Rheumatology 2000;39:34–42

Disease-modifying anti-rheumatic drug use according to the 'sawtooth' treatment strategy improves the functional outcome in rheumatoid arthritis: results of a long-term follow-up study with review of the literature

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Abstract

Objectives. To investigate long-term functional outcomes of early rheumatoid arthritis (RA) patients treated actively with disease-modifying anti-rheumatic drugs (DMARDs) from diagnosis, according to the 'sawtooth' principle, and to compare the results to historical data.

Methods. The surviving 46 and 65 patients from two early RA cohorts were examined on average 13.0 (cohort 1) and 8.5 (cohort 2) yr, respectively, after onset of disease. Functional outcome was measured by the Health Assessment Questionnaire (HAQ) and compared with the HAQ scores of 57 RA patient cohorts found through a Medline computer search.

Results. The respective cross-sectional mean HAQ scores of cohorts 1 and 2 were 0.75 and 0.55, and were more favourable than the mean HAQ scores of 1.27 (27 cohorts, disease duration >10 yr) and 1.13 (13 cohorts, disease duration 5–10 yr) of the comparator cohorts. The median time that our patients were treated with DMARDs out of the total follow-up period was 88%, while in the majority of comparator cohorts the use of DMARDs was less extensive or poorly described.

Conclusions. The observation of better preserved function in patients with RA over 13 and 8.5 yr, compared to earlier reports which indicated more severe declines, is a hopeful sign for the rheumatology community.

KEY WORDS: Rheumatoid arthritis, Functional capacity, Health Assessment Questionnaire, Early RA, Long-term outcome.

Preservation of function is a major goal of treatment in rheumatoid arthritis (RA) as patients generally experience functional declines from the beginning of the disease and throughout the disease course [1–9].

One approach to preservation of function is the 'sawtooth' strategy proposed by Fries [10], which includes early disease-modifying anti-rheumatic drug (DMARD) therapy with continual and serial use of one or multiple DMARDs. It would be optimal to analyse this strategy according to a randomized, controlled (double-blind) clinical trial. However, such a trial is not feasible over the many years required to measure possible effects of sustained DMARD therapy on long-term outcomes of RA, and effectiveness must be analysed through longitudinal observational studies [11].

Self-report questionnaires provide a formal, highly valid and reliable method to assess patients' functional status. Pincus *et al*. [12], and Hawley and Wolfe [13], have demonstrated that the Stanford Health Assessment Questionnaire (HAQ) [14] is more effective than any other available method in documenting functional decline over 5–10 yr in RA.

In the present paper, we report cross-sectional HAQ scores of 46 and 65 early RA patients at 13 and 8.5 yr after disease onset, treated with DMARDs continually and serially from the diagnosis, later designated by Fries as the 'sawtooth' strategy. We also compare our results to historical data.

Submitted 15 September 1998; revised version accepted 6 July 1999.

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Patients and methods

The study included a total of 135 newly diagnosed RA patients initially recruited to two separate cohorts [15, 16] monitored from the first visit <24 months after disease onset at Jyväskylä Central Hospital. The first cohort of 58 early RA patients was assembled in 1983–85 to study early erosiveness in recent-onset RA (cohort 1). The second cohort of 78 patients was started in the

beginning of 1988 as a case–control study to investigate the efficacy and tolerability of sulphasalazine (SASP) in the treatment of early RA (cohort 2). At enrolment of these early RA cases, all met the American Rheumatism Association (ARA) 1958 criteria [17] for definite or classical RA. One initially enrolled patient was later diagnosed as suffering from reactive arthritis and was excluded.

Demographic and clinical characteristics of the patients at outset are shown in Table 1. Only one patient was lost to follow-up 1 yr after the diagnosis; demographic and clinical variables of this patient are not included in Table 1.

All patients were enrolled in a prospective, longitudinal study to evaluate the 'sawtooth' strategy. In cohort 1, DMARD therapy with i.m. gold was started immediately after the diagnosis, whereas in cohort 2 patients were initially treated with SASP or placebo. In spite of the lag period due to the study setting, the mean symptomatic period before the first genuine DMARD initiation was compatible in both cohorts (8.4 *vs* 7.5 months for cohorts 1 and 2, respectively). Only one patient has never needed DMARDs due to a self-remitting disease.

All new starts of individual DMARDs or their combinations, as well as the proportion of time the patients were on DMARDs out of the total follow-up time, were recorded.

A total of 23 (17%) patients died during the observation period. At baseline, those who subsequently died were older, and their disease was more active (Table 1). The most common cause of death was cardiovascular disease.

The patients were clinically assessed every 3 months for the first 2 yr, and at least yearly thereafter. In January 1997, the surviving 46 and 65 patients were re-examined, when the mean (range) disease duration from the onset of symptoms was 13.0 (11.7–15.3) and 8.5 (7.2–9.6) yr, respectively.

In this paper, we refer to the cross-sectional findings of the 111 examined cohort patients with special emphasis on the patients' functional outcome and the factors related to it. The examination included assessment of the number of tender and swollen joints, a blood test for erythrocyte sedimentation rate (ESR), radiographs of hands and feet, as well as patients' self-assessed pain, general well-being (GH) and functional status.

