

New Approaches to Prevent Heart Disease In Women

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Disclosures

- **Research grants:** Ionis Pharma, Servier Canada, NIH, CIHR, HSFC
- **Industry relations:** Sanofi, Amgen, Ionis, Servier, Boehringer-Ingelheim, Novartis, Silence



Learning Objectives


1. Demonstrate the relationship between early risk factors and cardiovascular disease in women
2. Identify strategies for early primary prevention in women
3. Role of advanced lipoprotein testing (apoB, Lp(a)) in determining cardiovascular risk



Case



Lisa

- 50 years old, non-smoker
 - 2 children, pre-eclampsia with 2nd pregnancy
 - BMI = 28 kg/m²
 - BP 135/80 mm Hg
 - No diabetes
 - Total cholesterol = 6.4 mmol/L
 - HDL cholesterol = 1.2 mmol/L
 - TG = 1.7 mmol/L
 - LDL-C = 4.5 mmol/L
- 

Lisa

Risk Factor	Risk Points			
	Men		Women	
Age				
30-34	0		0	
35-39	2		2	
40-44	5		4	
45-49	7		5	
50-54	8		7	
55-59	10		8	
60-64	11		9	
65-69	12		10	
70-74	14		11	
75+	15		12	
HDL-C (mmol/L)				
>1.6	-2		-2	
1.3-1.6	-1		-1	
1.2-1.29	0		0	
0.9-1.19	1		1	
<0.9	2		2	
Total Cholesterol				
<4.1	0		0	
4.1-5.19	1		1	
5.2-6.19	2		3	
6.2-7.2	3		4	
>7.2	4		5	
Systolic Blood Pressure (mmHg)				
	Not Treated	Treated	Not Treated	Treated
<120	-2	0	-3	-1
120-129	0	2	0	2
130-139	1	3	1	3
140-149	2	4	2	5
150-159	2	4	4	6
160+	3	5	5	7
Smoker	Yes	4		3
	No	0		0
Diabetes	Yes	statin-indicated condition		
	No	0		0
Total Points				

50 F

BMI = 26 kg/m²

BP 135/80 mm Hg

No diabetes

Total cholesterol = 6.4 mmol/L

HDL cholesterol = 1.2 mmol/L

TG = 1.7 mmol/L

What's her risk?

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Smoker	Yes	4	3	
	No	0	0	
Diabetes	Yes	statin-indicated condition		
	No	0	0	
Total Points				

50 F, prior pre-eclampsia

BMI = 28 kg/m²

BP 135/80 mm Hg

No diabetes

Total cholesterol = 6.4 mmol/L

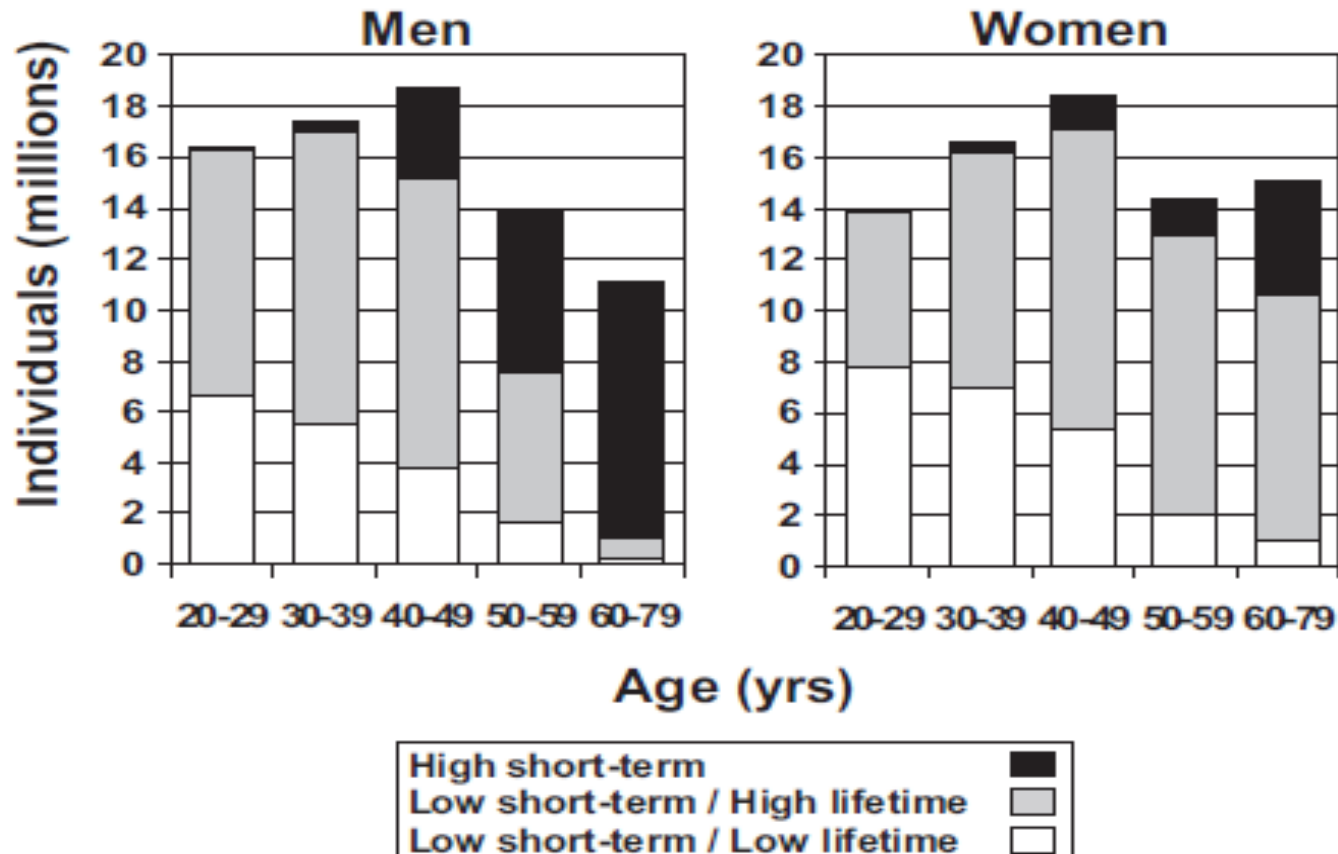
HDL cholesterol = 1.2 mmol/L

TG = 1.7 mmol/L

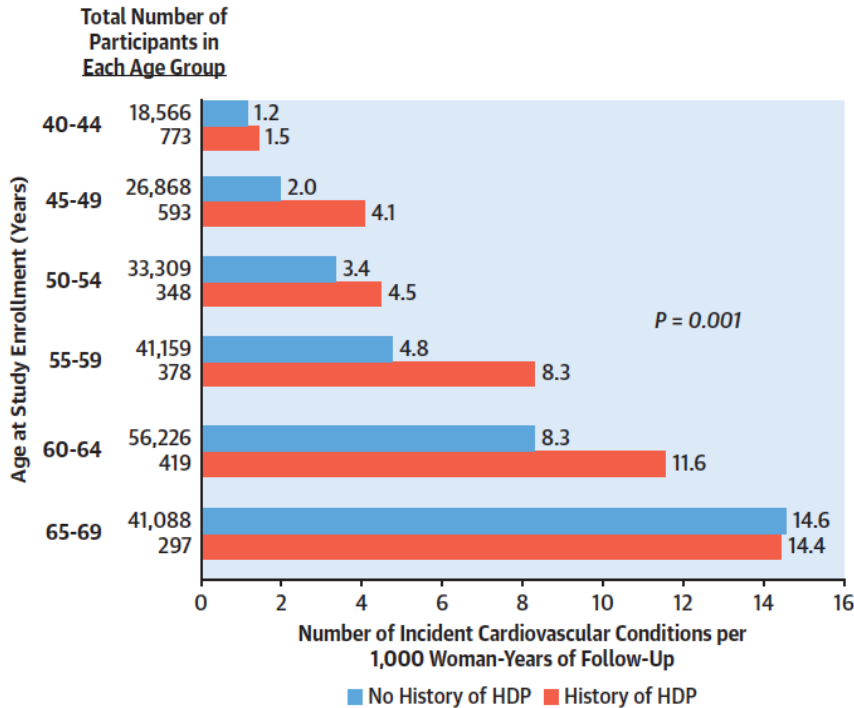
What's her risk?

