Fitting a Model of the Mortality Reductions Produced by One/Several Rounds of Cancer Screening:

Time and Sample Size Considerations

James A. Hanley[1], Zhihui (Amy) Liu[2,3],Olli Saarela[3]

[1]McGill University
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Statistical Society of Canada Annual Meeting
Brock University, St. Catharines, Ontario
2016-05-31

Dedication

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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

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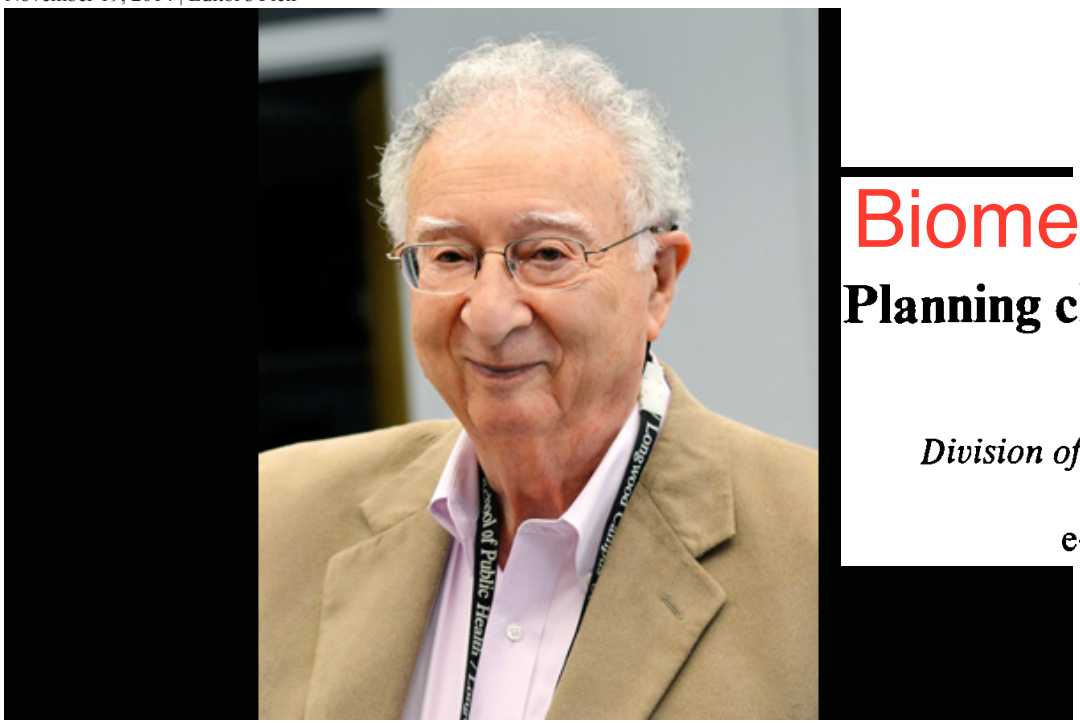

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BY PING HU AND MARVIN ZELEN

Division of Biostatistics, Dana Farber Cancer Institute, 44 Binney Str
Massachusetts 02115, U.S.A.

e-mail: phu@jimmy.harvard.edu zelen@jimmy.harvard.e

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Biometrics 2008

Mortality Modeling of Early Detection H

Sandra J. Lee* and Marvin Zelen

Harvard School of Public Health and the Dana-Farber Cancer
Boston, Massachusetts 02115, U.S.A.

Outline: non-proportional hazards, in 2 time scales

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- A condn'l approach to fit HR models to Lexis array of Counts & Population-Times
- No. of years of screening and follow-up needed to fit 2-parameter model and (scalar) resultant?
- Which Lexis cells provide the most information on these?
- Implications of findings

Number-of-Events-based Sample Size Planning

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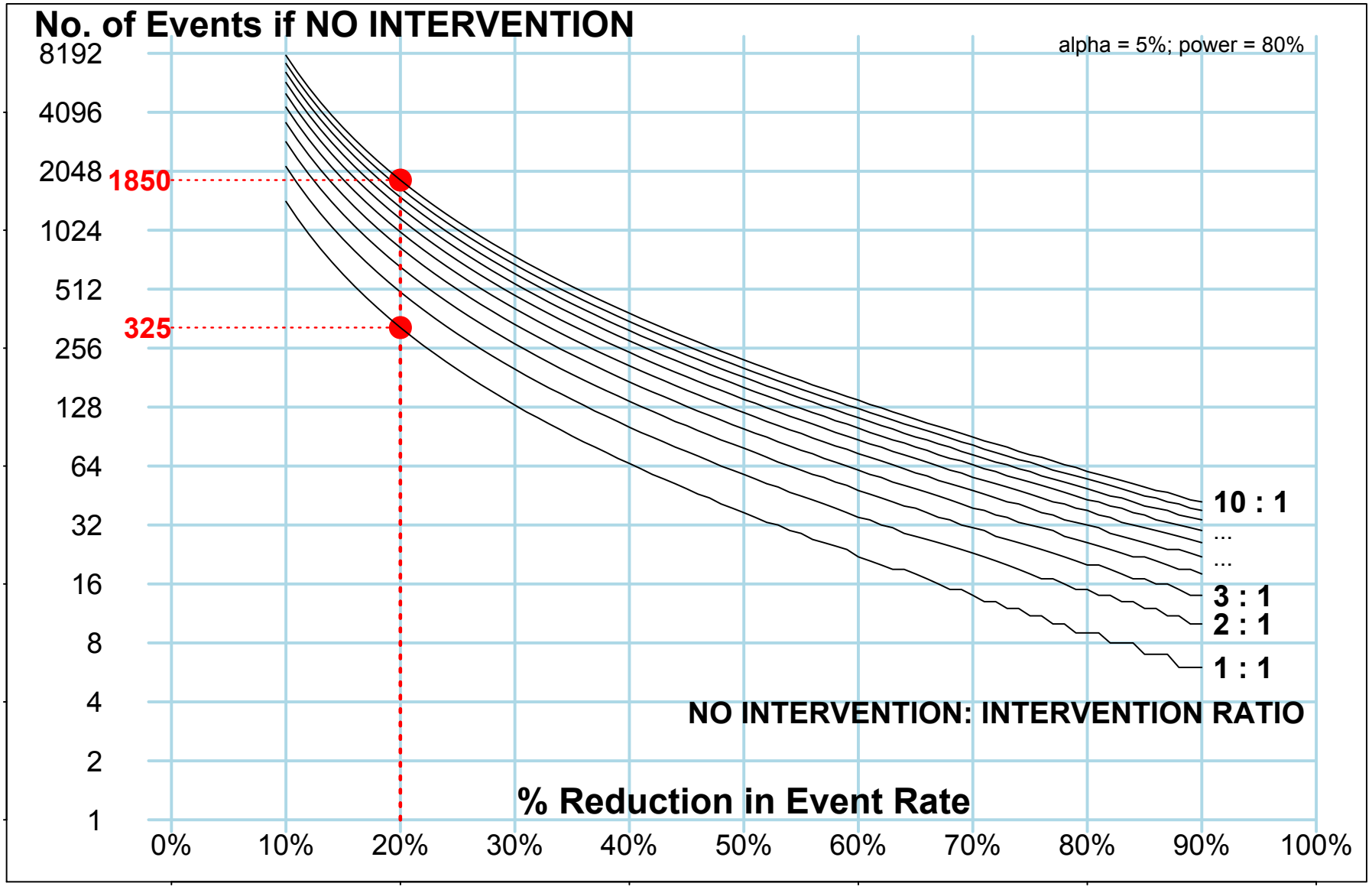

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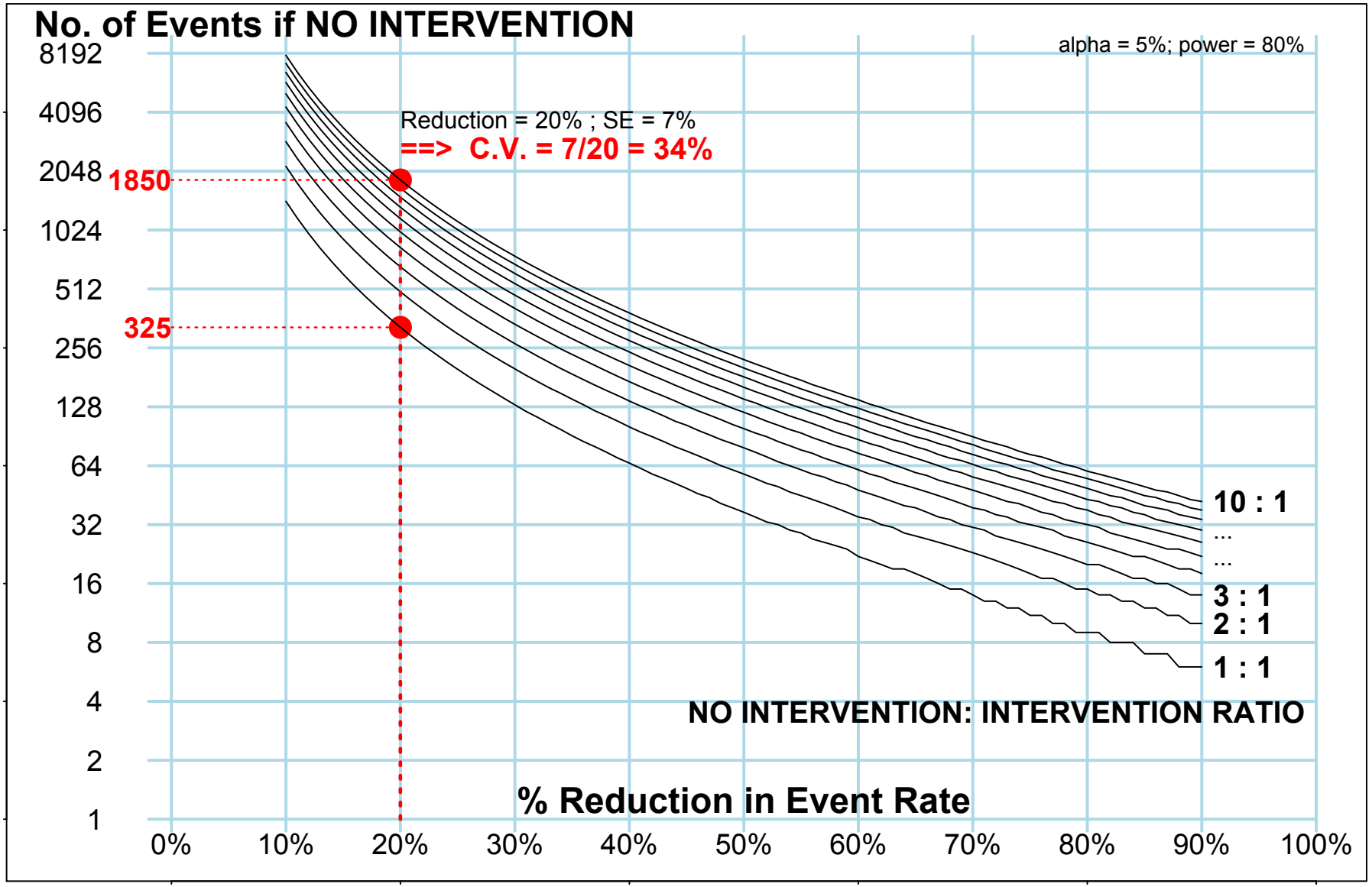

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or...

- STOP COUNTING AS SOON AS PROTECTION STOPS
  - **Blood thinners**
  - **beta blockers**

Reduction is CONSIDERABLY DELAYED in ...

