Clinical Journal of the American Society of Nephrology

Cardiovascular Risk Assessment Tools in Chronic Kidney Disease

--Manuscript Draft--

Manuscript Number:	CJASN-2025-001978R3
Full Title:	Cardiovascular Risk Assessment Tools in Chronic Kidney Disease
Short Title:	CV calculators in CKD
Article Type:	Review - Invited
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Manuscript Classifications:	Cardiovascular Disease; Cardiovascular Events; CKD Non-Dialysis; End-Stage Renal Disease (ESRD); Mortality Risk; Risk Factors
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Funding Information:	
Additional Information:	
Question	**Response**
Study Group: Does your paper include study group(s)? If yes, please provide a list of study group(s) and members that have contributed to or participated in the submitted work in some way. This list may contain either a collaboration of individuals (e.g., investigators) and/or the name of an organization (e.g., a laboratory, educational institution, corporation, or department) and its members.	No
Preprint Server Posting of unrefereed manuscripts to a community preprint server by the author will not be considered prior publication provided that the conditions included within the Instructions for Authors are met. Has this paper already been posted on a preprint server such as arXiv or bioRxiv?	This research was not posted on a preprint server.

Clinical Journal of the American Society of Nephrology

DOI: 10.2215/CJN.0000001025

Cardiovascular Risk Assessment Tools in Chronic Kidney Disease

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Abstract

Cardiovascular (CV) risk calculators estimate the likelihood of CV events by integrating factors such as age, sex, blood pressure, lipids, smoking, and diabetes. Commonly used tools in the general population include the Framingham Risk Score, SCORE2, Atherosclerotic Cardiovascular Disease (ASCVD)Pooled Cohort Equations, and **QResearch Cardiovascular Risk Algorithm** (QRISK), the latter being regularly updated using large-scale United Kigdom (UK) health records and including a wider range of variables such as chronic kidney disease (CKD). CKD is a strong, independent risk factor for CV disease, but most standard models omit kidney function and CKD-specific factors (e.g., inflammation, vascular calcification, mineral metabolism disorders). Consequently, they often underestimate CV risk in CKD, particularly in advanced stages and among dialysis patients, where competing risks (e.g., non-CV death) further complicate risk estimation. To overcome these limitations, enhanced and CKD-specific models have been developed. Systematic Coronary Risk Evaluation (SCORE2) Add-ons incorporate estimated glomerular filtration rate (eGFR) and albuminuria to refine prediction in CKD. QRISK includes CKD as a variable. The CKD Prognosis Consortium (CKD-PC) and Predicting Risk of Cardiovascular Disease EVENTs (PREVENT) models are tailored to CKD populations and leverage large, diverse datasets to improve discrimination and calibration. Reflecting this evidence, the 2024 Kidney Disease Global Outcomes (KDIGO) guidelines recommend QRISK, CKD-PC, and PREVENT for CV risk prediction in CKD. Artificial intelligence and machine learning approaches may further enhance risk prediction by exploiting complex clinical and laboratory data, but they require external validation, transparency, and assessment of clinical utility before broad implementation. CV risk calculators should support, not replace, clinical judgment and must be embedded within individualized, multifactorial management strategies. This narrative review summarizes the main characteristics, strengths, and limitations of currently available CV risk tools for CKD, focusing on those endorsed by major international guidelines and used in routine practice. We adopt a global perspective, while acknowledging that most evidence derives from high-income settings, which limits generalizability.

Why cardiovascular risk calculators?

Cardiovascular (CV) risk calculators are essential tools in clinical practice, revolutionizing how healthcare professionals assess and manage the risk of cardiovascular diseases (CVD) (1). By integrating multiple risk factors—such as age, sex, blood pressure, cholesterol, smoking, and diabetes—these calculators provide an evidence-based estimate of a patient's likelihood of experiencing a cardiovascular event within a defined period, usually ten years. Their significance is underscored by the World Health Organization's (WHO) direct involvement in developing such tools (2).

Unlike approaches that target individual risk factors, CV risk calculators synthesize the cumulative effect of multiple, interacting variables. For example, a patient with mildly elevated cholesterol may seem low-risk in isolation. However, if combined with hypertension, smoking, and a family history of heart disease, the overall risk can be much higher. These tools thus offer a more accurate, individualized risk profile.

Properly validated calculators facilitate shared decision-making between clinicians and patients (3). Quantifying risk—for example, a 15% chance of a heart attack over ten years—makes the consequences of unhealthy behaviors more tangible and can motivate positive lifestyle changes. They also help clinicians target interventions, such as statin therapy, to those most likely to benefit, aligning with guideline recommendations and ensuring efficient resource use (4) (5).

Risk prediction models serve several purposes: they raise awareness of absolute risk, guide therapy, and improve clinician-patient communication. By categorizing patients into risk strata (low, moderate, high, very high) (6), these models inform decisions on drug therapy and lifestyle interventions. High-risk individuals receive intensive treatment, while those at lower risk are encouraged to make lifestyle changes. Importantly, CV risk calculators also help avoid overtreatment in low-risk individuals (7), minimizing unnecessary medication and potential side effects.

Cardiovascular (CV) risk prediction is now central to clinical practice and prevention guidelines[8]. However, interpreting risk calculator results requires nuance. A 10-year risk of 7% does not mean an individual has a 7% chance of a cardiovascular event; rather, among 100 people with similar risk factors, about seven would be expected to experience an event over 10 years. This reflects the population-based nature of these tools[9]. While such estimates guide clinical decisions, they must be contextualized within each patient's unique circumstances and preferences.

This narrative review describes the main characteristics, strengths, and limitations of currently available tools, with particular attention to those endorsed by major international guidelines and used in clinical practice. We adopt a global perspective by considering models derived in different geographic regions and discussing their generalizability; nonetheless, the evidence base is largely drawn from studies conducted in high-income countries, which represents an important limitation.

