

Cardiovascular Risk Assessment Across the Lifespan: Too Soon, Too Late, or Just Right?

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Disclosure

Consultant: Amgen; Esperion Therapeutics;
Medtronic (Renal Denervation Program);
Novartis

Speaker Bureau: Esperion Therapeutics



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Learning Objectives

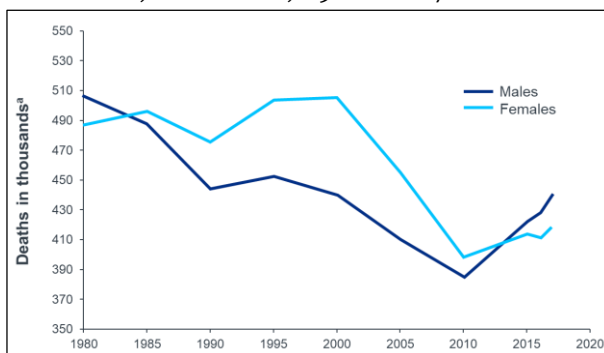
1. To discuss the role of individualized cardiovascular risk assessment to guide primary prevention of ASCVD
2. Describe risk enhancing factors and sex specific ASCVD risk factors
3. Identify tools for cardiovascular risk assessment and shared decision-making for optimal preventive care



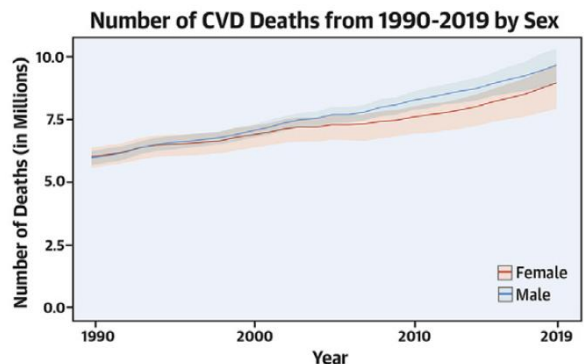
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DEATHS ATTRIBUTABLE TO CVD

US; CDC data; 1980-2017



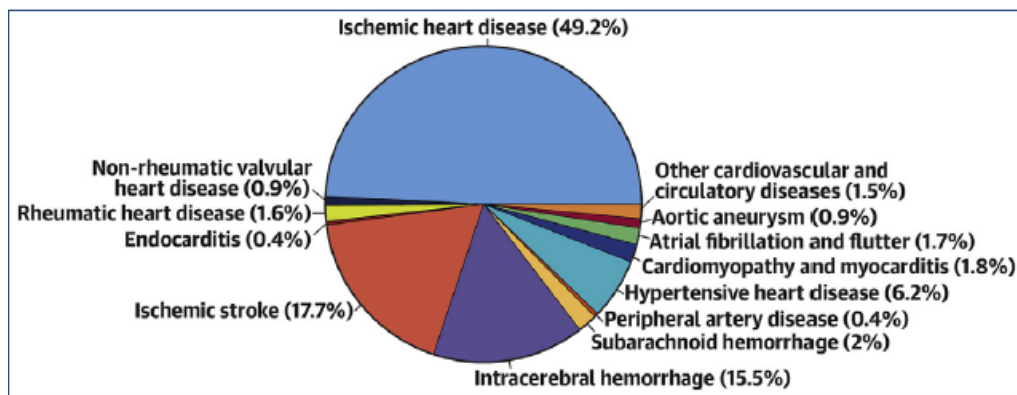
Global Burden



Virani SS, et al., American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee (2020). *Circulation*, 141(9), e139–e596. Roth GA, et al. *J Am Coll Cardiol* 2020;76:2982–3021)

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Global CVD Deaths by Cause, 2019



Roth GA, et al. J Am Coll Cardiol 2020;76:2982–3021

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AHA/ACC SPECIAL REPORT

Use of Risk Assessment Tools to Guide Decision-Making in the Primary Prevention of Atherosclerotic Cardiovascular Disease

A Special Report From the American Heart Association and American College of Cardiology

- *Individualized risk assessment:*
 - Guides shared-decision discussions for evidence-based primary prevention strategies to reduce CVD
 - Educates patients about their CVD risk
 - Assists with risk/benefit discussion of pharmacotherapy
 - Can motivate patients to adhere to risk-reduction therapies

Lloyd-Jones DM, et al. *Circulation*. 2019;139:e1162–e1177

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Evolution of CVD Risk Assessment

Article | 1 July 1961

Factors of Risk in the Development of Coronary Heart Disease—Six-Year Follow-up Experience

The Framingham Study

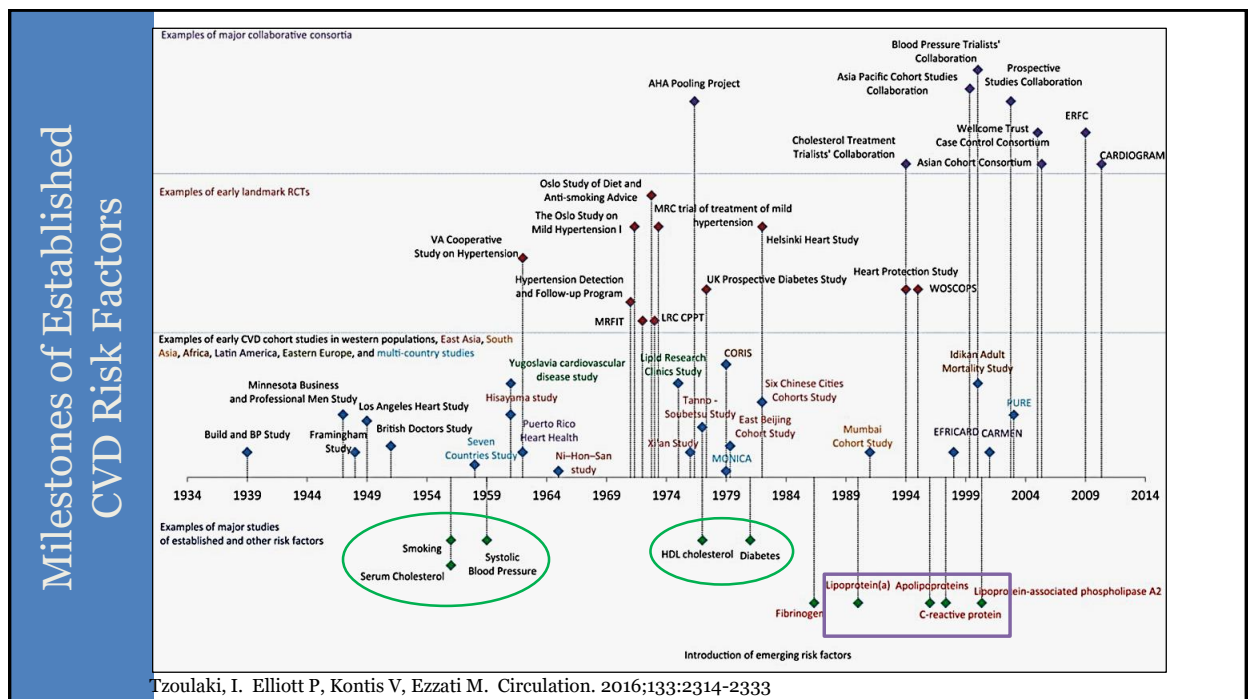
WILLIAM B. KANNEL, M.D., THOMAS R. DAWBER, M.D., F.A.C.P., ABRAHAM KAGAN, M.D., F.A.C.P.,

