Clinical Rheumatology (2021) 40:3411–3418
https://doi.org/10.1007/s10067-021-05841-1

REVIEW ARTICLE

Psoriatic arthritis in Africa

Ajesh B. Maharaj[1] · **Adewale Adebajo**[2]

Received: 19 October 2020 / Revised: 7 June 2021 / Accepted: 22 June 2021 / Published online: 28 June 2021

Abstract
Psoriatic arthritis is a chronic immune-mediated inflammatory arthritis associated with the skin condition psoriasis. Although there is a large body of evidence regarding epidemiology, outcomes, and response to therapy from the Western world, there is a dearth of published literature from the African continent. There are many challenges responsible for this. Lack of resources, both human and financial, an enormous disease burden, and a focus on communicable diseases leave an unmet need for this important disease. This review explores and identifies these challenges and proposes ways to improve and overcome these deficiencies. We discuss the epidemiology of psoriatic arthritis in Africa, postulating the role of genetic and environmental factors, looking at the role of HLA-B 23, HLA-B 17, and HLA-B 8. Dietary intake as a contributing factor to the low prevalence of psoriatic arthritis and psoriasis is also discussed. Challenges on the African continent regarding limited access to specialised units/specialists, delay in diagnosis, limited attention by healthcare authorities to non-communicable diseases, and the difficulties in implementing international recommendations on the African continent are discussed. We also discuss a relative lack of data from the African continent, the cost of specialised medication in resource-poor countries, and comorbidities of psoriatic arthritis. The lack of validated questionnaires relevant to the African continent is also important and discussed. Finally, we discuss a proposed research agenda that will improve care, quality of life, and outcomes for patients with psoriatic arthritis on the African continent.

Keywords Africa · Comorbidities · HIV · Psoriasis · Psoriatic arthritis

Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory arthritis associated with the skin disease psoriasis. Data from most studies show the prevalence of psoriasis (PsO) to be approximately 1 to 3% of the general population, although a much higher prevalence has been reported in some populations [1–3]. About 30% of patients with PsO develop PsA; however, various studies have shown a prevalence of between 6 and 42%, depending on the classification criteria used [4]. In approximately 70 to 80% of patients, the onset of arthritis follows the cutaneous manifestations. In 10 to 15%, there is a simultaneous onset of musculoskeletal and cutaneous manifestations, and in about 10 to 15% of patients, arthritis may antedate psoriasis [4].

PsA is a heterogeneous disease, both in its musculoskeletal and cutaneous manifestations. The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) have divided psoriatic arthritis into the five domains:

a) Peripheral arthritis.
b) Skin and nail disease.
c) Axial arthritis.
d) Enthesitis.
e) Dactylitis.

Following on from older criteria, such as the Moll and Wright criteria, the development of the CASPAR criteria (ClASsification criteria for Psoriatic Arthritis) has helped to standardise the reporting of PsA worldwide [4, 5]. The development of these CASPAR criteria involved patients

This article is part of the Topical Collection on *Rheumatology in Africa*

✉ Ajesh B. Maharaj
maharaja30@ukzn.ac.za

[1] Department of Internal Medicine, Prince Mshiyeni Memorial Hospital, Nelson R Mandela School of Medicine, University of Kwazulu-Natal, Durban, South Africa

[2] Faculty of Medicine, Dentistry, and Health, University of Sheffield, South Yorkshire, UK

derived globally, including from Africa. The CASPAR criteria were reported to have a specificity of 98.7% and a sensitivity of 91.4% for PsA compared to a group of patients with other forms of inflammatory arthritis [5].

Epidemiology of psoriatic arthritis in Africa

Psoriatic arthritis appears to be uncommon in the African black population. There are currently no published data on population-based studies on the prevalence and incidence of PsA in Africa, to the best of our knowledge. The few studies on PsA in Africa that exist are hospital-based. In South Africa, hospital-based prevalence studies, almost all done in dermatology departments, show PsO prevalence to be about 2.8 to 3.5% in whites [6]. This is similar to those reported in Caucasians in Western populations. However, there was a much lower prevalence of PsO in African Blacks [6]. In a study undertaken in 5 academic hospitals serving the public sector in Johannesburg, 5355 consecutive African black patients with dermatological problems were assessed, of which 112 (2.1%) were diagnosed with PsO [6]. Psoriasis prevalence was 0.4% of 2254 patients with newly diagnosed skin abnormalities in a clinic in Ghana [7]. A similar low prevalence of PsO was noted in the dermatology outpatient department clinic in Ibadan, Nigeria, where the prevalence of PsO was reported to be 0.9% of 1091 new patients [8]. A study by Green et al. was published in the Annals of Rheumatic Diseases in 1981 with a cohort of 61 unselected PsO patients attending the dermatology clinic in Cape Town. Their study showed the prevalence of PsA to be 41.6% based on the Moll and Wright criteria [9]. Peripheral arthritis was present in 15.5% and sacroiliitis in 43% of this cohort. The study also showed an association of HLA-B 23 and HLA-B 17 in Caucasian patients, while a haplotype of HLA B8 was increased in the mixed-race population [9].

Socio-economic status and psoriatic arthritis

In a population-based study of African Americans, there was a significant difference between PsO prevalence in Caucasians and African Americans (2.5 vs. 1.3%; $p < 0.0001$). The disease's impact on quality of life and treatment satisfaction were similar in both groups [10].

