Methotrexate, glucocorticoids and DMARDs in the treatment of rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis in the next decade

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Methotrexate as the "anchor drug" for the treatment of early rheumatoid arthritis.

T Pincus, Y Yazici, T Sokka,
D Aletaha, JS Smolen

Clin Exp Rheumatol 21:S179-S185, 2003.

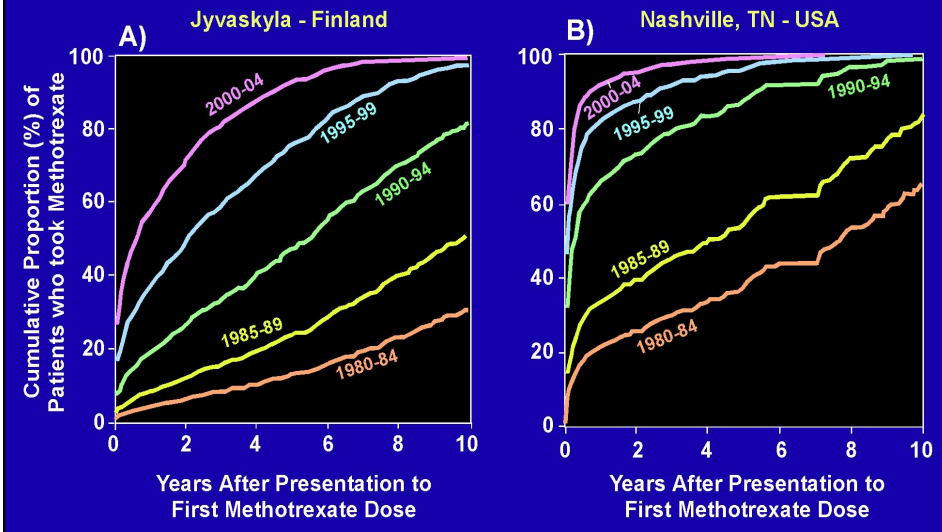
QUEST-RA From January 2005 to December 2008: 7568 patients from 83 clinics in 30 countries

QUEST-RA: Medications in 4,363 patients in 15 countries

Medication	All 4,363 patients in 15 countries	301 Danish patients
Methotrexate Ever	83%	85%
Leflunomide Ever	21%	11%
Sulfasalazine Ever	43%	64%
Biological Agent Ever	23%	23%

Sokka , Kautiainen, Toloza, Mäkinen, Verstappen, Lund Hetland, et al QUEST-RA: Ann Rheum Dis 66:1491-1496, 2007.

Methotrexate in RA Care: 1980-2005 Jyvaskyla, Finland & Nashville, TN



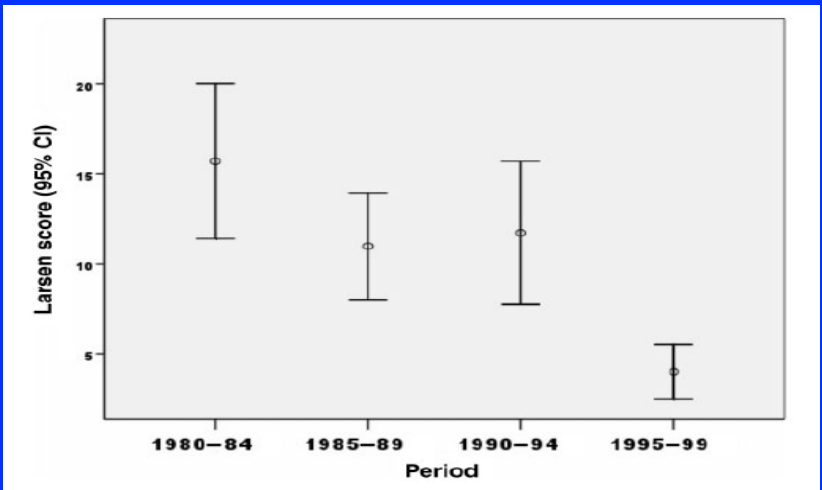
Sokka and Pincus. *Rheumatology* (Oxford). 2008:47:1543-1547

First DMARD at presentation per 5-year period since 1980

	1980-84	1985-89	1990-94	1995-99	2000-04
Jyväskylä, Finland					
Number of patients	219	305	363	508	497
I.M. Gold, *n* (%)	139 (64%)	171 (56%)	51 (14%)	12 (2%)	1 (<1%)
HCQ, *n* (%)	72 (33%)	35 (12%)	29 (8%)	44 (9%)	70 (14%)
SSZ, *n* (%)	2 (1%)	92 (30%)	257 (71%)	366 (72%)	257 (52%)
MTX, *n* (%)	0	0	15 (4%)	77 (15%)	154 (31%)
Nashville, TN, USA					
Number of patients	216	185	141	93	103
I.M. Gold, *n* (%)	59 (27%)	18 (9%)	5 (4%)	3 (2%)	1 (1%)
HCQ, *n* (%)	23 (11%)	12 (7%)	35 (18%)	10 (11%)	4 (4%)
MTX, *n* (%)	22 (10%)	48 (26%)	80 (57%)	66 (71%)	80 (78%)

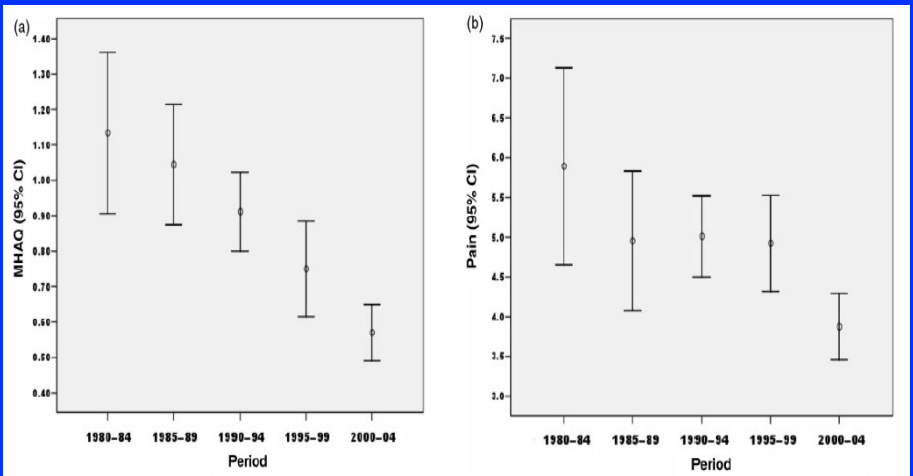
Sokka T, Pincus T. *Rheumatology (Oxford)* 2008; 47:1543-7

