

Decreasing Mortality in Patients with Rheumatoid Arthritis: Results from a Large Population Based Cohort in Sweden, 1964–95

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ABSTRACT. Objective. To assess changes in mortality in patients with rheumatoid arthritis (RA) from 1964 to 1995.

Methods. A population based cohort of 46,917 patients with RA was identified from 1964 to 1994, using the Swedish Hospital Discharge Register, and followed until 1995 through linkage to the Cause of Death Register. Mortality was separately analyzed in each inclusion period (1964–75, 1975–84, 1985–94). The relative risk of death was estimated as standardized mortality ratio (SMR) using the Swedish population as a reference

Results. All-cause mortality was increased twice the expected (SMR = 2.03, 95% CI 2.00, 2.05). Coronary artery disease was the major cause of death and mortality was increased by 80% (SMR = 1.79, 95% CI 1.75, 1.83). Females with RA aged 20–39 at first discharge had a more than 5-fold increased risk of coronary death (SMR = 5.48, 95% CI 3.45–5.71). From 1975 patients with RA had decreasing all-cause mortality. This decline was most pronounced in patients aged 40–59 at first discharge, where SMR was 2.68 (95% CI 2.45, 2.92) from 1964 to 1974 compared to SMR 1.63 (95% CI 1.37, 1.92) from 1985 to 1994.

Conclusion. The elevated mortality rates in RA patients compared to the general population have decreased during the last 20 years, possibly due to an increased access to specialized rheumatology care. An excess risk for death in coronary artery disease was, however, present in RA patients, especially patients with early onset of disease. (J Rheumatol 2002;29:906–12)

Key Indexing Terms:

RHEUMATOID ARTHRITIS
CORONARY HEART DISEASE

MORTALITY
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OUTCOME

A number of studies from different populations and in different settings have confirmed increased mortality among patients with rheumatoid arthritis (RA)^{1–7}. Severe disease and bad functional status have been shown to be important predictors for this excess mortality^{1,4}.

To improve the prognosis of RA, the concept of a more aggressive drug therapy earlier in the disease course started to form in the mid 1980s, and during the 1990s this regimen became an established part of rheumatology care. However, the changes in treatment of RA have been a continuous

process. Today the pharmacological treatment and subsequent rehabilitation in patients with RA is different to that in the 1960s in both extent and accomplishment.

Very little is known to what extent changes in care^{7,8} and/or in natural history have had an influence on excess mortality. To address this question, we identified a population based cohort of patients with RA using nationwide Swedish health care registers. Mortality was assessed separately for patients who had their first hospital discharge in different periods (1964–74, 1975–84, and 1985–94) in order to analyze any changes over time for different causes of death.

MATERIALS AND METHODS

The Hospital Discharge Register. Since 1964 the Swedish National Board of Health and Welfare has received annual reports from the medical institutions in the country. These data are gathered in the Hospital Discharge Register, which contains information on all individual discharges, including the date of admission and discharge, discharging department, and the discharge diagnoses. The discharge diagnoses consist of a main diagnosis and up to 5 secondary diagnoses coded according to the 7th revision of the International Classification of Diseases (ICD-7) throughout 1968, ICD-8 from 1969 to 1986, and ICD-9 from 1987 to 1995. Each record in The Hospital Discharge Register contains the National Registration Number (NRN), an individually assigned 10 digit number given to all Swedish residents.

Validations of the register by analyzing the medical data in the records

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both in 1986 and 1990 have demonstrated a correct ICD code at the 4 digit level in 86% of all principal discharge diagnoses⁹. Moreover, a previous study¹⁰ validated the discharge code of RA in the register by examining 276 different medical records in women aged 15–50 years discharged during 1975 to 1978 to estimate the number of criteria fulfilled for each case. They found that 91% fulfilled at least 2 of 4 New York criteria and that 92% fulfilled at least 3 of the Rome criteria for RA. The sensitivity of the Rome criteria to detect an already persistent RA seems higher than the American College of Rheumatology (ACR) criteria, whereas the ACR criteria predict a more severe disease¹¹. A recent study¹² also scrutinized the medical records in a sample of 162 patients and found that 131 or 81% fulfilled at least 4 ACR criteria for RA.

