

Focus on Lipid-Related Risk as a Component of Comprehensive Cardio-Kidney-Metabolic Health

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Disclosure

I have no financial interests or relationships to disclose.



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CKM Lipid Related Risk

- CKM Overview
- PREVENT / CPR
- Top 10
- Focus on Lipids in CKM
- Summary

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Cardiometabolic Think Tank- June 2014



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THE PRESENT AND FUTURE Sperling, LS, et al. JACC 2015;66:1050–67

STATE-OF-THE-ART REVIEW

The CardioMetabolic Health Alliance

Working Toward a New Care Model for the Metabolic Syndrome



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Laurence Sperling, MD
Focus on Lipid-Related Risk as a Component of CKM Health

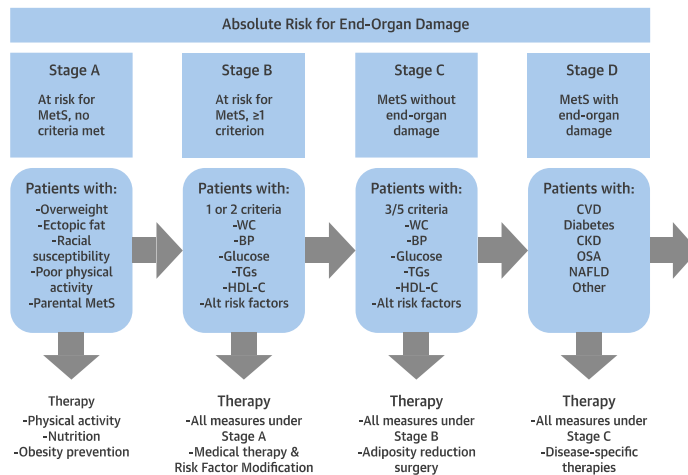
THE PRESENT AND FUTURE Sperling, LS, et al. JACC 2015;66:1050–67
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FIGURE 2 Stages in the Evolution of MetS and Recommended Therapy by Stage



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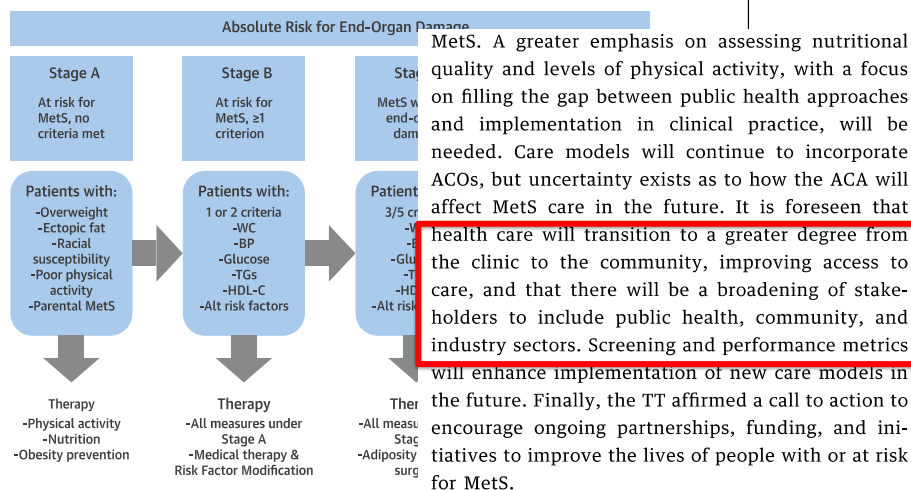
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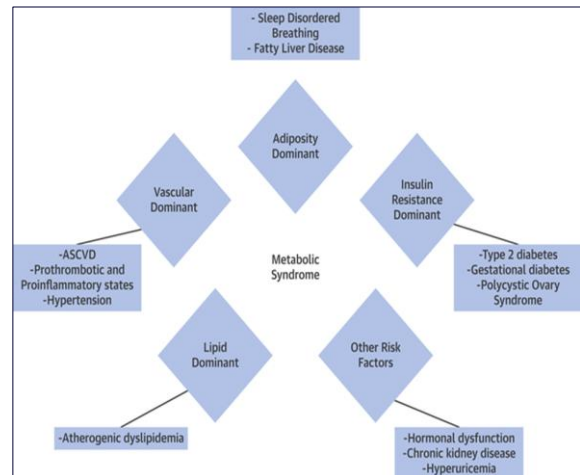


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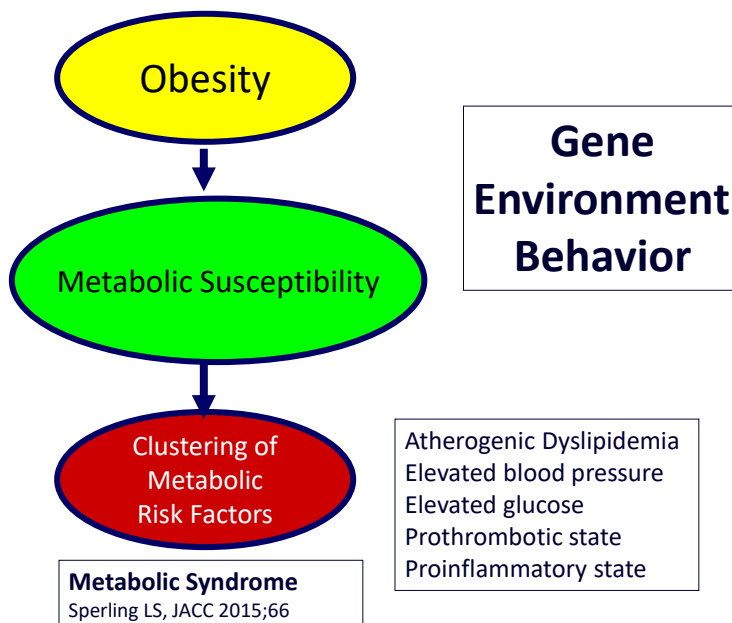
Paradigm for Subtyping MetS

- At risk for multi-end-organ damage
- CV & non-CV
- **Variability** in end-organ involvement
- **Overlap**
- Target preventive / therapeutic approaches

