RA treatment in an international perspective

Tuulikki Sokka-Isler, MD, PhD,
Head of Rheumatology
Jyväskylä Central Hospital
Jyväskylä, Finland

The goal of treatment

"...In our opinion gold treatment ought to be started in the early stages of RA, before the development of erosions. We are treating not only the actual inflammation of the joints but also the quality of the patient's life for many decades in the future"

Luukkainen R, Kajander A, Isomäki H. Treatment of rheumatoid arthritis (letter). Br Med J 1978; 2:1501.

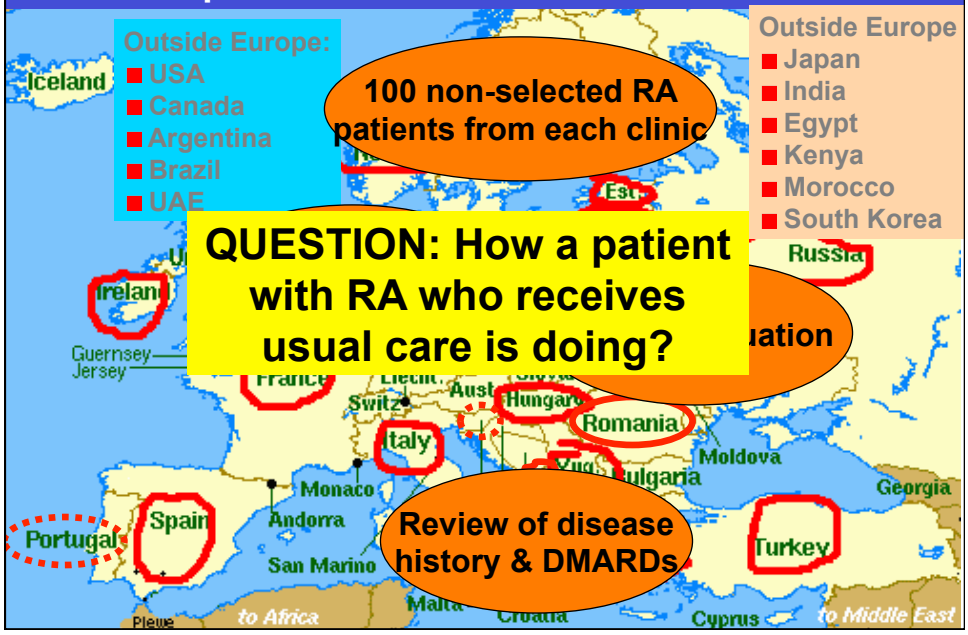
The ultimate goal of RA registers?

- To improve long-term outcomes of RA, by preventing
  - Disease activity
  - Damage
  - Disability
- How?
  - By opening the data in front of our eyes
    - To see mistakes
    - To see success

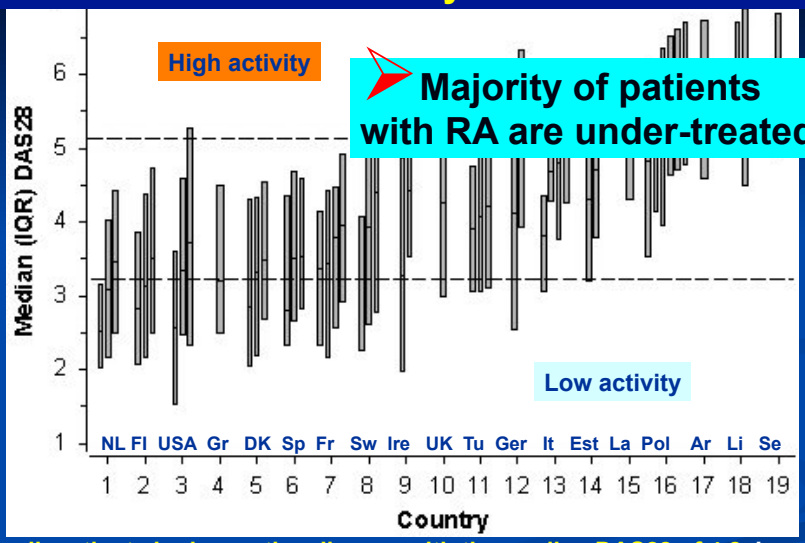
"clinicians may all too easily spend years writing 'doing well' in the notes of a patient who has become progressively crippled before their eyes …"

Verna Wright.
British Medical Journal.
1983;287:569.

QUEST-RA From January 2005 to Dec 2010: 8792 patients from 90 clinics in 33 countries



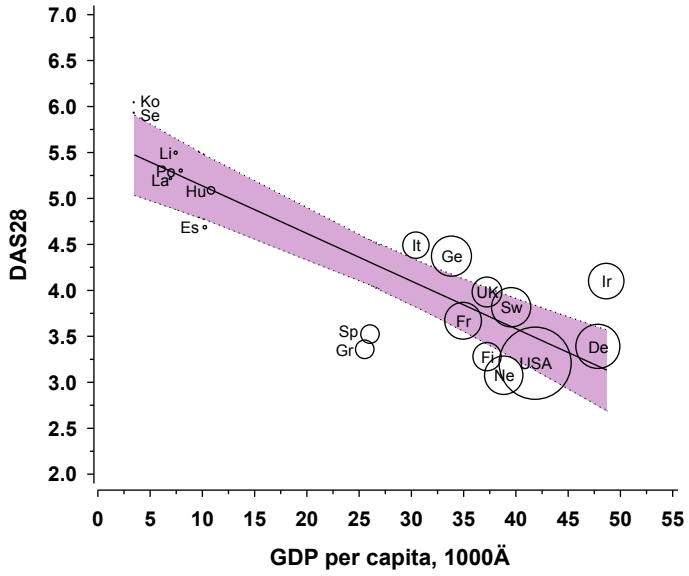
QUEST-RA: Disease activity of RA in 19 countries



Overall, patients had an active disease with the median DAS28 of 4.2. Low disease activity of DAS28≤3.2 was met by the majority of patients in 8 sites in 6 countries; in 11 sites in 7 other countries >50% of patients had high disease activity of DAS28>5.1.

Sokka et al. ARD 2007

Association between gross domestic product (GDP) and disease activity (DAS28) in 19 countries in QUEST-RA



Sokka et al ARD 2009

QUEST-RA: Medications for RA in 2005-06

Country	Patients	PrdEver	MTX Ever	Biol Ever	Biol Now
USA	301	76.7	85.4	32.6	27.9
Argentina	246	82.5	68.3	3.3	2.8
Denmark	301	43.5	85.7	23.3	20.6
Estonia	168	75.6	73.8	1.2	0.7
Finland	304	73.7	85.2	17.4	12.5
Germany	225	54.2	80.0	28.9	22.7
Greece	300	89.0	32.0	46.0	16.0
Hungary	153	58.2	85.0	15.7	19.0
Ireland	240	71.3	93.3	41.7	32.1
Italy	336	72.3	81.0	26.8	12.8
Lithuania	300	96.7	72.7	11.0	9.0
Netherlands	317	30.3	91.5	22.4	19.2
Poland	642	78.8	88.0	9.5	6.1
Serbia	100	88.0	69.0	2.0	0.0
Spain	302	68.2	85.4	27.2	15.3
Sweden	260	68.5	83.5	33.1	25.5
Turkey	309	75.4	89.3	7.1	5.8
UK	145	53.8	82.8	20.0	14.5
Total	5519	70.4	82.5	22.5	16.9

