Longitudinal and Observational Studies Module

Hard questions must have hard answers.

— Plutarch, AD 46-120

Longitudinal and observational studies (LOS) are both attractive and problematic. Compared with cross sectional data, case–control data, and randomized controlled trials, the appeal of LOS data derives from the richer set of analytic questions that can be addressed regarding etiology, pathogenesis, natural history, prognosis, and effects of intervention, often within the setting of clinical practice.

Although longitudinal and observational studies are potentially a valuable research source, it is regrettable that so many can be criticized for lack of specific data and for flaws in design and reporting characteristics. Many LOS omit valuable demographic or clinical data so that the comparisons between studies (by time, place, or person) are difficult or impossible. More importantly, various selection and measurement biases and the application of different analytical procedures can influence the internal validity and generalizability of the conclusions of a study.

This module has two objectives: the identification of a core set of variables for LOS and the identification and description of their design elements.

A selection of published LOS in rheumatoid arthritis (RA) since the 1930s is reviewed in Tables 1–3. Characteristics described include time and place, study design, sampling method, source population, sample size, response rate, disease ascertainment methods (including the RA classification criteria), demographic data (percentage male, age, and disease duration of the group), and clinical features (seropositivity, erosiveness status, and nodularity status of the group), as well as relevant bibliographic information.

LOS have appeared in many guises. Most early reports are based on convenient series of patients from a particular clinical setting. More recently inception cohort studies[1-11] have been specifically designed to investigate the natural history of RA and its prognosis, including studies on the mortality of RA. Other designs include LOS that have begun as a randomized controlled clinical trial (RCT)[12-17] or other type of study (such as a case–control study[18-22]). Some studies were initially conducted to examine the relationship of a particular etiological or pathogenetic measure in different subsets of patients. Sometimes no clear research objectives are indicated, or the stated research objectives were not the original research objectives for the assembly of patients and data collection, although, often, this is not made clear in the publication, and this may be important in drawing our conclusions regarding the generalizability of the results.

LOS have been influenced over the decades by: the different methods used to ascertain and classify RA (for example, prior to the 1958 American Rheumatism Association criteria, ankylosing spondylitis was included in RA studies[24-26]); our understanding of the etiology and pathogenesis of the disease; the laboratory and other diagnostic biotechnological methods available; and issues relating to the design of studies and the statistical analysis of longitudinal data, as well as the various methods that have been developed to measure functional status, structural status, and other measures of outcome in this disease. The nature of LOS over the decades has also been influenced by non-science factors such as the personalities, interests, and expertise (clinical, laboratory, or epidemiological based) of the authors, as well as the varied agendas of regulatory authorities, medical associations, and the health policies and the administration of health services at a local and national level.

The aim of setting and meeting standards in clinical longitudinal and observational research is not new. It has surfaced every so often in the rheumatological as well as the general literature. Although Mainland is best remembered for his work with the Co-operating Clinics Committee of the American Rheumatism Association, in 1955 he discussed all the critical issues regarding the use of clinical records in observational studies of chronic disease[27]. Regarding some design issues, Mainland states "the notion that a survey giving only 'approximate' results needs less care than a first-class experiment is erroneous" and he quotes Bradford-Hill: "I would therefore myself infinitely sooner have, say, a one in four [random] sample of the population of a size thereby which enabled me to pursue relentlessly, and complete the records for, all or nearly all persons in it, than have to interpret figures derived from a survey of the 'whole' population from which finally a quarter was missing."

I can only speculate why he and others[28] have failed to substantially influence such clinical research and why, to this day, many LOS still fail to meet criteria for internal validity and generalizability. Perhaps it was not due to lack of knowledge regarding scientific methods but due to the general perception that the value of medical information was immediately recognizable and "hard," and therefore required little proof, whereas the value of information from other research disciplines such as psychology and sociology was considered conceptual and "soft" and therefore required extensive proof. Another reason is the difficulty and cost required to meet such high standards, as I can affirm from my own experience[29]. However, the push for evidence based medicine and processes such as OMERACT appear to be

Table 1. Selected RA longitudinal and observational studies from North America.

