FULL THREAD | POSTS 1-558

Cardiovascular Health 2026

Global TL;DR from the first post through the latest visible post today

Verified endpoint	Post #558, published 19 July 2026
Evidence rule	Forum ideas are separated from guidelines, labels and cardiovascular outcome trials
Purpose	A one-stop, actionable summary of the entire discussion

Global verdict

The thread's strongest conclusion is that cardiovascular prevention is exposure management: reduce cumulative ApoB-containing particle burden, blood pressure, smoking, dysglycemia and kidney risk while preserving high fitness. The weak part is its recurrent leap from this sound model to universal targets, repeated high-tech imaging and self-experimentation. Risk should determine treatment intensity; outcome evidence should determine the tool.

The whole thread in ten points

- Atherosclerosis is driven mainly by the number and lifetime exposure of ApoB-containing particles, not by LDL-C concentration alone.

- Lower ApoB/LDL-C is generally better when achieved safely, but there is no evidence-based universal LDL-C below 50 mg/dL target for every adult.

- Absolute risk comes first: age, established plaque/ASCVD, blood pressure, smoking, diabetes, kidney disease, family history, ApoB and Lp(a) determine the likely benefit.

- Lp(a) should usually be measured once. hsCRP can refine risk if persistently elevated, but low hsCRP does not neutralize high ApoB or Lp(a).

- HDL-C, LDL/HDL ratios, NHHR and small-dense LDL are usually secondary or redundant once ApoB/non-HDL-C and global risk are known.

- Statins remain the outcomes-first drug anchor when tolerated. Ezetimibe, bempedoic acid and PCSK9 therapies close the remaining gap according to risk and tolerance.

- CAC can help when a treatment decision is uncertain. CCTA is for a specific question; routine serial plaque scans are not validated prevention.

- Aerobic fitness, resistance training, Mediterranean-pattern food quality, sleep and no smoking are foundational, even when drugs are needed.

- Aspirin, nattokinase, chelation, fibrinolytic supplements, berberine or high-dose vitamins should not be used as substitutes for proven primary prevention.

- The newest posts add real high-risk PCSK9 outcome evidence and the first oral PCSK9 inhibitor, but they do not validate the thread's experimental naltrexone-plus-rapamycin myalgia protocol.

This is educational synthesis, not a diagnosis or prescription. Medication and imaging decisions require a clinician with the complete record.

EVIDENCE MAP

What survives critical review

Status	Thread claim	Global conclusion
KEEP	Cumulative ApoB exposure is causal	Strong. Earlier and longer reduction lowers lifetime atherosclerotic burden. ApoB is especially helpful when LDL-C is discordant with triglycerides, diabetes or metabolic syndrome.
KEEP	Blood pressure, glucose, smoking, kidney function and fitness matter	Strong. Cardiovascular prevention is multi-axis; favorable weight or insulin does not cancel risk elsewhere.
KEEP	Lp(a) once; hsCRP as a modifier	Strong with nuance. Lp(a) is inherited and largely stable. Repeat hsCRP when well if elevated; it is downstream and nonspecific.
CONDITION	Very low LDL-C is safe and desirable	Trial safety is reassuring, especially in high-risk patients. The target must still reflect absolute risk, treatment burden and patient preference.
CONDITION	Pitavastatin is the best statin	It may help with tolerability, glycemia or interactions, but is not universally superior and the FDA maximum is 4 mg/day.
CONDITION	CCTA detects plaque missed by CAC	True anatomically, but detection is not the same as outcome benefit. Use only when the result will change care.
CONDITION	PCSK9 drugs lack an all-cause mortality signal	Some trials were not powered or long enough for mortality. Clear reductions in MI/stroke/revascularization are clinically meaningful; absence of proof is not proof of no benefit.
REJECT	Everyone should target LDL-C below 50 mg/dL	Overreach. High- and very-high-risk targets are lower; lower-risk primary prevention needs formal risk assessment and modifiers.
REJECT	HDL or lipid ratios should drive treatment	Raising HDL-C has not reliably reduced events. ApoB/non-HDL-C and absolute risk are more actionable.
REJECT	Serial CCTA/Cleerly should track prevention	No outcome validation for routine surveillance; measurement noise, incidental findings, radiation and contrast can create false precision.
REJECT	Nattokinase, chelation, DMSA, serrapeptase or naltrexone plus rapamycin treat plaque or myalgia	No credible clinical-outcome evidence supports these protocols; several introduce bleeding, toxicity or interaction risk.

Mechanistic shorthand

ApoB particles enter and become retained in the arterial wall, where modified lipoproteins provoke inflammatory repair and plaque formation. Blood pressure accelerates endothelial injury; glucose and kidney disease amplify vascular damage. Exercise improves endothelial function, muscle glucose disposal, mitochondrial capacity and cardiorespiratory fitness. These mechanisms support action, but hard outcomes determine which interventions deserve priority.

DECISION DASHBOARD

Measure, classify, then act

Priority	What to obtain	How it changes the plan
1. Baseline	7-day home BP; fasting lipid panel plus ApoB; HbA1c/glucose; creatinine/eGFR; UACR; smoking and family history.	Defines the main modifiable axes and permits SCORE2/SCORE2-OP risk calculation in Europe.
2. Once	Lp(a), preferably reported in nmol/L.	High Lp(a) strengthens the case for aggressive control of every modifiable exposure. Do not convert units using a fixed factor.
3. Conditional	hsCRP when well; repeat if >=2 mg/L. ALT before drug therapy; CK for significant muscle symptoms/history.	Risk refinement and treatment safety, not routine biomarker chasing.
4. Imaging	CAC only if the medication decision remains uncertain. CCTA only for symptoms, high suspicion or a defined discordance.	Imaging must answer a treatment question. CAC=0 lowers near-term risk but does not erase lifetime risk or noncalcified plaque.

