Diagnose en therapie van artritis

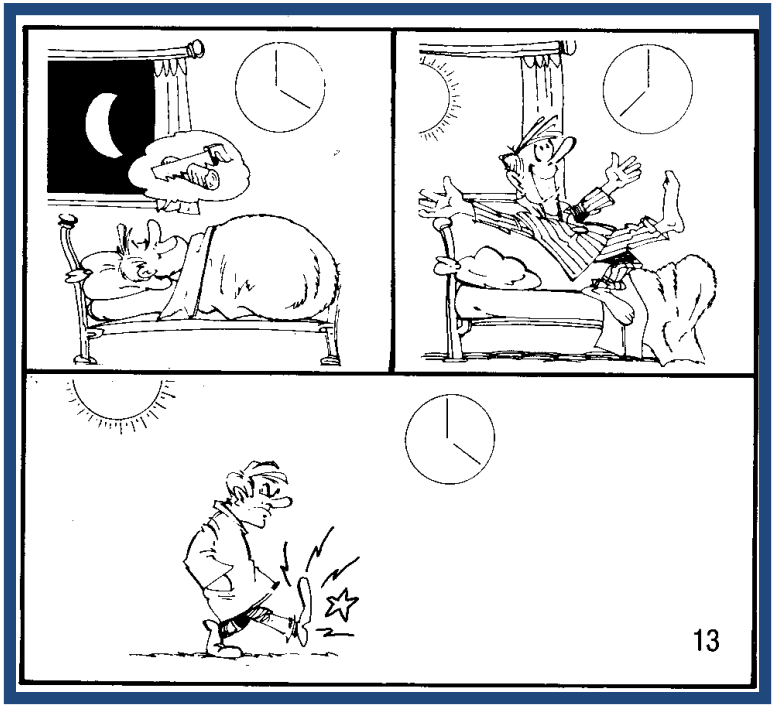
Patrick Verschueren MD, PhD

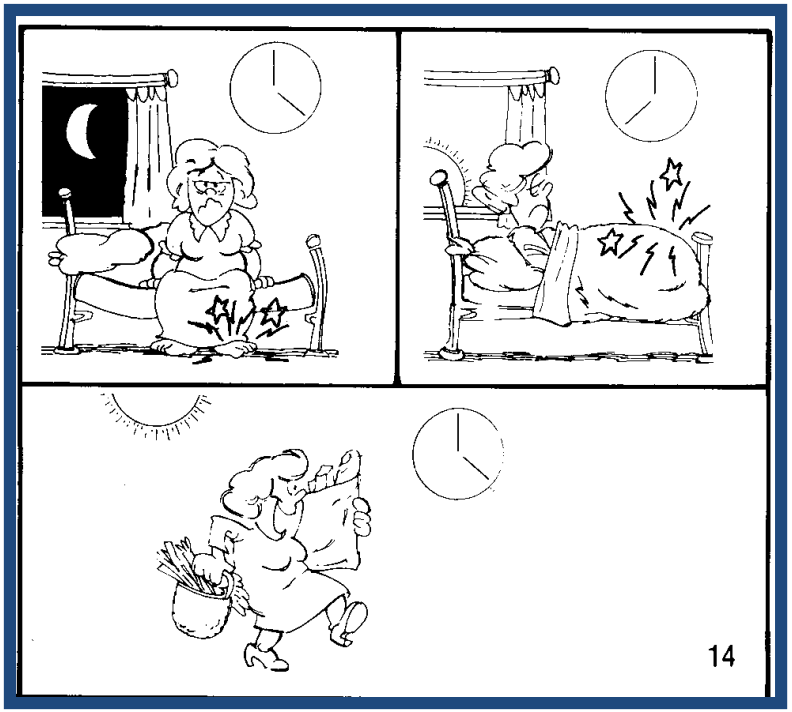
What's in a name ?

The diagnostic process

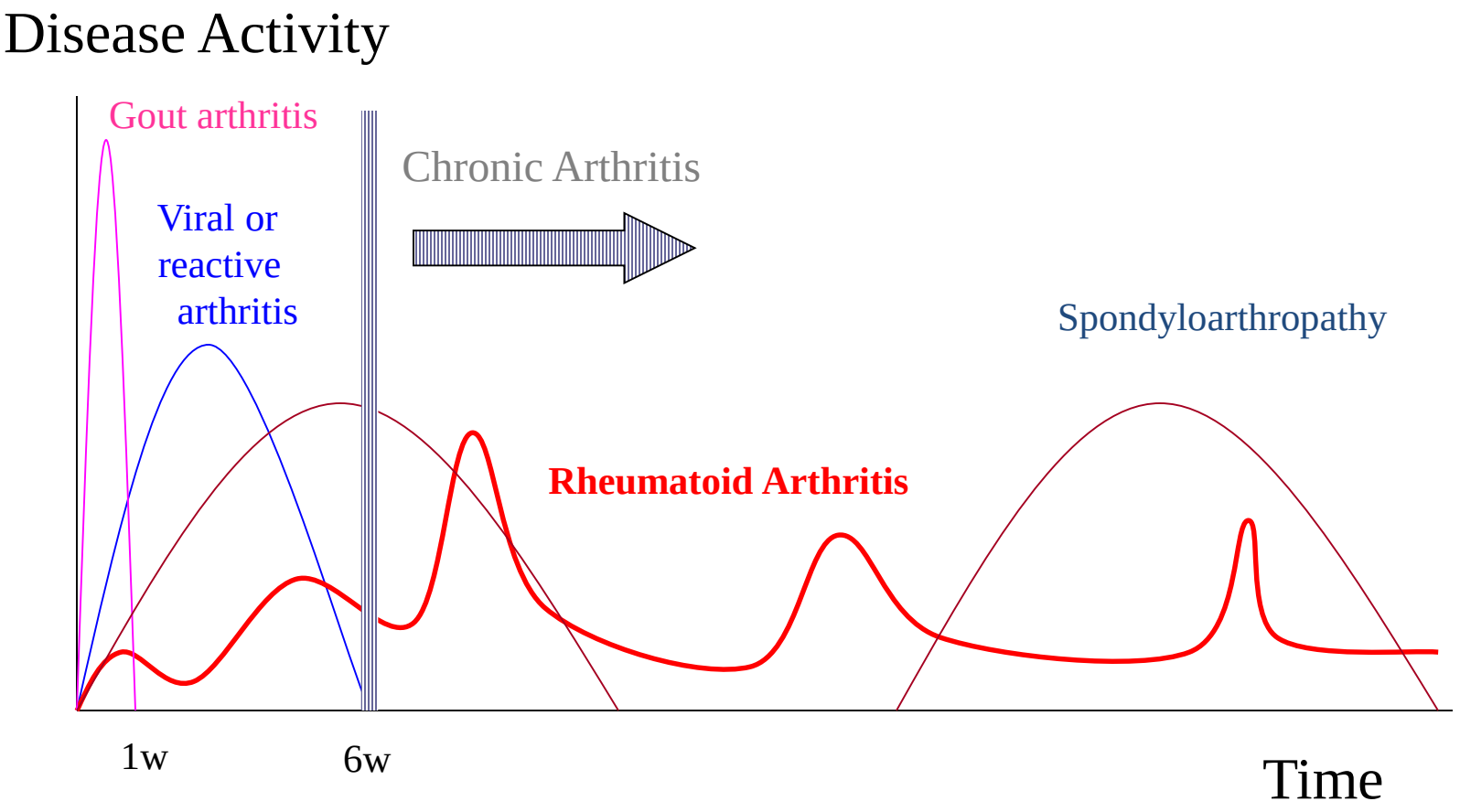
- **Anamnesis is key !**
  - presenting symptom: pain, swelling, stiffness…
  - symptom character: inflammatory/mechanical
  - time course: (sub)acute or chronic, circadian
  - joint type: small, medium or large
  - distribution: number of joints, symmetry
  - other articular problems: enthesitis, dactylitis
  - axial complaints: buttock, neck or back pain
  - extra-articular manifestations: gut, skin, mouth, eye…
  - global setting: context, history, organ function…

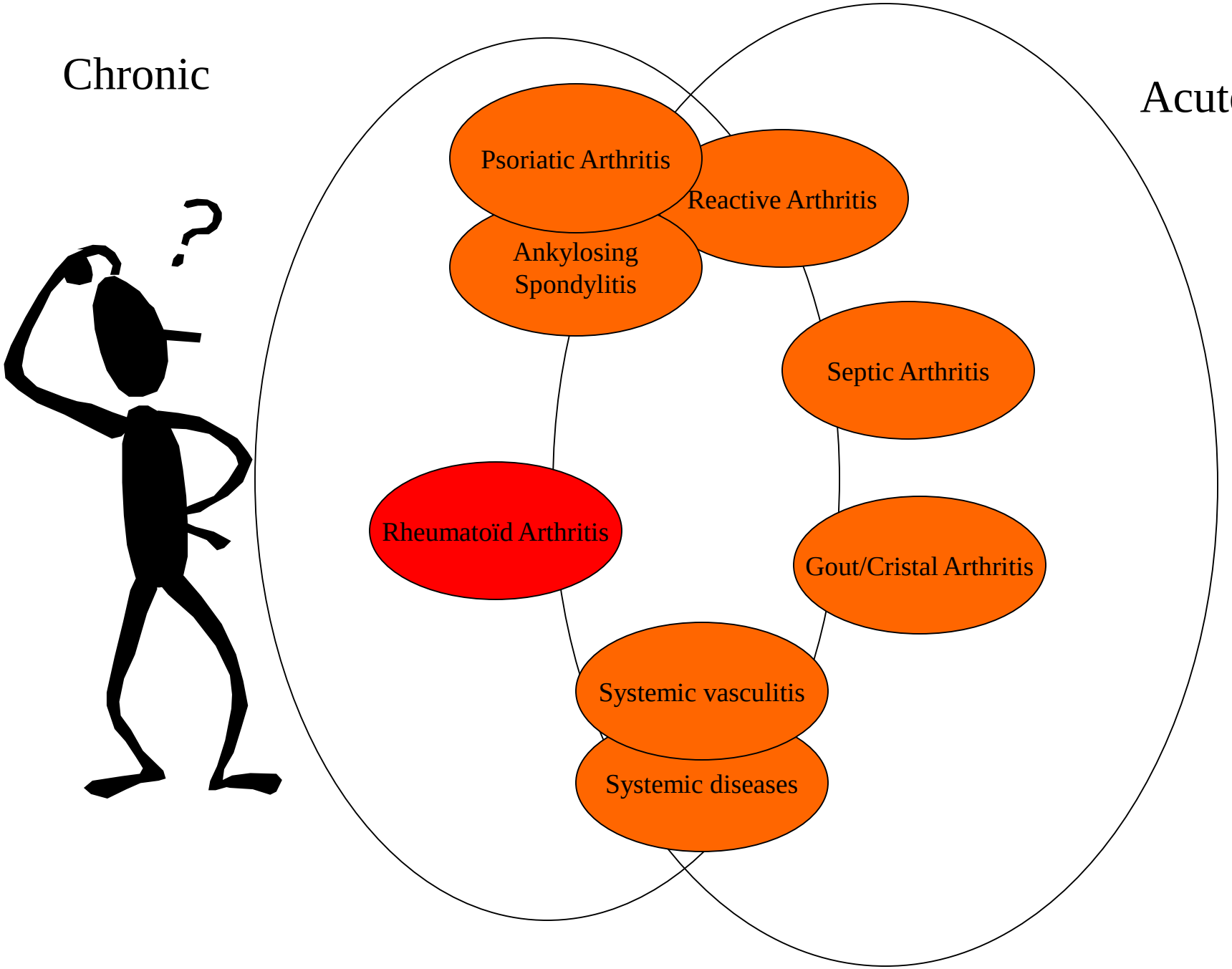
Joint pain:
Mechanical versus Inflammatory

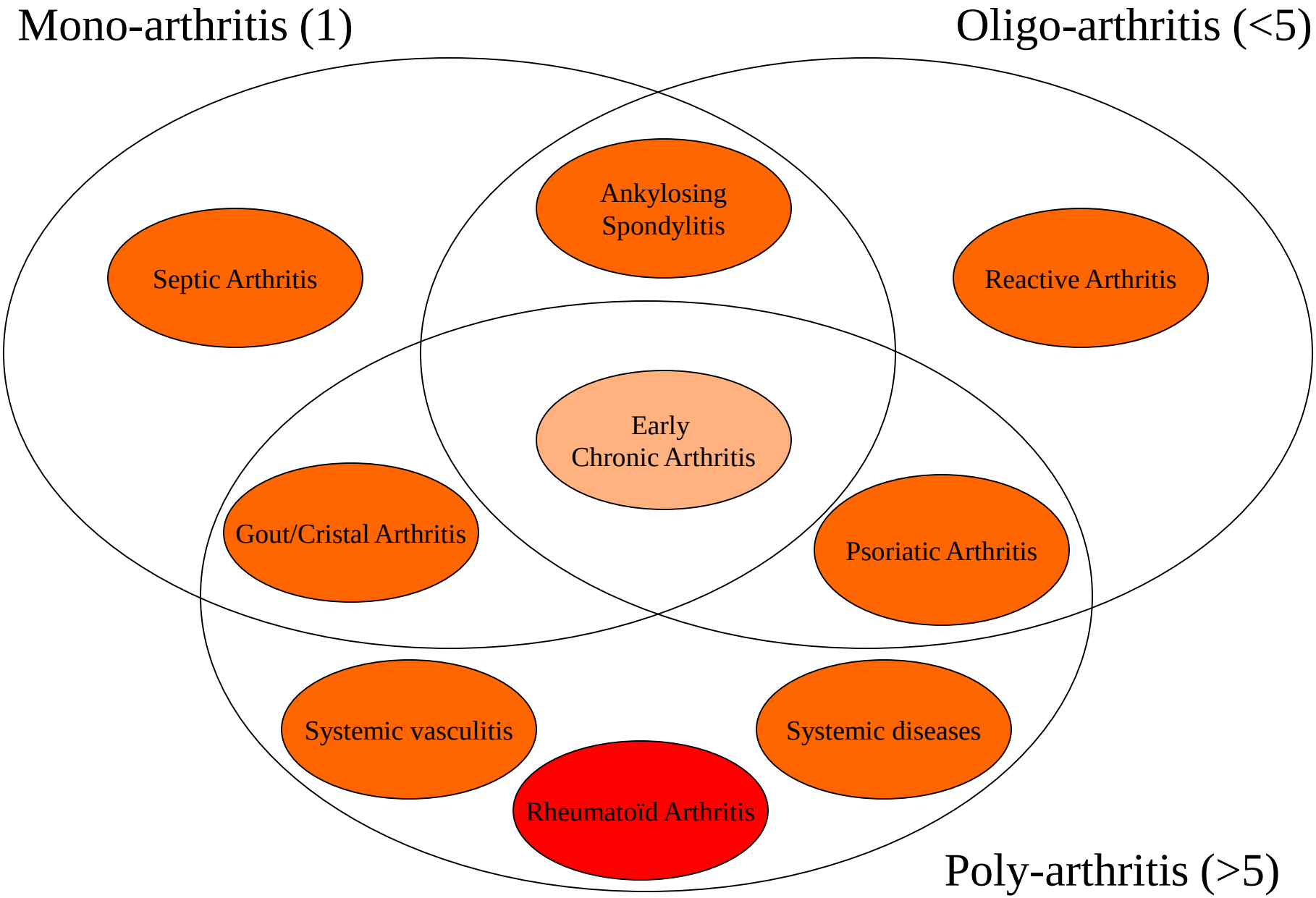




Acute versus chronic arthritis




Chronic
Acute
Psoriatic Arthritis
Reactive Arthritis
Ankylosing Spondylitis
Septic Arthritis
Rheumatoïd Arthritis
Gout/Cristal Arthritis
Systemic vasculitis
Systemic diseases


Mono-arthritis (1)
Oligo-arthritis (<5)
Ankylosing Spondylitis
Septic Arthritis
Reactive Arthritis
Early Chronic Arthritis
Gout/Cristal Arthritis
Psoriatic Arthritis
Systemic vasculitis
Systemic diseases
Rheumatoïd Arthritis
Poly-arthritis (>5)

The diagnostic process

- **Clinical examination: be systematic !**
  - make sure the patient is comfortable
  - look your patient in the eyes
  - start carefully with the culprit joint
  - go step by step: inspection > palpation > function
  - examine all joints, one by one, including the back
  - look for skin/nails, vascular/neurologic signs
  - do a general physical examination

