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PERSPECTIVE

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Rethinking cardiovascular prevention beyond short term risk scores in low and middle income countries

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Abstract

Cardiovascular disease remains the leading cause of death worldwide, accounting for more than 20 million deaths each year, over 75% of which occur in low- and middle-income countries (LMICs). Despite this burden, contemporary cardiovascular prevention continues to rely largely on short-term risk scores developed in high-income settings, prioritising a relatively small proportion of individuals at high predicted risk. According to the PURE study, more than 40% of cardiovascular events, and over 50% in LMICs, occur among individuals classified as low or intermediate risk (calculated using the World Health Organization 10-year cardiovascular risk score), highlighting a critical gap in current prevention paradigms. Cardiovascular risk in LMICs accumulates across the life course through sustained exposure to biological, social, and environmental determinants that are insufficiently captured by conventional risk models. In parallel, the geographic concentration of cardiovascular evidence generation in high-income countries has shaped prevention frameworks that are poorly calibrated to the populations bearing the greatest disease burden. The aim of this Perspective is to argue for a more inclusive and anticipatory framework for cardiovascular prevention, integrating social determinants of health, cumulative and lifespan-based risk assessment, and scalable population-level strategies alongside traditional high-risk approaches. Aligning clinical prevention with public policy and health system capacity may enable earlier, more equitable, and more effective cardiovascular prevention in settings where the global cardiovascular burden is highest.

Keywords Cardiovascular Diseases prevention and control, Risk Assessment, Social Determinants of Health, Public Health Policy, Life Course, Low- and Middle-Income Countries

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1 Introduction

Cardiovascular disease remains the leading cause of death worldwide, accounting for more than 20 million deaths annually, with over three-quarters occurring in low- and middle-income countries (LMICs) [1, 2]. This disproportionate burden reflects not only differences in exposure to traditional cardiovascular risk factors, but also profound demographic and social transitions unfolding unevenly across regions. Importantly, low- and middle-income countries represent a heterogeneous group, with substantial variation in epidemiology, healthcare infrastructure, and access to preventive services. Many LMICs are experiencing rapid urbanisation and population aging without parallel development of robust preventive health infrastructures [3]. Currently, more than 55% of the global population lives in urban areas, a proportion projected to reach 68% by 2050; by the same year, approximately 80% of individuals aged ≥ 60 years will reside in LMICs, intensifying cumulative cardiovascular risk where preventive capacity remains limited [4, 5].

Contemporary prevention strategies focus primarily on secondary prevention and on primary prevention among individuals classified as high risk [6, 7]. Despite this epidemiological reality, cardiovascular prevention continues to rely largely on short-term risk stratification tools developed in high-income countries, typically based on 10-year predicted risk of cardiovascular events using models such as the Framingham Risk Score, the Pooled Cohort Equations, or the World Health Organization risk charts, which primarily include age, sex, blood pressure, cholesterol levels, smoking status, and diabetes [8]. These models prioritise intensive interventions in a relatively small segment of the population identified as high risk over a 10-year horizon. However, in many settings, cardiovascular events arise predominantly from individuals outside these high-risk categories, reflecting the fact that individuals at low and intermediate risk represent the majority of the population and therefore contribute substantially to the overall burden of events [9].

Across populations, a consistent paradox has emerged: most cardiovascular events occur among individuals not classified as high risk by conventional prediction scores [9]. This observation reflects a population distribution effect, whereby individuals at low or intermediate predicted risk represent the majority of the population and therefore contribute substantially to the overall burden of events [10]. This phenomenon is particularly pronounced in LMICs, where demographic transition, limited access to care, and socioeconomic disadvantage amplify long-term cardiovascular vulnerability [11]. Together, these observations underscore the limitations of prevention frameworks anchored exclusively to short-term risk estimation. Importantly, this does not imply that existing risk prediction models are inherently flawed or should be abandoned, but rather that reliance on short-term, threshold-based stratification alone may be insufficient as it does not fully capture cumulative risk shaped by social, environmental, and contextual determinants.