Place, Time	*Study Design, Sampling*	*Source population*	*RA Criteria*	*Size of sample, Response rate (RR)(%)*	*% male age (yrs) DD* (yrs)*	*% RF +ve Erosive Nodular*	*Refs*
New York, USA, 1920's, 1930's? (Ragan)	Prospective, mean follow-up 11 yrs, no data as to sampling	Hospital clinic	AS excluded, used clinical xray	374	?male ?age DD 1-2 yr (28% <1 yr)	agg'tn 50% ?eros ?nod	(30)
New York, 1930's, 1940's and 1950's	Case series, Retrospect, longitudinal >5 yrs of data, 5 assessments of records or mail at 3-5 yr intervals, Convenient	Cinic in voluntary hospital ? since 1932	Diagnosis of RA by two clinicians, later met ACR 1958 criteria for class or definite RA)	500 Visit 1, 403 at visit 2 (81%), 301 > 10 yrs FU (60%)	n=301 21% male ? age 47% <2 yrs DD at visit 1	n=301 45%RF+ ?eros 11%nod	(31)
Boston, USA 1931-36	Prospective, mean follow up 9.5 years, consecutive, excluded deaths	Hospital admissions	Usual clinical criteria 262 RA, 38 with AS (included with RA) 250 82% RR	Of the 250 20% FU < 5yrs, 32% 5-10 yrs and 46% 10-15 yrs, 56 died	38% (29% male if exclude patients with AS) ? age ?DD	?RF + ?eros ?nod	(24) (25)
Boston, USA 1930's?	Prospective, mean follow up 9.5 years, ?consecutive	Hospital admissions for RA or some other condition but patient also had RA	No data but would have included patients with AS	538 137 deaths analysed	44% male ?age ?DD	?RF + ?eros ?nod	(26)
Memphis, TN; 1960s	Prospective cohort 3-5 yrs, young adults, convenient sample (patient included if FU > 1 yr)	University clinic & referred private practice	FU > 1 yr Dx Rheum ARA criteria 1958: 76% def/class ARA 1958	50 ?%	22% ~30 yrs < 6mth at visit 1	40% RF+ 22% eros 6% nod	(32) (33)
ARAMIS Database Phoenix, Wichita, Saskatoon, Santa Clara & Stanford USA; 1978+	Prospective cohort, Consecutive patients with minimum 1yr FU	Hospital clinic & referred private practice, some primary referred community		2006 ?%	22.4% M:60.5 yrs F:56.4 yrs M:16.0 yrs F: 15.7 yrs	?RF+ ?eros ?nod	(34) (35)[1] (36) (37) (38) (39)
Nashville, TN, USA; 1982-1986	Cross-sectional, consecutive	Hospital clinic & referred private practice	ARA 1958	385[2] ?95%	37% 56 yrs 11 yrs	87% RF+ ?eros ?nod	(40) (41) (42) (43)[3]
Nashville, TN, USA; 1973	Prosp cohort 9 yrs, convenient	University clinic & private practice	ARA 1958	75 73%	29% 54.7 yrs 11.2 yrs	?RF + ?eros ?nod	(44)

Table 1 (cont)

Place, Time	Study Design, Sampling	Source population	RA Criteria	Size of sample, Response rate (%)	% male age (yrs) DD (yrs)	% RF+ve Erosive Nodular	Refs
Multiple USA centres, 1978-1986 (Boston-centre)	Prospective cohort 5 yrs, (some analysis cross-sectional), convenient	Hospital clinic & private practice, clinical trial subjects	ARA 1958	410[4] ?%	30% 50 yrs ?DD	?RF + ?eros ?nod	(45) (46)
Multiple USA centres, 1980's (Boston-centre)	Prospective cohort 1 yr, convenient	Hospital clinic & private practice	ARA 1958	1920 83%	22% 57 yrs 13 yrs	?RF + ?eros ?nod	(47)
Wichita, KN, USA, 1976+	Prospective cohort, minimum 2 visits, consecutive, some exclusions	Referred private practice	ARA 1958	1274 89.7%	29.5% 54.8 yrs 7.4 yrs	82% RF+ ?eros ?nod	(48) (49) (50) (51)[5]
Hanover, NH, USA 1980's	Cross-sectional, consecutive; some exclusions	Hospital clinic	ARA 1958	166 79%	32.5% 57.8 yrs 11 yrs	62 ?eros ?nod	(52) (53)
Edmonton, Alberta, Canada, 1985-1992	Sampling frame: cross-sectional analysis of a retrospective cohort onset in 1985	Hospital clinic & referred private practice	ACR 1987	128 69.6%	30% ?age 6.5 yrs	60% RF+ 90% eros 34% nod	(54) (55)

[a]DD: disease duration; eros: erosive; nod: nodular; ?: the data was not provided or not reported for the entire group, i.e., the result was stratified by some other measure (e.g., disease duration category, HLA-DR, SAARD usage, education category; no summary result was provided for the group as a whole, or, the variable was changed from a continuous to a categorical variable.

[1]The ARAMIS database has ongoing recruitment of patients with RA. It has been the source of numerous publications. The Leigh, *et al* 1991 publication is the source for the data in this table.

[2]Subset of patients (n = 200) from the hospital clinic.

[3]The results are from Callahan 1988.

[4]410 patients were seen at baseline; 5 years later 299 were followed up (RR 85% with known outcome).

[5]Ongoing recruitment of patients. Wolfe 1991 publication of all patients (first visit) shown.

changing some of these perceptions, and it is timely that we have the opportunity to tackle longitudinal and observational studies within OMERACT.

Fred Wolfe will consider the critical issues in longitudinal and observational studies. Importantly, he will show how LOS research objectives, design, and analysis and study variables specifically differ from RCT, illustrating why different core sets are required for RCT and LOS. Ted Pincus will discuss the concept of damage in rheumatoid arthritis LOS and appraise the various damage measures available. Desiree van der Heijde will summarize the preliminary core sets of variables for LOS developed from the results of a small pre-conference mail survey. Finally, Alan Silman will consider the design, analysis, and reporting elements of LOS and suggest the core items required for the design and reporting of LOS.

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Table 2. Selected RA series from Europe.

