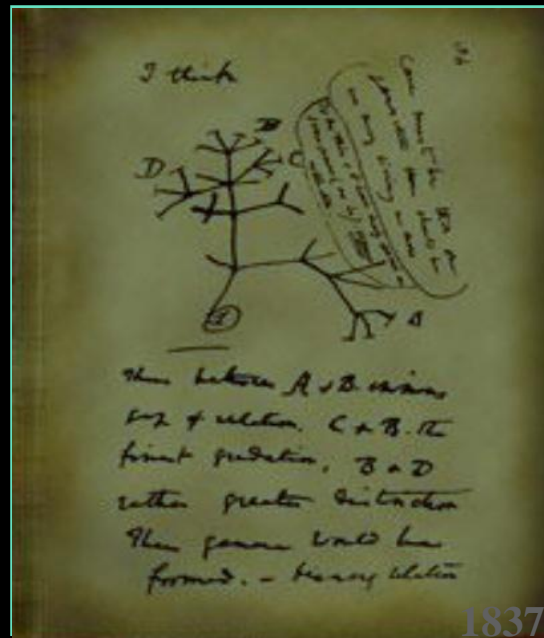


Vascular Healthcare

Focused on Evolving Issues

회성수술
수술



울산의대
서울아산병원
심장병원
심장내과
이철환

Where did the first life come from?
(Universal common ancestor (oldest fossils-3.5 billion years))

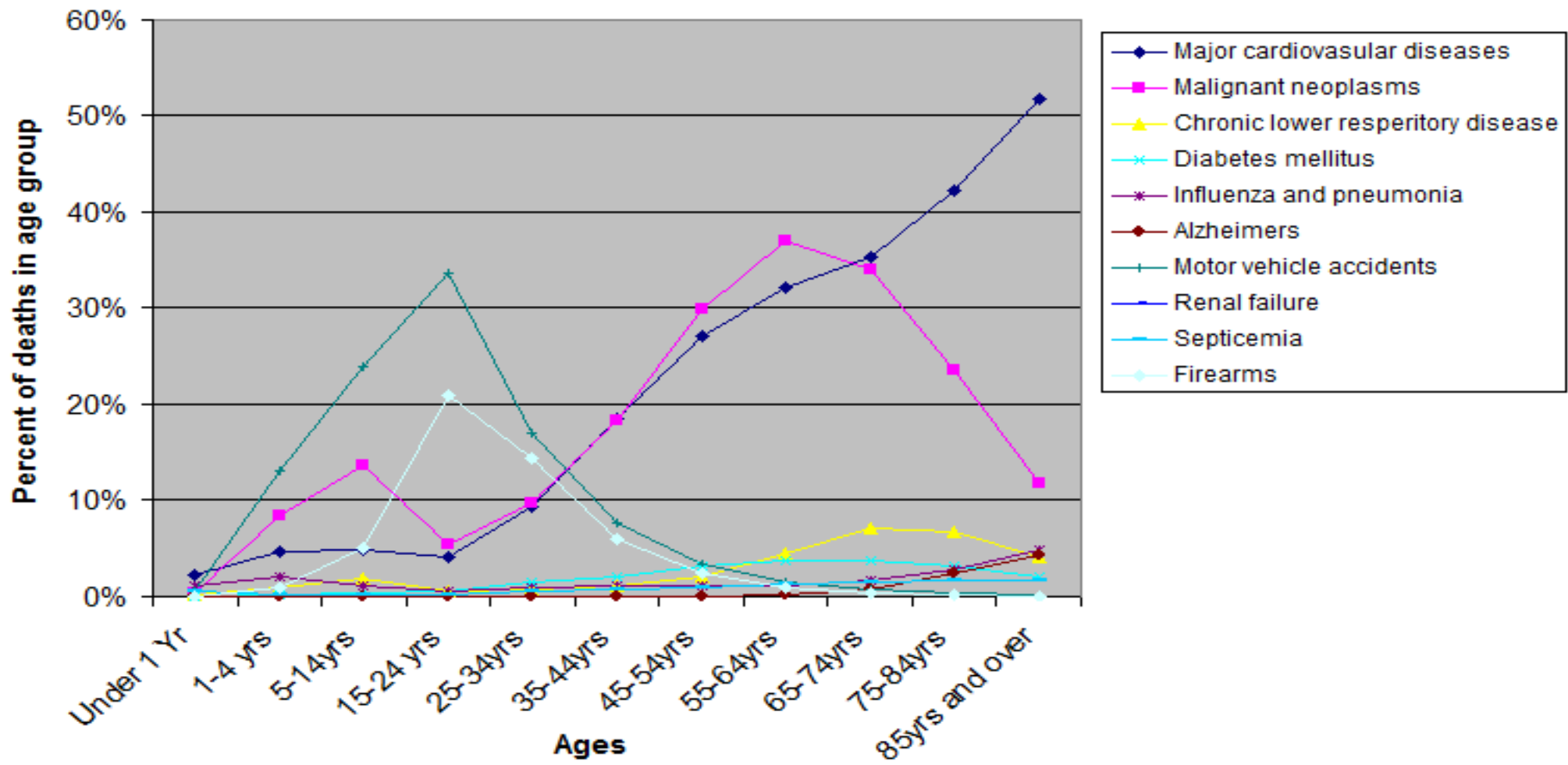
Presentation

- **Why Atherosclerosis Matter?**
- **Statins: Riddle to Magic Pill**
- **Goodbye to Old Solutions**
- **Unsettled Issues**
- **PCI and Vascular Health**

[속보] 황수관 박사 사망 원인 밝혀져! '충격'

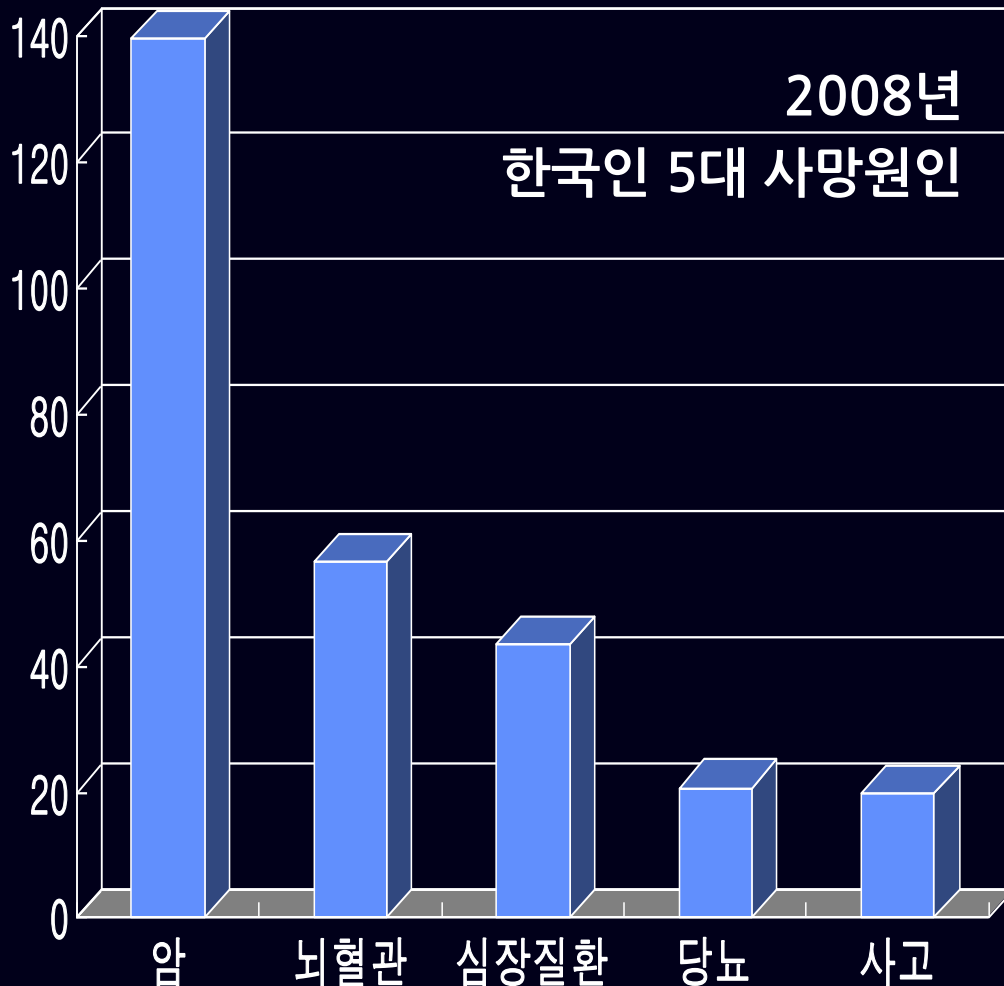
'신바람 박사' 황수관 연세대 의대 외래교수가 30일 오후 1시 서울 도곡동 강남세브란스 병원에서 향년 67세로 별세했습니다. 사망 원인은 급성 패혈증입니다.

Leading causes of death in the United States



Causes of Death Worldwide, 2008

사망/인구10만

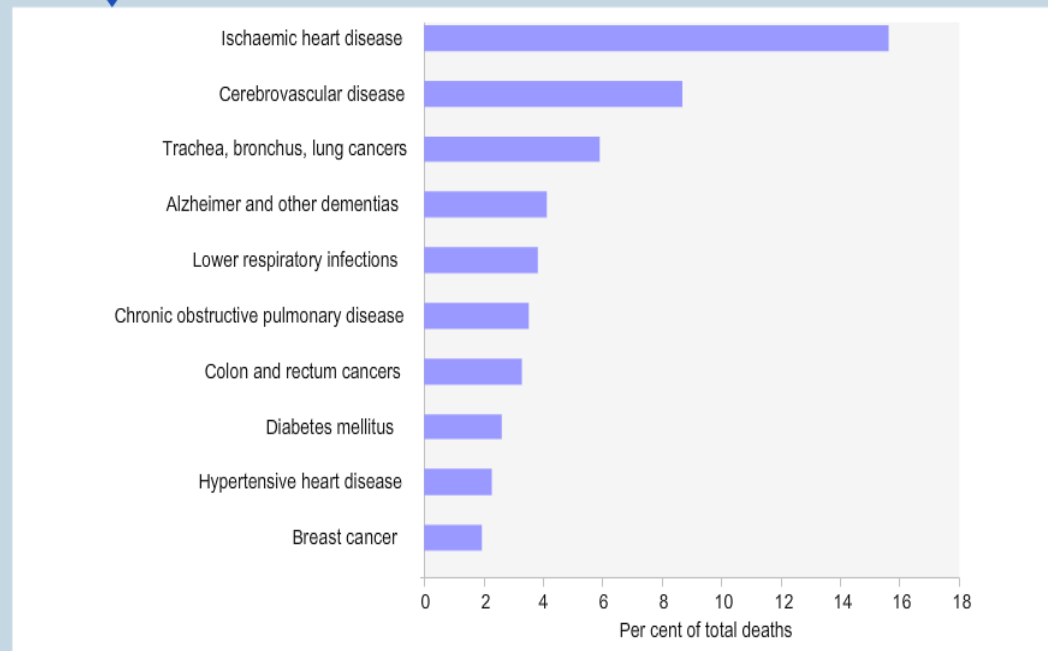


World Health Organization

Ten leading causes of deaths in 2008
High-income and low- and middle-income countries