Sperling LS, et al. JACC 2015;66(9):1050-67



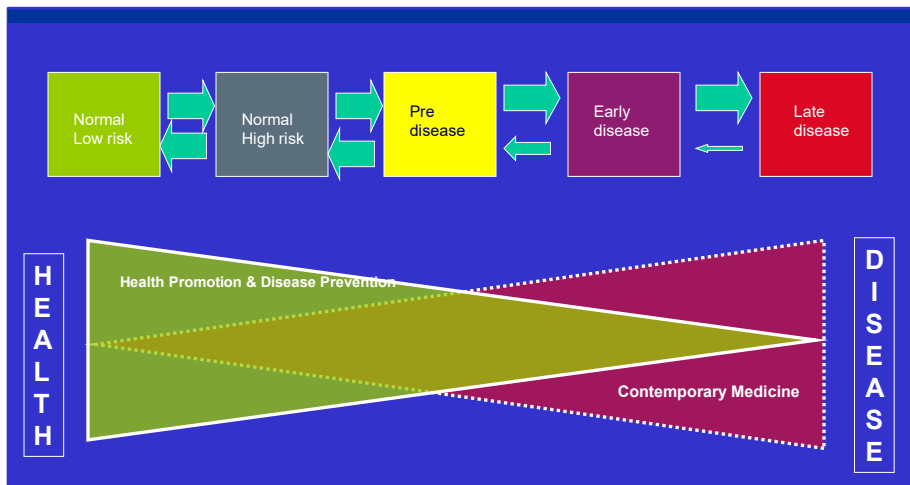
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Focus on CV Population Health: The Health/Disease Continuum

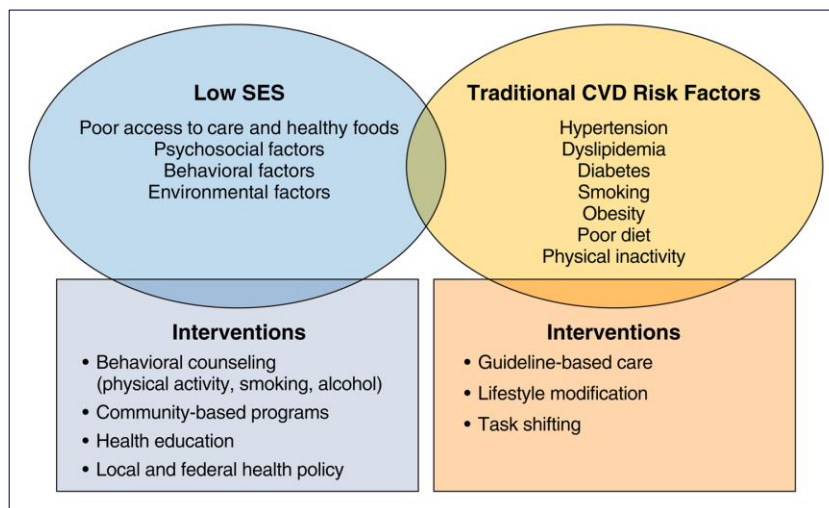
Knapper JT, Quyyumi AA, Mensah GA, Sperling LS. JACC 2015;66:960-7



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SDOH and CV Outcomes: Challenges & Interventions

Schultz WM, Kelli HM, Sandesara P, Quyyumi AA, Mensah GA, Sperling LS. Circulation, May 2018.137;2166-2178



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Letters

RESEARCH LETTER
Prevalence of the
Cardiovascular-Kidney-
Metabolic Syndrome in
the United States

What is the clinical question being addressed?

What is the prevalence of the CKM syndrome in the United States?

What is the main finding?

Most of the U.S. population, including those without clinical cardiovascular disease, meets criteria for stages 1 to 3 of the CKM syndrome, indicating an urgent need for population-wide risk-reduction measures.

- Data from 4 NHANES cycles (2011-2018)
- **CKM 1-3 prevalence**
 - Age 20-44 81%
 - Age 45-64 86%
 - > age 65 72%
 - **Only 1.8% age > 65 have no CKM syndrome**

Minhas AMK, Mathew RO, Sperling LS, Abramov D. JACC 2024. 83(18): 1824-1826

TABLE 1 Prevalence of Different Stages of Cardiovascular-Kidney-Metabolic Syndrome

CKM Stage	Population	Overall	Male	Female	American Hispanic	Other Hispanic	Non- Hispanic White	Non- Hispanic Black	Non- Hispanic Asian	Other Race, Including Multiracial	2011- 2012	2013- 2014	2015- 2016	2017- 2018
Age 20-44 years, unweighted n = 3,568, population n = 104,113,793														
Stage 0	18,063,743	17.35	13.3	21.63	7.13	18.73	20.02	13.36	20.99	15.09	19.25	18.08	16.39	15.58
Stage 1	39,125,963	37.58	35.71	39.57	39.95	39.38	37.22	39.56	33.57	31.87	32.77	37.53	41.18	38.96
Stage 2	44,945,504	43.17	49.58	36.37	50.95	39	41.11	44.51	44.57	50.15	45.27	42.92	40.4	44.08
Stage 3	197,816	0.19	0.14	0.23	0.98	0.22	0	0.29	0.15	0	0.22	0.25	0.27	0
Stage 4	1,780,346	1.71	1.26	2.19	0.98	2.68	1.64	2.27	0.73	2.9	2.49	1.22	1.75	1.38
Age 45-64 years, unweighted n = 3,118, population n = 82,640,261														
Stage 0	4,503,894	5.45	3.11	7.6	1.51	3.83	6.8	1.54	3.88	3.76	3.56	6.93	5.85	5.45
Stage 1	17,346,191	20.99	20.02	21.9	20.25	20.24	21.77	14.49	23.93	25.21	21.8	22.81	20.27	19.28
Stage 2	52,716,222	63.79	65.55	62.16	69.11	64.7	63.11	67.34	66.23	49.77	65.26	61.4	64.45	63.95
Stage 3	966,891	1.17	1.81	0.59	1.23	3	0.58	3.21	1.67	2.3	1.62	1.41	0.77	0.93
Stage 4	7,107,062	8.6	9.51	7.76	7.9	8.23	7.73	13.42	4.29	18.96	7.76	7.45	8.66	10.4
Age ≥65 years, unweighted n = 2,012, population n = 44,836,799														
Stage 0	807,062	1.8	0.39	3	0.83	0.84	2.11	0.52	1.2	0	1.77	2.18	1.77	1.51
Stage 1	3,784,226	8.44	6.72	9.9	7.82	5.99	9.55	2.84	5.24	1.35	8.76	4.22	11.68	8.72
Stage 2	17,481,868	38.99	31.25	45.57	44.86	41.15	38.62	35.96	50.34	29.17	35.54	39.55	40.08	40.24
Stage 3	11,029,853	24.6	28.76	21.07	28.48	32.84	32.05	34.1	27.54	19.65	24.77	25.3	23.84	24.49
Stage 4	11,733,790	25.17	32.87	20.47	18.01	19.09	26.66	26.57	15.68	49.83	29.15	28.76	22.63	24.92