As private inpatient care in Sweden is almost nonexistent, patients are obliged to use the public hospitals in their own county. Thus, the data in the Hospital Discharge Register refers to the whole population in each county. The register covers virtually all discharges in the population, as the non-reporting rate was estimated to be 2% or less¹³. The Hospital Discharge Register has gradually expanded to cover 20% of all the Swedish counties in 1967, 85% by the end of 1983¹⁴, and 100% from 1987.

The Causes of Death Register. The Swedish National Board of Health and Welfare administers the Causes of Death Register, which comprises all deaths from 1952 among persons registered as Swedish residents. In addition to the NRN, the register contains the underlying (primary) and contributing causes of death, injuries, date of death, home county of the deceased, and sex, all obtained from the death certificates. Reporting by death certificate has been at almost 100% for several decades. Validation studies^{15,16} of the cause of death certification for myocardial infarction from the 1970s as well as the late 1980s reported a confirmation rate of 92–96%.

The cohorts. All patients who were discharged for the first time with a diagnostic code for RA (ICD-7 722, 00; ICD-8 712, 38–712, 39; and ICD-9 714A–C, 714W) between 1964 and 1994, served as the basis for the study. The NRN allowed us to select the first recorded discharge for each individual patient. Through linkage through the Swedish Cancer Register, we excluded 4964 patients with a malignancy diagnosed prior to first discharge. We excluded 2861 patients because of a discharge diagnosis of inflammatory rheumatic diseases other than RA, irrespective of whether this diagnosis was obtained before or after first discharge diagnosis of RA. Also, 1085 patients were excluded because of age younger than 20. A total of 2415 patients died at first discharge and were thus not available for followup. Finally, 3428 patients were excluded due to incomplete or erroneous NRN, leaving 61,899 patients for followup.

In addition, a second cohort was identified, as we wanted a cohort of RA patients without a prior cardiovascular disease (CVD). Therefore 18,767 patients were excluded due to a discharge diagnosis of CVD prior to or at first discharge of RA. The second cohort consisted of 46,917 patients.

Followup. The cohorts were followed through computerized linkage by the NRN in the Hospital Discharge Register and the Cause of Death Register. The person-years at risk in the cohorts were calculated from the date of the first discharge and until death or the end of the observation period, December 31, 1995. All underlying causes of death were studied.

The cohorts were stratified for sex, age at first discharge (20–39, 40–59, 60 or older), number of years of followup, periods of first discharge (1964–74, 1975–84, 1985–94), and frequency of discharges (1, 2–3, 4 or more).

Statistical methods. SMR, the ratio of observed to expected number of deaths, was used as an indicator of risk. Nationwide statistics from the Cause of Death Register includes annual sex- and age-specific mortality rates for different ICD codes. The number of expected deaths in the observed population was calculated by multiplying the numbers of person-years at risk according to each 5 year age group, sex, and calendar year, by the corresponding age-, sex-, and year-specific mortality rates in the general population. The 95% confidence interval (CI) of the SMR was then calculated on the assumption that deaths in different categories followed a Poisson distribution¹⁷.

To compare the influence of different calendar periods on excess

mortality, we separately analyzed the first 5 and 10 years of followup for the first discharge in each calendar period. When assessing the calendar period effects we chose to restrict the followup to 5 and 10 years in order to avoid confounding between followup and calendar period. In the analysis of 5 years of followup we included all patients in the last period (1985–94) but allowed for different mortality rate in the first year after discharge. Statistically significant differences in SMR with respect to age at entry, calendar time, and sex were investigated by means of Poisson regression. The observed number deaths were stratified according to all the combinations of age at entry, calendar time, and sex and were analyzed by Poisson regression with the logarithm of the expected number as an offset term. The standard errors and tests were adjusted to allow for overdispersion. The interaction terms between age at entry and calendar period were assessed to investigate differences in period effects between the different age groups. Likelihood ratio tests for homogeneity and trend tests were used to assess statistical significance. The results are presented as relative risks representing SMR ratios with 95% CI. The statistical analyses were performed using PROC GENMOD in the Statistical Analysis System (SAS[®]) package¹⁸.

