



## ORIGINAL RESEARCH

# Characterisation of patients with axial psoriatic arthritis and patients with axial spondyloarthritis and concomitant psoriasis in the SCQM registry

Adrian Ciurea <sup>1</sup>, Andrea Götschi,<sup>2</sup> Seraphina Kissling,<sup>2</sup> Alexander Bernatschek,<sup>1</sup> Kristina Bürki,<sup>1</sup> Pascale Exer,<sup>3</sup> Michael J Nissen <sup>4</sup>, Burkhard Möller,<sup>5</sup> Almut Scherer,<sup>2</sup> Raphael Micheroli <sup>1</sup>

**To cite:** Ciurea A, Götschi A, Kissling S, *et al.* Characterisation of patients with axial psoriatic arthritis and patients with axial spondyloarthritis and concomitant psoriasis in the SCQM registry. *RMD Open* 2023;**9**:e002956. doi:10.1136/rmdopen-2022-002956

Received 21 December 2022  
Accepted 18 May 2023



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<sup>1</sup>Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland

<sup>2</sup>DataScience, Swiss Clinical Quality Management in Rheumatic Diseases, Zurich, Switzerland

<sup>3</sup>Praxis Rheuma-Basel, Basel, Switzerland

<sup>4</sup>Department of Rheumatology, Geneva University Hospitals, Geneva, Switzerland

<sup>5</sup>Department of Rheumatology and Immunology, University Hospital Bern, Bern, Switzerland

**Correspondence to**  
Prof Adrian Ciurea;  
adrian.ciurea@usz.ch

## ABSTRACT

**Background** Within the spectrum of spondyloarthritis, axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) present with overlapping features. Axial involvement in PsA (axial PsA) is treated according to recommendations for axSpA, as specific studies in axial PsA are scarce. We compared characteristics of patients with axSpA (particularly of patients with axSpA and concomitant psoriasis (pso)) with those of patients with axial PsA.

**Methods** Patients with axSpA and PsA in the Swiss Clinical Quality Management (SCQM) registry were included if information on pso and axial involvement was available. Patients with AxSpA were stratified by axSpA with and without pso (axSpA±pso) and patients with PsA were stratified to axial PsA or strictly peripheral PsA.

**Results** Previous or current psoriasis was observed in 479/4489 patients with axSpA (10.7%). Of 2631 patients with PsA, 1153 (43.8%) presented with axial involvement (opinion of the treating rheumatologist). Compared with patients with axSpA+pso, patients with axial PsA were older at symptom onset and at inclusion in SCQM, were less frequently HLA-B27 positive, had back pain less frequently and a higher prevalence of dactylitis and peripheral arthritis. A positive family history of pso or PsA was more frequent in axial PsA, while a positive family history of axSpA was more frequent in patients with axSpA+pso. Disease activity, function and mobility were comparable in axSpA+pso versus axial PsA.

**Conclusion** Patients with axial PsA differ from patients with axSpA+pso in important demographic and clinical characteristics, and genetically, but present with a comparable disease burden. Treatment studies specifically dedicated to axial PsA seem warranted.

## INTRODUCTION

The spectrum of spondyloarthritis (SpA) encompasses a group of overlapping inflammatory rheumatic diseases: ankylosing spondylitis (extended to axial spondyloarthritis (axSpA) to include earlier and milder disease forms), psoriatic arthritis (PsA), enteropathic

## WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ There is a substantial overlap in manifestations between axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) as part of the spectrum of the spondyloarthritis.
- ⇒ Patients with PsA and axial involvement (axial PsA) are treated according to the recommendations for axSpA.

## WHAT THIS STUDY ADDS

- ⇒ Patients with axSpA and concomitant psoriasis differ substantially from those with axial PsA regarding genetics, demographics and clinical phenotype.
- ⇒ The differences persisted in HLA-B27 positive individuals.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ The findings suggest that axSpA and axial PsA might be distinct entities.
- ⇒ Treatment studies specifically dedicated to axial PsA need to be conducted as soon as a consensus is found on the definition of axial involvement in PsA.

SpA and reactive arthritis.<sup>1</sup> These disorders feature common musculoskeletal manifestations to differing degrees and with different emphases (inflammatory axial involvement at the level of the sacroiliac joints and the spine, proximal or peripheral arthritis, enthesitis and dactylitis). The diseases also share some extramusculoskeletal manifestations (EMM): uveitis, psoriasis and inflammatory bowel disease (IBD). The overlapping nature of the diseases within the SpA spectrum led to the development of classification criteria by the Assessment of SpondyloArthritis international Society (ASAS), which mainly differentiates between predominantly axial and predominantly peripheral manifestations.<sup>2 3</sup>

A patient with inflammatory axial involvement and psoriasis can be classified as having axSpA through the ASAS classification criteria<sup>2</sup> or having PsA according to the CLASSification for Psoriatic ARthritis (CASPAR) criteria.<sup>4</sup> The terminology used to describe axial involvement in PsA has been diverse: psoriatic spondylitis, psoriatic SpA and axial PsA, among others.<sup>5–7</sup> Moreover, there is no consensus on a definition of axial involvement in PsA.<sup>8</sup> Whether axSpA and axial PsA represent the same or different disorders remains controversial.<sup>9</sup> The suggestion that, in contrast to axSpA, axial PsA might respond to treatment with interleukin-23 inhibitors (IL-23i) has brought the issue into the spotlight.<sup>10–11</sup> Awaiting a consensus on the definition of axial PsA,<sup>8</sup> we compared the phenotype of patients with axial PsA versus axSpA in two different cohorts within a large national observational registry of patients with inflammatory rheumatic diseases (axSpA and PsA cohorts, respectively).

