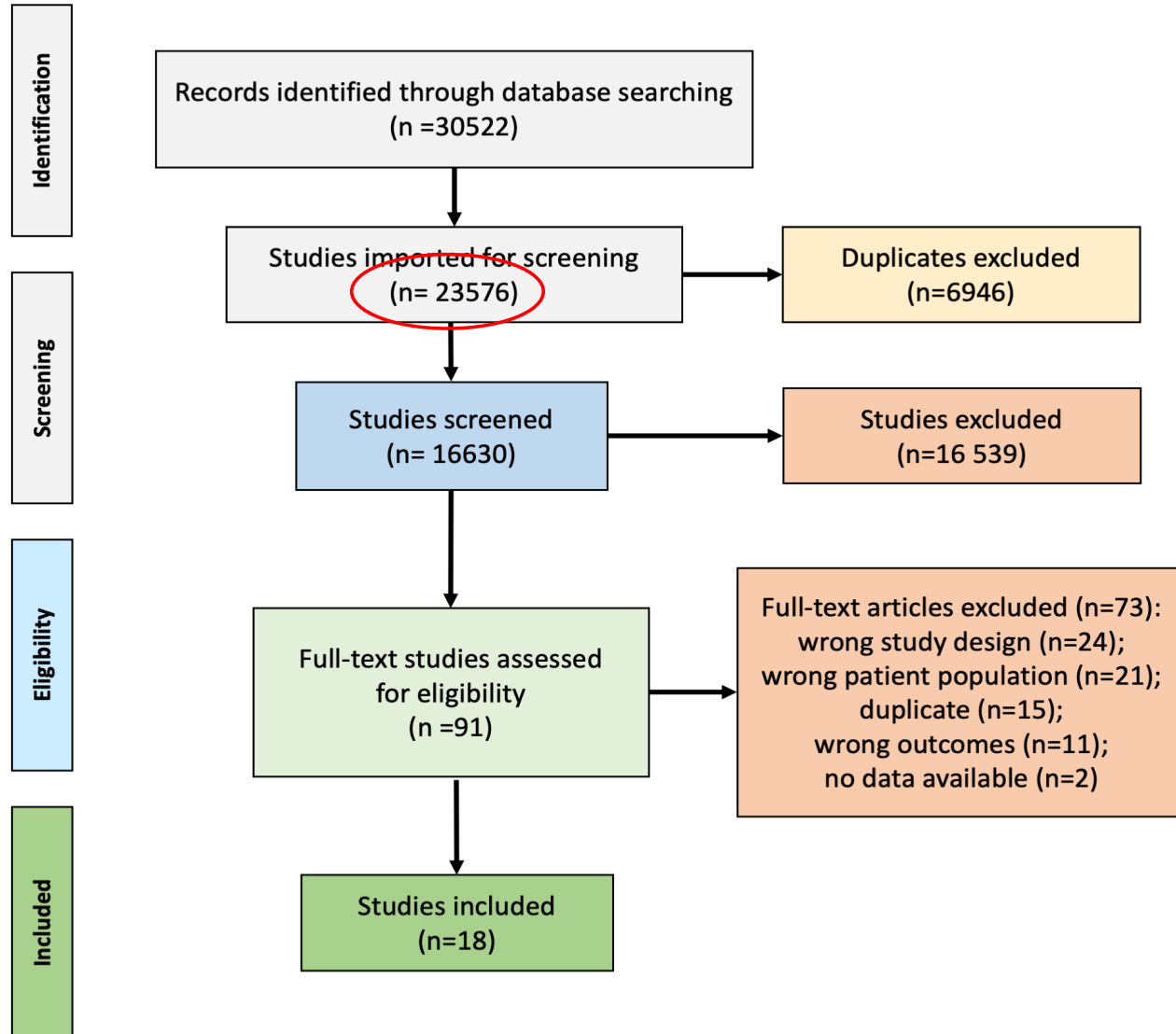


PRISMA FLOW-CHART «PsO to PsA» SLR for question # 1



18 studies included:

- 10 cohort studies (6 prospective, 4 retrospective);
- 1 case-control study;
- 1 Bayesian network study;
- 4 abstracts (2 from ACR and 2 from EULAR);
- 2 SLRs (to check references)

BREAKDOWN PRESENTATION OF THE INCLUDED STUDIES

Study (year)	Design	Data Source	Population (n=)	Incident PsA (n=)	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Simon et al. 2022	Cohort Prospective	OPD	114*	24**	2.3	PsO patients with arthralgia: PsA incidence 12.5 per 100 patient-years; without arthralgia: 5.9 per 100 patient-years.	PsA onset: 17/24 (71%) clinical arthritis**; 1/24 (4%) clinical dactylitis; 1/24 (4%) axial involvement; 5/24 (21%) ultrasound proven enthesitis	Structural enthesal lesion at the MCP joints*** corresponded to a HR of 4.9 (95% CI 2.0-11.9) for PsA development. Patients progressing to PsA had a lower enthesal, cortical and trabecular volumetric BMD	Incidence of PsA according to the baseline characteristics

NOS score 7

* 47/114 (41%) reported arthralgia at BL with an overall intensity of 18.8 for VAS pain and a mean tender joints of 0.8. ** PsA was defined as the presence of inflammatory musculoskeletal involvement (arthritis as defined by joint swelling, enthesitis as defined by enthesal pain plus power Doppler ultrasound signal, dactylitis as determined by clinical examination, or axial involvement as determined by inflammatory back pain and radiographic/magnetic resonance imaging [MRI] evidence of sacroiliitis or spondylitis) assessed by an experienced rheumatologist and a score of ≥ 3 points on the CASPAR criteria.

*** detected by peripheral quantitative computed tomography

BMD: bone mineral density

Simon et al, *Arthritis Rheumatol.* 2022 Feb;74(2):253-262

Study (year)	Design	Data Source	Population (n=)	Incident PsA (n=)	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Eder et al. 2016	Cohort Prospective	OPD	464	51 *: **	4.1	Not reported	<p>Pattern of presentation: peripheral arthritis (64%, among peripheral 73% was oligoarthritis), axial involvement alone (18%), combined peripheral and axial involvement (16%), and enthesitis (2%) .</p> <p>PsA diagnosis: TJC 2.8; SJC 1.5; Dactylitis 6%; Enthesitis 20%.</p> <p>HAQ score, mean 0.34; VAS pain 3.28</p>	<p>41% of the patients had signs of sacroiliitis or spondylitis on imaging (radiographs or MRI). 23% patients showed at least one periarticular joint erosion. 10% had periarticular new bone formation.***</p>	Predictor/risk factors for PsA development

NOS score 8

* The diagnosis of PsA was determined by at least 2 rheumatologists after reviewing the clinical, laboratory, and imaging data. Participants were classified as having PsA if they fulfilled the Classification of Psoriatic Arthritis (CASPAR) criteria. Patients were instructed to contact the clinic prior to their annual assessment if they developed symptoms suggestive of PsA (e.g., joint pain or swelling). ** Patients with incident PsA = 51 with diagnosis, 9 with suspected PsA excluded from the analysis. *** 39/51 patients performed X-ray at the baseline

Eder et al, Arthritis Rheumatol. 2016 Apr;68(4):915-23

Study (year)	Design	Data Source	Population (n=)	Incident PsA (n=)	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Faustini et al. 2014	Cohort Prospective	OPD	41*	12**	1.2	BL presence of higher VAS pain (4.4 vs 1.7 joint tenderness (4.0 vs 1.0) and VAS global health (4.1 vs 1.7)	Not reported	No differences related to MRI*** findings were found between PsA developer and non developer	Combination of MRI+ and TJC>0 predict PsA progression. PsO with TJC>0 and MRI+ presented a LR of 55% vs 15% (TJC =0 and MRI neg)

NOS score 7

*41/55 PsO patients completed the follow-up and were included in the longitudinal analysis; 21/55 (38.8%) presented at baseline at least one tender joint; the mean tender joint count was 1.6. No patients with swollen joints, dactylitis, enthesitis.