The patients' functional capacity was assessed by the Stanford HAQ, scoring from 0 to 3 [14]. The current disease activity was measured by the 28-joint-based Disease Activity Score [$DAS = 0.56 \times SQRT$ (tender joint count) $+ 0.28 \times SQRT$ (swollen joint count) $+ 0.70 \times \ln$ (ESR) $+ 0.014 \times GH$], ranging from 0 to 10 [18]. The method described by Larsen *et al.* [19] was used to grade radiographic damage. Indices for the wrists were multiplied by five. These and the indices for the I–V PIP as well as MCP joints of the hands and the IP joints of the big toes, and the I–V MTP joints, were added together to form an index from 0 to 210. Pain and GH were assessed by the patient-completed 100 mm horizontal visual analogue scales (VAS) [14]. Arthritis was judged seropositive if rheumatoid factor was positive at any time during the observation period.

The data were entered into a microcomputer and analysed by using the Statistical Package for the Social Sciences (SPSS) [20]. Patients with mild disability ($HAQ \leqslant 1$) were compared to other patients ($HAQ > 1$) with regard to other clinical variables. Statistical significance of differences was determined using the Mann–Whitney test for continuous measures and the χ^2 test for dichotomous variables.

A Medline computer search was performed to identify reports which included HAQ or modified HAQ (MHAQ) (scales 1–4 changed to 0–3) scores of cohorts of patients with RA who had had disease for longer than 5 yr, published in English after 1988. Our results were compared with these historical data.

TABLE 1. Comparison of mean (range) demographic and clinical variables between the cohort groups at baseline (seropositivity during the follow-up)

	Cohort 1		Cohort 2	
	Alive ($n = 46$)	Died during follow-up ($n = 12$)	Alive ($n = 65$)	Died during follow-up ($n = 11$)
Age (yr)	43.5 (17–72)	65.3 (41–79)	49.9 (23–78)	64.1 (54–74)
Duration of symptoms (months)	7.6 (1–24)	10.1 (1–24)	5.1 (2–12)	5.3 (2–12)
Sex, female, no. (%)	34 (74)	7 (58)	42 (65)	7 (64)
Seropositive, no. (%)	36 (78)	10 (83)	43 (66)	10 (91)
Larsen score	2.8 (0–30)	7.8 (0–33)	2.3 (0–21)	3.8 (0–26)
ESR (mm/h)	38.1 (7–122)	46.4 (9–115)	38.6 (2–91)	41.6 (12–68)
CRP (mg/l)	25.7 (0–99)	31.5 (2–124)	22.8 (1–102)	42.6 (6–152)
Ritchie index	9.6 (2–22)	13.0 (7–19)	9.3 (3–23)	12.8 (7–23)
Functional class, no. (%)				
Class I	0 (0)	0 (0)	7 (11)	0 (0)
Class II	43 (94)	10 (83)	57 (88)	10 (91)
Class III	3 (6)	2 (17)	1 (1)	1 (9)
Class IV	0 (0)	0 (0)	0 (0)	0 (0)

Results

The present cohort

The mean (median) HAQ scores were 0.75 (0.63) for cohort 1 and 0.55 (0.25) for cohort 2 after an average duration of disease of 13.0 and 8.5 yr. A total of 39 (35.1%) patients had an HAQ score of 0, while 86 (77.5%), 21 (18.9%) and 4 (3.6%) patients scored between 0 and 1.0, 1.01–2.0 and 2.01–3.0, representing mild, moderate and severe functional impairment, respectively (Fig. 1).

Patients with mild functional disability (HAQ $\leqslant 1$) differed statistically significantly from other patients (HAQ > 1) according to disease activity, age, pain score VAS, Larsen score, number of DMARD starts and joint replacement. No significant differences were seen between the groups in seropositivity, gender and extra-articular disease (Table 2).

The median time that our patients were treated with DMARDs out of the total follow-up time was 88%, and the mean (range) counts of new starts of individual DMARDs or combinations of DMARDs were 6.5 (1–16) and 3.5 (0–12) for the patients in cohorts 1 and 2, respectively. Figure 2 details the distribution of the proportion of cohort patients on individual DMARDs 1–10 yr after the diagnosis. The proportion of DMARD non-recipients, as well as the proportion of those who used combinations, increased over time. At the final visit, a total of 21 patients did not use DMARDs due to a long-lasting remission.

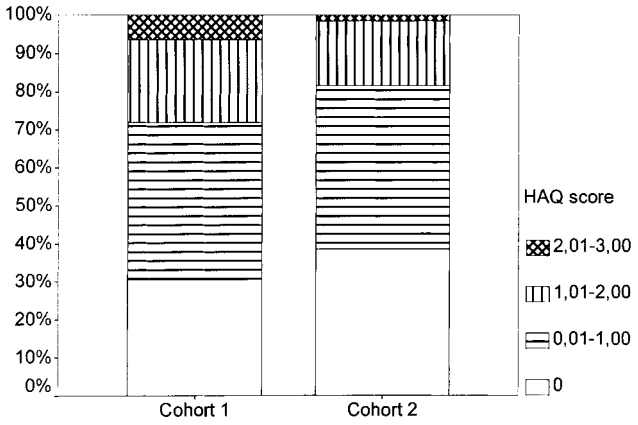

FIG. 1. Percentage distribution of the cohort patients in HAQ score groups.