## METHODS

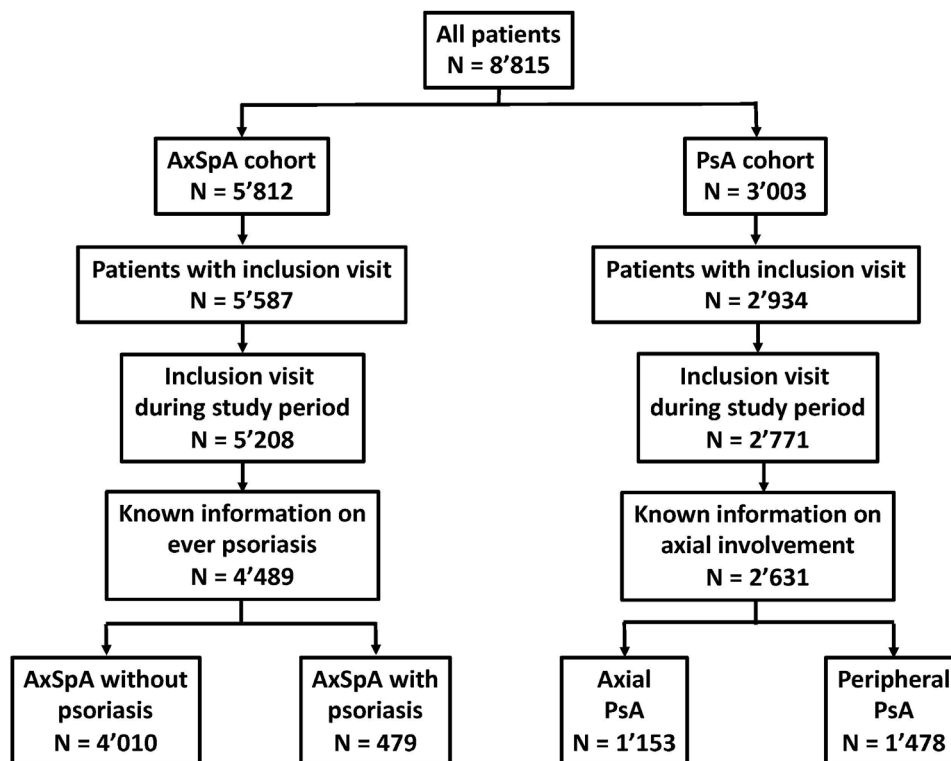
### Study population

The Swiss Clinical Quality Management (SCQM) Foundation initiated an ongoing cohort of patients diagnosed as having axSpA in 2005 and a parallel cohort of patients diagnosed as having PsA in 2006.<sup>12–13</sup> The primary aim of the registry is to provide direct feedback to the treating rheumatologist in private practice or a non-academic or academic institution on validated disease measures and assist with treating the respective disease to target. Criteria for inclusion in SCQM are a clinical diagnosis by the rheumatologist for the respective disease, informed consent for participation and ability to fill out questionnaires in one of the official Swiss languages (German, French or Italian). The individual items of the ASAS classification criteria are collected for the axSpA cohort and the items of the CASPAR classification criteria are collected for the PsA cohort.<sup>2–4</sup> The study represents a cross-sectional comparison of the two ongoing cohorts at the time-point of inclusion of each patient into the SCQM registry. Prior to 2006, the rheumatologists had no choice to include patients with inflammatory axial disease and concomitant psoriasis in either the axSpA cohort or the PsA cohort. Therefore, inclusions were only considered after initiation of the PsA cohort in January 2006 and up to the end of February 2023. Moreover, we excluded patients with missing data on the presence of psoriasis or axial involvement from the primary analyses. These patients were added to the comparison of the two cohorts in a sensitivity analysis. Assessment of patients with axSpA was performed according to the recommendations of ASAS.<sup>14</sup> Data on the Bath Ankylosing Spondylitis Disease Activity, Functional and Mobility Indices (BASDAI, BASFI and BASMI, respectively) as well as the Patient Assessment of Global Disease Activity were available for two-thirds of the axSpA population but only in a minority of patients with PsA, as this information was only collected in the PsA cohort from 2021. Information on the Physician Global

Assessment of Disease Activity, Short-Form 12 questions (SF-12) and the European Quality of Life with 5 dimensions questionnaire (EQ-5D) was collected since cohort initiation and was available in a comparable proportion of patients in both cohorts, as was information on C reactive protein (CRP) levels and human leucocyte antigen B27 (HLA-B27). Peripheral disease was assessed with regard to the previous or current presence of peripheral arthritis, previous or current presence of enthesitis (Maastricht Ankylosing Spondylitis Enthesitis Score (MASES), and ever dactylitis. While the 44-joint count was used in axSpA and the 66/68-joint count in PsA, the former was used for comparative analyses of both cohorts. The MASES score used was modified to include the proximal insertion of the plantar fasciae bilaterally. EMMs included the presence of ever uveitis, ever IBD and ever psoriasis, with information on current psoriatic involvement of skin and nails available only in the PsA cohort. Missing characteristics at the time-point of inclusion were mapped from visits closest to inclusion if within a range of 100 days (only 10 days for disease activity variables). Family history and information on HLA-B27 status were mapped from any visit. Medication start and stop dates were available for all conventional-synthetic, targeted-synthetic or biological disease-modifying antirheumatic drugs (cs/ts/bDMARDs). Specific data were available for tumour necrosis factor inhibitors (TNFi), interleukin-17 inhibitors (IL-17i), interleukin-23 inhibitors (IL-23i), Janus kinase inhibitors (JAKi) and phosphodiesterase-4 inhibitors. Data on nonsteroidal anti-inflammatory drugs (NSAIDs) were collected as yes/no. Written informed consent was obtained from all patients prior to inclusion into SCQM.

