Fag og anbud

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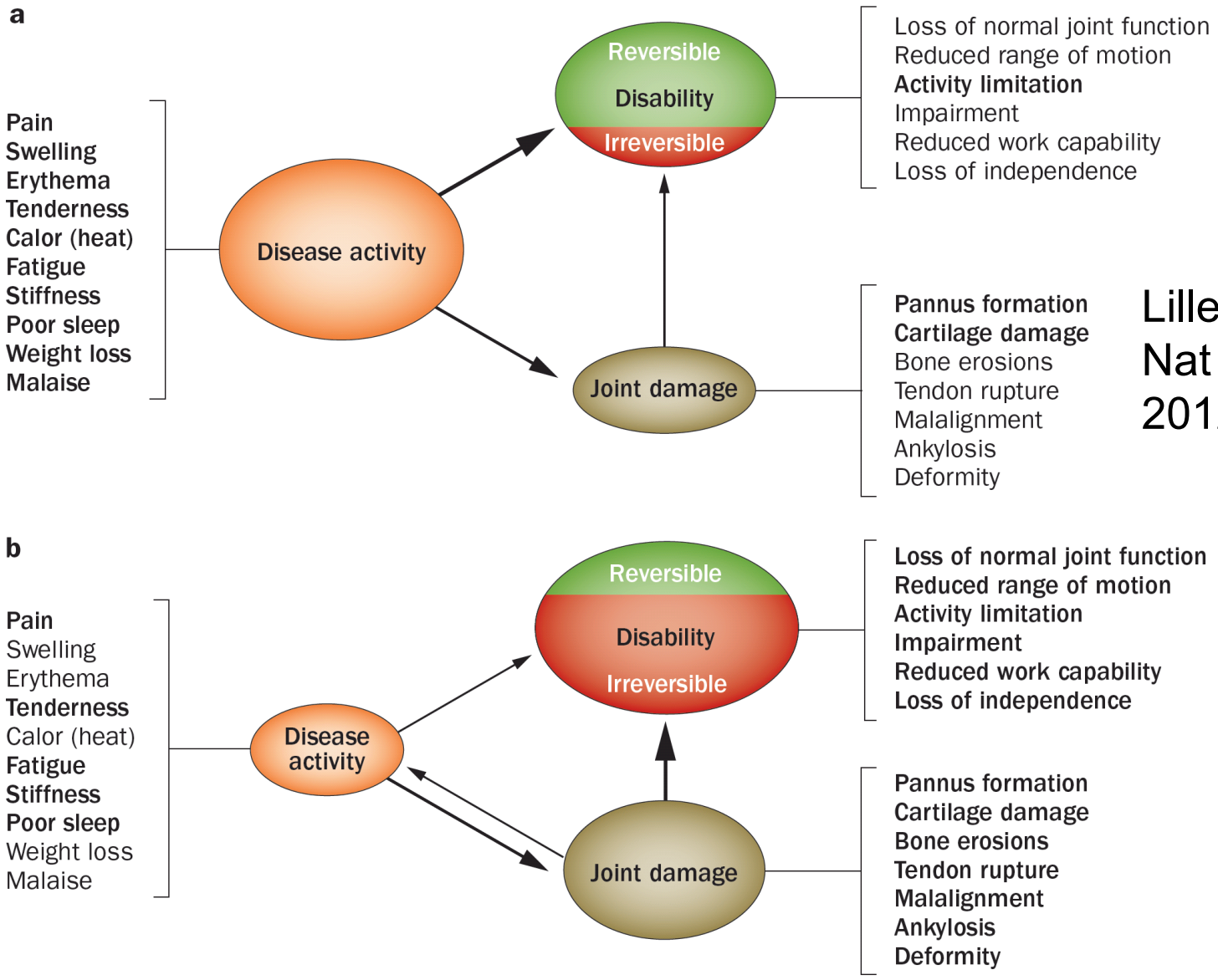
Main inflammatory joint diseases (IJD)

- Rheumatoid arthritis (RA)
- Spondyloarthritis (SpA)
- Psoriatic arthritis (PsA)

