Η ποιότητα ζωής στο επίκεντρο

...

at_kout@yahoo.com

Σύγκρουση συμφερόντων

Τιμητική αμοιβή από την εταιρεία AbbVie

Την τελευταια διετία τιμητική αμοιβή απο τις εταιρείες Genesis Pharma, UCB, Pfizer

QoL

What is it?

Does it matter?

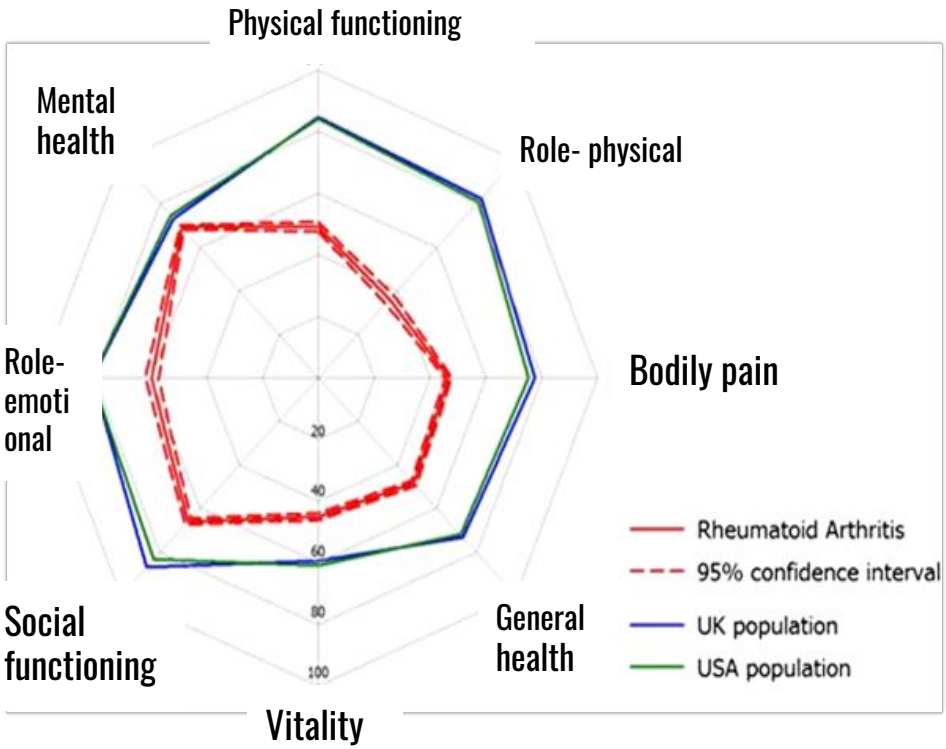
What influences it?

What to do?

Aspects of HrQoL

Physical functioning
Bodily pain
Role-physical
General health
Vitality
Social functioning
Role-emotional
Mental health
Fatigue
Sleep

Rheumatoid arthritis: Impact on QoL



Matcham, Semin Arthritis Rheum 2014

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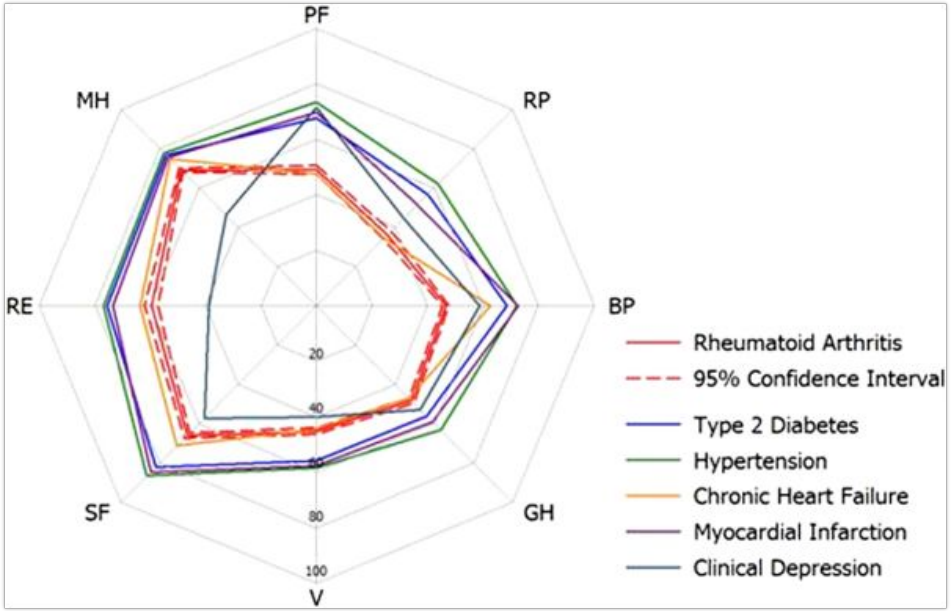
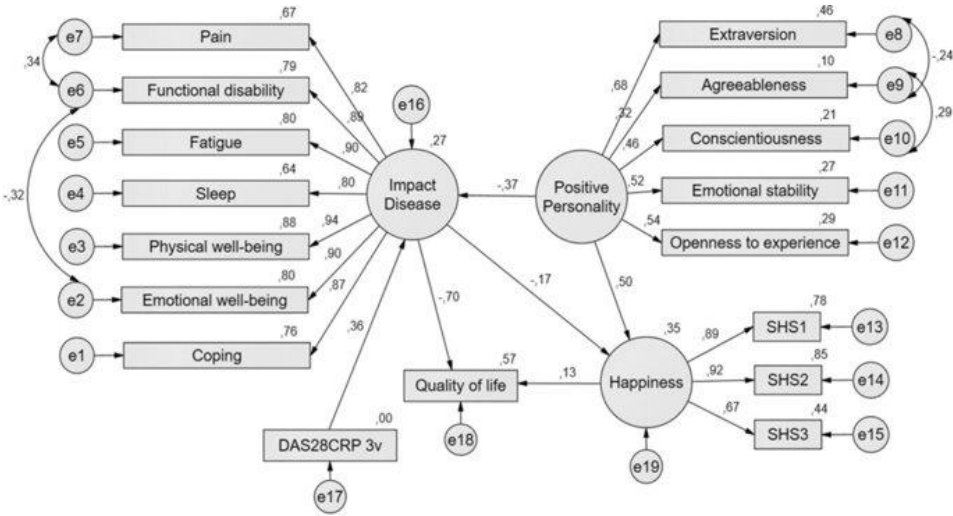


