"Cardiologia Pratica: integrazione Ospedale-Territorio"

Roma 28 marzo 2009
Best Western Globus Hotel Roma

Dai fattori di rischio all'aterosclerosi: nuovi dati dallo studio JUPITER

Giuseppe Ferraiuolo

"Cardiologia Pratica: integrazione Ospedale-Territorio"

08:30 Registrazione dei partecipanti, ritiro dei materiali congressuali e del questionario di valutazione

SESSIONE I

Dall'Ipertropfia Ventricolare allo Scompenso Cardiaco

Moderatori: Giuliano Altamura – Francesco D'Agostino

09:00 **Lettura**: Analisi di modelli di gestione integrata Ospedale-territorio
Biagio Valente

09:40 Dai fattori di rischio all'aterosclerosi: nuovi dati dallo studio Jupiter
Giuseppe Ferraiuolo

10:00 Tiroide e scompenso cardiaco
Aldo Fierro

10:20 Cardiopatia ischemica e scompenso cardiaco
Fabrizio Castelli

10:40 Diabete mellito e scompenso cardiaco
Concetta Suraci

11:00 Discussione

11:20 Coffee Break

SESSIONE II

Monitoraggio dei pazienti sottoposti a PTCA

Moderatori: Paolo Loschiavo – Fiorella Basta

11:40 Indicazioni all'angioplastica coronarica
Pasquale Silvestri

12:10 Ptca: lo stato dell'arte e linea di confine con le indicazioni cardiochirurgiche
Stefano Rigattieri

12:40 La doppia antiAggregazione: quali problematiche?
Cristian Di Russo

13:10 Gestione clinco-strumentale del follw up nei pazienti sottoposti ad angioplastica
Silvio Fedele

13:40 Discussione

14:00 Lunch

SESSIONE III

La fibrillazione atriale

Moderatori: Antonello Castro – Claudio Ippoliti

15:00 Modello di gestione integrata Ospedale-Territorio (Dalla gestione territoriale all'ablazione della FA attraverso la telemedicina)
Federico Turreni

15:30 La fibrillazione atriale: contesti clinici e trattamento
Luca D'Antonio

16:00 Fibrillazione atriale: parametri eco di elevato rischio tromboembolico
Paolo Trambaiolo

17:00 Questionario finale
Giuseppe Ferraiuolo

17:30 Termine dei lavori

La parola serendipità è un neologismo coniato nel 1754 dallo scrittore Horace Walpole (esattamente il 28 gennaio del 1754, Walpole lo usò in una lettera scritta a Horace Mann, un suo amico inglese che viveva a Firenze) ed è la traduzione letterale del termine inglese è *serendipity*.

Serendipità ha origine dalla parola Serendip, l'antico nome dell'isola di Ceylon (Sri Lanka). La storia da cui si ispirò Walpole per coniare il termine era una fiaba persiana e si intitolava "*Tre principi di Serendippo*". La fiaba narra di tre principi che nel loro cammino trovano alcuni indizi che li salvano in più occasioni. Le loro scoperte sono ovviamente casuali, ma il loro grande merito consiste nel loro notevole spirito di osservazione.

Dal punto di vista filosofico la serendipità è quella situazione in cui si trova qualcosa di importante mentre se ne sta cercando un'altra.

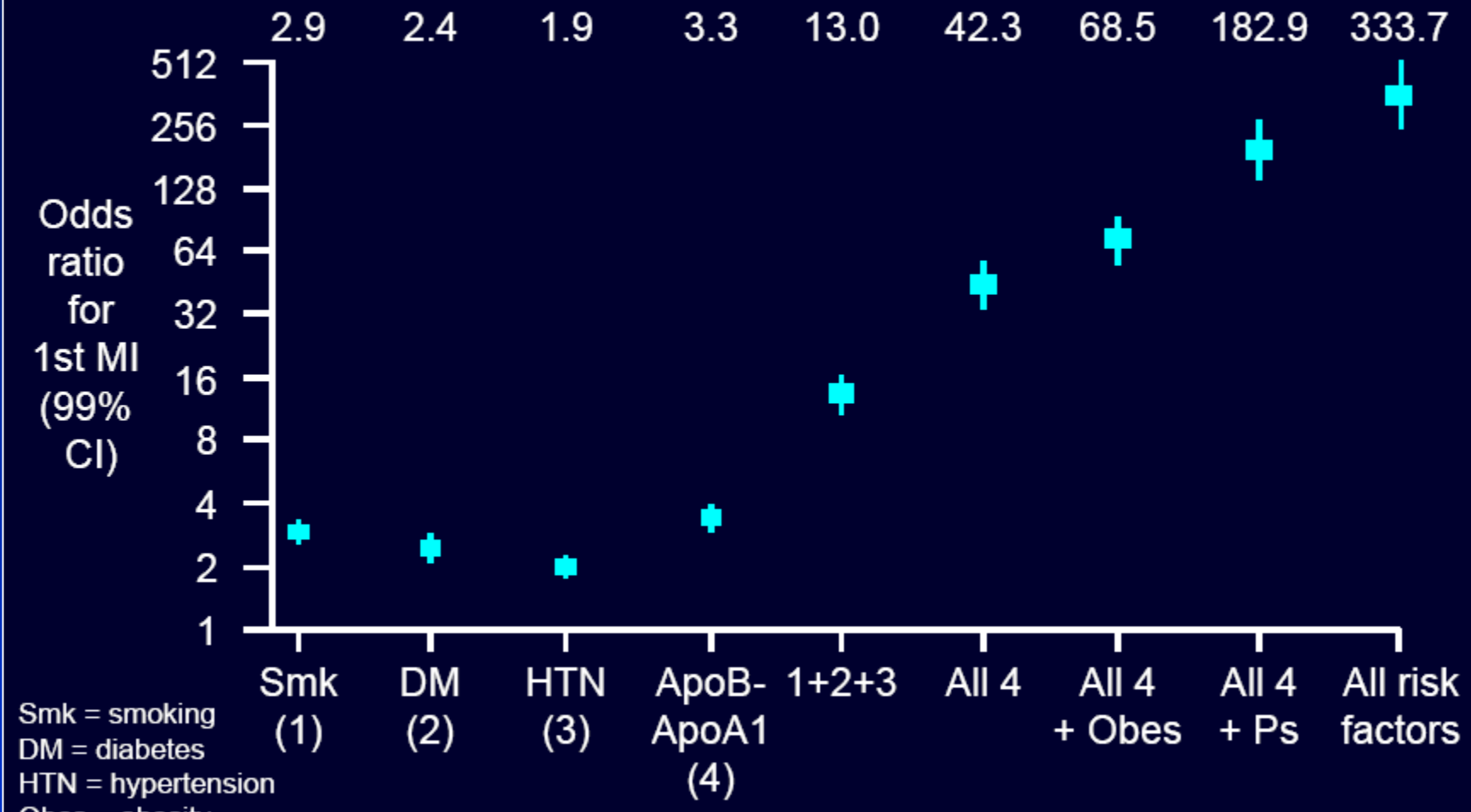
La serendipità è molto importante nella ricerca scientifica, dove molte grandi scoperte sono state fatte per serendipità.

Scoperte ed invenzioni:

- L'America da parte di Cristoforo Colombo che cercava le Indie.
- La dinamite da parte di Alfred Nobel
- La penicillina da parte di Alexander Fleming
- Gli effetti psichedelici dell'LSD (dietilamide-25 dell'acido lisergico) da parte di Albert Hofmann nel 1938: gliene era caduta per caso una goccia su una mano.
- Il ruolo del pancreas nel diabete mellito da parte di Joseph von Mering ed Oscar Minkowsky che in realtà cercavano di individuare il compito dell'organo sulla digestione.
- Le radiazione cosmica di fondo a microonde dell'universo da parte di Arno Penzias e Robert Woodrow Wilson
- I riflessi condizionati dei cani di Pavlov che stava conducendo ricerche sulla salivazione di questi animali
- La struttura del benzene da parte di Kekulé che scoprì la conformazione della molecola sognando un serpente che si morde la coda.La molecola in questione ha una struttura che la fa assomigliare ad una forma circolare (infatti, è un esagono regolare).
- Il cellophane inventato nel 1908 da Jacques Edwin Brandenberger, un ingegnere chimico svizzero.
- La Rosa DALLAS
- Il Prozac (fluoxetina ossalato), altro esempio di serendipità. Il farmacologo David Wong nel giugno 1974 annunciò pubblicamente che la fluoxetina è un inibitore del reuptake della serotonina.
- Il Teflon (PTFE, politetrafluoroetilene) nel 1938 da parte del chimico della Du Pont R.J. Plunkett che stava usando il tetrafluoroetilene come intermedio per la sintesi di nuovi refrigeranti.
- La colla dei Post-it, il cui inventore in realtà stava cercando di realizzare un collante estremamente forte ottenendo, invece, un collante debole, che non macchiava e che si poteva attaccare e staccare con facilità.
- ……
- Il Viagra (citrato di sildenafil), scoperto per caso dalla compagnia farmaceutica Pfizer mentre cercava un farmaco per curare l'angina pectoris.

da: Wikipedia; voce: Serendipità

INTERHEART: Impact of multiple risk factors on CV risk



Smk = smoking
DM = diabetes
HTN = hypertension
Obes = obesity
Ps = psychosocial factors
Note: odds ratio plotted on a doubling scale

Yusuf S et al. *Lancet*. 2004;364:937-52.

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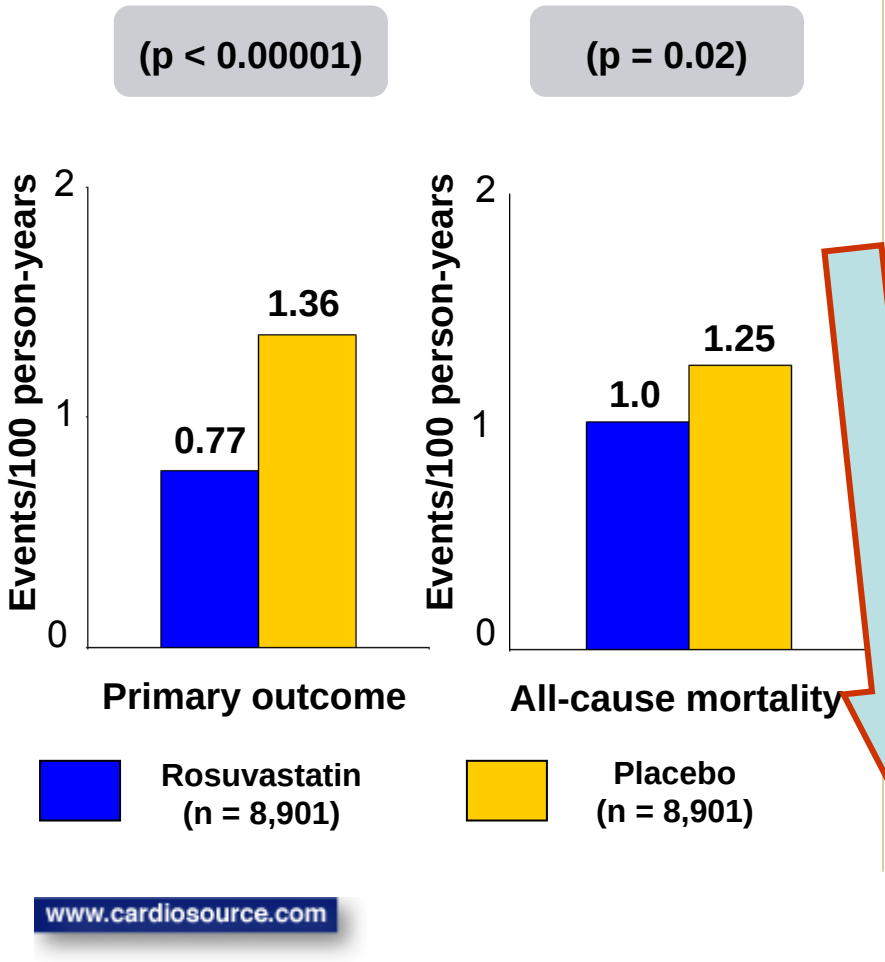
Trial design: Apparently healthy patients with LDL cholesterol <130 mg/dl and hs-CRP ≥2 mg/L were randomized to rosuvastatin 20 mg daily or placebo. Clinical outcomes were compared at a median of 1.9 years.