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PROSTATE CANCER SCREENING

Screening & Prostate-Ca Mortality in Randomized European Study ’92-’08 (“ERSPC” nejm2009.04)

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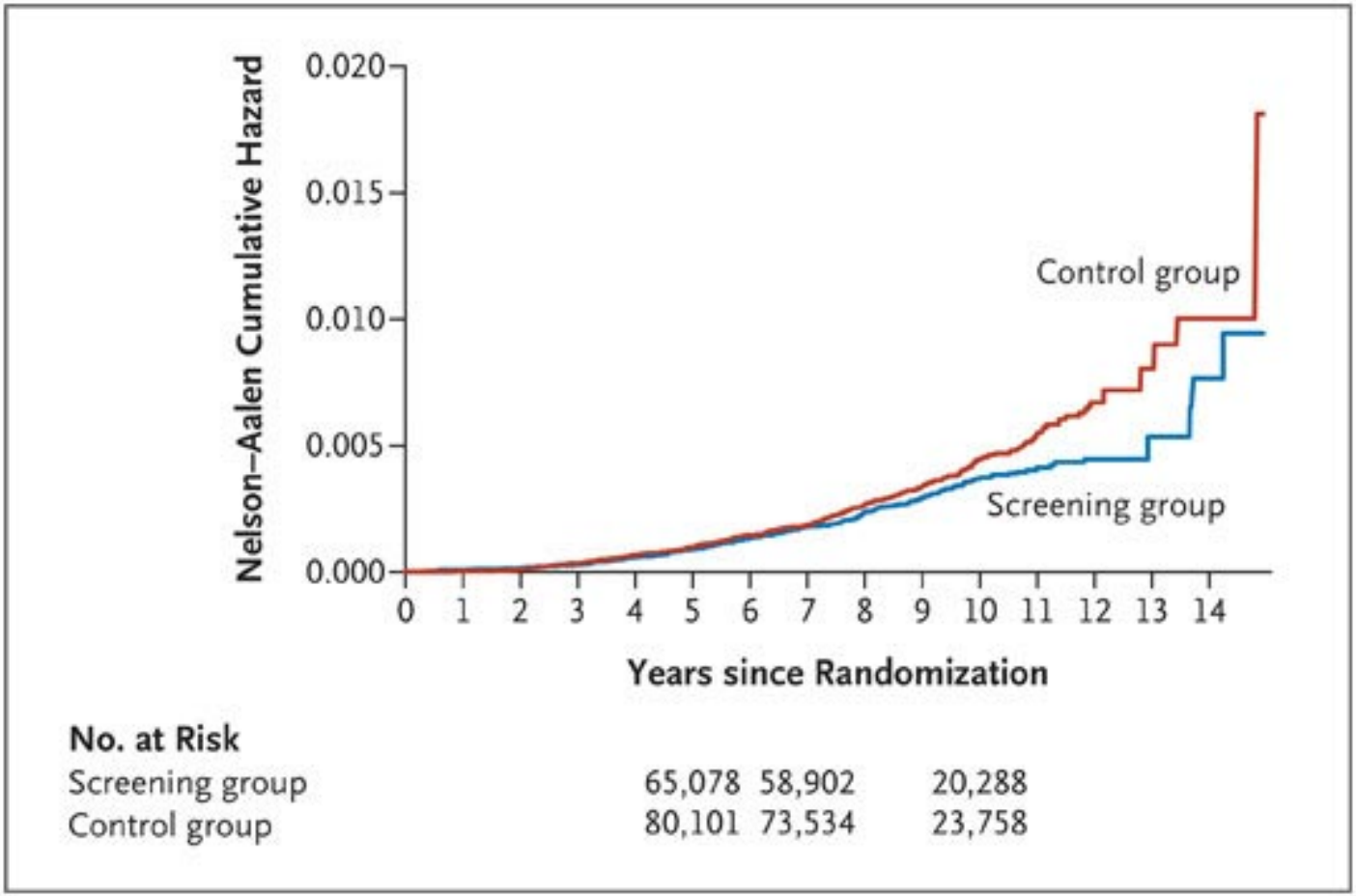

RE-ANALYSIS OF ERSPC DATA
using
year-specific prostate cancer mortality ratios

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

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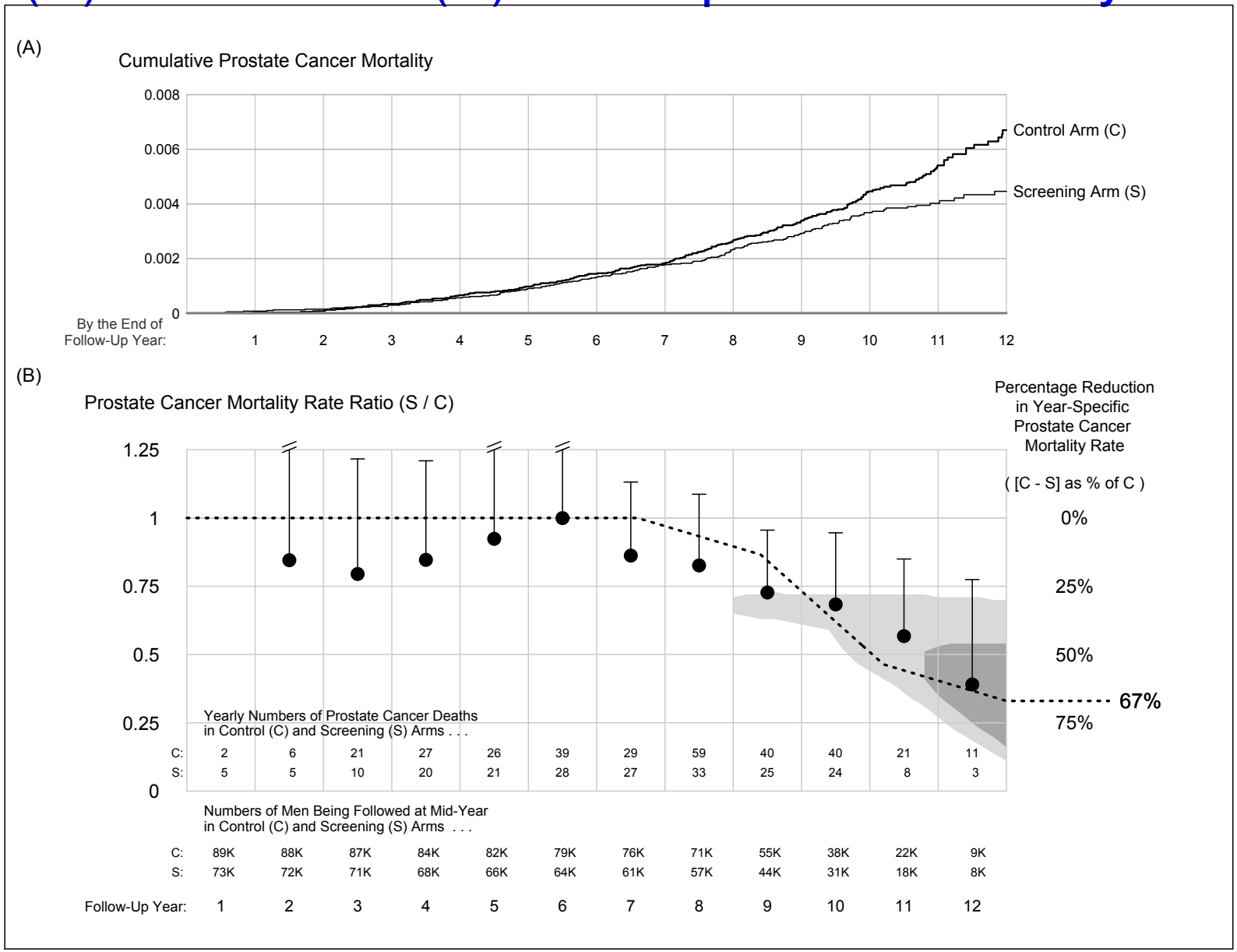

Hanley, *J Medical Screening*, 2010.

Reductions EVENTUALLY CEASE:

30-year follow-up in Minnesota Trial

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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

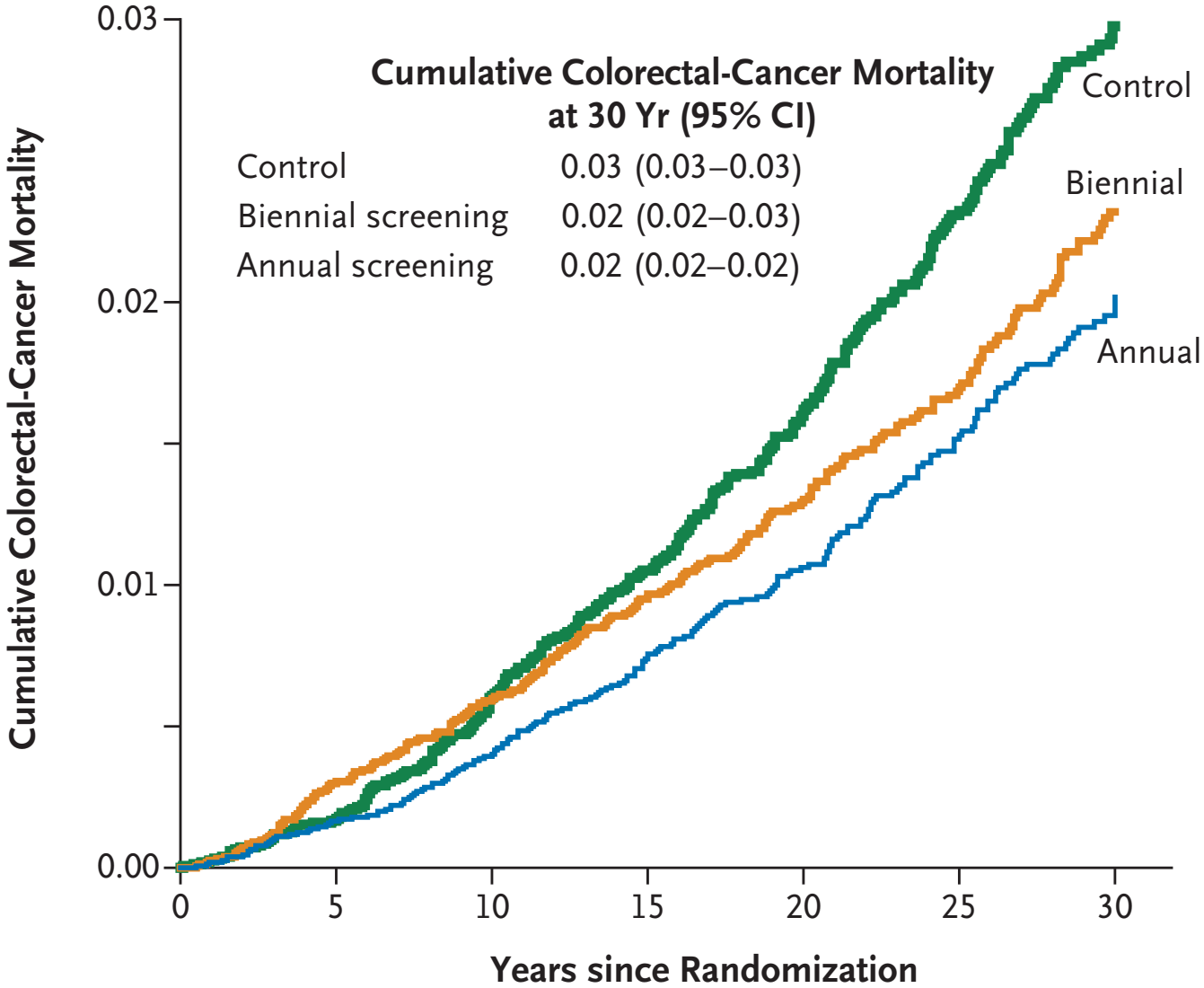
In randomized trials, fecal occult-blood testing reduces mortality from colorectal cancer. However, the duration of the benefit is unknown, as are the effects specific to age and sex.

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.