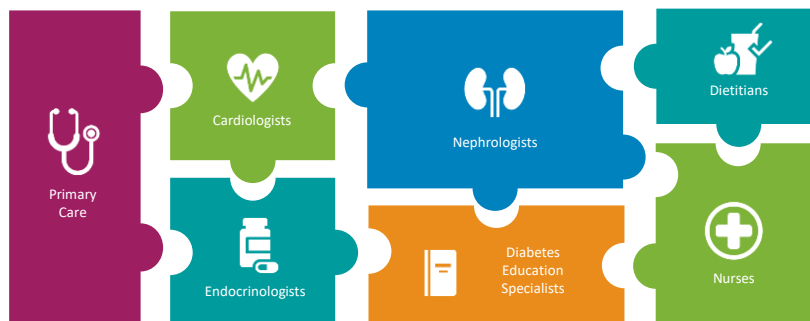
Values are weighted percentages.

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Fragmented Patient Care

Multiple providers + lack of comprehensive/cohesive treatment plans



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December 27, 2023

What to Know About PREVENT, the AHA's New Cardiovascular Disease Risk Calculator

Howard Larkin

Article Information

JAMA. Published online December 27, 2023. doi:10.1001/jama.2023.25115

JAMA Medical News

PREVENT™ Online Calculator

Welcome to the American Heart Association Predicting Risk of cardiovascular disease EVENTS (PREVENT™). This app should be used for primary prevention patients (those without atherosclerotic cardiovascular disease or heart failure) only.

Sex: ☒ Male ☐ Female

Age: years

Total Cholesterol: mg/dL

HDL Cholesterol: mg/dL

SBP: mmHg

BMI:

a professional heart.org

eGFR:

Diabetes: ☒ No ☐ Yes

Current Smoking: ☒ No ☐ Yes

Anti-hypertensive medication: ☒ No ☐ Yes

Lipid-lowering medication: ☒ No ☐ Yes

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

HbA1c: ☒ No ☐ Yes

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

Calculate **Reset**

☒ Risk of CVD ☐ Risk of ASCVD ☐ Risk of Heart Failure

Intended Use of PREVENT:
This calculator is intended for primary prevention patients (those without coronary heart disease, stroke, or heart failure) who are between the ages of 30-79 years. Estimating absolute risk may assist and guide clinicians and patients in shared decision-making for interventions targeting lifestyle behaviors and consideration of pharmacotherapies.

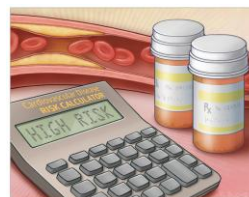
Description of the PREVENT models:

- Primary Prevention
 - Ages 30-79
- Risk of
 - CVD
 - ASCVD
 - Heart Failure

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PREVENT Risk Calculator

- **10 and 30-year** risk of **ASCVD, CVD, and HF; age 30-79**
- Incorporates kidney and metabolic diseases (CKMH)
- Eliminates race / factors in SDOH
 - Social deprivation index (**SDI**) based on zip code
 - Incorporates measures of income, education, employment, housing, household characteristics, transportation
- Based on data from **6.6M from 46 datasets** including population and health system data
- Goal is to incorporate into EMR / ease of use
- Complete model available online
 - February 2024



Larkin H. JAMA 2023.doi:10:1001

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Refining Risk Estimates- “CPR”

- **Calculate**
- **Personalize**
- **Reclassify**

Donald Lloyd-Jones, ACC 2019

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Figure 3. Rationale for New 10-Year Risk Thresholds in Lipid-Lowering Therapy Using PREVENT-ASCVD

Rationale for New 10-y Risk Thresholds in Lipid Lowering Therapy Using PREVENT-ASCVD

Rationale to start LLT in patients at borderline (3% to <5%), intermediate (5% to <10%), and high (≥10%) predicted 10-y risk

Estimates from contemporary PREVENT-ASCVD equations ~40%–50% lower than older PCE
Similar numbers of US adults recommended to consider statin therapy using PCE ≥5% or PREVENT-ASCVD ≥3% 10-y risk
Net benefit (benefit > potential harm) for statin therapy ≥3% 10-y event rate in primary prevention RCTs



2026 Dyslipidemia

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ASCVD indicates atherosclerotic cardiovascular disease; LLT, lipid-lowering therapy; PCE, pooled cohort equations; RCTs, randomized controlled trials; and US, United States.

Adapted from Khan et al and Khan et al.

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Table 12. Crosswalk Between 10-Year Risk ASCVD Estimates From PCE and PREVENT-ASCVD Equations

Risk Group	Approximate Equivalent Ranges of 10-Year ASCVD Risk Estimates*	
	PCE	PREVENT-ASCVD
Low	<5%	<3%
Borderline	5% - <7.5%	3% to <5%
Intermediate	7.5% - <20%	5% to <10%
High	≥20%	≥10%

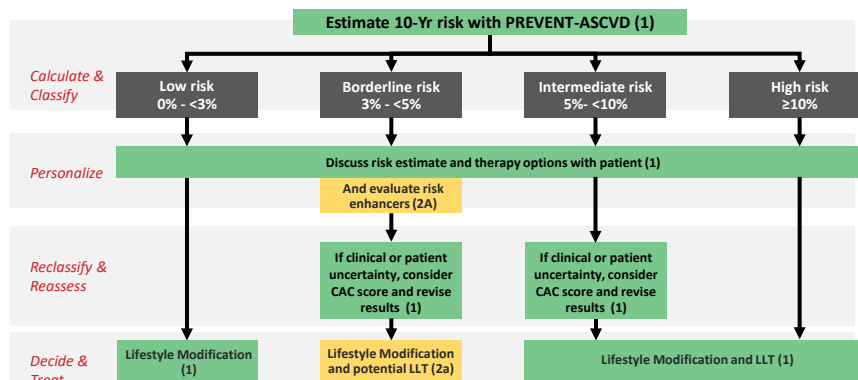
*The PREVENT-ASCVD equations generally provide 10-year risk estimates that are 40% to 50% lower than the PCE estimates because the PCE calculator often overestimated the risk for adults.

ASCVD denotes atherosclerotic cardiovascular disease; and PCE, pooled cohort equations.

Adapted from Khan et al.

