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CLINICAL SCIENCE

EULAR points to consider for the definition of clinical and imaging features suspicious for progression from psoriasis to psoriatic arthritis

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ABSTRACT

Background The transition from psoriasis (PsO) to psoriatic arthritis (PsA) and the early diagnosis of PsA is of considerable scientific and clinical interest for the prevention and interception of PsA.

Objective To formulate EULAR points to consider (PtC) for the development of data-driven guidance and consensus for clinical trials and clinical practice in the field of prevention or interception of PsA and for clinical management of people with PsO at risk for PsA development.

Methods A multidisciplinary EULAR task force of 30 members from 13 European countries was established, and the EULAR standardised operating procedures for development for PtC were followed. Two systematic literature reviews were conducted to support the task force in formulating the PtC. Furthermore, the task force proposed nomenclature for the stages before PsA, through a nominal group process to be used in clinical trials.

Results Nomenclature for the stages preceding PsA onset, 5 overarching principles and 10 PtC were formulated. Nomenclature was proposed for three stages towards PsA development, namely people with PsO at higher risk of PsA, subclinical PsA and clinical PsA. The latter stage was defined as PsO and associated synovitis and it could be used as an outcome measure for clinical trials evaluating the transition from PsO to PsA. The overarching principles address the nature of PsA at its onset and underline the importance of collaboration of rheumatologists and dermatologists for strategies for prevention/interception of PsA. The 10 PtC highlight arthralgia and imaging abnormalities as key elements of subclinical PsA that can be used as potential short-term predictors of PsA development and useful items to design clinical trials for PsA interception. Traditional risk factors for PsA development (ie, PsO severity, obesity and nail involvement) may represent more long-term disease predictors and be less robust for short-term trials concerning the transition from PsO to PsA.

Conclusion These PtC are helpful to define the clinical and imaging features of people with PsO suspicious to progress to PsA. This information will be helpful for identification of those who could benefit from a therapeutic intervention to attenuate, delay or prevent PsA development.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Given that psoriasis (PsO) typically predates psoriatic arthritis (PsA) by a decade or more, then skin involvement offers the opportunity to investigate risk factors and predictors of PsA development and to study PsA preclinical phases.

WHAT THIS STUDY ADDS

⇒ Three distinct stages were relevant to the prevention of PsA: (a) people with PsO at higher risk of PsA; (b) subclinical PsA; (c) clinical PsA.

⇒ The presence of PsO and clinical synovitis not explained by other diagnoses was considered as diagnostic for new-onset PsA in the setting of clinical trials focusing on prevention and/or interception of PsA.

⇒ Five overarching principles and 10 points to consider were developed in order to cover the key areas for conducting clinical research in people with PsO at higher risk for PsA development.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study will facilitate research investigating the stages preceding clinical PsA and the opportunity to prevent PsA development by modifying lifestyle habits or using systemic treatment that could act both on the skin and the joint to prevent PsA development.

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INTRODUCTION

The clinical onset of inflammatory rheumatic musculoskeletal diseases, including rheumatoid arthritis (RA), is usually preceded by a preclinical phase encompassing immunological abnormalities, arthralgia and imaging abnormalities prior to formal diagnosis[1–4] The major advantage for healthcare professionals assessing the preclinical stage of RA is that many 'at-risk' individuals have well-defined autoantibodies that antedate symptoms. In addition, the formal recognition and diagnosis of early RA is well defined.[5] Indeed, such is the state of advancement of the RA field that experience in clinical prevention trials has already been gathered, with several conducted or in progress.[1] Psoriatic arthritis (PsA) affects up to a third of people with psoriasis (PsO) and, similarly to RA, there is emergent evidence on the occurrence of arthralgia and imaging abnormalities preceding the diagnosis of PsA.[6–10] However, data in this space are limited with the field being controversial with a lack of established serological markers and a standardised working definition for early phase PsA for PsA prevention studies.[11] A specific practical advantage of undertaking prevention trials for PsA, unlike RA, is that many patients would qualify for therapy aimed at controlling the existing cutaneous manifestations of their disease, thus avoiding both added costs and/or toxicity.[12–16] The environmental, genetic, clinical and immunological predictors for PsA development remain poorly understood, although such factors are crucial for standardised and cost-effective trials in PsA prevention. Recently, expert consensus emerged on strategies for setting up/conducting prevention trials in PsA, initially proposing the distinction of three clinically quiet stages preceding PsA onset (ie, preclinical PsA, subclinical PsA and prodromal PsA).[10] Subsequently, a Delphi exercise evaluating evidence pertaining to people with PsO at increased risk for PsA identified factors such as synovio-entheseal imaging abnormalities as well as musculoskeletal complaints not explained by other diagnoses occurring in people with PsO.[11] In contrast to RA, where revised classification criteria (American College of Rheumatology/EULAR 2010) allow for classification of patients with early disease,[5] this is not the case for PsA which thus hampers definitions of the evolution to early PsA as an outcome measure for prevention trials. Therefore, an unmet need exists to further explore and characterise the transition of PsO to PsA. To this extent, EULAR convened a task force with the goal of providing data-driven guidance and consensus for use in trials aimed at the prevention/interception of PsA and at the management of people with PsO at risk for PsA development.

