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Alberto Cauli

Psoriatic Arthritis:
Patient burden, diagnosis and therapeutics.

Overview *on patient burden of disease and current unmet needs* (except therapeutic).

Definition of PsA

- Inflammatory arthritis
- Associated with psoriasis
- Usually negative for rheumatoid factor and anti-CCP
- Associated features:
    - Spondylitis,
    - Enthesitis,
    - Dactylitis,
    - Iritis
    - Mucous membrane ulcers
    - Urethritis
    - Other extra-articular features of SpA.

Moll JM, Wright V. *Semin Arthritis Rheum* 1973;3:55–78

Epidemiology

- Affects Caucasians more than other races
- 30–50 years of age, can occur earlier
- Familial aggregation, 5-10 x increased risk in 1st degree relatives of patients with PsA
- Female/Male ratio 1:1 (except axial M>F)
- Prevalence:
  - Range from 6% to 42% of psoriasis patients (psoriasis prevalence in general population 2% to 3%)
  - Estimates range from 0.04% (Faroe Islands) to 0.1% (Mayo Clinic) of general population

Zachariae H et al. Am J Cli Dermatol 2003; 4:441-7.

Onset of disease

In 75% of cases skin psoriasis precedes arthritis

In 15% of cases the onset of skin and joint disease is at the same time

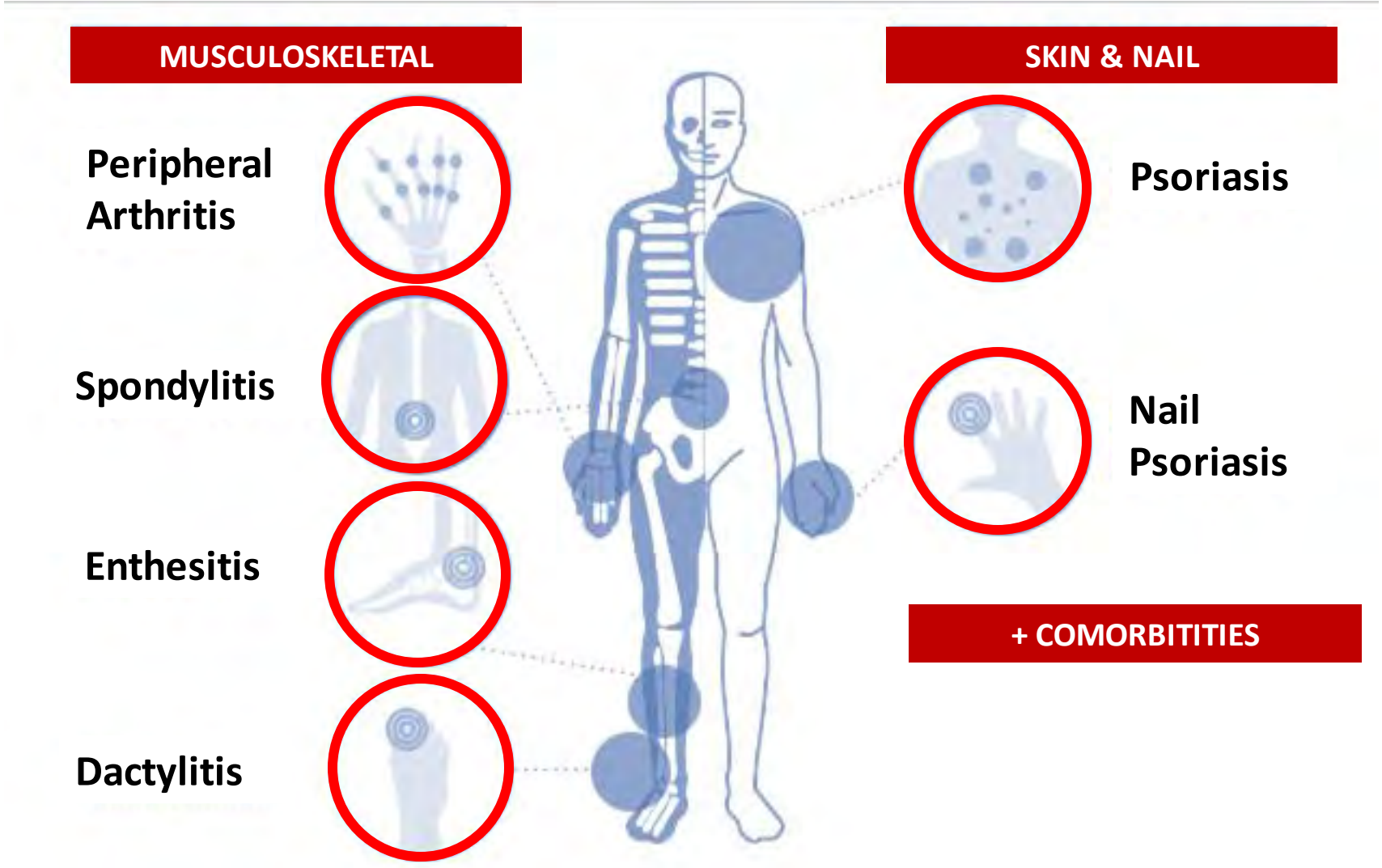
In 10% of cases arthritis precedes psoriasis

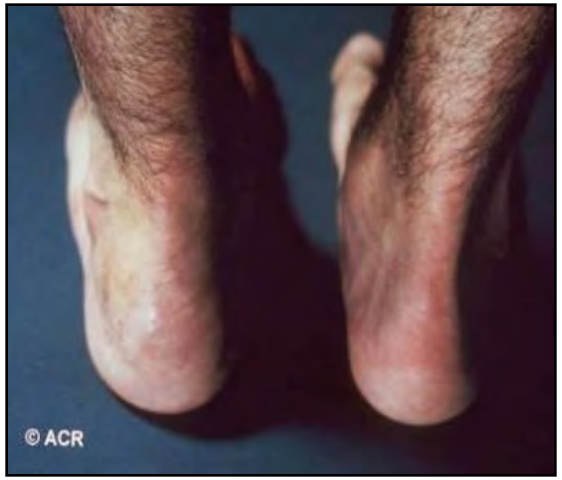
Swelling, stiffness, pain and tenderness of peripheral joints and surrounding soft tissue. Inflammatory back pain in axial involvement.

No pattern of psoriasis associated with arthritis

Gladman DD. *Rheum Dis Clin North Am* 1992;18:247–56

Psoriatic Arthritis (PsA): a multifaced disease

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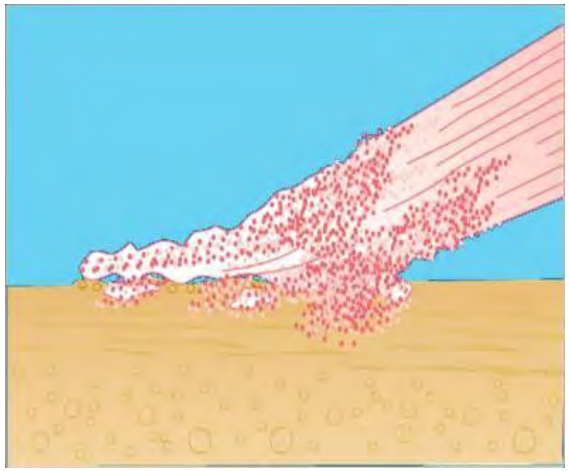


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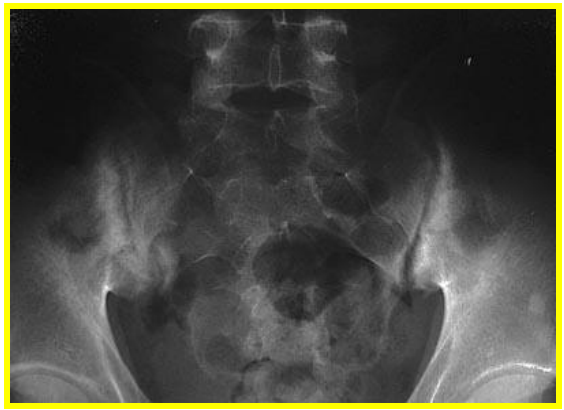
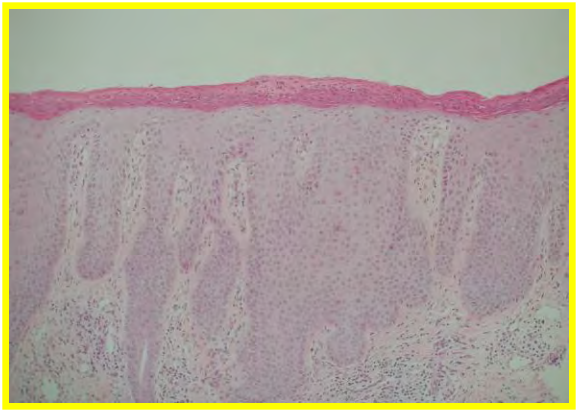
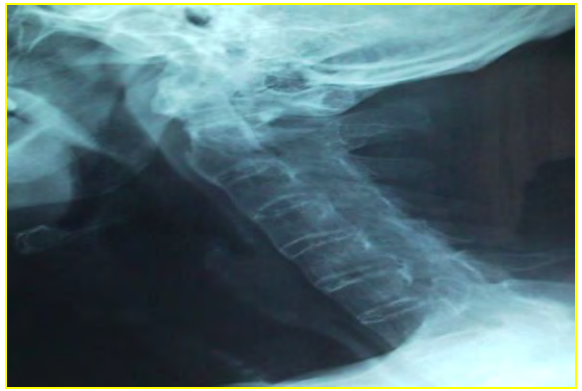
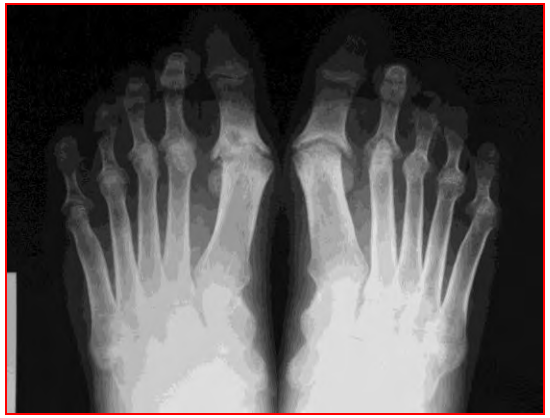
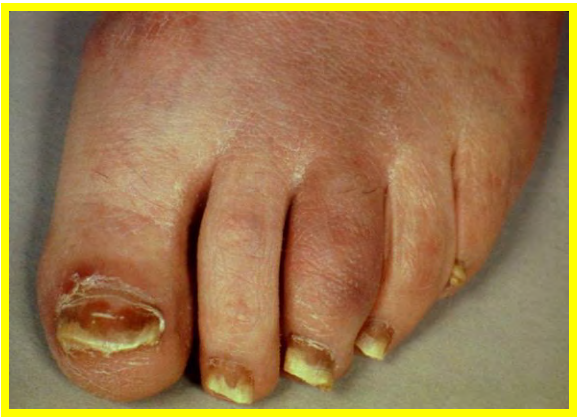
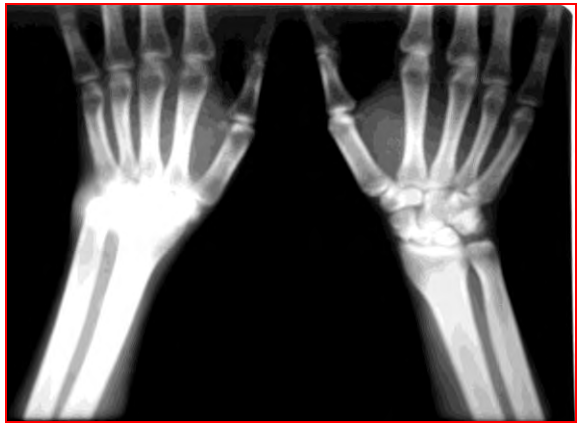






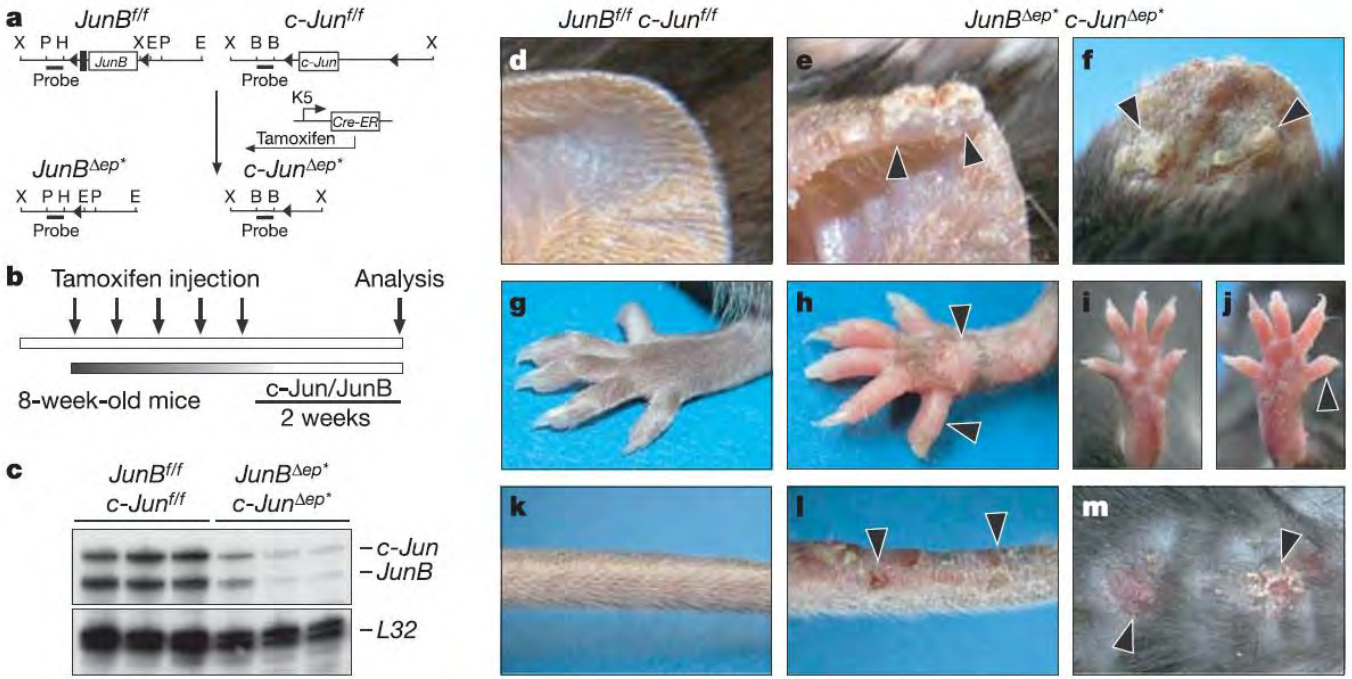


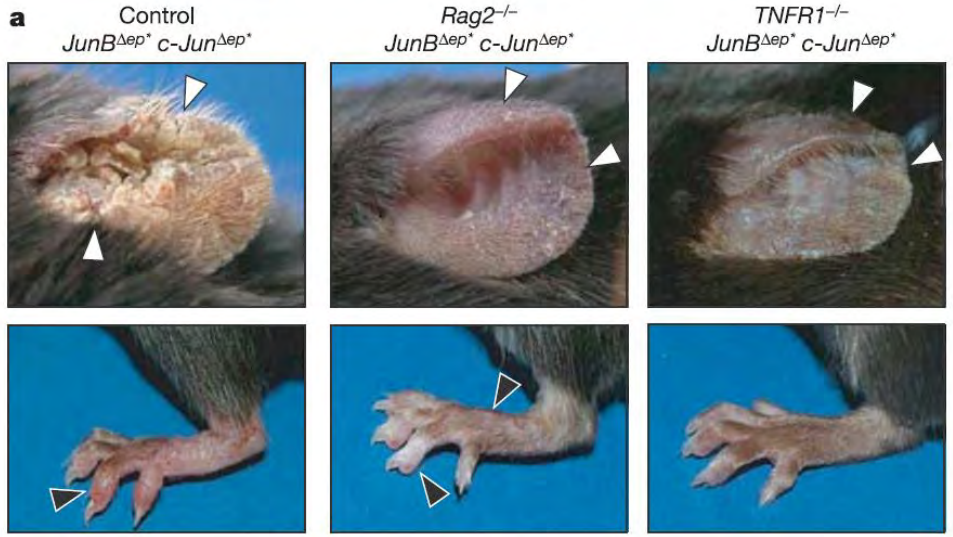




Psoriasis-like skin disease and arthritis caused by inducible epidermal deletion of Jun proteins