Larsen radiographic scores in 295 patients in Jyväskylä, Finland, 5 years after presentation (dx), according to the period of presentation



Sokka T, Pincus T. *Rheumatology (Oxford)* 2008; 47:1543-7

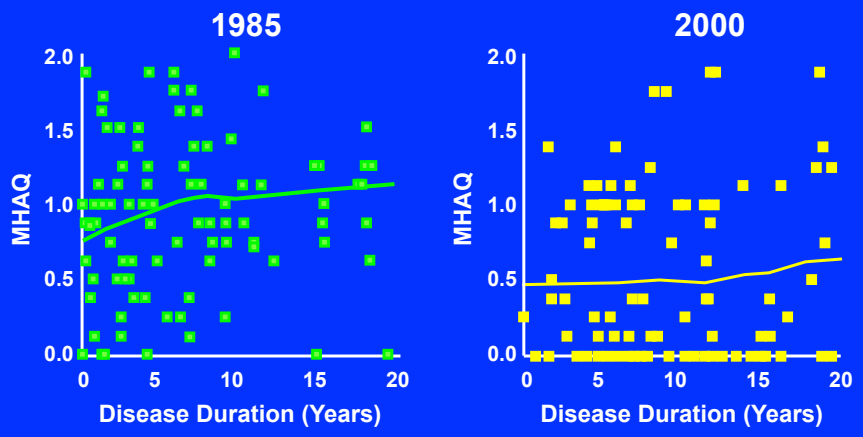
Patient functional status according to (a) MHAQ physical function score and (b) pain, in 596 patients in Nashville, TN, USA at final visit, according to the period when last visit occurred



Sokka T, Pincus T. *Rheumatology (Oxford)* 2008; 47:1543-7

Cross-Sectional Data: All RA Patients seen by TP in 1985 (n=125) and in 2000 (n=150):

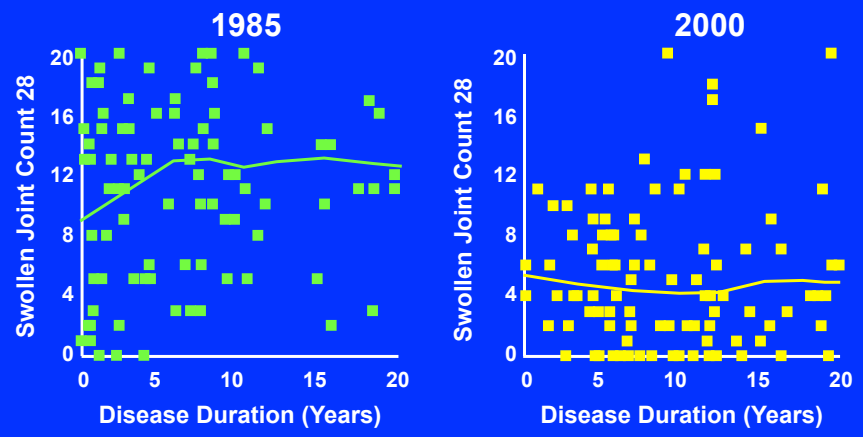
Multidimensional Health Assessment Questionnaire (MDHAQ) scores



Pincus, Sokka, Kautiainen, Arthritis Rheum 52:1009, 2005

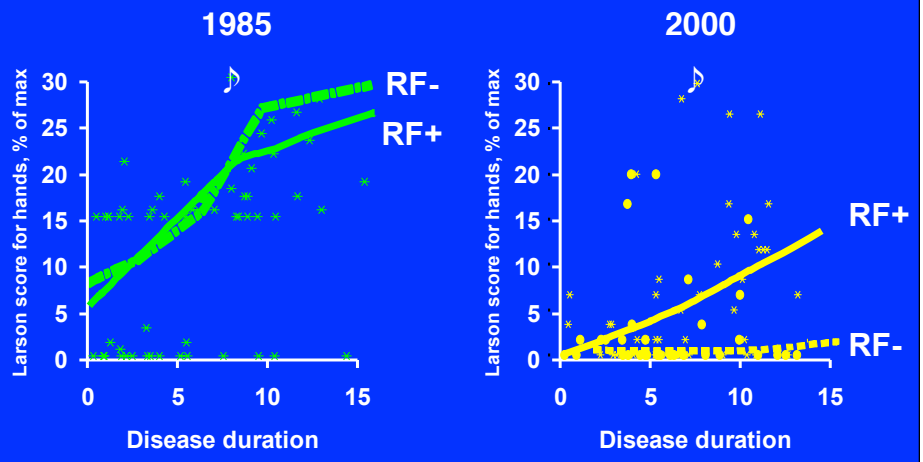
Cross-Sectional Data: All RA Patients seen by TP in 1985 (n=125) and in 2000 (n=150):

Swollen Joint Count Scores



Pincus, Sokka, Kautiainen, Arthritis Rheum 52:1009, 2005

Cross-Sectional Data: All RA Patients seen by TP in 1985 (n=125) and in 2000 (n=150): : Larsen X-Ray score,% of Maximum



Pincus, Sokka, Kautiainen, Arthritis Rheum 52:1009, 2005

Better status of patients with rheumatoid arthritis in 2005 versus 1980

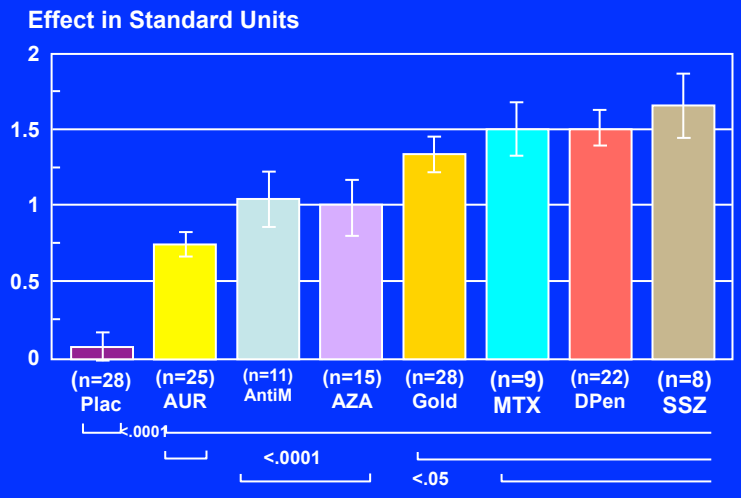
1. Weekly low-dose methotrexate
2. Early treatment
3. Treat-to-target –quantitative monitoring
4. Low-dose Prednisone/prednisolone
5. Biological agents