Another study that evaluated clinical disease measures in patients with PsO and PsA in Caucasian and African American patients seen at four urban academic institutions in the USA showed a lower prevalence of PsA in African Americans as compared to Caucasians (30 vs. 64.5% respectively, $p < 0.001$) [11]. The study also noted that African Americans had more severe skin disease than their Caucasian counterparts (psoriasis area and severity index 8.4 vs. 5.6, respectively $p = 0.06$) [11]. The study showed that only 25% of African American patients achieved minimal disease activity. There was a disparity in the care of PsO and PsA patients in terms of treatment. This suggests that people with PsA from lower socio-economic backgrounds have a greater burden of disease and tend to do worse with disease activity and response to treatment. In a more recent study from Leeds, UK, Helliwell and his group studied the clinical and radiological differences between people of South Asian and North European origin. Psoriatic arthritis patients of South Asian origin had a greater burden and worse impact of the disease as compared to PsA patients of North European ancestry [12].

Environmental and genetic factors

The interplay between genetic and environmental factors seems to be important in the onset of PsO and PsA. However, the effect of genetic factors is uncertain in the African black population. One of the risk alleles for PsO in Caucasians, HLA Cw6, has a high frequency amongst black Africans of 15.1% compared to 9.6% of Caucasians in the Western world [13]. Consequently, it is unclear whether African black patients have certain, yet unidentified, protective genetic factors. The role of dietary factors that may have a protective effect in PsO in the black African population is also unclear. In general, Africans have a low intake of polyunsaturated fatty acids and a high intake of maize, which appears to be the staple diet in Africa. The diet in these populations is high in linoleic acid, a precursor of prostaglandin E2, which suppresses cellular immunity and reduces psoriasis risk [14].

Challenges on the African continent

There are various diagnostic challenges of PsA on the African continent, as follows:

1) Limited access to specialists

   There is a shortage of rheumatologists on the African continent. There are no rheumatologists in several African countries, and where rheumatologists exist, they are usually limited to the urban areas. Even in South Africa, one of the most developed countries on the continent, there is one rheumatologist for every 630,000 inhabitants, with most of these rheumatologists being concentrated in large cities. Apart from specialist rheumatologists, there is a general lack of physicians with only 2.7 physicians per 10,000 population in Africa compared to 5.9 in Southeast Asia, 12.7 in the eastern Mediterranean,

15.5 in the western Pacific, 21.5 in the Americas, and 32.1 in the European region [15].

2) Delay in diagnosis

Due to the shortage of specialised personnel, there is a delay in diagnosis and referral to specialised centres. This delay in diagnosis leads to a delay in the institution of appropriate therapies for PsA patients, subsequently leading to worse outcomes. Many countries in Africa, some supported by the Western world, are now using specially trained nurses and community-based healthcare workers to screen patients and expedite their referral to specialised centres. It is vitally important that all healthcare professionals, including medical students, are trained to identify PsO as well as the musculoskeletal manifestations in Africans. The late presentation of patients with inflammatory arthritides is a major problem in many African countries. The late presentation is multifactorial, including lack of qualified rheumatologists, lack of resources from a community perspective, high unemployment rate, and lack of infrastructure. Patients have to travel large distances to consult a rheumatologist, which is not always possible. Lower socioeconomic status has a worse prognosis and outcomes [12]. With this in mind, general practitioners and primary care physicians are forced to manage patients in rural settings, albeit inadequately.

3) Lack of specialised services

Many countries on the continent have a lack of specialised musculoskeletal ultrasound-trained radiologists. There is also limited access to MRI scanning for patients with inflammatory arthropathies.

4) The main focus of African healthcare is currently on infectious diseases, maternal, and child health. The resultant effect is that there is a considerable increase in non-communicable diseases, with Africa being at risk of the challenges of both increased communicable and noncommunicable diseases. The increase in noncommunicable diseases is estimated to cause a 60% mortality by 2030, as estimated by the World Health Organisation (WHO) [16]. Population-based studies on the prevalence of psoriatic arthritis in Africa are, therefore, urgently needed.

Challenges in implementing international recommendations

Most rheumatology centres the world over use international PsA treatment recommendations, such as the GRAPPA or EULAR treatment recommendations for psoriatic arthritis.

There are various challenges to the implementation of international PsA treatment recommendations in Africa. These include:

I. A lack of trained personnel to both institute and monitor therapy, where required.

As alluded to earlier, there is a lack of specially trained personnel in managing PsA on the continent. This leads to a delay in instituting appropriate therapy, with the resultant increase in avoidable morbidity and mortality. The institution of appropriate treatment and the regular monitoring of drug therapy for toxicity are problematic due to financial and human constraints.

II. A lack of relevant data

There is a dearth of published data on PsA from the African continent. Prevalence and incidence rates of PsA on the continent are not well defined. Problems specific to Africa have not been reported through community-based studies. Response rates to the various PsA therapies are extrapolated from Western data, making it problematic at a local African level. There are no specific treatment recommendations from the African continent, with most rheumatologists relying on treatment recommendations from the Western world. Evidence-based recommendations, such as those from the European League Against Rheumatism (EULAR), Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA), and American College of Rheumatology/National Psoriasis Foundation (ACR/NPF), have to be balanced with the patient's individual needs and local factors, due to the lack of African published data [17–19]. The International League of Association of Rheumatologists (ILAR) has recently published their adapted recommendations for PsA treatment in resource-poor countries, based on the EULAR and GRAPPA PsA treatment recommendations [20]. This is an important step in the right direction to improve PsA therapies and outcomes on the African continent.