NICHOLAS REVOTSKIE, M.D., JOSEPH STOKES III, M.D. See Less

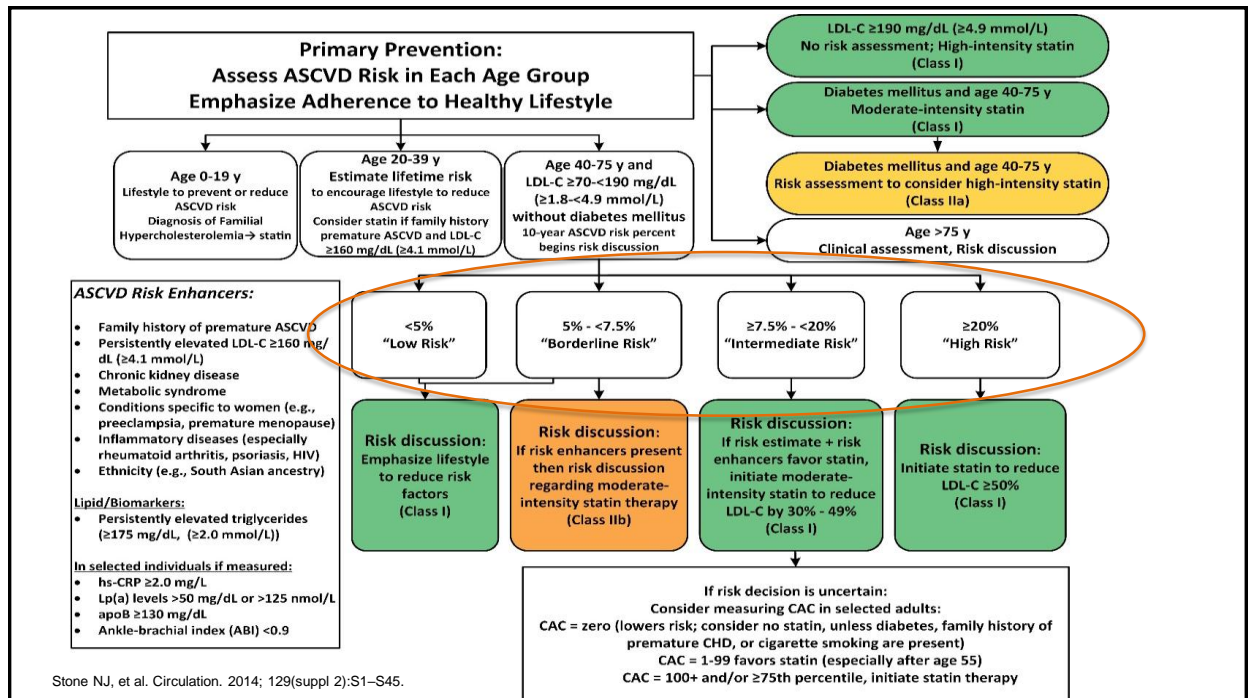
1. Intensity of treatment should match a person's CVD risk
2. Clinician's personal estimate usually underestimates risk
3. CVD risk assessment improves the use of guideline therapy

Kannel WB, et al. Annals of Internal Medicine; July 1961;55:33-50; Grundy SM, et al. Circulation. 1999;100:1481-1492

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10-year & Lifetime ASCVD Risk Assessment

ASCVD Risk Estimator Plus

Estimate Risk **Therapy**

0.9% **Current 10-Year ASCVD Risk** Low

Lifetime ASCVD Risk: 39% **Optimal ASCVD Risk: 0.4%**

Current Age Age must be between 20-79

Sex ☐ Male ☒ Female

Race ☒ White ☐ African American ☐ Other

Systolic Blood Pressure (mm Hg) Value must be between 90-200

Diastolic Blood Pressure (mm Hg) Value must be between 60-130

Total Cholesterol (mg/dL) Value must be between 130 - 320

HDL Cholesterol (mg/dL) Value must be between 20 - 100

LDL Cholesterol (mg/dL) Value must be between 30-300

History of Diabetes? ☐ Yes ☒ No

Smoker? ☐ Current ☒ Former ☐ Never

How long ago did patient quit smoking?

On Hypertension Treatment? ☐ Yes ☒ No

On a Statin? ☐ Yes ☒ No

On Aspirin Therapy? ☐ Yes ☒ No

More than half of the US adult population has a 10-year ASCVD risk estimate $<10\%$ and a lifetime risk estimate $\geq 39\%$

Berger JS, et al. J Am Coll Cardiol 2010;55:1169-77

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Development and Validation of the American Heart Association's PREVENT Equations

- Predicting Risk of cardiovascular disease EVENTS (PREVENT)
- 30-79 yrs old:
 - 10-year risk estimates: 30-79 yrs old
 - 30-year risk estimates: 30-59 yrs old
- Outcomes: ASCVD (CHD + stroke), HF
- 10-year risk for ASCVD is categorized as:**
 - Low risk (<5%)
 - Borderline risk (5% to 7.4%)
 - Intermediate risk (7.5% to 19.9%)
 - High risk ($\geq 20\%$)

Base PREVENT Model		Optional
30-79 years Age	no or yes Current Smoking	0-25,000 mg/g UACR
female or male Sex	18.5-39.9 kg/m ² Body Mass Index	3-15% HbA1c
90-200 mmHg Systolic Blood Pressure	no or yes Antihypertensive Tx	zip code SDI
130-320 mg/dL Total Cholesterol	no or yes Statin Tx	
20-100 mg/dL HDL-Cholesterol	15-140 mL/min/1.73m ² eGFR	
no or yes Diabetes		

<https://professional.heart.org/en/guidelines-and-statements/prevent-calculator>; Garba DL, Razavi AC, et al. American Journal of Preventive Cardiology 19 (2024) 100705

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PREVENT Risk Equation

https://www.linkedin.com/posts/american-heart-association_the-american-heart-associations-new-total-activity-7151207093583151104-y06F; <https://professional.heart.org/en/guidelines-and-statements/prevent-calculator>

Sex ☒ Male ☐ Female

Age 30-79 years **1**

Total Cholesterol 130-320 mg/dL **1**

HDL Cholesterol 20-100 mg/dL **1**

SBP 90-200 mmHg **1**

BMI 18.5-39.9 **1**

eGFR 15-140 **1**

Diabetes ☒ No ☐ Yes **1**

Current Smoking ☒ No ☐ Yes **1**

Anti-hypertensive medication ☒ No ☐ Yes **1**

Lipid-lowering medication ☒ No ☐ Yes **1**

The following three predictors are optional for further personalization of risk assessment. When they are clinically indicated or available, please click on yes and enter the value

UACR ☒ No ☐ Yes **1**

HbA1c ☒ No ☐ Yes **1**

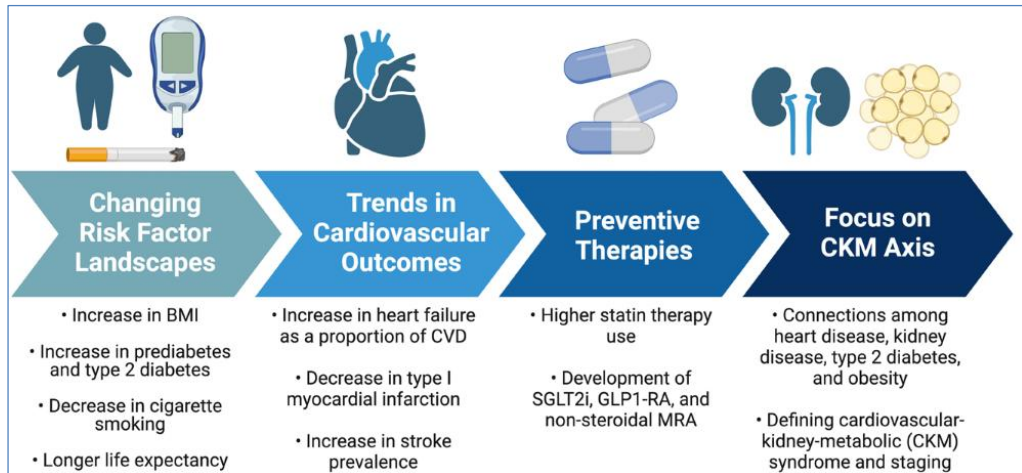
Zip Code (for estimating social deprivation index [SDI]) ☒ No ☐ Yes **1**