This Perspective examines the limitations of current risk-based approaches in global cardiovascular prevention and argues for a shift toward a more inclusive and anticipatory framework. Integrating life-course trajectories, social determinants of health, and population-level policy strategies alongside traditional high-risk prevention may better align clinical practice with the realities shaping cardiovascular risk worldwide (Fig. 1).

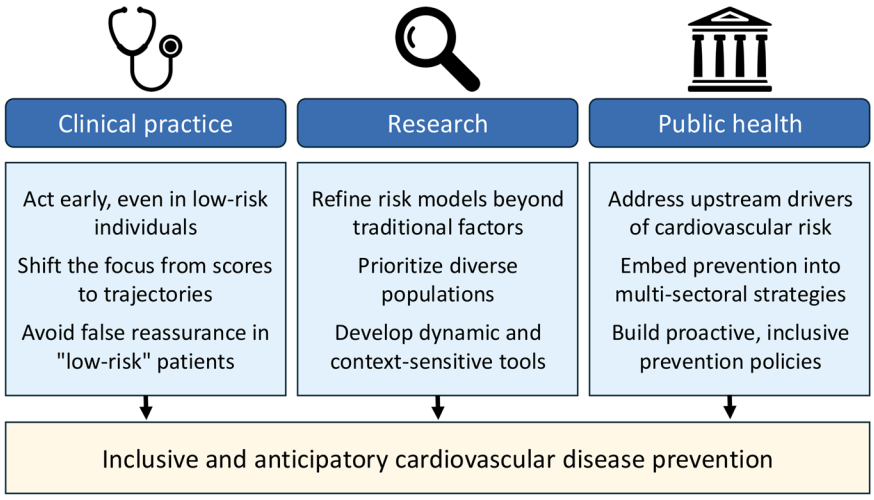

Fig. 1 Clinical, research, and policy strategies for a more inclusive and proactive approach to cardiovascular prevention

1.1 The low-risk paradox and its amplification in low- and middle-income countries

In the PURE (Prospective Urban Rural Epidemiology) study, approximately 40% of major cardiovascular events occurred among individuals without prior cardiovascular disease who were classified as low risk, with this proportion increasing from 32% in high-income countries to 54% in low-income countries [9, 12]. Similar patterns have been reported in European and US cohorts [13].

Several mechanisms contribute to this paradox. Populations in low- and middle-income countries are younger on average, resulting in lower short-term predicted risk despite substantial lifetime exposure to adverse determinants. At the same time, major cardiovascular risk factors such as hypertension, diabetes, and dyslipidaemia are frequently underdiagnosed and undertreated [14, 15]. Limited access to healthcare and delayed presentation to medical services further increase event severity and fatality [16]. Crucially, social deprivation and contextual disadvantage, rarely incorporated into conventional risk scores, contribute to systematic risk underestimation [17–19].

Because individuals classified as low risk represent the majority of the population, even relatively low event rates translate into a substantial absolute burden. This distribution of risk and the resulting concentration of events across the population are illustrated in Fig. 2 and are consistent with the well-described prevention paradox, in which a large number of events arise from a large group at modest risk rather than a small group at high risk [10]. In LMICs, particularly in settings with limited or fragmented access to primary care, preventive services are often reserved for overt disease or extreme risk profiles, contributing to a persistent prevention gap among disadvantaged populations.

1.2 Static scores in dynamic life courses

Conventional cardiovascular risk scores remain useful clinical tools, but important limitations emerge when they are applied across diverse global contexts. Most models are derived from a restricted set of traditional risk factors measured at a single point in time and are therefore intrinsically static in their structure, even though periodic reassessment is recommended in clinical practice [20, 21]. This design reflects the historical

