

Cross-sectional study of rheumatoid arthritis treatment in a university hospital

W T FRIESEN,¹ Y A HEKSTER,² L B A VAN DE PUTTE,³ AND F W J GRIBNAU⁴

From the ¹School of Pharmacy, University of Tasmania, Hobart, Australia; and Departments of ²Clinical Pharmacy, ³Rheumatology, and ⁴Pharmacology, Sint Radboud University Hospital, Nijmegen, the Netherlands

SUMMARY Drug prescribing patterns for the management of inpatients and outpatients with rheumatoid arthritis (RA) were investigated. The population of patients resembled published epidemiological descriptions of RA patients with respect to age and sex distribution. Multiple drug therapy was common in the treatment of both hospitalised and clinic patients. 90% of all patients with RA received non-steroidal anti-inflammatory drug (NSAID) therapy, indomethacin and naproxen being the two most frequently prescribed NSAIDs for both in- and outpatients. The vast majority of inpatients (85%) and outpatients (79%) received slow-acting anti-rheumatic drug (SAARD) treatment. 13% of hospitalised patients received H₂-antagonist drugs in addition to their NSAIDs. A high proportion of inpatients (46%) received oral corticosteroids in the management of their rheumatoid arthritis, while only 15% of clinic patients were prescribed corticosteroids.

Key words: anti-rheumatic drugs, drug utilisation, drug prescribing, non-steroidal anti-inflammatory drugs, slow-acting antiarthritic drugs, outpatients, inpatients.

The prevalence of chronic disease in modern industrialised nations is increasing, and among these intractable conditions rheumatoid arthritis stands out as a major cause of multiple medical problems.¹ An estimated 1-3% of the population is affected by this disease, while about two-thirds of cases suffer significant social and economic disadvantages.^{1,2}

Although some therapeutic measures appear to improve the clinical picture, the influence of drug therapy on the course of the disease is still uncertain.^{2,3} The twofold goals of treatment are well established,⁴ i.e., firstly, suppression of pain and inflammation with non-steroidal anti-inflammatory drugs (NSAID) and secondly, induction of remission of the disease with disease modifying drugs if the disease progresses. There is a bewildering array of NSAIDs available, and by comparison the repertoire of disease modifying slow-acting anti-rheumatic drugs (SAARD) is small.

Considerable differences exist in prescribing practices, for example between countries⁵⁻⁷ and between hospital and community-based practice.⁸ Although data are available on the drug utilisation of different classes of antiarthritic drugs, only limited information is available on prescribing practices specifically for rheumatoid arthritis.

This paper describes the results of a study establishing baseline data on the drug treatment patterns for rheumatoid arthritis patients in the rheumatology ward and the rheumatology outpatient clinic of a Dutch university hospital.

Patients and methods

INPATIENT DATA COLLECTION

Patient data

All patients admitted to the rheumatology ward over a one-year period (June 1983 to May 1984) were surveyed retrospectively. Patient details such as age, sex, diagnosis details, and duration of hospitalisation were determined from medical records. Only patients with probable, definite, or

Accepted for publication 4 December 1984.
Correspondence to Dr W T Friesen, School of Pharmacy, University of Tasmania, PO Box 252C, Hobart, Tasmania 7001, Australia.

classical rheumatoid arthritis according to the American Rheumatism Association (ARA) criteria⁹ were admitted to the survey.

Drug prescribing data

Individual medication registration sheets are stored in the pharmacy department by ward specialty (i.e., rheumatology) and per time period (quarter). Drug prescribing details were compiled directly from these sheets as follows: antiarthritic drug or drug combinations, prescribed daily dosages, and all coprescribed drugs for each patient.

OUTPATIENT DATA COLLECTION

Patient data

A one-month prospective survey of rheumatoid arthritis patients treated in the Sint Radboud Hospital Outpatient Clinic was conducted. Only patients with definite or classical rheumatoid arthritis⁹ were admitted to the survey. The data represent a cross-sectional definition of a clinic population. The following patient information was compiled: age, sex, and the current patient disability status based on the ARA functional class¹⁰ as assessed by the physician during the consultation.