Results

- Rosuvastatin associated with a significant ↓ in the primary outcome of MI, stroke, unstable angina, revascularization, or cardiovascular death (HR 0.56, 95% CI 0.46-0.69, p < 0.00001)
- All-cause mortality ↓ with rosuvastatin (p = 0.02)
- Serious adverse effects were similar (p = 0.60)

Conclusions

- Rosuvastatin was associated with a significant reduction in major cardiovascular events, including death, in patients with LDL <130 mg/dl, but high hs-CRP (≥2.0 mg/L)
- May require revision of current guidelines

Ridker PM, et al. NEJM 2008;359:2195-207

Presented by Dr. Paul Ridker at AHA 2008

The NEW ENGLAND JOURNAL of MEDICINE

Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein

Ridker et al., for the JUPITER Study Group; N Engl J Med, 2008; 359:2195-207

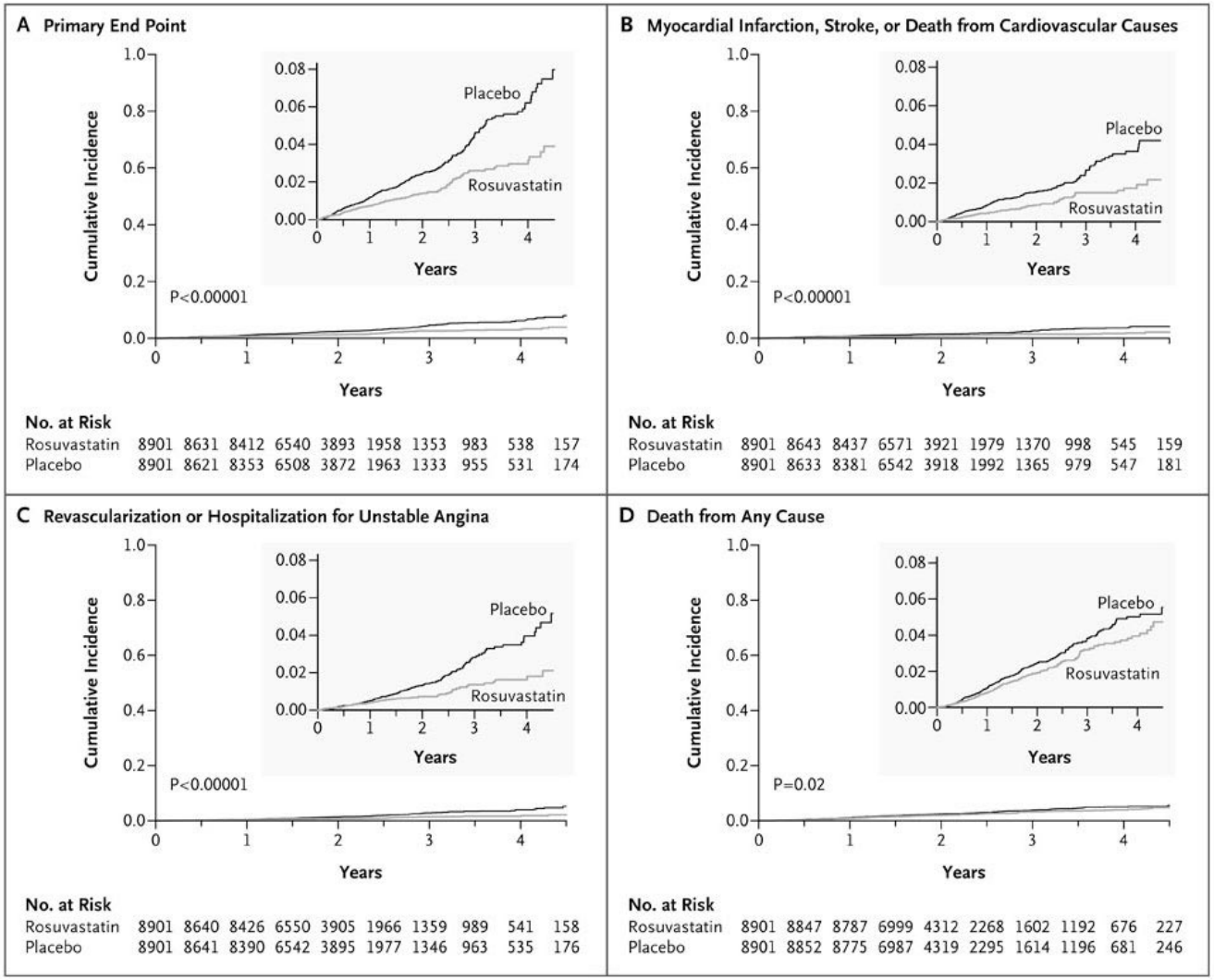


Figure 1. Cumulative Incidence of Cardiovascular Events According to Study Group.

Panel A shows the cumulative incidence of the primary end point (nonfatal myocardial infarction, nonfatal stroke, arterial revascularization, hospitalization for unstable angina, or confirmed death from cardiovascular causes). The hazard ratio for rosuvastatin, as compared with placebo, was 0.56 (95% confidence interval [CI], 0.46 to 0.69; P<0.00001).

Panel B shows the cumulative incidence of nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes, for which the hazard ratio in the rosuvastatin group was 0.53 (95% CI, 0.40 to 0.69; P<0.00001).

Panel C shows the cumulative incidence of arterial revascularization or hospitalization for unstable angina, for which the hazard ratio in the rosuvastatin group was 0.53 (95% CI, 0.40 to 0.70; P<0.00001).

Panel D shows the cumulative incidence of death from any cause, for which the hazard ratio in the rosuvastatin group was 0.80 (95% CI, 0.67 to 0.97; P=0.02). In each panel, the inset shows the same data on an enlarged y axis and on a condensed x axis.

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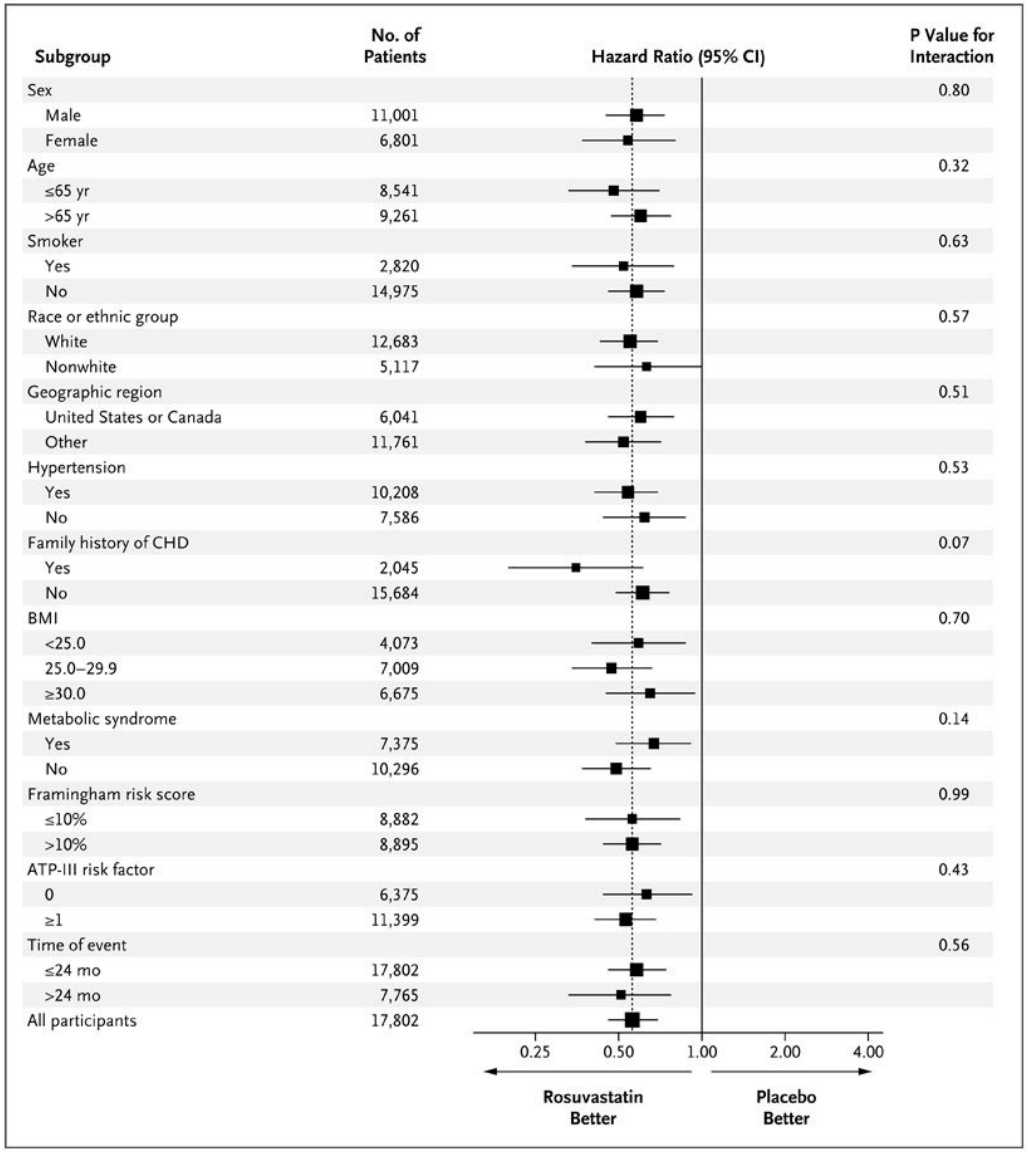
Figure 2. Effects of Rosuvastatin on the Primary End Point, According to Baseline Characteristics.



The primary end point was the combination of nonfatal myocardial infarction, nonfatal stroke, arterial revascularization, hospitalization for unstable angina, or confirmed death from cardiovascular causes. The relative hazard ratios for rosuvastatin as compared with placebo are shown, with the size of each black square proportionate to the number of participants who had an occurrence of the primary end point in the subgroup; the horizontal lines indicate 95% confidence intervals. The dashed vertical line indicates the overall relative risk reduction for the complete trial cohort. Also shown are the P values for the test of an interaction between the primary end point and the categories within each subgroup. For the ordinal variables, interaction tests considered a trend across the subgroup categories with integer scores applied to these categories. Data were missing for some participants in some subgroups. The body-mass index (BMI) is the weight in kilograms divided by the square of the height in meters. CHD denotes coronary heart disease. The metabolic syndrome was defined according to 2005 consensus criteria of the American Heart Association and the National Heart, Lung, and Blood Institute.21 ATP-III risk factors refer to major risk factors, other than increased age, according to the Adult Treatment Panel III of the National Cholesterol Education Program. Race or ethnic group was self-reported.

JUPITER

Why Consider Statins for Low LDL, high hsCRP Patients?

In 2001, in an hypothesis generating analysis of apparently healthy individuals in the AFCAPS / TexCAPS trial*, we observed that those with low levels of both LDL and hsCRP had extremely low vascular event rates and that statin therapy did not reduce events in this subgroup (N=1,448, HR 1.1, 95% CI 0.56-2.08). Thus, a trial of statin therapy in patients with low cholesterol and low hsCRP would not only be infeasible in terms of power and sample size, but would be highly unlikely to show clinical benefit.

In contrast, we also observed within AFCAPS/TexCAPS that among those with low LDL but high hsCRP, vascular event rates were just as high as rates among those with overt hyperlipidemia, and that statin therapy significantly reduced events in this subgroup (N=1,428, HR 0.6, 95% CI 0.34-0.98).

