

ECONOMIC VALUE AND RESOURCE ALLOCATION IN CARDIOVASCULAR PREVENTION: AN INTEGRATED FRACTAL AND MULTISCALE RISK FRAMEWORK

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Abstract

Cardiovascular diseases remain the leading cause of mortality worldwide and impose a substantial economic burden on healthcare systems, households, and society. Cardiovascular risk is influenced by biological, behavioural, socioeconomic, environmental, healthcare, and geographic factors. Although conventional risk scores have improved preventive decision-making, they may not fully capture temporal variability, nonlinear interactions, physiological complexity, or spatial heterogeneity, potentially limiting their capacity to inform the efficient allocation of preventive resources. This paper proposes an interdisciplinary framework integrating fractal analysis, cardiovascular risk prediction, spatial epidemiology, and health economics to provide a theoretical basis for adaptive cardiovascular prevention and improved economic evaluation of preventive strategies. Based on a structured narrative synthesis of literature spanning cardiovascular risk prediction, fractal physiology, spatial and social epidemiology, and health economics, we develop a four-layer conceptual architecture linking clinical risk, physiological complexity, contextual vulnerability and economic evaluation. Designed as a complementary layer to established models such as SCORE2, the Fractal Cardiovascular Risk and Economic Prevention Framework (FCREPF) extends conventional risk assessment from static estimates toward dynamic and spatially adaptive prevention while linking cardiovascular risk to healthcare expenditure, productivity losses, informal care, and potentially avoidable costs. By connecting multidimensional risk information with economic consequences, the framework is intended to support future assessment of economic value, cost-effectiveness, and prevention-resource allocation. The framework additionally conceptualises prevention-resource allocation as the maximisation of expected net health and economic benefit under budget constraints. Prospective validation, external calibration, reproducibility assessment, evaluation of incremental predictive value, and formal health-economic analysis are required before clinical or policy implementation.

Keywords: fractal analysis; multiscale modelling; cardiovascular risk; health economics; socioeconomic determinants; risk prediction

JEL Classification: I10; I14; I18

1. Introduction

Cardiovascular diseases (CVDs) remain the leading cause of death worldwide and represent one of the major challenges for contemporary healthcare systems. According to the Global Burden of Disease (GBD) 2023 study, approximately 19.2 million people died from CVDs worldwide in 2023 (95% uncertainty interval [UI], 17.4–20.4 million), while the number of prevalent CVD cases reached approximately 626 million. CVDs remained the leading cause of both death and disability-adjusted life years globally, with ischemic heart disease, intracerebral hemorrhage, ischemic stroke, and hypertensive heart disease among the major contributors to the cardiovascular disease burden (GBD 2023 Collaborators, 2025). Beyond mortality and disability, CVDs generate substantial social and economic consequences through healthcare expenditure, long-term care, informal care, productivity losses, and premature mortality. In the European Union, the total annual economic

burden of CVD was estimated at approximately €282 billion in 2021, of which €155 billion was attributable to health and social care expenditure, while informal care and productivity losses accounted for €79 billion and €48 billion, respectively (Luengo-Fernandez et al., 2023). These figures highlight the need for prevention strategies that are not only clinically effective but also capable of identifying where preventive resources may generate the greatest health and economic benefit.

Current cardiovascular prevention strategies rely extensively on established risk factors and validated prediction models. The 2021 European Society of Cardiology (ESC) prevention guidelines recommend systematic cardiovascular risk assessment and the use of risk estimation to support treatment decisions and prevention strategies (Visseren et al., 2021). Among the principal tools used in European practice, SCORE2 was developed to estimate the 10-year risk of fatal and non-fatal cardiovascular disease in individuals without previous CVD or diabetes and aged 40–69 years, using routinely available clinical variables and region-specific calibration (SCORE2 Working Group & ESC Cardiovascular Risk Collaboration, 2021). Such models have important strengths, including clinical interpretability, relatively limited data requirements, validation in large populations, and direct applicability to preventive decision-making. Nevertheless, cardiovascular risk is not determined exclusively by a fixed set of conventional clinical variables. Biological processes evolve over time, physiological systems exhibit complex and nonlinear dynamics, and cardiovascular vulnerability is influenced by social, economic, environmental, and geographic conditions (Sperti et al., 2022). These limitations highlight the need for approaches capable of integrating a broader range of interacting determinants of cardiovascular risk and may provide a rationale for the development of more flexible and data-intensive predictive models.