METHODS

This study was conducted using the updated EULAR standardised operating procedures for developing points to consider (PtC)/recommendations.[17] After approval from the EULAR Council (March 2021), the convenor (DMG) and the co-convenor (JSS) formed the Steering Committee (SC) and set up a task force, inviting members representing 13 European countries. The SC included the convenors, one methodologist (LG) and one co-methodologist (XB), two fellows (AZ, GDM), two rheumatologists (AI, DA) and one dermatologist (PG). The task force comprised the SC members plus 21 additional researchers, including 14 rheumatologists (with two Emerging EULAR Network representatives and 7/14 rheumatologists were also experts of imaging in the field of PsA), 4 dermatologists, 2 patient research partners and 1 non-MD healthcare professional.

Due to COVID-19 pandemic restrictions, the task force meetings took place via virtual online platforms, with the first meeting in June 2021 and four subsequent online meetings between April and June 2022. At the time of the first meeting, the task force discussed the background and agreed on three key objectives:

1. To define the major features (ie, musculoskeletal symptoms and imaging features) of individuals transitioning from PsO to PsA.
2. To characterise the phenotype of people with PsO at risk for development of PsA.
3. To develop definitions of preclinical and *very early* PsA.

To address these objectives, the task force performed a systematic review of the literature (*see accompanying systematic literature reviews (SLR)*).

Table 1 Overarching principle and points to consider for the definition of clinical and imaging features suspicious for progression to PsA

2022 EULAR points to consider for the definition of clinical and imaging features suspicious for progression to PsA		
Overarching principle	**LoE**	**LoA**
A. People with PsO may develop PsA at different time-points.	n.a.	9.7 (± 0.7) 95.8% >8
B. Close collaboration between dermatologists and rheumatologists is important to understand and optimise PsA prevention, interception and early diagnosis.	n.a.	9.7 (± 0.6) 91.6% >8
C. The identification of risk factors for PsA development in people with PsO may influence therapy choices for PsO.	n.a.	8.9 (± 1.3) 75.0% >8
D. The rheumatologist has a key role in the diagnosis and management of PsA.	n.a.	9.7 (± 0.6) 91.6% >8
E. Certain systemic treatments of PsO may reduce the risk of transition to PsA.	n.a.	8.4 (± 1.8) 56.0% >8
Specific points to consider		
1. Arthralgia in people with PsO should be considered as a risk factor for PsA development, taking into account alternative diagnoses such as osteoarthritis and fibromyalgia.	3a	9.2 (± 1.3) 75.0% >8
2. In people with PsO, joint and entheseal pain and functional limitation should be enquired about regularly and, if present, referral to a rheumatologist should be considered.	3b	9.3 (± 0.9) 83.3% >8
3. Imaging (including ultrasound and MRI) in people with PsO could be used to help identify those at risk for PsA; in particular to detect synovio-entheseal involvement/abnormalities.	3b	9.1 (± 1.2) 75.0% >8
4. Imaging abnormalities in the absence of musculoskeletal symptoms should be considered carefully in order to avoid the risk of inappropriate treatment.*	3b	9.5 (± 0.9) 83.3% >8
5. The combination of musculoskeletal symptoms and imaging abnormalities in people with PsO, without a diagnosis of PsA, should be considered as an entry criterion for clinical trials to prevent the transition to PsA.	5	8.8 (± 1.2) 58.3% >8
6. In the context of clinical trials, people with PsO and clinically evident synovitis should be considered to have PsA, when alternative diagnoses have been excluded.	5	9.3 (± 0.8) 83.3% >8
7. In people with PsO who require systemic treatment, the risk of transition to PsA should be taken into account in the choice of treatment.	5	9.1 (± 1.3) 75.0% >8
8. People with PsO with obesity, nail disease and/or extensive PsO should be considered at increased risk for PsA development over the longer term.	3a	9.3 (± 0.9) 83.3% >8
9. People with PsO should be informed about the risk of developing PsA and prompted to report their symptoms to facilitate early PsA recognition.	5	9.5 (± 0.8) 83.3% >8
10. In people with PsO, risk factors for PsA development should be regularly assessed over time.	5	9.5 (± 0.8) 87.5% >8

*In the event that physicians incidentally perform musculoskeletal imaging (eg, ultrasound and MRI) in people with PsO without joint symptoms and the imaging is abnormal, then this in itself is not an impetus to consider therapy as such abnormalities are not uncommon in healthy individuals and consequently also PsO.[30 31 49] The task force agreed that musculoskeletal imaging should be performed in people with PsO without joint symptoms only in research setting and not in clinical practice.
LoA, level of agreement; LoE, level of evidence; n.a., not available; PsA, psoriatic arthritis; PsO, psoriasis.