11 pts = 7% risk of CV event in 10 years
(low risk)

Low Short-term but High Lifetime Risk



What are we missing?

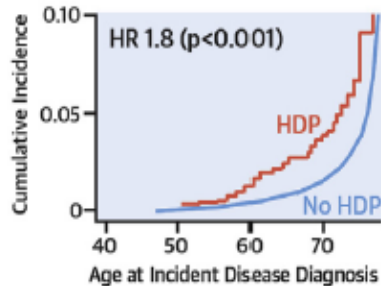
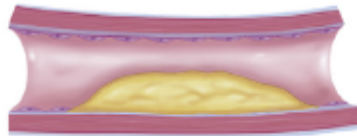


Cardiovascular Condition	HR	95% CI	P-Value
Coronary artery disease	1.8	1.3-2.6	<0.001
Heart failure	1.7	1.04-2.6	0.03
Aortic stenosis	2.9	1.5-5.4	<0.001
Mitral regurgitation	5.0	1.5-17.1	0.01
Atrial fibrillation	1.1	0.8-1.6	0.56
Ischemic stroke	0.8	0.4-1.8	0.57
Peripheral artery disease	1.0	0.4-2.3	0.94
Venous thromboembolism	1.0	0.6-1.7	0.97

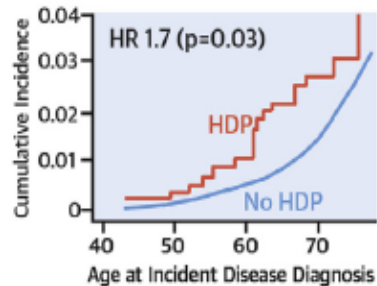
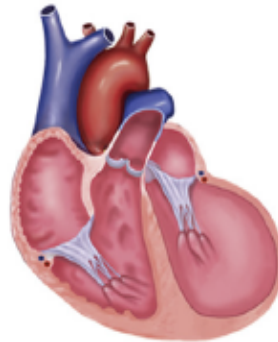
Honigsberg M et al JACC 2020

What are we missing?

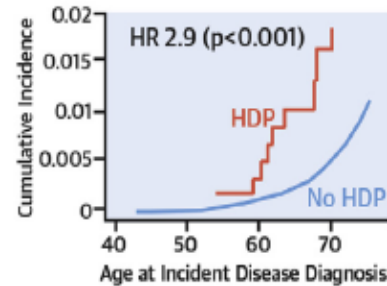
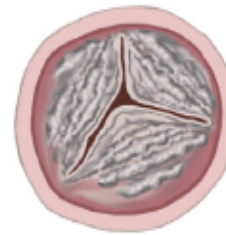
Coronary Artery Disease



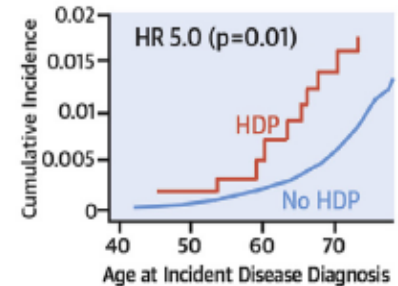
Heart Failure



Aortic Stenosis



Mitral Regurgitation




Honigberg, M.C. et al. *J Am Coll Cardiol.* 2019;74(22):2743-54.


What (else) are we missing?



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 - ApoB = 1.3, Lp(a) = 75 mg/dL
- 

Low Short-term but High Lifetime Risk

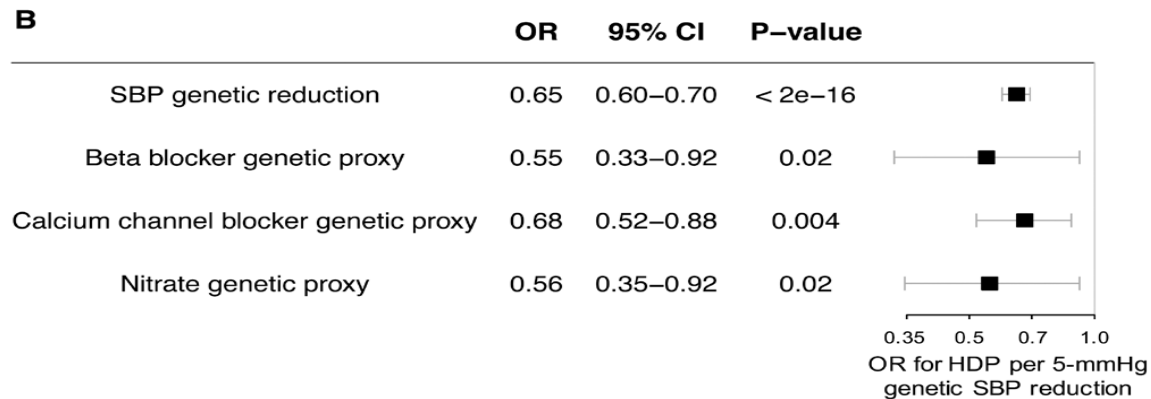
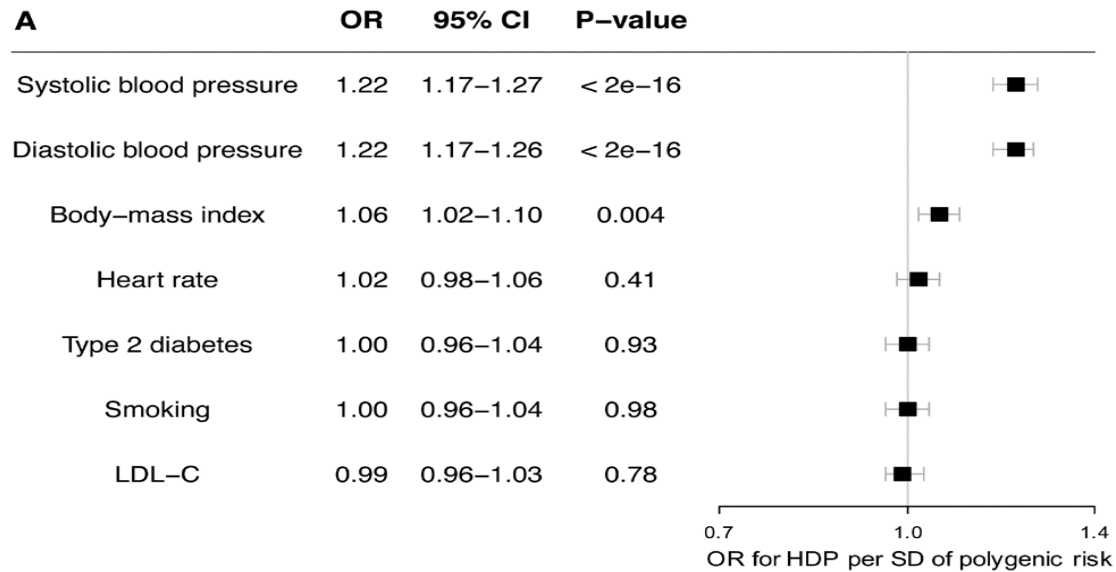
- A large proportion have low short-term BUT high lifetime risk, but what can we do?
 - Identify high risk women
 - HTN disorders of pregnancy, lipoprotein testing, etc
 - Improve CV risk models for women
 - Counselling with focus on **lifestyle change**
 - Target optimal risk factors
 - Consider **EARLY** preventative treatment?