TABLE 2. Comparison of the patients with mild functional disability and the other patients

	HAQ 0–1 ($n = 86$)	HAQ > 1 ($n = 25$)	P
DAS	2.8 (0.6–6.7)	4.0 (1.6–6.1)	<0.001
Age (yr)	54.0 (30–83)	67.4 (38–87)	<0.001
No. of DMARD starts	4.2 (1–12)	6.6 (0–16)	0.003
Patients with artificial joints, no. (%)	6 (7)	8 (32)	0.003
Pain VAS	26 (0–99)	46 (0–99)	0.003
Larsen's score	28 (0–141)	53 (0–192)	0.03
RF+, no. (%) of patients	58 (67)	19 (76)	0.47
Sex, female, no. (%)	56 (65)	20 (80)	0.22
Patients with extra-articular disease, no. (%)	9 (10)	6 (24)	0.10

Values are means (range).

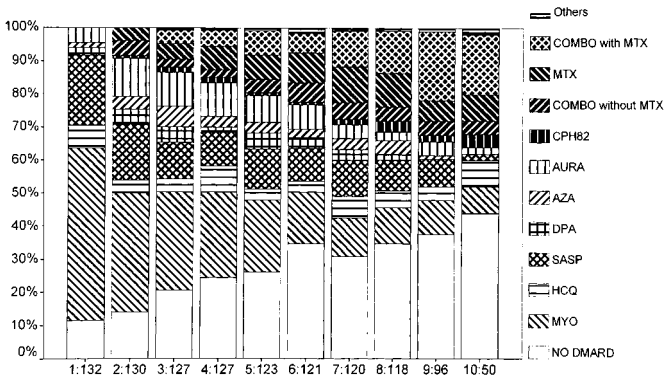

FIG. 2. Proportion of patients on individual DMARDs or combinations of DMARDs 1–10 yr after the diagnosis. Year, with the number of patients, is shown on the horizontal axis. DMARD, disease-modifying anti-rheumatic drug; MYO, i.m. gold; HCQ, hydroxychloroquine; SASP, sulphasalazine; DPA, D-penicillamine; AZA, azathioprine; AURA, auranofin; CPH82, podophyllotoxin derivatives; MTX, methotrexate; COMBO, combination of DMARDs.

Historical control cohorts

Table 3 summarizes the characteristics and the HAQ or the MHAQ scores of 57 RA cohorts including a total of 13 591 patients with >5 yr disease duration that we were able to find in 30 reports published in English after 1988 [5, 21–49]. Most of the studies were cross-sectional, and the patient recruitment had varied from advertisement calls to clinical in-patients. Several studies consisted of subgroups classified according to status at outset, therapy and care given or the subsequent outcome of the patients, as detailed in Table 3. Only three studies consisted of patients with early RA and a follow-up period of several years [26, 30, 36]. Indeed, the cohorts and the patients included were very heterogeneous. Furthermore, the MHAQ scores are recognized to be somewhat lower than the HAQ scores, and thus are not entirely comparable with each other.

In the cohorts with disease duration between 5 and 10 yr, the mean ($n = 13$) or median ($n = 9$) HAQs and the mean MHAQs ($n = 3$) ranged from 0.5 to 1.8 or from 1.3 to 2.3 and from 0.5 to 1.0, respectively. The respective corresponding figures in cohorts with disease duration >10 yr were 0.8–2.4 ($n = 27$), 1.8 ($n = 1$) and 0.6–1.3 ($n = 3$). Table 3 also shows that the median MHAQ of an additional cohort with disease duration >10 yr was 1.4.

A statement regarding DMARD treatment was found in 24 out of the 57 referred cohorts. The mean number of prescribed DMARDs was mentioned in seven [27, 42, 45], the point [24] and period [26, 30, 40, 43]

prevalence of DMARD use in two and five, respectively, and the proportion of the follow-up time on DMARDs in two [44] cohorts. In the study by Munro *et al.* [36], the DMARD was defined to be i.m. gold.

In Fig. 3, originally sketched by Fries, we have summarized the HAQs of the historical cohorts found as well as our present results.

Discussion

The primary observation in the present study was that the functional capacity of 111 patients with RA who were initially seen after <2 yr of disease was well preserved after 13 and 8.5 yr. Scores for our patients were 0.75 after 13 yr and 0.55 after 8.5 yr of disease, in contrast to scores >1 for most studies.

Fries proposed the figure concerning different courses of RA to illustrate the failure of traditional 'pyramidal' DMARD use to alter the long-term disability status of RA patients. However, long-term outcome of RA depends on variables beyond therapy given. Since the course of epidemiological RA is more favourable than that of clinical disease [50], one has to know how the patient cohort is assembled and how the disease is defined [51]. The referred cohorts with patients with the poorest outcome seemed to represent clinical cases in whom DMARD therapy had been started with long delays, if not at all [28, 29, 33, 37]. Furthermore, some of the series with conspicuously good functional outcome appeared to consist of 'community based inception cohorts' [21, 23, 38, 40, 41, 43, 44].

We regard our patients as representing good examples of population-based clinical RA cohorts. The hospital in Jyväskylä is the only rheumatological centre in the region, which has 260 000 inhabitants. Based on the common consensus, all new RA cases are referred to our centre for diagnostic and therapeutic purposes. Our cohorts also have negligible drop-out rates. Indeed, only one male patient in these two cohorts was lost to follow-up.