Ridker et al N Engl J Med 2001;344:1959-65

JUPITER
Primary Objectives

Ridker et al NEJM 2008

Justification for the Use of statins in Prevention: an Intervention Trial Evaluating Rosuvastatin

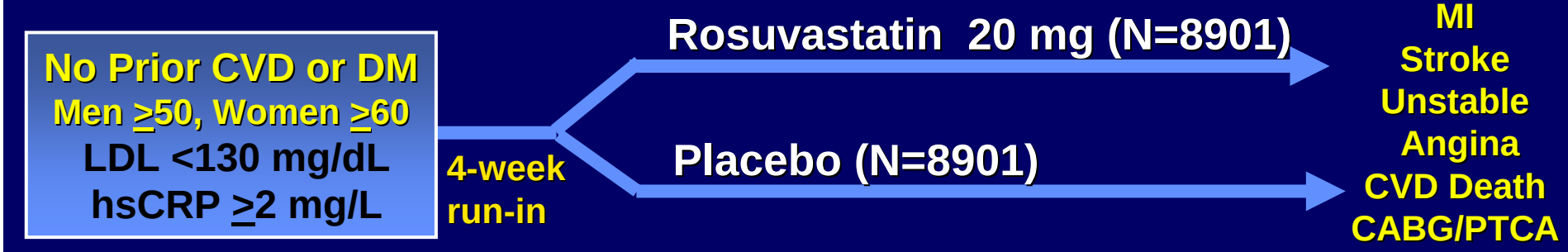
To investigate whether rosuvastatin 20 mg compared to placebo would decrease the rate of first major cardiovascular events among apparently healthy men and women with LDL < 130 mg/dL (3.36 mmol/L) who are nonetheless at increased vascular risk on the basis of an enhanced inflammatory response, as determined by hsCRP ≥ 2 mg/L.

To enroll large numbers of women and individuals of Black or Hispanic ethnicity, groups for whom little data on primary prevention with statin therapy exists.

JUPITER
Trial Design

JUPITER

Multi-National Randomized Double Blind Placebo Controlled Trial of Rosuvastatin in the Prevention of Cardiovascular Events Among Individuals With Low LDL and Elevated hsCRP



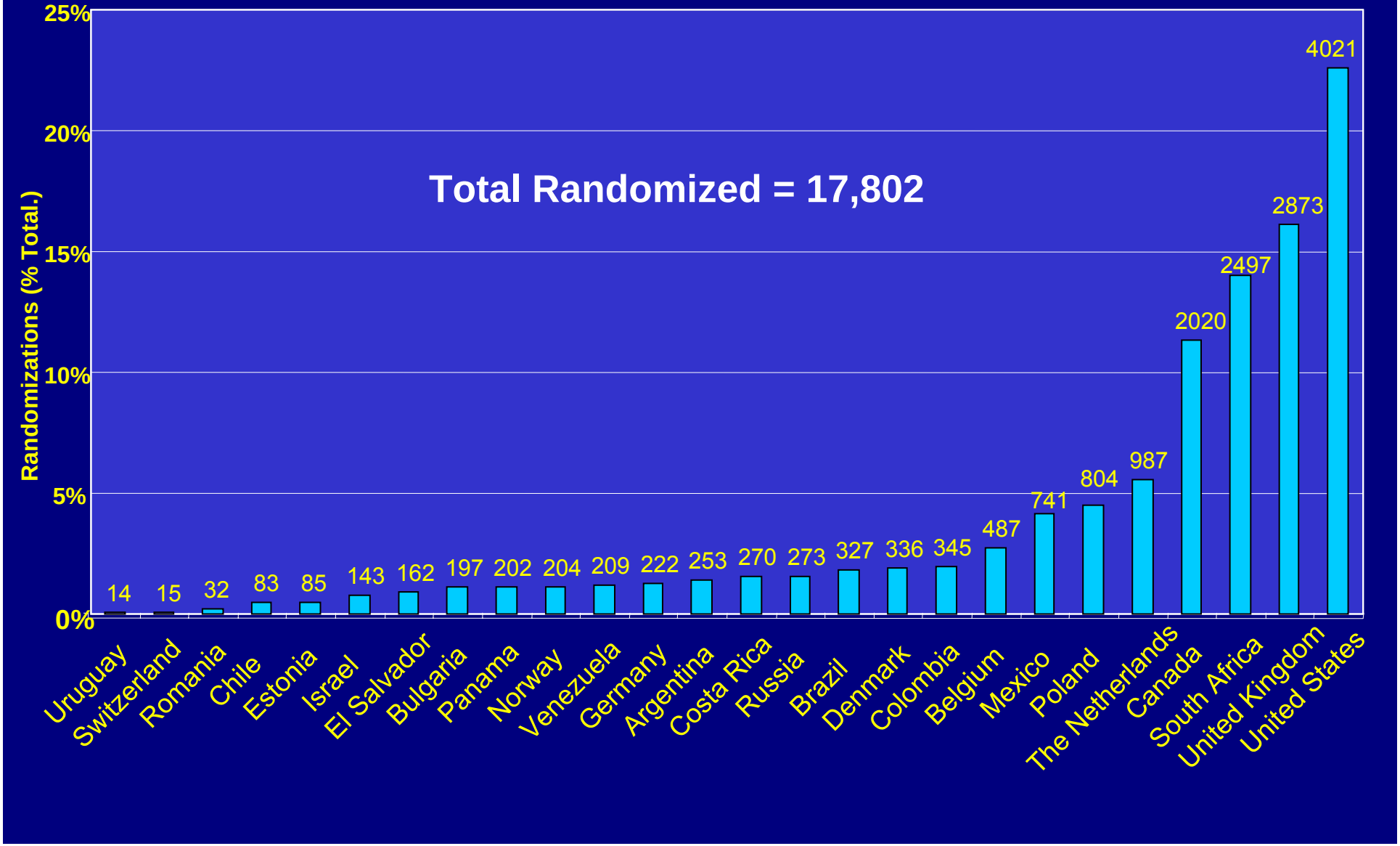
Argentina, Belgium, Brazil, Bulgaria, Canada, Chile, Colombia, Costa Rica, Denmark, El Salvador, Estonia, Germany, Israel, Mexico, Netherlands, Norway, Panama, Poland, Romania, Russia, South Africa, Switzerland, United Kingdom, Uruguay, United States, Venezuela

Ridker et al, Circulation 2003;108:2292-2297.

JUPITER

17,802 Patients, 1,315 Sites, 26 Countries

Ridker et al NEJM 2008



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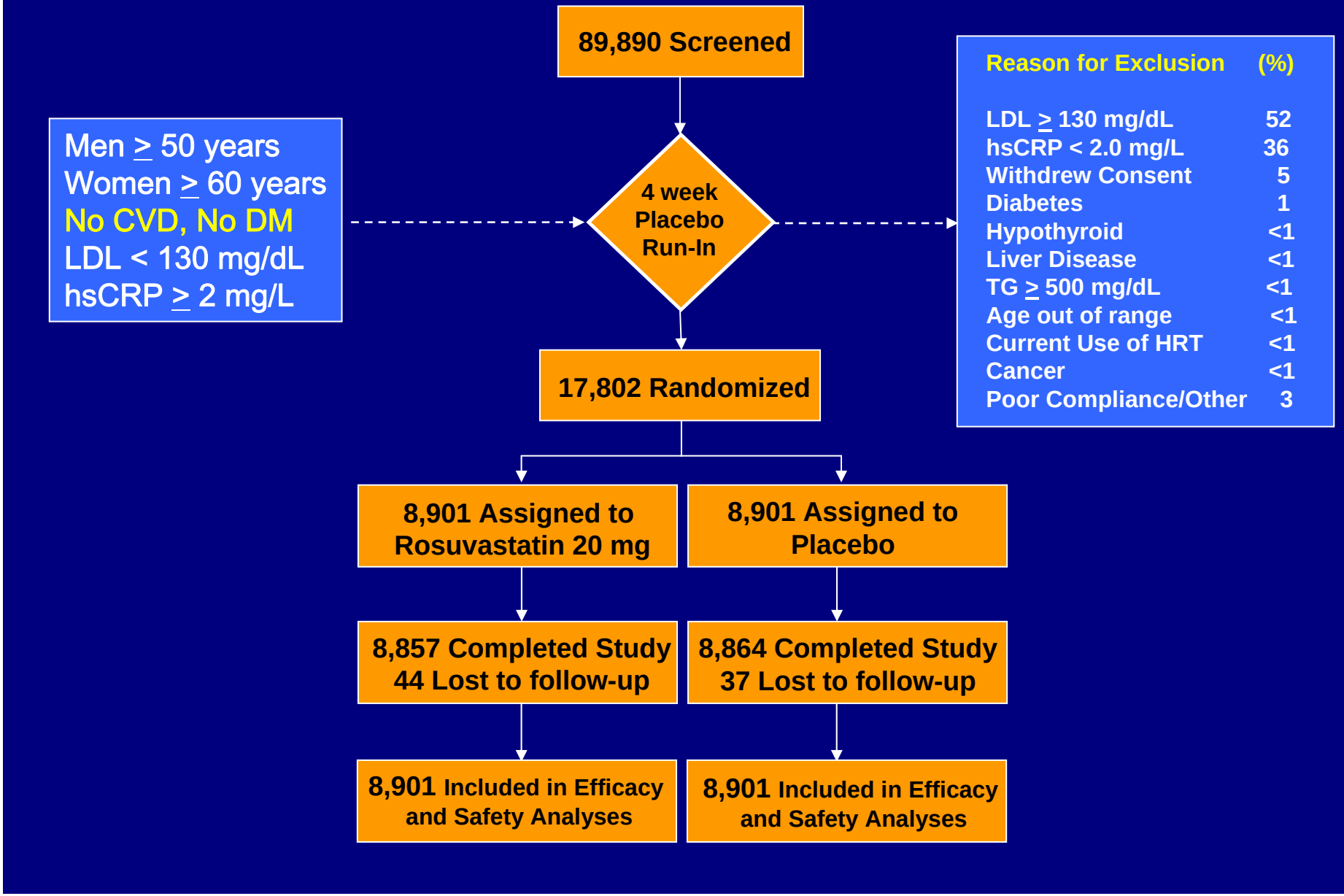
Inclusion and Exclusion Criteria, Study Flow

Ridker et al NEJM 2008



JUPITER
Baseline Clinical Characteristics

Ridker et al NEJM 2008

	Rosuvastatin (N = 8901)	Placebo (n = 8901)
Age, years (IQR)	66.0 (60.0-71.0)	66.0 (60.0-71.0)
Female, N (%)	3,426 (38.5)	3,375 (37.9)
Ethnicity, N (%)		
Caucasian	6,358 (71.4)	6,325 (71.1)
Black	1,100 (12.4)	1,124 (12.6)
Hispanic	1,121 (12.6)	1,140 (12.8)
Blood pressure, mm (IQR)		
Systolic	134 (124-145)	134 (124-145)
Diastolic	80 (75-87)	80 (75-87)
Smoker, N (%)	1,400 (15.7)	1,420 (16.0)
Family History, N (%)	997 (11.2)	1,048 (11.8)
Metabolic Syndrome, N (%)	3,652 (41.0)	3,723 (41.8)
Aspirin Use, N (%)	1,481 (16.6)	1,477 (16.6)

All values are median (interquartile range) or N (%)

JUPITER

Ridker et al NEJM 2008

Baseline Blood Levels (median, interquartile range)

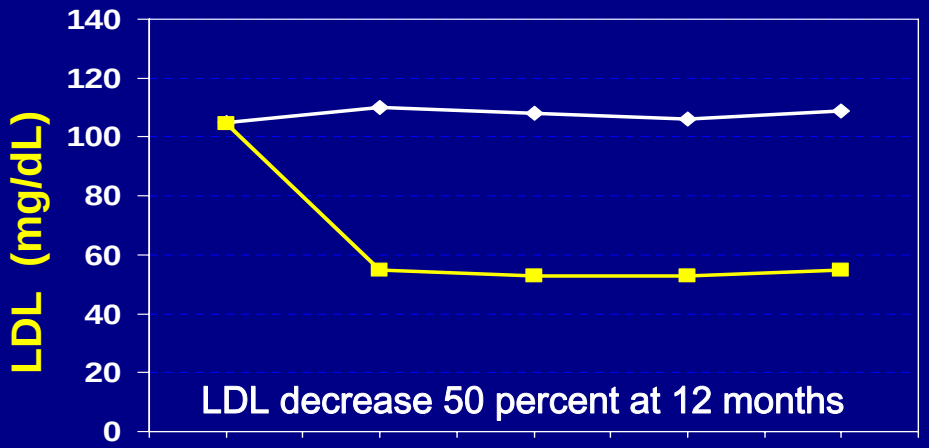
	Rosuvastatin (N = 8901)		Placebo (n = 8901)	
hsCRP, mg/L	4.2	(2.8 - 7.1)	4.3	(2.8 - 7.2)
LDL, mg/dL	108	(94 - 119)	108	(94 - 119)
HDL, mg/dL	49	(40 – 60)	49	(40 – 60)
Triglycerides, mg/L	118	(85 - 169)	118	(86 - 169)
Total Cholesterol, mg/dL	186	(168 - 200)	185	(169 - 199)
Glucose, mg/dL	94	(87 – 102)	94	(88 – 102)
HbA1c, %	5.7	(5.4 – 5.9)	5.7	(5.5 – 5.9)