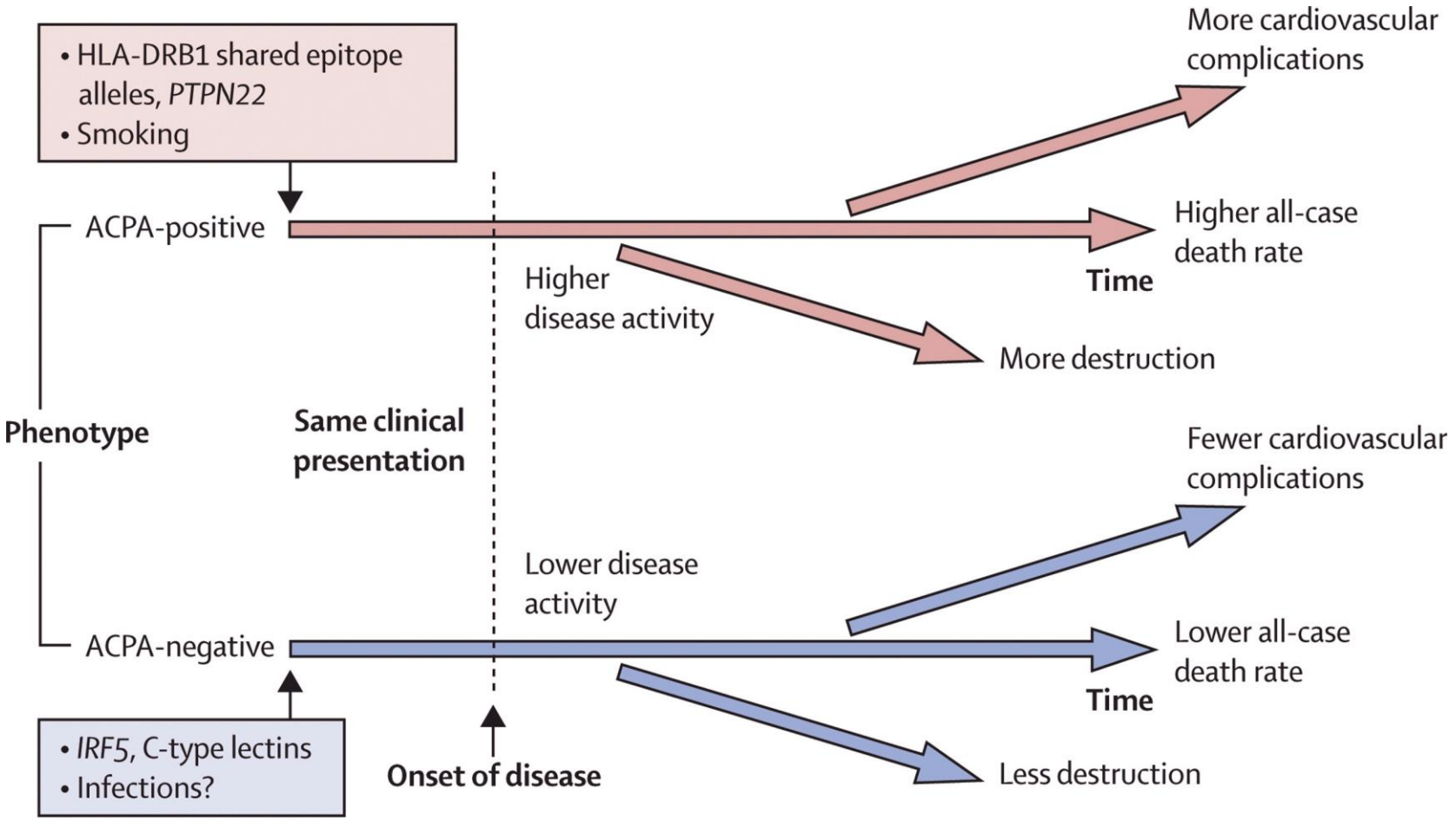
The diagnostic process

- **Technical examinations: be selective !**
  - blood : CRP/BSE, biomarkers, function tests
  - ultrasound: confirmation of synovitis, tendinosis
  - X-ray: culprit joint + both sides + hands/feet
  - CT: differential diagnosis bone problems
  - MRI: clinical uncertainty and suspicion of SpA
  - scintigraphy: suspicion of cancer, widespread pain

Meta-analysis of 86 studies: diagnostic accuracy of anti-cyclic citrullinated peptide antibody and rheumatoid factor for rheumatoid arthritis

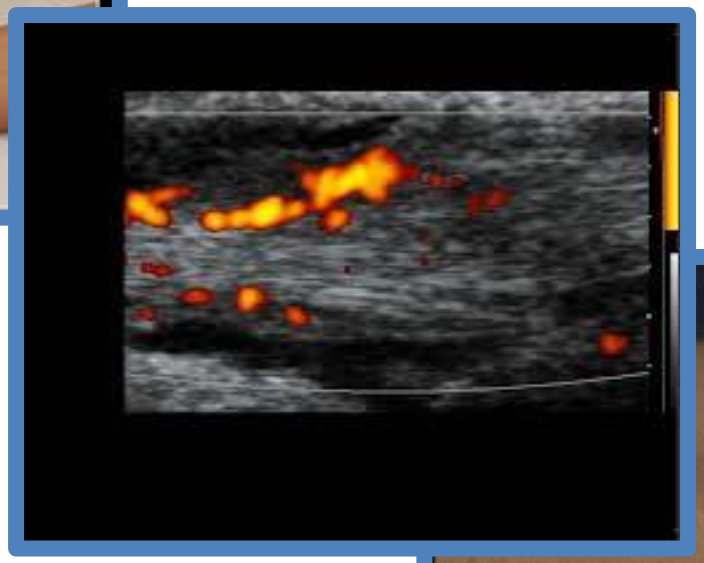
	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio
Anti-CCP	67% (CI, 62% to 72%)	95% (CI, 94% to 97%)	12.46 (CI, 9.72 to 15.98)	0.36 (CI, 0.31 to 0.42)
RF	69% (CI, 65% to 73%)	85% (CI, 82% to 88%)	4.86 (CI, 3.95 to 5.97)	0.38 (CI, 0.33 to 0.44)

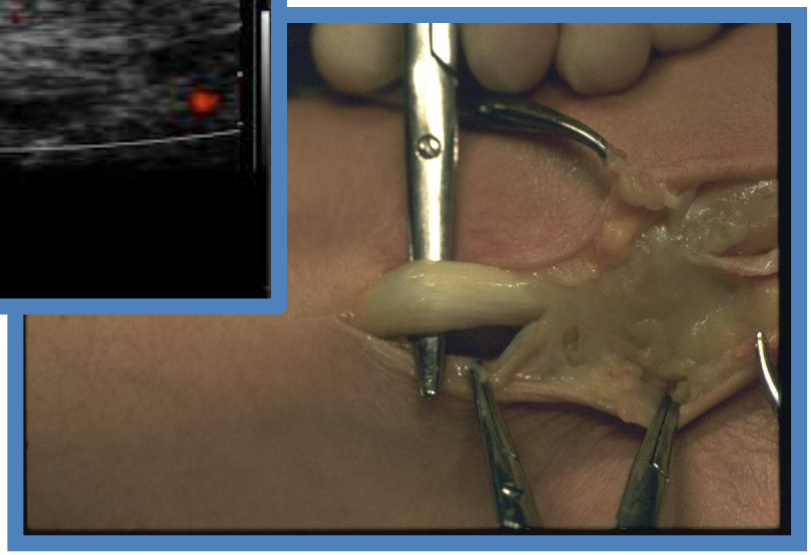
Nishimura K et al. Ann Intern Med 2007; 146(11):797-808



Klareskog et al. Lancet 2009 feb 21;373(9664):659-72

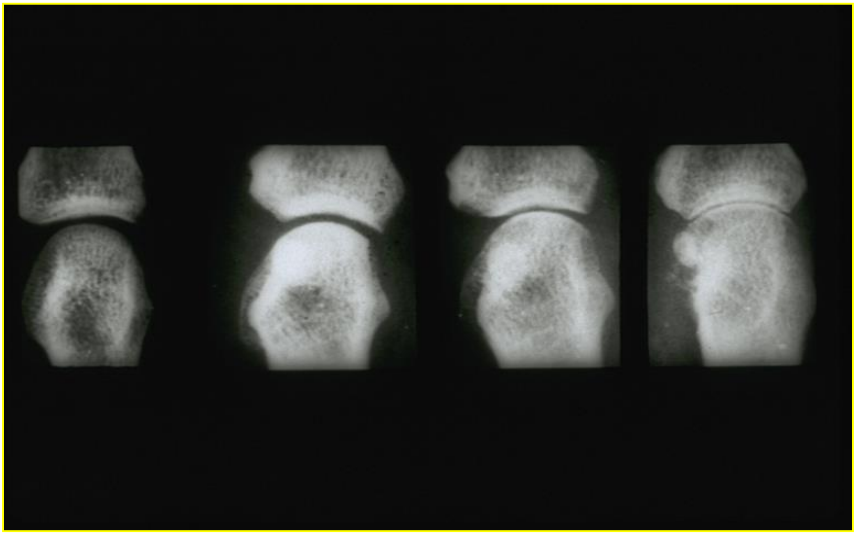
Ultrasound examination of soft tissue: (teno)synovitis





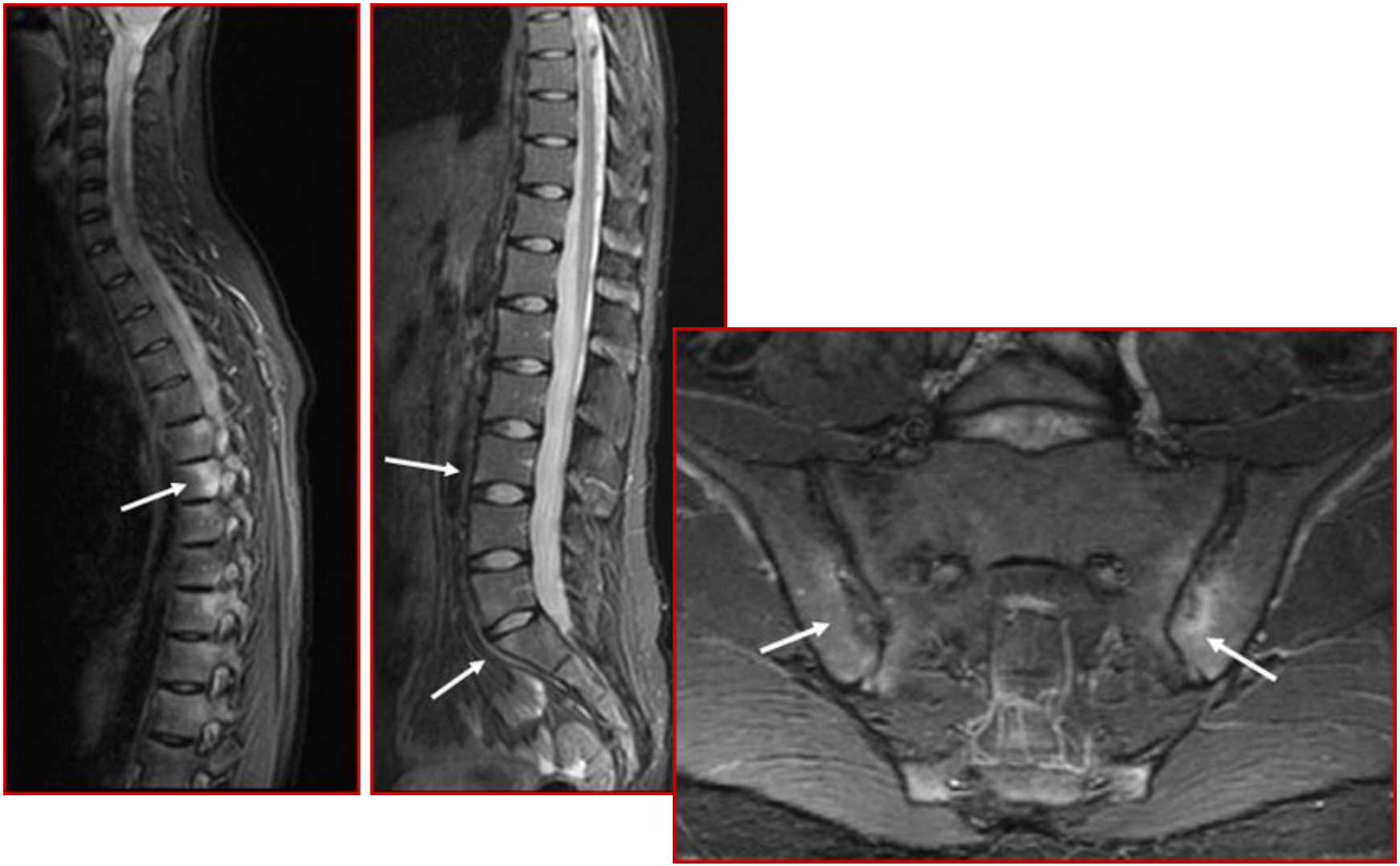
X-ray examination of hard tissue: cartilage loss and bone erosions

- Early RA
  - Soft tissue swelling
- Progressive RA
  - Juxta-articular osteoporosis
  - Jointspace narrowing and erosion
- Established RA
  - Progressive erosion, functional ankylosis
  - Axis deviation, subluxation, deformities

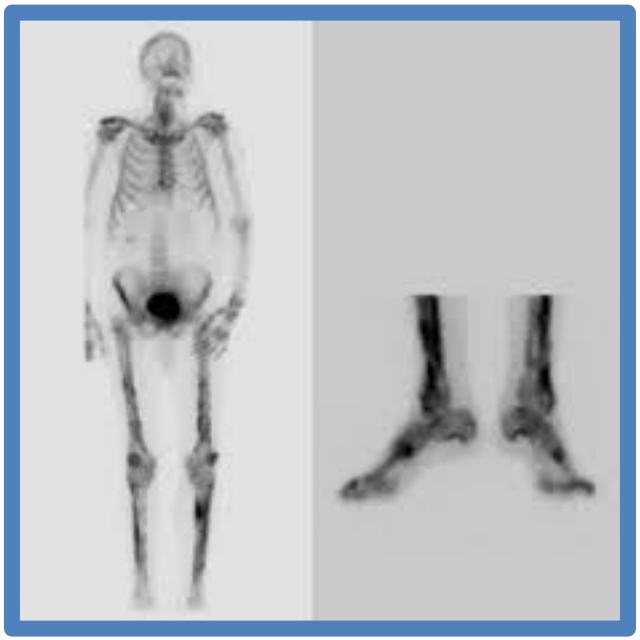


Bower AC. In: Klippel JH, Dieppe PA, eds. *Rheumatology*. Vol 1. 2nd ed. 1998;5:5.1–5.8.
Resnick D et al. In: Kelley WN et al, eds. *Textbook of Rheumatology*. 5th ed. 1997:626–685.

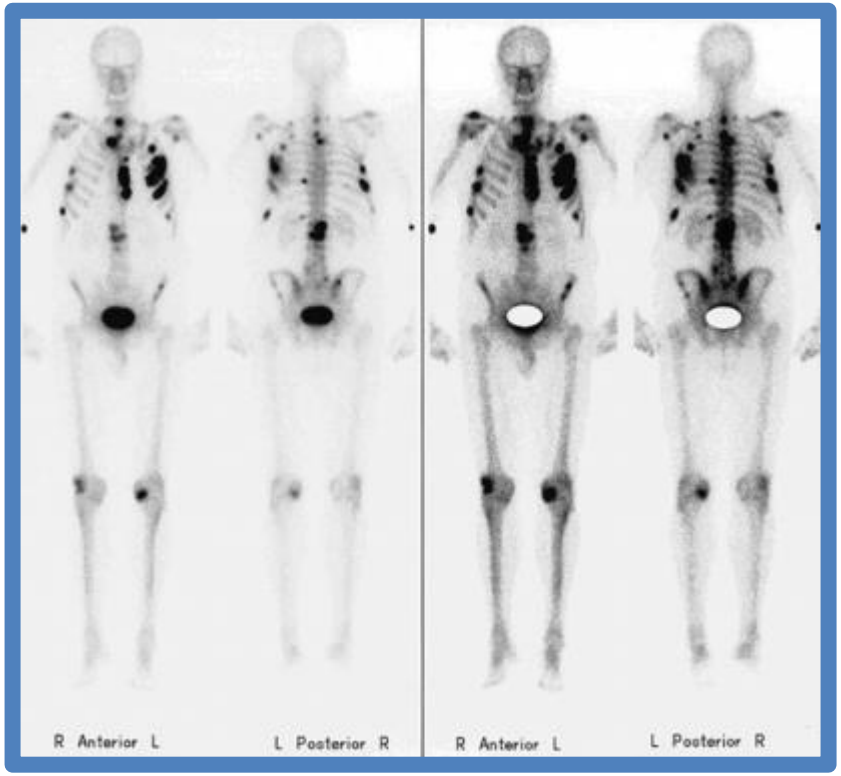
MRI examination: axial inflammation



Bone scintigraphy: atypical presentation



Pierre-Marie Bamberger
hypertrophic osteoarthropathy



Diffuse skeletal metastasis

Acute monoarthritis

Differential diagnosis:

- First rule out septic arthritis
- Think about crystal arthritis

Diagnostic procedure number one: arthrocentesis

-Gram staining and culture

-WBC count and microscopic examination for crystals

Acute monoarthritis

Circumstantial evidence

- Calor-rubor-dolor-tumor
- Fever, illness
- Skin lesions
- Tophi

Diagnostic procedure: bloodsample

- Bloodculture
- CRP +++
- Serum uric acid (lowered in aute phase)

Acute monoarthritis: septic arthritis

- Treatment
  - ubi pus ibi evacua
  - antibiotics (6w) according to culture/abiogram

- Prognosis
  - destructive arthropathy
  - cave contractures
  - cave osteomyelitis

Acute monoarthritis: crystal arthropathy

- Treatment (acute phase)
  - Colchicine 1mg followed by 0.5mg/12 hours
  - Strong NSAID at anti-inflammatory dosages
  - In case of kidney problems: moderate dose GC

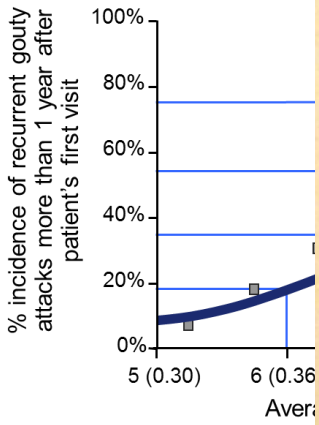
- Prognosis
  - Spontanuous resolution acute phase 4-7 days
  - Repeated arthritis attacks are destructive
  - Longstanding gout can become chronic/polyarticular