Risk Prediction: Interpretation of models and methodological aspects

Risk model performance is evaluated using calibration (how well predicted risks match observed outcomes) and the C-statistic (discrimination ability) (8). **Figure 1**. Reclassification assesses whether new models or biomarkers improve risk stratification (9). This concept is illustrated in **Figure 2**.

A limitation of 10-year risk models is their strong emphasis on age, which can underestimate risk in younger adults with significant risk factor burdens (10). This limitation has spurred interest in lifetime or long-term risk estimation, which better captures the cumulative effects of risk factors. Individuals with optimal risk factors at age 50 have significantly lower lifetime CVD risk and longer survival (11), highlighting the value of lifetime risk models in motivating prevention, especially among younger or low short-term risk individuals.

Effective prevention requires both individualized, high-risk strategies and broad, population-level approaches. The optimal balance between these remains debated, as each has unique strengths and limitations in different health contexts. Ultimately, robust risk prediction models underpin both strategies, aiming to reduce the overall burden of CVD.

Cardiovascular Risk Calculators in the General Population

Risk calculators are now central to both population-level and individual-based cardiovascular disease (CVD) prevention strategies (1). The Framingham Risk Score (FRS), derived from the Framingham Heart Study, is a foundational tool estimating 10-year CVD risk using factors such as age, sex, cholesterol, blood pressure, smoking, and diabetes (12). Over time, FRS has evolved to include more variables

and predict broader outcomes, and some versions substitute BMI for cholesterol when lab data are unavailable. However, FRS's accuracy is limited outside its original, predominantly white American cohort, and it does not account for family history, socioeconomic status, or newer biomarkers. Its predictive value is also reduced in older adults and those with comorbidities, so clinicians often supplement it with other models or clinical judgment.

The Atherosclerotic Cardiovascular Disease (7) Pooled Cohort Equation was developed to estimate 10-year risk of a first hard event—nonfatal myocardial infarction, coronary heart disease death, or stroke—using variables including age, sex, race, cholesterol, blood pressure, diabetes, and smoking. It is primarily used for adults aged 40–79 and guides preventive interventions such as statin therapy (13).

The World Health Organization (WHO) /International Society of Hypertension (ISH) risk charts are designed for simplicity and use in low-resource settings, requiring fewer variables and sometimes no lab data. However, earlier versions lacked validation in many populations and could underestimate risk, especially in high-risk groups. The 2019 WHO models, calibrated for 21 global regions, aim to improve accuracy and applicability (2).

In the United Kingdom UK, Qresearch Risk,(QRISK®) is the most accurate and widely validated tool, incorporating a broad range of demographic, clinical, and laboratory variables, and is updated using large-scale electronic health records. The latest QR4 algorithm further refines risk estimates for men and women using data from millions of adults (14). However, QRISK® requires robust digital infrastructure and comprehensive clinical data, limiting its use outside the UK.

Effective CVD risk calculators are distinguished by their variable selection, predictive accuracy, discrimination index, applicability, understandability, and cost-effectiveness **(TABLE 1)**. QRISK® offers superior accuracy but at a higher cost and data requirements, while WHO/ISH charts prioritize accessibility over precision. No single calculator is universally applicable; genetic, cultural, and lifestyle differences require population-specific validation. Digital health platforms can expand reach and accuracy if tailored and validated for local contexts.

In summary, the choice of a CVD risk calculator should consider accuracy, feasibility, and relevance to local populations and health systems. Tools validated for the intended population and supported by digital infrastructure offer the best performance.

Issues related to CV risk factors peculiar to CKD

The most widely used models, like the Framingham Risk Score, were developed in general populations and do not account for CKD's specific pathophysiology and risk profiles. CKD is a strong, independent risk factor for CVD, yet it is not included in most traditional risk scores (15). As a result, CKD patients—especially those at early stages—experience far more cardiovascular events than general models predict (16). This underestimation arises because standard models focus on traditional risk factors, whereas CKD introduces additional, nontraditional ones, such as inflammation, oxidative stress, vascular calcification, and disturbances in mineral metabolism (17) (**Figure 3**). Calibration and discrimination of standard models are poor in CKD, consistently underestimating risk (16), particularly in advanced disease or dialysis. Competing risks, such as non-cardiovascular mortality, further complicate risk estimation (18). CKD patients may also have atypical CVD presentations, like silent ischemia or sudden cardiac death, which standard models may miss (19). Attempts to improve prediction by adding biomarkers or kidney function measures have yielded only modest gains (20).

In summary, general population CV risk calculators are inadequate for CKD patients due to unique risk factors, higher baseline risk, poor calibration, and competing risks. There is a clear need for CKD-specific models that integrate both traditional and nontraditional risk factors to guide prevention and treatment more effectively.

CKD-Specific Risk Assessment Tools

Recent advances in CV risk prediction have led to the development of tools tailored for individuals with CKD, addressing limitations of general population models. The "Add-ons" for the SCORE2 and SCORE2-OP algorithms (21) represent a significant step forward. While the original SCORE2 and SCORE2-OP did not include direct kidney function measures, the Add-ons now allow clinicians to incorporate estimated glomerular filtration rate (eGFR), albumin-to-creatinine ratio (ACR), or dipstick

proteinuria into risk calculations. Developed and validated using data from nearly nine million participants across 68 datasets, these enhancements improve the accuracy of CV risk prediction in CKD, as shown by measurable gains in the C-statistic and net reclassification improvement (NRI). Unlike the previous qualitative approach of categorizing CKD as high- or very-high-risk, the Add-ons provide greater granularity. However, while they improve statistical prediction, the absolute gain in discrimination is modest.