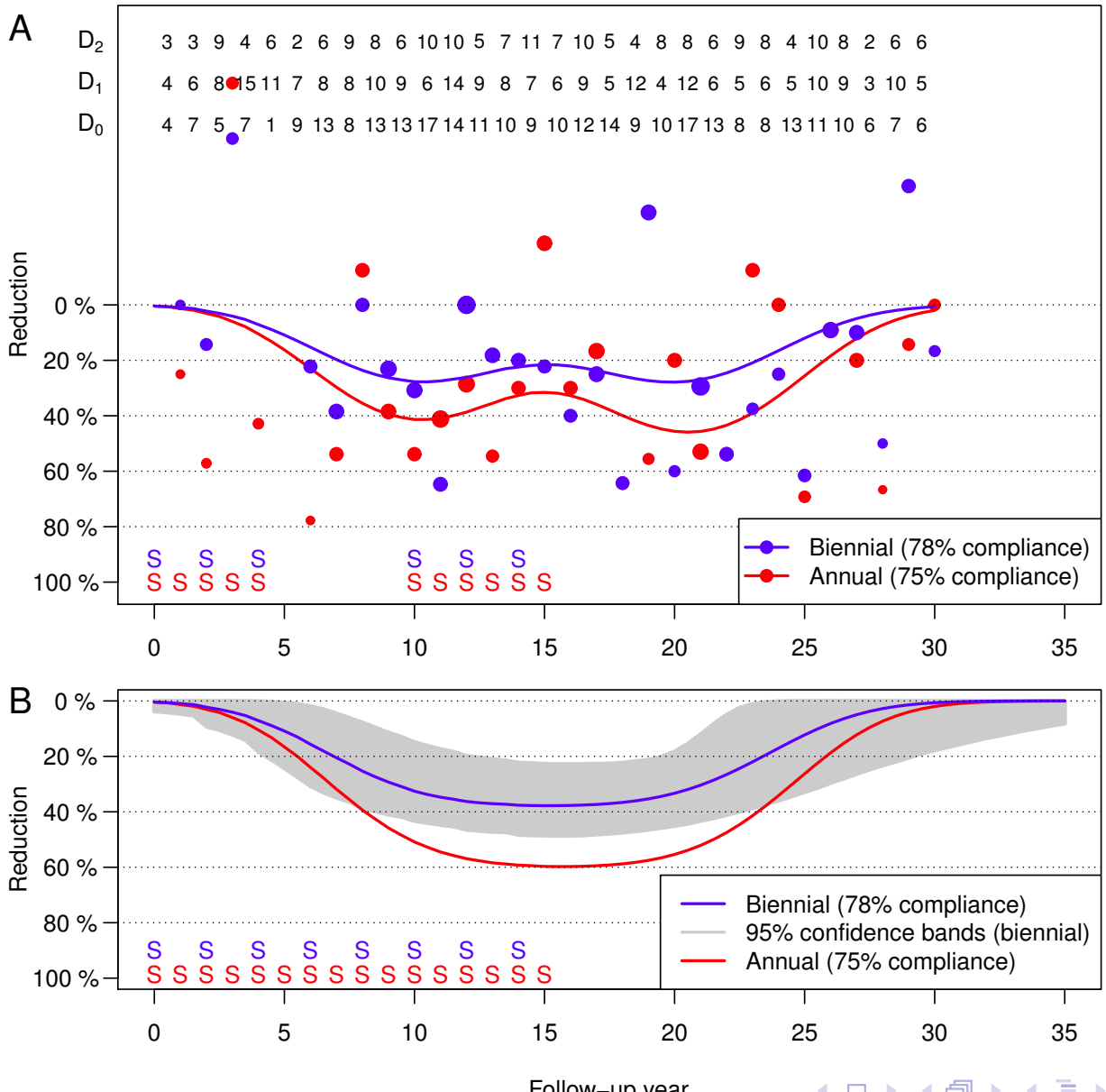
N Engl J Med 2013;369:1106-14.
DOI: 10.1056/NEJMoa1300720



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

Liu Model: A Fitted to Data; B Projected i.e., no interruption. 6 & 11 Rounds



SCREENING for BREAST CANCER

???

Magnitude of reductions being achieved with contemporary mammography

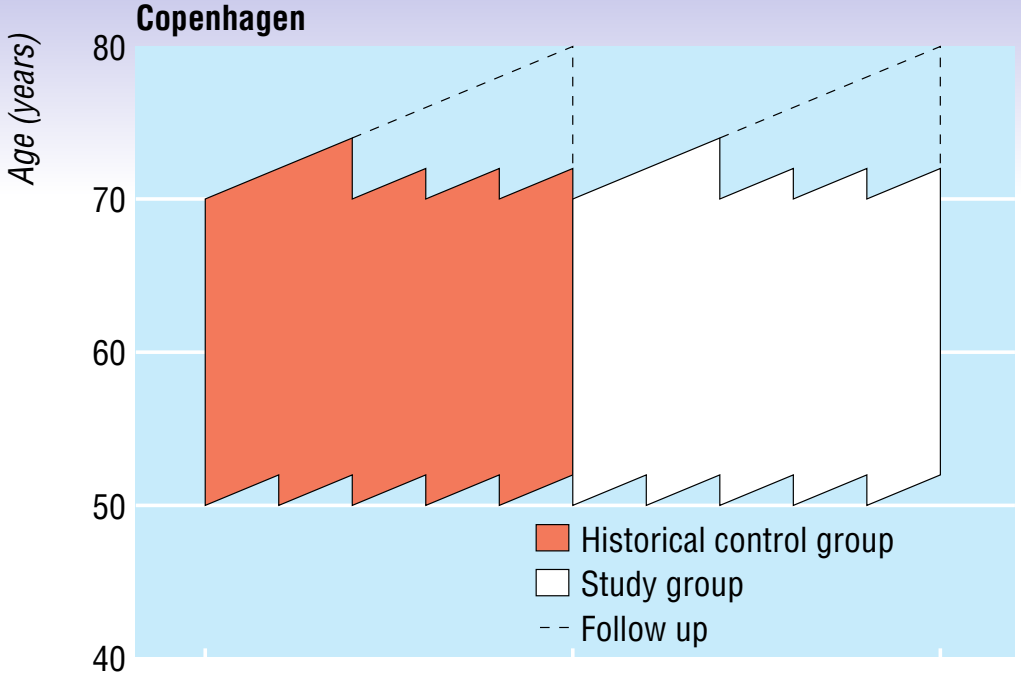
Estimates from (non-experimental) population-based studies

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

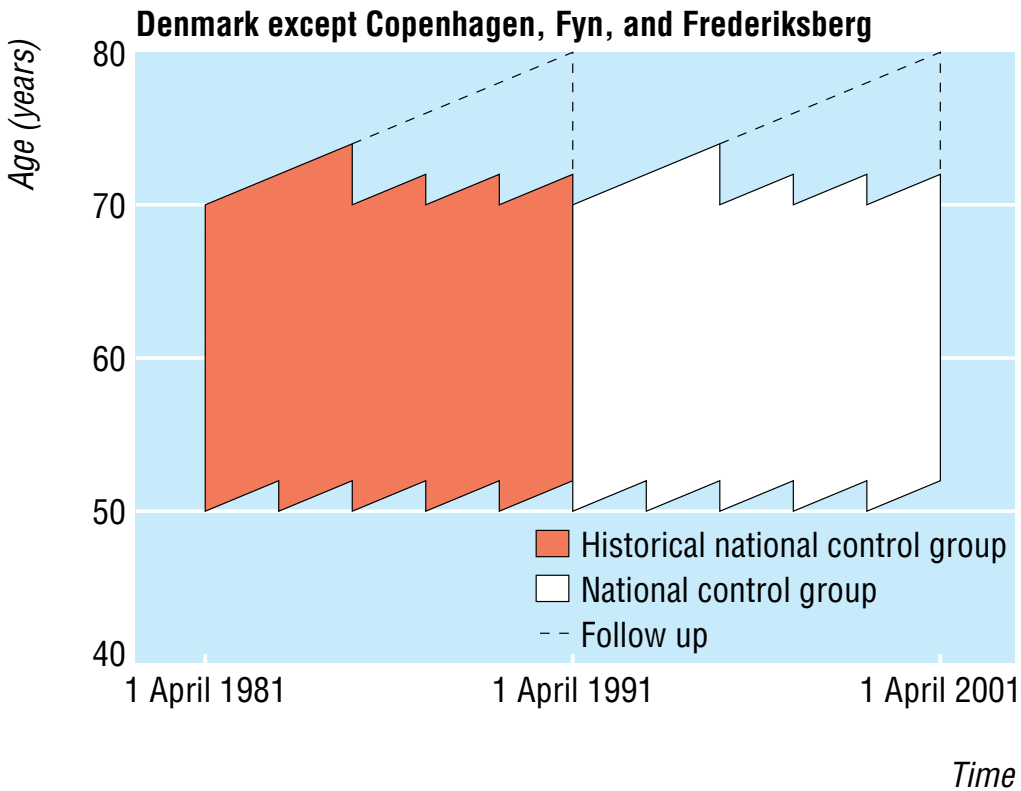
Papers

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



Copenhagen
0.43 Million WY; ??? deaths



Rest of Denmark (10 x)
4.3 Million WY; 2,300 deaths

1-D time-pattern of mortality deficits (HRs) if NO screening

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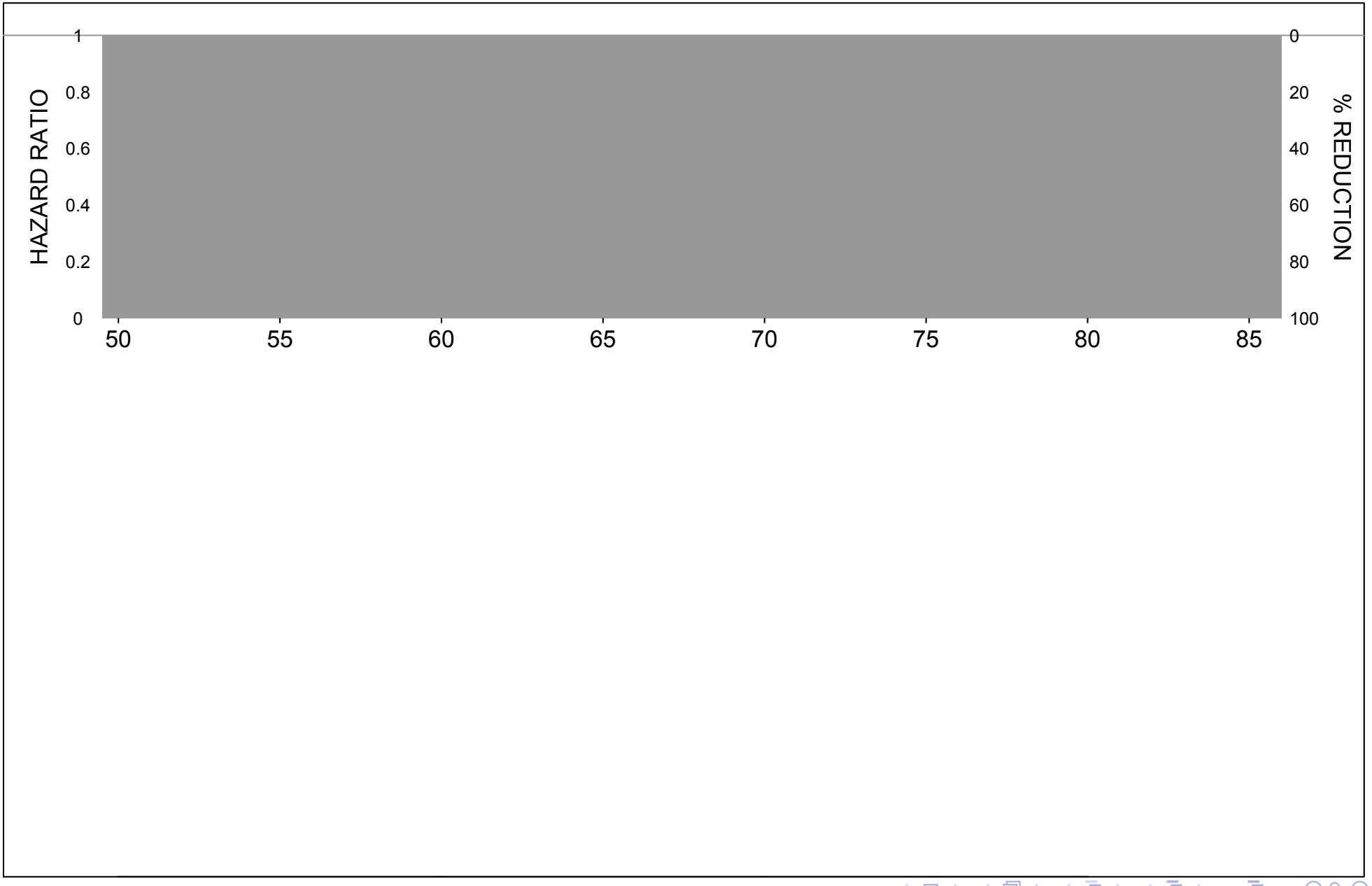