Acute

opathy

Urinezuur > 6mg/dl

Ura



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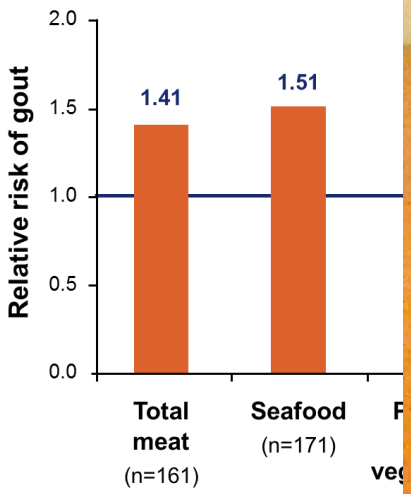
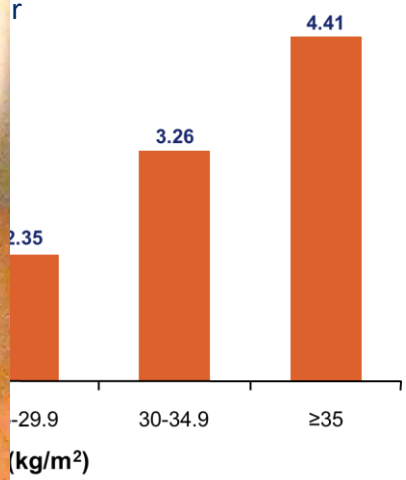
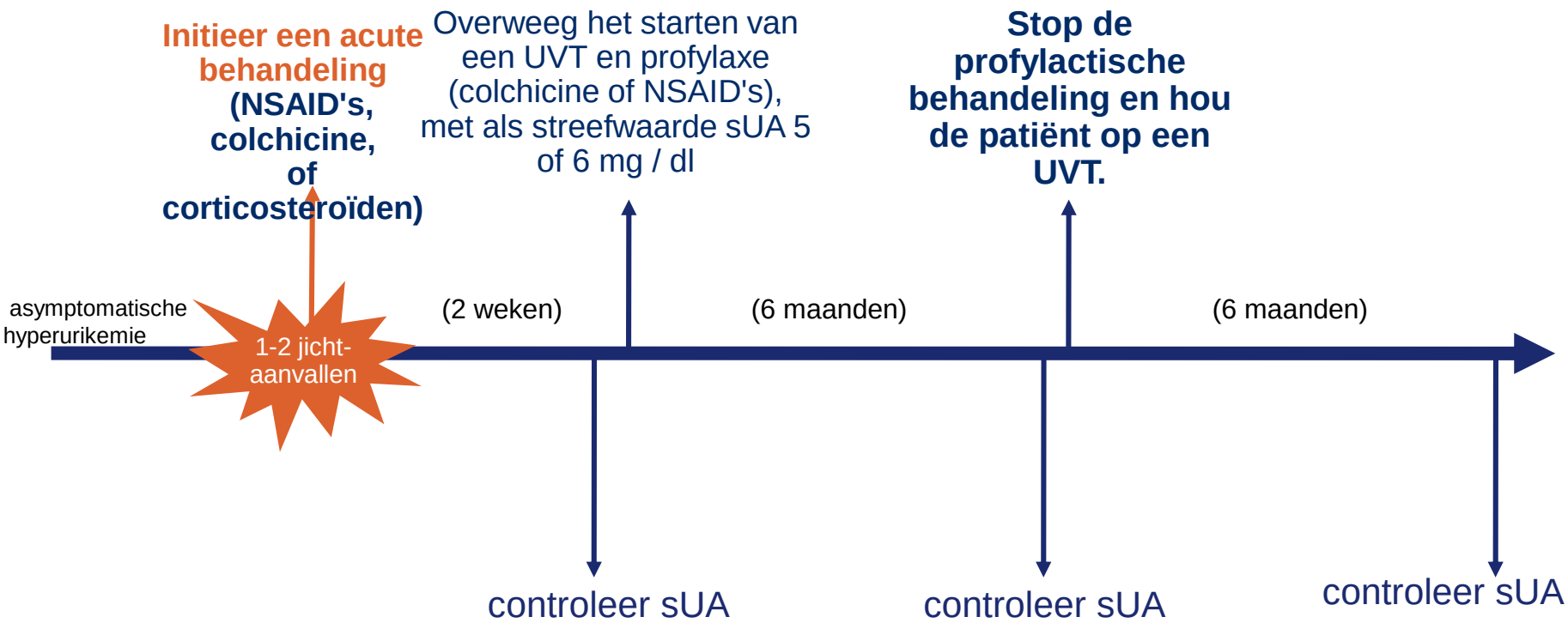




heum 2004; 51(3):321-325.

Acute monoarthritis: crystal arthropathy

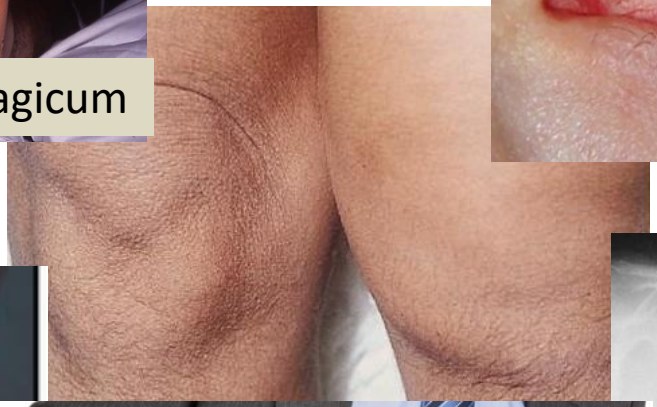


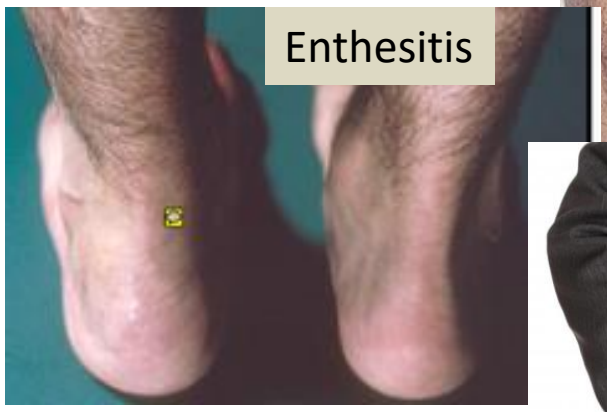
** Net zoals het cholesterolgehalte regelmatig opgevolgd dient te worden, moet ook de sUA regelmatig gemeten worden om een sUA onder de 5 of 6 mg/dl te bekomen .*

Subacute mono- oligoarthritis

Keratoderma Blenorhagicum

Conjunctivis





Enthesitis

Gastroenteritis

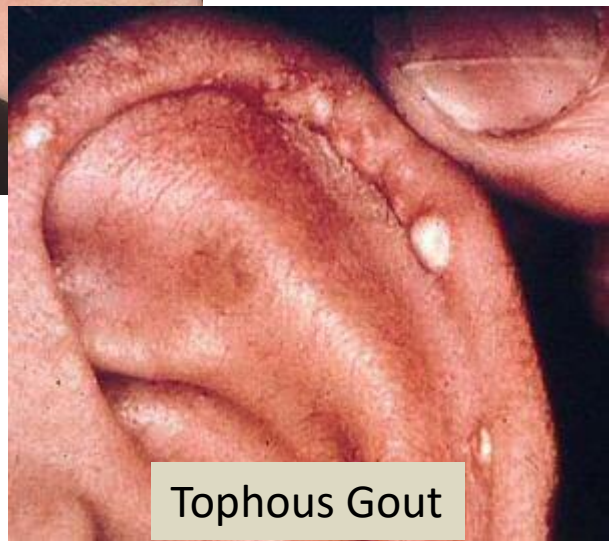
Sarcoidosis arthritis

Subacute polyarthritis

SLE

Parvovirus B19

RS3PE, McCarthy Syndrome


Tophous Gout

Chronic mono- oligoarthritis

Chronic polyarthritis

2010 ACR/EULAR classification criteria for RA

- ✓ Patients with at least one joint with definite clinical synovitis (swelling).
- ✓ The synovitis cannot be better explained by another disease
- ✓ A score of > or = 6/10 is needed for classification as definite RA

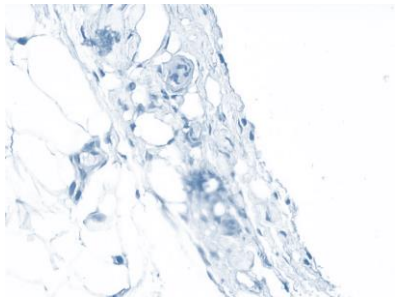
A	**Joint involvement**	**Score**
	1 large joint	0
	2-10 large joints	1
	1-3 small joints (with or without large joints)	2
	4-10 small joints (with or without large joints)	3
	> 10 joints (at least 1 small joint)	5
B	**Serology**	
	Negative RF and negative ACPA	0
	Low positive RF or low positive ACPA	2
	High positive RF or high positive ACPA	3
C	**Acute phase reactants**	
	Normal CRP and normal ESR	0
	Abnormal CRP or abnormal ESR	1
D	**Duration of symptoms**	
	< 6 weeks	0
	> or = 6 weeks	1

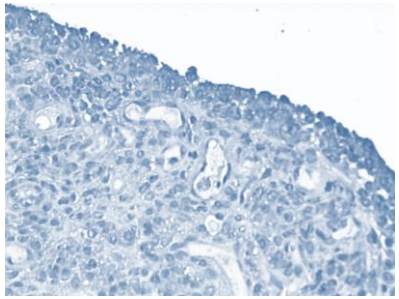
RA: an inflammatory disease of the synovium

