Seminars in Arthritis and Rheumatism 72 (2025) 152694

Contents lists available at ScienceDirect

Seminars in Arthritis and Rheumatism

journal homepage: www.elsevier.com/locate/semarthrit

Evaluating the reliability of cardiovascular risk scales in patients with chronic inflammatory rheumatic diseases

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ARTICLE INFO

Keywords:
Chronic inflammatory rheumatic diseases
Cardiovascular risk
SCORE2
PREVENT
QRISK3

ABSTRACT

Objective: To compare the performance of the QRESEARCH risk estimator version 3 (QRISK3), the Systematic COronary Risk Evaluation (SCORE) 2, and Predicting Risk of cardiovascular disease EVENTs (PREVENT) equationin a cohort of individuals with chronic inflammatory rheumatic diseases (CIRD) enrolled in the Spanish prospective CARdiovascular in RheuMAtology (CARMA) project.

Methods: Between July 2010 and January 2012, the study recruited CIRD patients from 67 hospitals across Spain. It included individuals diagnosed with rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis. At the 10-year follow-up, data for all patients included in the initial cohort were assessed. We estimated four 10-year cardiovascular disease (CVD) incidence risk scores using data recorded at recruitment.

Results: 2080 patients were included in this analysis. QRISK3 and PREVENT-CVD predicted an average of approximately 10 % CV events across the entire cohort, while SCORE2 and PREVENT-Atherosclerotic

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https://doi.org/10.1016/j.semarthrit.2025.152694

Available online 24 February 2025

Cardiovascular Disease (ASCVD) predicted an average of only 6.3 %. The linear correlation coefficients between each pair of scales were consistently above 0.8, with an average of 0.9074. Notably, lower correlations were observed between QRISK3 and the other scales. When identifying patients with higher CV risk, the kappa index was higher between SCORE2, PREVENT-CVD, and PREVENT-ASCVD than between QRISK3 and any other scale. These findings suggest that most patients identified as high-risk by SCORE2 would also be classified as high-risk when using PREVENT-CVD or PREVENT-ASCVD.

Conclusions: The higher correlation and reliability observed between SCORE2, PREVENT-CVD, and PREVENT-ASCVD in our series of CIRD patients followed over a 10-year period suggest that these scales may be largely interchangeable for identifying high-risk CIRD patients.

Introduction

Individuals with chronic inflammatory rheumatic diseases (CIRD) have an elevated risk of cardiovascular (CV) complications, which remain the leading cause of mortality in this population. This increased risk is partly attributed to inflammatory mechanisms that drive the development and progression of CV disease (CVD) [1]. Additionally, traditional CV risk factors and genetic predisposition also contribute to the heightened risk of CVD in these patients [2].

The European Society of Cardiology developed the Systematic COronary Risk Evaluation (SCORE) scale in 2003 as a tool to estimate the 10-year risk CVD-related death [3]. Subsequently, the European Alliance of Associations for Rheumatology (EULAR) recommended an adaptation of the SCORE for patients with CIRD. This modified version, known as the EULAR-modified SCORE, multiplies the original SCORE by a factor of 1.5 and is applied in both high- and low-CV-risk countries [4, 5].

Over time, new CV risk assessment scales have been developed, shifting the focus from predicting CV mortality to estimating the overall incidence of CV events. For example, the SCORE2 scale, introduced in 2021, estimates the 10-year risk of both fatal and non-fatal CV events in individuals without prior CVD or diabetes across Europe [6]. Similarly, the QRESEARCH risk estimator (QRISK) series—QRISK, QRISK2, and QRISK3—was developed to estimate 10-year CV risk specifically in England [7]. In this regard, in previous studies, we have highlighted differences in the performance of QRISK3 and SCORE2 among patients with psoriatic arthritis and ankylosing spondylitis [8–10].

In 2023, the American Heart Association introduced the Predicting Risk of CVD EVENTs (PREVENT) scale, designed to estimate 10-year CV risk [11]. However, this scale has generated some controversy, as its risk estimates tend to be lower than those of earlier models. This could potentially reduce the proportion of individuals classified as having high CV risk and, consequently, decrease the number of people eligible for primary prevention with statins [12].

