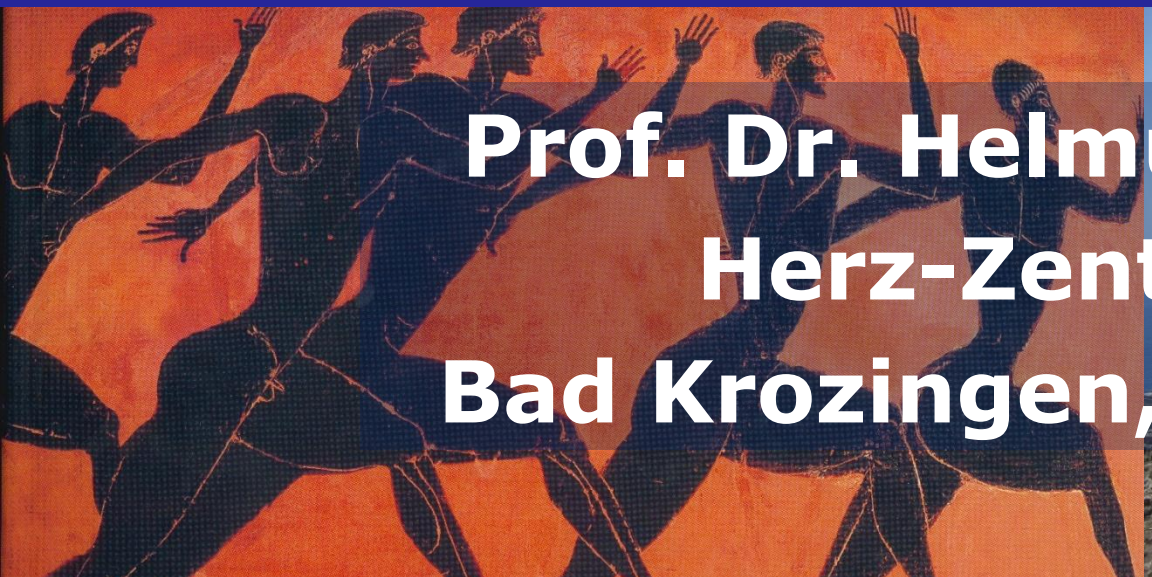


Is it ever too late for cardiovascular prevention and rehabilitation?



Prof. Dr. Helmut Gohlke

Herz-Zentrum

Bad Krozingen, Germany

The demographic issue

Life expectancy is increasing

➔Patients are getting older:

80 + -year old patients with unstable angina are not unusual any more.

Is it ever too late for prevention?

- **Life expectancy at age 65 and age 80**
- Smoking cessation after CABG*
- Lipid lowering after ACS and in the elderly (65-82yrs)*
- Exercise in stable CAD and in CHF
- Mediterranean diet
- Influenza vaccination*
- Too late: dialysis patient

*aspects of costeffectiveness will be covered

Is it worthwhile to worry about secondary prevention in a 65 yrs old patient?

Is there enough life expectancy for secondary prevention to be effective?

Question 1

The average life expectancy of a 65 year old European man (in 2006) is :

1. 7- 9 years
2. 10-12 years
3. 13-16 years
4. 17-19 years
5. 20-23 years

Germany 17,2 yrs
France 18,2 yrs

OECD Health Data

What is the average life expectancy of an 80 year old European person ?

male	female
8,0 - 8,5	9,0 - 11,0

Thus : There is enough time for preventive measures to take effect, even in an 80 year old person !

Saving lives by changing life!
Is it ever too late for prevention?

- Life expectancy at age 65 and age 80
- **Smoking cessation after CABG***
- Lipid lowering after ACS and in the elderly (65-82yrs)*
- Exercise in stable CAD and in CHF
- Mediterranean diet
- Influenza vaccination*
- Too late: dialysis patient

*aspects of costeffectiveness will be covered

Prevention and Rehabilitation

Three life-years gained from smoking cessation after coronary artery bypass surgery: A 30-year follow-up study

Ron T. van Domburg, PhD, Wilma Scholte op Reimer, PhD, Sanne E. Hoeks, Msc, Arie Pieter Kappetein, MD, PhD, and Ad J.J.C. Bogers, MD, PhD *Rotterdam, The Netherlands*

Van Domburg et al Am Heart J 2008;156:473-6

Cumulative Life expectancy in years with smoking cessation and persisting smoking by age

	Quitters Life expectancy (y)	Persistent smokers Life expect.(y)	Gain of LE	%
Total	20.0	17.0	3.0	15%
Age				
<50 yrs	21.7	18.2	3.5	16%
50-60 yrs	16.4	13.6	2.8	17%
>60 yrs	14.2	12.5	1.7	12%

Van Domburg et al Am Heart J 2008;156:473-6

Conclusions

Smoking cessation turned out to have a greater effect on reducing the risk of mortality than any other intervention or treatment..

….and it saves money!*

Van Domburg et al Am Heart J 2008;156:473-6

*** Kahn et al Circulation. 2008;118:576-585**

Statins at higher age

Is it really beneficial for the elderly vascular patient to have his/her LDL-Cholesterol lowered by statins?

Statins for Secondary Prevention in Elderly Patients

A Hierarchical Bayesian Meta-Analysis

19,569 patients
with an age range of 65 to 82 years

Jonathan Afilalo, MD,* Gustavo Duque, MD, PHD,*† Russell Steele, PHD,‡
J. Wouter Jukema, MD, PHD,§ Anton J. M. de Craen, PHD,‖ Mark J. Eisenberg, MD, MPH*¶

Montreal, Canada; and Leiden, the Netherlands

Afilalo et al JACC 2008;51:37–45

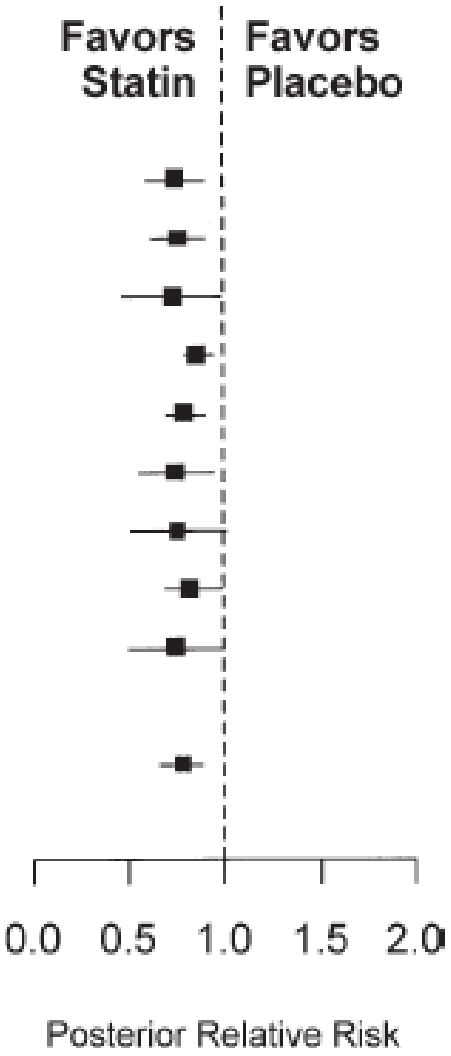
Statins for Secondary Prevention in Elderly Patients: 65-82yrs

Bayesian Forest Plot for

All-Cause Mortality

Study	No. Events/ Total No. of Patients: Statin	Placebo	Posterior Median Relative Risk (95% Credible Interval)
4S	67 / 518	96 / 503	0.75 (0.59 , 0.89)
CARE	77 / 640	108 / 643	0.76 (0.61 , 0.90)
FLARE	2 / 179	6 / 187	0.74 (0.47 , 0.97)
HPS	963 / 5366	1089 / 5331	0.87 (0.80 , 0.93)
LIPID	287 / 1741	365 / 1773	0.80 (0.71 , 0.90)
LIPS	23 / 324	32 / 299	0.75 (0.55 , 0.94)
PLAC I	1 / 42	2 / 52	0.76 (0.51 , 1.00)
PROSPER	110 / 934	128 / 899	0.82 (0.69 , 0.98)
REGRESS	1 / 75	1 / 63	0.75 (0.49 , 0.99)
Pooled (5 year)	**1531 / 9819**	**1827 / 9750**	**0.78 (0.65 , 0.89)**

15,6% vs 18,7%➔ NNT 161

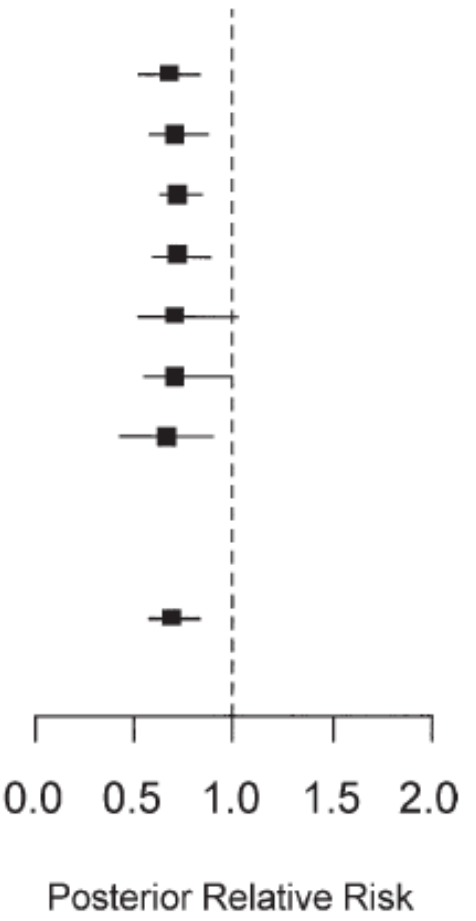


Afilalo et al J Am Coll Cardiol, 2008; 51:37-45

Statins for Secondary Prevention in Elderly Patients: 65-82yrs

Revascularization

Study	No. Events/ Total No. of Patients: Statin	Placebo	Posterior Median Relative Risk (95% Credible Interval)
4S	51 / 518	80 / 503	0.68 (0.53 , 0.83)
CARE	73 / 640	104 / 643	0.71 (0.58 , 0.86)
LIPID	205 / 1741	284 / 1773	0.73 (0.63 , 0.84)
LIPS	57 / 324	76 / 299	0.73 (0.59 , 0.88)
PLAC I	5 / 42	7 / 52	0.71 (0.52 , 1.02)
PROSPER	29 / 934	31 / 899	0.71 (0.55 , 0.99)
REGRESS	1 / 75	5 / 63	0.66 (0.42 , 0.90)
Pooled (5 year)	**422 / 4274**	**586 / 4232**	**0.70 (0.53 , 0.83)**



