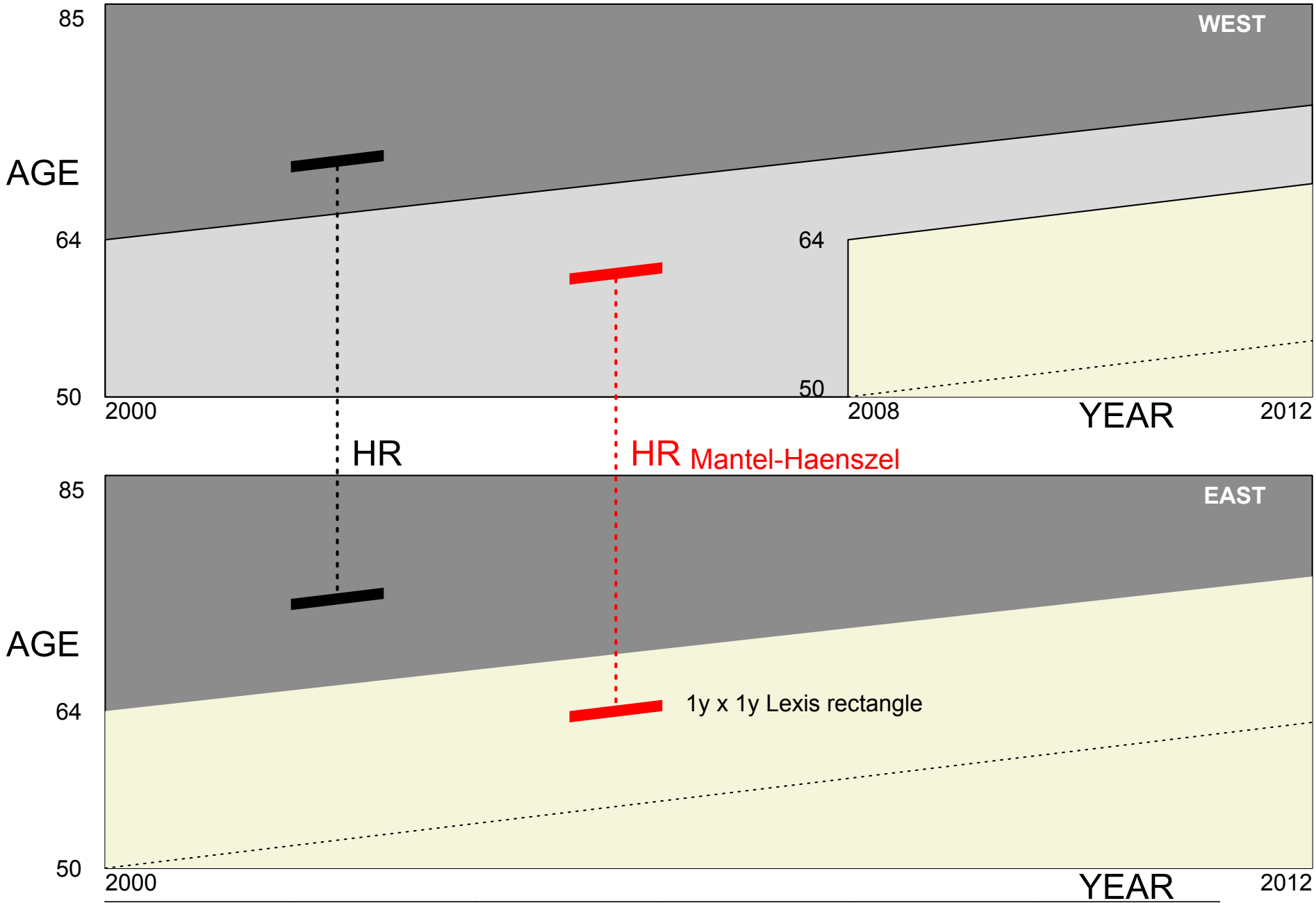
IRELAND

IRELAND


BreastCheck
An Clár Náisiúnta Scagthástála Cioch
The National Breast Screening Programme
FREEPHONE 1800 45 45 55
Search
SCREENING NEWS
Breast Screening
Self Search & Register Online
Screening Locations
Publications
Contact
About Us
Accessibility
JOIN THE MANY WOMEN
ALREADY PART OF BREASTCHECK
BreastCheck is the quick and easy way
for women aged 50 - 64 to have a free
mammogram every two years.
Welcome
BreastCheck is a Government-funded programme providing breast screening and invites women aged 50 to 64 for a free mammogram on an area-by-area basis every two years. The aim of BreastCheck is to reduce deaths from breast