### Definition of axial involvement in the PsA cohort

Axial involvement was considered in the PsA cohort if the following question in the rheumatologist's questionnaire was answered with yes: 'Does your patient currently have or has he/she ever had axial involvement?' Additional information on axial involvement was derived from the manifestations tab, where the treating rheumatologist can indicate the presence of sacroiliitis and spinal involvement separately as either clinically and/or radiographically and/or by MRI. The grade or the symmetry of sacroiliitis and the exact features of spinal involvement on X-rays (eg, typical syndesmophytes vs coarse non-marginal syndesmophytes) are not collected.<sup>15</sup> When the respective imaging item is not reported, differentiation between 'imaging negative' or 'imaging not performed' is not possible. Data on back pain for at least 3 months and of IBP were collected independently of the question on axial involvement of SpA. However, the questionnaire did not include information regarding the localisation of back pain (cervical, thoracic or lumbar). Pelvis radiographs were collected in the axSpA cohort, but not in the PsA cohort. Central scoring of the sacroiliac joints according to the modified New York classification criteria performed at regular intervals as a service to the treating



**Figure 1** Disposition of patients in the axSpA and PsA SCQM cohorts, particularly with regard to axial and psoriatic involvement. axSpA, axial spondyloarthritis; PsA, psoriatic arthritis; SCQM, Swiss Clinical Quality Management.

rheumatologist was, therefore, only available in the axSpA population in patients with radiographs sent to SCQM or uploaded to the online database.

### Statistical analyses

R statistical software was used for the statistical analyses. Patient characteristics were compared using the Fisher's exact test for categorical variables and the Kruskal test for continuous variables. All tests were two-sided with the significance level set at 0.05.

## RESULTS

### Comparison of the two SCQM cohorts (axSpA vs PsA)

Patient disposition in the SCQM cohort is displayed in [figure 1](#). From 8815 patients (5812 axSpA and 3003 PsA) recruited into SCQM, 604 patients with axSpA and 232 patients with PsA were excluded, as their inclusion visit predated the initiation of the PsA cohort. Comparison of baseline characteristics at the time-point of recruitment into SCQM of the remaining 5208 patients with axSpA and 2771 patients with PsA is shown in [table 1](#). The proportion of women was higher and patients were older in PsA compared with axSpA. Axial symptoms, enthesitis, uveitis and IBD were more frequent in axSpA, while peripheral arthritis and dactylitis were more prevalent in PsA. Patient and physician global disease activity levels were higher in axSpA, paralleling a worse generic health status as assessed by the mental and the physical component summary scores of the SF-12 questionnaire, as well as a more impaired health-related quality of life. Regarding

medication, a higher proportion of patients with axSpA were on treatment with NSAIDs and with TNFi, while more patients with PsA were treated with IL-17i, IL-23i and tsDMARDs. In light of the higher percentage of patients with a history of peripheral arthritis in the PsA cohort, more patients were on treatment with csDMARDs in this group, compared with patients with axSpA. Similar results were found for the comparison of the two cohorts when only patients with available information on the presence or history of psoriasis and of axial involvement were considered (N=4489 for axSpA and N=2631 for PsA; [table 1](#)). The proportion of patients fulfilling the respective classification criteria was 75% for axSpA (ASAS) and 87% for PsA (CASPAR).

### Comparison of patients with axSpA with and without psoriasis

The proportion of patients with a history of or current psoriasis in the axSpA cohort was 11%. Comparison of characteristics of patients with axSpA without psoriasis (N=4010) and patients with axSpA with psoriasis (axSpA+pso) are shown in detail in [tables 2–5](#). While sex distribution was comparable between the two groups, HLA-B27 positivity was less prevalent in patients with psoriasis, leading to a slightly lower proportion of patients fulfilling the ASAS classification criteria in this group. Patients with AxSpA+pso were older and had longer symptom duration, despite a later onset of symptoms in comparison to patients without psoriasis ([table 2](#)). No differences between the groups could







**Table 2** Demographic and defining characteristics of patients with axSpA (without and with psoriasis) and PsA (with and without axial involvement)

Parameter	Axial spondyloarthritis				Psoriatic arthritis				P value A vs B	P value B vs C	P value C vs D
	A. AxSpA without psoriasis N=4010		B. AxSpA with psoriasis N=479		C. Axial psoriatic arthritis N=1153		D. Strictly peripheral psoriatic arthritis N=1478				
	N	N	N	N	N	N	N	N			
Female sex, N (%)	4010	1881 (46.9)	479	230 (48.0)	1153	588 (51.0)	1478	715 (48.4)	0.68	0.30	0.20
Age, years	4010	41.4 (12.7)	479	44.7 (12.4)	1153	48.6 (12.4)	1478	51.0 (12.6)	<0.001	<0.001	<0.001
Age at first symptoms, years	3892	30.5 (11.8)	469	32.6 (13.3)	1122	38.7 (13.6)	1415	42.3 (14.1)	0.002	<0.001	<0.001
Symptom duration, years	3892	10.9 (10.6)	469	12.1 (11.0)	1122	9.8 (9.6)	1415	8.6 (9.3)	0.01	<0.001	<0.001
Duration since start back pain, years	3274	8.9 (10.5)	366	10.1 (10.8)	611	9.8 (10.9)	124	10.2 (11.7)	0.01	0.96	<0.001
Diagnostic delay, years	3859	5.6 (7.7)	464	6.2 (8.3)	1114	4.5 (7.3)	1403	3.2 (6.4)	0.53	<0.001	<0.001
HLA-B27 positivity, N (%)	3596	2357 (65.5)	401	222 (55.4)	674	150 (22.3)	669	113 (16.9)	<0.001	<0.001	0.02
Family history axSpA, N (%)	3418	770 (22.5)	396	92 (23.2)	996	35 (3.5)	1269	20 (1.6)	0.80	<0.001	0.01
Family history PsA, N (%)	3418	30 (0.9)	396	21 (5.3)	996	140 (14.1)	1269	127 (10.8)	<0.001	<0.001	0.02
Family history psoriasis, N (%)	3418	147 (4.3)	396	89 (22.5)	996	367 (36.8)	1269	406 (32.0)	<0.001	<0.001	0.02
Family history other SpA, N (%)	3418	78 (2.3)	396	14 (3.5)	996	21 (2.1)	1269	17 (1.3)	0.17	0.18	0.21
Body mass index, kg/m <sup>2</sup>	3491	25.6 (4.7)	407	26.0 (4.8)	1012	26.9 (5.1)	1277	27.5 (5.6)	0.10	0.002	0.01
Obesity, N (%)	3491	555 (15.9)	407	79 (19.4)	1012	241 (23.8)	1277	342 (26.8)	0.19	0.01	0.13
Smoking status	3889		417		925		1162		0.001	0.001	0.03
Current		1076 (31.0)		140 (33.6)		229 (24.8)		262 (22.5)			
Former		863 (24.9)		131 (31.4)		285 (30.8)		423 (36.4)			
Never		1533 (44.2)		146 (35.0)		411 (44.4)		477 (41.0)			
ASAS axSpA classification pos.	3340	2541 (76.1)	393	278 (70.7)	-	-	-	-	0.02	-	-
CASPAR classification pos.	-	-	-	-	908	799 (88.0)	1259	1080 (85.8)	-	-	0.15