III. Cost of advanced therapies

The cost of biological therapies makes access to these drugs difficult in developing countries. Affordability in public healthcare systems is a major concern. Tumour necrosis factor-alpha (anti-TNF) therapies, interleukin-17 antagonists, the interleukin 12/23 antagonists, and targeted synthetic disease-modifying antirheumatic drugs (tsDMARDs) are out of reach of most PsA patients in Africa. Most countries on the continent do not have a government-funded scheme, such as a central insurance scheme, to provide their populations with access to these therapies.

IV. Validated questionnaires

There is a lack of patient-based validated questionnaires from the African continent. Psoriatic arthritis

questionnaires such as the Psoriasis Epidemiology Screening Tool (PEST) and Dermatology Life Quality Index (DLQI) require validation in Africans to improve patient outcomes.

Comorbidities

Comorbidities in patients with PsA in general would apply to the African continent. There are no comorbidities that are specific to patients from Africa.

Human immunodeficiency virus infection

The prevalence of human immunodeficiency virus (HIV) infection in sub-Saharan Africa remains of concern. The prevalence rates of PsO and PsA appear to have increased in the African black population due to the HIV pandemic. The pathogenesis of PsO and PsA in patients with concomitant HIV infection is complex and revolves around three main dilemmas:

PsO/PsA is a T-cell-mediated disease with increased prevalence in the background of decreasing T-cell counts in patients with HIV infection [21].
Although in immuno-competent patients, targeting T cells are effective therapies in the management of PsO; PsO seems to be worse in patients with HIV infection with decreasing CD4 T-cell counts [22, 23].
HIV infection is characterised by a Th2 cytokine profile, and PsO is characterised by a more pronounced Th1 pattern [24–27].

The prevalence rates of both PsO and PsA have increased following the HIV pandemic [28]. The prevalence of PsO appears to have increased post-HIV pandemic (5.15% amongst HIV-positive individuals as compared to 1–3% of the general population) [29]. Psoriasis's prevalence rate on the African continent is even lower than reported in the Western world [6–8]. Several PsA cases were identified in HIV-positive individuals (40 to 96%) in hospital-based studies, many of which had small sample sizes [29, 30]. HLA Cw6 confers a greater risk for PsO in Caucasian populations. Even though the prevalence of HLA Cw6 is higher in Africans than Caucasians, the prevalence of PsO is lower [13]. Mallon et al. studied the risk of HLA Cw6 in patients with HIV with and without PsO. They provided evidence of a possible link between this immunogenetic association. Their study compared genomic DNA isolated from the lymphocytes of 14 men with HIV and psoriasis compared to HIV-positive men without PsO. The HLA-Cw6 antigen (HLA-Cw*0602 allele) was detected in 79% (11/14) of the HIV-1–positive psoriatic patients, while the allele was present in only 24.5% (36/147) of HIV-1–positive controls (95% CI, 2.73–65.36; P5.0001) [31]. This could explain the increased prevalence and severity of PsO in African patients with HIV.

HIV-associated psoriasis can be clinically confusing because of several skin disorders present in patients with concomitant HIV infection. A similar hyperkeratotic psoriasiform rash can be difficult to distinguish from true PsO in patients who have HIV infection [32]

Most of the proven effective therapies for the treatment of PsA are contraindicated in patients with concomitant HIV infection. There are no published data regarding the use of these therapies in HIV-positive PsA patients. The high incidence of tuberculosis on the African continent increases the risk of either the development or the reactivation of tuberculosis in PsA patients treated with anti-TNF therapy. Local African screening protocols have to be rigidly adhered to.

Various comorbidities impact negatively on patient outcomes in PsA. Patients with inflammatory diseases, including PsA and PsO, are associated with an increased risk of atherosclerotic vascular disease, with increased morbidity and mortality [33–38]. There is an increased risk of hypertension in patients with PsA [39]. Han et al. showed that the prevalence ratio of hypertension was 1.3 times higher in PSA patients as compared to controls [40]. In addition to the independent effect of the inflammatory disease, PsA patients have added risk factors (such as chronic ingestion of non-steroidal anti-inflammatory drugs (NSAIDs) associated with an increased prevalence of hypertension [41]. Patients with PsA have a significantly higher blood pressures than psoriasis alone [42]. A direct correlation between the degree of psoriasis and elevation of blood pressure has also been observed. The higher the PASI scores, the more elevated the blood pressure [43]. Treatment targets for hypertension in patients with inflammatory joint disease are similar to those of the general population [44–46]. There is a greater risk for dyslipidaemias in patient with psoriatic disease [47–53]. Regular monitoring of lipid profile must be undertaken in these patients.

Patients with psoriatic disease have an increased prevalence of obesity as well as metabolic syndrome [50, 54]. Not only do these comorbidities increase the risk for the development of PsO and PsA, but obese patients may have a poor response to therapy as compared to non-obese patients, and have more disease activity, including higher PASI scores [54]. Weight loss in obese patients is associated with improved response to therapy [50, 54]. Metabolic syndrome is often associated with more severe PsA. A study published in the International Journal of Dermatology noted a high metabolic syndrome burden in South Africans with psoriasis compared to controls. The prevalence of metabolic syndrome was 52.4 vs. 33.7% ($p=0.007$) in patients with psoriasis compared to controls [55]. They also noted a higher

prevalence of type II diabetes (25.2 vs. 4.1%; p = < 0.0001), and hypertension (70.9 vs. 46.6% p = 0.001) in psoriasis as compared to controls. High school education was associated with a better prognosis in this cohort [55]. Diabetes mellitus (DM) is more common in patients with PsA compared to the general population [56, 57]. Aggressive treatment of the PsA improves glycaemic control [58–60].