Those who died may have been severely disabled and could have worsened the final HAQ scores. However, we suppose that this bias does not differ from other reported clinical cohorts.

One may argue that superior long-term outcomes of our patients were the result of less aggressive disease than in comparator studies—some patients in cohorts with early RA patients might not have progressive disease seen in other long-term studies [52]. A conspicuous shortage of most of the referred comparator studies was the absence of clinical data at the outset, which hampers adequate comparisons. Only in three other reports did the cohort patients consist of early RA cases and their clinical data at the baseline could be found [26, 30, 36]. The data are demonstrated in Table 4. In comparison to our results, the most striking differences were the remarkably higher HAQ outcome scores and very modest use of DMARDs in two of them [26, 30].

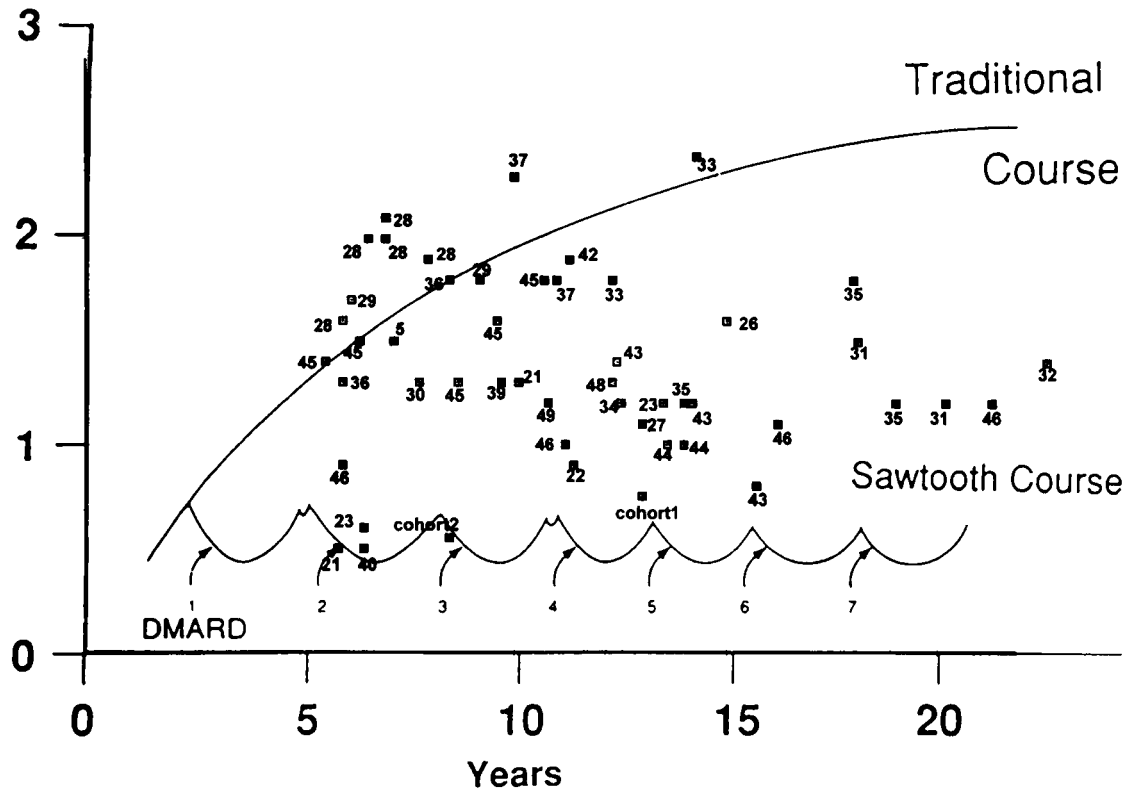

FIG. 3. 'The sawtooth strategy', as illustrated by Fries [10], supplied with mean or median HAQ scores of 50 cohorts as well as the mean HAQ scores of the present study. Each number corresponds to a study in the reference list (and Table 3). Permission for the use of the figure was granted by the *Journal of Rheumatology* and Professor Fries.

TABLE 3. Characteristics and the mean [median] HAQ (MHAQ) scores in the 57 RA patient cohorts with a disease duration of at least 5 yr