Place, Time	*Study Design, Sampling*	*Source population*	*RA Criteria*	*Size of sample RR (%)*	*% male age (yrs) DD (yrs)*	*% RF +ve Erosive Nodular*	*Refs*
Leyden, Netherlands 1958-62	Mixed prospective cohort, 6-8 years & case control design RF- vs RF+ RA, consecutive?, first visit	Hospital clinic, 2 visits	ARA 1958	130 RF-ve (from 153) 85% & 130 RF +	27% 61yrs male 55 yrs female 11 yrs male 14 yrs female	First visit 50% 62% xray abn 11%	(56)
Heinola, Finland, 1970-1973 1973-1975	Prospective cohort 0, 3, 7, 8 yrs; convenient	Referred community	ARA 1958	235 & 107	16-34% 45 (11) <6mths	71-82% RF+ 91% eros (at 3 years) ?nod	(57)** (58)** (59)** (60) (61) (62) (63)
Lund, Sweden, 1980's	Prospective cohort 2 & 5 yrs, convenient	Primary care referred community	ARA 1958	113 97%	33.6% 53 (13) yrs 11.2 mths	70% RF+ 91% eros ?nod	(64) (65) (66) (67) (68) (69)**
Jyvaskyla, 1983; Helsinki, 1986; Finland	Prospective cohort 6 yrs, consecutive	Hospital clinic	ARA 1958	142 98%	24.6% 45.6 yrs 7.9 mths	63% RF+ 94% eros 12% nod (current)	(70) (71) (72)
Nimegin, Netherlands 1985+	Prospective cohort 3 yrs, consecutive	Hospital clinic, (early disease)	ARA 1958/ ACR 1987	149 ?100 %	37% 53 yrs 0.5 yrs	81% RF+ ? eros ? nod	(4) (5) (6;73) (74) (75) (76)
Kuusamo, Finland' 1989	Cross-sectional, Drug registry	Community		103 88%	36.9% 59 (11.7)yrs 16 (9.5) yrs	88% RF+ 96% eros ?nod	(77) (78) (79)**
Enschede, Netherlands 1990	Cross-sectional, Patient registry	Rheumatology clinic	ACR 1987 66% Ú 4/7	282 71%	30% 61 (15.5) yr 8.8 (4.4) yr	51% RF+onset 37% eros onset 4% nod onset	(80)
Leiden, Netherlands 1954-81	Prospective cohort 25 yrs, convenient	Hospital clinic	ARA 1958	209	34% 54 yrs 8 yrs	~72% RF+ ?eros ?nod	(81)
Leiden, Netherlands 1982-1986	Prospective cohort 6 yrs, convenient	Hospital clinic, follow-up of case-control study	ARA 1958	132 95.6 %	0% ? age ? DD	84% RF+ 87% eros 9% nod (current)	(18) (19) (20) (21) (22)
Lorraine district, France, 1990	Cross-sectional, longitudinal data to follow, sampling frame of patients who met EURIDISS criteria	Primary & referred community, hospital inpatients, exclusion criteria	ACR 1987	116 70%	29% 54 yrs 1.9 (1.1) yrs	62 %RF+ ?eros 14% nod	(82)
Ancona, Italy, 1990's	Cross-sectional, convenient	University clinic		228 ?%	20% 59 (10.5) yr 6.4 (4.9) yr	72% RF+ ?eros ?nod	(83)
Milan, Italy, 1982-83	Cross-sectional, consecutive	Rheumatology clinic		315	29% 47.6 yrs 12 mths	46% RF+(current) 60% eros ?nod	(84)

Table 2 (cont)

Place, Time	Study Design, Sampling	Source population	RA Criteria	Size of sample, RR (%)	% male age (yrs) DD (yrs)	% RF +ve Erosive Nodular	Refs
Utrech, Netherlands 1990	Prospective cohort 6 yrs, consecutive	Hospital clinic in clinical trial	ACR 1987	128 ?100%	34% 57 (15) yrs < 1 yr	66 RF+ ?eros ?nod	(12) (13) (14)**
Groningen, Netherlands 1987-1992	Cross-sectional, longitudinal data to follow, sampling frame of patients who met EURIDISS criteria	Referred hospital outpatients		221, 283, 292, 80%	36% 54 yrs 21% <12 mths DD	81% RF+ ?eros 15% nod	(85) (86) (87)
Oslo, Norway, 1990's	Cross-sectional and longitudinal data, registry of patients who met EURIDISS criteria	Primary and referred community, hospital inpatients	ACR 1987	238 82% 1992, 75% 1994	26.2% 52(13.6) yr 2.3 (1.2) yr	73% RF+ ?eros 14% nod	(85) (88) (89) (90) (91) (92)
Oslo, Norway, 1991+,	Cross-sectional and longitudinal (retrospective and prospective), registry of all patients seen since 1980	Referred community, hospital inpatients, included patients aged 20-79 yrs	ACR 1987	1333 ~86% complete	20% 61 yrs 13.2 yrs	48% RF+ ?eros ?nod	(93) (94)

*DD: disease duration; eros: erosive; nod: nodular; ?: the data was not provided or not reported for the entire group, i.e., the result was stratified by some other measure (e.g., disease duration category, HLA-DR, SAARD usage, education category; no summary result was provided for the group as a whole, or, the variable was changed from a continuous to a categorical variable.
**Published report that was used for the table summary.

Table 3. Selected RA series from the United Kingdom and Republic of Ireland.

Place, Time	Study Design, Sampling	Source population	RA Criteria	Size of sample, RR (%)	% male age (yrs) DD (yrs)	% RF +ve Erosive Nodular	Refs
Droitwich, 1964-1966	Prospective cohort 10 yrs, consecutive	Hospital in-patients	1958 ARA class/def	112 80% RR at 10 yrs (15% dead at 10yrs 35% dead at 20 yrs)	28.6% 60%>50 yrs 64%< 5yrs (at time$_0$)	66% RF+ ?eros ?nod	(95;96)
Edinburgh and Aberdeen, UK, 1935-40	Retrospective case series, convenient	Hospital admissions	~ 3 of the 7 1958 ARA criteria, did not exclude AS	388	30.5% 59% 35-54 yr 21% <12 mths	?RF + ?eros ?nod	(97)

Table 3 (cont)

