

# Underperformance of clinical risk scores in identifying imaging-based high cardiovascular risk in psoriasis: results from two observational cohorts

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Aims	We aimed to evaluate whether traditional risk scores [short-term, 'psoriasis-modified' (multiplied by 1.5) and life- time] were able to capture high cardiovascular disease (CVD) risk as defined by the presence of atherosclerotic plaques in coronary, femoral, or carotid arteries in psoriasis.
Methods and results	We used two prospectives obseravational cohorts. European cohort: femoral and carotid atherosclerotic plaques were evaluated by ultrasound in 73 psoriasis patients. Lifetime CVD risk (LTCVR) was evaluated with QRISK-LT; short-term CVD risk was evaluated with SCORE and psoriasis-modified SCORE. American cohort: 165 patients underwent coronary computed tomography angiography to assess presence of coronary plaques. LTCVR was eval- uated with atherosclerotic cardiovascular disease (ASCVD-LT) lifetime; short-term CVD risk was evaluated with ASCVD and psoriasis-modified ASCVD. European cohort: subclinical atherosclerosis was present in 51% of patients. QRISK-LT identified 64% of patients with atherosclerosis missing a high proportion (35%) with atheroma plaque ( $P < 0.05$ ). The percentage of patients with atherosclerosis identified by QRISK-LT was significantly higher than those detected by SCORE (0%) and modified SCORE (10%). American cohort: subclinical atherosclerosis was present in 54% of patients. ASCVD-LT captured 54% of patients with coronary plaques missing a high proportion (46%) with coronary plaque ( $P < 0.05$ ). The percentage of patients with atherosclerosis with atheroma plaque ASCVD were only 20% and 45%, respectively.
Conclusions	Application of lifetime, short-term and 'psoriasis-modified' risk scores did not accurately capture psoriasis patients at high CVD risk.
Keywords	Psoriasis • Lifetime risk • Atherosclerotic plaque • Cardiovascular disease • Atherosclerosis

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### Introduction

Psoriasis is a chronic inflammatory, immune-mediated skin disease associated with accelerated subclinical as well as clinical atherosclerosis leading to incident cardiovascular events inclusive of myocardial infarction, stroke, and peripheral artery disease.<sup>1,2</sup> Thus, the prompt detection of cardiovascular disease (CVD) at earliest stages is crucial for implementing preventive measures in patients at higher risk. Traditional cardiovascular risk scoring systems are a cornerstone in the prediction of adverse cardiovascular events as they play a significant role to accurately predict and stratify a patient's CVD risk and thus can be instrumental in implementing treatment guidelines. Although traditional scoring systems are widely used method for estimating CVD risk in the general population, it is well established that they underestimate the actual CVD risk in patients with chronic inflammatory disease states such as psoriasis especially since a high proportion of patients with psoriasis experience adverse cardiovascular events earlier in their life.<sup>2</sup> Additionally, recognizing the burden of increased CVD risk in inflammatory disease states such as psoriatic arthritis and rheumatoid arthritis, the European League Against Rheumatism had recommended multiplying traditional risk scores by 1.5.3 This was also reflected in the recent American Academy of Dermatology Guidelines in moderate to severe psoriasis patients.<sup>4</sup> Nonetheless, it is currently unknown whether these modified equations predict presence of prevalent CVD beyond traditional risk scores in psoriasis patients.

Moreover, these traditional models may not identify younger patients at risk, because short-term CVD risk models are strongly age-dependent and do not capture younger patients' longer-term risk. Furthermore, because these patients are of young age, the majority are usually in the low-risk category, which would not warrant aggressive risk reduction strategies despite recent American College of Cardiology/American Heart Association (ACC/AHA) guidelines<sup>5</sup> recommending early initiation of statin therapy in inflammatory disease states. Thus, estimating lifetime cardiovascular risk (LTCVR) using algorithms which measure the cumulative risk of developing a cardiovascular event during the remainder of a patient's life,<sup>6</sup> such as QRISK lifetime score (QRISK-LT) or atherosclerotic cardiovascular disease (ASCVD) lifetime score (ASCVD-LT)<sup>6,7</sup> may be beneficial in psoriasis patients. Estimates of the lifetime risk of CVD provide a more comprehensive assessment of the overall burden of the disease as it does not consider age as the main determinant of CVD, and as a result young psoriasis patient at higher cardiovascular (CV) risk may be identified.