Other associated comorbidities that impact negatively on patients with PSA include smoking [61–69], myocardial infarction [34, 69], congestive cardiac failure [70, 71], cerebro-vascular disease [38, 72–75], liver disease including non-alcoholic fatty liver disease (NAFLD) [76–82], depression [83–85], and osteoporosis [86, 87]. The risk of development of malignancies in patients with PsA is low. However, there is a relative dearth of information in this regard. In general, the rates of malignancy in patients with PsA are no different from that of the general population [88–91].

Impact of comorbidities on treatment response

The presence and burden of comorbidities have an adverse impact on treatment response and persistence. In the DANBIO registry, patients with comorbidities had higher baseline disease activity scores, inadequate response to therapy, and decreased persistence rates of anti-TNF therapy [85]. Comorbidities also have a negative impact on achieving minimal disease activity (MDA)—a state of near remission. Cohort studies have reported that patients with obesity and metabolic syndrome are less likely to achieve MDA [92, 93]. In an interventional study, Di Minno et al. showed that regardless of the dietary intervention, successful weight loss of ≥ 5% from baseline was associated with a higher rate of achievement of MDA in overweight/obese patients with PsA who start treatment with TNFi [94].

Therapeutic aspects of PsA in Africa

The use of conventional synthetic disease-modifying antirheumatic drugs (cs DMARDs) is available in most countries on the continent. These include methotrexate, sulphasalazine, and leflunomide. The early initiation of therapy should be stressed to improve long-term outcomes. However, long-term monitoring of complete blood count and liver function tests, and disease activity markers are often problematic in resource-poor settings. Physicians should be trained in the use of these medications and their monitoring. Aggressive and appropriate escalation of therapy should be emphasised to target low disease activity or remission in most patients. Due to resource limitations, aggressive treatment with csDMARDs either as sequential monotherapy or combination therapy has to be emphasised. The jury is still out on whether sequential monotherapy or combination therapy has better long-term outcomes and reduced adverse effects in the long term. Treat to target recommendations should be adhered to attain and maintain low disease activity or remission.

Conventional synthetic disease modifying anti-rheumatic drugs are widely used as first-line therapy on the African continent. Methotrexate is the anchor drug in most treatment regimens. Although methotrexate is commonly used in the treatment of PsA, one of the initial studies on the use of methotrexate in PsA was a negative study [95]. A more recent study from India shows that methotrexate is efficacious in the treatment of PsA [96]. Other csDMARDS, including sulphasalazine, and leflunomide, are used as add-on therapy if patients do not achieve minimal disease activity/remission on methotrexate monotherapy. In Africa, these drugs should be initiated as early as possible to achieve good outcomes. Due to cost constraints in resource-poor settings, biologic disease-modifying antirheumatic drugs (bDMARDs) are not widely used on the continent. Hopefully, with the advent of biosimilars, the penetrance of biologics into Africa will increase. As alluded to earlier, the high prevalence of tuberculosis, hepatitis B and C, and human immunodeficiency virus (HIV) infections also limits the use of these drugs.

Treat-to-target paradigms need to be adhered to, to improve patient outcomes. Due to the lack of published data from Africa, we are reliant on data from the Western world, which does not necessarily apply to the African setting. It is imperative that more epidemiological and other clinical studies are undertaken and published from the continent. Treatment recommendations from the various African countries need to be formalised by local experts. This will provide a valuable tool for local primary care physicians and general physicians to follow. Clinical trials/research from a local perspective needs to be encouraged from Africa. Pharmaceutical companies should be encouraged to involve greater participation of African centres in phase III/IV PsA clinical trials.

Proposed research agenda

Large-scale observational studies from the entire African continent comparing data from the different regions would assist in understanding the different phenotypes as well as in determining the burden of disease and response to therapy on the continent. Studies analysing outcome measures in patients treated by primary care physicians vs. rheumatologists to identify deficiencies in optimum healthcare for these patients will help to address quality of care issues. Regional-based studies outlining the optimal frequency of appropriate monitoring in resource poor settings to optimise outcomes

without compromising safety would be helpful. Evaluation of monotherapy vs. combination therapy/sequential monotherapy on the continent is also important to ensure effective treatment. Another important part of the research agenda would be to study the question of HIV associated PsA and different treatment modalities, as well as response to therapy. It is also important to develop region-specific treatment recommendations, tailoring the existing recommendations to fit resource poor countries so that appropriate standards of care can be achieved.

Conclusion

In conclusion, early diagnosis, and aggressive treatment with appropriate management, will improve the quality of life and long-term outcomes of African patients with PsA. Finally (and perhaps most important of all), the public, all healthcare professionals, and the relevant healthcare officials and health policymakers in Africa need to be educated about the importance of PsA in Africa to ensure early diagnosis, early treatment interventions, and a good outcome, for all African patients with psoriatic arthritis.

Declarations

Disclosures None.