RESULTS

The cohort of all RA cases including 61,899 patients constituted 574,561 person-years. Previous studies on RA prevalence have reported varying estimates, with ranges from 0.4% to 0.8% in different studies^{19,21} of Nordic origin. Assuming a prevalence in the high range (0.8%) and an annual incidence of 25/100,000²², 79% of all patients with RA in the study population were included in this cohort. With assumptions of lower prevalence figures, an even higher number of patients with RA would have been identified through the Hospital Discharge Register.

The second cohort of RA patients, including only those without a history of CVD, consisted of 46,917 patients with RA. There were 489,048 person-years of followup until December 31, 1995. Descriptive data of this cohort are shown in Table 1. Calculations on mortality were made for both the larger cohort of 61,899 patients and for the smaller cohort that excluded patients with a prior CVD. We have chosen to present all data further in this text and in the tables in a conservative way, i.e., by using the cohort excluding the prior CVD cases, unless otherwise stated.

Patterns of all-cause mortality in patients with RA. Fifty-four percent or 25,353 of all patients in the cohort died during followup. All-cause mortality was double (Table 2) that of the background population. CVD infections and causes of death attributed to RA were the major underlying causes of death. There were 12,853 excess deaths (Table 2) during more than 30 years of followup and 55% of these (7034) was due either to CVD (5582) or various infections, especially pneumonia (950).

Mortality remained increased during all years of followup after first discharge, and even increased after more than 10 years of duration (Table 3). There were no changes in the pattern of different underlying causes of death associated with the duration of followup, except for coronary artery disease (CAD), where mortality was increased with an increasing duration of followup.

Table 1. Characteristics of patients with rheumatoid arthritis (RA) in the cohort by inclusion period.

	All, n (%)	1964–74, n (%)	1975–84, n (%)	1985–94, n (%)
All	46,917 (100)	14,828 (32)	17,931 (38)	14,158 (30)
Sex				
Male	13,554 (29)	4321 (29)	5250 (29)	3983 (28)
Female	33,363 (71)	10,507 (71)	12,681 (71)	10,175 (72)
Age at first discharge, yrs				
20–39	4482 (10)	1512 (10)	1642 (9)	1328 (9)
40–59	16,476 (35)	6125 (41)	5877 (33)	4474 (32)
60 or older	25,959 (55)	7191 (49)	10,412 (58)	8356 (59)

Table 2. Mortality in patients with RA by different causes of death from 1964 to 1995.

Causes of death (ICD7:ICD8:ICD9)	Percentage	No. of Deaths	No. of Excess Deaths	SMR	95% CI
All causes	100	25,353	12,853	2.03	2.00, 2.05
Cardiovascular including stroke (330–334, 400–455:390–458: 390–459)	49	12,431	5582	1.81	1.78, 1.85
Coronary artery disease (420, 0, 420, 2, 420, 9: 410–414: 410–414)		6991	3089	1.79	1.75, 1.83
Stroke (330–334: 430–438: 430–438)		2202	736	1.50	1.44, 1.57
Malignancy (140–239)	12	2986	130	1.05	1.01, 1.08
RA	11	2730		81.00	78.0, 84.1
Respiratory (240–245, 470–527: 460–519:460–519)	10	2448	1580	2.82	2.71, 2.93
Pneumonia (490–493: 480–486:480–486)		1481	950	2.79	2.65, 2.94
Obstructive pulmonary disease (500–502, 241:490–493: 490–493, 496)		604	364	2.51	2.32, 2.72
Gastrointestinal (530–587:520–577:520–579)	5.6	1419	1016	3.53	3.34, 3.71
Peptic ulcer disease (540–542:531–534, 707:531–534)		421	335	4.90	4.44, 5.39
Chronic liver disease (581, 583: 571:571)		120	39	1.48	1.23, 1.78
Urogenital (590–637:580–629:580–629)	3.2	811	633	4.55	4.24, 4.87
Nephritis/nephrosis (590–539:580–584:580–589)		305	256	6.26	5.58, 7.00
Pyelitis (600:590:590)		217	162	3.94	3.44, 4.50
Trauma and Intoxication (800–999:800–995:800–995)	2.4	618	175	1.40	1.29, 1.51
Infection (001–138:000–136:001:139)	1.6	409	323	4.77	4.32, 5.26
Neurology (340–398:320–389:320–389)	0.8	191	61	1.46	1.26, 1.69
Meningitis (340:320:320–322)		22	17	4.44	2.78, 6.73
Psychiatric (300–326:290–315:290–315)	0.8	191		0.91	0.78, 1.05
Dementia (305:290:290)		148		0.90	0.76, 1.06
Hematological (malignancies excluded) (290–299:280–289:280–289)	0.4	100	69	3.27	2.66, 3.98
Endocrine (250–289:240–246, 250–279:240–246, 250–279)		24	12	2.08	1.33, 3.09