The REACH (Reduction of Atherothrombosis for Continued Health) risk calculator, derived from a large international registry of over 68,000 patients (22), estimates the risk of recurrent CV events in patients with established vascular disease, including those with CKD as a comorbidity (22). Its multinational derivation enhances generalizability, and a web application is available (23). REACH is particularly relevant for secondary prevention but is less widely used in routine practice and may be affected by changes in CV event rates and management since its development in 2006.

The ADVANCE study, involving over 11,000 people with type 2 diabetes, produced a calculator for major CV events and all-cause mortality, as well as nephropathy and microvascular complications (24). It incorporates eGFR and albuminuria, making it directly relevant for CKD or at-risk patients. Its use in routine practice is limited, and its derivation from a clinical trial population may affect generalizability.

QRISK (https://qrisk.org/) is a widely used UK-based CV risk tool developed from data on about 10 million patients (14). It estimates 10-year CV risk using a broad range of variables, including CKD, thereby improving risk estimation for this population. However, its development in the UK may limit its applicability in other settings and ethnicities.

The CKD Prognosis Consortium (CKD-PC) risk equation (25) was developed from over four million adults and specifically targets CKD patients (https://ckdpcrisk.org/ckdpatchpce/). It incorporates age, sex, estimated Glomerular Filtration Rate (eGFR), albuminuria, and traditional CV risk factors to predict all-cause mortality, CV mortality, and major CV events. Its strength lies in development and validation within large, diverse CKD cohorts, enhancing accuracy and relevance, especially for capturing graded risk with declining kidney function and increasing albuminuria.

The American Heart Association PREVENT model (https://professional.heart.org/en/guidelines-and-statements/prevent-risk-calculator/prevent-calculator) (26) is a recent tool derived from data on over 6.5 million US adults, including a significant representation of individuals with CKD. It incorporates clinical and laboratory variables, including kidney function markers, and predicts a broad range of CV outcomes, including heart failure and arrhythmias—conditions particularly relevant in CKD. Its main strength is its validation in contemporary, diverse cohorts, but its performance outside the US population remains to be fully established.

For primary CVD prevention in adults without prior CVD, 2024 KDIGO guidelines provide a strong recommendation to base treatment intensity on multivariable absolute CVD risk. These guidelines (27) recommend the QRISK, CKD-PC, and PREVENT calculators (see **Table 2**). However, these models have not been directly compared in large, prospective head-to-head studies. Because they use different variables and were validated in distinct populations, risk estimates for the same individual can differ substantially. Indirect comparisons suggest that CKD-specific models, such as CKD-PC, tend to outperform general models in discrimination and calibration among CKD patients, but this is not universal, and performance varies by population. The generalizability of these models across healthcare settings and ethnic groups remains debated. In brief, while Kidney Disease Global Outcomes (KDIGO) recommends all three models, clinicians should recognize that risk estimates may vary for the same patient due to differences in model design and validation populations. The choice of tool should take into account the specific clinical context and patient population. Further comparative research is needed to determine which model offers the most accurate and clinically useful predictions for diverse CKD populations. Multiple calculators should not be indiscriminately applied. For CVD prevention, clinicians should anchor decisions to a single, validated contemporary CVD tool (preferably PREVENT where available). If another tool is used, it should serve only as a secondary check; when estimates differ, priority goes to the model best validated and calibrated for the patient's stage of CKD and clinical setting. In cases of residual, plausible disagreement, clinicians should present a risk range, verify data and inclusion criteria, and then use clinical judgment and shared decision-making rather than averaging or "voting" across calculators.

Attempts to develop dialysis-specific cardiovascular risk scores, such as the Analyzing Data, Recognizing Excellence and Optimizing Outcomes (AROii) risk score (28), have not resulted in tools that are widely adopted in clinical practice. More recently, the CV Event Risk Test 2 (CERT2), which incorporates plasma ceramides and selected phosphatidylcholine species (29), has been evaluated in hemodialysis patients from the AURORA and 4D trials. This calculator showed better discrimination for cardiovascular outcomes than traditional markers such as LDL cholesterol and commonly used general-population risk estimators. However, both AROii and CERT2 lack sufficiently large and diverse external validation, are methodologically complex, or depend on biomarkers that are not routinely available. At present, therefore, no cardiovascular risk calculator can be considered validated or standard for patients on dialysis. KDIGO does not recommend the routine use or comparison of multiple different CV risk scores in this population. In End Stage Kidney Disease (ESKD)CVD risk is universally high, which explains why treatment strategies in this population remain aggressive.

Emerging Biomarkers and Artificial Intelligence-Based Risk Calculators in CKD

Despite advances, current CKD-specific cardiovascular (CV) risk models such as CKD-PC and PREVENT achieve C-statistics in the 0.70–0.80 range, which is acceptable but not exceptional discrimination[32]. The latest QRISK version shows higher discrimination, but it is tailored to the British population. The limited discrimination of these models has spurred interest in new strategies to enhance CV risk prediction in CKD.

While the search for novel biomarkers continues, the most significant recent studies in CV risk prediction have come from AI applied to existing data(30). These models, with discrimination abilities similar to CKD-PC and PREVENT, could be further improved by leveraging additional variables from electronic health records, larger datasets, and, in the future, new biomarkers. However, enthusiasm for AI-based calculators must be tempered by important limitations that currently hinder widespread clinical adoption. First, most high-performing models operate as “black boxes,” providing little insight into which predictors drive individual risk estimates; this lack of explainability can reduce clinicians’ trust and complicate shared decision-making with patients. Second, artificial intelligence (AI) models are highly

dependent on the data on which they are trained and validated: under-representation of specific CKD subgroups (e.g., women, ethnic minorities, or patients with advanced CKD) raises concerns about algorithmic bias and inequitable performance across populations, and model performance may degrade over time because of data drift as practice patterns, therapies, and baseline risk change. Third, although the underlying algorithms may be open-source or nominally free, their integration into electronic health records, maintenance, monitoring for drift and bias, regulatory compliance, and user-interface development typically incur substantial financial and organizational costs. These issues underscore the need for transparent, well-validated, and continuously monitored AI-based tools before they can be safely and equitably incorporated into routine CV risk assessment in CKD.