Due to the increased risk of CVD observed in patients with CIRD, it is essential for clinicians managing these patients to have updated recommendations for CV risk assessment. Therefore, in the present study, we compare the performance of QRISK3, SCORE2, and PREVENT in a cohort of approximately 2000 individuals with rheumatoid arthritis, ankylosing spondylitis, or psoriatic arthritis, enrolled in the Spanish prospective CARdiovascular in RheuMAtology (CARMA) project and followed over a 10-year period [13]. We excluded the original SCORE and its EULAR modification from this analysis, as they are designed to estimate CV mortality risk rather than the combined risk of fatal and

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non-fatal CV events.

Patients and methods

Study design

The CARMA project is a prospective cohort study designed to assess the CV risk profile in patients with CIRD. Between July 2010 and January 2012, the study recruited patients from 67 hospitals across Spain. It included individuals diagnosed with rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis, as well as a cohort of people without inflammatory diseases. This paper focuses on patients with CIRD who had no prior CV events at the time of recruitment [13].

Data collected at recruitment were obtained through personal interviews, medical examinations, and medical records. These included demographic information, details about the inflammatory disease diagnosis, disease activity, and treatment, as well as traditional CV risk factors, medical history, and current treatments. Results from various laboratory tests were also recorded, along with assessments using CV risk scales.

The study was conducted in accordance with the principles outlined in the Declaration of Helsinki, with a strong emphasis on ethical considerations. Full written informed consent was obtained from all participants prior to their inclusion in the study. The study was approved by the Clinical Research Ethics Committee of Lugo, Galicia (Spain), under protocol number 2009/077. In addition, approval was sought and granted by the Ethics Committee of each participating hospital.

The spectrum of CV events included diagnoses of ischemic heart disease, heart failure, transient ischemic attack, stroke, and limb claudication/peripheral arterial disease, all confirmed by a physician during follow-up. The operational definitions for the parameters of the variables under analysis are detailed in a separate report [13].

We estimated four 10-year CVD incidence risk scores using data recorded at recruitment.

Operational scales used in this study

QRISK3 was developed through collaboration between academics and clinicians associated with the UK National Health Service [7]. It includes factors such as age, sex, ethnicity, smoking status, diabetes, family history, chronic kidney disease, atrial fibrillation, use of antihypertensive medication, migraine, rheumatoid arthritis, systemic lupus erythematosus, severe mental illness, atypical antipsychotic medication, regular steroid use, erectile dysfunction, cholesterol/HDL ratio, systolic blood pressure, and body mass index.

Since QRISK3 was developed for use in England, it also incorporates UK postcode to estimate the Townsend score (a measure of material deprivation) [14]. As the Townsend score is not available for the Spanish population, we did not include this information in our calculations. We calculated QRISK3 using the algorithm published at https://qrisk.org/src.php

SCORE 2 [6] includes age, sex, systolic blood pressure, total cholesterol, HDL-cholesterol and smoking. SCORE2 has different formulas to use in countries with low, moderate, high and very high risks. In this study, we used that for low-risk countries, as is the case of Spain (reference). Information on SCORE2 has previously been reported [8,9]. For patients aged 70 or more, we use the SCORE2-OP (old people) algorithm. The SCORE2 calculation was carried out using the "score-2r-isk" user command for Stata, available at http://www.phpc.cam.ac.uk/ceu/erfc/programs/.

PREVENT equations were developed following an American Heart Association Statement [15] with the purpose of predicting risk of CV events in US adults 30 to 79 years of age without CVD at baseline. PREVENT equations include PREVENT-CVD to estimate risk of total CVD, as well as PREVENT-Atherosclerotic Cardiovascular Disease (ASCVD) to estimate risk of atherosclerotic cardiovascular disease and PREVENT-HF referring to risk of heart failure. In this article we only include PREVENT-CVD and PREVENT-ASCVD. To accomplish this, we use the equations for the 10-year risk provided in Table S24 of the study published by Khan SS et al. [15].