Click on the country income groups below to view the related graphs

High-income countries | Low- and middle-income countries



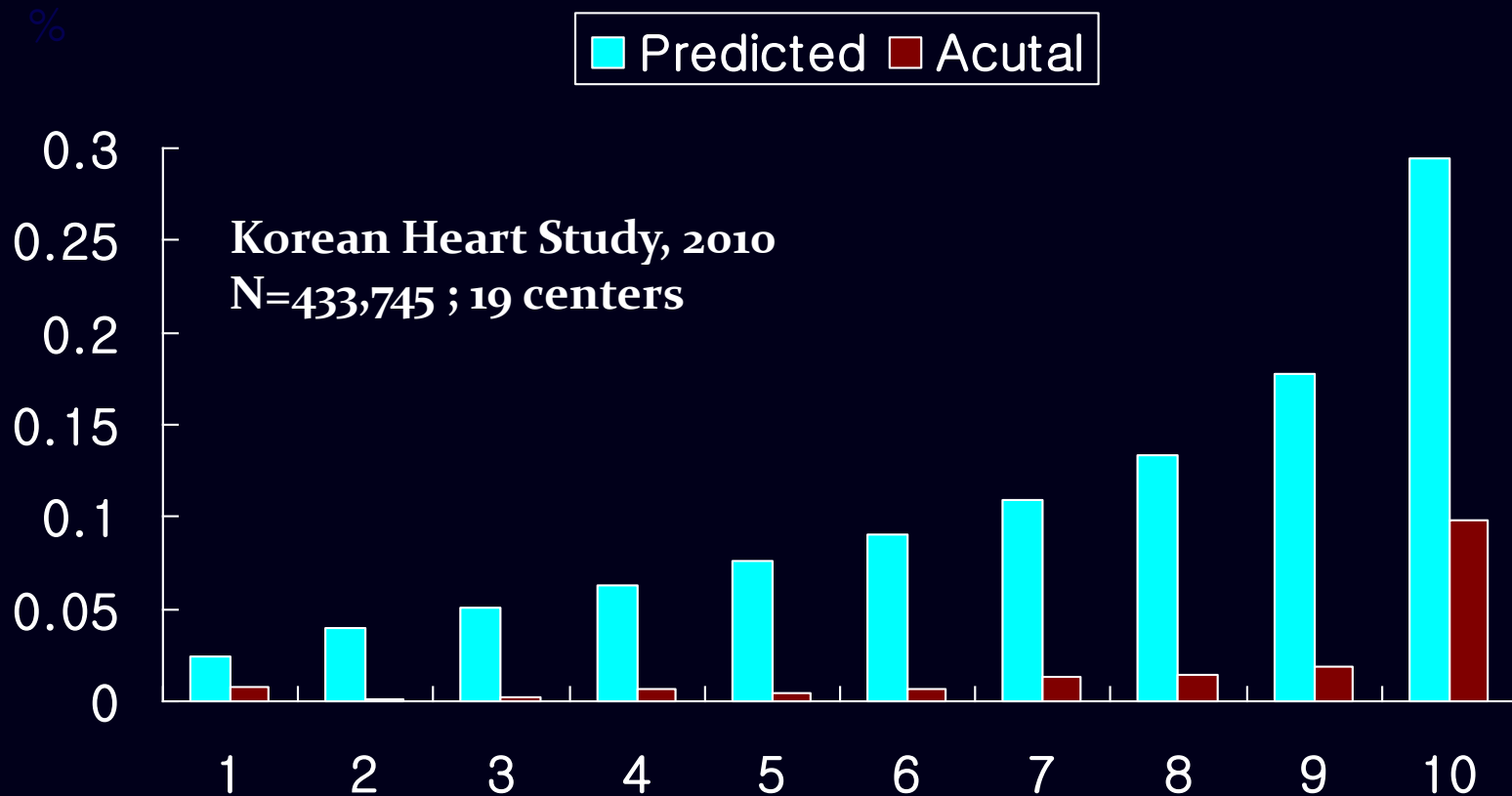
© WHO. All rights reserved.

유전 vs. 환경



The origin of sexual reproduction is still a hot topic

10 Year CHD Risk in Korean Men Using FHS Functions, 30-74



FHS: Framingham Heart Study

10-year probability: Men (3× women); Men (1/10 USA), Women (1/7 USA)

ENVIRONMENTAL AND HERITABLE FACTORS IN THE CAUSATION OF CANCER

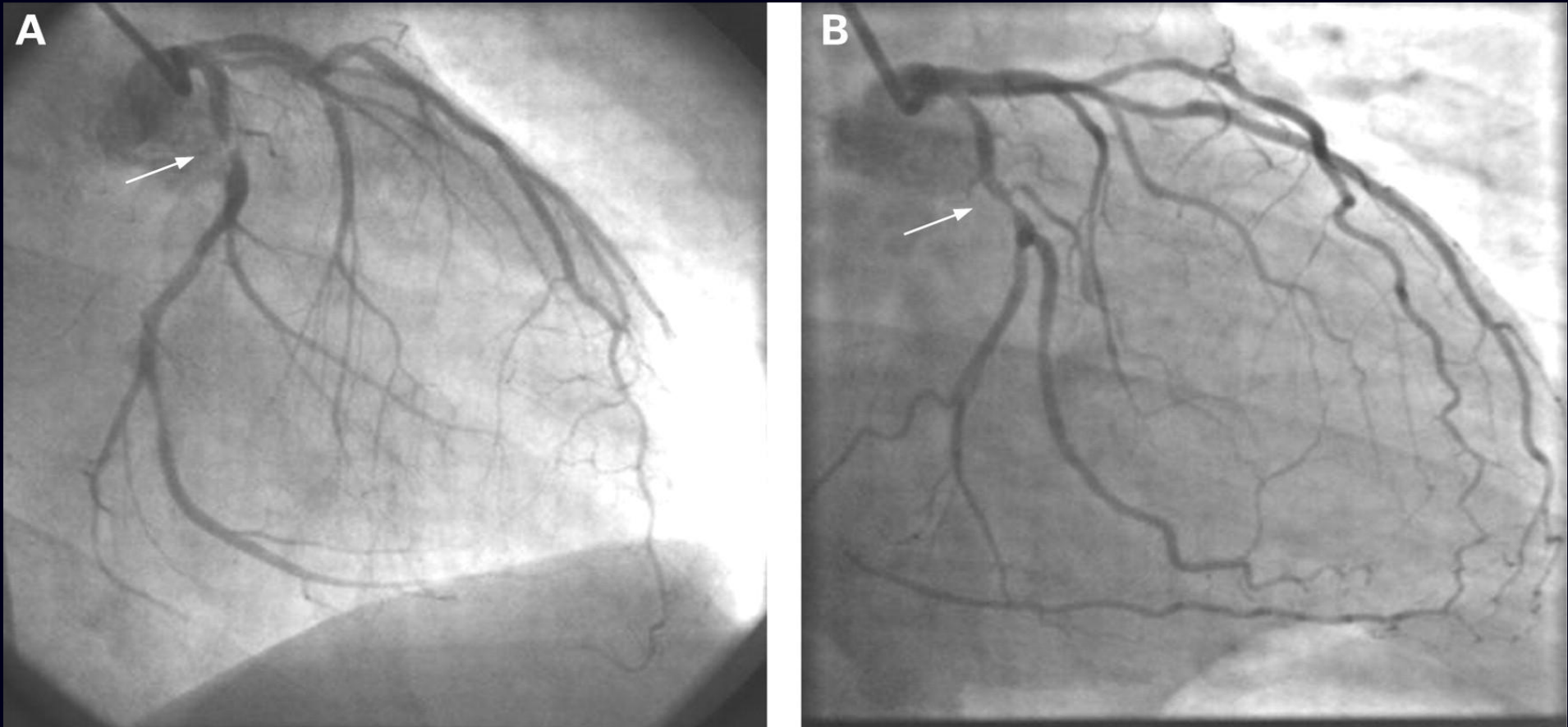
Analyses of Cohorts of Twins from Sweden, Denmark, and Finland

Concordance Rates in Twins of an Affected Person up to the Age of 75 Years (44,788 pairs)

Site of Cancer	Monozygotic	Dizygotic
Colorectum	0.11	0.05
Breast (women)	0.13	0.09
Prostate	0.18	0.03

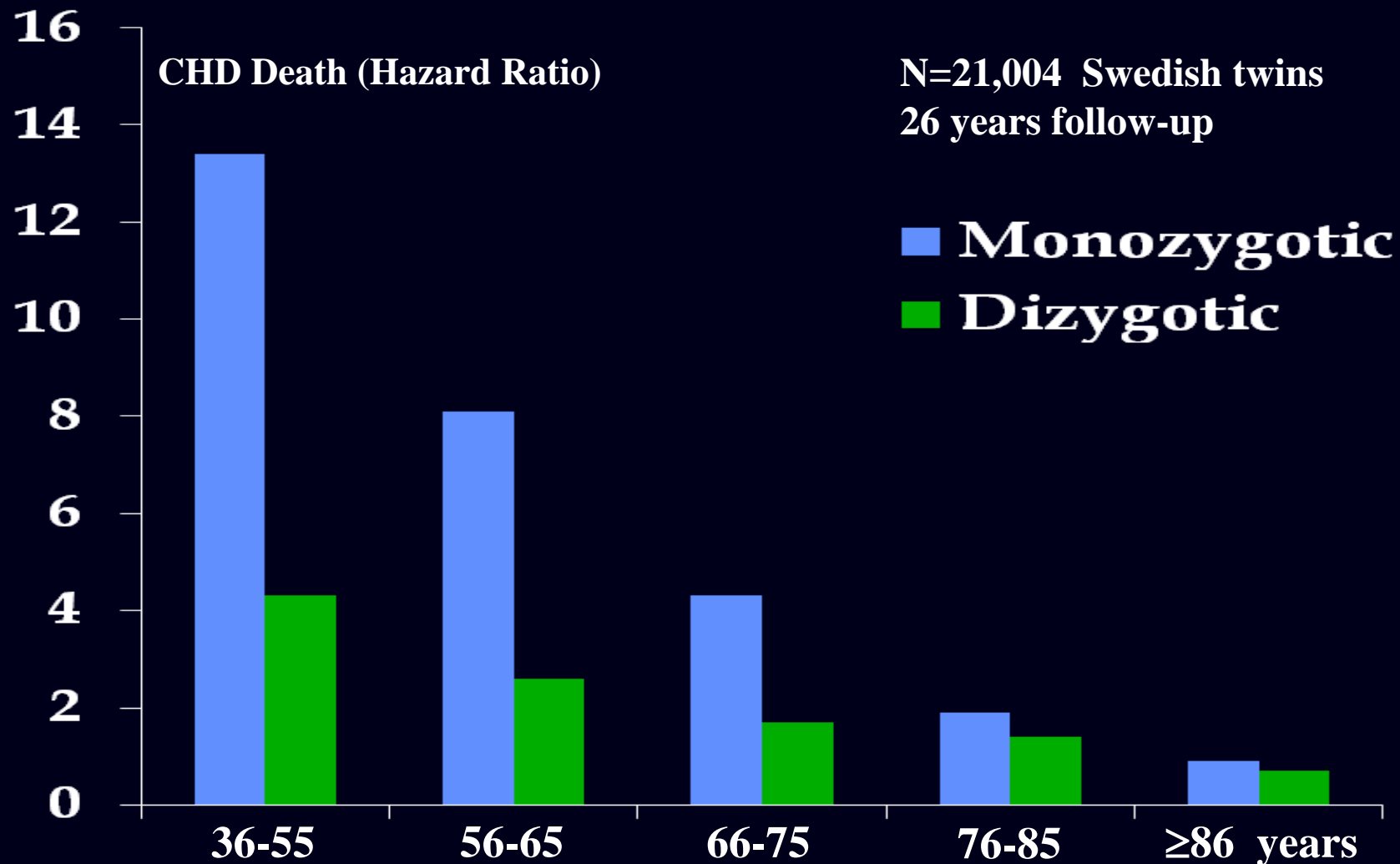
Inherited genetic factors make a minor contribution to susceptibility to most types of neoplasms.