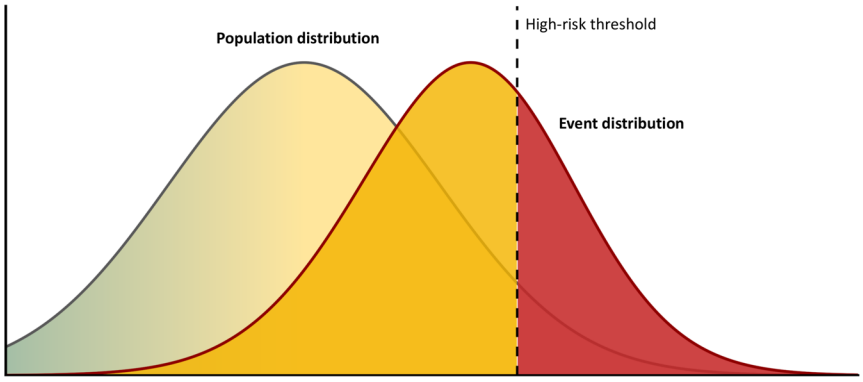

Fig. 2 The prevention paradox in cardiovascular disease: distribution of risk and population burden of events. This figure illustrates the prevention paradox in cardiovascular disease. The background curve represents the population distribution across predicted cardiovascular risk, with low and intermediate risk shown in a green-to-yellow gradient and high risk in red. The overlaid curve represents the corresponding distribution of cardiovascular events. Although individual event probability increases with higher predicted risk, a substantial proportion of events still occurs below conventional high-risk thresholds because most individuals are distributed within low and intermediate risk ranges

development of risk prediction in relatively stable epidemiological settings, where risk factor trajectories and healthcare access have been more consistent over time. This approach may be less suited to populations experiencing rapid social, environmental, and behavioral change, where cardiovascular risk trajectories evolve dynamically across the life course. In such contexts, risk accumulation is shaped not only by the presence of conventional clinical risk factors, but also by the timing, duration, and interaction of multiple exposures acting from early life onward.

In LMICs, cardiovascular risk often accumulates through pathways insufficiently captured by traditional metrics. Early-life adversity, including undernutrition, limited access to education, and constrained social mobility, can influence long-term cardiometabolic regulation and vascular health. Social disadvantage, chronic psychosocial stress, environmental exposures, and job insecurity exert persistent biological effects through neuroendocrine activation, systemic inflammation, and adverse behavioral adaptations, often acting upstream of conventional risk factors [5, 17, 22]. These processes may contribute to earlier onset of hypertension, metabolic dysfunction, and vascular aging, even when short-term predicted risk remains low.

Environmental exposures represent an additional dimension of cardiovascular vulnerability. Chronic exposure to air pollution, water contamination, and environmental noise has been linked to endothelial dysfunction, oxidative stress, autonomic imbalance, and accelerated atherosclerosis. These exposures disproportionately affect socioeconomically disadvantaged urban communities, contributing to inequalities in cardiovascular outcomes across and within countries [22–26]. Framing cardiovascular risk within the broader concept of the exposome highlights how cumulative environmental and social exposures interact with biological susceptibility over time.

Socioeconomic inequalities also shape health-related behaviours across the life course, constraining access to healthy foods, physical activity, adequate housing, and healthy sleep environments [27–32]. These structural constraints influence behavioral risk factors long before clinical thresholds are reached, reinforcing trajectories of cardiovascular

vulnerability. Together, these mechanisms contribute to cumulative cardiovascular risk that extends beyond what is captured by conventional risk scores.

When contextual exposures are not incorporated into risk assessment, prognostic estimates may underestimate true cardiovascular susceptibility and provide unintended reassurance to individuals whose long-term risk trajectories are unfavorable. Recent efforts to integrate contextual information into prediction models, including area-level social deprivation indices and measures of environmental burden, represent an important step toward more equitable and accurate risk estimation [33, 34]. Such approaches may improve calibration across heterogeneous populations while avoiding biologically imprecise proxies such as race.

However, the adoption of context-sensitive risk prediction remains limited in routine prevention strategies, particularly in some LMICs, where data availability, health system infrastructure, and implementation capacity may constrain their use. Bridging this gap will require both methodological innovation in risk modelling and greater investment in longitudinal population data capable of capturing life-course exposures in diverse settings.