References

1. Gelfand JM, Weinstein R, Porter SB et al (2005) Prevalence and treatment of psoriasis in the United Kingdom: a population-based study. Arch Dermatol 141:1537–1541
2. Brandrup F, Green A (1981) The prevalence of psoriasis in Denmark. Acta Derm Venereol 61:344–346
3. Ferrandiz C, Bordas X, Garcia-Patos V et al (2001) Prevalence of psoriasis in Spain (Epiderma Project: phase I). J Eur Acad Dermatol Venereol 15:20–23
4. Moll JM, Wright V (1973) Psoriatic arthritis. Semin Arthritis Rheum 3:55–78
5. Taylor W, Gladman D, Helliwell P et al (2006) CASPAR Study Group. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. Arthritis Rheum 54:2665–73
6. Hartshorne ST (2003) Dermatological disorders in Johannesburg, South Africa. Clin Exp Dermatol 28:661–665. https://doi.org/10.1046/j.1365-2230.2003.01417.x
7. Doe PT, Asiedu A, Acheampong JW, Rowland Payne CM (2001) Skin diseases in Ghana and the UK. Int J Dermatol 40(5):323–326. https://doi.org/10.1046/j.1365-4362.2001.01229.x (PMID: 11554993)
8. Ogunbiyi AO, Daramola OO, Alese OO (2004) Prevalence of skin diseases in Ibadan. Nigeria Int J Dermatol 43(1):31–36. https://doi.org/10.1111/j.1365-4632.2004.01967.x
9. Green L, Meyers OL, Gordon W et al (1981) Arthritis in psoriasis. Ann Rheum Dis 40:366–369
10. Gelfand JM, Stern RS, Nijsten T et al (2005) The prevalence of psoriasis in African Americans: results from a population-based study. J Am Acad Dermatol 52(1):23–26. https://doi.org/10.1016/j.jaad.2004.07.045
11. Kerr GS, Qaiyumi S, Richards J, Vahabzadeh-Monshie H, Kindred C, Whelton S, Constantinescu F (2015) Psoriasis and psoriatic arthritis in African-American patients–the need to measure disease burden. Clin Rheumatol 34(10):1753–1759. https://doi.org/10.1007/s10067-014-2763-3 (Epub 2014 Aug 28 PMID: 25164561)
12. Aslam Tariq, Mahmood Farrouq, Sabanathan Anetha, Waxman Robin, Helliwell Philip S (2021) A clinical and radiographic comparison of patients with psoriatic arthritis from different ethnic backgrounds. Rheumatology. 60(1):340–345. https://doi.org/10.1093/rheumatology/keaa298
13. Ouédraogo DD, Meyer O (2012) Psoriatic arthritis in Sub-Saharan Africa. Joint Bone Spine 79(1):17–19. https://doi.org/10.1016/j.jbspin.2011.06.007
14. Namazi MR (2004) Paradoxical exacerbation of psoriasis in AIDS: proposed explanations including the potential roles of substance P and gram-negative bacteria. Autoimmunity 37(1):67–71. https://doi.org/10.1080/08916930310001637986 (PMID: 15115314)
15. Scheffler RM, Liu XJ, Yohannes Kinfuc J et al (2008) Forecasting the global shortage of physicians: an economicand needs-based approach. Bull World Health Organ 86:516–523
16. WHO (2013) GBD 2010 country results: a global public good. Lancet 381(9871):965–70
17. Coates Laura C, Kavanaugh Arthur, Mease Philip J, at, (2016) Group for Research and Assessment of Psoriasis and Psoriatic Arthritis 2015 Treatment Recommendations for Psoriatic Arthritis. Arthritis Rheumatol. 68(5):1060–71. https://doi.org/10.1002/art.39573
18. Gossec L, Baraliakos X, Kerschbaumer A et al (2020) EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. Ann Rheum Dis 79(6):700–712. https://doi.org/10.1136/annrheumdis-2020-217159.PMID:32434812;PMCID:PMC7286048
19. Singh JA, Guyatt G, Ogdie A et al (2019) 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. Arthritis & Rheumatology 71:5–32. https://doi.org/10.1002/art.40726
20. Elmamoun M, Eraso M, Anderson M et al (2020) International league of associations for rheumatology recommendations for the management of psoriatic arthritis in resource-poor settings. Clin Rheumatol 39:1839–1850. https://doi.org/10.1007/s10067-020-04934-7
21. Fife DJ, Waller JM, Jeffes EW et al (2007) Unraveling the paradoxes of HIV-associated psoriasis: a review of T-cell subsets and cytokine profiles. Dermatol Online J 13:4
22. Ortonne JP, Lebwohl M, Griffiths C; Alefacept Clinical Study Group (2003) Alefacept-induced decrease in circulating blood lymphocyte counts correlate with clinical response in patients with chronic plaque psoriasis. Eur J Dermatol 13:117–123
23. Ellis CN, Krueger GG, Alefacept Clinical Study Group (2001) Treatment of chronic plaque psoriasis by selective targeting of memory effector T lymphocytes. N Engl J Med 345:248–255
24. Klein SA, Dobmyer JM, Pape M et al (1997) Demonstration of the Th1 to Th2 cytokine shift during the course of HIV-1 infection using cytoplasmic cytokine detection on single cell level by flow cytometry. AIDS 11(9):1111–1118. https://doi.org/10.1097/00002030-199709000-00005 (PMID: 9233457)
25. Austin LM, Ozawa M, Kikuchi T et al (1999) The majority of epidermal T cells in psoriasis vulgaris lesions can produce type 1