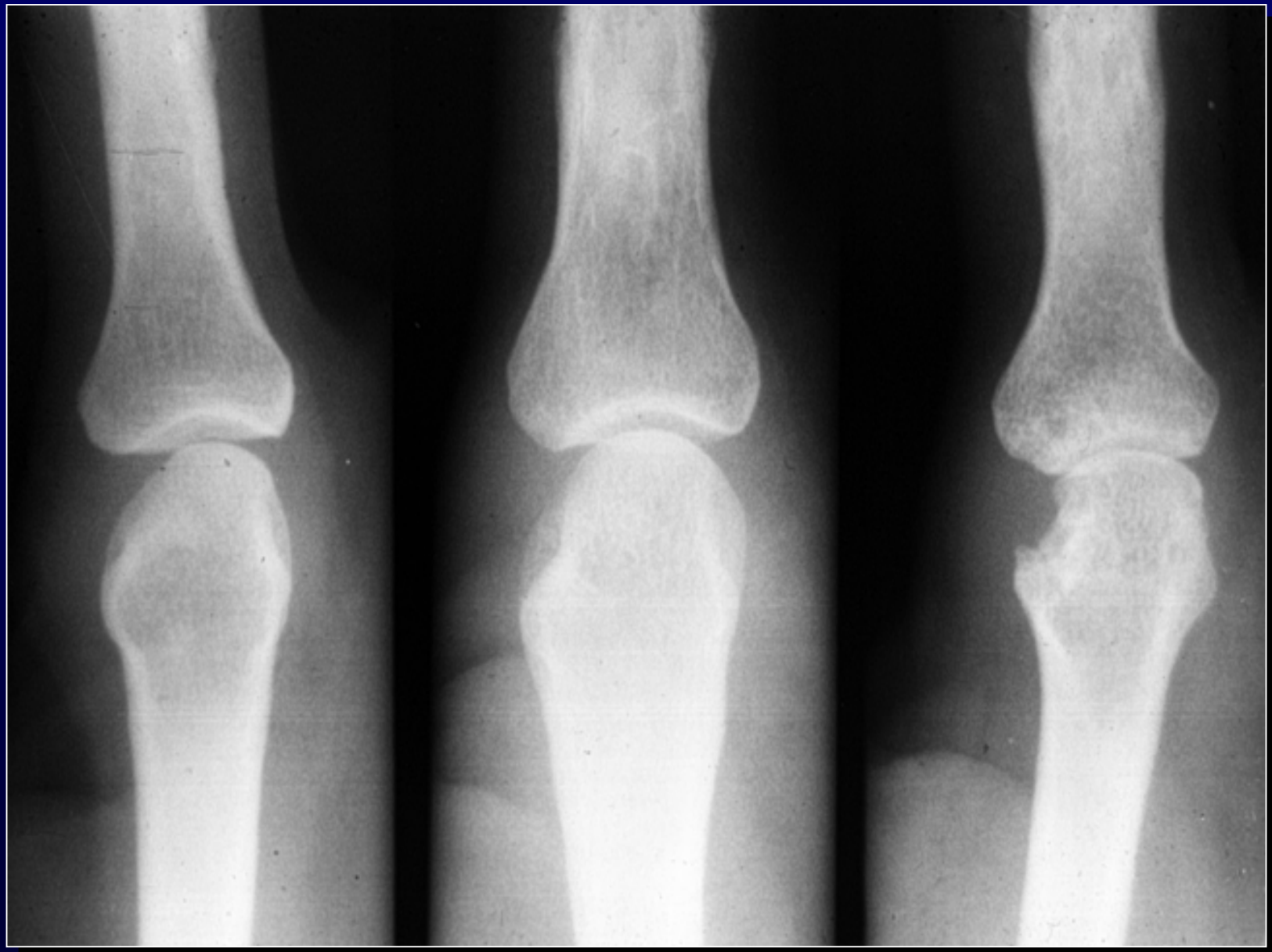
2019 RA treatment strategy

- early diagnosis
- early use of synthetic disease modifying therapies (Methotrexate)
- identify a treatment target (remission)
- monitor (tight control) and adjust disease-modifying therapy according to the target
- add biological DMARD if target is not achieved
- continue to monitor and adjust therapy as long as the target is not achieved



Lillegraven et al
Nat Rev Rheumatol
2012;8:117-20

Figure 1 | Hypothesized link between disease activity, functional disability and structural joint damage in RA. **a** | Early disease. **b** | Advanced disease. The magnitude and direction of associations are depicted by the size of arrows and circles. The signs and symptoms associated with each main feature are listed, with the more prominent features in early or late disease shown in bold.



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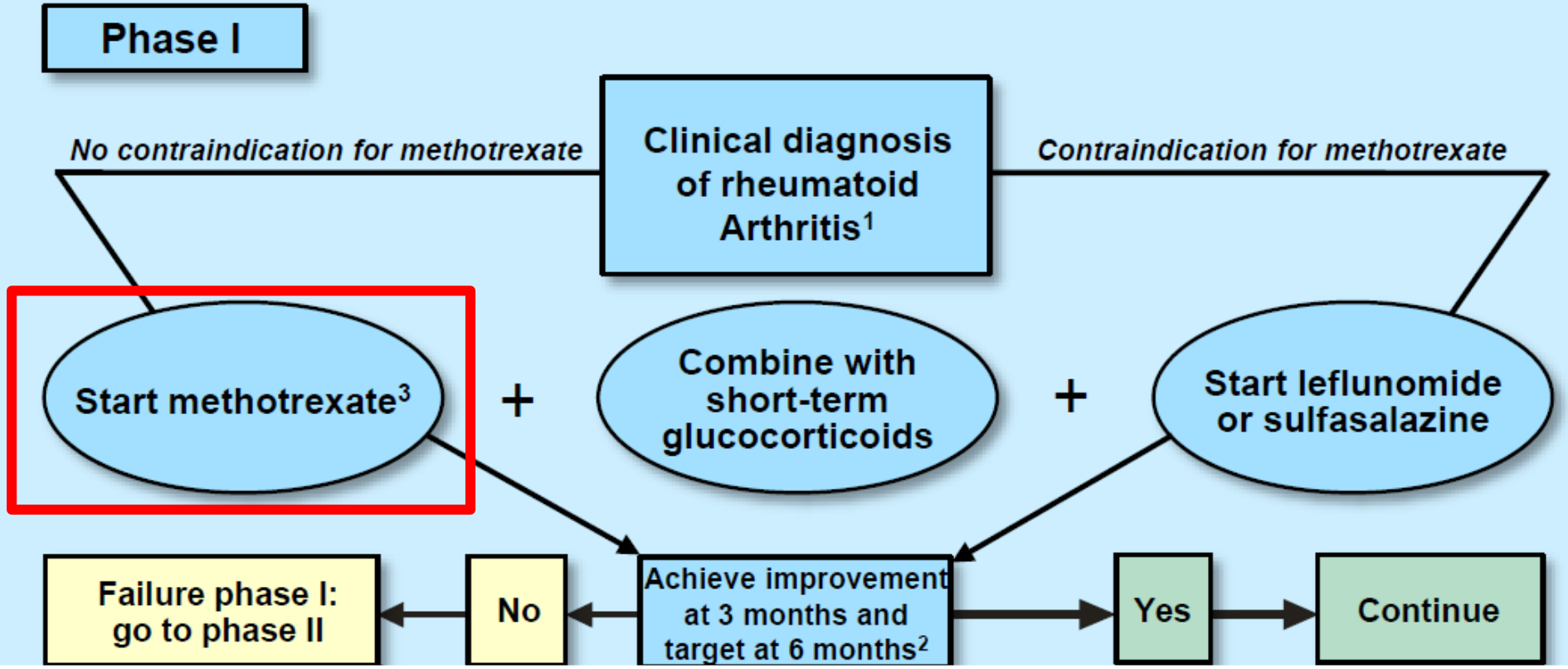

