Systematic review of studies of productivity loss due to rheumatoid arthritis

Wayne Burton¹, Alan Morrison², Ross Maclean³ and Eric Ruderman¹

Background  Rheumatoid arthritis (RA) is a chronic, debilitating disease with a significant impact on workplace productivity.

Aim  To perform a systematic review of studies of the relationship between RA and reduced workplace productivity.

Methods  Screening of 307 titles identified in bibliographic database searches resulted in 38 articles subject to systematic review. Productivity loss was expressed by three different measures: work disability, work loss (synonymous with absenteeism or short-term sick leave) and work limitation (reduction in productivity while present at work).

Results  A median of 66% (range 36–84%) of employed RA subjects experienced work loss due to RA in the previous 12 months, for a median duration of 39 days (range 7–84 days). The times from RA diagnosis until a 50% probability of being work disabled varied from 4.5 to 22 years. In inception cohort studies, the baseline variables consistently predictive of subsequent work disability were a physically demanding work type, more severe RA and older age.

Conclusions  RA-related work-disability rates were similar in the USA and European countries. An apparent decrease in the prevalence of RA-related work disability since the 1970s may be related to a decrease in physically demanding work rather than to epidemiologic changes in RA. The majority of the literature addresses permanent disability and temporary work loss; none of the studies reviewed reported the effect of RA on presenteeism, i.e. work limitation from the employer perspective, and there are few published studies of the effectiveness of disease-modifying anti-rheumatic drugs in reducing work-related productivity loss.

Key words  Economics; employment; epidemiology; rheumatoid arthritis; risk factors.

Introduction  Rheumatoid arthritis (RA) is a chronic, systemic, inflammatory disorder of unknown aetiology. Its prevalence in North America and Europe is 0.4–3.0% and the annual incidence in North America is 24–75/100 000 [1]. Both prevalence and incidence rates are 2–4-fold higher in women than in men [1]. The prevalence increases and the women-to-men ratio decreases with age [1].

Many researchers have estimated the costs of RA from a societal perspective [2–11]. Given that most sufferers develop the disease between 35 and 50 years of age and many experience functional loss that translates into reduced productivity and work disability, employers have a vested interest in understanding the relationship between RA and productivity loss. Our objective, therefore, was to perform a systematic review of studies of the relationship between RA and reduced workplace productivity from an employer perspective.

AND lost) OR work-loss OR ‘work loss’). HealthStar, CINAHL and International Pharmaceutical Abstracts were searched with the algorithm (limited to human subjects): ‘arthritis, rheumatoid’[MeSH term] AND (productivity or (work and LOST) or work-loss or ‘work loss’ or presenteeism or absenteeism). The Cochrane database of systematic reviews was searched with the title word ‘rheumatoid arthritis’. The Medline search yielded 272 records and the other searches identified 9 additional records. Articles not in English were identified by repeating the Medline search without the language limitation. The electronic database searches were supplemented by titles identified in the bibliographies of reviews [1,3,5, 12–24] and by titles known to the authors.

Titles were screened and full-text copies retrieved if the article was a primary report in the peer-reviewed literature of a study in which subjects ≥18 years of age were selected on the basis of a diagnosis of RA and a measure of work productivity loss was a study outcome or the article was a narrative or systematic review of such studies and the article was in English or had a sufficiently detailed abstract in English. Full-text copies were screened and articles excluded if ‘arthritis’ was not defined [25] or if ‘arthritis’ referred to a broad spectrum of forms of the disease [26]. The latter included studies in which the data source was the National Health Interview Survey [22,27] and other national surveys [23,28–31]. Articles about symmetrical polyarthritis, which is a simulated definition computed from responses to the 1978 Social Security Survey of Disability and Work, were also excluded [32,33]. Duplicate articles were excluded. After exclusions, 38 titles remained for data abstraction [2,4,7,8,34–67]. Two of the authors carried out this process, which is summarized in Figure 1.

Data from the primary studies were collected using data abstraction forms. Productivity loss was expressed by three different measures: work limitation, work loss and work disability. Work limitation is synonymous with presenteeism, defined as time lost because of a diminished capacity while at work, and work loss is synonymous with absenteeism, defined as time off work [68,69]. Work disability is the permanent partial or complete disablement for work purposes.

The specific statistics abstracted and the corresponding study selection criteria were as follows.

(i) Period estimate of the proportion of RA patients with work loss. Studies were included if they reported the proportion of subjects with work loss, the corresponding time period, that the work loss was due to RA and that all patients were gainfully employed. Point estimates of the proportion of patients with work loss (i.e. on sick leave at the time of interview) were not included [37,44].

(ii) Period estimate of the mean duration of work loss. Studies were included if they reported the mean duration of work loss due to RA per employee over a 1-year period among gainfully employed subjects. An estimate of work loss per month since RA onset was excluded [52].

