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Derivation of a Multivariable Psoriatic Arthritis Risk Estimation Tool (PRESTO): A Step Towards Prevention

Lihi Eder,[1] Ker-Ai Lee,[2] Vinod Chandran,[3] Jessica Widdifield,[4] Aaron M. Drucker,[5] Christopher Ritchlin,[6] Cheryl F. Rosen,[3] Richard J. Cook,[2] and Dafna D. Gladman[3]

Objective. A simple, scalable tool that identifies psoriasis patients at high risk for developing psoriatic arthritis (PsA) could improve early diagnosis. We aimed to develop a risk prediction model for the development of PsA and to assess its performance among patients with psoriasis.

Methods. We analyzed data from a prospective cohort of psoriasis patients without PsA at enrollment. Participants were assessed annually by a rheumatologist for the development of PsA. Information about their demographics, psoriasis characteristics, comorbidities, medications, and musculoskeletal symptoms was used to develop prediction models for PsA. Penalized binary regression models were used for variable selection while adjusting for psoriasis duration. Risks of developing PsA over 1- and 5-year time periods were estimated. Model performance was assessed by the area under the curve (AUC) and calibration plots.

Results. Among 635 psoriasis patients, 51 and 71 developed PsA during the 1-year and 5-year follow-up periods, respectively. The risk of developing PsA within 1 year was associated with younger age, male sex, family history of psoriasis, back stiffness, nail pitting, joint stiffness, use of biologic medications, patient global health, and pain severity (AUC 72.3). The risk of developing PsA within 5 years was associated with morning stiffness, psoriatic nail lesion, psoriasis severity, fatigue, pain, and use of systemic nonbiologic medication or phototherapy (AUC 74.9). Calibration plots showed reasonable agreement between predicted and observed probabilities.

Conclusions. The development of PsA within clinically meaningful time frames can be predicted with reasonable accuracy for psoriasis patients using readily available clinical variables.

INTRODUCTION

Psoriatic arthritis (PsA) is an inflammatory musculoskeletal disease affecting up to a third of patients with psoriasis (1). Early diagnosis and treatment are critical to prevent or reduce the severity of adverse PsA-related outcomes (2). In approximately 75% of patients, the development of PsA follows the diagnosis of psoriasis (1). As such, patients with psoriasis serve as a high-risk population for PsA on whom early detection and prevention efforts can be focused. There is an essential need to optimize risk prediction for PsA among patients with psoriasis, which should improve care delivery for high-risk patients. However, no such prediction tool currently exists. A simple, scalable tool that identifies patients with psoriasis who are at high risk for developing PsA will be an important step towards improving early detection enabling opportunities for early interventions, which may halt progression from psoriasis to PsA.

Recent research efforts are focused on revealing risk factors in psoriasis patients to identify individuals at increased risk for PsA. The most consistent evidence suggests that obesity, extensive psoriasis,

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[1]Lihi Eder, MD, PhD: Women's College Research Institute, Women's College Hospital, Toronto, Ontario, Canada, and Department of Medicine, University of Toronto, Toronto, Ontario, Canada; [2]Ker-Ai Lee, MMath, Richard J. Cook, PhD: Department of Statistics and Actuarial Science, University of Waterloo, Waterloo, Ontario, Canada; [3]Vinod Chandran, MBBS, MD, DM, PhD, Cheryl F. Rosen, MD, Dafna D. Gladman, MD: Department of Medicine, University of Toronto, and Schroder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Toronto, Ontario, Canada; [4]Jessica Widdifield, PhD: Sunnybrook Research Institute, Sunnybrook Hospital, and Institute for Clinical Evaluative Sciences (ICES), and Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Ontario, Canada; [5]Aaron M. Drucker, MD, SCM: Women's College Research Institute, Women's College Hospital, and Department of Medicine, University of Toronto, and ICES, and Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Ontario, Canada; [6]Christopher Ritchlin, MD, MPH: Division of Rheumatology, University of Rochester, Rochester, New York.

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Address correspondence via email to Lihi Eder MD, PhD, at lihi.eder@wchospital.ca.

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and psoriatic nail lesions predict the development of PsA among psoriasis patients (3–7). Other, less consistent risk factors include the location of psoriasis (intergluteal or scalp) (6), history of uveitis (4), comorbidities, such as thyroid disease and depression (4,8), and a recent history of physical trauma (9,10). In addition, the presence of nonspecific musculoskeletal symptoms, such as pain, fatigue, and stiffness, predicts the development of overt PsA among psoriasis patients (11,12). Although those individual risk factors for PsA are somewhat clinically useful, no unifying prediction tool currently exists.

Risk estimation using prediction tools plays an important role in shaping treatment plans, based on the ability of the risk score to accurately predict and stratify a patient's risk (13). A prognostic model for PsA could assist clinicians in identifying susceptible psoriasis patients for screening or interventional purposes and facilitate informed decision-making by both the treating physician and patient. Such a prediction tool would enable tailored management of individuals with psoriasis (eg, referral to rheumatology and close monitoring of high-risk individuals), which is expected to foster timely diagnosis of PsA, ultimately improving disease outcomes. The development of prediction tools for PsA was identified as a research priority by the American Academy of Dermatology and the Group for Research and Assessment of Psoriasis and PsA (14,15). In addition, the advent of novel immune-modulating therapies that target shared proinflammatory cytokines for psoriasis and PsA brings new opportunities for interventional studies aiming to prevent or delay the onset of PsA in susceptible psoriasis patients who do not yet have joint involvement. Thus, a prediction tool that identifies patients with psoriasis at high-risk for PsA will be an important first step in the development and testing of interventional strategies that may ultimately halt disease progression.