PREVENT-CVD [15] includes age, sex, systolic blood pressure, total cholesterol, HDL-cholesterol, diabetes, smoking, glomerular filtration rate, use of anti-hypertensive medication and use of statins.

PREVENT-atherosclerotic CVD (ASCVD) [15] is a part of PREVENT-CVD, which only includes atherosclerotic CVD. It includes the same variables indicated in PREVENT-CVD.

It is important highlight that each factor contributes to each scale with a different coefficient. This ensures that all factors have some impact and contribute to the correlation, but, naturally, they do not have the same influence on every scale. If all factors had the same influence across all scales, the scales would essentially be identical. Moreover, for a clinician, it is crucial to have a single scale that can be applied to all patients, rather than separate scales for smokers, overweight individuals, those with high cholesterol or left-handed people. The purpose of each scale is to combine all relevant factors into one framework, eliminating the need for separate evaluations.

Table 1
Characteristics at recruitment of patients included in this analysis.

Variable	Total (n = 2080)	Rheumatoid arthritis (n = 708)	Ankylosing spondylitis (n = 692)	Psoriatic arthritis (n = 680)
Age (years)	58.7 ± 13.2	63.5 ± 12.9	54.4 ± 12.7	58.0 ± 12.2
Women	1052 (50.6)	548 (77.4)	191 (27.6)	313 (46.0)
BMI (kg/m^2)	27.3 ± 4.6	26.7 ± 4.7	27.3 ± 4.4	28.1 ± 4.6
Duration of the disease (years)	9.9 ± 8.6	8.9 ± 8.2	12.0 ± 10.0	9.0 ± 7.5
Smoking	579 (27.8)	184 (26.0)	242 (35.0)	153 (22.5)
Hypertension	535 (25.7)	192 (27.1)	163 (23.6)	180 (26.5)
Diabetes mellitus	143 (6.9)	46 (6.5)	46 (6.7)	51 (7.5)
Hypercholesterolemia	593 (28.5)	206 (29.1)	163 (23.6)	224 (32.9)
Taking statins	338 (16.3)	128 (18.1)	85 (12.3)	125 (18.4)
Receiving biological therapies	905 (43.5)	282 (39.8)	334 (48.3)	289 (42.5)
QRISK3	10.0 ± 11.0	14.0 ± 13.1	7.2 ± 8.2	8.4 ± 9.7
SCORE2	6.3 ± 5.1	7.2 ± 5.7	5.6 ± 4.7	6.0 ± 4.7
PREVENT-CVD	9.8 ± 8.8	11.5 ± 9.5	8.4 ± 8.1	9.5 ± 8.5
PREVENT-ASCVD	6.3 ± 5.9	7.2 ± 6.1	5.5 ± 5.7	6.1 ± 5.7

Abbreviations: BMI: Body mass index; QRISK: QRESEARCH risk estimator series; SCORE: Systematic COronary Risk Evaluation; PREVENT: Predicting Risk of cardiovascular disease EVENTs; CVD: cardiovascular disease; ASCVD: atherosclerotic cardiovascular disease.
All data are represented as mean±standard deviation or number (percentage).

Statistical analysis

We first measured the reliability of the CV risk scales as continuous variables by estimating the linear correlation coefficient (Pearson) between all four scales. We also represented this correlation in scatter plots, using both the original scales (i.e., percentage of CV risk for each patient in each scale) and the percentile distribution of each scale.