9,9% vs 13,8% ➔ NNT 128

Afilalo et al J Am Coll Cardiol, 2008; 51:37-45

Statins for Secondary Prevention in Elderly Patients: 65-82yrs

Endpoint	Eventrate in % Statin	vs	Control	HR	NNT
CAD Mortality	8,7%	vs	11,3%	0.77	192
Nonfatal MI	8,0%	vs	10,5%	0.76	200
Stroke	5,2%	vs	7,0%	0.74	277

Conclusions: Statins reduce all-cause and CAD mortality in elderly patients and the magnitude of this effect is substantially larger than had been previously estimated

Afilalo et al J Am Coll Cardiol, 2008; 51:37-45

cost-effectiveness of statins

- A quality-adjusted life-year costs $18,800 in 75 to 84 y/o patients

  - comparable to the cost of commonly accepted treatments such as treating hypertension in adults aged 35 to 64 years.

Afilalo et al JACC 2008;51:37–45

Cardiovascular Benefit of Magnitude of Low-Density Lipoprotein Cholesterol Reduction

A Comparison of Subgroups by Age

Catherine R. Rahilly-Tierney, MD, MPH; Elizabeth V. Lawler, MPH, ScD;
Richard E. Scranton, MD, MPH; J. Michael Gaziano, MD, MPH

Rahilly-Tierney et al Circulation 2009;120:1491-1497

20 132 male veterans at high risk for an acute CV event and who had 2 or **more LDL-C measurements before their first documented acute MI, revascularization, death, or censoring date.**

Unadjusted and Multivariate-Adjusted* HRs (95% CI) For: first acute MI, revascularization, death for Each Category of LDL-C Reduction, by Age Quartile

Category of LDL-C Reduction	<61 y	61-69 y	69-75 y	>75 y
Small: 10–40 mg/dL				
Unadjusted	0.87 (0.76–1.00)	0.69 (0.59–0.79)	0.77 (0.66–0.90)	0.72 (0.61–0.85)
Multivariate adjusted	0.73 (0.64–0.84)	0.67 (0.58–0.78)	0.70 (0.60–0.82)	0.64 (0.54–0.76)
Moderate: 40–70 mg/dL				
Unadjusted	0.68 (0.59–0.79)	0.57 (0.48–0.67)	0.65 (0.55–0.77)	0.73 (0.60–0.87)
Multivariate adjusted	0.50 (0.43–0.58)	0.45 (0.37–0.52)	0.45 (0.39–0.56)	0.53 (0.44–0.64)
Large: ≥70 mg/dL				
Unadjusted	0.73 (0.61–0.87)	0.57 (0.47–0.68)	0.53 (0.42–0.66)	0.54 (0.42–0.0.70)
Multivariate adjusted	0.37 (0.31–0.45)	0.29 (0.24–0.37)	0.26 (0.20–0.34)	0.38 (0.30–0.49)

*Adjusted for age, gender, current smoking status, body mass index, statin use, nonstatin cholesterol-modifying therapy use, hypertension, cerebrovascular disease, thyroid disease, and renal disease.

Rahilly-Tierney et al Circulation 2009;120:1491-1497

Conclusions

—In a cohort of veterans at high risk for CV events, patients of all ages, including those 80 years or older, benefitted the most from large reductions in LDL-C.

Rahilly-Tierney et al Circulation 2009;120:1491-1497

Do we increase
the risk of cancer
by statin treatment ??

Cardiovascular and Cancer Mortality in Very Elderly Post-Myocardial Infarction Patients Receiving Statin Treatment

Klas Gränsbo, MD,* Olle Melander, MD,* Lars Wallentin, MD,† Johan Lindbäck, PHD,† Ulf Stenestrand, MD,‡ Jörg Carlsson, MD,§ Jan Nilsson, MD*

Malmö, Lund, Uppsala, Linköping, and Kalmar, Sweden

J Am Coll Cardiol 2010;55:1362–9)

Cardiovascular and Cancer Mortality in Very Elderly Post-Myocardial Infarction Patients Receiving Statin Treatment

Methods:
all patients **≥ 80 years** admitted with the diagnosis of AMI in the Register of Information and Knowledge About Swedish Heart Intensive Care Admissions between 1999 and 2003 (n 21,410).

Complete covariate and follow-up data available for 14,907 patients (**population A**).

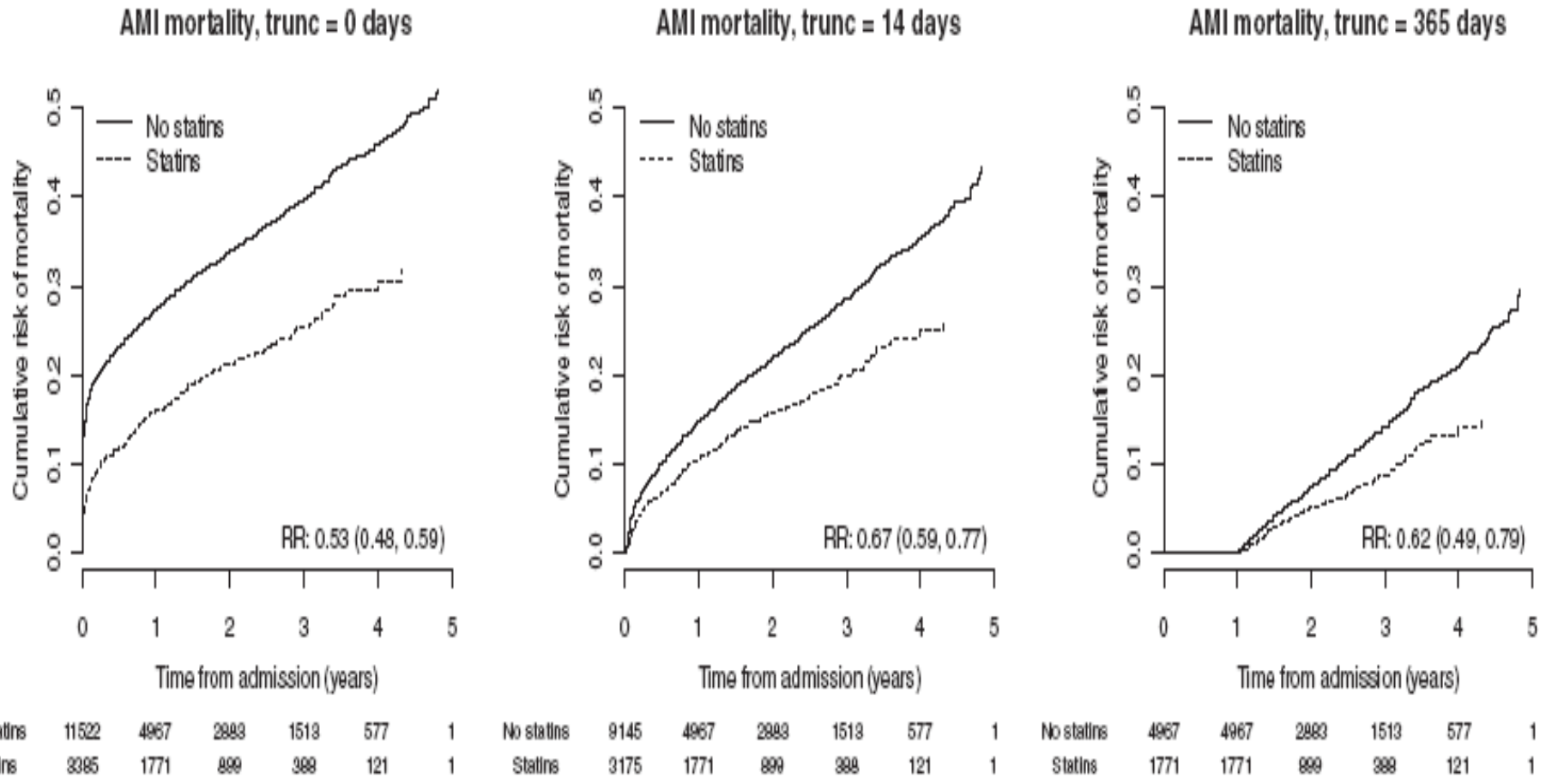
To limit the bias related comorbidity on statin therapy, analyses were performed **excluding**
-patients who died within 14 days of the acute event (**population B**)
- patients who **died within 365 days** (**population C**).

A propensity score was used to adjust for initial differences between treatment groups.