Drug prescribing data

At the time of the consultation the drug prescribing data were recorded as follows: antiarthritic drug or drug combinations, dosage form, prescribed daily dosage, frequency, and all coprescribed drugs. Patterns of drug prescribing of individual drugs and particular drug combinations were then determined.

Results

PATIENT CHARACTERISTICS

Inpatients

A total of 166 patients were admitted to the rheumatology ward during the 12-month survey period. Of these, 108 patients (65%) had a diagnosis of probable, definite, or classical rheumatoid arthritis and were included in the study. The age and sex distribution of the RA patients admitted to the rheumatology ward is shown in Fig. 1a. The duration of hospitalisation averaged 34.6 days and ranged between two and 206 days. The female: male ratio for inpatients is 2.2:1.

Outpatients

A total of 153 definite or classical rheumatoid arthritis patients treated in the outpatient clinic during the month of June 1984 were surveyed. The age and sex distribution of these patients is shown in Fig. 1b. The female: male ratio for outpatients is 2.8:1.

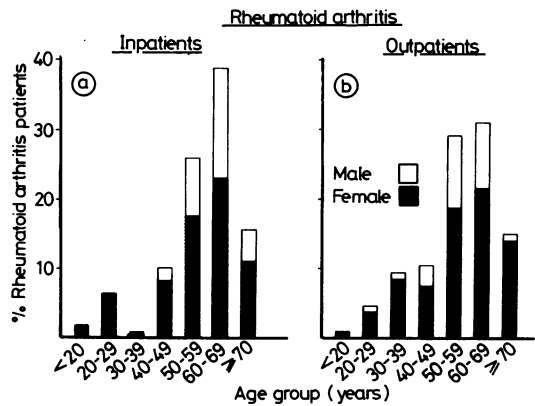


Fig. 1 (a) The age and sex distribution of rheumatoid arthritis inpatients admitted to the rheumatology ward during a 12-month period (June 1983 – May 1984). n=108. (b) The age and sex distribution of rheumatoid arthritis outpatients treated in the rheumatology clinic during a one-month period. n=153.

The disability distribution of outpatients by age and sex according to the ARA functional capacity rating is shown in Fig. 2. It can be seen that the majority of patients fall into disability rating 2, and no patient under the age of 40 had a disability rating of 3. No patient had a disability rating of 4.

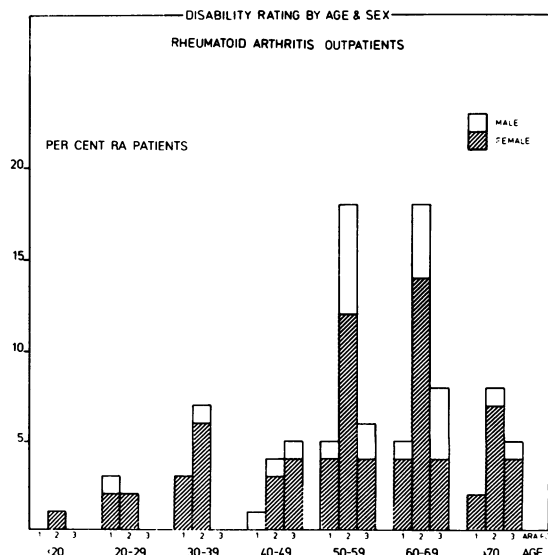


Fig. 2 The disability rating (ARA functional class) by age and sex for rheumatoid arthritis outpatients treated in the rheumatology clinic during a one-month period. n=153.

DRUG UTILISATION DATA

Patterns of drug treatment

Fig. 3a outlines the current use of antirheumatic drug therapy for rheumatoid arthritis inpatients, indicating that polypharmacy is a common practice in the management of a hospitalised RA population. About 90% of the RA inpatients received NSAID therapy (10% receiving a two-drug NSAID combination usually as one drug administered orally and the second one rectally at night; see Fig. 4a). 11% of the patients did not receive any NSAID therapy during their hospital stay.