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Table 2 Risk factors for PsA development

Risk factors for PsA development	
Medium to long term	**Short term**
Nail involvement	Arthralgia
Obesity	Subclinical imaging-determined disease (eg, sonographic entheseal changes)
Psoriasis severity	
Familial history of PsA*	

*'Mainly having a first-degree relative with PsA' citing points to consider 8.
PsA, psoriatic arthritis.

During the virtual meetings held in 2022, task force members appraised the evidence from the literature and then formulated the overarching principles (OAP), the PtC and the nomenclature for the stages preceding PsA onset, through a nominal group process. As per EULAR methodology, consensus was accepted in the first round of discussion if ≥75% of the members voted in favour of a statement, and in the second round if >two-thirds voted in favour. Within 1 month of the end of the virtual meetings, each member—online and anonymously—indicated their level of agreement (LoA) to each OAP or PtC statement using Research Electronic Data Capture (RedCap) (LoA, 0–10 numeric rating scale ranging from 0='completely disagree' to 10='completely agree'). The mean and SD of the LoA, alongside the percentage of members with an agreement ≥8, are presented. The level of evidence was defined based on the Oxford system.[18]

RESULTS

The task force developed and agreed on 5 OAP and 10 PtC (table 1). When formulating OAP, task force discussions focused on the involvement of dermatologists in at-risk population identification and recruitment, and the key role of rheumatologists in diagnosing PsA at early stage. Mirroring the scenario of early RA,[1] the members agreed that three distinct stages were relevant to the prevention of PsA. Namely, people with PsO at higher risk of PsA; subclinical PsA; and finally, the clinical PsA. Informed by the SLR, the task force also proposed a definition of PsA as an outcome measure for clinical trials in PsA prevention.

Proposed nomenclature for research trials in subjects with PsO at risk of PsA

People with PsO at higher risk of PsA

Although at least 70% of PsO cases do not develop PsA,[19 20] theoretically all people with PsO remain at risk due to the incomplete understanding of the immunogenetic and other factors linked to disease evolution (*see accompanying SLR*).[10 11 20 21]

Among risk factors, some are associated with a short-term risk and others with a risk in the medium term/long term (table 2). Risk factors, including nail disease, obesity and PsO severity, may be more associated with a risk of PsA in the medium-term/long-term period and these clinical features characterised the stage here defined as 'people with PsO at higher risk of PsA'. These risk factors are less relevant for trials that enrich for subjects 'at risk' of imminent PsA development, since their mere presence is not indicative of imminent PsA.

The familial predisposition, mainly having a first-degree relative with PsA, can also be considered a risk factor for PsA development.[22 23] Future studies on genetics[24] and prediction models for PsA development[25] may overcome the use of single risk factors and offer new clinical tools including different risk factors estimating the real risk of PsA development in people with PsO.

Due to the paucity of evidence available, it is not possible at present to provide any clear definition of the timings pertaining to 'short-term' or 'medium-term to long-term' risk of PsA onset. Limited evidence suggests an approximate cut-off of 2 years to define 'short-term risk of PsA onset'.[26]

Subclinical PsA

Joint symptomatology, mainly arthralgia and imaging abnormalities or their combination were considered for the definition of subclinical PsA and these, particularly when combined, can be considered as short-term risk factors for PsA development. The term subclinical refers to the absence of clinical arthritis, not to the absence of clinical symptoms as such. Therefore, similarly to RA, the presence of arthralgia in PsO is considered a subclinical sign of PsA, as it has been shown to be associated with increased risk of subsequent development of clinical PsA.[6 7 27] Furthermore, and again akin to the preclinical phases of RA, arthralgia (not specifically defined) in PsO has been associated with increased imaging detected synovitis and enthesitis.[7 27 28] In turn, these imaging features were linked to PsA development (*see accompanying SLR*).[7 27–29] Some task force members supported the view that arthralgia associated with imaging evidence of inflammation would be tantamount to the presence of actual PsA and would be inclined to treat such patients as PsA in the real-world setting.