According to recent European Society of Cardiology (ESC) guidelines,<sup>8</sup> patients with documented high-grade atherosclerotic plaques on imaging have the same level of CVD risk as patients with documented clinical CVD. Therefore, in this study, we aim to evaluate traditional (short-term, modified and lifetime) risk scores to identify imaging-documented atherosclerotic plaques in coronary, femoral, and carotid arteries in patients with psoriasis.

### Methods

We used a two-cohort approach, utilizing an American cohort and a European cohort with their validated and recommended scores to better

### **European cohort**

patients).

### Study design and population

We conducted a cross-sectional study in 73 patients with moderate to severe chronic plaque psoriasis (psoriasis area and severity index and body surface area > 10). Patients were consecutively recruited from May through September 2017 at the Department of Dermatology of Complejo Hospitalario de Toledo in Toledo, Spain. Participants signed their informed consent before study enrolment. The study protocol was approved by the ethical committee of our institution.

#### Vascular analyses

Subjects underwent B-Mode and Doppler ultrasound examination with a MyLab 25 Gold ultrasound system (Esaote, Florence, Italy). Ultrasound images were acquired with linear high-frequency two-dimensional probe (Esaote LA435). All participants underwent the same vascular ultrasound examination as previously described.<sup>9,10</sup> Atherosclerotic plaque was defined as a focal structure encroaching at least 0.5 mm into the arterial lumen or having a thickness >50% of the surrounding intima media thickness. Atherosclerosis was defined by the presence of any plaque in carotid or femoral arteries. Three measurements were made of each atherosclerotic plaque thickness, calculating the mean value. A single experienced radiologist physician performed all ultrasound examinations, blinded to the patient characteristics.

#### CV risk assessment

Long-term CV risk was estimated using QRISK-LT calculator https://qrisk.org/lifetime/,<sup>7</sup> an online validated tool developed with QResearch database and included in the National Institute for Health and Care Excellence (2014) *Cardiovascular disease: risk assessment and reduction, including lipid modification* (NICE clinical guideline 181). As previously reported,<sup>11</sup> patients were stratified into two groups, high and low longterm CV risk, according to the median long-term CV risk value of 35.5%, which was close to the cut-off value with best overall accuracy (highest Youden index). Short-term CVR was calculated using the SCORE risk model,<sup>8</sup> and 'psoriasis-adapted' modified SCORE (mSCORE) was calculated according to the 2019 AAD-NPF guidelines recommendations (SCORE multiplied by 1.5)<sup>12</sup> with adherence to pre-set cut-offs for population application. In patients stratified as non-high-risk by the clinical risk scores, risk reclassification was applied based on the presence of atherosclerotic plaques.

#### **American cohort**

### Study design and population

A total of 165 consecutive psoriasis patients were examined from our ongoing cohort study of psoriasis (The Psoriasis Atherosclerosis Cardiometabolic Initiative). Study protocols were approved by the institutional review board at the National Institutes of Health. Research was conducted in accordance with the Declaration of Helsinki. All participants included in the study were >18 years of age at the time of recruitment and provided written informed consent after a full explanation of the procedures.

#### Coronary artery analyses

Acquisition: Guidelines implemented by the National Institutes of Health Radiation Exposure Committee were followed. Coronary computed tomography angiography (CCTA) scans were performed with prospective EKG gating, 100 or 120 kV tube potential, tube current of 100–850 mA adjusted to the patient's body size, with a gantry rotation time of 275 ms. All CCTA scans were performed using similar settings. Images were acquired at a slice thickness of 0.5 mm with a slice increment of 0.25 mm. Psoriasis patients underwent CCTA on the same day as blood draw, using the same CT scanner (320-detector row Aquilion ONE ViSION, Toshiba, Japan). The scans were then visually read by two cardiologists to adjudicate presence or absence of coronary plaque blinded to the patient characteristics.