The initial DMARD in selected early RA cohorts, according to period of time

			Percentage of patients who started selected DMARDs					
Country	Cohort	Enrollment Period	IM gold	AM	SSZ	MTX	Other DMARD	No DMARDs
Finland	Heinola Cohort, Jantti et al 2001	1973-75	56%	36%	0	0	4%	4%
Finland	Jyvasyla Cohort1983-5 Sokka et al 2004	1983-85	70%	30%	0	0	0	0
Austria	Aletaha et al 2002	1985	87%	7%	0	0	6%	
NL	Welsing et al. 2005	1985-90	na	na	60%	2%	38%	
Austria	Aletaha et al 2002	1992	20%	46%	22%	4%	8%	
NL	Welsing et al. 2005	1991-95	na	na	82%	9%	9%	
UK	ERAS, Young et al. 2000	Before 1994	8%	2%	61%	2%	11%	16%
UK	*NOAR, Bukhari et al 2003	Early 1990's	3%	4%	37%	3%	1%	52%
Greece	Papadopoulos et al. 2002	1987-1995	5%	30%	0%	21%	44%	0
USA	Western Consortium, Paulus et al. 1999	1993-1996	4%	17%	7%	36%	0	36%
Sweden	BARFOT, Forslind et al. 2004	1993-1997	0	0	34%	24%	8%	34%
Finland	Jyvaskyla Cohort1995-6, Sokka et al 2004	1995-96	3%	1%	95%	1%	0	0
Finland	Jyvaskyla 1997, Makinen et al 2005	1997	na	na	73%	20%	6%	1%
Sweden	Carli et al. 2006	1997	na	na	30%	23%	11%	33%
Austria	Aletaha et al 2002	1998	1%	40%	29%	29%	1%	
NL	Welsing et al. 2005	1996-2000	na	na	76%	10%	14%	
USA	ERATER, Sokka&Pincus, 2002	1998-2003	0	7%	1%	82%	3%	7%
Sweden	Carli et al. 2006	2001	na	na	20%	54%	6%	17%
USA	SONORA, Bombardier et al. 2002	Early 2000's	0	16%	5%	27%	17%	35%
Italy	GIARA, CER 2003	#2001-02	na	18%	1.2%	19%	11%	51%

Sokka, Envalds, Pincus. Mod Rheumatol 2008

RA treatment – an international perspective

- Received medications are dictated by:
  - Traditions
  - Beliefs
  - Money
  - Rheumatologists' personality
  - etc

→ Patients with the same disease receive different treatments in different parts of the world – which leads to different outcomes

CPG / recommendations, e.g.

- 2 – Canada 2002
- 14 – Australian 2010
- 15 – Latin American 2006
- 17 – British 2006
- 18 – NICE 2009
- 20 – T2T 2010
- 21 – EULAR 2010
- 22 – Spanish 2010
- 23 – Australian 2008
- 24 – Wolfe, Cush, O' dell et al 2001
- 25 – British 2008
- 26 – Inidian 2008
- 27 – Scottish 2000
- 28 – EULAR early 2007
- 29 – South African 2003
- 30 – NICE biol 2007
- 31 – ACR 2008
- 34 – French biol 2007
- 35 – British biol 2010
- 45 - British biol/derm 2008
- 54 – French early 2006
- 56 – Pavy et al MTX 2006
- 57 – 3E MTX 2009
- 80 – Canada 2011

Current overarching principles in treatment of RA include:

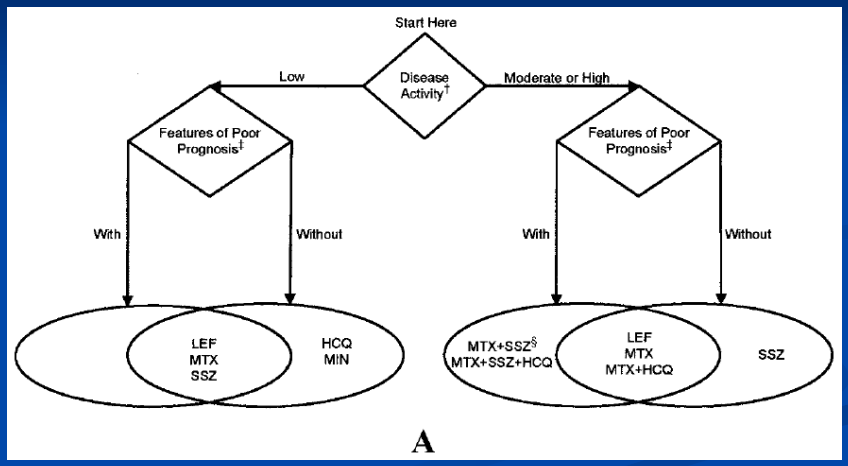
- Treatment target
- Remission
- Patient in a central role

ACR recommendations consider…

- Disease duration thresholds were chosen to help with clinical decision-making
  - 6 months (considered to be equivalent to early disease)
  - 6–24 months (considered to be equivalent to intermediate disease duration)
  - 24 months (considered to be long or longer disease duration)
- Disease activity low/ moderate/ high according to one of:
  - DAS28
  - SDAI
  - CDAI
  - RADAI
  - PAS
  - RAPID
- Poor prognostic factors:
  - Functional limitation (HAQ)
  - Extra-articular disease
  - RF/CCP +
  - Bone erosions

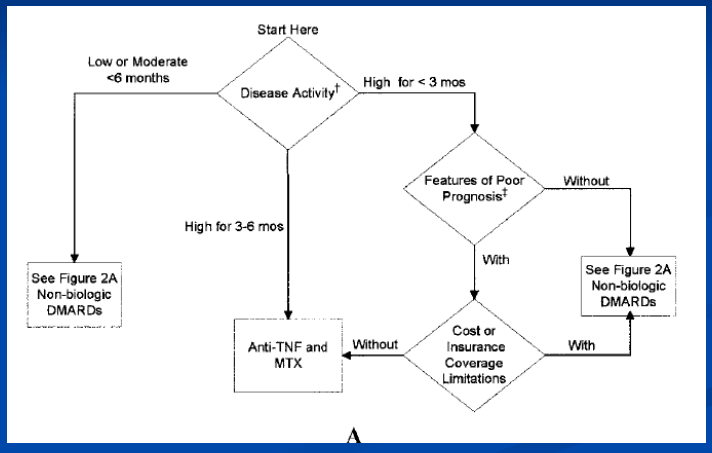
Saag et al. A&R 2008

Treatment algorithm for DMARD naïve patients, disease duration <6 months



Saag et al. A&R 2008

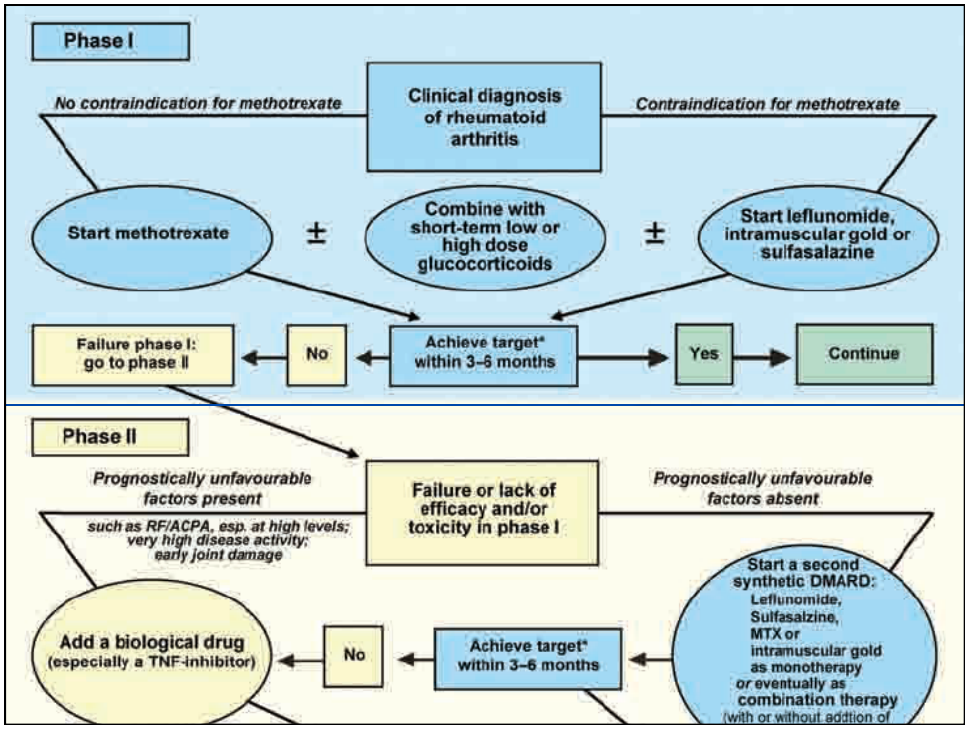
ACR: When to start a biologic?



Saag et al. A&R 2008

EULAR recommendations in short:

- Start MTX
- In addition, start glucocorticoids p.o. and taper down
- If treatment target not achieved within 3-6 months, add a biologic



NICE 2009

- In people with newly diagnosed active RA, NICE recommends a combination of DMARDs (including MTX and at least one other DMARD, plus short-term glucocorticoids)
- NICE recommendations emphasize fast escalation of a DMARD to a clinically effective dose rather than the choice of DMARD.
- In mild or less-active RA, NICE offers an option to treat a patient with monotherapy.
- TNF-α are recommended as options for the treatment of patients who have:
  - Active rheumatoid arthritis as measured by disease activity score (DAS28) greater than 5.1 confirmed on at least two occasions, 1 month apart, and
  - Have undergone trials of two disease-modifying anti-rheumatic drugs (DMARDs), including MTX (unless contraindicated).