** The diagnosis of PsA was clinical and made by rheumatologists if CASPAR criteria were fulfilled.

*** MRI: image analysis focused on the detection of synovitis, tenosynovitis, osteitis, erosions on MCP, PIP and DIP of the second to fifth fingers

BL: baseline; GS tenosynovitis; LR: likelihood ratio.

Faustini F, et al. Ann Rheum Dis 2016;75:2068–2074

Study (year)	Design	Data Source	Population (n=)	Incident PsA (n=)	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Zabotti et al. (2019)	Cohort prospective	OPD	102*	6*	1.2	BL presence of arthralgia, higher VAS pain (5.9 vs 2.6), HAQ (0.4 vs 0.2), joint tenderness (6.8 vs 1.7)	Not reported	BL active enthesitis associated with later PsA; BL GS tenosynovitis was associated with arthralgia but not later PsA	Correlation between the sonographically detected inflammation and the BL variables.

NOS score 7

* 54 Psoriatic arthralgia patients + 48 PsO patients. Arthralgia was defined as recent onset (≤ 12 months) of non-inflammatory joint and/or enthesal pain, without current or past inflammatory signs/symptoms, and with CASPAR ruled out.

** The diagnosis of PsA was clinical and made by rheumatologists if CASPAR criteria were fulfilled. The follow-up was set every 6 months and patients were instructed to contact the rheumatologist prior to their scheduled assessment if they developed inflammatory symptoms

BL: baseline; GS tenosynovitis;

Zabotti A, et al. RMD Open 2019;5:e001067

Study (year)	Design	Data Source	Population (n=)	Incident PsA (n=)	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Elnady et al. 2019	Cohort Prospective	OPD	109	9*	2**	BL CRP was higher in newly diagnosed PsA patients (10 mg/l vs 1.4 mg/l)	9/9 showed clinical arthritis at baseline. 1/9 also developed unilateral axial sacro-ileitis	Higher PDUS score (2.44 vs 0.23) GSUS score (0.77) and subclinical enthesitis	Comparison between psoriatic patients with and without MSUS manifestation according to demographic, clinical and lab variables

NOS score 5

*Diagnosis of PsA: clinical arthritis in the form of hot, tender and/or swollen joints or enthesitis, with or without dactylitis, that satisfied CASPAR criteria

** follow-up of 2 years with clinical evaluation every 3 months by two experts rheumatologists

GSUS (greyscale) and power Doppler (PD) at 34 joints level, 8 enthesitis

Elnady et al, Clin Rheumatol. 2019 Jun;38(6):1627-1635

Study (year)	Design	Data Source	Population (n=)	Incident PsA (n=)	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Eder et al. 2017	Cohort Prospective	OPD	410	57 *	3.8	The intensity and the number of symptoms increases in the period prior to the diagnosis of PsA. The presence of arthralgia in women, morning joint and back stiffness and fatigue was associated with PsA development.	Pattern of presentation: peripheral arthritis (64%-73% oligoarthritis), axial involvement alone (18%), combined peripheral and axial involvement (16%), and enthesitis (2%).	At the PsA onset 25% showed periarticular erosions at the x-ray of hands and feet	Prevalence of musculoskeletal symptoms at baseline; correlation between patient-reported symptoms at baseline

NOS score 8

* The diagnosis of PsA was determined by at least 2 rheumatologists after reviewing the clinical, laboratory, and imaging data. Participants were classified as having PsA if they fulfilled the Classification of Psoriatic Arthritis (CASPAR) criteria. Patients were instructed to contact the clinic prior to their annual assessment if they developed symptoms suggestive of PsA (e.g., joint pain or swelling).