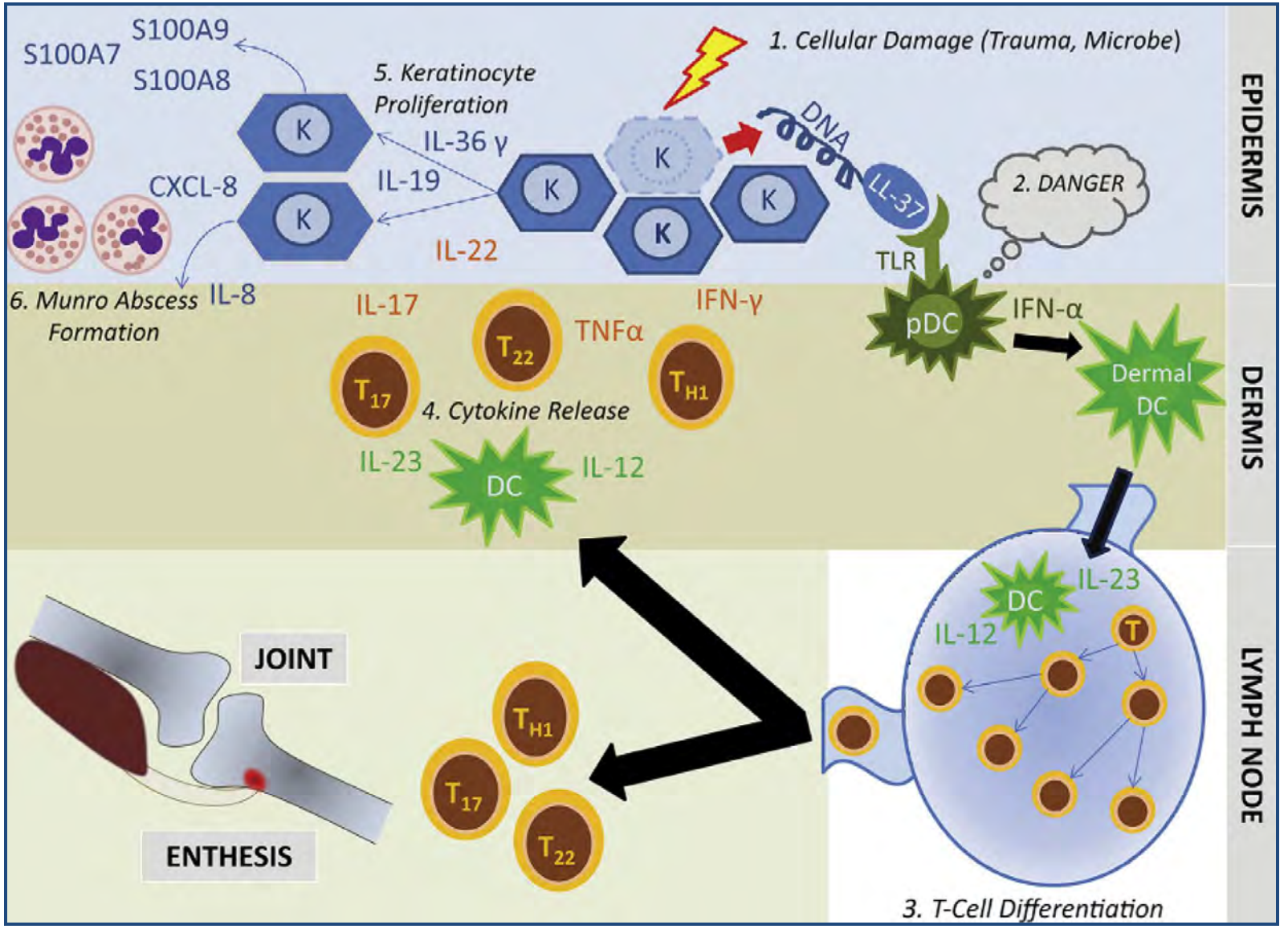
Rainer Zenz[1], Robert Eferl[1], Lukas Kenner[1], Lore Florin[2], Lars Hummerich[3], Denis Mehic[4,5], Harald Scheuch[1], Peter Angel[2], Erwin Tschachler[4,5] & Erwin F. Wagner[1]





Zenz R et al Nature 2005

Relationship between skin and joint disease



Ritchlin Chypothesis

Patient Global Assessment in Psoriatic Arthritis: A Multicenter GRAPPA and OMERACT Study

ALBERTO CAULI, DAFNA D. GLADMAN, ALESSANDRO MATHIEU, IGNAZIO OLIVIERI, GIOVANNI PORRU, PAUL P. TAK, CLAUDIA SARDU, ILONA UJFALUSSY, RAFFAELE SCARPA, ANTONIO MARCHESONI, WILLIAM J. TAYLOR, ANTONIO SPADARO, JOSE L. FERNÀNDEZ-SUEIRO, CARLO SALVARANI, JOACHIM R. KALDEN, ENNIO LUBRANO, SUELI CARNEIRO, FRANCESCA DESIATI, JOHN A. FLYNN, SALVATORE D'ANGELO, ALESSANDRA VACCA, ARNO W.R. VAN KUIJK, MARIA GRAZIA CATANOSO, MATHIAS GRUENKE, ROSARIO PELUSO, WENDY J. PARSONS, NICOLA FERRARA, PAOLO CONTU, PHILIP S. HELLIWELL, and PHILIP J. MEASE; for the GRAPPA 3PPsA Study Group

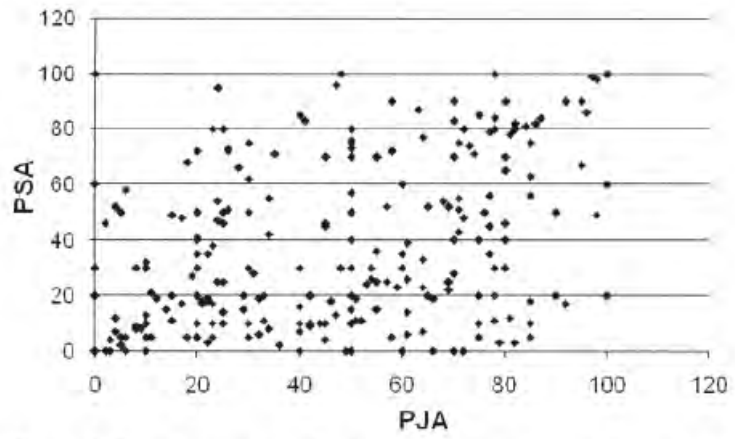
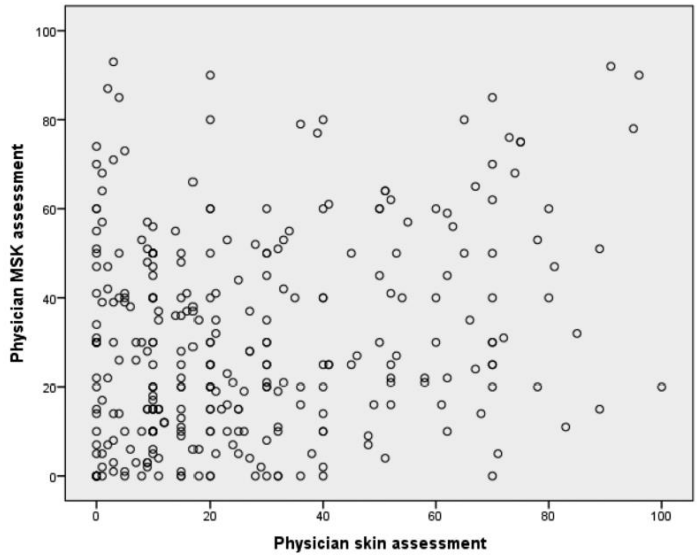


Figure 1. Patient perception of joint disease versus patient perception of skin disease. A scattered pattern is clearly visible.

Cauli et al J Rheumatol. 2011

Physician's Global Assessment in Psoriatic Arthritis: A Multicenter GRAPPA Study

Alberto Cauli, Dafna D. Gladman, Alessandro Mathieu, Ignazio Olivieri, Giovanni Porru, Paul P. Tak, Claudia Sardu, Raffaele Scarpa, Antonio Marchesoni, William J. Taylor, Carlo Salvarani, Joachim Kalden, Ennio Lubrano, Sueli Carneiro, Matteo Piga, Alberto Floris, Francesca Desiati, John A. Flynn, Salvatore D'Angelo, Arno W.R. van Kuijk, Maria Grazia Catanoso, Francesco Caso, Paolo Contu, Ilona Ujfalussy, Philip S. Helliwell, and Philip J. Mease, for the GRAPPA 3PPsA Study Group



Cauli et al J Rheumatol. 2018

ARD

Psoriasis, psoriatic arthritis and increased risk of incident Crohn's disease in US women

Wen-Qing Li, Jia-Li Han, Andrew T Chan and Abrar A Qureshi

*Ann Rheum Dis*2013 72: 1200-1205 originally published online August 31, 2012

Table 4 The relative risk of Crohn's Disease by diagnosis of psoriasis with or without psoriatic arthritis

Psoriasis	Person-years	Cases	Age-adjusted RR	Multivariate-adjusted RR*
Nurse's Health Study				
Crohn's disease				
No psoriasis	911944	66	1.00	1.00
Psoriasis	17070	5	4.07 (1.64 to 10.09)	3.80 (1.53 to 9.48)
Psoriasis/psoriatic arthritis	2021	1	6.76 (0.94 to 48.80)	5.94 (0.82 to 43.15)
Nurse's Health Study II				
Crohn's disease				
No psoriasis	1490002	108	1.00	1.00
Psoriasis	24890	6	3.50 (1.54 to 7.98)	3.25 (1.43 to 7.43)
Psoriasis/psoriatic arthritis	3640	2	8.70 (2.14 to 35.32)	6.87 (1.67 to 28.17)
Nurse's Health Study/Nurse's Health Study II				
CD				
No psoriasis	2401946	174	1.00	1.00
Psoriasis	41960	11	3.74 (2.03 to 6.89)	3.49 (1.89 to 6.44)
Psoriasis/psoriatic arthritis	5661	3	7.99 (2.55 to 25.08)	6.54 (2.07 to 20.65)
Ulcerative colitis				
No psoriasis	2399440	236	1.00	1.00
Psoriasis	25569	4	1.73 (0.43 to 6.97)	1.60 (0.39 to 6.65)

*Adjusted for age, body mass index (<18.5, 18.5–24.9, 25–29.9, ≥30 kg/m^2), smoking (never, past, current with 1–14, 15–24, ≥25 cigs/day), alcohol drinking (no, <4.9, 5.0–9.9 or ≥10.0 g/d), physical activity (<3, 3.0–8.9, 9.0–17.9, 18.0–26.9 or ≥27.0 metabolic equivalent hours/week), post menopausal hormone (premenopausal, never, past or current use), oral contraceptive (never, past or current use), aspirin (never, past or current use), and non-aspirin, non-steroidal anti-inflammatory drugs (never, past or current use).
CD, Crohn's Disease; RR, relative risk.

ARD

Prevalence and characteristics of uveitis in the spondyloarthropathies: a systematic literature review

N Zeboulon, M Dougados and L Gossec

*Ann Rheum Dis*2008 67: 955-959 originally published online October 25, 2007

Table 1 Prevalence of uveitis by type of spondyloarthritis (SpA)

Type of SpA	No of patients (No of articles)	Prevalence of uveitis (%) Mean (SD)	Disease duration (years) Mean (SD)
All SpA	29 877 (126)	32.7 (0.5)	17.7 (1.0)
Ankylosing spondylitis	12 768 (65)	33.2 (0.8)	17.0 (1.0)
Psoriatic arthritis	1341 (10)	25.1 (2.3)	17.4 (1.0)
Arthritis associated with IBD	453 (3)	36.9 (4.4)	22.0 (10.0)
Reactive arthritis	516 (9)	25.6 (3.8)	5.8 (0.6)
Undifferentiated SpA	532 (9)	13.2 (2.9)	5.8 (0.7)

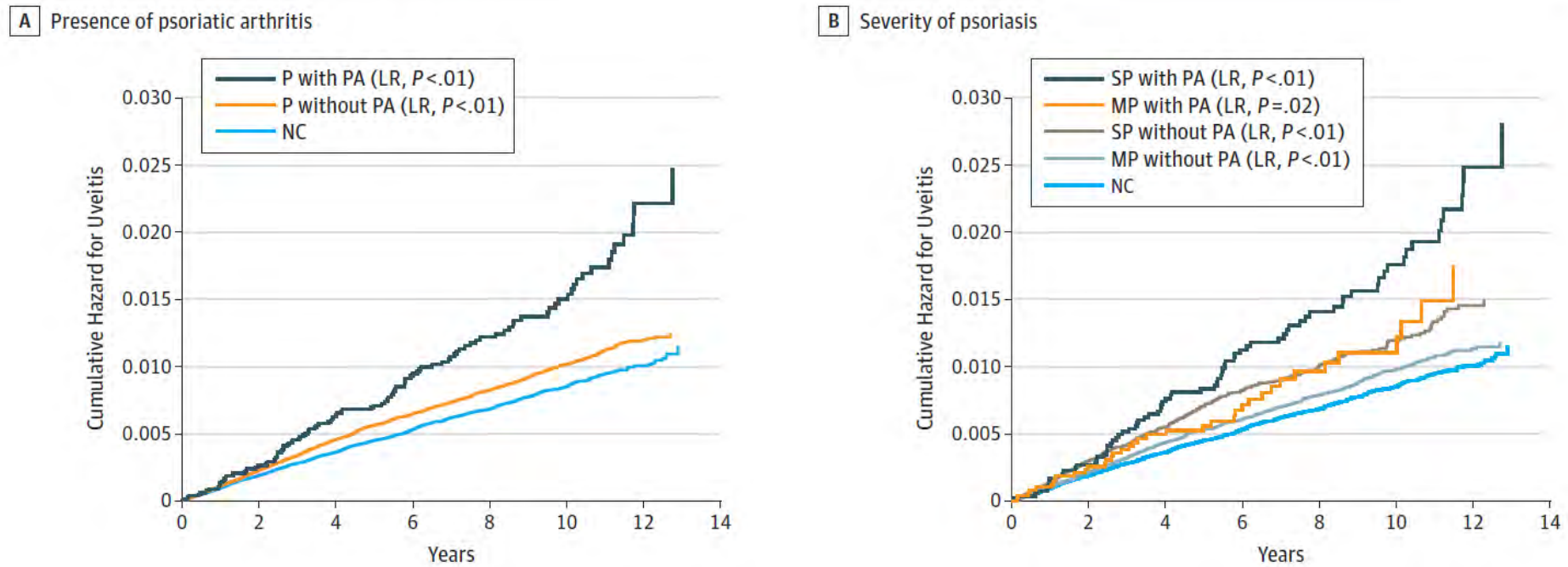
IBD, inflammatory bowel disease.

JAMA Ophthalmology | Original Investigation

Risk of Uveitis Among People With Psoriasis
A Nationwide Cohort Study

Ching-Chi Chi, MD, MMS, DPhil; Tao-Hsin Tung, PhD; Jui Wang, MPH; Yu-Sheng Lin, MD; Yu-Fen Chen, MSN; Tsui-Kan Hsu, MD, MPH; Shu-Hui Wang, MD, MS

Figure 2. Cumulative Incidence Curves for Uveitis



ROLE OF OBESITY

- Obesity, or overabundance of adipose tissue, is an inflammatory state characterized by a type 1 immune response.
- Adipocyte produce adipokines such as Resistin and Leptin (but also IL-6 and TNF-α)
- Leptin inhibits T-regulatory cells, promotes naive T cells and NK proliferation, monocytes proliferation, macrophage production TNF-α , IL-6 and IL-12, increase neutrophil chemotaxis. Leptin deficient mice die by infection.
- Obesity as a risk factor for PsV (odd ratio 2.23) and PsA
- Weight loss improve response to anti-TNFα treatment

Versini M et al. Autoimmun Rev 2014;13:981-1000

Cardiovascular morbidity in psoriatic arthritis

D D Gladman,[1] M Ang,[1] L Su,[2] B D M Tom,[2] C T Schentag,[1] V T Farewell[2]

Table 2 Standardised prevalence ratio of CVD events

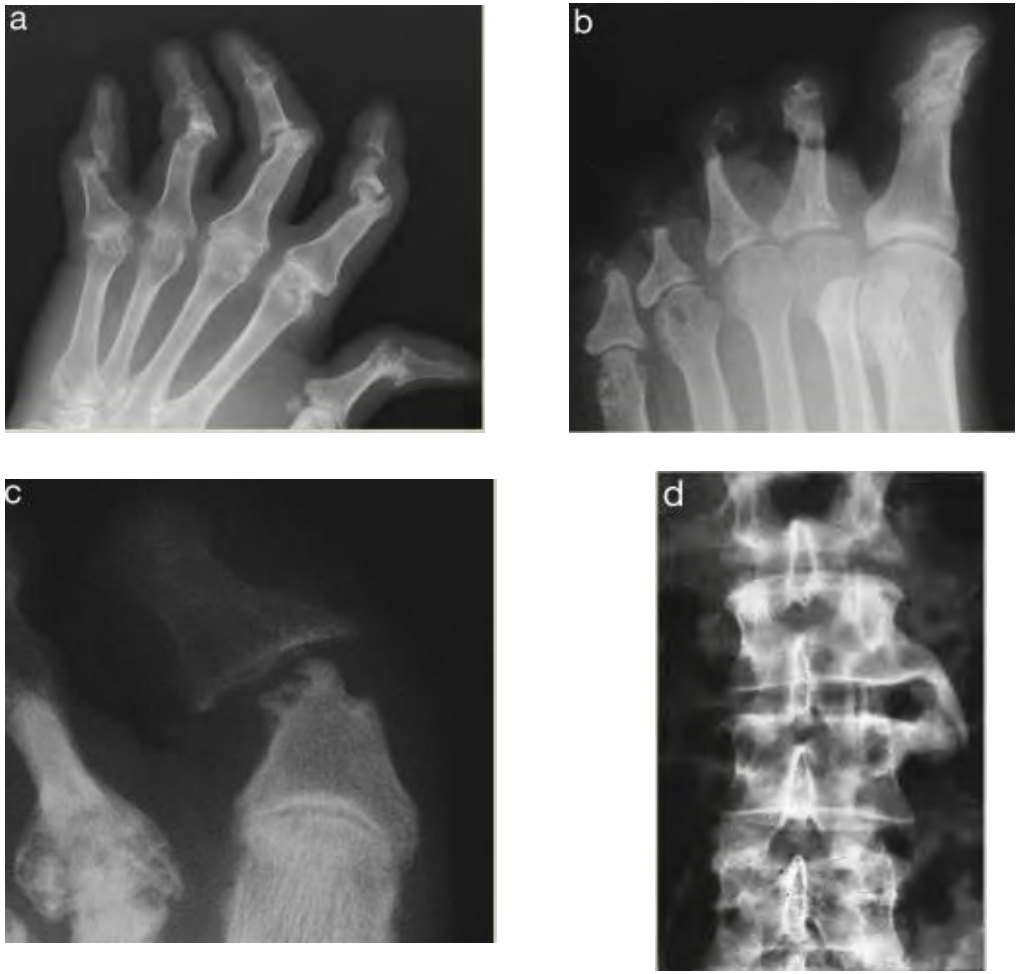
CVD events	SPR*	LCL	UCL	p Value
Hypertension	1.90	1.59	2.27	<0.01
Cerebrovascular accident	0.91	0.34	2.43	0.85
Myocardial infarction	2.57	1.73	3.80	<0.01
Angina	1.97	1.24	3.12	<0.01
Congestive heart failure	1.19	0.50	2.86	0.69

*Time range: 1 January 2000 to 31 December 2001; reference rates calculated for Ontario, 2000–1 CCHS, separately by gender and age where relevant.
CCHS, Canadian Community Health Survey; CVD, cardiovascular disease; LCL, lower 95% confidence limit; SPR, standardised prevalence ratio; UCL, upper 95% confidence limit.

