Summary

The burden of illness in chronic diseases such as rheumatoid arthritis (RA) can be expressed in measures of outcome. Ideally, these measures should reflect all suffering throughout the course of the disease. The impact of RA on the patient's health and well-being has often been expressed by the 'five Ds' of death, disability, drug side effects, discomfort, and dollar costs. However, these outcome measures do not fully reflect the burden of illness in the RA patient. Aim of this thesis was to evaluate some generally used outcome measures as well as a number of more patient-centered outcome measures giving a better reflection of the burden of illness in a cohort of patients with recent onset RA at the start of the study during six years of follow-up. The study was performed at the University Hospitals of Groningen and Nijmegen and at the Medical Center of Leeuwarden.

In chapter 2, an assessment of the onset of radiographic damage in the large joints (hips, knees, shoulders, elbows, ankles and tarsus) and the onset of atlantoaxial subluxation was performed. Large joint damage appeared to be an early phenomenon with 20% of the patients having some damage in at least one large joint within one year, and 50% of the patients within six years after disease onset. The progression of large joint damage was most pronounced in the patients with the largest progression of damage in their hands and feet, and these patients had more functional impairment, and had suffered the largest cumulative disease activity. The disease activity at study entry was the only predictor of large joint damage that reached statistical significance. Atlanto-axial subluxation did occur early in the disease, particularly in patients with progressive erosive disease in their hands and feet.

Radiographic progression of damage in hands and feet is considered an important and objective outcome measure in RA, and is used as a measure of drug effectiveness. In chapter 3, we evaluated whether the reported largest increase of radiographic damage in the first years of the disease is a real phenomenon, or due to a ceiling effect caused by reaching maximum scores for erosions and/or joint space narrowing in individual joints, inherent to the scoring system. Using the Van der Heijde modification of Sharp's method to assess radiographic damage, a ceiling effect influenced significantly the mean radiographic progression after a disease duration of six years. In some individual patients the ceiling effect appeared to occur earlier. After six years, the maximum scores were distributed over 50% of the patients, and 20% of the patients had
maximum scores in more than ten joints without preference for specific localisation. Therefore, the ceiling effect appeared to be clinically relevant and should be taken into account when interpreting the effects of DMARDs on radiographic progression in RA during the first years of the disease. Furthermore, it must be accounted for when describing the relationship between radiographic progression and process variables, which are used to assess the effect of DMARDs.

Antirheumatic drugs have to be taken daily by most patients with RA, and often patients have to attend the outpatient clinic and/or laboratory for monitoring purposes. In chapter 4, the burden of illness related to the use of antirheumatic drugs was evaluated. Inefficacy appeared to be the main reason for DMARD discontinuation. The mean number of different DMARDs used was 3.1, and the mean number of different NSAIDs 2.4. The median duration of use for the first five DMARDs ranged from 0.7-2.8 years. The time consumption due to antirheumatic drug treatment was mainly caused by monitoring for adverse drug reactions. The patients who had the largest radiographic progression and who suffered the largest cumulative disease activity and physical disability, had the largest number of DMARD changes.

Having a chronic disease such as RA can be very time consuming. In chapter 5, we tried to quantify the time consumption due to treatment and monitoring activities as well as the extra time needed to perform activities of daily living. RA patients were compared with a group of asthma and COPD patients. RA as well as asthma and COPD appeared indeed to be time consuming diseases. In particular the activities of daily living and daily disease-related activities were taking much (extra) time. For the RA patients, there was a reduction of effective life expectancy, i.e. that part of life that a patient can live according to his own wishes, ideals or ambition, of at least 11.6%. The time consumption was most pronounced for the patients with the largest (progression of) radiographic damage in hands and feet, the largest physical disability, and the largest cumulative disease activity after six years. RF-positivity at study entry was the only variable that reached statistical significance as a prognostic factor for time consumption. Suggestions were provided for a reduction of the time consumption caused by RA.

One possible way to reduce time consumption of patients and doctors is the use of self-administered forms filled in by patients. The self-administration of joint involvement has already been investigated, however a comparison between several of these joint counts has never been performed. In chapter 6, the
reproducibility and the validity to measure disease activity of several self-administered joint counts was evaluated. The joint involvement measured by patients was reproducible, however, the correlation with the joint examination of the assessors was moderate. The relation of the self-administered scores and the assessors' scores with other disease activity variables was comparable. Therefore, at the present time the assessors' joint examination can not be replaced by self-administered joint involvement. The value of the self-administered joint involvement in the evaluation of disease activity should be investigated further in the future.

The literature addressing the socioeconomic consequences of RA for the patient has mainly been focussed on work disability. However, the socio-economic impact should not be restricted to changes in work and income, but also comprehend fatigue, recreation, transport mobility, housing facility and social support. These items were studied in chapter 7, focussing on the impact in the first years of the disease. Observed socio-economic changes varied from nine percent (removals) to 59% of the cohort (reduced recreation pattern). Concrete effect magnitudes showed work disability to increase by 4-15 times, whereas, after three years, 42% of the patients was registered 'work disabled'. Due to fatigue, patients needed extra bedrest (during daytime), recreation changed towards a lower joint loading pattern and social dependency increased (with frequencies varying from monthly to daily support). Multiple regression analyses showed socioeconomic changes to be influenced by age, gender, household composition and work situation. Furthermore, physical limitation appeared to be predictive for work related income reduction, reduced transport mobility and development of social dependency.

The prediction of longterm outcome in RA is important for many reasons, both for the individual patient and for the health care providers as well as for health economics. In chapter 8 prognostic factors for the different outcome measures and the interrelationship if these outcomes were studied. There was good relationship between measures of joint damage in small and large joints, cumulative disease activity (as expressed by markers of the acute phase response), physical disability, and (for most of them) psycho-social consequen-

ces. The strongest correlations were found between the objective outcome measures joint damage and markers of the acute phase response. One third of the patients could be correctly classified as having a 'poor' or a 'good' outcome for all respective outcome measures which shows that the discrimination of outcome measures in two classes only ('good' or 'poor') has its limitations. C-reactive
protein, an objective indicator of disease activity, appeared to be the best single predictor of outcome, both when measured at study entry and when measured serially throughout the course of the disease. The accuracy of the prediction of physical disability and AIMS (including psycho-social consequences), using the factors which appeared to be predictive for radiographic damage, was lower than for the other measures of outcome reflecting the multi-dimensional nature of disease outcome in RA.

Conclusion: the burden of illness in rheumatoid arthritis is impressive, particularly for the group of patients with persistent disease activity leading to progressive joint destruction and functional impairment. Recognition of this burden is important with respect to e.g. the handling of work (dis)ability assessments in patients with RA, as well as with respect to the development of (new) treatment and counselling strategies for these patients and the concomitant monitoring activities. At all times, we should bear in mind that our patients 'have rheumatoid arthritis' instead of 'are rheumatoid arthritis'.