Next, we assessed the reliability of the four scales in identifying patients with high CV risk. To do this, we dichotomized each scale

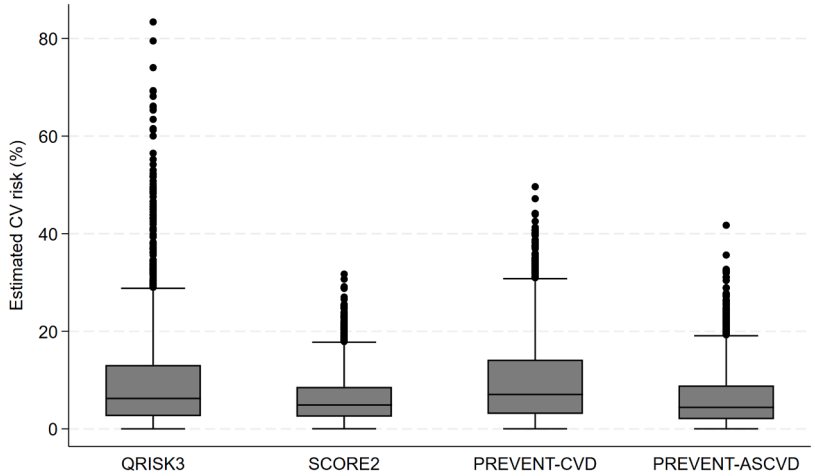

Fig. 1. Estimated CV risk in the whole cohort using each scale. QRISK3 and PREVENT-CVD estimated higher risk than SCORE2 and PREVENT-ASCVD. Note the over dispersion of estimates by QRISK3.
Footnotes: Abbreviations: CV: cardiovascular; QRISK: QRESEARCH risk estimator series; SCORE: Systematic COronary Risk Evaluation; PREVENT: Predicting Risk of cardiovascular disease EVENTs; CVD: cardiovascular disease; ASCVD: atherosclerotic cardiovascular disease.

Table 2
Linear correlation coefficient (Pearson) of four CV risk scores.

	QRISK3	SCORE 2	PREVENT-CHD	PREVENT-ASCVD
QRISK3	1			
SCORE 2	0.8313	1		
PREVENT-CVD	0.8726	0.9490	1	
PREVENT-ASCVD	0.8807	0.9308	0.9801	1

Average correlation coefficient = 0.9074.
Abbreviations: CV: cardiovascular; QRISK: QRESEARCH risk estimator series; SCORE: Systematic COronary Risk Evaluation; PREVENT: Predicting Risk of cardiovascular disease EVENTs; CVD: cardiovascular disease; ASCVD: atherosclerotic cardiovascular disease.

according to its 90th percentile and estimated the kappa coefficient for this cut-off point across all four scales. The kappa coefficient is a measure of agreement beyond what would be expected by chance. The result can be interpreted as the agreement between each pair of scales in classifying patients as having a risk above or below the 90th percentile. The same procedure was repeated using the 70th and 50th percentiles as cut-off points. All statistical analyses were conducted using the Stata SE/18 package.

Results

This analysis included a total of 2080 patients: 708 with rheumatoid arthritis, 692 with ankylosing spondylitis, and 680 with psoriatic arthritis. Their main characteristics are shown in Table 1. The average age was 58.7 ± 13.2 years (standard deviation), and 50.6 % of the patients were women. The average time since diagnosis was 9.9 ± 8.6 years. More than 40 % of the patients were receiving biological treatment.

QRISK3 and PREVENT-CVD predicted an average of approximately 10 % CV events across the entire cohort, while SCORE2 and PREVENT-ASCVD predicted an average of only 6.3 %. All four scales showed high standard deviation in their predictions (Table 1). Predictions using QRISK3 displayed overdispersion, as indicated by the outliers in Fig. 1. These characteristics were observed not only in the overall cohort but also within each of the individual diseases studied (Table 1 and Supplementary Figure 1). Notably, all four scales predicted higher CV risk in patients with rheumatoid arthritis compared to those with ankylosing spondylitis or psoriatic arthritis (Table 1 and Supplementary Figure 1).