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Calculate, Personalize, Reclassify (CPR) Framework



Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; CAC, coronary artery calcium; LLT, lipid-lowering therapy; and PREVENT, Predicting Risk of cardiovascular disease EVENTS.

Blumenthal, R.S., Morris, P.B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. Circulation.

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Table 13. Risk Enhancers

Risk Enhancers	
•	History of premature ASCVD in a parent or sibling (onset age <55 y for men, <65 y for women)
•	Higher risk ancestry (eg, South Asian, Filipino)
•	High polygenic risk (if measured) (Section 4.2.3.5, "Polygenic Risk Scores")
•	Chronic inflammatory diseases (eg, systemic lupus, rheumatoid arthritis, advanced psoriasis, inflammatory arthritis)
•	Lp(a) ≥125 nmol/L or ≥50 mg/dL
•	hsCRP ≥2 mg/L on >1 occasion (if measured)
•	TG persistently ≥175 mg/dL (2 mmol/L) (if nonfasting) and ≥150 mg/dL (1.7 mmol/L) (if fasting)
•	CKM syndrome
•	LDL-C persistently ≥160-189 mg/dL (4.1-4.9 mmol/L), non-HDL-C ≥190-219 mg/dL or apoB ≥120 mg/dL*
•	Reproductive risk markers (premature menopause, preeclampsia, gestational diabetes, gestational hypertension, preterm delivery; Section 4.2.3.4, "Reproductive Risk Marker")

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ApoB indicates apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; CKM, cardiovascular-kidney-metabolic; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein-cholesterol; hsCRP, high-sensitivity C-reactive protein; LDL-C, low-density lipoprotein-cholesterol; Lp(a), lipoprotein (a); and TG, triglycerides.



Note that all available information should be included in risk estimates derived from the PREVENT-ASCVD equations, including albuminuria, HbA1c, and zip code for assessment of neighborhood-level social determinants of health. Given the recent publication of the PREVENT-ASCVD equations, it remains to be demonstrated for most risk enhancers that risk is incremental to the PREVENT-ASCVD equations.

*Although LDL-C is not included in the PREVENT-ASCVD equations (total cholesterol and HDL-C are included), it is included here because persistent elevation of LDL-C may be a useful factor to include in risk-benefit discussions about LDL-C-lowering therapy, given that it is the target of that therapy. See Section 4.2.3.4, "Reproductive Risk Marker," for more detail regarding reproductive risk factors.

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Table 14. Reproductive Risk Markers Associated With ASCVD Events



Adverse Pregnancy Outcomes* That Have a Stronger Association With ASCVD Events

- Hypertensive disorders of pregnancy (preeclampsia, gestational hypertension)
- Gestational diabetes
- Small-for-gestational age (birthweight below the 10th percentile²⁴)
- Preterm delivery (before 37 weeks' gestation)
- Recurrent spontaneous pregnancy loss

Other Reproductive Risk Markers

- Early menarche (<10 y old)
- Early menopause (<45 y old), especially premature menopause (<40 y old)
- Polycystic ovarian syndrome and irregular menses

*Reference: Parikh NJ, Gonzalez JM, Anderson CAM, et al. Adverse pregnancy outcomes and cardiovascular disease risk: unique opportunities for cardiovascular disease prevention in women: a Scientific Statement from the American Heart Association. *Circulation*. 2021;143:e502–e916.

ASCVD indicates atherosclerotic cardiovascular disease; and y, years.



Table 17. Diabetes-Specific Risk Enhancers Independent of Other Diabetes-Related Risk Factors



Risk Enhancers

- Long duration (≥10 y for type 2 diabetes or ≥20 y for type 1 diabetes)
- Albuminuria ≥30 µg of albumin/mg creatinine
- eGFR <60 mL/min/1.73 m²
- Retinopathy
- Neuropathy
- ABI <0.9

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ABI indicates ankle-brachial index; eGFR, estimated glomerular filtration rate; and y, years.

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**1**

Start Earlier: Reduce Lifetime Exposure to LDL-C

Start Statin Therapy for:

- All Adults with HeFH
- Age ≥ 30 :
 - LDL-C ≥ 160 mg/dL **OR**
 - Strong family history of premature ASCVD **OR**
 - High 30-year risk of ASCVD



Treat these groups early even if 10y risk is low to prevent long-term exposure to high LDL-C

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2a

Use PREVENT-ASCVD for Risk Assessment

- Calculate Risk (if no ASCVD or FH)
 - 10-yr ASCVD risk if age 30-79
 - 30-yr ASCVD risk if age 30-59
- Personalize risk assessment
 - Evaluate Risk Enhancers
 - CAC if intermediate risk or LLT decision uncertain
- Reassess need for LLT



PCE risk estimates were known to overestimate 10-year risk. PREVENT-ASCVD 10-y risk estimates are generally lower than PCE results. Approximate equivalent ranges for PCE and PREVENT ASCVD are shown here:

10-yr risk Category	PCE	PREVENT ASCVD
Low	<5%	<3%
Borderline	5-<7.5%	3-<5%
Intermediate	7.5-<20%	5-<10%
High	≥20%	≥10%

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2b

ASCVD Risk Enhancers to Guide Primary Prevention Risk Assessment

ASCVD Risk Enhancers

Demographic, Genetic and Family History	Family history of premature ASCVD Sibling or parent <55y if M, <65y if F
	Higher risk ancestry South Asian, Filipino
Clinical Conditions that Increase ASCVD Risk	High polygenic risk
	Chronic inflammatory diseases Systemic lupus, inflammatory arthritis, psoriasis
	CKM Syndrome Reproductive risk markers Early menopause (<45 y), preeclampsia, gestational DM
Biomarkers	hsCRP ≥2 mg/L on >1 measurement
	Elevated TGs ≥150 mg/dL fasting, ≥175 mg/dL nonfasting
	Persistently elevated LDL-C (≥160 mg/dL), non-HDL-C (≥190 mg/dL) or ApoB (≥120 mg/dL) Lp(a) ≥125 nmol/L or ≥50 mg/dL



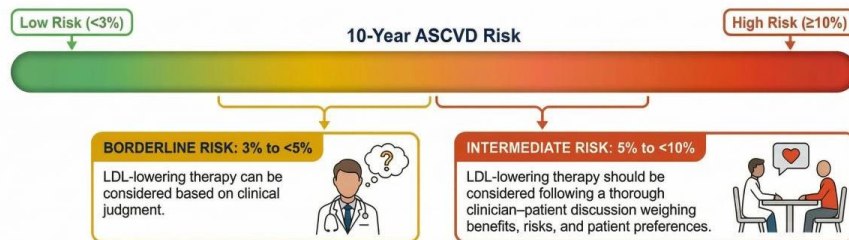
If present, risk enhancers favor statin therapy in borderline to intermediate risk individuals (10-year ASCVD risk 3-<10%)