Smolen et al, Ann Rheum Dis 2017 (online)

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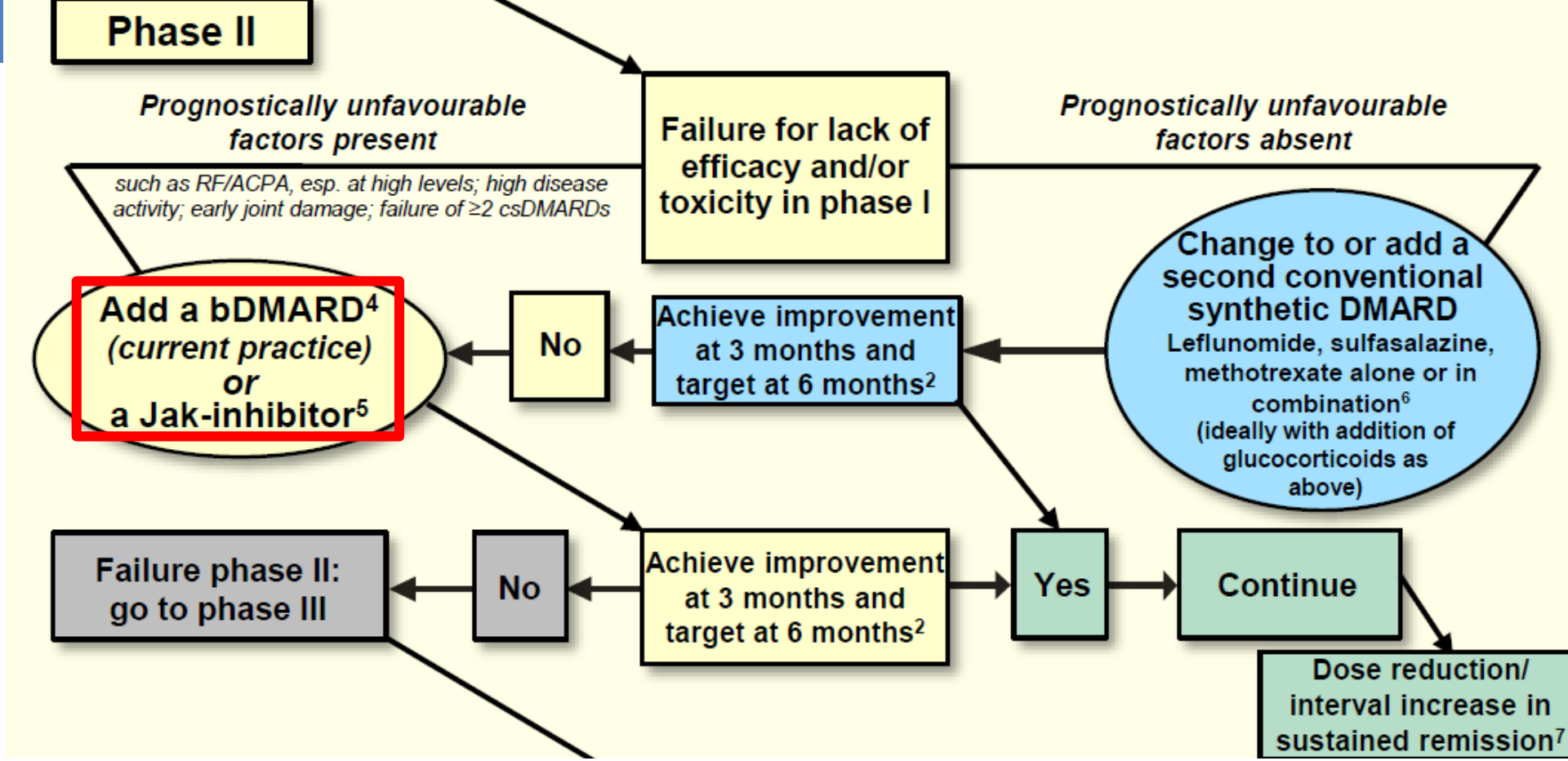

Phase II
Prognostically unfavourable factors present
such as RF/ACPA, esp. at high levels; high disease activity; early joint damage; failure of ≥2 csDMARDs
Failure for lack of efficacy and/or toxicity in phase I
Prognostically unfavourable factors absent
Add a bDMARD[4] (current practice) or a Jak-inhibitor[5]
No
Achieve improvement at 3 months and target at 6 months[2]
Change to or add a second conventional synthetic DMARD
Leflunomide, sulfasalazine, methotrexate alone or in combination[6]
(ideally with addition of glucocorticoids as above)
Failure phase II: go to phase III
No
Achieve improvement at 3 months and target at 6 months[2]
Yes
Continue
Dose reduction/ interval increase in sustained remission[7]

Types of Treatments for RA: Nomenclature

Disease Modifying Antirheumatic Drugs (DMARDs)			
Synthetic DMARDs (sDMARDs)		**Biological DMARDs (bDMARDs)**	
Conventional synthetic (csDMARDs	**Targeted synthetic (tsDMARDs)**	**Biological originator (boDMARDs)**	**Biosimilar (bsDMARDs)**
MTX, SSZ, LEF	*Tofacitinib* *Baricitinib*		

Smolen JS, et al. Ann Rheum Dis 2014 Jan;73(1):3-5.

bDMARDs - targets

- TNF-alpha (5 different (etanercept, adalimumab, infliximab, golimumab, certolizumab + biosimilar infliximab and etancercept)
- IL-6 (tocilizumab)
- B-cells (rituximab)
- T-cells (abatacept)
- IL-1(anakinra, canakinumab)

….and more to come

Targeted synthetic DMARDS (tsDMARDs)

