Course of Patient-Reported Health Outcomes in Rheumatoid Arthritis: Comparison of Longitudinal and Cross-Sectional Approaches

INES RUPP, HENDRIEK C. BOSHUIZEN, LEO D. ROORDA, HUIBERT J. DINANT, CATHARINA E. JACOBI, and GEERTRUDIS A.M. van den BOS

ABSTRACT. ***Objective.*** To describe health outcomes reported by patients with rheumatoid arthritis (RA), i.e., pain, disability and health-related quality of life, as a function of disease duration in a longitudinal approach, and to compare the course of patient-reported health outcomes by a longitudinal versus a cross-sectional approach.

Methods. Data were collected with 4 series of questionnaires between 1997 and 2002 among patients with RA (maximum number = 882) of varying disease duration. The course of patient-reported health outcomes as a function of disease duration was evaluated using both longitudinal data and cross-sectional data of the first series.

Results. The course of RA shows a different pattern for various health outcomes. We observed similar trends in health outcomes in this large patient sample using the longitudinal and the cross-sectional approach.

Conclusion. Although longterm consequences of RA are preferably assessed in longer duration followup studies, cross-sectional studies, including patients with a broad range of disease durations, seem to provide fairly reliable estimates of the course of health outcomes. (J Rheumatol 2006; 33:228–33)

Key Indexing Terms:
RHEUMATOID ARTHRITIS | PAIN | DISABILITY
HEALTH-RELATED QUALITY OF LIFE | LONGITUDINAL | CROSS-SECTIONAL

Rheumatoid arthritis (RA) is a chronic progressive inflammatory disease confronting patients with varying health problems. Specific insights into the course of health outcomes and prognosis are essential in guiding treatment and management. Preferably, the courses of health outcomes and prognosis are investigated in longitudinal studies[1]. Several extensive followup studies among patients with RA are reported in the literature[2-10]. However, longterm followup is generally hard to achieve, because of practical reasons, among others, such as loss to followup of patients and costs. Cross-sectional studies, on the other hand, are less expensive to perform, and data are more readily available. However, we might expect that longitudinal studies with repeated measurements would provide more reliable estimates on the course of health outcomes than cross-sectional studies with one single measurement. Cross-sectional studies are, in particular, considered to be less reliable because selection processes, e.g., selective mortality, might have been active.

We followed patients with varying disease durations, i.e., from 0 to more than 20 years, for 5 years. Through this approach we were able to substantially prolong our observation window, enabling us to study short-term as well as longterm health outcomes. Our aim was to describe patient-reported health outcomes as a function of disease duration in a longitudinal approach, and to compare the course of patient-reported health outcomes by a longitudinal versus a cross-sectional approach. Cross-sectional studies including patients of varying disease durations might be seen as substitutes for assessing the course of health outcomes if they yield results that are similar to longitudinal studies.

MATERIALS AND METHODS

Participants and procedure. In 1997 we started with a longitudinal study on health and health-related quality of life (HRQOL) among patients with

From the Department of Social Medicine, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands.

Supported by the Jan van Breemen Institute, the Dutch Arthritis Association (het Nationaal Reumafonds), and the Netherlands Organization for Health Research and Development—Medical Sciences (ZonMw; grant 940-32-002).

I. Rupp, MD; G.A.M. van den Bos, PhD, Professor of Social Medicine, Department of Social Medicine, Academic Medical Center; H.C. Boshuizen, PhD, National Institute of Public Health and the Environment, Bilthoven; L.D. Roorda, MD, PT, Department of Rehabilitation Medicine, Institute for Research in Extramural Medicine, VU University Medical Center, Jan van Breemen Institute, Center for Rheumatology and Rehabilitation, Amsterdam; H.J. Dinant, MD, Jan van Breemen Institute, Center for Rheumatology and Rehabilitation, Department of Clinical Immunology and Rheumatology, Academic Medical Center, University of Amsterdam; C.E. Jacobi, PhD, Department of Medical Decision Making, Leiden University Medical Center, Department of Social Medicine, Academic Medical Center, University of Amsterdam.