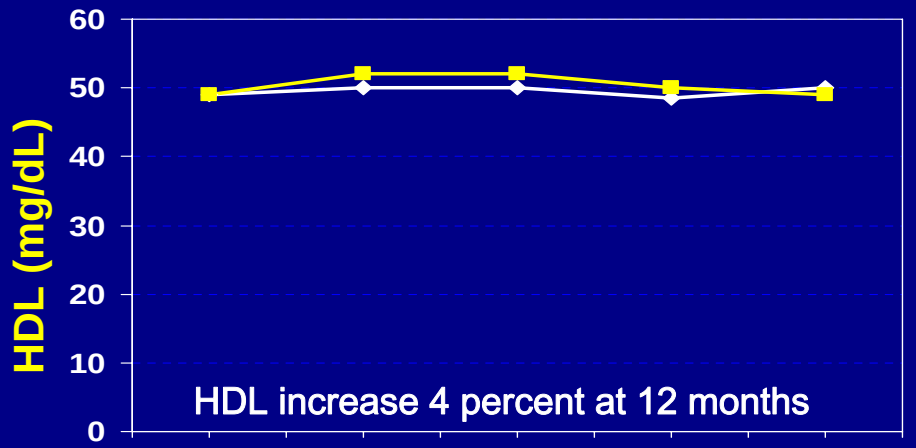
All values are median (interquartile range). [Mean LDL = 104 mg/dL]

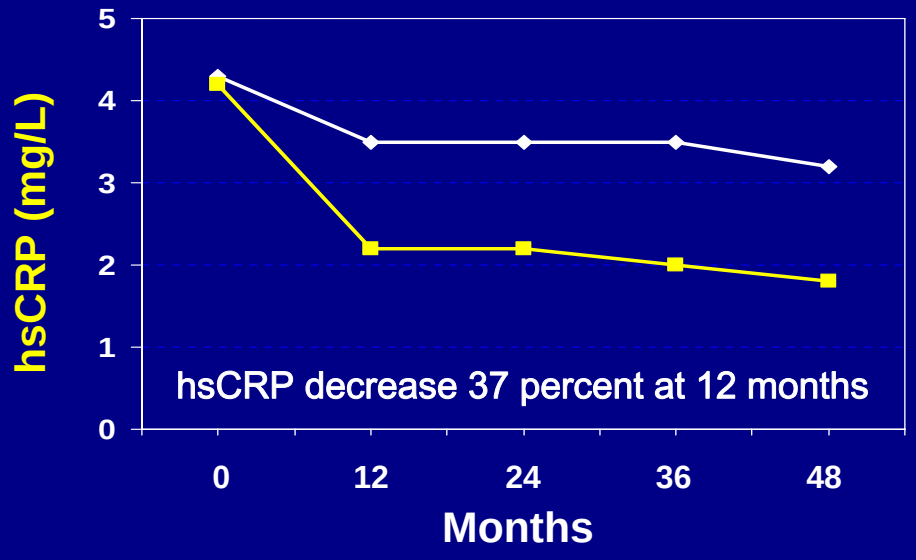
JUPITER

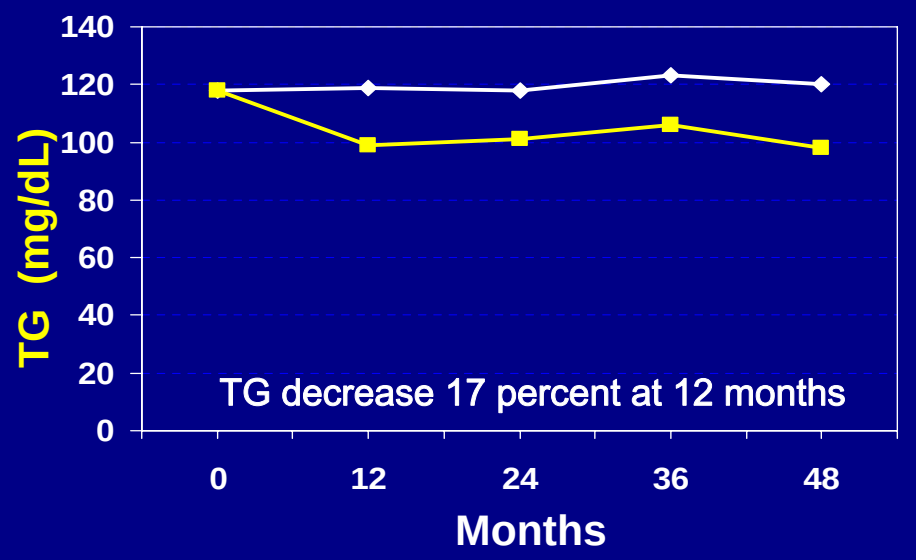
Ridker et al NEJM 2008

Effects of rosuvastatin 20 mg on LDL, HDL, TG, and hsCRP





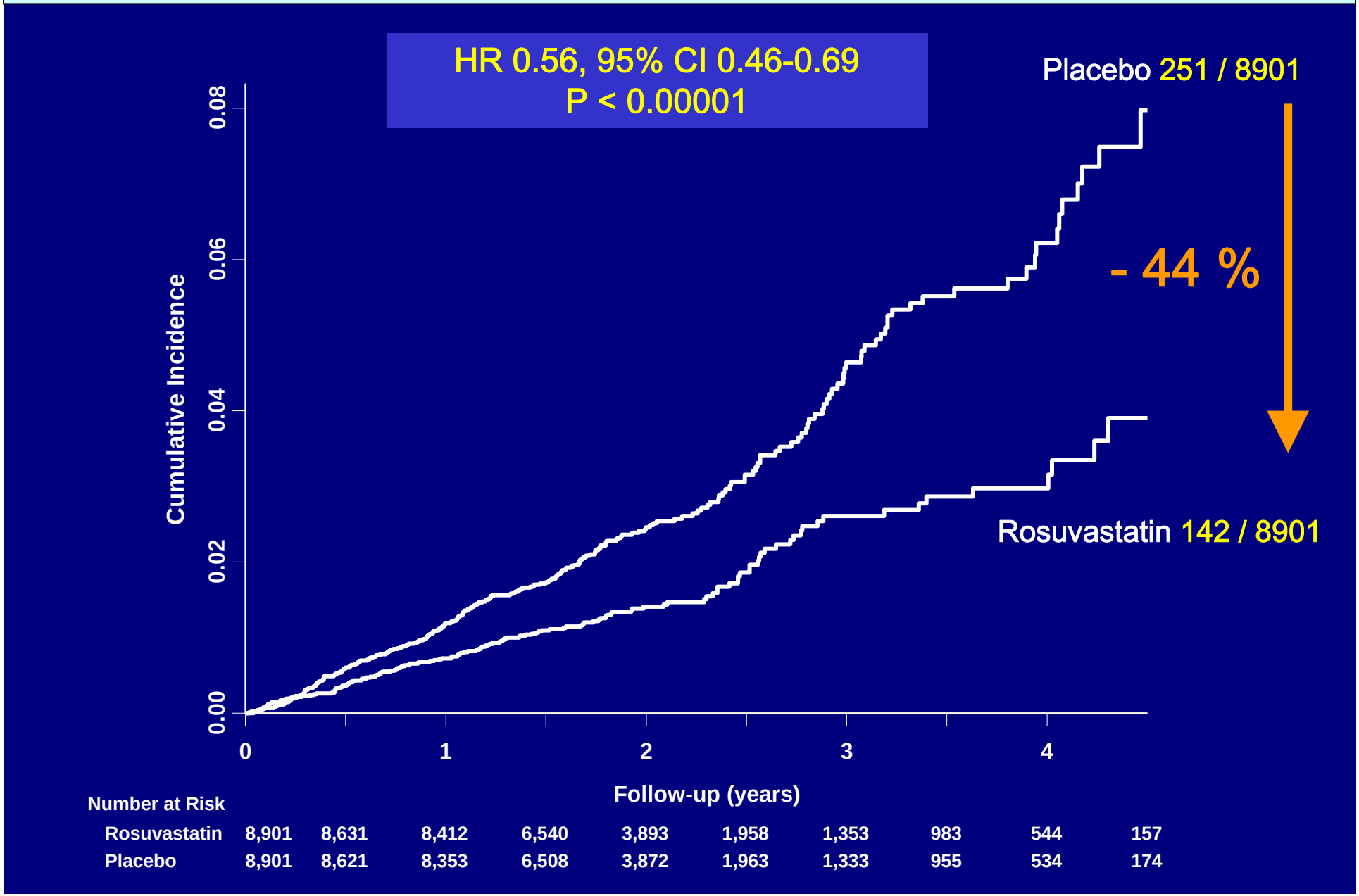




JUPITER

Ridker et al NEJM 2008

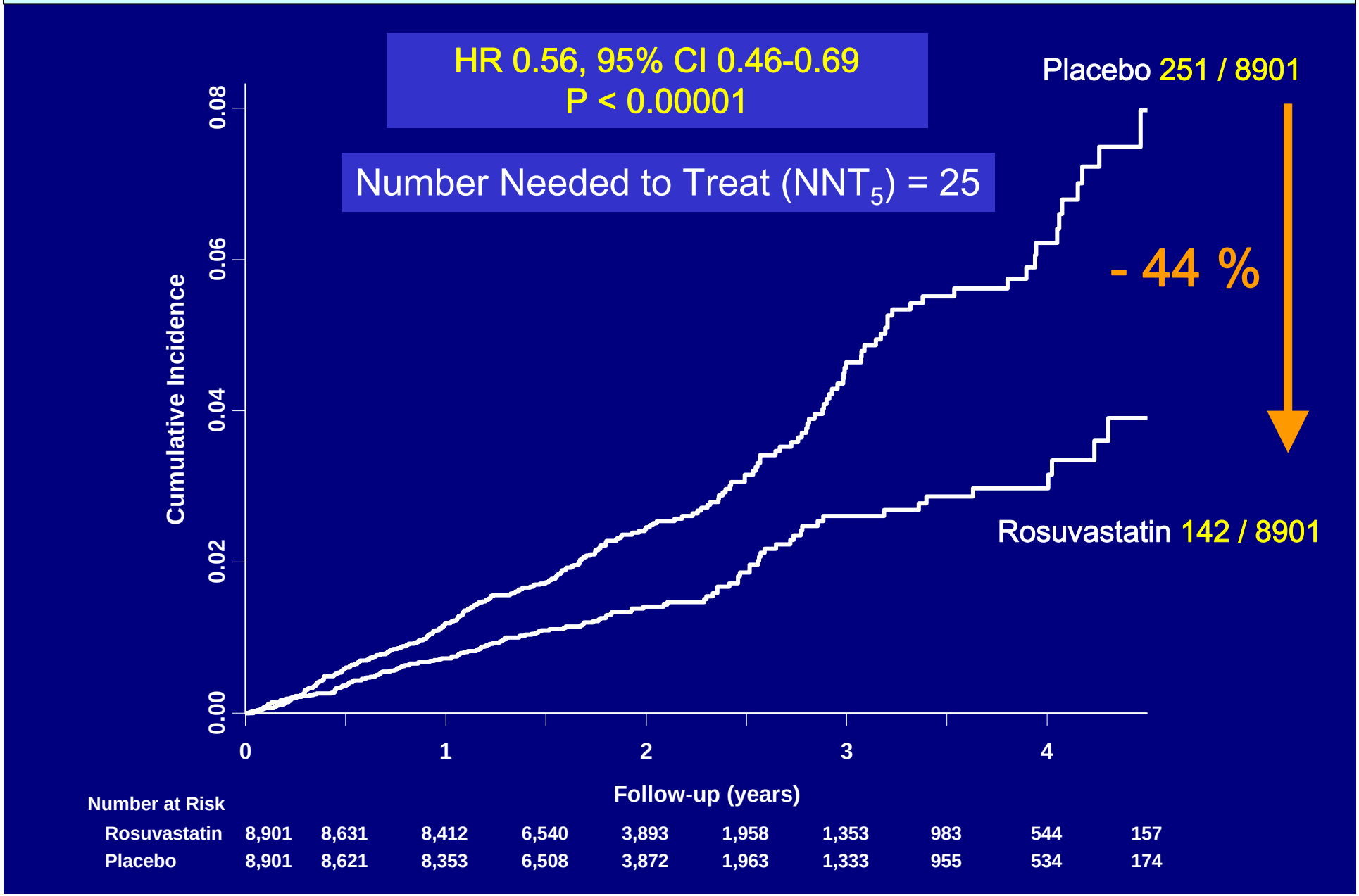
Primary Trial Endpoint：MI, Stroke, UA/Revascularization, CV Death