One potentially relevant but comparatively underused dimension is the complexity of physiological dynamics. Cardiovascular physiology is characterised by fluctuations across multiple temporal scales rather than by strictly periodic behaviour. Heart-rate variability (HRV), for example, reflects the interaction of autonomic regulation, respiration, haemodynamics and other physiological mechanisms. Research in complexity science and fractal physiology has suggested that healthy physiological systems may exhibit scale-dependent organisation and complex variability, while alterations in such dynamics may accompany ageing and disease [6,7]. More recent clinical evidence supports the potential prognostic relevance of nonlinear and advanced HRV measures. In the population-based HypnoLaus cohort, several advanced nocturnal HRV indices were independently associated with incident cardiovascular events during approximately four years of follow-up, suggesting that information contained in the organisation of physiological signals may complement conventional measures (Berger et al., 2022). However, fractal and nonlinear measures should not currently be regarded as established clinical biomarkers because their reproducibility, standardisation and incremental predictive value require further investigation. (Goldberger et al., 2002; Lipsitz & Goldberger, 1992; Berger et al., 2022; Delgado-Aranda et al., 2024).

Cardiovascular risk is also strongly shaped by the social and environmental context in which individuals live. An umbrella review of 70 systematic reviews found consistent evidence linking socioeconomic circumstances and other social determinants of health with cardiovascular disease and mortality, including factors related to income, education, occupation, neighbourhood socioeconomic conditions, social isolation, food insecurity and environmental characteristics (Teshale et al., 2023). These findings suggest that cardiovascular risk assessment based exclusively on individual clinical characteristics may overlook important contextual determinants. Similarly, geographic variation in healthcare accessibility, environmental exposure, socioeconomic deprivation and population structure may contribute to substantial spatial heterogeneity in cardiovascular risk (Teshale et al., 2023; Wang et al., 2023).

The economic dimension introduces a further consideration. Identifying individuals or populations at elevated cardiovascular risk is clinically important, but prevention also requires

decisions concerning the intensity, timing and allocation of interventions. A prediction model may improve statistical discrimination without necessarily improving health outcomes or representing good value for money. Consequently, cardiovascular prevention should increasingly consider not only who is at risk, but also where risk is concentrated, how it changes over time, which intervention is most appropriate, and whether the expected health benefits justify the resources required. This perspective is particularly relevant in health systems with limited preventive capacity and substantial regional inequalities.

These considerations reveal a conceptual gap between conventional cardiovascular risk prediction and the broader, multiscale nature of cardiovascular vulnerability. Existing approaches generally address clinical risk prediction, physiological complexity, socioeconomic determinants, spatial epidemiology and health economics as partially separate domains. Although each domain is supported by an expanding evidence base, their integration into a single cardiovascular prevention framework remains insufficiently developed. The present paper addresses this gap by proposing the Fractal Cardiovascular Risk and Economic Prevention Framework (FCREPF), a conceptual interdisciplinary model designed to complement rather than replace established cardiovascular risk algorithms such as SCORE2.

The novelty of the proposed framework lies not simply in introducing fractal metrics into cardiovascular prediction, but in combining physiological complexity, conventional clinical risk, temporal dynamics, socioeconomic and spatial context, and economic consequences of prevention within a unified analytical architecture. In this framework, fractal and multiscale indicators are conceptualised as a potential source of incremental physiological information, while socioeconomic and geographic variables provide contextualisation and the economic layer links risk estimation to prevention costs, expected benefits, cost-effectiveness and resource allocation. The framework therefore shifts the conceptual objective from estimating cardiovascular probability alone toward supporting adaptive prevention and prevention-resource stratification. Importantly, FCREPF is proposed as a research hypothesis and complementary analytical layer; it does not claim that fractal variables currently outperform validated cardiovascular risk models.