SMR: Standardized mortality ratio, 95% CI: confidence interval.

Table 3. Mortality in patients with RA due to all causes of deaths and coronary deaths by the duration of followup.

	All Causes of Deaths			
	Observed	Expected	SMR	95% CI
No. of years after first discharge				
0–1	2072	987.45	2.10	2.01, 2.19
1–4	6566	3635.90	1.81	1.76, 1.85
5–9	7082	3513.87	2.02	1.97, 2.06
10–14	4911	2249.85	2.18	2.12, 2.24
15–20	2863	1298.51	2.20	2.12, 2.29
20+	1859	813.91	2.28	2.18, 2.39
Deaths in Coronary Artery Disease				
No. of years after first discharge				
0–1	474	317.58	1.49	1.36, 1.63
1–4	1799	1169.57	1.54	1.47, 1.61
5–9	2017	1120.88	1.80	1.72, 1.88
10–14	1382	693.88	1.99	1.89, 2.10
15–20	815	378.96	2.15	2.01, 2.30
20+	504	221.30	2.28	2.08, 2.49

SMR: Standardized mortality ratio, 95% CI: confidence interval.

Young age at first discharge and at multiple discharges was associated with additional risks. Patients aged 20–39 and 40–59 years at first discharge had risk of death (SMR = 2.62, 95% CI 2.36, 2.90 and SMR = 2.49, 95% CI 2.42, 2.55, respectively) higher than that of patients aged 60 or older (SMR = 1.90, 95% CI 1.87, 1.93) at first discharge. Patients who had 4 or more discharges during followup had a greater risk of death (SMR = 2.26, 95% CI 2.22, 2.30) compared with those who had only one discharge (SMR = 1.55, 95% CI 1.51, 1.59). There were only small sex differences in SMR, women having a SMR of 2.09 (95% CI 2.06, 2.12) and men a SMR of 1.91 (95% CI 1.87, 1.95).

Women with onset of RA in young age had a prominent increased risk for death in CAD. CAD was the main cause of death and the risk was increased by 80% in patients with RA (Table 2). This risk was present many years after onset of disease, i.e., even after 20 years after first discharge, RA patients had a more than doubled risk of death from CAD compared with the general population (Table 3).

An especially high risk was observed in female patients with RA who were discharged at a young age. Those 20–39 years of age at first discharge had a more than 5-fold increased risk of death in CAD (SMR = 5.48, 95% CI 3.45, 5.71).

Decreasing mortality in RA patients included during the last decades. All-cause mortality was then compared between patients who had their first discharge at different calendar periods. In multivariate analysis, we analyzed interactions of calendar period, sex, and age. Patients included from 1975 and forward had a decreased mortality during both 5 (Tables 4 and 5) and 10 years (Table 6) of followup

compared with those included before 1975. The calendar-specific decline in mortality was most pronounced in patients aged 40–59 at the first discharge. Mortality at 5 years of followup was decreased by 29 and 39% in patients included 1975–84 and 1985–94, respectively, compared with those included before 1975 (Table 5). Mortality at 10 years of followup was decreased by 22% in patients included 1975–84 compared with those included before 1975 (Table 6).

The interactions of calendar period, sex, and age were also analyzed in specific causes of death, such as CVD, respiratory, peptic ulcer, and infections. During the first 5 years of followup, mortality in CVD was decreased by 16% in patients included 1985–94 compared with those included before 1975. However, when we compared the specific causes of deaths by 10 years of followup, there was no difference in any of the causes whether the patients had been included before or after 1975 (data not shown).