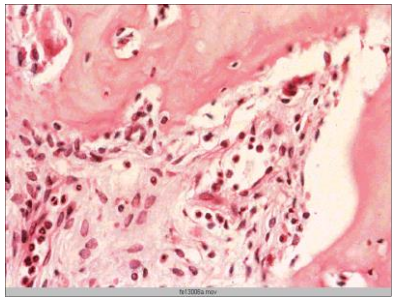
Early RA

Progressive RA

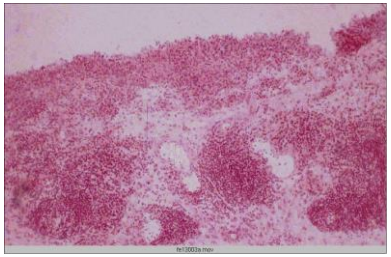
Established RA

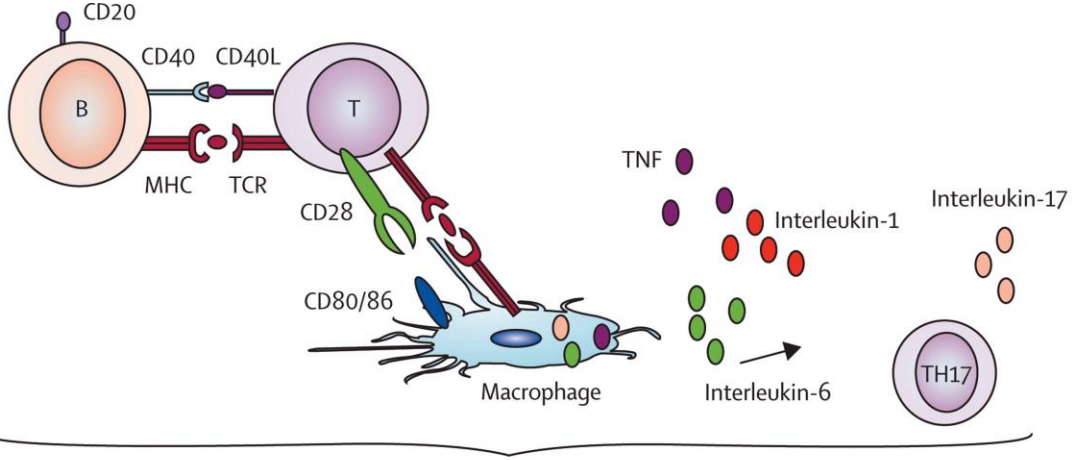


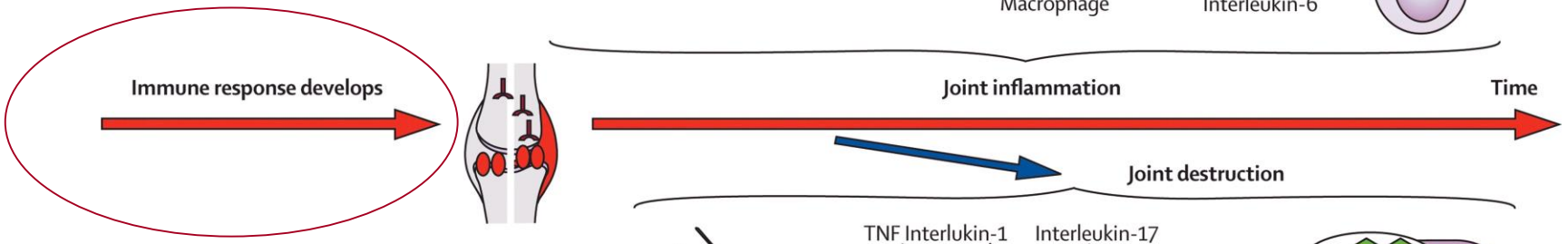




The synovium as a lymfoid organ



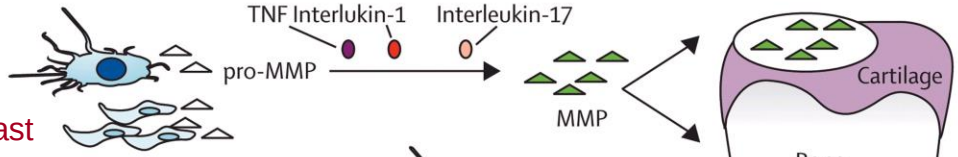


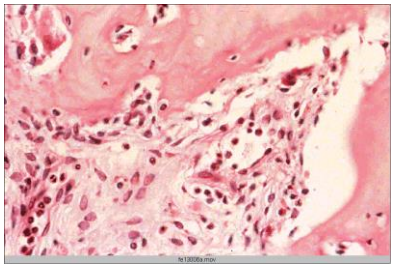


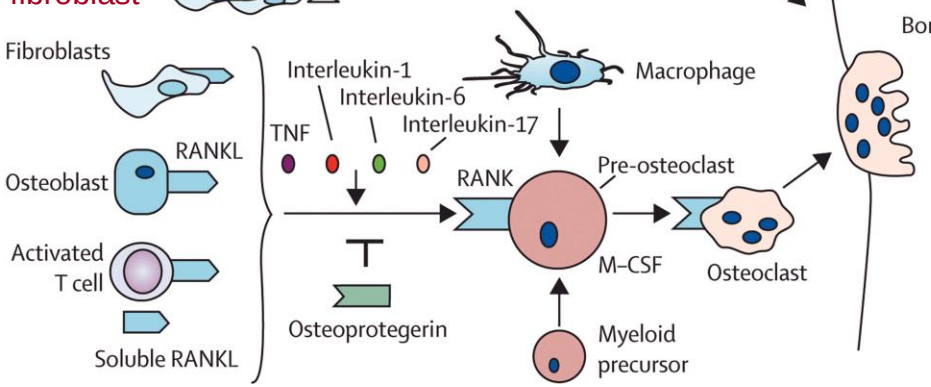
Synovial macrophage

Pannus

Synovial fibroblast

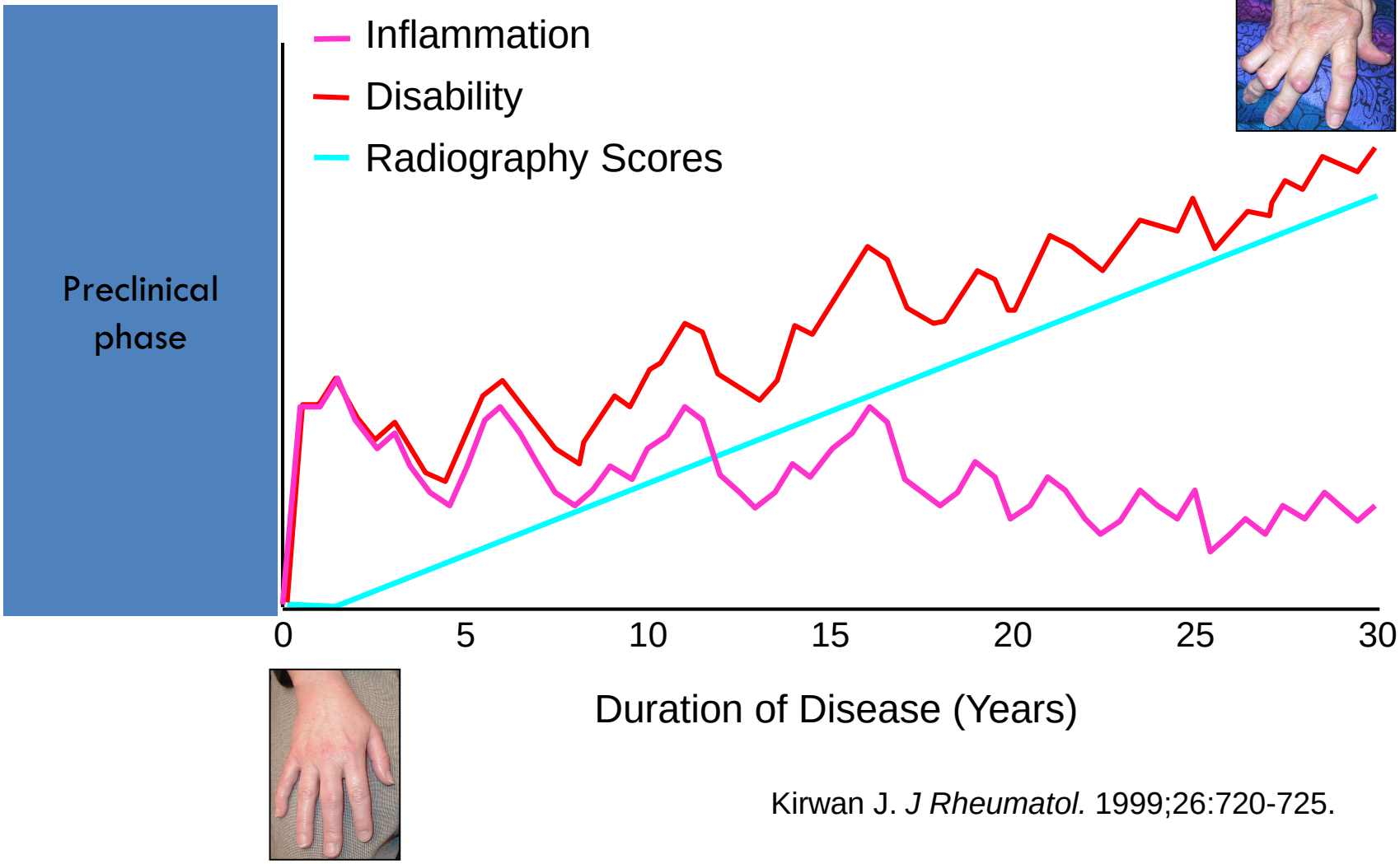






Klareskog et al. Lancet 2009 feb 21;373(9664):659-72

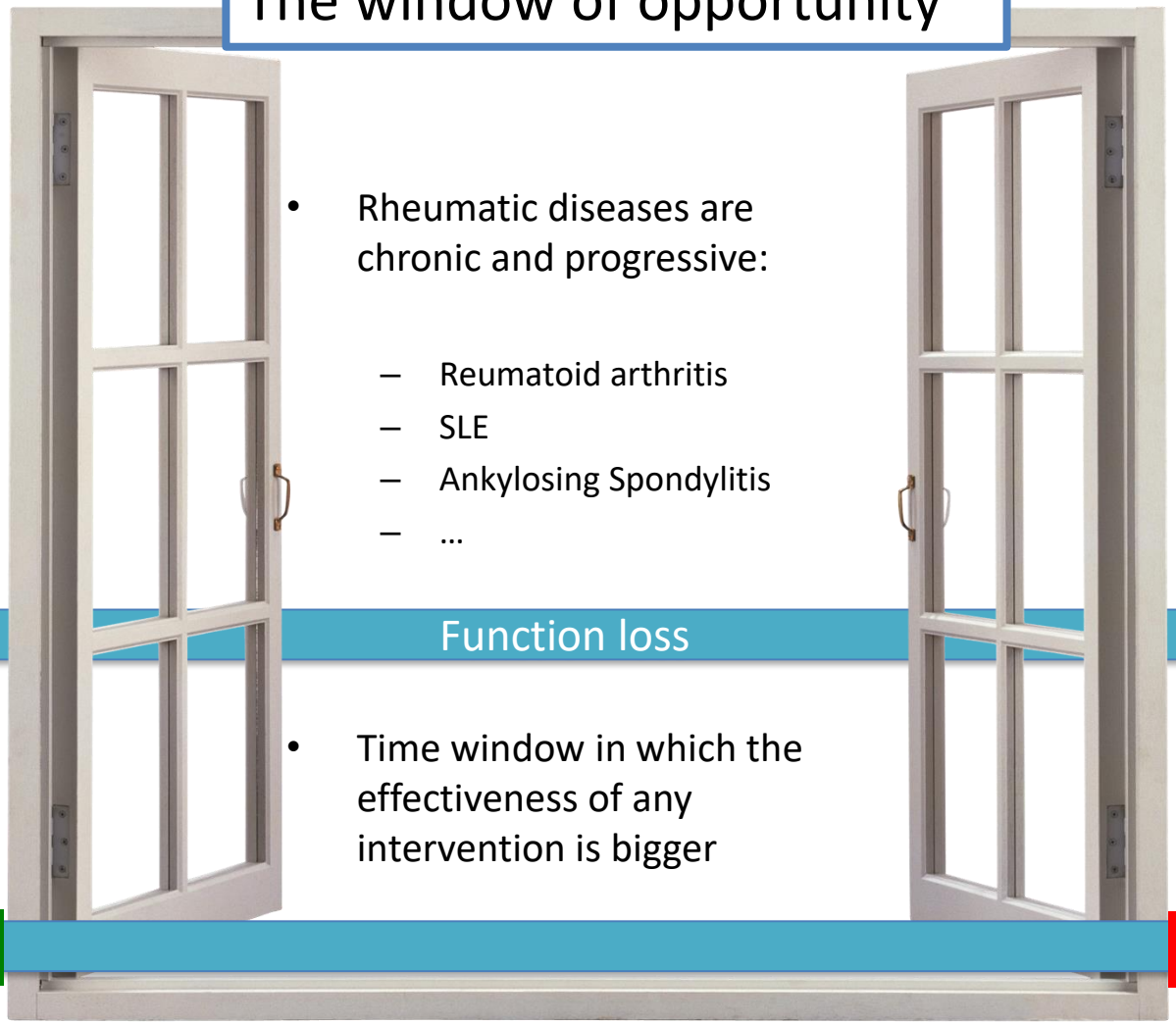
Inflammation / Loss of function



Kirwan J. *J Rheumatol.* 1999;26:720-725.

“No time to waste”

The window of opportunity



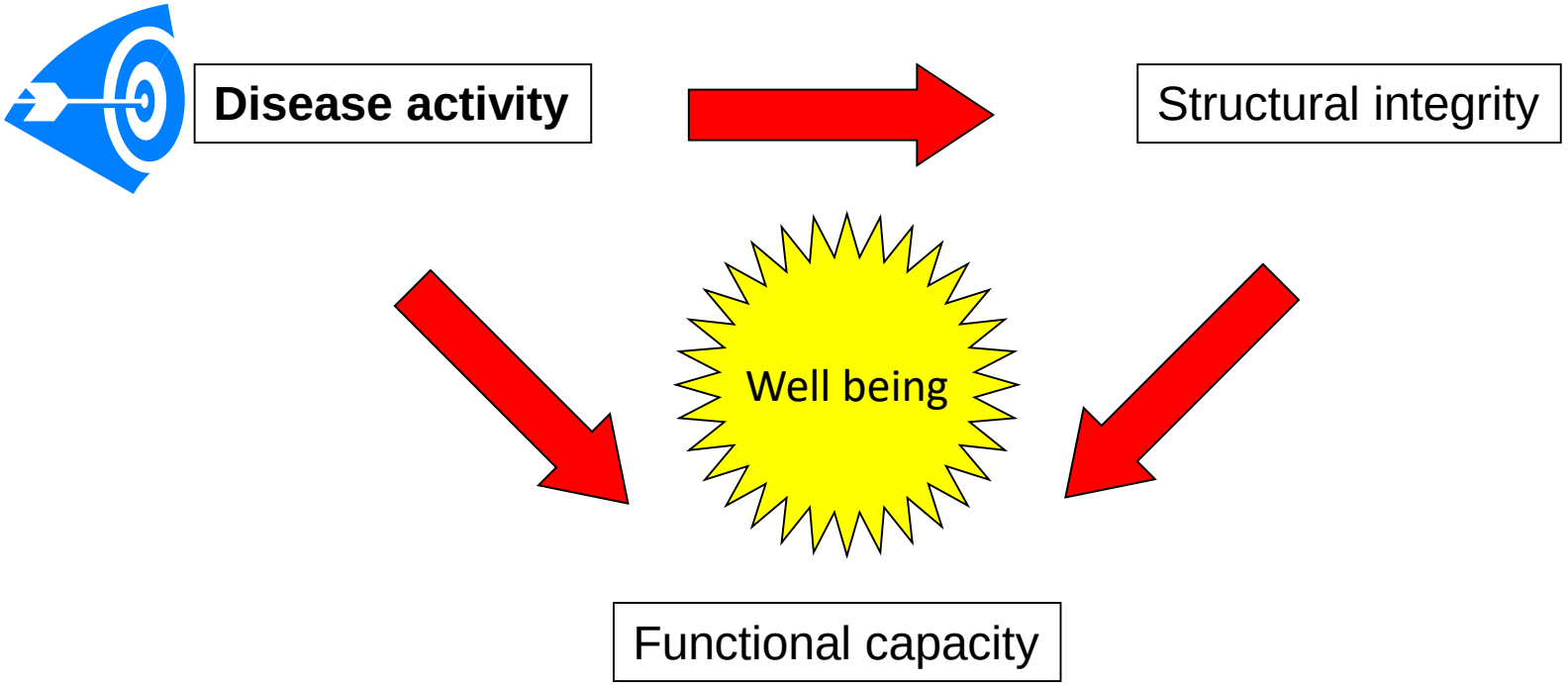
- Rheumatic diseases are chronic and progressive:
  - Reumatoid arthritis
  - SLE
  - Ankylosing Spondylitis
  - …

Inflammation → Function loss → Damage

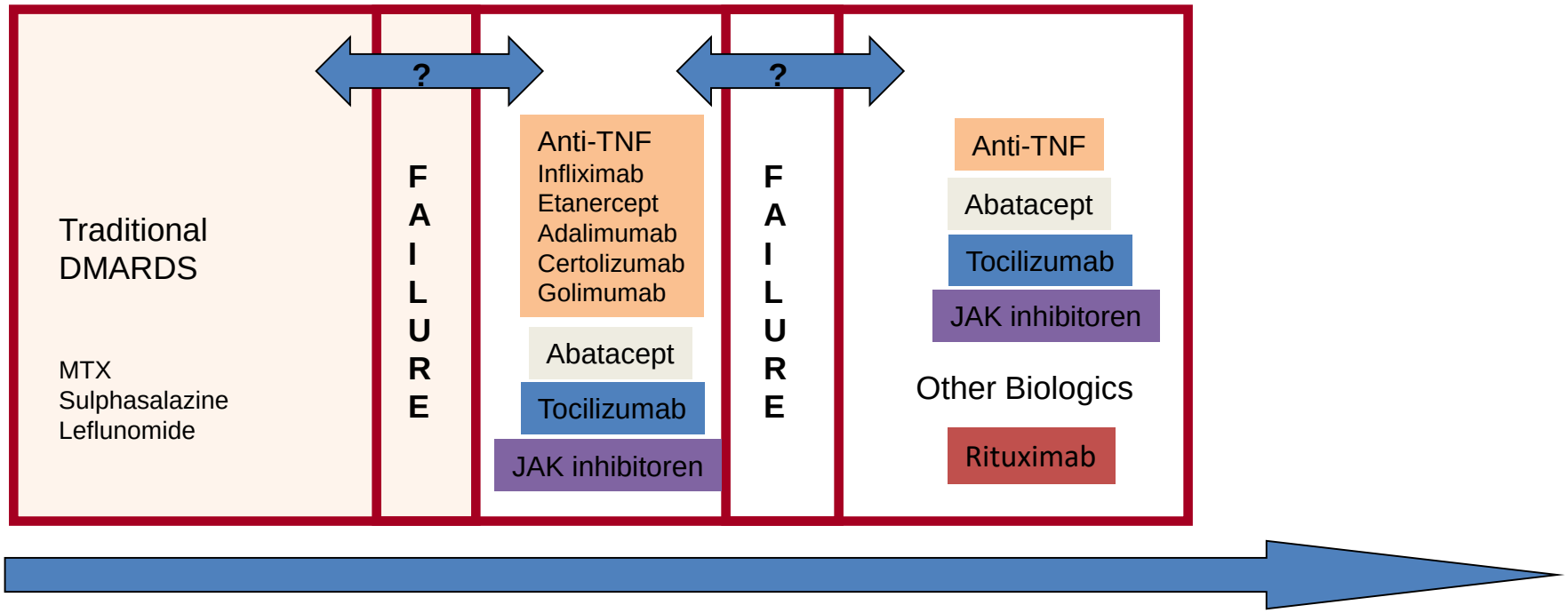
- Time window in which the effectiveness of any intervention is bigger

Reversible → Definitive

The target


Disease activity
Structural integrity
Well being
Functional capacity

The arsenal: disease modifying antirheumatic treatment



Current treatment paradigm for RA based on Belgian reimbursement criteria

Traditional DMARDs versus Biologics

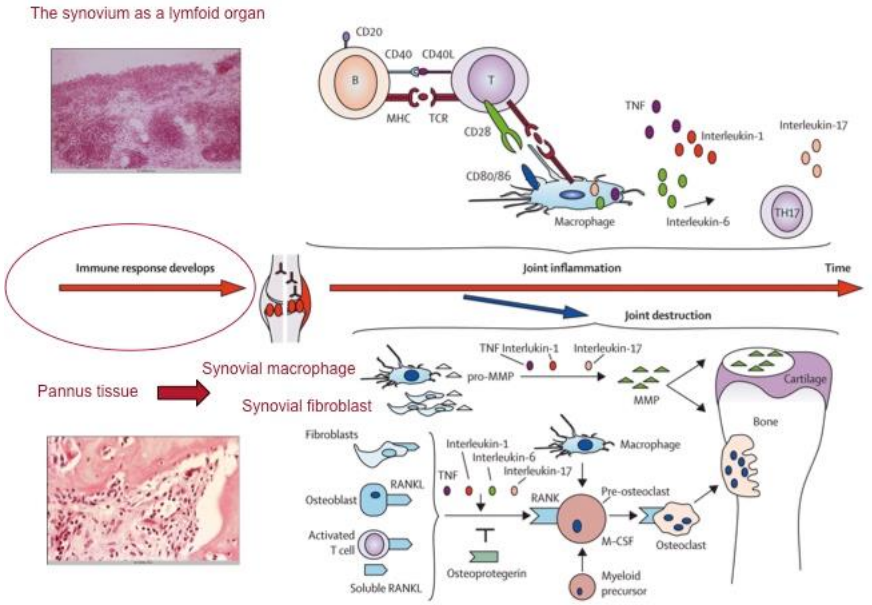
Traditional DMARDS

- Chemical compounds
- Use based on experience
- Mode of action largely unknown

Biologics

- Biosynthesized Proteins
- Use based on insight in pathology
- Sophisticated targeted therapy

- Improve symptoms slowly
- Control inflammation slowly
- Improve function slowly
- Slow down radiographic damage
- Specific toxicity profile
- Mostly cheap
- Available for everyone



Klareskog et al. Lancet 2009 feb 21;373(9664):659-72

Reimbursement criteria for biologicals in RA

First request for reimbursement:

- Severe rheumatoid arthritis
- Having failed 2 DMARDs (MTX + other)
  - Insufficient response at optimal dosage for at least 3 months
  - Intolerance
- DAS28 score ≥ 3.7
- Absence of active tuberculosis

Prolongation of reimbursement:

- After six months and yearly afterwards
- First treatment was efficacious: moderate to good EULAR response

Additional criteria for rituximab:

- Insufficient response/toxicity on anti-TNF therapy for rituximab

The arsenal: glucocorticoids

Ann Rheum Dis. 2010 Jun;69(6):1015-21. doi: 10.1136/ard.2009.114579.

Status praesens

✧ Future for newly onset RA patients looks bright

…at least through the **window of opportunity** for therapeutic intervention

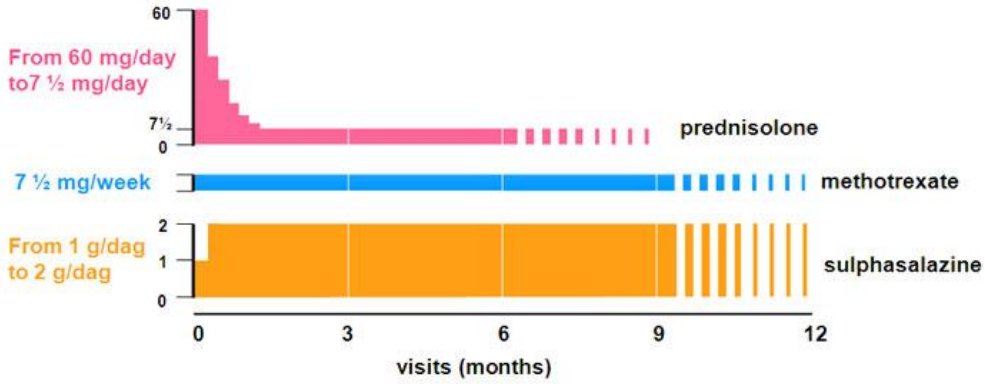
✧ Two basic strategic principles

- ➢ rapid remission induction
- ➢ treat to target

Boers (1997) Randomised comparison of combined step-down prednisolone, MTX and sulphasalazine with sulphasalazine alone in early RA (Cobra Trial)
Grigor (2004) Effect of a treatment strategy of tight control for rheumatoid arthritis: a single-blind randomised controlled trial (Ticora Trial)
Goekoop-Ruiterman (2007) Comparison of treatment strategies in early rheumatoid arthritis (BeST trial)

Remission induction with Cobra

- **Cobra-like** induction therapies
  - ✓ efficacious (=biologicals)
  - ✓ cost-effective (>biologicals)
  - ✓ feasible in daily practice



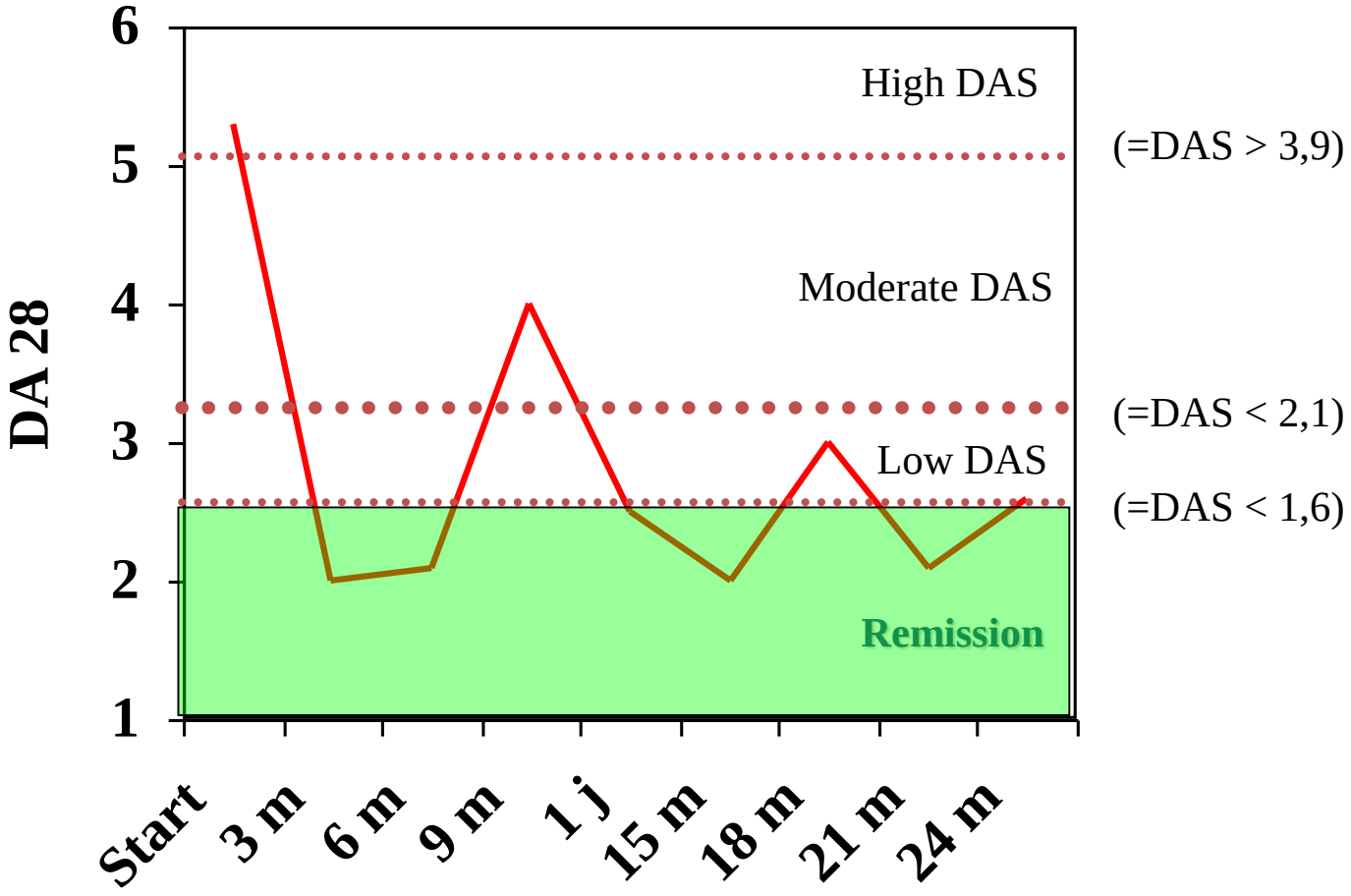
- However **not widely used** in clinical practice
  - ➢ Doubts about the ideal DMARD combination
  - ➢ Doubts about initial high prednisone dosage
  - ➢ Many other barriers for implementation…

Not for everybody ?!