However, isolated imaging abnormalities, that is, in absence of joint symptoms, were also associated with subsequent PsA development in some publications appraised by the task force.[28 29] Yet, given the high prevalence of imaging abnormalities, in the range of 40%–50% in people with complete asymptomatic PsO, but even in the healthy population,[8 30 31] it was considered that isolated imaging abnormalities can be considered a less strong predictor of imminent PsA development. Hence, the task force considered that the combination of arthralgia and imaging abnormalities were both part of the subclinical phase of PsA, representing a subset group at particularly high risk for PsA development in the short term (*see accompanying SLR*). Furthermore, the members considered that regression of arthralgia in people with PsO, coupled with resolution of subclinical joint inflammation, could be considered as a potential outcome measure for clinical trials representing surrogates for PsA interception.

Clinical PsA

For randomised controlled trials in PsA prevention, the development of clinical PsA or its prevention is an obvious outcome, so the task force suggested a definition for new-onset PsA to be used within the context of clinical trials focused on PsA prevention. Such definition is not intended for the clinical diagnosis of new-onset PsA in the standard real-world clinical setting. The limited data available (*see accompanying SLR*) describing people with PsO followed up longitudinally and until the clinical development of PsA illustrated that the majority of subjects presented with clinical synovitis (ie, the presence of swollen joints), with enthesitis, or axial disease being uncommon[6 7 32–34] in the early clinical stage. Therefore, the presence of PsO and clinical synovitis was considered the clinical hallmark of new-onset PsA. Since dactylitis is associated with both synovitis and tenosynovitis and is a characteristic feature of PsA it can be included in the joint swelling that is linked to PsA presentation.

Hence, the presence of PsO and clinical synovitis, including synovitis and swelling that accompanies dactylitis, not explained by other diagnoses was considered as diagnostic for new-onset PsA.

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The limited data suggested a mean low swollen joint count (ranged from 1.5 to 3.2) at diagnosis, which could be used as an outcome measure for the trials on prevention or interception of PsA.[6 7 21 33 34] Furthermore, this could also provide a starting point for studies of therapy initiation in the earliest phases of PsA. It is important to underscore that the task force members recognised that the definition proposed may occasionally miss instances of purely enthesitic presentation of PsA, or that it would not capture isolated axial disease development/evolution. However, these recognisable clinical patterns of presentations are uncommon at this stage of the disease.

The task force acknowledged that synovitis, once diagnosed, could be transient, but for a trial for prevention new unexplained synovitis could represent an end point. The usual cut-off for chronicity in RA is 6 weeks of synovitis duration.[5 35] Once other possible causes of synovitis in people with PsO are excluded, acute onset of arthritis (ie, usually defined as a sudden onset of mono-oligoarthritis) should be considered as possible PsA. Indeed, after triggering infections or after an acute musculoskeletal injury PsA can present as an acute onset of mono-oligoarthritis or oligoarthritis.[15 36] This led the task force to not specify a minimum duration of synovitis and leave the differential diagnosis of a new-onset synovitis to the clinical expertise of rheumatologists.

Overarching principles

People with PsO may develop PsA at different time-points

This principle emphasises that arthritis usually develops in a setting of an established diagnosis of PsO, in approximately 70% of cases.[19 20] Some individuals may develop PsO or have a diagnosis of PsO (particularly in the case of minimal skin involvement) at the time of, or subsequent to, PsA clinical onset.

When rheumatological manifestations antedate the onset of the cutaneous lesions, often in combination with family history of PsO, such patients tend to be diagnosed as PsA 'sine psoriasis'.[37] Furthermore, the task force members highlighted that, at the time of onset of PsA, arthritis severity may range from mild to severe disease, or it can change over time, and different therapeutic approaches may be needed.

Close collaboration between dermatologists and rheumatologists is important to understand and optimise PsA prevention, interception and early diagnosis

Since PsO precedes PsA in about 70% of cases and it represents an easily identifiable clinical biomarker on clinical examination, there is a potentially identifiable at-risk pool of people that could benefit from prevention, interception of PsA and/or from an early diagnosis of PsA.[12 38]

The task force agreed that prevention and interception are not interchangeable terms, since the former should be applied to people with PsO with risk factors for PsA (eg, severe skin involvement, nail involvement, obesity) but no features or symptoms of PsA, while the latter to subclinical PsA or new-onset PsA.

In this scenario, this OAP highlights the importance of close collaboration between dermatologists and rheumatologists, in clinical and research settings, aimed at improving knowledge of the transition from PsO to PsA and timely referral of new-onset PsA cases.

The early diagnosis of PsA is an important cornerstone in the management of PsA, since even a diagnostic delay as short as 6 months can lead to significantly more severe radiographic joint damage, worse physical function and decrease the changes of therapeutic success.[39 40]

Therefore, developing the concept of transition from PsO to PsA, early PsA detection and management within the dermatology clinic should be prioritised, in order to improve the clinical outcomes of patients and facilitate early combined intervention in cooperation with rheumatologists.[13] Furthermore, a substantial number of people with limited PsO (ie, not requiring systemic therapy in dermatology settings) remain under the care of their primary care practitioners, suggesting the importance of involving general practitioners (GPs) in the diagnostic pathways for the early referral of people with PsO affected by musculoskeletal symptoms.