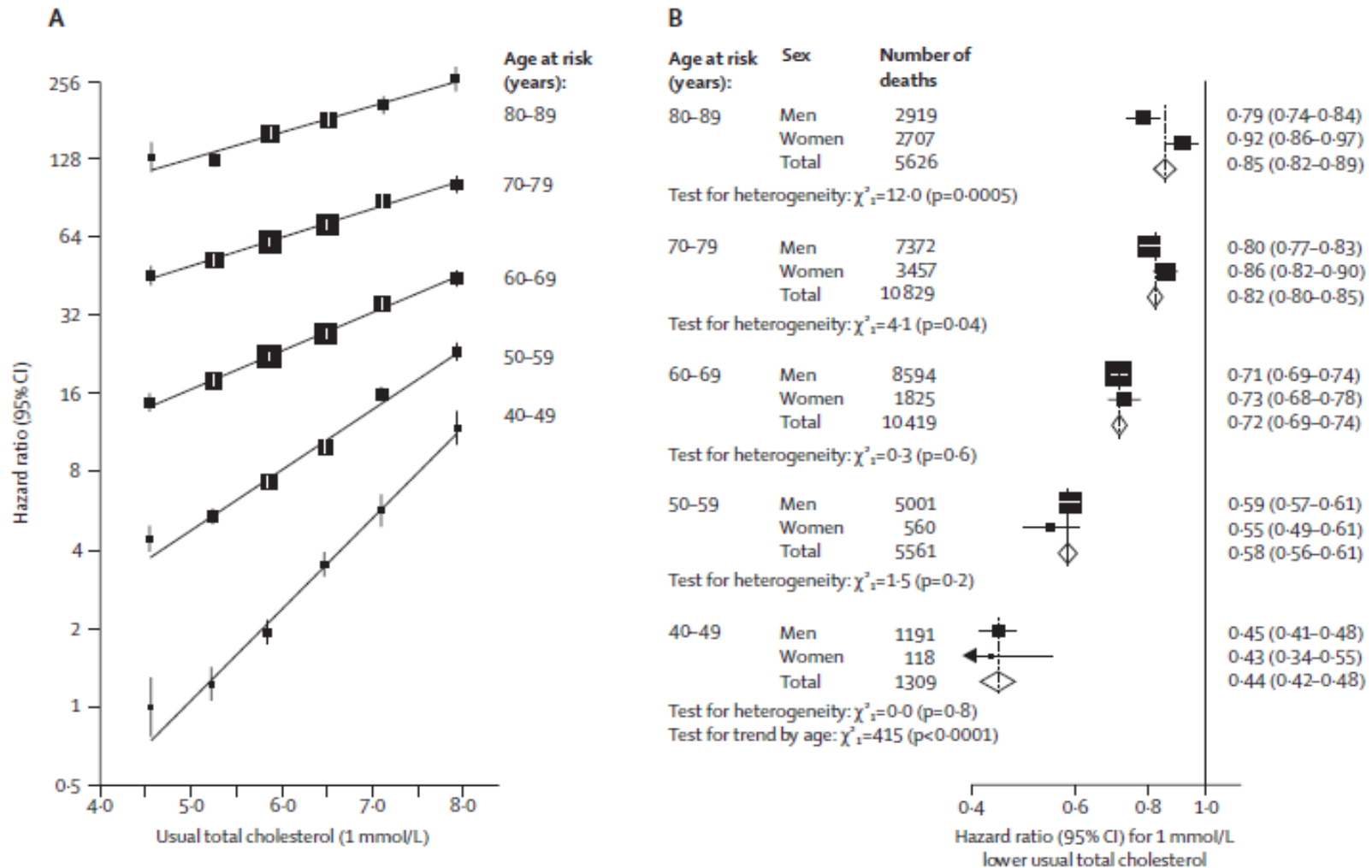
Early preventative treatment?



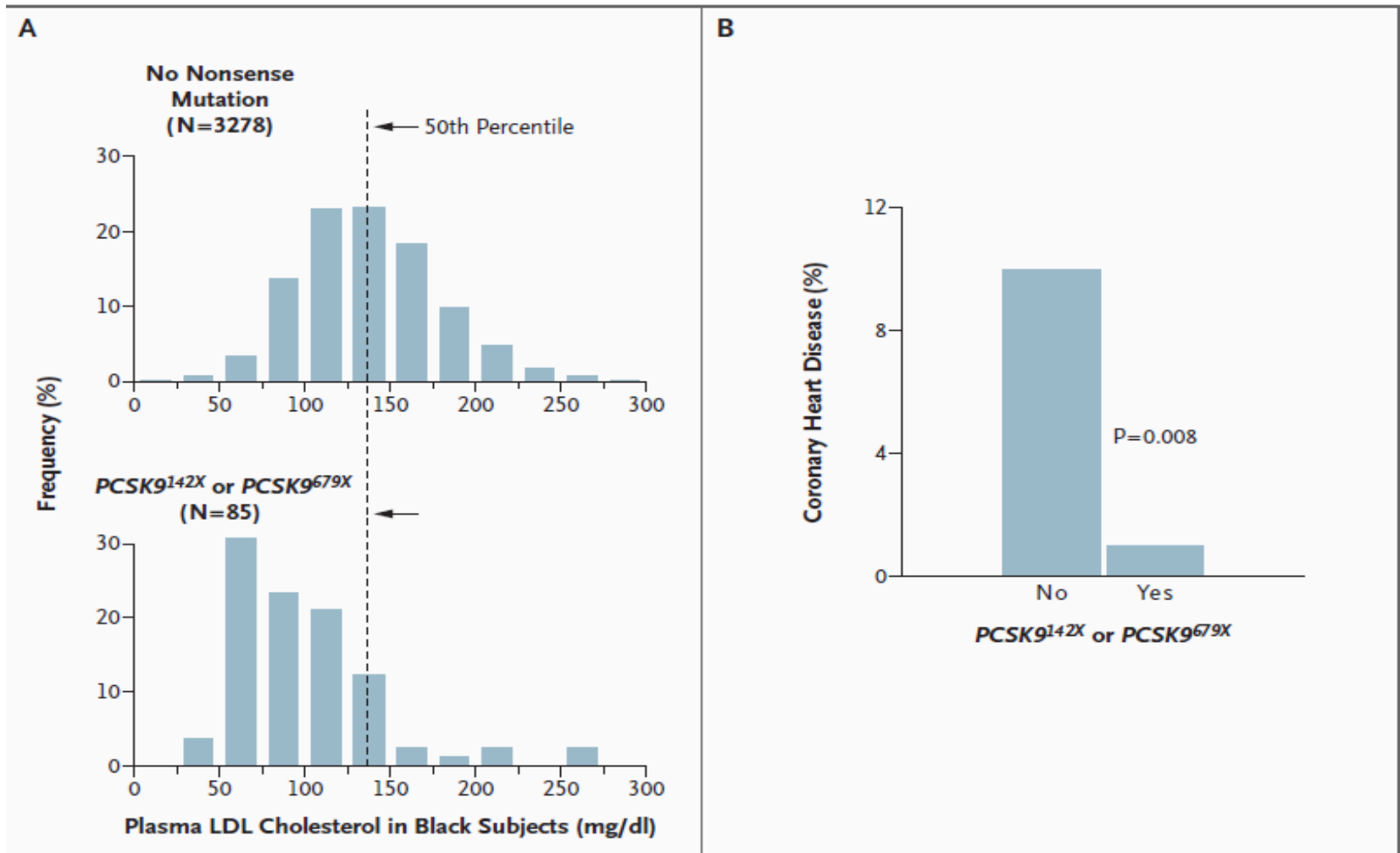
EARLY hypertension treatment?



