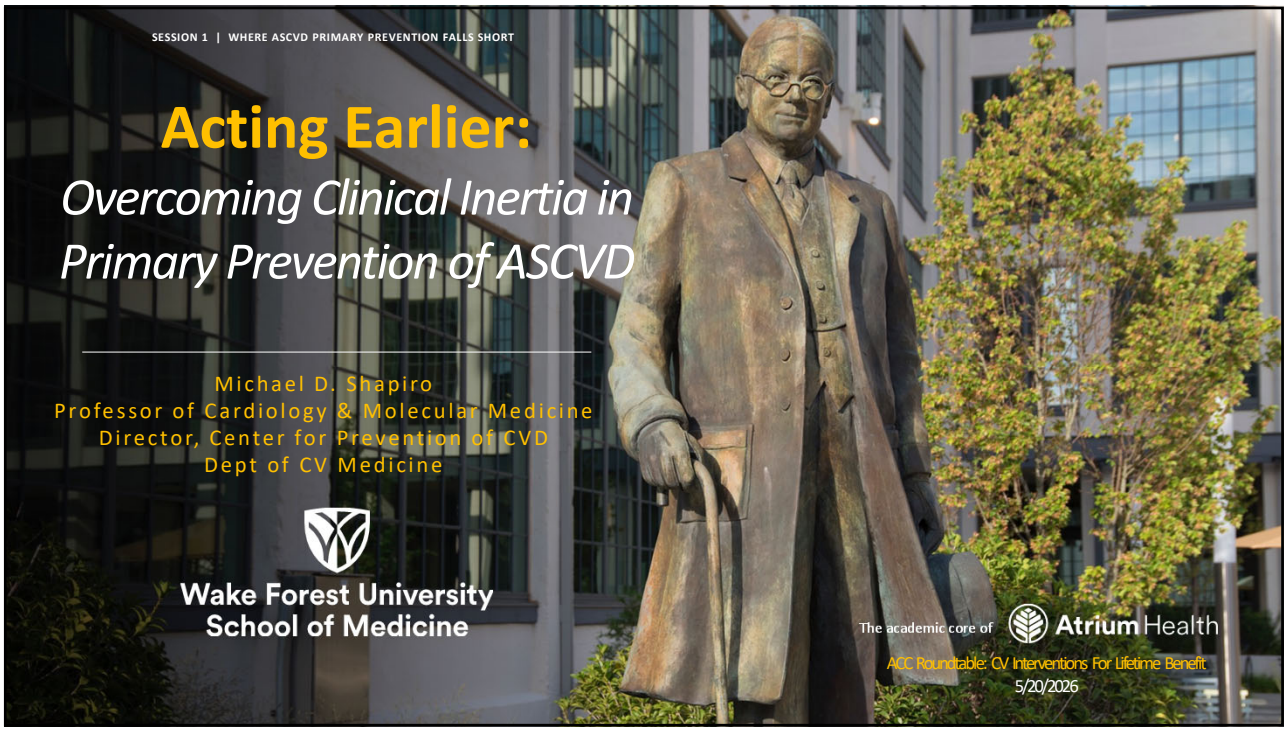

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Disclosures

Research Grants

- Amgen, Boehringer Ingelheim, Cleerly, Novartis, Ionis, Lilly, Merck, New Amsterdam, Astra Zeneca, Alnylam, Nanox

Scientific Advisory Boards

- Amgen, Esperion Novartis, Lilly, Merck, Regeneron

Consultant

- Ionis, Novartis, Regeneron, Merck, Esperion Tourmaline, Astra Zeneca, Alnylam

Writing Committee Member

- 2026 ACC/AHA Dyslipidemia Guideline

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Objectives

- Drivers of delayed action despite available risk indicators (for primary prevention)
- Explore uncertainty in early or borderline-risk scenarios
- Discuss limitations of guidelines in practice

The Prevention Paradox

ASCVD is simultaneously the most preventable and the most lethal condition in medicine