Matcham, Semin Arthritis Rheum 2014

Impact on QoL: what matters most?



Ferreira Santos, Ann Rheum Dis 2017

What counts most

for health care providers and patients
when choosing a treatment?

High discrepancy rates between physician and patients ratings

Desthieu, Arthritis Care Res 2016

What physicians want

Low swollen counts
Low DAS
X-ray progression slowing

What patients want

Less pain and fatigue
Better coping with daily life
Ability to work

Studenic, Arthritis Rheum 2012

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Studenic, Arthritis Rheum 2012

What physicians want

Low swollen counts
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X-ray progression slowing

Explain

65%

of discrepancy between PhGA and PGA

What patients want

Less pain and fatigue
Better coping with daily life
Ability to work

Studenic, Arthritis Rheum 2012

What physicians want

Table 2. Ten of the most important reasons to escalate care from a rheumatologist's perspective*

	Relative importance score, mean ± SD		Ranking	
	Rheumatologists	Patients	Rheumatologists	Patients
Swollen joints	5.24 ± 0.39	2.57 ± 1.63	1	12
DAS28	5.19 ± 0.54	2.40 ± 1.56	2	17
Rheumatologist's impression of overall disease activity	5.17 ± 0.55	3.03 ± 1.61	3	8
Worsening erosions in the past year	5.15 ± 0.53	2.12 ± 1.62	4	27
Disease activity now compared to 3 months ago	5.12 ± 0.60	2.37 ± 1.69	5	19
Risk factors for more severe RA	4.58 ± 1.04	2.17 ± 1.49	6	22
Physical functioning and mobility	4.38 ± 0.97	4.30 ± 1.07	7	1
Presence of erosions on most recent radiographs	4.21 ± 1.44	2.17 ± 1.59	8	23
Worsening of deformities last year	3.86 ± 1.19	1.88 ± 1.63	9	30
Patient's willingness to change DMARDs	3.61 ± 1.24	1.13 ± 1.21	10	37

* DAS28 = Disease Activity Score in 28 joints; RA = rheumatoid arthritis; DMARDs = disease-modifying antirheumatic drugs.

Van Hulst, Arthritis Care Res 2011

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Van Hulst, Arthritis Care Res 2011

What patients want

Table 1 Seventeen domains of health ranked for importance by 96 patients with RA

Domain*	Mean (SD) rank	Median rank	Order of domains by median	Patients giving rank 1–7 to the domain (%)	Patients giving rank 1–3 to the domain (%)
Pain	4.3 (4.2)	2	1	78.1	59.4
Functional disability	6.3 (3.9)	5.5	2	64.6	30.2
Fatigue	6.7 (4.2)	6	3	61.4	26.0
Physical well-being	8.3 (4.9)	9	5	44.8	24.0
Coping	8.8 (4.4)	9	5	41.7	16.7
Sleep	8.9 (4.8)	8	4	45.8	13.5
Emotional well-being	8.9 (4.0)	9	5	33.3	8.3
Being a burden to others	9.0 (4.6)	9.5	9	40.6	15.6
Family life	9.3 (5.3)	10	11	38.5	20.8
Satisfaction with health care	9.5 (5.1)	9	5	37.5	18.7
Anxiety	9.5 (4.5)	9.5	9	37.5	12.5
Ability to fulfil social role	9.5 (4.6)	10	11	35.4	11.5
Depression	10.0 (4.5)	10	11	32.3	9.4
Drug side effects	10.1 (4.8)	11	15	33.3	8.3
Professional life	10.2 (4.8)	10	11	33.3	12.5
Sexuality	11.2 (5.2)	12	16	23.9	10.4
Socioeconomic issues	11.5 (4.6)	13	17	27.1	5.2

*Domains are ordered by mean rank.

Gossec, Ann Rheum Dis 2009

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Gossec, Ann Rheum Dis 2009

Pain is a major factor contributing to QoL in RA, PsA and AS.