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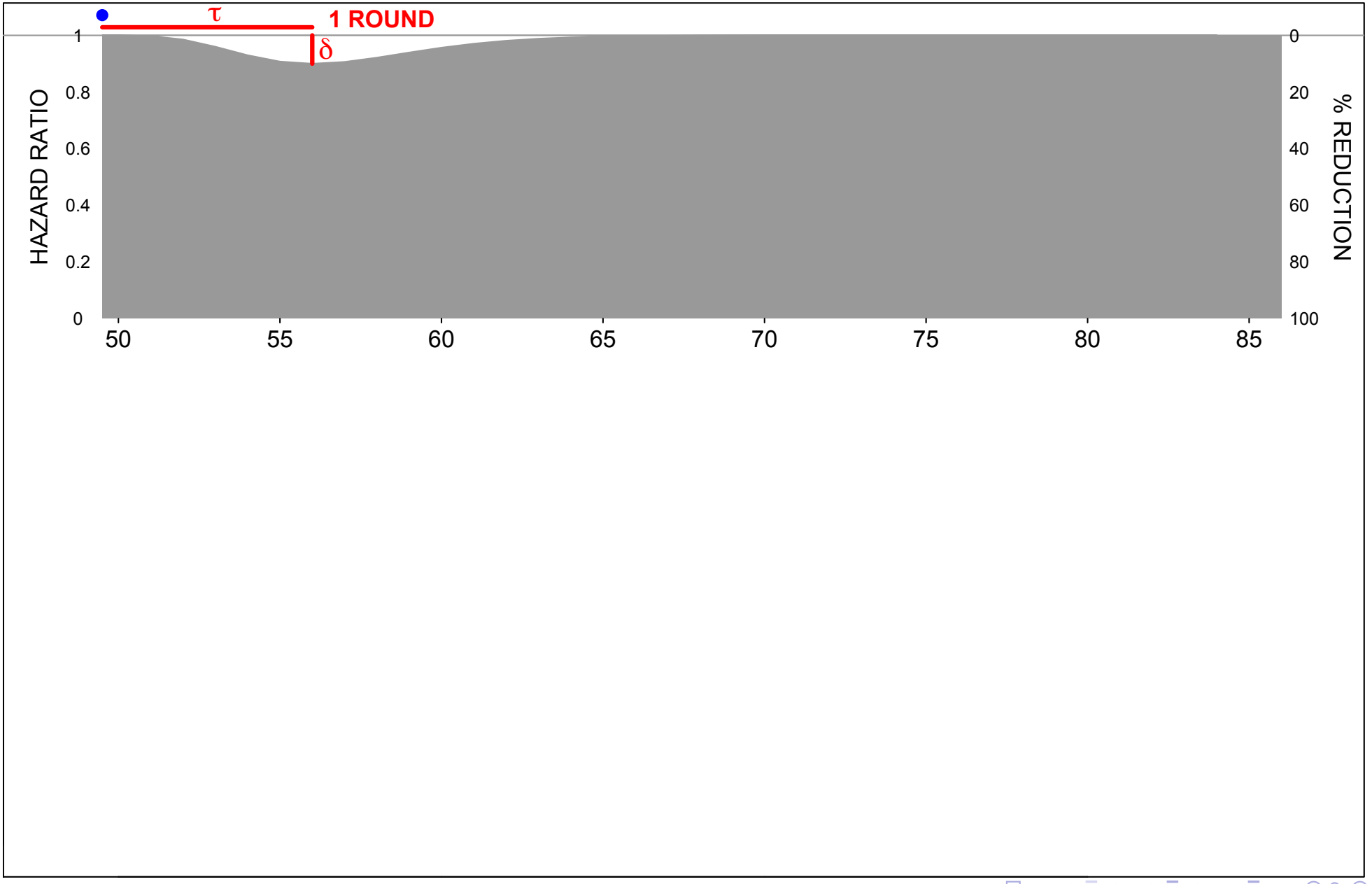
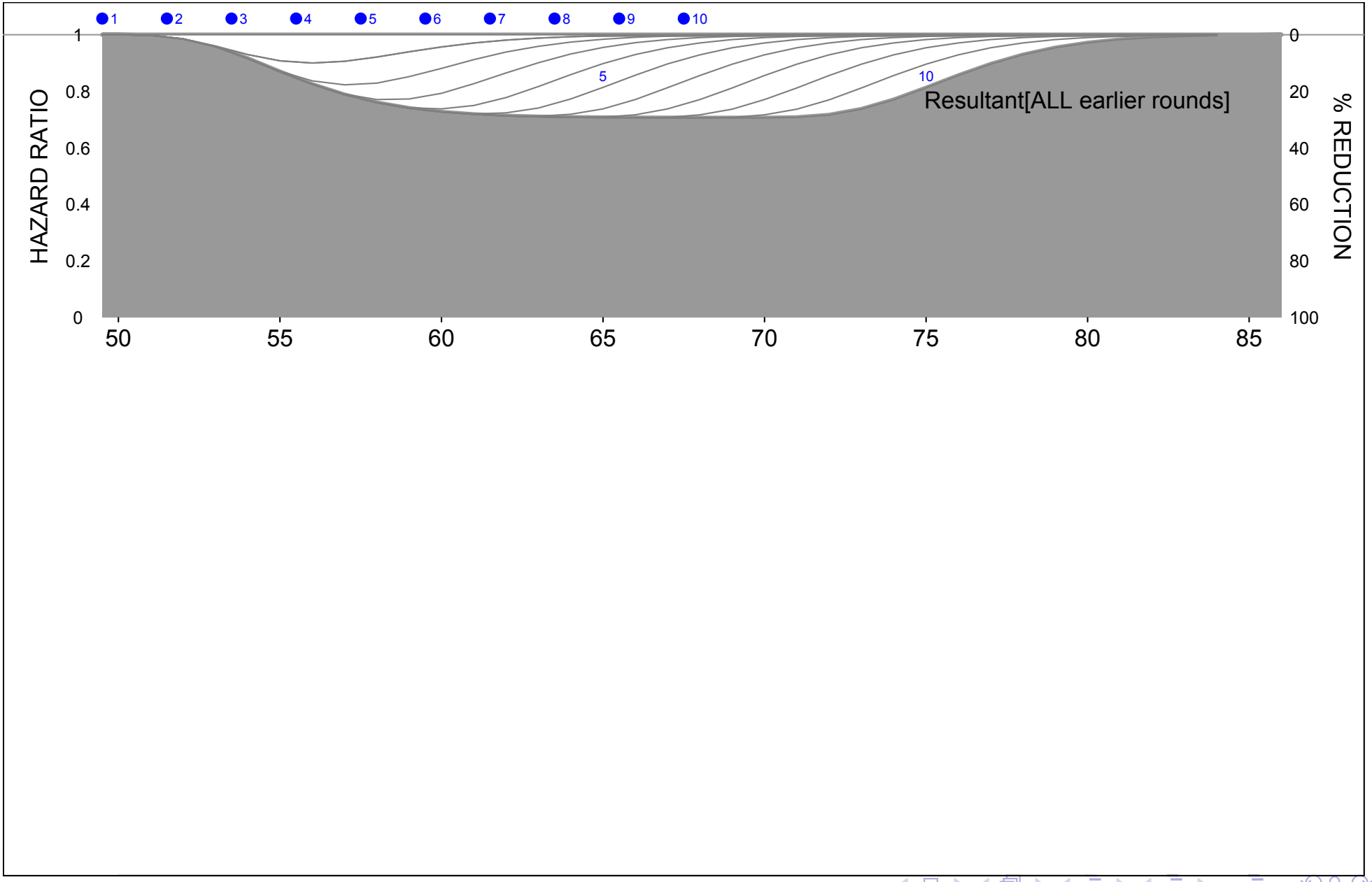


1-D HR pattern if • • • • • • • • • • rounds

1-D HR pattern if ● ● ● ● ● ● ● ● ● ● rounds



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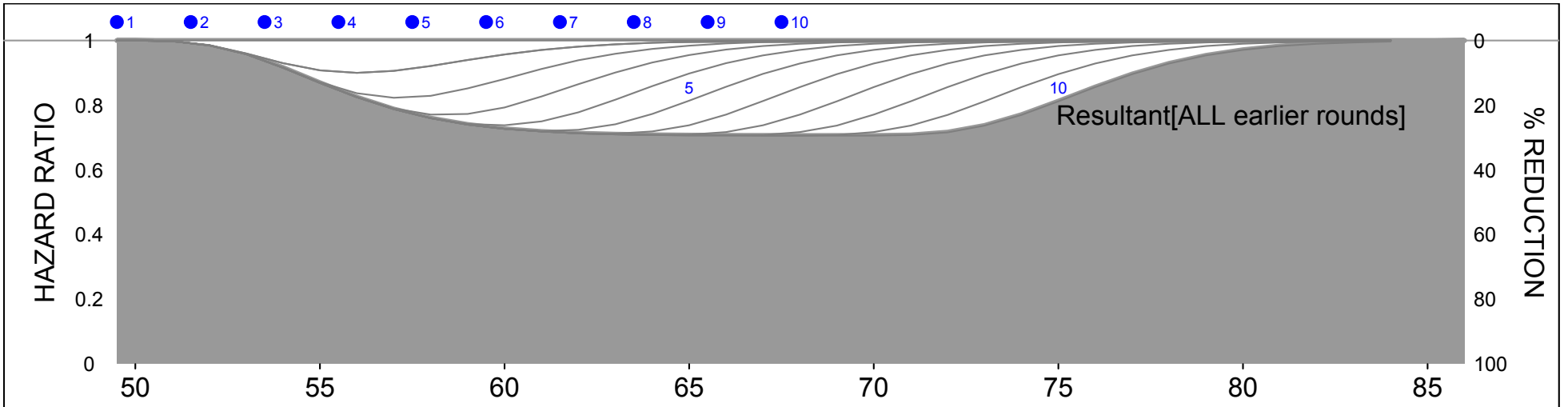

Zhihui (Amy) LIU **PhD Thesis** 2104

Zhihui (Amy) LIU, James A. Hanley , Olli Saarela and Nandini Dendukuri
A Conditional Approach to Measure Mortality Reductions Due to Cancer Screening
International Statistical Review (2015), 0, 0, 1?18 doi:10.1111/insr.12088