Except where indicated otherwise, values represent the mean and SD.

ASAS, Assessment in SpondyloArthritis international Society; axSpA, axial spondyloarthritis; CASPAR, CIASSification for Psoriatic ARthritis criteria; HLA-B27, human leucocyte antigen B27; PsA, psoriatic arthritis; SpA, spondyloarthritis.

**Table 3** Musculoskeletal and extramusculoskeletal clinical manifestations in patients with axSpA (without and with psoriasis) and PsA (with and without axial involvement)

Parameter	Axial spondyloarthritis N=4489				Psoriatic arthritis N=2631						
	A. AxSpA without psoriasis N=4010		B. AxSpA with psoriasis N=479		C. Axial psoriatic arthritis N=1153		D. Strictly peripheral psoriatic arthritis N=1478				
	N	N (%)	N	N (%)	N	N (%)	N	N (%)			
Back pain $\geq$ 3 months, N (%)	3874	3545 (91.5)	448	409 (91.3)	984	698 (70.9)	1279	158 (12.4)	0.95	<0.001	<0.001
Inflammatory back pain, N (%)	3730	2570 (68.9)	418	282 (67.5)	945	380 (40.2)	1272	33 (2.6)	0.59	<0.001	<0.001
Spine involvement ever (all modalities), N (%)	3771	3525 (93.5)	426	400 (93.9)	1093	993 (90.9)	1233	0 (0.0)	0.82	0.07	–
Clinical opinion, N	2244		281		570		0				
Radiographic assessment; including CT*, N	406		62		79		0				
MRI assessment*, N	969		123		161		0				
Other (eg, nuclear medicine imaging)*, N	28		4		15		0				
Sacroiliitis ever (all modalities), N (%)	3607	2785 (77.2)	406	314 (77.3)	842	468 (55.6)	899	0 (0.0)	1.00	<0.001	–
Clinical assessment, N	2308		274		386		0				
Radiographic assessment; including CT*, N	955		108		137		0				
MRI assessment*, N	1695		177		210		0				
Other (eg, nuclear medicine imaging)*, N	48		8		26		0				
Radiographic axSpA (central scoring)†	1660	1126 (67.8)	175	117 (66.9)	–	–	–	–	0.86	–	–
Dactylitis ever, N (%)	3999	336 (8.4)	475	87 (18.3)	1142	493 (43.2)	1458	753 (51.6)	<0.001	<0.001	<0.001
Peripheral arthritis ever, N (%)	4005	1774 (44.3)	477	277 (58.1)	1151	998 (86.7)	1475	1417 (96.1)	<0.001	<0.001	<0.001
Peripheral arthritis current, N (%)	3988	1283 (32.2)	477	201 (42.1)	1136	844 (74.3)	1467	1229 (83.8)	<0.001	<0.001	<0.001
Number of swollen joints (44-joint count)	3527	0.6 (2.1)	424	1.0 (2.4)	992	2.2 (3.8)	1292	2.7 (4.0)	<0.001	<0.001	<0.001
Coxitis current, N (%)	3835	372 (9.7)	456	49 (10.7)	1074	91 (8.5)	1347	38 (2.8)	0.53	0.19	<0.001
Enthesitis current, N (%)	3963	2271 (57.3)	464	279 (60.1)	1087	605 (55.7)	1360	521 (38.3)	0.27	0.12	<0.001
MASES	3837	1.9 (2.8)	435	2.4 (3.2)	518	2.1 (3.0)	712	1.0 (2.1)	0.01	0.31	<0.001
Uveitis ever, N (%)	3968	623 (15.7)	442	70 (15.8)	1049	65 (6.2)	1354	47 (3.5)	0.99	<0.001	0.001
Psoriasis ever, N (%)	4010	0 (0.0)	479	479 (100.0)	1150	1026 (89.2)	1472	1316 (89.5)	–	–	0.93
Inflammatory bowel disease ever, N (%)	3901	327 (8.4)	410	62 (15.1)	983	55 (5.6)	1270	22 (1.7)	<0.001	<0.001	<0.001

Except where indicated otherwise, values represent the mean and SD.  
 \*Information provided by the local rheumatologist with unknown total number of patients with imaging performed.  
 †Patients with pelvis radiographs sent to SCQM or uploaded to the SCQM database (only available for a subpopulation of the axSpA cohort).  
 axSpA, axial spondyloarthritis; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score, modified to include the insertion of the plantar fasciae; mNYc, radiographic criterion of the modified New York classification.