cytokines, interferon-g, interleukin-2, and tumor necrosis factor-a, defining TC1 (cytotoxic T lymphocye) and TH1 effector populations: a type 1 differentiation bias is also measured in circulating blood T cells in psoriatic patients. J Invest Dermatol 113:752–759
26. Szabo SK, Hammerberg C, Yoshida Y et al (1998) Identification and quantitation of interferon-gamma producing T cells in psoriatic lesions: localization to both CD41 and CD81 subsets. J Invest Dermatol 111:1072–1078
27. Friedrich M, Krammig S, Henze M et al (2000) Flow cytometric characterization of lesions T cells in psoriasis: intracellular cytokine and surface antigen expression indicates an activated, memory/effector type 1 immunophenotype. Arch Dermatol Res 292:519–521
28. Ouédraogo D-D, Meyer O. Psoriatic arthritis in Sub-Saharan Africa. Joint, Bone, Spine: Revue du Rhumatisme 79(1):17–9. https://doi.org/10.1016/j.jbspin.2011.06.007
29. Gabla A, Eti E, Nebavi Z et al (1997) Psoriatic arthritis in Ivory Coast - a report of 10 cases. Rhumatologie 49(3):91–94
30. SteinP Davis CM (1996) Arthritis associated with HIV infection in Zimbabwe. J Rheumatol 23(3):506–511
31. Mallon E, Young D, Bunce M et al (1998) HLA-Cw*0602 and HIV-associated psoriasis. Br J Dermatol 139:527–533
32. Morar N, Willis-Owen SA, Maurer T et al (2010) HIV-associated psoriasis: pathogenesis, clinical features, and management. Lancet Infect Dis. 10(7):470–8. https://doi.org/10.1016/S1473-3099(10)70101-8
33. Jamnitski A, Symmons D, Peters MJ et al (2013) Cardiovascular comorbidities in patients with psoriatic arthritis: a systematic review. Ann Rheum Dis 72:211–216
34. Polachek A, Touma Z, Anderson M et al (2017) Risk of cardiovascular morbidity in patients with psoriatic arthritis: a meta-analysis of observational studies. Arthritis Care Res (Hoboken) 69(1):67–74
35. Ogdie A, Schwartzma S, Eder L et al (2014) Comprehensive treatment of psoriatic arthritis: managing comorbidities and extraarticular manifestations. J Rheumatol 41:2315–2322
36. Dommasch ED, Troxel AB, Gelfand JM (2013) Major cardiovascular events associated with anti-IL 12/23 agents: a tale of two meta-analyses. J Am Acad Dermatol 68:863–865
37. Lebwohl M (2012) Interleukin 12/23 agents and major adverse cardiovascular events. Arch Dermatol 148:1329
38. Eder L, Joshi AA, Dey AK et al (2018) Association of tumor necrosis factor inhibitor treatment with reduced indices of subclinical atherosclerosis in patients with psoriatic disease. Arthritis Rheumatol 70(3):408–416
39. Molto A, Etcheto A, van der Heijde D et al (2016) Prevalence of comorbidities and evaluation of their screening in spondyloarthritis: results of the international cross-sectional ASAS-COMOSPA Study. Ann Rheum Dis 75(6):1016–1023
40. Han C, Robinson DW Jr, Hackett MV et al (2006) Cardiovascular disease and risk factors in patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. J Rheum 33(11):2167–2172
41. Roubille C, Richer V, Starnino T et al (2015) The effects of tumour necrosis factor inhibitors, methotrexate, non-steroidal anti-inflammatory drugs and corticosteroids on cardiovascular events in rheumatoid arthritis, psoriasis and psoriatic arthritis: a systematic review and meta-analysis. Ann Rheum Dis 74(3):480–489
42. Bellou E, Verstappen SMM, Cook M, et al (2016) Increased rates of hypertension in patients with psoriatic arthritis compared to psoriasis alone: results from the UK Biobank [abstract]. Arthritis Rheumatol 68(suppl 10). http://acrabstracts.org/abstract/increased-rates-of-hypertension-in-patients-with-psoriatic-arthritis-compared-to-psoriasis-alone-results-from-the-uk-biobank. Accessed 28 Sept 2016