Fig. 3a also shows that the vast majority of inpatients (85%) received specific remittive therapy in the form of slow-acting antirheumatic drugs, and that almost half of the inpatients (46%) received oral corticosteroid therapy (usually in a 5.0–7.5 mg daily maintenance dose of prednisolone) during their hospital stay. About one-third of all RA inpatients (36%) were treated with a NSAID+SAARD+oral corticosteroid combination, while an additional 40% of patients were prescribed NSAID+SAARD drug regimens. Only 1% of admitted patients had no specific antirheumatic therapy.

Fig. 3b outlines the use of antirheumatic drug therapy for rheumatoid arthritis outpatients in the rheumatology clinic during the sample period. Like the inpatients 90% of these patients also received

NSAID therapy. 79% of clinic patients received SAARD therapy, and the most frequently prescribed drug regimen (63% of clinic patients) was NSAID+SAARD combination therapy. 15% of all clinic patients were prescribed oral corticosteroids in addition to NSAID or SAARD therapy, or both. A further 15% of outpatients received NSAID drugs alone. 4% of patients received SAARD therapy alone, while only 3% of patients were not prescribed any specific antirheumatic treatment.

NSAID prescribing data

Fig. 4a presents a complete summary of NSAID prescribing frequency for inpatients. Indomethacin was the most frequently prescribed NSAID (36% of patients), and together with naproxen (24% of patients) these two drugs accounted for about two-thirds of the NSAIDs prescribed. 9% of hospitalised patients received piroxicam, while only 5% of patients were prescribed ibuprofen.

Fig. 4b shows the frequency distribution of NSAID prescribing for outpatients. The largest single NSAID used was indomethacin (41% of patients), and together with naproxen (22% of patients) these two drugs made up about 70% of the total use of NSAIDs in clinic patients. Ibuprofen was prescribed for 12% of outpatients, while newer agents accounted for a further 14% of NSAID usage.

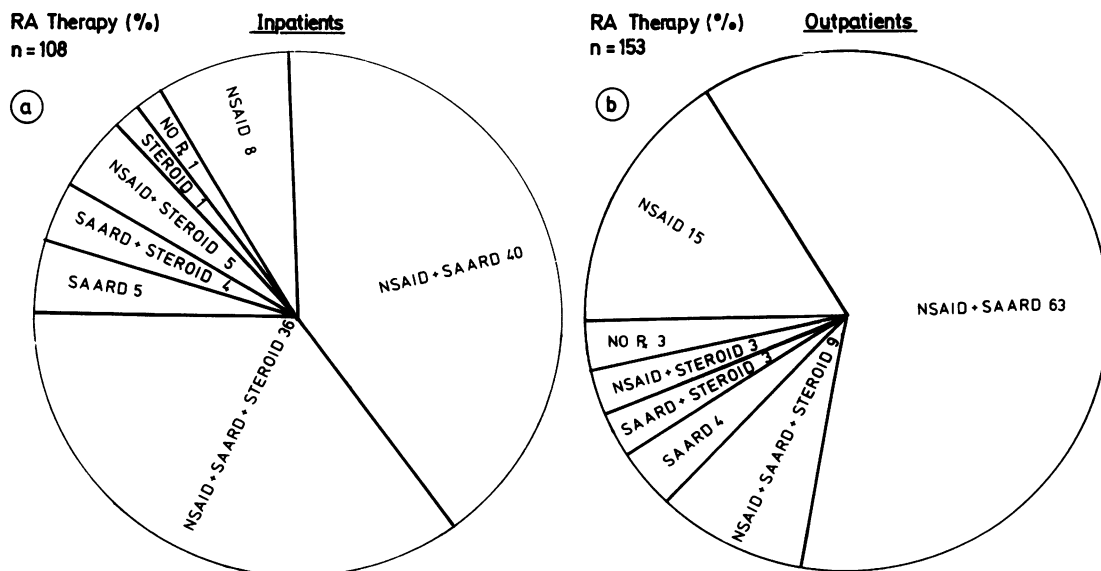


Fig. 3 Prescribing pattern of antirheumatic drug usage for the treatment of RA (a) inpatients and (b) outpatients. The numbers refer to the percentage of patients receiving a particular drug category or combination.