Eder et al, *Arthritis Rheumatol.* 2017 Mar;69(3):622-629

Study (year)	Design	Data Source	Population (n=)	Incident PsA (n=)	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Belman et al. 2021	Cohort Retrospective	OPD	627	128*	7.7 years	Not reported	Not reported	Not reported	<p>Predictors and risk factors of PsA development.</p> <p>Differential diagnosis: 21% presented at with uncertain PsA (no other data useful)</p>

NOS score 5

*Definitive PsA classification required PsA diagnosis by a rheumatologist, defined by 1) patient-reported diagnosis of PsA from a rheumatologist, 2) PsA diagnosis reported by a UPI study rheumatologist after an evaluation with the patient, or 3) a diagnosis code for PsA or ankylosing spondylitis (AS) by a rheumatologist in an EMR

Belman et al, J Rheumatol. 2021 Oct;48(10):1559-1565.

Study (year)	Design	Data Source	Population (n=)	Incident PsA (n=)	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Acosta Felquer et al. 2022	Cohort Retrospective	OPD	1719	*239	7.3 **,***	Not reported	Not reported	Not reported	Identification of predictors and risk factors of PsA development treatment with biologics was significantly associated with a reduced risk of developing PsA

NOS score 6

* The diagnosis of PsA was confirmed by a rheumatologist and/or fulfilled the CASPAR criteria; PsA diagnosis was recorded by rheumatologists in 87% of the cases, by dermatologists in 3% and by others or not recorded in 10% of the cases

** follow up every 6 months and rapid referral to rheumatologist if musculoskeletal symptoms were present or if EARP-10 questionnaire was positive

*** All medical appointments were reviewed, with special attention to pain-related problems or musculoskeletal symptoms and orthopedists, physiotherapists and rheumatologists visit

SJC: swollen joint count; TJC: tender joint count

Acosta Felquer et al, Ann Rheum Dis 2022;81:74–79

Study (year)	Design	Data Source	Population (n=)	Incident PsA (n=)	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Gisoni et al. 2022	Cohort Retrospective	OPD	464	51*	6.9**	Not reported	<p>The most frequent pattern of PsA was peripheral arthritis (84%), followed by dactylitis (20%), enthesitis (16%) and axial involvement (6%). More than one pattern could be observed in a single psoriatic patient.</p> <p>At the PsA diagnosis: SJC, 2.6 in bDMARDs and 3.2 in phototherapy; TJC 2.3 in bDMARDs and 2.9 in phototherapy</p>	Not reported	<p>Predictors and risk factors of PsA development</p> <p>treatment with biologics was significantly associated with a reduced risk of developing PsA</p>

NOS score 6

* The diagnosis of PsA was determined by one rheumatologist if the patient fulfilled CASPAR criteria;

** follow up very 6 months and rapid referral to rheumatologist if musculoskeletal symptoms were present or if EARP-10 questionnaire was positive

SJC: swollen joint count; TJC: tender joint count

Gisoni et al, Ann Rheum Dis. 2022 Jan;81(1):68-73

Study (year)	Design	Data Source	Population (n=)	Incident PsA (n=)	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Balato et al. 2021	Cohort Retrospective	OPD	285	22*	Not reported**	Not reported	Pattern of presentation: Peripheral arthritis in 50%; Axial involvement in 9%; Enthesitis in 28%; Dactylitis in 41%; Peripheral + Axial in 4.5%	In 27 suspected PsA cases (22 then diagnosis confirmed) imaging was used: ultrasound examination in 48.5%, followed by X-ray (30.8%) and magnetic resonance (20.7%).	Predictors and risk factors for PsA development

NOS score 4

* 22/285; in the text it is reported as 22/236, but 41 were lost to follow-up visits. PsA diagnosis was clinical and confirmed by a rheumatologist.

** Screening frequency was 7.2 months

Balato et al, G Ital Dermatol Venereol. 2020 Dec;155(6):733-738

Study (year)	Design	Data Source	Population (n=)	Incident PsA (n=)	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Abji et al. 2021	Case-Control (Case: incident PsA)	OPD	24 PsA converters and 16 non converters	24*	Not reported	Not reported	The median number of active joints was 1.5 (0-3.3)	Not reported	<u>Declining levels of CXC (Ligand)10</u> in new onset of PsA in patients during the transition from PsO to PsA **

NOS score 5

* Converters selected from the Toronto cohort of 644 patients. The diagnosis was clinical and made according to CASPAR.