The comparative efficacy and toxicity of second-line drugs in rheumatoid arthritis: results of two metaanalyses

Felson DT, Anderson JJ, Meenan RF

Arthritis Rheum 33:1449-1461, 1990

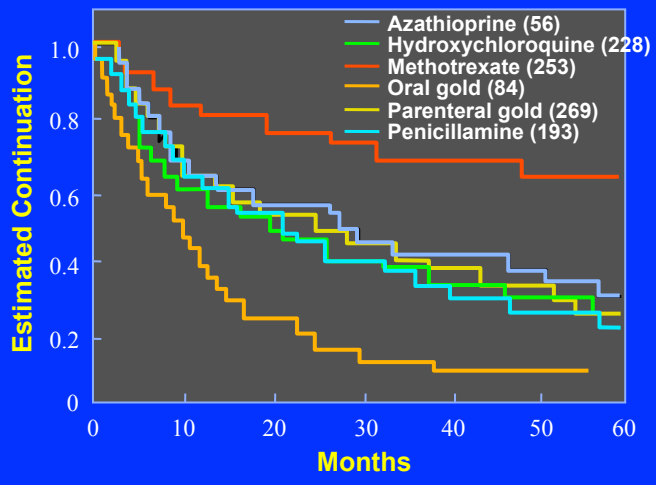
Standard Composite Treatment Effect*



*Composite of grip strength (adjusted for disease duration and trial length), tender joint count (adjusted for initial TJC and blinding and ESR

Felson, Anderson, Meenan. *Arthrit Rheum.* 1990;33:1449.

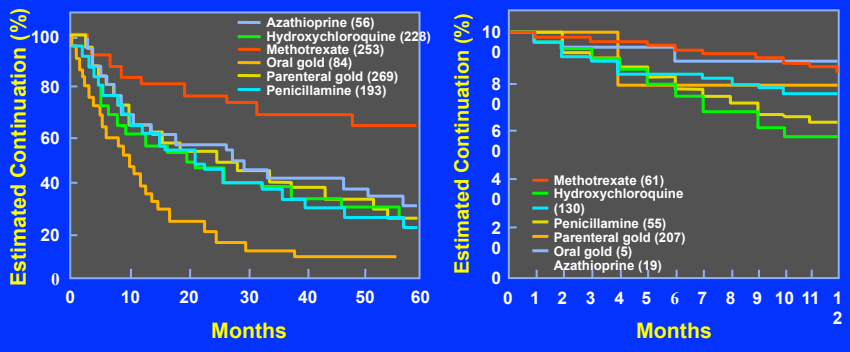
Estimated Continuation of Courses of 2nd Line Therapies Over 60 Months in RA Patients



Pincus, Marcum, Callahan. *J Rheumatol.* 1992;19:1885.

Estimated Continuation of Courses of 2nd-Line Therapy

All Courses Over 60 Months Initial Course Over 12 Months



Pincus, Marcum, Callahan. *J Rheumatol.* 1992;19:1885.

Randomized Controlled Clinical Trials

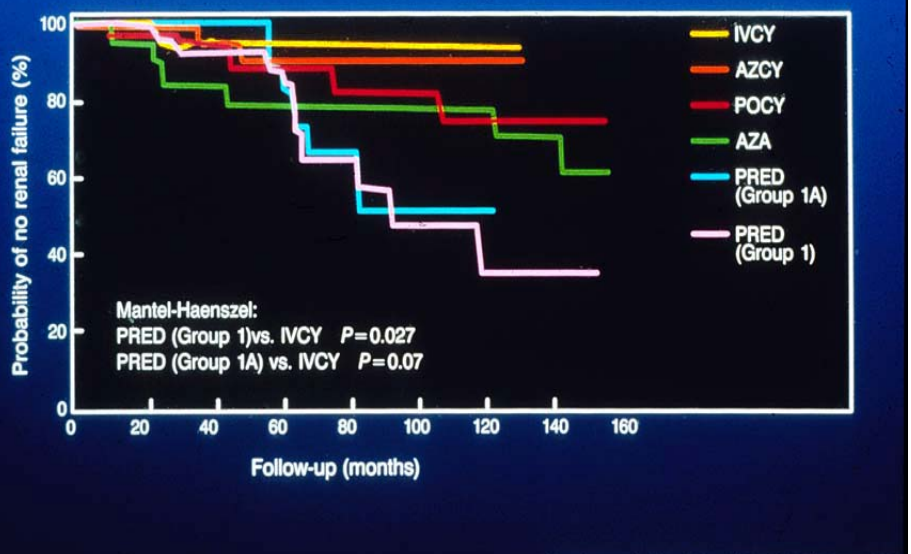
1. Optimal method to analyze efficacy and safety of any therapy
2. Mimics lab experiment with control group
3. Foundation of "evidence-based medicine"
4. Required by FDA to market new therapy
5. Nonetheless, many limitations, particularly in chronic diseases
6. Rarely informs clinician how to treat an individual patient

Some Pragmatic Limitations of Randomized Controlled Clinical Trials in Chronic Diseases

J Clin Epidemiol 41:1037,1988; Arthritis Rheum 48:313, 2003

1. Relatively short observation period
2. Inclusion and exclusion criteria – most patients ineligible in most trials
3. Surrogate markers often suboptimal for actual outcomes
4. Inflexible dosage schedules and concomitant drug therapies
5. Variables other than randomization (eg, socioeconomic status) affect outcome
6. Statistically significant results may be clinically unimportant, and vice versa

THERAPY OF LUPUS NEPHRITIS: CONTROLLED TRIAL OF PREDNISONE & CYTOTOXIC DRUGS: RENAL SURVIVAL



Austin et al. New Eng J Med; 314:614, 1986

Some Intrinsic Limitations of Randomized Controlled Clinical Trials in Chronic Diseases

J Clin Epidemiol 41:1037,1988; Arthritis Rheum 48:313, 2003

1. Design of a clinical trial influences results - control group does not eliminate bias
2. Data from clinical trials reported in groups - individual variation generally ignored
3. Balance of efficacy versus adverse effects not standardized - individual views of risks vs benefits differ widely among individuals
4. Format of a clinical trial compromises the "placebo effect" by not informing patients that they may receive the "best" therapy.