- Janus kinas (JAK) inhibitors («Jakinibs»)
  - Tofacitinib
  - Baricitinib

Time trends 2000–2010

Baseline characteristics TNFi+MTX

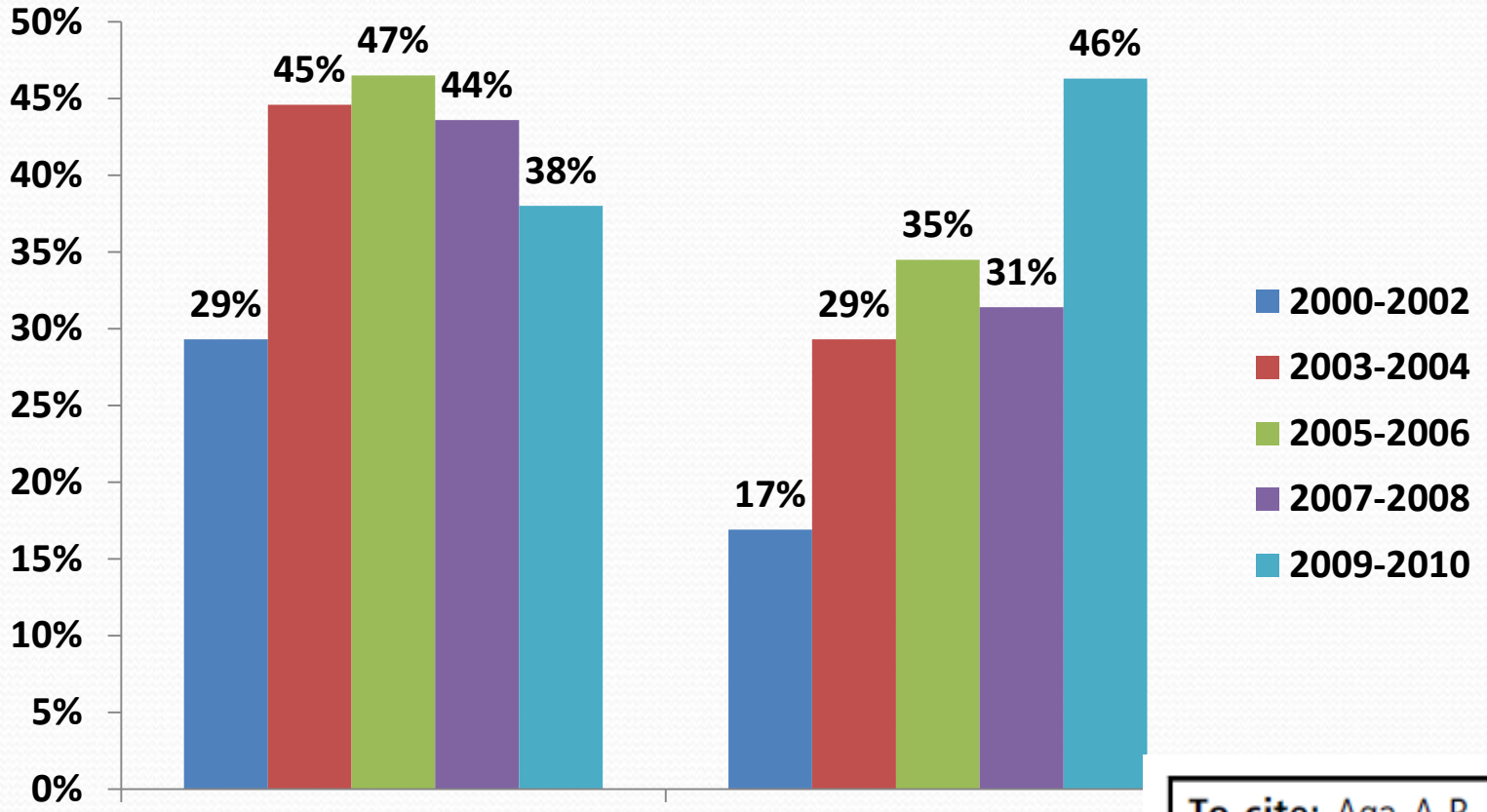
To cite: Aga A-B, Lie E, Uhlig T, *et al*. *Ann Rheum Dis* 2015;**74**:381–388.

	2000-2002	2003-2004	2005-2006	2007-2008	2009-2010	P-value
	n=85	n=184	n=143	n=160	n=134	
Duration, yrs*	8.0	6.5	6.3	4.2	3.8	<0.001
DAS28†	5.88	5.25	5.21	4.87	4.64	<0.001
MHAQ†	1.00	0.75	0.71	0.625	0.625	<0.001
28-SJC*	10	8	7	5	5	<0.001
28-TJC*	10	7	8	7	6	<0.001
ESR*	34	24	20	19	20	<0.001
CRP*	27	19	12	9	7	<0.001
SF-6D†	0.54	0.56	0.57	0.57	0.56	0.195

Values are expressed as means (†) or medians (*).