** CXCL10 levels were compared over time in converters prior to PsA onset and nonconverters over a minimum of two visits.

Abji et al. British Journal of Dermatology (2020) 183, pp920–927

Study (year)	Data Design	Source	Population (n=)	Incident PsA (n=)	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Green et al. 2021	Cohort study. Bayesian network	CPRD*	90189*	1409	Not reported	Musculoskeletal symptoms requiring medical attention** Arthritis and swelling and arthralgia, back pain, fatigue, finger pain, hand pain, hip pain, knee pain, myalgia, non-specific arthritis, unspecified swelling were identified as direct predecessors of PsA.	Not reported	Not reported	The BN with the best accuracy was BN-2: BN consisting of baseline demographics and only those musculo-skeletal symptom subgroups identified as influencing the development of PsA ***

NOS score 5

*Data from the Clinical Practice Research Datalink (CPRD)

** Over one-fifth of the psoriasis patients who went on to develop PsA visited their GP with musculoskeletal-related symptoms during the 5- years prior to their diagnosis of PsA. This proportion gradually increased and reached over 57% in the 6 months immediately preceding the diagnosis.

*** symptom subgroups identified as influencing the development of PsA (arthralgia, back pain, fatigue, finger pain, hand pain, hip pain, knee pain, myalgia, non-specific arthritis, unspecified swelling)

Green et al, Rheumatology (Oxford) 2022 Feb 2;61(2):581-590

Study (year)	Design	Data Source	Population (n=)	Incident PsA (n=)	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Pollock Presented as abstract EULAR 2019	Case-Control	OPD	120*	60		Not reported	Not reported	Not reported	DNA methylation changes occur early in PsA pathogenesis and can potentially serve as prognostic biomarkers of future onset of arthritis in psoriasis patients

*epigenome-wide comparison of DNA methylation in baseline whole blood samples from psoriasis converters (n=60) and non-converters (n=60) from a longitudinal cohort.

NOS score 2

Abstract number OP0203 at EULAR congress 2019.

Study (year)	Design	Data Source	Population (n=)	Incident PsA (n=)	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Eder et al. 2020 Presented as abstract EULAR 2020	Cohort Prospective	OPD	250 PsO patients with MSK symptoms	17	1 year*	Not reported	Not reported	Not reported	The authors tested the performance of the genetic essay in predicting PsA at 1 year

NOS score 2

* All patients who were classified as not PsA but with MSK symptoms at baseline were reassessed 1 year later to determine whether they have developed PsA.

Abstract number SAT 0414 at EULAR congress 2020.

Study (year)	Design	Data Source	Population (n=)	Incident PsA (n=)	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Chiu et al. 2012 Presented as abstract ACR 2012	Cohort Prospective	OPD	132	6*	1 year	Not reported	Not correctly reported***	2/6 (33.3%) had radiographic erosions	The progression of PsO to PsA was associated with a dramatic increase in circulating OCP numbers accompanied with an elevated DC STAMP+CD14+ monocyte frequency.

NOS score 3 *** Tender Joint Counts were 8.3±6.7 (prior) and 16±15 (after), Swollen Joint Counts were 3.9±4.1 (prior) and 7.1±9.6 (after);

Abstract number 2616 at ACR congress 2012.

Study (year)	Design	Data Source	Population (n=)	Incident PsA (n=)	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Thiele et al. 2013 Presented as abstract ACR 2013	Cohort Prospective	OPD	39	5*	3 years**	Not reported	Not reported	38% of patients with inflammation at imaging developed PsA	The Osteoclast Precursor frequency was highest in patients with new onset PsA.

NOS score 3 * Diagnosis of PsA was clinical and confirmed by CASPAR; ** follow-up every 3 months

Abstract number 307 at ACR congress 2013.