Gränsbo et al J Am Coll Cardiol 2010;55:1362–9

Adjusted Cumulative Risk of **AMI Mortality** Estimated at the Mean of Each Covariate Included in the Model

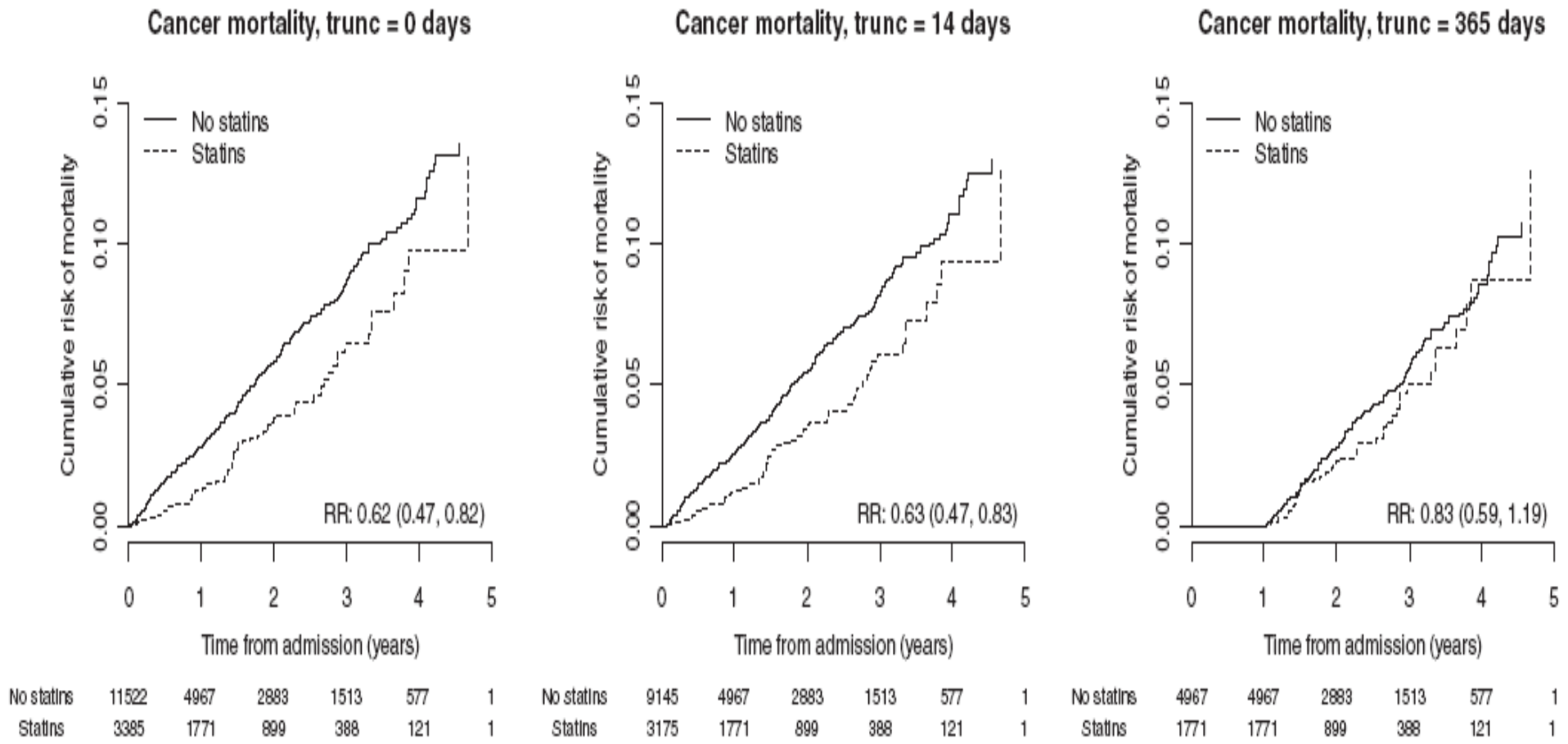
Pts who died within 14 days or 365 days after discharge were excluded from analysis



Gränsbo et al J Am Coll Cardiol 2010;55:1362–9

Adjusted Cumulative Risk of **Cancer Mortality** Estimated as the Mean of Each Covariate Included in the Model

Pts who died within 14 days or 365 days after discharge were excluded from analysis



Gränsbo et al J Am Coll Cardiol 2010;55:1362–9

Statin treatment is associated with lower cardiovascular mortality in very elderly post-infarction patients **without** increasing the risk of the development of cancer.

Gränsbo et al J Am Coll Cardiol 2010;55:1362–9

Unresolved question
(until recently)

Whether the treatment of patients with hypertension who are 80 years of age or older is beneficial is unclear.

Is it treatment or stroke prevention?

Isn't reaching the age of 80 yrs a success-story in itself, that can't be improved by lowering BP?

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 1, 2008 VOL. 358 NO. 18

Treatment of Hypertension in Patients 80 Years of Age or Older

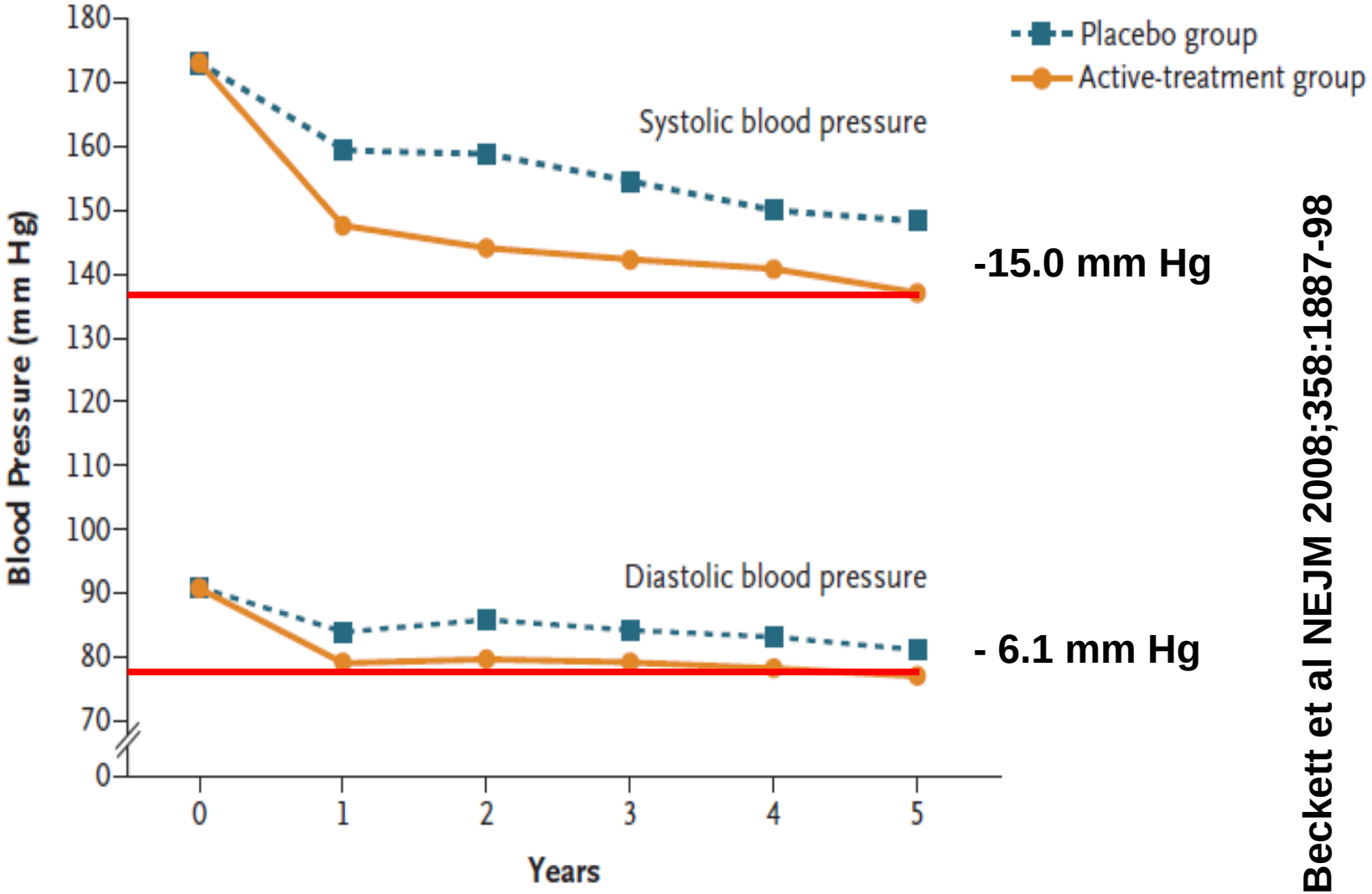
Nigel S. Beckett, M.B., Ch.B., Ruth Peters, Ph.D., Astrid E. Fletcher, Ph.D., Jan A. Staessen, M.D., Ph.D., Lisheng Liu, M.D., Dan Dumitrascu, M.D., Vassil Stoyanovsky, M.D., Riitta L. Antikainen, M.D., Ph.D., Yuri Nikitin, M.D., Craig Anderson, M.D., Ph.D., Alli Belhani, M.D., Françoise Forette, M.D., Chakravarthi Rajkumar, M.D., Ph.D., Lutgarde Thijs, M.Sc., Winston Banya, M.Sc., and Christopher J. Bulpitt, M.D., for the HYVET Study Group*

N Engl J Med 2008;358:1887-98

Table 1. Baseline Characteristics of the Patients.*

Characteristic	Active Treatment (N=1933)	Placebo (N=1912)
Age — yr	83.6±3.2	83.5±3.1
Female sex — no. (%)	1174 (60.7)	1152 (60.3)
Blood pressure — mm Hg		
While sitting	173.0±8.4/90.8±8.5	173.0±8.6/90.8±8.5
While standing	168.0±11.0/88.7±9.3	167.9±11.1/88.6±9.3
Orthostatic hypotension — no. (%)†	152 (7.9)	169 (8.8)
Isolated systolic hypertension — no. (%)	625 (32.3)	623 (32.6)
Heart rate — beats/min	74.5±9.1	74.5±9.3
Cardiovascular history		
Cardiovascular disease — no. (%)	223 (11.5)	229 (12.0)
Hypertension — no. (%)	1737 (89.9)	1718 (89.9)
Antihypertensive treatment — no. (%)	1241 (64.2)	1245 (65.1)
Stroke — no. (%)	130 (6.7)	131 (6.9)
Myocardial infarction — no. (%)	59 (3.1)	62 (3.2)
Heart failure — no. (%)	56 (2.9)	55 (2.9)
Cardiovascular risk factors		