Types of questions that cannot be answered by "evidence-based medicine" from randomized controlled clinical trials

1. Which medication do I give to an individual patient?
2. When do I begin or stop Medication A (or B or C) in a particular individual patient?
3. Which laboratory test or imaging study should I order to make a diagnosis or monitor safety?

2008 "systematic analysis" in Ann Int Med suggests that efficacy of Mtx is similar to other DMARDs

There is "moderate evidence that sulfasalazine and leflunomide are equivalent to methotrexate in efficacy," with "no obvious major differences in adverse events and discontinuation rates" among these 3 DMARDs

– Donahue KE, Gartlehner G, Jonas BE et al. *Ann Intern Med* 2008; 148:124-34

QUEST-RA: Medications in 4,363 patients in 15 countries

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Methotrexate Ever	83%	85%
Leflunomide Ever	21%	11%
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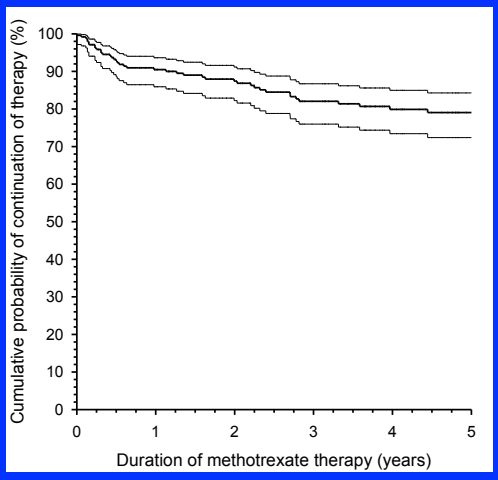
Sokka , Kautiainen, Toloza, Mäkinen, Verstappen, Lund Hetland, et al QUEST-RA: Ann Rheum Dis 66:1491-1496, 2007.

The series of consecutive cases as a device for assessing outcomes of intervention

LE Moses

New Engl J Med 1984;311:705–710

Methotrexate continuation in TP clinic standard care: 1990–2003



Yazici Y, Sokka T, Kautiainen H, Swearingen C, Kulman I, Pincus T
Ann Rheum Dis 2005;64:207–211.

Quantitative Clinical Rheumatology

N-of-1 Trial of Low-dose Methotrexate and/or Prednisolone in Lieu of Anti-CCP, MRI, or Ultrasound, as First Option in Suspected Rheumatoid Arthritis?

T Pincus, TWJ Huizinga, Y Yazici

J Rheumatol. 34:250-252, 2007

Is weekly low-dose methotrexate one of the safest medications available in clinical medicine, far safer than (almost) all antibiotics, anti-depressants, statins, etc.?

3 organic molecules which may be of great benefit in small doses, but severely toxic in high doses

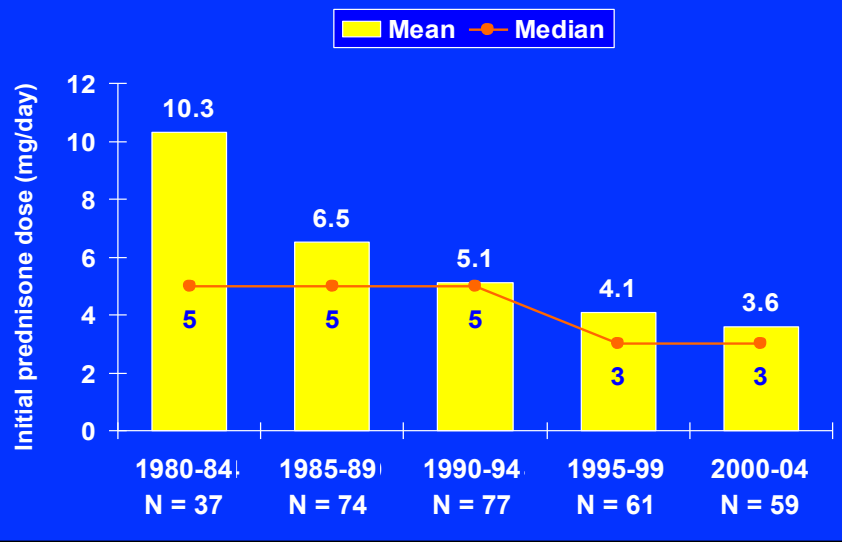
1. Methotrexate
2. Alcohol
3. Prednisone/prednisolone

QUEST-RA: Medications in 4,363 patients in 15 countries

Medication	All 4,363 patients in 15 countries	301 Danish patients
Prednisone Ever	66%	43%
Methotrexate Ever	83%	85%
Leflunomide Ever	21%	11%
Sulfasalazine Ever	43%	64%
Biological Agent Ever	23%	23%

Sokka , Kautiainen, Toloza, Mäkinen, Verstappen, Lund Hetland, et al QUEST-RA: Ann Rheum Dis 66:1491-1496, 2007.

Mean and median initial prednisone dose in 308 patients with rheumatoid arthritis (RA) seen from 1980 through 2004, computed in 5-year periods



Initial Prednisone Dose in 308 Patients with RA: 1980-2004

Year first seen	N	Mean (median) initial dose: mg/d	Percentage of patients taking initial dose: mg/d		
			<5	=5	>5
1980-1984	37	10.3 (5)	0	51%	49%
1985-1989	74	6.5 (5)	4%	80%	16%
1990-1994	77	5.1 (5)	23%	70%	7%
1995-1999	61	4.1 (3)	67%	26%	7%
2000-2004	59	3.6 (3)	86%	10%	3%
TOTAL	308	5.6 (5)	37%	50%	13%

Percent change (Δ) over 12 months in MDHAQ-FN (0-10) in 308 patients treated with prednisone 1980-2004 ("+" indicates improvement and "-" worsening)

Year First Seen	N	Initial dose <5 mg/d		Initial dose ≥5 mg/d	
		Baseline FN	12-mo Δ	Baseline FN	12-mo Δ
1980-84	37	None	--	4.1	+33%
1985-89	74	1.4	-5%	3.3	+45%
1990-94	77	1.7	+26%	3.2	+44%
1995-99	61	2.7	+33%	3.9	+27%
2000-04	59	2.6	+37%	4.3	+25%
TOTAL	308	2.4	+34%	3.5	+40%

Editorial: Are long-term very low doses of prednisone for patients with rheumatoid arthritis as helpful as high doses are harmful?