STATISTICAL MODEL

2-D [year-and- age-specific] time-pattern of mortality deficits

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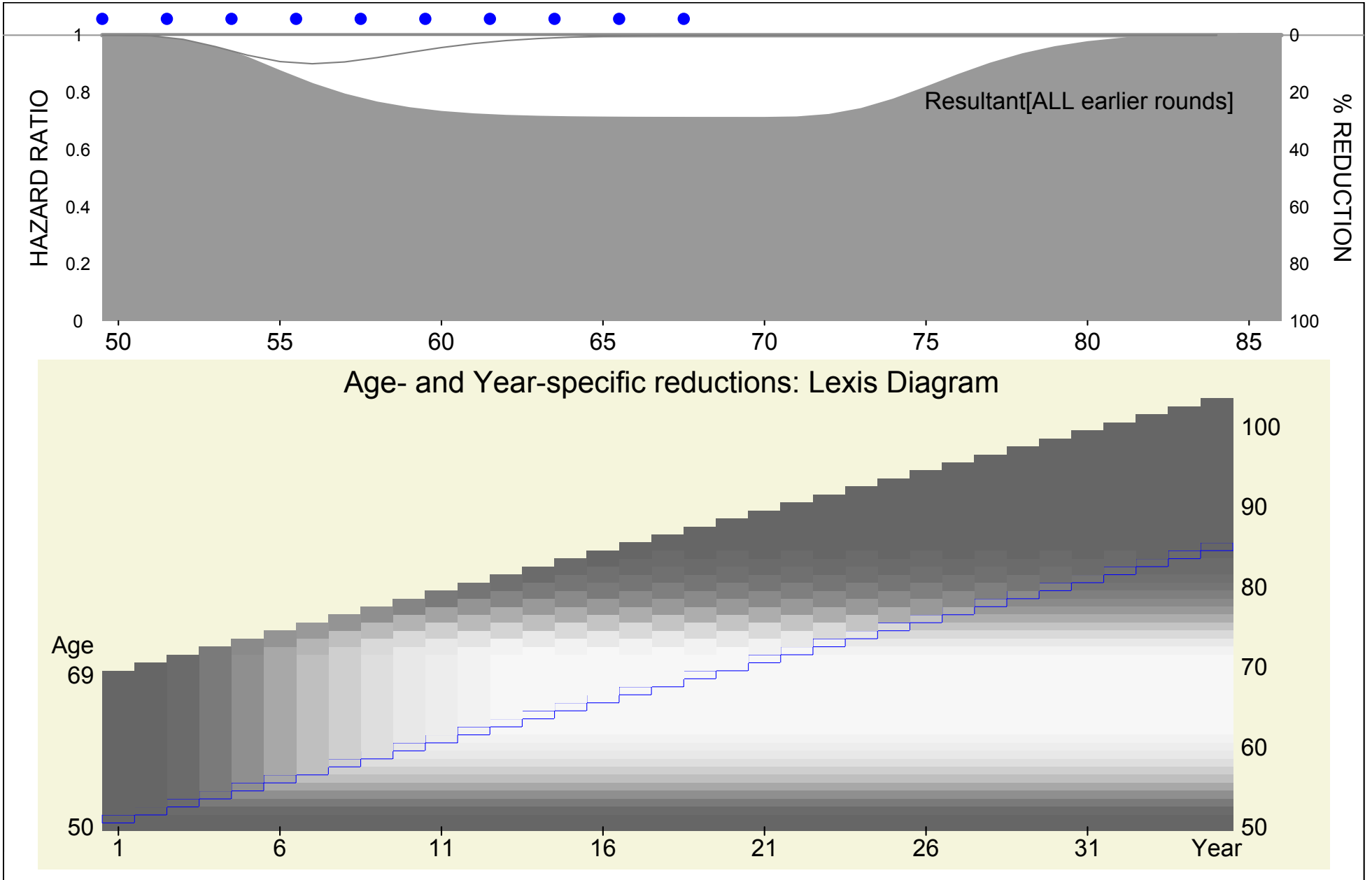

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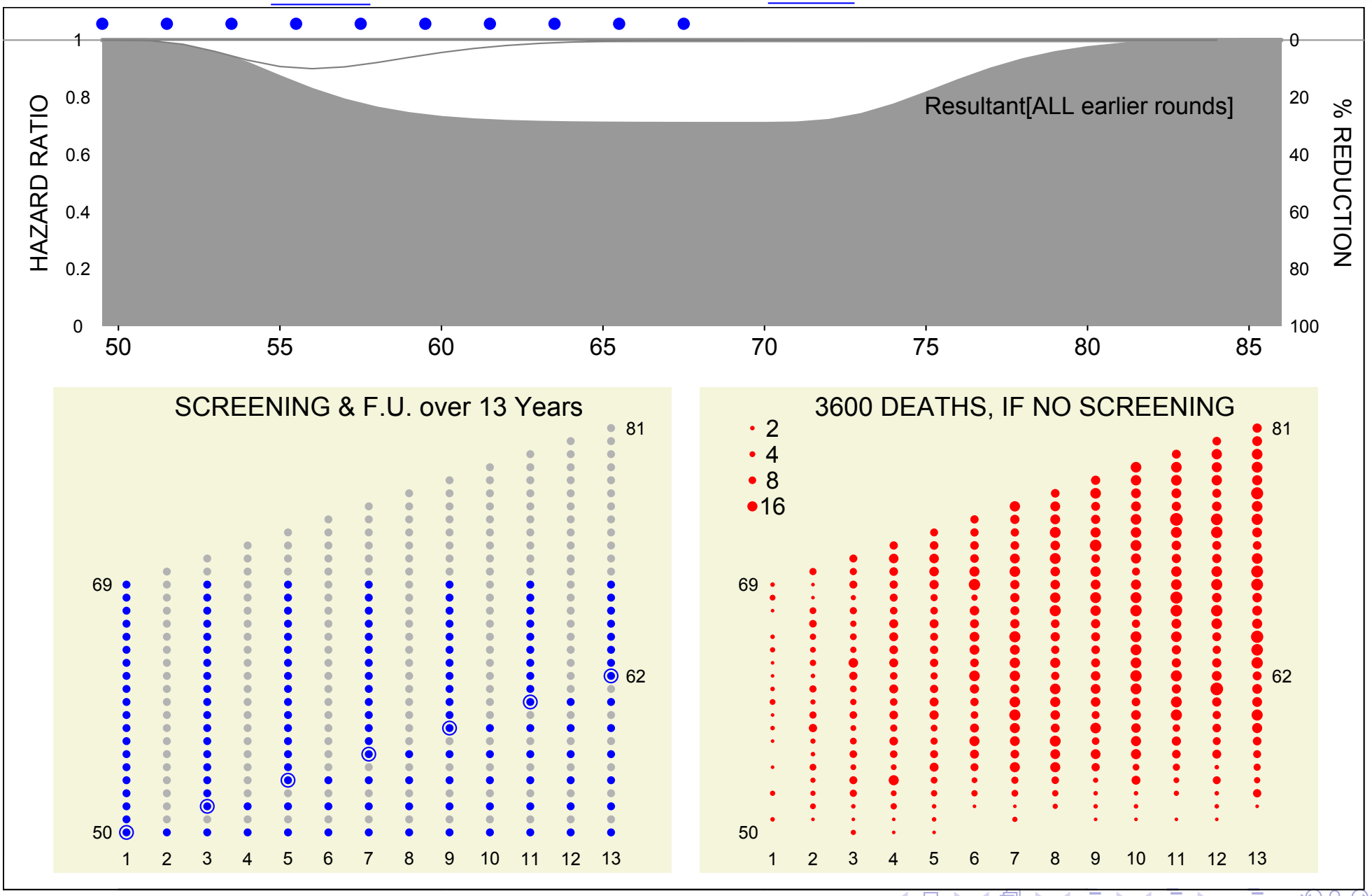

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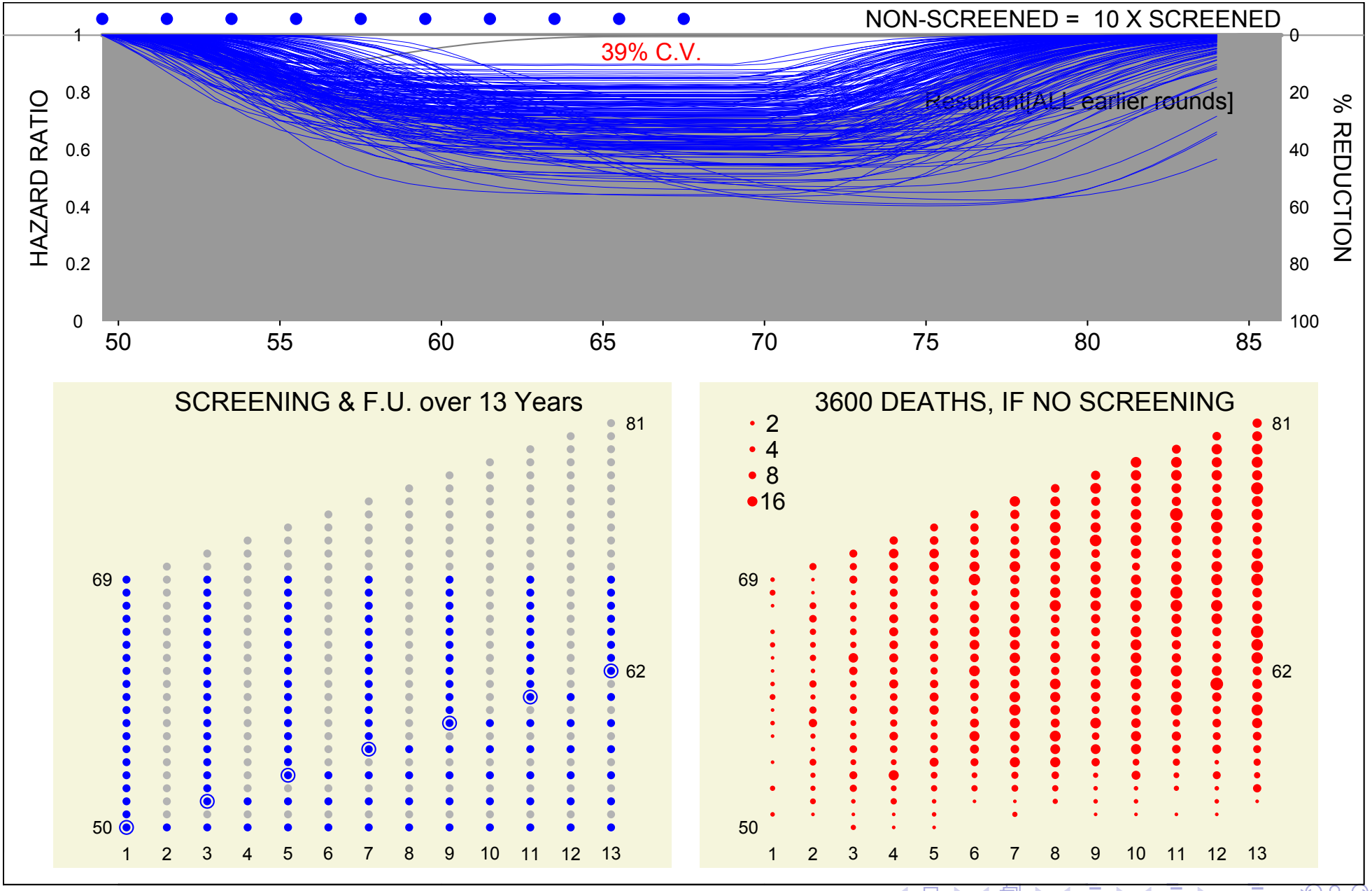

Info. re 2 model parameters provided by each death

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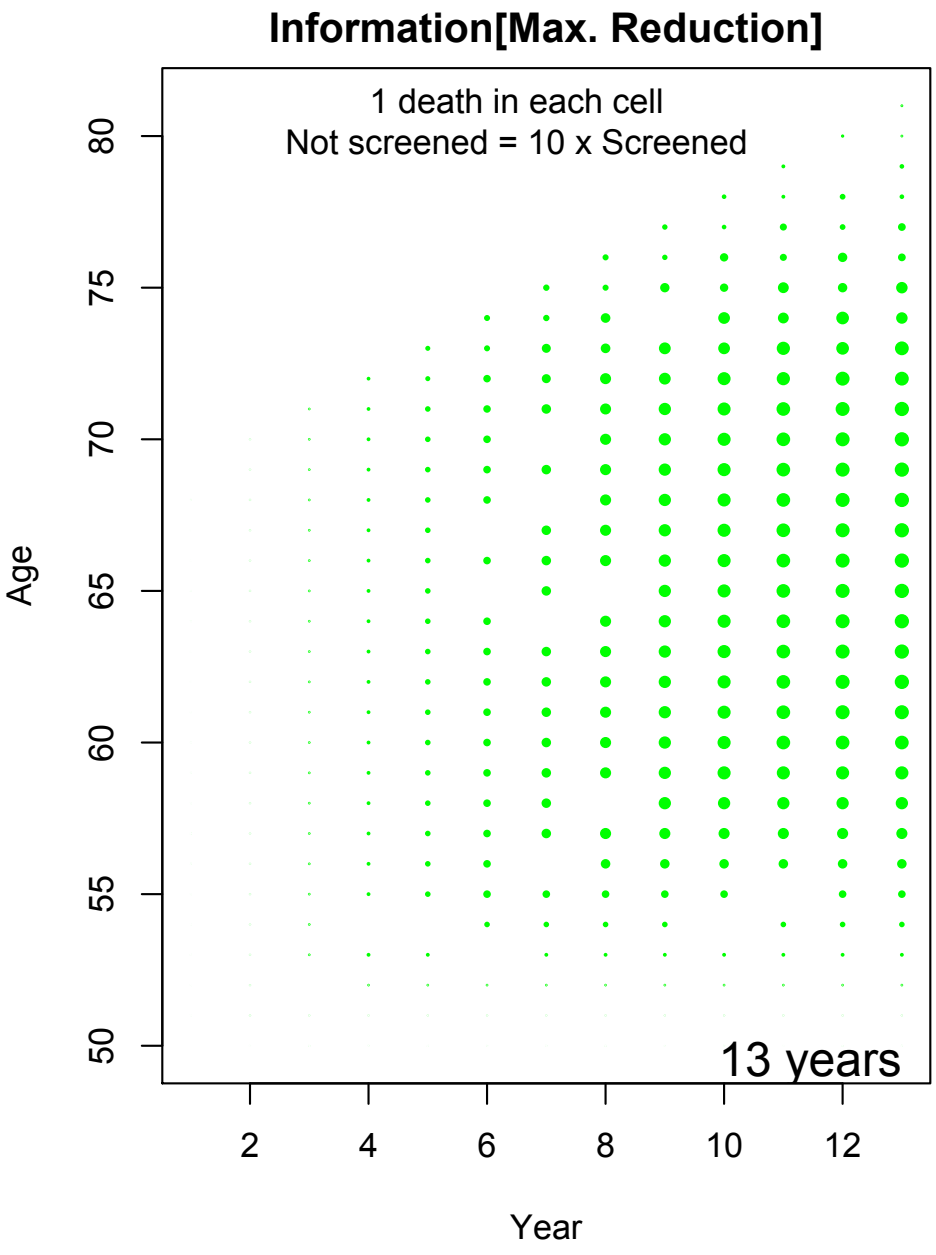