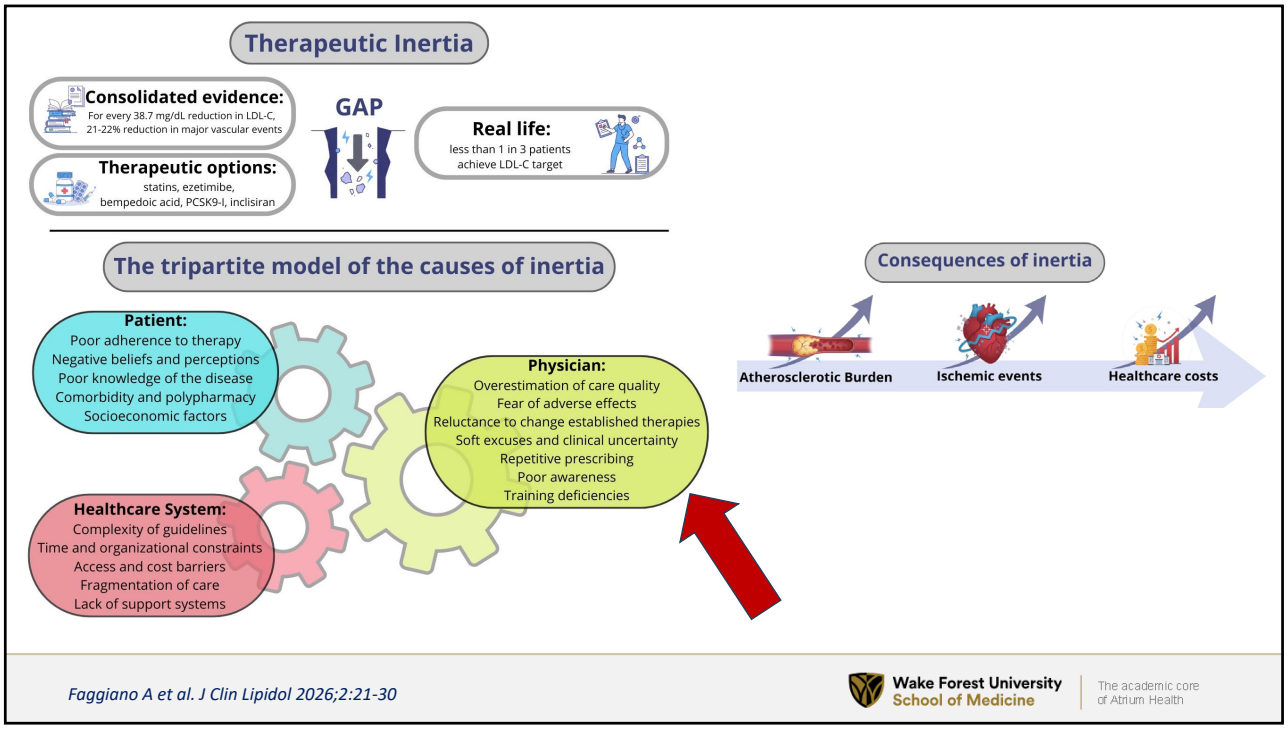
PREVENTABLE

- Causal evidence: unambiguous and replicated
- Effective therapies: accessible and well-tolerated
- Risk identifiable: decades before first events
- Guidelines: comprehensive and regularly updated

AND YET

- #1 cause of death and disability worldwide
- <1 in 3 high-risk patients at LDL-C goal
- 47% at BP target despite being on therapy
- Median 2.9 years before DM intensification

Roth et al. Global Burden of Disease 2019; Kotseva et al. Eur J Prev Cardiol 2020
Khunti et al. Diabetes Care 2013; Faggiano et al. J Clin Med 2025



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Defining Clinical Inertia in ASCVD Prevention

Clinical inertia is the failure of clinicians to initiate or intensify therapy when indicated, even when evidence, guidelines, and risk data support action

Recognition failure

Clinician does not recognize that the patient's risk level warrants preventive intervention

Decision failure

Risk is recognized but the clinician decides not to act, often due to uncertainty or competing priorities

Implementation failure

Decision to act is made but therapy is never initiated, referral not completed, or follow-up is missed

Even when clinicians act, they under-intensify.
Proposed regimen changes are frequently insufficient to reach goals