Identical Twins, Identical Coronary Disease

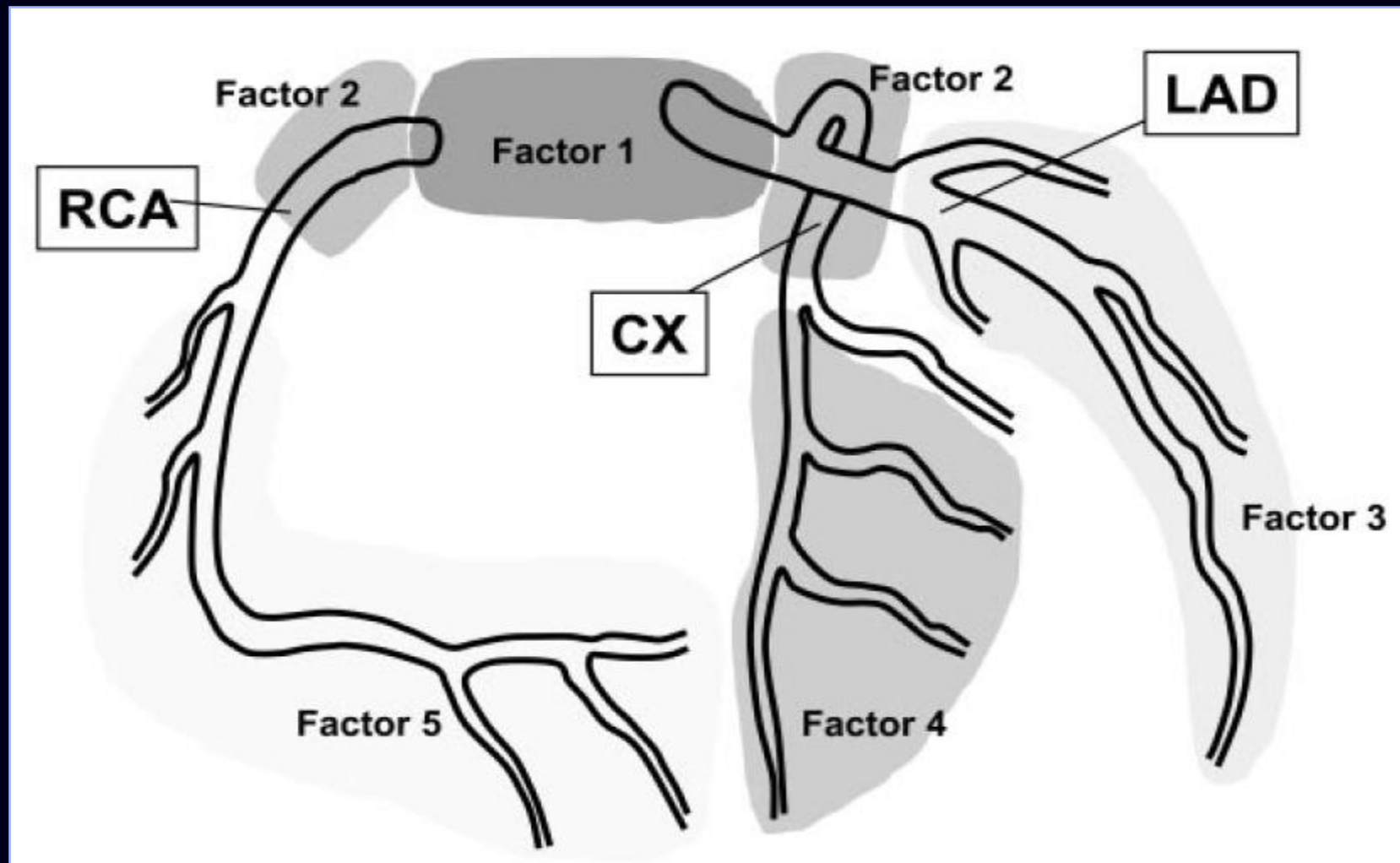


A pair of monozygotic identical twins presenting near simultaneously with CAD and identical atherosclerotic lesions despite significant differences in environmental risk factors & being divided geographically by 12 000 miles (England, Malaysia; 46/M).

Relative Hazard of CHD Death in Subjects according to the Age of Their Twins at CHD Death



Distinct Heritable Patterns of Angiographic Coronary Artery Disease in Families With Myocardial Infarction



The most hazardous localizations, like left main or proximal disease, display a high heritability.

Like Father, Like Son

Y-chromosome Variant May Explain CAD

No Hope for **Y**'s Future

End of Sexual Reproduction

Y So Lonely!

Scientists theorize that the X and Y chromosome started out with about the same amount of genes -- about 1,000. Today, the Y chromosome has less than 80 genes.

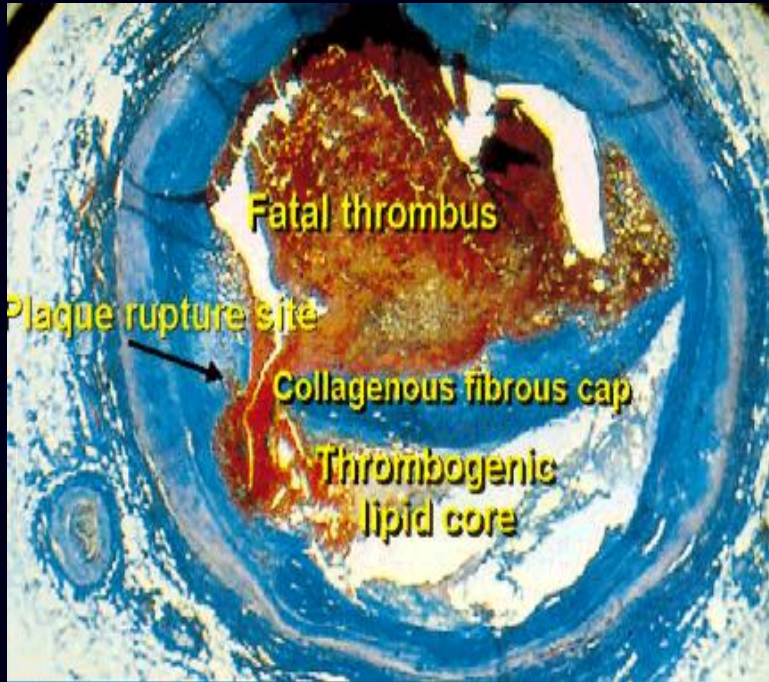
Carriers of one **haplogroup I** had about a 50% higher age-adjusted risk of CAD than did men with other Y chromosome lineages. Specifically, in the BHF study, the odds ratio was 1.75 (p=0.004); in WOSCOPS it was 1.45 (p=0.012); and in a joint analysis of both populations it was 1.56 (p=0.0002).

Presentation

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Two Great Drugs

Statins and Anti-platelet Agents



THE HUMAN PROTEIN ATLAS 
ABOUT & HELP

HMGCoA reductase: statins

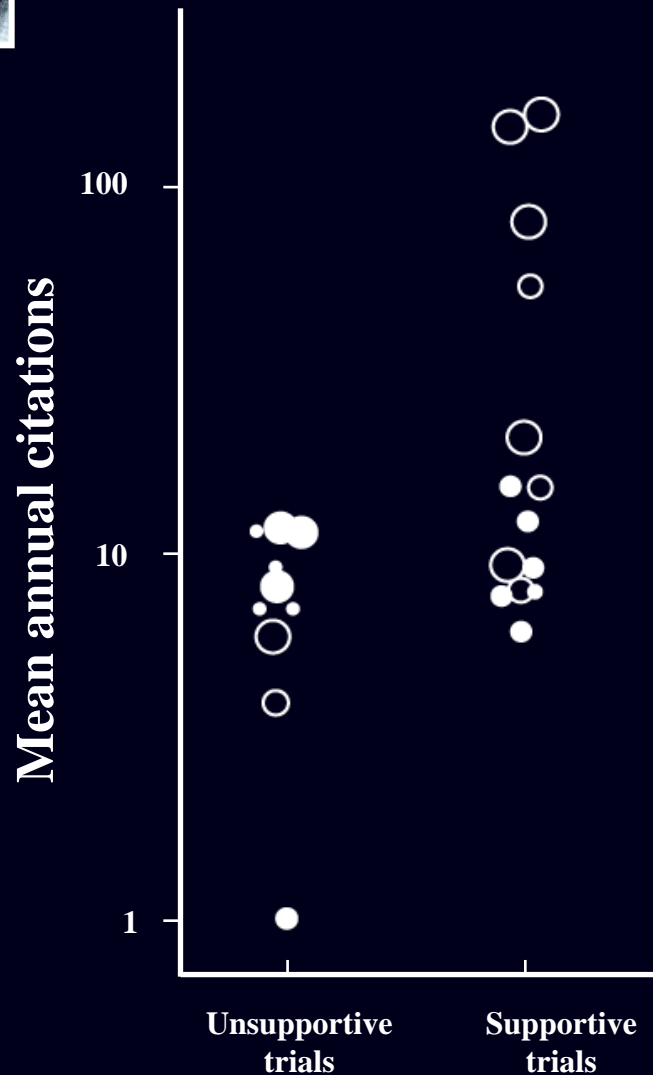
P2Y₁₂ receptor: clopidogrel, prasugrel, ticagrelor



1898

The initial road to cholesterol treatments was rather bumpy.