cancer by finding and treating the disease at an early stage. **BreastCheck encourages all women who receive an invitation to attend their appointment.** Women who have any concerns regarding their appointment can contact BreastCheck on **Freephone 1800 45 45 55. BreastCheck encourages women aged 50 to 64 to check they are on the BreastCheck register and their details are correct.**


WEST
85
AGE
64
50
64
50
2000
2008
YEAR
2012
EAST
85
AGE
64
50
2000
YEAR
2012

2 age- & year-matched EAST:WEST contrasts

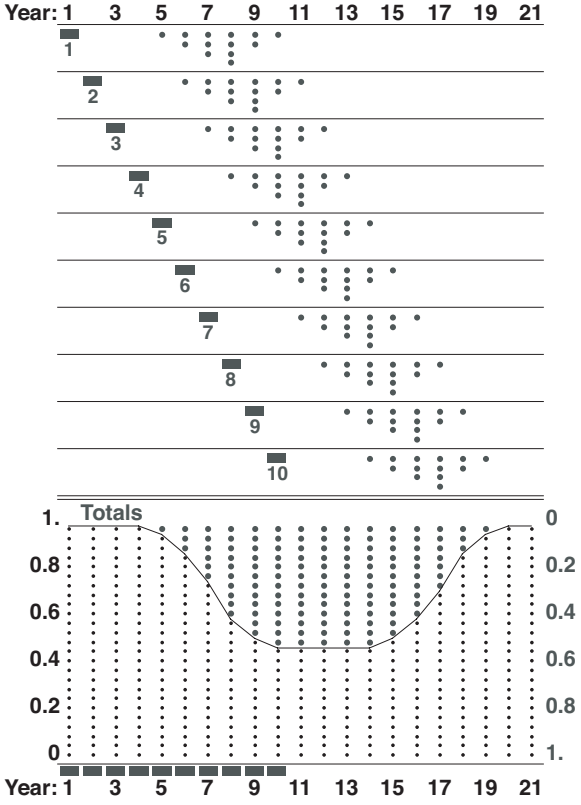


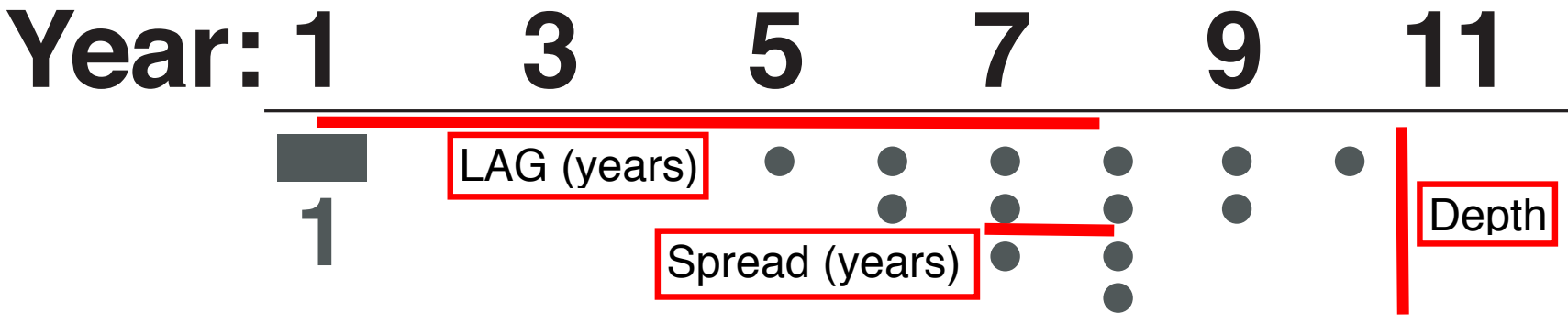
Incorporating NO. & TIMING of Screens

Estimate impact of (each) single round of screening:

Liu, Hanley, et al. parametrization, in RCT context, easily extended to population-based studies

Single-Round Model and its 3 Parameters





Our Model ... in more detail

Webpage: screening

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

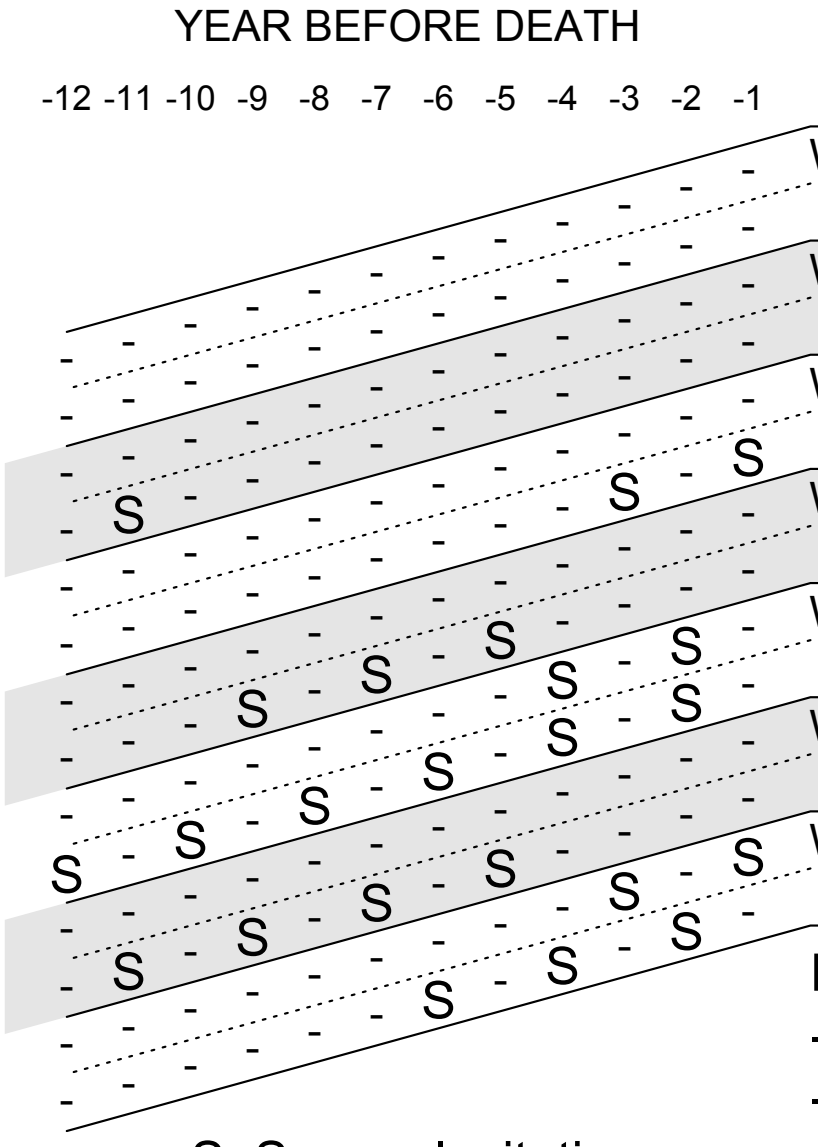
Methods

`http://www.biostat.mcgill.ca/hanley/screening/section2.mov`

Applications: Lung Cancer; Colon Cancer

`http://www.biostat.mcgill.ca/hanley/screening/section3.mov`

Design Matrix, Mortality Data, Parameter Fitting



	AGE	YEAR	No. Deaths
WEST	80	2003	2
EAST	80	2003	5
WEST	75	2011	7
EAST	75	2011	5
WEST	64	2003	5
EAST	64	2003	2
WEST	68	2009	4
EAST	68	2009	2
WEST	62	2012	6
EAST	62	2012	3
WEST	68	2011	4
EAST	68	2011	5
WEST	56	2011	5
EAST	56	2011	2

} Binomial

S: Screen Invitation

Binomial P = function of
- Region, Relative Population Sizes,
- NUMBER & TIMING of Screens
- IMPACT of each ROUND of SCREENING
- Participation Rate

Some References

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9. Weedon-Fekjaer, et al. Modern mammography screening and breast cancer mortality: population study BMJ 2014;348:g3701 doi: 10.1136/bmj.g3701 (Published 17 June 2014)
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11. Njor SH, Schwartz W, Blichert-Toft M, Lynge E. Decline in breast cancer mortality: how much is attributable to screening? J Med Screen. 2015 Mar;22(1):20-7.