#### **CV** risk assessment

We used the AtheroSclerotic CardioVascular Disease (ASCVD) Risk Estimator Plus, an online tool developed by the ACC/AHA based on the Pooled Cohort Equations and included in recent ACC/AHA clinical guidelines<sup>5</sup> for short-term (ASCVD) and LT (ASCVD-LT) CVR estimation. 'psoriasis-adapted' modified ASCVD (mASCVD) was calculated according to the 2019 AAD-NPF guidelines recommendations (SCORE multiplied by 1.5).<sup>12</sup> For ASCVD and mASCVD, we used the pre-set cutoff value ( $\geq$ 7.5%). Since the threshold for high ASCVD-LT is not clearly stated, we stratified patients according to the median ASCVD-LT value. In patients stratified as non-high-risk by the clinical risk scores, risk reclassification was applied based on the presence of atherosclerotic plaques.

#### **Statistical analyses**

In both cohorts, data were reported as mean with standard deviation for parametric variables, median with interquartile range for non-parametric variables and percentages for categorical variables. In baseline analyses, parametric and non-parametric variables were compared between the two groups using Student's *t*-test and Mann–Whitney *U* test, respectively. Dichotomous variables were analysed using Pearson's  $\chi^2$  test. The diagnostic values of the different risk score models for the detection of subclinical atherosclerosis were analysed calculating the area under curve. Logistic regression models were used to assess atherosclerotic plaque determinants. Variables included in the multivariate analyses were those statistically significant in the univariate analysis and/or clinically relevant. A cut-off value of *P* < 0.05 was set to denote statistical significance. All statistical analyses were performed using STATA 12 (Stata Corp., College Station, TX, USA) by National Institutes of Health staff, blinded to clinical demographics and imaging characteristics.

### Results

The baseline characteristics of our two cohorts are shown in *Table* 1. In the European cohort, patients with moderate-severe psoriasis underwent arterial ultrasound to identify femoral and/or carotid atheroma plaque as previously described.9,10 Psoriasis patients were middle-aged, predominantly male, with low cardiovascular risk by SCORE and severe psoriasis disease severity at baseline. On estimating, plague prevalence we found that 50% of the patients had atheroma plaques in both femoral and carotid arteries, however, atherosclerotic plaques in femoral arteries (45.2%) were significantly more prevalent than in carotid arteries (21.9%), P < 0.01. No significant difference was found between the percentage of patients with atheroma plaque in both, femoral and carotid arteries (50.6%) compared with percentage of patients who had only plaque in the femoral arteries. In the European cohort, age, measure of insulin resistance and CV risk scores were significant predictors of subclinical atherosclerosis (Supplementary material online, Table S1). Scoring systems values are exhibited in *Table 2*. The mean SCORE (0.7) and mSCORE (1.1) values were in the low-risk range and the mean QRISK-LT (35.9) was borderline between low and high risk. The SCORE algorithm was unable to classify any patient as high risk, in fact all patients were in the low category, although half of the patients (50.6%) had atherosclerotic plaques. With the m-SCORE model, 94.5% of the patients were in the low-risk category, however, almost half: 47.8% of them had atheroma plaques. The QRISK-LT performed better, 50.7% of the patients were classified as high risk by this algorithm, and 24 of them (64.9%) had an atheroma plaque (Figure 1). Performance measures for all risk scores models are shown in *Table 2*. Area under the curve values for all risk scores were between 0.67 and 0.74 for plaque presence (Supplementary material online, *Table S2*).