Urine albumin creatinine ratio, HgbA1c, social deprivation index

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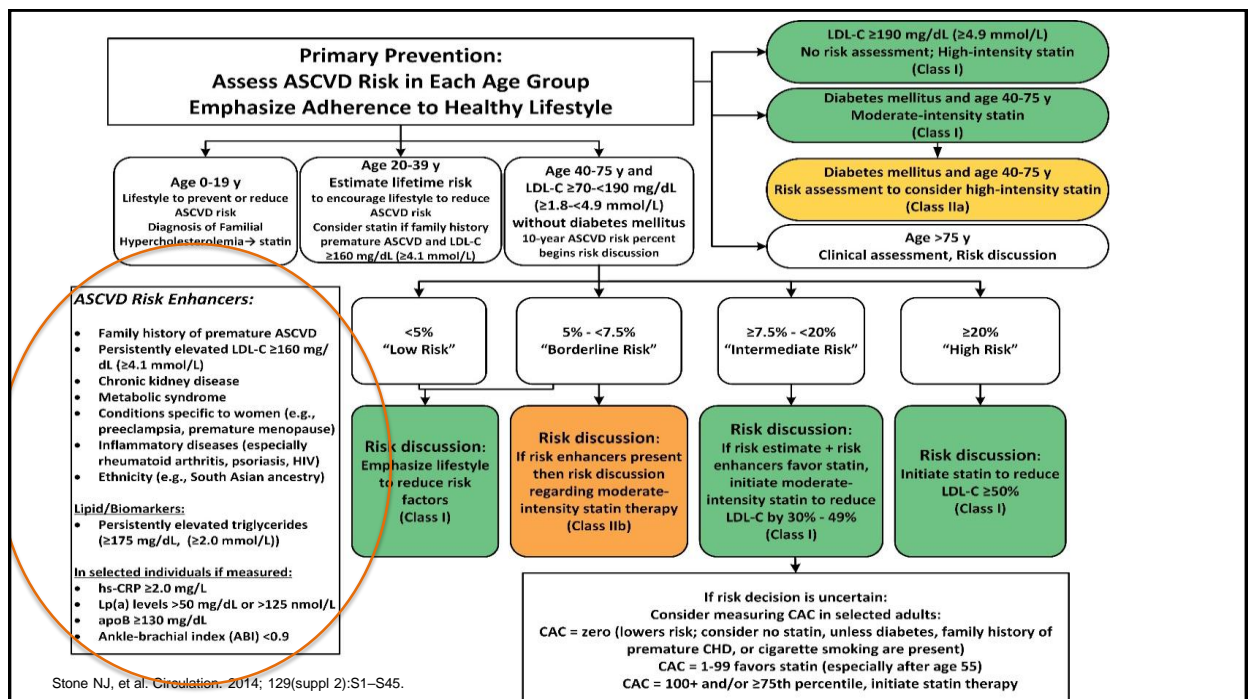
CARDIOVASCULAR PERSPECTIVE

PREVENT Equations: A New Era in Cardiovascular Disease Risk Assessment



Ravazi AC, et al. Circ Cardiovasc Qual Outcomes. 2024;17:e010763. DOI: 10.1161/CIRCOUTCOMES.123.01076

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Stone NJ, et al. Circulation. 2014; 129(suppl 2):S1-S45.

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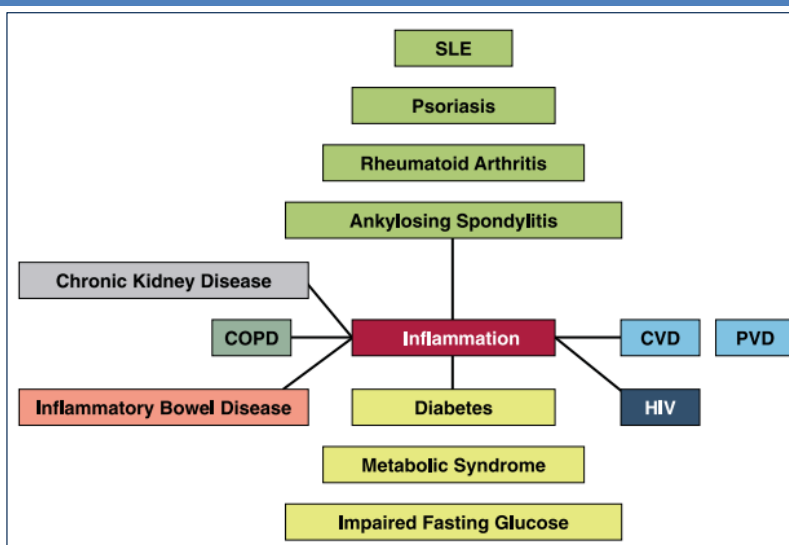
Cardiovascular Disease Risk Enhancers

Family History of Premature CAD	Male <55yo, and Female <65 yo.
Primary hypercholesterolemia	LDL-c 160-189 mg/dL; non-HDL-c 190-219 mg/dL
Metabolic syndrome	Any 3: increased WC (>40 in. men; >35 in. women), TGs >150 mg/dL, HTN, elevated glucose, low HDL-c (<40 men, <50 women)
Chronic kidney disease	eGFR 15-59 mL/min/1.73m ² +/- albuminuria
Inflammatory Disease	Psoriasis, rheumatoid arthritis, HIV/AIDS
Female-specific risks	Premature menopause (<40 yrs. old); pregnancy conditions
ABI	<0.9
Elevated hs-CRP	≥2.0 mg/dL
High-risk race/ethnicities	Ex: South Asian Ancestry
Lipid biomarkers	Triglycerides ≥175 mg/dL; ApoB Levels ≥130 mg/dL, Lp(a) ≥50 mg/dL; ≥125 nmol/L

Arnett DK, et al. Circulation. 2019;140:e563–e595

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Inflammatory Disease and CVD



Hecht HS. J Am Coll Cardiol Img 2015;8:579–96

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Unique CVD Risk Factors in Women

Risk factors for cardiovascular disease in women

Well-established, sex-specific, and under-recognised risk factors

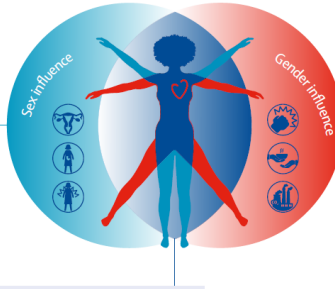
Sex-specific risk factors

Premature menopause
Gestational diabetes
Hypertensive disorders of pregnancy
Preterm delivery
Polycystic ovary syndrome
Systemic inflammatory and autoimmune disorders



Well-established risk factors

Hypertension Obesity Smoking or tobacco use
Dyslipidaemia Unhealthy diet
Diabetes Sedentary lifestyle



Under-recognised risk factors

Psychosocial risk factors
Abuse and intimate partner violence
Socioeconomic deprivation
Poor health literacy
Environmental risk factors

Acknowledging the effects of these risk factors is crucial to understanding cardiovascular disease in women.

Read more: *The Lancet women and cardiovascular disease Commission: reducing the global burden by 2030*

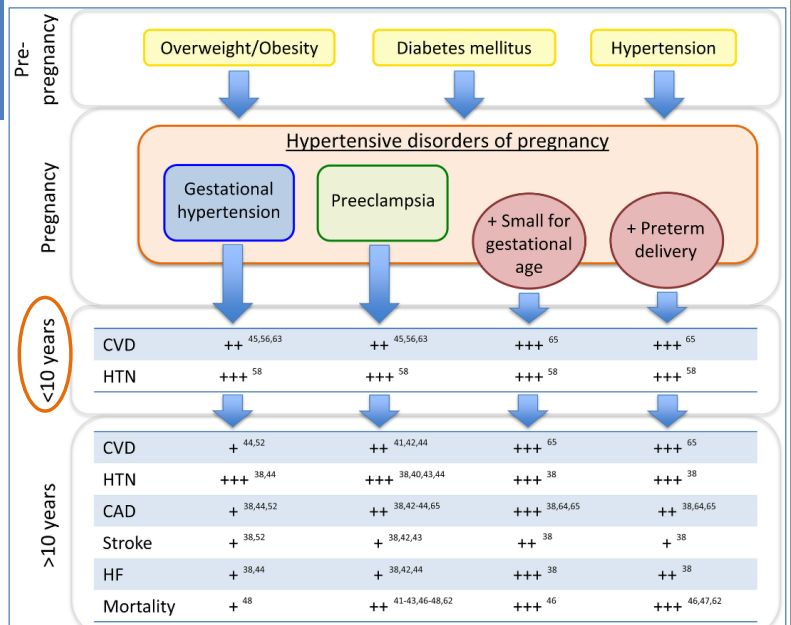
Vogel, B., Acevedo, M., Appelman, Y., Bairey Merz, C. N., et al. (2021). *The Lancet women and cardiovascular disease Commission: reducing the global burden by 2030*. *Lancet* (London, England), 397(10292), 2385–2438. [https://doi.org/10.1016/S0140-6736\(21\)00684-X](https://doi.org/10.1016/S0140-6736(21)00684-X)