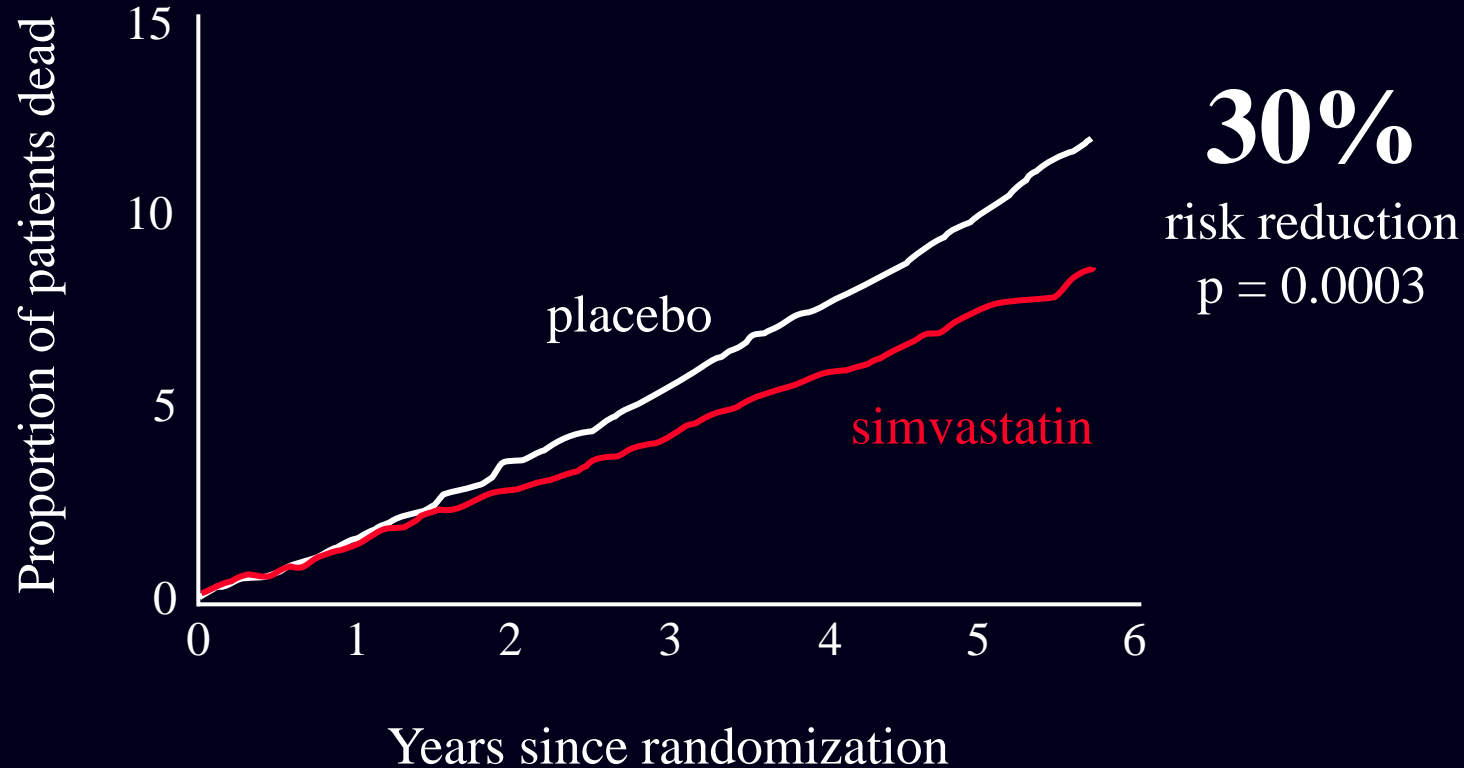
Cholesterol Lowering Trials before Statin Era



Lowering serum cholesterol concentrations does not reduce mortality and is unlikely to prevent coronary heart disease.

Revolution

Pre-S & S Era 4S



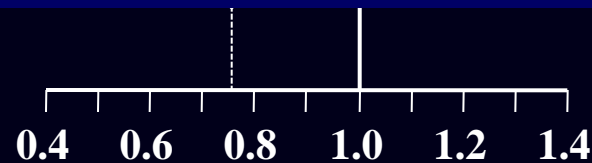
Heart Protection Study

Baseline	STATIN	PLACEBO	Risk ratio and 95% CI	
Feature	(10269)	(10267)	STATIN better	STATIN worse

Every patients with atherosclerosis has LDL-C that is too high for him or her.

(19.9%)

(25.4%)



JUPITER *Trial*

STUDY POPULATION

As described in detail elsewhere,^{17,18} men 50 years of age or older and women 60 years of age or older were eligible for the trial if they did not have a history of cardiovascular disease and if, at the initial screening visit, they had an LDL cholesterol level of less than 130 mg per deciliter (3.4 mmol per liter) and a high-sensitivity C-reactive protein level of 2.0 mg per liter or more. Other require-

N=17,802

1.9 years follow-up

**Rosuvastatin 20mg/d
Vs. Placebo**

“seemingly healthy people”
normal LDL-C & high CRP

Ailing to JUPITER

**A home run
for the public health!**

LDL 50%↓
CRP 37%↓

No doubt, it is definitively positive!

Relative Risk

Primary endpoint	44% ↓
Secondary endpoints	
CV Death/MI/Stroke	47% ↓
Total death	20% ↓
Myocardial infarction	54% ↓
Stroke	48% ↓

...the only proven medicine

Statin is Anti-atherosclerotic Drug!

Landmark Statin Trials

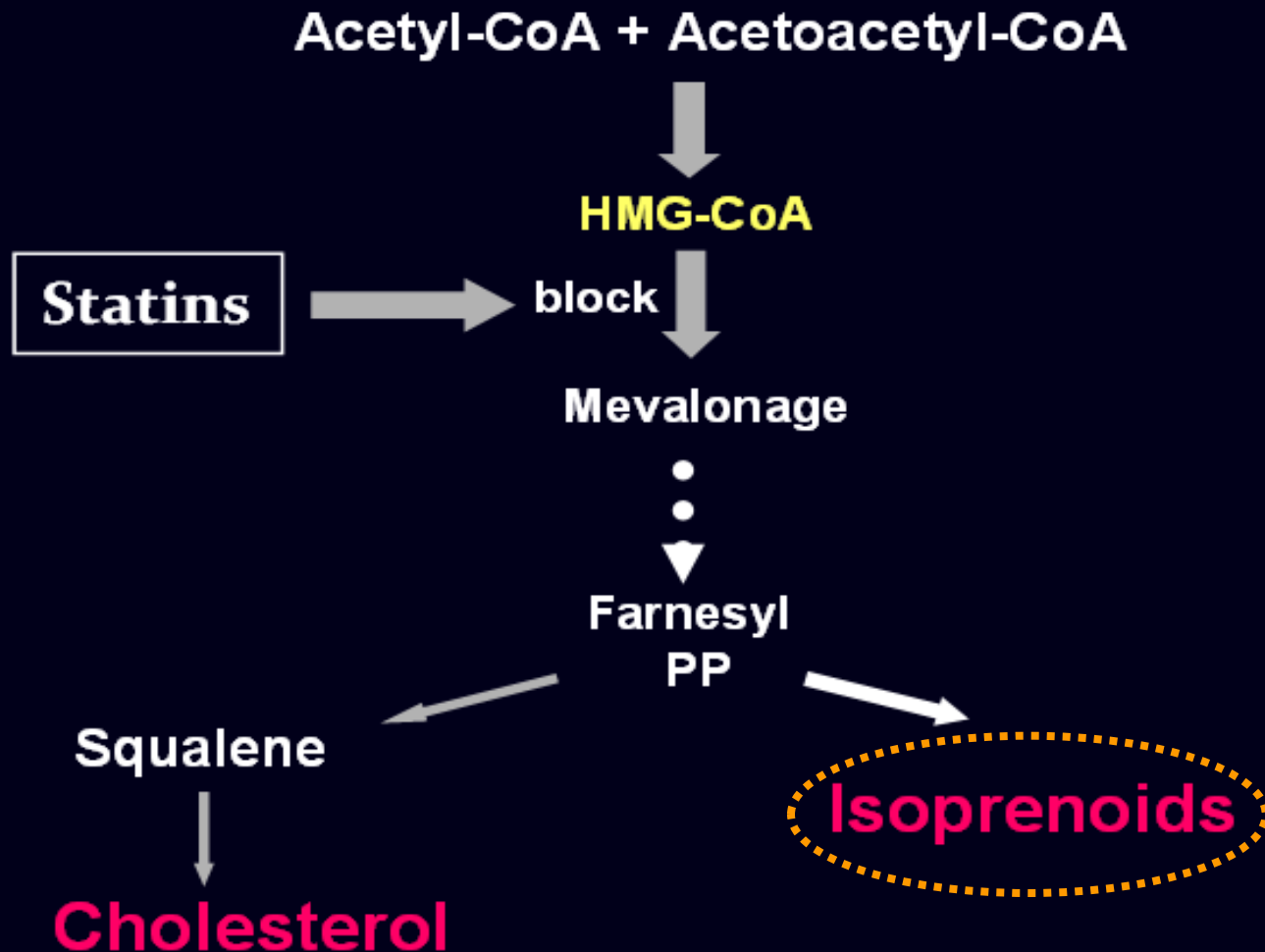
So Luxurious ...

Clinical End-Point Trials: “The Only One_Statin Trials”

AFCAPS/TexCaps, WOSCOPS, ALLHAT, CARE, LIPID, PROSPER, 4S, HPS, A-to-Z, MIRACL, CARDS, PROVE-IT, ALLIANCE, 4D, ASCOT-LLA, IDEAL, TNT, SPARCL, AURORA, CORONA, GISSI-HF, JUPITER, SEAS, SHARP, IMPROVE-IT (ongoing).