An example patient

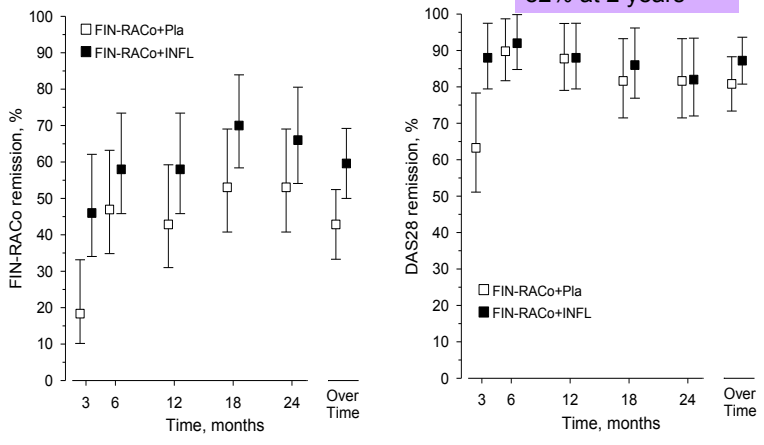
- A 60-years old otherwise healthy woman
- symmetric polyarthritis in 2 MCPs, 3 PIPs, 5 MTPs a wrist and a knee
- first symptoms two months ago
- HAQ=1
- no erosions
- 5x elevated CCP, normal RF
- CRP=20 and ESR=30
- DAS28=5.2

Which therapy is recommended to this patient?

- ACR: preferably a combination of MTX+SSZ or MTX+SSZ+HCQ, alternatively MTX or LEF. ACR recommendations do not cover the use of glucocorticoids, NSAIDs and analgesics.
- NICE: a MTX-based combination of DMARDs, oral glucocorticoids for short term, and analgesics if needed.
- EULAR: MTX (or other DMARD) monotherapy, oral glucocorticoids for short term.

NEO-RACo – remissions during 2 years

DAS28 remissions: 82% at 2 years



Leirisalo-Repo et al: EULAR2008

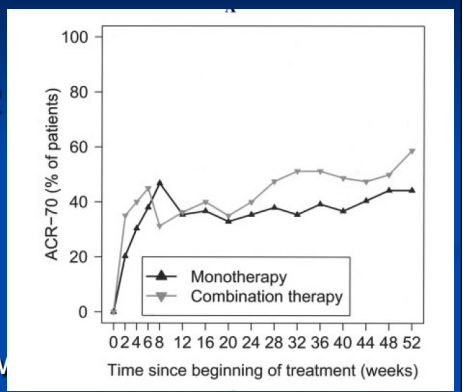
Lesson from SWEFOT

- 487 patients with early RA <1 year included
- MTX started with initial dose 10mg, dose increased every 2 weeks by 5mg – at week 5 patients took MTX20mg per os
- Only 6-8% took Pred
- Patients seen at 3-4 months later:
- 147/487 (30%) with DAS28≤3.2 (low activity)

van Vollenhoven et al. Lancet 2009

CIMESTRA

- 160 patients with RA<6months 1999-2002
  - MTX7.5+CyA 2.5mg/kg
  - MTX7.5+placebo
  - i.a. betamethasone wk 0,2,4,6,8, every 4 wk
  - After wk8 MTX could be increased 2.5mg every 4w up to 20mg by half year



Active treatment strategy includes joint injections!

Hetland et al A&R 2006

Did patient did not respond treatment?

- By ACR recommendations, she would receive a TNF-α inhibitor if her insurance covers it.
- According to NICE recommendations, she would possibly not receive biologics as she most probably would have DAS28<5.1.
- EULAR recommendations are a highway to biologics.

Conclusions

- MTX is an anchor drug for RA
- What about MTX injections as a starter?
- Differences in recommendations are confusing to a regular rheumatologist

Conclusions: to do

- Registers:
  - To collect data on
    - Medications
    - Outcomes
  - To observe which treatment strategies lead to the best outcomes long term in real world settings

EXTENDED REPORT

EULAR recommendations for the management of early arthritis: report of a task force of the European Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT)

B Combe, R Landewe, C Lukas, H D Bolosiu, F Breedveld, M Dougados, P Emery, G Ferraccioli, J M W Hazes, L Klareskog, K Machold, E Martin-Mola, H Nielsen, A Silman, J Smolen, H Yazici

Ann Rheum Dis 2007;**66**:34–45. doi: 10.1136/ard.2005.044354

5. **Patients at risk of developing persistent or erosive arthritis should be started with DMARDs as early as possible, even if they do not yet fulfill established classification criteria for inflammatory rheumatological diseases.**

EULAR recommendations for early arthritis (Combe et al 2007)

7. NSAIDs have to be considered in symptomatic patients after evaluation of gastrointestinal, renal, and cardiovascular status.
8. Systemic glucocorticoids reduce pain and swelling and should be considered as adjunctive treatment (mainly temporary), as part of the DMARD strategy. Intra-articular glucocorticoid injections should be considered for the relief of local symptoms of inflammation.
9. Among the DMARDS, methotrexate is considered to be the anchor drug, and should be used first in patients at risk of developing persistent disease.
10. The main goal of DMARD treatment is to achieve remission.

EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs

Josef S Smolen, Robert Landewé, Ferdinand C Breedveld, et al.

1. Treatment with synthetic DMARDs should be started as soon as the diagnosis of RA is made.

2. Treatment should be aimed at reaching a target of remission or low disease activity as soon as possible in every patient; as long as the target has not been reached, treatment should be adjusted by frequent (every 1–3 months) and strict monitoring

EULAR recommendations….

3. MTX should be part of the first treatment strategy in patients with active RA

4. When MTX contraindications (or intolerance) are present, the following DMARDs should be considered as part of the (first) treatment strategy: leflunomide, SSZ or injectable gold

5. In DMARD naïve patients, irrespective of the addition of GCs, synthetic DMARD monotherapy rather than combination therapy of synthetic DMARDs may be applied

Red flag

EULAR recommendations….

6. GCs added at low to moderately high doses to synthetic DMARD monotherapy (or combinations of synthetic DMARDs) provide benefit as initial short-term treatment, but should be tapered as rapidly as clinically feasible

Red flag

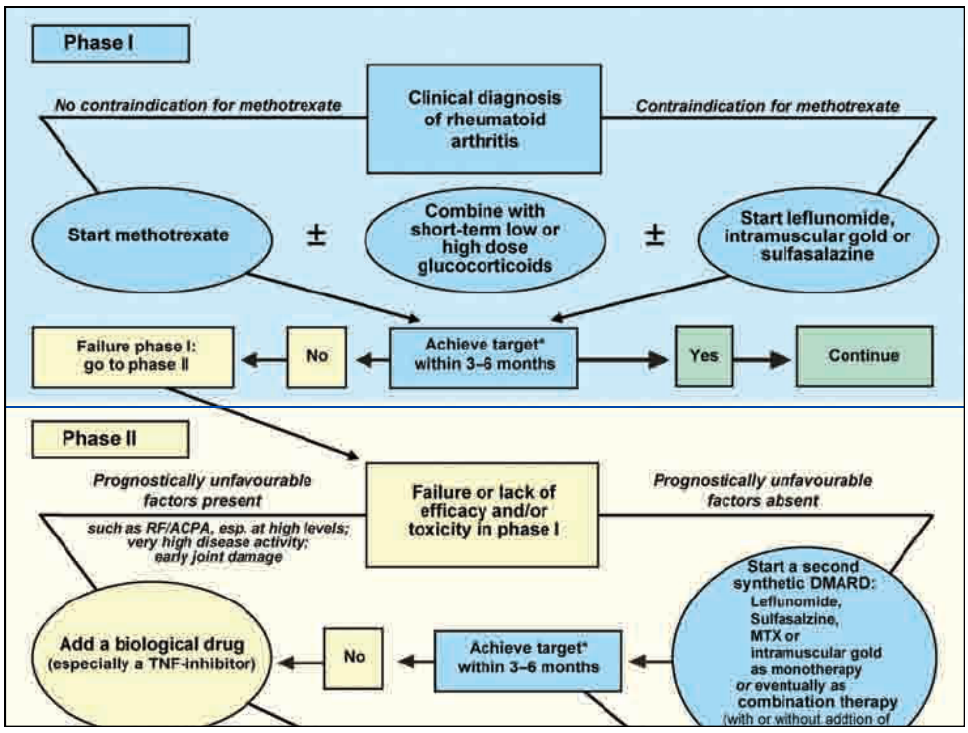
7. If the treatment target is not achieved with the first DMARD strategy, addition of a biological DMARD should be considered when poor prognostic factors are present; in the absence of poor prognostic factors, switching to another synthetic DMARD strategy should be considered