The objective of the study was to develop and internally validate a Psoriatic Arthritis Risk Estimation Tool (PRESTO) in patients with psoriasis.

PATIENTS AND METHODS

The Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis framework guided the development of the methodology and reporting for this study (16).

Setting

The ongoing University of Toronto Psoriasis Cohort started in 2006 as a prospective longitudinal cohort study aiming to study risk factors for the development of PsA among patients with psoriasis. Patients enrolled in the cohort have a dermatologist-confirmed diagnosis of psoriasis. They are recruited mainly from dermatology clinics and phototherapy centers in the Greater Toronto Area but also from family medicine clinics and through advertisements in hospitals and local media. All patients are assessed prior to enrollment by a rheumatologist to exclude those with inflammatory arthritis in the past or at the time of assessment. Rheumatologists examine the joints for the presence of tenderness, swelling and deformities, and signs of dactylitis, enthesitis, and tenosynovitis and evaluate the spine for restriction in movements. If definitive clinical findings of PsA are found, the patient is excluded from the study prior to enrollment. Imaging modalities, such as radiographs, MRI, or ultrasound, are performed only in cases of clinical doubt to investigate the nature of existing abnormalities. Patients with noninflammatory musculoskeletal conditions, such as osteoarthritis, are allowed to be enrolled. This process ensures that all study participants are free of clinical inflammatory arthritis at the time of enrollment. In this study, we used data from January 2006 to December 2019. We excluded patients without any follow-up study visits. The study was approved by the University Health Network Research Ethics Board. All patients signed an informed consent form.

Data collection

All study participants were reassessed annually by a rheumatologist who determined whether PsA had developed since the last study visit and to collect information on potential risk factors for PsA. Information was collected using standard protocols that record information about lifestyle habits, medical family history, musculoskeletal symptoms, comorbidities, medications, and skin examination findings. The presence of musculoskeletal symptoms was recorded by the rheumatologist at each visit. Physical examination included the evaluation of their height and weight, and skin assessment for psoriasis type, location, and activity (using psoriasis area and severity index [PASI]). The presence of psoriatic nail lesions was also documented. The rheumatologist also examined 66 and 68 joints for swelling and tenderness, respectively, and evaluated 18 entheseal sites for tenderness, and assessed for signs of dactylitis.

Musculoskeletal symptom severity was recorded using self-reported questionnaires. Stiffness level was measured on a 0- to 10-cm visual analogue scale. Pain level was measured on a numeric rating scale ranging from 0 (no pain) to 10 (severe pain). Current pain severity was also measured on a five-category Likert scale ranging from 1 = none to 5 = very severe. Fatigue was measured by functional assessment of chronic illness therapy–fatigue (FACIT-F), with lower scores indicating higher level of fatigue. The subject's self-reported global health status was measured on a five-category Likert scale ranging from 1 = very good to 5 = Vvry poor. Ability to function compared with 1 year ago was also assessed on a Likert scale ranging from 1 = much better to 5 = much worse. The presence of human leukocyte antigen (HLA)-B*27 allele was assessed. See Supplementary Information 1, available on the *Arthritis & Rheumatology* website at http://onlinelibrary.wiley.com/doi/10.1002/art, for detailed information on collection of study variables.

Case definition

A comprehensive assessment of symptoms and signs of PsA was performed at each study visit by a rheumatologist

experienced in assessing patients with PsA. The diagnosis of PsA was based on clinical findings, as described above. Imaging modalities were ordered only if clinically indicated to investigate abnormalities that may suggest PsA. The diagnosis of PsA was determined after reviewing the clinical, laboratory, and imaging data (if available). Information on HLA-B*27 status was not considered as part of the diagnostic process.

To address the issue of lost to follow-up, we contacted patients who failed to return for their yearly follow-up (missed two or more consecutive annual visits) to determine if they are alive and whether they have seen a physician for musculoskeletal symptoms. We also reviewed all relevant medical records from rheumatologists and other specialists outside of our research group to determine whether they received a new diagnosis of PsA.

Statistical analysis

We calculated descriptive statistics, including mean (SD) for continuous variables and frequencies (percentages) for categorical variables. Data on up to 10% of patient-reported outcome variables and body mass index (BMI) were missing. We used multiple imputation to handle missing data (via proc MI in SAS) based in predictive mean matching using full conditional specification; five complete data sets were generated by imputation.