The multi-marker approach—combining several biomarkers reflecting different disease pathways in CKD, such as inflammation, fibrosis, cardiac stress, and mineral metabolism —holds theoretical promise. Tamarappoo et al.(31) applied a gradient-boosting machine learning algorithm (XGBoost) that combined traditional clinical risk factors with quantitative CT measures—specifically coronary artery calcium (CAC) score, number of coronary lesions, aortic valve calcium score, and epicardial adipose tissue (EAT) volume and attenuation—to predict long-term cardiac events (myocardial infarction or cardiac death) over ~15 years of follow-up. In this prospective cohort, the machine learning model integrating clinical and imaging variables significantly outperformed standard clinical risk assessment, with an area under the ROC curve of 0.82 for the prediction of myocardial infarction and cardiac death. In the UK Biobank cohort, retinal biomarkers (the Reti-CVD score) have been shown to identify individuals with ≥10% 10-year CVD risk and to significantly ($P<0.001$) but modestly (0.013-0.023 gain in c-statistics) increase risk discrimination when added to QRISK3) (32). Nonetheless, AI-based CV risk models remain in early development and are not yet ready for widespread clinical use.

A Cautionary Note

To maximize clinical utility, prediction tools—especially for high-risk groups like CKD patients—must meet several criteria. First, they should be freely accessible to all clinicians, regardless of resources or geography, to promote equity and facilitate integration into routine care. Second, these tools require rigorous validation in the

populations for which they are intended, ideally through prospective clinical trials. Without robust validation, there is a risk of misclassification and inappropriate management, potentially harming patients. Third, prediction tools should be subject to ongoing evaluation and refinement, incorporating new evidence and real-world feedback. Only through this cycle of accessibility, validation, and continuous improvement can prediction tools reach their full potential. More research is needed on differences in CV risk between men and women and among ethnic groups.

While the search for novel biomarkers continues, the most significant recent improvements in CV risk prediction have come from AI applied to existing data. These models, with discrimination abilities similar to CKD-PC and PREVENT, could be further improved by leveraging additional variables from electronic health records, larger datasets, and, in the future, new biomarkers. AI-based calculators are generally free for users, as they are software-driven and accessible via the internet or digital devices.

Conclusion

Traditional CV risk assessment tools are a helpful starting point, but are insufficient for optimal management of CKD patients. Tools like QRISK, which include CKD as a risk factor, represent progress but do not fully capture the complexity of CV risk in this population. The 2024 KDIGO guidelines emphasize that risk calculators should inform, not dictate, clinical decisions. Given the high baseline risk in CKD, clinicians must adopt a vigilant, multifaceted approach—aggressively modifying all risk factors and individualizing care based on comprehensive clinical evidence and patient preferences. The ultimate aim is a precise, personalized model of care that leverages risk prediction tools while recognizing their limitations and the indispensable value of clinical expertise and patient engagement.

Acknowledgements: Because Francesca Mallamaci is an editor of the Clinical Journal of the American Society of Nephrology, she was not involved in the peer review process for this manuscript. Another editor oversaw the peer review and decision-making process for this manuscript.

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TABLE 1 Cardiovascular risk calculators developed for the general population

Name of the Calculator	Development dataset	Validation dataset(s)	External validation outside original study population	Variables included (summary)	Study population characteristics (including ethnic groups)	Endpoints predicted	Sex-specific performance reported	Strenghts C-statistics and Net Reclassification Improvement (NRI)	Weaknesses
Framingham Risk Score (12)	Original Framingham Heart Study cohort (community-based US population, predominantly White, middle-aged adults)	Internal validation within Framingham cohorts; later recalibrations and validations in other US and non-US cohorts	Yes, numerous external validations in Europe, Asia, Latin America, and other regions	Age, sex, total and HDL cholesterol, systolic BP, antihypertensive treatment, smoking, diabetes (variables differ slightly by version)	Community-dwelling adults, predominantly White US population in mid-20th century; later validations in more diverse populations	10-year risk of coronary heart disease (MI and CHD death) in original score; later versions include broader CVD endpoints	Yes (separate equations for men and women; sex-specific coefficients)	Well-validated, large cohort data; simple to use; widely adopted C-statistics in the 0.70–0.80 range , depending on population, endpoint, and whether it's recalibrated. NRI is not an intrinsic property of the Framingham risk score. It is reported only in comparative studies (e.g. Framingham vs. Framingham plus additional predictors), so no single NRI value can be given for the score itself.	Population specificity (mostly White US). Over/underestimation in some groups; limited endpoints (coronary heart disease only in original version)
SCORE (33)	>200,000 individuals without prior CVD from multiple	Internal validation and temporal	Yes, but largely within European populations with	Age, sex, smoking status, systolic BP, total cholesterol (or total/HDL-cholesterol ratio in	European general population cohorts, predominantly White; data stratified by high- and	10-year risk of fatal cardiovascular events (CVD	Yes (separate risk charts/coefficients for men and	European focus; country-specific charts; estimates	Only fatal events. Not recommended for treated patients in original