When we analyzed the proportion of causes of deaths by 10 years of followup, patients aged 40–59 included 1975–84 had an increase in cardiovascular causes from 34 to 41%, and a decline in causes attributed to RA from 20 to 13% compared with those included before 1975 (Table 7).

Exclusion of patients with a history of CVD did not affect the risk estimates of longterm followup. The cohort of patients with RA, including those with prior CVD, had a

Table 4. Overall mortality in different inclusion periods by age at first discharge during the first 5 years of followup in patients with RA.

	Inclusion Period	Observed	Expected	SMR	95% CI
Age at First Discharge, yrs					
40–59	1964–74	508	189.65	2.68	2.45, 2.92
	1975–84	326	171.84	1.90	1.70, 2.11
	1985–94	142	87.22	1.63	1.37, 1.92
60+	1964–74	2255	1143.68	1.97	1.89, 2.05
	1975–84	3222	1742.75	1.85	1.79, 1.91
	1985–94	2116	1266.57	1.67	1.60, 1.74

Table 5. Overall mortality in patients with RA during the first 5 years of followup by SMR^a 95% CI as a function of calendar time and patient age at first discharge^b.

	All Ages	40–59 yrs	60+ yrs
Period of inclusion			
1964–74	1.00	1.00	1.00
1975–84	0.90 (0.83, 0.97)	0.71 (0.59, 0.86)	0.94 (0.84, 1.05)
1985–94	0.81 (0.74, 0.88)	0.61 (0.47, 0.79)	0.84 (0.74, 0.96)
p trend	< 0.001	< 0.001	0.006
p homogeneity	< 0.001	< 0.001	0.02

^a In Poisson regression model SMR is adjusted to 1.00 in 1964–74.

^b Interaction between age at entry and period p = 0.03.

Table 6. Overall mortality in patients with RA during the first 10 years of followup by SMR^a as a function of calendar time and patient age at first discharge^b.

	All Ages	40–59 yrs	60+ yrs
Period of inclusion			
1964–74	1.00	1.00	1.00
1975–84	0.93 (0.88–0.98)	0.78 (0.69–0.88)	0.93 (0.89–1.03)
p homogeneity	0.006	< 0.001	0.28

^a In Poisson regression model SMR is adjusted to 1.00 in 1964–74.

^b Interaction between age at entry and period p = 0.01.

Table 7. The number of deaths (percentage) due to different causes in patients aged 40–59 years at first discharge by inclusion period, during the first 10 years of followup.

	1964–74	1975–84
All deaths	1192 (100)	837 (100)
Cardiovascular disease	406 (34)	341 (41)
RA	238 (20)	105 (13)
Respiratory	70 (6)	66 (8)
Infection	18 (2)	17 (2)
Peptic ulcer	28 (2)	9 (1)
Remainder	432 (36)	299 (36)

higher all-cause mortality during the first 10 years after discharge (SMR = 2.18, 95% CI 2.16, 2.21) compared with those without a prior CVD (SMR = 1.93, 95% CI 1.90, 1.96). However, after a duration of 10 or more years of followup, no differences were found whether a cohort included patients with a history of prior CVD (SMR = 2.24, 95% CI 2.20, 2.28) or not (SMR = 2.21, 95% CI 2.16, 2.25).

As for the calendar-specific trends in mortality, patients in the cohort including those with a prior CVD also had a decline in mortality since 1975 without a decline in any specific cause of death, whether followed for the first 5 or 10 years after discharge.

DISCUSSION

Our data in this large population based study covering deaths from the 1960s to the 1990s confirm a reduced life expectancy in patients with RA. Coronary artery disease was one of the major causes of the excess number of deaths. Early disease onset and female sex further increased the risk of death. We also observed a progressive decrease in all-cause mortality in patients included since 1975 compared with those included before 1975, particularly in patients aged 40–59 at first discharge. Previous studies on RA mortality have presented a wide range of risk estimates, with SMR varying from 2.48² to 1.30³. The present risk estimate of all-cause mortality falls between these figures. The risk estimate for CVD was in accord with a population based study³ in Pima Indians with extensive followup. Our findings of a declining mortality in RA patients included since

the mid-1970s is in agreement with results of Savolainen, *et al*²³ on patients with chronic inflammatory disease, as young women treated 1990–93 had a decreased mortality compared with those treated 1977–80. These findings are in contrast to data in a Minnesota, USA, study⁶. However, the results from our study are difficult to compare with the US study, since the authors analyzed a mixture of incident and prevalent cases.