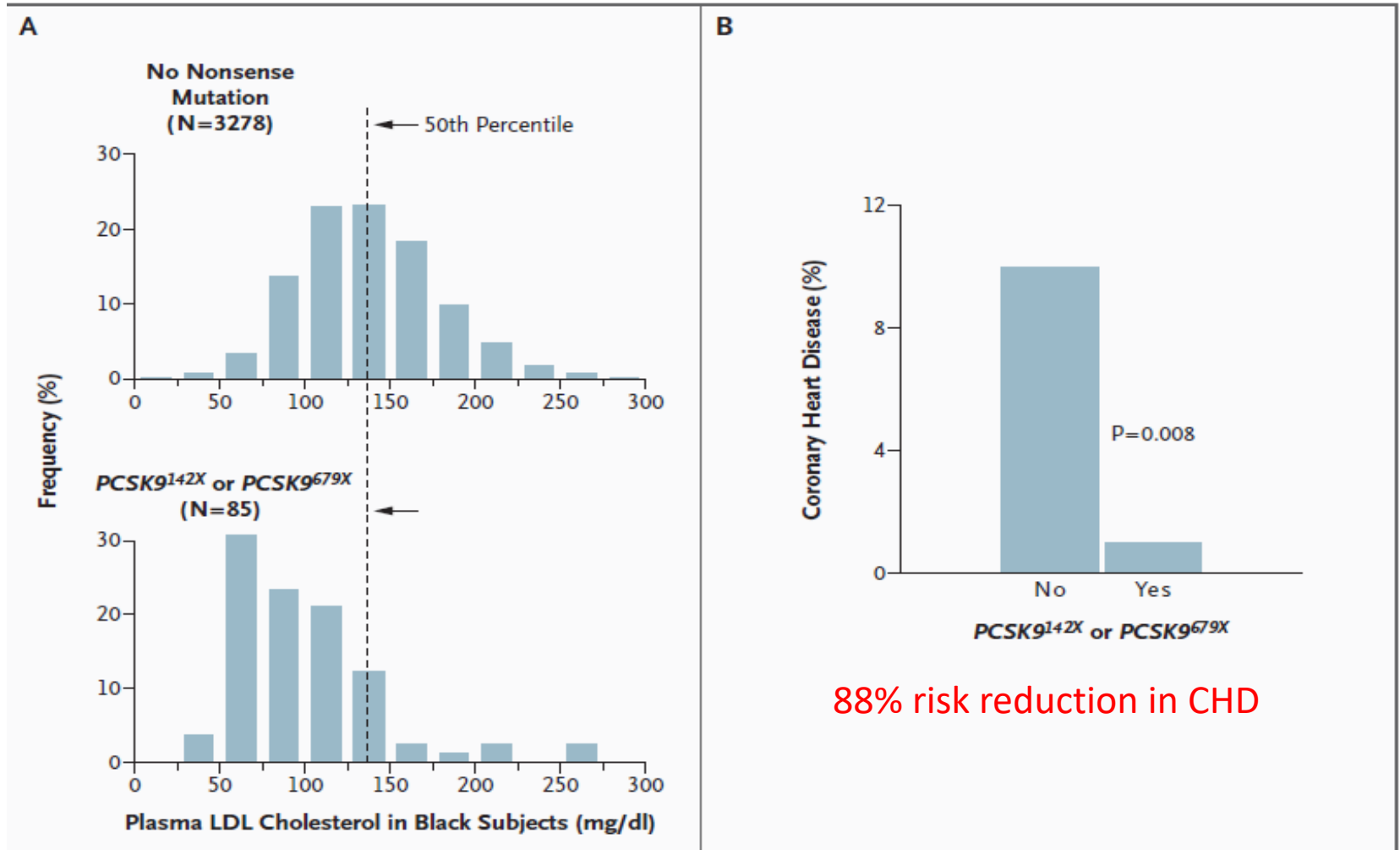
EARLY cholesterol treatment?