Pain in inflammatory arthritis.

Multiple etiology of pain in AxSpA

Table III. Causes of back pain in patients with SpA.

Axial inflammation including sacroiliitis, spondylitis, spondylodiscitis, enthesitis
Structural damage (new bone formation, ankylosis, hyperkyphosis)
Vertebral fractures
Spinal instability due to atlantoaxial dislocation
Subarachnoidal cysts
Degenerative spinal changes
Disc herniation
Spinal stenosis
Fibromyalgia, myofascial pain syndromes
Muscular dysbalance
Non-specific (low) back pain
All other causes of back pain (myocardial infarction, aneurysm, pleuritis, paptic ulcer, etc.

Kiltz, Clin Exp Rheumatol 2017

Which factors are related to poor QoL in AxSpA?

Table 3 Validation of a model predicting poor quality of life

Variable	Model derived from SIRAS study	
		Relative risk (95% CI)
Disease activity (BASDAI)	BASDAI<4	1.00
	BASDAI≥4	1.52 (1.09 to 2.12)
Physical function (BASFI)	BASFI<4	1.00
	BASFI≥4	3.46 (1.76 to 6.82)
Spinal mobility (BASMI)	BASMI<4	1.00
	BASMI≥4	1.52 (0.93 to 2.50)
Fatigue	None/mild	1.00
	Moderate/severe	1.60 (1.13 to 2.28)
Widespread Pain Index‡	No	1.00
	Yes	1.92 (1.33 to 2.75)

McFarlane, Ann Rheum Dis 2020

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Inflammation

McFarlane, Ann Rheum Dis 2020

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Inflammation

Chronic changes

McFarlane, Ann Rheum Dis 2020

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Inflammation

Chronic changes

Chronic pain

McFarlane, Ann Rheum Dis 2020

High percentage of pain in patients in remission.

A considerable percentage of patients in remission still experience pain and fatigue

Table: Number (%) of 734 patients in the ESPOIR early RA cohort who are in remission according to each of 8 descriptions, and number (%) of patients within each description category having residual symptoms according to specific measures and joint counts.

	8 Descriptions of Remission in Rheumatoid Arthritis							
	Boolean	SDAI ≤3.3	DAS28 ≤2.6	CDAI ≤2.8	RAPID3R [RAPID3 ≤3]	RAPID3R+J1 [RAPID3 ≤3; SJC ≤1]	RAPID3R+J1D1 [RAPID3 ≤3; SJC ≤1; DOCGL ≤1]	RAPID3R+J0D1 [RAPID3 ≤3; SJC=0; DOCGL ≤1]
N (% of all pts)*	**96 (13%)**	**127 (17%)**	**238 (32%)**	**138 (18%)**	**194 (26%)**	**141 (19%)**	**121 (16%)**	**100 (13%)**
Measures: N (%) of patients in remission by each description								
TJC28 >1	0 (0%)	4 (3%)	26 (11%)	4 (3%)	46 (24%)	22 (16%)	18 (15%)	13 (13%)
SJC28 >1	0 (0%)	3 (2%)	38 (16%)	3 (2%)	53 (27%)	0 (0%)	0 (0%)	0 (0%)
CRP >1	0 (0%)	4 (3%)	14 (6%)	10 (7%)	14 (8%)	8 (6%)	7 (6%)	5 (5%)
DOCGL >1	7 (7%)	10 (8%)	90 (37%)	11 (8%)	44 (23%)	20 (14%)	0 (0%)	0 (0%)
PATGL >1	0 (0%)	24 (19%)	117 (49%)	29 (21%)	40 (21%)	25 (18%)	13 (11%)	10 (10%)
Pain >1	15 (16%)	29 (23%)	100 (46%)	29 (21%)	33 (17%)	19 (13%)	14 (12%)	9 (9%)
Fatigue >1	55 (57%)	75 (59%)	156 (65%)	81 (59%)	103 (53%)	76 (54%)	57 (47%)	53 (53%)
HAQ-FN >0.5	5 (5%)	12 (9%)	29 (12%)	13 (9%)	3 (1%)	3 (2%)	3 (2%)	2 (2%)
Swollen Joints: N (%) of patients in remission by each description								
Knees ≥1	0 (0%)	0 (0%)	7 (3%)	1 (1%)	9 (4%)	2 (1.5%)	1 (1%)	0 (0%)
Shoulders ≥1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Elbows ≥1	0 (0%)	0 (0%)	5 (2%)	0 (0%)	2 (1%)	0 (0%)	0 (0%)	0 (0%)
Wrists ≥1	5 (5%)	5 (4%)	19 (8%)	5 (4%)	22 (11%)	6 (4%)	6 (5%)	0 (0%)
MCPs ≥1	9 (9%)	11 (9%)	46 (21%)	10 (7%)	52 (27%)	13 (9%)	10 (8%)	0 (0%)
PIPs ≥1	3 (3%)	5 (5%)	24 (11%)	5 (4%)	14 (19%)	4 (3%)	4 (3%)	0 (0%)

*Top row indicates number (%) of 734 patients who are in remission according to each of 8 descriptions. All other values are number (%) of patients within each column (remission description category) who have residual symptoms.