Risk of death from CAD was most pronounced in young women, a group of individuals otherwise with few established cardiovascular risk factors. These findings indicate that the disease itself or the treatment might be in the causal pathway. Low grade inflammatory processes are presently considered a feature of CAD²⁴, and inflammatory markers in plasma have been associated with future risk of CAD²⁵. In RA patients⁷, a high last-registered value for erythrocyte sedimentation rate was associated with an increased risk of cardiovascular event or death.

Many of the different components of the inflammatory response characterizing atherogenesis²⁶ can also be found within the inflammatory process of RA²⁷. The presence of proinflammatory cytokines in both synovial fluid and sera²⁸ of RA patients has been associated with disease activity and severity. Moreover, concentrations of these proinflammatory cytokines in plasma have recently been reported to be associated with the outcome of CAD in samples from individuals from the general population^{29,30}.

Our findings of increasing cardiovascular risk with longer followup imply that chronic inflammation might be an important predictor for clinical consequences of CAD in patients with RA.

The major strengths of this study are the population based setting, the size of the cohort, and the extended followup. There are, however, some limitations.

First, as the study was confined to hospitalized patients, selection bias might hamper the generalizability of our results. However, in 1981 Allebeck, *et al*¹ found in a community based study that 75% of all RA patients had sometimes been hospitalized at one time. This finding reflects the comprehensive inpatient care of RA patients in Sweden, at least to the end of the 1980s. Moreover, these figures are in accord with our estimates built on available figures for incidence and prevalence of RA in Sweden.

Second, the specificity of the underlying RA diagnosis is a concern. However, studies^{2,12} using the Hospital Discharge Register have found a high specificity for the discharge diagnosis of RA. Moreover, a low specificity of the discharge diagnosis cannot explain these high risk estimates. As misclassification of the discharge diagnosis is nondifferential, it will, if anything, lead to an underestimation of the true risk estimates. Similarly, any misclassification of the underlying cause of death in the Swedish Causes of Death Register should be nondifferential and will not create false positive findings.

Our finding of calendar-specific decline in mortality mainly confined to young ages is probably due to more than one underlying mechanism.

A more liberal admission policy for inpatient care from 1975 onwards could lead to a selection of patients with milder disease. The descriptive data argue against that, as the proportion of middle-aged patients was smaller from 1975 compared with that before. A reduction of hospital beds in the 1990s substantially reduced the number of inpatients in rheumatology units. However, despite this restrained policy, RA patients included since 1985 still had decreased mortality.

Longer disease duration in patients included before 1975 compared with those included afterwards might affect the outcome. Although we could not assess disease duration, according to a random sample of patients in another Swedish study¹² utilizing the Hospital Discharge Register, no differences were found for disease duration between RA patients included before 1975 and those included afterwards.

A change in the disease characteristics of RA to milder course was proposed earlier^{31,32}. One study³² reported a decline in the number of erosions in patients with RA included between 1972 and 1982 compared to those in 1962, which corresponds to the calendar time during which we found the most apparent decline in mortality. In a recent Swedish study³³, a significant decrease in disease activity as well as disability was found in RA patients included in 1995 compared with those included between 1972 and 1978. The reason for this decrease in disease severity is unclear, but the group of patients included 1995 had been taking more extensive disease modifying antirheumatic drugs (DMARD). Moreover, Wallberg-Jonsson, *et al*⁷ found that both DMARD treatment and joint prosthesis were associated with a decreased risk of death in RA patients. There is, however, no firm answer to whether changes in treatment or in the natural history of the disease account for the decreased disease severity.