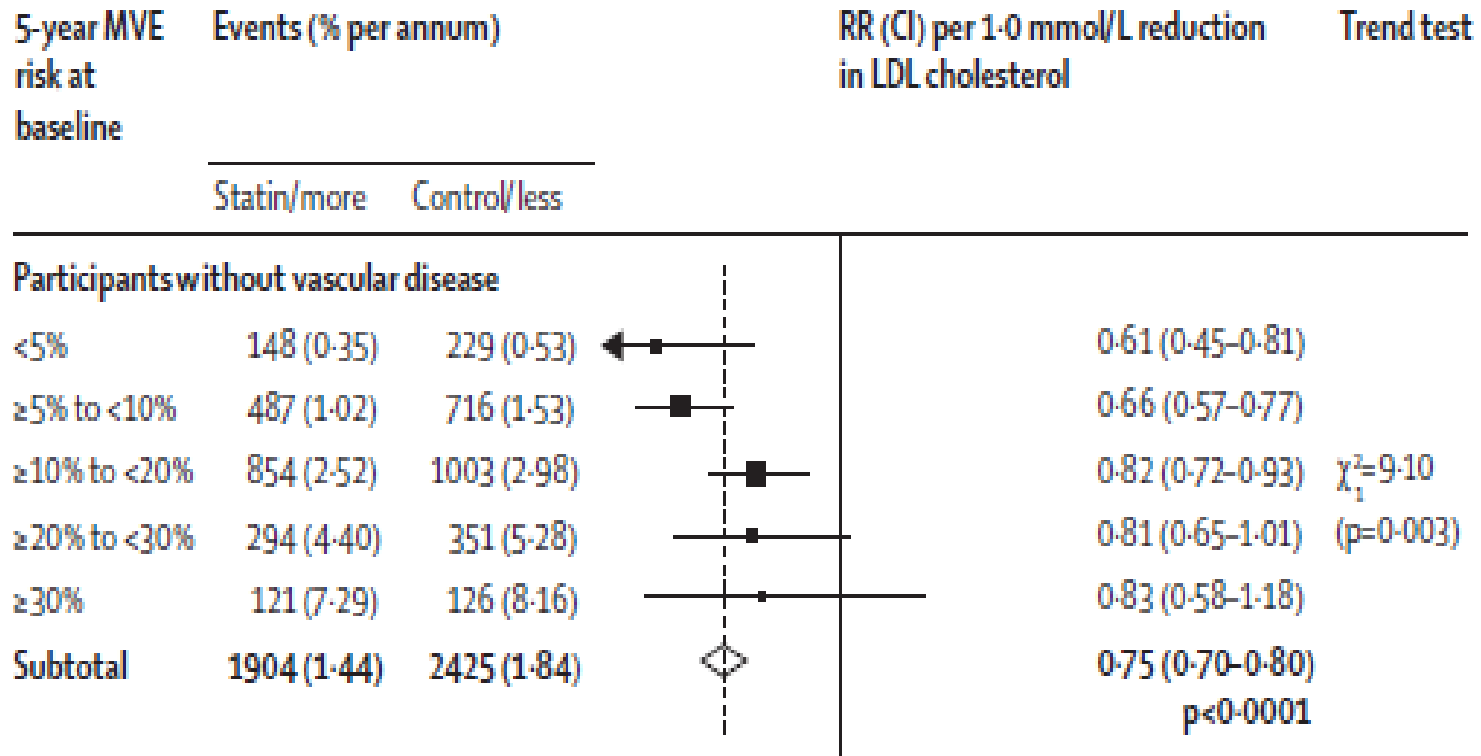
Life-long lipids and Risk of CHD



Life-long lipids and Risk of CHD



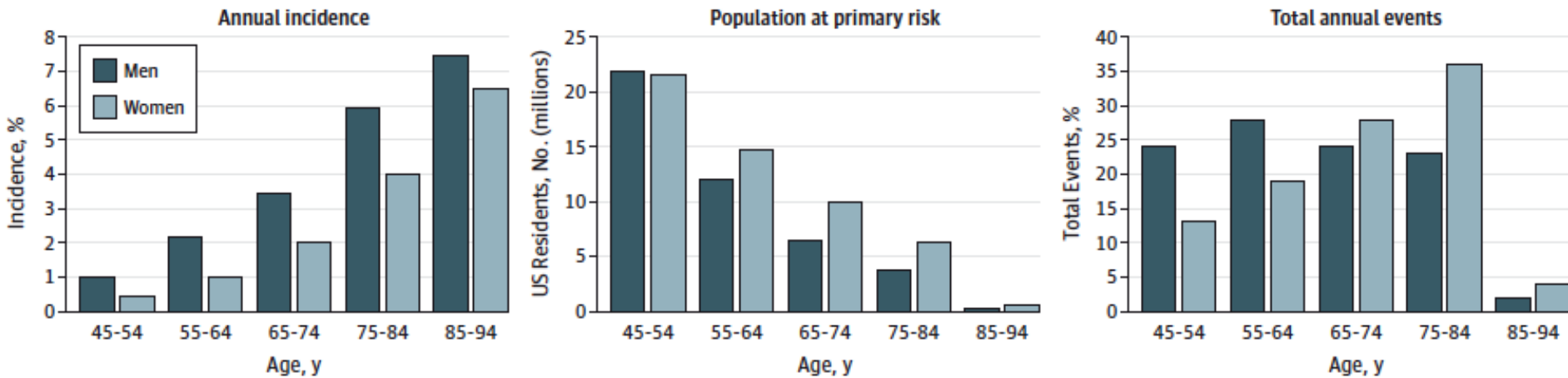
Cholesterol Treatment Trialists



CTT collaboration *Lancet* 2010

Earlier is better

Figure. Event Rates, Population at Risk, and Event Numbers by Sex and Age Groups



A, Average primary annual incidence rates of coronary heart disease, heart failure, stroke, or intermittent claudication. B, Numbers of US residents without clinical atherosclerotic cardiovascular disease represented in the 2005-2010 National Health and Nutrition Examination Survey. C, Percentage of the expected total of 930 621 annual primary events in men and 702 105 in women by age group.

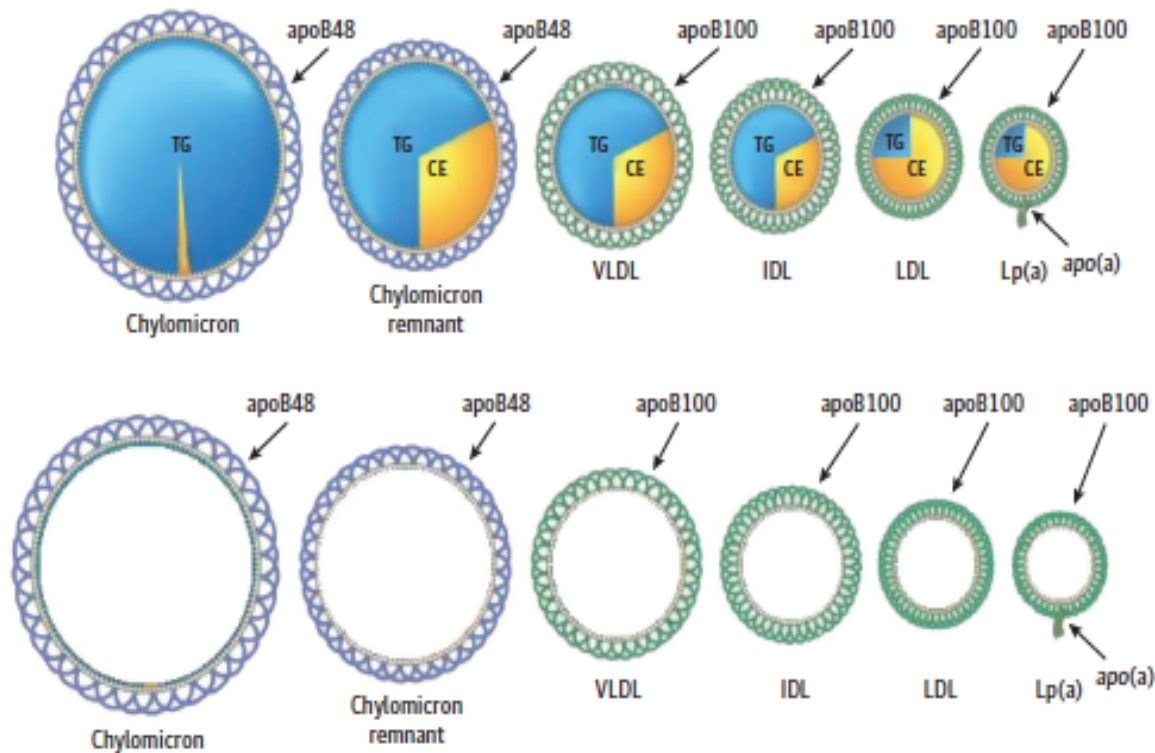
1 in 2 CV events in men and 1 in 3 CV events in women occur before 65 years of age.