Name of the Calculator	Development dataset	Validation dataset(s)	External validation outside original study population	Variables included (summary)	Study population characteristics (including ethnic groups)	Endpoints predicted	Sex-specific performance reported	Strenghts C-statistics and Net Reclassification Improvement (NRI)	Weaknesses
	European countries. Coordinated by the European Society of Cardioilogy	validation within contributing European cohorts	varying baseline risk; limited data from non-European regions	some versions)	low-risk European regions	mortality)	women)	fatal CV risk C-statistic for SCORE/SCORE2: usually moderate in external validations; in some high-risk or special populations, values can be as low as ~0.5–0.6, as seen in a rheumatoid arthritis cohort where the C-statistic for SCORE was 0.53. A single NRI for SCORE versus Framingham cannot be provided.	form. Limited age range (40–65 years in classic SCORE)
QRISK (14)	QResearch primary care database (UK electronic health records; ≈10 million adults aged 25–84 years)	Internal and temporal validation within QResearch; validation in independent UK primary care datasets	Some external validation within UK settings; limited robust validation in non-UK health systems	Age, sex, ethnicity, deprivation index, smoking, systolic BP, cholesterol/HDL ratio, BMI, diabetes, CKD, atrial fibrillation, rheumatoid arthritis, migraine, corticosteroid use, severe mental illness, family history of CVD, and other comorbidities	General UK primary care population with broad ethnic representation (White, South Asian, Black, and other ethnic groups); includes individuals with multiple comorbidities	10-year risk of first major CVD event (non-fatal MI, CHD death, stroke/TIA and related outcomes, depending on version)	Yes (sex-specific equations and performance indicators)	Inclusive (ethnicity, comorbidities); regularly updated; UK population-based In general population cohorts, QRISK2/QRISK3 typically show good discrimination, often in the	UK-specific. Complexity (many variables) and risk of overfitting

Name of the Calculator	Development dataset	Validation dataset(s)	External validation outside original study population	Variables included (summary)	Study population characteristics (including ethnic groups)	Endpoints predicted	Sex-specific performance reported	Strenghts C-statistics and Net Reclassification Improvement (NRI)	Weaknesses
								mid-0.7 range, similar to or slightly better than Framingham-type models, depending on cohort and endpoint. In the key UK validation study, QRISK2 reclassified about 10–12% of men (and a smaller proportion of women) across the 20% 10-year risk threshold compared with the NICE-Framingham equation, with observed risks in the reclassified groups supporting QRISK2's categorisation.	
ASCVD Pooled Cohort Equations (13)	US cohort pooling project: multiple community-based and observational studies (e.g., ARIC, CHS, CARDIA, Framingham Offspring), largely from the US	Internal validation within pooled US cohorts; temporal validation in similar US data	External validation in several non-US cohorts, with variable performance; recalibration often needed	Age, sex, race (White/Black in original form), total and HDL cholesterol, systolic BP, antihypertensive treatment, diabetes, smoking	US adults aged 40–79 years, including White and Black populations; limited representation of other ethnic groups	10-year risk of "hard" ASCVD events (non-fatal MI, CHD death, and stroke)	Yes (sex-specific and race-specific equations in original model)	Broader endpoints (MI, stroke, CV death); includes race. Typically ~0.70–0.80 in external validations; in some direct comparisons, ASCVD pooled cohort and	Overestimation in low-risk groups. Limited age range (40–79 years). Not for secondary prevention

Name of the Calculator	Development dataset	Validation dataset(s)	External validation outside original study population	Variables included (summary)	Study population characteristics (including ethnic groups)	Endpoints predicted	Sex-specific performance reported	Strenghts C-statistics and Net Reclassification Improvement (NRI)	Weaknesses
								contemporary Framingham scores have very similar C-indices (e.g. both ≈0.72)	
World Health Organization/International Society of Hypertension (WHO/ISH) risk charts (2)	Pooled epidemiologic data and risk factor distributions from 21 Global Burden of Disease regions, combined with relative risks from large international cohort and case–control studies	Indirect (model-based) validation using regional data; limited classical cohort-based validation in some regions	Some regional and country-level validations, but still limited for many low- and middle-income countries	Age, sex, smoking status, systolic BP, presence of diabetes, total cholesterol (omitted in non-laboratory version)	Adults aged 40–80 years in 21 Global Burden of Disease regions; designed to be applicable to diverse resource settings with varying ethnic and socioeconomic backgrounds	10-year risk of major cardiovascular events (mainly myocardial infarction and stroke)	Yes, separate charts for males and females	Simple charts; can be applied with or without cholesterol; designed for use in low- and middle-income settings. C-statistic: Harrell's C ≈0.69–0.83 (external validations, WHO 2019 CVD charts). NRI vs Framingham: Not established; formal NRI comparisons WHO vs Framingham have not been consistently reported.	Potential inaccuracies within diverse regions. Focus only on myocardial infarction and stroke. Regional calibration may not reflect local sub-populations

2 **TABLE 2** Cardiovascular risk models in pre-dialysis CKD recommended in 2024 KDIGO guidelines (27)