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3 LDL-Lowering in Primary Prevention: Risk-Guided Decision Making

Based on 10-Year PREVENT-ASCVD Risk Estimates



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4/ LDL-C & Non-HDL-C Goals Are Back + ApoB Goals Are Included

	Patient Examples	LDL-C mg/dL	Non-HDL-C mg/dL	ApoB mg/dL
Borderline to Intermediate Risk	3-<5% or 5-<10% 10y ASCVD Risk <3% 10y ASCVD risk + (LDL-C ≥160 mg/dL or Fam Hx or 30y risk ≥10%) - T2DM without ASCVD or Risk Factors - CAC 1-99 or mild incidental CAC	<100	<130	<90
High Risk	>10% 10-yr ASCVD Risk - T2DM + Risk Factors - HeFH without ASCVD - CAC ≥100 – 999 AU - Moderate to severe incidental CAC	<70	<100	<70
Very High Risk	- ASCVD (optional if not very-high risk) - CAC ≥1000 AU (optional if ≥300 AU)	<55	<85	<55

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Use ApoB to Assess Residual Lipid-Related Risk

Consider ApoB when

- LDL-C & non-HDL-C goals are met, especially in patients with:
 - Cardiovascular-Kidney-Metabolic syndrome
 - Diabetes
 - TG ≥ 200 mg/dL
- If ApoB above goal, Rx should be intensified



About ApoB:

All atherogenic lipoproteins have a single apoB100 protein. ApoB reflects the total # of atherogenic lipoproteins. ApoB is not affected by fasting.

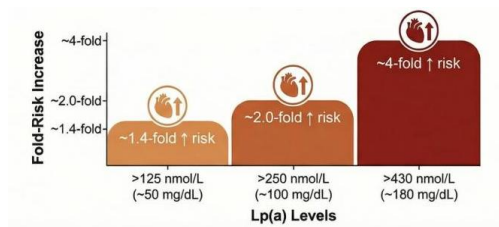
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Measure Lp(a) Once in All Adults

Increased ASCVD Risk By Lp(a) Levels



About Lp(a):

Lp(a) particles consist of an LDL particle bound to an apo(a) protein. Lp(a) levels largely genetically determined & mostly stable over a lifetime. Repeat testing generally not needed.

If Lp(a) is elevated, LDL-C lowering should be intensified and other ASCVD risk factors aggressively controlled

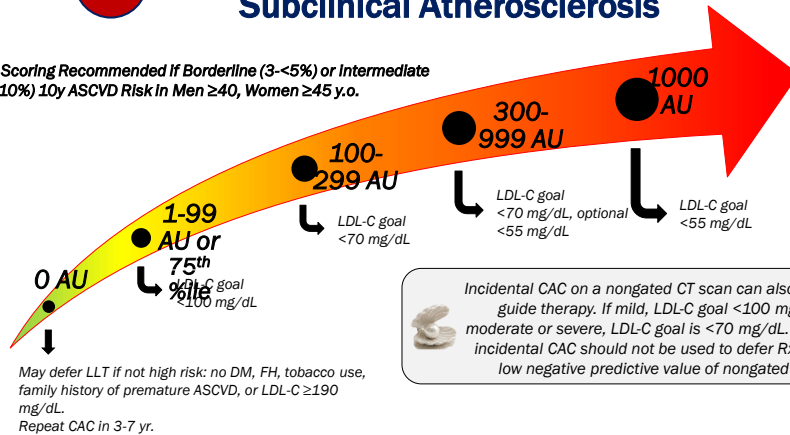
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CAC Score Guided Rx of Subclinical Atherosclerosis

CAC Scoring Recommended If Borderline (3-5%) or Intermediate (5-10%) 10y ASCVD Risk in Men ≥ 40 , Women ≥ 45 y.o.



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Special Considerations in Therapy



CKD

Stage 3-4
All Ages

Statin Therapy Recommended if
LDL-C ≥ 70 mg/dL



HIV

Age ≥ 40



Diabetes

Age ≥ 40



Cancer

Continue LLT
unless
contraindicated



Pregnancy

Consult a dietitian and
defer most LLT

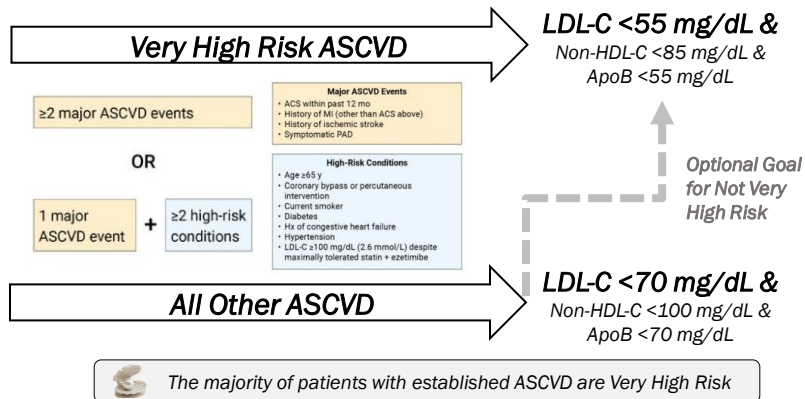
If TG are ≥ 500 mg/dL
(after 1st trimester),
consider fibrate
or omega-3 FA

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Lipid Goals in Established ASCVD

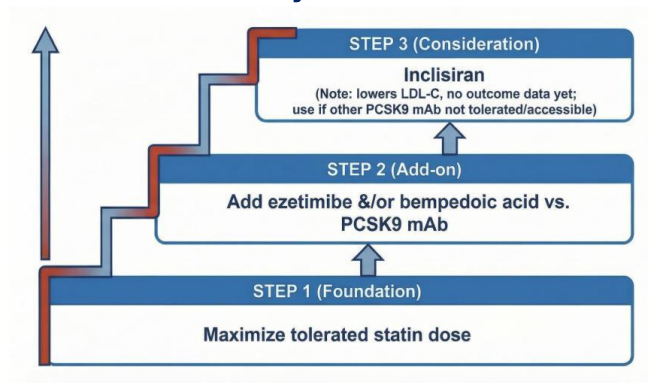


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Lipid-Lowering Therapy Beyond Statins



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Dietary Interventions for Hypertriglyceridemia