Address reprint requests to Dr. I. Rupp, Department of Social Medicine, Academic Medical Center/University of Amsterdam, PO Box 22700, 1100 DE Amsterdam, The Netherlands. E-mail: i.rupp@amc.uva.nl

Accepted for publication September 12, 2005.

RA[11,12]. Patients (n = 1200) registered at an outpatient center for rheumatology and rehabilitation in Amsterdam or at one of its affiliated outpatient clinics were randomly selected from different strata of disease duration, ranging from 0 to more than 20 years, in order to cover the heterogeneity of RA within the group selected. Because of this random sampling procedure, we assume that the selected patients are a representative sample of patients in the database.

Inclusion criteria were the following: RA according to the 1987 revised American College of Rheumatology criteria[13], age > 16 years, and sufficient command of the Dutch language. The medical ethical committee approved the study design. Patients were asked to participate and to sign a letter of informed consent. The followup period was 5 years (1997–2002).

Data collection. Data were collected in 1997, 1998, 1999, and 2002 by a self-administered postal questionnaire. These questionnaires included questions on sociodemographic characteristics, comorbidity, clinical RA-specific outcomes, and patient-reported health outcomes.

Health outcomes. *RA-related pain*. The degree of RA-related pain was measured with a visual analog scale (VAS–pain) ranging from 0 (no RA-related pain) to 100 (RA-related pain as bad as it could be).

Disability. Disease impact in terms of disability was assessed with the validated Dutch capacities of daily life questionnaire (VDF)[14]. The VDF, similar to the Health Assessment Questionnaire, consists of 20 items measuring the degree of difficulty a patient has in performing activities of daily living (ADL) in 8 areas (dressing and grooming, arising, eating, walking, hygiene, gripping, reaching, and other activities). Responses to each item can range from 0 (no difficulty) to 3 (unable to do). The score is not influenced by the use of aids needed for certain ADL. We averaged the scores to create an overall mean score (range 0–3, higher scores indicating more disability).

Health-related quality of life. HRQOL was assessed with a validated Dutch version of the RAND-36[15]. The RAND-36 is a validated, internationally used questionnaire measuring health status on different dimensions. Given the reported minimal differences in final subscales scores of the RAND-36 and Medical Outcome Study Short Form-36[16], physical (PCS) and mental component summary (MCS) scales were computed according to the manual for SF-36 health summary scales[17], using Dutch SF-36 population means, standard deviations, and factor score coefficients[18,19]. Higher scores indicate better HRQOL.

Statistical analyses. Analyses were carried out using SPSS v. 11.5.2 for Windows (SPSS Inc., Chicago, IL, USA) for the cross-sectional analyses, and SAS v. 8.02 (SAS Inc., Cary, NC, USA) for longitudinal analyses. Results were considered statistically significant when p values were less than 0.05. The longitudinal course of RA-related pain, disability, and HRQOL over 5 years as a function of disease duration was evaluated by means of the mixed-effect modeling procedure Proc Mixed of SAS, using a random intercept model. The advantage of the mixed-effect modeling procedure is that cases are not rejected from analyses because of missing data.

Pain, disability, and HRQOL were the dependent variables, while disease duration classified in cohorts was the independent variable. We defined the following cohorts for our analyses:< 1, 1–2, 2–3, 3–5, 5–7, 7–10, 10–15, 15–20, and > 20 years. We classified duration in relatively narrow cohorts, especially in the first years of the disease, in order to allow patients to change from one cohort to another during followup.

Data from the first series (1997) were used for the cross-sectional approach to assure that all cohorts were filled with respondents, because in any later year at least the disease duration category "< 1 year" would have been empty. Moreover, some respondents did not respond to questionnaires for later series; so using the first wave assures the same subjects are included in both analyses.