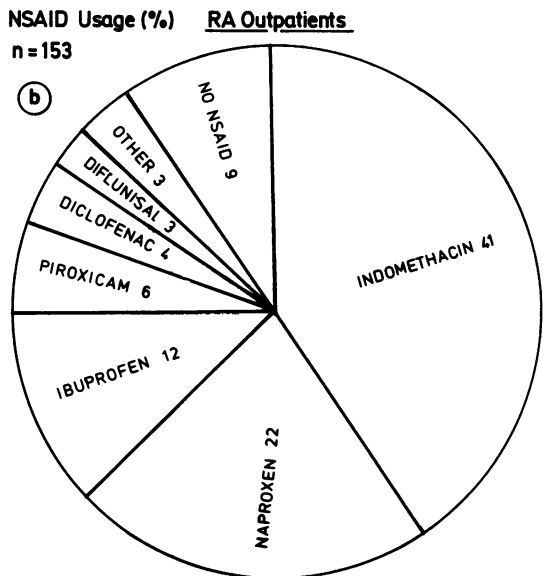
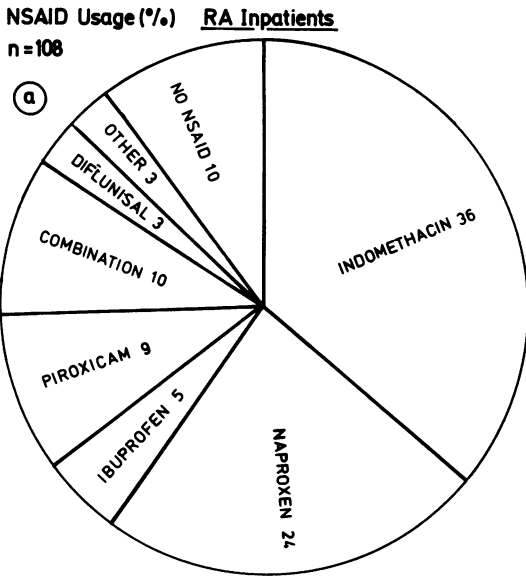


Fig. 4 Prescribing pattern of non-steroidal anti-inflammatory drug (NSAID) usage for the treatment of rheumatoid arthritis inpatients and outpatients. The numbers refer to the percentage of patients receiving a particular drug or combination.

SAARD prescribing data

The prescribing frequency of the SAARDs for inpatients, which from Fig. 3a can be seen to be used mostly in multiple drug therapy, is summarised in

Fig. 5a. Azathioprine had the highest usage (38% of SAARD-treated patients), followed by aurothioglucose (34%), and D-penicillamine (26%).

The outpatient prescribing frequency of indi-

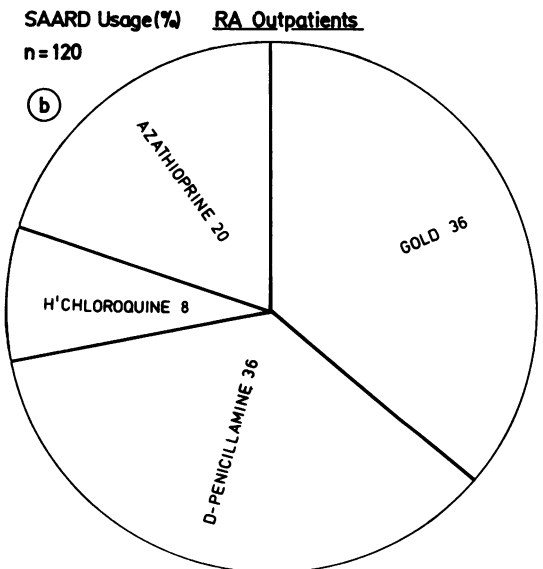
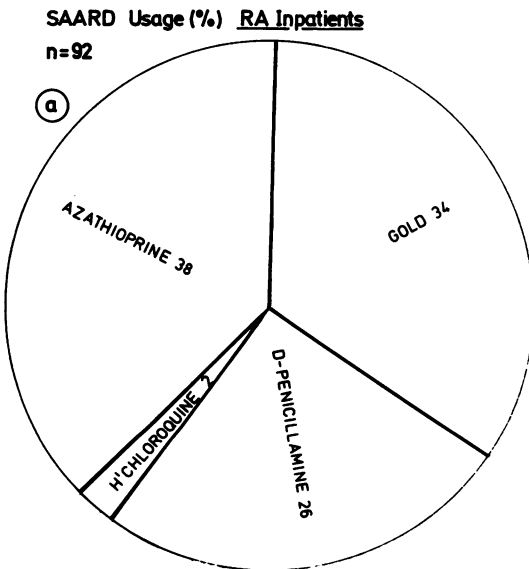


