Difficult-to-treat psoriatic arthritis (D2T PsA): a scoping literature review informing a GRAPPA research project

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ABSTRACT
Background Psoriatic arthritis (PsA) is a multifaceted condition with a broad spectrum of manifestations and a range of associated comorbidities. A notable segment of patients with PsA remains resistant to even advanced therapeutic interventions. This resistance stems from myriad causes, including inflammatory and non-inflammatory factors.

Objectives To collate and critically assess the various definitions and criteria of difficult-to-treat (D2T) PsA present in the literature.

Methods Using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines, we conducted a scoping review in July 2023, searching PubMed, American College of Rheumatology Convergence 2022, European Alliance of Associations for Rheumatology Congress 2023, Google Scholar and cited articles. Selection was made by two independent authors using Rayyan software, and conflicts were adjudicated by a third author. Eligibility criteria for PubMed focused on all article designs that were written in English, with full-text available, from the past decade, excluding only those not defining D2T PsA or targeting other populations.

Results From the 565 references sourced, 15 studies were analysed, revealing considerable variations in defining both ‘active disease’ and ‘resistant PsA’, which was most often termed ‘D2T’ PsA.

Conclusion The definitions and criteria for D2T PsA and for ‘active disease’ are notably heterogeneous, with considerable variation across sources. The ongoing Group for Research and Assessment of Psoriasis and Psoriatic Arthritis initiative stands to bridge these definitional gaps and aims to provide guidance for clinicians and illuminate a path for pharmaceuticals and regulatory agencies to follow.

INTRODUCTION
Psoriatic arthritis (PsA) is an immune-mediated disease with a heterogeneous presentation. It typically presents with a broad spectrum of clinical phenotypes, including peripheral arthritis, axial disease, dactylitis, enthesitis, and skin and nail involvement. Several manifestations are subsumed as associated conditions due to their increased prevalence in the PsA population, such as uveitis, Crohn’s disease, ulcerative colitis and subclinical colitis. In addition, several comorbidities are known to coexist with PsA, including obesity, type 2 diabetes, hypertension, metabolic syndrome, fatty liver disease, cardiovascular diseases and fibromyalgia.

PsA is also associated with a number of psychosocial conditions, including sleep disorders, anxiety, depression and mood/behavioural changes, negative body image and reduced work productivity. In a study conducted by Coates et al., 69% of patients with PsA reported that the disease had a significant impact on their emotional and mental well-being, 56% reported effects on
romantic relationships and intimacy and 44% indicated an impact on relationships with family and friends.

Over the years, treatment options for patients with PsA have evolved, expanding from non-steroidal anti-inflammatory drugs, glucocorticoids, conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) to biological DMARDs (bDMARDs) and targeted synthetic DMARDs (tsDMARDs). This evolution has provided clinicians with a growing armamentarium to manage this multifaceted disease.6 Despite the availability of these treatment options and their proven benefits of achieving remission, less than 50% of patients achieve an American College of Rheumatology (ACR) 50 response and typically fewer than 40% achieve a state of minimal disease activity (MDA) on consecutive visits.7–9 Furthermore, up to 40% may experience only a partial response or fail to respond at all to DMARD therapies altogether.10

Several factors may contribute to this inadequate response (IR). Clinical trials often focus on persistent inflammatory activity, which would be referred to as difficult-to-treat (D2T) PsA. However, factors other than inflammation are the reason for treatment failure in numerous patients, creating a complex, multifaceted landscape of challenges. These include failure due to the presence of pre-existing conditions (eg, nociceplastic pain secondary to fibromyalgia), complications related to immunotherapy (eg, side effects and opportunistic infections), non-adherence to therapy, limited access to healthcare, discrepancies between patient-reported outcomes (PROs) and physician assessments of remission rates, among multiple others.11,12

Given the complexities outlined above, it is paramount to recognise the specific reasons for failure to achieve remission and to clearly delineate subsets within the PsA population. Notably, this challenge is not unique to PsA. The broader field of rheumatology is grappling with similar issues in other diseases. The European Alliance of Associations for Rheumatology (EULAR) has established clear criteria to define D2T rheumatoid arthritis (RA),15 and the Assessment of Spondyloarthritis international Society (ASAS) is spearheading a project focused on defining D2T axial spondyloarthritis.16 Meanwhile, in the field of PsA, the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) has taken the initiative to establish these comprehensive definitions.