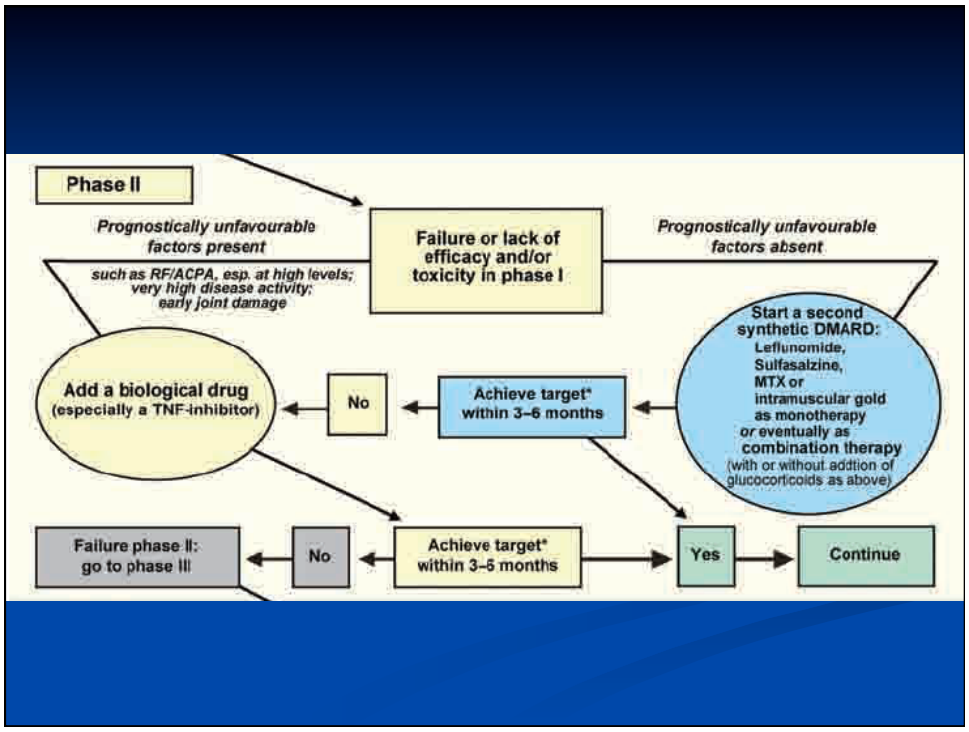
EULAR recommendations….

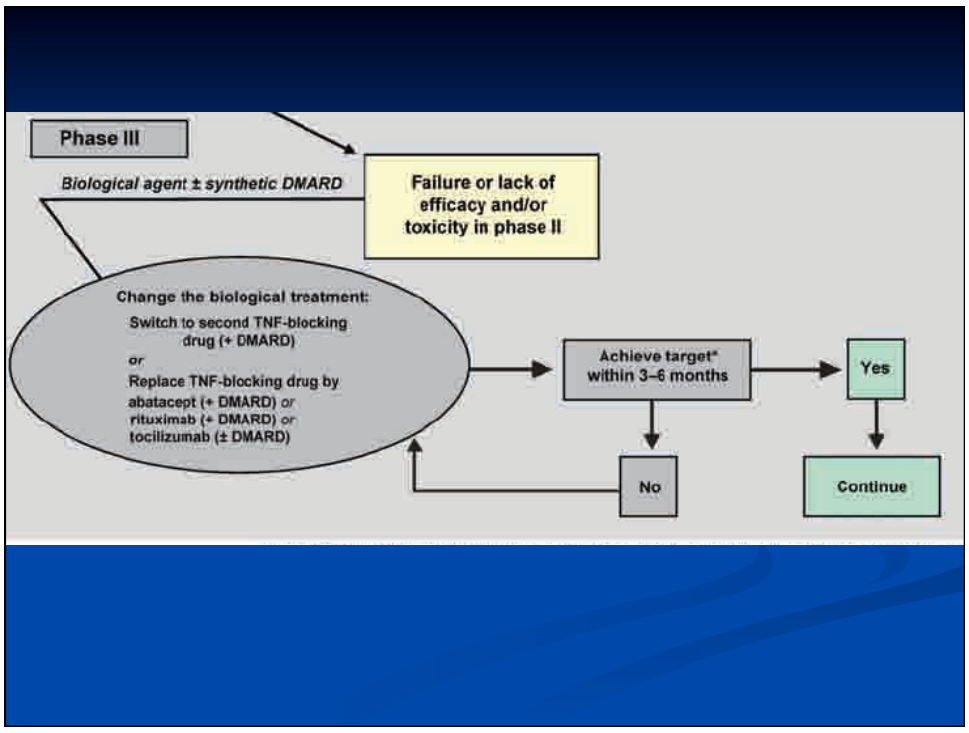
8. In patients responding insufficiently to MTX and/or other synthetic DMARDs with or without GCs, biological DMARDs should be started*; current practice would be to start a TNF inhibitor (adalimumab, certolizumab, etanercept, golimumab, infliximab)† which should be combined with MTX*

9. Patients with RA for whom a first TNF inhibitor has failed, should receive another TNF inhibitor, abatacept, rituximab or tocilizumab

14. DMARD naïve patients with poor prognostic markers might be considered for combination therapy of MTX plus a biological agent




Phase II
Prognostically unfavourable factors present
such as RF/ACPA, esp. at high levels; very high disease activity; early joint damage
Failure or lack of efficacy and/or toxicity in phase I
Prognostically unfavourable factors absent
Start a second synthetic DMARD:
Leflunomide, Sulfasalzine, MTX or intramuscular gold as monotherapy
or eventually as combination therapy
(with or without addition of glucocorticoids as above)
Add a biological drug
(especially a TNF-inhibitor)
No
Achieve target* within 3–6 months
Failure phase II: go to phase III
No
Achieve target* within 3–6 months
Yes
Continue

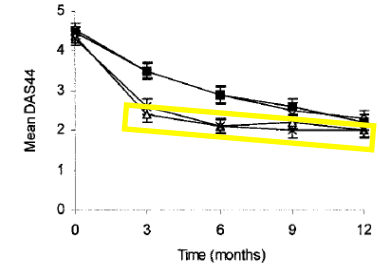

Phase III
Biological agent ± synthetic DMARD
Failure or lack of efficacy and/or toxicity in phase II
Change the biological treatment:
Switch to second TNF-blocking drug (+ DMARD)
or
Replace TNF-blocking drug by abatacept (+ DMARD) or rituximab (+ DMARD) or tocilizumab (± DMARD)
Achieve target* within 3–6 months
Yes
No
Continue

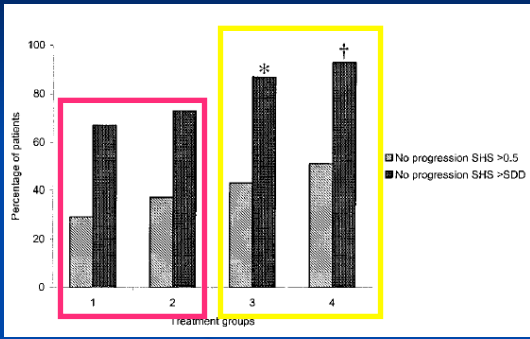
EULAR recommendations - critique:

- Is "window of opportunity" lost while waiting effects of MTX?
  - Escalation of MTX to full dose may take weeks
- Is this current "wait and see" strategy???
  - With consequences on
    - Work productivity while waiting?
    - Long-term joint damage?
- Why not hit hard immediately:
  - Combination of DMARDs?
  - Role of Pred diluted?
  - Intra articular glucocorticoids?