Mean Blood Pressure, Measured while Patients Were Seated, in the Intention-to-Treat Population, According to Study Group



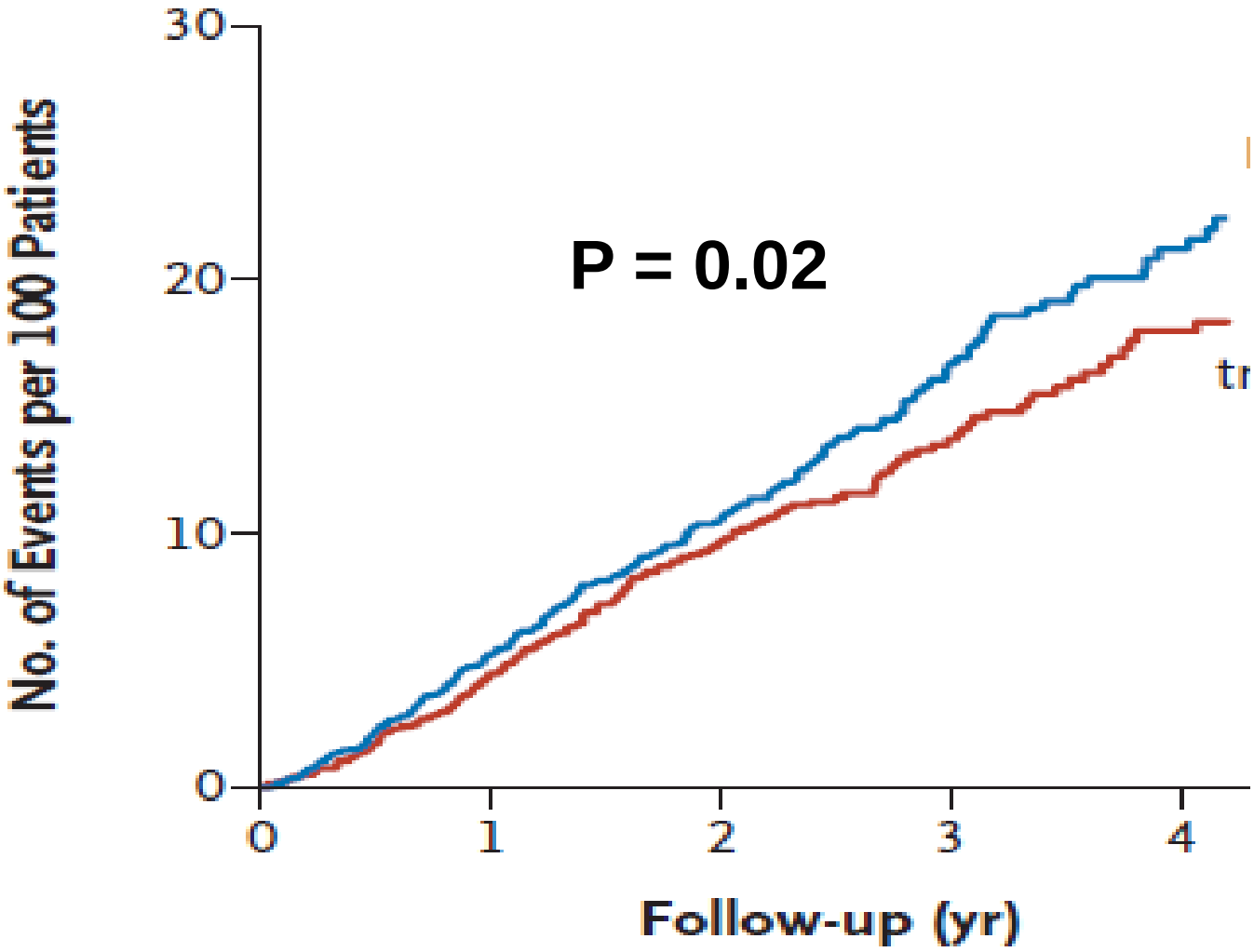
Beckett et al NEJM 2008;358:1887-98

No. at Risk

Placebo group	1912	1468	701	330	191	116
Active-treatment group	1933	1540	754	373	207	118

B

Death from Any Cause

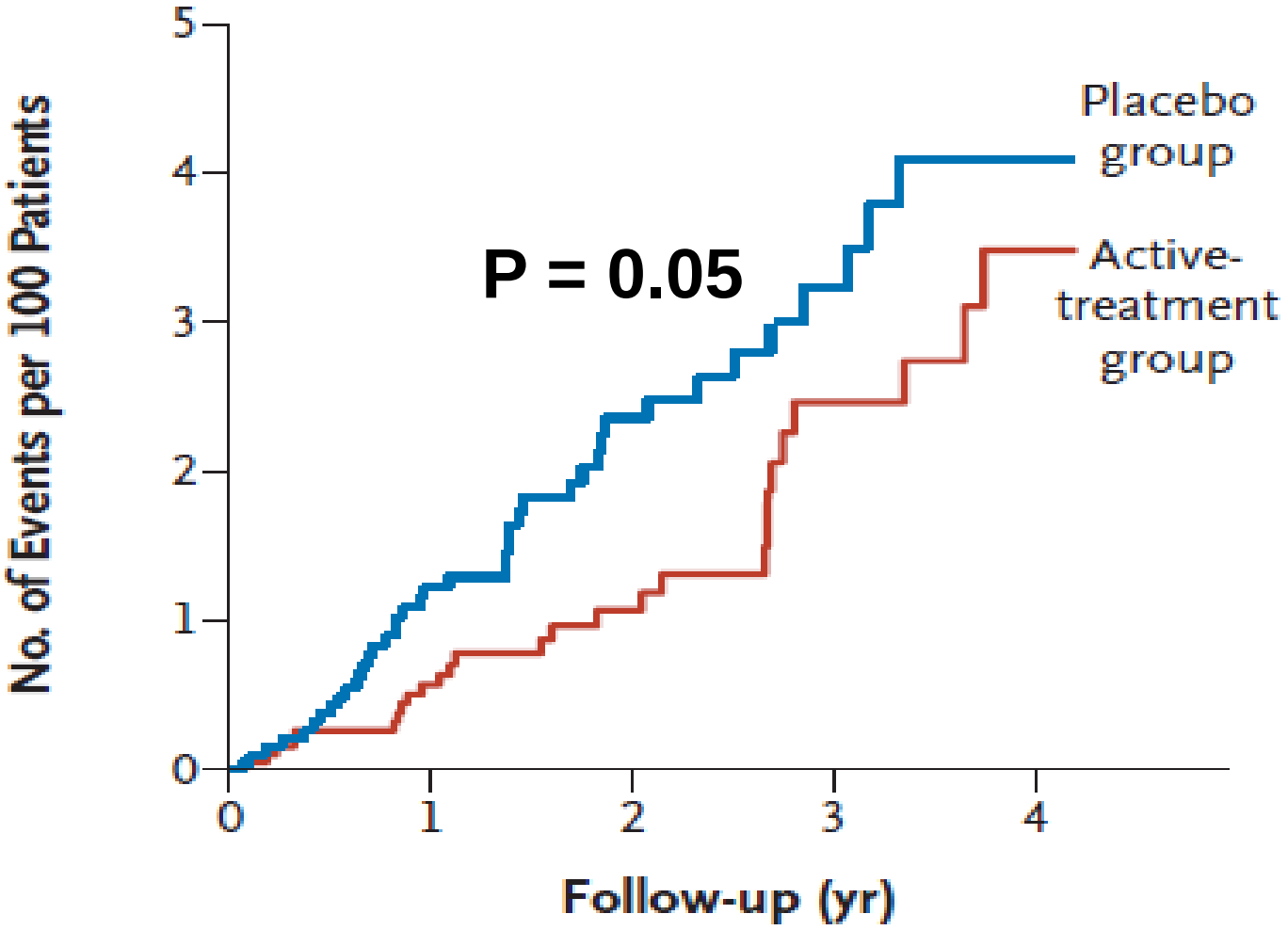


No. at Risk					
Placebo group	1912	1492	814	379	202
Active-treatment group	1933	1565	877	420	231