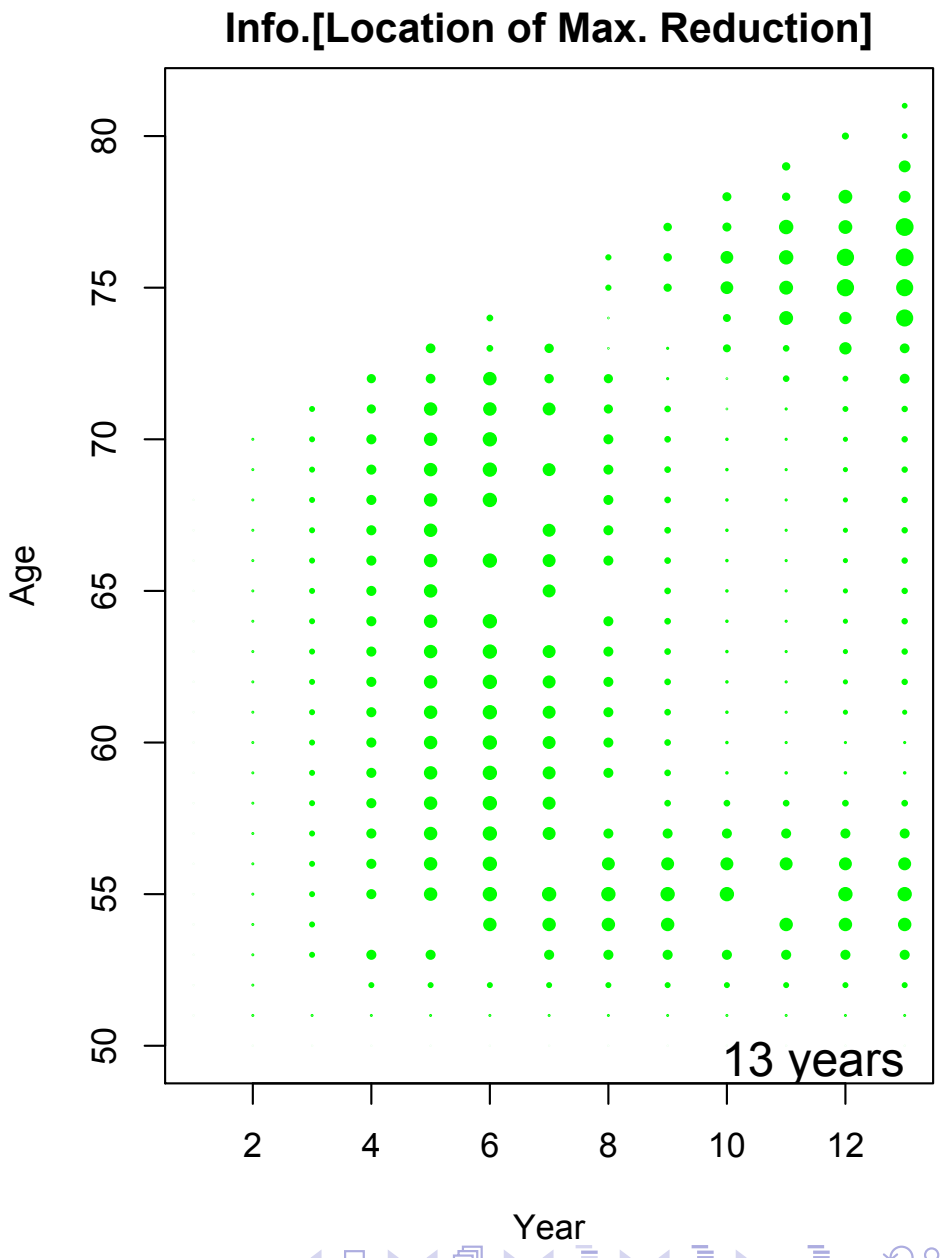

WHAT IF **20 yrs**. of screening & F.U., and **7,200** deaths in unscreened?

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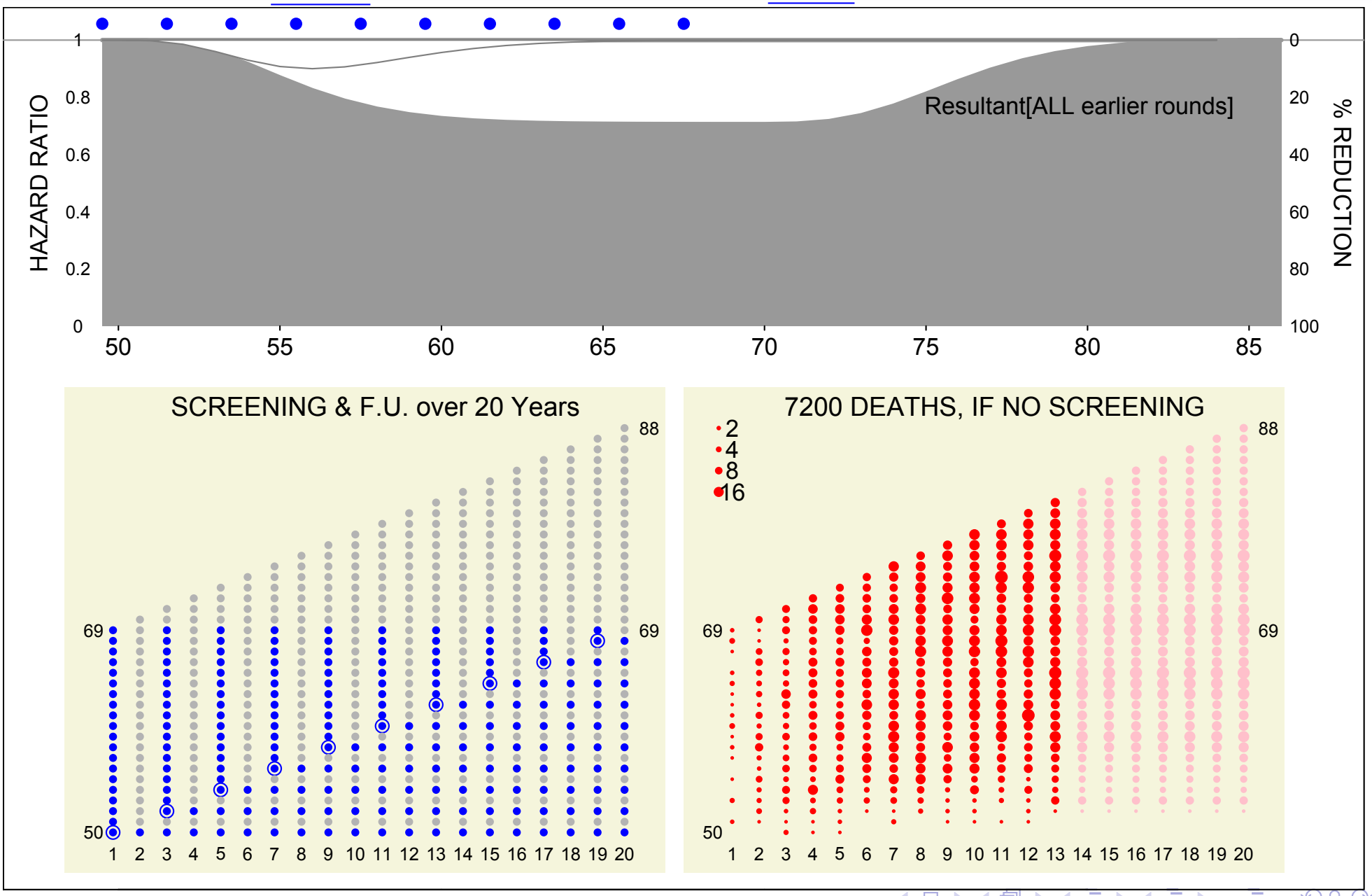

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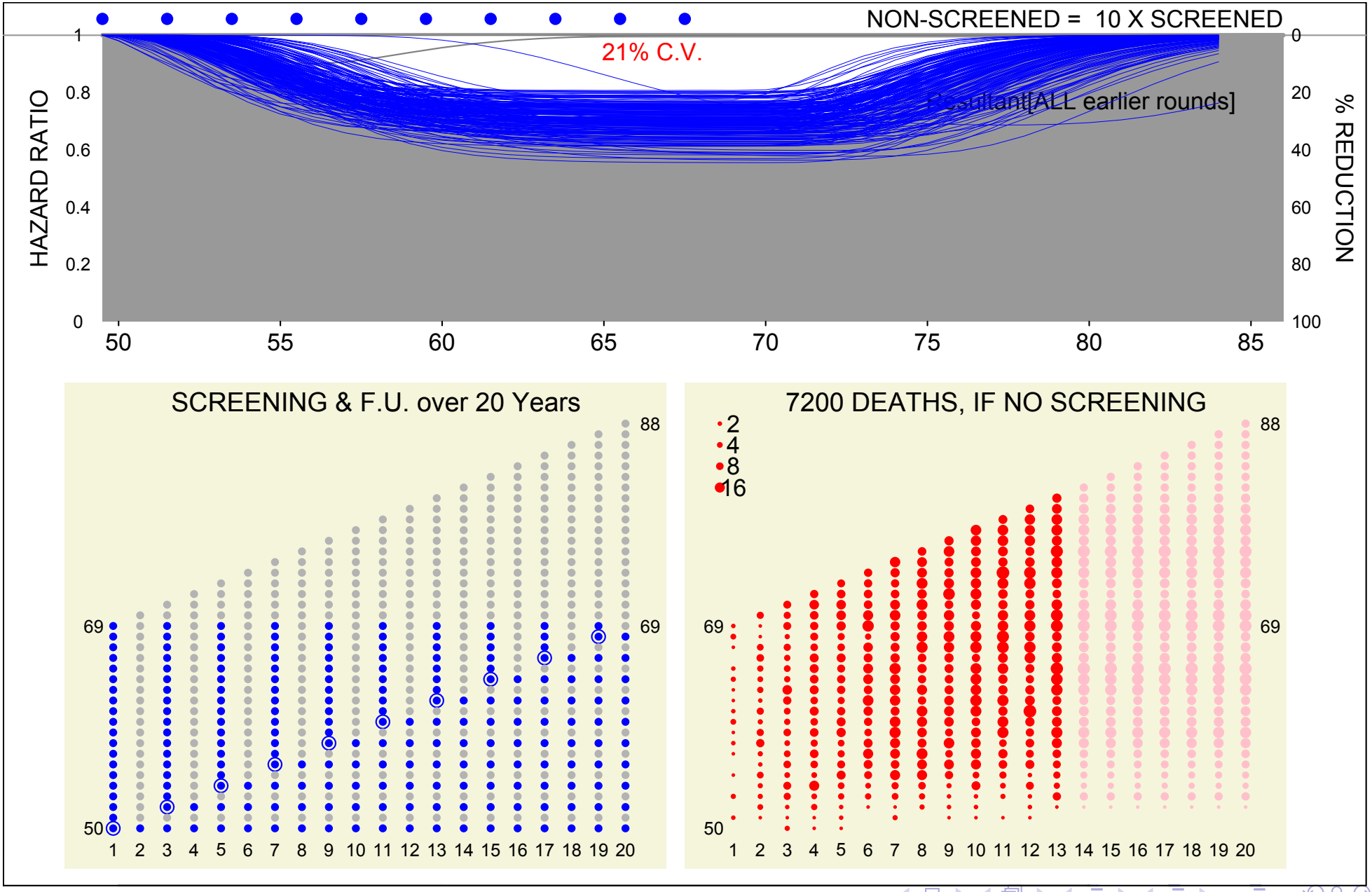