(iii) Point estimate of the proportion of RA patients with work disability. Cross-sectional studies reporting the proportion of RA-related work disability at the time of the review and the mean duration of RA were included. The denominator (the patient set
at RA onset) was either employed subjects only or all subjects regardless of employment status. The 'year of study' was the year in which the study was carried out, the most recent year if a range of study dates was provided or the year of publication if the study date was not reported.

(iv) Survival analyses of work disability. Studies were included if patients were employed at baseline (or, in one study, working during the course of their RA) work disability was due to RA and a Kaplan–Meier survival analysis was performed.

(v) Factors associated with work disability. Multivariate regression analyses with a sample size ≥250 and dependent variable work disability due to RA were included. An inception cohort study was defined as one in which the mean duration of RA of patients entering the study was ≤1 year. Studies were excluded if the dependent variable was ‘no longer working outside the home for pay’ [59,60] or ‘leaving the work force’ [60], or if ‘work disability’ was not defined [45]. There was insufficient information in the English abstracts of two foreign-language articles for data abstraction [52,70]. Results from different studies were described using simple summary statistics and no statistical pooling was attempted. Dixon’s test for statistical outliers was applied to investigate the significance of the difference between a suspicious extreme value and other values in the sample [71].

Results

Most studies were cross-sectional in design but six were inception cohort studies. With few exceptions, the patients were identified via a physician diagnosis of RA, usually according to American College of Rheumatology or American Rheumatology Association criteria. In the US and UK studies, the source for productivity loss information was patient self-report. Data were collected via a questionnaire completed at the clinic [40,57,65,66], a mailed questionnaire [35,43] or via a structured interview given either at home [54] or by telephone [55]. Work disability was defined in these studies as self-reported work disabled [43,54,57,66], unemployed due to RA [35] or retired early or no longer working due to RA [55,65,67]. In one US study, the definition of work disability was ‘receiving work-disability payments’ [40].

In Northern European countries, work disability is covered by statutory national insurance schemes and databases containing this information were used as the information source in Finland [51], Germany [62] and Norway [46]. In other European studies, work disability was measured by a questionnaire but was based on a validated definition: subjects were recipients of a disability pension in Germany [56], while in the Netherlands [34,41], Lithuania [42] and Finland [63] work disability was described as registered [34] or officially recognized [41,42] or was confirmed from disability certificates [63].

From 22 to 76% (median 54%) of employed subjects with RA had experienced work loss due to RA in the previous 6 months and 36–84% (median 66%) in the previous 12 months (Figure 2A). The median of estimates of the mean duration of work loss in the previous 12 months was 39 days (range 7–84 days; Figure 2B).

About 20–70% of people who were employed at RA onset were work disabled after 7–10 years (Figure 3A). The corresponding range of values for all subjects (employed or otherwise at RA onset) was 19–52%. There appears to be a time trend to increasing work disability when outliers are excluded [points outside the shaded area in Figure 3(A)—see caption to Figure 3]. In addition, there appears to have been a decrease in the proportion of RA subjects with work disability from the 1970s until the present (Figure 3B).

In survival analyses, the times from RA onset until 50% probability of being work disabled varied widely,
from 4.5 to 22 years, with a median of 13 years (Figure 4). In several analyses, the biggest jump in work disability occurred in the first year after diagnosis and fall off was roughly linear for the next 4–9 years.

Factors associated with work disability are presented in Table 1. In cohort studies, the baseline variables that were consistently predictive of subsequent work disability were a physically demanding work type, greater RA severity—e.g. expressed as score on the Health Assessment Questionnaire (HAQ), which measures functional disability in the activities of daily living, joint count—and older age. Other demographic and socioeconomic variables (female, less education) were predictive of work disability in some studies but not others. A study of the Norwegian population, examining only demographic and socioeconomic variables, confirmed that older age, female and less education were predictive of work disability due to RA [46]. Results from cross-sectional studies were similar [35,43]. Demographic and disease variables were controlled for in one study so that work and patient factors could be examined [41]. In that analysis, personal factors (coping style) and organizational factors (e.g. attitudes of management) were associated with work disability.