STEPs-UP in BeST

STEP-UPs inferior in disease activity, radiology





1 – monotherapy: MTX15 - SSZ – LEF – MTX+INF – gold+mPr – other
2 – STEP-UP: MTX15 – add SSZ – add HCQ – add Pr – MTX+INF – other
3 – TOP: MTX7.5+SSZ+Pr – MTX+CSA+Pr – MTX+INF – LEF – AZA+Pr – Other
4 – TOP: MTX25+INF – SSZ – LEF – MTX+CSA+Pr – AZA+Pr - Other

Goekoop-Ruiterman et al A&R 2005

Lesson from SWEFOT

- 487 patients with early RA <1 year included
- MTX started with initial dose 10mg, dose increased every 2 weeks by 5mg – at week 5 patients took MTX20mg per os
- Only 6-8% took Pred
- Patients seen at 3-4 months later:
- 147/487 (30%) with DAS28≤3.2 (low activity)

Can we accept recommendation of a therapy that may be ineffective in 2/3 of patients for early RA?

van Vollenhoven et al. Lancet 2009

EULAR recommendations were based on (interpretation) of:

- EVIDENCE: 5 systematic literature reviews (SLR) concerning
  1. Synthetic DMARDs as mono/combination therapy without glococorticoids (GC)
  2. GCs alone and in combination with synthetic DMARDs
  3. Biological DMARDs
  4. Treatment strategies
  5. Economic issues

EULAR recommendations were based on (interpretation) of:

- EVIDENCE: 5 systematic literature reviews concerning

1. **Synthetic DMARDs as mono/combination therapy without glococorticoids (GC)**
2. GCs alone and in combination with synthetic DMARDs
3. Biological DMARDs
4. Treatment strategies
5. Economic issues

Synthetic DMARDs as mono/combination therapy without GCs

- Efficacy was assessed by the change in signs and symptoms or disability status between baseline and week 24 or closest time point, and radiographic joint damage between baseline and week 48. **Reported results had to fit in pre-defined time frames**
- Efficacy: 97 (13%) of 759 articles
- Long-term safety: 39 (5%) of 821 article

A minority of papers included

-is a systematic (non-analytical) literature review an appropriate method to find EVIDENCE for treatment recommendations in clinical care?

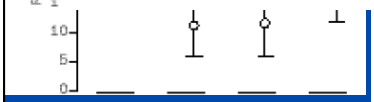
Gaujoux-Viala et al. ARD 2010

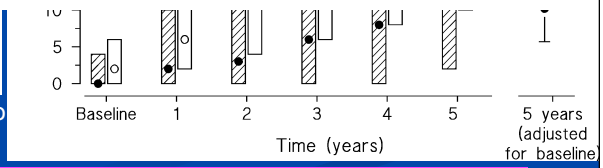
Where is FIN-RACo with excellent results?

Inte

Sulfasalazine monotherapy versus sulfasalazine combination

In six trials (657 patients), there was no difference for SJC, function, ACR20, 50 and 70 response criteria. The only significant result was for structural damage in one trial favouring the combination MTX+sulfasalazine+hydroxychloroquine: SRM=−1.70 (95% CI −2.03 to −1.37)[25] and for pain in one trial favouring sulfasalazine monotherapy: SRM=4.10 (2.91 to 5.29)[10] (online supplementary file table K). Other combinations are detailed in the online supplementary material.





NOT included because "no initial MTX monotherapy arm"

Möttönen et al Lancet 1999 Korpela et al A&R 2004

FIN-RACo did not contribute to EULAR recommendations of management of RA

Arthritis & Rheumatism (Arthritis Care & Research)
Vol. 59, No. 6, June 15, 2008, pp 762–784
DOI 10.1002/art.23721

SPECIAL ARTICLE

American College of Rheumatology 2008 Recommendations for the Use of Nonbiologic and Biologic Disease-Modifying Antirheumatic Drugs in Rheumatoid Arthritis

KENNETH G. SAAG,[1] GIM GEE TENG,[1] NIVEDITA M. PATKAR,[1] JEREMY ANUNTIYO,[2] CATHERINE FINNEY,[2] JEFFREY R. CURTIS,[1] HAROLD E. PAULUS,[2] AMY MUDANO,[1] MARIA PISU,[1] MARY ELKINS-MELTON,[1] RYAN OUTMAN,[1] JEROAN J. ALLISON,[1] MARIA SUAREZ ALMAZOR,[3] S. LOUIS BRIDGES, JR.,[1] W. WINN CHATHAM,[1] MARC HOCHBERG,[4] CATHERINE MACLEAN,[5] TED MIKULS,[6] LARRY W. MORELAND,[7] JAMES O'DELL,[5] ANTHONY M. TURKIEWICZ,[1] AND DANIEL E. FURST[2]

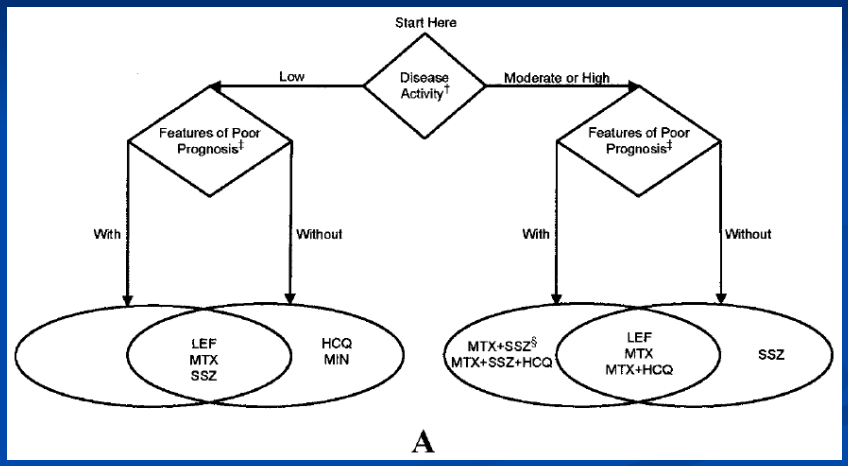
Smolen et al ARD 2010: "ACR has provided therapeutic recommendations for several years. However, its most recent 2008 recommendations are complex and may not fully cover several aspects of drug treatments and therapeutic strategies and goals…."

ACR recommendations:

- Recommendations on indications for the use of non-biologic DMARDs in patients with RA who have never received DMARDs.
- Recommendations on indications for the use of biologic drugs in patients with RA.
- These recommendations do not specifically include the potential role of glucocorticoids or nonsteroidal antiinflammatory drugs in the management of patients with RA.