Ann Rheum Dis 2009;**68**:1131–1135.

PsA is a potentially progressive disease, that may result in…

Joint damage accrual



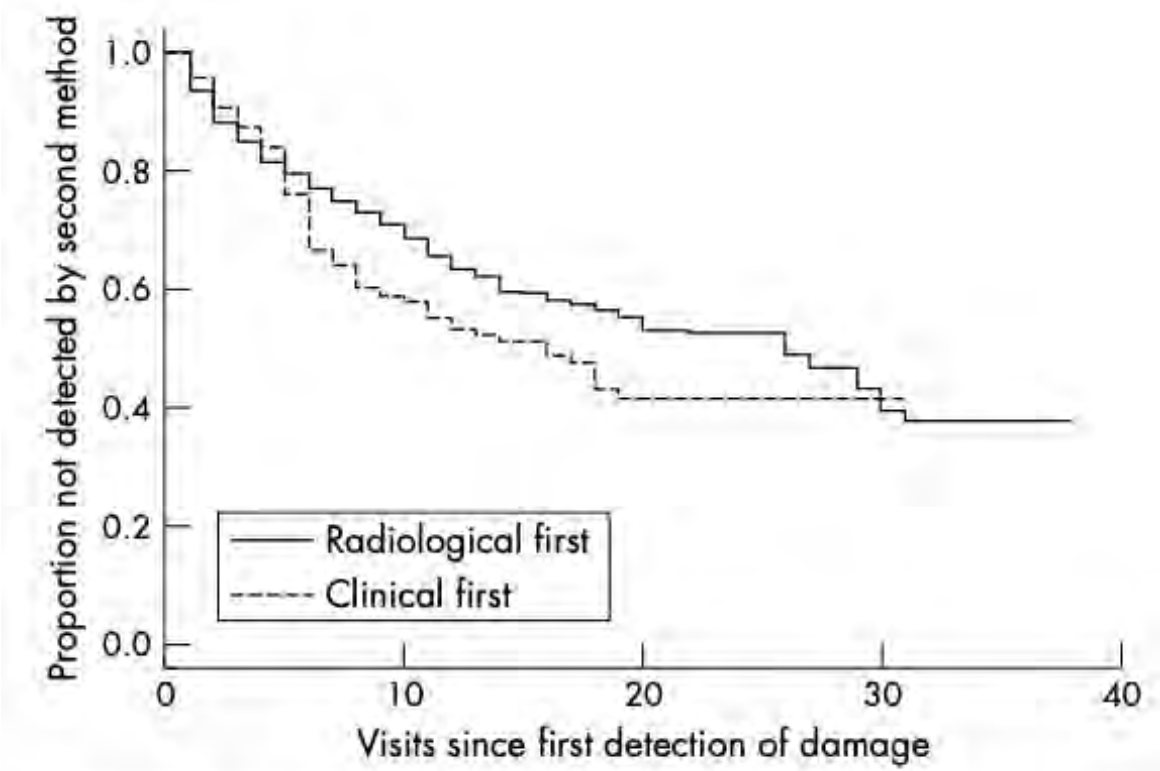


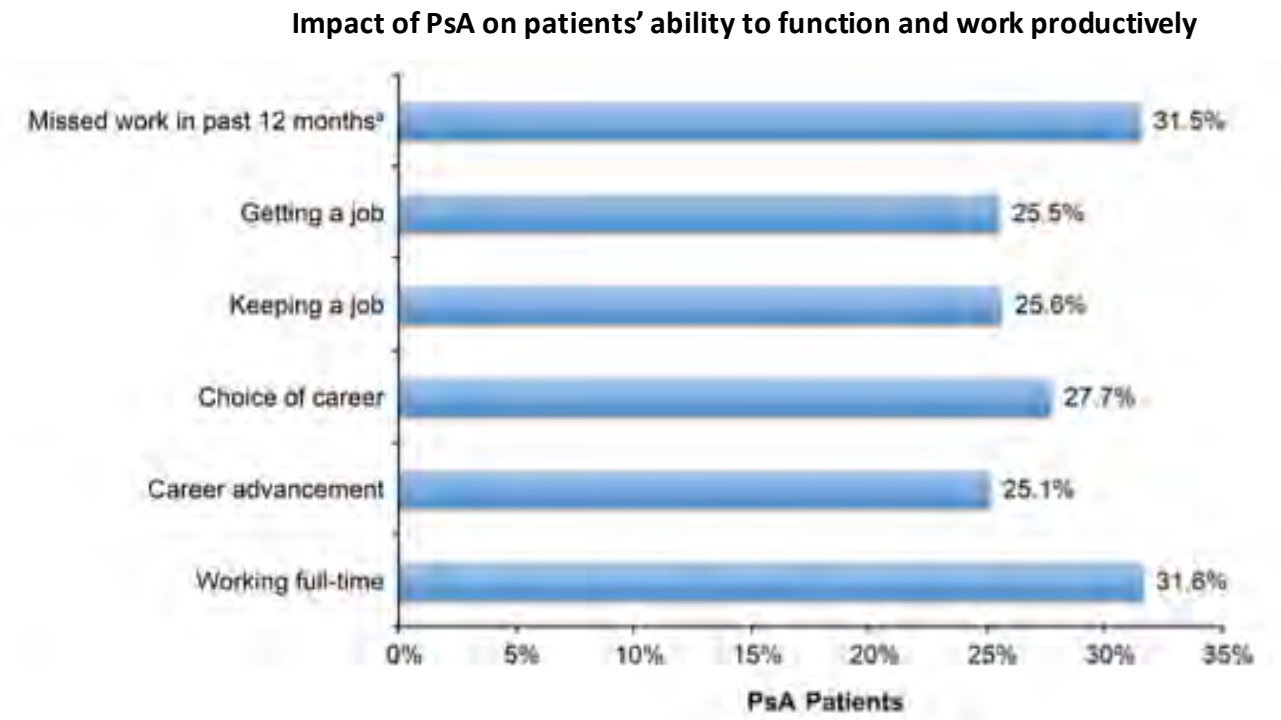
Figure 2 Survival of damage-free joints over time (in visits) in a psoriatic arthritis clinic.

(1) Siannis F et al. Ann Rheum Dis 2006;65:478–481 (2) images from Jadon DR et al. Medicine 2022;50:167-172

PsA is a potentially progressive disease, that may result in…

Development of disability

Impaired work ability (socioeconomic costs)



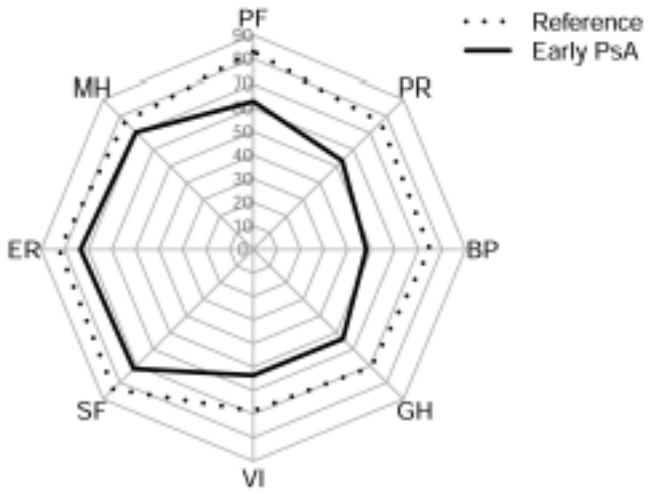
Proportion of patients who responded with yes; all other responses represent the proportion of patients reporting 'a lot' or 'some' impact of PsA

Kavanaugh A, et al. Rheumatol Ther. 2016;3:91-102

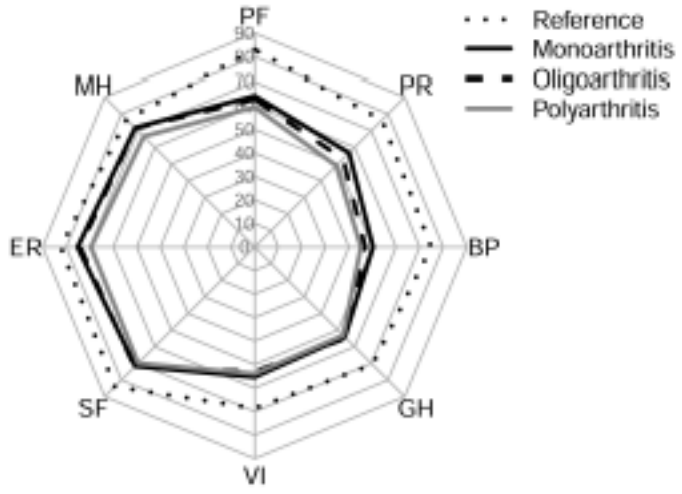
PsA is a potentially progressive disease, that may result in…

Impairment of Quality of Life

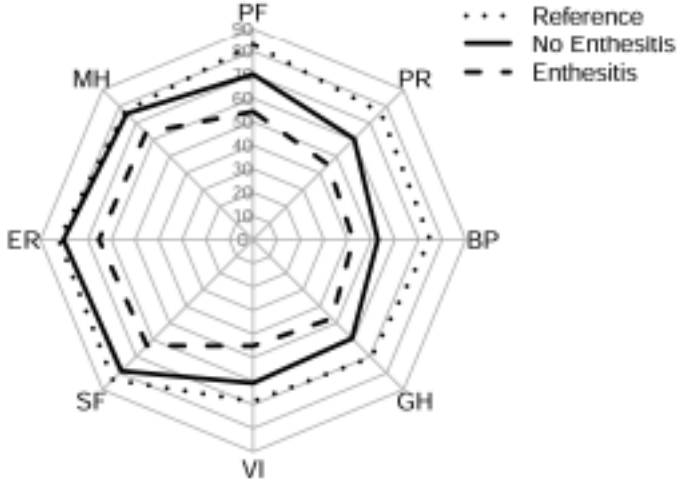
All patients



Arthritis subgroups



Enthesitis subgroups



Health-related quality of life measured by these domains of the SF-36:

- physical functioning (PF),
- physical role functioning (PR),
- bodily pain (BP),
- general health (GH),
- vitality (VI),
- social functioning (SF),
- emotional role functioning (ER),
- and mental health (MH).

	PCS (Component Summary)		MCS (Mental Component Summary)	
	β	95% CI	**β**	95%CI
Age, yrs	−0.05	−0.12 to 0.01	1.3	−6.03 to 8.63
Sex (male vs female)	**−2.39**	**−4.24 to −0.55**	**−292**	**−499 to −85**
Swollen joint count (66)	−0.07	−0.37 to 0.23	27	−6 to 61
Tender joint count (68)	**−0.25**	**−0.44 to −0.05**	**−38**	**−59 to −16**
No. enthesitis locations	**−0.84**	**−1.25 to −0.43**	**−38**	**−83 to 7**
Dactylitis (no vs yes)	−0.97	−3.63 to 1.69	104	−195 to 402
PASI	−0.12	−0.36 to 0.11	−16	−43 to 10
Chronic back pain (no vs yes)	**−5.33**	**−9.56 to −1.1**	**−298**	**−580 to −16**

Wervers K et al. J Rheumatol 2018;45:1526-1531

Do patients with psoriatic arthritis who present early fare better than those presenting later in the disease?

Dafna D Gladman,[1] Arane Thavaneswaran,[2] Vinod Chandran,[1] Richard J Cook[3]

Results of different multivariate analysis models on disease duration as predictor for progression of clinical joint damage in patients with PsA (stratifed according disease duration)

Duration of disease at first visit	No of patients	Relative rate of joint damage progression (95% CI)	p Value
1–2 years vs <1 year	212	1.53 (0.99 to 2.36)	0.05
2–4 years vs <1 year	248	1.70 (1.11 to 2.62)	0.01
5–9 years vs <1 year	201	1.83 (1.16 to 2.88)	0.009
10–20 years vs <1 year	204	1.83 (1.14 to 2.96)	0.01
>20 years vs <1 year	86	2.96 (1.64 to 5.34)	0.0003

Ann Rheum Dis 2011;70:2152–2154.

CONCISE REPORT

Smoking and delay to diagnosis are associated with poorer functional outcome in psoriatic arthritis

William Tillett,[1] Deepak Jadon,[1] Gavin Shaddick,[2] Charlotte Cavill,[3] Eleanor Korendowych,[1] Corinne S de Vries,[4] Neil McHugh[1,4]

Summary of associations with HAQ score at a minimum of 10 years' PsA disease duration (235 pts)

Variable	Proportion (%)	Effect on HAQ* (median disease duration 13 years)	SE	p Value	95% CI
Baseline†		0.09	0.140	0.51	(−0.18 to 0.37)
Male sex	52.8				
Female sex	47.2	0.39	0.095	<0.01	(0.20 to 0.57)
<50 years of age at diagnosis	77.9				
>50 years of age at diagnosis*	22.1	0.27	0.121	0.03	(0.03 to 0.51)
<1 year symptom duration prior to diagnosis	69.4				
>1 year symptom duration prior to diagnosis*	30.6	0.22	0.102	0.03	(0.02 to 0.42)
Never smoked	43.0				
Smoker (current or ever)	57.0	0.23	0.097	0.02	(0.04 to 0.42)
Never had DMARD or anti-TNF	16.2				
History of DMARD use (ever)	60.0	0.26	0.135	0.06	(−0.01 to 0.52)
History of anti-TNF use (ever)	23.8	0.63	0.154	<0.01	(0.32 to 0.93)

*Effect on HAQ is the difference from baseline, associated with the variable adjusted for calendar effect using a smoothing spline.
†Baseline is the estimated HAQ score for when all variables are zero, that is, male gender, ≤50 years of age, diagnosis in year of symptom, non-smoker, no history of DMARD or anti-TNF.

Ann Rheum Dis 2013;72:1358–1361

EXTENDED REPORT

Diagnostic delay of more than 6 months contributes to poor radiographic and functional outcome in psoriatic arthritis

Factors associated with the delayed rheumatological consultation of >6 mths

	Univariate model			Multivariate model		
	OR	95% CI	p Value	OR	95% CI	p Value
Low education status	1.66	0.84 to 3.2	0.14			
Oligoarthritis	0.44	0.18 to 1.10	0.08			
PsA duration	1.04	1.01 to 1.07	0.009			
Deformed joints	2.28	1.35 to 3.85	0.002			
Number of deformed joints	1.06	1.01 to 1.10	0.006			
DMARDs/TNFi free	0.42	0.21 to 0.85	0.01			
No. of DMARDs/TNFi failures	1.47	1.11 to 1.95	0.007			
Erosions	4.58	2.5 to 8.2	<0.001	4.25	2.32 to 7.99	<0.001
Osteolysis	3.6	1.3 to 9.5	0.01			
Sacroiliitis	2.28	1.17 to 4.44	0.01			
Arthritis mutilans	10.6	1.4 to 80.6	0.02			
PCS.SF-36	0.99	0.97 to 1.02	0.73			
MCS.SF-36	1.01	0.99 to 1.03	0.15			
HAQ	2.17	1.30 to 3.61	0.003	2.20	1.29 to 3.74	0.004

DMARDs, disease-modifying antirheumatic drugs; HAQ, Health Assessment Questionnaire; MCS.SF-36, mental health factors of quality of life; PCS.SF-36, physical health factors of quality of life; PsA, psoriatic arthritis.

Haroon M et al. Ann Rheum Dis 2015;74:1045–1050.

The main challenges for early diagnosis of PsA are:

- Diagnostic and classification criteria
- Differential diagnosis
- Influence of sociodemographic factors, such as sex and gender
- Biomarkers
- Screening tools for PsA in psoriasis patients

CASPAR Criteria

Taylor W, et al. A&R 2006;54:2665-73

Inflammatory musculoskeletal disease (joint, spine, or entheseal) With 3 or more of the following:		
1. Evidence of psoriasis (one of a, b, c)	a. Current psoriasis*	*Psoriatic skin or scalp disease present today as judged by a dermatologist or rheumatologist*
	b. Personal history of psoriasis	*A history of psoriasis that may be obtained from patient, family doctor, dermatologist or rheumatologist*
	c. Family history of psoriasis	*A history of psoriasis in a first or second degree relative according to patient report*
2. Psoriatic nail dystrophy		*Typical psoriatic nail dystrophy including onycholysis, pitting and hyperkeratosis observed on current physical examination*
3. A negative test for rheumatoid factor		*By any method except latex but preferably by ELISA or nephelometry, according to the local laboratory reference range*
4. Dactylitis either a or b	a. Current Dactylitis	*Swelling of an entire digit*
	b. History of Dactylitis	*Recorded by a rheumatologist*
5. Radiological evidence of juxta-articular new bone formation		*Ill-defined ossification near joint margins (but excluding osteophyte formation) on plain xrays of hand or foot*

Specificity 98.7%, sensitivity 91.4%. *Current psoriasis scores 2, others 1.

NEWS & VIEWS

SPONDYLOARTHRITIS

CASPAR criteria in early psoriatic arthritis

Vinod Chandran

The performance of the CASPAR criteria, which are known to have high specificity and sensitivity in classifying patients with long-standing psoriatic arthritis, has now been evaluated in early disease. Whereas the findings are likely to boost clinical research, implications for daily practice—and diagnosis—are less certain.

Chandran, V. *Nat. Rev. Rheumatol.* **8**, 503–504 (2012); published online 24 July 2012; doi:10.1038/nrrheum.2012.121

Previous studies have tested the sensitivity of these criteria in early PsA, reporting values ranging from 77.3 to 99.1%.3,4 However, these studies did not include a control group of patients with other inflammatory arthritides; therefore, specificity was not estimated.

Chandran, V. *Nat. Rev. Rheumatol.* 8, 503–504 (2012);

Sensitivity and Specificity of the Classification of Psoriatic Arthritis Criteria in Early Psoriatic Arthritis

Laura C. Coates,[1] Philip G. Conaghan,[1] Paul Emery,[1] Michael J. Green,[2] Gamal Ibrahim,[3] Helen MacIver,[3] and Philip S. Helliwell[1]

The CASPAR Study Group and Moll and Wright criteria were applied to patients with early PsA (<24 months symptom duration) and to control patients with other new-onset inflammatory arthritides.