Dougados, ACR/ARHP Annual Meeting 2012

A considerable percentage of patients in remission still experience pain and fatigue

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Shoulders ≥1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Elbows ≥1	0 (0%)	0 (0%)	5 (2%)	0 (0%)	2 (1%)	0 (0%)	0 (0%)	0 (0%)
Wrists ≥1	5 (5%)	5 (4%)	19 (8%)	5 (4%)	22 (11%)	6 (4%)	6 (5%)	0 (0%)

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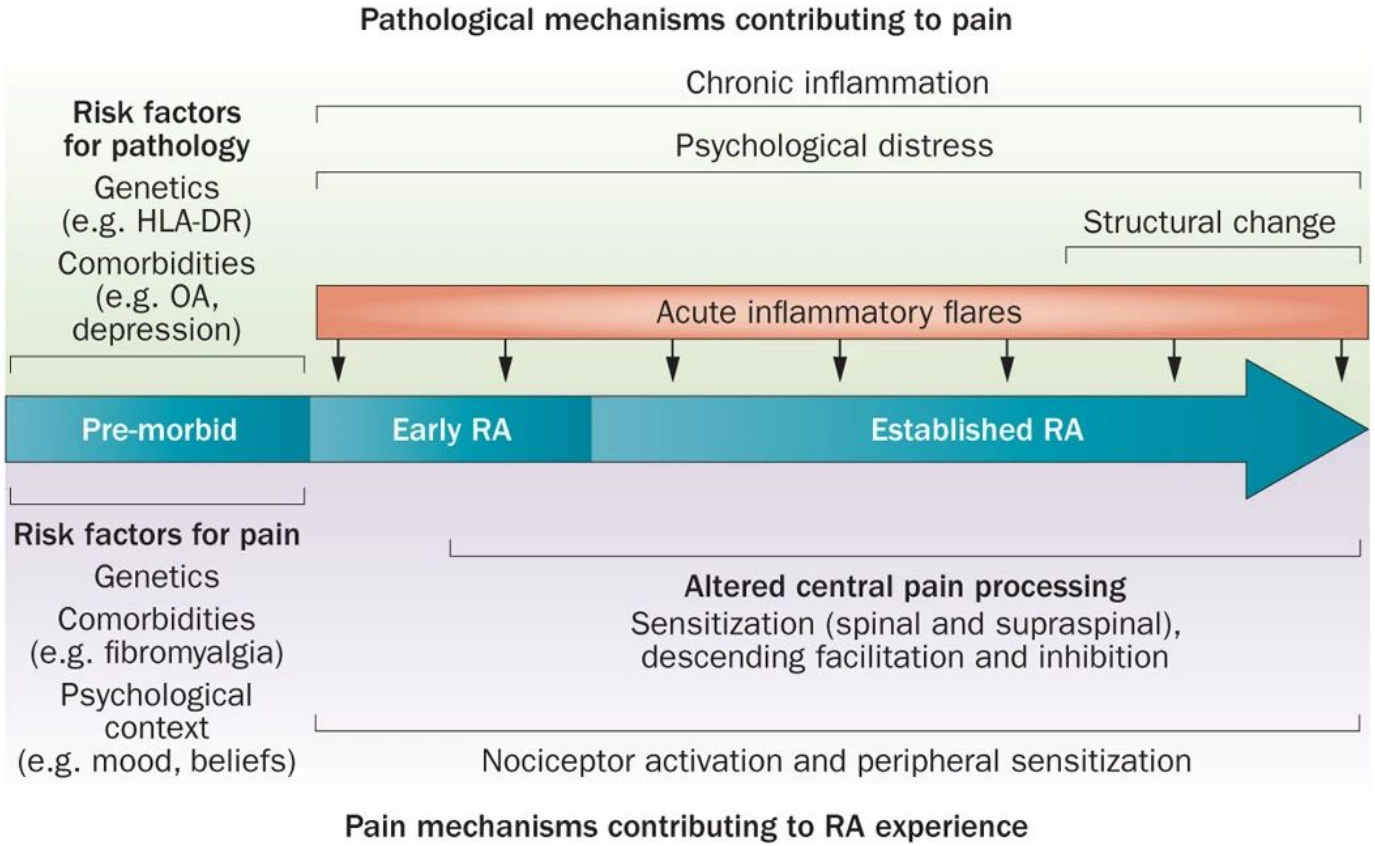
Dougados, ACR/ARHP Annual Meeting 2012