Lifestyle is 1st Line for All With Elevated TGs:

≥5% weight loss, ≥150 min/week moderate intensity activity

Implemented shared decision-making intervention	TG ≥150 to 499 mg/dL* (1.7 to <5.7 mmol/L)	TG ≥500 to 999 mg/dL* (5.7 to <11.3 mmol/L)	TG ≥1000 mg/dL† (≥11.3 mmol/L)
Added sugars (percent calories)	<6%	<5%	Eliminate
Total fat (percent calories)	30%–35%	20%–25%‡	10%–15%§¶
Alcohol	Avoid	Abstain completely	Abstain completely
Physical activity	At least 150 minutes/week of accumulated moderate-intensity or 75 minutes/week of vigorous intensity aerobic activity (or equivalent combination of both) and 2 days/week of upper and lower body resistance exercise¶		
Weight loss (percent body weight)	Recommended weight loss goal of 5%–10% for patients who are overweight or obese with elevated TG		

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Screening for CKM Syndrome

Early Life Screening Age <21 years



- » Annual screening for overweight and obesity using sex- and age-specific CDC growth charts
- » Mental and behavioral health screening
- » Blood pressure assessment at least annually, and at every visit starting at age 3
- » Fasting lipid panel between ages 9-11 and again between ages 17-21
- » Positive family history of dyslipidemia- begin screening at age 2
- » Screen for glucose intolerance and monitor alanine aminotransferase
- » Assign appropriate CKM Syndrome stage and begin recommended prevention

Abbreviations: CDC indicates Centers for Disease Control and Prevention; and CKM, Cardiovascular-Kidney-Metabolic.



Ndumele, C.E. et al., Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association, 2023. Circulation.

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Screening for CKM Syndrome

Adult Screening Age ≥21 years



- » BMI and waist circumference annually
- » Blood pressure, HbA1c and lipid panel at stage-determined intervals
- » Microalbumin and creatinine measurements at stage-determined intervals
- » Screening for MASLD every 1-2 years as directed by guidelines
- » CAC measurements as directed by guidelines

Abbreviations: BMI indicates body mass index; CAC, coronary artery calcium; CKM, Cardiovascular-Kidney-Metabolic; Hb A1c, hemoglobin a1c; and MASLD, metabolic dysfunction-associated steatotic liver disease.



Ndumele, C.E. et al., Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association, 2023. Circulation.

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LDL-C (Non HDL-C) Lowering

- LDL-C (and Non HDL-C) levels closely tied to ASCVD risk
- While LDL-C less closely tied to metabolic risk factors (non-HDL), intensity of LDL-C lowering tied to global CVD risk in guidelines and clinical practice
- Many in stage 4 of CKM syndrome fall into the category of very high-risk ASCVD, where more intensive lipid lowering favored
- key question is whether there is a primary prevention population where more intensive LDL-C lowering with considerations beyond statins and ezetimibe, is warranted. Potential investigation of the CKM Stage 3 population for such consideration



Ndumele, C.E. et al., A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic Syndrome: A Scientific Statement From the American Heart Association. 2023. *Circulation*.

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Diabetes Without ASCVD

- Most adults 40–75 years with diabetes = **intermediate or high ASCVD risk**
- First events in diabetes carry **higher morbidity and mortality**

Primary LDL Treatment Strategy

- Moderate-intensity statin indicated for ages 40–75 yrs
 - **Goal:** ≥30–49% LDL mg/dL reduction, LDL <100 mg/dL
- High-intensity statin reasonable if multiple ASCVD risk factors
 - **Goal:** ≥50% LDL reduction, LDL <70 mg/dL

COR	RECOMMENDATIONS
1	Age 40–75 years → moderate statin (LDL<100 mg/dL).
1	Statin-intolerant: ezetimibe/PCSK9/bempedoic.
2a	Multiple risk factors → high-intensity statin (LDL<70 mg/dL).
2b	TG 150–499 mg/dL → consider icosapent ethyl.
2b	10-year risk ≥10% → consider ezetimibe/PCSK9.
2b	Age >75 years → moderate statin reasonable.
2b	Age 20–39 years with long-duration diabetes → consider statin.

Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; LDL, and low-density lipoprotein cholesterol.



Blumenthal, R.S., Morris, P.B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. *Circulation*.

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Adults with Chronic Kidney Disease



Adults with CKD	
COR	RECOMMENDATIONS
1	In adults 40 to 75 years of age with CKD Stage 3 or higher and an LDL-C of 70-189 mg/dL (1.8-4.9 mmol/L), moderate-intensity statin therapy (± ezetimibe) is recommended to reduce ASCVD risk.
1	In adults with CKD Stage 3 or higher and clinical ASCVD, LLT with high-intensity statin therapy (± ezetimibe) and/or a PCSK9 mAb, is recommended to achieve ≥50% reduction in LDL-C levels and a goal of LDL-C <55 mg/dL (1.4 mmol/L) and non-HDL-C <85 mg/dL (2.2 mmol/L) to reduce ASCVD risk.
2b	In adults with CKD who require maintenance hemodialysis, it may be reasonable to continue statin therapy to reduce the risk of ASCVD events. Treatment decisions should be individualized, considering expected survival, other comorbidities, and severity of ASCVD.

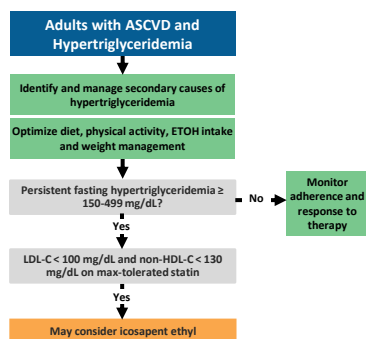
Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; CKD, chronic kidney disease; HDL-C, high-density lipoprotein cholesterol; HFrEF, heart failure with reduced ejection fraction; LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy; and PCSK9, proprotein convertase subtilisin/kexin type 9.



Blumenthal, R.S., Morris, P.B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. Circulation.

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Management of Hypertriglyceridemia



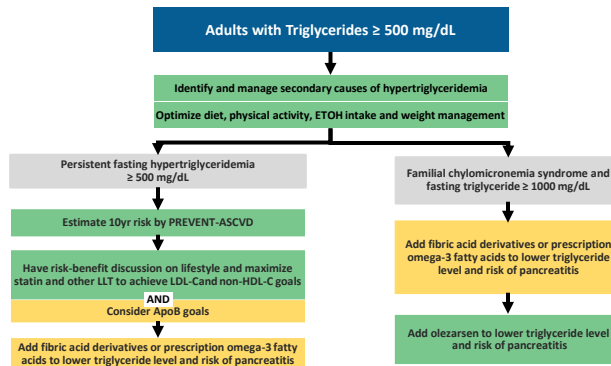
Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; ETOH, ethyl alcohol; HDL-C, high-density lipoprotein cholesterol; and LDL-C, low-density lipoprotein-cholesterol.