Criteria	Score	Sensitivity	Specificity
Moll and Wright	Positive	80.2	99.1
CASPAR Study Group criteria score			
≥1		100	42.3
≥2		99.1	94.6
≥3		87.4	99.1
≥4		42.3	100
≥5		15.3	100

* CASPAR = Classification of Psoriatic Arthritis.

Coates LC.Arthritis Rheum 2012 Oct;64(10):3150-5

PsA: an inflammatory disease with several differential diagnoses

Clinical and imaging features that may help differentiate psoriatic arthritis from osteoarthritis, rheumatoid arthritis and gout.

Feature	OA	RA	Gout	PsA
Erosion type	absent	Marginal	Uncommon; erosion with overhanging margins in tophaceous gout	Marginal and Para marginal in proximal plate, marginal periostitis at DIP "mouse ear" appearance
Joint involved	DIP, PIP, CMC	All, DIP not involved	DIP less common	DIP classically involved
Periarticular osteoporosis	Uncommon	Frequent	Uncommon	Uncommon; lack of periarticular osteoporosis described as characteristic
Ankylosis	Rare	Rare	Rare	Frequent and characteristic
Periostitis	Rare	Rare	Uncommon	Frequent
Symmetry	Common	Common	Uncommon	Less common
Axial involvement	Common but non-inflammatory	Not involved except for atlanto-axial involvement	Rare	Common
Dactylitis	Uncommon	Uncommon	Rare	Frequent
Enthesitis	Enthesopathy common	Uncommon	Uncommon	Frequent
Skin lesions	Uncommon	Uncommon	Uncommon	Defining feature
Nail lesions	Uncommon	Not involved	Not involved	Frequent

OA: Osteoarthritis, RA: Rheumatoid arthritis, IP: Interphalangeal joint, CMC: Carpometacarpal joint, DIP: Distal interphalangeal joint.
Modified from Gladman *et al* [21].

Rida MA, et al. Clinical Immunology 214 (2020) 108390

Axial Involment in Psoriatic Arthritis (AXIS)

- Expert agreed to develop data driven criteria for axial involvement in PsA
- GRAPPA/ASAS project
- 50 centers across 20 countries
- Extensive clinical and imaging evaluation (MRI spine and hips, Xray hips, cervical and lumbar spine)
- Local assessment vs central assessment

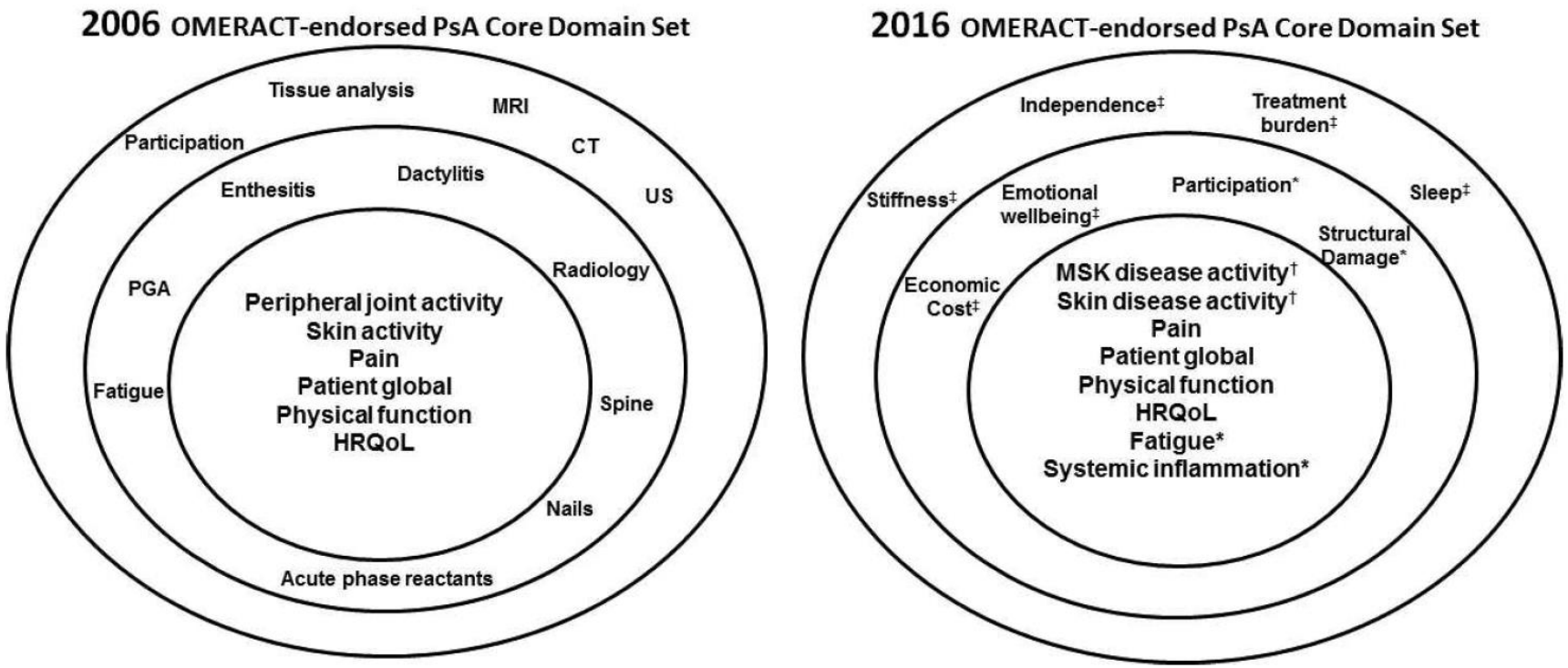
The main objectives of the planned study are

1. to determine the frequency of axial involvement in patients with PsA (based on local and central assessments) in the studied patient population;
2. to identify the frequency of active inflammatory and structural changes on imaging (MRI and radiographs) suggestive of axial involvement (SIJ and spine) in PsA; and
3. to identify factors (clinical, laboratory, imaging) associated with the presence of axial involvement in PsA, which will be determined based on the local and central assessments.

Development of classification criteria for axPsA

Poddubnyy et al Therp Adv Musk Dis 2021

Defining Outcome Measures for Psoriatic Arthritis: A Report from the GRAPPA-OMERACT Working Group



GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

Ogdie A J Rheumatol 2017

Domains and instruments

Alberto Cauli

Table 23.4 Domains of PsA and main instruments in the assessment

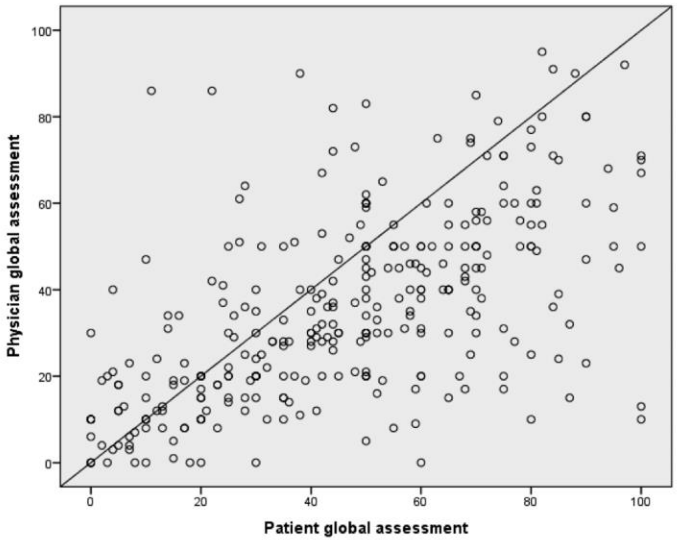
Core set domains	Instruments
Peripheral joints	Tender and swollen joint counts (68/66)
Skin	Psoriasis Activity and Severity Index (PASI) Physician Global Assessment (static/dynamic) Target lesion assessment Body Surface Area (BSA) PGA of skin activity (VAS skin) Psoriasis Symptom Inventory (PSI)
Patient global	Patient Global Assessment (VAS skin + joint)
Pain	VAS pain
Physical function	Health Assessment Questionnaire (HAQ or modified HAQ) Short Form-36 (SF-36)
Health related quality of life	PsA Quality of Life (PsAQoL) Dermatology Life Quality Index (DLQI)
Outer circle domains	
Spinal	Schober test, finger to floor, spine lateral flexion, chest expansion, tragus to wall, cervical rotation. BASMI (summary of five measurements) BASFI BASDAI
Dactylitis	Count of dactylitis digits Leeds Dactylitis Index (LDI)
Enthesitis	Mander Enthesitis Index (MEI) Spondyloarthritis Research Consortium of Canada (SPARCC) Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) Leeds Enthesitis Index (LEI)
Nails	Nail Psoriasis Severity Index (NAPSI)
Fatigue	Functional Assessment of Chronic Illness Therapy (FACIT)
Physician global	Physician Global assessment (VAS skin + joint)
Radiology	Sharp/Van der Heijde score of hand and feet PASRI
Acute phase reactants	Erithrocyte sedimentation rate (ESR) C-reactive protein (CRP)
Research agenda domains	
Participation	To be determined
Tissue analysis	To be determined
Imaging (MRI, US, CT)	PsA Magnetic Resonance Image Scoring System (PsAMRIS) Glasgow Ultrasound Enthesitis Scoring System (GUESS)

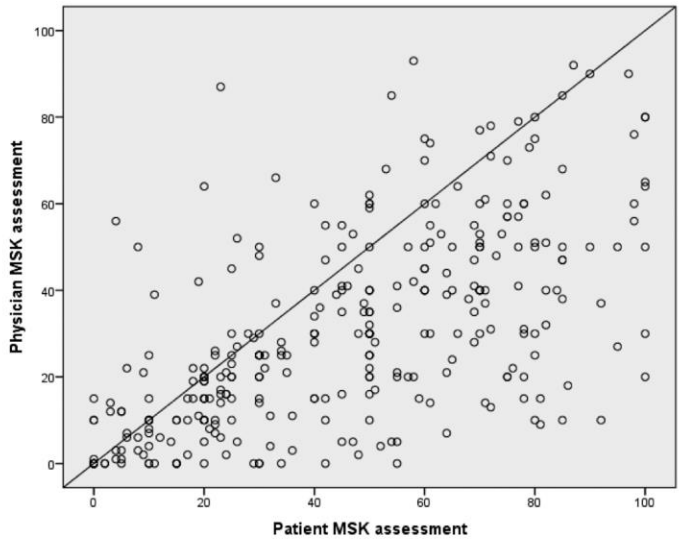
Patient Global Assessment in Psoriatic Arthritis: A Multicenter GRAPPA and OMERACT Study

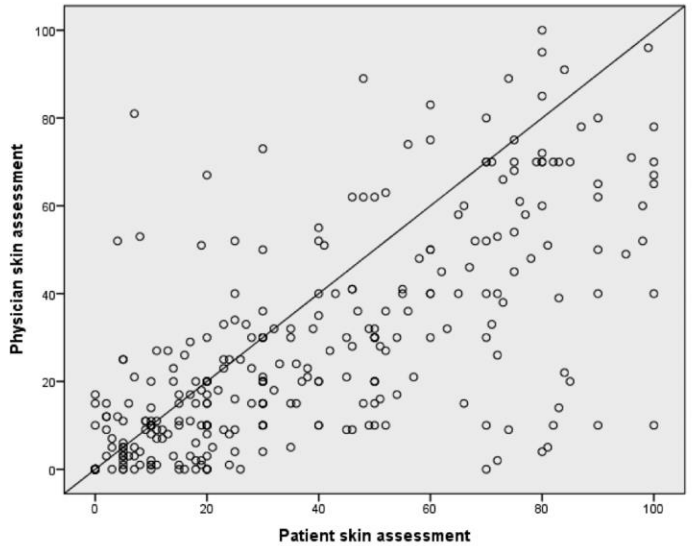
ALBERTO CAULI, DAFNA D. GLADMAN, ALESSANDRO MATHIEU, IGNAZIO OLIVIERI, GIOVANNI PORRU, PAUL P. TAK, CLAUDIA SARDU, ILONA UJFALUSSY, RAFFAELE SCARPA, ANTONIO MARCHESONI, WILLIAM J. TAYLOR, ANTONIO SPADARO, JOSE L. FERNÀNDEZ-SUEIRO, CARLO SALVARANI, JOACHIM R. KALDEN, ENNIO LUBRANO, SUELI CARNEIRO, FRANCESCA DESIATI, JOHN A. FLYNN, SALVATORE D'ANGELO, ALESSANDRA VACCA, ARNO W.R. VAN KUIJK, MARIA GRAZIA CATANOSO, MATHIAS GRUENKE, ROSARIO PELUSO, WENDY J. PARSONS, NICOLA FERRARA, PAOLO CONTU, PHILIP S. HELLIWELL, and PHILIP J. MEASE; for the GRAPPA 3PPsA Study Group

Physician's Global Assessment in Psoriatic Arthritis: A Multicenter GRAPPA Study

Alberto Cauli, Dafna D. Gladman, Alessandro Mathieu, Ignazio Olivieri, Giovanni Porru, Paul P. Tak, Claudia Sardu, Raffaele Scarpa, Antonio Marchesoni, William J. Taylor, Carlo Salvarani, Joachim Kalden, Ennio Lubrano, Sueli Carneiro, Matteo Piga, Alberto Floris, Francesca Desiati, John A. Flynn, Salvatore D'Angelo, Arno W.R. van Kuijk, Maria Grazia Catanoso, Francesco Caso, Paolo Contu, Ilona Ujfalussy, Philip S. Helliwell, and Philip J. Mease, for the GRAPPA 3PPsA Study Group



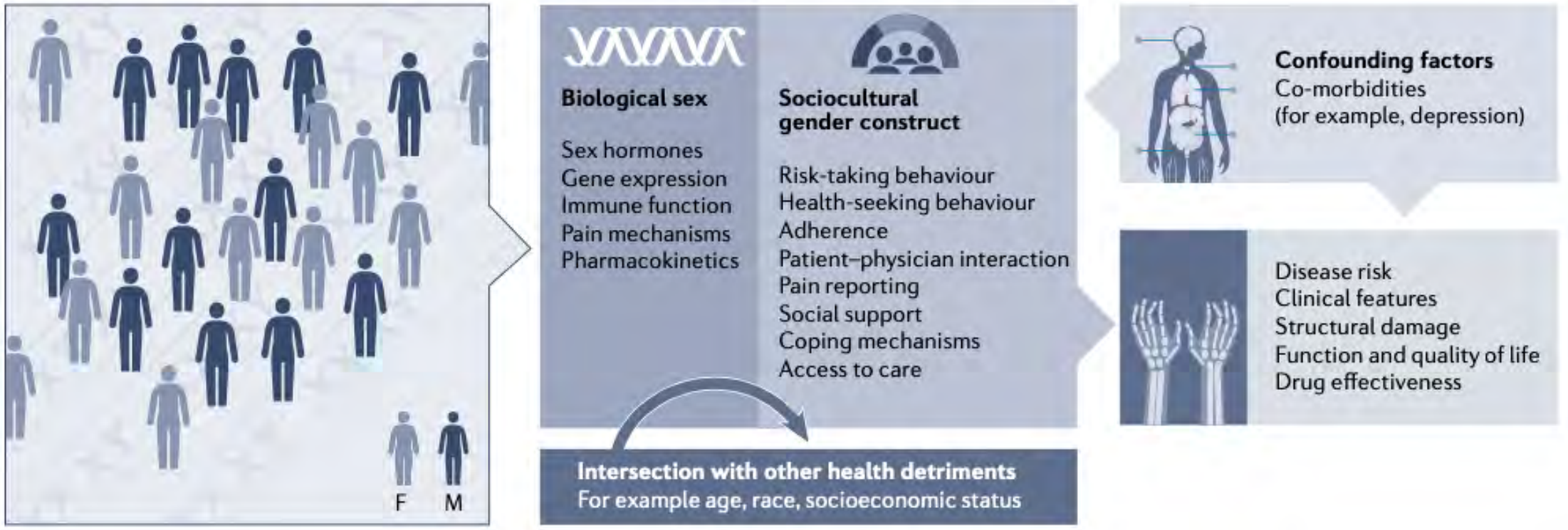




Cauli et al J Rheumatol. 2011, Cauli et al. J Rheumatology 2018

Sex and gender influence clinical features, disease course and response to treatment

Sex- and gender-related mechanisms and disease outcomes in PsA.



Tarannum S, et al. Nat Rev Rheumatol. 2022 Sep;18(9):513-526

Sex- and gender-related differences in clinical features of PsA

Male patients have more axial involvement, and more severe skin and nail psoriasis

Female patients frequently have peripheral joint involvement

This emphasizes the need for specific sex-gender considerations in diagnosis and treatment selection.

Tarannum S, et al. Nat Rev Rheumatol. 2022 Sep;18(9):513-526

Sex- and gender-related differences in QoL and function

Male patients typically have a **better quality of life** and **less of a work disability**

Female patients suffer from more pain, fatigue and poor functional status

These worse patient outcomes in women might be related to PsA or, alternatively, to co-existing conditions that are more common in females (e.g. fibromyalgia).

Tarannum S, et al. Nat Rev Rheumatol. 2022 Sep;18(9):513-526

Sex- and gender-related differences in QoL and function

Male patients develop more severe structural changes both in axial and in peripheral joints

Female patients exhibit less structural damadge

Tarannum S, et al. Nat Rev Rheumatol. 2022 Sep;18(9):513-526

Sex / gender and age at the diagnosis

Higher age at diagnosis of PsA in women

This may not only indicate a biological difference between women and men, but may also suggest delays in diagnosis possibly because of:

- misinterpretation of early symptoms of PsA
- delayed access to rheumatology care in female patients
- higher prevalence of confounding conditions such as fibromyalgia
- related to mental health disorders, such as depression, rather than reflecting disease manifestations

Tarannum S, et al. Nat Rev Rheumatol. 2022 Sep;18(9):513-526

Markers differentiating PsA from PsO

Soluble factors

Previous studies on "candidate biomarkers" : [1, 2]

- **CRP**
- IL- 6
- IL-23
- TNF-a
- Osteoprotegerin (OPG)
- MMP-3
- Markers of bone or cartilage damage
- Adipokines
- CXCL10
- Combination of ITGβ5, M2BP CRP

The emerging proteomic approach: [2.3,4]

- **ITGβ5** and **periostin** the most notably porteints that were higher in PsA than in PsO patients In a mass spectrometry analysis of skin biopsy samples (also higher in serum of PsA patients)

- A broad screen of 951 serum proteins using an affinity-based proteomic platform concluded that **PsO and PsA patients shared a broadly similar serum proteomic signature**. A significant correlation was found between PI3 and IL-17 receptor A and PsA disease activity (PASI) and between ICAM-1 and CCL-8 and PsA disease activity.