In its pursuit to define D2T PsA, GRAPPA’s pivotal project is laying the groundwork with this review, which is the first step in a three-tiered approach. The subsequent phase will capture real-world perspectives through surveys targeting both healthcare professionals (HCPs) and patients, highlighting the importance of patient viewpoints and perspectives. Building on this foundational knowledge, the initiative will culminate in a Delphi exercise that will synthesise all the data gathered to formulate a data-driven and expert-supported definition. The overarching goal is to clarify what constitutes the failure in achieving those pre-defined treatment targets. In doing so, this initiative aims to address this prevailing unmet need in PsA and thereby aiding clinicians and researchers in the field.

METHODS

In July 2023, two independent investigators (AR, SS) conducted a scoping review according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines.15 The objective was to compile and analyse articles defining ‘D2T’ PsA. The primary search was conducted using PubMed, with specific criteria detailed in online supplemental table S1.

Eligibility for inclusion consisted of full-text articles written in English within the last 10 years. The only exclusion criteria were articles that either failed to define ‘D2T’ PsA or focused on other populations, such as patients with psoriasis.

To expand the scope of the search, both investigators independently searched abstracts from the most recent major international rheumatological conferences held in the past year, specifically ACR Convergence 2022 and EULAR Congress 2023, using the Web of Science. Thereafter, a final search was conducted manually using PubMed, Google Scholar and the citations from the included articles. The terms used for these additional searches were similar to those used in the initial PubMed search.

Articles were selected through a hierarchical screening process conducted by AR and SS using the Rayyan Qatar Computing Research Institute software (https://www.rayyan.ai). Disagreements in article selection were adjudicated by a third investigator (FP).

Data were systematically extracted to highlight key characteristics of the studies, including their definitions of treatment failure, criteria for active disease and the specific terminology used for D2T PsA. The subsequent analysis was primarily descriptive in nature and aimed to synthesise the different definitions and criteria used across studies.

RESULTS

The initial PubMed search yielded 542 references. After applying predetermined filters and discarding duplicates, 395 abstracts were excluded, leaving 147 records for screening. Subsequently, 42 of these records were selected for a comprehensive full-text review, resulting in eight articles that met our inclusion criteria and that were therefore incorporated into the final review. In addition to the PubMed search, we assessed 11 abstracts from EULAR 2023, of which 4 were included and 9 abstracts from ACR 2022, none of which met our inclusion criteria. The manual search yielded an additional 3 articles, while the citation search produced no additional entries. Ultimately, a total of 15 articles were included in the final review. The complete flowchart detailing the study selection process is summarised in figure 1.
The characteristics of the studies are summarised in Table 1. Of note, most studies were conducted between 2020 and 2023 and encompassed a variety of methodologies, ranging from case reports to randomised controlled trials (RCTs). Specifically, our review covered eight retrospective cohort studies, four RCTs, two review articles and a single case report.

Definitions for both ‘active disease’ and ‘D2T’ PsA were highly variable across the studies and are summarised in Figures 2 and 3. The criteria for D2T were diverse; in some cases, it was vaguely described as multiple treatment attempts,11 16 while in others, it spanned from resistance to ≥1 tumour necrosis factor inhibitors (TNFi)9 17–22 or even extending to ≥2 bi/tsDMARDs23–25 or even ≥3 b/tsDMARDs.26 27 Only one study included patients with prior corticosteroid use as part of the definition of D2T.20 The review by Lubrano et al11 was distinct, being the only study that proposed dividing into refractory disease secondary to persistent inflammation (‘refractory to treatment’ PsA) and non-remission due to pre-existing comorbidities (‘D2T’ PsA).11

In terms of nomenclature, the reviewed studies employed a variety of terms for cases with an inadequate treatment response. The term ‘D2T’ emerged as the most prevalent (n=8), followed by ‘refractory PsA’ (n=5). The criteria for active disease were diverse as well. It spanned from number of swollen and painful joints combined with skin disease activity to more holistic definitions encompassing composite outcome measures. Of note, Perrotta et al25 and Kumthekar et al26 proposed detailed lists of signs signalling active or progressive disease, encompassing metrics from composite measures to perceived decline in quality of life attributed to PsA.25 26