T Pincus, T Sokka, CM Stein

Ann Internal Med 136:76-78, 2002

Clinical Trials Documenting Value of Low-dose Prednisone in Rheumatoid Arthritis

1st author	Reference	Dose/day	Outcome
Harris	*J Rheumatol* 1983; 10:713	5mg	FN, X-Ray
Kirwan	*NEJM* 1995; 333:142	7.5 mg	X-ray
Boers	Lancet 1997; 350: 309	60>5 mg	ACR crit X-ray
van Everdingen	*Ann Intern Med* 2002; 136:1	10mg	TJC,X-ray
Svensson	*Arth Rheum* 2005; 52:3360	7.5mg	X-ray
Wassenberg	*Arth Rheum* 2005; 52:3371	5mg	X-ray
Pincus	*Ann Rheum Dis* 2009; 68:1715	3mg	Withdrawal
Todoerti	Ann NY Acad Sci2010;139:1193	12.5>7.5mg	Remission
Malysheva	J Rheumatol. 2008, 35:979	7.5	X-ray

Efficacy of prednisone 1-4 mg/day in patients with rheumatoid arthritis: a randomised, double-blind, placebo controlled withdrawal clinical trial

Pincus T, Swearingen CJ, Luta G, Sokka T

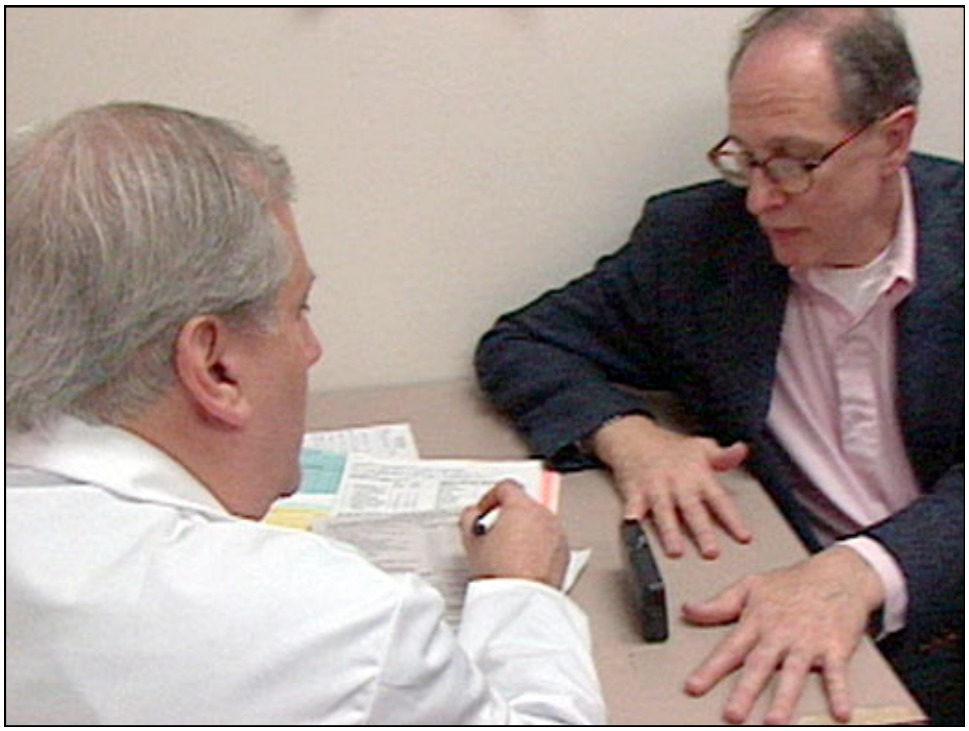
Ann Rheum Dis 2009; 68:1715-20

Clinical trial results in 31 participants who were randomized to prednisone or placebo, following gradual withdrawal of prednisone, according to baseline prednisone dose

Study group	Clinical trial results	Baseline prednisone dose				Total
		1 mg	2 mg	3 mg	4 mg	
Prednisone	Number randomized	1	2	10	2	15
	Withdrew – lack of efficacy	0	0	3	0	3*
	Completed trial	1	2	6	1	10*
	Withdrew – administrative	0	0	1	1	2
Placebo	Number randomized	0	1	12	3	16
	Withdrew – lack of efficacy	0	1	9	1	11*
	Completed trial	0	0	2	2	4*
	Withdrew – administrative	0	0	1	0	1
TOTAL		1	3	22	5	31

*For 28 participants who either completed the trial or withdrew because of lack of efficacy, p = 0.021
For all 31 randomized participants, p= 0.032 by Fisher's exact test (prednisone vs placebo).


Concerned about the treatment of RA during pregnancy?



MDHAQ/RAPID3:
04 Nov 2003
3 RA Core Data Set scores
FN (0–10) = 2.7
PN (0–10) = 9.5
PTGL (0–10) = 9.0

RAPID3 (0–30) = 21.2

Severity:
12.1-30 = High
6.1-12 = Moderate
3.1-6 = Low
0-3 = Near remission

Multi-Dimensional Health Assessment Questionnaire (R808-NP2)

This questionnaire includes information not available from blood tests, X-rays, or any source other than you. Please try to answer each question, even if you do not think it is related to you at this time. Try to complete as much as you can yourself, but if you need help, please ask. There are no right or wrong answers. Please answer exactly as you think or feel. Thank you.