43. Salihbegovic EM, Hadzigrahic N, Suljagic E et al (2015) Psoriasis and high blood pressure. Med Arch. 69(1):13–5. https://doi.org/10.5455/medarh.2015.69.13-15
44. Recarti C, Unger T (2013) Prevention of coronary artery disease: recent advances in the management of hypertension. Curr Atheroscler Rep 15:311
45. American Heart Association, Diet, and Lifestyle Recommendations 2014 [Internet. Accessed August 7, 2014]; Available from: http://www.heart.org/HEARTORG/GettingHealthy/NutritionCenter/HealthyEating/The-American-Heart-Associations-Diet-and-LifestyleRecommendations_UCM_305855_Article.jsp
46. Perk J, De Backer G, Gohlke H et al (2012) The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). Eur Heart J 2012(33):1635–1701
47. Akhyani M, Ehsani AH, Robati RM et al (2007) The lipid profile in psoriasis: a controlled study. J Eur Acad Dermatol Venereol 21(10):1330–1332
48. Jones S, Harris C, Lloyd J et al (2000) Lipoproteins and their subfractions in psoriatic arthritis: identification of an atherogenic profile with active joint disease. Ann Rheum Dis 59(11):904–909
49. Tam LS, Tomlinson B, Chu TT et al (2008) Cardiovascular risk profile of patients with psoriatic arthritis compared to controls–the role of inflammation. Rheumatology (Oxford) 47(5):718–723
50. Li W, Han J, Qureshi AA (2012) Obesity and risk of incident psoriatic arthritis in US women. Ann Rheum Dis 71:1267–1272
51. Popescu C, Pintilie AM, Bojinca V, Balanescu A, Ionescu R (2014) Cardiovascular risk in psoriatic arthritis - a cross-sectional study. Maedica (Bucur). 9(1):19–24
52. Myasoedova E, Akkara Veetil BM, Matteson EL et al (2013) Cardiovascular risk in psoriasis: a population-based analysis with assessment of the framingham risk score. Scientifica 371569. https://doi.org/10.1155/2013/371569
53. Eder L, Chandran V, Gladman DD (2014) The Framingham Risk Score underestimates the extent of subclinical atherosclerosis in patients with psoriatic disease. Ann Rheum Dis 73(11):1990–1996
54. Caso F, Del Puente A, Oliviero F, et al (2018) Metabolic syndrome in psoriatic arthritis: the interplay with cutaneous involvement. Evidences from literature and a recent cross-sectional study. Clin Rheumatol 37(3):579–586
55. Goolam Mahyoodeen N, Crowther NJ, Snyman T et al High burden of the metabolic syndrome and its component disorders in South Africans with psoriasis. Int J Dermatol 58:557–562. https://doi.org/10.1111/ijd.14348
56. Dreiher J, Freud T, and Cohen AD. Psoriatic arthritis and diabetes: a population-based cross-sectional study. Dermatol Res Pract. 2013; 2013: 580404. Published online 2013 Jun 17
57. Solomon DH, Love TJ, Canning C et al (2010) Risk of diabetes among patients with rheumatoid arthritis, psoriatic arthritis, and psoriasis. Ann Rheum Dis 69:2114–2117
58. Kumar S, Han J, Li T, Qureshi AA (2013) Obesity, waist circumference, weight change and the risk of psoriasis in US women. J Eur Acad Dermatol Venereol 27:1293–1298
59. Shapiro J, Cohen AD, David M et al (2007) The association between psoriasis, diabetes mellitus, and atherosclerosis in Israel: a case-control study. J Am Acad Dermatol 56(4):629–634
60. Eder L, Chandran V, Cook R et al (2017) The risk of developing diabetes mellitus in patients with psoriatic arthritis: a cohort study. J Rheumatol 44(3):286–291
61. Kavli G, Forde OH, Arnesen E et al (1985) Psoriasis: familial predisposition and environmental factors. Br Med J (Clin Res Ed) 291:999–1000
62. Braathen LR, Botten G, Bjerkedal T (1989) Psoriatics in Norway. A questionnaire study on health status, contact with paramedical