apolipoprotein B



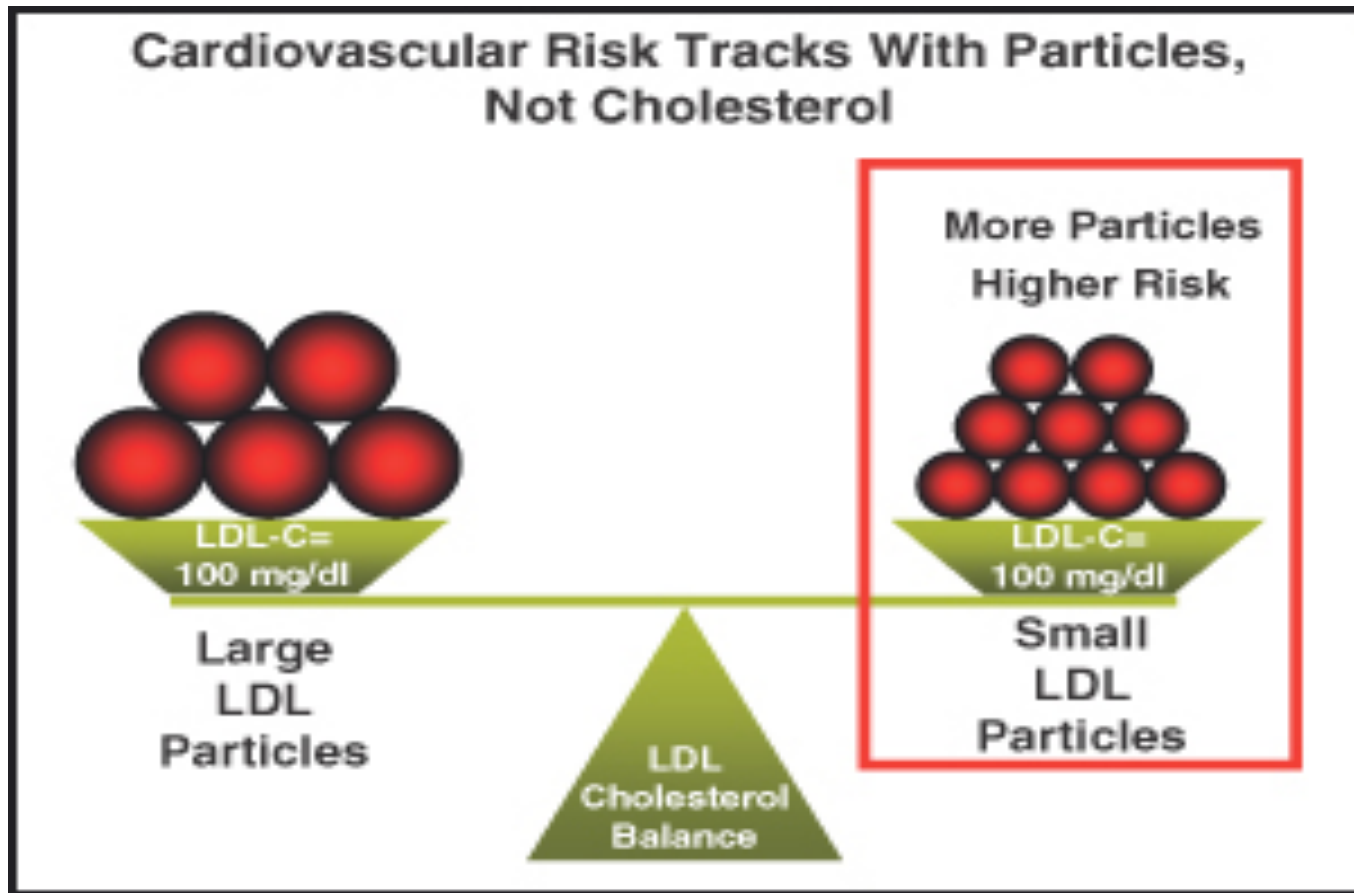
ApoB

Figure 1. Apolipoprotein B48 and B100 Lipoprotein Particles

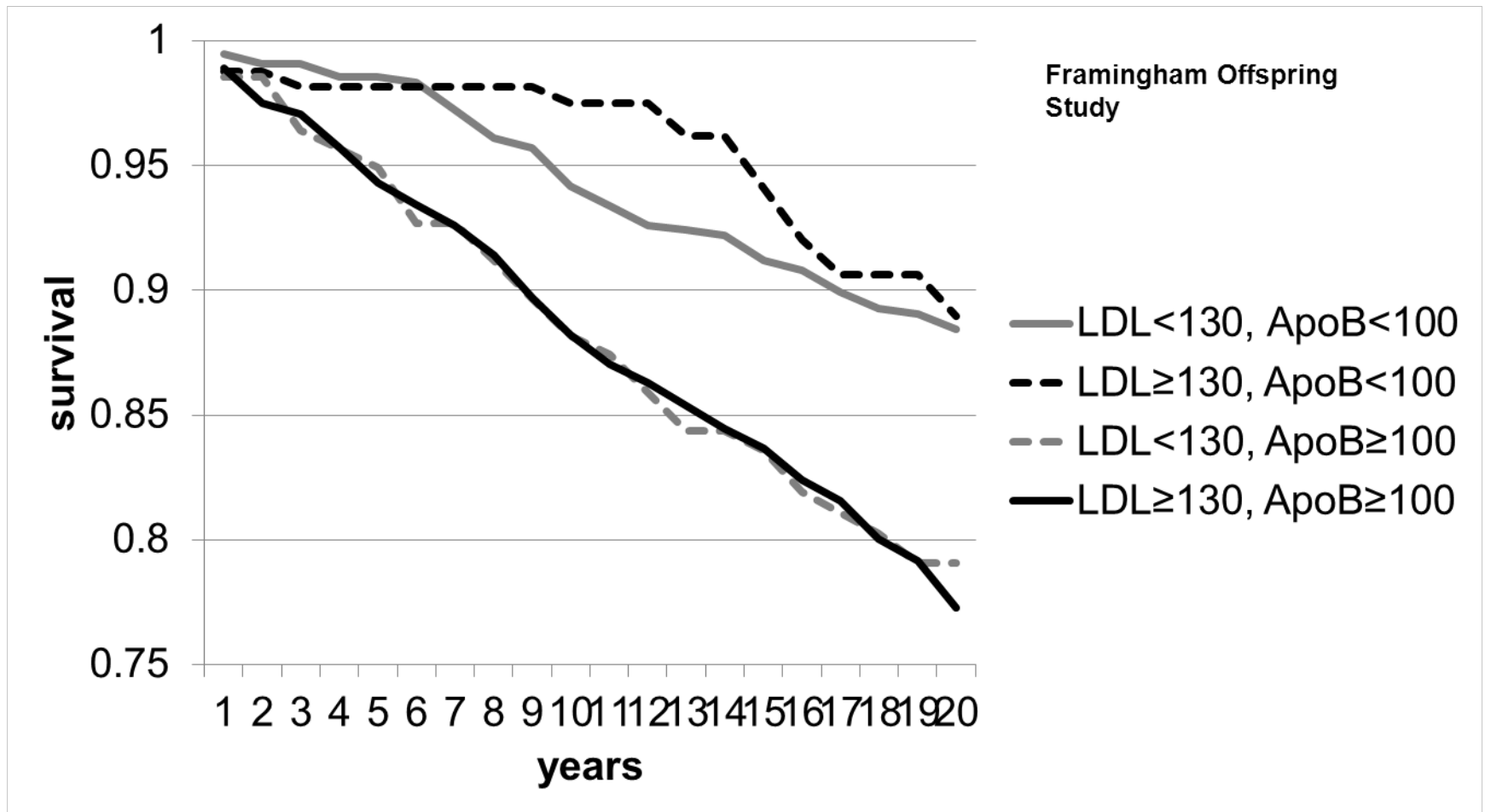


1 apoB molecule = 1 lipid particle.
Therefore, apoB plasma concentration = total number of atherogenic lipid particles. apo indicates apolipoprotein; CE, cholesterol ester; IDL, intermediate-density lipoprotein; LDL, low-density lipoprotein; Lp(a), lipoprotein(a); TG, triglyceride; VLDL, very low-density lipoprotein.