Beckett et al NEJM 2008;358:1887-98

D

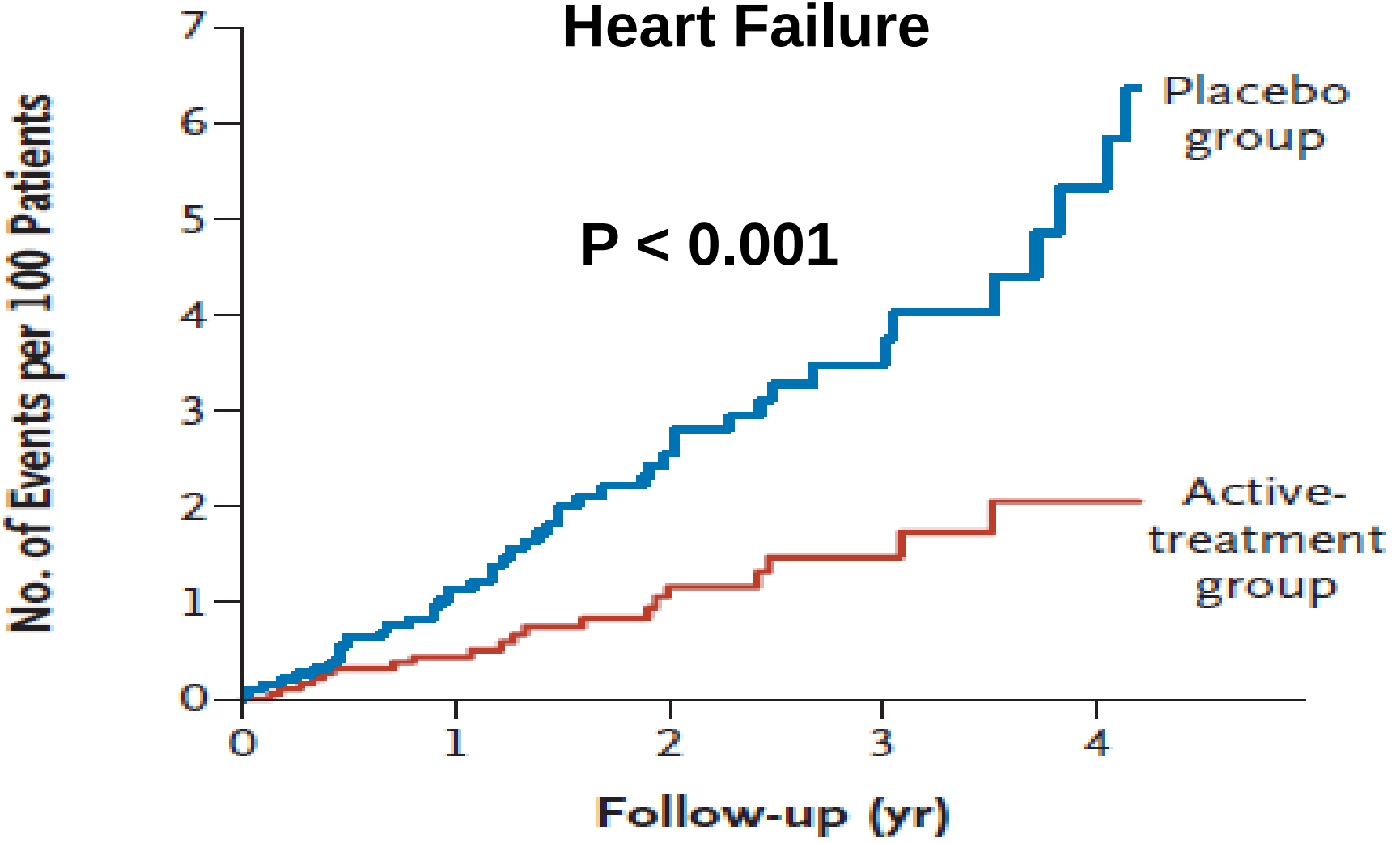
Death from Stroke



No. at Risk					
Placebo group	1912	1492	814	379	202
Active-treatment group	1933	1565	877	420	231

Beckett et al NEJM 2008;358:1887-98

Heart Failure



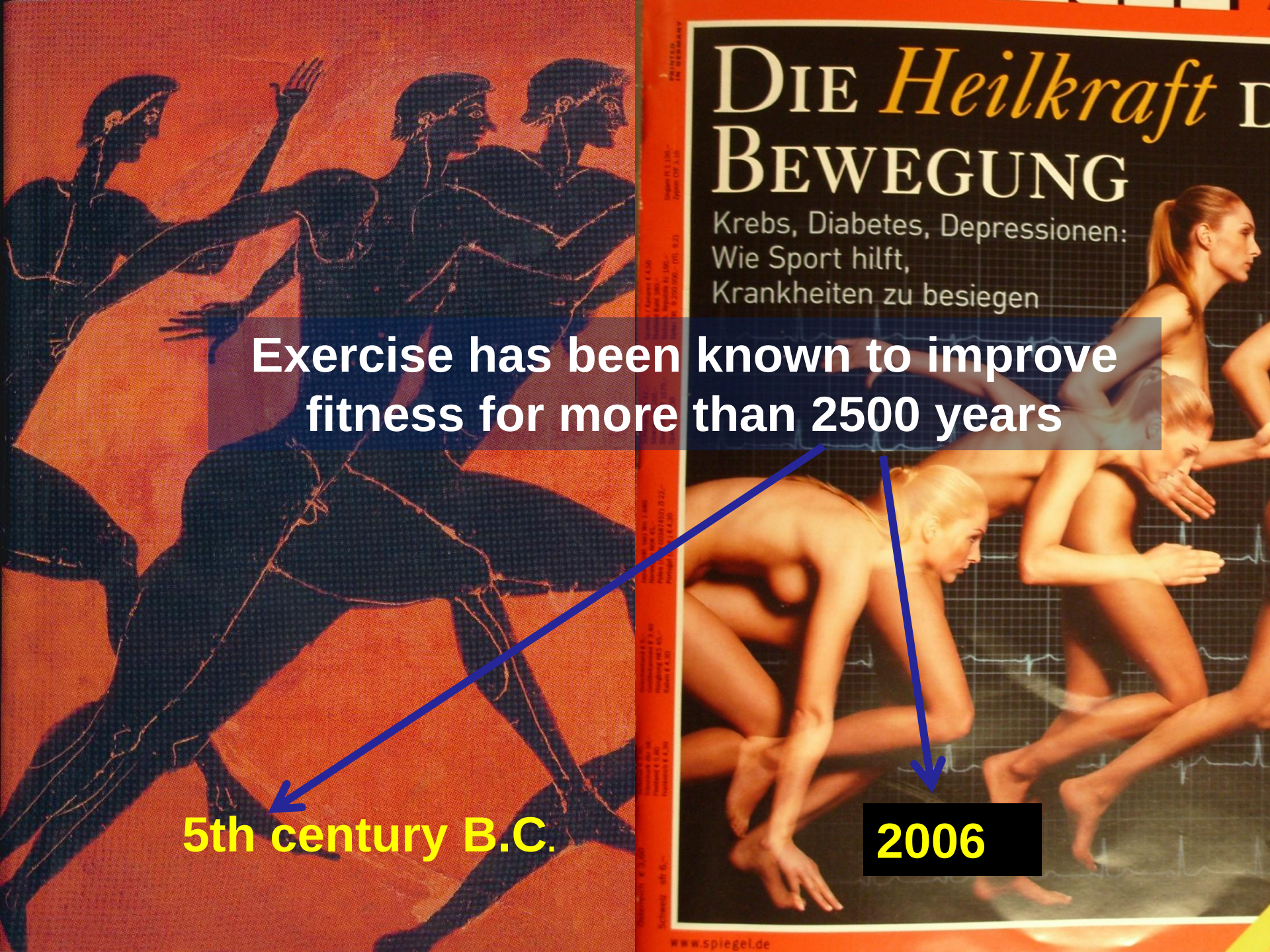
Placebo	1912	1480	794	367	188
Active Rx	1933	1559	872	416	228

Beckett et al NEJM 2008;358:1887-98

Conclusion

Hypertension treatment in the very elderly, aimed to achieve a **target blood pressure of 150/80 mm Hg**, is beneficial and is associated with reduced risks of:
death from **any cause**,
death from **stroke** and
of **heart failure**.
Whether further reduction is beneficial still needs to be established.

Beckett et al NEJM 2008;358:1887-98



Exercise has been known to improve fitness for more than 2500 years

5th century B.C.

2006

Percutaneous Coronary Angioplasty Compared With Exercise Training in Patients With Stable Coronary Artery Disease