Blumenthal, R.S., Morris, P.B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. Circulation.

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Management of Hypertriglyceridemia (Continued)



Abbreviations: ApoB indicates apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; ETOH, ethyl alcohol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LLT, lipid lowering therapy; and PREVENT, Predicting Risk of CVD Events.



Blumenthal, R.S., Morris, P.B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. Circulation.

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Recommendations for Management of Hypertriglyceridemia

COR	RECOMMENDATIONS
1	In adults with persistently elevated triglyceride levels ≥ 150 mg/dL (1.7 mmol/L), after evaluation and management of secondary causes, lifestyle management (consuming a diet that consists of low added sugars, as well as reduced alcohol and saturated fat intake, routine exercise, and weight loss of 5-10% of body weight if overweight or obese) is recommended as first-line approach to reduce triglyceride levels.
1	In adults with clinical ASCVD and LDL-C ≥ 55 mg/dL (1.4 mmol/L) and non-HDL-C ≥ 85 mg/dL on maximally tolerated statin with persistently elevated triglyceride levels ≥ 150 to 999 mg/dL (1.7 to 11.3 mmol/L), intensification of LDL-C lowering therapy is recommended to reduce ASCVD risk.
1	In adults aged 40 to 75 years without a history of ASCVD or diabetes who have persistently elevated triglyceride levels ≥ 150 to 499 mg/dL (1.7 to 5.6 mmol/L), it is recommended to estimate 10-year ASCVD risk by the PREVENT-ASCVD equations to guide the benefit-risk discussion regarding further optimization of diet and lifestyle management as well as the potential initiation of statin therapy to reduce ASCVD risk.

Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; and PREVENT, Predicting Risk of CVD Events.



Blumenthal, R.S., Morris, P.B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. Circulation.

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Recommendations for Management of Hypertriglyceridemia (Continued)

COR	RECOMMENDATIONS
2b	In adults with clinical ASCVD or with diabetes ≥50 years of age and 1 or more ASCVD risk factors, with persistently elevated triglyceride levels ≥150 to 499 mg/dL (1.7 to 5.6 mmol/L), and LDL-C <100 mg/dL (2.6 mmol/L) on maximally tolerated statin, the addition of icosapent ethyl may be reasonable to lower ASCVD risk.
1	In adults aged 40 to 75 years without a history of ASCVD or diabetes who have persistently elevated triglyceride levels ≥150 to 499 mg/dL (1.7 to 5.6 mmol/L), it is recommended to estimate 10-year ASCVD risk by the PREVENT-ASCVD equations to guide the benefit-risk discussion regarding further optimization of diet and lifestyle management as well as the potential initiation of statin therapy to reduce ASCVD risk.
2a	In adults with severe hypertriglyceridemia (persistently elevated triglyceride levels ≥500-999 mg/dL (5.7 to 11.3 mmol/L) and especially with triglyceride levels ≥1,000 mg/dL (11.3 mmol/L) despite dietary intervention, the use of fibric acid derivatives or prescription omega-3 fatty acids is reasonable to lower triglyceride levels and reduce the risk of pancreatitis.
2a	In adults with hypertriglyceridemia (TG ≥150 mg/dL), measurement of non-HDL-C or apoB is preferred over LDL-C to guide clinical decision-making.

Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein cholesterol; and PREVENT, Predicting Risk of CVD Events.



Blumenthal, R.S., Morris, P.B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. Circulation.

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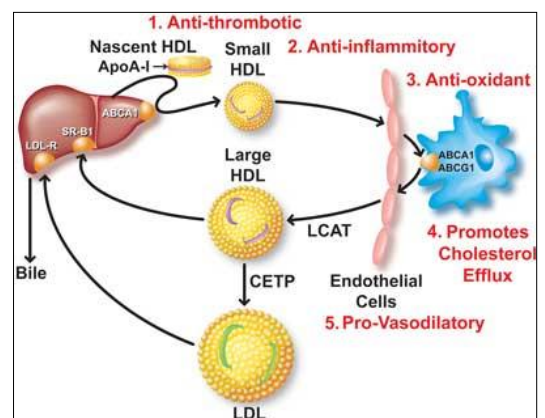
HDL - The “Good” Cholesterol

- Risk for ASCVD inversely related to HDL-C
 - < 40 mg/dL (men)
 - < 50 mg/dL (women)
- Increased risk even when LDL-C well controlled (TNT)
- For every 1 mg/dL rise in HDL-C risk for CVD decreases 2-3%

Toth PP. Circulation 2005. 111(5) e89-91

Barter P, et al. NEJM 2007. 357(13): 1301-10

Cooney MT, et al. Atherosclerosis 2007. (206): 611-616



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Associated with Low HDL-C

- Overweight / obesity
- Metabolic Syndrome
- Diabetes
- Tobacco use
- Very low-fat diets
- Systemic inflammation
- Anabolic steroids / b-blockers, diuretics, progestins

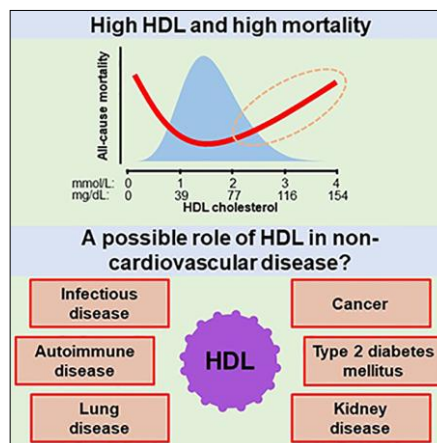
Schaefer EJ, et al. J Lipid Res 1994; 35(5): 871-82

Gotto AM. Circulation 2001; 103(17): 2213-2218

Sun L, et al. Lipids in Health and Disease 2021; 20(149)

51

U-Shaped Curve and HDL-C



ATVB 2021; 41: 128-140

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CKM Lipid Related Risk

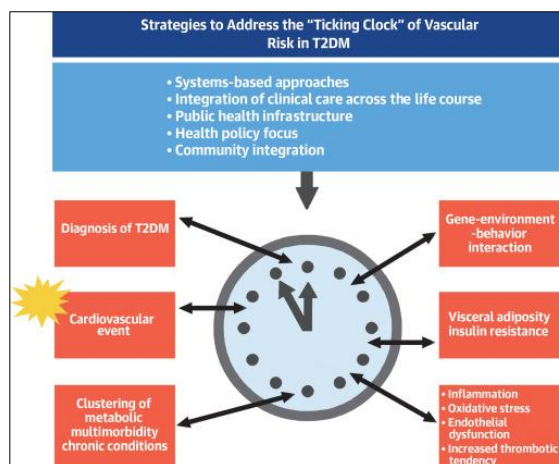
- CKM Overview
- PREVENT / CPR
- Top 10
- Focus on Lipids in CKM
- **Summary**

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The “Ticking Clock” of Impending Diabetes: Cause for Concern or Window of Opportunity?