Name of the calculator	Key Features	Development dataset	Validation dataset(s)	External validation	Variables included (summary)	Study population characteristics (including ethnic groups)	Endpoints predicted	Sex-specific stratification and prognostic performance.	Strengths and CKD stage applicability	Weaknesses
QRISK (34).	10-year CVD risk; includes CKD as a variable; developed in the UK	UK primary care electronic health records (QResearch database; ≈10 million adults)	Internal and temporal validation within QResearch; additional UK cohorts	Yes (primarily within UK; limited data from other countries)	Age, sex, ethnicity, deprivation index, smoking status, systolic BP, cholesterol/HDL ratio, BMI, diabetes, CKD, atrial fibrillation, rheumatoid arthritis, corticosteroid use, severe mental illness, family history of CVD, other comorbidities	General UK primary care population with broad ethnic representation (White, South Asian, Black, and other groups); includes individuals with CKD	10-year risk of first non-fatal MI, CHD death, stroke/TIA and related outcomes (depending on version)	Yes (sex-specific equations and performance). C statistics:Men: QRISK2 ≈ 0.79, vs Framingham ≈ 0.76. Women: QRISK2 ≈ 0.82, vs Framingham ≈ 0.79. Net reclassification Improvement (NRI) vs Framingham. Men ≈ 5–6% Women ≈ 7–8%	Broad inclusion of risk factors; regularly updated; widely used; explicitly adjusts for CKD. Applicable for primary prevention in stage G3a-5 pre-dialysis patients.	Developed in a UK health-care setting (generalizability to other regions uncertain); CKD often modeled as categorical variable with limited granularity; relatively complex with many predictors
CKD-PC risk equations (25)	Predict all-cause and CV mortality/events, commonly focusing on 10-year risk; use age, sex, eGFR, albuminuria, and traditional risk factors	Pooled individual-participant data from multiple CKD cohorts worldwide (>4 million adults)	Internal validation within pooled datasets; validation across independent CKD cohorts	Yes (multiple cohorts from different regions and settings)	Age, sex, eGFR, albuminuria, BP, diabetes, smoking, lipids, prior CVD (exact set varies by equation)	Adults with CKD (typically stages 3–5) from North America, Europe, Asia, and other regions; mixed clinical settings; ethnic composition varies by cohort	All-cause and CV mortality and major CV events (composite CVD outcomes, depending on equation)	No sex-stratified equations. Gain in c-statistics for CVD mortality beyond the SCORE calculator 0.027 (95% CI 0.018–0.036). NRI gain vs SCORE for CVD mortality 0.080 (8.0%; 95% CI 0.032–0.127).	Developed/validated in large CKD cohorts; captures graded risk across eGFR and albuminuria; high relevance for CKD patients. Applicable for primary prevention in stage G3a-5 pre-dialysis patients.	More complex than general population scores; requires precise laboratory measurements; heterogeneity in cohorts and outcome definitions; implementation in routine practice still limited
PREVENT (26)	Predicts a broad range of CV outcomes on 10 to 30 year risk; includes kidney function markers; derived from contemporary US data	Large US EHR-based datasets (>6.5 million adults from multiple health systems)	Internal and temporal validation across participating US health systems	Yes (the UK Biobank, the National Health and Nutrition Examination Survey (NHANES) the MESA cohort, and specific populations like those in the United Arab Emirates (UAE),	Age, sex, race/ethnicity (in some implementations), BP, lipids, diabetes, smoking, kidney function markers (eGFR, albuminuria), and other clinical variables	Contemporary US adult population with inclusion of high-risk groups (including CKD); racially and ethnically diverse, mainly high-income setting	10-year risk of MI, stroke, heart failure, atrial fibrillation, and CV death	Yes, sex-specific, race-free models for total CVD and its subtypes. c-statistics 0.79 in women and 0.76 in men across validation cohorts. NRI gain vs Pooled Cohort Equations 0.093 (9.3%) (95% CI 0.073–0.115),	High-risk groups; modern, diverse validation cohorts; includes heart failure and arrhythmias; incorporates kidney function. Applicable for primary prevention in stage G1-5 pre-dialysis patients.	Newer model with less real-world experience; validation largely limited to US systems; data-intensive; generalizability to other regions and healthcare settings remains to be fully established

Legend to Figures

Figure 1

Risk calibration. In this plot, the orange line labeled "How the Model Predicts Risk" shows how often the event actually happened for different levels of predicted risk from the model. The blue dashed line labeled "Ideal: Predictions Match Reality" represents perfect calibration, where the model's predicted risk matches the observed risk exactly. When the orange line closely follows the blue dashed line, it means the model's predictions are well-calibrated and reliable for decision-making. If the orange line deviates from the blue dashed line, it indicates that the model may be overestimating or underestimating risk for certain probability ranges.

Risk discrimination. In this plot, the orange line shows how well the model can tell apart people who will experience the event from those who will not. The closer the orange line is to the top left corner, the better the model is at distinguishing between high and low risk. The blue dashed line represents a model that cannot discriminate at all and is no better than random guessing. In this example, the value in the legend, area under the curve (AUC=0.98), summarizes the model's exceptional ability to separate risk. In other words, the closer is the AUC to 1, the better the discrimination.

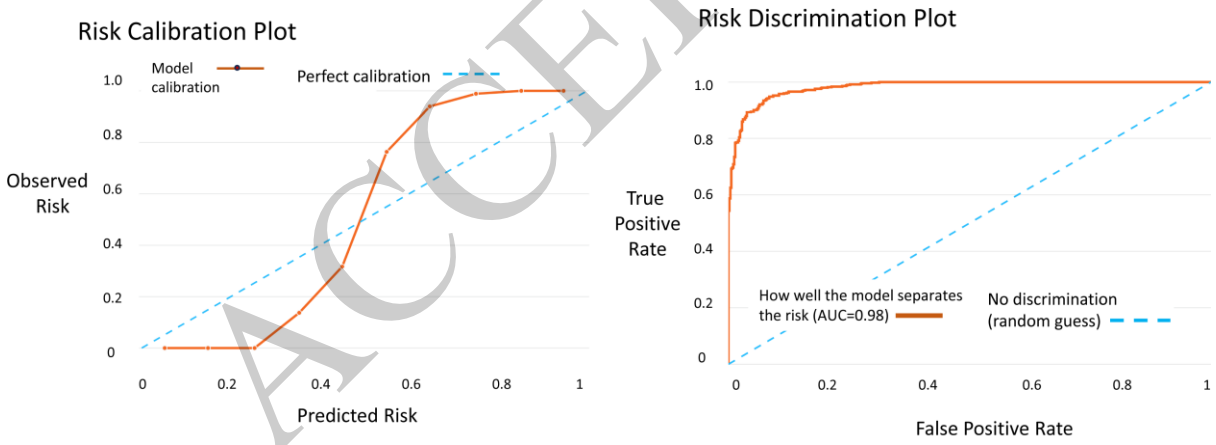

Figure 1

Figure 2

In this diagram, each colored bar on the left represents the number of people in each risk category according to the old model, and each bar on the right shows the categories according to the new model. The flows connecting them illustrate how many people move from one category to another. Blue flows represent people who stay in the same category, while orange flows show those who are reclassified. This helps non-experts see at a glance whether the new model is changing risk assignments and by how much, making it easier to judge if the new approach is likely to improve risk stratification in practice