The time at risk was the time from clinic entry to the development of PsA or, for those not developing PsA, to the earliest of the dates of death, moving out of province, or loss to follow-up. For the development of the PRESTO predictive tool, the risk of developing PsA was estimated over 1- and 5-year moving, overlapping time windows (see Supplementary Information 2, available on the *Arthritis & Rheumatology* website at http://onlinelibrary.wiley.com/doi/10.1002/art). That is, baseline covariates were used separately to predict the development of PsA within 1 and 5 years. Information on baseline covariates was updated in subsequent visits along with an update of the prediction windows. For the 5-year prediction model, this update often resulted in overlapping prediction windows. Thus, individual patients can contribute multiple observation windows with different index dates to the analysis, depending on their length of follow-up and number of visits. Based on our prior studies that showed an increase in nonspecific musculoskeletal symptoms closer to the time of diagnosis (11), we hypothesized that different variables would predict PsA at each of these two time windows. Therefore, we aimed to develop two separate prediction models to estimate the shorter- and longer- term PsA risk within two clinically meaningful time periods.

We selected 29 variables as potential predictors for the models based on existing literature on risk factors for the development of PsA in psoriasis patients. Additional guiding principles for the selection of potential predictors were availability of information in our cohort and their typical availability in routine clinical practice. The following time-varying covariates were considered as possible prognostic variables for PsA: age, sex, family history of psoriasis, family history of PsA or ankylosing spondylitis, arthralgia, morning joint stiffness, heel pain, back pain, morning back stiffness, BMI, flexural psoriasis, pustular psoriasis, palmoplantar psoriasis, PASI score, psoriasis body surface area, psoriatic nail lesions, pitting, onycholysis, iritis, inflammatory bowel disease (IBD), joint stiffness severity, FACIT-F, patient global health, current pain severity, ability to function compared with 1 year ago, and pain level (numeric rating scale [NRS]), HLA-B*27, phototherapy or use of nonbiologic systemic therapy, and use of biologic therapy. Because of software limitations for the handling of multilevel categorical variables, all covariates measured on Likert scales were converted to binary variables (see Supplementary Information 1, available on the *Arthritis & Rheumatology* website at http://onlinelibrary.wiley.com/doi/10.1002/art).

To avoid sparse data situations arising from covariates with low frequencies, the baseline distribution of all potential binary predictors by PsA conversion status were examined using 2×2 contingency tables. Predictors with less than five cell counts for at least one of the imputed data sets were excluded from the analysis prior to fitting the regression models.

We fitted multivariable logistic regression models adjusting for covariates, the duration of psoriasis, and the log duration at risk to estimate the probability of developing PsA within each of 1-year and 5-year time windows from consecutive study visits. If an individual considered at risk of PsA did not develop PsA before their next study visit, the covariates were updated and used to predict PsA onset within the next future time window. Individuals not observed to develop PsA over the entire duration of follow-up gave censored conversion times.

The penalized regression method using weighted stacked objective function and least absolute shrinkage and selection operator penalty function for binary response with 5-fold cross-validation is used for variable selection and to minimize overfitting (17). Because we have five imputed data sets, and each imputed data set may lead to different sets of selected predictors, the stacked approach was applied to pool the objective functions across imputations. This is a way to pool the penalized regression estimates across imputed data sets. Because stacking five imputed data sets can be viewed as artificially increasing the sample size by five times, a weight is added to each subject to address the increase in sample size. We assign an observation weight of 1/5 to a visit that has some missing covariates; otherwise, the observation weight is 1. The models were internally validated by 5-fold cross-validation.

We assessed model performance using metrics for discrimination and calibration, including the area under the curve (AUC) and calibration plots, respectively. To calculate AUC and its confidence interval, we used Rubin's combining rule to aggregate estimates on five imputed data sets (18). Two hundred bootstrap samples were used, sampling individuals' entire courses, to obtain a nonparametric bootstrap standard error of the aggregate AUC. A priori, we considered an AUC of greater than 70% acceptable. We

calculated sensitivity and specificity for varying cutoff values for each model based on averages of five imputed data sets.

RESULTS

A total of 786 patients with psoriasis were screened. Of those, 84 patients were excluded because of the presence of PsA and other rheumatic conditions at baseline. A total of 702 patients with psoriasis without clinical evidence of musculoskeletal inflammatory disease enrolled in the Toronto Psoriasis Cohort were followed from January 1, 2006 to December 31, 2019. Of these patients, 67 patients were excluded from the analysis because they only had a single visit and did not contribute any follow-up data. Of 635 patients included in the analysis, 51 and 71 patients developed PsA within the 1-year and 5-year time windows, respectively (Table 1).