The aim of this paper is therefore to develop and theoretically describe FCREPF, examine its relationship with established cardiovascular risk prediction, and outline a pathway for future empirical and health-economic validation. The remainder of the paper first discusses the transition from conventional cardiovascular risk scores to broader cardiovascular risk systems and introduces the role of fractal dynamics in cardiovascular physiology. It then conceptualises cardiovascular risk across physiological, clinical, socioeconomic, geographic, temporal and economic scales and presents the four-layer FCREPF architecture. Subsequent sections examine the economic dimension, spatially adaptive prevention, the potential integration with artificial intelligence and digital health, and the proposed empirical validation strategy. The paper then considers the potential contribution of the framework to health economics and health equity, followed by a discussion of limitations and a future research agenda. Finally, the paper summarises the theoretical contribution and the conditions required for prospective clinical and policy evaluation.

2. Methodological approach and framework development

This study adopts a structured narrative synthesis approach to develop an interdisciplinary conceptual framework for cardiovascular prevention and resource allocation. The framework was informed by literature from four complementary domains: cardiovascular risk prediction, fractal and nonlinear physiological analysis, social and spatial epidemiology, and health economics. Priority was given to established risk-prediction models, systematic reviews, major cardiovascular guidelines, studies addressing fractal or multiscale physiological indicators, and economic evaluations relevant to cardiovascular prevention.

Relevant literature was identified through searches of major scientific databases and complementary reference screening. Search concepts included combinations of terms related to

cardiovascular risk prediction, SCORE2, heart-rate variability, fractal and multifractal analysis, socioeconomic determinants, spatial epidemiology, cardiovascular prevention, cost-effectiveness, QALYs, healthcare costs and resource allocation. Particular attention was given to recent systematic reviews, major clinical guidelines and seminal methodological studies relevant to the conceptual foundations of the framework.

The literature was synthesised conceptually rather than quantitatively because the objective was not to estimate a pooled effect size or compare the predictive performance of individual biomarkers, but to identify theoretically compatible dimensions that could be integrated within a common analytical architecture. The development process involved three stages: identification of the principal dimensions influencing cardiovascular vulnerability; mapping these dimensions to potential measurable variables and data sources; and linking multidimensional risk assessment to economic evaluation and prevention-resource allocation.

On this basis, FCREPF was structured around four interacting analytical layers: conventional clinical risk, physiological complexity, socioeconomic and spatial context, and economic evaluation. The resulting framework should therefore be interpreted as a testable conceptual model intended to guide future empirical validation rather than as an already validated cardiovascular prediction algorithm.

3. From conventional cardiovascular risk prediction to a multiscale risk system

. Conventional cardiovascular risk models estimate the probability of cardiovascular events over a defined period using measurable clinical predictors. SCORE2, for example, was developed and externally validated to estimate 10-year risk of first-onset fatal and non-fatal cardiovascular disease in European populations, using age, smoking status, systolic blood pressure, total cholesterol and HDL cholesterol, with region-specific recalibration (SCORE2 Working Group & ESC Cardiovascular Risk Collaboration, 2021). Its clinical value derives from interpretability, relatively limited data requirements and compatibility with preventive decision-making.

However, cardiovascular risk is dynamic. Clinical risk factors change over time, physiological systems exhibit complex temporal organisation, and exposure to social, environmental and healthcare conditions varies across individuals and places. These considerations do not imply that conventional risk models are inadequate; rather, they suggest that additional dimensions could be evaluated as complementary information. FCREPF is therefore conceived as an augmentation layer rather than a replacement for validated risk algorithms.

Conceptually, conventional risk can be expressed as

$$R_i = \Pr(Y_{i=1} | X_i)$$

where R_i denotes the estimated probability that individual i will experience a predefined cardiovascular event within a specified time horizon, y_i denotes the corresponding outcome, and X_i represents a vector of established clinical predictors.

FCREPF extends this representation to:

$$R_i^{FCREPF} = f(X_i, P_i, S_i, T_i, G_i)$$

where X_i represents established clinical risk factors; P_i represents physiological complexity and fractal characteristics; S_i represents socioeconomic characteristics and social determinants of health; T_i represents temporal and longitudinal dynamics; and G_i represents geographic, environmental and healthcare-access characteristics.