In the American cohort, consecutive patients with moderatesevere psoriasis underwent CCTA to identify presence of coronary plaque. Psoriasis patients were middle-aged, predominantly male, with low cardiovascular risk by ASCVD score and moderate-tosevere disease severity at baseline. On estimating, plaque prevalence we found that 54% of the patients had atheroma plagues in the coronary arteries (Figure 2). The mean ASCVD (4.2) and mASCVD (6.3) values were in the low-risk range and the mean ASCVD-LT (38.9) was borderline between low and high risk. In the American cohort, age, sex, hypertension, HDL cholesterol, and CVD risk scores were all significant determinants of subclinical atherosclerosis. With ASCVD, only 15% of the patients were classified as high risk, however, 75% of them had an atheroma plague. mASCVD performed incrementally better: 30% of the patients were in the high-risk category, and 80% of them had atheroma plaques. Finally, with ASCVD-LT, 41% of the patients were classified as high risk, and 70% of them had atheroma plaques. Performance measures for all risk scores models are shown in Table 2. Area under the curve values for all risk scores were between 0.67 and 0.74 for plague presence (Supplementary material online, Table S2).

Finally, *Figure 1* shows ultrasound-based risk reclassification of non-high-risk patients in both cohorts. For SCORE and ASCVD models, non-high-risk patients were reclassified to high-risk according to plaque presence in 50% of cases. Risk reclassification was noticed to be lower for QRISK-LT (36%), ASCVD-LT (42%), and mASCVD (42%). QRISK-LT identified a significantly higher proportion of patients with subclinical atherosclerosis than the others scores but it still missed a large group of at-risk patients (36%).

### Discussion

To our knowledge, this is the first study that compares the performance of multiple types (short-term, lifetime and modified) risk scores to identify high CVD risk as defined by the presence of imagingdocumented atherosclerotic plaques in multiple vascular territories (coronary, femoral, and carotid) in psoriasis. Our results demonstrate that assessing lifetime CVD risk in patients with moderate to severe psoriasis doesn't adequately identify patients with subclinical atherosclerosis (coronary, femoral, and carotid atheroma plaques), which is considered to be the highest CV risk category in the 2019 ESC guidelines.<sup>8</sup> We also found that applying a 1.5 multiplication

Table I	<b>Baseline characteristics of both cohorts</b>
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Parameter	American cohort	European cohort	
Demographics	(n = 165)	(n = 73)	
Age (years)	50.6 ± 11.5	45.1 ± 11.5	
Males	113 (56.0)	50 (68.4)	
Cardiovascular risk factors			
Body mass index (kg/m <sup>2</sup> )	29.6 ± 6.4	29.8 ± 4.9	
Waist circumference (cm)		101.47 ± 14.2	
Waist-to-hip ratio	0.95 ± 0.08		
Systolic blood pressure (mmHg)	122.9 ± 14.4	132.3 ± 12.6	
Diastolic blood pressure (mmHg)	73.4 ± 10.8	81.3 ± 8.2	
Current smoker	25 (12.0)	25 (34.2)	
Hypertension	56 (28.0)	19 (26.0)	
Hyperlipidaemia	86 (43.0)	19 (26.0)	
Type 2 diabetes	15 (7.0)	0 (0.0)	
Total cholesterol (mg/dL)	187.7 ± 38.7	191.1 ± 39.6	
HDL-C (mg/dL)	57.6 ± 20.3	49.5 ± 13.6	
LDL-C (mg/dL)	105.9 ± 31.5	110.1 ± 69.6	
Non-HDL-C (mg/dL)	127.0 ± 38.0	140.1 ± 32.5	
LDL-C/HDL-C ratio	1.9 ± 0.8	$2.3 \pm 0.7$	
Total cholesterol /HDL-C ratio	3.4 ± 1.1	4.0 ± 1.1	
Triglycerides/HDL-C ratio	2.3 ± 2.0	$3.3 \pm 2.8$	
Triglycerides (mg/dL)	122.3 ± 71.7	143.1 ± 87.3	
Metabolic syndrome	55 (33.0)	17 (23.2)	
Glucose (mg/dL)	100.4 ± 14.8	99.8 ± 15.4	
Cardiovascular drug use			
Statin therapy	57 (28.0)	3 (5.4)	
Anti-hypertensive drugs	44 (22.0)	18 (24.6)	
Psoriasis characterization		× ,	
Psoriasis area severity index score	6.0 (3.0–10.3)	$12.7 \pm 5.0$	
, Disease duration (years)	20.0 (10.0–31.0)	$14.4 \pm 9.8$	
High-sensitivity C-reactive protein (mg/L)	1.8 (0.8–4.3)	$4.9 \pm 4.6$	
Cardiovascular risk scores			
ASCVD	4.2 ± 3.6		
mASCVD	6.3 ± 5.3		
ASCVD lifetime	38.9 ± 15.3		
SCORE		0.7 ± 1.1	
mSCORE	_	1.1 ± 1.7	
QRISK lifetime risk score	_	35.9 ± 8.9	
Artery atheroma plaque			
Subclinical atherosclerosis	89 (54.0)	37 (50.6)	
Coronary atheroma plaques	89 (54.0)		
Carotid atheroma plaques		16 (21.9)	
Femoral atheroma plaques		33 (45.2)	
		55 (15.2)	