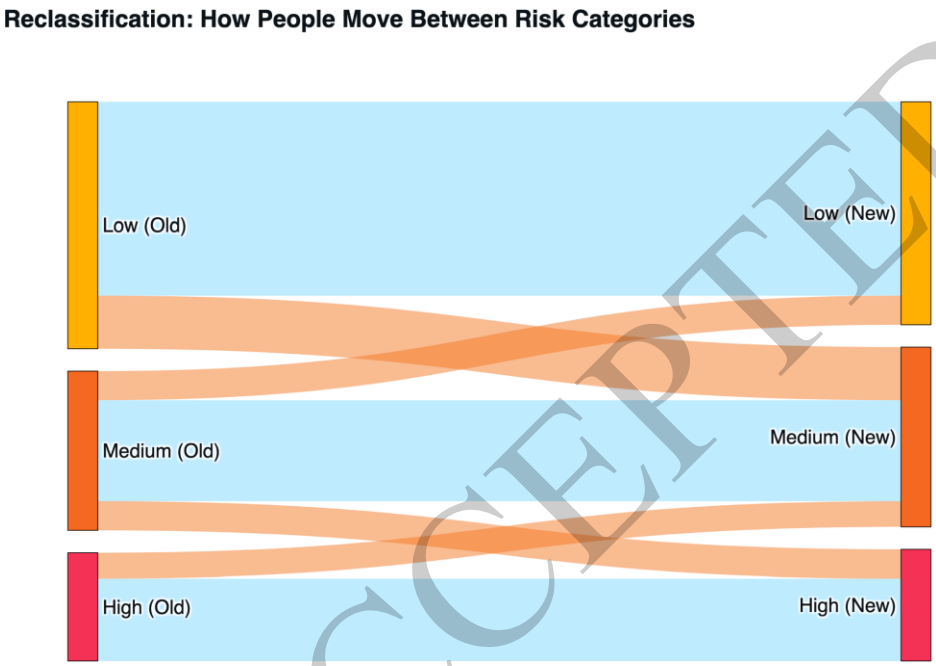

Figure 2

Figure 3

This figure illustrates the complex interplay between traditional and CKD-specific risk factors in the development of cardiovascular events and mortality in patients with CKD.. Clinical outcomes, namely cardiovascular events and mortality, are indicated in orange. The arrows in the diagram illustrate both direct and indirect causal pathways from these risk factors to clinical outcomes, emphasizing that CKD not only increases risk directly but also acts as a driver for nontraditional risk pathways. This conceptual diagram underscores why standard cardiovascular risk calculators may underestimate risk in CKD patients and highlights the importance of models that incorporate both traditional and nontraditional risk factors.