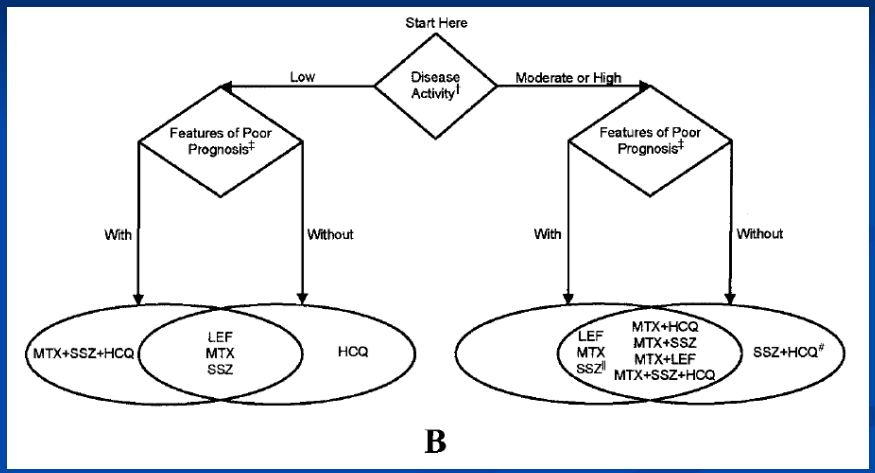
Saag et al. A&R 2008

Treatment algorithm for DMARD naïve patients, disease duration <6 months



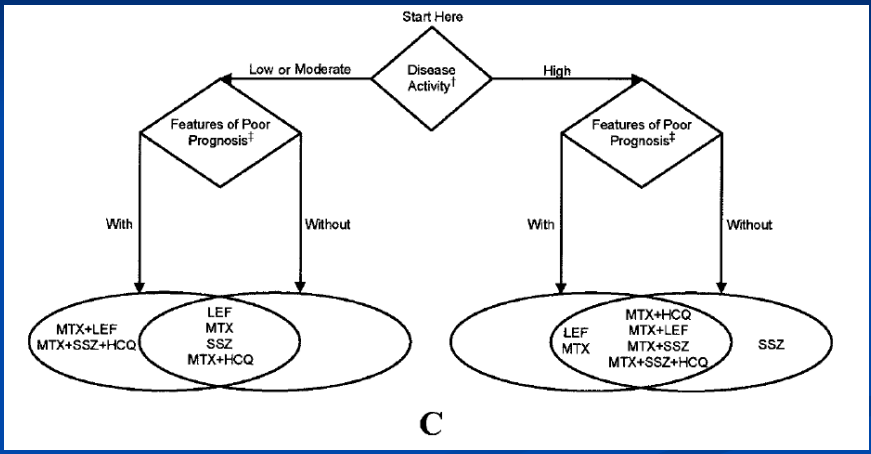
Saag et al. A&R 2008

Treatment algorithm for DMARD naïve patients, disease duration of 6-24 months



Saag et al. A&R 2008

Treatment algorithm for DMARD naïve patients, disease duration >24 months

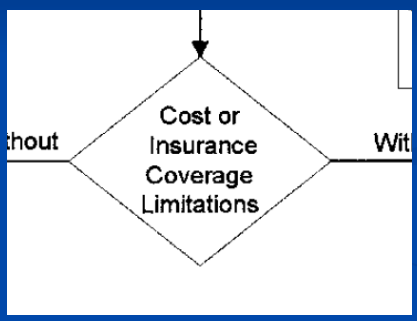


Saag et al. A&R 2008

ACR recommendations in short "TOP":

- **Monotherapy** to patients with
  - Short disease duration
  - Low disease activity
  - Without poor prognostic factors
- **Combination** of DMARDs to most patients with early RA
- **Biologic treatments** after failed mono/combination of DMARDs

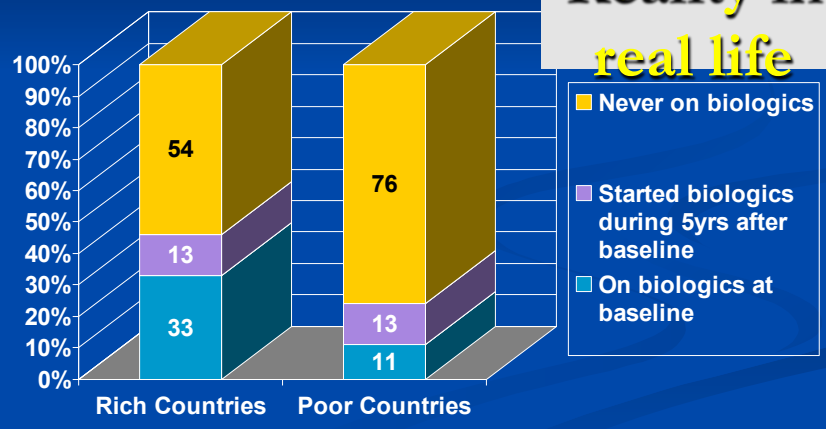
In addition, ACR recommendations consider…



Biologic agents in the QUEST-RA study at baseline and over follow-up of 4-5 years

Proportion of patients on biologic treatments in rich and poor countries

Reality in real life



Sokka et al. EULAR 2010

What patient pays / year:

	MTX 20 + SSZ 2g + HCQ + Pr5	Biol self-admin +MTX	Biol at hospital +MTX
Finland	340 Eur	673 Eur	250 Eur
Sweden	200 Eur	200 Eur	160 Eur
Norway	240 Eur	"Cheap"	240 Eur
Denmark	"cheap"	"cheap"	"cheap"
Other "rich" countries	?	?	?
"Poor" countries	?	?	?

Canadian recommendations 2011

- "The panel recognized that different highly rated guidelines came to different conclusions regarding the same literature. The panel felt that while the body of evidence supporting combination therapy has some limitations, there is sufficient evidence to consider the use of specific DMARD combinations as initial therapy and/or after inadequate response to monotherapy, particularly in the clinical situations highlighted in the
- recommendation."

Different recommendations of treatment for RA, WHY?

- 2008 vs. 2010?
- Different study questions in literature review?
- Different interpretation of literature?
- Personal beliefs of opinion leaders?
- Hidden role of industry?

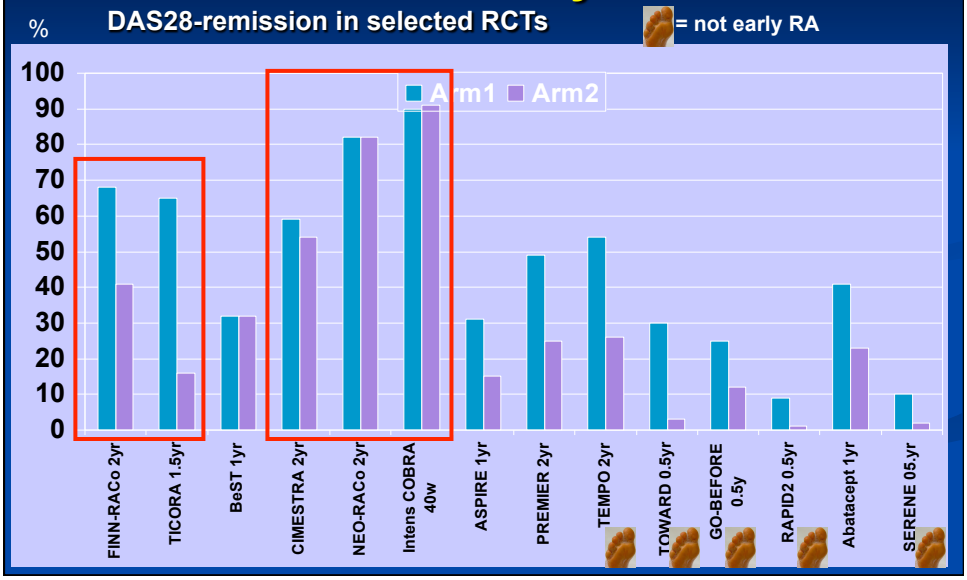
"Multinational evidence-based recommendations to X Y Z"

- Extensive literature review (only a sum of published work not more)
- Expert opinion (golden memories of grey hair professors)
- Delphi process (voting of those who did not leave for lunch yet)

Another approach

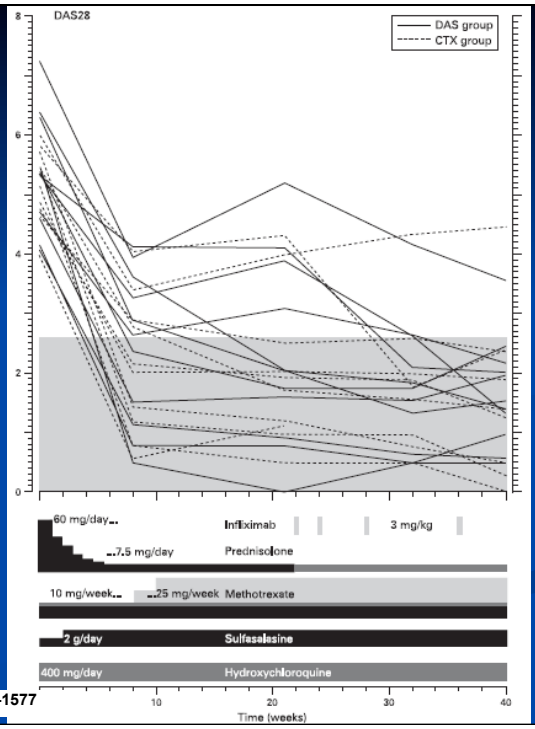
- To identify studies with best results
- To define what is special in these studies
- To use an analytical approach: what is useful and feasible to clinical care in these studies

Another approach: how to get best results in early RA?