Author	Country	Setting	Number of patients and special characteristics	HAQ	Disease duration	Age (yr)	F (%)	RF+ (%)	DMARDs
Allaire [21]	USA, 1996	Mail survey	367 (employed)	0.5	5.9	45.6	78	NR	NR
			102 (work disabled)	1.3	10.1	50.0	75	NR	NR
Callahan [22]	USA, 1989	Clinical	134	0.9	11.4	55.0	66	NR	NR
Callahan [23]	USA, 1992	Various	36 (working full-time)	0.6	6.5	48.3	44	89	NR
			55 (receiving disability payments)	1.2	13.5	55.1	38	89	NR
Callahan [24]	USA, 1996	Cohort from private practices	943 (alive after 5 yr)	(0.6)	11.5	55.1	78	NR	70% taking DMARDs
			126 (died during 5 yr follow-up)	(1.0)	12.6	67.6	72	NR	63% taking DMARDs
Callahan [25]	USA, 1997	Various	169 (alive after 5 yr)	(1.0)	9.1	55.1	NR	NR	NR
			37 (subsequently died)	(1.3)	12.7	65.5	NR	NR	NR
Corbett [26]	UK, 1993	Clinical early RA	64	1.6	15	61	61	NR	55% of the patients during the follow-up
Van den Ende [27]	The Netherlands, 1995	Clinical	51	1.1	13	55	53	84	Mean number of prescribed DMARDs 2.3
McEntegart [28]	UK, 1997	Clinical	Three deprivation groups						
			440	[1.8]	4	58	NR	NR	NR
				[2.0]	7	57	NR	NR	NR
				[2.0]	6.6	58	NR	NR	NR
			374	[1.6]	6	60	NR	NR	NR
				[1.9]	8	60	NR	NR	NR
				[2.1]	7	60	NR	NR	NR
Ferraz [29]	Brazil, 1994	Clinical	34	1.8	9.2	49.7	82	71	At least one DMARD previously
			34	1.7	6.2	43.6	85	77	At least one DMARD previously
Fex [30]	Sweden, 1998	Clinical early RA	106	1.3	7.8	59	67	81	65% of the patients during the follow-up
Fries [31]	USA, Canada, 1996	ARAMIS database	2437	1.5	18.1	61.9	76	86	At least one visit with DMARD use during the follow-up time of on average 9 yr
			408	1.2	20.2	65.8	74	70	No DMARDs during the follow-up of 9 yr
Fries [32]	USA, Canada, 1997	ARAMIS database	663	1.4	22.6	63.0	81	NR	NR
Gardiner [33]	Ireland, 1993	Clinical	37 in-patients	2.4	14.3	64.2	89	NR	NR
			208 out-patients	1.8	12.3	55.4	80	NR	NR
Guillemin [5]	France, 1992	Clinical	82	1.5	7.2	55.3	70	NR	NR
Hawley [34]	USA, 1992	Private out-patients	572	1.2	12.5	59.6	75	NR	NR
Leigh and Fries [35]	USA, 1992	ARAMIS	209 (alive after 9 yr)	1.2	19	60	86	NR	NR
			54 (subsequently died)	1.8	18	66	63	NR	NR
			67 (lost to follow-up)	1.2	14	55	85	NR	NR
Munro [36]	UK, 1998	Clinical, early RA	44	[1.3]	5–7	58	75	77	i.m. gold 100%
		Clinical	37	[1.8]	7–10	59	85	81	i.m. gold 100% after disease duration of 2–5 yr

TABLE 3. (*Continued*)

Porter [37]	UK, 1994	Clinical	41 (subsequently died)	[2.3]	10	62	NR	NR	NR
			444 (stopped therapy)	[2.1]	7	57	NR	NR	NR
			190 (continued therapy)	[1.8]	11	58	NR	NR	Last 5 yr on DMARDs
Reisine [38]	USA, 1995	Private out-patients	392 employed	(0.5)	8.7	48	72	NR	NR
Stein [39]	USA, 1997	Clinical	92	1.3	9.7	54	75	NR	Several previous DMARDs
Suarez-Almazor [40]	Canada, 1994	Inception cohort	128	0.5	6.5	58.5	70	59	85% of the patients during the follow-up
Tuttleman [41]	USA, 1997	Cross-sectional	207	(0.6)	9.3	53.7	78	NR	NR
Vliet Vlieland [42]	The Netherlands, 1995	Clinical	63 hospitalized for active RA	1.9	11.3	61.7	75	89	Median no. of DMARDs 2.8
Ward [43]	USA, 1993	ARAMIS	Groups based on the amount of rheumatology care						
			69 (continuous care)	1.4	12.4	54.6	83	86	83% of the patients during the follow-up
			161 (intermittent care)	1.2	14.2	53.8	83	75	70% of the patients during the follow-up
			52 (no specialist care)	0.8	15.7	55.9	86	68	NR
Ward [44]	USA, 1998	UCSF RA panel	125 (FFS care)	1.0	13.6	52.5	84	73	35% of the time of observation
			57 (PGP care)	1.0	14.0	52.6	77	76	35% of the time of observation
Wolfe [45]	USA, 1990	Private out-patients	Groups based on current DMARD						
			187	1.8	10.7	56.7	64	90	Current DMARD: methotrexate Prior DMARD count 1.7 per patient
			303	1.5	6.4	55.0	69	86	Current: i.m. gold Prior 0.15
			64	1.4	5.6	57.2	64	83	Current: oral gold Prior 0.36
			269	1.3	8.7	56.5	80	80	Current: hydroxychloroquine Prior 0.52
			194	1.6	9.6	55.5	74	87	Current: penicillamine Prior 0.96
Wolfe [46]	USA, 1991	Private out-patients	Groups based on disease duration						
			143	0.9	6.0	55.0	73	81	NR
			67	1.0	11.2	55.4	82	89	NR
			57	1.1	16.2	54.9	63	87	NR
			30	1.2	21.3	62.5	80	86	NR
Wolfe [47]	USA, 1996	Private out-patients	628	([1.4])	12.0	61.9	75	NR	NR
Wolfe and Hawley [48]	USA, 1993	ARAMIS	713	1.3	12.3	59.5	71	86	NR
Yelin [49]	USA, 1996	UCSF RA panel	798 (FFS care)	1.2	10.8	57.5	77	73	NR
			227 (PGP care)	1.2	10.8	55.1	70	78	NR

F, female; RF, rheumatoid factor; NR, not reported; DMARDs, disease-modifying anti-rheumatic drugs; FFS, fee-for-service; PGP, prepaid group practice. UCSF, University of California, San Francisco.