**Table 4** Disease activity, function and quality of life in patients with axSpA (without and with psoriasis) and PsA (with and without axial involvement)

Parameter	Axial spondyloarthritis N=4489				Psoriatic arthritis N=2631						
	A. AxSpA without psoriasis N=4010		B. AxSpA with psoriasis N=479		C. Axial psoriatic arthritis N=1153		D. Strictly peripheral psoriatic arthritis N=1478				
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)			
Elevated CRP level, N (%)	3586	1175 (32.8)	433	152 (35.1)	997	291 (29.2)	1256	372 (29.6)	0.36	0.03	0.86
CRP, mg/l, median (IQR)	3591	4.0 (1.2; 9.0)	434	5.0 (2.0; 9.0)	1022	5.0 (1.9; 8.0)	1292	5.0 (1.5; 8.0)	0.06	0.45	0.15
Patient global disease activity*	3151	4.8 (2.8)	354	5.2 (2.8)	144	4.5 (2.7)	154	3.3 (2.2)	0.03	0.02	<0.001
Physician global disease activity	3808	3.5 (2.3)	452	3.5 (2.2)	1092	3.7 (2.3)	1398	3.1 (2.2)	0.52	0.22	<0.001
BASDAI*	2866	4.5 (2.3)	346	4.9 (2.3)	172	5.1 (2.3)	132	4.5 (2.4)	0.01	0.34	0.04
BASDAI-1 (fatigue)	2898	5.2 (2.6)	347	5.5 (2.5)	178	5.5 (2.6)	137	4.9 (2.8)	0.10	0.83	0.07
BASDAI-2 (back pain)	2894	5.5 (2.8)	347	5.7 (2.9)	178	5.3 (2.9)	137	3.3 (3.2)	0.12	0.14	<0.001
BASDAI-3 (joint pain/swelling)	2890	3.5 (3.0)	347	4.0 (3.0)	175	5.2 (2.9)	137	5.3 (3.0)	0.001	<0.001	0.64
BASDAI-4 (tender areas)	2892	4.0 (3.1)	347	4.4 (3.1)	175	4.9 (3.1)	135	4.9 (3.3)	0.03	0.12	0.84
BASDAI-5 (stiffness intensity)	2892	4.9 (3.0)	347	5.3 (3.1)	178	5.2 (2.9)	137	4.6 (3.2)	0.01	0.52	0.07
BASDAI-6 (stiffness duration)	2892	3.9 (2.9)	346	4.3 (3.0)	178	4.4 (3.0)	134	3.7 (2.7)	0.04	0.59	0.03
ASDAS*	2667	2.8 (1.0)	305	3.0 (1.1)	32	2.9 (1.1)	10	2.5 (1.2)	0.01	0.64	0.28
BASFI*	2825	3.0 (2.5)	340	3.4 (2.5)	176	3.5 (2.7)	136	2.6 (2.5)	0.001	0.91	0.003
BASMI*	3432	1.8 (1.8)	382	2.2 (1.9)	102	1.7 (1.3)	65	1.7 (1.4)	<0.001	0.18	0.71
SF-12 physical component	2646	39.2 (10.3)	331	37.1 (10.5)	764	39.4 (10.8)	931	42.5 (10.5)	<0.001	0.001	<0.001
SF-12 mental component	2646	44.0 (11.4)	331	43.4 (11.6)	764	44.6 (11.6)	931	47.4 (10.8)	0.32	0.10	<0.001
EQ-5D	2794	63.4 (22.0)	323	61.1 (21.9)	579	65.3 (20.3)	745	72.1 (18.8)	0.09	0.01	<0.001

Except where indicated otherwise, values represent the mean and SD.

\*Only added to the assessment of PsA in early 2021.

ASDAS, Axial Spondyloarthritis Disease Activity Score using C reactive protein levels; axSpA, axial spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Mobility Index; CRP, C reactive protein; EQ-5D, European Quality of Life questionnaire 5 domains; SF-12, Short Form 12 questions.



**Table 5** Pharmacological treatment in patients with axSpA (without and with psoriasis) and PsA (with and without axial involvement)

Parameter	Axial spondyloarthritis N=4489						Psoriatic arthritis N=2631					
	A. AxSpA without psoriasis N=4010		B. AxSpA with psoriasis N=479		C. Axial psoriatic arthritis N=1153		D. Strictly peripheral psoriatic arthritis N=1478		P value A vs B	P value B vs C	P value C vs D	
	N	N (%)	N	N (%)	N	N (%)	N	N (%)				
History of TNFi, N (%)	4003	1567 (39.1)	478	182 (38.1)	1150	438 (38.1)	1478	475 (32.1)	0.69	1.00	0.002	
History of csDMARD, N (%)	4003	860 (21.5)	479	115 (24.0)	1150	672 (58.4)	1478	1050 (71.0)	0.23	<0.001	<0.001	
Current NSAID, N (%)	4010	3006 (75.0)	479	360 (75.2)	1153	771 (66.9)	1478	815 (55.1)	0.97	0.001	<0.001	
Current csDMARD, N (%)	4000	528 (13.2)	478	87 (18.2)	1149	494 (43.0)	1477	786 (53.2)	0.003	<0.001	<0.001	
Current systemic steroids, N (%)	4009	87 (2.2)	479	12 (2.5)	1153	83 (7.2)	1474	125 (8.5)	0.76	<0.001	0.26	
Current TNFi, N (%)	3999	1802 (45.1)	479	206 (43.0)	1150	530 (46.1)	1476	564 (38.2)	0.42	0.28	<0.001	
Current IL-17i, N (%)	4008	63 (1.6)	479	15 (3.1)	1150	57 (4.9)	1476	65 (4.4)	0.02	0.14	0.58	
Current IL-23i, N (%)	4009	5 (0.1)	477	1 (0.2)	1151	23 (2.0)	1478	33 (2.2)	1.00	0.01	0.78	
Current JAKi, N (%)	4010	6 (0.1)	479	0 (0.0)	1153	3 (0.3)	1477	10 (0.7)	0.85	0.63	0.22	
Current PDE4i, N (%)	4010	2 (0.0)	479	4 (0.8)	1152	33 (2.9)	1477	60 (4.1)	<0.001	0.02	0.12	

Except where indicated otherwise, values represent the mean and SD.

axSpA, axial spondyloarthritis; b/tsDMARD, biological or targeted-synthetic disease modifying antirheumatic drug; csDMARD, conventional synthetic disease modifying antirheumatic drug; IL-17i, interleukin-17 inhibitor; IL-23i, interleukin-23 inhibitor; JAKi, Janus kinase inhibitor; NSAID, nonsteroidal anti-inflammatory drug; PDE4i, phosphodiesterase-4 inhibitor; TNFi, tumour necrosis factor inhibitor.

be observed for axial involvement and uveitis, while a higher proportion of patients with axSpA+pso had peripheral musculoskeletal manifestations (table 3). Disease activity was higher, and function as well as spinal mobility was more severely impaired in patients with axSpA+pso (table 4). More patients in the axSpA+pso group were already treated with csDMARDs at inclusion, reflecting the higher prevalence of peripheral arthritis in this group (table 5).