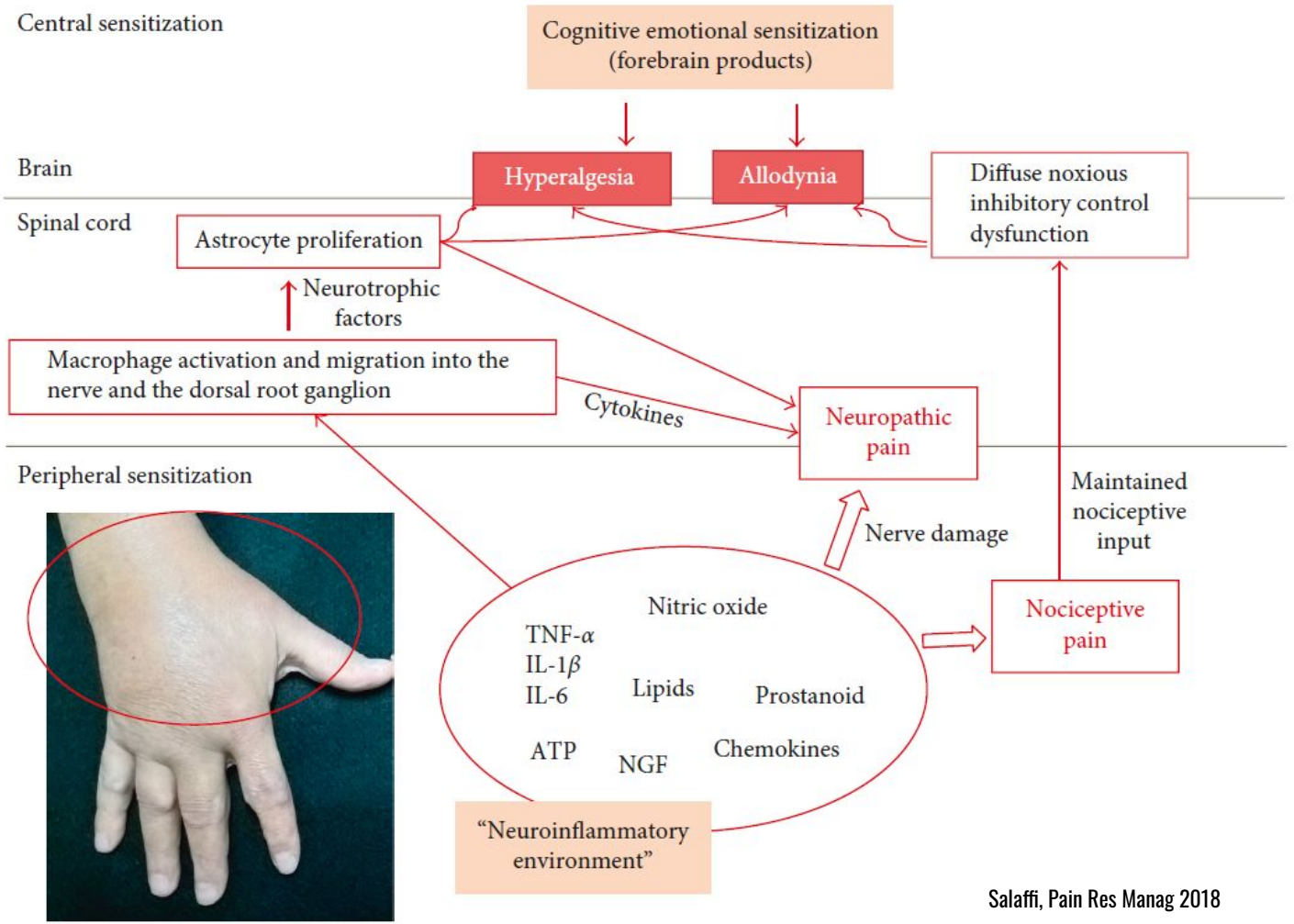
Pain in inflammatory arthritis: basic pathophysiologic considerations

Pain mechanisms in RA



Walsh, Nat Rev Rheumatol 2014

Mechanisms of peripheral and central sensitization in inflammatory arthritis



Salaffi, Pain Res Manag 2018

Table 1
Cytokine interactions with the Jak/STAT pathway and likely involvement in pain.

Cytokine (ligand/receptor)	Elements of Jak/STAT pathway affected	Association with pain mechanisms
GM-CSF/GM-CSFR	Jak2 [31,71] STAT3 [71], STAT5 [11]	Induces hyperalgesia [36,40,71] Upregulates sodium channel expression (Nav1.7-Nav1.9) [71]
IFN-γ/IFN-γR	Jak1/Jak2 [9,11] STAT1 [9,11] STAT3 [72]	Initiation or maintenance of pain [73,74] IFN-γ– and IFN-γ receptor–deficient mice demonstrate social dysfunction [75] Can signal through inhibitory (GABAergic-specific) neurons [75]
IL-1β/IL-1R	Indirect via IL-6/STAT3 {Ahmed, 2000 #295}	Initiation of pain [19] Can have detrimental effect on cognitive function [76]
IL-4/IL-4R	Jak1, Jak3 [31] STAT1, STAT3, STAT6 [11,77]	Overexpression of IL-4 can decrease hyperalgesia [34] IL-4–deficient mice show improved social function, may have mechanical allodynia, and demonstrate cognitive deficits [75,78,79]
IL-6/IL-6R, sIL-6R	Jak1, Jak2, TYK2 [9,80] STAT3 [9,31]	Pro-nociceptive factor [21] Contributes to development of hyperalgesia/allodynia in rats [81] Can have detrimental effect on cognitive function [82]
IL-10/IL-10R	Jak1 STAT3 [9]	Mitigates pain (anti-nociceptive effects) [19, 21]
IL-12/IL-12R	TYK2 and STAT4 [34]	Leads to release of pro-nociceptive cytokines TNF and IFN-γ [34]
IL-15/IL-15Rα, IL-2Rβ,γ_C	Jak1/Jak3 STAT5 [11]	Associated with severity of pain in osteoarthritis [83] Induces neuropathic pain [84]
IL-17/IL-17RA	Jak2 [38] STAT1, STAT3 [38]	Causes allodynia [85]
IL-18/IL-18R	TYK2 and STAT4 [34]	Pro-nociceptive factor [21]
IL-22/IL-22R	Jak1 [86] STAT3 [86]	Increased expression level is noted in experimental arthritis [87] Inhibiting IL-22 reduces pain [87]
IL-27/gp130	TYK2 [88] STAT1, STAT3, STAT5a/b [32] gp130-signaling subunit [32]	Diminished expression of gp130 can attenuate pain [89]
TNF-α/TNFR1, TNFR2	Indirect via IFN-β–Jak/STAT expression and STAT1 [69]	Can initiate pain and induce pain-receptor sensitization (both mechanical and thermal hyperalgesia) [90] Is associated with neuropathic pain [91,92] and has detrimental effect on cognitive function [93,94]