THE LANCET

The best science for better lives

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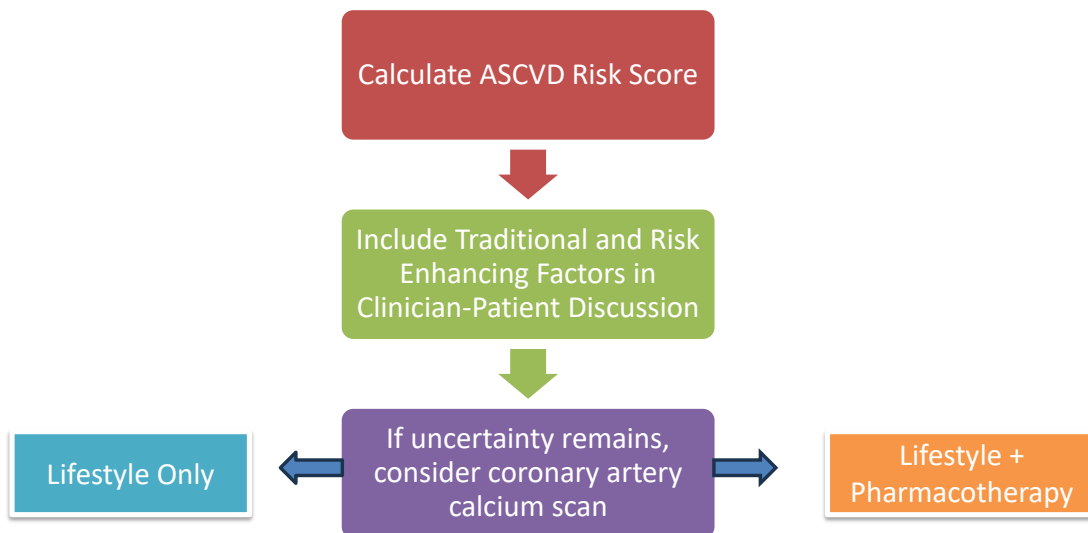
Hypertension Disorders of Pregnancy & CVD Risk



Ying W, et al. *Journal of the American Heart Association*. 2018;7:e009382

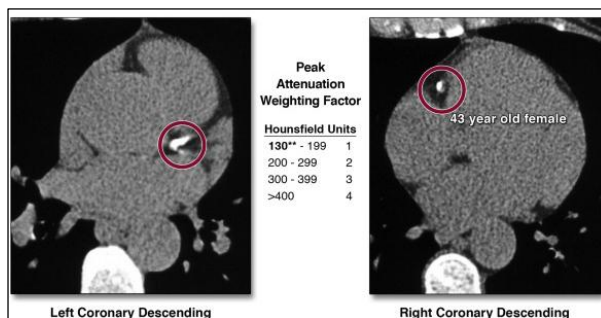
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CVD Risk Assessment to Guide Primary Prevention Treatment



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CAC Score: The Agatston Method



- Volume of calcified area
- Density Weighting Factor: ≥ 130 HU to detect calcium
- Lesion Score = Area x density weighting factor

- 1) Score for each vessel (Left main, LAD, LCx, RCA)
- 2) Total score (sum of all vessels)
- 3) Percentile

Kalra DK, et al. Arterioscler Thromb Vasc Biol. 2014;34:1144-1154

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Coronary Calcium Scoring: Older Thresholds

Table 1. Agatston score, plaque burden and degree of coronary artery obstruction

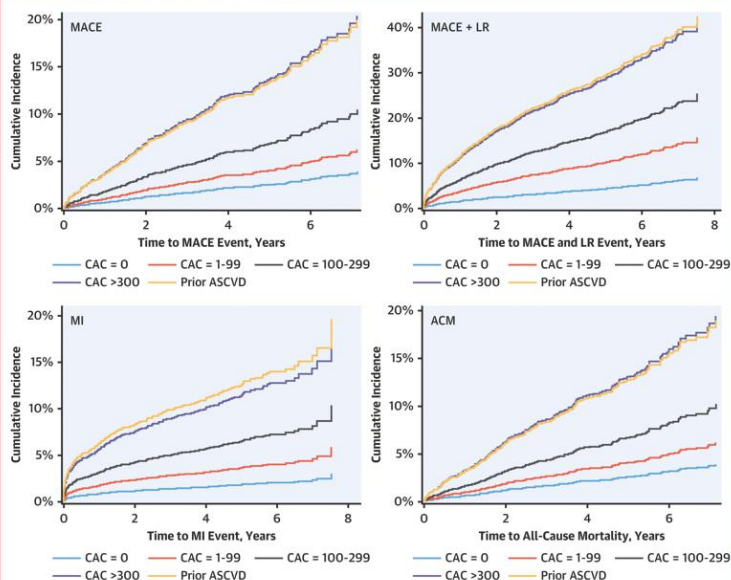
Agatston score	Plaque burden	Probability of significant CAD
0	No plaque	Very low
1–10	Minimal plaque	Low
11–100	At least mild atherosclerotic plaque	Mild or minimal coronary artery stenosis
101–400	At least moderate atherosclerotic plaque	Nonobstructive CAD likely, although obstructive disease possible
>400	Extensive atherosclerotic plaque	High likelihood of at least one significant coronary artery stenosis

Kalra DK, et al. *Arterioscler Thromb Vasc Biol.* 2014;34:1144-1154; Greenland P, et al. *J Am Coll Cardiol.* 2018;72:434-47

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Coronary Calcium Scoring and Risk of Major Adverse Cardiovascular Events (MACE)

CENTRAL ILLUSTRATION: Event Rates by CAC Score Categories for MACE Compared to Prior ASCVD Patients



Budoff MJ, et al. *J Am Coll Cardiol Img.* 2023;16(9):1181-1189.

Mean age: 57.6 ± 12.4 years (56% male)

Median follow-up: 4 yrs (IQR: 1.7-5.7 yrs)

Patients with CAC scores >300 are at an equivalent risk of MACE as those treated for established ASCVD

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Coronary Calcium Scoring: Percentile Matters!

Amount of calcium:	None	Mild	Moderate	Severe
	0	1-99	100-299	300 or more
Chance of heart disease, heart attack or stroke is:	<div> <div></div> <div></div> <div></div> <div></div> </div>			
	Low			High

Greenland P, et al. *J Am Coll Cardiol*. 2018;72:434-47; <https://www.cardiosmart.org/assets/infographic/what-is-a-calcium-heart-scan>

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Amount of calcium:	None	Mild	Moderate	Severe
	0	1-99	100-299	300 or more
Chance of heart disease, heart attack or stroke is:	<div> <div></div> <div></div> <div></div> <div></div> </div>			
	Low			High

i) Score for each vessel ii) Total score iii) Percentile

The following are scores for the individual vessels-

LMA- 0; LAD- 1; LCX- 0; RCA- 0;

IMPRESSION-

The total coronary calcium score of 1 places the patient in the approximate 89th percentile for an apparently healthy person of the same age and gender, and indicates minimal atherosclerotic plaque burden.