Fig. 5 Prescribing pattern for slow-acting antiarthritic drug (SAARD) usage for the treatment of rheumatoid arthritis inpatients and outpatients. The numbers refer to the percentage of patients receiving a particular drug.

Table 1 *Rheumatoid arthritis coprescribing data for inpatients*

<i>Drug combination</i>	<i>Percentage of patients (no. of patients)</i>
NSAID + cimetidine	10.2 (11)
NSAID + cimetidine + antacid	2.8 (3)
NSAID + antacid	14.8 (16)
NSAID + other GI therapy	1.9 (2)
NSAID + iron supplement	17.6 (19)
NSAID + benzodiazepine	38.9 (42)
NSAID + diuretic	10.2 (11)
NSAID + analgesic	45.4 (49)

vidual SAARDs used principally in combination therapy is shown in Fig. 5b. Aurothioglucose and D-penicillamine were prescribed in equal frequency (36% of SAARD-treated patients each), while in contrast to the inpatient prescribing pattern, azathioprine accounted for only 20% of SAARD usage.

Additional prescribing data

Table 1 outlines the principal drugs coprescribed with antirheumatic therapy for inpatients. It can be seen that 13% of hospitalised patients received a combination of cimetidine and NSAID treatment, and overall about 30% of patients received some form of drug therapy to control gastric symptoms while on NSAID treatment.

A significant proportion of inpatients (17.6%) received iron supplementation, and over one-third of admitted patients with RA (38.9%) received benzodiazepine medication.

A large proportion of hospitalised patients (45.4%) received analgesic therapy in addition to their antirheumatic drugs. About 10% of patients were taking a diuretic in conjunction with NSAID drugs.

There was very little in the way of coprescribed drug therapy in the clinic patients. Only 3% of patients received H₂-antagonist drugs and only 7% of outpatients were prescribed benzodiazepines in addition to their antirheumatic treatment.

Prescription instructions for clinic patients were also noted. About 19% of patients received non-specific instructions regarding the dosage of their treatment, i.e., 8% of prescriptions were to be 'used as required', and 11% of prescriptions gave patients instructions to use the NSAID treatment within a dosage range.

Discussion

Our sample statistics were consistent with

epidemiological data on age and sex distribution in rheumatoid arthritis,^{11 12} there being a two to three times greater prevalence in females than in males for both inpatients and clinic patients. The majority of cases were over the age of 50 (about 80% of inpatients and about 75% of outpatients). Among younger patients with rheumatoid arthritis the overwhelming majority were female, as no male patients under the age of 40 were admitted to the rheumatology ward during the one-year survey period, and only 10% of patients under the age of 40 among the RA outpatients were male.

The functional capacity data for the clinic patients indicate that a relatively lower proportion of outpatients (24%) developed severe handicap (categories 3 or 4 in the ARA classification) than was reported for clinic-treated patients elsewhere. Rasker and Cosh¹³ reported 45% of their patients to be in categories 3 or 4; however, no reference was made to relationships between functional class and treatment. The widespread use of second-line drugs in our treatment regimens and the ready access to orthopaedic surgery could well account for a disability profile in this study, which is similar to that reported for rheumatoid arthritis patients treated in community practice⁸ who would not be expected to have such a severe disease as clinic-treated patients.