101

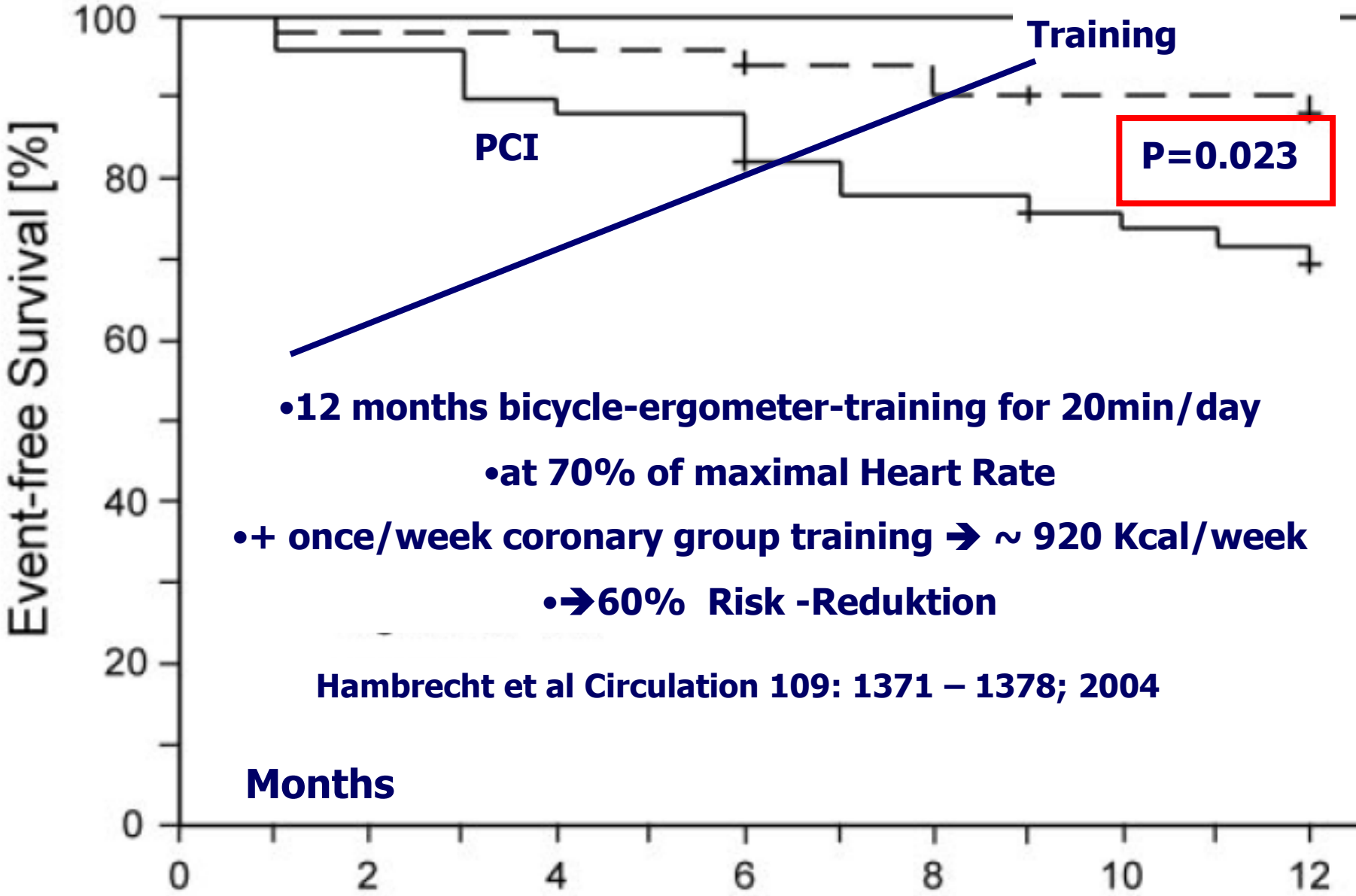
A Randomized Trial

Aged 70 yrs

Rainer Hambrecht, MD; Claudia Walther, MD; Sven Möbius-Winkler, MD; Stephan Gielen, MD; Axel Linke, MD; Katrin Conradi, MD; Sandra Erbs, MD; Regine Kluge, MD; Kai Kendziorra, MD; Osama Sabri, MD; Peter Sick, MD; Gerhard Schuler, MD

Circulation, 2004; 109: 1371 - 1378.

Event-free survival after 12 months was significantly superior in exercise training group versus PCI group



- 12 months bicycle-ergometer-training for 20min/day
- at 70% of maximal Heart Rate
- + once/week coronary group training ➔ ~ 920 Kcal/week
- ➔60% Risk -Reduktion

Hambrecht et al Circulation 109: 1371 – 1378; 2004

Cite this article as: BMJ, doi:10.1136/bmj.37938.645220.EE (published 16 January 2004)

Papers

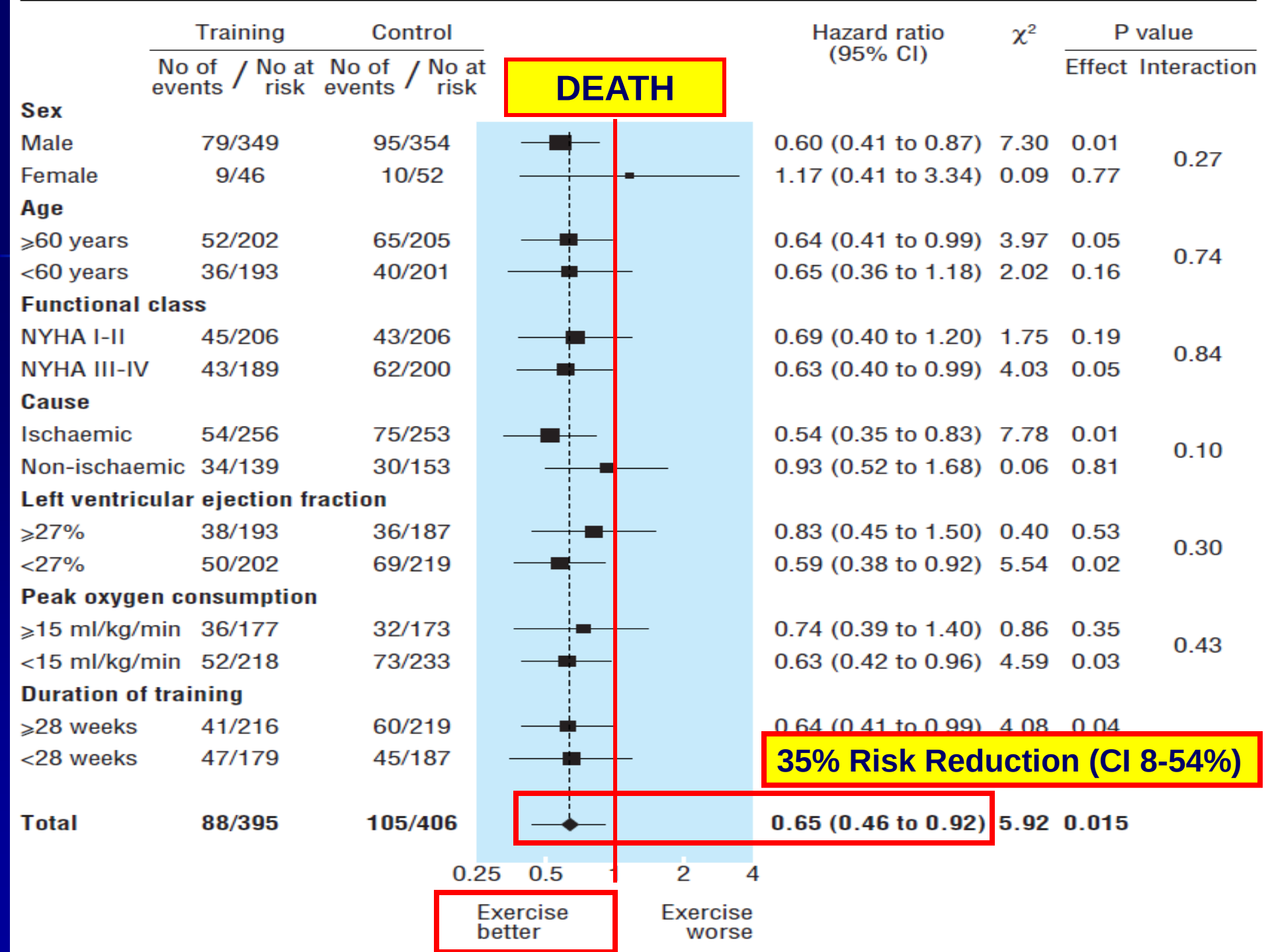
Heart failure - the end stage of cardiac diseases:

Mean age ~60yrs

Exercise training meta-analysis of trials in patients with chronic heart failure (ExTraMATCH)

ExTraMATCH Collaborative

BMJ Jan 2004; 328: 189;


DEATH
Training
Control
No of events / No at risk
No of events / No at risk
Hazard ratio (95% CI)
χ²
P value
Effect
Interaction
Sex
Male 79/349 95/354 0.60 (0.41 to 0.87) 7.30 0.01
Female 9/46 10/52 1.17 (0.41 to 3.34) 0.09 0.77
0.27
Age
≥60 years 52/202 65/205 0.64 (0.41 to 0.99) 3.97 0.05
<60 years 36/193 40/201 0.65 (0.36 to 1.18) 2.02 0.16
0.74
Functional class
NYHA I-II 45/206 43/206 0.69 (0.40 to 1.20) 1.75 0.19
NYHA III-IV 43/189 62/200 0.63 (0.40 to 0.99) 4.03 0.05
0.84
Cause
Ischaemic 54/256 75/253 0.54 (0.35 to 0.83) 7.78 0.01
Non-ischaemic 34/139 30/153 0.93 (0.52 to 1.68) 0.06 0.81
0.10
Left ventricular ejection fraction
≥27% 38/193 36/187 0.83 (0.45 to 1.50) 0.40 0.53
<27% 50/202 69/219 0.59 (0.38 to 0.92) 5.54 0.02
0.30
Peak oxygen consumption
≥15 ml/kg/min 36/177 32/173 0.74 (0.39 to 1.40) 0.86 0.35
<15 ml/kg/min 52/218 73/233 0.63 (0.42 to 0.96) 4.59 0.03
0.43
Duration of training
≥28 weeks 41/216 60/219 0.64 (0.41 to 0.99) 4.08 0.04
<28 weeks 47/179 45/187
35% Risk Reduction (CI 8-54%)
Total 88/395 105/406 0.65 (0.46 to 0.92) 5.92 0.015
0.25
0.5
1
2
4
Exercise better
Exercise worse