Once cardiovascular risk has been estimated and potential prevention strategies have been identified, the FCREPF framework introduces an economic decision layer to assess whether the expected benefits of a preventive intervention justify the resources required for its implementation.

$$NB_i(a) = \Delta B_i(a) - C_i(a)$$

where $NB_i(a)$ denotes the expected net benefit of preventive intervention a for individual i , $\Delta B_i(a)$ represents the expected health and/or economic benefit associated with the intervention, and $C_i(a)$ represents its incremental cost.

This formulation provides a conceptual link between cardiovascular risk stratification and the allocation of preventive resources, allowing interventions to be evaluated not only according to their potential clinical effectiveness but also according to their expected economic consequences.

At the health-system level, the economic value of FCREPF-guided prevention can be assessed by comparing its costs and health outcomes with those associated with standard risk-based prevention. A commonly used measure for this purpose is the incremental cost-effectiveness ratio (ICER), which expresses the additional cost required to obtain one additional unit of health benefit under the alternative prevention strategy.

$$ICER = (C_{FCREPF} - C_{standard}) / (QALY_{FCREPF} - QALY_{standard})$$

where the ICER represents the incremental cost-effectiveness ratio comparing FCREPF-guided prevention with standard risk-based prevention.

In this formulation, C_{FCREPF} and $C_{standard}$ denote the costs associated with FCREPF-guided and standard prevention, respectively, while $QALY_{FCREPF}$ and $QALY_{standard}$ represent the corresponding quality-adjusted life years. The ICER therefore provides a comparative measure of the additional resources required to achieve an additional health benefit through FCREPF-guided prevention relative to conventional risk-based prevention.

It should be emphasised that these equations represent the proposed conceptual structure of the FCREPF framework rather than validated economic prediction or cost-effectiveness models. Their empirical application would require prospective data, explicit costing methods, specification of the relevant health outcomes, uncertainty analysis, and comparison with established prevention strategies. The proposed framework consequently treats cardiovascular risk as a multiscale system in which established clinical predictors remain the foundation, while physiological, contextual and economic information can be tested for incremental predictive and decision-making value.

4. Physiological complexity and cardiovascular dynamics

Cardiovascular physiology contains variability across multiple temporal scales. Heart-rate dynamics, for example, reflect interactions among autonomic regulation, respiration, haemodynamics and other physiological processes. Fractal and complexity-based methods provide mathematical tools for describing scale-dependent organisation in physiological signals. Goldberger and colleagues described complex, fractal-like dynamics as characteristic of healthy physiological regulation and discussed alterations in physiological complexity with ageing and disease (Goldberger et al., 2002). Earlier work likewise proposed loss of complexity as a possible feature of ageing and pathological states (Goldberger et al., 2002). (Goldberger et al., 2002; Lipsitz & Goldberger, 1992; Mitchell, 2009).

Cardiovascular studies have investigated nonlinear and heart-rate-variability measures as potential markers of autonomic function and prognosis. A meta-analysis of cohort studies reported associations between HRV measures and mortality or cardiovascular events in patients with cardiovascular disease (Lipsitz & Goldberger, 1992). In the population-based HypnoLaus study, advanced nocturnal HRV measures were associated with incident cardiovascular events during follow-up (Berger et al., 2022). These findings support the hypothesis that the organisation of physiological signals may contain information complementary to conventional risk factors. (Fang et al., 2020; Huikuri & Stein, 2013; Berger et al., 2022; Delgado-Aranda et al., 2024).

Nevertheless, fractal metrics should not currently be considered established cardiovascular biomarkers. Their values may depend on signal quality, recording duration, preprocessing, sampling characteristics and the mathematical method applied. Associations with outcomes also do not establish incremental clinical utility. FCREPF therefore proposes fractal dimension, scaling/Hurst exponents, multifractal parameters and temporal variability as candidate variables for empirical testing rather than validated predictors.