- T2DM usually component of Metabolic Multi-morbidity Chronic Conditions (MMMCC)
- Impact across the life course
- Need to tackle root causes / complex contributing factors

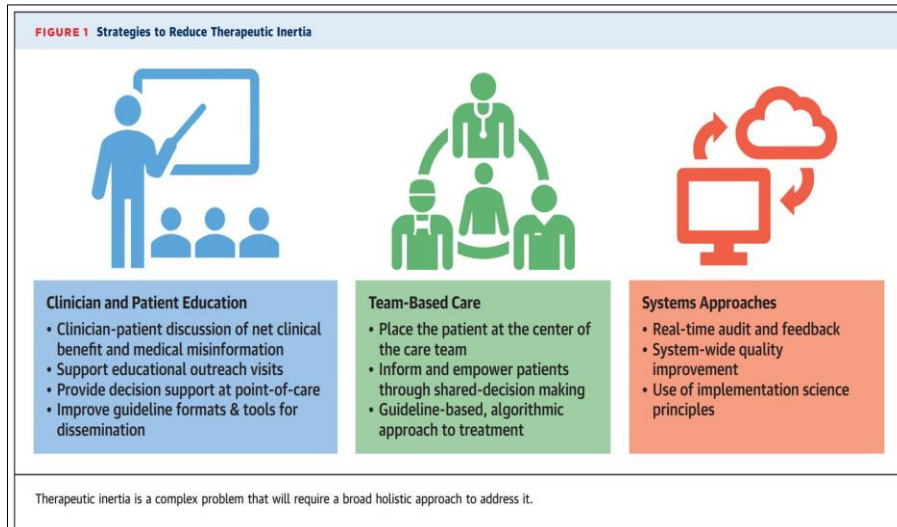
Sperling LS JACC 2024. 84 (23)



54

Therapeutic Inertia in CVD Prevention

Dixon DL, Sharma G, Mensah GA, Sperling LS, Deedwania, PC, Virani SS JACC 2019;74(13)



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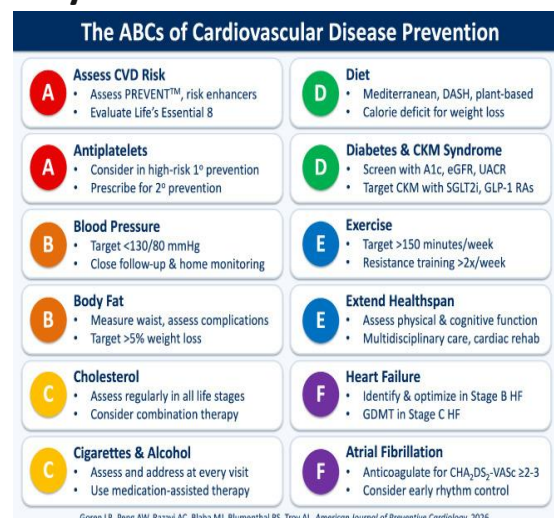
Goal Is Comprehensive CVD Prevention- ABC's and Beyond.....

Prevention Across Life Course

Prevention of:

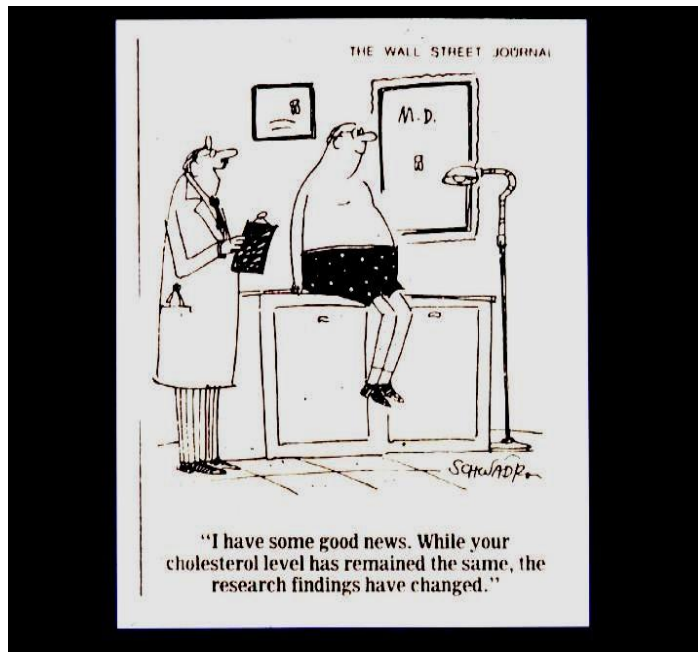
- ASCVD
- total CVD
- heart failure
- atrial fibrillation
- CKM syndrome
- dementia?

Goren L, et al. AJPC 2026. 101570



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Laurence Sperling, MD
Focus on Lipid-Related Risk as a Component of CKM Health



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CKMH Lipid Related Risk

- CKM syndrome is prevalent
- Life course approach needed
- Lifestyle / behavioral approaches foundational
- PREVENT / CPR
- Typical pattern of metabolic dyslipidemia
- Diabetes and CKD signal high risk
- Approach to hypertriglyceridemia
- Implementation, implementation, implementation

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ARS Question #1

All Are Components of the Complete PREVENT Risk Score Except:

- A. Systolic BP
- B. BMI
- C. UACR
- D. LDL-C
- E. Zip code



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ARS Question #2

Target LDL-C, Blood Pressure, and A1C Goals for a 60-year-old Patient with T2DM and Cardiac RF's Would Be:

- A. < 55; < 110/70; < 6.0
- B. < 130; < 135/85; < 7.5
- C. < 70; < 130/80; < 7.0
- D. < 100; < 140/85; < 8.0



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