40 weeks of intensified COBRA:

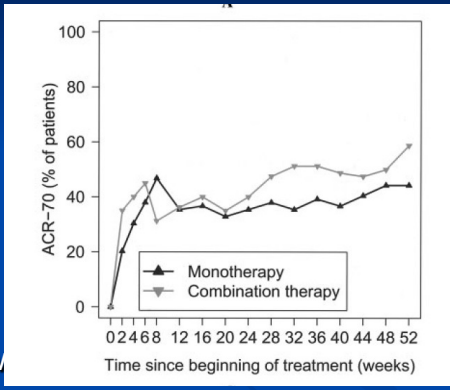
All but 2 patients in DAS28 remission!



van Tuyl L H D et al. Ann Rheum Dis 2008;67:1574-1577

CIMESTRA

- 160 patients with RA<6months 1999-2002
  - MTX7.5+CyA 2.5mg/kg
  - MTX7.5+placebo
  - i.a. betamethasone wk 0,2,4,6,8, every 4 wk
  - After wk8 MTX could be increased 2.5mg every 4w up to 20mg by half year

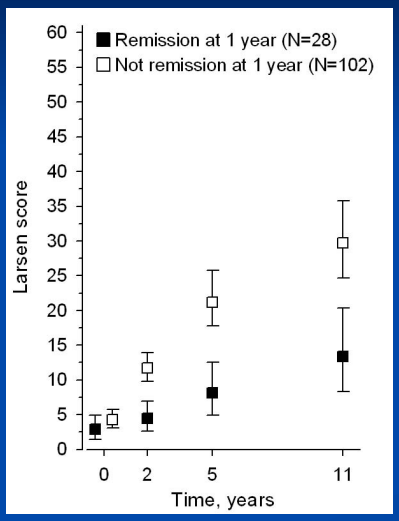


Active treatment strategy includes joint injections!

Hetland et al A&R 2006

It is not only how to start, but: how to FINISH!

FIN-RACo: radiographic outcomes at 11 years

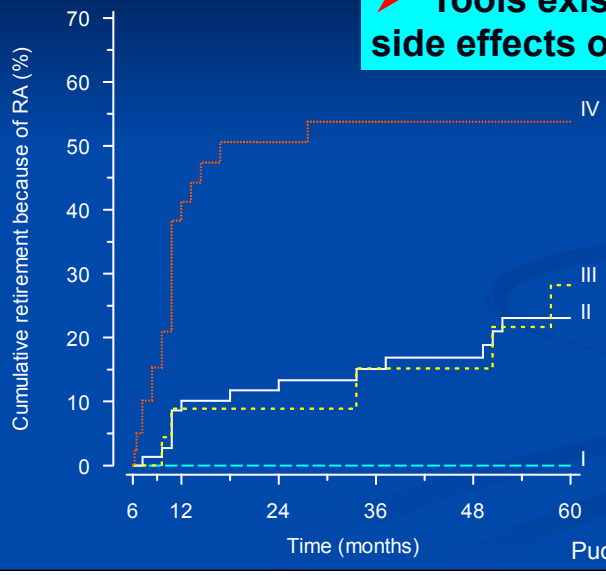


FAST remission at one year provides benefits over 11 years

Rantalaiho et al. ART 2010,12:R112

Early remission prevents work disability

Tools exist to prevent side effects of RA



FIN-RACo - Response at 6 months:

IV: no ACR20

III: ACR20, no ACR50

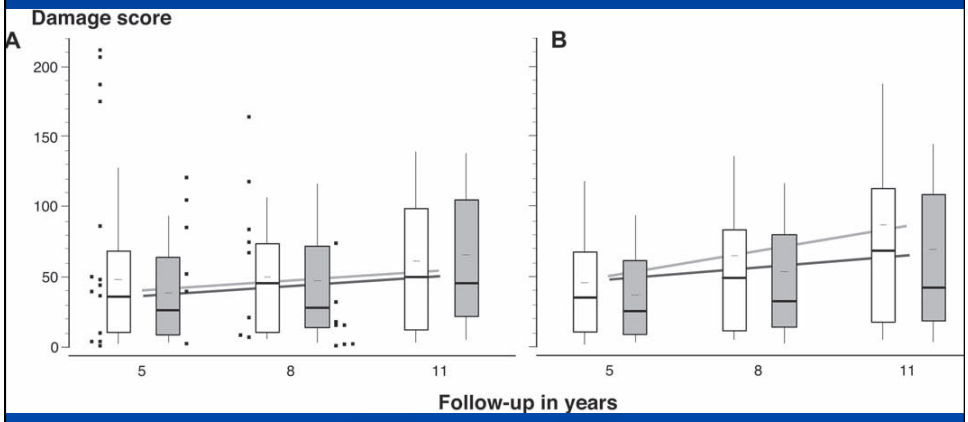
II: ACR50, no remission

I: remission

Puolakka et al. A&R 2005

COBRA: radiographic outcomes at 11 years

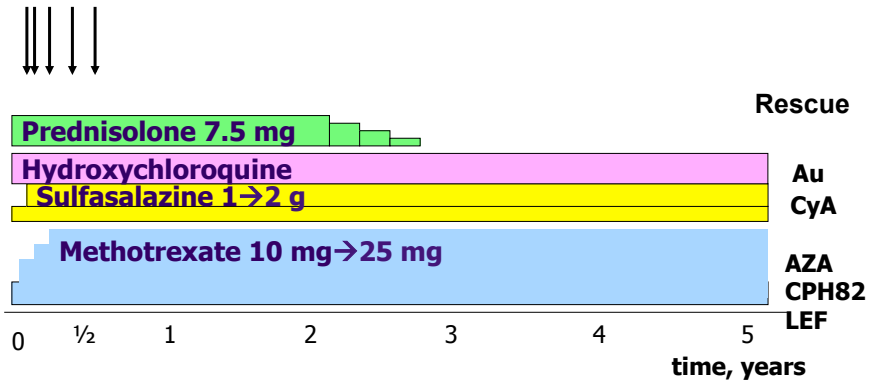
COBRA-intervention (Pred 60→0 + MTX 7,5+ SSZ2g) over ½+ yrs provides benefits over 11yrs



Van Tuyl et al ARD 2010

NEO-RACo Treatment

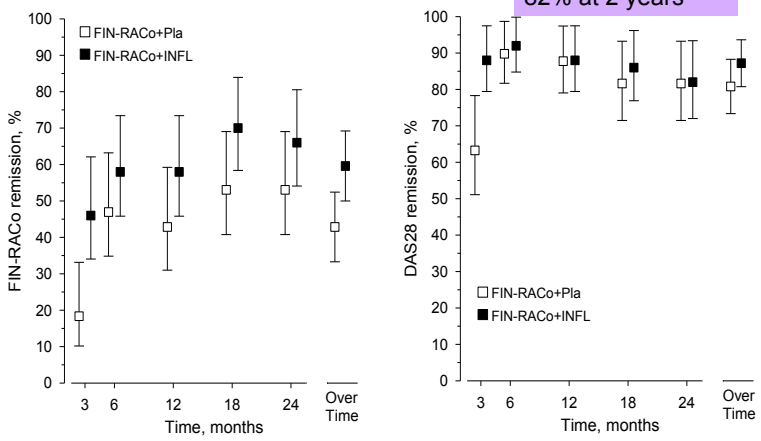
Infliximab 3 mg/kg/placebo weeks 4, 6, 10, 18, 26



Leirisalo-Repo et al: EULAR2008

NEO-RACo – remissions during 2 years

DAS28 remissions: 82% at 2 years



Leirisalo-Repo et al: EULAR2008

2 year results – radiology

	Baseline median (IQR)	At 2-year Change * (mean, 95% CI)
FIN-RACo+PLA	0 (0 , 2)	1.4 (0.8 to 2.2)
FIN-RACo+INF	0 (0 , 3)	-0.2 (-1.1 to 0.4)

* p=0.005

Modified Sharp-van der Heijde

Leirisalo-Repo et al: EULAR2008

NEO-RACo, CIMESTRA vs. usual RCTs What makes the difference?