Place, Time	Study Design, Sampling	Source population	RA Criteria	Size of sample, RR (%)	% male age (yrs) DD (yrs)	% RF +ve Erosive Nodular	Refs
London??, UK, 1940's?	Prospective?, mean 6 yr follow-up, 4 visits	Hospital clinic?	?	250 No data	?male ?age ?DD	?RF + ?eros ?nod	(98)
Edinburgh, UK, 1948-1951	Prospective 2 yrs (1-4 yrs), 4 yrs, 6 yrs, 9 yrs, consecutive, first visit (some inception)	Hospital in-patients	?	307 at visit 1 92% 80% 65%	27% 50 yrs 7 yrs (31% <12 mths)	67% RF+ ?eros 13.5% nod at visit 4	(99) (100) (101) (102)
Bath, 1957-1963	Prospective cohort 3, 11, 15, 18, 20 and 25 yrs, consecutive	Hospital clinic	ARA 1958	100 65% (at 15 yrs)	36% 50.6 yrs 3.7 mths	88% RF+ ?eros ?nod	(7;8) (9;10) (103;104)
Middlesex1966-1971	Prospective cohort 4.5 and 15 yrs, consecutive	Hospital clinic	ARA 1958	102 79.7%	43% 50.5 yrs <1 yr	68% RF+ 71% $eros_{5yr}$ 81% $eros_{15yr}$ 20% nod	(1) (2) (3) (105)
London 1970's	Prospective cohort, 2 yrs,	Hospital clinic	ARA 1958	72 95%	33% 51 yrs 11 months	100% RF+ ?eros ?nod	(106)
London, 1970-80	Cross-sectional, consecutive (patient register)	Hospital clinic	ARA 1958	2088	29% ?age ?DD	71% RF+ 68% eros 24% nod	(107)
Middlesex 1970's (?)	Prospective cohort 3-15 yrs, consecutive	Hospital clinic	ARA 1958	151 ?%	35% 49.4 yrs <12 mths	~50 % RF+ ~65% eros ?nod	(108;109) (110)
London, England, 1976-79	Mixed prospective / case control, 8 yrs	Hospital clinic and inpatients	ARA 1958	108	? ? ?	?RF + ?eros ?nod	(23)
London 1980's	Cross-sectional, Consecutive	Hospital clinic	ARA 1958	85 ?100%	26% M:59(11) yrs F:56(13) yrs M:10(7) yrs F: 6(9) yrs	M F 10 14 RF+ 73 71 eros 50 19 nod	(111)
Glasgow, 1978-9	Prospective cohort 10 yrs, convenient, exclusion criteria	Hospital clinic, clinical trial	ARA 1958	123 75%	20% male 49 yrs 5 yrs	89% RF+ ?eros ?nod	(15)
Oxford 1980's	Cross-sectional, consecutive	Hospital clinic and in-patients	ARA 1958	102 ?98%	23% 56 (12) yrs 12.9 (8.9) yrs	?RF + ?eros ?nod	(112) (113)
Newcastle, 1984	Prospective cohort:: 5 yrs. Consecutive	Referred Hospital clinic	ARA 1958	201 71%	18% 55.4 yrs 12.7 yrs	?RF + ?eros ?nod	(114)
Stoke-on-Trent, 1980's	Prosp cohort: 5-9 yrs Consecutive	Hospital clinic in clinical trial	ARA 1958	127 ?%RR	32% 51 yrs 5 yrs	64 ? 29	(115)
UK, 1989	Cross-sectional, Convenient (from a twin study of RA)	Primary & referred community	ACR 1987	201	~21% ~53 yrs ?DD	87% RF+ 81% eros ?nod	(116;117)

Table 3 (cont)

Refs	Place, Time	Study Design, Sampling	Source population	RA Criteria	Size of sample, RR (%)	% male age (yrs) DD (yrs)	% RF +ve Erosive Nodular	Refs
(98)	UK 1988-	Prospective cohort, consecutive	Nine hospital clinics	ACR 1987	421 ?%RR	81%	81% RF+ 72% eros 21% nod	(118)
(99) (100) (101) (102)	Norwich 1990-1993	Prospective cohort 1 yr, consecutive	Primary & referred community	ACR 1987	175 73%	29% 59 yrs < 6 mths	?RF+ 36 (1 yr) ?nod	(11)
(7;8) (9;10) (103;104)	Dublin 1984-1987	Prospective cohort 6 yrs, consecutive	Hospital clinic *exclusions: Steroids or SAARDS	ARA 1958	40 70%	30% 46.4(13.3) yrs 2.4 (2.9) yrs	93% RF+ ?eros ?nod	(119)

*DD: disease duration; eros: erosive; nod: nodular; ?: the data was not provided or not reported for the entire group, i.e., the result was stratified by some other measure (e.g., disease duration category, HLA-DR, SAARD usage, education category; no summary result was provided for the group as a whole, or, the variable was changed from a continuous to a categorical variable.