Calcium score: 1

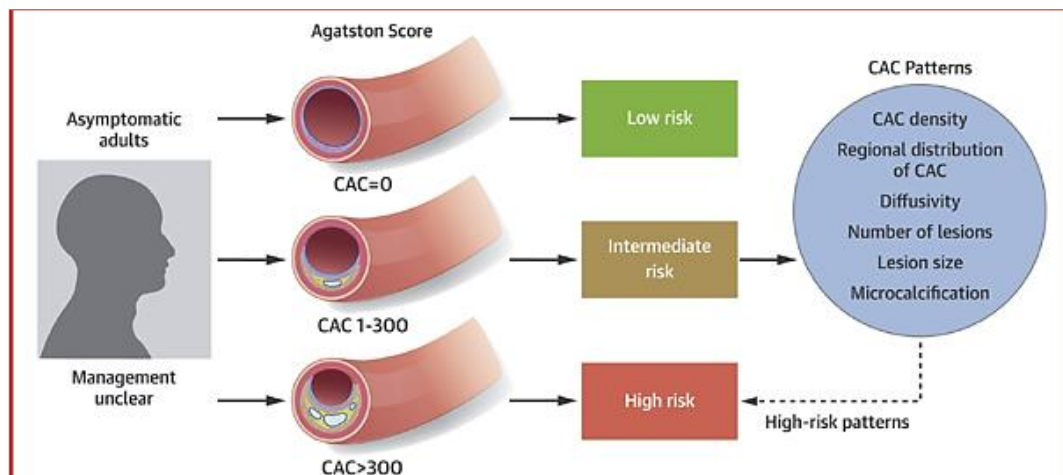
Percentile: 89th

Calculate percentile: <https://www.mesa-nhlbi.org/calcium/input.aspx>

Greenland P, et al. *J Am Coll Cardiol*. 2018;72:434-47; <https://www.cardiosmart.org/assets/infographic/what-is-a-calcium-heart-scan>

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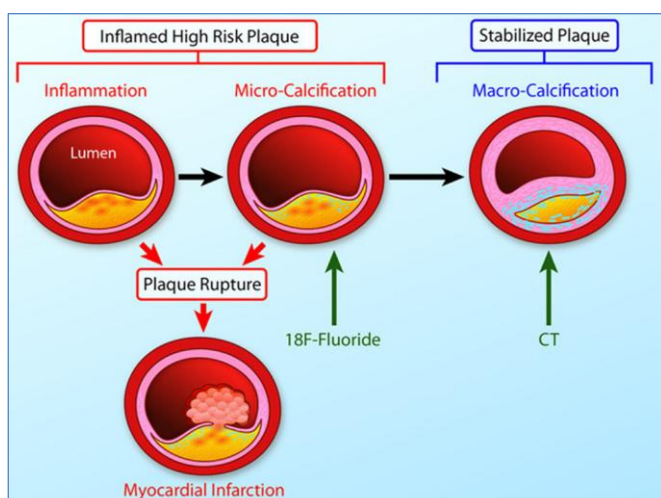
Higher CAC Score...Higher ASCVD Risk



Blaha MJ, et al. J Am Coll Cardiol Img 2017;10:923-37

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Calcified vs. Non-Calcified Plaque




Yaming Li. *Journal of the American Heart Association*. 2018 Jun 28;7(13):e008564.

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10-year CHD Risk Assessment with Coronary Artery Calcium


The Multi-Ethnic Study of Atherosclerosis

MESA 10-Year CHD Risk with Coronary Artery Calcification [Back to CAC Tools](#)

1. Gender Male ☐ Female ☒

2. Age (45-85 years) Years

3. Coronary Artery Calcification Agatston

4. Race/Ethnicity **Choose One**

Caucasian ☒
Chinese ☐
African American ☐
Hispanic ☐

5. Diabetes Yes ☐ No ☒

6. Currently Smoke Yes ☐ No ☒

7. Family History of Heart Attack (History in parents, siblings, or children) Yes ☒ No ☐

8. Total Cholesterol mg/dL or mmol/L

9. HDL Cholesterol mg/dL or mmol/L

10. Systolic Blood Pressure mmHg or kPa

11. Lipid Lowering Medication Yes ☐ No ☒

12. Hypertension Medication Yes ☒ No ☐

[Calculate 10-year CHD risk](#)

The estimated 10-year risk of a CHD event for a person with this risk factor profile including coronary calcium is 12.3%. The estimated 10-year risk of a CHD event for a person with this risk factor profile if we did not factor in their coronary calcium score would be 7.0%.

<https://www.mesa-nhlbi.org/MESACHDRisk/MesaRiskScore/RiskScore.aspx>

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The Power of Zero

TABLE 2 Summary of CAC Absolute Event Rates From 14,856 Patients in 5 Prospective Studies (11,19,21,24,25)

CAC Score	FRS Equivalent	10-Year Event Rate, %
0	Very low	1.1-1.7
1-100	Low	2.3-5.9
101-400	Intermediate	12.8-16.4
>400	High	22.5-28.6
>1,000	Very high	37.0

CAC = coronary artery calcium; FRS = Framingham Risk Score.

CAC has a sensitivity for obstructive CAD: 88% to 100%

CAC=0, with negative predictive values approaching 100%

Arnett DK, et al. *Circulation*. 2019;140:e563-e595. Hecht H. *JACC Cardio. Imaging*. 2015;8:579-96
Hecht HS. *J Am Coll Cardiol Img* 2015;8:579-96

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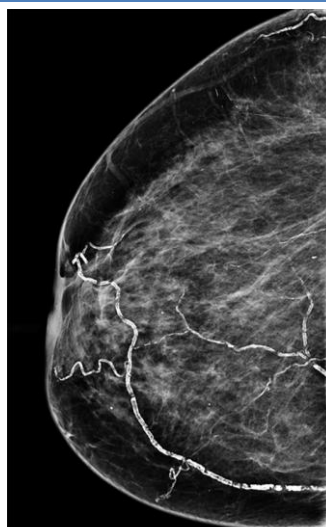
Absence of coronary artery calcium demonstrates a low 10-year CVD event rate.

Reasonable to withhold statin therapy and reassess if there is an absence of: diabetes mellitus, family history of premature CAD, cigarette smoking

Arnett DK, et al. *Circulation*. 2019;140:e563–e595. Hecht H. *JACC Cardio. Imaging*. 2015;8:579-96

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Emerging: Breast Artery Calcification

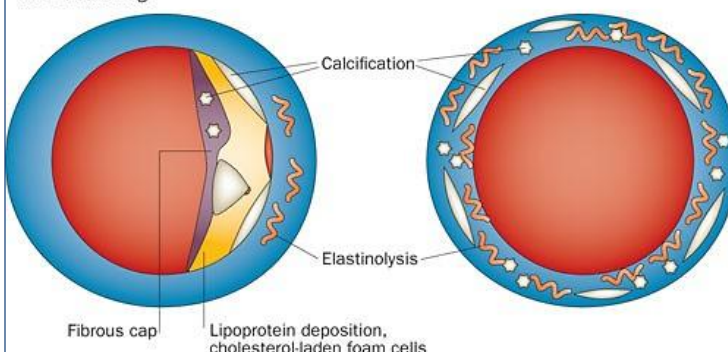


Atherosclerotic calcification

- Eccentric
- Lumen deforming
- Fibrous intimal cap
- Focal elastinolysis
- Vessel stiffening

Medial calcification

- Concentric
- Vessel stiffening
- Medial fibrosis and elastinolysis
- Adventitial inflammation



Bui, Q. M., & Daniels, L. B. (2019). *Circulation*, 139(8), 1094–1101. <https://doi.org/10.1161/CIRCULATIONAHA.118.038092>; Quispe, R., et al. *JACC: Cardiovascular Imaging*, 12(12), 2538–2548.

Thompson B, Towler DA. *Nat Rev Endocrinol* 8, 529–543 (2012). <https://doi.org/10.1038/nrendo.2012.36>

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CVD Risk and Prevalent BAC

Risk Factors for BAC:

- Age: OR 2.98; 95% CI: 2.31 -3.85
- HTN: OR 1.20; 1.00–1.42
- Diabetes mellitus: OR: 1.88; 1.36-2.59
- Parity: OR 3.43; 2.23 - 5.27

2024: Presence of BAC (adj HR):

- Mortality: 1.49; 95%CI:1.33-1.67
- Composite (acute MI, HF, CVA, mortality): 1.56; 95%CI:1.41-1.72
- Highest risk: 40-59 year olds
- Young adults at highest risk!

Bui, Q. M., & Daniels, L. B. (2019). Circulation, 139(8), 1094–1101. Hendriks, E. J., et al. (2015). Atherosclerosis, 239(1), 11–20. Quispe, R., et al. (2019). JACC: Cardiovascular Imaging, 12(12), 2538–2548; Trimboli, R. M., et al. (2019). European journal of radiology, 119, 108636; Allen ST, et al. JACCAdv.2024;3:101283

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Relationship Between Breast Artery and Coronary Artery Calcification

- Women 39-59 yrs. old with BAC:
 - 52% with CAC; 13% moderate to severe CAC
- Women 60-69 yrs. old with BAC:
 - 67% with CAC; 31% moderate to severe CAC

Additional CVD risk assessment is needed!