On detailed examination of the RCTs, a common criterion emerged.17–19 28 All deemed patients to have active disease if they displayed three or more swollen and tender joints, complemented by evident skin disease. When it came to defining D2T PsA, most RCTs centred on the patient’s past response to TNFi, particularly highlighting those with either an IR or an intolerance to TNFi. It is noteworthy that only one RCT considered csDMARDs resistance when defining D2T PsA.17

The eight retrospective cohort studies demonstrated varying inclusion criteria based on drug resistance. Specifically, four studies emphasised patients who had previously been on a regimen involving at least 2 TNFi, often combined with other medications like csDMARDs. The criteria for active disease in these studies primarily hinged on established scoring methods, such as Disease Activity in Psoriatic Arthritis (DAPSA), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), The Clinical Disease Activity Index (CDAI), Routine Assessment
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Study type</th>
<th>Definition of treatment failure</th>
<th>Definition of active disease</th>
<th>Term in text</th>
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<tbody>
<tr>
<td>Nash et al</td>
<td>2017</td>
<td>RCT</td>
<td>≥1 csDMARD+1 or 2 TNFi failure and/or intolerance</td>
<td>≥3/68 tender and ≥3/66 swollen joint counts and active psoriatic skin lesion</td>
<td>TNFi inadequate response and/or intolerance</td>
</tr>
<tr>
<td>Gladman et al</td>
<td>2017</td>
<td>RCT</td>
<td>≥1 TNFi or other (non-TNFi) bDMARD</td>
<td>Active plaque psoriasis and ≥3/68 tender and ≥3/66 swollen joint counts</td>
<td>D2T PsA</td>
</tr>
<tr>
<td>Kirkham et al</td>
<td>2020</td>
<td>RCT</td>
<td>Inadequate response to 1 or 2 TNFi</td>
<td>≥3/68 tender and ≥3/66 swollen joint counts and active psoriatic skin lesion or a documented history of plaque psoriasis</td>
<td>TNFi inadequate response</td>
</tr>
<tr>
<td>Merola et al</td>
<td>2023</td>
<td>RCT</td>
<td>Inadequate response or intolerance to 1 or 2 TNFi</td>
<td>≥3 TJC and ≥3 SJC and one psoriatic lesion or history of psoriasis or both psoriatic lesion</td>
<td>TNFi inadequate response and/or intolerance</td>
</tr>
<tr>
<td>Cincinelli et al</td>
<td>2023</td>
<td>Retrospective</td>
<td>csDMARD+≥2 b/tsDMARDs with different MoA</td>
<td>Presence of three criteria: (1) failure of ≥2 b/tsDMARDs (with different MoA) after failing csDMARD therapy; (2) signs suggestive of active/progressive disease (defined either as a DAPSA&gt;14 or not achieving MDA; signs or symptoms suggestive of active disease; a rapid radiographic progression; a reduction of quality of life due to PsA symptoms); (3) disease management perceived as problematic by rheumatologists or patients (all three criteria must be met to define D2T patients)</td>
<td>D2T PsA</td>
</tr>
<tr>
<td>Galíndez-Agirregoikoa et al</td>
<td>2023</td>
<td>Retrospective</td>
<td>Prior corticosteroid (71.3%) + csDMARD/apremilast (mean; 1.8±0.9) + ≥1 bDMARD (3.4±2.2)</td>
<td>Did not achieve low disease activity or remission by DAS28 or DAPSA</td>
<td>Refractory PsA</td>
</tr>
<tr>
<td>Philippoteaux et al</td>
<td>2023</td>
<td>Retrospective</td>
<td>≥3 b/tsDMARDs with different MoA</td>
<td>Persistence of disease activity by BASDAI</td>
<td>D2T PsA</td>
</tr>
<tr>
<td>Braña-Abascal et al</td>
<td>2023</td>
<td>Retrospective</td>
<td>≥2 bDMARDs and/or tsDMARDs (present in 90% of patients)</td>
<td>Not available</td>
<td>Refractory PsA</td>
</tr>
<tr>
<td>Tillet et al</td>
<td>2023</td>
<td>Retrospective</td>
<td>Prior bDMARD, with 2/3 receiving ≥2 bDMARD≥csDMARD</td>
<td>High CDAI and RAPID3</td>
<td>D2T PsA</td>
</tr>
<tr>
<td>Elgaard et al</td>
<td>2023</td>
<td>Retrospective</td>
<td>Prior methotrexate +≥1 bDMARDs</td>
<td>Disease activity with joint swelling and/or disease progression on X-ray or MRI</td>
<td>D2T PsA</td>
</tr>
<tr>
<td>Perrotta et al</td>
<td>2022</td>
<td>Retrospective</td>
<td>Treatment according to EULAR recommendation and/or GRAPPA recommendations and failure of ≥2 b/ tsDMARDs (with different MoA) after failing csDMARD therapy (unless contraindicated)</td>