At the individual level, these variables would remain integrated with conventional characteristics such as age, sex, smoking, blood pressure, lipid profile, diabetes, obesity, renal

function, medication and previous disease. The central hypothesis is that physiological complexity may provide information about cardiovascular vulnerability that complements the absolute level of conventional risk factors.

5. Social, spatial and temporal context

Cardiovascular risk is embedded within social and geographic environments. Evidence from an umbrella review indicates consistent associations between social determinants of health and cardiovascular disease across multiple domains, including socioeconomic circumstances and neighbourhood conditions (Teshale et al., 2023). These determinants may influence cardiovascular risk through material conditions, health behaviours, chronic stress, healthcare access and the ability to maintain preventive interventions (Teshale et al., 2023; Wang et al., 2023; Diez Roux, 2001).

Spatial epidemiology provides an additional perspective because populations in different areas may experience different combinations of deprivation, environmental exposure, healthcare accessibility, food environments, employment conditions and population ageing. Area-level characteristics should not be treated as direct substitutes for individual socioeconomic variables because ecological inference can introduce bias. Within FCREPF, spatial information is therefore considered contextual information that can modify interpretation and prioritisation rather than replace individual-level assessment. (Cromley & McLafferty, 2012; Diez Roux, 2001).

The temporal dimension is equally important. Cardiovascular risk factors and physiological characteristics can change with ageing, treatment, medication adherence, sleep, weight, blood pressure and recurrent acute events. A future dynamic implementation could represent risk as $R(t) = f[X(t), P(t), S, G]$, allowing repeated observations to update risk rather than relying exclusively on a single baseline assessment.

The integration of physiological, social, spatial and temporal information leads to a broader definition of cardiovascular vulnerability. The objective is not to substitute geographic or socioeconomic indicators for clinical variables, but to determine whether contextual and dynamic information provides useful incremental information and improves prevention targeting.

6. FCREPF architecture and the economic dimension

FCREPF is organised into four analytical layers. The first is the clinical-risk layer, in which an established model such as SCORE2 provides the baseline estimate, $R_{base} = SCORE2(X)$. The second is the complexity layer, in which physiological measures are evaluated as potential incremental predictors, conceptually represented as $R_{complex} = g(R_{base}, D_f, H, \Delta\alpha)$. The third is the spatial and socioeconomic layer, which contextualises risk using socioeconomic status, deprivation, healthcare accessibility and environmental exposure. The fourth is the economic layer, which connects risk and prevention to expected costs and benefits. The main conceptual differences between the established SCORE2 approach and the proposed FCREPF framework are summarised in Table 1.

Table 1. Conceptual comparison: SCORE2 vs. FCREPF

Dimension	SCORE2	FCREPF (proposed)
Primary purpose	Estimate 10-year cardiovascular risk	Extend risk estimation toward economic and prevention-resource evaluation
Nature	Clinical risk algorithm	Integrated clinical-economic framework
Key inputs	Age, sex, smoking, blood pressure, lipids and other clinical variables	Clinical risk + physiological complexity + socioeconomic/spatial context + intervention costs
Output	Risk probability/category	Risk estimate + economic value + prevention priority
Time dimension	Defined prediction horizon	Potentially dynamic and multiscale
Spatial dimension	Not a core component	Explicit spatial and regional context

Economic dimension	Not directly incorporated	Costs, QALYs, cost-effectiveness and budget impact
Policy use	Clinical decision support	Clinical + population + resource-allocation decision support
Main strength	Validated and widely adopted	Potentially richer representation of complexity and resource constraints
Main limitation	Limited explicit representation of economic/spatial complexity	Requires more data, validation and methodological standardisation

Note. SCORE2 refers to the European cardiovascular risk prediction framework developed by the SCORE2 Working Group and ESC Cardiovascular Risk Collaboration (2021). FCREPF is a conceptual framework proposed in the present manuscript and is not yet clinically validated.

The proposed architecture of FCREPF and the relationships among its clinical, physiological, spatial, socioeconomic, and economic components are summarised in Figure 1.