GABA: γ-aminobutyric acid; GM-CSF: granulocyte-macrophage colony-stimulating factor; gp: glycoprotein; IFN: interferon; IL: interleukin; Jak: Janus kinase; R: receptor; STAT: signal transducer and activator of transcription; TNF: tumor necrosis factor; TYK: tyrosine kinase.

Treatment with jak-inhs rapidly reduces central sensitization and pain catastrophizing

Variable	Baseline	4 weeks	p
Central sensitization inventory	36.73	32.57	<0.0001
Pain Catastrophizing scale	32.46	28.72	0.0001
SDAI	44.3	27.83	<0.0001
US score	5.25	5.03	0.226
Pain Detect Questionaire	17.65	15.66	0.0005

Salaffi, Immunopharmacol 2022

Upadacitinib improves pain in RA- the SELECT-COMPARE TRIAL

TABLE 2 LSM changes from baseline at weeks 12 and 2 following UPAD initiation

PRO measures	LSM change (95% CI)		
	UPAD 15 mg ($n = 651$)	PBO ($n = 651$)	ADA 40 mg ($n = 327$)
Week 12			
PtGA	−30.39 (−32.62, −28.16)[a,b]	−15.24 (−17.44, −13.04)	−23.55 (−26.43, −20.67)[c]
Pain VAS	−31.76 (−33.96, −29.56)[a,b]	−15.46 (−17.63, −13.29)	−25.31 (−28.16, −22.47)[c]
HAQ–DI	−0.61 (−0.66, −0.56)[a,b]	−0.30 (−0.35, −0.25)	−0.51 (−0.57, −0.44)[c]
AM stiffness duration	−92.63 (−103.03, −82.23)[a]	−48.59 (−58.84, −38.34)	−82.71 (−95.80, −69.62)[c]
AM stiffness severity	−3.37 (−3.59, −3.15)[a,b]	−1.83 (−2.05, −1.61)	−2.86 (−3.14, −2.57)[c]
FACIT-F	8.95 (7.98, 9.93)[a,b]	4.81 (3.85, 5.77)	7.44 (6.25, 8.64)[c]
RA-WIS (among employed patients)	−5.16 (−6.10, −4.23)[a]	−1.98 (−2.87, −1.10)	−4.45 (−5.61, −3.28)[c]
SF-36 Summary Scores			
PCS	7.89 (7.11, 8.68)[a,b]	3.56 (2.79, 4.33)	6.27 (5.31, 7.23)[c]
MCS	6.39 (5.50, 7.29)[a]	3.67 (2.78, 4.55)	5.39 (4.29, 6.49)[c]
SF-36 domains			
Physical functioning	7.31 (6.45, 8.18)[a,b]	3.59 (2.74, 4.45)	6.18 (5.12, 7.25)[c]
Role-physical	6.85 (6.06, 7.65)[a,b]	3.63 (2.85, 4.41)	5.16 (4.19, 6.14)[c]
Bodily pain	9.85 (9.02, 10.68)[a,b]	4.61 (3.80, 5.43)	8.03 (7.02, 9.05)[c]
General health	7.27 (6.49, 8.05)[a,b]	3.12 (2.35, 3.89)	5.67 (4.72, 6.63)[c]
Vitality	8.24 (7.38, 9.10)[a,b]	4.26 (3.41, 5.10)	6.79 (5.74, 7.84)[c]
Social functioning	7.19 (6.32, 8.06)[a,b]	3.40 (2.54, 4.25)	5.75 (4.69, 6.82)[c]
Role-emotional	6.24 (5.31, 7.18)[a]	3.60 (2.68, 4.53)	5.21 (4.05, 6.36)[c]
Mental health	6.99 (6.11, 7.87)[a]	4.02 (3.15, 4.88)	5.91 (4.83, 6.99)[c]
Week 2			
Pain VAS	−17.57 (−19.53, −15.60)[a]	−7.10 (−9.04, −5.17)	−17.94 (−20.41, −15.46)[c]
AM stiffness duration	−49.09 (−61.46, −36.71)[a]	−16.73 (−28.98, −4.47)	−41.79 (−57.98, −25.61)[c]
AM stiffness severity	−1.62 (−1.82, −1.42)[a]	−0.65 (−0.85, −0.45)	−1.65 (−1.90, −1.39)[c]