- Therapy is adjusted according to patient response – ZERO disease activity tolerated vs. usual RCTs: strict protocol
- Injections MUST be used for active joints vs. usual RCTs: avoid injections
- It is possible to achieve DAS remission in >80% of patients –requires treat to target

= extra lessons, not learned from RCTs that were reviewed for official recommendations

Official recommendations should NOT lead clinicians:

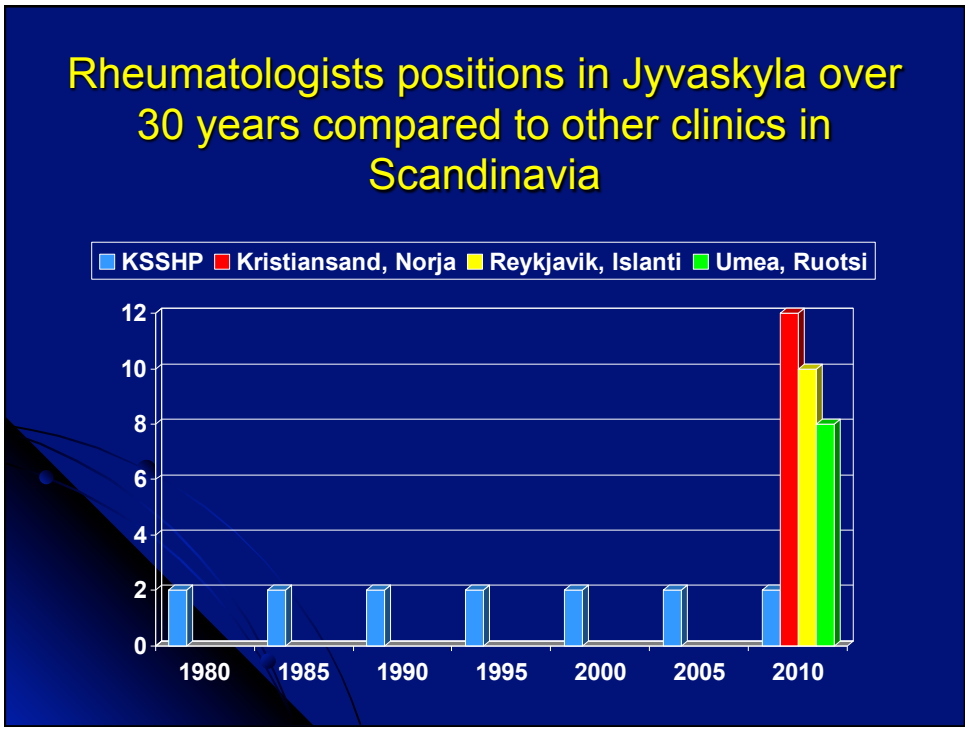
- To blindly follow recommendations
- To rely only on information from clinical trials, meta-analyses or systematic literature reviews – which, and interpretation of which, may exclude highly relevant information
- To ignore trying to assess results of treatments in their own care

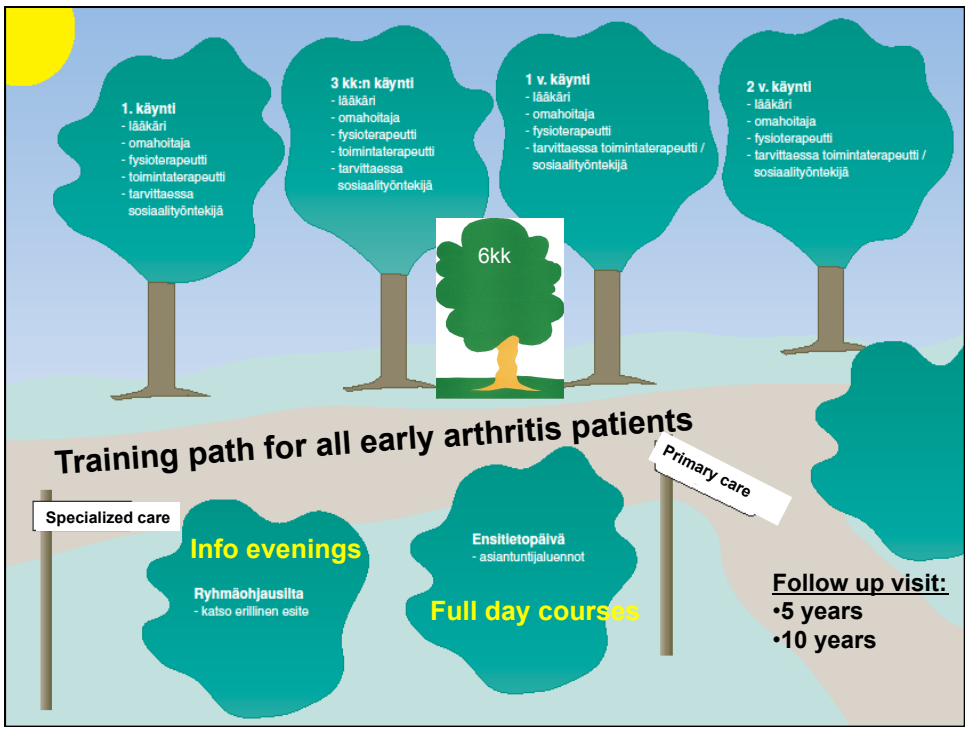
Remaining issues: Escalation of MTX

- 6 guidelines: a starting dose of 5-10mg with a maximum dose of 20-25mg
- 1 recommended a starting does of 10- 15mg with a maximum dose of 20-30mg
- 5 guidelines advised schedule for dose escalation; 2 recommended escalating by 2.5-5mg every 2-6 wks
- 1 recommended escalating by 5mg every 2-4 weeks
- 1 recommended escalating every 6 weeks without specifying the dose increment
- 1 simply recommended rapid dose escalation

Remaining issues: Escalation of MTX

- Canadian Recommendations 2011
  - Dosing of methotrexate should be individualized to the patient
  - Methotrexate should be started PO or SC and titrated to a usual maximum dose of 25 mg per week by rapid dose escalation.
  - In patients with inadequate response or intolerance to oral methotrexate, parenteral administration should be considered
  - The panel agreed with starting with higher doses of MTX with rapid dose escalation, including in certain situations starting directly at target dose.


Rheumatologists positions in Jyvaskyla over 30 years compared to other clinics in Scandinavia
KSSHP
Kristiansand, Norja
Reykjavik, Islanti
Umea, Ruotsi
12
10
8
6
4
2
0
1980
1985
1990
1995
2000
2005
2010


1. käynti
- lääkäri
- omahoitaja
- fysioterapeutti
- toimintaterapeutti
- tarvittaessa sosiaalityöntekijä
3 kk:n käynti
- lääkäri
- omahoitaja
- fysioterapeutti
- toimintaterapeutti
- tarvittaessa sosiaalityöntekijä
1 v. käynti
- lääkäri
- omahoitaja
- fysioterapeutti
- tarvittaessa toimintaterapeutti / sosiaalityöntekijä
2 v. käynti
- lääkäri
- omahoitaja
- fysioterapeutti
- tarvittaessa toimintaterapeutti / sosiaalityöntekijä
6kk
Training path for all early arthritis patients
Primary care
Specialized care
Info evenings
Ryhmäohjausilta
- katso erillinen esite
Ensitietopäivä
- asiantuntijaluennot
Full day courses
Follow up visit:
•5 years
•10 years

Patient self report every visit

Date	EXAMPLE OF A PATIENT FLOW SHEET
ID	
Age, Gender	44, Female
Work status	Full-time job
Diagnosis	Rheumatoid Arthritis
	- Symptoms: Polyarticular 7.2010
	- Clinical diagnosis date: 9.2010
Highest RF (IgM)	Positive (760) 29.09.2010
Highest aCCP	Positive (128) 29.09.2010
Erosions	Negative 29.09.2010
DMARD (now)	Sulfasalazine 9.2010
	- 2 000,00 mg Peroral Every day
	Prednisolone 9.2010
	- 5,00 mg Peroral Every day
	Methotrexate 9.2010
	- 25,00 mg Subcutaneous Once a week
	Hydroxychloroquine 9.2010
	- 300,00 mg Peroral Every day
Comorbidity	Arterial hypertension 9.2010
Data confirmed	29.09.2010, sokkat (Sokka, Tuulikki)

Latest score

Date				29.09.2010	12.01.2011
Pain				35	0
Fatigue				38	0
Patient global				23	0
Morning stiffness				1,50	0,08
Rheumatic activity				47	0
Physical exercise				1-2/month	1-2/week
M-HAQ (0-3)				0,50	0,00
MDHAQ (FN) (0-3)				1,4	0,0
MDHAQ (PS) (0-3)				1,00	0,00
HAQ (0-3)				1,00	0,00
Raw HAQ (0-24)				7	0
Inv. global				80	0
ESR				93	27
CRP				59	10
TJC 28/32				7/9	0/0
SJC 28/32				1/1	0/0
TJC 46				16	0
SJC 46				1	0
DAS28 (4)				5,3	2,3
DAS28 (3)				5,5	2,7
DAS28-CRP(4)				4,5	1,8


”light through the tunnel”
thank you