Margolies, L., (2016). Digital mammography and screening for coronary artery disease. JACC: Cardiovascular Imaging, 9(4), 350–360.

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CVD Risk Assessment After Breast Artery Calcification

What Next after BAC?

1. Notify the patient
2. CVD Risk assessment
3. Lifestyle management
4. Risk-guided pharmacotherapy
5. IF appropriate, consider CAC

Yoon YE, et al. Curr Atheroscler Rep 23, 21 (2021)

Radiologist

Include BAC findings as a part of standard mammography report.

- Presence or absence of BAC
- Semiquantitative assessment of BAC (i.e., mild, moderate, severe)

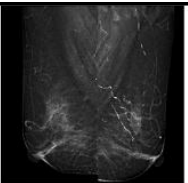
Clinician

Initiate personalized approach for risk stratification and preventive treatment.

- Evaluate 10-year ASCVD risk and initiate statin therapy in women classified as high-risk.
- Consider further testing, such as CAC scan, in women with BAC but are not classified as high risk.

Patient

Recognize personal risk for ASCVD and optimize lifestyle to control risk factors, such as diet, smoking, physical activity, blood pressure, diabetes mellitus, and cholesterol.



Presence of BAC, severe

ASCVD Risk Factors


Please check all that apply.

☒ High cholesterol

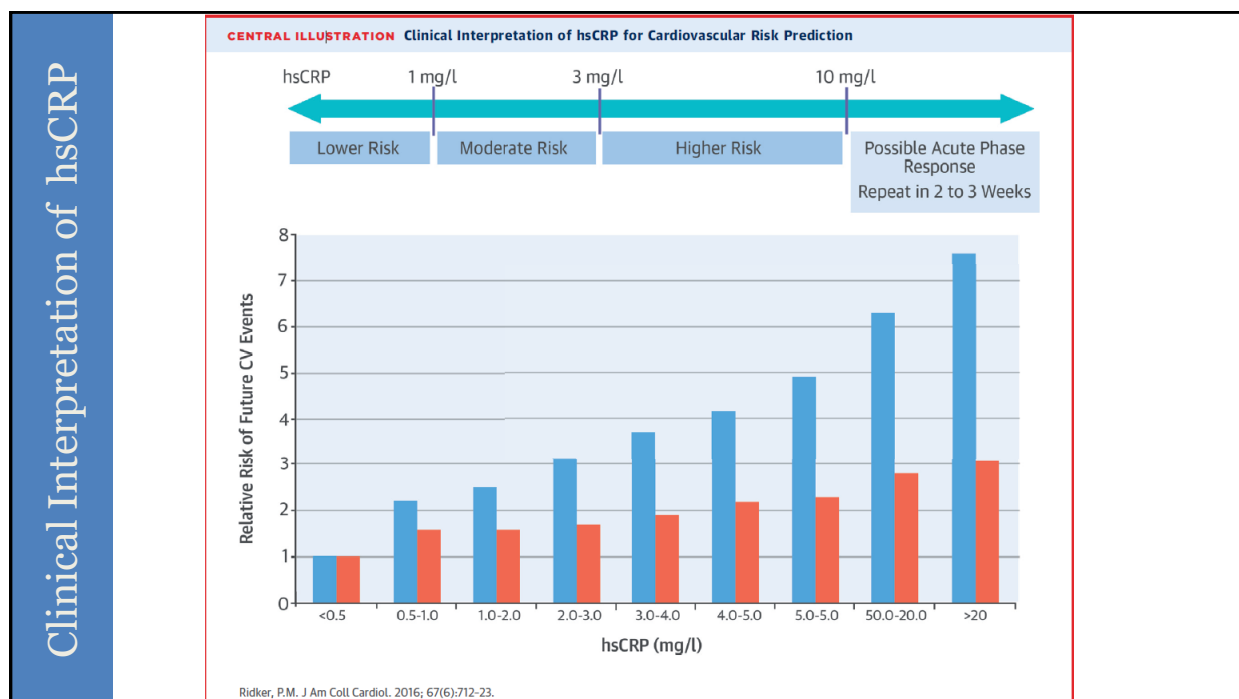
☐ High blood pressure

☒ Diabetes

☐ Smoking

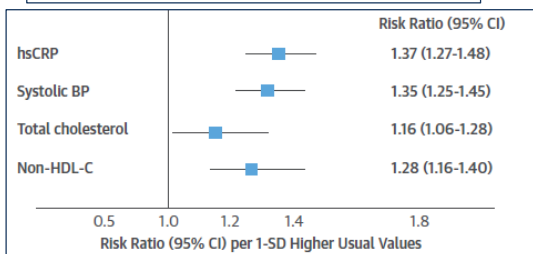
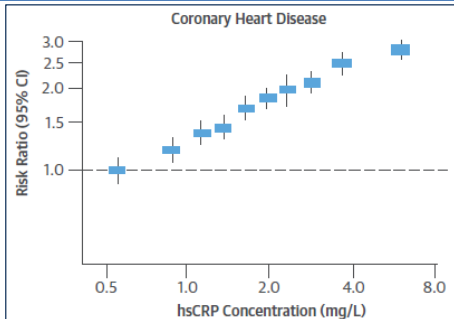


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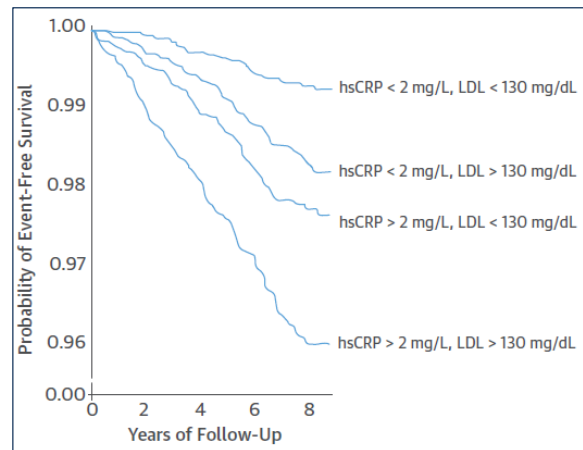


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High-Sensitivity C-Reactive Protein



Residual Risk

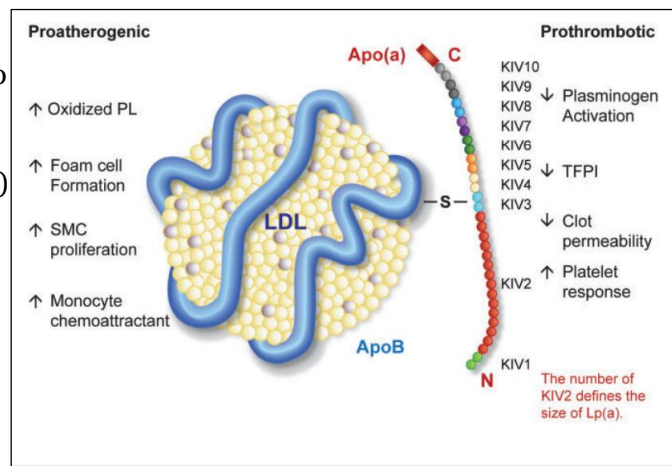


Ridker P. J Am Coll Cardiol 2016;67:712-23

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What Is Lipoprotein(a)?