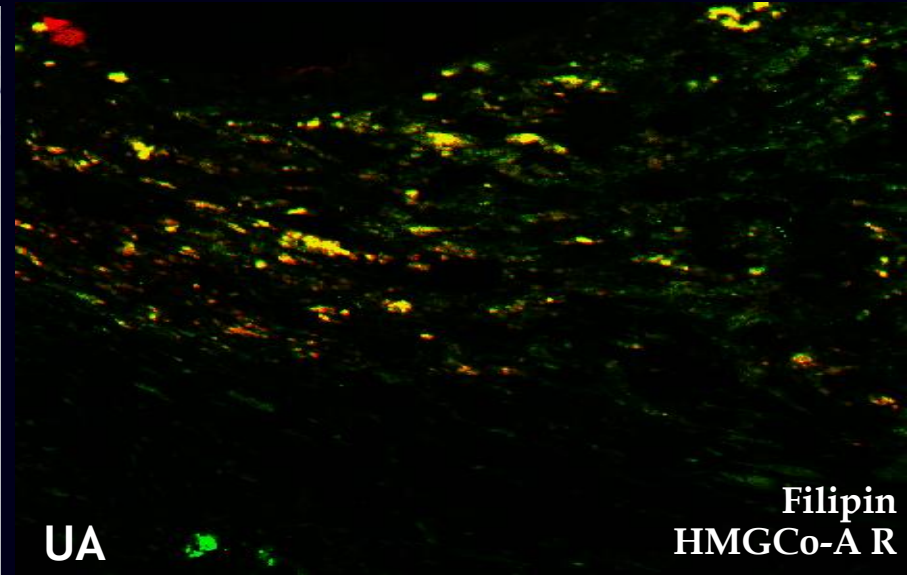
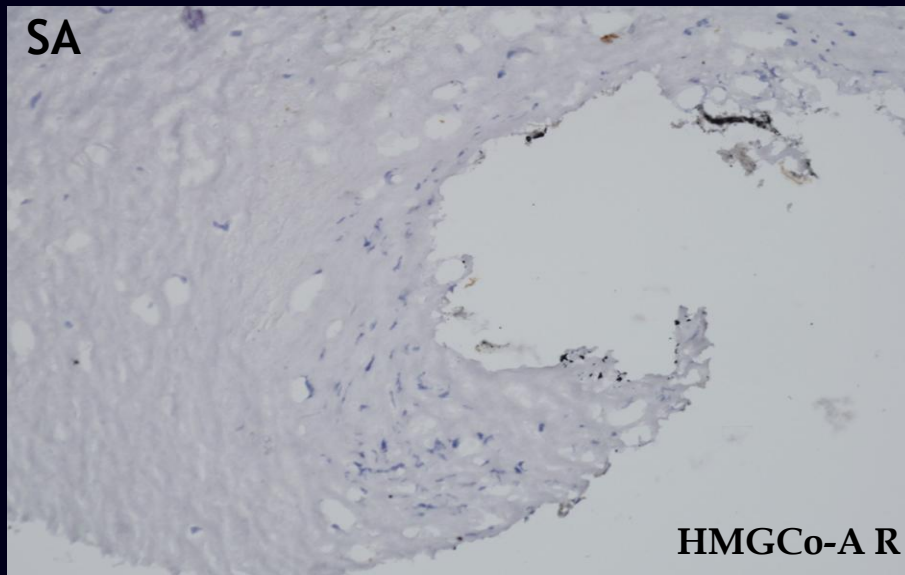
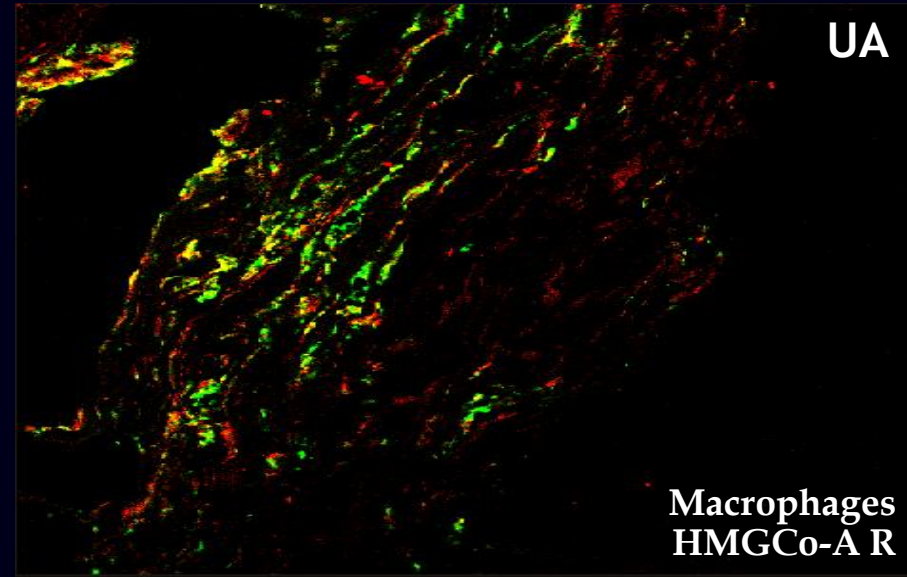
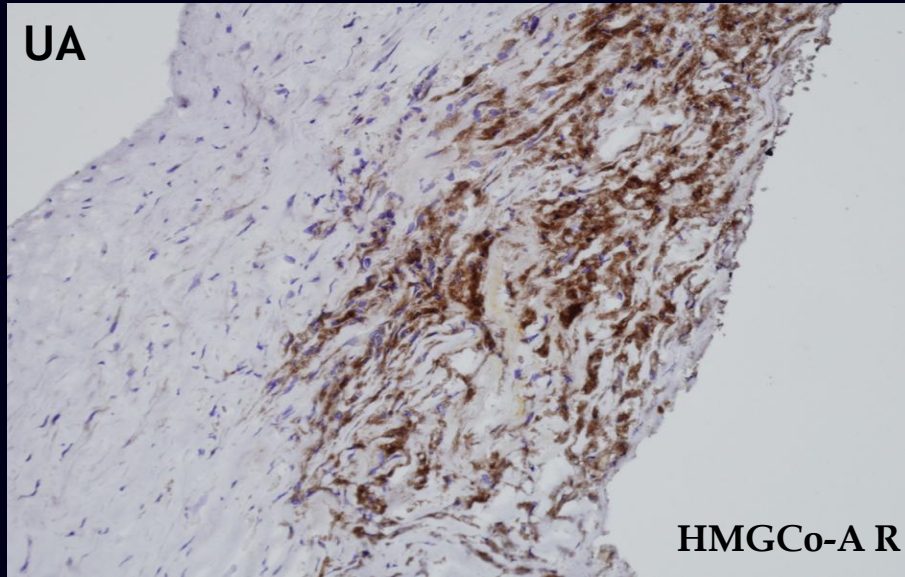
Save life!: The only proven medicine in 1° & 2° prevention

Statin Benefits, Why?



Expression of HMG-CoA Reductase in Human Coronary Atherosclerotic Plaques & Relationship to Plaque Destabilization

Heart 2011;97:715-20



Presentation

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Vitamins Therapy

Primary prevention

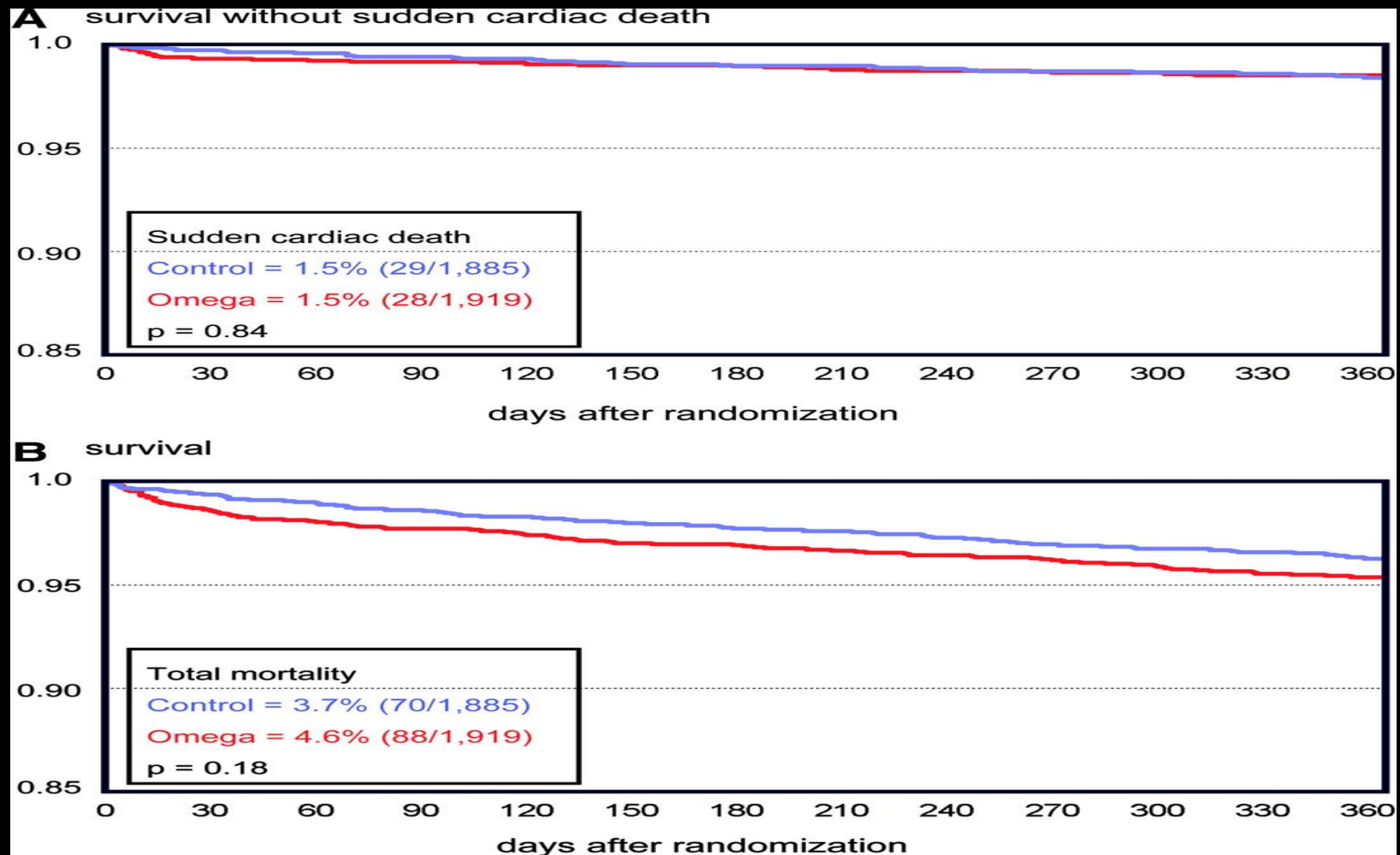
Secondary prevention

“Potential Harm, No Benefit”

It's time to **forget** about the saying
“a vitamin a day keeps heart attack/cancer away”

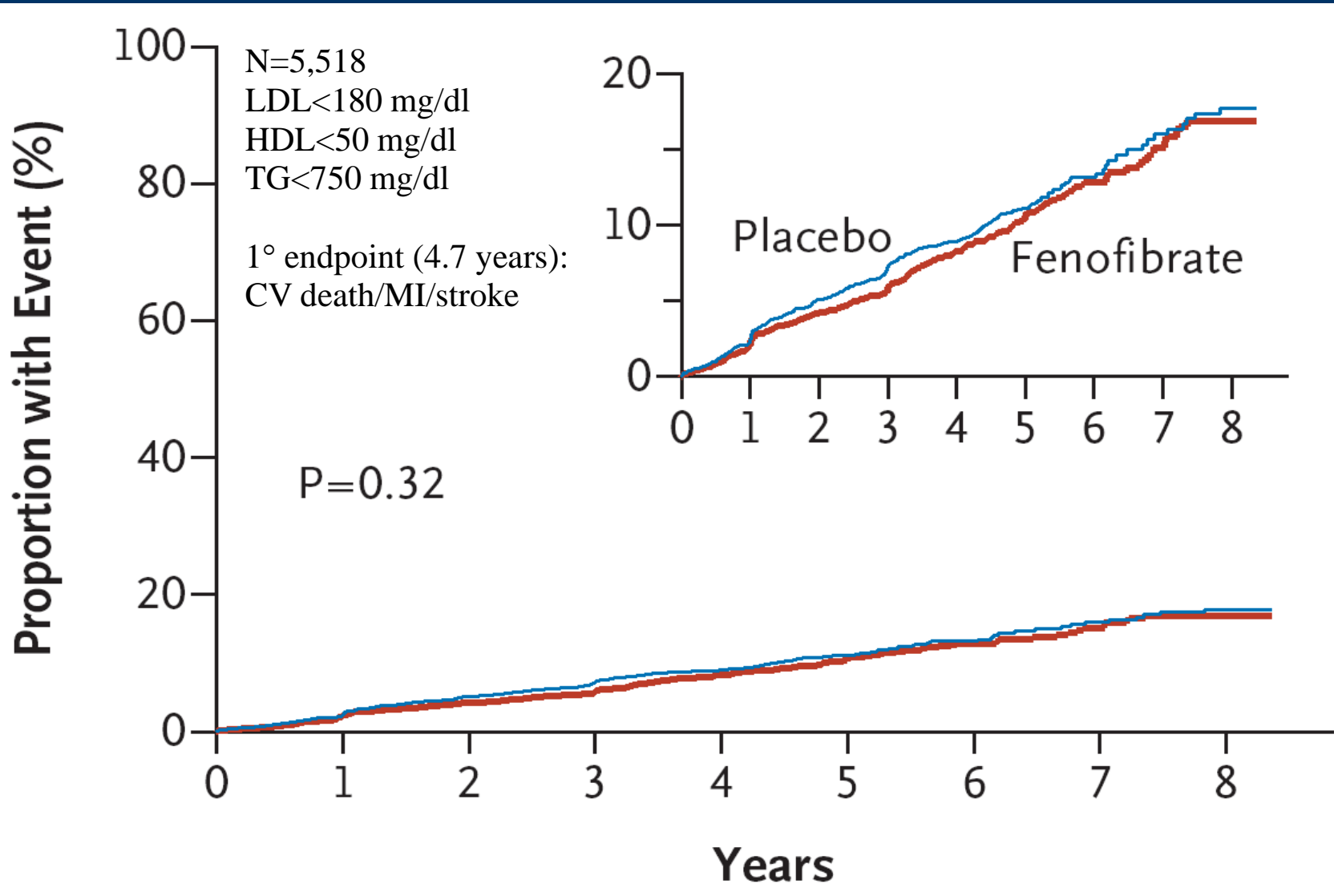
Medical decisions should be guided by
“science, and not by strongly held opinion”.