* `http:www.medicine.mcgill.ca/epidemiology/hanley/` (reprints/talks)

FUNDING, CO-ORDINATES, DOWNLOADS

Natural Sciences and Engineering Research Council of Canada

Canadian Institutes of Health Research (2011-2015)

.....

James.Hanley@McGill.CA

www.med.mcgill.ca/epidemiology/hanley

→ **r e p r i n t s / talks**

EXTRA SLIDES

Why do statisticians commonly limit their inquiries to Averages?

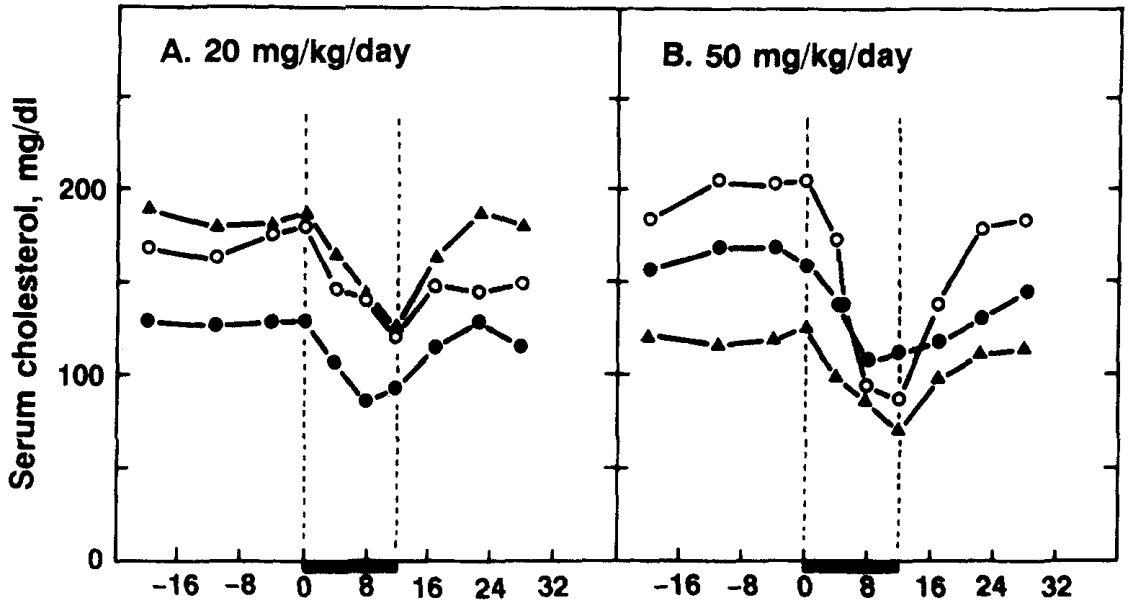
F. Galton, Natural Inheritance, 1889.

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

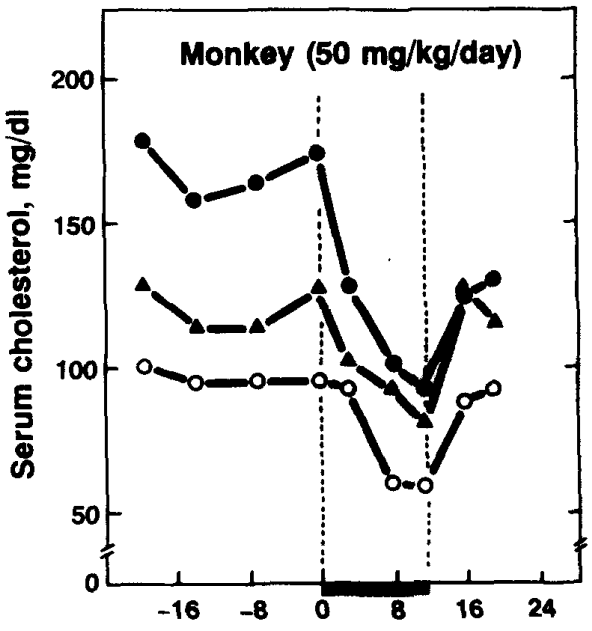
Their souls seem as dull to the charm of variety as that of the native of one of our flat English counties, whose retrospect of Switzerland was that, if its mountains could be thrown into its lakes, two nuisances would be got rid of at once.”