For the comparison of longitudinal and cross-sectional data we used predicted values from the random-intercept model in the longitudinal approach and group means in the cross-sectional approach. The random-intercept procedure models trajectories in time after diagnosis (disease duration) that run parallel for all patients, but with a different intercept (height) for each patient. The predicted values from the random-intercept model give the values of the trajectory modelled for the average patient. For both analyses 95% confidence intervals are provided.

It should be noted that we did not compare a cross-sectional design with a purely longitudinal design since not all patients were followed from diagnosis.

RESULTS

A total of 882 patients (net response rate 74%) enrolled in 1997 in our study. The majority were women (71.9%), and the mean age at the start of the study was 59.8 (SD 14.8) years (Table 1). The effect of RA on all domains of HRQOL was indicated by the relatively unfavorable scores on all subscales of the RAND-36. The summary scales showed that physical health was more affected than mental health.

Response. In the first year of the study 882 patients participated. Of the 1200 invited patients, 14 could not be reached because of relocation to an unknown address and 304 refused to participate. With respect to potential systematic differences between respondents and nonrespondents we conducted a specific study of nonresponders[20] to determine the extent of bias with respect to key items under study. This nonresponse study showed that respondents were younger than nonrespondents (on average 5 years). The most important predictors of nonresponse were self-reported pain and

Table 1. Characteristics of study population at baseline.

	Total Population (N = maximum 882)
Women, no. (%)	634 (71.9)
Age, yrs, mean (range), SD	59.8 (18.5–91.6), 14.8
Disease duration, yrs, mean (range), SD	8.9 (0–66.7), 9.8
No. of patients per disease duration, yrs	
< 1	102
1–2	165
2–3	98
3–5	58
5–7	62
7–10	88
10–15	135
15–20	71
> 20	103
Disability, mean (range), SD	0.66 (0–2.75), 0.62
VAS-pain, mean (range), SD	40.6 (0–100), 28.1
RAND-36, mean (range), SD	
Physical functioning	49.0 (0–100), 27.2
Social functioning	68.8 (0–100), 27.6
Role physical	39.7 (0–100), 42.4
Role emotional	70.8 (0–100), 41.5
Mental health	70.5 (4–100), 19.5
Vitality	53.8 (0–100), 20.6
Pain	54.8 (0–100), 23.1
General health	49.7 (0–100), 20.3
PCS	35.8 (9.0–61.7), 10.8
MCS	49.2 (16–72.6), 11.4

RAND-36: RAND 36-Item Health Survey; PCS: physical component summary scale; MCS: mental component summary scale.

health care utilization, with respondents reporting pain more often and using healthcare services additional to rheumatology care more often.

In 1998, 755 patients (87% of the eligible respondents of 1997) took part in the questionnaire survey. In 1999, 683 patients (81% of the eligible respondents) returned the questionnaire. In 2002, 529 of 720 patients still eligible (73%) participated in the followup.

Health outcomes as a function of disease duration: longitudinal approach. Our results from the longitudinal approach indicated that in the first years after diagnosis, pain did not increase. Indeed, there were indications of a statistically significant decline of pain between 2 and 3 years of disease duration. After 3 years, pain increased constantly (Figure 1A). With regard to disability, patients started to experience statistically significantly progressive deterioration of functional capacity after 3 years of disease (Figure 1B).