Faggiano et al. J Clin Med 2025 Phillips et al. Ann Fam Med 2001

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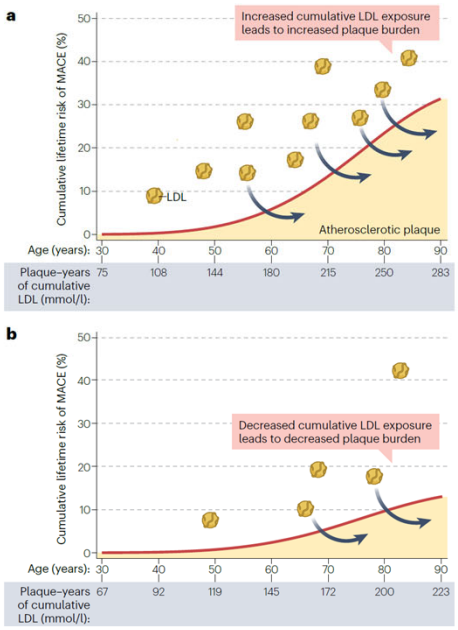

Clinical inertia has consequences

Every year of delay is compounding atherosclerotic burden that only partially offset by later treatment

Ference BA et al. Nat Rev Cardiol. 2024;21:701-716

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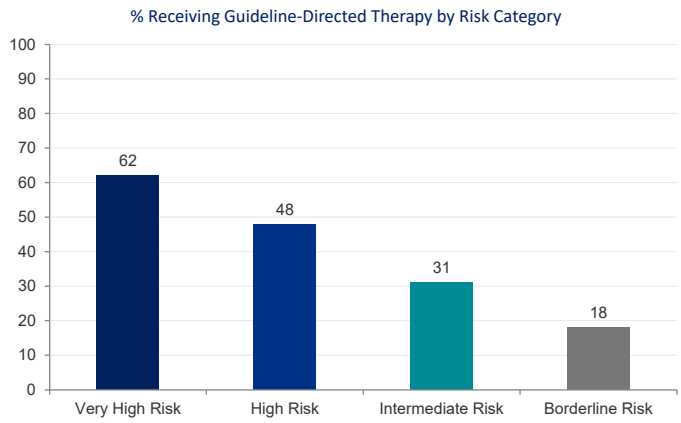
The Treatment Gap: How Large Is the Problem?



~80% of borderline-risk patients receive no statin or lifestyle counseling

~52% of high-risk patients remain undertreated at 12-month follow-up

>60% of primary care visits with elevated PCE scores result in no management change

Mortensen 2022; Pencina et al., NEJM Evid 2022; Navar et al. JAMA Cardiol 2017

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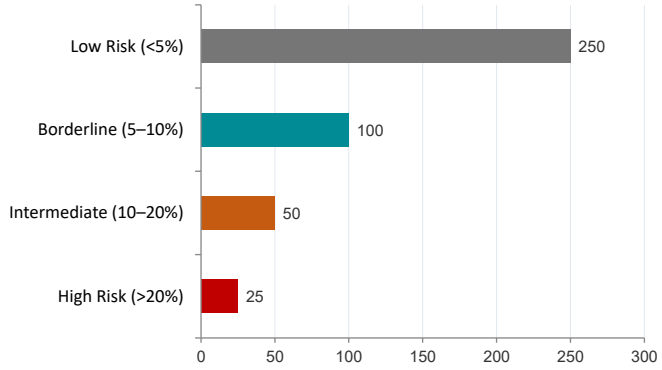
The NNT Problem: How Numbers Shape Clinical Decisions

NNT for statins in primary prevention varies widely, and how it's framed significantly influences both physician and patient decision-making



NNT is not the whole story

Absolute risk reduction is small per patient, but population-level impact is enormous, similar to vaccines

Framing effect matters

'1 in 50 patients will benefit' vs. '2% absolute risk reduction', both accurate but elicit different responses

Lifetime NNT is more persuasive

Reframing NNT over a patient's lifetime significantly improves the perceived value of preventive therapy