professions, and alcohol and tobacco consumption. Acta Derm Venereol Suppl (Stockh) 142:9–12
63. Mills CM, Srivastava ED, Harvey IM et al (1992) Smoking habits in psoriasis: a case control study. Br J Dermatol 127:18–21
64. Li W, Han J, Qureshi AA (2012) Smoking and risk of incident psoriatic arthritis in US women. Ann Rheum Dis 71(6):804–808. https://doi.org/10.1136/annrheumdis-2011-200416
65. Eder L, Shanmugarajah S, Thavaneswaran A et al (2012) The association between smoking and the development of psoriatic arthritis among psoriasis patients. Ann Rheum Dis 71(2):219–224. https://doi.org/10.1136/ard.2010.147793
66. Nguyen UDT, Zhang Y, Lu N et al (2018) Smoking paradox in the development of psoriatic arthritis among patients with psoriasis: a population-based study. Ann Rheum Dis 77(1):119–123
67. Kaine J, Song X, Kim G, Hur P, Palmer JB (2019) Higher incidence rates of comorbidities in patients with psoriatic arthritis compared with the general population using U.S. Administrative Claims Data. J Manag Care Spec Pharm 25(1):122–132. https://doi.org/10.18553/jmcp.2018.17421
68. Højgaard P, Glintborg B, Hetland ML et al (2015) Association between tobacco smoking and response to tumour necrosis factor α inhibitor treatment in psoriatic arthritis: results from the DANBIO registry. Ann Rheum Dis 74(12):2130–2136
69. Egeberg A, Thyssen JP, Jensen P et al (2017) Risk of myocardial infarction in patients with psoriasis and psoriatic arthritis: a nationwide cohort study. Acta Derm Venereol 97(7):819–824
70. Khalid U, Ahlehoff O, Gislason GH et al (2014) Psoriasis and risk of heart failure: a nationwide cohort study. Eur J Heart Fail 16(7):743–748
71. Chung ES, Packer M, Lo KH et al (2003) Randomized, double-blind, placebo-controlled, pilot trial of infliximab, a chimeric monoclonal antibody to tumor necrosis factor-alpha, in patients with moderate-to-severe heart failure: Results of the anti-TNF Therapy Against Congestive Heart Failure (ATTACH) trial. Circulation 107:3133–3140
72. Gelfand JM, Dommasch E, Shin BD et al (2009) The risk of stroke in patients with psoriasis. J Invest Dermatol 129(10):2411–2418. https://doi.org/10.1038/jid.2009.112
73. Semb AG, Kvien TK, DeMicco DA et al (2012) Effect of intensive lipid-lowering therapy on cardiovascular outcome in patients with and those without inflammatory joint disease. Arthritis Rheum 64:2836–2846
74. Boehncke WH, Boehncke S, Tobin AM et al (2011) The 'psoriatic march': a concept of how severe psoriasis may drive cardiovascular comorbidity. Exp Dermatol 20:303–307
75. Eder L, Harvey P, Chandran V et al (2018) Gaps in diagnosis and treatment of cardiovascular risk factors in patients with psoriatic disease: an international multicenter study. J Rheumatol 45(3):378–384
76. O'Connor N, Dargan PI, Jones AL (2003) Hepatocellular damage from non-steroidal anti-inflammatory drugs. QJM 96:787–791
77. Sokolove J, Strand V, Greenberg JD et al (2010) Risk of elevated liver enzymes associated with TNF inhibitor utilisation in patients with rheumatoid arthritis. Ann Rheum Dis 69:1612–1617
78. Seitz M, Reichenbach S, Moller B et al (2010) Hepatoprotective effect of tumour necrosis factor alpha blockade in psoriatic arthritis: a cross-sectional study. Ann Rheum Dis 69:1148–1150
79. Amital H, Arnson Y, Chodick G et al (2009) Hepatotoxicity rates do not differ in patients with rheumatoid arthritis and psoriasis treated with methotrexate. Rheumatology 48:1107–1110
80. Curtis JR, Beukelman T, Onofrei A et al (2010) Elevated liver enzyme tests among patients with rheumatoid arthritis or psoriatic arthritis treated with methotrexate and/or leflunomide. Ann Rheum Dis 69:43–47
81. Tilling L, Townsend S, David J (2006) Methotrexate and hepatic toxicity in rheumatoid arthritis and psoriatic arthritis. Clin Drug Invest 26:55–62
82. Ogdie A, Grewal SK, Noe MH, Shin DB, Takeshita J, Chiesa Fuxench ZC, Carr RM, Gelfand JM (2018) Risk of incident liver disease in patients with psoriasis, psoriatic arthritis, and rheumatoid arthritis: a population-based study. J Invest Dermatol 138(4):760–767
83. Lewinson RT, Vallerand IA, Lowerison MW et al (2017) Depression is associated with an increased risk of psoriatic arthritis among patients with psoriasis: a population-based study. J Invest Dermatol 137(4):828–835
84. McDonough E, Ayearst R, Eder L et al (2014) Depression and anxiety in psoriatic disease: prevalence and associated factors. J Rheum 41(5):887–896
85. Ballegaard C, Højgaard P, Dreyer L et al (2018) Impact of comorbidities on tumor necrosis factor inhibitor therapy in psoriatic arthritis: a population-based cohort study. Arthritis Care Res (Hoboken) 70(4):592–599
86. Magrey MN, Lewis S, Asim KM (2016) Utility of DXA scanning and risk factors for osteoporosis in ankylosing spondylitis—a prospective study. Semin Arthritis Rheum 46(1):88–94
87. Chandran S, Aldei A, Johnson SR et al (2016) Prevalence and risk factors of low bone mineral density in psoriatic arthritis: a systematic review. Semin Arthritis Rheum 46(2):174–182
88. Thompson AE, Rieder SW, Pope JE (2011) Tumor necrosis factor therapy and the risk of serious infection and malignancy in patients with early rheumatoid arthritis: a meta-analysis of randomized controlled trials. Arthritis Rheum 63(6):1479–1485. https://doi.org/10.1002/art.30310
89. Rohekar S, Tom BD, Hassa A et al (2008) Prevalence of malignancy in psoriatic arthritis. Arthritis Rheum 58:82–87
90. Ogdie A, Maliha S, Love T, et al (2017) Cause-specific mortality in patients with psoriatic arthritis Rheumatology (Oxford) 56(6):907–911
91. Hellgren K, Dreyer L, Arkema EV et al (2017) Cancer risk in patients with spondyloarthritis treated with TNF inhibitors: a collaborative study from the ARTIS and DANBIO registers. Ann Rheum Dis 76:105–111
92. Eder L, Thavaneswaran A, Chandran V et al (2015) Obesity is associated with a lower probability of achieving sustained minimal disease activity state among patients with psoriatic arthritis. Ann Rheum Dis 74(5):813–817
93. Chimenti MS, Triggianese P, Conigliaro P et al (2017) A 2-year observational study on treatment targets in psoriatic arthritis patients treated with TNF inhibitors. Clin Rheumatol 36(10):2253–2260
94. Di Minno MN, Peluso R, Iervolino S, et al (2014) CaRRDs Study Group. Weight loss and achievement of minimal disease activity in patients with psoriatic arthritis starting treatment with tumour necrosis factor α blockers. Ann Rheum Dis 73(6):1157–62
95. Kingsley GH, Kowalczyk A, Taylor H et al (2012) A randomized placebo-controlled trial of methotrexate in psoriatic arthritis. Rheumatology (Oxford). 51(8):1368–77. https://doi.org/10.1093/rheumatology/kes001
96. Appani SK, Devarasetti PK, Irlapati RVP, al. et al (2019) Methotrexate achieves major cDAPSA response, and improvement in dactylitis and functional status in psoriatic arthritis. Rheumatology 58(5):869–873. https://doi.org/10.1093/rheumatology/key369