Timing of cholesterol reductions produced by statins

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

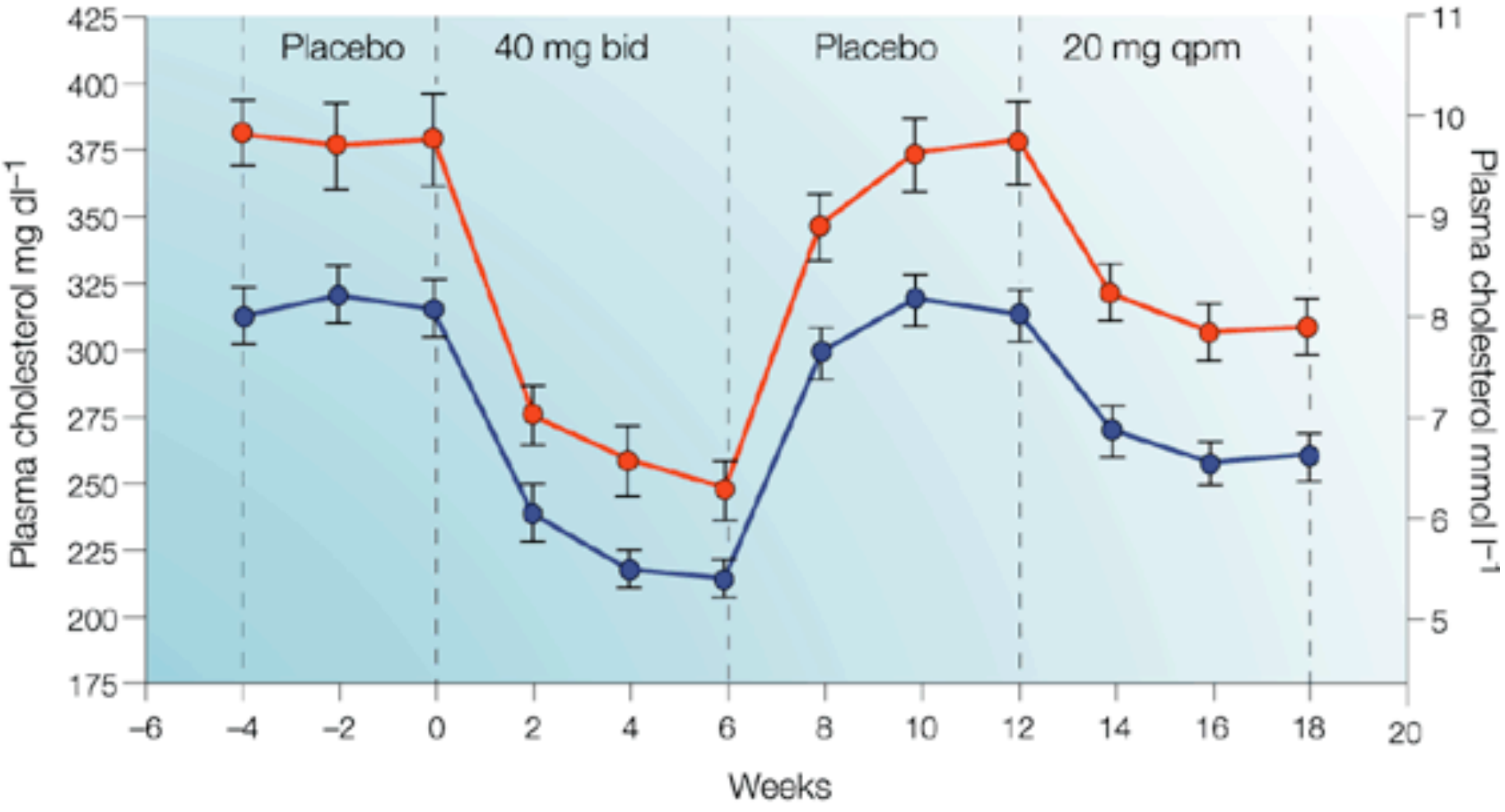


3 monkeys at 50