Time trends 2000–2010

Response and remission rates TNFi+MTX

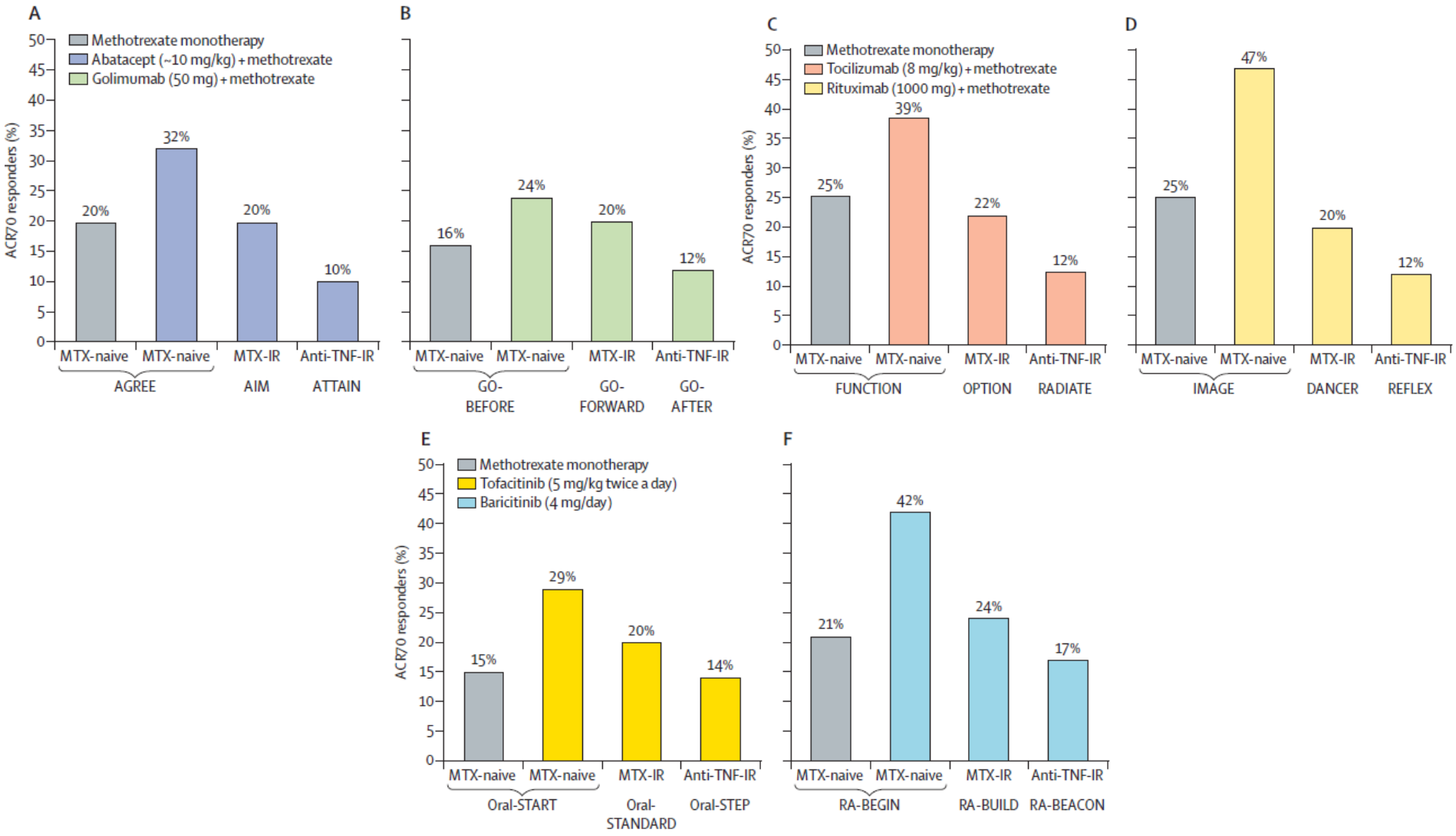


Time trend:	NA	p=0.003
First vs. last period:	p=0.34	p=0.001

To cite: Aga A-B, Lie E, Uhlig T, *et al. Ann Rheum Dis* 2015;**74**:381–388.

Which bDMARD?

Efficacy of Various Agents



Smolen JS, Aletaha D & McInnes I. Lancet 2016; 388:2023-2038

Why Biosimilars?

- Similar to the originator product
  - Not better
  - Not worse
  - But less expensive!

Could improve accessibility to good therapies for more people with RMDs

EXTENDED REPORT

Inequities in access to biologic and synthetic DMARDs across 46 European countries

Polina Putrik,[1] Sofia Ramiro,[2] Tore K Kvien,[3] Tuulikki Sokka,[4] Milena Pavlova,[5] Till Uhlig,[6] Annelies Boonen,[7] Working Group 'Equity in access to treatment of rheumatoid arthritis in Europe'

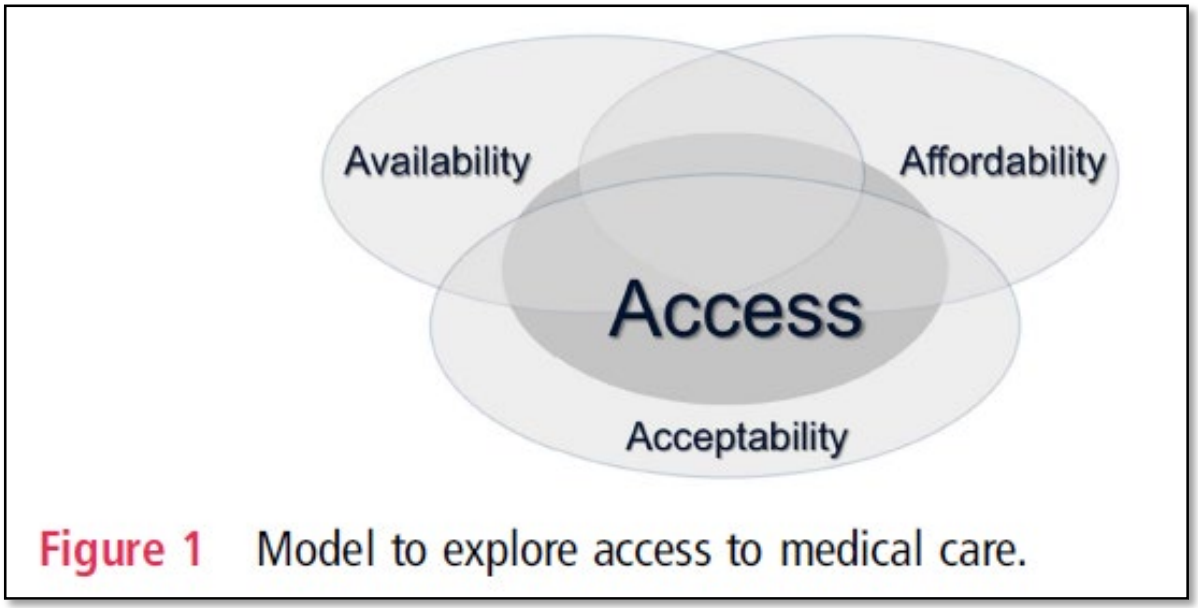


Figure 1 Model to explore access to medical care.

Putrik P, et al. Ann Rheum Dis 2014;73:198-206.