Clinical risk (SCORE2)	Physiological layer Fractal dimension • Hurst/scaling • HRV • temporal dynamics
Economic layer Costs • QALYs • Budget impact	Spatial/social layer SES • deprivation • access • environment

Figure 1. Conceptual architecture of the FCREPF framework

Conceptual flow: clinical risk → physiological and spatial/social context → economic layer → FCREPF. The model is proposed as a complementary analytical layer, not as a replacement for validated cardiovascular risk algorithms.

Table 2 illustrates how the conceptual components of FCREPF could be translated into measurable variables for future empirical studies. The specific variables included in an operational implementation should depend on data availability, population characteristics, clinical context and the cardiovascular outcome being predicted.

Table 2. Proposed operationalisation of FCREPF domains and analytical components

Analytical layer	Candidate variables	Level	Potential data source	Proposed contribution
Clinical risk	age, sex, smoking, SBP, lipids, diabetes	Individual	Clinical records / SCORE2	Baseline cardiovascular risk
Physiological complexity	HRV, fractal dimension, DFA/scaling exponents, Hurst exponent, multifractal parameters	Individual / temporal	ECG / wearable devices	Dynamic physiological vulnerability
Temporal	repeated BP, HRV, weight, treatment adherence	Individual longitudinal	Clinical monitoring / digital devices	Dynamic risk updating
Socioeconomic	income, education, deprivation, employment	Individual / area	Administrative / census data	Social vulnerability
Spatial	healthcare accessibility, environmental exposure, geographic clustering	Area / regional	GIS / administrative data	Geographic contextualisation
Economic	intervention costs, healthcare costs, productivity losses, QALYs	Individual / system	Health-economic datasets	Economic value
Allocation	NMB, budget impact, budget constraint	Health system	Model-derived outputs	Prevention prioritisation

The economic component is central to the proposed framework. CVD was estimated to cost the European Union €282 billion in 2021, including healthcare and long-term care, productivity losses and informal care (Luengo-Fernandez et al., 2023). This burden illustrates why risk prediction should ultimately be connected to decisions about prevention intensity and resource allocation. A model may identify higher-risk individuals, but decision-makers must also consider which intervention should be offered, when it should be offered, what resources it requires and

whether expected benefits justify those resources. (Luengo-Fernandez et al., 2023; Luengo-Fernandez et al., 2024; Leal et al., 2006).

Accordingly, FCREPF proposes linking risk estimates to healthcare costs, productivity losses, informal care, QALYs, cost-effectiveness and budget impact. A conceptual net-benefit expression is $\Delta CVD_events \times C_{avoided} - C_{intervention}$. A future empirical analysis could additionally estimate an incremental cost-effectiveness ratio,

$$ICER = (C_{FCREPF} - C_{standard}) / (QALY_{FCREPF} - QALY_{standard}).$$

These expressions are illustrative and require formal economic modelling before being used for decisions.

Cost-effectiveness alone, however, does not determine how limited preventive resources should be allocated across individuals or population groups. To represent this decision problem, the economic layer of FCREPF can be extended using the concept of net monetary benefit:

$$NMBi(a) = \lambda \Delta QALYi(a) - \Delta Ci(a)$$

where $NMBi(a)$ represents the expected net monetary benefit of preventive intervention a for individual or population subgroup i , λ represents the decision-maker's willingness-to-pay threshold per QALY, $\Delta QALYi(a)$ represents the expected incremental health gain, and $\Delta Ci(a)$ represents the incremental cost of the intervention.

At the health-system level, preventive resource allocation can then be conceptualised as:

$$\max_i \sum E[NMBi(ai)]$$

subject to:

$$\sum_i Ci(ai) \leq B$$

where B represents the available prevention budget. Under this formulation, the objective is to allocate preventive resources to the combination of interventions expected to generate the greatest aggregate net benefit within the available budget.