With regard to HRQOL our analyses showed mainly

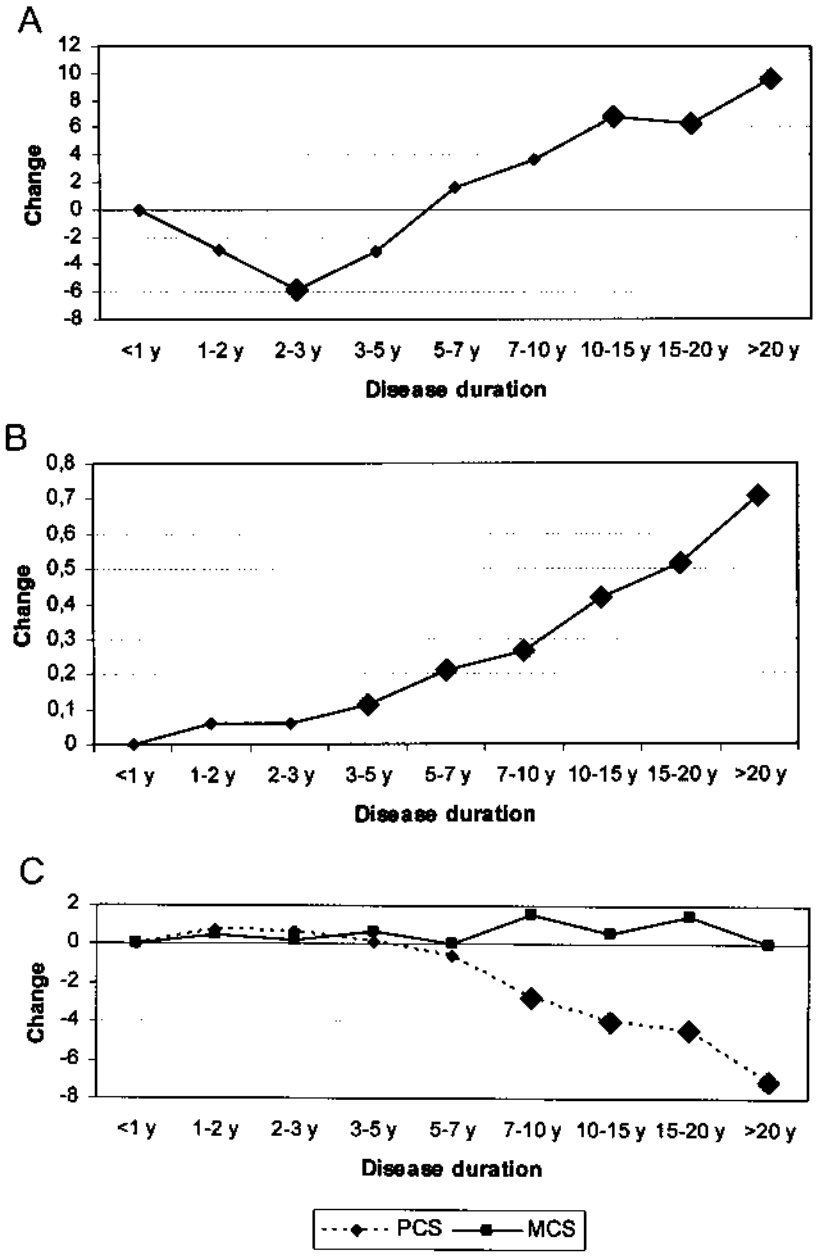

Figure 1. Change of health outcomes in relation to disease duration: results from the random-intercept model. A. Change in RA-related pain (VAS) by disease duration. B. Change in disability (VDF) by disease duration. C. Change in physical (PCS) and mental (MCS) component summary scales by disease duration. Bold markings indicate significant changes with regard to "< 1 year."

longterm consequences for physical health (Figure 1C). Physical health (PCS) declined significantly after 7 years of disease duration. With respect to mental health (MCS), no statistically significant changes during followup could be detected. Predicted estimates of change are shown in Table 2.

Health outcomes as a function of disease duration: Comparison of longitudinal vs cross-sectional approach. The cross-sectional approach matched the longitudinal approach rather well. Results of cross-sectional analyses of data of the first series (1997) and of the longitudinal approach with the random-intercept model are given in Table 2 and illustrated in Figure 2. Results are highly comparable. The longitudinal approach yielded slightly smoother curves with fewer fluctuations.