Despite the clear need for better (even some) diagnostic tools, there have been relatively few biomarker studies undertaken using well clinically phenotyped cohorts of PsO and PsA patients. Further research applying proteocmic strategies is needed to develop protetin biomarker that might have clinical utility in the management of PsA

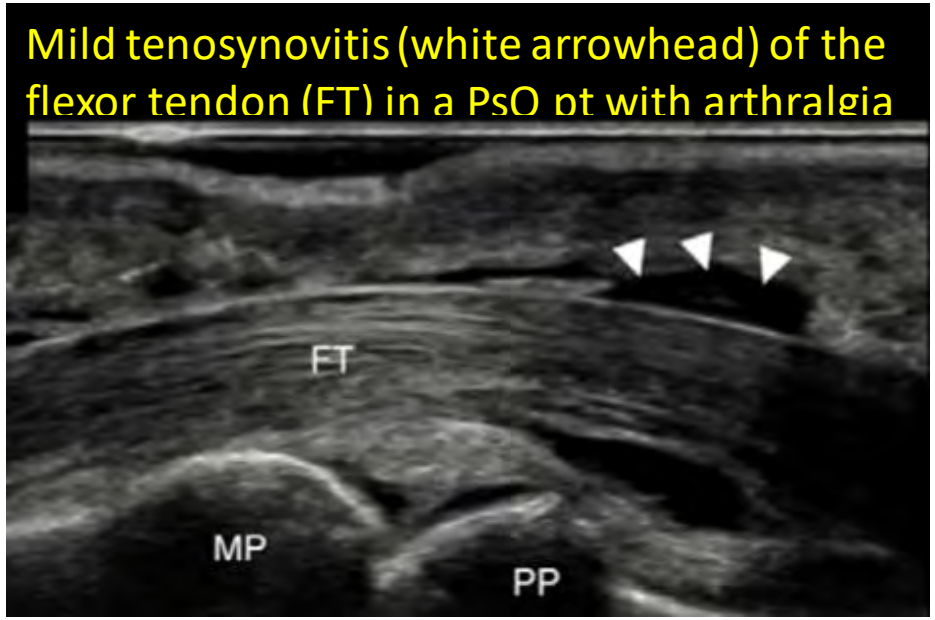
(1) Chandran V et al. Curr Rheumatol Rep 2014;16:453. (2) Scher JU et al. Nat Rev Rheumatol 2019. (3) Certu D et al Clin. Proteomics 2015; 12: 1. (4) Leijten E et al. Rheumatol. (2021) 60:751–61

Lack of new biomarkers in routine clinical practice.

Imaging as biomarker of subclinical PsA

Active enthesitis of the common extensor tendon enthesis in the elbow [1]

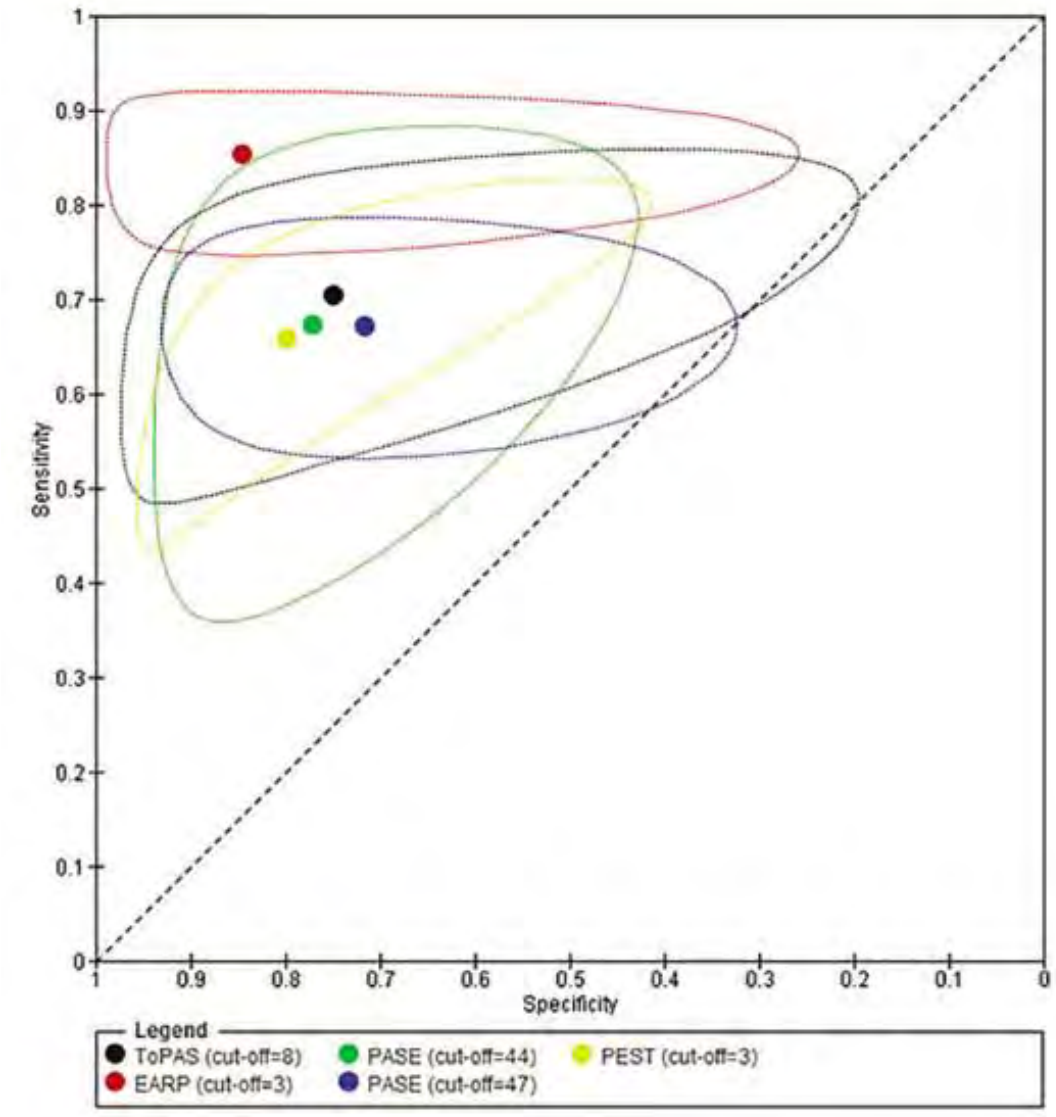
Mild tenosynovitis (white arrowhead) of the flexor tendon (FT) in a PsO pt with arthralgia



- PsO patients has higher prevalence of enthesitis in ultrasonography (US) than healthy controls, despite being asymptomatic. [1]
- US tenosynovitis is one of the most prevalent findings in PsO patients with aspecific arthralgia. [2]
- US enthesopathy is the US finding with higher evidence for a predictive role of transition from Pso to PsA. [3]
- In MRI, up to 47% PsO pts showed ≥1 inflammatory lesion (60% risk of PsA in pts with synovitis + arthralgia).[4]

(1) Zabotti A. Current Rheumatology Reports 2020;22: 24. (2) Zabotti A et al. RMD Open. 2019;5:e001067.
(3) Zuliani F et al. Clin Exp Rheumatol. 2018;37:593–9. (4) Faustini F et al . Ann Rheum Dis. 2016; 75:2068–74.

The questionnaire-based PsA screening tools



- **EARP:** Early Psoriatic Arthritis Screening Questionnaire
- **PASE:** Psoriatic Arthritis Screening and Evaluation
- **PEST:** Psoriasis Epidemiology Screening Tool
- **ToPAS:** Toronto Psoriatic Arthritis Screening Tool

Questionnaire-based tools have moderate accuracy (particularly low specificity) to identify PsA among psoriasis patients. The EARP appears to have slightly better accuracy

Iragorri N et al. Rheumatology 2019;58:692– 707

Multisciplinary management of psoriasis and psoriatic arthritis in combined dermatology-rheumatology clinic

Some benefits…

Identification of undiagnosed PsA among PsO pts

Results form meta-analysis

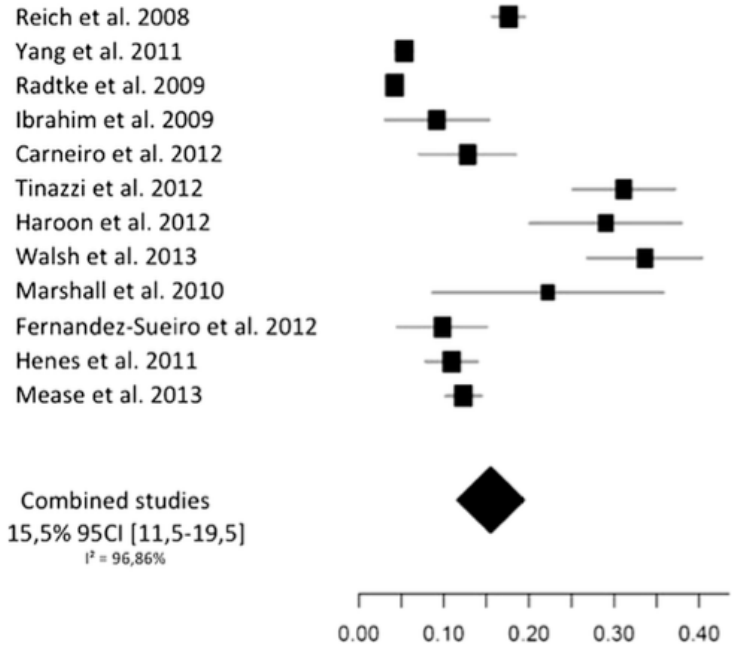


Fig 2. Prevalence of undiagnosed psoriatic arthritis: meta-analysis *95CI*, 95% confidence interval.

Accurate differential diagnosis of MSK symptoms in PsO patients

Diagnosis of arthropathy in patients with PsO and MSK symtoms in a combined dermatology-rheumatology clinic (n = 173)

Diagnosis	Percentage (%)
Indeterminate (%)	26.6
PsA (%)	53.2
OA (%)	13.9
Gout (%)	0.6
PsA + OA (%)	5.2
Gout + OA + PsA (%)	0.6

PsA psoriatic arthritis, *OA* osteoarthritis

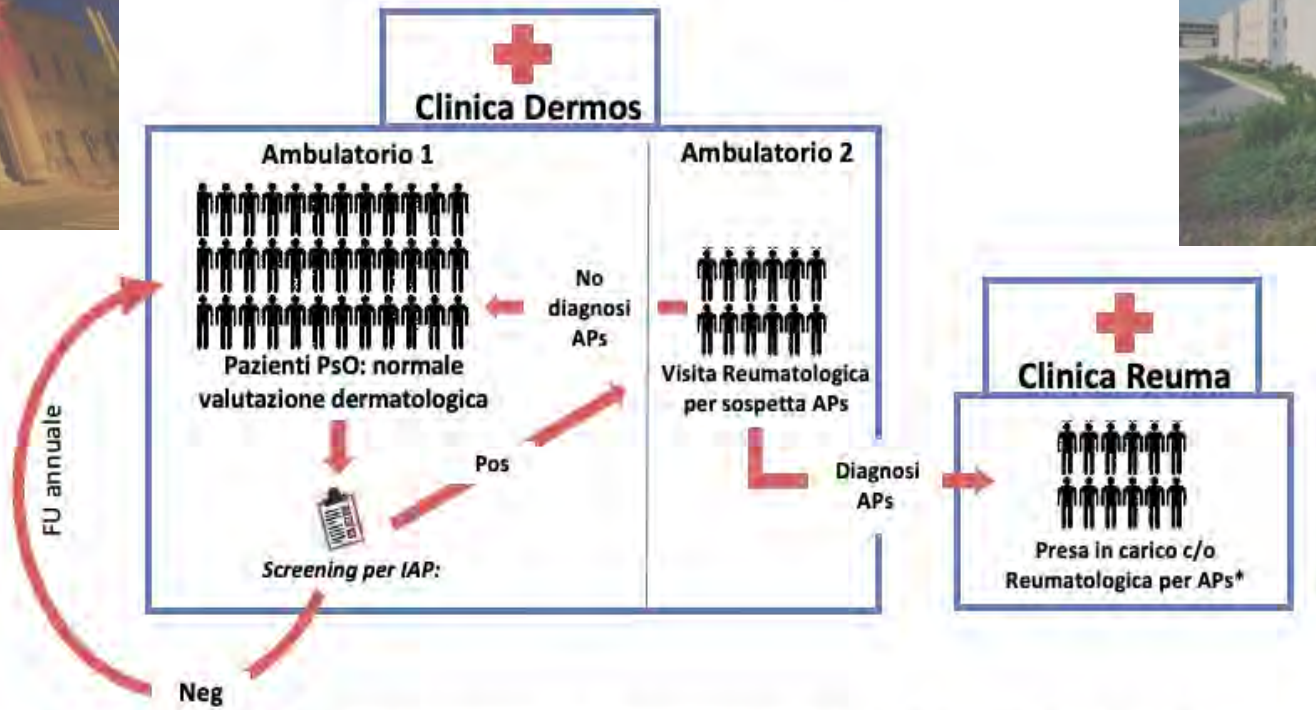
High patient's satisfaction

- Rate of satisfaction from 0 to 5 with the multidisciplinary vs. separate assessment: 4.91 vs.2.85
- High level of satisfaction regarding:
  - amount of information provided
  - involvement in decisions

Villani et al. J AM ACAD DERMATOL 2015

DIAPASON

Diagnosi precoce di artrite psoriasica in una coorte prospettica di pazienti affetti da psoriasi cutanea.

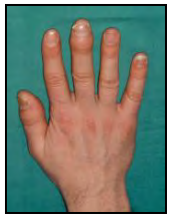


Disegno della studio. PsO, psoriasi cutanea. IAP, interessamento articolare a possibile evoluzione artritica, individuato sulla base di questionario di screening. APs, artrite psoriasica. FU: follow-up. * Prosecuzione follow-up sia in ambito reumatologico che dermatologico.

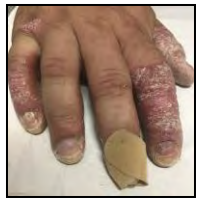
Remission in PsA

Possible definition:

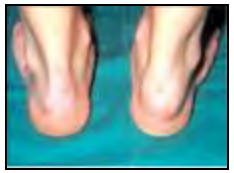
- Complete lack of disease activity in all domains:



o Joint



o Skin/Nails



o Enthesis

o Axial

Editorial

The Difficult Task of Assessing Psoriatic Arthritis

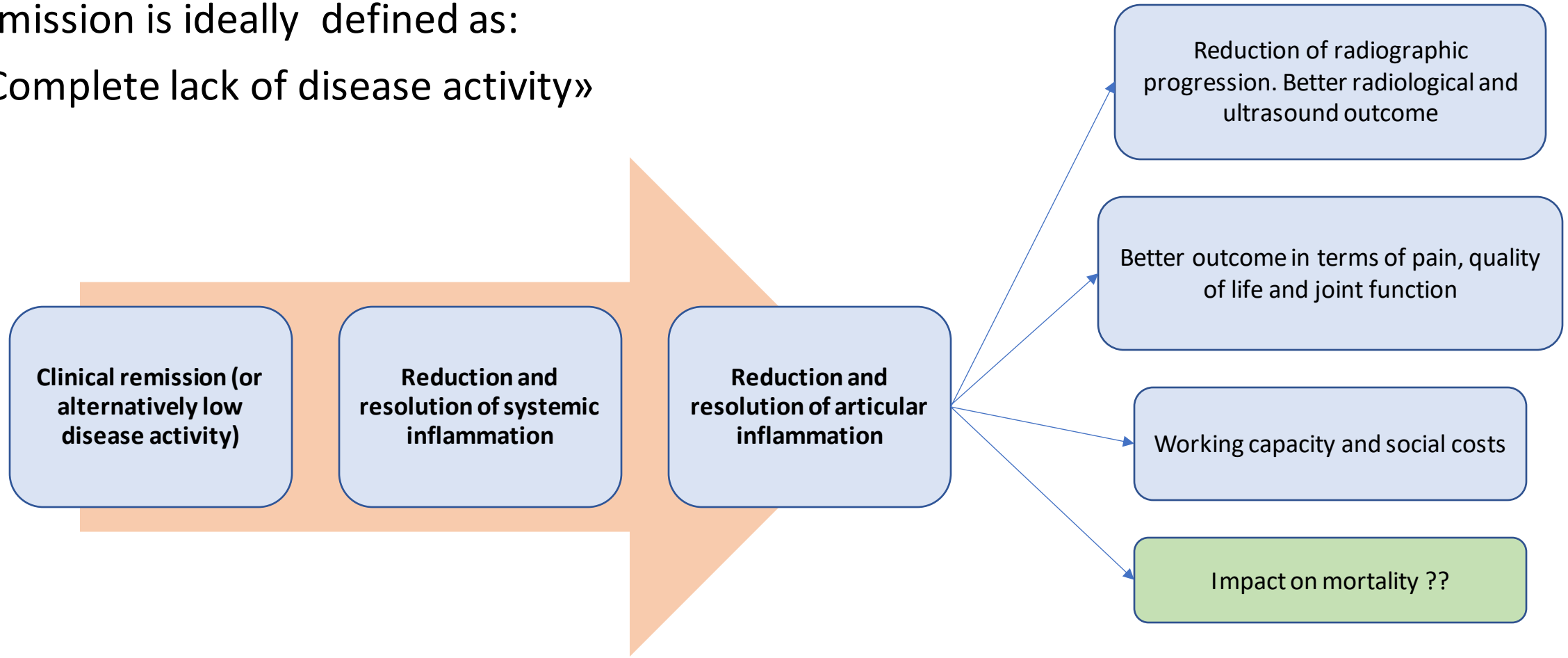
- Although it may appear logical and practical to embrace all PsA clinical domains in a composite disease activity and responder index summarizing the heterogeneous manifestations of PsA, this approach remains controversial.
- The need for detailed information on specific domains appears strong and therefore should be obtained by means of several domain-specific instruments, not only in RCT but also in routine clinical practice