**Discussion**

Population-based studies have shown the labor force participation of people with RA to be substantially less than that in the population at large. In Lithuania, the age- and sex-adjusted employment rate was 24% lower in RA patients than in the general population [42]. Similar results were reported in two studies set in the Netherlands [64,75]. (In a third Netherlands study, the labor force participation of persons with RA was only slightly less than that of the general population [76]. The reason for this discrepancy is unclear.) This substantial differential effect of RA was confirmed in a UK
<table>
<thead>
<tr>
<th>Citation</th>
<th>Dependent variable</th>
<th>Associated factors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cohort studies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Holte et al. 2001 [46]</td>
<td>Becoming a disability pensioner with RA in the next 10-year period</td>
<td>c</td>
</tr>
<tr>
<td>Puolakka et al. 2005 [74]</td>
<td>RA-related disability pension within 5 years</td>
<td>—</td>
</tr>
<tr>
<td>Young et al. 2002 [67]</td>
<td>Permanent work disability at 5 years</td>
<td>Manual or semi-manual work type</td>
</tr>
<tr>
<td>Yelin et al. 1987 [66]</td>
<td>Work disabled (as opposed to working) in 1985</td>
<td>Work characteristics</td>
</tr>
<tr>
<td>Wolfe and Hawley 1998 [65]</td>
<td>Work disability</td>
<td>Moderate/heavy versus light/sedentary work type</td>
</tr>
<tr>
<td><strong>Cross-sectional studies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chorus et al. 2001 [41]</td>
<td>Withdrawal from the labor force</td>
<td>Limitations coping style, pain coping style, coaching of management, career opportunities within company, accessibility of workplace, mobility in transportation and temporary job position</td>
</tr>
<tr>
<td>Allaire et al. 1996 [35]</td>
<td>RA-related work disability</td>
<td>Non-professional or non-administrative job, job physical demand, commuting difficulty and less co-worker support.</td>
</tr>
<tr>
<td>De Roos and Callahan 1999 [43]</td>
<td>Work disabled versus working</td>
<td>Non-professional or non-managerial occupation</td>
</tr>
</tbody>
</table>

BMI, body mass index; ESR, erythrocyte sedimentation rate; RADAR, rapid assessment of disease activity in rheumatology; RF, rheumatoid factor; VAS, visual analogue scale.

*aCohort studies analyzed patient factors measured at baseline (the first clinic visit). In cross-sectional studies, the independent variables referred to the current or recalled status of subjects. The article by Puolakka et al. [74] appeared after completion of the systematic review but has been added since it met the inclusion criteria.

*bStudy of the population of Norway. Work disability with RA was measured for the 10-year periods 1971–80 and 1981–90 among persons identified in the 1970 and 1980 censuses, respectively. Only factors significant in both decades analyzed are presented here.

*cOnly demographic and economic variables were available. Type of work (manual or routine non-manual as opposed to professional) was significant in 1981–90 but not 1971–80.

*dService industry work, more physical activities and fewer discretionary activities.

*eDisease and demographic variables were controlled for in the model.
inception cohort study [37]. All subjects with RA and matched controls were initially economically active. At the 4-year follow-up, 33% of RA cases were economically inactive because of permanent disability compared with only 2.7% of controls. Similar proportions of RA cases and controls, however, experienced work loss [37].

Estimates of RA-related work loss varied substantially. The proportion of employees with RA-related work loss was greater in Germany than in Lithuania or the USA/Mexico (Figure 2A). This cannot be explained by demographic differences (in age or sex). The differences among countries other than Germany could plausibly be related to the HAQ score or duration of disease (HAQ scores were not available for the studies set in Germany). The mean number of days of work loss was also greater in Germany than in other countries (Figure 2B), though this might reflect an inverse relationship between work loss and RA duration. The relatively low number of work loss days in the Canadian study (C1997 in Figure 2B) could be due to the age of the subjects (60 years) [7]. It is conceivable that the greater durations of work loss in Germany are related to social policy, but no definitive explanation can be given.

Differences in social policy have been suggested as influencing RA work-disability rates [19]. There is no indication, however, that work-disability rates vary systematically by country (Figure 3). The variability in survival time until work disability (Figure 4) might be due to differences in the patient populations. Variations in patient age, degree of disability and job type can produce times to 50% work disability that range from 2 to ≥12 years [53]. Whether such factors entirely explain the variations seen in Figure 4 is unclear. However, the study ranking in the time to 50% work disability corresponds to the rankings in (i) mean HAQ score at study entry (0.6 [34] and 0.27 [63]) and (ii) the proportion of subjects with moderate or demanding work type (0.73 [63] and 0.35 [65]).

Consistent with previous suggestions [12], the data in Figure 3(B) seem to show that the prevalence of RA-related work disability has decreased over time. This temporal decline is not related to changes in RA patient demographics (which remained constant) or in patient disability (HAQ scores, reported for studies done in the last 10–15 years, were unchanged). Although a temporal decline in the incidence of RA in the USA and Europe has been suggested [77–79], a comprehensive review of studies indicates that the RA prevalence rate has remained constant over the last several decades (Figure 3C) [72]. Figure 3(C) also indicates that there has been a decrease in the proportion of US workers engaged in goods-producing work, which we take as a surrogate for manual or physically demanding work. It is possible, therefore, that the apparent temporal decrease in RA-related work disability reflects a decrease in the proportion of subjects doing physically demanding work. The data in Figure 3(B) are consistent with this hypothesis. If only those studies in which 29–45% of subjects performed manual work are examined (shaded in Figure 3B), there is no evident decrease in work disability over time. [The highest—and earliest—value for the proportion of work disability in Figure 3(B)—0.66 in US1978 [54]—occurred in the study with the greatest proportion of manual workers: 0.45; median 0.35 for the other estimates, range 0.29–0.35.] Furthermore, the apparent time trend in the two studies labeled F1982 and S2003 in Figure 3(B) could be explained by a difference in the proportion of subjects performing moderate or heavy physical work—0.81 in the earlier study and 0.54 in the later one [2,51]. [Comparable statistics were not available for the other studies shown in Figure 3(B).]