1. Please check (√) the ONE best answer for your abilities at this time:

OVER THE LAST WEEK, were you able to:	Without **ANY** Difficulty	With **SOME** Difficulty	With **MUCH** Difficulty	**UNABLE** To Do
a. Dress yourself, including tying shoelaces and doing buttons?	0	√ 1	2	3
b. Get in and out of bed?	0	√ 1	2	3
c. Lift a full cup or glass to your mouth?	√ 0	1	2	3
d. Walk outdoors on flat ground?	√ 0	1	2	3
e. Wash and dry your entire body?	√ 0	1	2	3
f. Bend down to pick up clothing from the floor?	0	1	√ 2	3
g. Turn regular faucets on and off?	√ 0	1	2	3
h. Get in and out of a car, bus, train, or airplane?	0	√ 1	2	3
i. Walk two miles or three kilometers, if you wish?	0	√ 1	2	3
j. Participate in recreational activities and sports as you would like, if you wish?	0	1	√ 2	3
k. Get a good night's sleep?	0	√ 1.1	2.2	3.3
l. Deal with feelings of anxiety or being nervous?	0	1.1	√ 2.2	3.3
m. Deal with feelings of depression or feeling blue?	0	√ 1.1	2.2	3.3

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1.a. **FN** (0-10): **2.7**

1=0.3 16=5.3
2=0.7 17=5.7
3=1.0 18=6.0
4=1.3 19=6.3
5=1.7 20=6.7
6=2.0 21=7.0
7=2.3 22=7.3
8=2.7 23=7.7
9=3.0 24=8.0
10=3.3 25=8.3
11=3.7 26=8.7
12=4.0 27=9.0
13=4.3 28=9.3
14=4.7 29=9.7
15=5.0 30=10

2.**PN** (0-10): **9.5**

4.**PTGL** (0-10): **9.0**

RAPID 3 (0-30): **21.2**

Cat:
HS = >12
MS = 6.1-12
LS = 3.1-6
R = ≤3

2. How much pain have you had because of your condition OVER THE PAST WEEK? Please indicate below how severe your pain has been:

NO PAIN ○ 0 ○ 0.5 ○ 1.0 ○ 1.5 ○ 2.0 ○ 2.5 ○ 3.0 ○ 3.5 ○ 4.0 ○ 4.5 ○ 5.0 ○ 5.5 ○ 6.0 ○ 6.5 ○ 7.0 ○ 7.5 ○ 8.0 ○ 8.5 ○ 9.0 ● 9.5 ○ 10 PAIN AS BAD AS IT COULD BE

3. Please place a check (√) in the appropriate spot to indicate the amount of pain you are having today in each of the joint areas listed below:

	None	Mild	Moderate	Severe		None	Mild	Moderate	Severe
a. LEFT FINGERS	□ 0	□ 1	√ 2	□ 3	i. RIGHT FINGERS	□ 0	□ 1	□ 2	√ 3
b. LEFT WRIST	□ 0	□ 1	√ 2	□ 3	j. RIGHT WRIST	□ 0	□ 1	□ 2	√ 3
c. LEFT ELBOW	□ 0	√ 1	□ 2	□ 3	k. RIGHT ELBOW	□ 0	√ 1	□ 2	□ 3
d. LEFT SHOULDER	√ 0	□ 1	□ 2	□ 3	l. RIGHT SHOULDER	√ 0	□ 1	□ 2	□ 3
e. LEFT HIP	√ 0	□ 1	□ 2	□ 3	m. RIGHT HIP	√ 0	□ 1	□ 2	□ 3
f. LEFT KNEE	□ 0	√ 1	□ 2	□ 3	n. RIGHT KNEE	□ 0	□ 1	√ 2	□ 3
g. LEFT ANKLE	√ 0	□ 1	□ 2	□ 3	o. RIGHT ANKLE	□ 0	√ 1	□ 2	□ 3
h. LEFT TOES	□ 0	√ 1	□ 2	□ 3	p. RIGHT TOES	□ 0	□ 1	√ 2	□ 3
q. NECK	□ 0	□ 1	√ 2	□ 3	r. BACK	□ 0	√ 1	□ 2	□ 3

4. Considering all the ways in which illness and health conditions may affect you at this time, please indicate below how you are doing:

VERY WELL ○ 0 ○ 0.5 ○ 1.0 ○ 1.5 ○ 2.0 ○ 2.5 ○ 3.0 ○ 3.5 ○ 4.0 ○ 4.5 ○ 5.0 ○ 5.5 ○ 6.0 ○ 6.5 ○ 7.0 ○ 7.5 ○ 8.0 ○ 8.5 ○ 9.0 ● 9.5 ○ 10 VERY POORLY

Please turn to the other side

MDHAQ/RAPID3: 13 Jan 2004

3 RA Core Data Set scores

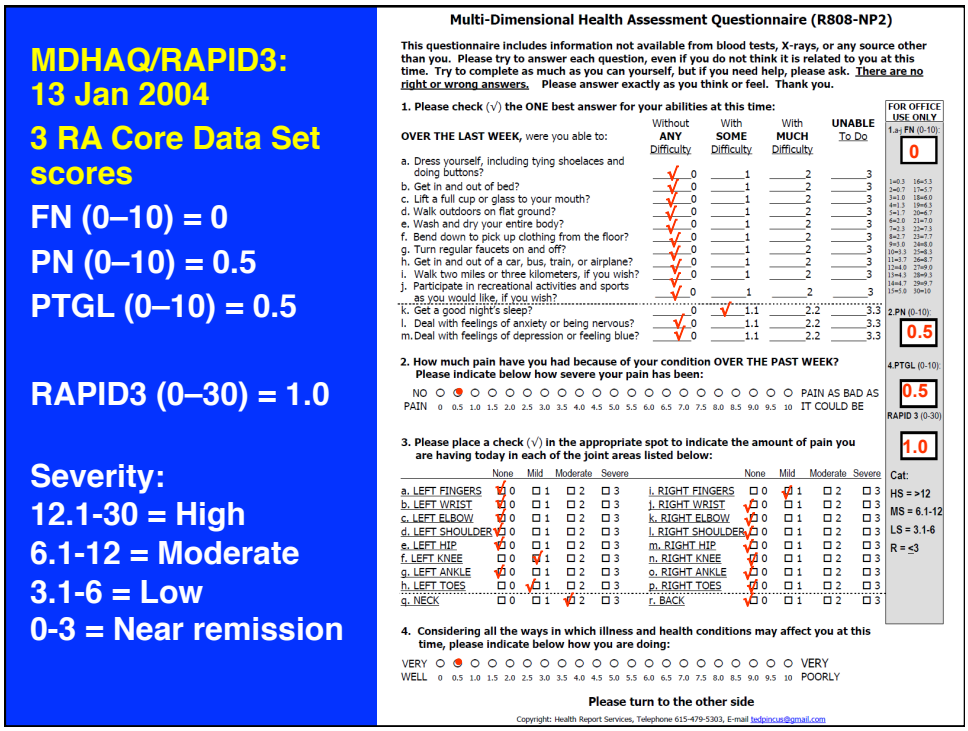
FN (0–10) = 0

PN (0–10) = 0.5

PTGL (0–10) = 0.5

RAPID3 (0–30) = 1.0

Severity:
12.1-30 = High
6.1-12 = Moderate
3.1-6 = Low
0-3 = Near remission



Multi-Dimensional Health Assessment Questionnaire (R808-NP2)