Inequities in Access to Biologic and Synthetic DMARDs Across 46 European Countries

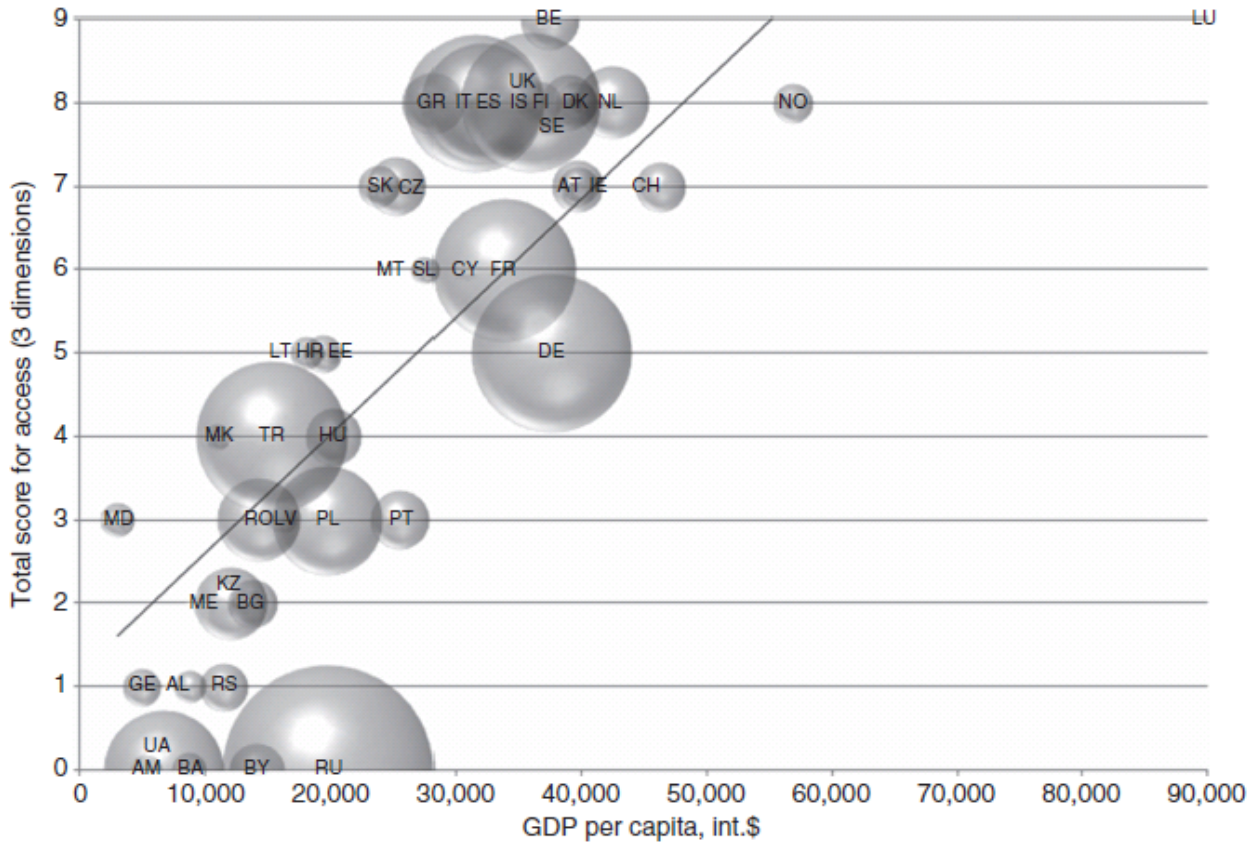
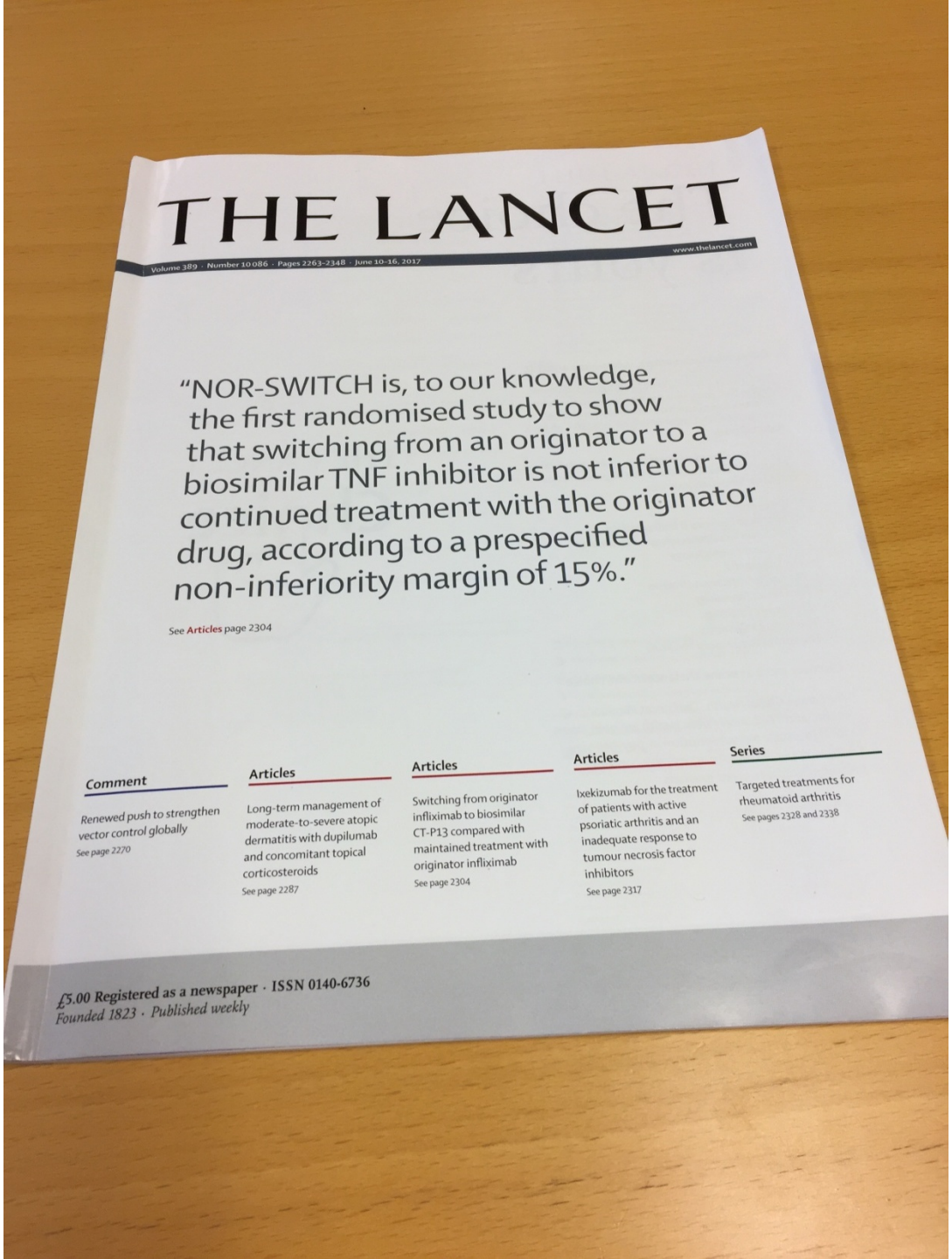