<td>Signs suggestive of active/progressive disease, defined as ≥1 of: (1) at least moderate disease activity (according to validated composite measures including joint counts, eg, DAPSA&gt;14 or not achieving the MDA criteria); (2) signs (including acute phase reactants and imaging) and/or symptoms suggestive of active disease (joint related or other); (3) rapid radiographic progression (with or without signs of active disease); (4) well-controlled disease according to above standards, but still having PsA symptoms that are causing a reduction in quality of life.</td>
<td>D2T PsA</td>
</tr>
<tr>
<td>Galíndez-Agirregoikoa et al</td>
<td>2021</td>
<td>Retrospective</td>
<td>≥1 bDMARD or csDMARD+apremilast</td>
<td>Not achieve clinical low disease activity or remission despite the use of bDMARDs or apremilast (DAS28 ESR or DAPSA)</td>
<td>Refractory PsA</td>
</tr>
<tr>
<td>Costa et al</td>
<td>2014</td>
<td>Case report</td>
<td>PsA refractory to csDMARDs and bDMARDs (in this case, 3 TNFi)</td>
<td>High scores of TJC, SJC, PASI, HAQ, VAS, ESR, CRP</td>
<td>Refractory PsA</td>
</tr>
<tr>
<td>Author</td>
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<td>Kumthekar et al</td>
<td>2023</td>
<td>Review</td>
<td>Treatment according to internationally accepted recommendations (such as ACR-NPF, GRAPPA, or EULAR) and failure of ≥3 b/tsDMARDs (with different MoA) after failing csDMARD therapy (unless contraindicated) + fulfilling one of the following: the signs and/or symptoms are perceived as problematic by the rheumatologist and/or the patient even in the absence of active disease as described on the left OR presence of signs suggestive of active/progressive disease</td>
<td>Signs suggestive of active/progressive disease are defined as ≥one of the following: (1) at least moderate disease activity (DAPSA&gt;14 or PASDAS&gt;3.2); (2) signs and symptoms suggestive of active disease in musculoskeletal system (&gt;1 swollen and painful joint(s) despite local corticosteroid injections, persistent dactylyitis, verifiable enthesitis); (3) intractable axial symptoms which in the opinion of rheumatologist are caused by inflammatory axial PsA; (4) signs and symptoms suggestive of active skin or nail psoriasis (in the opinion of a dermatologist); (5) inability to taper glucocorticoid treatment (&lt;7.5 mg/d prednisone or equivalent); (6) persistently high sedimentation rate or CRP which are related to the PsA activity when other causes have been ruled out; (7) Rapid radiographic progression (with or without signs of active disease).</td>
<td>D2T PsA</td>
</tr>
<tr>
<td>Lubrano et al</td>
<td>2023</td>
<td>Review</td>
<td>Multiple treatment strategies</td>
<td>Refractory-to-treatment PsA: persistent tissue inflammation, as assessed by physical examination and/or imaging, despite multiple treatment strategies. D2T PsA: patients with PsA in which the presence of pre-existing clinical conditions (such as comorbidities, fibromyalgia, and other) may lead to a reduced treatment response with difficult management of the patient’s symptoms</td>
<td>Refractory to treatment PsA D2T PsA</td>
</tr>
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ACR-NPF, American College of Rheumatology-National Psoriasis Foundation; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; bDMARD, biological DMARD; CDAI, The Clinical Disease Activity Index; CRP, C reactive protein; csDMARD, conventional synthetic DMARD; DAPSA, Disease Activity in Psoriatic Arthritis; DAS28, Disease Activity Score in 28 Joints; DMARD, disease-modifying antirheumatic drug; D2T, difficult-to-treat; ESR, Erythrocyte Sedimentation Rate; EULAR, European Alliance of Associations for Rheumatology; GRAPPA, Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; HAQ, Health Assessment Questionnaire; MDA, minimal disease activity; MoA, mechanisms of action; PASDAS, Psoriatic Arthritis Disease Activity Score; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; RAPID3, Routine Assessment of Patient Index Data 3; RCT, randomised controlled trial; SJC, Swollen Joint Count; TJC, Tender Joint Count; TNFi, tumour necrosis factor inhibitors; tsDMARD, targeted synthetic DMARD; VAS, Visual Analogue Scale.
of Patient Index Data 3 (RAPID3), Disease Activity Score in 28 Joints (DAS28) and MDA. In contrast to the RCTs, three of those studies incorporated radiographic progression in the definition of D2T PsA.