DISCUSSION

Although health outcomes generally deteriorated over time, different patterns for various health outcomes were found. The observed improvement of RA-related pain in the early years of the disease might be explained by optimal response to medication, which is subsequently lost with further progression of the disease. It also might be that after 3 years another pain pathway, i.e., structural damage, becomes more important than inflammation, leading to the increase of pain. Disability started to deteriorate significantly only after 3 years of disease duration. Whereas the PCS deteriorated with longer disease duration, the MCS remained fairly stable over time.

We expected that the longitudinal approach with repeated measurements would provide divergent and more reliable results with respect to estimates on the course of health outcomes than the cross-sectional approach with one single measurement. However, both approaches yielded highly comparable results. The slightly smoother curves of the longitudinal approach with repeated measurements are to be expected as more data are included. Thus, although

Table 2. Pain, disability, and HRQOL (PCS and MCS): means (M) and predicted (P) values (95% confidence intervals) from the random-intercept model, by disease duration cohort.

	< 1 Year	1–2 Years	2–3 Years	3–5 Years	5–7 Years
Pain					
Cross-sectional (M)	35.53 (30.08; 40.98)	32.19 (27.90; 36.48)	36.51 (31.22; 41.80)	46.44 (39.46; 53.42)	40.77 (34.20; 47.34)
Longitudinal (P)	37.27 (32.78; 41.76)	34.38 (31.32; 37.44)	31.48 (28.65; 34.31)	34.16 (31.49; 36.83)	38.90 (36.12; 41.69)
Change (P)		–2.89 (–7.61; 1.83)	–5.79 (–10.51; –1.08)	–3.11 (–7.91; 1.68)	1.63 (–3.18; 6.44)
Disability					
Cross-sectional (M)	0.40 (0.32; 0.49)	0.48 (0.40; 0.56)	0.49 (0.39; 0.59)	0.63 (0.49; 0.76)	0.58 (0.44; 0.72)
Longitudinal (P)	0.44 (0.36; 0.52)	0.50 (0.44; 0.56)	0.50 (0.44; 0.56)	0.55 (0.50; 0.61)	0.65 (0.60; 0.71)
Change (P)		0.06 (–0.01; 0.13)	0.06 (–0.01; 0.13)	0.11 (0.04; 0.19)	0.21 (0.14; 0.29)
PCS					
Cross-sectional (M)	39.06 (37.08; 41.04)	39.42 (37.82; 41.02)	38.65 (36.45; 40.85)	35.76 (33.04; 38.49)	37.10 (34.32; 39.87)
Longitudinal (P)	38.10 (36.58; 39.61)	38.85 (37.75; 39.94)	38.76 (37.73; 39.80)	38.18 (37.19; 39.17)	37.52 (36.52; 38.53)
Change (P)		0.75 (–0.72; 2.22)	0.67 (–0.82; 2.16)	0.08 (–1.44; 1.61)	–0.57 (–2.09; 0.94)
MCS					
Cross-sectional (M)	47.49 (45.13; 49.85)	50.16 (48.42; 51.90)	48.95 (46.67; 51.23)	45.01 (41.65; 48.37)	48.12 (45.23; 51.01)
Longitudinal (P)	47.96 (46.11; 49.81)	48.45 (47.17; 49.74)	48.21 (47.01; 49.41)	48.64 (47.50; 49.78)	47.97 (46.80; 49.15)
Change (P)		0.50 (–1.40; 2.39)	0.25 (–1.66; 2.17)	0.68 (–1.26; 2.62)	0.02 (–1.92; 1.96)