Chou et al., JAMA 2022; CTTC, Lancet 2012

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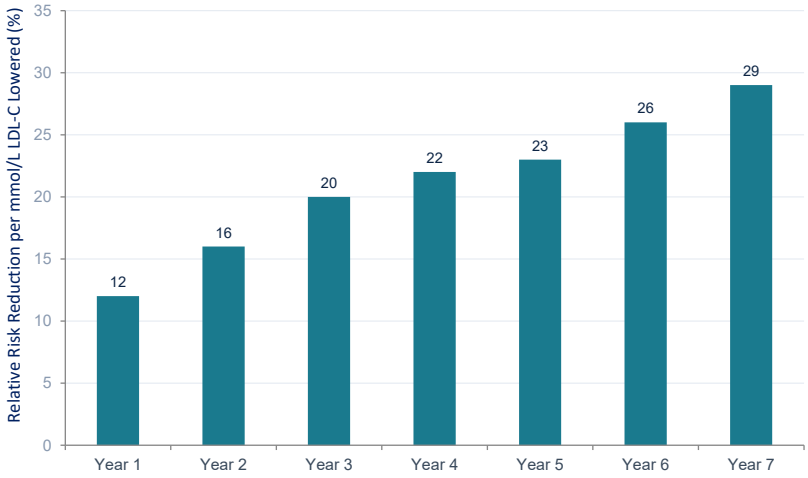
Why Earlier Means Exponentially More

RRR per unit LDL-C lowered grows substantially with treatment duration (Wang et al., 21 RCTs, n=184,012



Lifelong LDL lowering produces ~3× the per-unit CV risk reduction of short-term trial treatment

Wang N et al. Circ Cardiovasc Qual Outcomes 2022

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Where Guidelines Leave Clinicians Uncertain

Risk Score Proliferation
- Multiple quantitative risk scores
- Discordant results in up to 40% of borderline-risk patients
- 2026 ACC AHA Dyslipidemia GL endorses PREVENT, but most EHR's still default to PCE

Threshold Ambiguity
- The 10-year ASCVD risk cutoffs are population-derived and do not reflect individual patient context or competing comorbidities

Frequent Updates
- Guideline updates (2013, 2018, 2026 ACC/AHA) require re-learning and re-calibration. Each revision introduces new risk enhancers, decision pathways, etc

Competing Guideline Sources
- ACC/AHA, ESC, USPSTF, and ADA issue overlapping but sometimes conflicting recommendations, creating decision paralysis at point-of-care

Cosin-Sales et al. Atherosclerosis. 2023

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Physician-Level Barriers to Timely Action

Anticipated patient non-adherence
Clinicians sometimes defer prescribing based on their own prediction that a patient won't take the medication (removing the patient's agency to try)

Statin side-effect concerns
Real and perceived statin side effects disproportionately influence prescribing decisions relative to actual incidence data

Fear of medicalizing healthy patients
In younger, asymptomatic patients, there is reluctance to label or treat individuals perceived as 'healthy'

Uncertainty about NNT
Clinicians often underestimate absolute risk reduction and overestimate the NNT, biasing against preventive prescribing

Competing clinical priorities
During time-constrained visits, ASCVD risk discussion is often displaced by acute concerns or administrative burden

Lack of decision support
Integrated cardiovascular risk calculators and risk-based prompts remain absent in many EHR systems

Koskinas C et al. Eur J Prev Cardiol. 2021

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The CKM Patient: Multiple COR 1, No Sequencing Framework

Therapy	Guideline Recommendation	Clinical Friction
Statin	2026 GL COR 1 (CKD Stage 3–4, any LDL)	LDL-C already 74 mg/dL, patient asks 'why?'
SGLT2 inhibitor	KDIGO 2024 COR 1 (DM + CKD, eGFR ≥20)	Cost, access, education burden
GLP-1 RA	ADA 2024 COR 1 (DM + high CV risk)	GI tolerance, cost, injection, shortage
Finerenone	KDIGO 2024 COR 1 (DM + CKD + albuminuria)	Limited clinician familiarity
Antihypertensive	ACC/AHA COR 1 (BP >130/80)	Already on ACEi, which add-on?

? For discussion: When multiple COR 1 recommendations from different guidelines converge on the same patient , how do you prioritize meds?

Blumenthal et al. JACC 2026; KDIGO 2024; ADA Standards of Care 2024; ACC/AHA 2023 CKM Framework

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Summary

- Atherosclerosis is related to cumulative exposure of risk factors, every year of delay has a biological cost that cannot be fully reclaimed
- Multiple clinician-level drivers delay action despite available risk indicators
- Clinical inertia is most prevalent in borderline and intermediate risk patients
- We have new tools, more evidence, contemporary guidelines, the opportunity to act earlier and prevent more has never been greater

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Thank you