High apoB = danger



Risk tracks ApoB - always



Lipoprotein(a)?

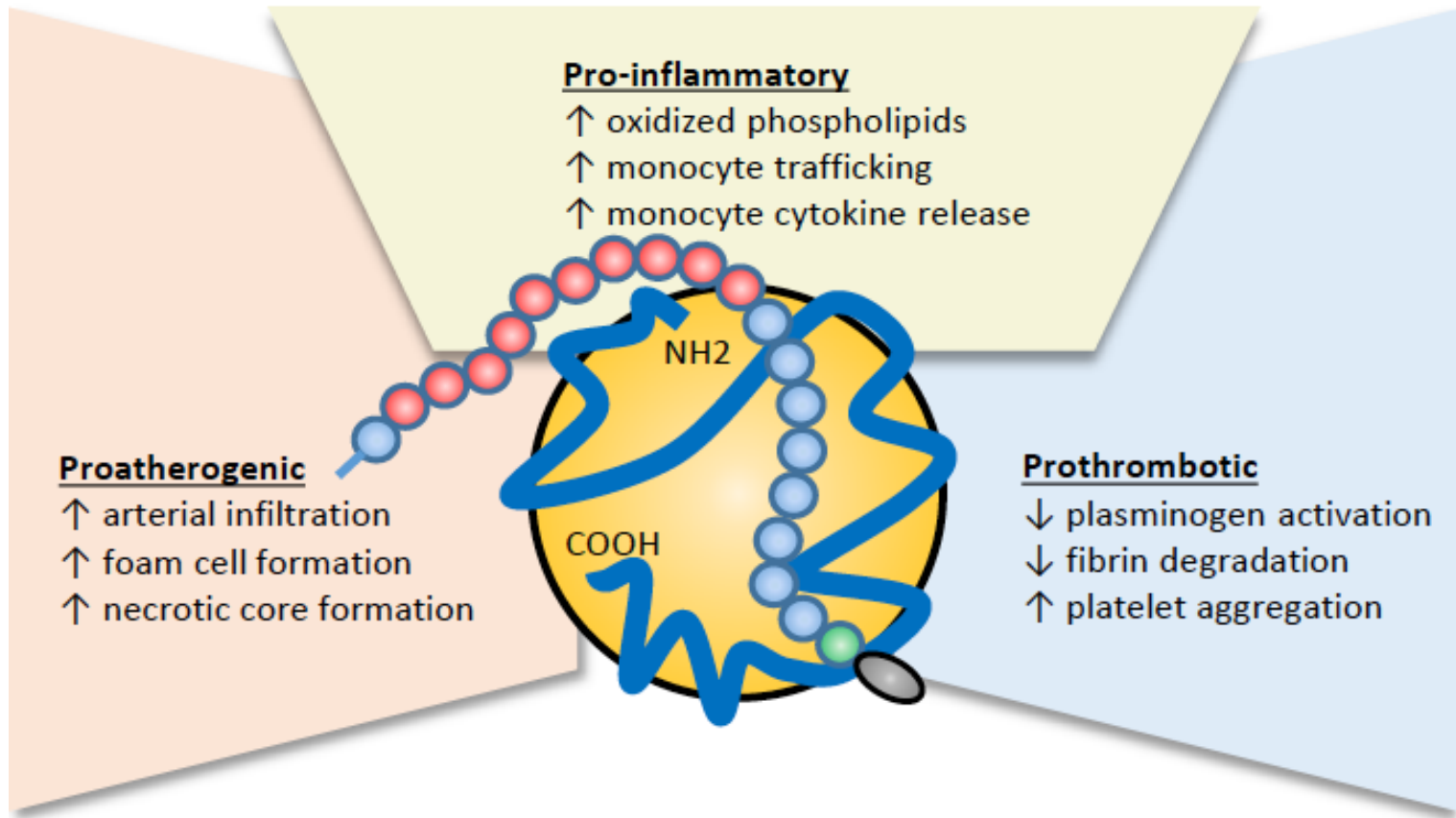


What is Lp(a)?

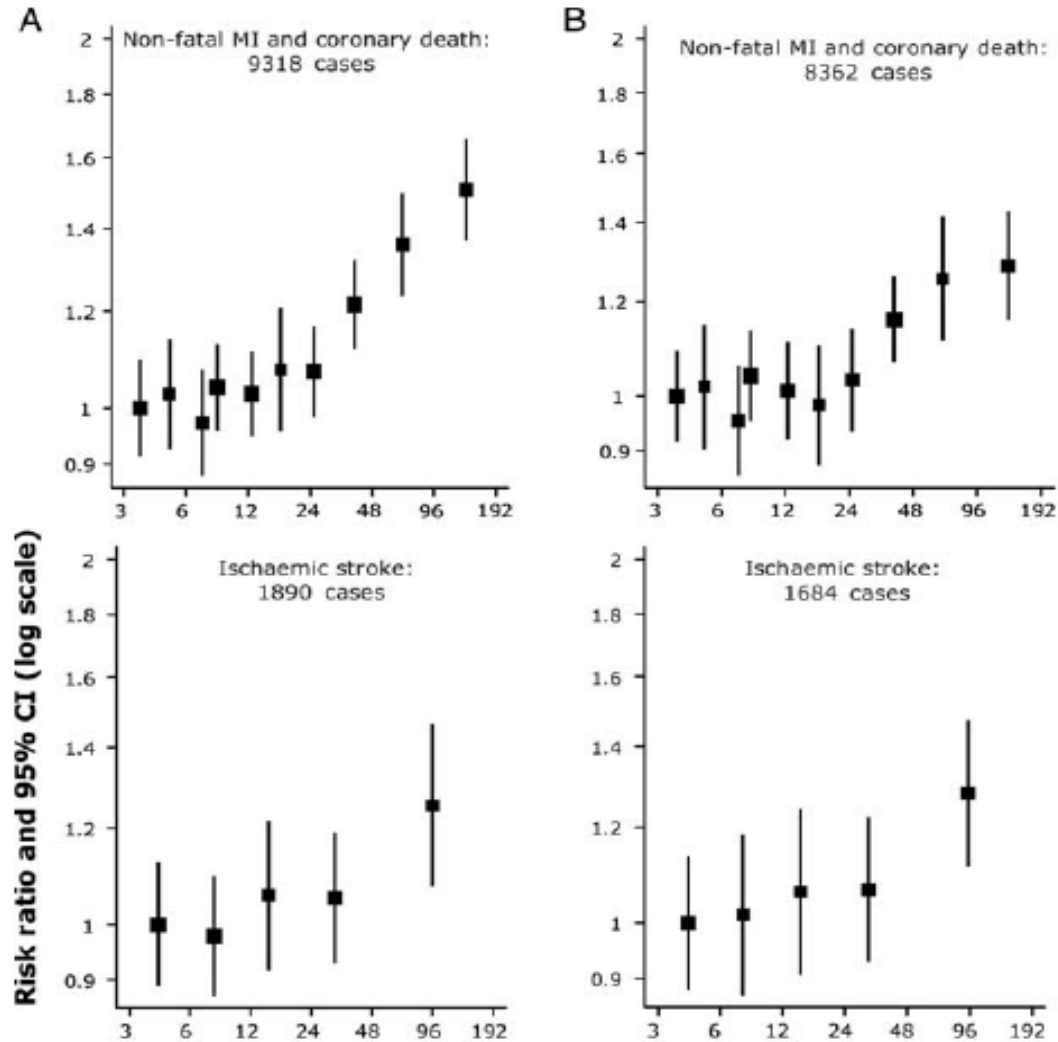
- ApoB+apo(a) → Lp(a)
- Lp(a) levels are almost entirely mediated by genetics
- Highly atherogenic, pro-calcific
- Most common genetic dyslipidemia
 - 6 million Canadians have high Lp(a)