The identification of risk factors for PsA development in people with PsO may influence therapy choices for PsO

Research in the field of the transition from PsO to PsA is rapidly evolving, but we are still unable to precisely identify people with PsO who ultimately develop PsA. The presence of defined risk factors for PsA development or the presence of subclinical arthritis could influence therapy for PsO in real-world settings, for example, a higher risk for PsA may modify the PsO treatment choice towards a compound that has proven efficacy in skin PsO and PsA. This OAP is particularly relevant to real-world dermatological practice where physician suspects the early stages of PsA but is keen to rapidly initiate therapy for PsO without further investigations.

Certain systemic treatments of PsO may reduce the risk of transition to PsA

Preliminary evidence, although from retrospective cohorts, suggests that PsO without defined risk factors for PsA that are treated with biological agents had a significantly lower risk of PsA development compared with those treated with phototherapy,[33] topical/no treatment[41] or no biological treatment.[42] In contrast, Meer *et al*,[43] using a retrospective electronic health record database, found a higher incidence of PsA among individuals treated with biologics for PsO than people on oral or phototherapy. However, the results of this last study appear inconsistent with clinical experience and may be biased by 'confounding by indication' and 'protopathic bias'.[12] Longitudinal prospective studies are needed to establish the potential impact of therapies given for the skin or nail in attenuating, delaying or intercepting PsA. In this scenario of PsA prevention and interception, the task force members emphasised the importance of close collaboration between dermatologists and rheumatologists at the time of subclinical PsA stage, to facilitate the early recognition of clinical PsA or to evaluate a potential musculoskeletal domain response in people with PsO that started systemic therapy for the skin/nail domains.

The rheumatologist has a key role in the diagnosis and management of PsA

In its simplest and the most common form, PsA is clinically recognised by clinical synovitis occurring in an individual affected by PsO. Nevertheless, PsA may present—or clinically evolve—in heterogeneous ways, affecting other musculoskeletal domains, simultaneously or not. Moreover, mimics of PsA (eg, osteoarthritis, fibromyalgia, gout) could complicate the diagnostic process.[44–47] In the absence of serum biomarkers, the diagnosis of PsA ultimately relies on the rheumatologists' clinical expertise that might entail a combination of clinical and imaging findings *(see accompanying SLR)*.

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Points to consider

PtC 1: arthralgia in people with PsO should be considered as a risk factor for PsA development, taking into account alternative diagnoses such as osteoarthritis and fibromyalgia

Arthralgia of otherwise unexplained origin should be considered the hallmark symptom preceding the onset of clinical PsA, and a risk factor for development of PsA in the short term.[6 7 27] The incidence rate of PsA development in people with PsO with arthralgia is significantly higher compared with PsO without such symptom, ranging from 10.9[7] to 34.3[27] per 100 patient-years.[26] However, any precise definition of arthralgia specifically predictive of progression to PsA is still lacking. The characterisation of arthralgia in terms of type of pain (eg, non-specific musculoskeletal pain vs inflammatory pain), sites involved (eg, Achilles tendon) and duration of symptoms will certainly be a matter of future studies focussing on the field of transition from PsO to PsA.

Fibromyalgia and osteoarthritis are relevant PsA mimickers, particularly at the early stages of PsA, when signs of articular inflammation are less easily detectable by clinicians.[44 46]

PtC 2: in people with PsO, joint and entheseal pain and functional limitation should be enquired about regularly and, if present, referral to a rheumatologist should be considered

This is the only PtC for which task force members needed a second round of voting. The members agreed that these three key clinical elements (ie, joint and entheseal pain and functional limitation) summarise the clinical musculoskeletal symptoms before PsA onset in people with PsO, nevertheless the evidence from SLRs was limited *(see accompanying SLR)*.

In prospective studies, people with PsO who later developed PsA had significantly higher baseline pain scores,[6 7 27] Health Assessment Questionnaire (HAQ) and joint tenderness.[7 27] Eder *et al*[6] reported that arthralgia-affecting women, morning joint and spine stiffness, fatigue and impaired physical function were associated with the development of PsA in PsO. The authors also observed that the intensity and number of musculoskeletal symptoms increased in the period prior to the diagnosis of PsA.

Furthermore, Green *et al*[48] reported that over one-fifth of the subjects ith PsO who went on to develop PsA consulted their GPs 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 of PsA. In this scenario, task force members felt it was appropriate to underline the important role of dermatologists, GPs and people with PsO themselves in monitoring the onset, severity and evolution of musculoskeletal symptoms—in particular joint and entheseal pain, especially if associated with functional limitation—in order to facilitate early referral to rheumatology.