- LDL-like particle with apolipoprotein(a) [Apo(a)] bound to apolipoprotein B-100 (ApoB)
- Apo(a): 10 different kringle IV (KIV)
- Apo(a) varies in size by the LPA gene, determines the number of kringle IV type 2 (KIV-2) repeats
- Lp(a) level is predominantly genetically determined

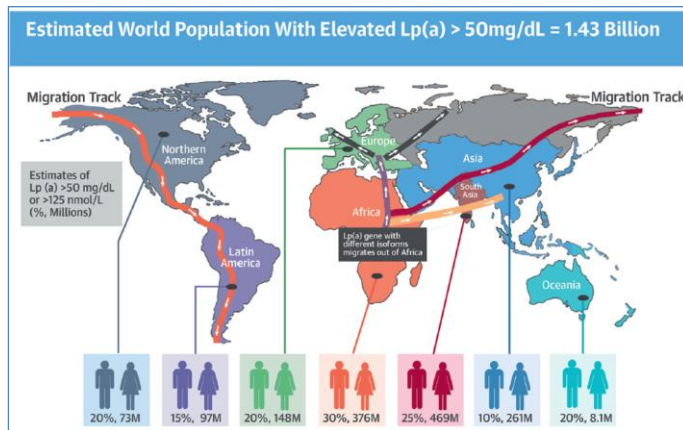


Witztum, J. L., & Ginsberg, H. N. (2016, March). J Lipid Res, 57(3), 336-339
 Gencer B, et al. European Heart Journal, Volume 38, Issue 20, 21 May 2017, Pages 1553-1560

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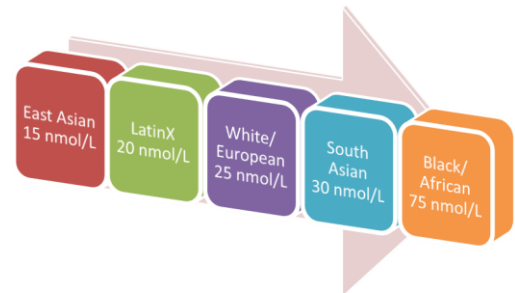
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Global Variation of Elevated Lp(a)



Mehta, A., et al. (2022). Lipoprotein (a) and ethnicities. *Atherosclerosis*, 349, 42-52
 Patel, N., Mittal, N., Choudhary, P.A. et al. Lipoprotein(a)—When to Screen and How to Treat. *Curr Cardiovasc Risk Rep* 16, 111–120 (2022).

Mean Lp(a) level By Ethnicity



- Global 10%-30% high Lp(a) > 50 mg/dL (> 100 nmol/L)

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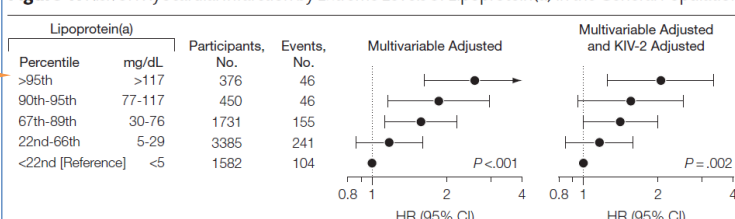
Genetically Elevated Lipoprotein(a) and Increased Risk of Myocardial Infarction

Table 1. Basic Characteristics of Participants (White Individuals of Danish Descent) in the 3 Studies

	CCHS	CGPS	CIHDS
Total, No.	8637	29 388	2461
Women, No. (%)	5302 (61)	15 260 (52)	566 (23)
Age, mean (SD), y	55 (17)	59 (13)	60 (10)
Diabetes mellitus, No. (%)	311 (4)	1346 (5)	242 (10)

Abbreviations: CCHS, Copenhagen City Heart Study; CGPS, Copenhagen General Population Study; CIHDS, Copenhagen Ischemic Heart Disease Study.

Figure 1. Risk of Myocardial Infarction by Extreme Levels of Lipoprotein(a) in the General Population



Adjusted: age, sex, T chol, TG, BMI, HTN, DM, smoking, use of lipid-lowering therapy; kringle IV type 2 genotype, HRT menopause

Kamstrup, P. R., et al. 2009. *Jama*, 301(22), 2331-2339.

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Independent Association of Lipoprotein(a) and Coronary Artery Calcification With Atherosclerotic Cardiovascular Risk



- MESA: n=4,512
- Dallas Heart Study: n=2,078
- Elevated Lp(a): highest race-specific quintile
- CAC score categories: 0, 1-99, ≥ 100

	All Participants (N = 4,512)	CAC = 0 (n = 2,377)	CAC 1-99 (n = 1,147)	CAC ≥ 100 (n = 988)	P Value
Age, y	61.9 \pm 10.4	57.9 \pm 9.3	64.1 \pm 9.8	69.2 \pm 8.7	<0.01
Men	2,145 (47.5)	891 (37.5)	612 (53.4)	642 (65.0)	<0.01
Race					<0.01
White	1,660 (36.8)	770 (32.4)	421 (36.7)	469 (47.5)	<0.01
Black	1,323 (29.3)	785 (33.0)	314 (27.4)	224 (22.7)	<0.01
Hispanic	1,002 (22.2)	565 (23.8)	256 (22.3)	181 (18.3)	<0.01
Chinese	527 (11.7)	257 (10.8)	156 (13.6)	114 (11.5)	0.27
Systolic BP, mm Hg	126.2 \pm 21.4	122.0 \pm 20.4	128.9 \pm 21.7	133.0 \pm 21.2	<0.01
Diastolic BP, mm Hg	72.0 \pm 10.3	71.3 \pm 10.4	72.8 \pm 10.3	72.9 \pm 10	<0.01
Antihypertensive use	1,485 (32.9)	612 (25.8)	418 (36.4)	455 (46.1)	<0.01
Diabetes	429 (9.5)	177 (7.5)	110 (9.6)	142 (14.4)	<0.01
Smoking	579 (12.8)	300 (12.6)	158 (13.8)	121 (12.3)	0.97
Total cholesterol, mg/dL	195.8 \pm 34.7	194.5 \pm 34.3	197.0 \pm 34.2	197.4 \pm 35.9	0.03
HDL cholesterol, mg/dL	51.3 \pm 15.1	52.7 \pm 15.2	49.7 \pm 14.5	49.8 \pm 15.3	<0.01
Triglycerides, mg/dL	107.0 (75.5-156.0)	102.0 (72.0-151.0)	113.0 (82.0-161.0)	111.5 (77.0-160.5)	<0.01
LDL cholesterol, mg/dL	119.7 \pm 31.4	117.8 \pm 30.7	121.7 \pm 31.8	122.1 \pm 32.1	<0.01
Family history of MI	1729 (47.2)	815 (42.2)	456 (49.7)	458 (56.3)	<0.01
Body mass index, kg/m ²	28.2 \pm 5.5	28.3 \pm 5.7	28.1 \pm 5.4	28.1 \pm 5.1	0.91
Lp(a), mg/dL	18.2 (8.2-40.5)	19.1 (8.4-41.5)	18.0 (8.4-38.5)	16.2 (7.3-39.4)	0.02

Mehta, A., et al. (2022). Journal of the American College of Cardiology, 79(8), 757-768.

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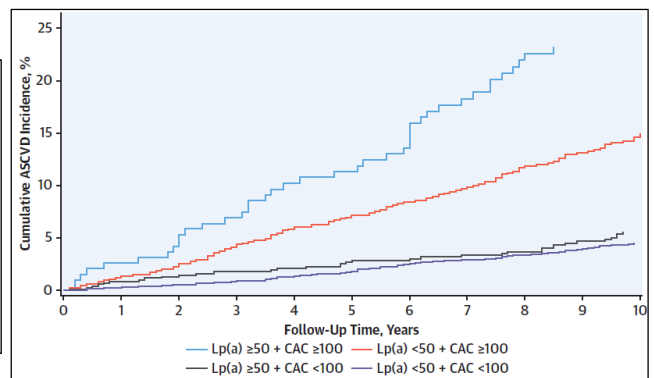
Independent Association of Lipoprotein(a) and Coronary Artery Calcification With Atherosclerotic Cardiovascular Risk



Elevated Lp(a) and CAC score were independently associated with incident ASCVD

TABLE 4 Joint Association of Elevated Lp(a) and CAC Score With Incident ASCVD Among MESA Participants

	HR (95% CI)	P Value
Lp(a) quintile 5 and CAC ≥ 100	4.71 (3.01-7.40)	<0.01
Lp(a) quintiles 1-4 and CAC ≥ 100	2.99 (2.06-4.33)	<0.01
Lp(a) quintile 5 and CAC 1-99	2.35 (1.36-4.08)	<0.01
Lp(a) quintiles 1-4 and CAC 1-99	2.17 (1.49-3.16)	<0.01
Lp(a) quintile 5 and CAC = 0	1.31 (0.73-2.35)	0.36
Lp(a) quintiles 1-4 and CAC = 0	Referent	



Mehta, A. et al. 2022. Journal of the American College of Cardiology, 79(8), 757-768