TABLE 4. Cohorts of early RA patients. Comparison of demographic data, ESR and joint damage scores at onset, the use of DMARDs and HAQ scores at the latest visit

	Corbett [26]	Fex [30]	Munro [36]	Cohort 1	Cohort 2
At baseline					
No. of patients	102	106	44	58	77
Symptomatic period before initiation of DMARD, months, mean (S.D.)	<12 NR	<24 11.4 (6.6)	<24 NR	<24 8.4 (6.3)	<12 7.5 (4.9)
Median age of patients (yr)	50.5	c. 51	53 (44–60)	50 (35–61)	52 (40–64)
Female (%)	57	67	75	71	64
RF+ (%)	NR	81 (at end)	77	79	69
ESR (mm/1st h)	NR	27 (12–47)	50 (40–99)	33 (22–50)	36 (24–51)
Joint damage score	NR	7 (3–11)/0–200	NR	0 (0–3)/0–210	0 (0–3)/0–210
At final assessment					
HAQ score at x yr	1.6 (60 pts) at 15 yr	1.3 (106 pts) at 7.8 yr	1.25 (44 pts) at 5 yr	0.63 (46 pts) at 13.0 yr	0.25 (65 pts) at 8.5 yr
DMARDs	55% of the pts ever on DMARDs	65% of the pts ever on DMARDs	i.m. gold 100% of the pts	Sawtooth 88% of the total follow-up time	

Continuous variables are given as median (interquartile range) and frequencies as percentages.
Mean (S.D.).
NR, not reported.

While all but one of our patients have been treated with DMARDs with a median coverage of 88% of the total follow-up time, only 65 and 55%, respectively, of the patients in the studies by Fex *et al.* [30] and Corbett *et al.* [26] had ever been treated with DMARDs.

Some reports of beneficial results of early DMARD initiation on relatively long-term outcome of RA have been published. Egsmose *et al.* [53] demonstrated that RA cases who had been treated early with DMARDs had a statistically significantly better 5 yr HAQ score than the other group with delayed DMARD initiation. The 6 yr HAQ of the patients of Möttönen *et al.* [54] (46 patients of that cohort are also included in the present study) was 0.64. Also, these patients had been treated with DMARDs from diagnosis, according to the 'sawtooth' strategy. A beneficial effect of early DMARD initiation could not be excluded either when the good functional outcome of 128 Canadian RA patients was considered [40]. In a recent report by Munro *et al.* [36], early i.m. gold therapy indicated long-lasting (at least for 5 yr) better functional capacity compared to delayed i.m. gold initiation, although the benefits were only modest when compared to other studies (Fig. 3).

The beneficial impact of sustained DMARD therapy on maintenance of long-term functional capacity is also supported by some reports. Increased DMARD use was associated with better long-term HAQ values in patients in the ARAMIS database [31]. Improved function was also seen in RA patients who tolerated i.m. gold, sulphasalazine or penicillamine for longer periods in a British study [37]. Furthermore, less progression of functional disability of the patients who had continuing care from rheumatologists in comparison to those who had only intermittent care [44] may, though not discussed, also have been influenced by the more extensive use of DMARDs in these patients.

In early RA, disease activity appears to be the most important explanatory factor for decreased functional capacity [1]. On the other hand, as RA advances, the contributive role of tissue damage reportedly grows [5]. In the present study, despite a longer disease duration, the current disease activity separated most strikingly the groups with poor or well-preserved functional capacity.

The increasing proportion of our patients treated with DMARD combinations over time demonstrates that in some RA patients even the 'sawtooth' treatment strategy is insufficient. We must emphasize that despite aggressive DMARD therapy, high clinical disease activity was present in some of our cases even 8–13 yr after the onset of RA. On the other hand, the number of patients without any DMARDs increased over time; 21 (19%) of the patients were in remission without DMARDs at the time of evaluation.

In conclusion, the observation of the improved functional outcome (compared to historical controls) in our 111 patients treated according to the 'sawtooth' strategy from diagnosis up to an average of 13 yr is promising. Aggressive therapy with traditional DMARDs appears to have a considerable impact on the result.

Acknowledgements

We thank the *Journal of Rheumatology* and Professor Fries for permission to use Fig. 3. This study was supported by grants from Central Finland Health Care District and Kuopio University Hospital (EVO-funding), Finland.

References

1. Guillemin F, Suurmeijer T, Krol B, Bombardier C, Briancon S, Doeglas D *et al.* Functional disability in early rheumatoid arthritis: Description and risk factors. J Rheumatol 1994;21:1051–5.
2. Pincus T, Callahan LF, Sale WG, Brooks AL, Payne LE, Vaughn WK. Severe functional declines, work disability and increased mortality in seventy-five rheumatoid arthritis patients studied over nine years. Arthritis Rheum 1984;27:864–72.