PtC 3: imaging (including ultrasound and MRI) in people with PsO could be used to help identify those at risk of PsA; in particular to detect synovio-entheseal involvement/abnormality

Imaging may be more sensitive than clinical examination for the detection of musculoskeletal inflammation.[30] Up to 40% of people with PsO, even if not affected by joint pain, show subclinical synovio-entheseal inflammation on imaging.[31 49] The role of subclinical inflammation detected by imaging as a predictor of later PsA development is a matter of ongoing research, mainly investigating peripheral involvement. Notably, the lack of bespoke studies in axial disease represents an unmet research need.[50] Imaging-determined subclinical entheseal involvement seems to be a promising predictive tool, however, contradictory results are reported for subclinical synovitis and tenosynovitis *(see accompanying SLR)*.

Subclinical enthesitis detected by ultrasonography and structural entheseal lesions detected by high-resolution peripheral quantitative CT seem to be a predictor of PsA development in a few recently published studies.[7 28 29] Overall, the evidence for the use of imaging to predict PsA development is limited, and further studies are needed to identify the best imaging predictors and potential 'sentinel sites' where imaging should better be performed. The task force concluded that this PtC should be applied only to research settings and not to the clinical management of people with PsO.

PtC 4: imaging abnormalities in the absence of musculoskeletal symptoms should be considered carefully in order to avoid the risk of inappropriate treatment

The detection of subclinical synovio-entheseal inflammation[8 31 49] in people with PsO is a common finding, even in patients without musculoskeletal complaints. The task force felt it was appropriate to underline that the identification, co-incidental or in a research setting, of subclinical musculoskeletal inflammation and/or damage needs to be interpreted carefully within the specific clinical context. Clinical examination and the symptoms reported by patients remain the cornerstones of PsA diagnosis and imaging remains an aid to the clinical diagnosis. Recently, interleukin (IL)-12/IL-23 inhibition for skin involvement demonstrated suppression of subclinical enthesopathy in people with PsO without clinical arthritis.[14] This study lays the foundation for further research studies on PsA interception and supports the hypothesis that inducing regression of subclinical enthesopathy with biological agents prescribed for skin involvement, and efficacious in joint disease, could modify the expression of subclinical enthesopathy that may be a very early feature of PsA.[14 16 51] Subclinical findings detected by imaging can be present in the subclinical PsA phase but there is no evidence that this should favour specific therapeutic choices in the management of people with PsO without musculoskeletal symptoms or be sufficient for the diagnosis of PsA.

PtC 5: the combination of musculoskeletal symptoms and imaging abnormalities in people with PsO without a diagnosis of PsA should be considered as an entry criterion for clinical trials to prevent the transition to PsA

The combination of musculoskeletal symptoms and imaging abnormalities emerged as predictor of PsA development in people with PsO.[27 28] Among musculoskeletal symptoms, arthralgia was the symptom most frequently reported in the literature and most often associated with later PsA development.[7 27] As for the discussion in PtC 1, the clear identification of musculoskeletal features and imaging findings preceding PsA development are key topics for a research agenda. The combination of clinical symptoms and subclinical imaging abnormalities could improve the characterisation of the subclinical PsA phase, allowing the identification of homogeneous cohorts of people with PsO at very high risk for PsA transition that could facilitate trials of PsA interception. To summarise, while subclinical PsA was defined as either arthralgia or imaging abnormalities, it was felt that the combination of these was most suitable for PsA prevention trials.

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PtC 6: in the context of clinical trials, people with PsO and clinically evident synovitis should be considered to have PsA, when alternative diagnoses are excluded