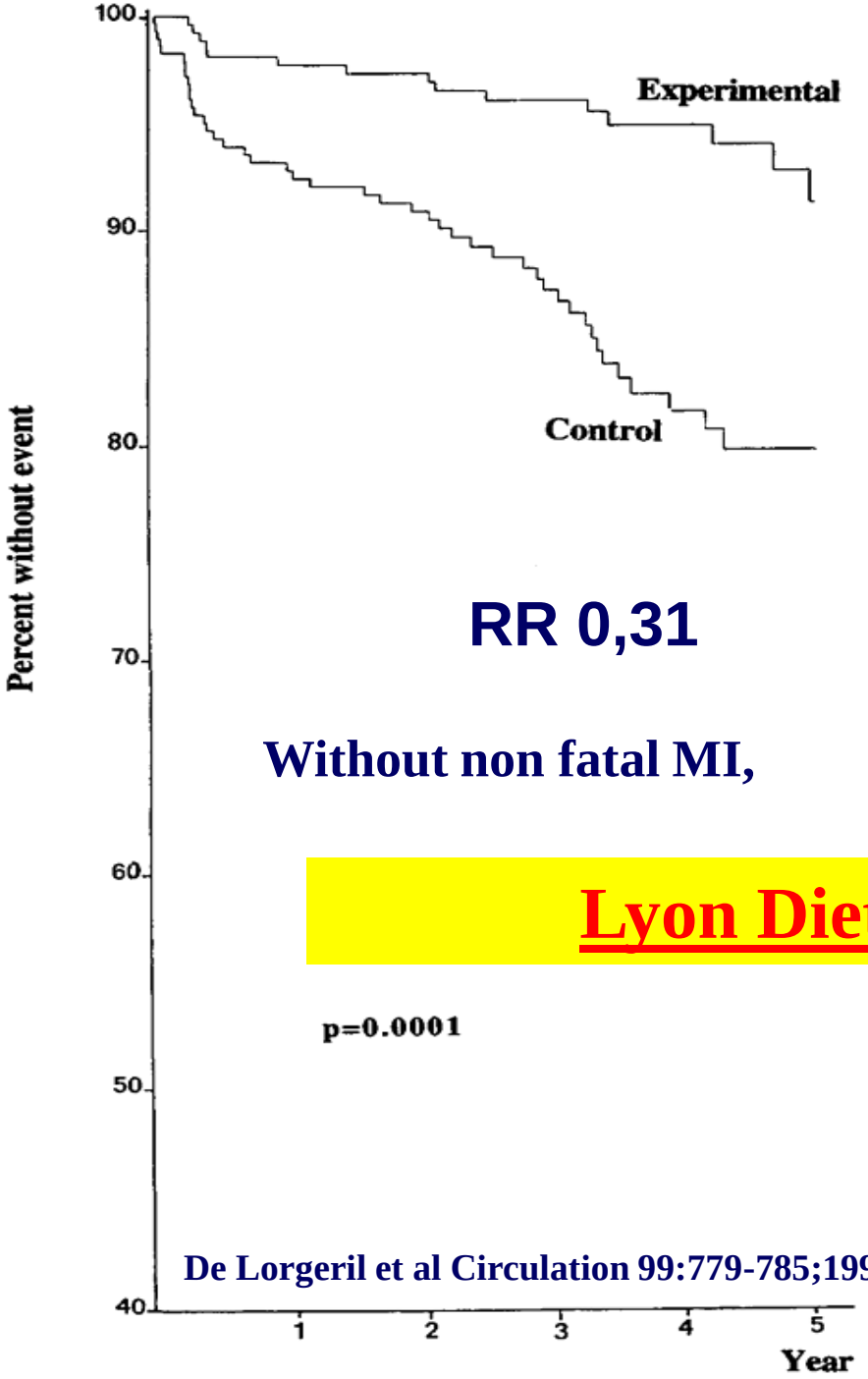
The Mediterranean Diet and Mortality -

Mediterranean Diet, Traditional Risk Factors, and the Rate of Cardiovascular Complications After Myocardial Infarction

Final Report of the Lyon Diet Heart Study

Michel de Lorgeril, MD; Patricia Salen, BSc; Jean-Louis Martin, PhD; Isabelle Monjaud, BSc; Jacques Delaye, MD; Nicole Mamelle, PhD

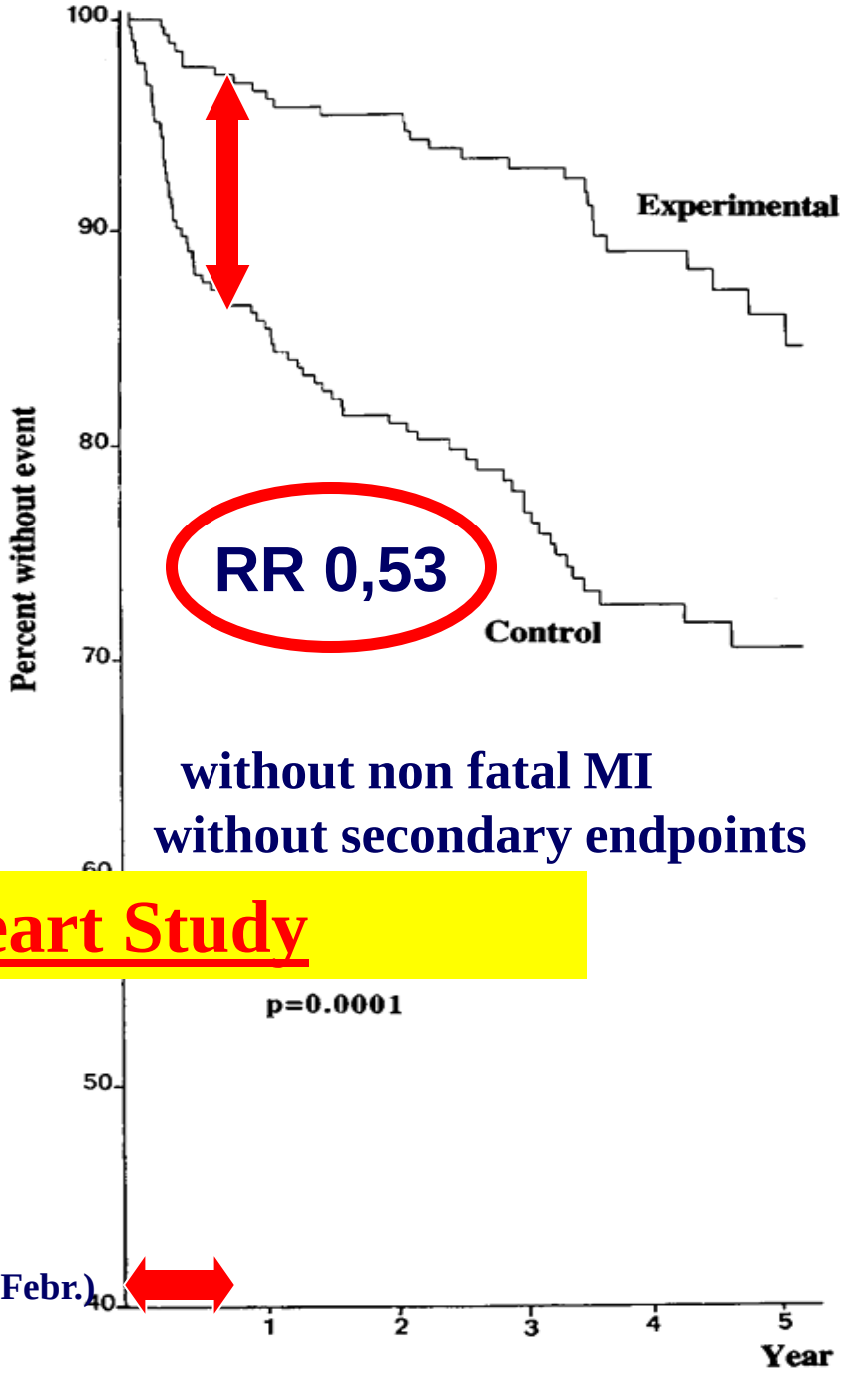
Circulation 1999; 99: 779-785



RR 0,31

Without non fatal MI,

p=0.0001



RR 0,53

without non fatal MI
without secondary endpoints

p=0.0001

Lyon Diet heart Study

De Lorgeril et al Circulation 99:779-785;1999 (16. Febr.)

AARP = (**American Association of Retired Persons**)

214 284 men and 166 012 women **= 380 296 persons**
~ 1.9 Mio person-years

Mediterranean Dietary Pattern and Prediction of All-Cause Mortality in a US Population

Results From the NIH-AARP Diet and Health Study

Panagiota N. Mitrou, PhD; Victor Kipnis, PhD; Anne C. M. Thiébaut, PhD; Jill Reedy, PhD; Amy F. Subar, PhD; Elisabet Wirfält, PhD; Andrew Flood, PhD; Traci Mouw, MPH; Albert R. Hollenbeck, PhD; Michael F. Leitzmann, MD, DrPH; Arthur Schatzkin, MD, DrPH

Arch Intern Med. 2007;167(22):2461-2468

Mediterranean Dietary Pattern (aMED) and cause-specific Mortality

Multivariate Rel Risk in 214.284 men

Score-Points

	0-3	4-5	6-9	p
			-17-23%	
• CV-Disease	1	0.95 (.86-1.04)	0.78 (.69- .87)	.001
• Cancer	1	0.86 (.80- .93)	0.83 (.76- .91)	.001
• Other causes	1	0.90 (.81-1.00)	0.77 (.70- .88)	.001

Mitrou et al Arch Intern Med. 2007;167(22):2461-2468

Mediterranean Dietary Pattern (aMED) and cause-specific Mortality

Multivariate Rel Risk in 166 012 women

	Score-points			
	0-3	4-5	6-9	p
			-19-28%	
• CV-Disease	1	0.85	0.81	.01
• Cancer	1	0.93	0.88	.04
• Other causes	1	0.82	0.72	.001

Mitrou et al Arch Intern Med. 2007;167(22):2461-2468

What's got a cardiologist to do with Influenza vaccination??