### Patients with AxSpA with psoriasis versus axial PsA

Comparison of the axSpA+pso group (N=479) versus the axial PsA group (N=1153) is also shown in tables 2–5. The axial PsA group in SCQM is characterised by an older age at first symptoms, older age at inclusion, shorter diagnostic delay and shorter symptom duration, as well as by a significantly lower prevalence of HLA-B27 positivity (22% vs 55.4% in axSpA+pso,  $p<0.001$ ; table 2). Significant differences between the two populations were also observed for the family history of axSpA, PsA and psoriasis, respectively (table 2). Body mass index as well as the prevalence of obesity was higher in axSpA+pso than in axial PsA. The following differences regarding axial involvement were detected: the proportion of patients with back pain  $\geq 3$  months, with IBP, as well as with ever sacroiliitis was significantly lower in axial PsA (table 3). Differences were also identified regarding peripheral musculoskeletal involvement: 43% vs 18% ever dactylitis, 87% vs 58% ever peripheral arthritis, for axial PsA vs axSpA+pso, respectively (table 3). In contrast, we did not detect differences in enthesitis between the two groups. Regarding disease activity assessments, physician global disease activity and the height of CRP elevation were comparable between the two groups, as were the parameters developed for axSpA (BASDAI and ASDAS), the latter being, however, only available in a minority of patients with axial PsA (table 4). Differences in the pharmacological treatment of the two groups reflected the respective differences in musculoskeletal involvement, with NSAIDs being more frequently used in axSpA+pso, while csDMARDs and steroids being more frequently used in axial PsA (table 5).

To investigate whether the differences in phenotype between axSpA+pso and axial PsA might be due to the distinct prevalence of HLA-B27 positivity, we compared the two groups after stratification for HLA-B27 (table 6). In HLA-B27-positive patients, as well as in HLA-B27-negative patients, differences between axSpA+pso and axial PsA persisted and encompassed a later onset of symptoms, an older age, a less important axial and a more frequent peripheral involvement in axial PsA (table 6). Against an HLA-B27 background, a positive family history of psoriasis was found in only 17% of patients with axSpA+pso vs 32% of patients with axial PsA ( $p=0.003$ ). A family history of axSpA was more often mentioned in axSpA+pso and a family history of PsA was more often found in axial PsA than vice versa (table 6).

### Axial versus peripheral PsA

Finally, we compared patients with axial versus strictly peripheral disease in the PsA cohort (N=1153 and N=1478, respectively, tables 2–5). Fulfilment of CASPAR classification criteria (88% vs 86%,  $p=0.15$ ) and sex distribution (female sex: 51% vs 48%,  $p=0.20$ ) were comparable between the two groups (table 2). Back pain of at least 3 months duration was found in 12% of patients with peripheral PsA, indicating that the rheumatologists had interpreted the back pain as not due to PsA in this group (table 3). Only a minority of patients in this group complained of IBP (2.6%). The majority of patients with peripheral PsA had a history of peripheral arthritis (96%) and 84% had current arthritis with a higher mean number of swollen joints compared with patients with axial PsA. Enthesitis was, however, less prevalent and the MASES lower in peripheral than in axial PsA (table 3).

### DISCUSSION

Our analysis of 4489 patients with axSpA and 1153 patients with axial PsA from a large national observational registry adds important data to earlier investigations to support the notion of two distinct entities.<sup>16–19</sup> Differences in inclusion criteria between the studies should be highlighted. In an analysis from Bath featuring 400 cases axSpA and PsA, only patients with radiographic disease were included.<sup>16</sup> Moreover, ankylosing spondylitis patients with psoriasis and patients with axial PsA were pooled together. Feld *et al* presented 1243 cases with axSpA and axial PsA identified by definite radiographic sacroiliitis from separate AS and PsA Clinics in Toronto.<sup>17</sup> The study from Madrid, by Benavent *et al*, included 352 cases of patients with axSpA and axial PsA, encompassing both the non-radiographic and the radiographic spectrum, but initiating treatment with bDMARDs.<sup>18</sup> Our analysis had a design comparable with the recent study from the German RABBIT-SpA registry of 1787 patients with axSpA and axial PsA.<sup>19</sup> Patients were diagnosed as having either axSpA or PsA by their treating rheumatologist and were included in the respective cohorts based on clinical grounds and imaging. Both our study and the study by Regierer *et al* focused on patients with axSpA+pso versus patients with axial PsA.<sup>19</sup> We have chosen the expert opinion of the treating rheumatologist based on all data available to define axial involvement in axial PsA, which was summarised by his/her confirmation that the patient with PsA had axial involvement. Additional validation of the definition came from information on sacroiliac joint or spinal involvement clinically or on imaging. The proportion of patients with PsA fulfilling the CASPAR classification criteria<sup>4</sup> was comparable in axial versus peripheral PsA.