Choy (2008) Factorial randomised controlled trial of glucocorticoids and combination disease modifying drugs in early rheumatoid arthritis (Cardera trial)
Van Tuyl LH (2008) Discordant perspectives of rheumatologists and patients on COBRA combination therapy in rheumatoid arthritis.
Verschueren (2008) Daily practice effectiveness of a step-down treatment in comparison with a tight step-up for early rheumatoid arthritis.
Meyfroidt (2014) Factors influencing the prescription of intensive combination treatment strategies for early rheumatoid arthritis.

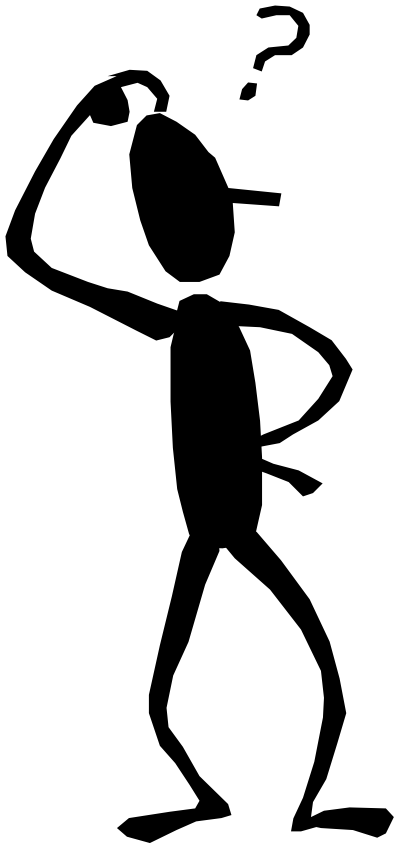
Treat to target: Disease Activity Score (DAS)

DAS (ESR) = 0.54*sqrt(**TJC RAI**) + 0.065*(**SJC 44**) + 0.33*Ln(**ESR**) + 0.0072***GH**



Prevoo MLL, van Gestel AM, van't Hof MA et al. British J Rheum 1996;35:1101-1105

Which intervention ?



Dose increase DMARD

Start corticosteroids

Social assistent

Change DMARD

Start physiotherapy

Start NSAID

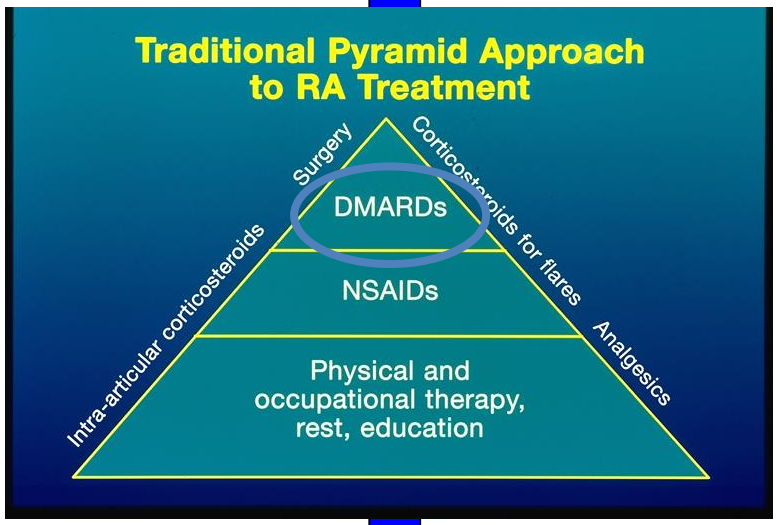
Plan operation

Local injection

= Flexible tight control

Can we do better than this ? Yes we can !

5 years



1995

Diagnosis

5 years

2005

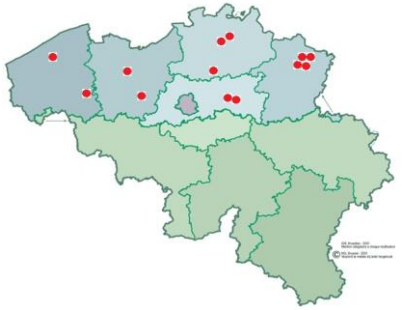
Diagnosis

CareRA trial

- ✧ 2 year multicenter investigator-initiated pragmatic RCT
  - ✓ Implementing Rapid Remission Induction + Treat to Target
  - ✓ Global Early RA Management = the CareRA “package”

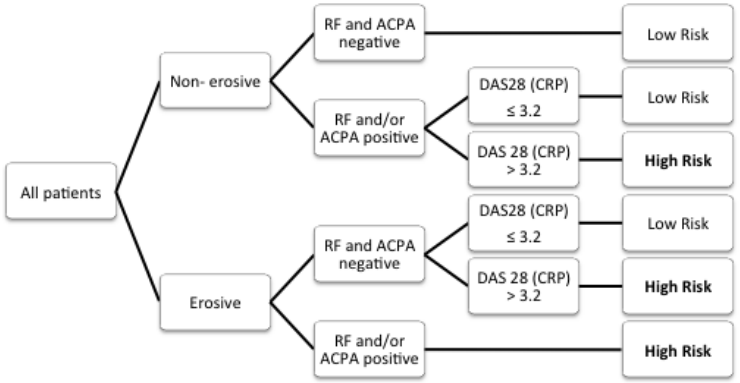
- ✧ Inclusion criteria:
  - **All** patients with early RA (<1 year, ACR 1987 criteria +)
  - Previously untreated with DMARDS
  - No contraindications for corticosteroids or DMARDS
  - Willing to give written informed consent

- ✧ 13 actively recruiting centers in Flanders

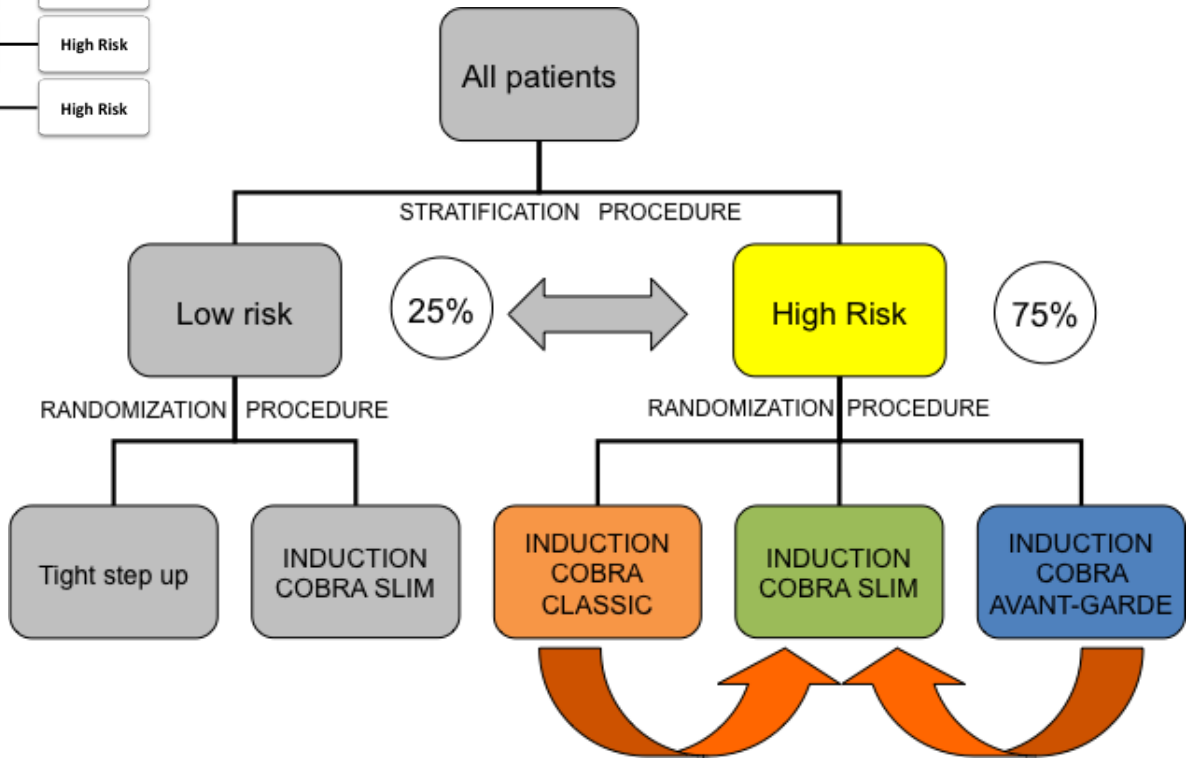


CareRA trial

Trial design



Stratification procedure



Randomization procedure

CareRA trial: high risk group

- High-Risk early RA patients were **randomized** to 3 treatment arms:

1. COBRA Classic

- Methotrexate 15mg weekly
- Sulphasalazine 2g daily
- Prednisone step down, from initially 60mg tapered to 7.5mg from W7

2. COBRA Slim

- Methotrexate 15mg weekly
- Prednisone step down, from initially 30mg tapered to 5mg from W6

3. COBRA Avant-Garde

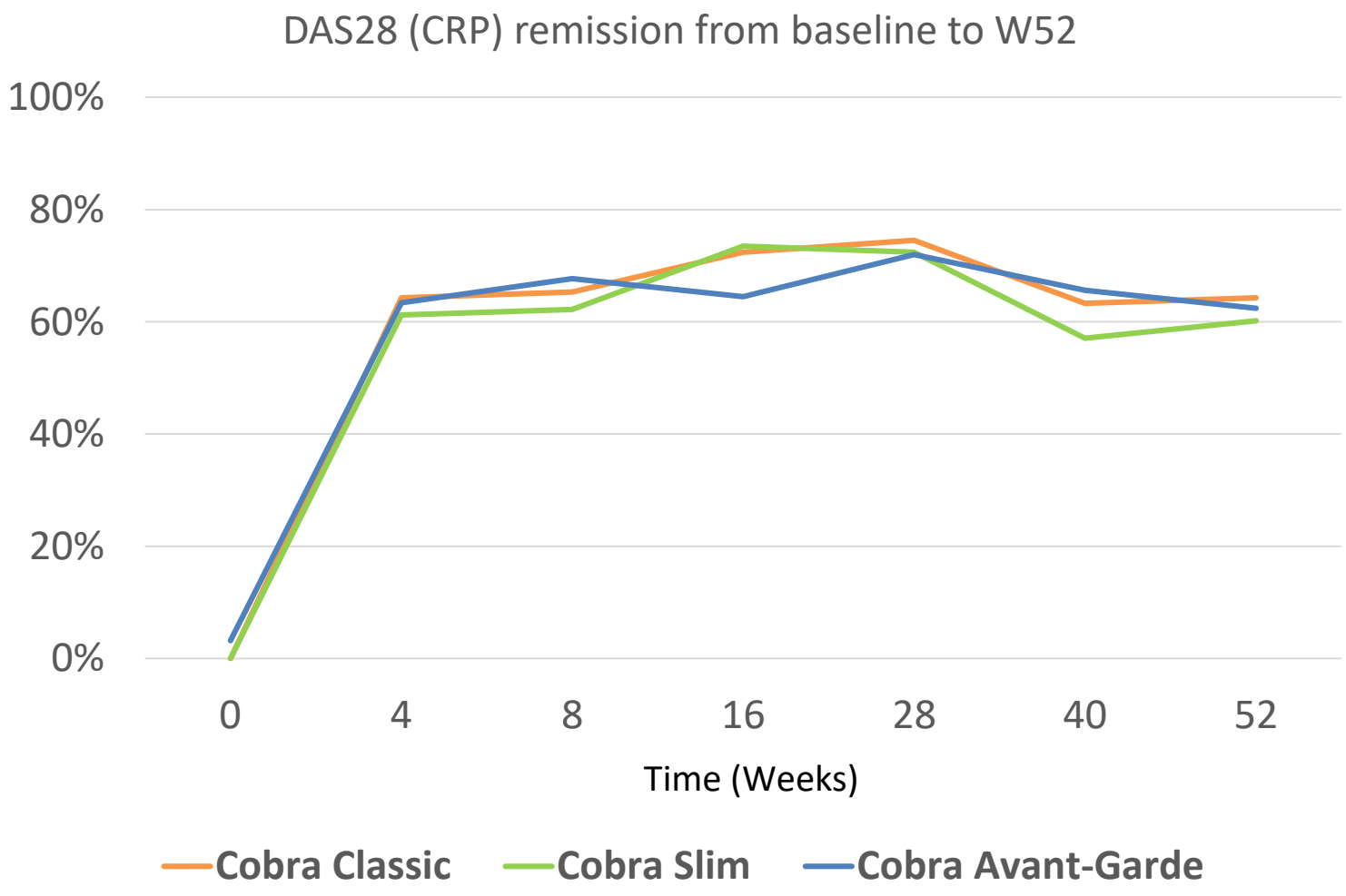
- Methotrexate 15mg weekly
- Leflunomide 10mg daily
- Prednisone step down, from initially 30mg tapered to 5mg from W6

- Treatment was **adjusted to a target** DAS28(CRP) ≤ 3.2 from W8
- Prednisone was further **tapered** from W28 and stopped at W34
- **DMARD monotherapy** was aimed for in all schedules from W40