Figure 3 Access to biologic disease modifying antirheumatic drugs and gross domestic product per capita, international dollars (n=44). Size of the bubbles is proportional to the population size of the country. AL, Albania; AM, Armenia; AT, Austria; BA, Bosnia and Herzegovina; BE, Belgium; BG, Bulgaria; BY, Belarus; CH, Switzerland; CY, Cyprus; CZ, Czech Republic; DE, Germany; DK, Denmark; EE, Estonia; ES, Spain; FI, Finland; FR, France; GE, Georgia; GR, Greece; HR, Croatia; HU, Hungary; IE, Ireland; IS, Iceland; IT, Italy; KZ, Kazakhstan; LT, Lithuania; LU, Luxemburg; LV, Latvia; MD, Moldova; ME, Montenegro; MK, Macedonia; MT, Malta; NL, Netherlands; NO, Norway; PL, Poland; PT, Portugal; RO, Romania; RS, Serbia; RU, Russia; SE, Sweden; SK, Slovakia; SL, Slovenia; TR, Turkey; UA, Ukraine; UK, United Kingdom.

Putrik P, et al. Ann Rheum Dis 2014;73:198-206.



THE LANCET

Volume 389 · Number 10086 · Pages 2263–2348 · June 10–16, 2017

www.thelancet.com

"NOR-SWITCH is, to our knowledge, the first randomised study to show that switching from an originator to a biosimilar TNF inhibitor is not inferior to continued treatment with the originator drug, according to a prespecified non-inferiority margin of 15%."

See **Articles** page 2304

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Spondyloarthritis

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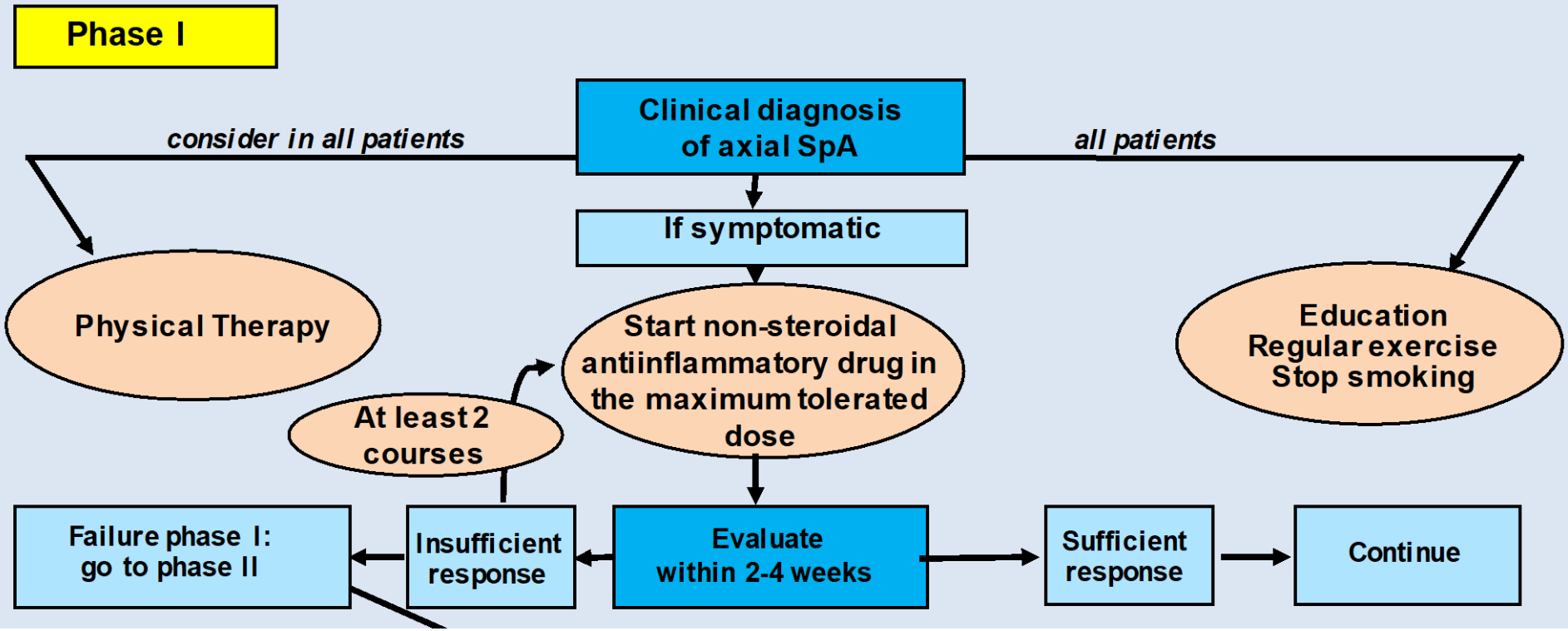
ASAS-EULAR 2016 RECOMMENDATIONS FOR THE MANAGEMENT OF AXIAL SPONDYLOARTHRITIS