Table 1. Baseline characteristics of study participants*

	All participants (N = 635)	Participants with PsA in 1-year window (N = 51)	Participants with PsA in 5-year window (N = 71)
Age (years)	47.0 (13.5)	47.6 (11.7)	46.8 (12.4)
Sex: male	360 (56.7%)	31 (60.8%)	43 (60.6%)
Race and ethnicity			
White	483 (76.1%)	41 (80.4%)	53 (74.6%)
South Asian	45 (7.1%)	3 (5.9%)	6 (8.5%)
Chinese	28 (4.4%)	2 (3.9%)	3 (4.2%)
Filipino	18 (2.8%)	1 (2.0%)	2 (2.8%)
Middle Eastern	14 (2.2%)	0 (0.0%)	2 (2.8%)
Black	11 (1.7%)	1 (2.0%)	2 (2.8%)
Southeast Asian	11 (1.7%)	0 (0.0%)	0 (0.0%)
Other	25 (3.9%)	3 (5.9%)	3 (4.2%)
Psoriasis duration (years)	16.0 (14.3)	20.3 (16.2)	17.6 (15.1)
Family history of psoriasis	268 (42.2%)	24 (47.1%)	33 (46.5%)
Family history of PsA	24 (3.8%)	3 (5.9%)	3 (4.2%)
Arthralgia	165 (26.0%)	7 (13.7%)	15 (21.1%)
Morning stiffness	66 (10.4%)	4 (7.8%)	6 (8.5%)
Heel pain	10 (1.6%)	1 (2.0%)	2 (2.8%)
Back pain	275 (43.3%)	23 (45.1%)	32 (45.1%)
Back stiffness	52 (8.1%)	2 (3.9%)	3 (4.2%)
BMI	28.0 (5.9)	28.5 (5.6)	28.6 (5.7)
Flexural psoriasis	14 (2.2%)	2 (3.9%)	3 (4.2%)
Pustular psoriasis	12 (1.9%)	0 (0%)	1 (1.4%)
Palmoplantar psoriasis	27 (4.3%)	0 (0%)	2 (2.8%)
PASI score	5.3 (6.0)	6.0 (5.9)	6.5 (6.3)
BSA (%)	8.6 (11.7)	7.1 (5.8)	9.7 (9.8)
Nail lesions	303 (47.7%)	29 (56.9%)	42 (59.2%)
Pitting	231 (36.4%)	23 (45.1%)	33 (46.5%)
Onycholysis	200 (31.5%)	20 (39.2%)	31 (43.7%)
Iritis	4 (0.6%)	1 (2.0%)	1 (1.4%)
IBD	2 (0.3%)	0 (0%)	0 (0%)
Stiffness level (VAS in mm)	18.3 (34.9)	23.0 (29.4)	20.1 (27.0)
FACIT-F	44.7 (7.2)	41.5 (7.8)	41.1 (7.7)
HLA-B*27	22 (3.5%)	0 (0%)	2 (2.8%)
Use of nonbiologic systemic therapies or phototherapy for psoriasis[a]	447 (70.4%)	41 (80.4%)	58 (81.7%)
Use of systemic biologic therapies for psoriasis[b]	32 (5.0%)	2 (3.9%)	2 (2.8%)
Patient's global health: very good or good vs. fair/poor/very poor	365 (79.2%)	31 (79.5%)	35 (72.9%)
Current pain severity: Any level of pain[c]	223 (48.5%)	27 (69.2%)	33 (68.8%)
Ability to function compared with previous year: much better or somewhat better[d]	94 (20.5%)	12 (30.8%)	13 (27.1%)
Pain level (NRS, 0–10)	1.5 (2.2)	1.9 (2.2)	2.0 (2.3)

* BMI = body mass index; BSA = body surface area; FACIT-F = functional assessment of chronic illness therapy—fatigue; HLA = human leukocyte antigen; IBD = inflammatory bowel disease; IL = interleukin; NRS = numeric rating scale; PASI = psoriasis area and severity index; TNF = tumor necrosis factor; VAS = visual analogue scale.
[a] Methotrexate, apremilast, cyclosporine, soriatane.
[b] IL-17, IL-12/23, IL-23, or TNF inhibitors.
[c] Current pain (Likert) very severe/severe/moderate/mild vs. none.
[d] Ability to function compared with previous year: much better or somewhat better vs. about the same/somewhat worse/much worse.

Of the 29 prespecified potential predictors, the following predictors were excluded because of low prevalence: family history of PsA, heel pain, flexural psoriasis, pustular psoriasis, iritis, IBD, and HLA-B*27. Use of biologic systemic therapy was excluded only for the 5-year prediction model.

One-year prediction model

The following variables were selected for the 1-year prediction model: age, male sex, family history of psoriasis, morning back stiffness, nail pitting, stiffness level, use of biologic systemic medications, patient global health, and pain (any level vs. none). These variables were associated with a higher risk of developing PsA except for age and patients' global health, which were associated with a reduced risk (see Figure 1A). The discriminatory ability of the model was acceptable with an AUC of 72.3% (95% confidence interval [95% CI] 65.5–79.1). Model calibration, qualitatively assessed by reviewing the calibration plot, was excellent with an almost perfect agreement between the observed versus predicted cases (Figure 2A and B). Sensitivity and specificity for various cutoff levels are shown in Figure 3.

Five-year prediction model

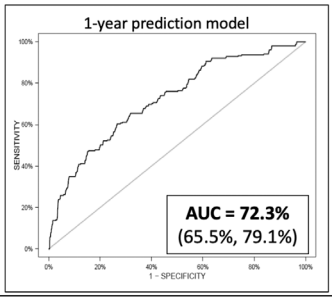
The following variables were selected for the 5-year prediction model: presence of morning joint stiffness, PASI, psoriatic nail lesions, FACIT-F, use of nonbiologic systemic medications/phototherapy, and pain (any level vs. none). The discriminatory ability of the model was acceptable with an AUC of 74.9% (95% CI 69.3–80.5; Figure 1B). Model calibration showed reasonable agreement between observed versus predicted cases in the first to fourth lower quantiles of predicted probability but more substantial disagreement in the fifth quantile, with underestimation of the actual risk by the prediction model (Figure 2C and D). Sensitivity and specificity for various cutoff levels are shown in Figure 3.