Lastly, a 2014 case report by Costa et al.\(^6\) detailed a patient with PsA who showed resistance to csDMARDs and three TNFi. The report highlighted an effort to treat the patient with tocilizumab, given the persistently high activity scores across various metrics, including joint counts, acute phase reactants, patient-reported outcomes and the Psoriasis Area and Severity Index score.

**DISCUSSION**

A clear and universally accepted definition of D2T PsA lays the foundation for optimal care, guiding clinicians towards the most effective interventions and mitigating the risks of undertreatment. Despite a comprehensive and thorough search that employed various search engines, spanning over a decade of research articles and incorporating conference abstracts, our scoping review yielded a limited number of studies that specifically aimed to define D2T PsA. Such scarcity is alarming, given PsA’s multifaceted nature, its wide-ranging symptomatic domains and the many challenges associated with its treatment, particularly the variable patient responses to existing therapeutic options.

Remarkably, the limited studies available do not provide a consensus on pivotal aspects such as the number of drugs to which a patient must fail to respond for their PsA to be classified as D2T. The number ranged from failing one csDMARD and one or two TNFi to failing multiple b/tsDMARDs. Similarly, there was no universally accepted criterion to define ‘active disease’, with some studies using composite measures like DAPSA or DAS28 and others resorting to tender/swollen joint counts and skin lesion evaluations. Even the terminology used to describe these cases varied among the studies, further complicating the clinical and academic discourse. The absence of well-defined criteria can lead to treatment delays and suboptimal outcomes due to uncertainties in escalating treatment. Conversely, it also risks overdiagnosis, such as wrongly categorising patients as resistant to therapy when they are not in remission due to other comorbidities (eg, fibromyalgia and depression), leading to overtreatment and unwarranted immunosuppression.\(^3\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^,\)\(^30\) Such overtreatment often involves prescribing aggressive combinations of b/tsDMARDs that not only expose patients to unnecessary risks and side effects but also inflate healthcare costs. Notably, while clear guidelines tend to align with improved medical care, it is essential to weigh them against growing time constraints and healthcare costs, always pursuing an optimal utilisation of health resources.\(^31\)\(^–\)\(^34\)
This lack of consensus and standardisation presents several key challenges that have far-reaching implications. First, the absence of universally accepted criteria may compromise patient care, making it difficult for clinicians to identify those who would benefit from more intensified treatment strategies, thereby potentially leaving this population with suboptimal disease management. Second, this lack of standardised definition also hampers the design of clinical trials aimed at these specific patient populations, ultimately stalling the development of new, potentially more effective treatment regimens. It will be important for regulatory officials to understand the existence and parameters of this D2T population to justify their consideration of trials of more intensified therapeutic regimes. It will be important for regulatory officials to understand the existence and parameters of this D2T population to justify their consideration of trials of more intensified therapeutic regimes. Lastly, the definitional ambiguities limit the consideration and implementation of advanced therapeutic approaches, like combinations of b/tsDMARDs, which could offer better disease control but are currently underutilised. Establishing clear criteria would pave the way for dedicated trials on combination therapies in PsA, akin to the VEGA trial for ulcerative colitis, and promote the widespread sharing of case series and cohorts that shed light on the effectiveness and safety of such treatments. Indeed, it is this trial that was the impetus for a similar trial now underway in patients with PsA who have failed one TNFi, the AFFINITY trial, which will provide evidence for the combination of a TNFi and IL-23 inhibitor. Also of high importance is the necessity to define the best method for assessing disease activity, given the considerable variation in remission rates across different tools, the domains that they incorporate and their prognostic value. This is the goal of the ongoing GRAPPA-OMERACT initiative, which seeks to identify the best composite measure for PsA contexts.