REFERENCES

1. Fleming A, Crown JM, Corbett M. Incidence of joint involvement in early rheumatoid arthritis. Rheumatol Rehabil 1976;15:92-6.
2. Fleming A, Crown JM, Corbett M. Early rheumatoid disease. I. Onset. Ann Rheum Dis 1976;35:357-60.
3. Brook A, Corbett M. Radiographic changes in early rheumatoid disease. Ann Rheum Dis 1977;36:71-3.
4. Van der Heijde DM, van't Hof M, van de Putte L, et al. Judging disease activity in clinical practice in rheumatoid arthritis: first step in the development of a disease activity score. Ann Rheum Dis 1990;49:916-20.
5. van der Heijde DM, van Riel PL, van Leeuwen MA, van't Hof M, van Rijswijk MH, van de Putte L. Older versus younger onset rheumatoid arthritis: results at onset and after 2 years of a prospective follow up study of early rheumatoid arthritis. J Rheumatol 1991;18:1285-9.
6. van der Heijde DM, van't Hof M, van Riel P, van Leeuwen M, van Rijswijk M, van de Putte L. Validity of single variables and composite indices for measuring disease activity in rheumatoid arthritis. Ann Rheum Dis 1992;51:177-81.
7. Jacoby RK, Jayson MI, Cosh JA. Onset, early stages, and prognosis of rheumatoid arthritis: a clinical study of 100 patients with 11-year follow-up. BMJ 1973;2(858):96-100.
8. Jacoby RK, Cosh JA, Jayson MI. Prognosis of rheumatoid arthritis. A prospective survey over 11 years. Ann Rheum Dis 1973;32:391.
9. Rasker JJ, Cosh JA. The natural history of rheumatoid arthritis: a fifteen year follow-up study. The prognostic significance of features noted in the first year. Clin Rheumatol 1984;3:11-20.
10. Rasker JJ, Cosh JA. The natural history of rheumatoid arthritis over 20 years. Clinical symptoms, radiological signs, treatment, mortality and prognostic significance of early features. Clin Rheumatol 1987;6 Suppl 2:5-11.
11. Brennan P, Harrison B, Barrett E, et al. A simple algorithm to predict the development of radiological erosions in patients with early rheumatoid arthritis: prospective cohort study. BMJ 1996;313:471-6.
12. van der Heide A, Jacobs JW, Schenk Y, Bijlsma JW. Endpoint measures in rheumatoid arthritis clinical trials: group summary and individual patient analysis. J Rheumatol 1994;21:2195-9.
13. van der Heide A, Jacobs JW, Albada-Kuipers G, Kraaimaat FW, Geenen R, Bijlsma JW. Physical disability and psychological well-being in recent onset rheumatoid arthritis. J Rheumatol 1994; 21:28-32.
14. van der Heide A, Remme CA, Hofman DM, Jacobs JW, Bijlsma JW. Prediction of progression of radiologic damage in newly diagnosed rheumatoid arthritis. Arthritis Rheum 1995;38:1466-74.
15. Capell HA, Murphy EA, Hunter JA. Rheumatoid arthritis: workload and outcome over 10 years. Q J Med 1991;79:461-76.
16. Dixon J, Bird H, Pickup M, Wright V. A human model screening system for the detection of specific antirheumatic activity. Semin Arthritis Rheum 1982;12:185-90.
17. Dixon JS, Hayes S, Constable PD, Bird HA. What are the "best" measurements for monitoring patients during short-term second-line therapy? Br J Rheumatol 1988;27:37-43.
18. van Zeben D, Hazes J, Zwinderman A, et al. Association of HLA-DR4 with a more progressive disease course in patients with RA. Results of a followup study. Arthritis Rheum 1991;34:822-30.
19. van Zeben D, Hazes JM, Breedveld FC, Zwinderman AH, Vandenbroucke JP. Which clinical variables contribute to the physician's assessment of medium term outcome in rheumatoid arthritis? J Rheumatol 1993;20:33-9.
20. van Zeben D, Hazes JM, Zwinderman AH, Vandenbroucke JP, Breedveld FC. Factors predicting outcome of rheumatoid arthritis: results of a followup study. J Rheumatol 1993;20:1288-96.
21. Vliet Vlieland TP, Buitenhuis NA, van Zeben D, Vandenbroucke JP, Breedveld FC, Hazes JM. Sociodemographic factors and the outcome of rheumatoid arthritis in young women. Ann Rheum Dis 1994;53:803-6.
22. van Zeben D, Hazes JH, Zwinderman AJ, Vandenbroucke JP, Breedveld FC. The severity of rheumatoid arthritis: a 6 year followup study of younger women with symptoms of recent onset. J Rheumatol 1994;21:1620-5.
23. Erhardt CC, Mumford PA, Venables PJ, Maini RN. Factors predicting a poor life prognosis in rheumatoid arthritis: an eight year prospective study. Ann Rheum Dis 1989;48:7-13.
24. Short C, Beckman W, Bauer W. Gold therapy in rheumatoid arthritis. New Engl J Med 1946;235:362-8.
25. Short C, Bauer W. The course of rheumatoid arthritis in patients receiving simple medical and orthopedic measures. New Engl J Med 1948;238:142-8.
26. Cobb S, Anderson F, Bauer M. Length of life and cause of death in rheumatoid arthritis. New Engl J Med 1953;249:553-6.
27. Mainland D. Use of case records in the study of therapy and other features in chronic disease. Ann Rheum Dis 1955;14:337-51.
28. Ali-Gombe A, Adebajo A, Silman A. Methodological problems in comparing the severity of rheumatoid arthritis between populations.