	7–10 Years	10–15 Years	15–20 Years	> 20 Years
Pain				
Cross-sectional (M)	43.01 (36.99; 49.03)	41.80 (37.10; 46.50)	48.99 (42.11; 55.87)	50.04 (43.98; 56.10)
Longitudinal (P)	40.90 (37.89; 43.90)	44.13 (41.37; 46.88)	43.52 (40.26; 46.78)	46.85 (43.23; 50.46)
Change (P)	3.62 (–1.61; 8.86)	6.85 (1.66; 12.05)	6.25 (0.73; 11.77)	9.57 (3.82; 15.33)
Disability				
Cross-sectional (M)	0.75 (0.61; 0.89)	0.70 (0.59; 0.81)	0.94 (0.80; 1.08)	1.11 (0.96; 1.25)
Longitudinal (P)	0.71 (0.65; 0.76)	0.86 (0.80; 0.92)	0.95 (0.89; 1.02)	1.15 (1.07; 1.23)
Change (P)	0.27 (0.18; 0.35)	0.42 (0.33; 0.51)	0.51 (0.42; 0.61)	0.71 (0.60; 0.82)
PCS				
Cross-sectional (M)	33.45 (31.14; 35.76)	34.19 (32.42; 35.96)	30.70 (28.22; 33.18)	30.19 (27.81; 32.57)
Longitudinal (P)	35.37 (34.29; 36.44)	34.14 (33.11; 35.18)	33.63 (32.42; 34.83)	30.99 (29.55; 32.42)
Change (P)	–2.73 (–4.44; –1.02)	–3.95 (–5.71; –2.20)	–4.47 (–6.36; –2.57)	–7.11 (–9.18; –5.04)
MCS				
Cross-sectional (M)	49.80 (47.21; 52.39)	49.44 (47.39; 51.50)	51.83 (49.32; 54.34)	49.64 (47.18; 52.11)
Longitudinal (P)	49.50 (48.22; 50.77)	48.55 (47.37; 49.74)	49.39 (47.99; 50.79)	48.04 (46.45; 49.63)
Change (P)	1.54 (–0.61; 3.68)	0.60 (–1.56; 2.75)	1.43 (–0.87; 3.73)	0.08 (–2.36; 2.52)

PCS: physical component summary scale; MCS: mental component summary scale.