The linear correlation coefficients between each pair of scales were consistently above 0.8, with an average of 0.9074. Notably, lower correlations were observed between QRISK3 and the other scales (Table 2). This trend is also illustrated in Fig. 2, which shows scatter plots of the predicted risk for each scale, and in Supplementary Figure 2, which presents similar plots but based on risk percentiles. Scatter plots comparing QRISK3 with other scales exhibit greater point overdispersion (i.e., the points are less aligned) compared to scatter plots between other pairs of scales. Correlation coefficients were of similar magnitude across the different inflammatory diseases, although they were slightly lower among patients with psoriatic arthritis (Supplementary Table 1).

When identifying patients with higher CV risk, the average kappa index was lower when using the 90th percentile (0.6250) compared to the 75th percentile (average kappa index=0.7443) or the 50th percentile (average kappa index=0.8055) (Table 3). The kappa index was higher between SCORE2, PREVENT-CVD, and PREVENT-ASCVD than between QRISK3 and any other scale. This pattern was consistent across all three cut points considered (90th, 75th, and 50th percentiles) (Table 3). These findings suggest that most patients identified as high-risk by SCORE2 would also be classified as high-risk when using PREVENT-CVD or PREVENT-ASCVD. However, this alignment was less apparent when using QRISK3 for classification.

When assessing reliability within patients with the same disease, the kappa index was higher in those with rheumatoid arthritis when using the 90th or 75th percentiles as cut points (Supplementary Tables 2, 3, and 4). The pattern of lower kappa indices for comparisons involving QRISK3 and other scales was consistent across all three diseases studied (Supplementary Tables 2, 3, and 4).

Discussion

Since CVD is one of the leading causes of mortality among patients with CIRD, identifying individuals at high risk of CVD is a major priority. However, to the best of our knowledge, there is limited information on studies focused on the agreement between CV risk scales in patients with CIRD, particularly regarding novel models like PREVENT. This gap in research motivates the current study, which aims to conduct a comprehensive comparison of four widely used CV risk prediction models. In this context, the present study evaluates the performance of four CV risk scales—QRISK3, SCORE2, PREVENT-CVD, and PREVENT-ASCVD—in a large cohort of Spanish individuals with CIRD who were prospectively followed over a 10-year period.

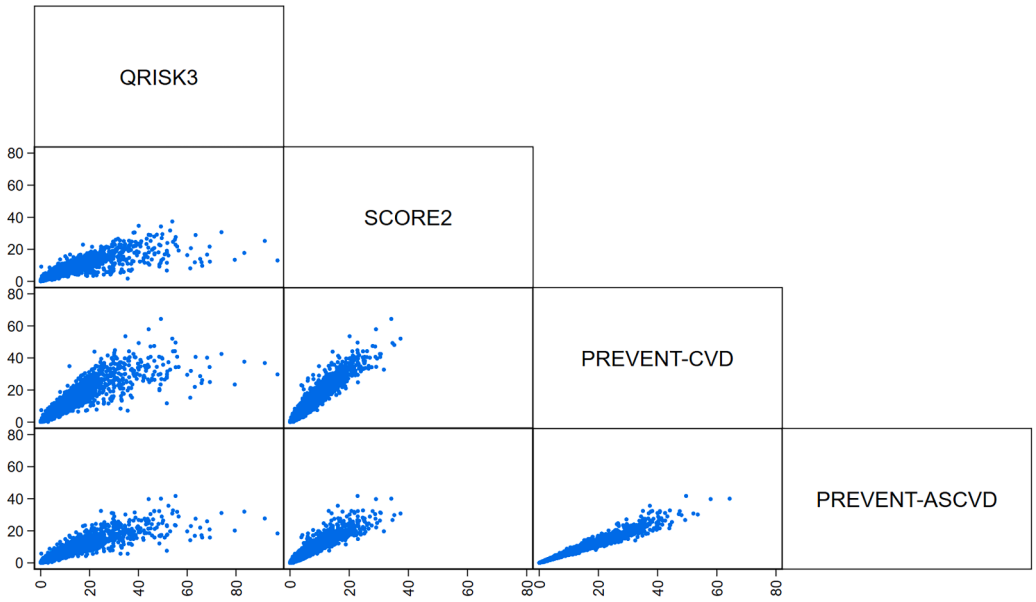

Fig. 2. Scatter plots for each pair of CV risk scales. Note that the scatter plots involving QRISK3 are more dispersed than those of the other scales.
Footnotes: Abbreviations: CV: cardiovascular; QRISK: QRESEARCH risk estimator series; SCORE: Systematic COronary Risk Evaluation; PREVENT: Predicting Risk of cardiovascular disease EVENTs; CVD: cardiovascular disease; ASCVD: atherosclerotic cardiovascular disease.

