From treatment to prevention: industry and regulatory partnership to deliver on the cardiometabolic promise

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Ola Vedin, MD, PhD

Executive Director, CVRM Late-Stage Clinical Development, AstraZeneca

Disclaimer

- Views expressed in this presentation are my own

Safe Hearts Plan: ambition is there – infrastructure isn’t

What the plan demands		What the system was built for
Prevention at population scale		Treatment of established disease
A cardiometabolic continuum	**VS**	Siloed indications
AI accelerated detection		No pathway for what is detected

The prevention evidence problem – endpoints

CV primary prevention trial: MACE endpoint

10-30,000 participants | 5-7 years | >1 EUR billion

Surrogate endpoints exist — none formally qualified, e.g.

- Lp(a) reduction, plaque regression, AI-enabled imaging
- In oncology, surrogates have defined acceptance criteria
- In CV prevention: case-by-case, less process, less predictability

Enrichment tools (PRS, SCORE2, AI stratification) make trials feasible —

but risk becoming label restrictions if not pre-agreed

Safety and access – the two other legs

Uncertainty costs years

Safety expectations in prevention are answerable questions:

- Database size? Follow-up duration? Scope for risk management plan? Comparators?
- Without early clarity → sponsors over-design → adds years and hundreds of millions

Misalignment costs patients

- Numbers needed to treat are inherently higher in prevention
- PCSK9 inhibitor precedent: full authorization → years of restricted access
- If regulatory and HTA expectations diverge → sponsors face a lose-lose
- Must be answered together, before Phase 3 — not sequentially after

Cardiometabolic convergence: one continuum vs separate silos

The science treats CV risk, diabetes, obesity, and renal disease as interconnected.
The regulatory system treats them as separate indications requiring separate evidence.

Approach	Time to CV Prevention claim	Challenge
Sequential (metabolic first → CVOT later)	+5–7 years	Delays patient access
Integrated (co-primary CV + metabolic)	Fastest	Larger, costlier, higher risk
Hybrid (metabolic → pragmatic CV study)	Moderate	No regulatory precedent

The guidance isn't missing, but from a different era

European Medicines Agency
Pre-Authorisation Evaluation of Medicines for Human Use

London, 25 September 2008
Doc. Ref. EMEA/CHMP/EWP/311890/2007

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

GUIDELINE ON THE EVALUATION OF MEDICINAL PRODUCTS FOR CARDIOVASCULAR DISEASE PREVENTION

Some new considerations since 2008

- Genetically validated targets (Lp(a), FH) as basis for surrogate acceptance
- If a metabolic program shows CV benefit: is there a path to a standalone CV prevention claim?
- AI-enabled endpoints and enrichment strategies
- How trial enrichment criteria relate to the final prescribing population
- Population screening context (Safe Hearts Plan)

If you screen for it, there must be an actionable plan for what you find

The gap today, examples:

- **Lp(a):** screening proposed → no authorized therapy
- **FH:** screening expanding → treatment authorized, access restricted
- **Novel markers** (PRS, AI imaging etc.): detection outpacing intervention

AI-enabled detection will only widen this gap faster.

What's needed:

- Proactive early EMA/developer interaction
- Surrogate qualification (Lp(a)) in parallel with screening rollout
- Formal link between Safe Hearts screening policy and regulatory readiness

Three things we can do together – now

1. Integrated early regulatory-HTA advice for CV prevention

- Work toward one consultation: endpoints, safety, HTA-relevant outcomes — together
- At pre-Phase 3 design lock
- Documented; deviation requires justification

2. Modernize the CV prevention regulatory framework

- Update the 2008 guideline
- Address: surrogate acceptance, sequencing, cross-continuum indications
- Reflection paper as immediate first step

3. Screen-to-treat alignment

- Link Safe Hearts Plan screening rollout to EMA regulatory readiness
- Surrogate qualification in parallel with screening — not after

The Safe Hearts Plan is a prevention plan. The system must be re-tooled to match

The science is ready.

The investment is ready.

Let’s make the system ready to meet them.