A further structural limitation concerns the global distribution of cardiovascular evidence generation. Most longitudinal cohorts, clinical trials, and risk prediction models informing contemporary prevention strategies have been conducted in high-income countries, reflecting their demographic profiles, healthcare systems, and social environments [14]. When such models are applied to LMICs without adequate recalibration, their predictive performance and clinical relevance may be reduced. Strengthening locally generated evidence and validating risk prediction tools across diverse populations are essential steps toward more equitable and context-sensitive cardiovascular prevention (Table 1).

1.3 Acting early: from thresholds to trajectories

These considerations support a shift in cardiovascular prevention from a narrow focus on risk thresholds to an emphasis on risk trajectories. Rather than relying on single-time-point estimates, prevention strategies should consider how cardiovascular risk evolves over time and which factors drive its progression. Lifetime approaches quantifying cumulative exposure to key risk factors, such as low-density lipoprotein cholesterol and blood pressure, expressed as mmol-years or mmHg-years, provide a biologically meaningful framework for prevention [35, 36].

Acting early among individuals classified as low risk does not imply indiscriminate pharmacological treatment. Instead, it emphasises timely and proportionate interventions targeting modifiable determinants before irreversible vascular damage occurs. Population-level strategies, including tobacco control, salt reduction, and promotion of physical activity, have consistently demonstrated substantial cardiovascular health benefits across diverse populations [37, 38]. Reducing environmental pollution across air, water, soil, and indoor settings has the potential to improve cardiovascular health, although longitudinal evidence directly linking pollution reduction to cardiovascular outcomes remains limited [23, 39–41].

Rather than abandoning risk prediction, which remains essential for individual-level decision-making, these limitations call for recalibration of existing models across

Table 1 Structural gaps between cardiovascular evidence generation and prevention needs in low- and middle-income countries

Dimension	Current paradigm	Structural limitation	Implications for LMICs	Policy-relevant shift
Evidence generation	Cardiovascular cohorts, trials, and risk models predominantly conducted in high-income countries	Limited representation of LMIC populations, contexts, and life-course exposures	Risk prediction and prevention frameworks poorly calibrated to populations bearing the highest burden of disease	Invest in locally relevant data generation and region-specific validation
Risk prediction models	Short-term, clinically focused models derived from high-income settings	Limited incorporation of social deprivation, environment, and access to care	Systematic underestimation of cardiovascular risk in disadvantaged populations	Integrate contextual and area-level determinants into risk assessment
Definition of high risk	Threshold-based categorisation based on 10-year predicted risk	Failure to capture cumulative and early-life risk accumulation	Delayed or missed prevention despite long-term vulnerability	Shift from threshold-based to anticipatory, life-course–oriented prevention
Research priorities	Emphasis on advanced biomarkers, -omics, and imaging technologies	Limited feasibility, scalability, and equity in resource-constrained settings	Low translational value for most LMIC health systems	Prioritise pragmatic, scalable prevention research
Policy translation	Guidelines largely extrapolated from high-income country evidence	Misalignment with LMIC health system capacity and population needs	Inefficient allocation of limited resources	Align prevention policy with local evidence and delivery models
Implementation capacity	Focus on guideline-based interventions assuming availability of structured healthcare delivery systems	Limited primary care infrastructure, variable density of community health workers, and inconsistent access to essential medications	Gap between risk identification and effective treatment delivery, leading to suboptimal implementation of preventive strategies	Strengthen primary care systems, expand community health worker programs, and ensure access to affordable essential medications

Abbreviations: *LMICs* Low- and middle-income countries

heterogeneous contexts and their integration with complementary approaches addressing population-level risk and life-course trajectories [34].

1.4 Prevention beyond the clinic: alignment with public policy

Cardiovascular prevention cannot be confined to clinical settings, particularly in LMICs where access to healthcare remains uneven both across and within countries. Many influential determinants of cardiovascular risk, including urban design, food systems, education, working conditions, and environmental regulation, lie outside the traditional scope of healthcare and align with the principles of a *Health in All Policies* approach [42].