Values are represented as mean  $\pm$  standard deviation or median (IQR) for continuous variables and as n (%) for categorical variables.

factor to traditional risk score models, did not significantly improve their ability to predict the presence of subclinical atherosclerosis.

Cardiovascular events inclusive of myocardial infarction, stroke, and peripheral artery disease occur prematurely in patients with psoriasis.<sup>1</sup> The goal of identifying these patients early is to provide treatment to reduce this incident risk. However, the initiation of treatment relies on cardiovascular risk scores to accurately carry out risk assessment in these patients. Our results confirm that current

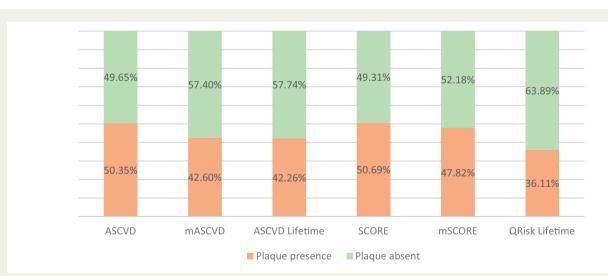
CVD risk scoring systems underestimate CVD risk in states of systemic inflammation such as psoriasis.<sup>13</sup> Psoriasis affects a high proportion of younger people and is associated with high systemic inflammation as well as high prevalence of obesity,<sup>14</sup> all these factors may contribute to accelerated atherosclerosis as well as earlier cardiovascular events described in psoriasis<sup>1</sup> and could be in part responsible for the lack of accuracy of traditional score models that rely on CV risk factors to properly predict CVD risk in these patients.

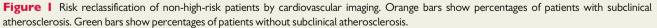
Risk scores	All patients	Psoriasis with	Psoriasis without	P-value
		subclinical atherosclerosis	subclinical atherosclerosis	
American cohort				
ASCVD	4.2 ± 3.6	5.3 ± 3.6	2.9 ± 3.0	0.028
High-risk	24 (14.6)	18 (20.2)	6 (7.9)	
Non-high-risk	141 (85.4)	71 (79.8)	70 (92.1)	
mASCVD	6.3 ± 5.3	7.9 ± 5.5	4.3 ± 4.5	<0.001
High-risk	50 (30.3)	40 (44.9)	10 (13.2)	
Non-high-risk	115 (69.7)	49 (55.1)	66 (86.9)	_
ASCVD LT	38.9 ± 15.3	43.4 ± 13.0	33.1 ± 15.9	< 0.001
High-risk	68 (41.2)	48 (53.9)	20 (26.3)	_
Non-high-risk	97 (58.8)	41 (46.1)	56 (73.7)	_
European cohort				
SCORE	0.7 ± 1.2	1.3 ± 1.4	$0.2 \pm 0.4$	< 0.001
High-risk	0 (0.0)	0 (0.0)	0 (0.0)	_
Non-high-risk	73 (100.0)	37 (100.0)	36 (100.0)	
mSCORE	1.1 ± 1.7	1.9 ± 2.1	0.3 ± 0.6	< 0.001
High-risk	4 (5.5)	4 (10.8)	0 (0.0)	_
Non-high-risk	69 (94.5)	33 (89.2)	36 (100.0)	_
QRisk LT	35.6 ± 8.9	38.5 ± 8.0	33.2 ± 9.3	0.026
High-risk	37 (50.7)	24 (64.9)	13 (36.1)	_
Non-high-risk	36 (49.3)	13 (35.1)	23 (63.9)	_