OMEGA, a Randomized, Placebo-Controlled Trial to Test the Effect of Omega-3 FA After MI

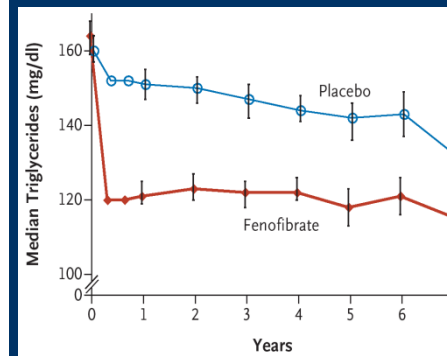
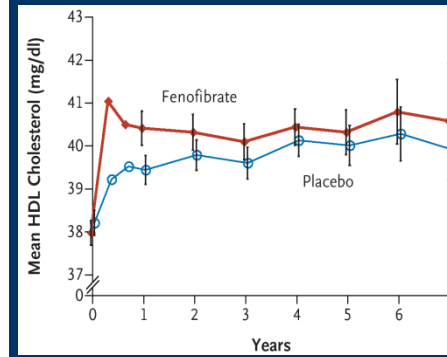


Guideline-adjusted treatment of AMI results in a low rate of SCD and other clinical events within 1 year of F/U, which could not be shown to be further reduced by the application of omega-3 fatty acids.

Effects of Combination Lipid Therapy in Type 2 DM ACCORD Trial - Lipid Arm



Market 1.3billion\$
Fenofibrate
- since 1974
- It lowers TG, but
no evidence that
lowering TG
affects outcomes



TIDE trial (2015: rosiglitazone vs pioglitazone vs placebo), >50 PPAR agonists failed (regulate TF & influence >100 genes)

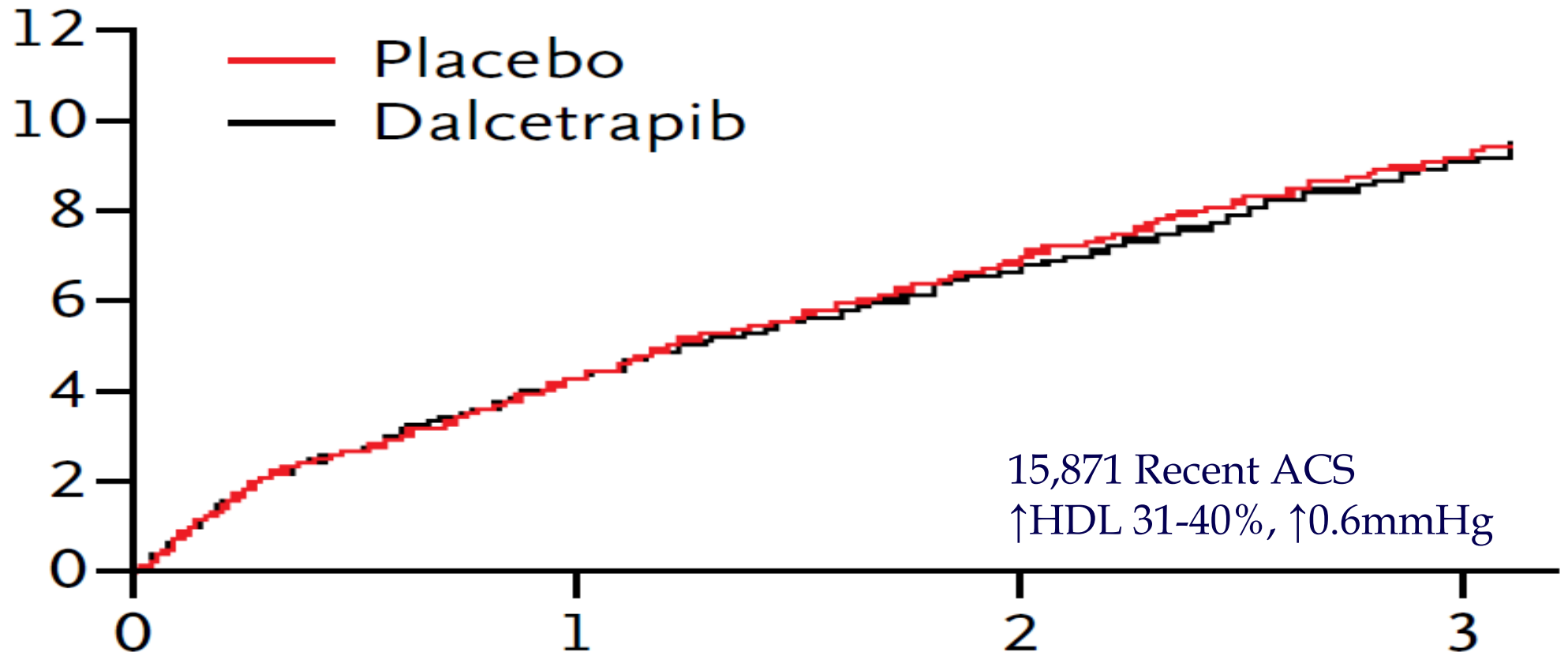
The Story So Far...

HDL-Targeted Therapies

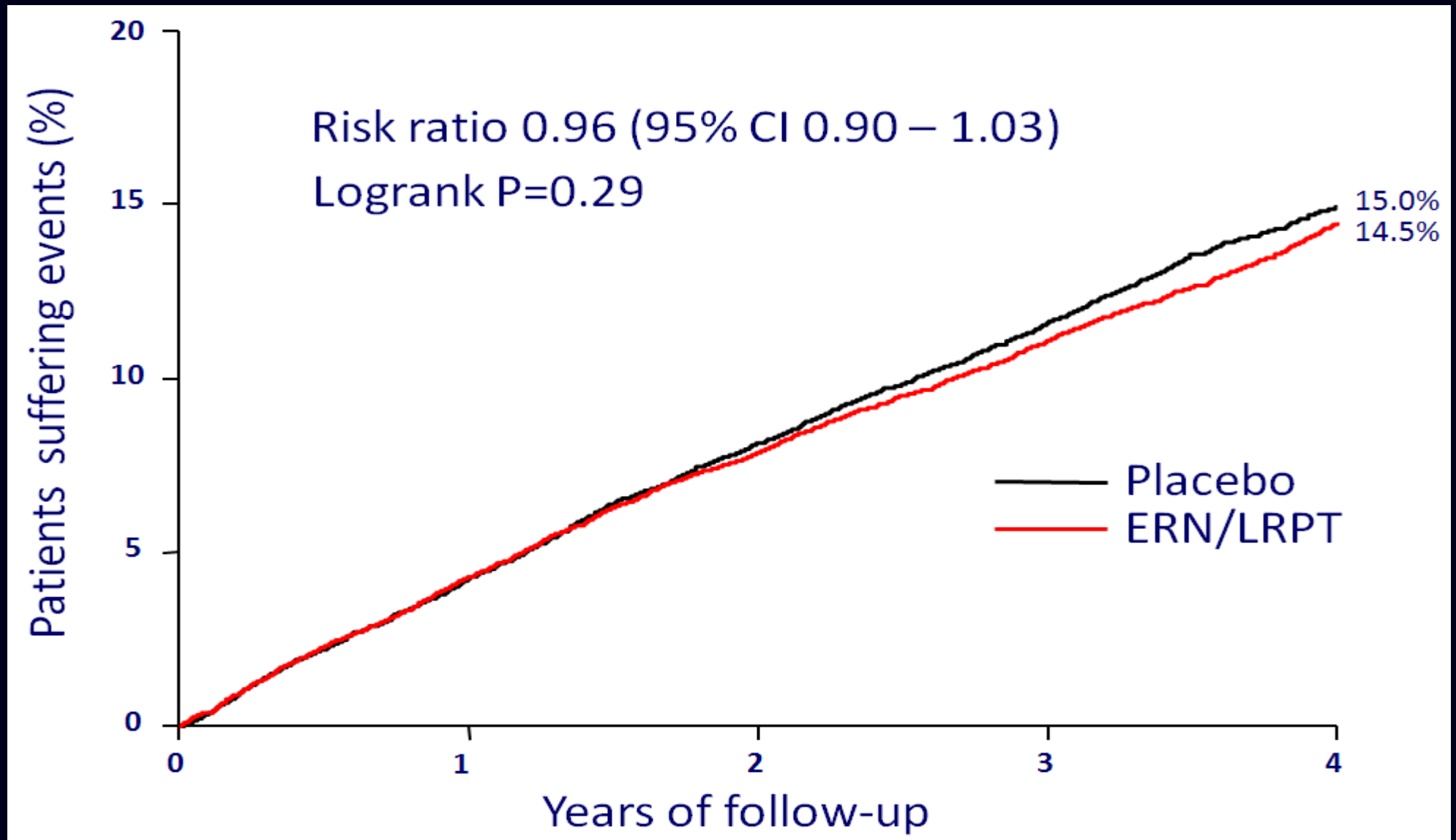
Roche stops dalcetrapib trial for lack of benefit

MAY 7, 2012 Reed Miller

high-risk project



HPS2-THRIVE: Randomized placebo-controlled trial of ER niacin & laropiprant in 25,673 pts with CV disease



lost its shine
but not its worth.

Things May Not Be as They Seem

Here today, gone tomorrow!

	Without Statin	With Statin
ACEI	Yes	No
Estrogen	No	-
Fibrate	No	No
Folate/B6,12/C,E	No	No
Glitazone	No	No
Omega-3*	Probable	No
Nicotinic acid	Yes	No

*Statin: GISSI-Prevention (5%, Lancet 1995;354:447), α -Omega trial (85%, NEJM 2010 on line)

Presentation

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- **Unsettled Issues**
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우리나라에서 장수하는 직업군은 종교인인데 반해 단명하는 직업군은 체육인, 작가, 언론인으로 집계됐다고 해요. 특히 두 직업군 간의 수명 차이는 무려 13년이나 되는 것으로 나타났다고 하네요.