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1. Please check (√) the ONE best answer for your abilities at this time:

OVER THE LAST WEEK, were you able to:	Without ANY Difficulty	With SOME Difficulty	With MUCH Difficulty	UNABLE To Do
a. Dress yourself, including tying shoelaces and doing buttons?	√ 0	1	2	3
b. Get in and out of bed?	√ 0	1	2	3
c. Lift a full cup or glass to your mouth?	√ 0	1	2	3
d. Walk outdoors on flat ground?	√ 0	1	2	3
e. Wash and dry your entire body?	√ 0	1	2	3
f. Bend down to pick up clothing from the floor?	√ 0	1	2	3
g. Turn regular faucets on and off?	√ 0	1	2	3
h. Get in and out of a car, bus, train, or airplane?	√ 0	1	2	3
i. Walk two miles or three kilometers, if you wish?	√ 0	1	2	3
j. Participate in recreational activities and sports as you would like, if you wish?	√ 0	1	2	3
k. Get a good night's sleep?	0	√ 1.1	2.2	3.3
l. Deal with feelings of anxiety or being nervous?	√ 0	1.1	2.2	3.3
m. Deal with feelings of depression or feeling blue?	√ 0	1.1	2.2	3.3

FOR OFFICE USE ONLY
1.FN (0-10): 0
2.PN (0-10): 0.5
4.PTGL (0-10): 0.5
RAPID 3 (0-30): 1.0
Cat: HS = >12 MS = 6.1-12 LS = 3.1-6 R = ≤3

2. How much pain have you had because of your condition OVER THE PAST WEEK? Please indicate below how severe your pain has been:

NO PAIN ○ ● ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ PAIN AS BAD AS IT COULD BE
0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0 8.5 9.0 9.5 10

3. Please place a check (√) in the appropriate spot to indicate the amount of pain you are having today in each of the joint areas listed below:

	None	Mild	Moderate	Severe		None	Mild	Moderate	Severe
a. LEFT FINGERS	√ 0	1	2	3	i. RIGHT FINGERS	0	√ 1	2	3
b. LEFT WRIST	√ 0	1	2	3	j. RIGHT WRIST	√ 0	1	2	3
c. LEFT ELBOW	√ 0	1	2	3	k. RIGHT ELBOW	√ 0	1	2	3
d. LEFT SHOULDER	√ 0	1	2	3	l. RIGHT SHOULDER	√ 0	1	2	3
e. LEFT HIP	√ 0	1	2	3	m. RIGHT HIP	√ 0	1	2	3
f. LEFT KNEE	0	√ 1	2	3	n. RIGHT KNEE	√ 0	1	2	3
g. LEFT ANKLE	√ 0	1	2	3	o. RIGHT ANKLE	√ 0	1	2	3
h. LEFT TOES	0	√ 1	2	3	p. RIGHT TOES	√ 0	1	2	3
q. NECK	0	1	√ 2	3	r. BACK	√ 0	1	2	3

4. Considering all the ways in which illness and health conditions may affect you at this time, please indicate below how you are doing:

VERY WELL ○ ● ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ VERY POORLY
0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0 8.5 9.0 9.5 10

Please turn to the other side

Visit 6: 8 Feb 2005

Visit date	4No03	13Ja04	20Ap04	28Se04	28De04	8Fe05
Q-Function (0–10)	2.7	0	0.3	0	0	0
Q-Pain (0–10)	9.5	0.5	0.0	0.5	6.0	0.0
Q-Global (0–10)	9.0	0.5	0.5	1.0	5.5	0.5
RAPID3 (0–30)	21.2	1.0	0.8	1.5	11.5	0.5
L-ESR	43	8	13	10	14	14
T-Prednisone	N3qd	3qd	3qd	3qd	3qd	3qd
T-Methotrexate	N10qw	C20qw	20qw	15qw	C25qw	C15qw
T-Folic acid	N1qd	1qd	1qd	1qd	1qd	1qd
T-acetamnphn/codn	30tid	30tid	D/C			
T-Naproxen	880q6h	440bid	440bid	440bid	440bid	D/C
T-Adalimumab					N40qow	40qow

N=new drug, C=change in dose, T=taper, D/C=discontinue

Editorial

Quantitative Clinical Rheumatology: "Keep It Simple, Stupid": MDHAQ Function, Pain, Global, and RAPID3 Quantitative Scores to Improve and Document the Quality of Rheumatologic Care

"The KISS principle (acronym for "Keep It Simple, Stupid") states that design simplicity should be a key goal and unnecessary complexity avoided.... Extra features are not needed; an approach that seems "too easy to be true" is in fact the best way."
— Wikipedia (http://en.wikipedia.org)

T Pincus, T Sokka

J Rheumatol. 36:1099-1100, 2009

Physician Form: Quantitative Assessment Scales for Global status, Inflammation, Damage, Neither, prognosis with and without therapy

a. MD GLOBAL ASSESSMENT today:	EXCELLENT	○ 0	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6	○ 7	○ 8	○ 9	○ 10	VERY POOR
b. CHANGE since last visit: (or over last month for new patients)	MUCH BETTER	○ 0	○ 1	○ 2	○ 3	○ 4	○ SAME	○ 6	○ 7	○ 8	○ 9	○ 10	MUCH WORSE
c. Degree of inflammation EVER:	NONE	○ 0	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6	○ 7	○ 8	○ 9	○ 10	HIGHEST
d. Degree of inflammation TODAY:	NONE	○ 0	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6	○ 7	○ 8	○ 9	○ 10	HIGHEST
e. Degree of joint/organ damage:	NONE	○ 0	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6	○ 7	○ 8	○ 9	○ 10	HIGHEST
f. Degree of fibromyalgia/somatization:	NONE	○ 0	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6	○ 7	○ 8	○ 9	○ 10	HIGHEST
g. Prognosis WITHOUT Rx:	Excellent,	Very Good,		Good,		Fair,		Poor					
h. Prognosis WITH Rx:	Excellent,	Very Good,		Good,		Fair,		Poor					