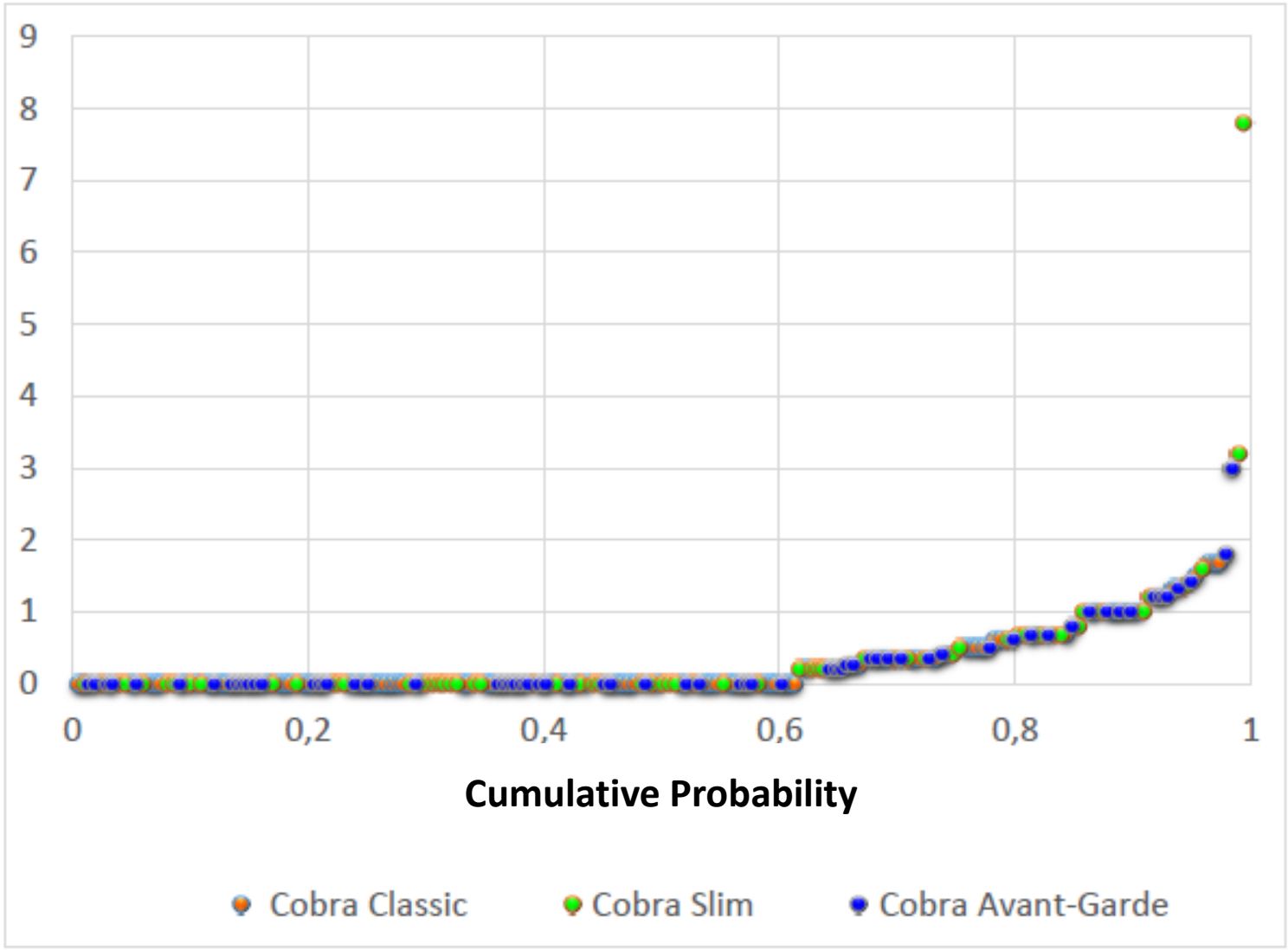
Results: Baseline Characteristics

	COBRA CLASSIC	COBRA SLIM	COBRA AVANT-GARDE
Number of patients	98	98	93
Age (years)	53.2 ± 11.9	51.8 ± 13.1	51.1 ± 12.8
BMI (kg/m²)	26.0 ± 4.3	26.8 ± 4.2	26.5 ± 4.2
Gender (female)	65.3%	64.3%	68.8%
Smoking Status (ever)	57.1%	59.2%	60.2%
Symptom Duration (weeks)	33.8 ± 35.5	33.2 ± 38.2	44.3 ± 65.9
RF (yes)	79.6%	83.7%	75.3%
ACPA (yes)	77.6%	79.6%	77.4%
Erosions (yes)	32.7%	32.7%	34.4%
Total TJC	14.7 ± 9.5	13.7 ± 8.2	14.1 ± 9.0
Total SJC	11.9 ± 8.9	10.8 ± 6.5	10.6 ± 6.7
PGA (0-100)	59.5 ± 21.7	56.2 ± 21.7	54.8 ± 24.2
Pain (0-100)	59.5 ± 23.6	56.5 ± 21.9	57.5 ± 23.8
Fatigue (0-100)	50.6 ± 26.0	49.0 ± 21.3	48.9 ± 23.7
PhGA (0-100)	54.7 ± 18.5	53.1 ± 18.1	51.7 ± 17.9
ESR (mm/h)	33.5 ± 25.2	32.1 ± 23.4	25.0 ± 17.6
CRP (mg/l)	19.7 ± 28.9	21.5 ± 33.2	14.5 ± 19.2
DAS28(ESR)	5.4 ± 1.3	5.2 ± 1.2	5.0 ± 1.3
DAS28(CRP)	5.0. ± 1.2	4.8 ± 1.1	4.7 ± 1.2
HAQ (0-3)	1.2 ± 0.7	1.0 ± 0.7	1.0 ± 0.6

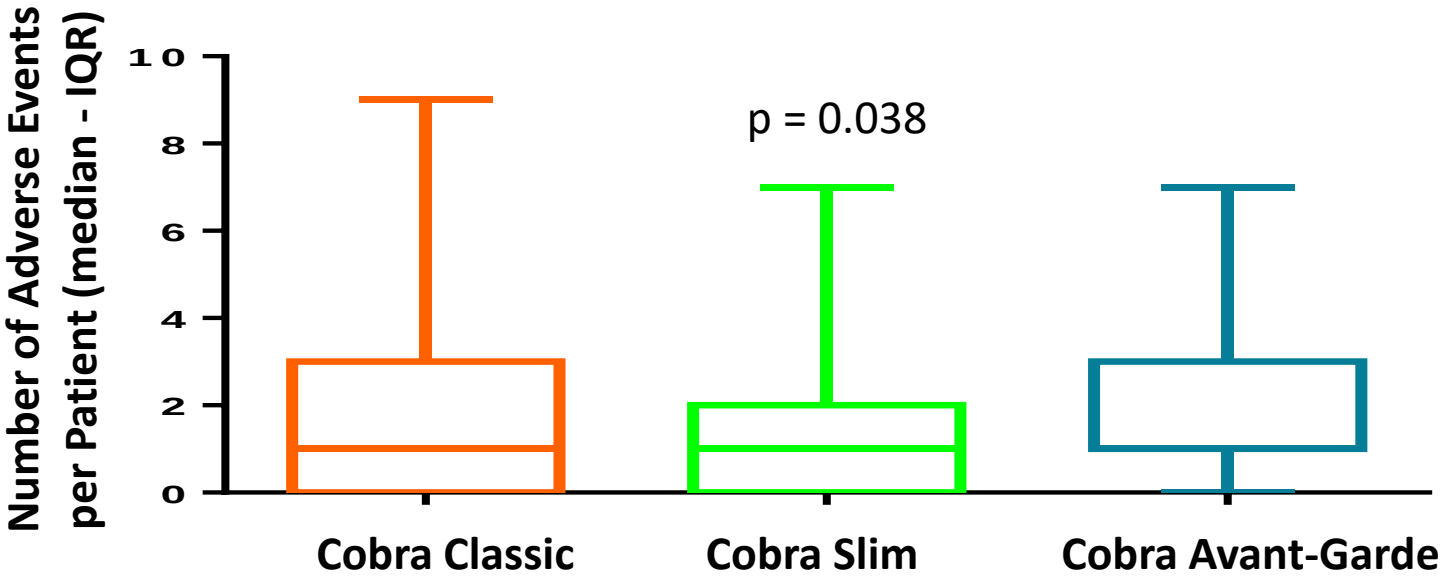
Results high risk group



Results: Radiographic Progression BL-W52



Results: Safety



	Cobra Classic	Cobra Slim	Cobra Avant-Garde
Patients with ≥ 1 AE (%)	66/98 (67.3%)	65/98 (66.3%)	71/93 (76.3%)
Discomfort Medication	143	100	137
Toxicity	24	20	26
Infection	12	9	10
Other	2	1	0

CareRA trial: low risk group

- Low-Risk early RA patients were **randomized** to 2 treatment arms:

1. Tight Step Up

- Methotrexate 15mg weekly
- Prednisone was not allowed in this treatment arm

2. COBRA Slim

- Methotrexate 15mg weekly
- Prednisone step down, from initially 30mg tapered to 5mg from W6
- Prednisone was further tapered from W28 and stopped at W34

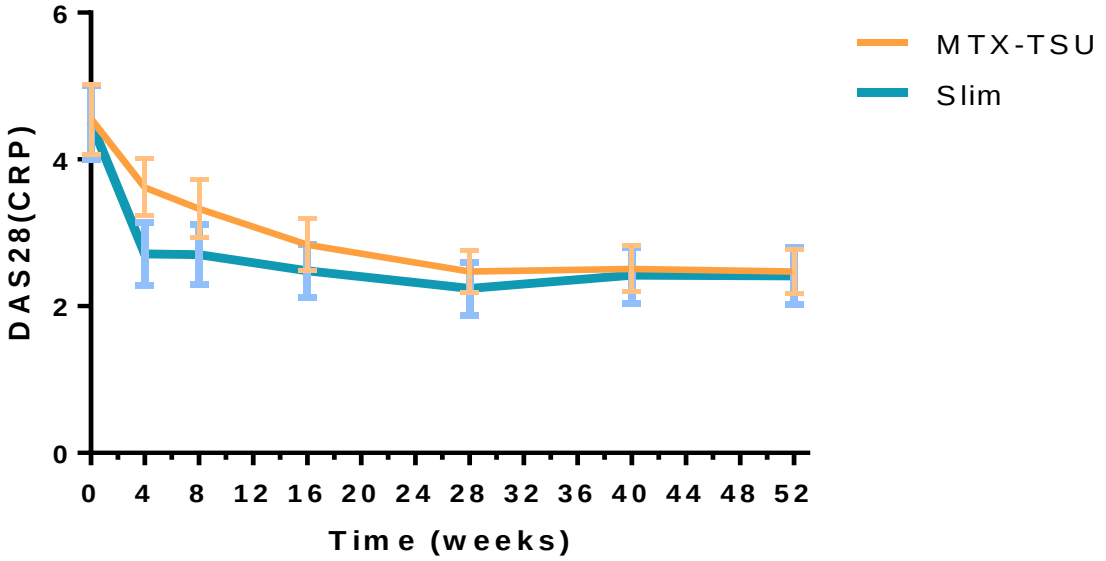
- Treatment was **adjusted to a target** DAS28(CRP) ≤ 3.2 from W8

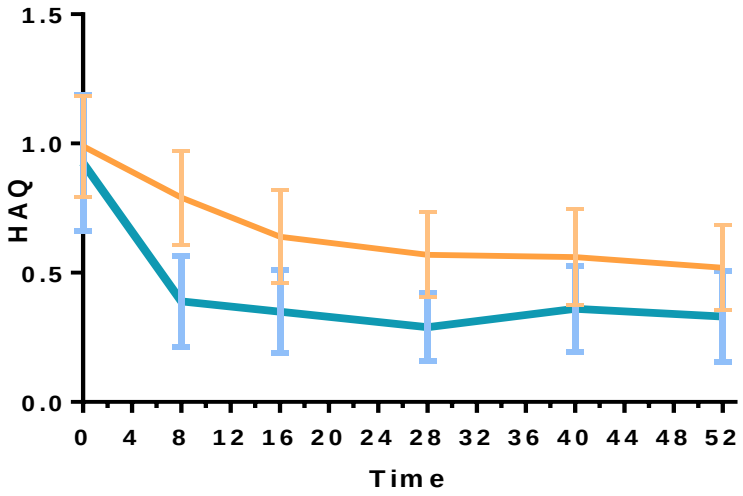
- First adjustment was a dose increase of MTX to 20 mg
- Second adjustment was the addition of leflunomide 10 mg daily
- Together with these adjustments one IM injection of depomedrol was allowed

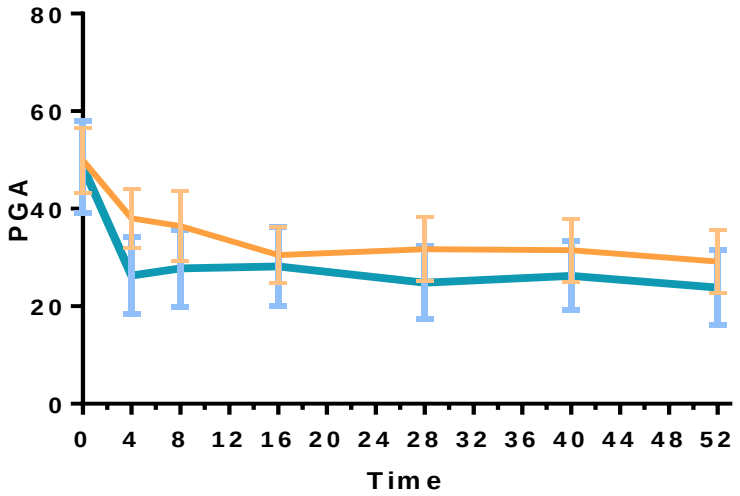
Results: Baseline Characteristics

	MTX TSU n=47	Cobra Slim n=43
Age (years)	51.02 ± 14.00	51.42 ± 14.42
BMI (kg/m²)	26.98 ± 4.22	25.40 ± 4.27
Women	80.9%	76.7%
Smokers (ever)	38.3%	48.2%
Alcohol users	61.7%	55.8%
Symptom duration (weeks)	33.11 ± 62.21	34.42 ± 68.16
RF positive	23.4%	25.6%
Anti-CCP positive	23.4%	27.9%
Erosions	0.0%	2.3%
TJC28	9.49 ± 7.46	8.51 ± 7.80
SJC28	6.89 ± 6.11	7.79 ± 6.03
PGA (0-100)	49.89 ± 22.99	48.60 ± 30.68
Pain (0-100)	52.09 ± 23.23	48.23 ± 31.19
Fatigue (0-100)	45.91 ± 22.07	39.40 ± 27.66
PhGA (0-100)	48.34 ± 23.37	48.63 ± 20.80
ESR (mm/hour)	23.04 ± 16.90	30.00 ± 29.40
CRP (mg/L)	13.53 ± 18.62	20.14 ± 39.25
DAS28(CRP)	4.55 ± 1.63	4.50 ± 1.63
HAQ (0-3)	0.99 ± 0.67	0.92 ± 0.85

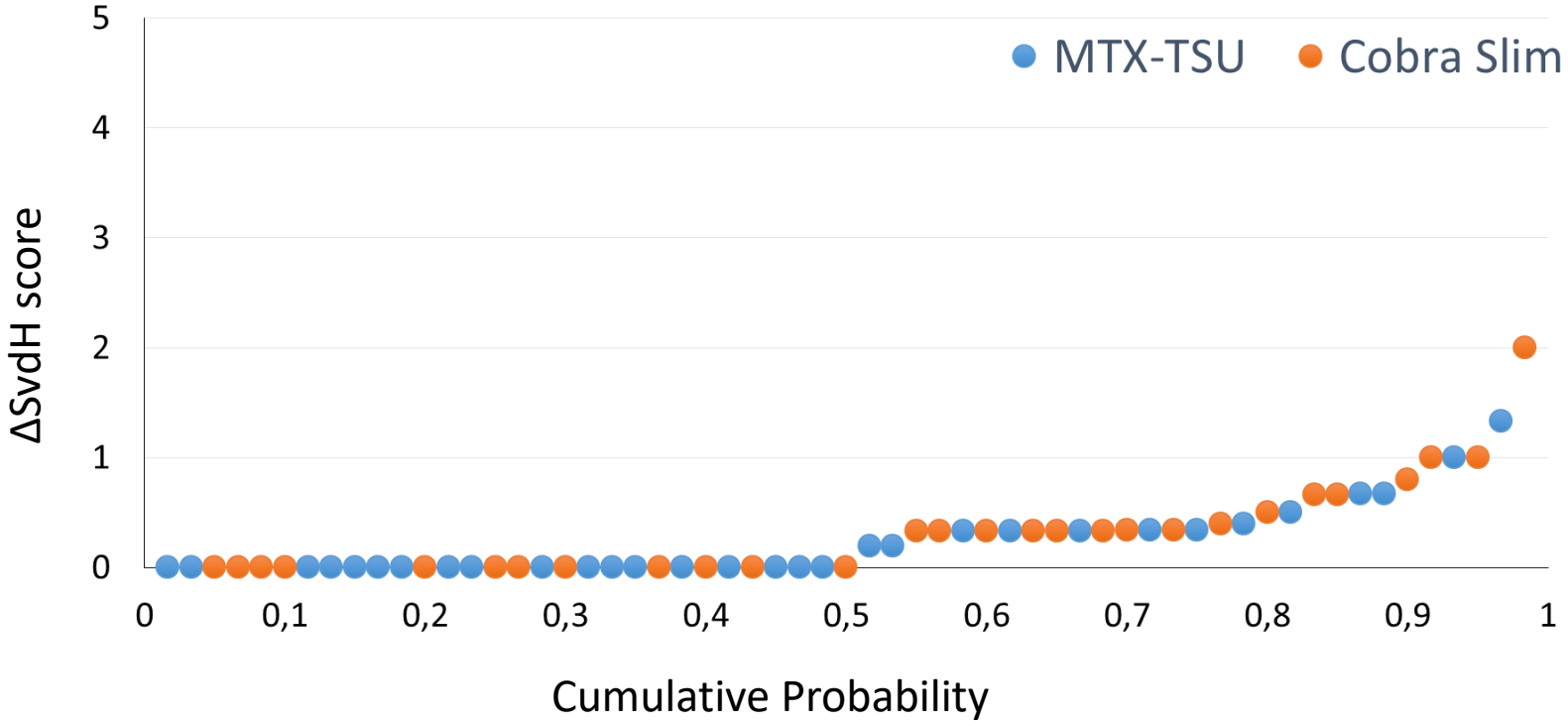
Results low risk group



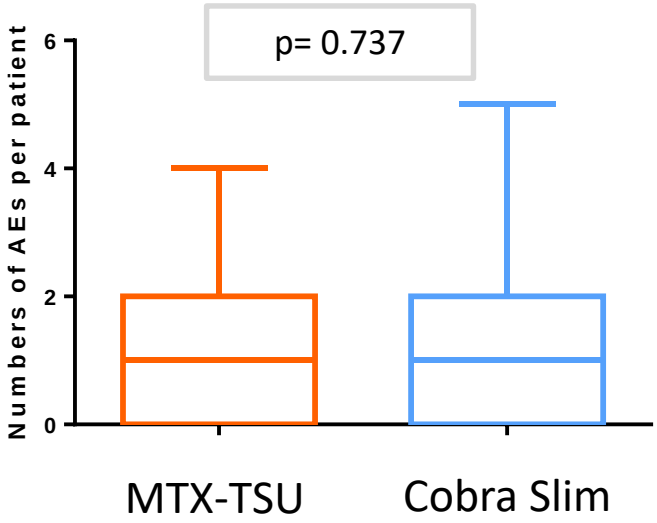




Results: Radiographic Progression BL-W52



Results: Safety



	MTX-TSU	Cobra Slim
Number of patients having AE	30/47 (63.8%)	22/43 (51.2%)
Discomfort medication (e.g. diarrhoea, general malaise)	39	43
Toxicity (e.g. abnormal liver function values)	11	6
Infection (e.g. pulmonary infections)	3	1
Other	1	0

Treatment at W52

Single DMARD (observed):
263/346 = 76%

Glucocorticoids (observed):
18/346 = 5%

Biologicals (observed):
26/346 = 7.5%

N= number of patients, GC= glucocorticoid, MTX=methotrexate, SSZ=sulphasalazine, LEF=leflunomide, NSAIDS=non-steroidal anti inflammatory drugs, HCQ=hydroxychlorquine, W52= week 52