직업별 평균 수명 (최근 10년 기준)

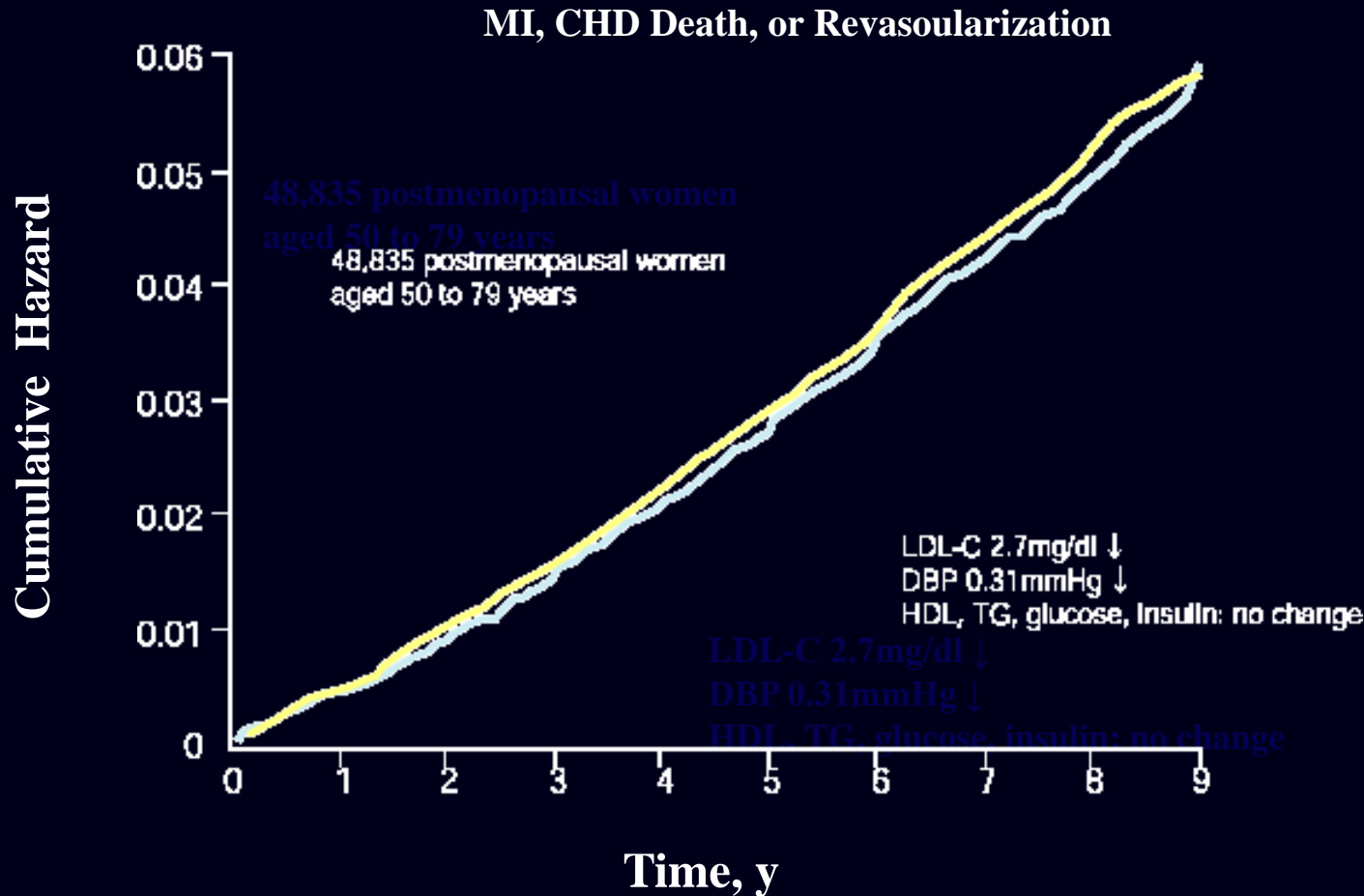


자료: 원광대 보건복지학부

연구팀은
종교인이 장수하는 이유로
가족관계로 인한
스트레스가 적고 **과욕이
없으며** 규칙적인 활동과
정신수양, **절식**, 금연,
금주의 실천 등이라고

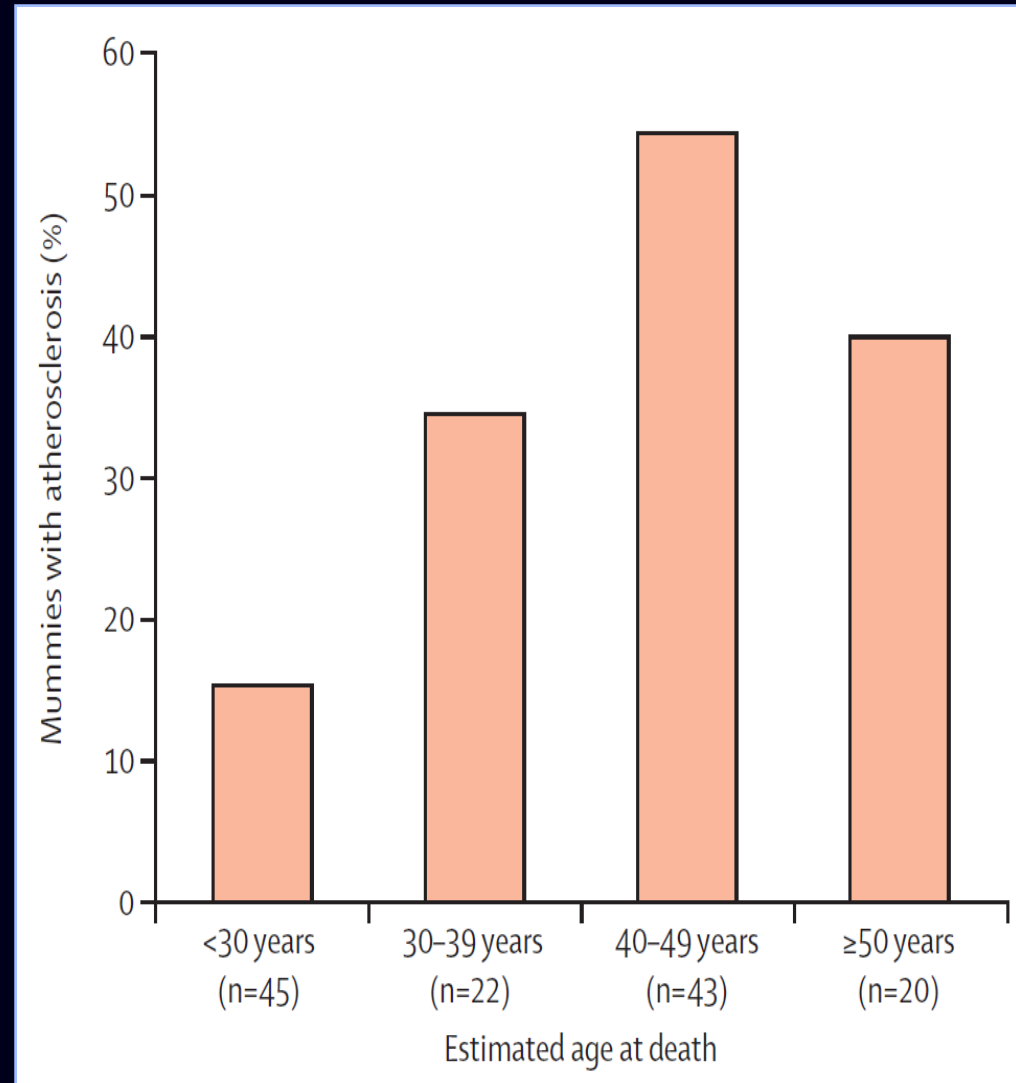
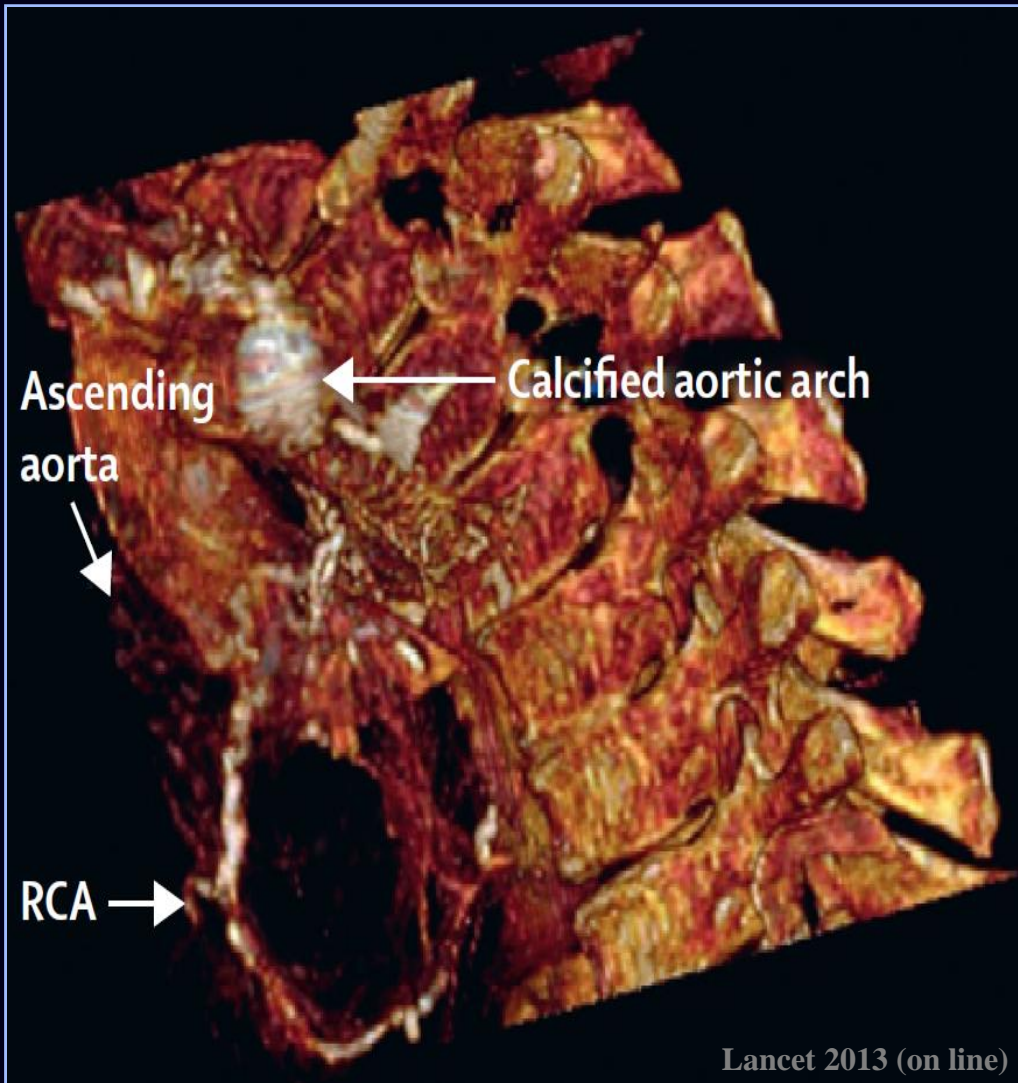
Unnecessary concern!

To E or Not to E



A dietary intervention that reduced total fat intake and increased intakes of vegetables, fruits, and grains did not significantly reduce the risk of CHD, stroke, CVD or breast, colorectal cancer in postmenopausal women (**no beneficial or adverse effects of the dietary changes**)

Atherosclerosis across 4000 years of human history: the Horus study of four ancient populations



Atherosclerosis was noted in 34% of 137 mummies in 4 preindustrial populations, suggesting that it is an inherent component of human ageing & not characteristic of any specific diet or lifestyle.

ECAD (Eliminate Coronary Artery Disease) Trial

■ Objective:

- ◆ To determine whether pharmacologic lowering of serum LDL-C, initiated in healthy middle-aged adults, can “eliminate”, or markedly reduce, all cause mortality, myocardial infarction (MI), or coronary revascularization.