### Table 2 Assessment of subclinical atherosclerosis by cardiovascular risk scores in psoriasis patients

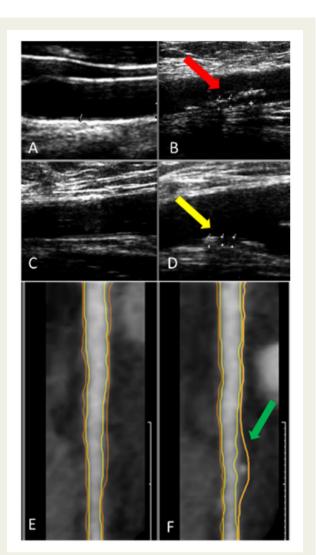
Results are shown as mean  $\pm$  standard deviation and frequencies (%).

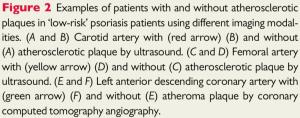
ASCVD LT, ASCVD lifetime; ASCVD, Pooled Cohort Risk Equations; mASCVD, modified ASCVD; mSCORE, modified SCORE; QRisk LT, QRisk lifetime; SCORE, Systematic Coronary Risk Evaluation.





In our study, ASCVD-LT and mASCVD had a similar ability to detect subclinical atherosclerosis, which was superior to SCORE, mSCORE and ASCVD, whereas QRISK-LT identified a significantly higher proportion of patients with subclinical atherosclerosis than the others scores. As age has such an important effect in short-term (ASCVD and SCORE) and modified scores (mASCVD and mSCORE) young adults at risk have higher chance to be missed with short-term risk scores. On the contrary, lifetime charts assess the risk of having a





cardiovascular event during their remaining lifetime,<sup>7</sup> which can be particularly useful for at-risk young psoriasis patients. In addition, other risk factors like obesity are underestimated by traditional risk scores and are only considered by QRISK-LT algorithm.<sup>15</sup> Nevertheless, QRISK-LT had certain limitations, as it missed onethird of patients with subclinical atherosclerosis in our study, probably because it does not take into account biomarkers of systemic inflammation, relevant in inflammatory diseases like psoriasis. Studies in the general population have shown that in a substantial proportion of individuals classified as non-high-risk by cardiovascular risk scores, subclinical atherosclerosis was detected using vascular ultrasound, in fact progression of sub-clinical atherosclerosis was detected in 36.5% of participants categorized as low risk.<sup>16</sup> Our findings support a recent study where traditional cardiac risk factors only partially contributed to the increased cardiovascular risk in rheumatoid arthritis patients, and thus cardiovascular risk assessment using traditional risk scores was suboptimal.<sup>17</sup> Our findings also support the results of a recent study showing underperformance of cardiovascular risk scores in identifying carotid and femoral atheroma plaques by ultrasound in patients with systemic lupus erythematosus (SLE), this is relevant since SLE similar to psoriasis is a high-risk state for increased cardiovascular events.<sup>18</sup>