Important changes in the external framework of rheumatology care took place in the mid-1970s. Until 1973, the inpatient care of disabled persons in Sweden was limited to a few units³⁴. The shift in 1973, when each county got full responsibility of rheumatology care, led to rapid expansion of rheumatology units over the next 10 years. The number of rheumatology units in Sweden increased from 11 in 1974 to 32 in 1984³⁴. A more active treatment earlier in disease course for patients with RA might have been a consequence of this extension. A recent study⁵ with longterm followup indicates also that patients attending rheumatological care earlier in the disease course do better in terms of mortality.

There was no decline in mortality of any specific cause of death. One interpretation of this is a decreasing disease severity in RA over time. As disease severity is linked to mortality^{1,4} and because the changes were confined to

middle-aged patients, a category of patients probably more suitable for active treatment in rheumatology units, improvements in the care of RA patients in Sweden might after all have had a positive effect.

In conclusion, all-cause mortality declined in RA patients over the last 20 years. This decline did not correspond to any specific cause of death. Increased accessibility to rheumatology care and more active and earlier treatment might be one of the reasons for this decrease in mortality.

Despite this decrease, our data confirm shorter life span in patients with RA and focus on the increased risk of coronary death, particularly evident in those with disease onset at an early age.

REFERENCES

1. Allebeck P, Ahlbom A, Allander E. Increased mortality among persons with rheumatoid arthritis, but where RA does not appear on death certificate. *Scand J Rheumatol* 1981;10:301-6.
2. Allebeck A. Increased mortality in rheumatoid arthritis. *Scand J Rheumatol* 1982;11:81-6.
3. Jacobsson L, Knowler W, Pillemer S, et al. Rheumatoid arthritis and mortality, a longitudinal study in Pima Indians. *Arthritis Rheum* 1993;8:1045-53.
4. Wolfe F, Mitchell D, Sibley J, et al. The mortality of rheumatoid arthritis. *Arthritis Rheum* 1994;4:481-94.
5. Symmons DPM, Jones MA, Scott DL, Prior P. Longterm mortality outcome in patients with rheumatoid arthritis: Early presenters continue to do well. *J Rheumatol* 1998;25:1072-7.
6. Gabriel SE, Crowson CS, O'Fallon WM. Mortality in rheumatoid arthritis: Have we made an impact in 4 decades? *J Rheumatol* 1999;26:2529-33.
7. Wallberg-Jonsson S, Johansson H, Ohman ML, Rantapaa-Dahlqvist S. Extent of inflammation predicts cardiovascular disease and overall mortality in seropositive rheumatoid arthritis. A retrospective cohort study from disease onset. *J Rheumatol* 1999;26:2562-71.
8. Lehtinen K, Isomäki H. IM gold therapy is associated with long-term survival in rheumatoid arthritis. *J Rheumatol* 1991;18:524-9.
9. Nilsson AC, Spetz CL, Carsjö K, Nightingale R, Smedby A. Slutenvårdsregistrets tillförlitlighet [The reliability of the Hospital Discharge Register]. *Diagnosuppgifterna bättre än sitt rykte. Läkartidningen* 1994;91:598-605.
10. Allebeck P, Ljungström K, Allander E. Rheumatoid arthritis in a medical system: How valid is the diagnosis? *Scand J Soc Med* 1983;11:27-32.
11. Jacobsson LT, Knowler WC, Pillemer S, et al. A cross-sectional and longitudinal comparison of the Rome criteria for active rheumatoid arthritis (equivalent to the American College of Rheumatology 1958 criteria) and the American College of Rheumatology 1987 criteria for rheumatoid arthritis. *Arthritis Rheum* 1994;37:1479-86.
12. Baecklund E, Ekblom A, Sparen P, Feltelius N, Klareskog L. Disease activity and risk of lymphoma in patients with rheumatoid arthritis: nested case-control study. *BMJ* 1998;317:180-1.
13. Naessen T, Parker R, Persson I, Zack M, Adami H-O. Time trends in incidence rates of first hip fracture in the Uppsala health care region, Sweden, 1965-1983. *Am J Epidemiol* 1989;130:289-99.
14. Nyren O, McLaughlin JK, Gridley G, et al. Cancer risk after hip replacement with metal implants: A population-based cohort study in Sweden. *J Natl Cancer Inst* 1995;87:28-33.
15. de Faire U, Friberg L, Lorich U, Lundman T. A validation of cause of death certification in 1156 deaths. *Acta Med Scand*