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Independent Association of Lipoprotein(a) and Coronary Artery Calcification With Atherosclerotic Cardiovascular Risk

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Even with a calcium score of zero:

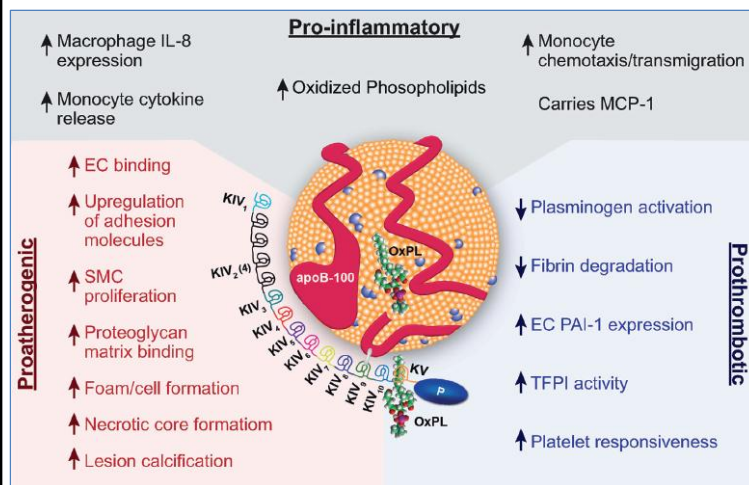
An elevated Lp(a) results in an increased risk of CVD

Mehta, A. et al. 2022. Journal of the American College of Cardiology, 79(8), 757-768

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Pathogenesis of Lipoprotein(a)



Tsimikas S. JACC. 2017 Feb 14;69(6):692-711.

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When Should We Screen for Lp(a)? (Recommended Units: nmol/L)

Guidelines Vary

FH of premature ASCVD (<55 years old men, <65 years old women)	A personal history of premature ASCVD
Familial Hypercholesterolemia (LDL-C \geq 190 mg/dL)	For cascade screening of family members with severe hypercholesterolemia and/or elevated Lp(a)
To aid discussion about whether to prescribe a statin in those aged 40-75 years with borderline (5.0%-7.4%) 10-year ASCVD risk	To identify those at risk for progressive valvular aortic stenosis

National Lipid Association (NLA), 2019; American College of Cardiology (ACC) / American Heart Association (AHA), 2018; European Atherosclerosis Statement, 2022; Canadian Guidelines, 2021; HEART UK Consensus 2019. Kronenberg, F., et al. (2022). Eur Heart J, 43(39), 3925-3946.*

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
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"Lp(a) should be measured at least once in adults to identify those with high cardiovascular risk."

National Lipid Association (NLA), 2019; American College of Cardiology (ACC) / American Heart Association (AHA), 2018; European Atherosclerosis Statement, 2022; Canadian Guidelines, 2021; HEART UK Consensus 2019. Kronenberg, F., et al. (2022). Eur Heart J, 43(39), 3925-3946.*

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Emerging Lp(a) Therapies

Emerging Lp(a) Therapeutics				
Antisense Oligonucleotides		Small-interfering RNA		Oral Agents
 Bind apo(a) mRNA preventing translation and production of Lp(a)		RNA-induced silencing complex (RISC) mediated degradation of apo(a) mRNA, preventing translation of protein and subsequent production		Disrupts noncovalent interaction between apo(a) & apoB100, preventing disulfide bond and Lp(a) formation
Pelacarsen		Olpasiran	SLN360	LY3819469
 Phase 3 completed enrollment		Phase 3	Phase 2 completed enrollment	Phase 1 & 2 ongoing
 In phase 2, mean percent reduction in Lp(a) ranged from 35-80%		In phase 2, mean percent reduction in Lp(a) ranged from 70.5%-100.5%	In phase 1, reduction in Lp(a) in dose dependent manner; well-tolerated	-
				 Phase 2 ongoing In phase 1, placebo adjusted Lp(a) reduction 63-65%

Kaur G, et al. American Journal of Preventive Cardiology 18 (2024) 100641

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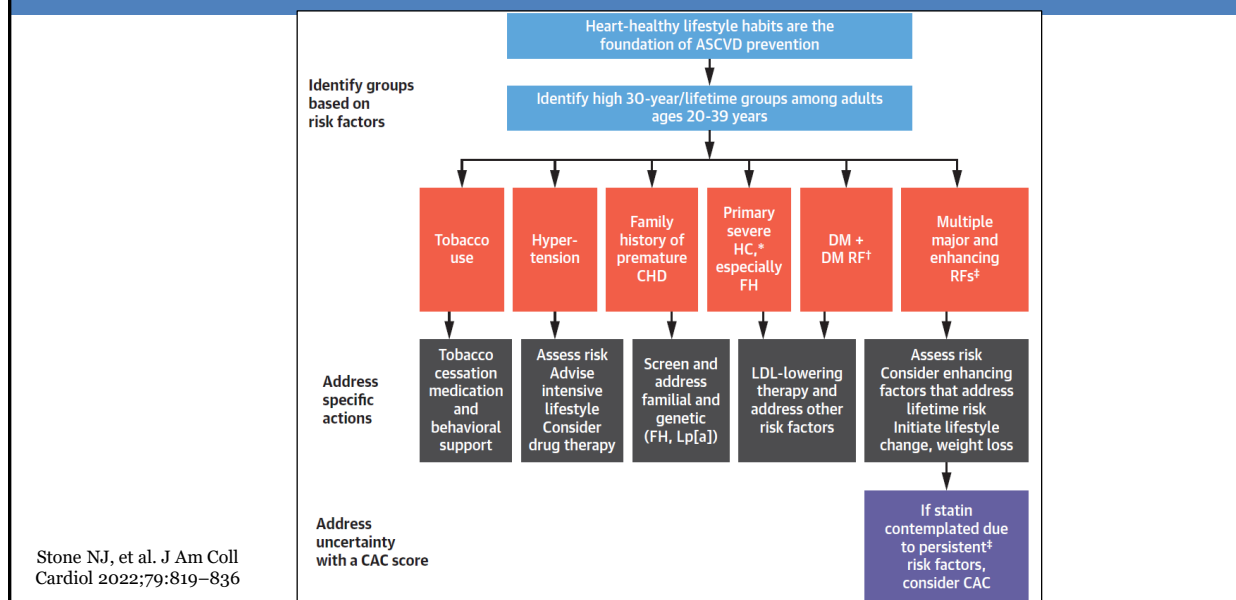
Lp(a) Summary

- Prevalent, genetically determined, causal risk factor for ASCVD and aortic stenosis
- Awareness of elevated Lp(a) improves ASCVD risk stratification
- Inform clinical decisions and shared decision-making for ASCVD risk management
- Measure Lp(a) at least once!

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CVD Risk Assessment in Young Adults



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Summary

- Cardiovascular risk assessment is essential to lower future risk of CVD events
- Risk enhancing factors and imaging improve CVD risk assessment beyond an ASCVD risk score
- Coronary artery calcification has excellent CVD risk prediction across race and ethnicity
- Measure lipoprotein(a) once in adulthood (nmol/L)

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Which of the Following Is False About Coronary Artery Calcium Scans?

- A. A score of >300 has an equivalent risk of major adverse cardiovascular events as someone with established ASCVD
- B. A calcium score of 1 with >75th percentile reflects advanced coronary artery calcium
- C. Cholesterol medication is not recommended for a 55yo female with current cigarette use and high LDLc if her coronary artery calcium score is zero
- D. Coronary artery calcium CT scans have a higher sensitivity to detect obstructive CAD than hs-CRP



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Which of the Following Is Not an AHA/ACC CVD Risk Enhancing Factor?

- A. Pre-eclampsia
- B. Homocysteine
- C. Rheumatoid arthritis
- D. High-sensitivity CRP ≥ 2.0 mg/dL



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Which of the Following Is False About Lipoprotein (a)?

- A. Lipoprotein (a) is a causal risk factor for atherosclerotic cardiovascular disease (ASCVD)
- B. Lipoprotein (a) levels are predominantly driven by lifestyle
- C. An individual with a high lipoprotein (a) and a calcium score of zero has an elevated ASCVD risk
- D. Lipoprotein (a) should be checked at least once in adults to assess ASCVD risk