3. Scott DL, Coulton BL, Symmons DPM, Popert AJ. Long-term outcome of treating rheumatoid arthritis: Results after 20 years. Lancet 1987;i:1108–11.
4. Sherrer YS, Bloch DA, Mitchell DM, Yourg DY, Fries JF. The development of disability in rheumatoid arthritis. Arthritis Rheum 1986;29:494–500.
5. Guillemin F, Briancon S, Pourel J. Functional disability in rheumatoid arthritis. Two different models in early and established disease. J Rheumatol 1992;19:366–9.
6. Wolfe F. 50 years of antirheumatic therapy: The prognosis of rheumatoid arthritis. J Rheumatol 1990;17(suppl. 22):24–32.
7. Wilske KR, Healey LA. Remodeling the pyramid—a concept whose time has come. J Rheumatol 1989;16:565–7.
8. Pincus T, Callahan LF. Taking mortality in rheumatoid arthritis seriously—predictive markers, socioeconomic status and comorbidity. J Rheumatol 1986;13:841–5.
9. Pincus T, Brooks RH, Callahan LF. Prediction of long-term mortality in patients with rheumatoid arthritis according to simple questionnaire and joint count measures. Ann Intern Med 1994;120:26–34.
10. Fries JF. Reevaluating the therapeutic approach to rheumatoid arthritis: the 'sawtooth' strategy. J Rheumatol 1990;17(suppl. 22):12–5.
11. Pincus T, Stein MC. What is the best source of useful data on the treatment of rheumatoid arthritis: Clinical trials, clinical observations, or clinical protocols? J Rheumatol 1995;22:1611–7.
12. Pincus T, Callahan LF, Brooks RH, Fuchs HA, Olsen NJ, Kaye JJ. Self-report questionnaire scores in rheumatoid arthritis compared with traditional physical, radiographic, and laboratory measures. Ann Intern Med 1989;110:259–66.
13. Hawley DJ, Wolfe F. Sensitivity to change of the Health Assessment Questionnaire (HAQ) and other clinical and health status measures in rheumatoid arthritis. Arthritis Care Res 1992;5:130–6.
14. Fries JF, Spitz PW, Kraines RG. Measurement of patient outcome in arthritis. Arthritis Rheum 1980;23:137–45.
15. Möttönen TT. Prediction of erosiveness and rate of development of new erosions in early rheumatoid arthritis. Ann Rheum Dis 1988;47:648–53.
16. Hannonen P, Möttönen T, Hakola M, Oka M. Sulphasalazine in early rheumatoid arthritis. Arthritis Rheum 1993;36:1501–9.
17. Ropes MW, Bennet GA, Cobb S, Jacox RA, Jessar R. 1958 revision of diagnostic criteria for rheumatoid arthritis. Arthritis Rheum 1959;2:16–20.
18. Prevoo MLL, van't Hof MA, Kuper HH, van Leeuwen MA, van de Putte LBA, van Riel PLCM. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. Arthritis Rheum 1995;38:44–8.
19. Larsen A, Dale K, Eek M. Radiographic evaluation of rheumatoid arthritis and related conditions by standard reference films. Acta Radiol Diagn 1977;18:481–91.
20. SPSS advanced statistics 7.5. Chicago, USA: SPSS Inc., 1997.
21. Allaire SH, Anderson JJ, Meenan RF. Reducing work disability with rheumatoid arthritis: Identification of additional risk factors and persons likely to benefit from intervention. Arthritis Care Res 1996;9:349–57.
22. Callahan LF, Smith WJ, Pincus T. Self-report questionnaires in five rheumatic diseases. Arthritis Care Res 1989;2:122–31.
23. Callahan LF, Bloch DA, Pincus T. Identification of work disability in rheumatoid arthritis: physical, radiographic and laboratory variables do not add explanatory power to demographic and functional variables. J Clin Epidemiol 1992;45:127–38.
24. Callahan LF, Cordray DS, Wells G, Pincus T. Formal education and five-year mortality in rheumatoid arthritis: Mediation by helplessness scale scores. Arthritis Care Res 1996;9:463–72.
25. Callahan LF, Pincus T, Huston JW, Brooks RH, Nance PE, Kaye JJ. Measures of activity and damage in rheumatoid arthritis: Depiction of changes and prediction of mortality over five years. Arthritis Care Res 1997;10: 381–94.
26. Corbett M, Dalton S, Young A, Silman A, Shipley M. Factors predicting death, survival and functional outcome in a prospective study of early rheumatoid disease over fifteen years. Br J Rheumatol 1993;32:717–23.
27. Van den Ende DHM, Hazes JMW, le Cessie S, Breedveld FC, Dijkmans BAC. Discordance between objective and subjective assessment of functional ability of patients with rheumatoid arthritis. Br J Rheumatol 1995;34:951–5.
28. McEntegart A, Morrison E, Capell HA, Duncan MR, Porter D, Madhok R *et al*. Effect of social deprivation on disease severity and outcome in patients with rheumatoid arthritis. Ann Rheum Dis 1997;56:410–3.
29. Ferraz MB, Pinheiro GRC, Helfenstein M, Rezende C, Roimicher L, Brandao L *et al*. Combination therapy with methotrexate and chloroquine in rheumatoid arthritis. Scand J Rheumatol 1994;23:231–6.
30. Fex E, Larsson BM, Nived K, Eberhardt K. Effect of rheumatoid arthritis on work status and social and leisure time activities in patients followed 8 years from onset. J Rheumatol 1998;25:44–50.
31. Fries JF, Williams CA, Morfeld D, Singh G, Sibley J. Reduction in long-term disability in patients with rheumatoid arthritis by disease-modifying antirheumatic drug-based treatment strategies. Arthritis Rheum 1996;39: 616–22.
32. Fries JF, Ramey DR. 'Arthritis specific' global health analog scales assess 'generic' health related quality-of-life in patients with rheumatoid arthritis. J Rheumatol 1997;24:1697–702.
33. Gardiner PV, Sykes HR, Hassey GA, Walker DJ. An evaluation of the health assessment questionnaire in long-term longitudinal follow-up of disability in rheumatoid arthritis. Br J Rheumatol 1993;32:724–8.
34. Hawley DJ, Wolfe F, Cathey MA. The sense of coherence questionnaire in patients with rheumatic disorders. J Rheumatol 1992;19:1912–8.
35. Leigh PJ, Fries JF. Predictors of disability in a longitudinal sample of patients with rheumatoid arthritis. Ann Rheum Dis 1992;51:581–7.
36. Munro R, Hampson R, McEntegart A, Thompson EA, Madhok R, Capell H. Improved functional outcome in patients with early rheumatoid arthritis treated with intramuscular gold: results of a five year prospective study. Ann Rheum Dis 1998;57:88–93.
37. Porter DR, McInnes I, Capell HA. Outcome of second line therapy in rheumatoid arthritis. Ann Rheum Dis 1994:53:812–5.
38. Reisine S, McQuillan J, Fifield J. Predictors of work disability in rheumatoid arthritis patients. A five-year followup. Arthritis Rheum 1995;38:1630–7.
39. Stein CM, Pincus T, Yucum D, Tugwell P, Wells G, Gluck O *et al*. Combination treatment of severe rheumatoid