Importantly, the highest estimated cardiovascular risk does not necessarily imply the highest economic priority. Resource-allocation decisions also depend on expected intervention effectiveness, intervention costs, opportunity costs and the potential health gain associated with prevention. This perspective changes the question from 'Who is at risk?' to a broader set of questions: where is risk concentrated, how is it changing, which intervention is likely to provide benefit, and where can prevention generate health value under resource constraints? It also permits prevention priorities to be considered at individual and regional levels. Economic efficiency, however, should not be the sole criterion; equity must be incorporated because cardiovascular risk and access to care are socially patterned. (Franco et al., 2007). Consequently, maximisation of aggregate net benefit should not be interpreted as the sole decision criterion within FCREPF. A health system may also assign value to reducing socioeconomic or geographic inequalities in cardiovascular outcomes. Future applications could therefore examine both conventional cost-effectiveness and distributional consequences, allowing decision-makers to identify potential trade-offs between efficiency and equity in preventive resource allocation.

The framework is compatible with digital health and machine-learning approaches. Physiological signals from ECGs or wearable devices could be transformed into fractal or multiscale features, while machine-learning methods could evaluate nonlinear associations. Spatial data could similarly generate contextual indicators. These are possible implementation pathways, not intrinsic requirements of FCREPF, and would require careful attention to interpretability, external validation, privacy, data quality and algorithmic fairness. (Sperti et al., 2022; Azmi et al., 2022; Ahsan & Siddique, 2022; Baashar et al., 2022).

Based on the proposed architecture, three principal empirical propositions can be derived:

P1. The addition of reproducible physiological complexity measures to established cardiovascular risk factors provides incremental predictive information beyond conventional clinical risk assessment alone.

P2. The integration of socioeconomic, spatial and temporal information improves the identification of cardiovascular vulnerability and the targeting of preventive interventions compared with individual clinical risk estimation alone.

P3. Under constrained preventive budgets, FCREPF-guided resource allocation generates greater expected net health and economic benefit than allocation based exclusively on conventional cardiovascular risk categories.

Together, these propositions establish a testable pathway from incremental risk prediction to prevention targeting and, ultimately, resource-allocation decisions. They also provide the basis for the staged empirical validation strategy proposed in the following section

Consider two individuals with comparable SCORE2 estimates and similar conventional clinical profiles. Under a conventional risk-based approach, both individuals could receive similar prevention recommendations. Within FCREPF, however, additional information may modify the interpretation of their cardiovascular vulnerability.

Individual A may exhibit relatively preserved physiological complexity, stable longitudinal measurements, low socioeconomic deprivation and good access to preventive healthcare. Individual B may present altered HRV complexity, increasing blood-pressure variability, higher socioeconomic deprivation and limited geographic access to preventive services. Although their baseline clinical risk may be comparable, the multidimensional profile of Individual B may indicate greater vulnerability or a higher probability that delayed prevention would result in avoidable cardiovascular and economic consequences.

The economic layer would subsequently evaluate alternative preventive strategies according to their expected costs, health gains and net benefit. Under a constrained budget, priority would not automatically be assigned to the individual with the highest physiological or socioeconomic vulnerability. Instead, allocation would depend on the combination of expected cardiovascular benefit, intervention effectiveness, costs, accessibility and equity considerations.

This example illustrates that FCREPF is not intended merely to generate a more complex risk score. Its principal purpose is to provide an analytical pathway linking clinical risk, dynamic vulnerability and contextual information with prevention choices and resource-allocation decisions.

7. Validation strategy, limitations and future research

The present paper is conceptual and does not report a patient-level empirical analysis. Its principal contribution is therefore the formulation of a testable framework. Future validation should determine whether the proposed components provide reproducible incremental information beyond established cardiovascular risk models.

A staged empirical programme is proposed. First, physiological validation should identify fractal and multifractal measures that are reproducible and associated with cardiovascular outcomes. Second, incremental prediction should compare a conventional SCORE2-based model with models augmented separately by socioeconomic variables, fractal physiological variables, and a combined set of physiological, socioeconomic and spatial variables. Third, spatial integration should assess whether contextual information improves prediction or prevention targeting. Fourth, health-economic modelling should evaluate costs, health outcomes, cost-effectiveness and budget impact. Finally, prospective implementation studies should assess whether dynamic risk updating changes clinical or public-health decisions.