The failure to achieve remission in PsA is influenced by an array of factors. These can be broadly classified into persistent inflammatory activity, non-adherence to treatment—which can be worsened by comorbid depression and anxiety—and challenges stemming from chronic pain due to structural damage or hypersensitisation. Moreover, numerous studies highlight the significance of addressing non-pharmacological factors, such as a poorer prognosis in female and patients with obesity. Drawing parallels to the differentiation proposed by Buch, for RA, a recent review by Lubrano et al advocated for differentiating between patients who remain refractory due to uncontrolled inflammation, termed refractory-to-treatment PsA, and those whose refractoriness is attributable to comorbidities, termed D2T PsA. This nuanced approach aligns with the clinical reasoning from GRAPPA, although with a slightly different terminology. It emphasises the need to address both inflammatory and non-inflammatory factors for...
effective PsA management, in addition to factoring in all comorbidities in therapeutic decision-making.2 45

Addressing the multifaceted challenges of achieving remission in PsA demands a coordinated effort from both clinicians and researchers. GRAPPA has already taken preliminary steps to confront this complex issue. A foundational step is to create a standardised, internationally recognised definition for D2T PsA which will include features of persistent inflammation indicating true biological and treatment refractory disease. Another goal is to differentiate D2T PsA from comorbidity-driven treatment-resistant PsA (termed as complex-to-manage PsA—C2M-PsA). The latter will focus on non-inflammatory factors that render the treatment ineffective. By integrating both patient perspectives and expert viewpoints via targeted surveys, a comprehensive understanding of the underlying factors contributing to treatment failures can be achieved. Building on this, the data and insights collected from these surveys and from the current review could be synthesised through a Delphi exercise to establish unified criteria.

Once these criteria are in place, a parallel goal, in addition to providing guidance to clinicians and improving patient outcomes, is to guide regulatory agencies to recognise the need for tailored studies of treatment intensification, including dose and frequency adjustment, combination therapies, sequential therapies (eg, more potent drugs with potentially higher adverse event rates for induction followed by milder drugs with lower adverse event rates for maintenance). Once regulatory agencies are involved, the focus can then shift to large, novel trials specifically designed to explore the unique phenotypes of D2T PsA and to address C2M PsA with non-immunomodulatory and non-pharmacological therapies.

There are some limitations to this review. First, we may have missed relevant studies that did not use the keywords used in our search. Second, we only included English language studies. It is also possible that we may have missed studies published in local language journals. Third, we did not critically appraise the included studies. Nevertheless, our review included a wider range of studies, including both high-impact RCTs and observational data. Finally, we did not perform critical appraisal of included studies. Nevertheless, our review included a wider range of studies, including both high-impact RCTs and observational data.

In conclusion, despite extensive efforts to compile research from various sources, the current literature on D2T PsA remains sparse. This paucity of research is particularly concerning given PsA’s heterogeneous nature, varying patient responses to existing therapies and the critical need for effective treatment strategies for such patients. The studies that do exist lack uniformity in pivotal aspects, such as the criteria for defining ‘active disease’ and number of failed therapies needed to classify PsA as D2T, thereby resulting in impaired patient care, stymied clinical research and underutilised advanced therapeutic options. As our review is the first step in a three-phase project aimed at defining these challenging cases more clearly, we believe that addressing these issues should be a priority for those involved in PsA research and treatment.

REFERENCES
Psoriatic arthritis