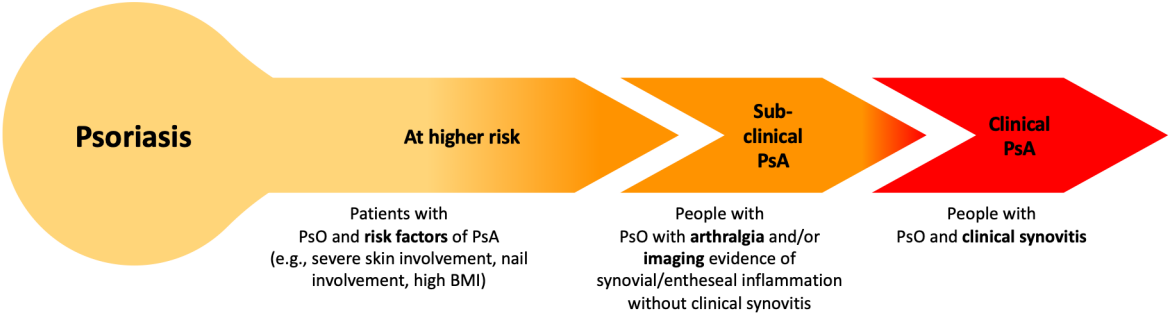
The prevention, or interception, of PsA development in people with PsO and the early recognition of PsA development are key topics in the research agenda.[52] When investigating subclinical and newly diagnosed PsA, an attempt to define the clinical aspect of new-onset PsA is crucial, since it is one of the outcomes of interest in clinical trials for prevention or interception of PsA development. The absence of serum biomarkers and the limited value of C reactive protein make the clinical examination as the cornerstone for the identification of new-onset PsA. The SLR performed as part of this EULAR activity provided evidence that peripheral arthritis, mainly in form of oligoarthritis *(see accompanying SLR)*, is the main pattern of presentation in individuals with new-onset PsA. Such findings led to the choice of the clinical evidence of synovitis, not explained by other possible diagnoses like gout, osteoarthritis, as the most likely specific clinical sign of new-onset PsA. In the literature, isolated enthesitis or isolated axial symptoms are uncommon patterns of PsA onset[7 21 33 34] and are currently difficult to clearly define, even with current advanced imaging methods. Accordingly, emphasis on clinical joint swelling, which is a simple and robust measure of articular inflammation, was agreed on.

PtC 7: in people with PsO that require systemic treatment, the risk of transition to PsA should be taken into account in the choice of treatment

The severity of PsO involvement is one of the main risk factors for PsA development in people with PsO[10 11 26 53] and recently three retrospective studies[33 41 42] reported that systemic treatment, mainly biologics, prescribed to ameliorate skin severity of PsO, may reduce the occurrence of PsA in people with PsO. On the contrary, Meer *et al*[43] reported that use of biological agents in PsO was actually associated with subsequent PsA development and not prevention. Recently, in a retrospective cohort of patients with PsO, Singla *et al*[54] identified that treatment with IL-23 inhibitors was associated with reduced risk of progression to PsA compared with tumor necrosis factor inhibitors. In the transition from PsO to PsA, retrospective studies should be considered as hypotheses-generating. The existing findings need to be validated in prospective randomised controlled trials.[55] In the absence of definitive data on the role of systemic treatment for PsO in prevention, mitigation or delay of PsA onset, the task force members agreed that in people with PsO requiring systemic treatment for their skin or nail involvement, the presence of risk factors for PsA development should favour the use of treatment that could ameliorate both skin and joint manifestations, particularly in the case of subclinical PsA.

PtC 8: people with PsO with obesity, nail disease and/or extensive psoriasis should be considered at increased risk for PsA development over the longer term

The risk factors for PsA development could be categorised into those linked to subclinical PsA (ie, imaging and arthralgia) and those usually not necessarily linked to subclinical PsA (ie, nail involvement, high Psoriasis Area Severity Index score, obesity) (figure 1). As expected, the former predict increased PsA development in the short-term period (usually within 2 years), while the latter are considered traditional risk factors for PsA development in people with PsO in the long-term, that is, with an average time between the onset of PsO and arthritis of 8–12 years.[56] Task force members agreed that among traditional risk factors for PsA development obesity, nail involvement and extensive PsO are



Nomenclature for research and prevention/interception trials in people with PsO at risk of PsA	
Phase	*Definition*
A. At higher risk	People with PsO at higher risk of PsA (i.e., severe skin involvement, nail involvement, obesity, familial history) of PsA.*
B. Sub-clinical	People with PsO with arthralgia and/or imaging evidence of synovial/entheseal inflammation without clinical synovitis
C. Clinical	People with PsO and clinical synovitis

Figure 1 Proposed nomenclature for the transition from PsO to PsA for clinical trials of PsA prevention. A simple three-stage scheme for progression from at risk of PsA to frank PsA. It is acknowledged that onset may be variable and could occur quickly in some subjects, for example, after trauma or following infection with a reactive arthritis type onset. Although arrows imply directionality and inevitable progression, it is acknowledged that some subjects may have spontaneous resolution of PsA and that subjects with arthralgia may regress and that strategies in at-risk people, for example, weight loss in obesity may lead to reduction of risk. This scheme recognises the importance of enthesitis in pathophysiology but for trials of interception suggest the use of synovitis development as an outcome measure since this was by far the most common manifestation of early disease from the accompanying systematic literature reviews. *Role of immunogenetics awaits definition. BMI, body mass index; PsA, psoriatic arthritis; PsO, psoriasis.

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those with the strongest evidence and people with PsO with at least one of these factors should be considered at higher risk.