Cauli et al. J Rheumatol. 2015

How to define the target of remission

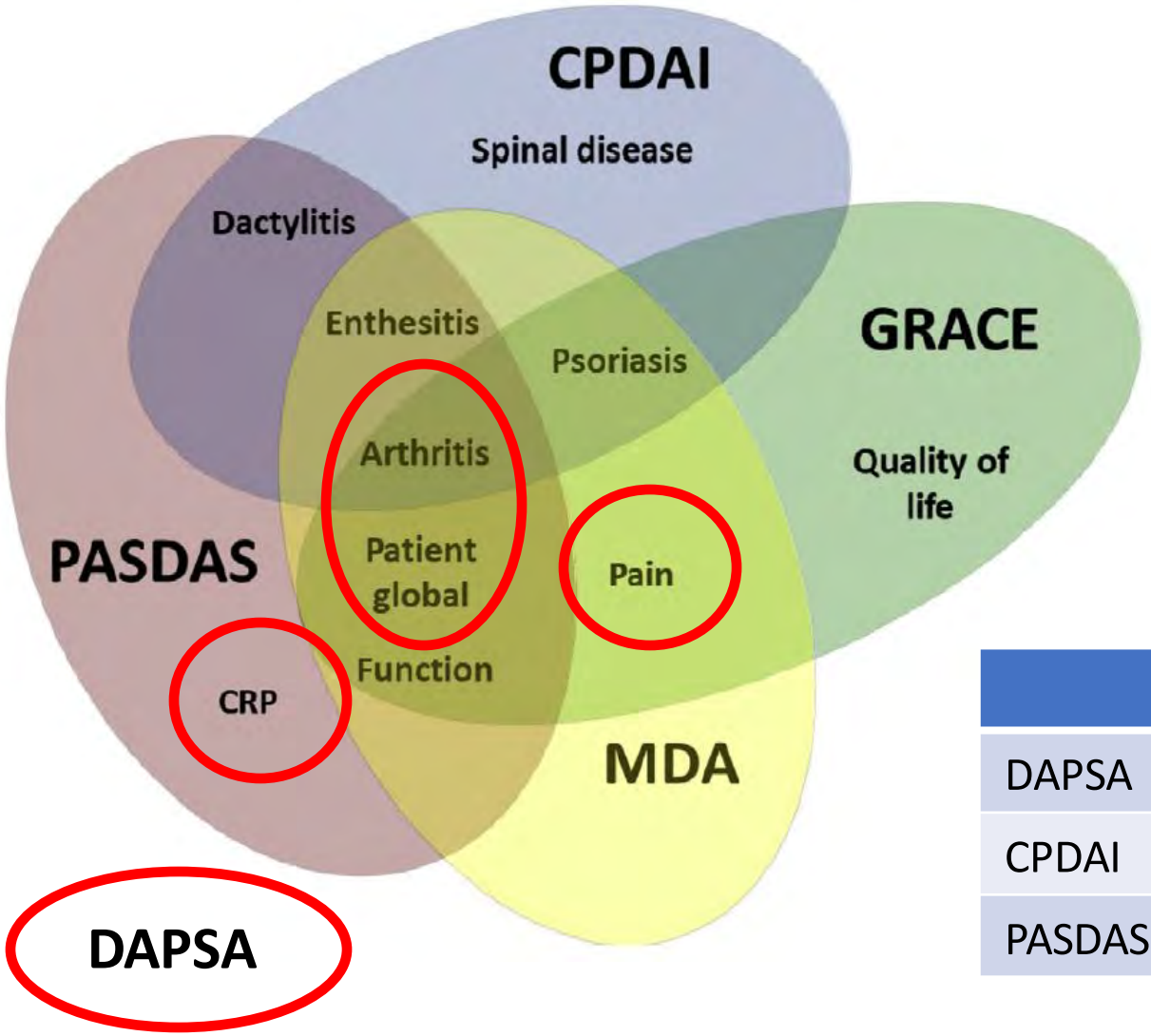
Remission is ideally defined as:

«Complete lack of disease activity»



Smolen JS, et al. Ann Rheum Dis 2017;0:1–15. doi:10.1136/annrheumdis-2017-211734

Composite measure of disease activity in PsA



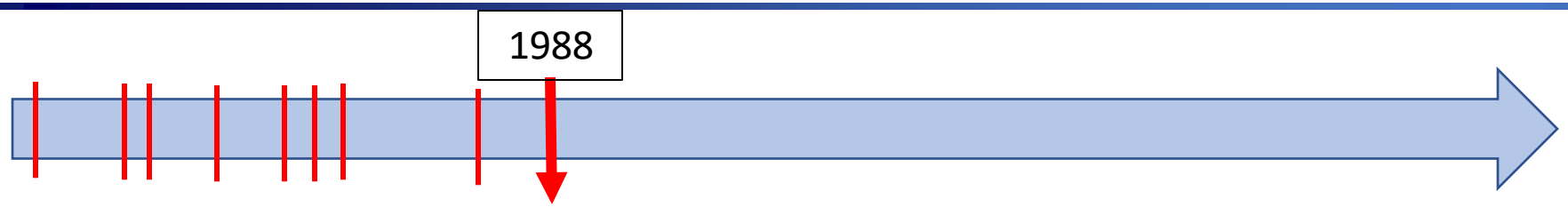
	Remission	Low DA	Moderate DA	High DA
DAPSA	≤ 4	>4 - 14	> 14-28	>28
CPDAI	Range 0-15 (0-3 for each domain)			
PASDAS	≤1.9	1.9-3.2	3.2-5.4	>5.4

Minimal Disease Activity (MDA)

- Tender Joint count ≤1
- Swollen Joint count ≤1
- PASI ≤1 or BSA ≤3%
- HAQ ≤0,5
- Pain VAS ≤15
- PGA ≤20
- Tender enthesal points <1

- VLDA 7/7
- MDA 5-6/7
- Active disease <5/7

- More stringet definition compared to DAPSA
- Used in TICOPA trial
- Included in T2T SpA recommendations



Article | Published: 24 March 1988

Reshaping human antibodies for therapy

Lutz Riechmann, Michael Clark, Herman Waldmann & Greg Winter

Nature **332**, 323–327(1988) | Cite this article

3286 Accesses | **1093** Citations | **18** Altmetric | Metrics

The Nobel Prize in Chemistry 2018

Frances H. Arnold
George P. Smith
Sir Gregory P. Winter

Share this

Sir Gregory P. Winter
Photo gallery

A milestone that changed the therapeutic scenario forever

Take home messages

- Early diagnosis and treatment are critical to prevent joint damage accrual, disability and impairment of QoL.
- Clinical heterogenicity, differential diagnosis, and lack of diagnostic criteria and validate biomarkers make early diagnosis of PsA challenging.
- Sex and gender may influence different aspects of PsA, including diagnosis
- The dermato-rheumatologic multidisciplinary approach may represent a key strategy for early diagnosis

ACKNOWLEDGEMENT

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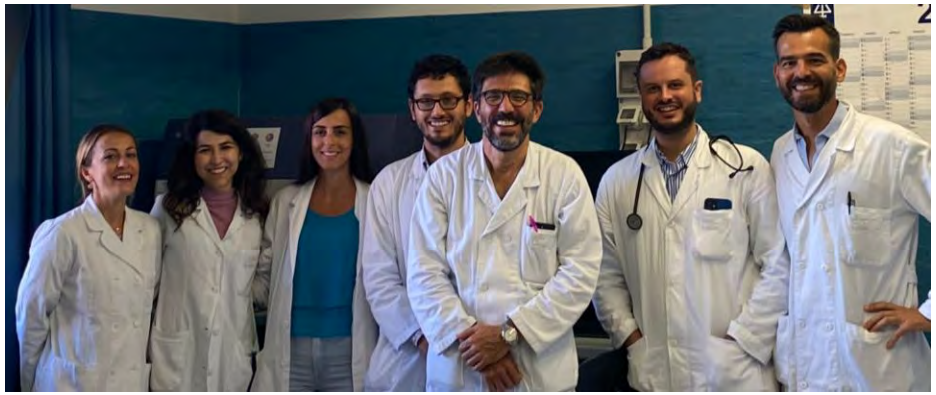
Unità di Reumatologia, Monserrato (CA), Italy
Direttore: Prof. Alberto Cauli



Policlinico Universitario di Monserrato

Cagliari, panoramica dal porto

Psoriatic Arthritis:

Patient burden, diagnosis and therapeutics

Dr James Galloway

Associate Professor in Rheumatology

King's College London

Bethany

- 74 years old
- 12 months MSK symptoms, hands, knees, feet, jaw
- Seen GP several times, NSAIDs and reassurance

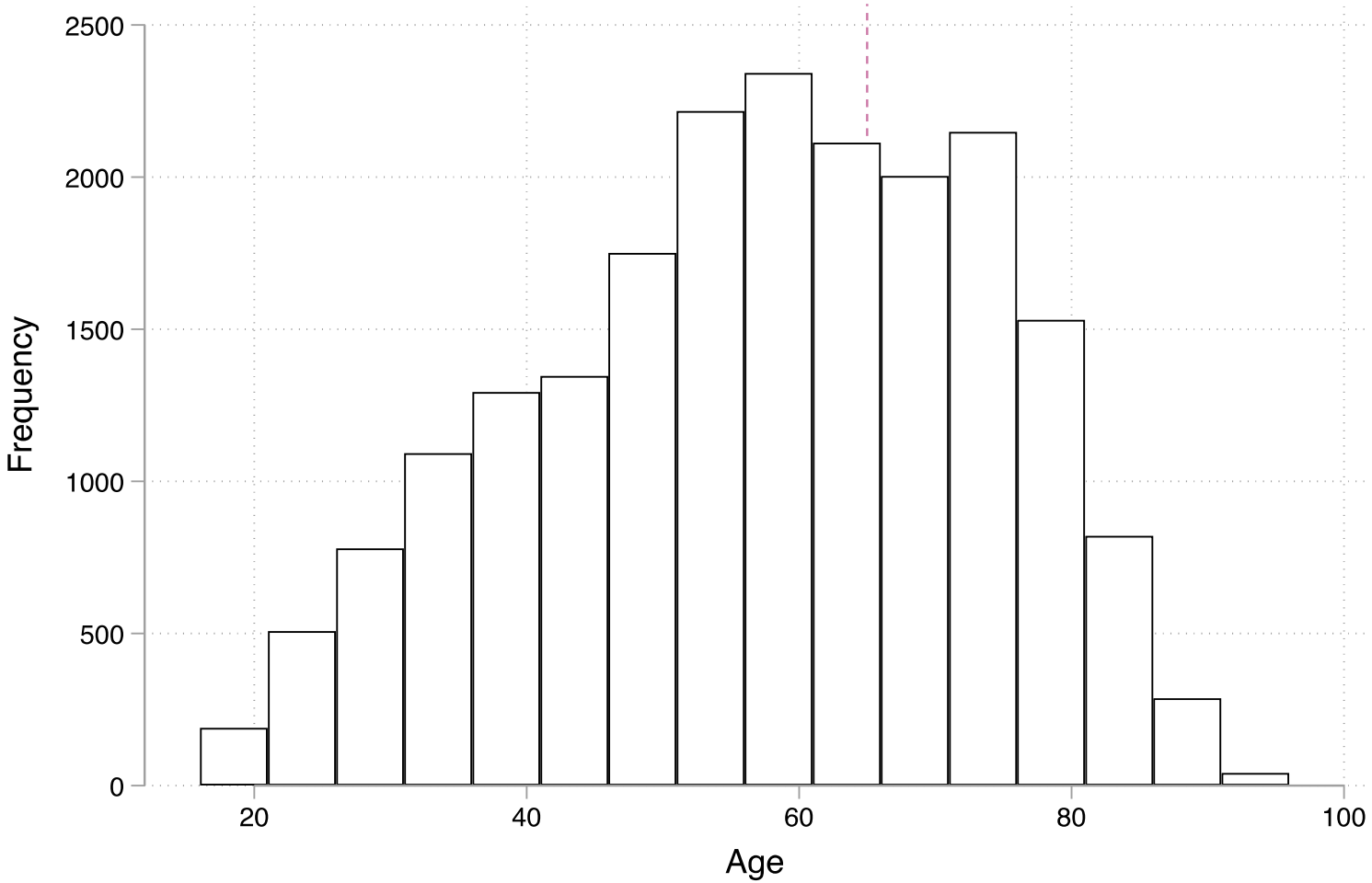
  (CRP normal)
- PMH: Eczema, hypertension, atrial fibrillation
- Retired photographer

Bethany

- **74 years old**
- 12 months MSK symptoms, hands, knees, feet, jaw
- Seen GP several times, NSAIDs and reassurance

  (CRP normal)
- PMH: Eczema, hypertension, atrial fibrillation
- Retired photographer

Age at PsA onset

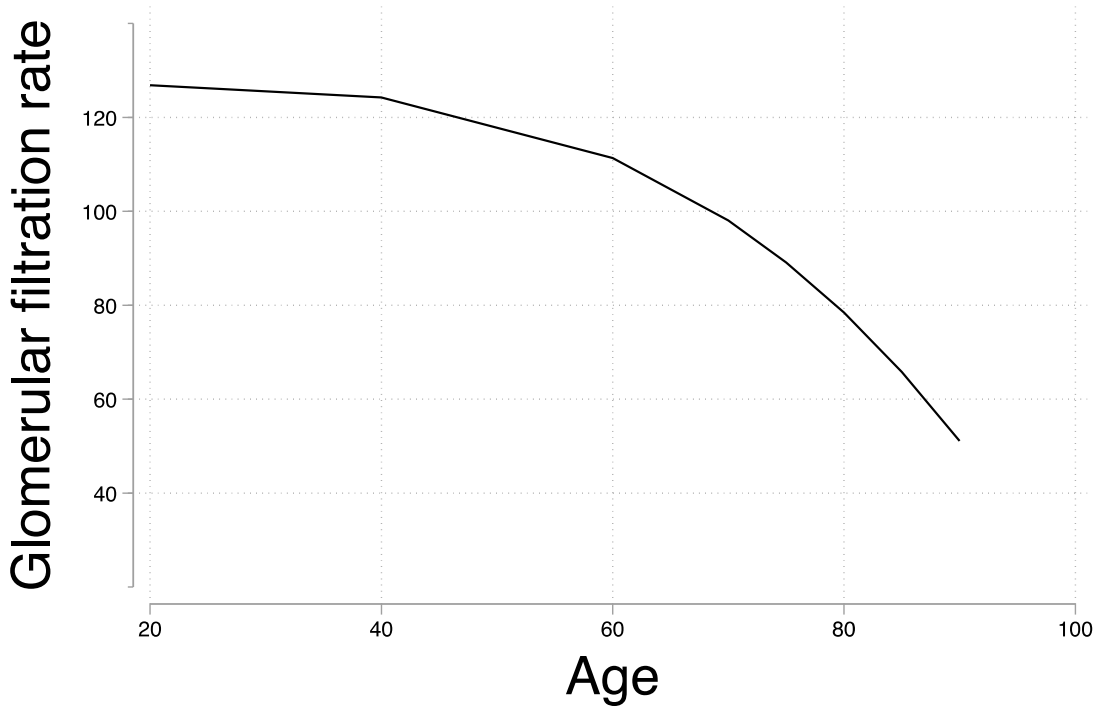


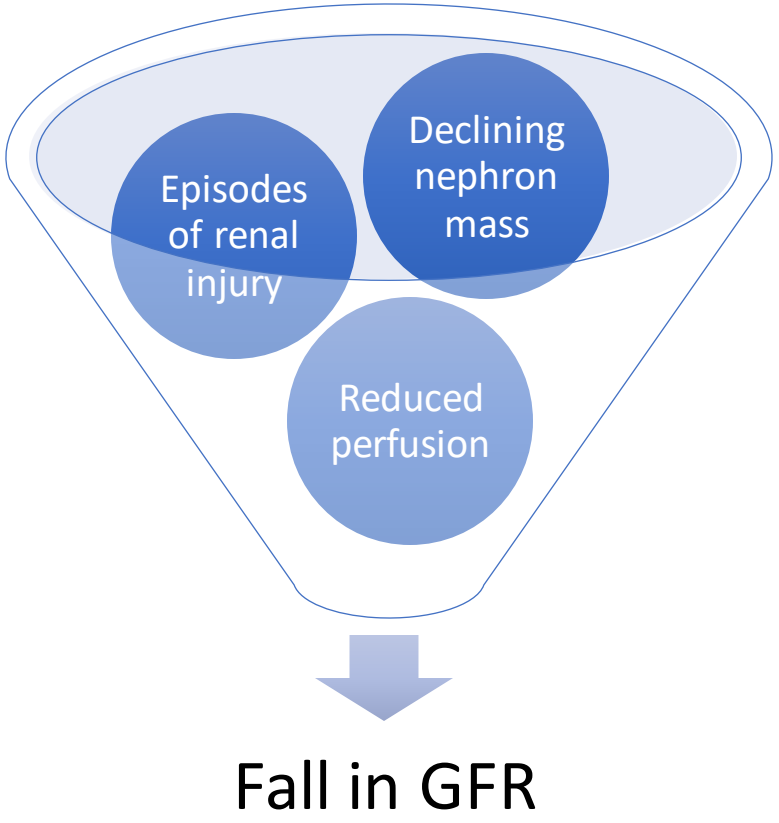
Age distribution in PsA cohort in NEIAA

Physiological changes with ageing

- Changes in lean body mass (↓35%)
  - More fat, less muscle
- Reduced circulating volume
  - Less water therefore higher concentration for water soluble drugs (alcohol, gentamicin)
- Reduction in liver volume (↓ 25-35%)
  - Reduced drug clearance, but also reduced 1st pass metabolism