JUPITER

Ridker et al NEJM 2008

Primary Trial Endpoint：MI, Stroke, UA/Revascularization, CV Death

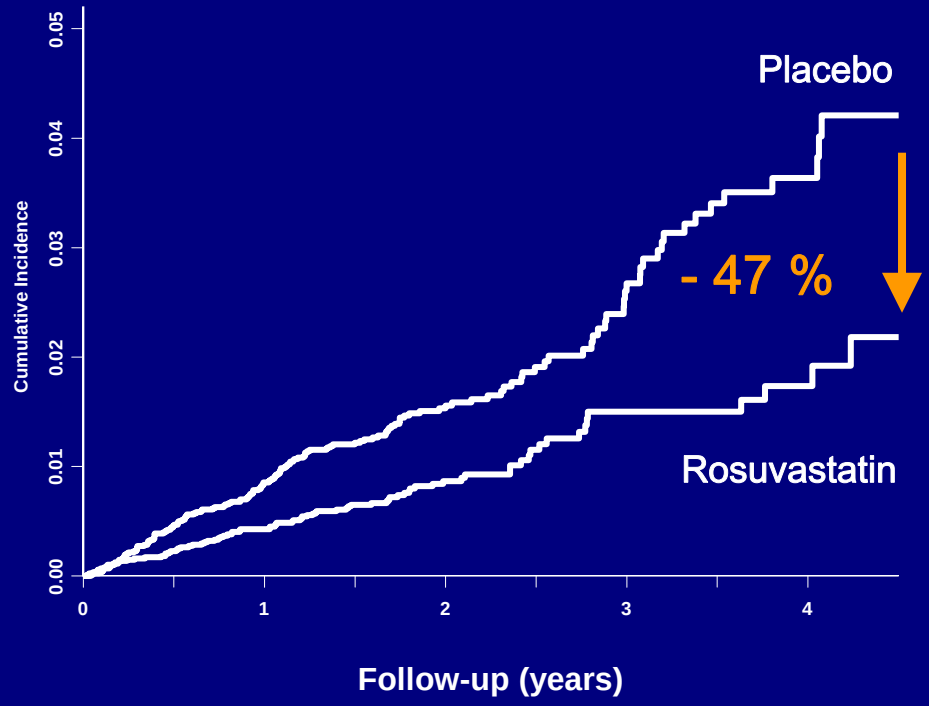


JUPITER
Grouped Components of the Primary Endpoint

Ridker et al NEJM 2008

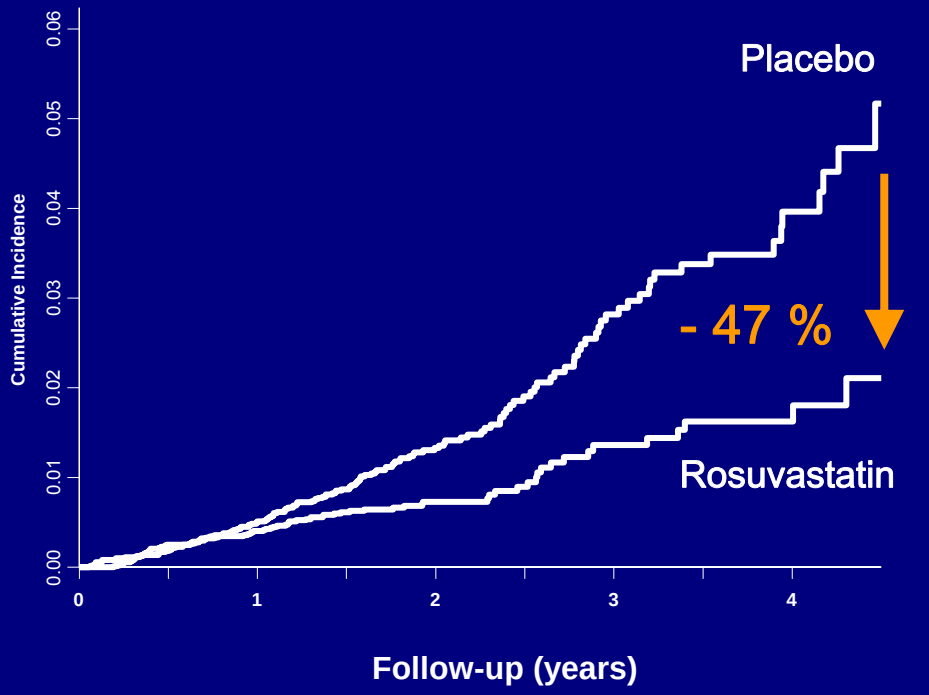
Myocardial Infarction, Stroke, or Cardiovascular Death

HR 0.53, CI 0.40-0.69
P < 0.00001



Arterial Revascularization or Hospitalization for Unstable Angina

HR 0.53, CI 0.40-0.70
P < 0.00001



JUPITER
Individual Components of the Primary Endpoint

Ridker et al NEJM 2008

Endpoint	Rosuvastatin	Placebo	HR	95%CI	P
Primary Endpoint*	142	251	0.56	0.46-0.69	<0.00001
Non-fatal MI	22	62	0.35	0.22-0.58	<0.00001
Any MI	31	68	0.46	0.30-0.70	<0.0002
Non-fatal Stroke	30	58	0.52	0.33-0.80	0.003
Any Stroke	33	64	0.52	0.34-0.79	0.002
Revascularization or Unstable Angina	76	143	0.53	0.40-0.70	<0.00001
MI, Stroke, CV Death	83	157	0.53	0.40-0.69	<0.00001

*Nonfatal MI, nonfatal stroke, revascularization, unstable angina, CV death

JUPITER

Adverse Events and Measured Safety Parameters

Ridker et al NEJM 2008

Event	Rosuvastatin	Placebo	P
Any SAE	1,352 (15.2)	1,337 (15.5)	0.60
Muscle weakness	1,421 (16.0)	1,375 (15.4)	0.34
Myopathy	10 (0.1)	9 (0.1)	0.82
Rhabdomyolysis	1 (0.01)*	0 (0.0)	--
Incident Cancer	298 (3.4)	314 (3.5)	0.51
Cancer Deaths	35 (0.4)	58 (0.7)	0.02
Hemorrhagic stroke	6 (0.1)	9 (0.1)	0.44
GFR (ml/min/1.73m^2 at 12 mth)	66.8 (59.1-76.5)	66.6 (58.8-76.2)	0.02
ALT > 3xULN	23 (0.3)	17 (0.2)	0.34
Fasting glucose (24 mth)	98 (91-107)	98 (90-106)	0.12
HbA1c (% at 24 mth)	5.9 (5.7-6.1)	5.8 (5.6-6.1)	0.01
Glucosuria (12 mth)	36 (0.5)	32 (0.4)	0.64
Incident Diabetes**	270 (3.0)	216 (2.4)	0.01

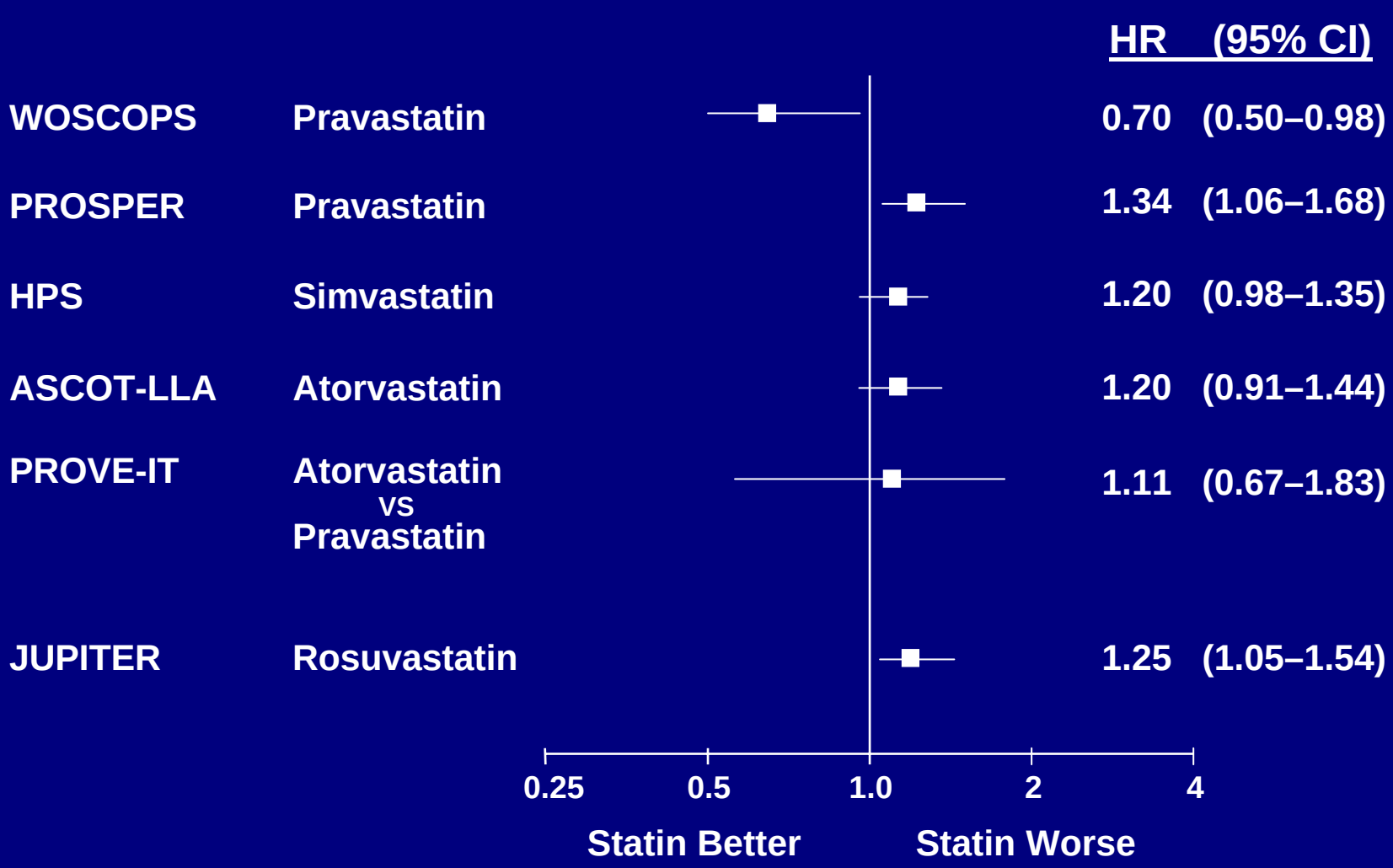
*Occurred after trial completion, trauma induced.