arthritis with cyclosporine and methotrexate for forty-eight weeks. Arthritis Rheum 1997;40:1843–51.
40. Suarez-Almazor ME, Soskolne CL, Saunders LD, Russell AS. Outcome in rheumatoid arthritis. A 1985 inception cohort study. J Rheumatol 1994;21:1438–46.
41. Tuttleman M, Pillemer SR, Tilley BC, Fowler SE, Buckley LM, Alarcon GS *et al.* A cross sectional assessment of health status instruments in patients with rheumatoid arthritis participating in a clinical trial. J Rheumatol 1997;24:1910–5.
42. Vliet Vlieland TPM, Zwinderman AH, Vandenbroucke JP, Breedveld FC, Hazes JMW. In-patient treatment for active rheumatoid arthritis: Clinical course and predictors of improvement. Br J Rheumatol 1995;34:847–53.
43. Ward MM, Leigh JP, Fries JF. Progression of functional disability in patients with rheumatoid arthritis. Arch Intern Med 1993;153:2229–37.
44. Ward MM, Lubeck D, Leigh P. Longterm health outcomes of patients with rheumatoid arthritis treated in managed care and fee-for-service practice settings. J Rheumatol 1998;25:641–9.
45. Wolfe F, Hawley DJ, Cathey MA. Termination of slow acting antirheumatic therapy in rheumatoid arthritis: A 14-year prospective evaluation of 1017 consecutive starts. J Rheumatol 1990;17:994–1002.
46. Wolfe F, Hawley DJ, Cathey MA. Clinical and health status measures over time: Prognosis and outcome assessment in rheumatoid arthritis. J Rheumatol 1991;18:1290–7.
47. Wolfe F, Hawley DJ, Wilson K. The prevalence and meaning of fatigue in rheumatic disease. J Rheumatol 1996;23:1407–17.
48. Wolfe F, Hawley DJ. The relationship between clinical activity and depression in rheumatoid arthritis. J Rheumatol 1993;20:2032–7.
49. Yelin EH, Criswell LA, Feigenbaum PG. Health care utilization and outcomes among persons with rheumatoid arthritis in fee-for-service and prepaid group practice settings. J Am Med Assoc 1996;276:1048–53.
50. Wolfe F. The natural history of rheumatoid arthritis. J Rheumatol 1996;23(suppl. 44):13–22.
51. Kirwan JR, Quilty B. Prognostic criteria in rheumatoid arthritis: Can we predict which patients will require specific anti-rheumatoid treatment. Clin Exp Rheumatol 1997;15 (suppl. 17):15–25.
52. Pincus T, Callahan LF. How many types of patients meet classification criteria for rheumatoid arthritis? J Rheumatol 1994;21:1385–9.
53. Egsmose C, Lund B, Borg G, Pettersson H, Berg E, Brodin U *et al.* Patients with rheumatoid arthritis benefit from early 2nd line therapy: 5 year followup of a prospective double blind placebo controlled study. J Rheumatol 1995;22:2208–13.
54. Möttönen T, Paimela L, Ahonen J, Helve T, Hannonen P, Leirisalo-Repo M. Outcome in patients with early rheumatoid arthritis treated according to the 'sawtooth' strategy. Arthritis Rheum 1996;39:996–1005.