Strand, Rheumatology 2021

Upadacitinib improves pain in RA- the SELECT-COMPARE TRIAL

TABLE 2 LSM changes from baseline at weeks 12 and 2 following UPAD initiation

PRO measures	LSM change (95% CI)		
	UPAD 15 mg ($n = 651$)	PBO ($n = 651$)	ADA 40 mg ($n = 327$)
Week 12			
Pain VAS	−31.76 (−33.96, −29.56)[a,b]	−15.46 (−17.63, −13.29)	−25.31 (−28.16, −22.47)[c]
AM stiffness duration	−92.63 (−103.03, −82.23)[a]	−48.59 (−58.84, −38.34)	−82.71 (−95.80, −69.62)[c]
AM stiffness severity	−3.37 (−3.59, −3.15)[a,b]	−1.83 (−2.05, −1.61)	−2.86 (−3.14, −2.57)[c]
FACIT-F	8.95 (7.98, 9.93)[a,b]	4.81 (3.85, 5.77)	7.44 (6.25, 8.64)[c]
RA-WIS (among employed patients)	−5.16 (−6.10, −4.23)[a]	−1.98 (−2.87, −1.10)	−4.45 (−5.61, −3.28)[c]
SF-36 Summary Scores			
PCS	7.89 (7.11, 8.68)[a,b]	3.56 (2.79, 4.33)	6.27 (5.31, 7.23)[c]
MCS	6.39 (5.50, 7.29)[a]	3.67 (2.78, 4.55)	5.39 (4.29, 6.49)[c]
SF-36 domains			
Physical functioning	7.31 (6.45, 8.18)[a,b]	3.59 (2.74, 4.45)	6.18 (5.12, 7.25)[c]
Role-physical	6.85 (6.06, 7.65)[a,b]	3.63 (2.85, 4.41)	5.16 (4.19, 6.14)[c]
Bodily pain	9.85 (9.02, 10.68)[a,b]	4.61 (3.80, 5.43)	8.03 (7.02, 9.05)[c]
General health	7.27 (6.49, 8.05)[a,b]	3.12 (2.35, 3.89)	5.67 (4.72, 6.63)[c]