**Physician reported

All values are median (interquartile range) or N (%)

JUPITER
Statins and the Development of Diabetes

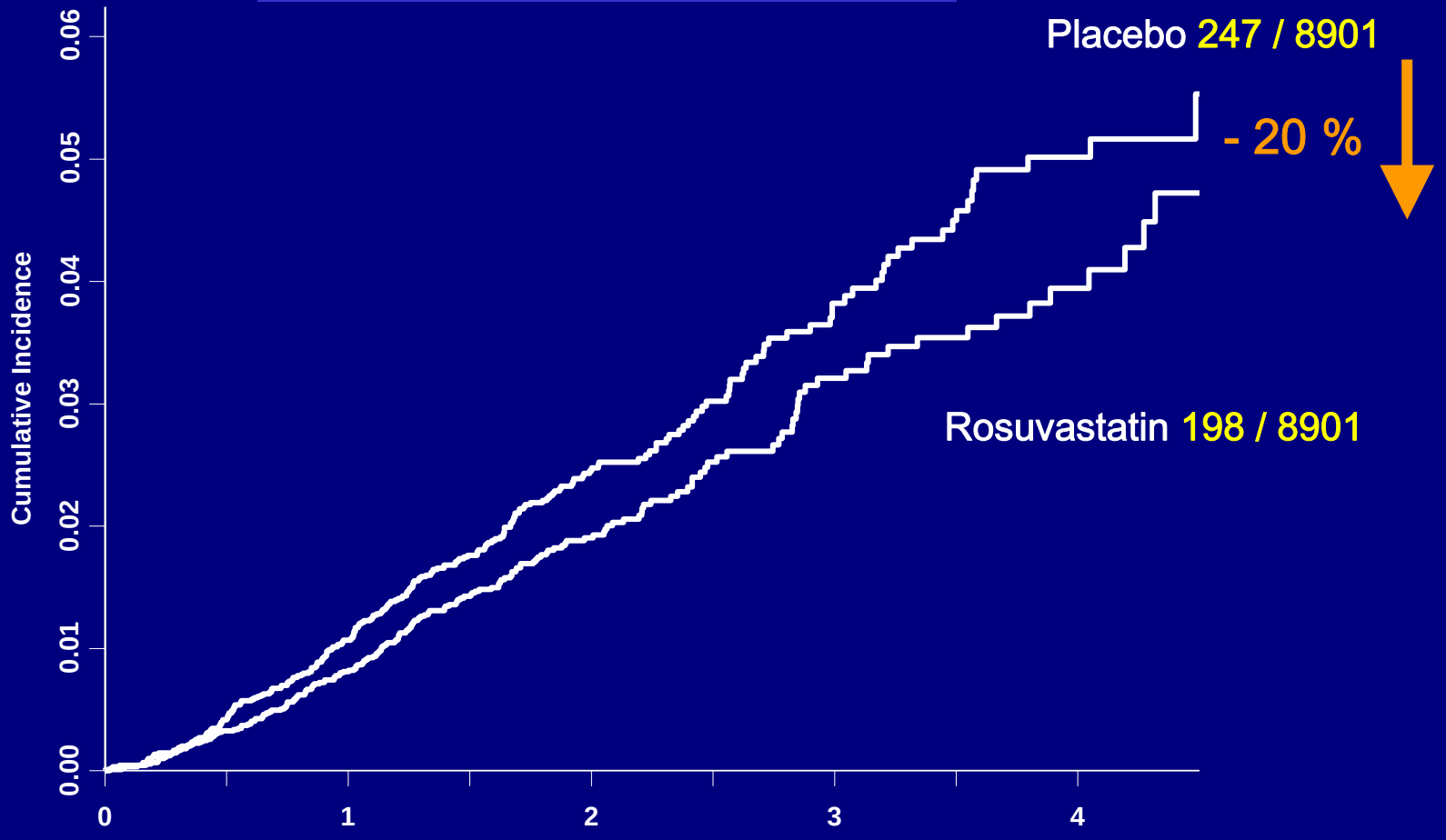
Ridker et al NEJM 2008



JUPITER
Secondary Endpoint – All Cause Mortality

Ridker et al NEJM 2008

HR 0.80, 95%CI 0.67-0.97
P= 0.02



Number at Risk										
Rosuvastatin	8,901	8,847	8,787	6,999	4,312	2,268	1,602	1,192	683	227
Placebo	8,901	8,852	8,775	6,987	4,319	2,295	1,614	1,196	684	246

JUPITER
Conclusions – Efficacy I

Ridker et al NEJM 2008

Among apparently healthy men and women with elevated hsCRP but low LDL, rosuvastatin reduced by 47 percent incident myocardial infarction, stroke, and cardiovascular death.

Despite evaluating a population with lipid levels widely considered to be “optimal” in almost all current prevention algorithms, the relative benefit observed in JUPITER was greater than in almost all prior statin trials.

In this trial of low LDL/high hsCRP individuals who do not currently qualify for statin therapy, rosuvastatin significantly reduced all-cause mortality by 20 percent.

JUPITER
Conclusions – Efficacy II

Ridker et al NEJM 2008

Benefits of rosuvastatin were consistent in all sub-groups evaluated regardless of age, sex, ethnicity, or other baseline clinical characteristic, including those with elevated hsCRP and no other major risk factor.

Rates of hospitalization and revascularization were reduced by 47 percent within a two-year period suggesting that the screening and treatment strategy tested in JUPITER is likely to be cost-effective, benefiting both patients and payers.

The Number Needed to Treat in JUPITER was 25 for the primary endpoint, a value if anything smaller than that associated with treating hyperlipidemia in primary prevention.

JUPITER
Conclusions - Safety

Ridker et al NEJM 2008

With regard to safety , the JUPITER results

- show no increase in serious adverse events among those allocated to rosuvastatin 20 mg as compared to placebo in a setting where half of the treated patients achieved levels of LDL< 55 mg/dL (and 25 percent had LDL < 44 mg/dL).
- show no increase in myopathy, cancer, hepatic disorders, renal disorders, or hemorrhagic stroke with treatment duration of up to 5 years
- show no increase in systematically monitored glucose or glucosuria during follow-up, but small increases in HbA1c and physician reported diabetes similar to that seen in other major statin trials

JUPITER

Implications for Primary Prevention

Ridker et al NEJM 2008

A simple evidence based approach to statin therapy for primary prevention.

Among men and women age 50 or over :

If diabetic, treat
If LDLC > 160 mg/dL, treat
If hsCRP > 2 mg/L, treat

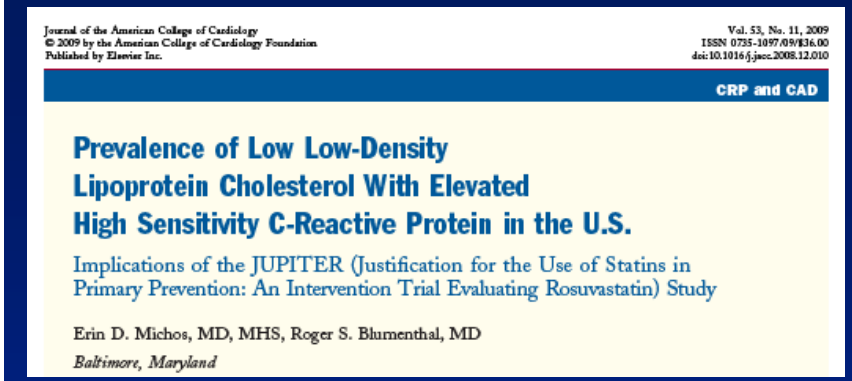
JUPITER
Public Health Implications

Ridker et al NEJM 2008

Application of the simple screening and treatment strategy tested in the JUPITER trial over a five-year period could conservatively prevent more than 250,000 heart attacks, strokes, revascularization procedures, and cardiovascular deaths in the United States alone.

We thank the 17,802 patients and the >1,000 investigators worldwide for their personal time, effort, and commitment to the JUPITER trial.

www.brighamandwomens.org/jupitertrial



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CRP and CAD

Prevalence of Low Low-Density Lipoprotein Cholesterol With Elevated High Sensitivity C-Reactive Protein in the U.S.

Implications of the JUPITER (Justification for the Use of Statins in Primary Prevention: An Intervention Trial Evaluating Rosuvastatin) Study

Erin D. Michos, MD, MHS, Roger S. Blumenthal, MD

Baltimore, Maryland

Conclusions: Extrapolating JUPITER eligibility to NHANES, an estimated 6.5 million additional adults could be potential candidates to initiate statin therapy

J Am Coll Cardiol, 2009; **53**:931–5

Continuation of Statin Treatment and All-Cause Mortality

A Population-Based Cohort Study

Varda Shalev et al., *Arch Intern Med.;* 2009; **169(3)**: 260-268

Methods

- **Retrospective cohort study;**
- Enrollees 229 918 adult in a health maintenance organization in Israel [Maccabi Healthcare Services (MHS)] who initiated statin treatment from 1998 through 2006 (mean age, 57.6 years; 50.8% female).
- ***Proportion of Days Covered*** (PDC) with statins was measured by the number of dispensed statin prescriptions during the interval between the date of the first statin prescription and the end of follow-up.
- The study assessed risk of mortality in 2 separate cohorts:
  1. a primary prevention cohort of subjects (n=136 052) with no indication of CHD or other cardiovascular disease, as evidenced by the absence of clinical diagnosis of cardiovascular disease at baseline, and
  2. a secondary prevention cohort of patients (n=93 866) with coronary artery disease who were identified from the MHS registry of cardiovascular diseases.

Continuation of Statin Treatment and All-Cause Mortality

A Population-Based Cohort Study

Varda Shalev et al., *Arch Intern Med.;* 2009; **169(3)**: 260-268

Results

- During the study period, 13 165 individuals (5.7%) died [4 259 among the primary prevention and and 8 906 among the secondary prevention cohorts] and 3 745 (1.6%) left MHS.
- In both cohorts, continuity of treatment with statins (PDC ≥ 90%) conferred at least a 45% reduction in risk of death compared with patients with a PDC of less than 10%.
- A stronger risk reduction was calculated among patients with high baseline low-density lipoprotein cholesterol level and patients.

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Results: PDC

Table 3. Proportion of Days Covered With Statins and All-Cause Mortality, Maccabi Healthcare Services, Israel, 1998-2006

	HR (95% CI)					
	Primary Prevention			Secondary Prevention		
PDC, %	Model 1[a]	Model 2[b]	Model 3[c]	Model 1[a]	Model 2[b]	Model 3[c]
<10	1 [Reference][d]	1 [Reference][d]	1 [Reference][d]	1 [Reference][d]	1 [Reference][d]	1 [Reference][d]
10-19	1.16 (1.04-1.28)	1.34 (1.21-1.49)	1.35 (1.22-1.50)	1.27 (1.17-1.37)	1.27 (1.17-1.38)	1.28 (1.18-1.39)
20-29	0.97 (0.86-1.09)	1.06 (0.94-1.20)	1.07 (0.95-1.21)	0.95 (0.87-1.04)	0.98 (0.89-1.07)	0.98 (0.90-1.08)
30-39	0.77 (0.67-0.87)	0.87 (0.77-1.00)	0.88 (0.77-1.00)	0.79 (0.72-0.87)	0.81 (0.74-0.89)	0.81 (0.74-0.89)
40-49	0.75 (0.66-0.86)	0.86 (0.75-0.98)	0.86 (0.75-0.98)	0.68 (0.62-0.75)	0.73 (0.66-0.80)	0.73 (0.66-0.80)
50-59	0.70 (0.62-0.81)	0.76 (0.67-0.87)	0.77 (0.67-0.88)	0.64 (0.58-0.70)	0.69 (0.63-0.76)	0.69 (0.63-0.76)
60-69	0.55 (0.48-0.64)	0.63 (0.54-0.72)	0.63 (0.55-0.73)	0.63 (0.58-0.69)	0.67 (0.61-0.73)	0.67 (0.62-0.74)
70-79	0.53 (0.47-0.61)	0.59 (0.52-0.68)	0.59 (0.51-0.68)	0.56 (0.51-0.61)	0.60 (0.55-0.66)	0.61 (0.56-0.67)
80-89	0.56 (0.49-0.64)	0.60 (0.53-0.69)	0.61 (0.53-0.69)	0.51 (0.47-0.55)	0.54 (0.50-0.59)	0.54 (0.50-0.59)
≥90	0.53 (0.47-0.58)	0.54 (0.49-0.60)	0.55 (0.49-0.61)	0.46 (0.43-0.49)	0.49 (0.46-0.52)	0.49 (0.46-0.53)

Abbreviations: CI, confidence interval; HR, hazard ratio; PDC, proportion of days covered.

[a] Adjusted for age and sex.

[b] Also adjusted for marital status, nationality, socioeconomic status, years of living in Israel, residence area, chronic condition, visits to primary care physician during the year before the index date, number of hospitalizations during the year before the index date, cancer, diabetes mellitus, and use of antihypertensives and diuretics during the year before the index date.

[c] Also adjusted for mean level of low-density lipoprotein cholesterol during the year before the index date.

[d] *P* for trend <.01.