In contrast to patients with axSpA+pso, patients with axial PsA have a significantly later symptom onset, a lower prevalence of back pain and sacroiliitis and a significantly higher prevalence of peripheral arthritis and dactylitis, but not enthesitis. Regarding the EMM, uveitis and IBD were more

**Table 6** Comparison of patients with axSpA and concomitant psoriasis vs axial PsA after stratification by HLA-B27 status

Parameter	AxSpA+pso N=222		Axial PsA N=150		AxSpA+pso N=179		Axial PsA N=524		P value
	HLA-B27 positive		HLA-B27 negative		HLA-B27 positive		HLA-B27 negative		
	N	N	N	N	N	N	N	N	
Female sex, N (%)	222	94 (42.3)	150	67 (44.7)	179	98 (54.7)	524	241 (54.0)	0.93
Age, years	222	41.2 (12.0)	150	45.9 (12.7)	179	46.0 (11.6)	524	47.8 (11.9)	0.05
Age at first symptoms, years	215	28.1 (11.0)	145	35.7 (13.6)	177	35.4 (13.5)	514	38.6 (13.1)	0.004
Symptom duration, years	215	13.2 (11.4)	145	10.0 (10.1)	177	10.6 (10.6)	514	9.2 (9.4)	0.18
Duration since start back pain, y	177	10.7 (11.4)	88	9.1 (11.5)	142	9.6 (10.5)	289	9.5 (10.6)	0.83
Family history axSpA, N (%)	192	64 (33.3)	126	12 (9.5)	147	19 (12.9)	456	13 (2.9)	<0.001
Family history PsA, N (%)	192	5 (2.6)	126	22 (17.5)	147	6 (4.1)	456	68 (14.9)	0.001
Family history psoriasis, N (%)	192	32 (16.7)	126	40 (31.7)	147	37 (25.2)	456	170 (37.3)	0.01
Back pain≥3 months, N (%)	213	200 (93.9)	131	102 (77.9)	173	157 (90.8)	453	327 (72.2)	<0.001
Inflammatory back pain, N (%)	196	142 (72.4)	127	59 (46.5)	163	107 (65.6)	435	182 (41.8)	<0.001
Sacroiliitis, clinically, N (%)	215	136 (63.3)	138	67 (48.6)	172	98 (57.0)	409	179 (36.5)	<0.001
Spine involvement, clinically, N (%)	216	135 (62.5)	138	69 (50.0)	174	106 (60.9)	492	277 (56.3)	0.33
Dactylitis ever, N (%)	222	39 (17.6)	150	53 (35.3)	177	34 (19.2)	521	229 (44.0)	<0.001
Arthritis current, N (%)	222	78 (35.1)	146	100 (68.5)	179	77 (43.0)	517	381 (73.7)	<0.001
Coxitis current, N (%)	215	29 (13.5)	137	15 (10.9)	172	16 (9.3)	490	43 (8.8)	0.96
Enthesitis current, N (%)	221	133 (60.2)	138	75 (54.3)	173	110 (63.6)	499	286 (57.3)	0.18
Uveitis ever, N (%)	209	51 (24.4)	137	29 (21.2)	167	14 (8.4)	481	18 (3.7)	0.03
IBD ever, N (%)	201	32 (15.9)	127	5 (3.9)	154	23 (14.9)	447	25 (5.6)	<0.001
Elevated CRP level, N (%)	203	79 (38.9)	123	45 (36.6)	164	52 (31.7)	462	133 (28.8)	0.55
CRP, mg/l, median (IQR)	203	5.0 (2.0; 11.0)	128	5.0 (2.0; 9.0)	164	5.0 (2.0; 8.0)	473	5.0 (1.8; 8.0)	0.95
Patient global disease activity	172	5.0 (2.9)	28	4.4 (2.9)	132	5.5 (2.7)	56	5.0 (2.9)	0.26
Physician global disease activity	212	3.3 (2.3)	141	3.3 (2.0)	166	3.8 (2.1)	494	3.8 (2.3)	0.94
BASDAI	167	4.7 (2.3)	33	4.3 (2.6)	128	5.1 (2.4)	72	5.4 (2.4)	0.34
ASDAS	148	2.9 (1.1)	16	2.7 (1.0)	116	3.0 (1.0)	12	3.3 (1.0)	0.36
BASFI	161	3.2 (2.6)	34	2.9 (2.7)	128	3.6 (2.5)	75	3.7 (2.7)	0.84
BASMI	190	2.1 (2.0)	20	1.6 (1.7)	138	2.3 (1.8)	42	1.9 (1.3)	0.40
SF-12 physical component	153	37.9 (11.0)	110	40.4 (10.9)	122	36.6 (10.6)	344	38.8 (10.8)	0.06
SF-12 mental component	153	44.2 (11.7)	110	46.7 (10.7)	122	42.4 (11.2)	344	43.6 (11.3)	0.21
EQ-5D	154	63.5 (21.7)	88	67.5 (20.0)	122	58.9 (22.3)	263	61.9 (21.3)	0.32

Continued

Table 6 Continued

Parameter	AxSpA+pso N=222		Axial PsA N=150		AxSpA+pso N=179		Axial PsA N=524		P value
	HLA-B27 positive	HLA-B27 negative	HLA-B27 positive	HLA-B27 negative	HLA-B27 positive	HLA-B27 negative	HLA-B27 positive	HLA-B27 negative	
Current csDMARD, N (%)	222 30 (13.5)	150 60 (40.0)	150 60 (40.0)	178 34 (19.1)	524 226 (43.1)	<0.001			<0.001
Current TNFi, N (%)	222 96 (43.2)	149 73 (49.0)	149 73 (49.0)	179 82 (45.8)	524 253 (48.2)	0.36			0.63
Current IL-17i, N (%)	222 8 (3.6)	150 11 (7.3)	150 11 (7.3)	179 5 (2.8)	524 20 (3.8)	0.17			0.69

Except where indicated otherwise, values represent the mean and SD. ASDAS, Axial Spondyloarthritis Disease Activity Score using C reactive protein levels; axSpA, axial spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Mobility Index; b/tsDMARD, biological or targeted-synthetic disease modifying antirheumatic drug; CRP, C reactive protein; csDMARD, conventional synthetic disease modifying antirheumatic drug; EQ-5D, European Quality of Life questionnaire 5 domains; IBD, inflammatory bowel disease; IL-17i, interleukin-17 inhibitor; IL-23i, interleukin-23 inhibitor; JAKi, Janus kinase inhibitor; NSAID, nonsteroidal anti-inflammatory drug; PDE4i, phosphodiesterase-4 inhibitor; PsA, psoriatic arthritis; pso, psoriasis; SF-12, Short Form 12 questions; TNFi, tumour necrosis factor inhibitor.