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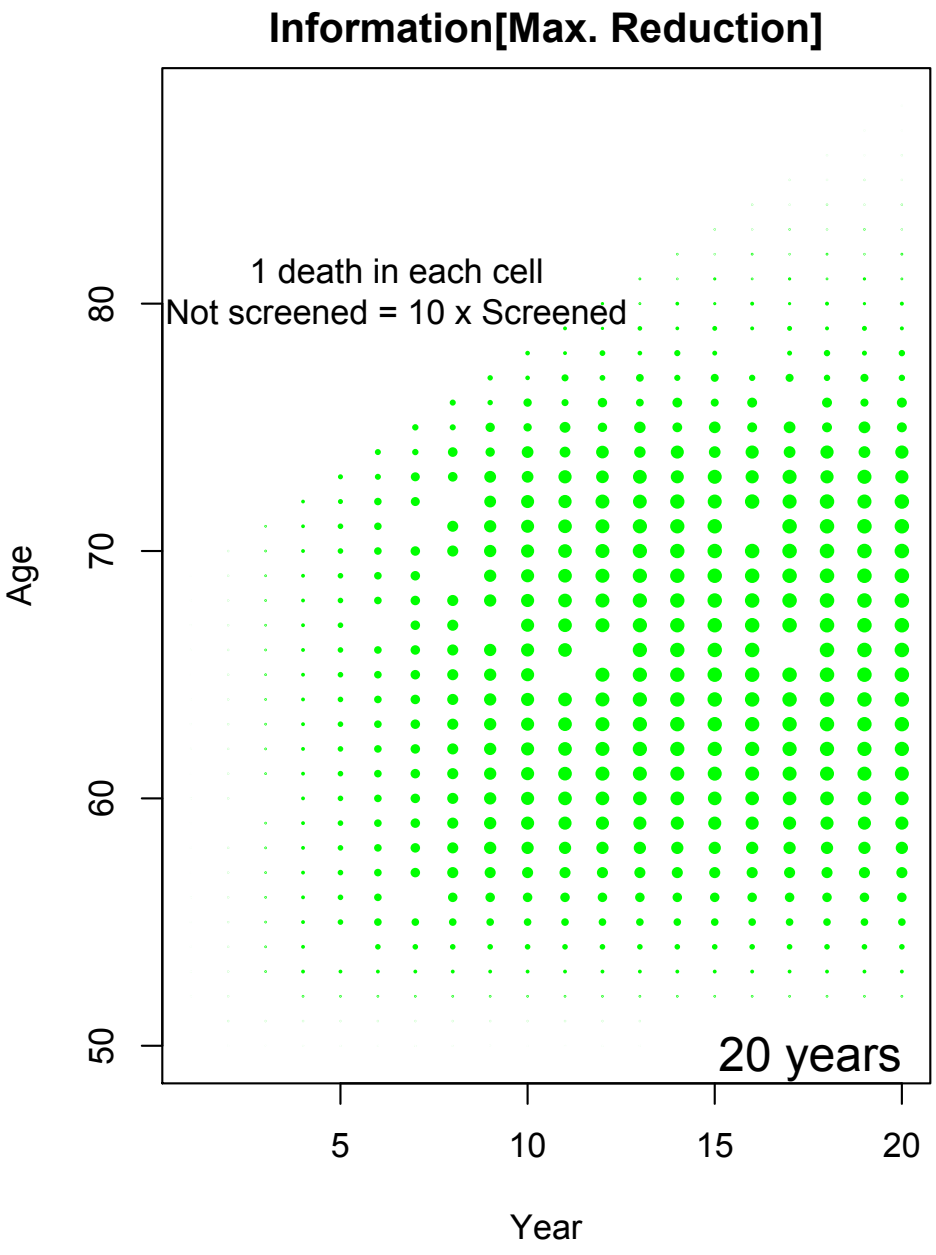

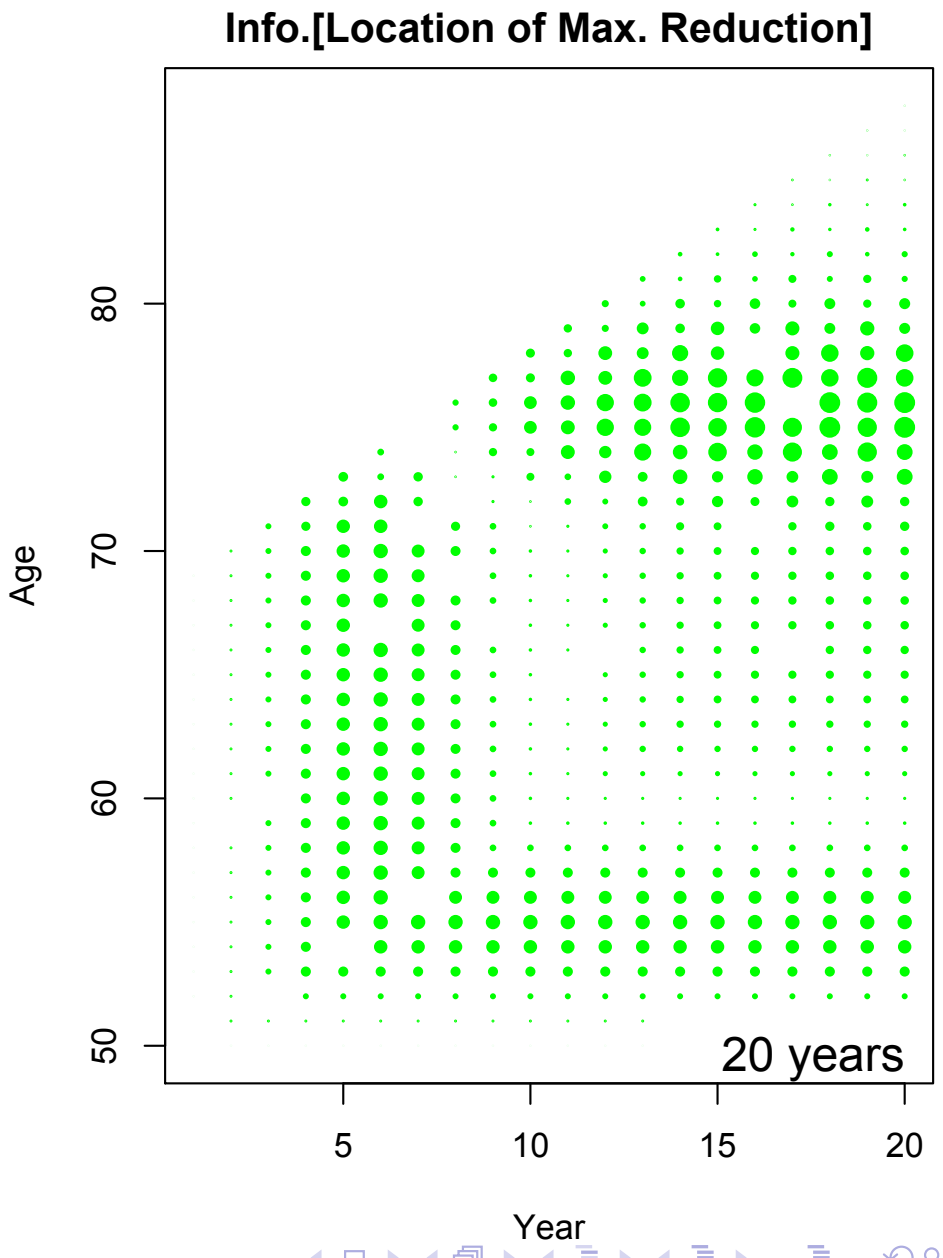

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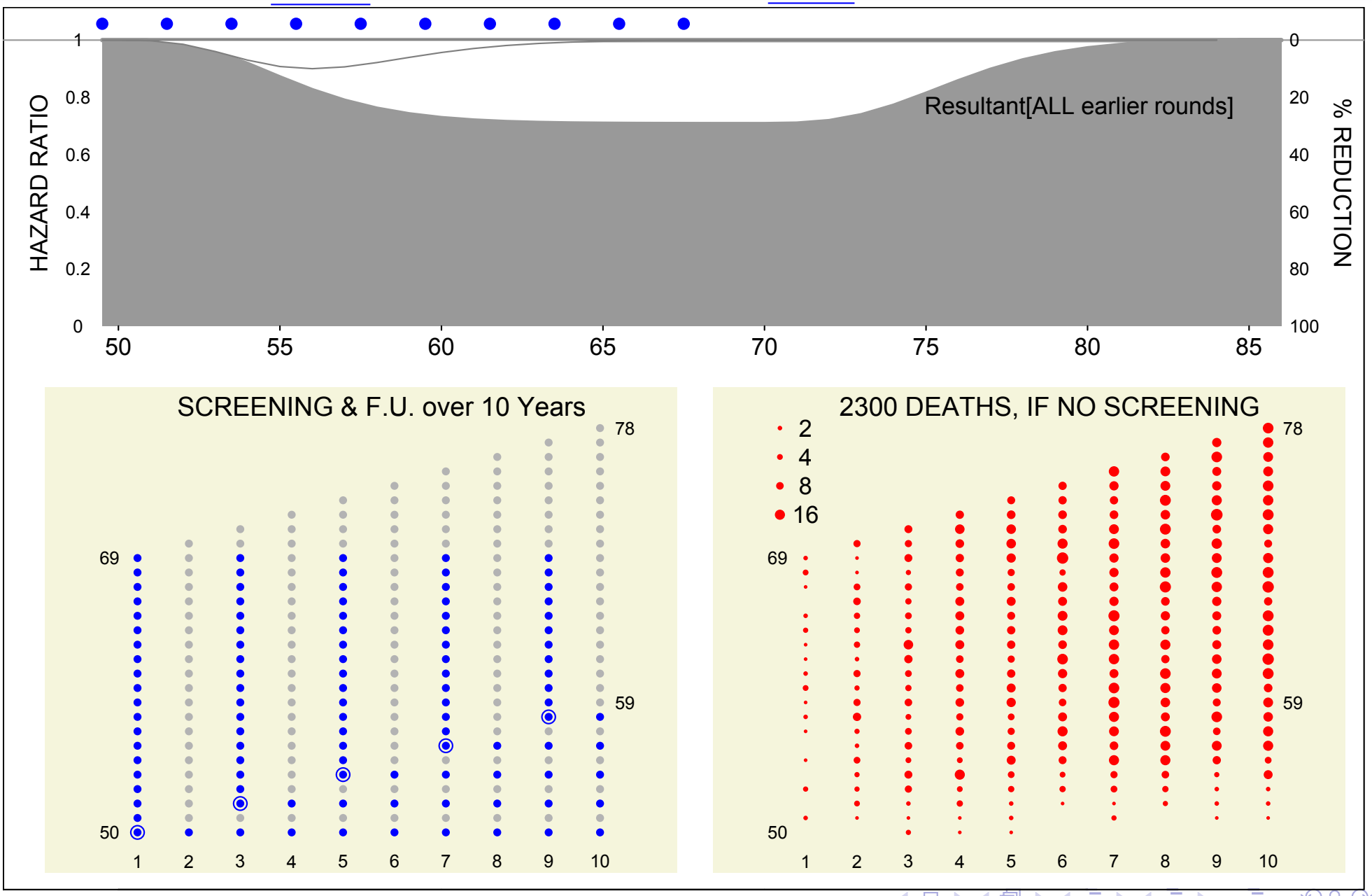