Future model assessment should include discrimination, calibration, Brier score, decision-curve analysis and appropriate internal and external validation. Reclassification measures may be reported where justified, but should not substitute for assessment of clinical utility. Economic evaluation should estimate intervention and implementation costs alongside avoided events and health outcomes.

Several limitations are inherent to the proposed approach. First, no empirical evidence is presented here that fractal variables improve prediction beyond SCORE2. Second, fractal measures

may be sensitive to acquisition and preprocessing choices, limiting comparability across studies. Third, cardiovascular disease is heterogeneous, and a complexity marker relevant to autonomic dysfunction may not have the same significance across atherosclerotic disease, heart failure or stroke. Fourth, area-level socioeconomic variables may introduce ecological bias. Fifth, additional predictors may increase complexity without producing clinically meaningful benefit. Finally, economic analyses depend on assumptions concerning costs, discounting, productivity, informal care and valuation of health outcomes.

Equity also requires explicit consideration. Data availability may itself be socially patterned: individuals with limited healthcare access may have fewer recorded measurements, while wearable-derived physiological data may be more available in populations with greater resources. Future studies should therefore evaluate model performance across socioeconomic and geographic groups and examine whether the framework reduces or inadvertently reproduces existing inequalities (Teshale et al., 2023; Wang et al., 2023; OECD, 2025).

The key empirical question is not simply whether a fractal model achieves a statistically higher area under the ROC curve, but whether adding multiscale information provides reproducible incremental value that improves prevention sufficiently to justify the additional data, complexity and implementation costs.

8. Discussion and conclusions

The principal contribution of FCREPF is the integration of four research domains that are commonly considered separately: cardiovascular risk prediction, fractal and complexity-based physiology, spatial and socioeconomic epidemiology, and health economics. The framework does not challenge the established clinical value of models such as SCORE2. Instead, it proposes that validated clinical prediction can serve as the foundation for a broader analytical system in which physiological dynamics, contextual vulnerability and economic consequences are evaluated as potential complementary dimensions. (Mitchell, 2009; Barabási, 2016).

The originality of the framework therefore lies in its integration rather than in the isolated use of fractal mathematics. Its conceptual progression is from clinical risk estimation toward multiscale risk characterisation and, ultimately, prevention-resource stratification. In principle, this could support a transition from asking only who is at risk to also considering where risk is emerging, how it changes over time, which interventions are appropriate and where preventive resources may generate the greatest health and economic value. (Goldberger et al., 2002; Luengo-Fernandez et al., 2023).

This proposition remains a research hypothesis. Before clinical or policy implementation, FCREPF requires prospective validation, external calibration, reproducibility assessment, evaluation of incremental predictive value, decision-curve analysis and formal health-economic evaluation. Particular attention should be given to fairness, data quality and the possibility that socioeconomic inequalities affect both cardiovascular risk and the availability of physiological measurements.

From a health-economic perspective, the proposed framework distinguishes between cardiovascular risk, intervention effectiveness and economic value. Individuals or regions with the highest predicted cardiovascular risk are not necessarily those in which additional preventive expenditure generates the greatest incremental health benefit. By linking multidimensional risk stratification to intervention costs, QALYs, budget impact and expected net benefit, FCREPF introduces opportunity cost explicitly into cardiovascular prevention. This distinction is particularly relevant when preventive budgets are constrained because resources allocated to one intervention cannot simultaneously be used elsewhere. FCREPF may therefore support future assessment not only of whether preventive interventions are cost-effective, but also of how competing interventions could be prioritised within a limited healthcare budget.

If future studies demonstrate that fractal and multiscale variables provide reproducible information beyond established predictors and that their integration improves decisions and health outcomes at acceptable cost, FCREPF could function as a complementary analytical layer connecting precision medicine, population health and economic decision-making. Its value should ultimately be determined by demonstrated clinical usefulness, economic value and equitable impact. Future economic evaluation should also consider the value and cost of acquiring additional information. Fractal physiological measurements, longitudinal monitoring and spatial-data integration may improve decision-making but also generate additional acquisition, processing and implementation costs. Value-of-information approaches could therefore help determine whether the expected decision benefit associated with additional FCREPF components justifies the resources required to collect and process such information.

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