Br J Rheumatol 1995;34:781-4.
29. Lassere M, Wells G, Tugwell P, Edmonds J. Percentile curve reference charts of physical function: rheumatoid arthritis population. J Rheumatol 1995;22:1241-6.
30. Ragan C. The general management of rheumatoid arthritis. JAMA 1949;141:124-7.
31. Ragan C, Farrington E. The clinical features of rheumatoid arthritis. JAMA 1962;181:663-7.
32. Masi A, Maldonado-Cocco J, Kaplan S, Feigenbaum S, Chandler R. Prospective study of the early course of rheumatoid arthritis in young adults: comparison of patients with and without rheumatoid factor positivity at entry and identification of variables correlating with outcome. Semin Arthritis Rheum 1976;5:299-326.
33. Feigenbaum SL, Masi AT, Kaplan SB. Prognosis in rheumatoid arthritis. A longitudinal study of newly diagnosed younger adult patients. Am J Med 1979;66:377-84.
34. Leigh JP, Fries JF. Predictors of disability in a longitudinal sample of patients with rheumatoid arthritis. Ann Rheum Dis 1992;51:581-7.
35. 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.
36. Sherrer YS, Bloch DA, Mitchell DM, Young DY, Fries JF. The development of disability in rheumatoid arthritis. Arthritis Rheum 1986;29:494-500.
37. Sherrer YS, Bloch DA, Mitchell DM, Roth SH, Wolfe F, Fries JF. Disability in rheumatoid arthritis: comparison of prognostic factors across three populations. J Rheumatol 1987;14:705-9.
38. Wolfe F, Mitchell DM, Sibley JT, et al. The mortality of rheumatoid arthritis. Arthritis Rheum 1994;37:481-94.
39. Leigh JP, Fries JF. Education level and rheumatoid arthritis: evidence from five data centers. J Rheumatol 1991;18:24-34.
40. Callahan LF, Pincus T. Formal education level as a significant marker of clinical status in rheumatoid arthritis. Arthritis Rheum 1988;31:1346-57.
41. 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.
42. Kaye JJ, Callahan LF, Nance EJ, Brooks RH, Pincus T. Rheumatoid arthritis: explanatory power of specific radiographic findings for patient clinical status. Radiology 1987;165:753-8.
43. Fuchs H, Kaye J, Callahan L, Nance P, Pincus T. Evidence of significant radiographic damage in rheumatoid arthritis in the first 2 years of disease. J Rheumatol 1989;16:589-91.
44. 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.
45. Mason J, Anderson J, Meenan R. A model of health status for rheumatoid arthritis. Arthritis Rheum 1988;31:714-20.
46. Guccione AA, Anderson JJ, Anthony JM, Meenan RF. The correlates of health perceptions in rheumatoid arthritis. J Rheumatol 1995;22:432-9.
47. Kazis LE, Callahan LF, Meenan RF, Pincus T. Health status reports in the care of patients with rheumatoid arthritis. J Clin Epidemiol 1990;43:1243-53.
48. Wolfe F, Kleinheksel SM, Cathey MA, Hawley DJ, Spitz PW, Fries JF. The clinical value of the Stanford Health Assessment Questionnaire Functional Disability Index in patients with rheumatoid arthritis. J Rheumatol 1988;15:1480-8.
49. Hawley DJ, Wolfe F. Anxiety and depression in patients with rheumatoid arthritis: a prospective study of 400 patients. J Rheumatol 1988;15:932-41.
50. 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.
51. Wolfe F, Cathey MA. The assessment and prediction of functional disability in rheumatoid arthritis. J Rheumatol 1991;18:1298-306.
52. Regan Smith MG, O'Connor GT, Kwoh CK, Brown LA, Olmstead EM, Burnett JB. Lack of correlation between the Steinbrocker staging of hand radiographs and the functional health status of individuals with rheumatoid arthritis. Arthritis Rheum 1989; 32:128-33.
53. Kwoh CK, O'Connor GT, Regan Smith MG, et al. Concordance between clinician and patient assessment of physical and mental health status. J Rheumatol 1992;19:1031-7.
54. Suarez Almazor ME, Soskolne CL, Saunders LD, Russell AS. Outcome in rheumatoid arthritis. A 1985 inception cohort study. J Rheumatol 1994;21:1438-46.
55. Suarez-Almazor M, Tao S, Moustarah F, Russell AS, Maksymowych W. HLA-DR1, DR4, and DRB1 disease related subtypes in RA. Association with susceptibility but not severity in a city wide community based cohort. J Rheumatol 1995;22:2027-33.
56. Cats A, Hazevoet H. Significance of positive tests for rheumatoid factors in the prognosis of RA. A follow up study. Ann Rheum Dis 1970;29:254-60.
57. Luukkainen R, Kaarela K, Isomaki H, et al. The prediction of radiological destruction during the early stage of rheumatoid arthritis. Clin Exp Rheumatol 1983;1:295-8.
58. Luukkainen R, Isomaki H, Kajander A. Prognostic value of the type of onset of rheumatoid arthritis. Ann Rheum Dis 1983;42:274-5.
59. Nissila M, Isomaki H, Kaarela K, Kiviniemi P, Martio J, Sarna S. Prognosis of inflammatory joint diseases. A three-year follow-up study. Scand J Rheumatol 1983;12:33-8.
60. Kaarela K, Sarna S. Correlations between clinical facets of outcome in rheumatoid arthritis. Clin Exp Rheumatol 1993;11:643-4.
61. Kaarela K, Luukkainen R, Koskimies S. How often is seropositive rheumatoid arthritis an erosive disease? A 17-year followup study. J Rheumatol 1993;20:1670-3.
62. Kaarela K. Prognostic factors and diagnostic criteria in early rheumatoid arthritis. Scand J Rheumatol 1985;57 Suppl:1-54.
63. Isomaki HA. An epidemiologically based follow-up study of recent arthritis. Incidence, outcome and classification. Clin Rheumatol 1987;6 Suppl 2:53-9.
64. Eberhardt K, Svensson B, Moritz U. Functional assessment of early RA. Br J Rheumatol 1988;27:364-71.
65. Eberhardt KB, Svensson B, Truedsson L, Wollheim FA. The occurrence of rheumatoid factor isotypes in early definite rheumatoid arthritis — no relationship with erosions or disease activity. J Rheumatol 1988;15:1070-4.
66. Eberhardt KB, Rydgren LC, Pettersson H, Wollheim FA. Early rheumatoid arthritis — onset, course, and outcome over 2 years. Rheumatol Int 1990;10:135-42.
67. Eberhardt K, Truedsson L, Pettersson H, et al. Disease activity and joint damage progression in early RA: relation to IgG, IgA, and IgM rheumatoid factor. Ann Rheum Dis 1990;49:906-9.
68. Eberhardt KB, Fex E. Functional impairment and disability in early rheumatoid arthritis development over 5 years. J Rheumatol 1995;22:1037-42.
69. Fex E, Johnson U, Johnson K, Eberhardt K. Development of radiographic damage during the first 5-6 years of rheumatoid arthritis. A prospective follow up study of a Swedish cohort. Br J Rheumatol 1996;35:1106-15.
70. Mottonen TT. Prediction of erosiveness and rate of development of new erosions in early rheumatoid arthritis. Ann Rheum Dis 1988;47:648-53.
71. Mottonen 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.
72. Paimela L, Leirisalo-Repo M, Helve T, Koskimies S. The prognostic value of HLA DR4 and B27 antigens in early rheumatoid arthritis. Scand J Rheumatol 1993;22:220-4.