DISCUSSION

We derived and internally validated a novel risk prediction tool for PsA: PRESTO. PRESTO estimates PsA risk within shorter and longer time horizons using easily collected information, including many variables that were previously reported as risk factors for PsA. PRESTO has demonstrated good model fit metrics, including discrimination and calibration, and its threshold could be adjusted depending on the purpose of its use (eg, higher sensitivity for screening, higher specificity for enrichment with high-risk patients for interventional studies). Accurate estimation of PsA risk using PRESTO among patients with psoriasis has important potential applications in clinical care, such as promoting early diagnosis and interventions to prevent progression from psoriasis to PsA.

1A. Summary of Regression Coefficients for 1-Year Period (N=635, 51 events)

Age (1 year increase)	-0.008
Sex (Male vs. Female)	0.179
Family history of psoriasis (Yes vs. No)	0.209
Back stiffness (Yes vs. No)	0.619
Nail pitting (Yes vs. No)	0.608
Stiffness level (VAS, 0-10)	0.036
Use of biologic systemic therapy* (Yes vs. No)	0.170
Patient Assessment of Global Health (Very good/Good vs. Fair/Poor/Very poor)	-0.168
Patient Pain Severity (Any level vs. None)	0.646



1B. Summary of Regression Coefficient for 5-Year Period (N=635, 71 events)

Morning joint stiffness (Yes vs. No)	0.014
PASI score (1 unit increase)	0.017
Psoriatic nail lesion (Yes vs. No)	0.099
FACIT – Fatigue score (1 unit increase)	-0.033
Use of non-biologic systemic therapy or phototherapy** (Yes vs. No)	0.145
Patient Pain Severity (Any level vs. None)	0.318

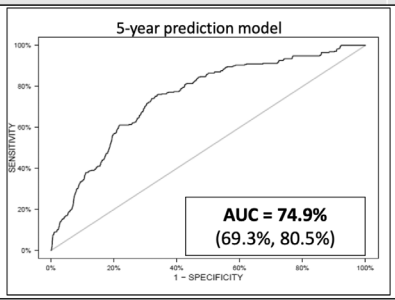


Figure 1. Prediction models for the development of PsA in psoriasis within 1-year period (**A**) and within 5-year period (**B**). Abbreviations: AUC = area under the curve; FACIT = functional assessment chronic illness therapy; PASI = psoriasis area and severity index; PsA = psoriatic arthritis; VAS = visual analogue scale. *Biologic systemic therapy includes current use of inhibitors of TNF, IL-17, IL-12/23 or IL-23. **Nonbiologic systemic therapies include current use of acitretin, apremilast, methotrexate, or cyclosporine.