■ Comparison:

- ◆ Standard therapy vs. standard therapy + Lipitor 40 mg daily

■ Target Study Population: 15,000 patients

- Men 35-50 years of age
- Women of non-child bearing potential, 35-59 years of age
- No prior history of CVD
- One additional risk factor (hypertension, family history of premature coronary atherosclerosis, smoking, or diabetes)
- LDL-C from 70 mg/dL (3.9 mmol/L) to the minimum LDL-C for which the current ACC/AHA Guidelines recommend pharmacologic treatment in the presence of a single additional risk factor

■ Primary Endpoint:

- ◆ Composite of death, MI or coronary revascularization

Presentation

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Therapeutic Approach



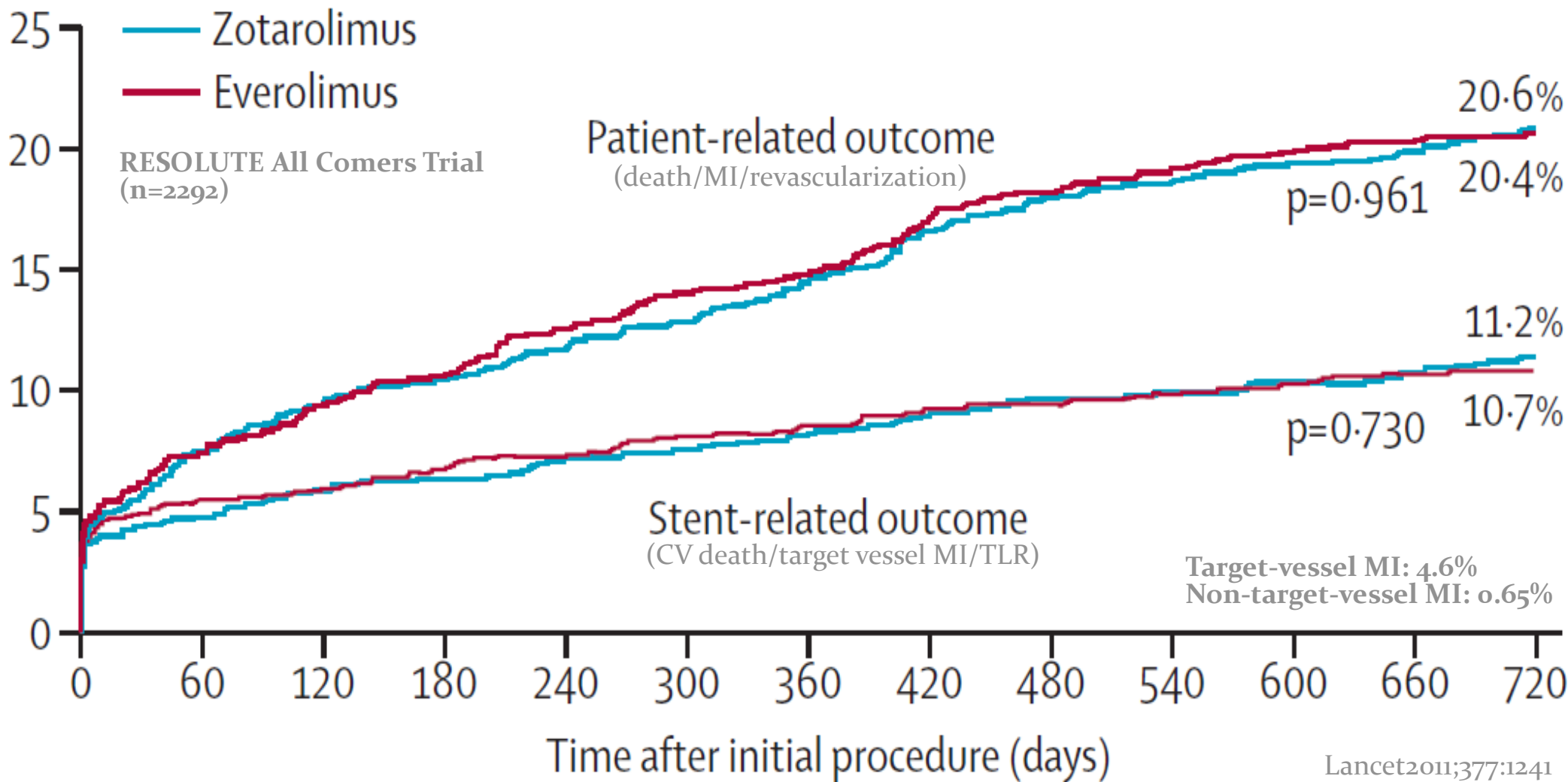
Revascularization
- stenting/bypass surgery



Infarct prevention
- medical treatment

The misconception: Coronary intervention of a coronary stenosis is "prevent an impending heart attack"

PCI/CABG I Fixed You?

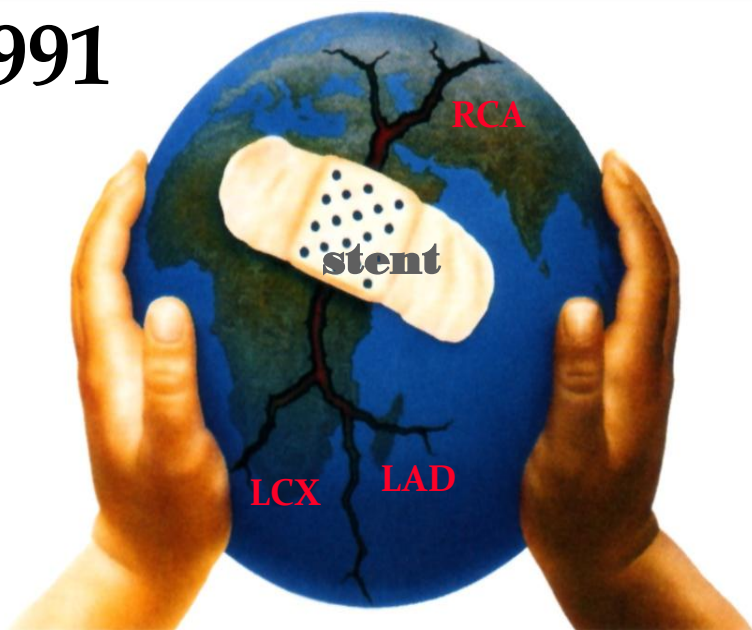


...the only proven medicine

How to Beat It?

MICHAEL JACKSON

1991



JUST BEAT IT!

Just Statin It!
Disease-Based Approach



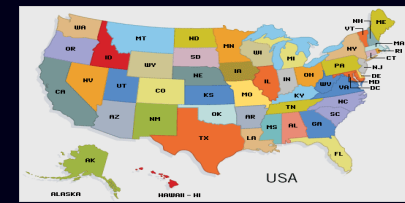
PREVENTION

The "MacStatin": Fast food with some ketchup, salt, and a statin to go

2 COMMENTS - AUG 13, 2010 16:30 EDT

They say it's a cheeky, mischievous

United Stain of America?



THE WALL STREET JOURNAL.
WSJ.com

JANUARY 23, 2012

Should Healthy People Take Cholesterol Drugs to Prevent Heart Disease?

Statin Nation

Facts on statin use
in the U.S. for 2009*

36 million

Number of Americans
who obtained prescriptions
for statin drugs

210.4 million

Total number of
statin prescriptions

\$17.1 billion

Total spending
on statin drugs

\$474

Annual spending for
statins for every person who
purchased at least one

\$81.37

The average prescription
cost of a statin drug

*The latest data available
Source: Agency for Healthcare Research
and Quality, Department of Health
and Human Services

Yes: They Save Lives

By Roger S. Blumenthal

Trials have shown reductions
in cardiovascular events of
30~40% with the use of a statin.

No: Harms Outweigh Benefits

By Rita Redberg

For most healthy people,
the data show that statins
do not prevent heart disease.

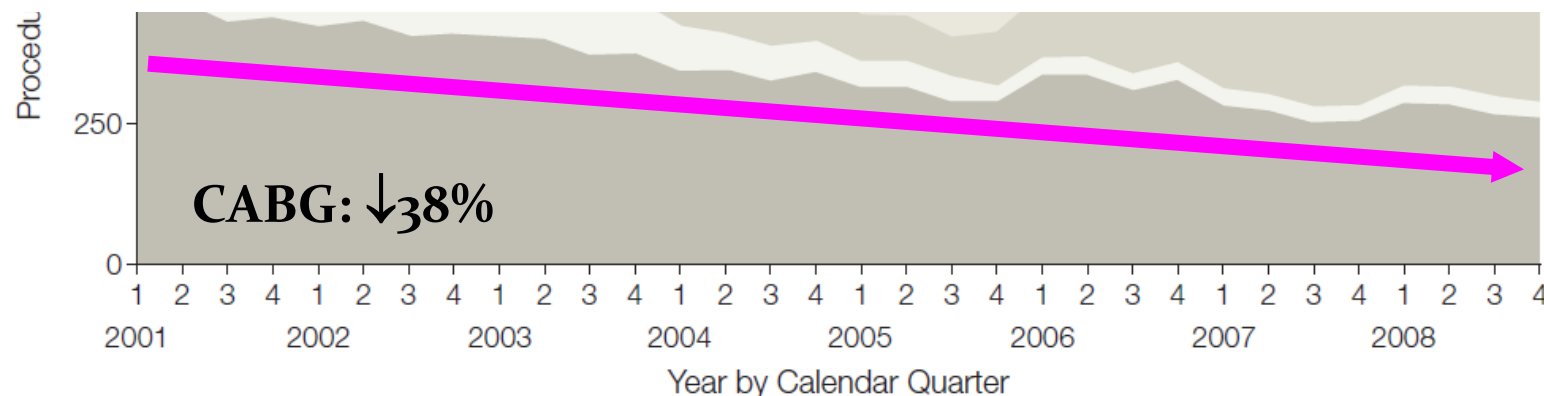
Trends in the USA: CABG Down, PCI Stable

흉부외과 어떻게 살릴 것인가? / 안혁 (대한흉부외과학회 이사장, 서울의대 흉부외과학)



젊은 의사들이 외과계열을 기피하는 현상이 십여 년 이상 지속되어온 상황에서 흉부심장혈관 환자들의 관리는 이미 크나큰 문제점으로 대두되어왔다. 이대로 가다가는 우리 국민들의 심장수술이나 폐수술을 해야 할 의사가 부족하여 외국인들을 초빙해야 할지도 모른다는 극단적인 위기의식까지 팽배되었다. 이러한 문제점에 대한 해결책으로 재작년 정부에서는 외과계열(흉부외과와 외과)의 수가를 인상해주는 획기적인 조치를 취하였음에도 불구하고 금년도 흉부외과 전공의의 지원율은 30% 정도에 머물고 있는 실정이다. 어떠한 해결책이 있는지 학회로서는 머리를 싸매고 고민 중이며 관계당국에 여러 가지로 협조를 구하는 바이다.

재작년 7월 이후 흉부외과 수가 100% 보전조치이후 전국의 흉부외과 전공의와 전문의들은 파격적인 처우 개선이 이루어질 것으로 기대했었다. 그러나 2년 가까이 시행되어온 수가 100% 인상 및 보전 조치의 혜택은 수도권의



My Personal Note

← ... born to love statin

People start life with clean arteries,
live with atherosclerosis and
die of acute vascular events.

감사합니다.