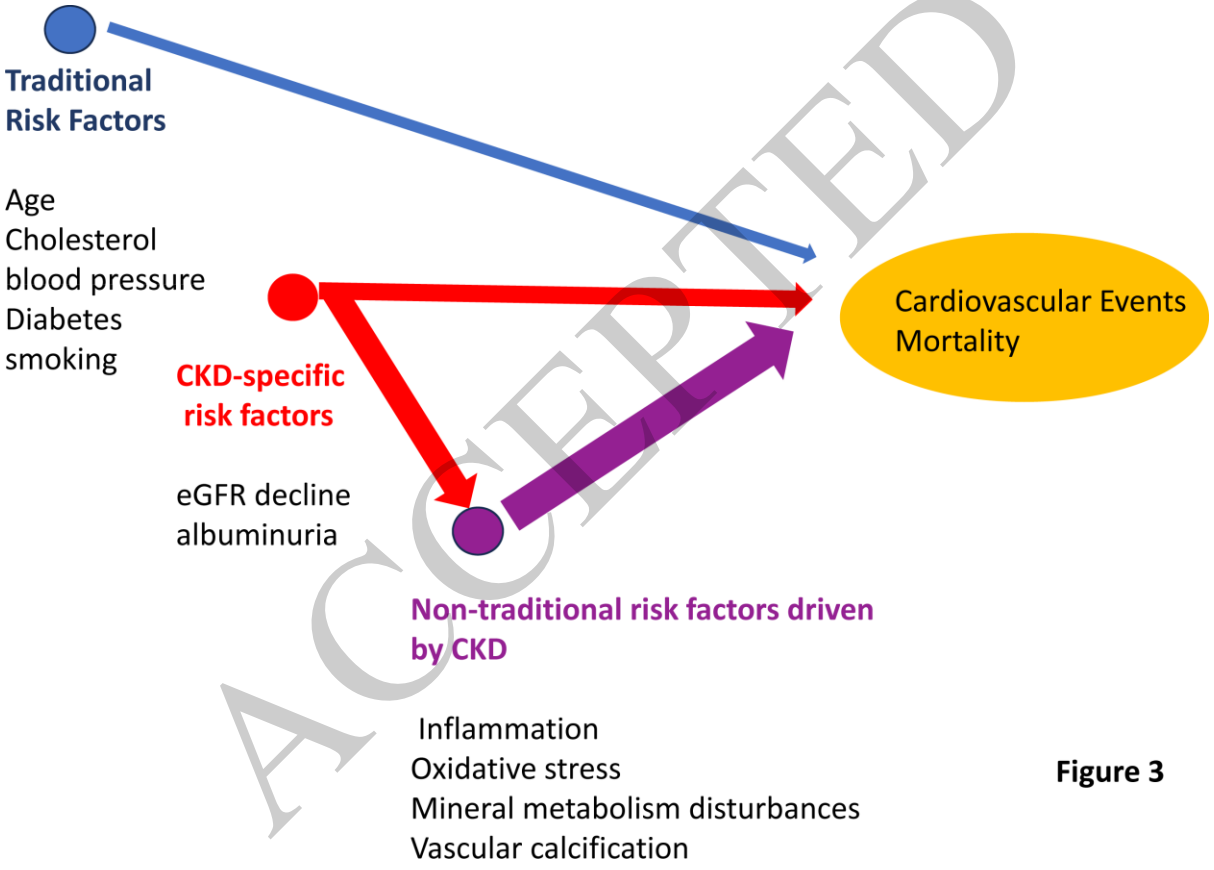

Figure 3

ASN American Society of Nephrology
JASN Journal of the American Society of Nephrology
KIDNEY360 Accessing Our World From Every Angle
CJASN Clinical Journal of the American Society of Nephrology

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Manuscript ID: CJASN-2025-001978R1
Manuscript Title: Cardiovascular risk calculators in chronic kidney disease
Date of Completion: December 23, 2025
Disclosure Updated Date: December 23, 2025

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K. Jager reports the following:
Employer: Amsterdam University Medical Center; and Advisory or Leadership Role: - Council Member European Renal Association; - Editorial Boards of Nephrology Dialysis Transplantation and African Journal of Nephrology; all unpaid.

I understand that the information above will be published within the journal article, if accepted, and that failure to comply and/or to accurately and completely report the potential financial conflicts of interest could lead to the following: 1) Prior to publication, article rejection, or 2) Post-publication, sanctions ranging from, but not limited to, issuing a correction, reporting the inaccurate information to the authors' institution, banning authors from submitting work to ASN journals for varying lengths of time, and/or retraction of the published work.

Name: Kitty J. Jager
Manuscript ID: CJASN-2025-001978
Manuscript Title: Cardiovascular risk calculators in CKD
Date of Completion: December 23, 2025
Disclosure Updated Date: December 23, 2025

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JASN Journal of the American Society of Nephrology
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M. Kanbay reports the following:
Employer: Koc University School of Medicine; and Advisory or Leadership Role: International Journal of Urology and Nephrology, Subject Editor of Clinical Kidney Journal, ERA working group EUROCA-M and CKD-MBD board member.

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Name: Mehmet Kanbay
Manuscript ID: CJASN-2025-001978R2
Manuscript Title: Cardiovascular risk calculators in chronic kidney disease
Date of Completion: January 23, 2026
Disclosure Updated Date: January 23, 2026

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F. Mallamaci reports the following:
Employer: I:P.N.E.T; Consultancy: Fresenius; Honoraria: Fresenius; Advisory or Leadership Role: Associate Editor of CJASN; Theme Editor of CKJ; Member of the Editorial Board of the International Journal of Nephrology ; Member of the Editorial Board of Turk Nefroloji, the Official Journal of the Turkish Society of Nephrology; Past Editor in Chief of the Journal of Nephrology; and Speakers Bureau: I am not aware of my spouse's details about being a paid speaker for a profit company. I was invited just once as a moderator in 2023 but I am not sure I received any payment.

I understand that the information above will be published within the journal article, if accepted, and that failure to comply and/or to accurately and completely report the potential financial conflicts of interest could lead to the following: 1) Prior to publication, article rejection, or 2) Post-publication, sanctions ranging from, but not limited to, issuing a correction, reporting the inaccurate information to the authors' institution, banning authors from submitting work to ASN journals for varying lengths of time, and/or retraction of the published work.

Name: Francesca Mallamaci
Manuscript ID: CJASN-2025-001978R3
Manuscript Title: Cardiovascular risk calculators in chronic kidney disease.
Date of Completion: February 3, 2026
Disclosure Updated Date: February 3, 2026

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V. Stel reports the following:
Employer: ERA Registry, Amsterdam UMC; Research Funding: ERA Registry is funded by ERA; and Advisory or Leadership Role: Editor of NDT.

I understand that the information above will be published within the journal article, if accepted, and that failure to comply and/or to accurately and completely report the potential financial conflicts of interest could lead to the following: 1) Prior to publication, article rejection, or 2) Post-publication, sanctions ranging from, but not limited to, issuing a correction, reporting the inaccurate information to the authors' institution, banning authors from submitting work to ASN journals for varying lengths of time, and/or retraction of the published work.

Name: Vianda S. Stel
Manuscript ID: CJASN-2025-001978R3
Manuscript Title: Cardiovascular risk calculators in chronic kidney disease
Date of Completion: February 3, 2026
Disclosure Updated Date: February 3, 2026

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G. Tripepi reports the following:
Employer: IFC-CNR

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Name: Giovanni Tripepi
Manuscript ID: CJASN-2025-001978R3
Manuscript Title: Cardiovascular risk calculators in chronic kidney disease,
Date of Completion: January 26, 2026
Disclosure Updated Date: January 26, 2026

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C. Zoccali reports the following:
Consultancy: I have a consultancy agreement with Fresenius Medical Care, Europe

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Name: Carmine Zoccali
Manuscript ID: CJASN-2025-001978R3
Manuscript Title: cardiovascular risk calculators in CKD
Date of Completion: February 3, 2026
Disclosure Updated Date: July 25, 2025