Study (year)	Design	Source	Population (n=)	Incident PsA (n=)	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Mulder et al. 2021	SLR*	Included in the SLR Cohort studies; Case-control studies, cross-sectional study**	N.A.	N.A.	N.A.	Arthralgia in women, heel pain, worsening of stiffness, worsening of pain were selected as moderate association with PsA development**	CRP was selected with a strong evidence for the presence of PsA in PsO patients ***	Not reported	An overview of most promising predictors for the development of PsA patients in PsO were showed.

*Quantitative synthesis was non performed

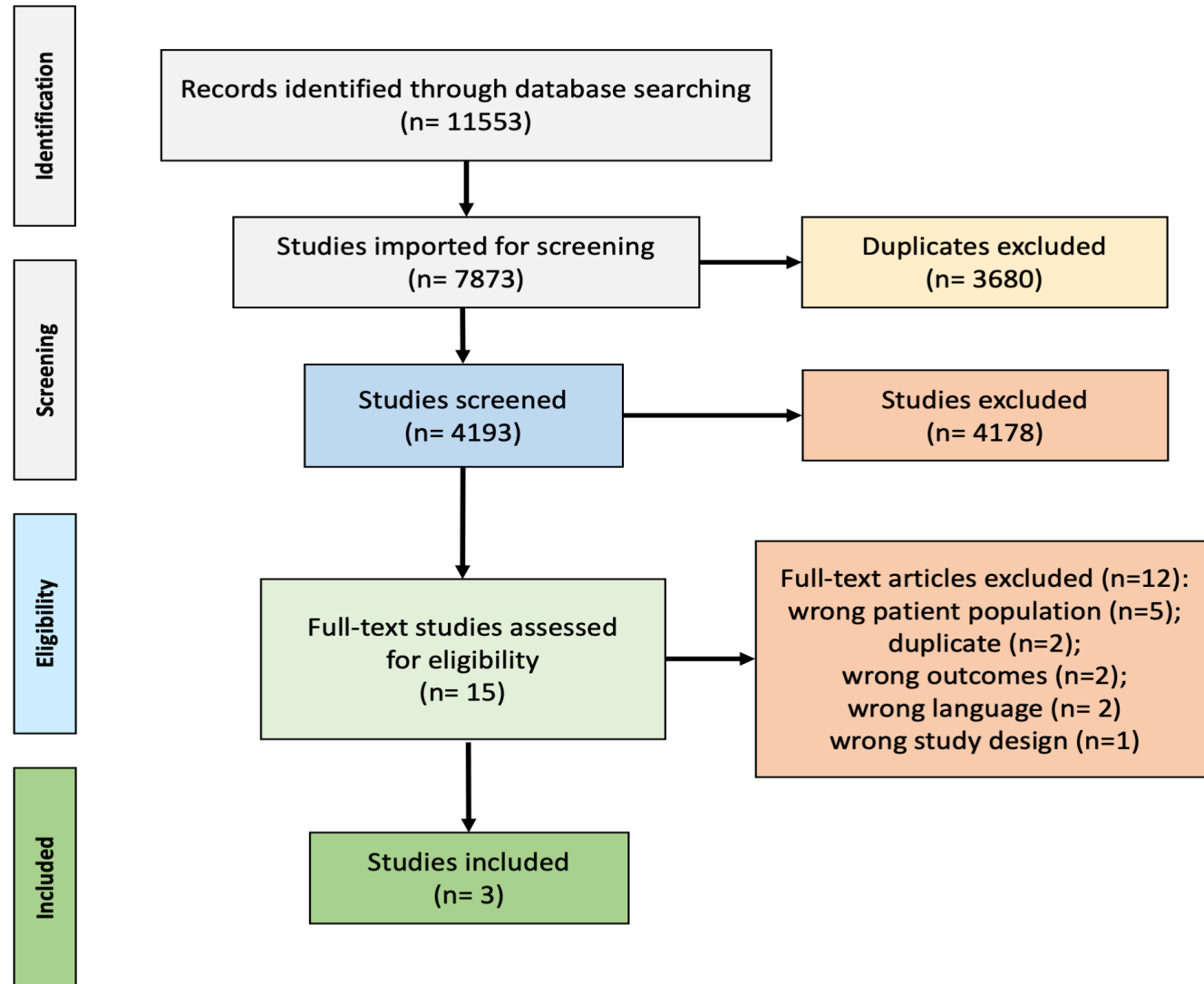
***to be considered as potential predictors

*** results obtained in the review only from cross-sectional studies (exclusion criteria of our SLR). No articles were selected in the SLR in which CRP was tested before PsA development and during the transition from PsO to PsA.