Risk-proportionate targets

Clinical state	LDL-C goal	ApoB secondary goal	Bottom line
Established ASCVD / very high risk	<55 mg/dL	Often <65 mg/dL	Combination therapy is commonly justified.
High risk	<70 mg/dL	Often <80 mg/dL	Treat the whole risk state, not LDL-C alone.
Lower/intermediate primary prevention	Calculator and modifier based	Useful when discordant	No universal <50 mg/dL rule.

A simple treatment ladder

Step	Use	Critical note
1	Maximally tolerated statin	Broadest outcomes history. Low dose, another statin or intermittent dosing can test/manage symptoms.
2	Add ezetimibe 10 mg/day	Usually 18-25% further LDL-C lowering with little CYP interaction burden.
3A	Bempedoic acid 180 mg/day	Useful in statin intolerance; watch uric acid/gout and tendon symptoms. Muscle effects are less frequent, not impossible.
3B	PCSK9 antibody	About 50-60% LDL-C lowering with outcome evidence. VESALIUS-CV supports high-risk prevention without prior MI/stroke, not indiscriminate low-risk use.
Alternative	Inclisiran or oral enlicitide	Inclisiran offers twice-yearly maintenance dosing but outcomes remain pending. Enlicitide lowers LDL-C about 56% but also lacks completed cardiovascular outcomes.

Do not start aspirin for routine primary prevention at age 66

Without established ASCVD or another indication, bleeding risk generally offsets benefit. This is one of the clearest 'do not extrapolate from the thread' conclusions.

ACTION

What the full thread means for you

Known profile used: male, about 66, BMI 22, body fat about 8%, fasting insulin about 5, regular upper-body resistance training and 20 minutes/day of incline treadmill in zones 3-5, with knee/ankle pain.

Area	Actionable conclusion
Largest unknowns	ApoB, Lp(a), home BP, eGFR/UACR, smoking/family history and documented plaque status matter more than additional supplement panels.
Body composition	Do not pursue further weight loss by default. Preserve energy availability, muscle and bone; low body fat and insulin do not exclude lipid or pressure risk.
Aerobic training	Keep the weekly volume, but make most work zone 2 to low zone 3. Limit hard zone 4-5 sessions to 1-2 per week and include recovery.
Strength and joints	Add two pain-compatible lower-body sessions using sit-to-stand, hip hinge, glute bridge, hamstring curl and calf isometrics. Substitute cycling, elliptical, rowing or pool work when impact hurts.
Food	Mediterranean pattern; replace saturated fats with olive oil, nuts, seeds and fish; add soluble fiber; keep protein roughly 1.2-1.6 g/kg/day unless kidney disease changes the plan.
Supplements	Do not use nattokinase, chelation, serrapeptase, berberine or megadose vitamins as substitutes for LDL/ApoB, BP and lifestyle treatment.

The only major new developments in the final posts

Development	What it really means
VESALIUS-CV	In 12,257 high-risk adults without prior MI/stroke, evolocumab reduced primary MACE from 8.0% to 6.2% over median 4.6 years (ARR 1.8%; approximate NNT 56). Most were not low risk.
Lipfendra (enlicitide)	FDA approved the first oral PCSK9 inhibitor on 17 July 2026. Trial LDL-C reduction was about 56% overall and 59% in HeFH. Take 20 mg fasting each morning and wait at least 30 minutes before food; cardiovascular outcomes are not yet established.
Inclisiran	A forum user's weak response is an anecdote. Expected LDL-C lowering is about 50%, but cardiovascular outcome data remain pending as of the cutoff.
Myalgia protocol	Low-dose naltrexone plus weekly rapamycin remains mechanistically speculative and clinically unvalidated. Use structured statin dechallenge/rechallenge and proven nonstatins instead.

Your next appointment should answer one question

What is your absolute cardiovascular risk, and how large is the gap between your current ApoB/LDL-C and the target justified by that risk? Bring home BP averages, ApoB, Lp(a), HbA1c, eGFR/UACR, family history and any prior imaging. Then choose the least burdensome proven therapy that closes the gap.

SOURCES

Evidence base and thread coverage

The complete forum thread was reviewed as a hypothesis-generating discussion. Recommendations were checked against current guideline, regulatory and trial sources. Links are clickable.

[1] Rapamycin.news - Cardiovascular Health 2026, thread start
[2] Rapamycin.news - page 28, latest visible page through post #558
[3] AHA - 2026 Guideline on the Management of Dyslipidemia: Top Things to Know
[4] ESC - 2025 focused update of the ESC/EAS dyslipidemia guidelines
[5] ACC - VESALIUS-CV trial summary
[6] US FDA - Approval of first oral PCSK9 inhibitor, Lipfendra
[7] Merck - Lipfendra (enlicitide) US Prescribing Information, July 2026
[8] ACC - Lipid Manager, including inclisiran outcomes-trial status
[9] ESC - 2024 blood pressure and hypertension guideline overview
[10] USPSTF - Aspirin use to prevent cardiovascular disease
[11] US FDA - Livalo (pitavastatin) Prescribing Information
[12] US FDA - Nexletol (bempedoic acid) Prescribing Information
[13] US FDA - Leqvio (inclisiran) Prescribing Information

Coverage note

The verified latest visible entry is post #558, dated 19 July 2026. Page 29 was not present at the time of checking. The thread may receive new posts after this PDF's cutoff.

Medical disclaimer

Educational summary only. Seek urgent care for chest pressure, new shortness of breath, fainting, stroke symptoms or other acute symptoms. Use a clinician for individualized risk calculation, medication selection, dosing and imaging decisions.