In patients with CIRD from the CARMA project, all cardiovascular risk scales showed a high correlation with one another; however, QRISK3 demonstrated lower correlations compared to the other scales. When identifying patients above the 90th percentile, the kappa index indicated moderate agreement across the whole cohort. However, kappa values involving QRISK3 were consistently lower than those involving the other scales. Conversely, kappa indices were relatively high between SCORE2 and both PREVENT-CVD and PREVENT-ASCVD. Agreement improved when using lower percentiles, likely due to the so-called "prevalence paradox of kappa". Notably, QRISK3 showed particularly low kappa values in patients with ankylosing spondylitis or psoriatic arthritis when applying the 90th percentile cut-off.

We also observed that, in patients with CIRD, QRISK3 and PREVENT-CVD predicted higher CV risk compared to SCORE2 and PREVENT-ASCVD. If the goal is to reliably identify patients at high CV risk, our findings highlight a problem with the reliability of some scales, particularly QRISK3. Despite their differences in formulas, all four scales rely on similar parameters, including age, sex, blood pressure, cholesterol, and HDL-cholesterol, which explains their overall high correlations. However, QRISK3 incorporates additional factors, such as rheumatoid arthritis, atrial fibrillation, and chronic kidney disease, which may partially account for its lower agreement with other scales. While this additional information could refine the identification of high-risk patients, it is not always routinely available, making QRISK3 less practical in some settings. It is also important to note that SCORE2 was specifically developed for European countries, and in this study, we used the version for low-risk countries, as applicable to Spain [6]. In contrast, QRISK3 was designed for use in England [7], and PREVENT was developed for use in the United States [11]. Differences in population-level CV risk profiles could reduce the applicability of QRISK3 and PREVENT in Spanish populations, potentially explaining some of the observed differences.

Table 3
Kappa index as measure of reliability of classifying patients over percentiles 90, 75 and 50. In this table, QRISK3 is the less reliable scale, as indicated by the lower kappa indices it has when compared with any other scale.

Cut point: percentile 90			
	QRISK3	**SCORE 2**	**PREVENT-CVD**
SCORE 2	0.4420		
PREVENT-CVD	0.4629	0.7816	
PREVENT-ASCVD	0.4714	0.7361	0.8562
Average kappa = 0.6250			
Cut point: percentile 75			
	QRISK3	**SCORE 2**	**PREVENT-CVD**
SCORE 2	0.5952		
PREVENT-CVD	0.6387	0.8370	
PREVENT-ASCVD	0.6397	0.8357	0.9195
Average kappa = 0.7443			
Cut point: percentile 50			
	QRISK3	**SCORE 2**	**PREVENT-CVD**
SCORE 2	0.6969		
PREVENT-CVD	0.7343	0.8666	
PREVENT-ASCVD	0.7201	0.8733	0.9415
Average kappa = 0.8055			

Abbreviations: QRISK: QRESEARCH risk estimator series; SCORE: Systematic COronary Risk Evaluation; PREVENT: Predicting Risk of cardiovascular disease EVENTs; CVD: cardiovascular disease; ASCVD: atherosclerotic cardiovascular disease.