What is Lp(a)?



Lp(a) is atherogenic



Who should I screen for Lp(a)?

In whom to measure Lp(a)

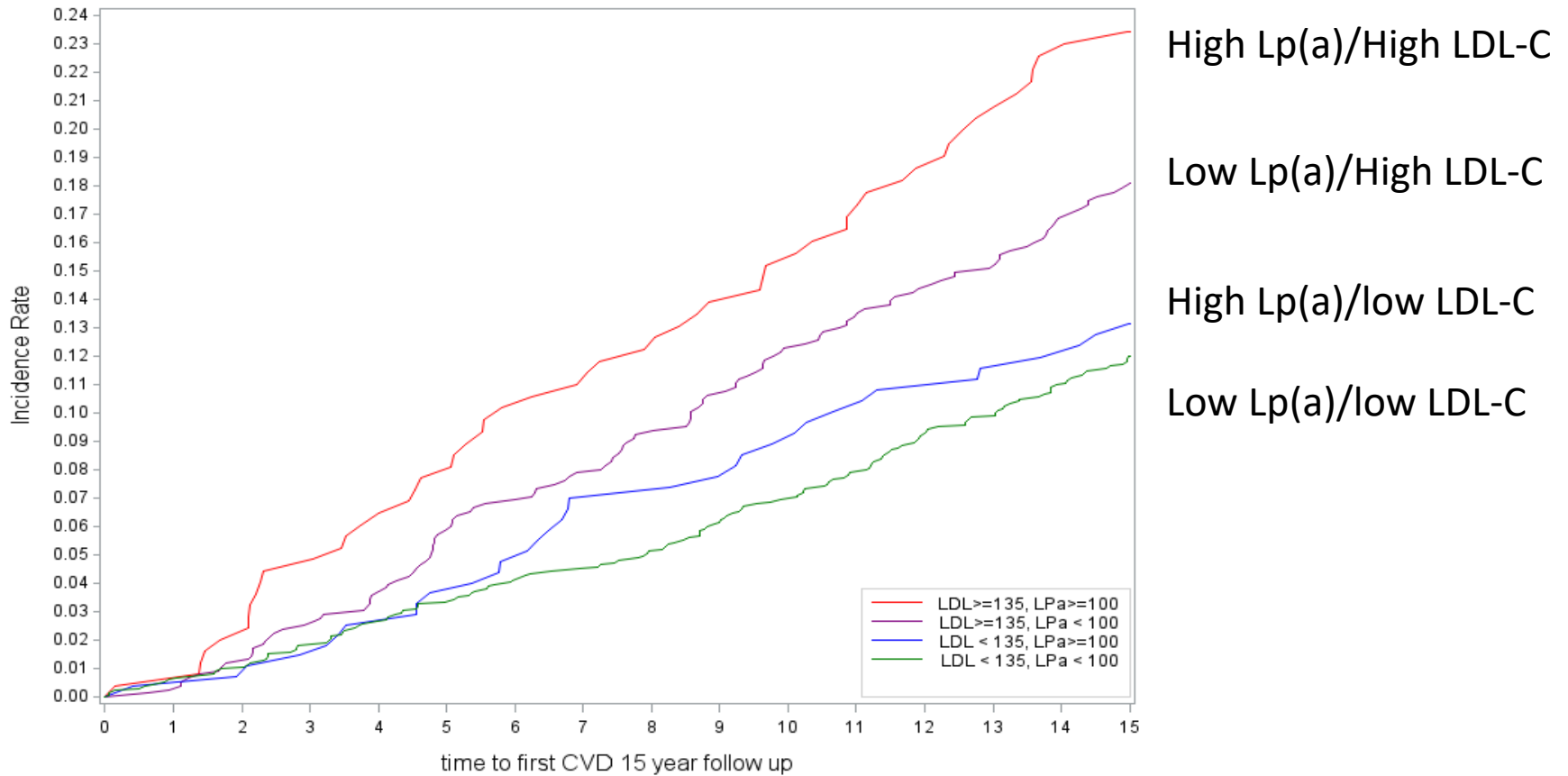
1. Personal or family history of premature atherosclerotic CVD
2. If first-degree relative has raised Lp(a) levels (>200 nmol/l)
3. Familial hypercholesterolemia
4. Calcific aortic valve stenosis
5. Borderline increased (but $<15\%$) 10-year risk of a cardiovascular event

What to do?


Treatment approaches for raised Lp(a)

1. Reducing overall atherosclerotic risk
2. Controlling dyslipidemia with a desirable non-HDL-cholesterol level of <100 mg/dl (2.5 mmol/l)
3. Consideration of lipoprotein apheresis

Lower LDL-C can reduce risk when Lp(a) is high




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- 

What's her REAL risk?

What's the REAL benefit?

- 7% risk at 10-year (probably **2 x**)
 - Atorvastatin 40 mg -> LDL-C from 4.5 to 2.7 mmol/L
 - $ARR = 15\% \times (0.66)^{1.8} = 7\%$
 - $NNT = 1/ARR =$ we need to treat 14 patients over 10 years to prevent 1 event

 - What about for 30 years?
- 

How much benefit?

Research

JAMA Cardiology | **Original Investigation**

A Long-term Benefit Approach vs Standard Risk-Based Approaches for Statin Eligibility in Primary Prevention

George Thanassoulis, MD, MSc, FRCPC; Allan D. Sniderman, MD; Michael J. Pencina, PhD

CONCLUSIONS AND RELEVANCE A long-term benefit approach to statin eligibility identifies nearly 1 in 6 individuals as having a high degree of expected long-term benefit of statins, with a number needed to treat of less than 7. This approach identifies younger individuals with higher LDL-C levels who would not be currently recommended for treatment and may provide a more optimal approach for determining statin eligibility in primary prevention.

Summary

- CV risk in women is frequently underestimated
 - High lifetime risk despite not eligible for statins
- Need to better assess all sources of CV risk
 - Hypertension disorders of pregnancy
 - Lipoproteins
- Emphasize lifestyle change in early life but consider preventative therapy when potential benefit is high
 - even if estimated risk is “low”