Study (year)	Design	Source	Population (n=)	Incident PsA (n=)	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Zabotti et al. 2021	SLR*	Included in the SLR Cohort studies; Case-control studies	N.A.	N.A.	N.A.	Quantitative synthesis: The risk of PsA development in PsO subjects with arthralgia was about two times greater than in subjects without arthralgia (pooled RR 2.15 [95% CI 1.16–3.99], I ² = 0.00%, p = 0.7797). *	Not reported	Quantitative synthesis: PsO patients with imaging evidence of inflammation or imaging detected structural damage were almost four times more likely to develop PsA (pooled RR 3.72 [2.12; 6.51], I ² = 0.00%, p = 0.6008) **	Predictors/risk factors for PsA development

* the definition of arthralgia among studies was different; ** imaging-detected MSK inflammation (e.g., synovitis, enthesitis, tenosynovitis) and imaging-detected structural damage (e.g., erosion and enthesela new bone formaation)

PRISMA FLOW CHART «UA to PsA» SLR for question # 2



Of 7873 references focusing on UA to PsA, 3 studies were included (2/3 were retrospective cohort and 1/3 was case control study). Meta-analysis was not done due to data heterogeneity.

BREAKDOWN PRESENTATION OF THE INCLUDED STUDIES

Study (year)	Design	Source	Population (n=)	UA->PsA	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Cuervo et al.	Case-Control retrospective	Outpatients		12*	7.0		SJC 1.33 (1-3); TJC 1.5 (1-3); Mono33%, Oligo58%; Poly 8%	Not reported	UA-PsA had more mono-oligoarthritis and the disease is more localized and intermittent when compared to UA-RA. UA evolving to PsA showed more CD117+ mast cells and Hsp47+ lining synovial fibroblasts

NOS score 3

* Undifferentiated arthritis (UA) was defined as an inflammatory arthritis that does not fulfill criteria for a definite diagnosis.

Cuervo et al, Front Med (Lausanne). 2021 Apr 9;8:656667

Study (year)	Design	Source	Population (n=)	UA->PsA	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Exposito Perez et al. 2018 Presented as abstract EULAR 2018	Cohort study Retrospective	Oupatient	45*	4*	13.7	Not reported	3/4 patients showed a peripeheral pattern; ¼ mixex (peripheral + axial)	Not reported	Within PsA, one developed skin psoriasis, another psoriatic onicopathy at 4 years after debut and 2 continue with- out skin involvement but with a family history of psoriasis.

NQS score 3

* UA defined as undifferentiated B27 negative oligo-arthritis.

* The diagnosis was made according to CASPAR criteria

EULAR 2018 AB1147

Study (year)	Design	Source	Population (n=)	UA->PsA	Follow-up (years)	Prodromal features before PsA onset	Objective Signs or PsA phenotypes at PsA onset	Imaging features before or at PsA onset	Other outcomes
Paalanen et al. 2019	Cohort study Retrospective	OPD	435**	46	10	Not reported	Dactylitis in 24% Assymmetric oligoarthritis or spinal disease in 26%.	PsA onset: Juxta-articular new bone formation in 20%; Pencil in cup deformities in 5%	

NOS score 3

* Mixed population at baseline, exclusion during the follow-up of the cases typical for RA. High number of diagnosis evolving during the follow-up. The cohort is typical for baseline UA.

Clin Exp Rheumatol. 2019 Jan-Feb;37(1):37-43