The ESC guidelines for CVD risk prediction consider that the presence of arterial atheroma plaque by imaging is the highest CVD risk category,<sup>8</sup> being therefore of pivotal importance in identifying at-risk patients. Nevertheless, most prior studies on CV risk prediction in patients with systemic inflammatory states use carotid, but not femoral ultrasound nor CCTA, when trying to capture arterial atheroma plaques.<sup>19–21</sup> In the general population, femoral atheroma plaques detection have been recently proposed as markers of early and/or generalized atherosclerosis and recommended in recent ESC guidelines for CVD risk assessment.<sup>22</sup> Furthermore, CCTA has enabled not only imaging of the coronary arteries to identify coronary plaque but also more comprehensive assessment of coronary plaque burden, both calcified and non-calcified and also evaluate whether pharmacologic interventions, particularly statins and other antipsoriatic systemic therapies, may have beneficial effects on coronary artery burden.<sup>2,23,24</sup> Considering that the events rate is predominantly driven by burden of atherosclerosis and that preventive interventions may reduce atherosclerotic burden, low-risk asymptomatic patients with atherosclerosis might benefit from early prevention as per a recent article.<sup>25</sup> In this context, a recent article summarized the clinical use of cardiac calcification, in risk stratification and prevention of clinical events in the primary prevention setting, our study adds to this growing body of literature regarding the benefit of multimodal imaging in capturing early sub-clinical vascular disease.<sup>26</sup>

Our study highlights how different traditional CVD risk scores underestimate actual CVD risk defined as presence of an atherosclerotic plaque in psoriasis and suggest personalized medicine, in the form of image-guided risk stratification, which in turn may better capture cardiovascular risk in inflammatory disease states that is missed by traditional risk scores.

### Limitations

Some important limitations must be considered. Our study population was comprised of a modest sample size and thus our results should be reproduced and validated in larger populations. Furthermore, we did not study hard cardiovascular events, for which these scores were developed to calibrate risk of major adverse cardiac events. However, in this study, we assessed presence of atherosclerotic plaque as the outcome of prediction. Second, this study is cross-sectional however, longitudinal studies are underway. Finally, absence of a control cohort makes it harder to contextualize our findings.

### **Future direction**

CVD risk assessment in psoriasis requires further research to assess whether image-guided risk stratification algorithms better capture CVD risk in this population at high risk for CVD.

## Conclusion

In conclusion, application of different lifetime, short-term as well as 'psoriasis-adapted' clinical risk scores did not accurately reflect CVD risk status as defined by presence of atherosclerotic plaque in patients with psoriasis.

# Supplementary material

Supplementary material is available at *European Journal of Preventive Cardiology* online.

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Conflict of interest: N.N.M. is a full-time US government employee and has served as a consultant for Amgen, Eli Lilly, and Leo Pharma receiving grants/other payments; as a principal investigator and/or investigator for AbbVie, Celgene, Janssen Pharmaceuticals, Inc, and Novartis receiving grants and/or research funding; and as a principal investigator for the National Institute of Health receiving grants and/or research funding. A.G.-C. has served as a consultant for Abbie, Janssen, Novartis, Almirall, Celgene, and Leo Pharma receiving grants/other payments. I.M.G. served as a consultant for BMS, Boehringer Ingelheim, Lilly, Janssen Biologics, Novartis Corp, UCB (DSMB), Neuroderm (DSMB). A.S.R. Labs, Pfizer Inc., and Sun Pharma, receiving honoraria; and receives research grants (to the Trustees of the University of Pennsylvania) from Abbvie, Boehringer Ingelheim, Janssen, Novartis Corp, Celgene, Ortho Dermatologics, and Pfizer Inc.; and received payment for continuing medical education work related to psoriasis that was supported indirectly by Lilly, Ortho Dermatologics and Novartis. J.M.G. is a co-patent holder of resiquimod for treatment of cutaneous T-cell lymphoma. J.M.G. is a Deputy Editor for the Journal of Investigative Dermatology receiving honoraria from the Society for Investigative Dermatology and is a member of the Board of Directors for the International Psoriasis Council, receiving no honoraria. All other authors declare no conflicts of interests in relation to the work presented in this manuscript.

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