Published data on prescribing patterns for rheumatoid arthritis are extremely limited. Information concerning NSAID drug utilisation is available but little of it is linked to morbidity (i.e., to specific forms of arthritis). Ibuprofen is currently the most widely prescribed NSAID in Britain,⁷ the Netherlands,¹⁴ and in the USA,⁵ excluding aspirin. Naproxen is the most widely prescribed NSAID in the Scandinavian countries⁶ and in Australia.¹⁵

In a more specific audit in a rheumatology clinic,¹⁶ where 77% of the patients had RA, indomethacin, naproxen, and ibuprofen accounted for 47% of the NSAID prescriptions. In an Australian community-based study dealing specifically with rheumatoid arthritis,⁸ naproxen (25%), aspirin (25%), and indomethacin (19%) together accounted for 69% of the NSAID usage. Our study showed indomethacin and naproxen to be the first and second ranking drugs prescribed for both inpatients (67% total) and outpatients (69% total), with ibuprofen having a relatively minor role and aspirin virtually not prescribed.

Statistics on consumption of SAARDs and their combination with other agents are even more scarce. Data on drug utilisation on national levels for SAARDs and corticosteroids⁶ are of limited value because they are not linked to diagnosis. In a British study,¹⁶ however, 32% of outpatients received gold therapy and 17% received D-

Table 2 Prescribed daily doses (PDD) versus defined daily doses (DDD) for non-steroidal anti-inflammatory drugs in the treatment of rheumatoid arthritis

Drug	Inpatients			Outpatients			
	n	PDD (mg)		DDD (mg)	n	PDD (mg)	
		Mean	Range			Mean	Range
Indomethacin	45	125	50-300	100	44	45	25-200
Naproxen	33	780	500-1000	500	24	653	125-1000
Piroxicam	10	18	10-30	20	6	23	20-30
Ibuprofen	7	771	400-800	800	13	1233	400-1600

penicillamine. Our study showed a similar prescribing rate for gold (28% of patients) but a higher use of D-penicillamine (28%) in the outpatient clinic.

No comparative data have been found for multiple-drug prescribing except for the community-based study⁸ which showed a considerably lower incidence of polypharmacy than in our hospital-based study. We found that on average about 82% of patients received SAARD therapy (85% of inpatients, 79% of outpatients), compared with only 18% in the community-based study. Although 46% of inpatients received oral corticosteroids in the management of acute phases of rheumatoid arthritis, only 15% of outpatients were prescribed oral corticosteroids. This compares with 23% of patients receiving corticosteroids therapy in the community-based study.⁸ Recently Million *et al.*¹⁷ have suggested that judicious use of steroids can greatly improve the mobility and welfare of many rheumatoid arthritis patients without the severe complications usually associated with steroid therapy. The need to prescribe H₂-antagonist therapy in conjunction with NSAIDs was considerably higher in inpatients (13%) than in outpatients (3%). This may be reflected in the generally higher prescribed daily doses of NSAIDs (Table 2) employed in the treatment of inpatients than in clinic patients.

A comparison of prescribed daily doses (PDD) between inpatients and outpatients (Table 2) shows that inpatients received higher doses of the principal NSAIDs, indomethacin and naproxen, well above the defined daily dose (DDD), an international unit of comparison for drug utilisation studies, being the average maintenance dose for the principal indication of a drug per day.¹⁸ This pattern of increased doses in inpatients may be expected because these patients would probably be hospitalised due to an acute exacerbation of rheumatoid arthritis, and higher doses of NSAID could be administered because, as inpatients, they could be more easily monitored for adverse effects than could clinic patients. Outpatients received doses of indomethacin

and naproxen which were closer to the DDDs, while ibuprofen and the non-formulary drug, piroxicam, were prescribed in less conservative doses, perhaps reflecting a confidence in their lower incidence of adverse effects.