73. van der Heijde D, van Leeuwen MA, van Riel PL, et al. Biannual radiographic assessments of hands and feet in a three-year prospective followup of patients with early rheumatoid arthritis. Arthritis Rheum 1992;35:26-34.
74. van Leeuwen MA, van Rijswijk MH, van der Heijde D, et al. The acute-phase response in relation to radiographic progression in early rheumatoid arthritis: a prospective study during the first three years of the disease. Br J Rheumatol 1993;32 Suppl 3:9-13.
75. van Leeuwen MA, van der Heijde D, van Rijswijk MH, et al. Interrelationship of outcome measures and process variables in early rheumatoid arthritis. A comparison of radiologic damage, physical disability, joint counts, and acute phase reactants. J Rheumatol 1994;21:425-9.
76. van Riel P, van der Heijde D, Nuver-Zwart I, van de Putte L. Radiographic progression in rheumatoid arthritis: results of 3 comparative trials. J Rheumatol 1995;22:1797-9.
77. Wolfe, F. Data collection and utilization: a methodology for clinical practice and clinical research. In: Wolfe F, Pincus T, editors. Rheumatoid arthritis: pathogenesis, assessment, outcome and treatment. New York: Marcel Dekker;1994:463-514.
78. Hakala M, Nieminen P, Manelius J. Joint impairment is strongly correlated with disability measured by self-report questionnaires. Functional status assessment of individuals with rheumatoid arthritis in a population based series. J Rheumatol 1993;21:64-9.
79. Hakala M, Nieminen P, Koivisto O. More evidence from a community based series of better outcome in rheumatoid arthritis. Data on the effect of multidisciplinary care on the retention of functional ability. J Rheumatol 1994;21:1432-7.
80. Borstlap M, van de Laar M, Zant J, van der Korst J. Components of health: an analysis in rheumatoid arthritis using quality of life questionnaires and clinical and laboratory variables. Ann Rheum Dis 1993;52:650-4.
81. Vandenbroucke J, Hazevoet H, Cats A. Survival and cause of death in rheumatoid arthritis: a 25 year prospective followup. J Rheumatol 1984;11:158-61.
82. Guillemin F, Suurmeijer T, Krol B, et al. Functional disability in early rheumatoid arthritis: description and risk factors. J Rheumatol 1994;21:1051-5.
83. Salaffi F, Ferraccioli G, Peroni M, Carotti M, Bartoli E, Cervini C. Progression of erosion and joint space narrowing scores in rheumatoid arthritis assessed by nonlinear models. J Rheumatol 1994;21:1626-30.
84. Caruso I, Santandrea S, Puttini PS, et al. Clinical, laboratory and radiographic features in early rheumatoid arthritis. J Rheumatol 1990;17:1263-7.
85. Smedstad L, Moum T, Guillemin F, et al. Correlates of functional disability in early rheumatoid arthritis: study of 706 patients in four European countries. Br J Rheumatol 1996;35:746-51.
86. 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.
87. Sanderman K, Suurmeijer T, Doeglas D, Van Rijswijk M, van Leeuwen M. Disease characteristics, level of self-esteem and psychological well-being in rheumatoid arthritis patients. Scand J Rheumatol 1994;23:8-12.
88. Smedstad L, Vaglum P, Kvien T, Moum T. The relationship between self-reported pain and sociodemographic variables, anxiety and depressive symptoms in rheumatoid arthritis. J Rheumatol 1995;22:514-20.
89. Smedstad L, Kvien T, Moum T, Vaglum P. Life events, psychosocial factors, and demographic variables in early rheumatoid arthritis: relations to one year changes to functional disability. J Rheumatol 1995;22:2218-25.
90. Smedstad L, Kvien T, Moum T, Vaglum P. Correlates of patients' global assessment of arthritis impact. Scand J Rheumatol 1997;26:259-65.
91. Smedstad L, Kvien T, Moum T, Vaglum P. The impact of early rheumatoid arthritis on psychosocial distress. A comparison of 238 patients with early RA and 116 matched controls. Scand J Rheumatol 1996;25:377-82.
92. Smedstad L, Vaglum P, Moum T, Kvien T. The relationship between psychological distress and traditional clinical variables: a 2 year prospective study of 216 patients with early rheumatoid arthritis. Br J Rheumatol 1997;36:1-8.
93. Kvien T, Glennas A, Knudsrod O, Smedstad LM, Mowinckel P, Forre O. The prevalence and severity of rheumatoid arthritis in Oslo. Scand J Rheumatol 1997;26:412-18.
94. Uhlig T, Kvien T, Glennas A, Smedstad LM, Forre O. The incidence and severity of rheumatoid arthritis. Results from a county register in Oslo, Norway. J Rheumatol 1998;25:1078-84.
95. Scott DL, Coulton BL, Chapman JH, Bacon PA, Popert AJ. The long-term effects of treating rheumatoid arthritis. J Roy Coll Physicians Lond 1983;17:79-85.
96. Scott DL, Symmons DP, Coulton BL, Popert AJ. Long-term outcome of treating rheumatoid arthritis: results after 20 years. Lancet 1987;1:1108-11.
97. Sclater J. An analysis of 388 cases of rheumatoid arthritis. Ann Rheum Dis 1943;3:195-206.
98. Bywaters E, Dresner E. The prognosis in rheumatoid arthritis. Q J Med 1952;21:463.
99. Duthie J, Thompson M, Weir MFW. Medical and social aspects of the treatment of rheumatoid arthritis. With special reference to factors affecting prognosis. Ann Rheum Dis 1955;14:133-49.
100. Duthie J, Brown P, Knox J, Thompson M. Course and prognosis in rheumatoid arthritis. Ann Rheum Dis 1957;16:411-24.
101. Brown P, Duthie J. Variations in the course of rheumatoid arthritis. Ann Rheum Dis 1958;17:359-64.
102. Duthie J, Brown P, Truelove L, Baragar F, Lawrie A. Course and prognosis in rheumatoid arthritis. A further report. Ann Rheum Dis 1964;23:193-204.
103. Reilly PA, Cosh JA, Maddison PJ, Rasker JJ, Silman AJ. Mortality and survival in rheumatoid arthritis: a 25 year prospective study of 100 patients. Ann Rheum Dis 1990;49:363-9.
104. Rasker J, Cosh J. Long-term effects of treating rheumatoid arthritis. Baillieres Clin Rheumatol 1992;6:141-60.
105. 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.
106. Reeback J, Silman A. Predictors of outcome at two years in patients with rheumatoid arthritis. J Roy Soc Med 1984;77:1002-5.
107. Silman A, Davies P, Currey HL, Evans SJ. Is rheumatoid arthritis becoming less severe? J Chronic Dis 1983;36:891-7.
108. Young A, Jaraquemada D, Awad J, et al. Association of HLA-DR4/Dw4 and DR2/Dw2 with radiologic changes in a prospective study of patients with rheumatoid arthritis. Preferential relationship with HLA-Dw rather than HLA-DR specificities. Arthritis Rheum 1984;27:20-5.
109. Young A, Bielawska C, Corbett M, Roitt I. A prospective study of early onset rheumatoid arthritis over fifteen years: prognostic features and outcome. Clin Rheumatol 1987;6 Suppl 2:12-9.
110. Young A, Corbett M, Winfield J, et al. A prognostic index for erosive changes in the hands, feet, and cervical spines in early rheumatoid arthritis. Br J Rheumatol 1988;27:94-101.
111. Thompson PW, Pegley FS. A comparison of disability measured by