Conclusions

1. Low-does Mtx and prednisone remain cornerstones of therapy for RA - optimal effectiveness and safety
2. Early treatment, Mtx, prednisone, & treat-to-target may be as important as biologicals in better status of RA patients now than in past
3. Evidence requires observations in usual clinical care, in addition to clinical trials – no apologies for observational studies
4. Patients can provide 80% of the data needed on simple self-report questionnaires
5. Data from clinical care may be an intellectual & ethical responsibility of doctors to patients

Some Suggestions for DANBIO next 10 years

1. Record data on all consecutive pains with all diagnoses
2. Record more simple physician data in each patient at each visit
3. Export database capabilities to rest of the world

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Sponsors
Arthritis Foundation
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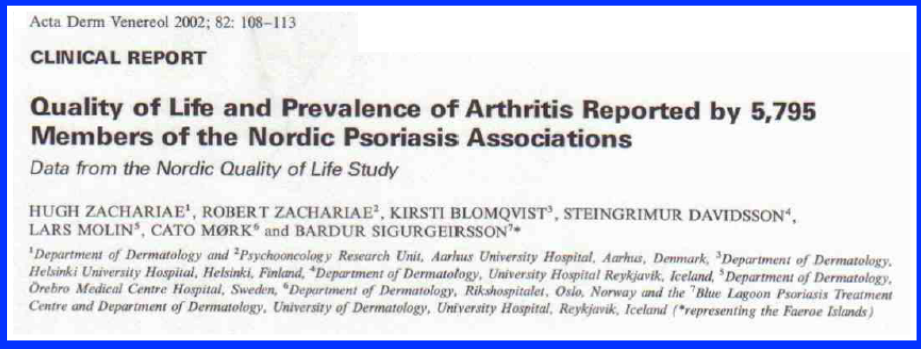
Amgen
Bristol-Meyers-Squibb
Centocor
Genentech
Jack C Massey Foundation
Novartis
Pfizer
UCB

Happy Birthday TAK

Low dose methotrexate and prednisone in psoriatic arthritis

1. Low-dose methotrexate is the treatment of choice for psoriasis
2. Low-dose methotrexate gives good results in psoriatic arthritis, similar to rheumatoid arthritis, in most patients
3. Low-dose prednisone may give similar results to rheumatoid arthritis in most patients, although some dermatologists avoid systemic glucocorticoids in patients with psoriasis
4. Low-dose methotrexate and prednisone likely to continue to be used a lot over the next 10 years, because of efficacy, effectiveness, safety, and low cost



Acta Derm Venereol 2002; 82: 108–113

CLINICAL REPORT

Quality of Life and Prevalence of Arthritis Reported by 5,795 Members of the Nordic Psoriasis Associations

Data from the Nordic Quality of Life Study

HUGH ZACHARIAE[1], ROBERT ZACHARIAE[2], KIRSTI BLOMQVIST[3], STEINGRIMUR DAVIDSSON[4], LARS MOLIN[5], CATO MØRK[6] and BARDUR SIGURGEIRSSON[7]*

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Low dose methotrexate and prednisone in ankylosing spondylitis

1. Low-dose methotrexate is not efficacious for axial involvement of AS, but sometimes effective for peripheral involvement
2. Low-dose methotrexate does not add to efficacy of biological agents for AS, unlike RA
3. Intra-articular glucocorticoids are quite effective in AS
4. Systemic glucocorticoids usually not efficacious for axial involvement of AS, sometimes effective for peripheral involvement
5. Low-dose methotrexate and prednisone are likely to be used less over the next 10 years for AS – ironically superiority of biological agents vs Mtx and glucocorticoids greater in AS than in RA, though they may be tried in individual patients due to low cost

Types of questions that cannot be answered by "evidence-based medicine" from randomized controlled clinical trials

1. Which medication do I give to an individual patient?
2. When do I begin or stop Medication A (or B or C) in a particular individual patient?
3. If the patient has elevated LFTs or mild GI distress, do I stop, reduce, or make no change in medication?
4. Which laboratory test or imaging study should I order to make a diagnosis?
5. Any question that requires longer to answer that the length of the trial (most questions in rheumatology).

Goodman and Gilman Textbook of Pharmacology, 2006 edition:

"Although aspirin is regarded as the standard against which other drugs should be compared for the treatment of rheumatoid arthritis, many clinicians favor the use of other NSAIDs perceived to have better gastrointestinal tolerability, even though this perception remains unproven by convincing clinical trials.

Patients with progressive or resistant disease require therapy with more toxic, second-line drugs, such as antimalarials, glucocorticoids, methotrexate, or immunosuppressive agents.

– (Section IV/Chapter 26, page 690)

Rethinking "best evidence" – not always from randomized controlled clinical trials, particularly in chronic diseases

1. Most chronic diseases clinical trials are too short, with too much patient selection, to provide definitive data – no difference over 1 year does not necessarily predict that there will be no difference over 5-10 years.
2. Most enigmas in medicine – perhaps 95% - cannot be solved through clinical trials.
3. Most patients cannot participate in trials but can provide data about results of therapies and outcomes.
4. The costs of futile clinical trials at this time in rheumatic diseases are far greater than costs to provide more progress through other methods.

Median Levels of All Patients at Initiation of MTX 1996-2001 and Mean of 2.6 Years Later in:

A. 63 "control" adequate responders continuing MTX
B. 30 incomplete responders initiating biologic agent

	63 Adequate Responders ("Controls")		30 Incomplete Responders	
	MTX Start	Follow-up (NO Biologic)	MTX Start	Biologic Start
ESR	24	16	28	18
MDHAQ-Function	2.3	1.0	3.2	3.3
Pain	4.1	1.4	5.2	6.8
Patient Global	4.2	0.9	5.5	5.5
RAPID3	10.6	3.6	14.9	16.2

Pincus T, Swearingen C.J. [Abstract #1627] *Arthritis Rheum* 2009;60(Suppl):S608. Presented at ACR, 2009.