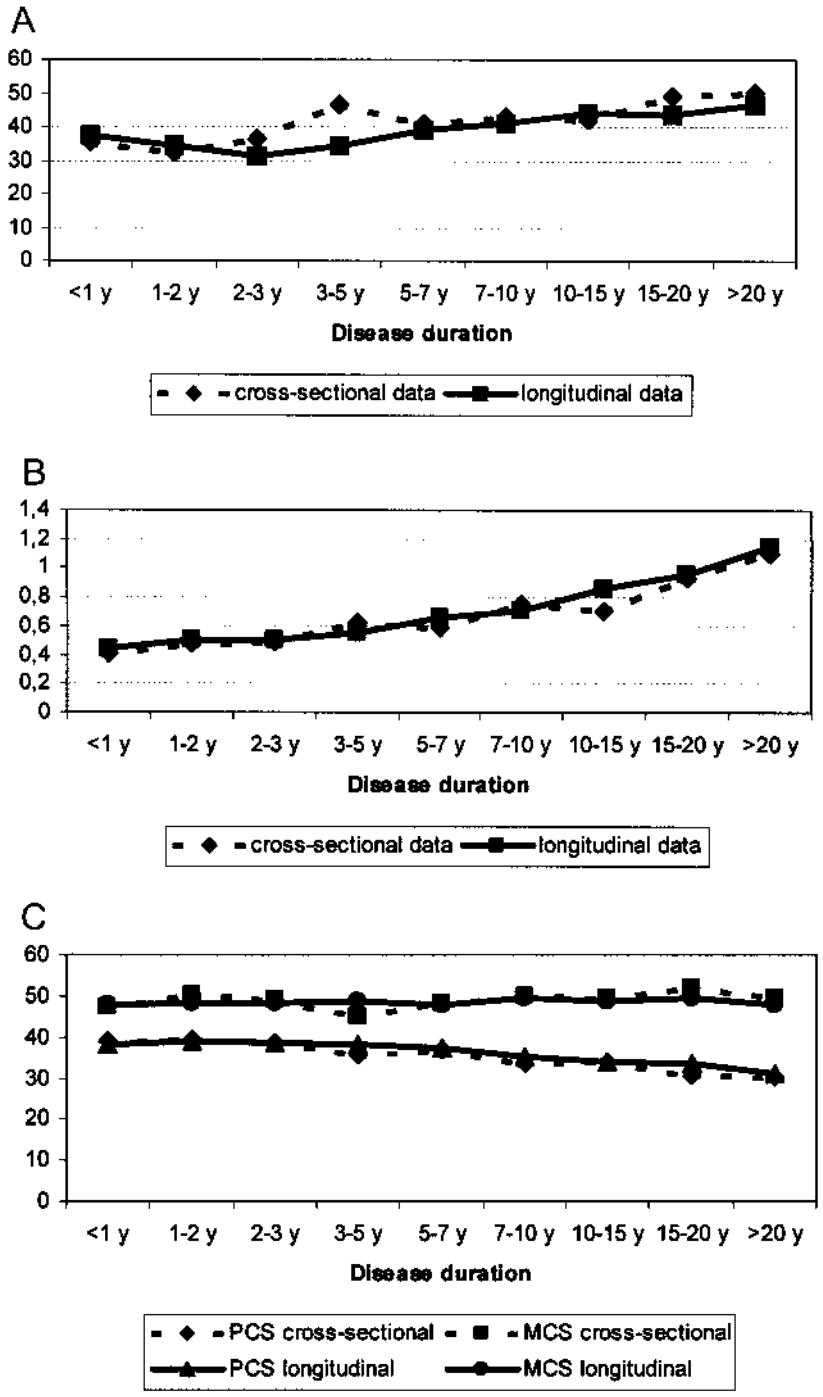

Figure 2. Comparison of cross-sectional data (group means of measurement in 1997) and longitudinal data (predicted values from the random-intercept model). A. RA-related pain (VAS) by disease duration. B. Disability (VDF) by disease duration. C. Physical (PCS) and mental (MCS) component summary scales by disease duration.

longterm health outcomes in RA are preferably assessed in long duration followup studies, cross-sectional studies that include patients with a broad range of disease durations seem to provide fairly reliable estimates of the course of health outcomes.

This conclusion holds particularly for chronic conditions and not for lethal conditions. In lethal diseases, e.g., cancer, cross-sectional studies including patients of varying disease durations might lead to an underestimation of deterioration as a consequence of selective mortality.

It should be noted that we did not compare a cross-sectional with a purely longitudinal data design. In a purely longitudinal approach, patients preferably enter the study at the same point in time. We started with a cohort of patients with a broad range of disease durations in which some selection bias cannot be ruled out.

Moreover not all changes in health outcomes might have been detectable — depending on their individual disease durations, not all patients needed to change between cohorts during followup.

Since we were especially interested in the course of health outcomes during followup, and not in the effect of explanatory variables on health outcomes, no multivariable adjusted models were generated. However, our findings are potentially subject to residual confounding.

Cross-sectional and longitudinal designs are certainly not fully interchangeable. Causal relationships and sequential order between variables can be assessed properly only by a longitudinal approach. Cross-sectional studies provide specific information about the burden of disease in various disease cohorts. Moreover, cross-sectional studies of patients of various disease durations appear to give reliable indications about the course of health outcomes of chronic conditions, and thus might be used as alternatives when real longterm followup is not feasible, and might help when investigators design more specifically targeted longitudinal followup studies.

ACKNOWLEDGMENT

We thank M. Kammeijer for her contribution in the data collection and M. Triemstra for her contribution to the study.