ASAS Assessment of Spondylo Arthritis International Society

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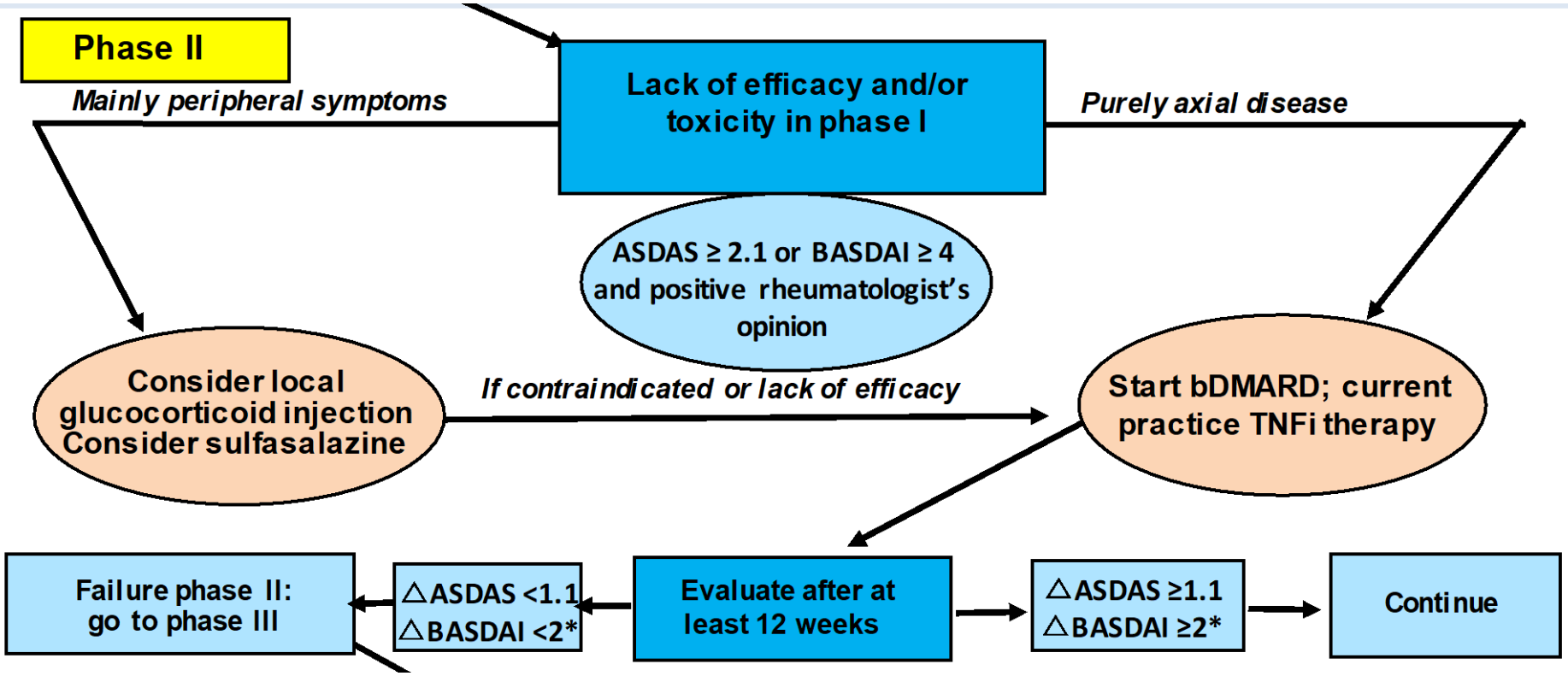

ASAS Assessment of Spondylo Arthritis International Society

eular

EXTENDED REPORT

European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update

L Gossec,[1,2] J S Smolen,[3,4] S Ramiro,[5] M de Wit,[6] M Cutolo,[7] M Dougados,[8,9] P Emery,[10,11] R Landewé,[12,13] S Oliver,[14] D Aletaha,[3] N Betteridge,[6] J Braun,[15] G Burmester,[16] J D Cañete,[17] N Damjanov,[18] O FitzGerald,[19] E Haglund,[20,21] P Helliwell,[22] T K Kvien,[23] R Lories,[24,25] T Luger,[26] M Maccarone,[27] H Marzo-Ortega,[10,11] D McGonagle,[10,11] I B McInnes,[28] I Olivieri,[29] K Pavelka,[30] G Schett,[31] J Sieper,[32] F van den Bosch,[33] D J Veale,[34] J Wollenhaupt,[35] A Zink,[36] D van der Heijde[5]

To cite: Gossec L, Smolen JS, Ramiro S, *et al*. *Ann Rheum Dis* 2016;**75**:499–510.

Kontakt med industri – fordeler og ulemper

Tore K. Kvien – disclosures

	Honorarium		Institutional support NOR-DMARD	
	Presentation	Advice	Previous	Current
AbbVie	X	X	X	
BMS	X	X	X	X
MSD	X	X	X	
Pfizer/Wyeth	X	X	X	
Roche	X	X	X	
UCB	X	X	X	
Hospira/Pfizer	X	X		
Mylan		X		
Orion	X	X		
Merck Serono		X		
Mundipharma	X			
Celltrion/Egis/Hikma	X	X		
Sandoz	X			
Samsung	X			
Biogen	X	X		
Amgen	X			

Conclusions

- Faglig innsikt viktig for konkurransegrunnlaget
- LIS anbefalingene må harmonisere med internasjonale (og nasjonale) anbefalinger for farmakoterapi
- Faglig kompetanse og internasjonal «standing» har vært ansett som viktig for å øke forståelsen for det norske anbudssystemet
- Målet for rabatter er i mange land 20-30% for biotilsvarende legemidler
- Vi har større ambisjoner og har lyktes! (Look to Norway!)