Regarding other studies aimed at comparing CV risk scales, Navickas et al. evaluated the inter-model agreement between nine risk prediction models: the PREVENT equation, the Australian CVD risk score, the Framingham Risk Score for Hard Coronary Heart Disease, the Multi-Ethnic Study of Atherosclerosis risk score, the Pooled Cohort Equation (PCE), the QRISK3 CV risk calculator, the Reynolds Risk Score, and SCORE2 in high-risk Lithuanian women [16]. In this population, PREVENT showed substantial concordance with models such as QRISK3 and PCE, while it exhibited complete discordance with SCORE2. These findings differ from our data. A possible explanation for this discrepancy lies in the different characteristics of the Lithuanian population and our Spanish cohort of patients with CIRD. In this regard, our study specifically focused on a population associated with potentially high CV risk due to chronic inflammation.

QRISK3 showed better reliability with the other scales in rheumatoid arthritis compared to ankylosing spondylitis or psoriatic arthritis. Whether any of these scales performs better in a particular disease would require a different approach, comparing predictions with actual event rates. However, it is noteworthy that QRISK3 includes rheumatoid arthritis as an additional risk factor, which may explain why its performance could differ in rheumatoid arthritis patients compared to those

with ankylosing spondylitis or psoriatic arthritis.

Atherosclerotic (ASCVD) and non-atherosclerotic (NASCVD) cardiovascular diseases share many risk factors, which may increase the risk for ASCVD and NASCVD with varying intensity. The PREVENT-ASCVD algorithm estimates the 10-year risk of an ASCVD event, while the PREVENT-CVD algorithm estimates the 10-year risk of both ASCVD and NASCVD. Despite their differences, the shared risk factors lead to equations that are highly correlated. Moreover, all the scales we studied included systolic blood pressure in their estimates, so it is undeniable that it influences the correlation among all four scales. However, this does not apply to congestive heart failure and other heart diseases, as patients who had experienced a CV event prior to recruitment were excluded from our analysis.

The higher correlation and reliability observed between SCORE2, PREVENT-CVD, and PREVENT-ASCVD in our series of patients followed over a 10-year period suggest that these scales may be largely interchangeable for identifying high-risk CIRD patients. However, our study focused solely on reliability. Therefore, further research with long-term follow-up is necessary to evaluate validity, which would help clinicians choose the most appropriate scale for patients with CIRD. In the meantime, our results support the use of SCORE2, PREVENT-CVD, and PREVENT-ASCVD as nearly interchangeable tools for identifying CIRD patients at high risk. Whether any of these scales could be complemented by QRISK3 warrants further investigation.

CRediT authorship contribution statement

Javier Llorca: Writing – original draft, Validation, Supervision, Methodology, Formal analysis, Conceptualization. **Iván Ferraz-Amaro:** Writing – review & editing, Validation, Methodology, Formal analysis. **Santos Castañeda:** Writing – review & editing, Validation, Supervision, Investigation, Conceptualization. **Enrique Raya:** Writing – review & editing, Investigation, Conceptualization. **Luis Rodríguez-Rodríguez:** Writing – review & editing, Investigation, Conceptualization. **Sergio Rodríguez-Montero:** Writing – review & editing, Investigation, Conceptualization. **Ginés Sánchez-Nievas:** Writing – review & editing, Investigation, Conceptualization. **Antonio López-Meseguer:** Writing – review & editing, Investigation, Conceptualization. **Zulema Plaza:** Writing – review & editing, Methodology, Conceptualization. **Fernando Sánchez-Alonso:** Writing – review & editing, Investigation, Conceptualization. **Carmen García-Gómez:** Writing – review & editing, Investigation, Conceptualization. **Carlos González-Juanatey:** Writing – review & editing, Visualization, Validation, Investigation, Data curation, Conceptualization. **Miguel Ángel González-Gay:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Role of the funding source

M.A. González-Gay research is supported by the Spanish Ministry of Health, Instituto de Salud Carlos III (ISCIII), Spanish Red de Investigación RICORS - RD24/0007/0031 and PI24/00554.

I. Ferraz-Amaro research is supported by the Spanish Ministry of Health, Instituto de Salud Carlos III (ISCIII), co-funded by the European Union (PI23/00046).

Acknowledgements

The authors thank the Spanish Society and Foundation of Rheumatology for supporting the development of CARMA research.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.semarthrit.2025.152694.

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