REFERENCES

1. Gladman DD, Farewell VT. Longitudinal cohort studies. J Rheumatol 2005;32 Suppl 72:30-2.
2. Kvien TK, Uhlig T. The population based studies in rheumatoid arthritis. A method of longterm followup studies. J Rheumatol 2004;31 Suppl 69:35-40.
3. Lindqvist E, Saxne T, Geborek P, Eberhardt K. Ten year outcome in a cohort of patients with early rheumatoid arthritis: health status, disease process, and damage. Ann Rheum Dis 2002;61:1055-9.
4. Minaur NJ, Jacoby RK, Cosh JA, Taylor G, Rasker JJ. Outcome after 40 years with rheumatoid arthritis: a prospective study of function, disease activity, and mortality. J Rheumatol 2004;31 Suppl 69:3-8.
5. Symmons DP, Silman AJ. The Norfolk Arthritis Register (NOAR). Clin Exp Rheumatol 2003;21 (5 Suppl 31):S94-S99.
6. Welsing PM, van Riel PL. The Nijmegen inception cohort of early rheumatoid arthritis. J Rheumatol 2004;31 Suppl 69:14-21.
7. Wolfe F, Hawley DJ. The longterm outcomes of rheumatoid arthritis: Work disability: a prospective 18 year study of 823 patients. J Rheumatol 1998;25:2108-17.
8. Wolfe F, Zwillich SH. The long-term outcomes of rheumatoid arthritis: a 23-year prospective, longitudinal study of total joint replacement and its predictors in 1,600 patients with rheumatoid arthritis. Arthritis Rheum 1998;41:1072-82.
9. Wolfe F, Sharp JT. Radiographic outcome of recent-onset rheumatoid arthritis: a 19-year study of radiographic progression. Arthritis Rheum 1998;41:1571-82.
10. Zink A, Huscher D. Longterm studies in rheumatoid arthritis — the German experience. J Rheumatol 2004;31 Suppl 69:22-6.
11. Rupp I, Boshuizen HC, Jacobi CE, Dinant HJ, van den Bos GAM. Comorbidity in patients with rheumatoid arthritis: effect on health-related quality of life. J Rheumatol 2004;31:58-65.
12. Rupp I, Boshuizen HC, Jacobi CE, Dinant HJ, van den Bos GAM. Impact of fatigue on health-related quality of life in rheumatoid arthritis. Arthritis Rheum 2004;51:578-85.
13. Arnett FC, Edworthy SM, Bloch DA, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988;31:315-24.
14. Bijlsma JW, Oude Heuvel CHB, Zaalberg A. Development and validation of the Dutch questionnaire capacities of daily life (VDF) for patients with rheumatoid arthritis. J Rehabil Sci 1990;3:71-4.
15. Van der Zee KI, Sanderman R. Measuring general health status with the RAND-36. User's manual. [Het meten van de algemene gezondheidstoestand met de RAND-36. Een handleiding]. Groningen: Northern Center for Healthcare Research, University of Groningen; 1993.
16. Hays RD, Sherbourne CD, Mazel RM. The RAND 36-Item Health Survey 1.0. Health Econ 1993;2:217-27.
17. Ware JE Jr, Kosinski MA, Keller SD. SF-36 Physical and Mental Health Summary Scales: a user's manual. Boston: The Health Institute, New England Medical Center; 1994.
18. Aaronson NK, Muller M, Cohen PD, et al. Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations. J Clin Epidemiol 1998;51:1055-68.
19. Ware JE Jr, Gandek B, Kosinski M, et al. The equivalence of SF-36 summary health scores estimated using standard and country-specific algorithms in 10 countries: results from the IQOLA Project. International Quality of Life Assessment. J Clin Epidemiol 1998;51:1167-70.
20. Rupp I, Triemstra M, Boshuizen HC, Jacobi CE, Dinant HJ, van den Bos GAM. Selection bias due to non-response in a health survey among patients with rheumatoid arthritis. Eur J Public Health 2002;12:131-5.