This paper provides baseline data concerning the drug prescribing patterns in the management of both hospitalised and clinic-treated rheumatoid arthritis patients. With the benefit of an insight into current prescribing patterns gained from an audit such as this it should be possible to evaluate prescribing practices and to develop policies or algorithms for the management of rheumatoid arthritis.

The authors gratefully acknowledge the assistance of the medical staff in the rheumatology outpatients clinic, Dr F Speerstra, Dr L Santen, and Dr H Houben.

References

- 1 Meenan R F, Yelin E H, Nevitt M, Epstein W V. The impact of chronic disease. A sociomedical profile of rheumatoid arthritis. *Arthritis Rheum* 1981; **24**: 544-9.
- 2 Scott D L, Couton B L, Chapman J H, Bacon P A, Popert A J. The long-term effects of treating rheumatoid arthritis. *J R Coll Physicians Lond* 1983; **17**: 79-85.
- 3 Wright W V, Amos R. Do drugs change the course of rheumatoid arthritis? *Br Med J* 1981; **280**: 964-6.
- 4 O'Duffy J D, Luthra H S. Current status of disease-modifying drugs in progressive rheumatoid arthritis. *Drugs* 1984; **27**: 373-7.
- 5 Baum C, Kennedy D L, Forbes M B, Jones J K. Drug utilization in the US. 1982: *Fourth Annual Review*. Department of Health and Human Services, Division of Drug Experience, National Center for Drugs and Biologics, Food and Drug Administration, Bethesda, 1983.
- 6 Kass E. Drugs used in rheumatic diseases. In: Sakshaug S, Marit A, Hjort P F, Lunde P K M, Oyvind K, eds. *Drug utilization in Norway during the 1970s: increases, inequalities, innovations*. Oslo: Norwegian Medicinal Depot, 1983.
- 7 Freeborn S F, Gibson P, Clinch D. Prescribing patterns for NSAIDs in a typical urban area. *Br J Pharm Pract* 1983; **5**: 20-5.
- 8 Owen S G, Friesen W T, Roberts M S, Flux W. Patient outcome and treatment data in a rheumatoid arthritis population (abstract). Australian Pharmaceutical Science Association Meeting, Melbourne, March 1984.
- 9 Ropes M W. Diagnostic criteria for rheumatoid arthritis: 1958

- revision by a committee of the American Rheumatism Association. *Ann Rheum Dis* 1959; **18**: 49-53.
- 10 Stenbrocker O, Traeger C H, Batterman R C. Therapeutic criteria in rheumatoid arthritis. *JAMA* 1949; **140**: 659-62.
 - 11 Hochberg M C. Adult and juvenile rheumatoid arthritis: current epidemiological concepts. *Epidemiol Rev* 1981; **3**: 27-41.
 - 12 Linos A, Worthington J W, O'Fallon W M, Kurland L T. The epidemiology of rheumatoid arthritis in Rochester, Minnesota. A study of incidence, prevalence and mortality. *Am J Epidemiol* 1980; **111**: 87-98.
 - 13 Rasker J J, Cosh J A. Cause and age at death in a prospective study of 100 patients with rheumatoid arthritis. *Ann Rheum Dis* 1981; **40**: 115-20.
 - 14 Zuidgeest L J B. Personal communication. Regional survey of NSAID use in the Nijmegen and Tilburg areas from health insurance data.
 - 15 Hall R C. Patterns of drug utilization - national and international aspects: drug use in Australia. *Acta Med Scand* 1982; **683** (suppl): 79-80.
 - 16 Takavarasha L, Scott D L, Constable T J. A pharmacist's audit of antirheumatic drugs. *Rheumatol Rehabil* 1982; **21**: 201-5.
 - 17 Million R, Kellgren J H, Poole P, Jayson M I V. Long-term study of management of rheumatoid arthritis. *Lancet* 1984; **i**: 812-6.
 - 18 Nordic Council of Medicines. *Nordic Statistics on Medicines, Parts I and II. Statistical Reports on the Nordic Countries (1978-1980)*. Nos. 8 and 9, Uppsala, 1982.