A study of the Norwegian population, however, did not provide consistent evidence of a temporal decline in the incidence of work disability due to RA [46]. This study reported the cumulative 10-year incidence of disability for those currently employed and without a disability pension in the index year (the year of the national census: 1970 or 1980). Compared with the 1971–80 period, the incidences of work disability due to RA in the 1981–90 period decreased by 24% for men 30–39 years of age and by 3.9% for those 40–49 years of age but increased by 21–44% for other demographic categories (men 50–56 years and women 30–39, 40–49 and 50–56 years) [46].

It has been suggested that RA duration is not consistently associated with the likelihood of work disability [80]. The time trends evident in survival curves (Figure 4) would then presumably reflect the relationship with patient age. However, both RA duration and age were independently associated with work disability in cross-sectional studies in which these variables were included (Table 1). The prevalence estimates of work disability shown in Figure 3(A) are consistent with a time trend, if studies with extreme values for patient age, percent females and mean HAQ score are excluded (see caption to Figure 3). It seems likely, therefore, that the duration of RA, rather than merely patient age, is related to the likelihood of work disability.

Several reviewers, using various methodological approaches, have concluded that physical job demands, HAQ disability, older age and low educational attainment are predictive of work disability [12,19,20,80]. As noted elsewhere [19,80], biomedical factors are inconsistently predictive of work disability: erythrocyte sedimentation rates were predictive of work disability in one inception cohort study and RF values were predictive in another (Table 1). Demographic characteristics are not alterable. Work-related factors can be modified within limits, either through a change in career path or through job accommodation (i.e. modification of the work environment or of the way the job function is performed) [12]. Disease status, however, ultimately determines work disability and is the primary target for intervention.
There is no evidence from the observational studies reviewed here that the use of disease-modifying anti-rheumatic drugs (DMARDs) affects work ‘disability.’ DMARD use was reported in several studies [41,43, 44,63,67], but did not appear as a significant independent variable in the multivariate regression models [41,43]. Similarly, there was no (inverse) relationship between DMARD use and work ‘loss.’ Even in studies in which intensive use of DMARDs was reported, 63–84% of employees experienced work loss [56,62]. DMARD use was associated with ‘greater’ work loss in one of these studies [56], possibly because of confounding between RA severity and DMARD use.

It may be that DMARD use has not generally been associated with increased productivity because available DMARDs have not been effective enough at improving function and reducing joint damage. Trials of biological therapies in RA show substantial impact on HAQ scores and inhibition of radiographic damage; these agents appear to be superior to traditional DMARDs in this regard [81,82]. Newer therapies, therefore, may offer the potential for a greater impact on productivity loss. In a trial of infliximab treatment, a clinically meaningful improvement in HAQ score was associated with increased employability and with fewer days lost from work [83]. Trials have shown that anakinra reduces work loss [84,85], and a retrospective analysis of studies of etanercept indicate that this drug is associated with increased workforce participation [86].

In summary, rates of work disability were similar in the USA and in Northern European countries, despite differences in social systems and study methodologies. Cohort studies show the progression of RA to be inexorable, with times from RA onset until 50% probability of being permanently work disabled varying from 4.5 to 22 years. Work loss was experienced by 36–84% of RA sufferers in the previous 12 months, for a median of 39 days. No studies met the inclusion criteria for analysis of factors associated with work loss and both the source of variability in estimates of work loss and the differential effect of RA on work loss remain unclear. Although several studies reported work limitation from the perspective of the patient (the outcome typically reported was working fewer hours due to RA) [36, 39,44,54,64], we found no published reports of work limitation from the perspective of the employer. In part, this reflects the challenge of defining and measuring work limitation [87]. In inception cohort studies, baseline variables consistently predictive of work disability were a physically demanding work type, more severe RA and older age. Disease status ultimately determines work disability and is the primary target for intervention. There are few published studies of the effectiveness of currently available DMARDs in reducing work-related productivity loss; this should be an area of importance for future research.

Acknowledgements

This study was funded by a grant from Bristol–Myers Squibb Company.

Conflicts of interest

None declared.

References