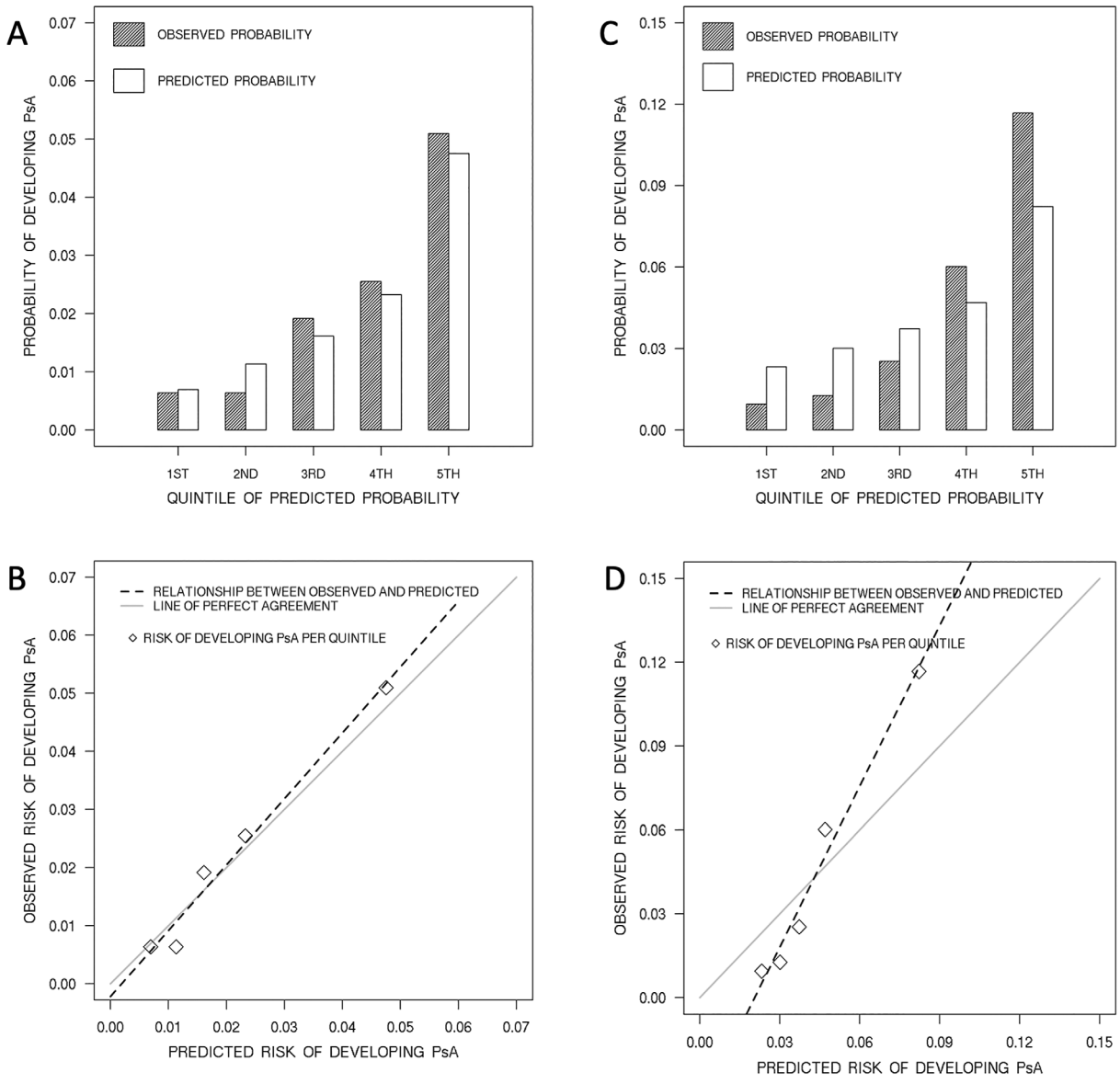


Figure 2. Calibration plots by quintile of predicted vs. observed probabilities for 1-year (**A** and **B**) and 5-year periods (**C** and **D**). Abbreviation: PsA = psoriatic arthritis.

PRESTO uses a mathematical model to estimate PsA risk. To facilitate its use, we developed a webpage with a PRESTO calculator (http://sharpmindtill120.x10host.com/PRESTO-PsA; see Supplementary Information 3, available on the *Arthritis & Rheumatology* website at http://onlinelibrary.wiley.com/doi/10.1002/art, for a calculator). We also created risk tables for various patient profiles (Figure 4). PRESTO builds upon existing literature on clinical risk factors for PsA. We purposely focused on assessing risk factors that are simple to measure in clinic setting via patient interview or physical examination. Our prediction tool includes many variables that have been previously associated with a higher risk of developing PsA, such as extensive psoriasis, psoriatic nail lesions, and nonspecific musculoskeletal symptoms (4,6,11,19,20). The inclusion of these variables in PRESTO strengthens its face validity. Interestingly, several previously reported risk factors for PsA, such as HLA-B*27, family history of PsA, uveitis, and flexural psoriasis, were not included in the risk prediction model because of their scarcity in our cohort. This finding may be due to immortal time bias, which can complicate the development of risk prediction models for PsA. Genetic factors or their surrogates (eg, family history of PsA) are associated with the development of PsA concurrently or shortly after the onset of psoriasis (21). Thus, our population of patients with longstanding psoriasis may have been depleted of patients carrying these risk factors, rendering these factors less useful for prediction of PsA among patients with longstanding psoriasis who are commonly seen in dermatology clinics.