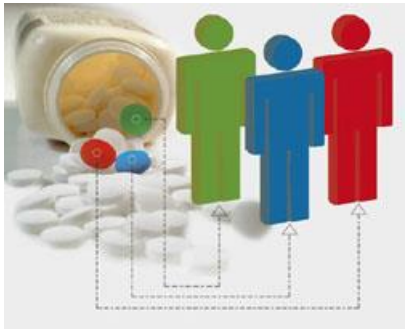
		COBRA CLASSIC	COBRA SLIM (High-Risk)	COBRA AVANT-GARDE	MTX-TSU	COBRA SLIM (Low-Risk)
Total patients in trial		N=98	N=98	N=93	N=47	N=43
Number of Treatment Adaptations	1	21 (21.4%)	38 (38.8%)	22 (23.7%)	17 (36.2%)	16 (37.2%)
	2	3 (3.1%)	16 (16.3%)	5 (5.4%)	9 (19.1%)	9 (20.9%)
cumulative prednisone dose (mg)		2597.2 ±666.8	1526.9 ±378.7	1585.6 ±422.9	36.3 ±49.6	1554.0 ±307.6
daily prednisone dose (mg)		6.5 ±2.7	3.8 ±1.6	4.0 ±1.6	0.1 ±0.1	3.8 ±1.6
Patients with GC injections		15 (15.3%)	31 (31.6%)	15 (16.1%)	17 (36.2%)	6 (13.9%)
Patients followed per protocol until W52		N=62 (63.2%)	N=75 (76.5%)	N=60 (64.5%)	N=36 (76.6%)	N=30 (69.9%)
Therapy at W52:	On MTX only	58 (93.5%)	68 (90.7%)	36 (60.0%)	31 (86.1%)	27 (90.0%)
	On LEF only	4 (6.5%)		20 (33.3%)		
	On MTX+SSZ		7 (9.3%)	4 (6.7%)	5 (13.9%)	3 (10.0%)
	On MTX+LEF					
Patients in remission at W52		49 (79.0%)	52 (69.3%)	45 (72.5%)	24 (66.7%)	25 (83.3%)
Patients in low disease activity at W52		55 (88.7%)	65 (86.7%)	53 (85.5%)	32 (88.9%)	29 (96.7%)
Patients not followed per protocol until W52		N=28 (28.6%)	N=14 (14.3%)	N=25 (26.9%)	N=8 (17.0%)	N=8 (18.6%)
Therapy at W52:	Biological therapy	10	2	6	4	4
	MTX+SSZ+GC	5	1			
	MTX+LEF+GC		1	1		
	MTX+LEF+HCQ		1			
	MTX+SSZ	5				
	MTX+LEF		3	4	1	1
	MTX+GC	2	2	2	1	2
	LEF+GC			1		
	MTX only	4	3	7	2	
	LEF only	1	1	4		
	SSZ only	1				
	NSAIDs					1
Patients in remission at W52		12 (42.9%)	2 (14.2%)	11 (44.0%)	3 (37.5%)	4 (50.0%)
Patients in low disease activity at W52		15 (53.6%)	4 (28.6%)	16 (64.0%)	5 (62.5%)	4 (50.0%)
Patient missing for evaluation at W52		N=8 (7.1%)	N=9 (9.2%)	N=8 (8.6%)	N=3 (6.4%)	N=5 (11.6%)

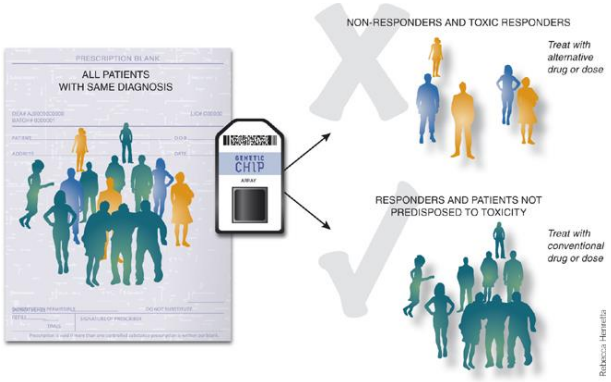
Take home messages

- Very high remission rates can be achieved in eRA patients with combinations of DMARDs and a step down regimen of glucocorticoids
- After Cobra induction therapy a large majority of patients achieves sustained remission, decreasing the need for sophisticated targeted biological therapies
- Cobra-like treatment strategies are feasible in daily practice
  - in high- as well as low-risk eRA patients
  - in different health care settings
- Cobra Slim could be considered a one-size-fits-all for initial eRA treatment
  - just as intensive as needed
  - less “collateral damage” as with combination therapies and with a better retention rate
- A flexible treat to target approach should be followed after remission induction
- There is an urgent need for biomarkers allowing better treatment allocation

Future = Personalized medicine ?

Initial therapeutic regimen à la carte
for each individual RA patient

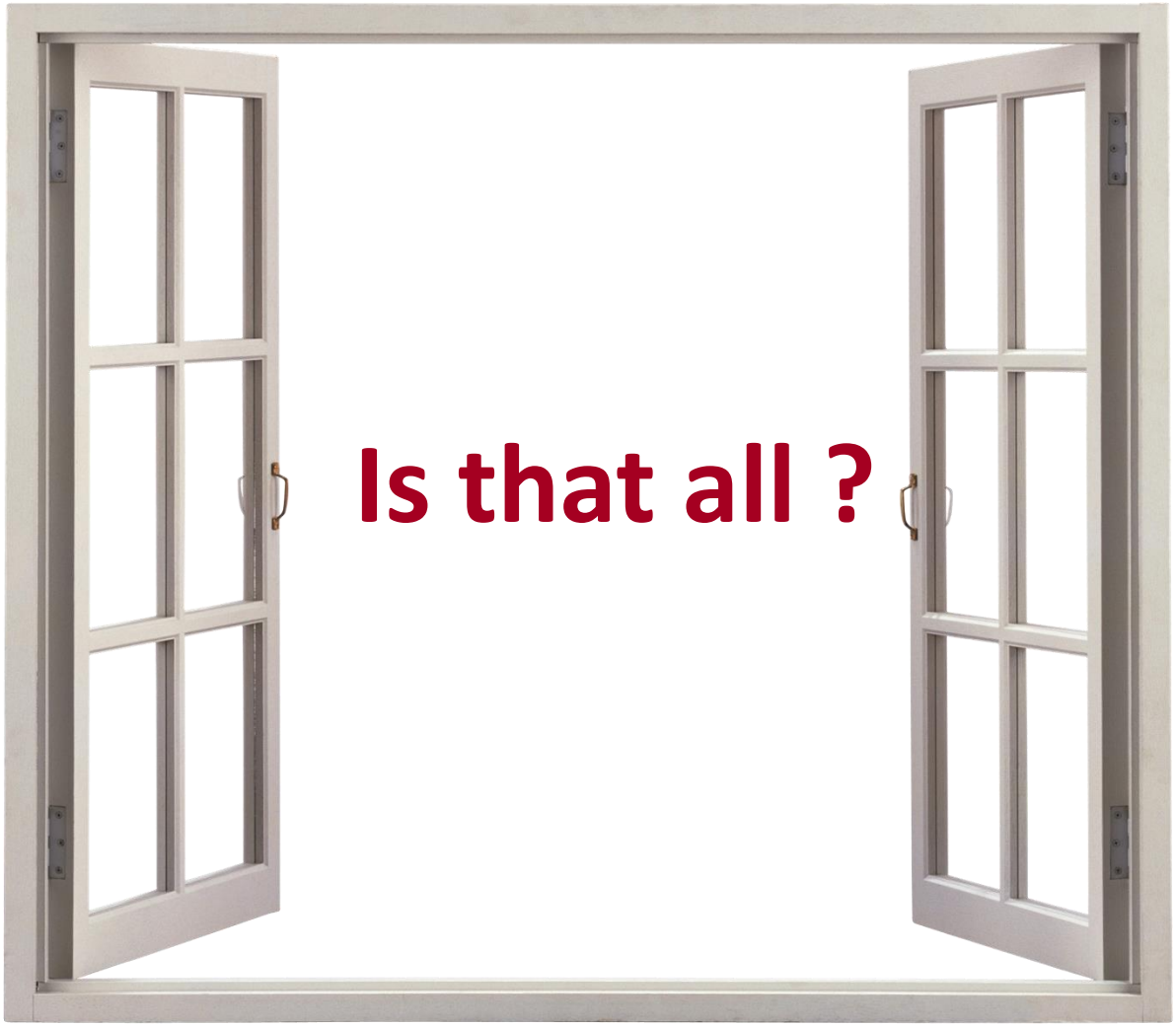




Based on biomarkers predicting disease severity and therapeutic response

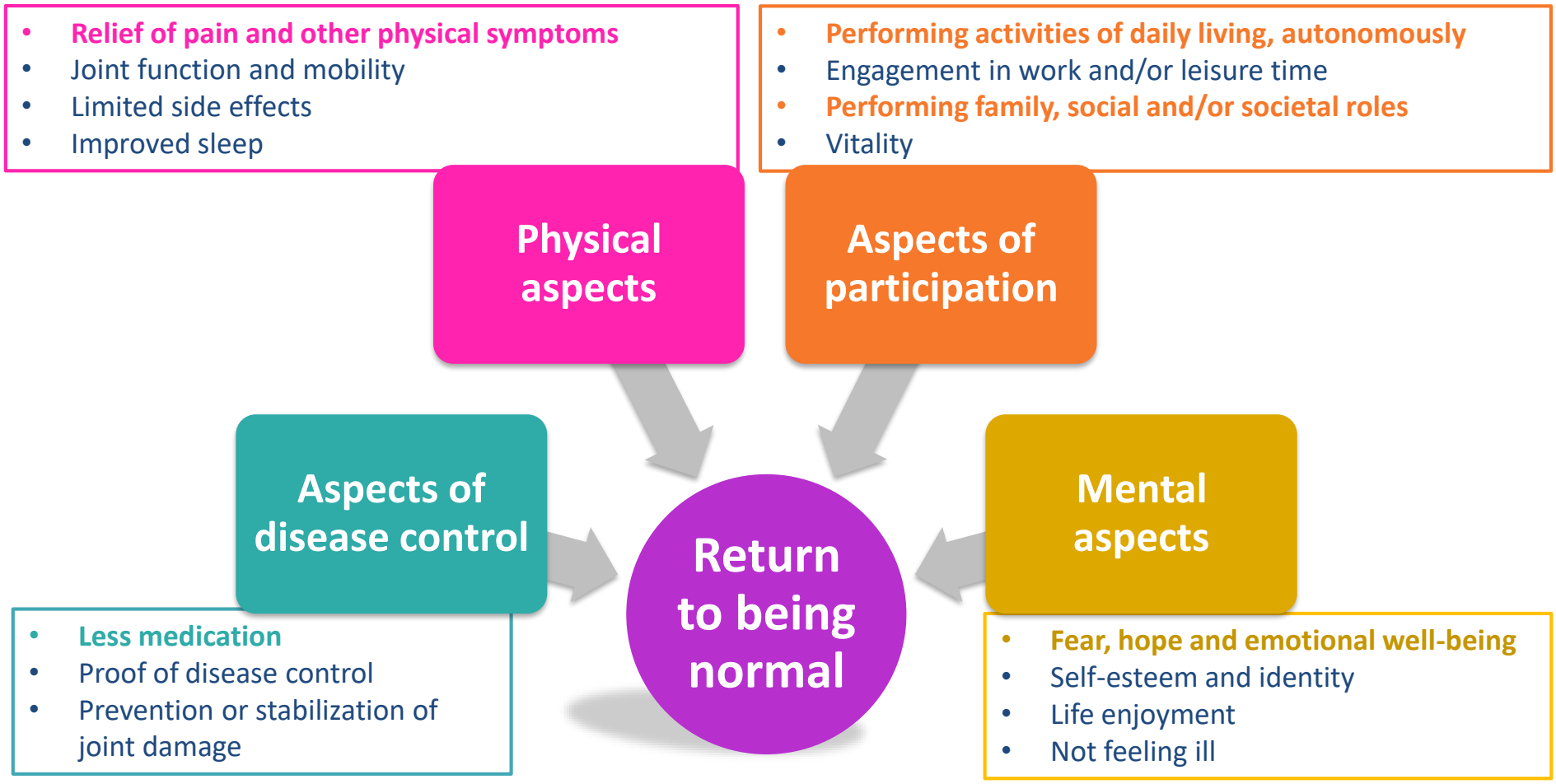
But there are no reliable biomarkers yet !

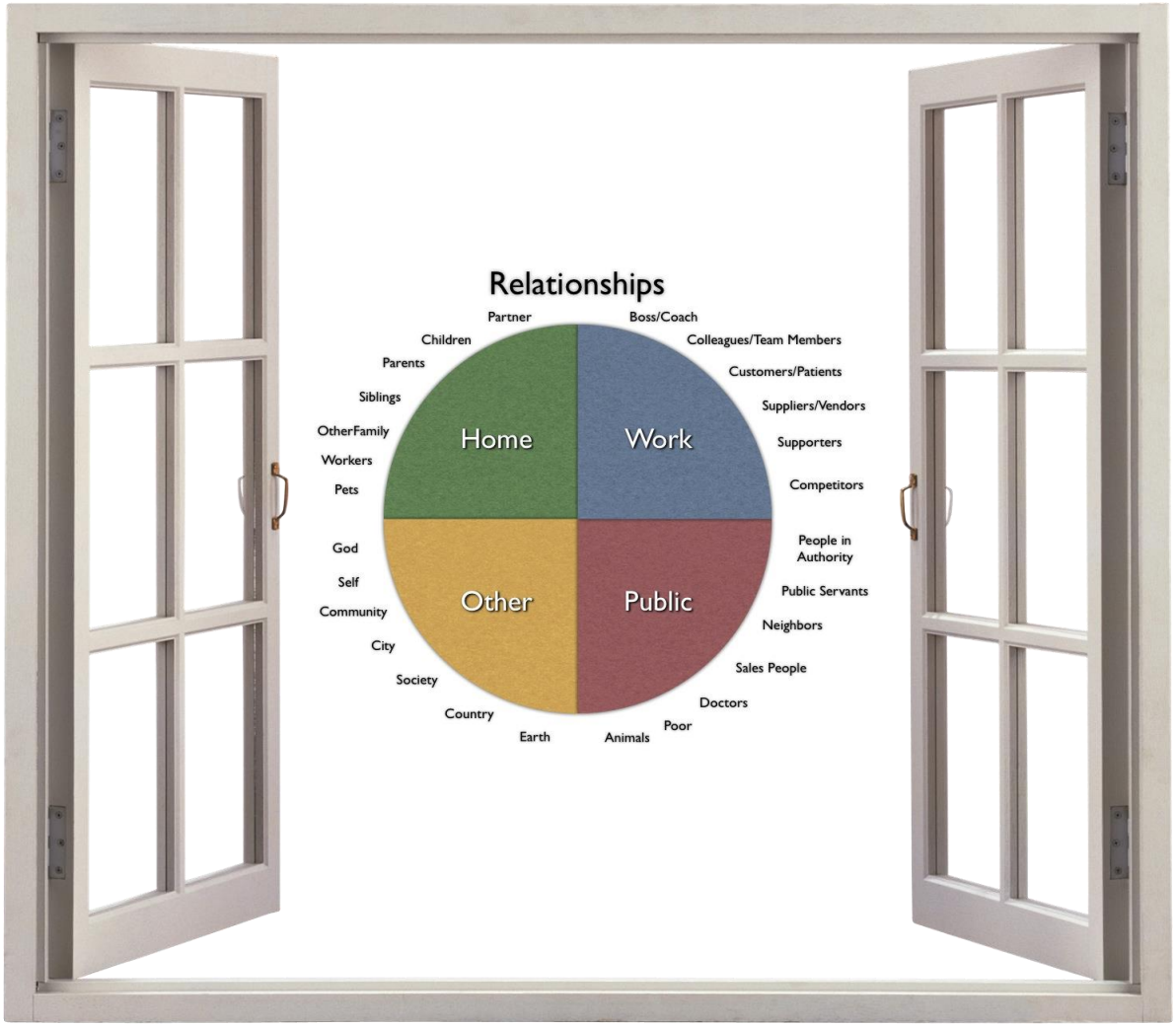
- therapy choice based on personal experience and patient preference
- trial and error : best predictor of long term response is short term response


Is that all ?