Vitality	8.24 (7.38, 9.10)[a,b]	4.26 (3.41, 5.10)	6.79 (5.74, 7.84)[c]
Social functioning	7.19 (6.32, 8.06)[a,b]	3.40 (2.54, 4.25)	5.75 (4.69, 6.82)[c]
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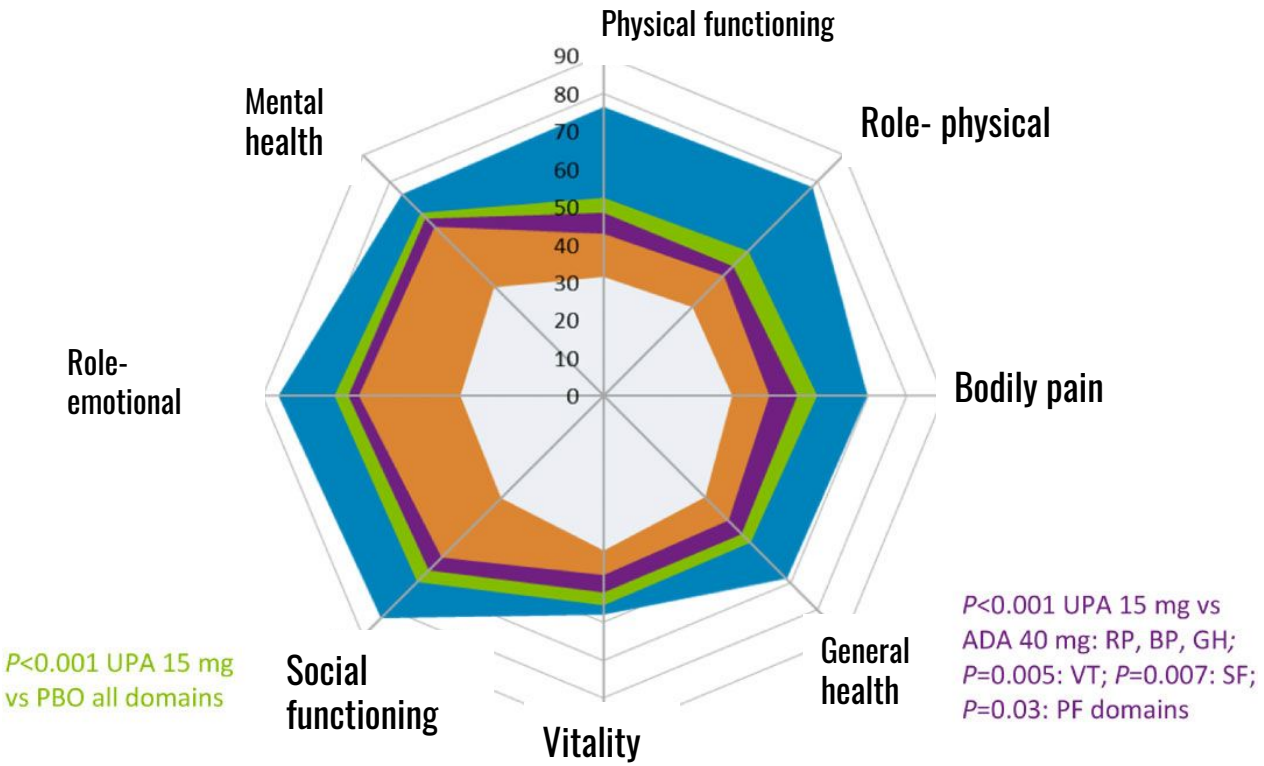
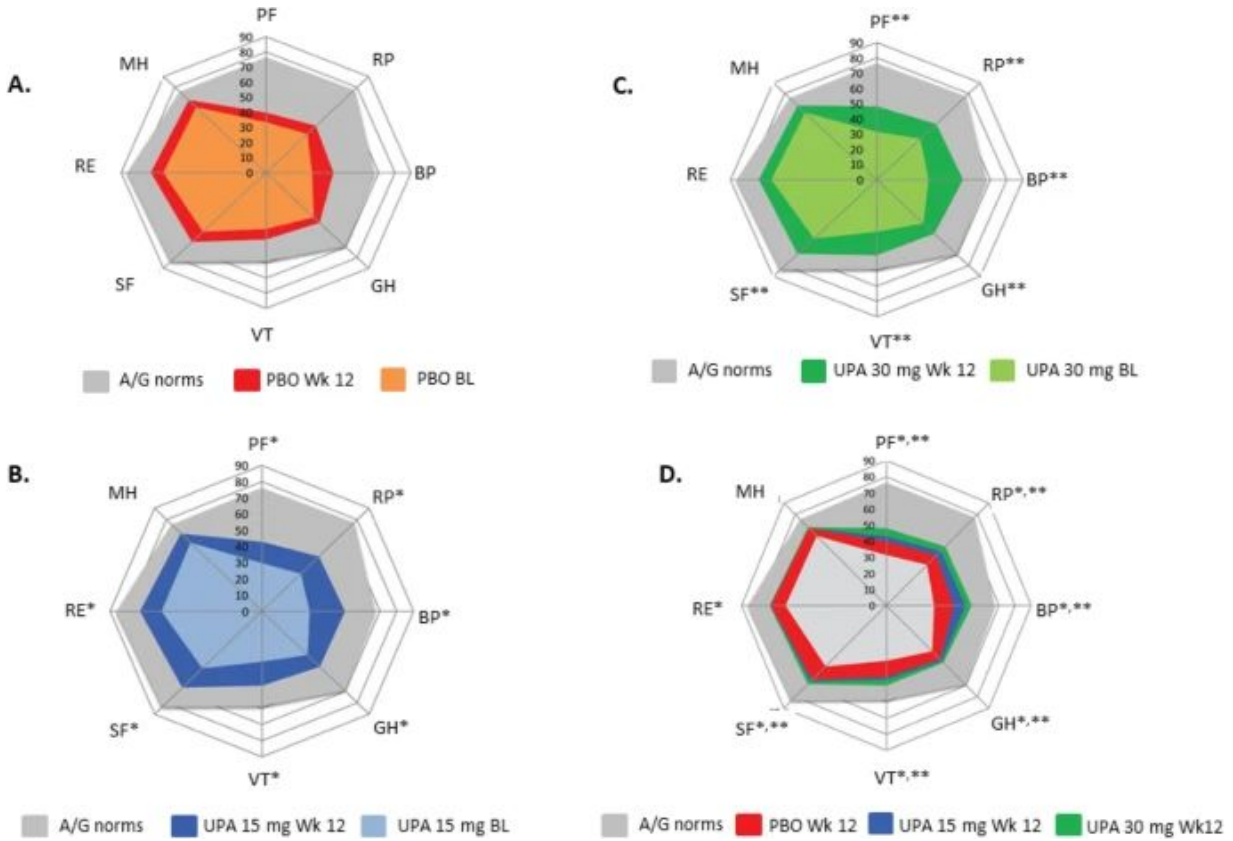
Strand, Rheumatology 2021

Upadacitinib improves PROs in RA: results from the SELECT- COMPARE trial



Strand, Rheumatology 2021

Upadacitinib improves PROs in RA: results from the SELECT- BEYOND trial



Strand, Arthritis Res Ther 2019

Pain in inflammatory arthritis: the hanging mobile toy model

Geenen, Ann Rheum Dis 2017

Pain in inflammatory arthritis: the hanging mobile toy model

Geenen, Ann Rheum Dis 2017

"...pain encompasses multiple and mutually interacting biological, psychological and social factors that include but are not limited to *pain severity, peripheral (inflammation and joint damage) and central neurophysiological processes, physical (dis)ability, resilience and vulnerabilities (emotions, cognitions, behaviour, lifestyle), social factors (work, support, facilities, economic), sleep quality*, obesity and other health risks (eg, smoking, alcoholism)."

Ευχαριστώ

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