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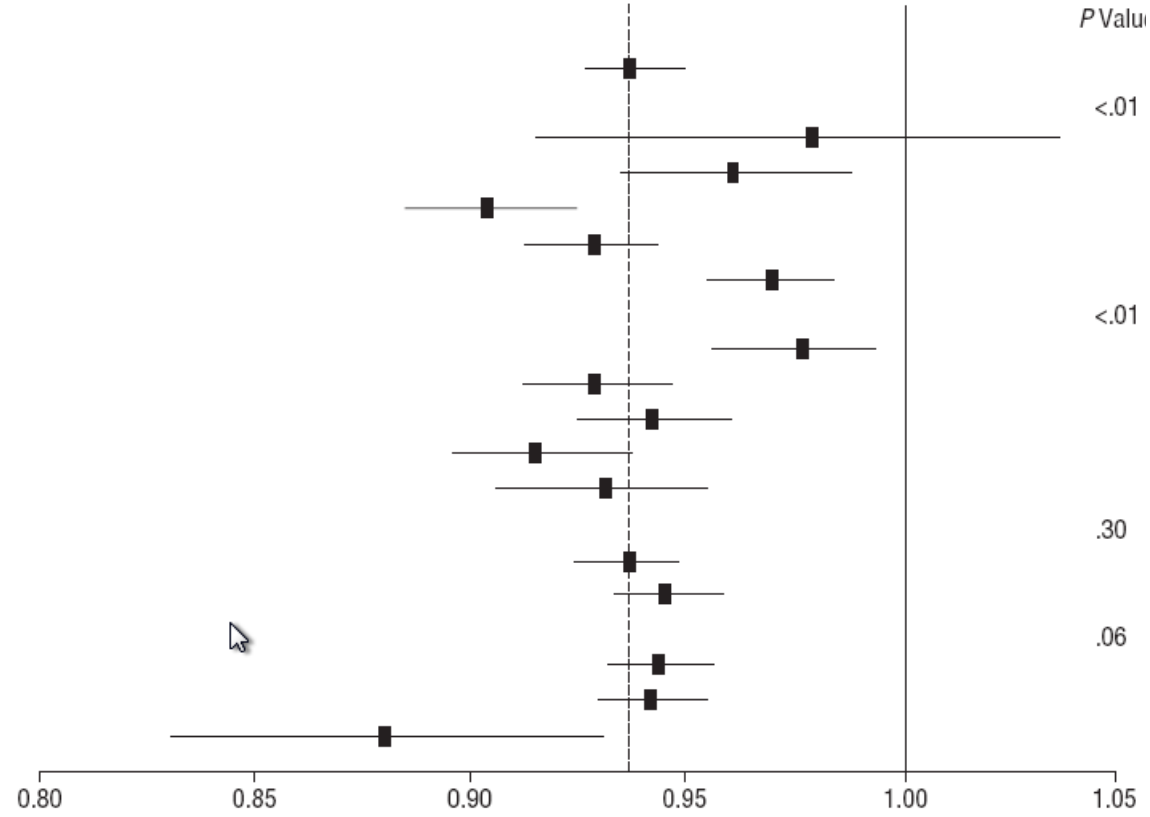
Results: Primary Prevention

Subgroup	No.	No. of Deaths	*P* Value
Total			
Age, y			<.01
<45	26 174	124	
45-54	46 614	471	
55-64	33 364	816	
65-74	21 614	1359	
≥75	8250	1489	
LDL-C, mg/dL			<.01
<130	18 882	849	
130-159	36 387	984	
160-189	44 296	1089	
≥190	24 734	771	
Missing	11 717	566	
Sex			.30
Male	60 680	1928	
Female	75 336	2331	
Statin efficacy			.06
Low	41 920	2064	
Moderate	86 795	2059	
High	7294	135	



Continuation of Statin Treatment and All-Cause Mortality

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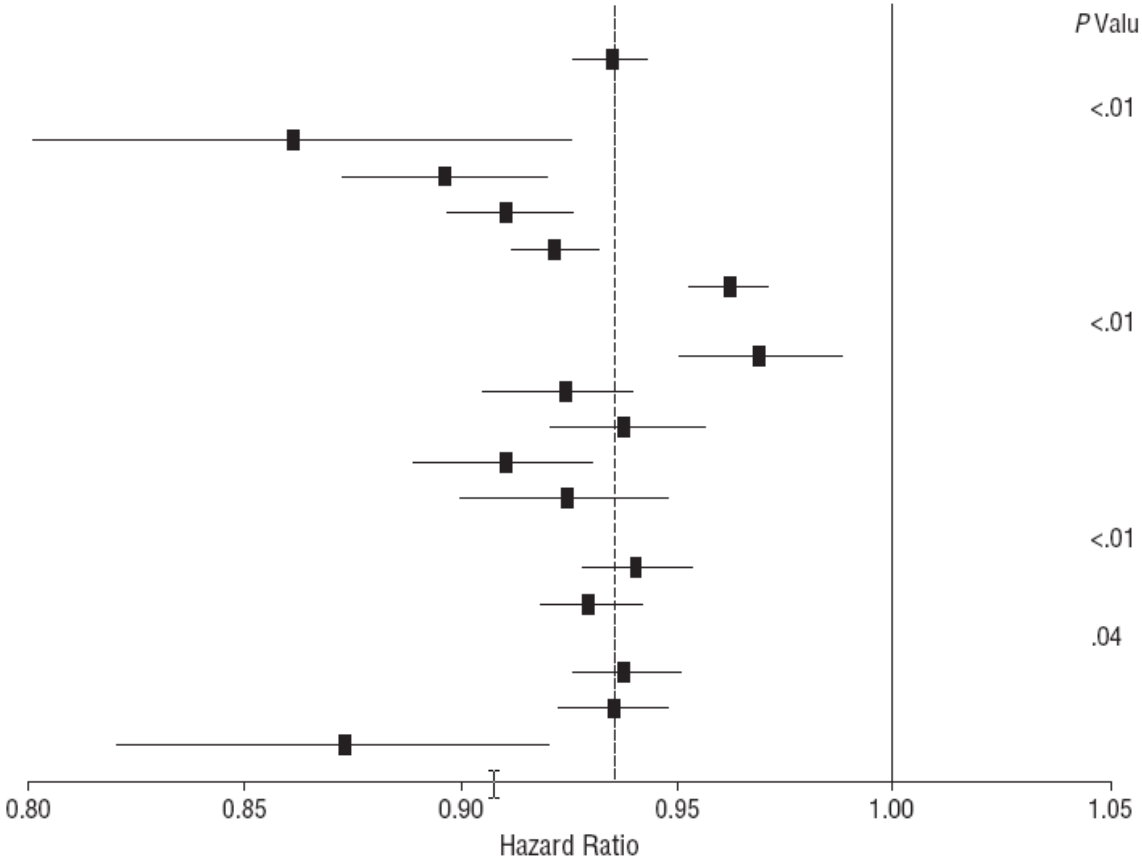
Results: Secondary Prevention

Subgroup	No.	No. of Deaths	*P* Valu
Total			
Age, y			<.01
<45	8558	97	
45-54	17 808	506	
55-64	31 434	1419	
65-74	23 240	3000	
≥75	12 826	3884	
LDL-C, mg/dL			<.01
<130	18 455	2188	
130-159	27 040	2355	
160-189	25 268	1917	
≥190	12 500	1155	
Missing	10 603	1291	
Sex			<.01
Male	52 322	5117	
Female	41 544	3789	
Statin efficacy			.04
Low	38 517	4508	
Moderate	48 657	4062	
High	6662	334	



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Conclusion

- The present study demonstrates a strong and independent association between statin therapy and the improved survival of patients with and without known CHD.
- Our findings confirm that the benefits of statins extend to unselected patients in community settings.
- Higher continuity of treatment and increased drug efficacy are associated with better survival among both primary prevention and secondary prevention cohorts.
- This study showed that continuation of statin treatment provided an ongoing reduction in all cause mortality for up to 9.5 years among patients with and without a history of CHD.
- The observed benefits from statins were greater than expected from randomized clinical trials, emphasizing the importance of promoting statin therapy and increasing its continuation over time for both primary and secondary prevention.

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Conclusion

While previous analyses of data from randomized clinical trials provided evidence that statin therapy produces only a modest (12%) reduction in all-cause mortality or no reduction at all, the present and other observational studies indicate a 40% to 50% reduction in mortality after consistent statin therapy and an even more dramatic reduction among older and hospitalized patients.

… … …

One possible explanation is that observational studies are usually conducted on unselected populations and may better capture the overall benefits of statins that may result from their anti-inflammatory, antithrombotic, or antiapoptotic effects as well as from their action on nitric oxide synthase, which may potentially contribute to lower overall morbidity and improved survival.

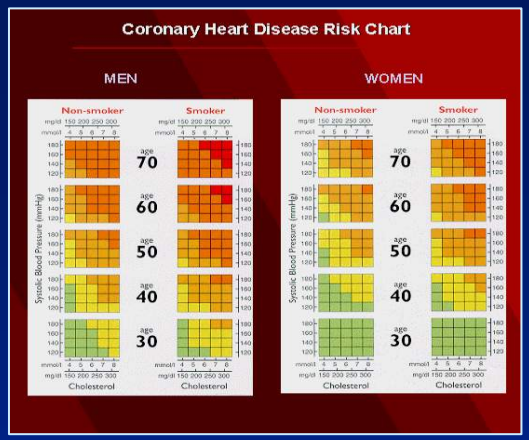
LE STATINE AGISCONO SOLO SUI LIPIDI?

- Numerosi studi di base hanno mostrato diversi effetti delle Statine indipendenti dalla loro azione sul metabolismo lipidico:
  - aumento della produzione di NO
  - riduzione delle proteine di fase acuta (PCR, citochine)
  - azione antiossidante (produzione e degradazione superossidi)
  - azione antitrombotica mediata da una attivazione della fibrinolisi e azione antiaggregante sulle piastrine
  - stabilizzazione della placca aterosclerotica
  - inibizione della proliferazione delle cellule muscolari liscie

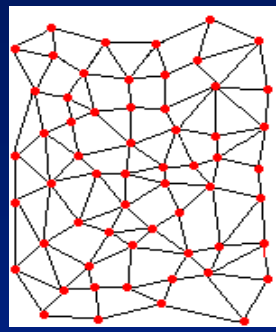
QUALE SIGNIFICATO CLINICO?

- Pur in assenza di grandi trials disegnati con lo scopo di valutare il significato clinico degli effetti extra-lipidici delle Statine,
- ci sono evidenze sufficienti per suggerire l'impiego delle Statine nelle sindromi coronariche acute e nell'immediato post-IMA,
- nel trattamento di pazienti trapiantati (cuore e rene)
- nei pazienti da sottoporre a endoarteriectomia carotidea.
- In tutte queste situazioni sembrano implicati più gli effetti extra-lipidici che l'effetto sul metabolismo lipidico che ha sicuramente bisogno di più tempo per manifestarsi

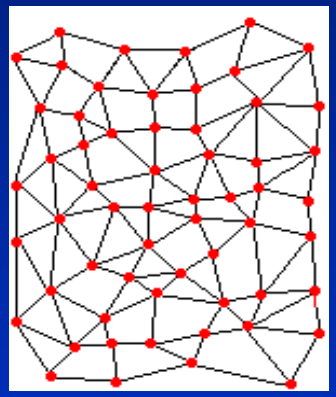
Medico di famiglia



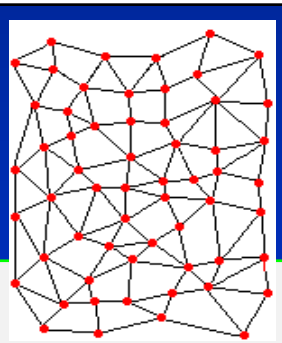
Alto rischio



Basso rischio



Ambulatorio di Cardiologia



Educazione sanitaria

Supporto psicocomp.

Stratificaz. Prognost.