- 1976;200:223-8.
16. Sundman L, Jakobsson S, Nyström L, Rosén M. A validation of cause of death certification for ischemic heart disease in two Swedish municipalities. *Scand J Prim Health Care* 1988;6:205-11.
 17. Bailar JC, Ederer F. Significance factors for the ratio of a Poisson variable to its expectation. *Biometrics* 1964;20:639-43.
 18. SAS Institute Inc. SAS/STAT® Software: Changes and enhancements through release 6.12. Cary, NC: SAS Institute Inc.; 1997:247-348.
 19. Kvien TK, Glennas A, Knudsrød OG, Smedsstad LM, Mowinckel P, Førre O. The prevalence and severity of rheumatoid arthritis in Oslo. Results from a county register and a population survey. *Scand J Rheumatol* 1997;26:412-8.
 20. Simonsson M, Bergman S, Jacobsson LTH, Petersson IF, Svensson B. The prevalence of rheumatoid arthritis in Sweden. *Scand J Rheumatol* 1999;28:340-3.
 21. Hakala M, Pollanen R, Nieminen P. The ARA 1987 revised criteria select patients with clinical rheumatoid arthritis from a population based cohort of subjects with chronic rheumatic diseases registered for drug reimbursement. *J Rheumatol* 1993;20:1674-8.
 22. Uhlig T, Kvien TK, Glennas A, Smedstad LM, Førre O. The incidence and severity of rheumatoid arthritis, results from a county register in Oslo, Norway. *J Rheumatol* 1998;25:1078-84.
 23. Savolainen A, Kautiainen H, Isomaki H, Myllykangas-Luosujarvi R, Aho K. Age specific mortality in Finnish women with chronic inflammatory joint disease during 1977-93 [letter]. *Ann Rheum Dis* 1997;56:754.
 24. Ross R. Atherosclerosis — an inflammatory disease. *N Engl J Med* 1999;2:115-26.
 25. Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH. Inflammation, aspirin and the risk of cardiovascular disease in apparently healthy men. *N Engl J Med* 1997;336:973-9.
 26. Jonasson L, Holm J, Skalli O, Bondjers G, Hansson GK. Regional accumulations of T-cells, macrophages and smooth muscle cells in the human atherosclerotic plaque. *Arteriosclerosis* 1986;6:131-8.
 27. Klareskog L, Forsum U, Kabelitz D, et al. Immune functions of human synovial cells. Phenotypic and T cell regulatory properties of macrophage-like cells that express HLA-DR. *Arthritis Rheum* 1982;25:488-501.
 28. Saxne T, Palladino MA Jr, Heinegård D, Talal N, Wollheim FA. Detection of tumor necrosis factor alpha but not tumor necrosis factor beta in rheumatoid arthritis synovial fluid and serum. *Arthritis Rheum* 1988;31:1041-5.
 29. Ridker PM, Rifai N, Stampfer M, Hennekens CH. Plasma concentrations of interleukin-6 and the risk of future myocardial infarction among apparently healthy men. *Circulation* 2000;101:1767-72.
 30. Ridker PM, Rifai N, Pfeffer M, Sacks F, Lepage S, Braunwald E, for the Cholesterol and Recurrent Events (CARE) Investigators. Elevation of tumor necrosis factor-alpha and increased risk of recurrent coronary events after myocardial infarction. *Circulation* 2000;101:2149-53.
 31. Silman A, Davies P, Currey HL, Evans SJ. Is rheumatoid arthritis becoming less severe? *J Chron Dis* 1983;36:891-7.
 32. Heikkilä S, Isomaki H. Long-term outcome of rheumatoid arthritis has improved. *Scand J Rheumatol* 1994;23:13-5.
 33. Bergstrom U, Book C, Lindroth Y, Marsal L, Saxne T, Jacobsson L. Lower disease activity and disability in Swedish patients with rheumatoid arthritis in 1995 compared with 1978. *Scand J Rheumatol* 1999;28:160-5.
 34. Leden I, Nived O. The 50th year of Anniversary of the Swedish Society of Rheumatology, 1996. The book of jubilee of the Swedish Society of Rheumatology. Solna: SmithKline Beecham AB; 1996.