In many LMICs, particularly where health systems are under-resourced or fragmented, high predicted cardiovascular risk does not translate into effective prevention when recommended therapies are financially or structurally inaccessible. The cost of novel agents such as glucagon-like peptide-1 receptor agonists or PCSK9 inhibitors remains prohibitive despite strong evidence of efficacy [43–45]. In this context, prioritising scalable strategies, including generic statins, antihypertensive combinations, fixed-dose polypills, and population-level policies, is likely to yield greater population benefit [46].

The excess cardiovascular mortality observed in LMICs reflects cumulative vulnerability shaped by social and environmental contexts, not merely delays in care [47–49]. Public policies that improve nutrition, education, environmental quality, and urban design

Table 2 Actionable strategies for a more inclusive and anticipatory cardiovascular prevention framework.

1. Expand risk assessment beyond short-term thresholdsIncorporate lifetime risk, cumulative exposure (e.g., blood pressure and lipid burden), and—where feasible—contextual factors such as socioeconomic conditions and environmental exposures alongside conventional risk scores.
2. Identify and act earlier in the risk trajectoryPrioritize early intervention in individuals classified as low or intermediate short-term risk but exposed to persistent adverse determinants, focusing on modifiable behaviors and upstream risk drivers.
3. Integrate individual and population-level prevention strategiesCombine high-risk approaches with population-wide interventions, including tobacco control, salt reduction, promotion of physical activity, and policies targeting environmental exposures.
4. Strengthen primary care and task-sharing modelsLeverage community health workers, simplified treatment algorithms, and fixed-dose combination therapies to improve access, adherence, and scalability of prevention in resource-limited settings.
5. Align prevention with health system capacityPrioritize cost-effective and scalable interventions (e.g., generic pharmacotherapy, polypills, mobile health platforms) over resource-intensive strategies that may not be broadly implementable.
6. Improve contextualization and calibration of risk toolsSupport local data generation and recalibration of risk prediction models to reflect regional epidemiology, social determinants, and healthcare access.
7. Foster cross-sectoral policy actionPromote a Health in All Policies approach addressing urban design, food systems, education, and environmental regulation to reduce cardiovascular risk across the life course.

can generate cardiovascular benefits across the life course, with a possible significant impact particularly in disadvantaged communities [50, 51].

At the interface between policy and practice, community health workers, mobile health platforms, simplified treatment algorithms, and fixed-dose combination therapies represent pragmatic strategies to bridge clinical prevention and public health delivery. Community health worker–led hypertension management programmes have improved treatment adherence and blood pressure control in several resource-limited settings through task-sharing models integrated into primary care [52]. Fixed-dose combination therapies ("polypills") have similarly demonstrated the potential to simplify treatment pathways and improve long-term adherence in both primary and secondary prevention [46]. Strengthening primary care networks, expanding telemedicine, and deploying mobile health clinics in underserved areas remain key priorities [53]. To facilitate translation of these concepts into practice, a set of pragmatic and scalable action points is summarized in Table 2.

2 Conclusion: towards an inclusive and anticipatory prevention framework

Converging global evidence supports the need for a dual cardiovascular prevention strategy. While targeted interventions for high-risk individuals remain essential, particularly for secondary prevention, and risk prediction tools remain central to clinical decision-making, they must be complemented by proactive population-level approaches that address cardiovascular risk earlier and more comprehensively. This is especially relevant in LMICs, where a substantial proportion of events arise outside traditionally defined high-risk groups. An inclusive and anticipatory prevention framework recognises that cardiovascular risk accumulates across the life course and is shaped by social, environmental, and contextual factors inadequately captured by static, short-term risk scores. Moving beyond isolated risk snapshots toward longitudinal trajectories, and aligning clinical prevention with integrated policy action, offers a more equitable and effective path to reducing the global burden of cardiovascular disease. These considerations should be interpreted in light of the substantial heterogeneity across LMICs, where

epidemiological patterns and health system capacity vary widely and require context-specific adaptation of prevention strategies.

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