Intervento strutturato sui FR con protocolli condivisi

Ambulatori di prevenzione inseriti in:
Centri cardiologici di alta specializzazione
o
U.O. Cardiologia Riabilitativa e Preventiva HUB

Progettazione dei Percorsi Clinici

- Identificazione di un problema clinico rilevante (gravità frequenza, criticità, novità);
- Formazione di un gruppo interdisciplinare rappresentativo delle diverse professionalità coinvolte;
- Identificazione e validazione di definite/specifiche *Linee Guida*;
- Revisione della pratica clinica attuale (revisione di cartelle cliniche);
- Definizione delle caratteristiche che determinano l'ingresso del paziente in un percorso;
- Definizione delle attività e della loro collocazione temporale e spaziale all'interno del percorso;
- Definizione del risultato atteso: stabilire quale stato di salute ci si attende che il paziente abbia al termine del percorso;
- Formazione degli operatori che dovranno utilizzare il percorso;
- Fase pilota di utilizzo;
- Regolare analisi della "*varianza*" da quanto atteso ed eventuale identificazione del processo assistenziale.

Ricostruzione dei Percorsi Clinici Effettivi

Struttura dei Percorsi Condivisi

1° Fase:

- Individuare i pazienti ad alto e medio rischio mediante le carte del rischio
- Avviarli al Centro di Prevenzione delle Malattie Cardiovascolari utilizzando:
  - Telefono con numero diretto (orario 8-14)
  - Fax (24 ore) con risposta entro 24 ore
  - E-mail (24 ore) con risposta entro 24 ore
  - …

2° Fase: Il percorso intraospedaliero

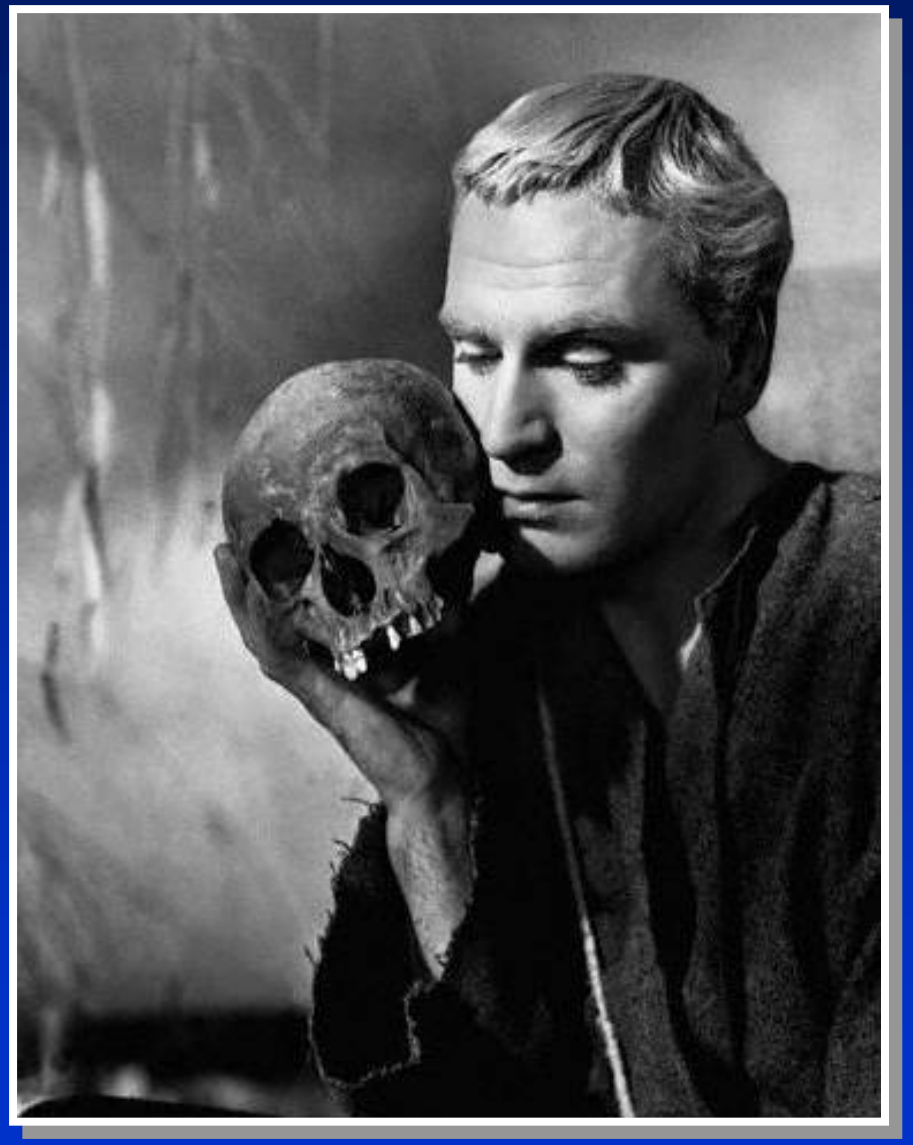
- Ambulatorio dedicato
- Accesso iniziale mediante impegnativa per visita ed ecg
- Possibilità di affrontare il rischio globale con interventi mirati su: ipertensione, dislipidemia, diabete, fumo, obesità
- Nei pazienti ad alto rischio avvio in day-hospital dei seguenti esami: ecocardiogramma, test da sforzo, spirometria, esami ematochimici.
- Possibilità di avvalersi di consulenze specialistiche (ad es. diabetologica, dietologica, psicologica)

3° fase: Percorso insieme

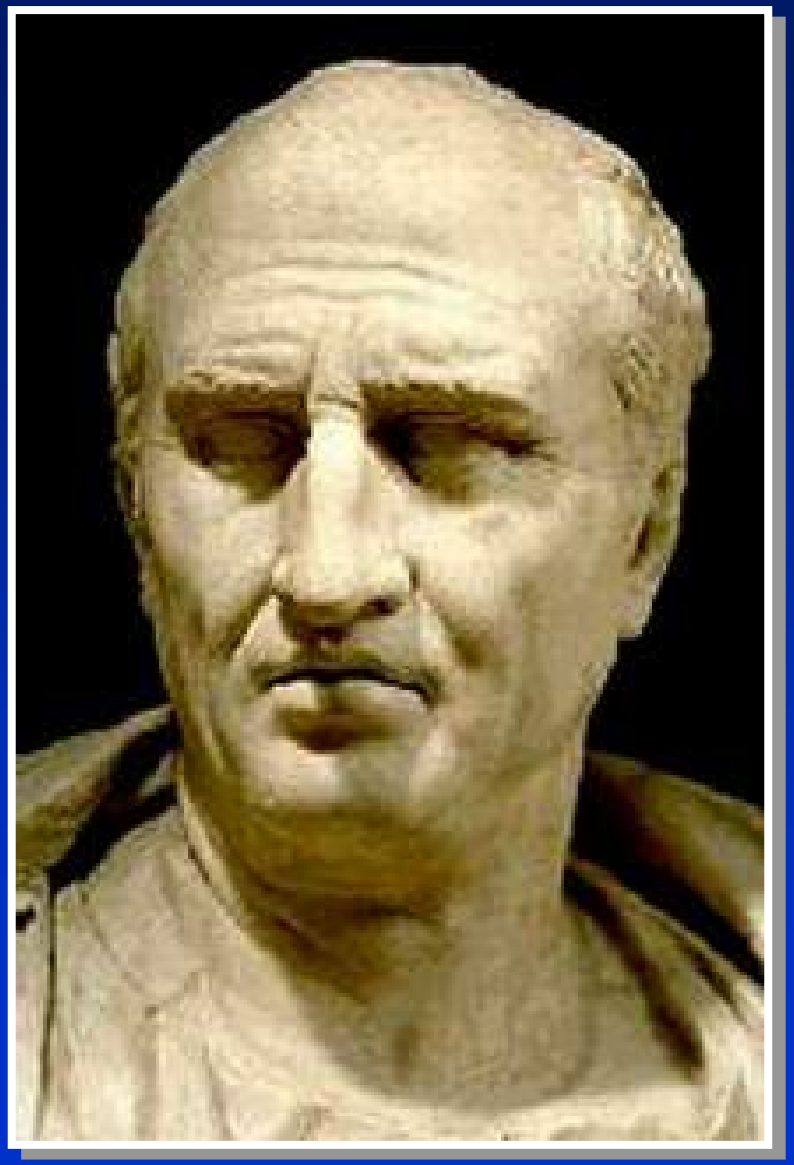
Definito il rischio del paziente concordare insieme:

- Obiettivi da raggiungere
- Terapie da avviare
- Ulteriori indagini
- Follow up

Statina o non statina ?

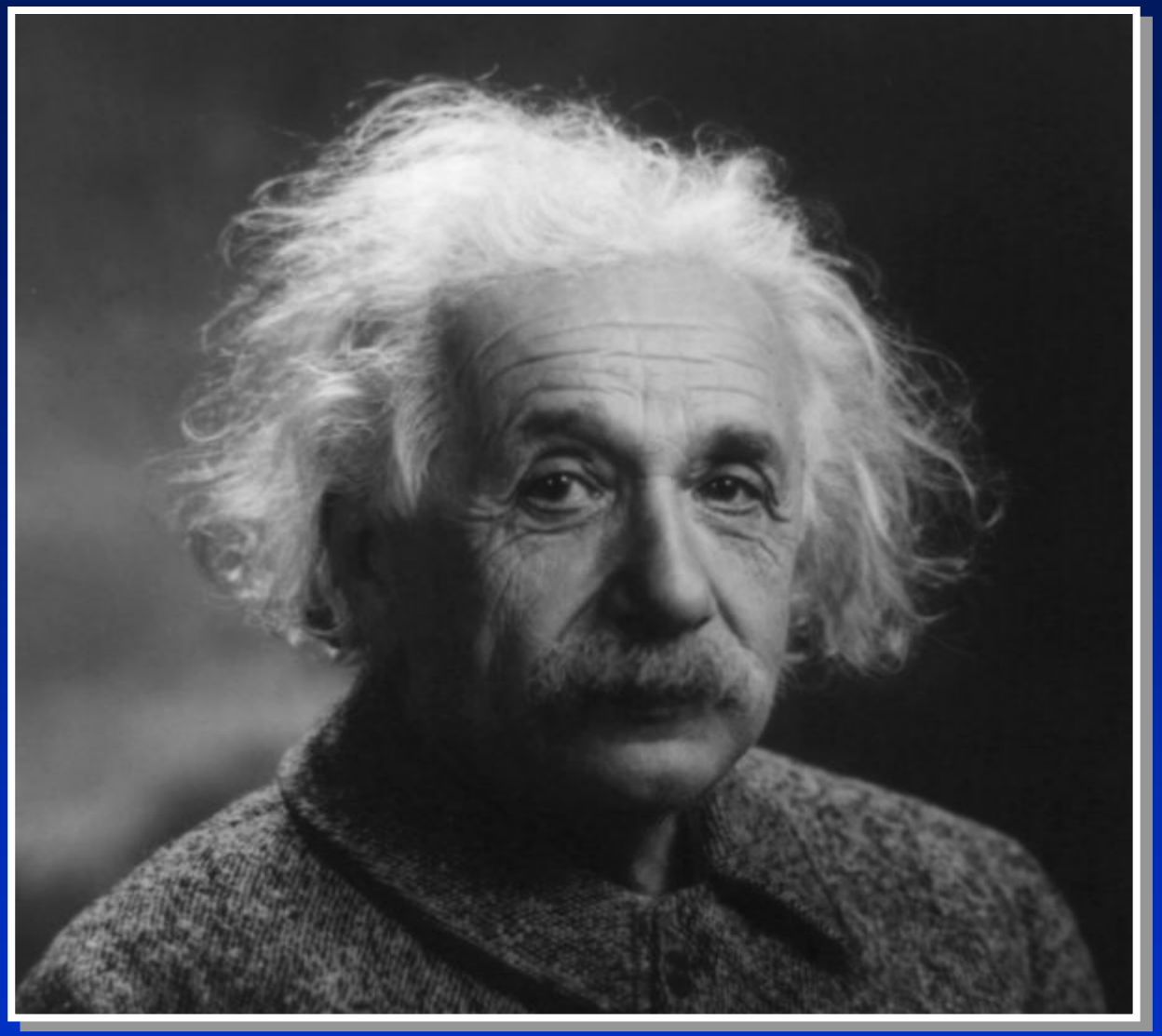


GRAZIE PER L'ATTENZIONE



Salus populi Suprema lex

De Legibus: Cicerone



la vita non si misura da quanti respiri facciamo,
ma dai momenti che ci tolgono il respiro.