Renal changes

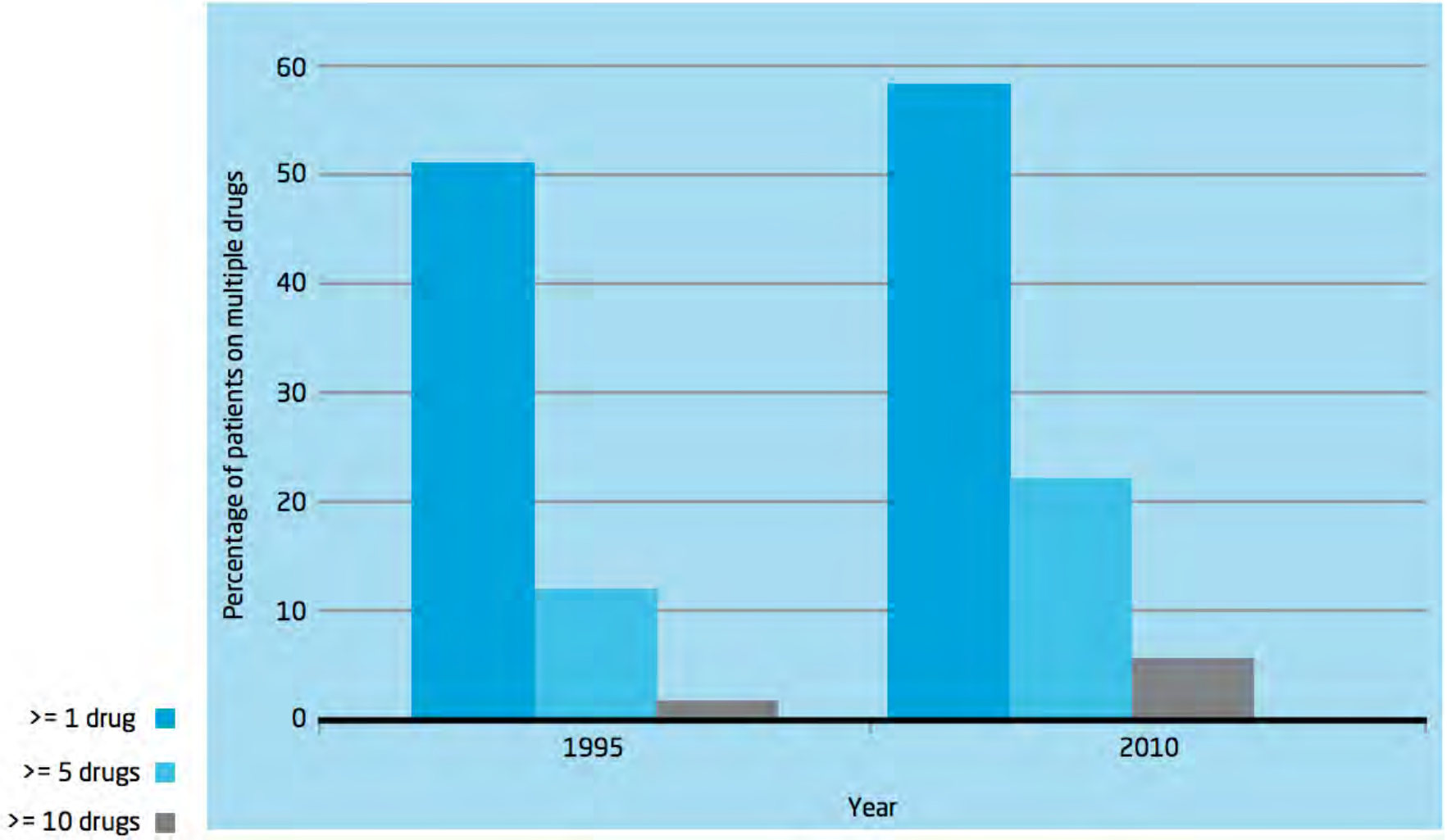




Bethany

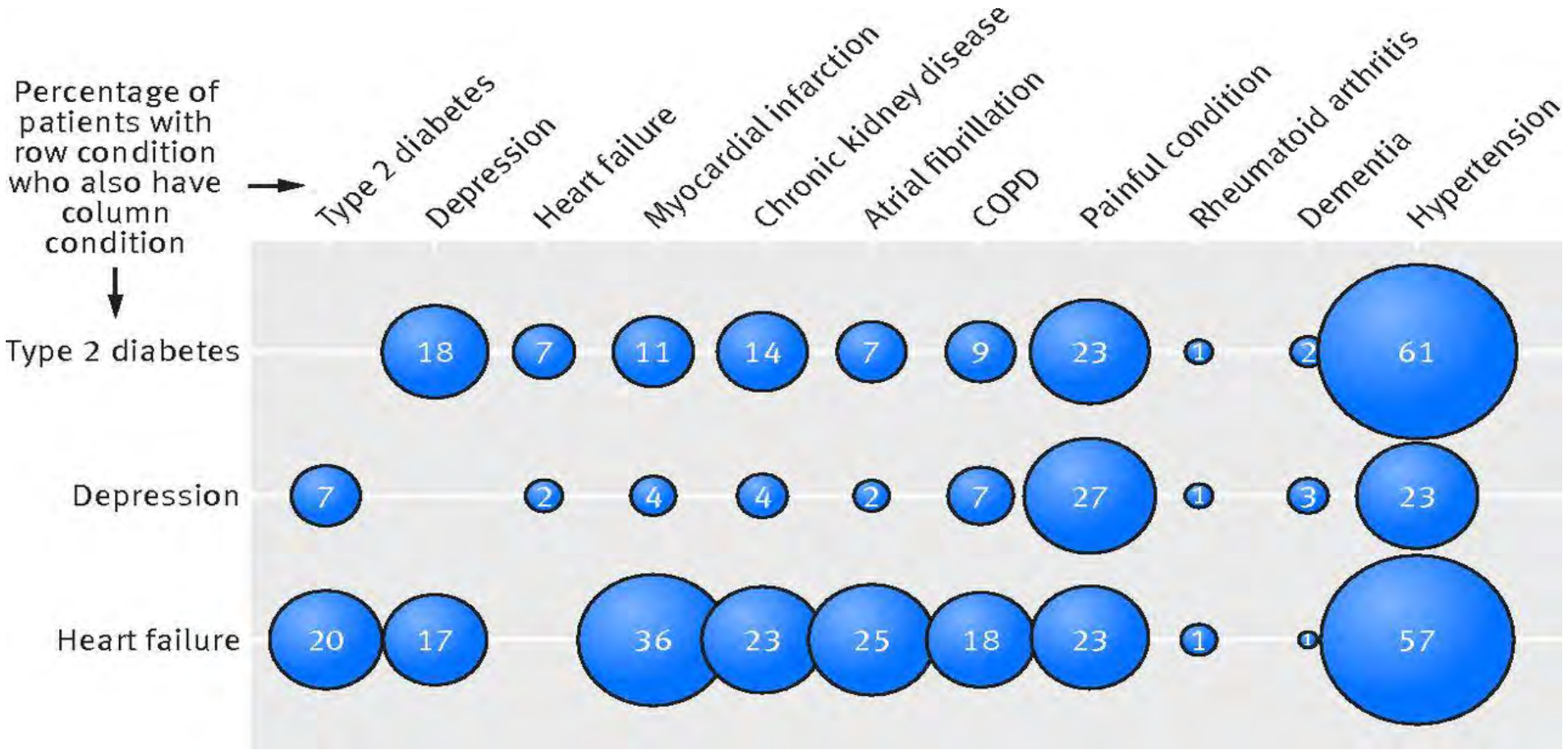
- Current medication
  - Aspirin
  - Ramipril
  - Bisoprolol
  - Simvastatin
  - Apixaban

The rising tide of polypharmacy



Primary Health Care Research & Development 13, supp S1: 45 2E.2

Drug interactions



BMJ 2015;350:h949

Drug interactions

- A Canadian case-control study explored frequent offenders in patients >65 years:
  - Co-trimoxazole and oral hypoglycaemics
    - **Odds ratio 6.6; 95% CI 4.5-9.7**
  - Clarithromycin and digoxin
    - **Odds ratio 11.7; 95% CI 7.5-18.2**
  - K^+ sparing diuretics and ACE inhibitors
    - **Odds ratio 20.3; 95% CI 13.4-30.7**

JAMA 2003; 289:1652.

Bethany

- Active dactylitis in toe
- Enthesitis L knee
- Synovitis in L wrist, L index PIPJ and L TMJ
- Psoriasis

Disease activity questions

- Joint counts? Include jaw? Toes?
  - *Avoid using DAS28*
- How should we assess enthesitis?
  - *Multiple scoring systems, Leeds Enthesitis Index is pragmatic*
- Skin severity?
  - *PASI scoring should be routine*

Treatment

- Bethany commences methotrexate 20mg once weekly
    - *Dactylitic toe is injected with corticosteroid*
- Topical treatment commenced for skin (PASI 3)
    - *Soap substitutes, emollient, steroid + vitamin D*

Progress

- 3-month review – dactylitis settled, but ongoing synovitis and enthesitis
- Nausea with methotrexate, and hair thinning
- PASI 0

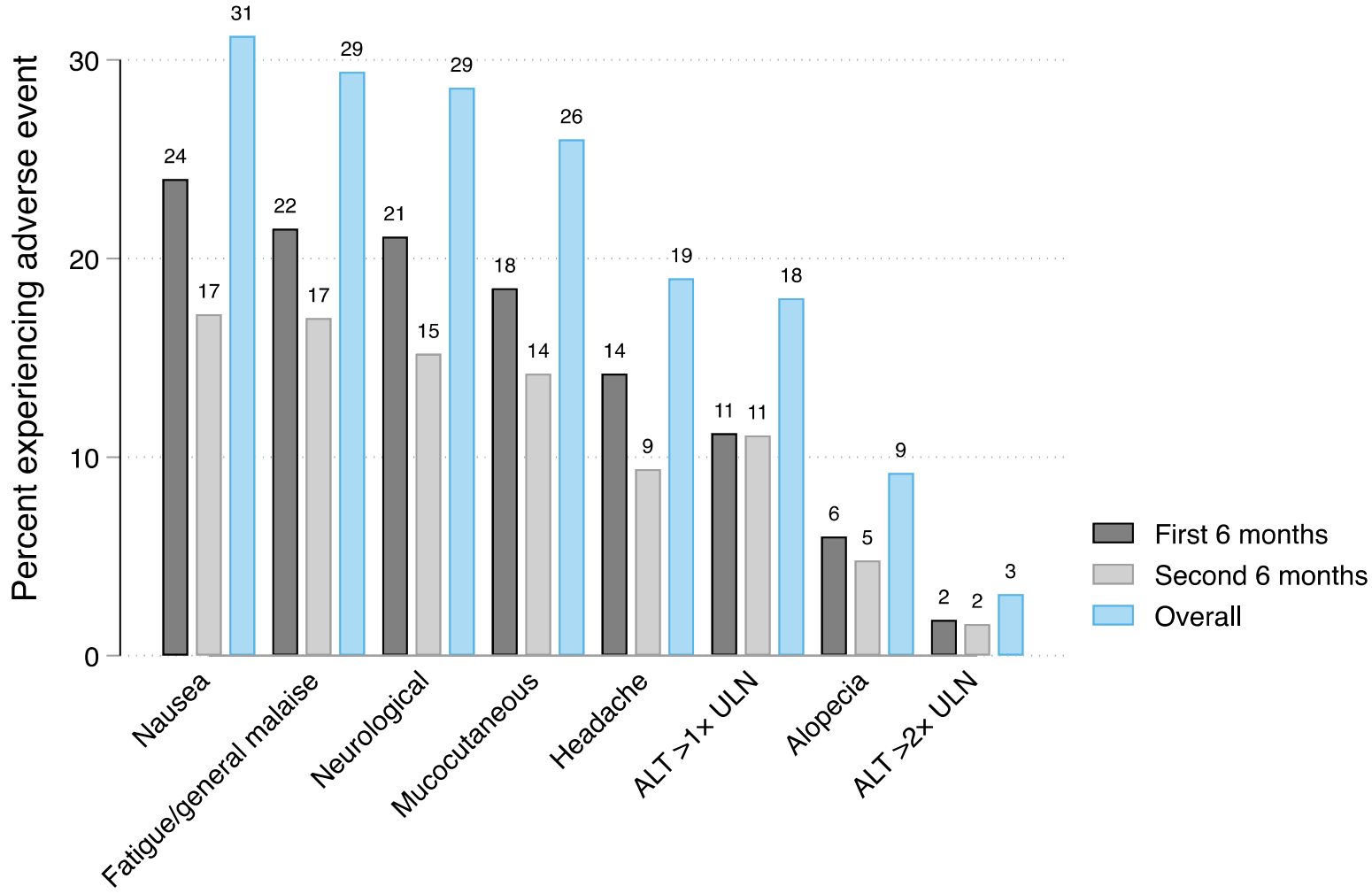
Barriers to treatment response

- Side effects from Methotrexate (adherence?)
- Comorbidities?

Barriers to treatment response

- **Side effects from Methotrexate (adherence?)**
- Comorbidities?

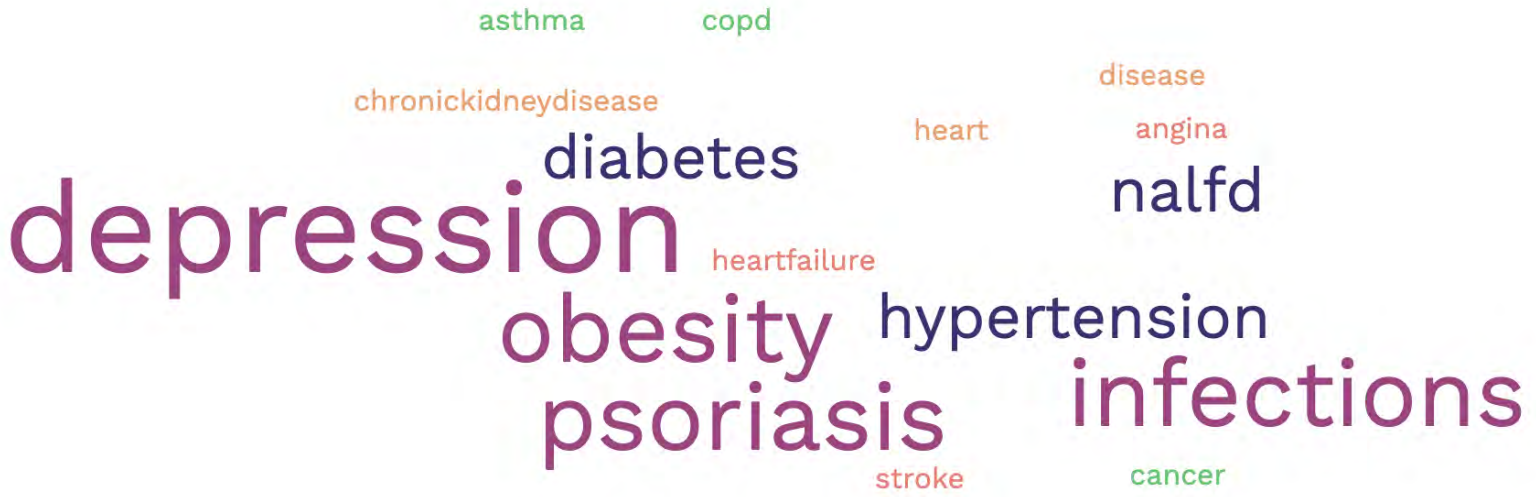
Methotrexate side effects



Rheumatology 2022: 3930–3938

Barriers to treatment response

- Side effects from Methotrexate (adherence?)
- **Comorbidities?**



Comorbidity and Psoriatic Arthritis

Diseases that arise directly because of PsA

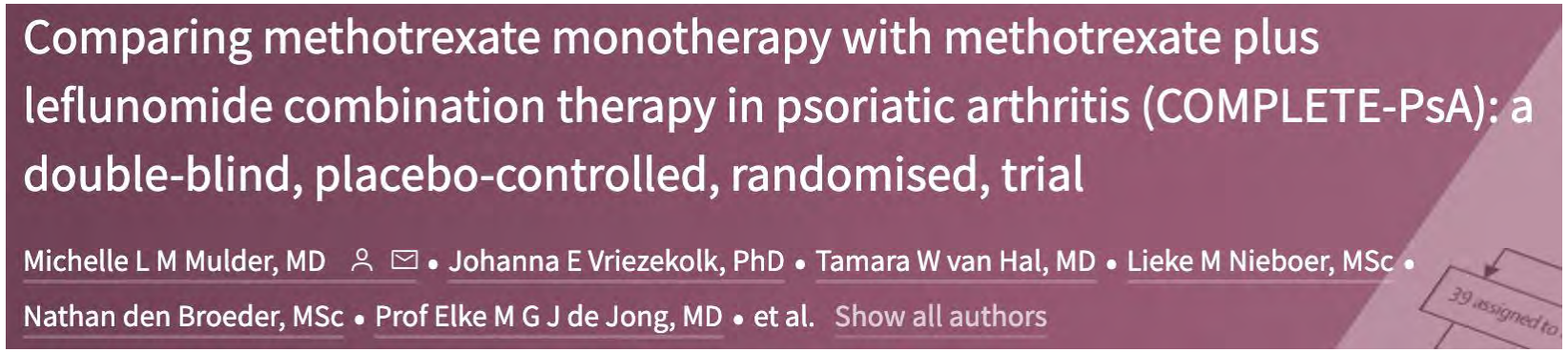
versus

Diseases that develop independently because of shared risk factors or coincidence