frequently seen in axSpA+pso than in axial PsA. In general, we confirm the differences between axial PsA and axSpA with concomitant psoriasis found in earlier studies.<sup>17 19</sup> Some of the mentioned differences are known to be associated with the presence of HLA-B27 positivity,<sup>20 21</sup> which was lower in axial PsA. However, HLA-B27 status did not fully explain the differences between patients with axSpA+pso and patients with axial PsA, as the amplitude of the differences remained after stratification for this genetic marker. However, HLA-B27 status might influence the radiographic phenotype in axial involvement of both axSpA and axial PsA, as demonstrated in a recent study.<sup>22</sup> Indeed, HLA-B27 positive patients had—in contrast to HLA-B27 negative patients—more severe radiographic damage, more marginal syndesmophytes and more frequent symmetrical syndesmophytes in a recent analysis. As radiographs of the axial skeleton were not collected in the PsA cohort in SCQM, we could not address this issue.

Might circular reasoning explain the clinical differences between the two entities, as the decision to include a patient with axial involvement in either the axSpA or the PsA cohort might be influenced by age or additional peripheral features? Although this issue might partly be valid, some important findings point to additional genetic differences between axSpA+pso and axial PsA, besides HLA-B27. First, the proportion of patients with a positive family history of axSpA on the one hand and the proportion of those with a positive family history of PsA and psoriasis on the other hand differed significantly between the two disorders, even in HLA-B27 positive individuals. Second, the presence of obesity was significantly higher in axial PsA than in axSpA+pso. A large-scale cross-trait genetic correlation analysis of psoriasis with multiple diseases has recently shown a significant association of psoriasis with obesity.<sup>23</sup> Taken together, these findings might indicate differences in underlying genetic correlations between axSpA and PsA.

Strengths of our analysis include the large number of patients with axSpA+pso and axial PsA across the whole spectrum of radiographic involvement recruited in a real-life observational registry by rheumatologists from private practices and secondary and tertiary institutions.<sup>24</sup> Patients in both cohorts were assessed according to comparable protocols by the same rheumatologists. We also acknowledge important limitations. There is no validated definition of axial PsA and we have chosen the expert opinion of the treating rheumatologist with regard to axial involvement. Additional information was available regarding back pain of at least 3 months duration, IBP as well as the imaging results that might have influenced the decision. Bath Indices for disease activity and severity of axial involvement were only available for a minority of patients in the PsA cohort. Imaging data were not collected to confirm the pattern of X-ray and MRI involvement indicated by the rheumatologist and/or to indicate alternative reasons for back pain (eg, degenerative changes).

In conclusion, we confirm demographic, clinical and genetic differences between axSpA and axial PsA, even when axSpA with concomitant psoriasis is used for the comparison.



**Twitter** Raphael Micheroli @ramicheroli

**Acknowledgements** We thank all rheumatologists and their patients for participation to SCQM and the entire SCQM staff for the continuous support. A list of rheumatology practices and hospitals contributing to the SCQM registries can be found at: <http://www.scqm.ch/institutions>.

**Contributors** AC and RM conceptualised and designed the study. AC, BM, KB, MSN, PE and RM substantially contributed to the acquisition of clinical data. AG, AB, SK and AS processed the data and performed the statistical analyses. All authors contributed to the interpretation of the data. AC wrote the article, and all coauthors revised the manuscript critically for important intellectual content. All authors agreed on the final content of the submitted manuscript. AC accepts full responsibility for the work and the conduct of the analyses, had access to the data, and controlled the decision to publish.

**Funding** This study was financially supported by Eli Lilly. Eli Lilly had no role in the study design or in the collection, analysis or interpretation of the data, the writing of the manuscript or the decision to submit the manuscript for publication. Publication of this article was not contingent on approval by Eli Lilly.

**Competing interests** The SCQM foundation is supported by the Swiss Society of Rheumatology and by Abbvie, AstraZeneca, Biogen, iQone, Janssen, Lilly, Merck Sharp & Dohme, Novartis, Pfizer, Samsung Bioepis, Sandoz. AC received honoraria for lectures or presentations from AbbVie, Merck Sharp & Dohme and Novartis. AG and SK are employees of SCQM and part of their salary in relation to statistical work performed for this study was financed through a research grant from Eli Lilly to SCQM (see funding). AS received consulting fees from Pfizer and support for attending meetings from Gilead. BM received speaking fees from Janssen, Eli Lilly, Novartis and Pfizer, support for attending meetings from Janssen and Pfizer and a research grant from Celgene. MSN received consulting and/or speaking fees from Abbvie, Eli Lilly, Janssen, Novartis and Pfizer, a research grant from Novartis. PE received financial support from UCB for attending a meeting. RM received honoraria for lectures or presentations from Abbvie, Eli Lilly, Janssen, Gilead and Pfizer. AB and KB declare they have no conflicts of interest.

**Patient consent for publication** Not applicable.

**Ethics approval** This study involves human participants and was approved by The Ethics committee of the Canton of Zurich (BASEC 2022-00272). Participants gave informed consent to participate in the study before taking part.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data may be obtained from a third party and are not publicly available. Restrictions apply to the availability of these data. Data are owned by a third party, the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) foundation. Data may be obtained after approval and permission from the license holder (SCQM). Contact information for data requests: [scqm@hin.ch](mailto:scqm@hin.ch).

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#### ORCID iDs

Adrian Ciurea <http://orcid.org/0000-0002-7870-7132>

Michael J Nissen <http://orcid.org/0000-0002-6326-1764>

Raphael Micheroli <http://orcid.org/0000-0002-8918-7304>

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