the Stanford Health Assessment Questionnaire disability scales (HAQ) in male and female rheumatoid outpatients. Br J Rheumatol 1991;30:298-300.
112. Ziebland S, Fitzpatrick R, Jenkinson C, Mowat A, Mowat A. Comparison of two approaches to measuring change in health status in rheumatoid arthritis: the Health Assessment Questionnaire (HAQ) and modified HAQ. Ann Rheum Dis 1992;51:1202-5.
113. Fitzpatrick R, Ziebland S, Jenkinson C, Mowat A, Mowat A. A comparison of the sensitivity to change of several health status instruments in rheumatoid arthritis. J Rheumatol 1993;20:429-36.
114. 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.
115. Hassell AB, Davis MJ, Fowler PD, et al. The relationship between serial measures of disease activity and outcome in rheumatoid arthritis. Q J Med 1993;86:601-7.
116. MacGregor A, Ollier W, Thomson W, Jawaheer D, Silman A. HLA-DRB1*0401/0404 genotype and rheumatoid arthritis: increased association in men, young age at onset, and disease severity. J Rheumatol 1995;22:1032-6.
117. MacGregor AJ, Bamber S, Silman AJ. A comparison of the performance of different methods of disease classification for rheumatoid arthritis. Results of an analysis from a nationwide twin study. J Rheumatol 1994;21:1420-6.
118. Young A. Short-term outcomes in recent-onset rheumatoid arthritis. Br J Rheumatol 1995;34 Suppl 2:79-86.
119. Fitzgerald O, Bresnihan B. Clinical improvement and radiological deterioration in rheumatoid arthritis: evidence that the pathogenesis of synovial inflammation and articular erosion may differ. Br J Rheumatol 1996;35:1263-8.

Papers presented at the OMERACT IV Conference, Cancun, Mexico, April 16–20, 1998:

Part 1: Outcome Measures in Rheumatology — Introductory Papers
Part 2: Measures and Methods in Longitudinal / Observational Studies
Systemic Lupus Erythematosus: Core Set and Response
Part 3: Rheumatoid Arthritis: Response and Imaging
Part 4: Ankylosing Spondylitis: Core Set and Response

Parts 3 and 4 will appear in the March and April issues of *The Journal.*