How to measure? Charleson / RCDI / polypharmacy…

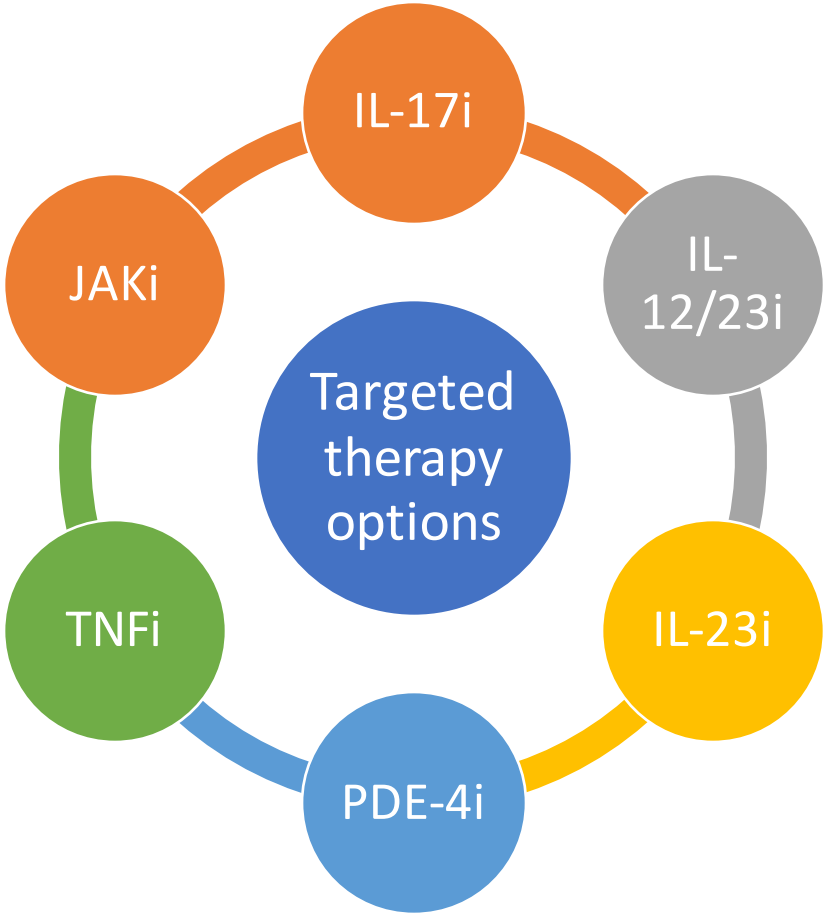
Plan

- Methotrexate switched to s/c
- Leflunomide added



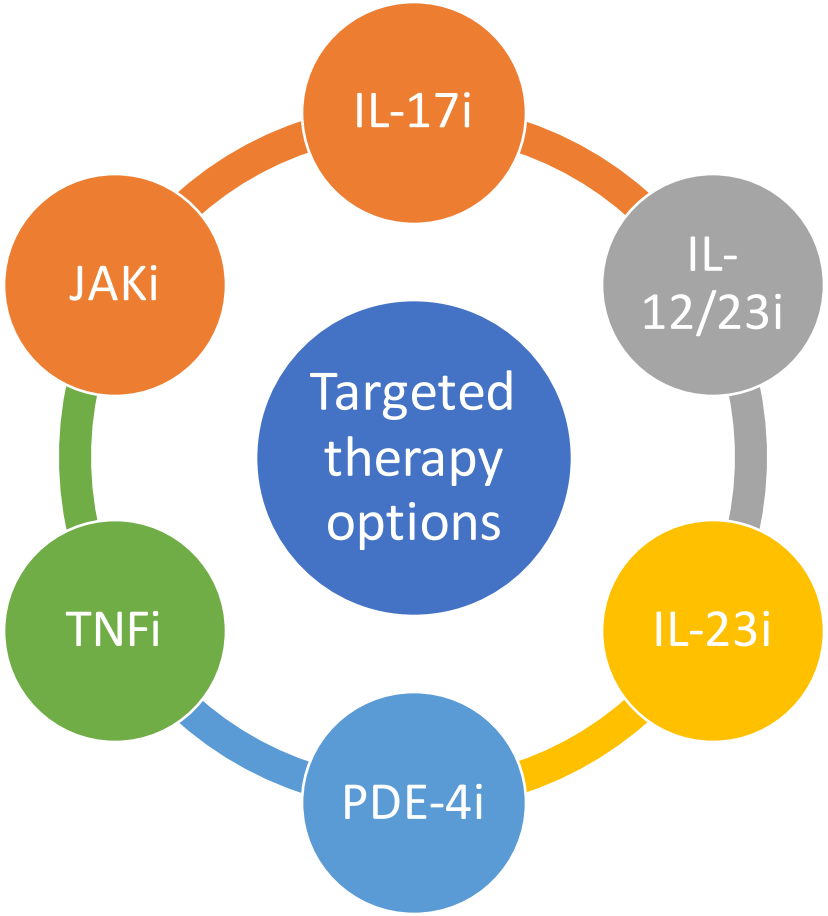
Lancet Rheum 2022: E252-E261

Failure to respond to DMARDs

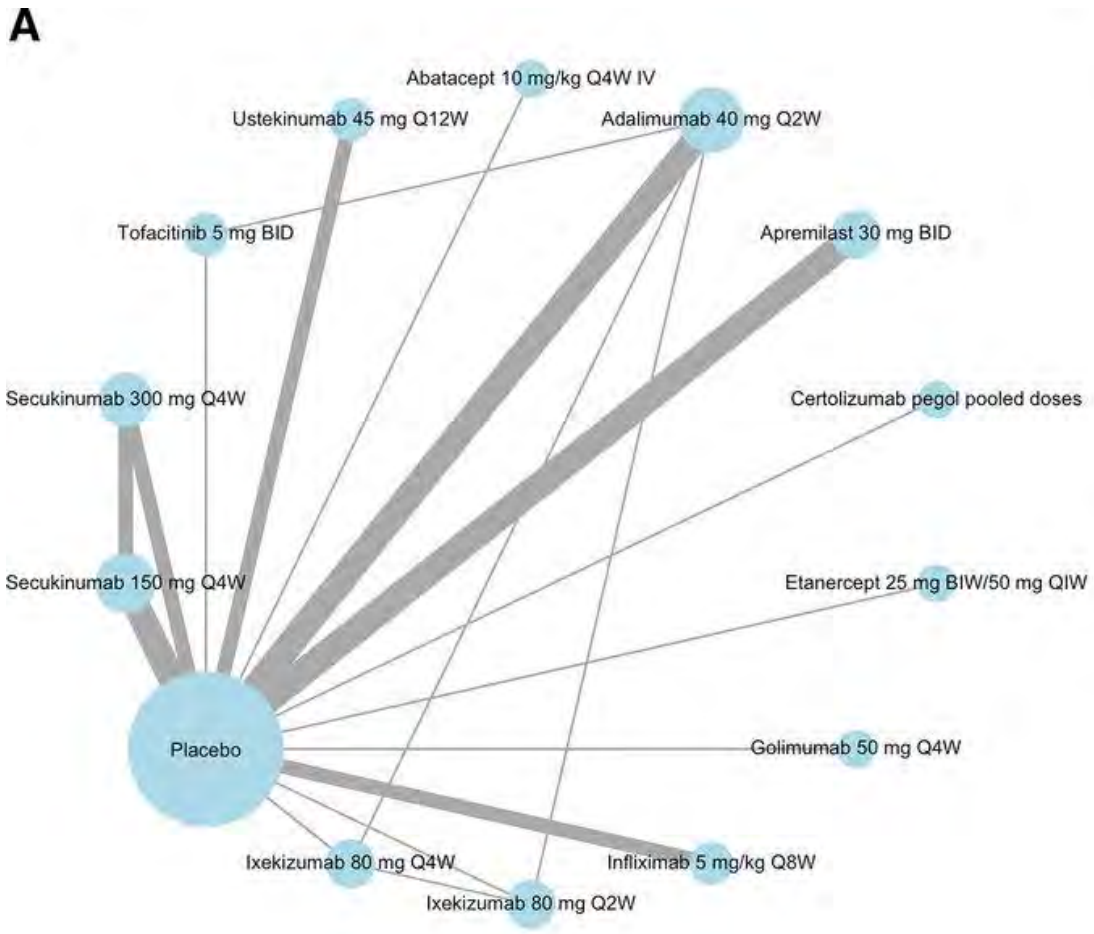


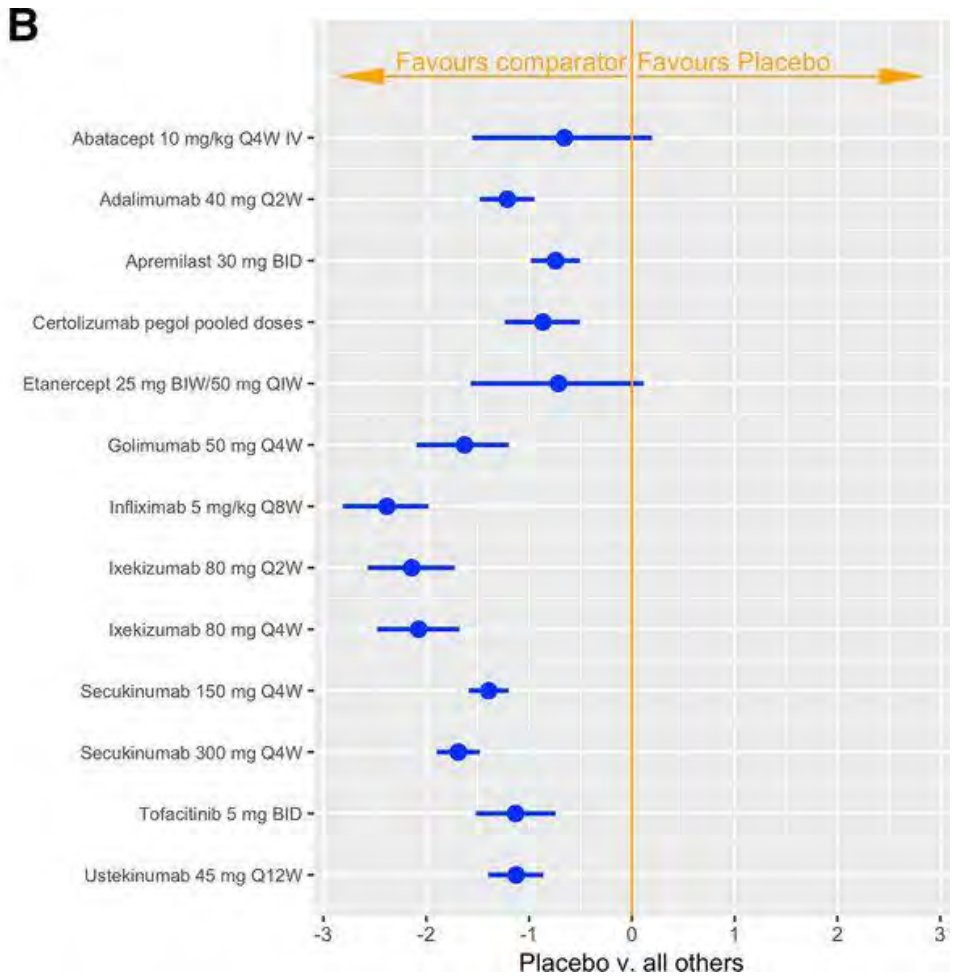
Failure to respond to DMARDs

Considerations:
Joint responses
Skin disease
Gut disease
Eye disease
Comorbidity



Network meta-analysis (PsARC response)

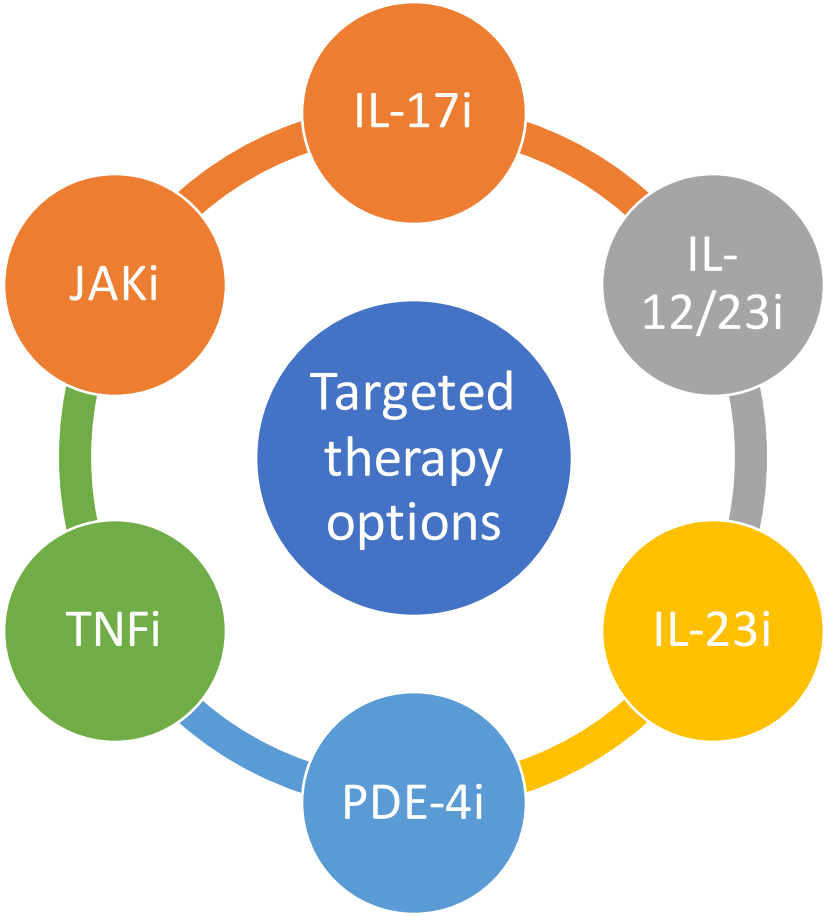




RMD Open 2020;6:e001117

Failure to respond to DMARDs

Considerations:
Joint responses
Skin disease
Gut disease
Eye disease
Comorbidity
Safety profile

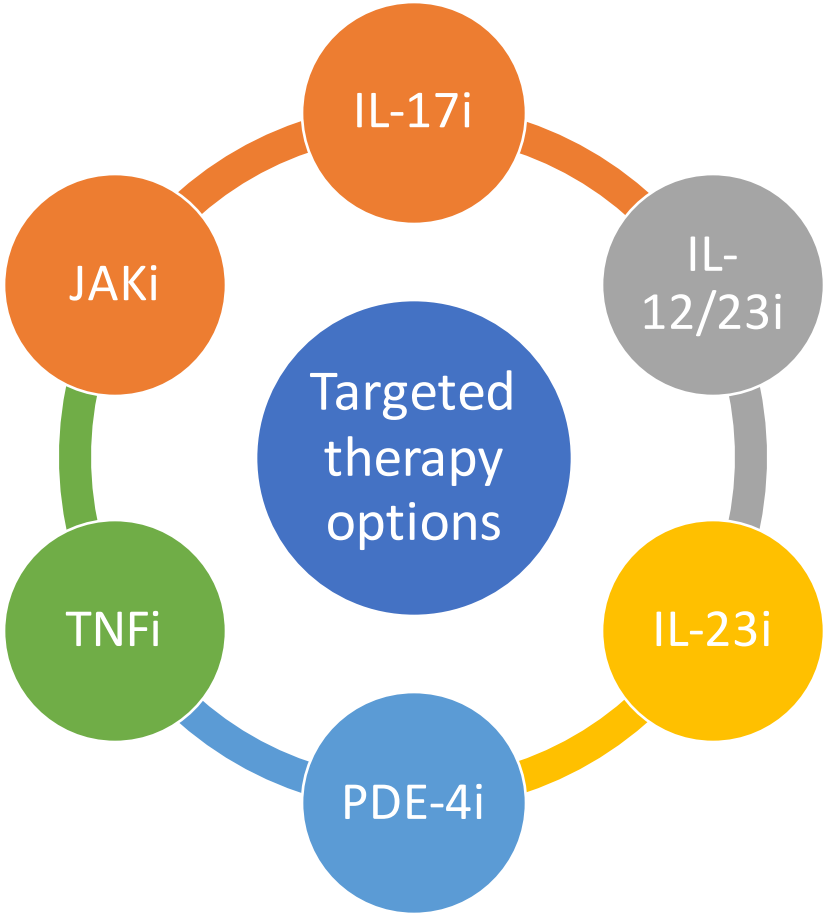


Safety profiles

CV risk

LV function

Prior malignancy



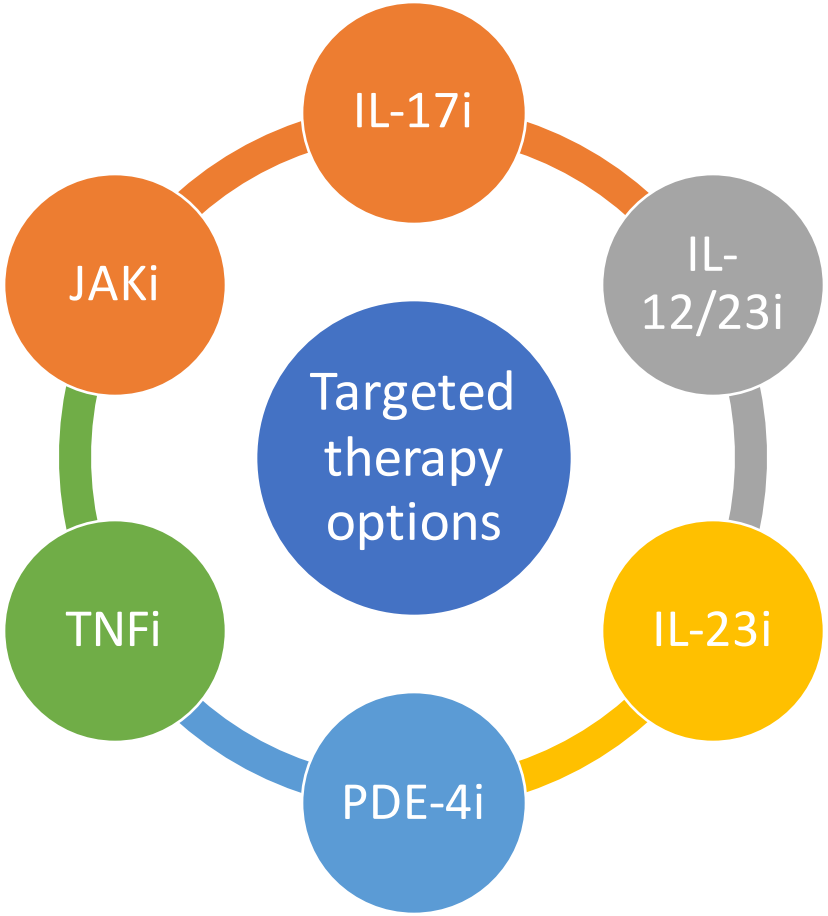
Diverticular disease

Recurrent infections

Demyelination

Failure to respond to DMARDs

Considerations:
Joint responses
Skin disease
Gut disease
Eye disease
Comorbidity
Safety profile



Switching considerations
Stay in class?
Oral or parenteral?
Dosing frequency?
Costs?

Summary

- PsA most commonly develops in younger adults, but can present at any age
- We need to consider patients as individuals
- Comorbidity and polypharmacy need to factor into decision making
- Fortunately, not many DMARDs (excluding NSAIDs and steroids) have serious drug interactions
- In the elderly, safety profiles often take priority when selecting treatments