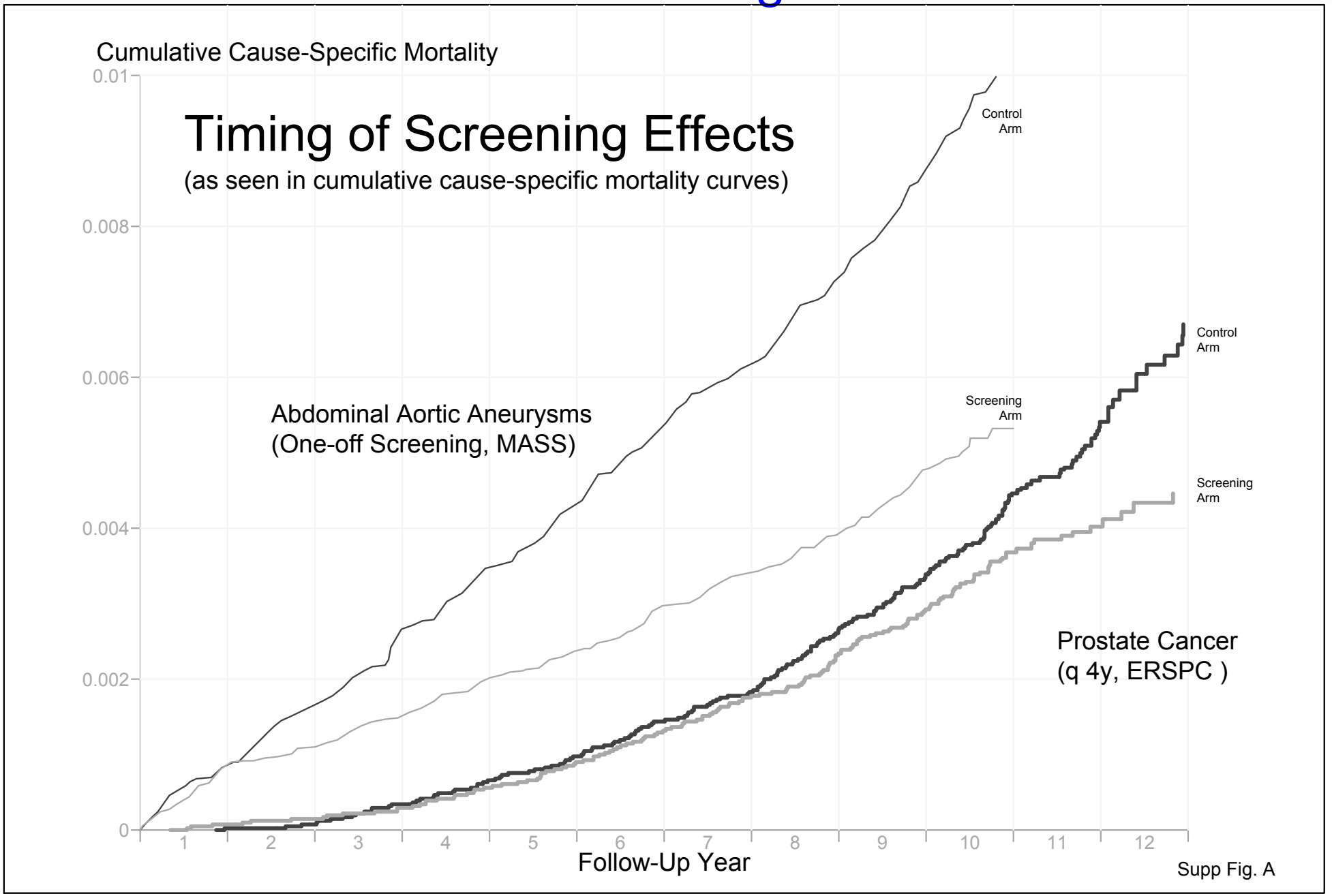


Timing of cholesterol reductions produced by statins

Humans



The loneliness of the long-distance trialist



Supp Fig. A