PtC 9: people with PsO should be informed about the risk of developing PsA and prompted to report their symptoms to facilitate early PsA recognition

The lifetime risk of PsA development in people with PsO is up to 30% and the chance of achieving remission of PsA symptoms appears to have a significant negative association with a diagnostic delay of >1 year, and a significant positive association with an early rheumatologist referral of <6 months.[39 40] People with PsO should be informed by dermatologists and primary care practitioners about this risk and about the importance of an early referral to rheumatologists when musculoskeletal symptoms develop. The education of people with PsO regarding their risk of PsA and symptoms and signs suspicious for PsA is a cornerstone for early PsA diagnosis.

PtC 10: in people with PsO, risk factors for PsA development should be regularly assessed over time

Recognising and assessing risk factors can favour PsA prevention, since a modification of these may alter the progression from PsO to PsA or the severity of the PsA presentation. Recently, Green *et al* reported on the association between reducing body mass index (BMI) and reduction in the risk of developing PsA over a 10-year period.[57] As discussed in the previous PtC, systemic treatment for nail involvement and severe PsO could reduce the risk of PsA development but there is no current clear evidence that a treat-to-remission strategy for PsO is superior to other strategies in reducing the risk of PsA development. Regarding short-term risk factors for PsA development, the onset of a musculoskeletal complaint should be assessed regularly (ideally every 6–12 months) in order to facilitate an early PsA diagnosis. Outside research studies, there is no evidence for the role of imaging to stratify the risk of PsA development among people with PsO.

DISCUSSION

The EULAR task force evaluated PtC for the definition of clinical and imaging features suspicious for progression to PsA, proposed nomenclature for the stages before PsA onset and a definition for early PsA as an outcome measure to be used in clinical trials aimed at PsA prevention. Unlike RA prevention, data on the transition phase from PsO to PsA are scarce. The task force agreed that people with PsO at higher risk for PsA should be defined for research purposes when predictors for PsA (eg, nail involvement) are present; subclinical PsA when people with PsO have arthralgia or imaging evidence of synovio-entheseal complex inflammation, or ideally both. Finally, clinical PsA is diagnosed when synovitis is present at the clinical examination. This proposed nomenclature reflects a temporal, although non-linear continuum of psoriatic disease: (a) the 'at higher risk' stage typically lasts on average 7–12 years before the PsA onset, (b) the 'subclinical stage', including imaging features typically linked to more imminent progression to PsA (1–3 years) and (c) the 'clinical' stage defined by the presence of clinical synovitis in an individual with PsO that has been longitudinally evaluated for synovitis, which is tantamount to early PsA (figure 1).

This nomenclature could be relevant for studies looking at PsA prevention or interception with two potential new outcomes in the field of transition: (i) the regression of joint symptoms and imaging features in people with PsO with subclinical PsA and (ii) reduction of new clinical PsA cases. In RA, the identification of early (<12 months) or very early (<3 months) disease is important, since this classification is linked to different chances of achieving remission.[58–61] Starting a conventional disease-modifying antirheumatic drug at early stages improves the rate of remission and drug-free remission. Preliminary data seem to confirm this point also in PsA.[39 40] The definition of early PsA is recognised by the task force as an important unmet need both for research studies and clinical practice but the definition of this term was considered beyond this Task Force's remit.

The 5 OAPs and 10 PtC set out a broad framework, covering the key areas for conducting clinical research in people with PsO at higher risk for PsA development and with subclinical PsA. This task force emphasises the essential role of collaboration between rheumatologists and dermatologists to achieve the goals of prevention and early diagnosis of PsA. Furthermore, these PtC provide to the dermatological community important insights that could inform clinical practice. The importance of regularly assessing risk factors, including musculoskeletal complaints or functional limitation, are key points for early PsA diagnosis, as well as the need to inform people with PsO about their risk of developing PsA, highlighting the importance of promptly reporting musculoskeletal symptoms.

The main limitation of these results lays in the limited evidence from prospective studies in the field of transition from PsO to PsA. This is not surprising, since the incidence rate of PsA development in people with PsO ranges from 0.3 to 3 events per 100 patient-years.[10 20 26 53 62] Therefore, prospective studies with many patients followed with a long follow-up (ie, >5 years) in unselected cases would be required. In the future, prospective studies[55] will be necessary to refine and update of these EULAR PtC and the comprehensive involvement of other specialists (eg, dermatologists, radiologists, dieticians) will require to produce new strategy of prevention and interception of PsA.

In conclusion, these PtCs will facilitate research investigating the stages preceding clinical PsA and the opportunity to prevent PsA development by modifying lifestyle habits or using systemic treatment that could act both on the skin and the joint to prevent PsA development. These findings set the scene for both PsA as an outcome in prevention studies and the regression of arthralgia and imaging abnormalities as bespoke strategy relevant to PsA cases, many of whom require chronic therapy for cutaneous PsO.

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