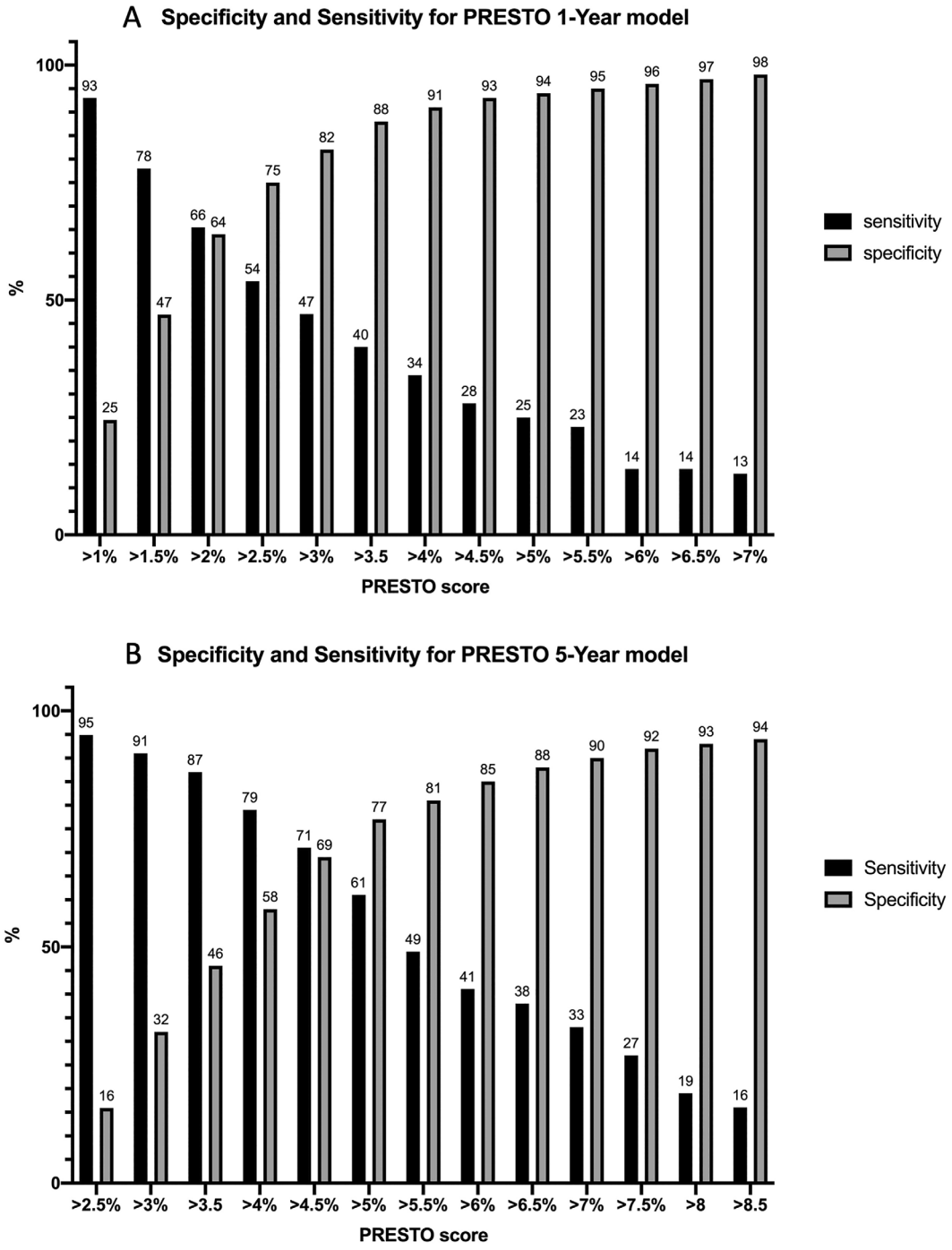


Figure 3. Sensitivity and Specificity of the model by selected cutoff point. (**A**) PRESTO score for 1 year window. (**B**) PRESTO score for 5-year window. The X axis in each graph depicts the probability of developing PsA for each model. The Y axis depicts the sensitivity and specificity (%) for each cut point. Abbreviations: PRESTO = Psoriatic Arthritis Risk Estimation Tool; PsA = psoriatic arthritis.

We have described a prodrome of nonspecific musculoskeletal symptoms occurring up to 5 years before the development of overt PsA (11,22). We found that the prevalence and severity of these symptoms increase closer to the diagnosis of PsA, which may lead to time-dependent effect sizes associated with these predictors. This result influenced our decision to develop two separate prediction models, one for estimating the short-term risk (within 1 year) and the other for longer-term risk estimation (within 5 years). Indeed, the composition of the two risk models differ, although both include a combination of patient-reported musculoskeletal symptoms and psoriasis features and therapies. An important strength of our study is the availability of prospectively