Unraveling Preferred Outcomes of Disease and Treatment in Patients with Early Rheumatoid Arthritis: a Longitudinal Qualitative Interview Study

Kristien Van der Elst, S Meyfroidt, A De Groef, E Binnard, D De Cock, P Moons, P Verschueren, R Westhovens



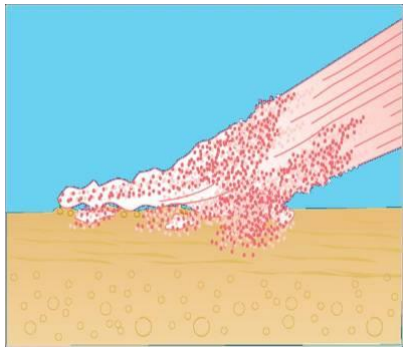


The psychosocial window of opportunity

Dougados M. J Rheumatol 2005;32:1-2

Psoriasis Artritis

- Prognose afhankelijk van het subtype: heterogeen !
  - **Oligoarticulair (5%)** >> fluctuerend verloop
  - **Polyarticulair symmetrisch (50%)** >> gelijkend op RA, minder destructief (?)
  - **Psoriatische artritis van de DIPs vd handen en voeten (5%)** >> gelokaliseerd
  - **Spondylitis (5%)** >> gelijkend op ankyloserende spondylitis
  - **Artritis mutilans (5%)** >> aggressief destructief verloop (telescoping fingers)



- Specifieke problemen als enthesitis en dactylitis
- Bijkomende moeilijkheden door cutane psoriasis

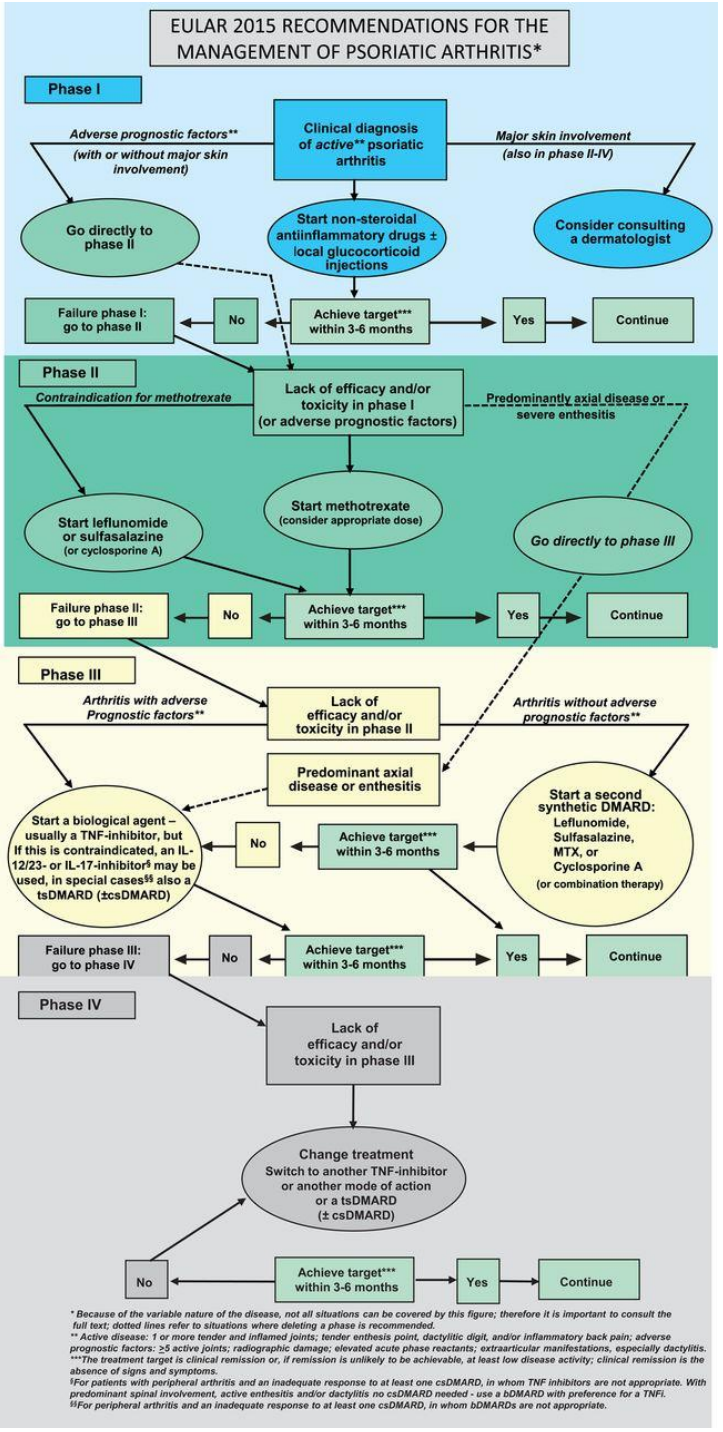
> In sommige gevallen zuiver symptomatisch beleid
> In andere gevallen intensief beleid met csDMARDs en/of bDMARDS

The EULAR 2015 algorithm for treatment of PsA with pharmacological non-topical treatments.

Available csDMARDs
- Methotrexate
- Leflunomide
- Sulphasalazine
- Cyclosporine A

Available bDMARDs
- TNF-alpha blockers
- IL-17 blocker: secukinumab
- IL-12/23 blocker: ustekinumab

Available tsDMARDs
- PDE4 blocker: apremilast



L Gossec et al. Ann Rheum Dis 2016;75:499-510

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ARD

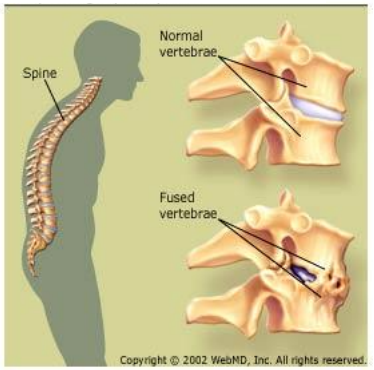
Management of psoriatic arthritis in 2016: a comparison of EULAR and GRAPPA recommendations.

Feature	EULAR[5]	GRAPPA[6]
General principles	Treatment target defined as remission or, alternatively, low or minimal disease activity	Treating to target recommended, but no specific target defined
	Overarching principle states that comorbidities should be considered	Specific literature review addressing prevalence of comorbidities, the need for screening, and potential effect on choice of therapy
Predominant axial or entheseal disease	bDMARDs without prior use of a csDMARD	
Drugs		
Methotrexate	Recommended as the csDMARD of choice	Considered alongside other csDMARDs with no specific preference
TNF inhibitors	Recommended for use after failure of csDMARDs for predominant peripheral disease or earlier in predominant axial or entheseal disease	
	• Recommended for use after failure of csDMARDs • Clear preference for TNF inhibitors as the first-line bDMARD	• Potential to use as a first-line therapy, before csDMARDs, in patients with severe active disease • No clear preference given to TNF inhibitors as the first-line bDMARD
Secukinumab and ustekinumab	Recommended for use after failure of methotrexate, but TNF inhibitors are preferred as the first-line bDMARD	Recommended alongside TNF inhibitors
Apremilast	Recommended for use after methotrexate if bDMARDs are contraindicated	• Recommended for use after failure of csDMARDs or if csDMARDs are contraindicated • Conditionally recommended before csDMARDs in certain cases

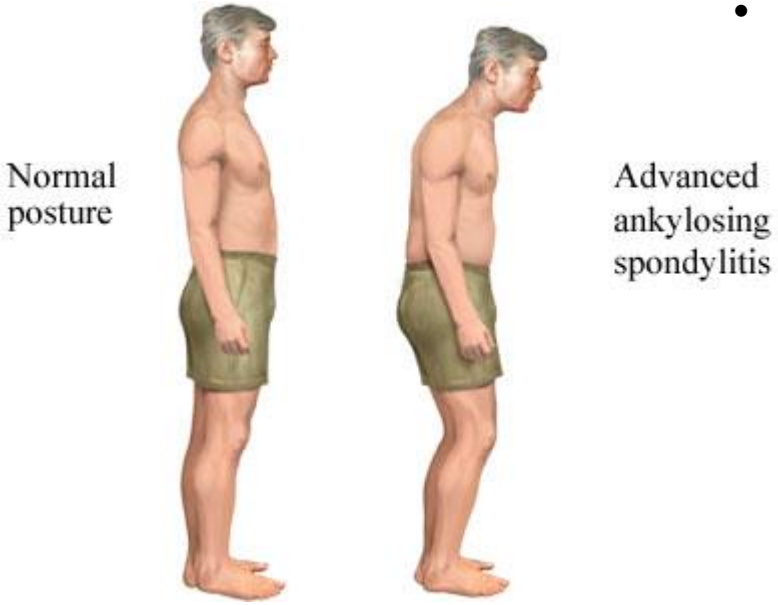
Nat Rev Rheumatol. 2016 Dec;12(12):743-750. doi: 10.1038/nrrheum.2016.183. Epub 2016 Nov 10.

Ankyloserende Spondylitis

- Meestal fluctuerend verloop, met goede en minder goede periodes
- Grote meerderheid heeft een zeer gunstige prognose
- Kleine minderheid ontwikkelt ankylose wervelkolom



- Sommigen ontwikkelen ook perifere artritis
- Sommigen ontwikkelen ook extra-articulaire problemen: oogontsteking, darmontsteking



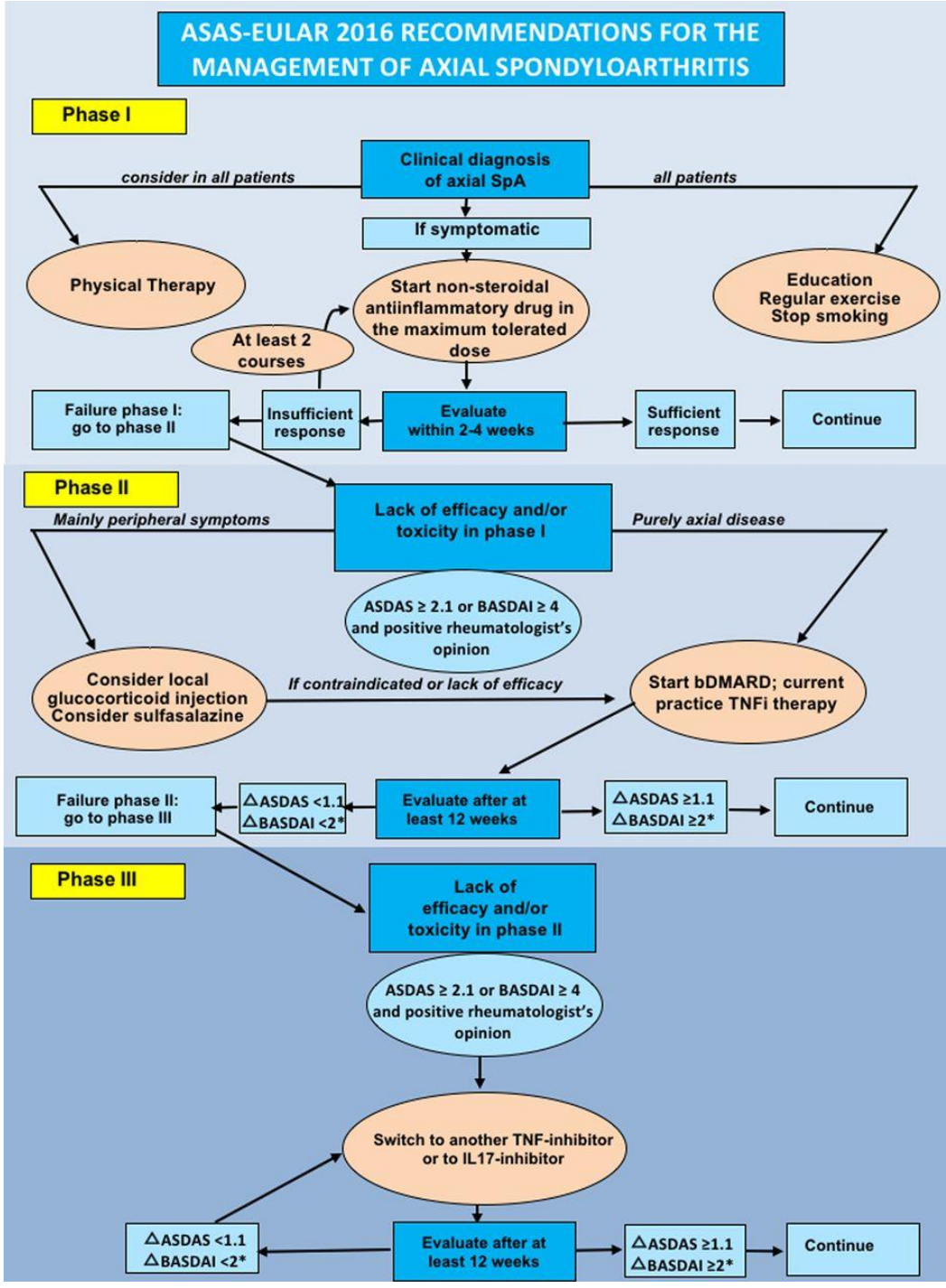
Meestal goede symptoomcontrole en behoud van functionaliteit mits oefening en NSAID

In bepaalde gevallen nood aan bDMARD: anti-TNF en anti-IL17

Algorithm based on the ASAS-EULAR recommendations for the management of axial spondyloarthritis.

Available csDMARDs
- Sulphasalazine

Available bDMARDs
- TNF-alpha blockers
- IL-17 blocker(s)



Désirée van der Heijde et al. Ann Rheum Dis 2017;76:978-991

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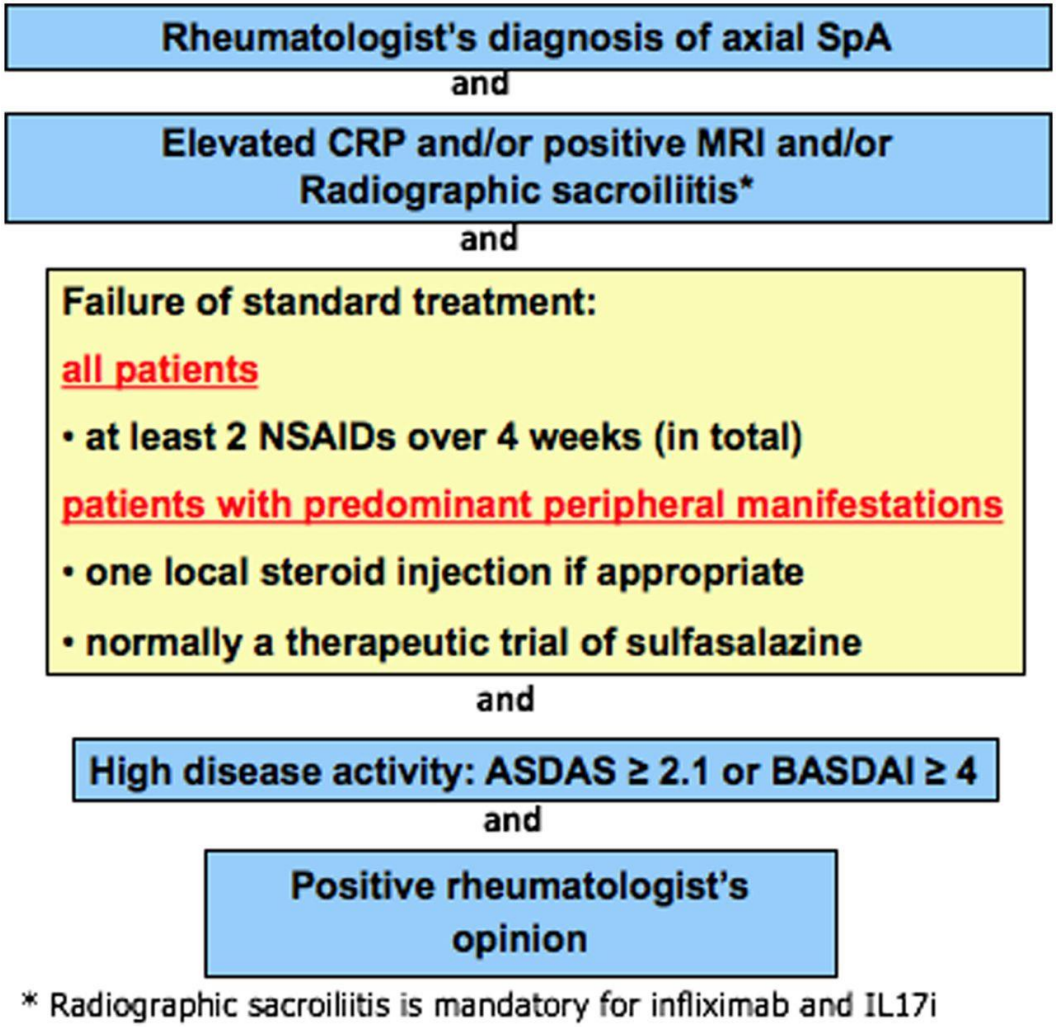
ASAS-EULAR recommendations for the treatment of patients with “axial spondyloarthritis” with bDMARDs.



Désirée van der Heijde et al. Ann Rheum Dis 2017;76:978-991

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ARD

Everything an internist needs to know about arthritis in daily practice anno 2018

- Acute monoarthritis > punction: cell count, crystals, culture
- Early polyarthritis: there is no time to waste !
  - Good response to NSAID is no reason to postpone referral
  - Refer to rheumatologist before starting glucocorticoids
- Established polyarthritis: stay alert and systematic !
  - DMARDs can be toxic products but are essential to treat RA
    - Discuss potential toxicity with rheumatologist as soon as possible
    - Beware of secondary toxicity in case of problems with renal or liver function
  - Patients on biologics are immune compromised
    - Increased risk of atypical severe infections: need for invasive diagnostic procedures
    - Increased risk of paradoxical autoimmune reactions: sometimes phenotype switch
  - A flare is not always simply a flare: beware of pitfalls
  - Like all systemic diseases RA can affect other organs than the joints

Rheumatology: for the happy few ?!

❖Preventie, diagnostiek en behandeling van ***niet traumatische musculoskeletale aandoeningen*** en ***systeemziekten***.
❖Diepgaande kennis van de kliniek en de pathofysiologie van aandoeningen zoals reumatoide artritis, systeemlupus, systeemsclerose en vasculitiden, spondyloartritis, infectieuze artritis, kristalartropathieën, (osteo)artrose, osteoporose.

❖Typisch competenties in de ***differentiaaldiagnostiek*** van musculoskeletale aandoeningen en het uitzetten van geïntegreerde ***therapiestrategieën*** bij diverse chronische reumatische aandoeningen.
❖Coördineert hierbij veelal een ***multidisciplinaire*** benadering.
❖Exclusiviteit in de indicatiestelling en het voorschrijven van gerichte ***biologische behandelingen*** voor chronische artritis.

❖Centrale rol in de evaluatie van de chronische inflammatoire gewrichtsaandoeningen.
❖Specifieke ***honorering voor evidence-based evaluatie*** van outcome, kostenefficaciteit en zorgkwaliteit
❖ Deelname aan klinisch wetenschappelijk ***onderzoek*** en registratie van de uitkomst van de nieuwe behandelingen is ook voor niet universitair werkende reumatologen een belangrijke taak.

❖De reumatoloog heeft hoofdzakelijk ***ambulante activiteiten***, meer en meer ***in associatie*** met meerdere collegae reumatologen. De nadruk ligt hierbij op consultaties maar ook op daghospitaal activiteiten voor toediening van gerichte biologische therapieën. Verder is er in grotere ziekenhuizen vaak een dienst reumatologie met ook opname faciliteiten.
❖Binnen ziekenhuizen kunnen reumatologen deel uitmaken van de pool ***interne geneeskunde*** of samenwerken met specialisten in de ***fysische geneeskunde en revalidatie***.