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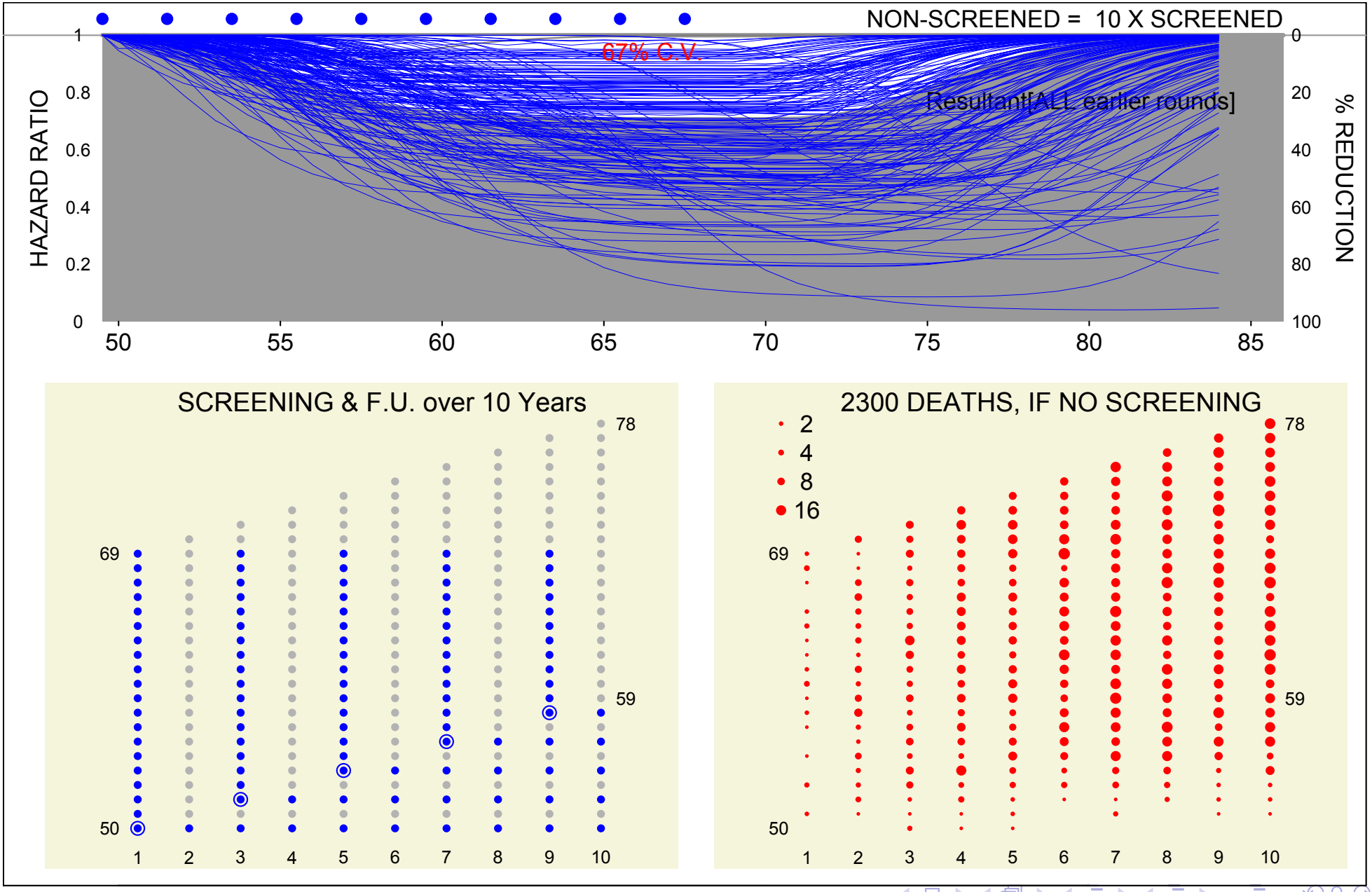

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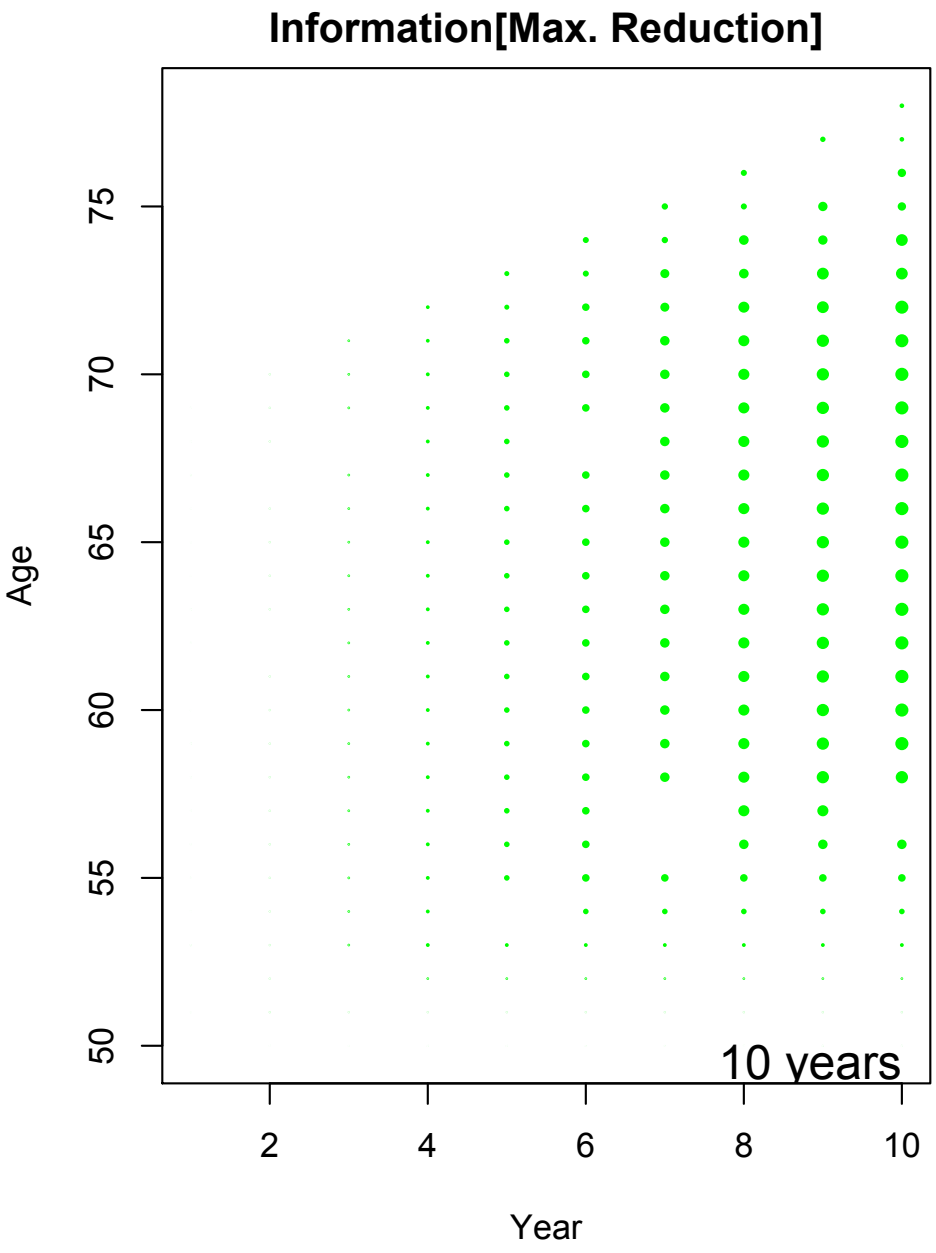

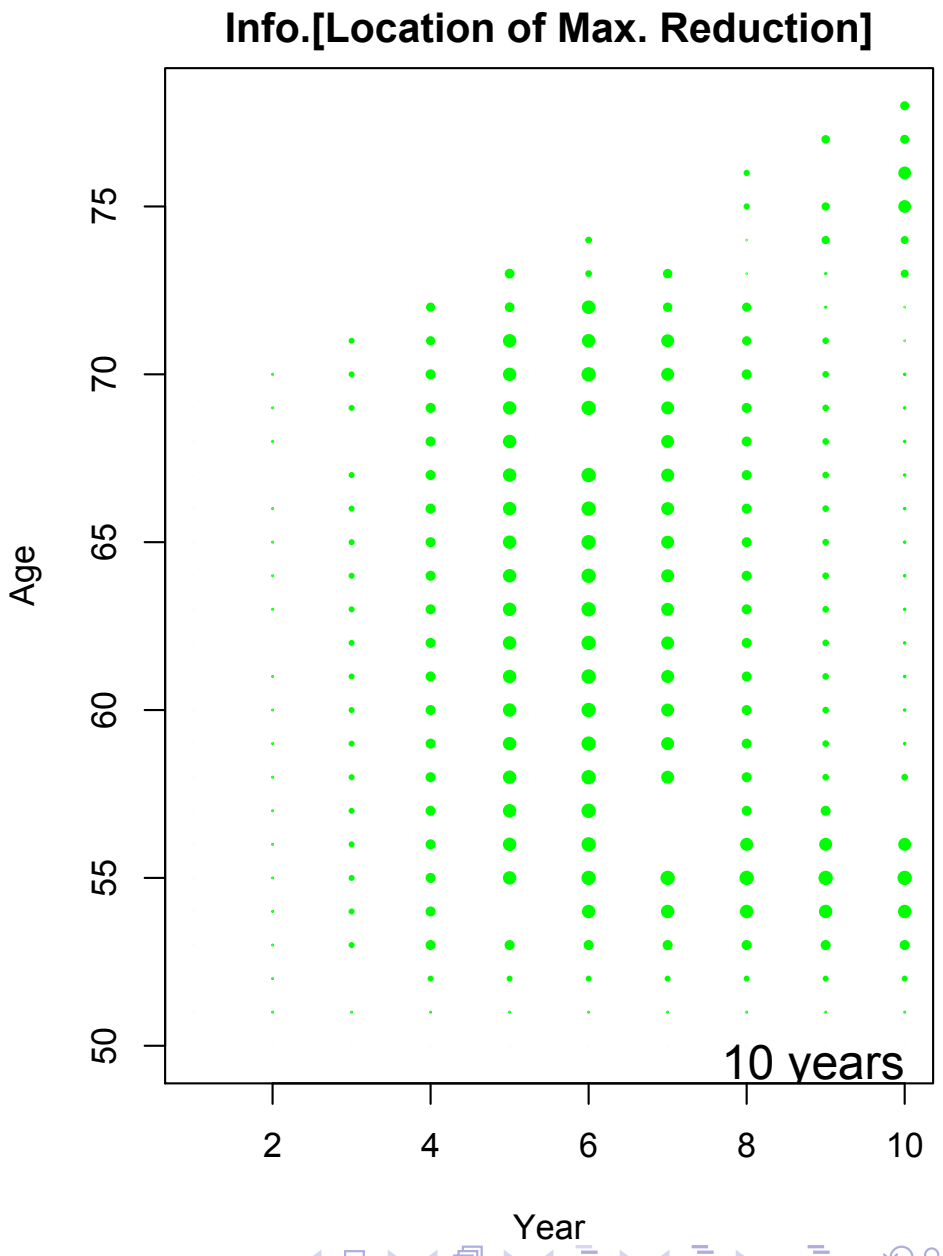

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- May have to limit to **just first half** of, rather than the full bathtub-shaped HR function
- Helps to study individual (Lexis Cell) contributions to the Information Matrix

DOWNLOADS / FUNDING

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

or Google "James Hanley McGill"

CIHR