ORIGINAL ARTICLE

Influenza Vaccination and Reduction in Hospitalizations for Cardiac Disease and Stroke among the Elderly

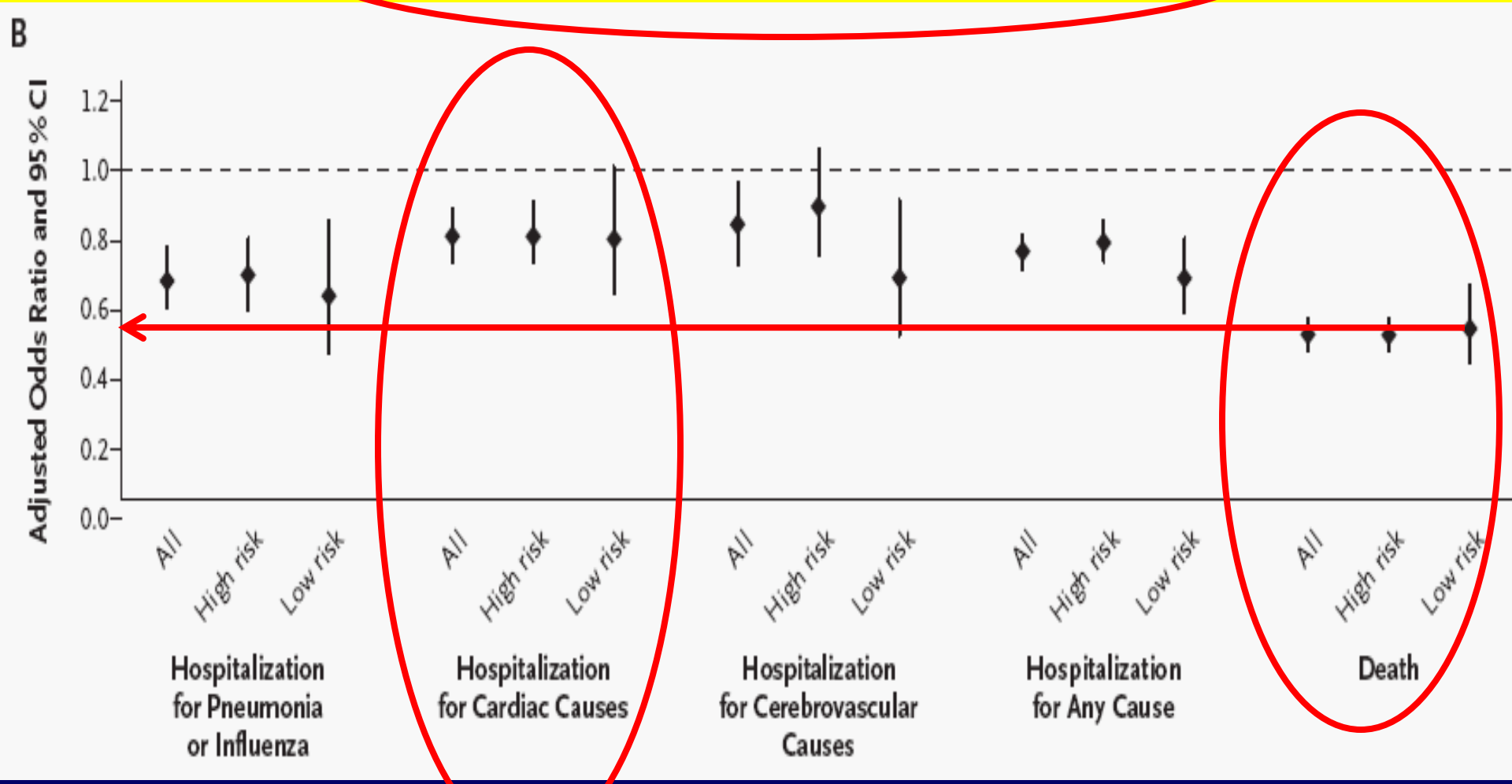
n => 286.000 >65 yrs

Kristin L. Nichol, M.D., M.P.H., M.B.A., James Nordin, M.D., M.P.H., John Mullooly, Ph.D., Richard Lask, M.D., Kelly Fillbrandt, B.S., and Marika Iwane, Ph.D.

NEJM 348:1322-32; 2003

Influenza vaccination and reduction in hospitalization

Adjusted for baseline risk



Nichol et al NEJM 348:1322-32; 2003

Review: Current Perspective

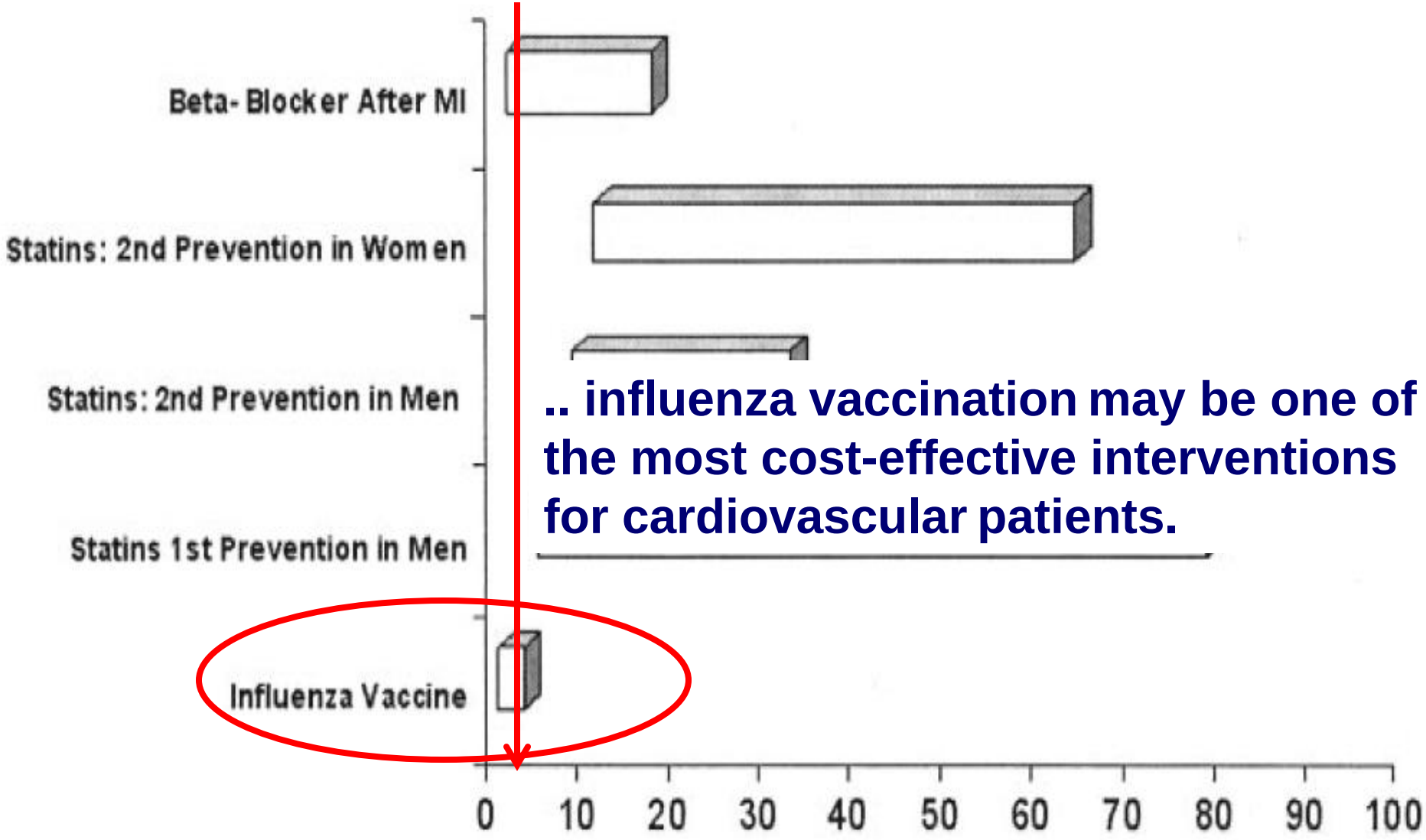
Influenza and Cardiovascular Disease

A New Opportunity for Prevention and the Need for Further Studies

Mohammad Madjid, MD; Morteza Naghavi, MD; Silvio Litovsky, MD; S. Ward Casscells, MD

Circulation 2003;108:2730 –2736

Direct costs of different Interventions per gained life year (in 1000 $US).



.. influenza vaccination may be one of the most cost-effective interventions for cardiovascular patients.

Madjid et al Circulation 2003;108:2730 –2736

Prevention :

In some instances –

it may be too late:

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Atorvastatin in Patients with Type 2 Diabetes Mellitus Undergoing Hemodialysis

CONCLUSIONS

Atorvastatin had no statistically significant effect on the composite primary end point of cardiovascular death, nonfatal myocardial infarction, and stroke in patients with diabetes receiving hemodialysis.

N Engl J Med 2005;353:238-48.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Rosuvastatin and Cardiovascular Events in Patients Undergoing Hemodialysis

CONCLUSIONS

In patients undergoing hemodialysis, the initiation of treatment with rosuvastatin lowered the LDL cholesterol level but had no significant effect on the composite primary end point of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke. (ClinicalTrials.gov number, NCT00240331.)

Ola Samuelsson, M.D., Ph.D., Sándor Sörkódi, M.D., Ph.D., D. Sci.,
Gultekin Süleymanlar, M.D., Dimitrios Tsakiris, M.D., Ph.D.,
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and Faiez Zannad, M.D., Ph.D., for the AURORA Study Group*

Fellström et al N Engl J Med 2009;360:1395-407.

Summary & take home message

- Life expectancy (LE) of elderly persons is often underestimated!

LE: 17-19/20-23yrs in a 65 yr old man/woman
8-9/9-11yrs in an 80yr old man/woman

- In the elderly patient with advanced vascular disease, preventive measures are of great benefit:
  - Smoking cessation: **More effective than anything else !!**
  - Lipid lowering with statins **Cost- effective : QALY for 18 800$**
  - Exercise training **Improves life expectancy and QoL !**
  - mediterranean diet **Small RCT- but large observational data base**
  - vaccination against influenza **Cost-effective: don‘t forget!!**
  - BP lowering (moderately) reduces stroke and all cause mortality even above age 80! **Target BP:150/80mmHg!**

It is hardly ever too late for [illegible] prevention and [illegible]

Thank you for your attention !

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