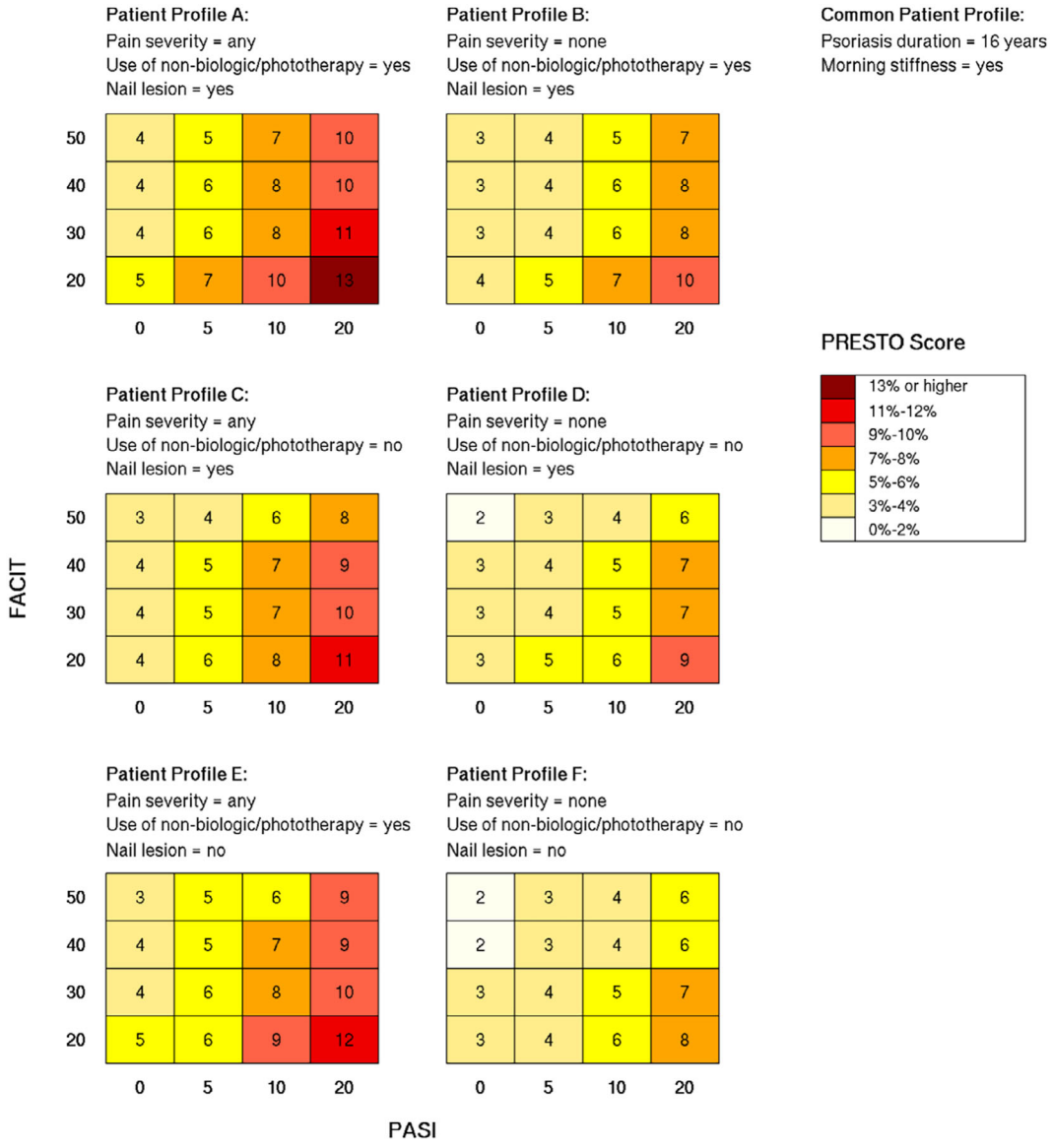


Figure 4. Estimated probability of developing PsA for six patient profiles based on the 5-year model. Abbreviations: FACIT = functional assessment of chronic illness therapy; PRESTO = Psoriatic Arthritis Risk Estimation Tool; PsA = psoriatic arthritis.

collected, time-varying information that estimated PsA risk within prespecified time frames, reflecting the dynamic nature of these factors in a real-life setting.

The relationship between the use of systemic therapies for psoriasis and future risk of PsA remains controversial. Use of biologic therapies and nonbiologic therapies or phototherapy were included in the 1-year and 5-year risk prediction models, respectively, both being associated with a higher risk of PsA. We showed that use of acitretin was associated with a higher risk of developing incident PsA among psoriasis patients (4). Similarly, Lindberg et al reported that use of systemic therapies or phototherapy was associated with an increased incidence rate of PsA among psoriasis patients (23). Studies that specifically assessed the question of whether use of biologic medications for psoriasis lowers the risk of developing PsA, showed conflicting results (24–26). It is important to note that our study was not designed to assess whether the use of systemic therapy modifies PsA risk; thus, interpretation of the direction of association between medication use and PsA risk in the context of a multivariable prediction model should be performed with great caution. The use of systemic therapy as a variable in a prediction model can be viewed as a surrogate for psoriasis severity, which has been associated with a higher risk of developing PsA.

Screening for at-risk individuals is an important part of preventive medicine. The rationale is to identify disease during an early and preclinical stage. Early disease may be easier and less expensive to treat, which positions screening strategies as potentially sound investments for health care systems. Risk estimation

using prediction tools plays an important role in tailoring treatment plans to fit the patient's individual risk factors. The assessment of a patient's absolute risk is integral to the assessment of major prevention and treatment targets in various medical fields, such as cardiology (Framingham Risk Score). In rheumatology, risk prediction tools have been developed to estimate the risk of developing rheumatoid arthritis (RA) in high-risk populations, such as family members. They combine clinical, serologic, and genetic data to provide an absolute risk estimation of developing RA with generally good predictive ability (AUC of 0.70 to 0.85) (27,28). These tools have been implemented in clinical and research settings as educational tools for high-risk populations and for selection of high-risk individuals for prevention trials (29,30). In PsA, a strong rationale exists for using a risk prediction tool, possibly more so than in RA, given the easily identifiable target population of patients with psoriasis. Indeed, the Preventing Arthritis in a Multicentre Psoriasis At-Risk cohort trial (NCT05004727) is the first randomized controlled prevention trial, aimed to assess the efficacy of guselkumab versus placebo for reducing rate of progression from psoriasis to PsA. The study uses some clinical and ultrasound parameters to enrich features associated with high risk of PsA. Future studies could use the PRESTO score to accurately estimate PsA risk for enrichment of prevention trials with at-risk patients and to inform sample size calculation. With more treatment options for both psoriasis and PsA combined with a better understanding of PsA pathophysiology, prevention trials using either targeted therapies or nonpharmaceutical interventions become more relevant.

This study has several limitations. First, the relatively small sample size may have reduced the precision of the model and prevented the inclusion of previously reported risk factors that were present in only a few patients but may have had a strong effect size. The small sample size also prevented analysis by sex and race and ethnic group. Second, the generalizability of the study may be somewhat limited because most of the patients were recruited from dermatology clinics, leading to overrepresentation of moderate-severe psoriasis. Therefore, PRESTO will require an external validation to assess its performance in other populations of psoriasis patients with different characteristics. Thirdly, because of the study design, patients who developed PsA prior or concurrently to psoriasis were excluded. Therefore, our incident cases of PsA may overrepresent certain subtypes of PsA that are associated with longer duration between the onset of psoriasis and PsA.

In summary, we derived and internally validated a novel risk prediction tool for PsA in patients with psoriasis. PRESTO has good model performance and can provide estimated risk of developing PsA within shorter and longer time periods that are relevant for both clinical and research purposes. If further validated, we anticipate that PRESTO may facilitate efforts to improve early detection of at-risk populations enabling opportunities for early interventions that may halt progression to PsA.

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