

The incidence of permanent work disability in patients with rheumatoid arthritis in Sweden 1990-2010: before and after introduction of biologic agents

Eva Hallert, Magnus Husberg and Lars Bernfort

Linköping University Post Print

N.B.: When citing this work, cite the original article.

Original Publication:

Eva Hallert, Magnus Husberg and Lars Bernfort, The incidence of permanent work disability in patients with rheumatoid arthritis in Sweden 1990-2010: before and after introduction of biologic agents, 2012, Rheumatology Int, (51), 2, 338-346.

<http://dx.doi.org/10.1093/rheumatology/ker332>

Copyright: Oxford University Press (OUP): Policy B

<http://www.oxfordjournals.org/>

Postprint available at: Linköping University Electronic Press

<http://urn.kb.se/resolve?urn=urn:nbn:se:liu:diva-75273>

The incidence of permanent work disability in patients with rheumatoid arthritis in Sweden 1990–2010: before and after introduction of biologic agents

Eva Hallert^{1,2}, Magnus Husberg¹ and Lars Bernfort¹

¹Center for Medical Technology Assessment, Department of Medical and Health Sciences, Faculty of Health Sciences, Linköping University

²Department of Cardiovascular Diseases and Speciality Medicine, University Hospital, Linköping, Sweden.

Correspondence to: Eva Hallert, Center for Medical Technology Assessment, Department of Medical and Health Sciences, Faculty of Health Sciences, Linköping University, SE-581 83 Linköping, Sweden. E-mail: eva.hallert@liu.se

Abstract

Objective. To explore the incidence of disability pension (DP) due to RA as an estimation of permanent work disability before and after introduction of biologic drugs.

Methods. The annual incidence of DP was derived from the Swedish National Social Insurance Register and rates of DP due to RA were compared with the total amount of new DPs.

Results. The incidence of DP due to RA has decreased over recent years, coinciding with earlier and more aggressive treatment with DMARDs and biologics. A similar declining incidence of DP was simultaneously seen in patients with all diagnoses in the general population. The decrease in DPs was, however, larger for RA and was evident even before introduction of biologics. In 1990, the proportion of DPs caused by RA was 1.9% out of total amount of DPs, decreasing to 1.5% in 2000 and to 1% in 2009. This may reflect effects of treatment, but may also be due to changing political policies as well as changes in age structure, increasing educational level and less physically demanding jobs.

Conclusion. The decrease in DPs due to RA coincides with new treatment strategies as well as with decreasing levels of DPs in patients with all diagnoses. Prevailing political and economic conditions have a large impact on permanent work disability and may affect patients with various diagnoses in different ways. To determine if the decline is a true effect of better treatment, there is a need for further investigations, taking possible confounding factors into account.

Key words rheumatoid arthritis, disability pension, permanent work disability, confounding factors, biologic drugs, disease-modifying anti-rheumatic drugs

Hallert E, Husberg M, Bernfort L. The incidence of permanent work disability in patients with rheumatoid arthritis in Sweden 1990-2010: before and after introduction of biologic agents. Rheumatology (Oxford). 2012 Feb;51(2):338-46. Epub 2011 Nov 16.

Introduction

RA is a chronic disease affecting patients and the society in many ways. Work disability is one of the most important outcomes of the disease and leads to substantial economic consequences for individuals, their families and society as a whole [1–3]. Work disability rates are already high early in the disease course and continue to increase with disease duration, and most studies report that loss of productivity constitutes the largest part of total costs in RA patients [3–6]. A number of studies have shown that as many as 20–40% of the patients had become permanently work disabled after a disease duration of 2–3 years [6–9]. After 5 years of disease, permanent work disability varied from 29 to 50% [10–13], and in an early cohort of RA patients followed over 20 years, work disability had increased to 80% [4].

The treatment strategies in RA patients have changed substantially over the past two decades. Until the late 1980s, a pyramid step-up approach was used. Patients were treated with NSAIDs and analgesics, and if they continued to have a progressive disease, single-therapy DMARD was instituted. In the early 1990s, treatment became more aggressive and the pyramid method was replaced by a step-down approach with more intensive use of DMARD monotherapy and with combinations of DMARDs early in the disease course, aiming at preventing joint damage and disease progression [14]. Around the year 2000, biologic drugs such as TNF inhibitors were introduced into the market. This has further improved the management of the disease, but has also substantially increased total costs, which are now predominantly driven by drug costs [15–17]. A challenging question is whether the increasing costs have been offset to some extent by a decrease in permanent work disability. The aim of the present study was to explore the yearly incidence of disability pension (DP) over 20 years in Sweden as an estimation of permanent work disability in RA patients before and after the introduction of biologic drugs, comparing rates of DP due to RA with rates of DP due to all diagnoses in the general population between 1990 and 2010.

Patients and methods

Sweden has a national tax-funded health insurance system, allowing all residents between 16 and 64 years sick leave benefits when they are unable to perform work because of illness or injury. If inability to work persists >1 year and is considered to be permanent and the employer is unable to find an adapted job, the patient can apply for a permanent DP. The pension can be granted as a full or partial benefit, depending on the degree of disability. Decisions with work DPs with International Classification of Diseases (ICD) codes are gathered in the National Social Insurance Register and information on DP was derived from this national register [18, 19; personal communication with Försäkringskassan (2007–9)]. Pensions due to RA were identified through ICD-10 codes M05 for RF-positive RA and M06 for RF-negative RA. Prior to 1997, the codes were ICD-9 and RA was registered as code 714. In Sweden, all persons are included in the social security system, and housewives, students and unemployed are entitled to disability benefits. All patients have equal access to medication, and after a charge of 1800 SEK (€190), all prescription medications, including biologic drugs, are free of charge during the rest of the year. In the present study, DP is defined as any level of work DP related to the disease. Official retirement age in Sweden is 65 years, but a number of individuals have received other types of pensions, retired early for other reasons, died or worked beyond the age of 65 years. In 2009, the average retirement

age was 64 years [20] (average exit age from the labour force by gender). A correct calculation of loss of productivity demands a life table calculation for each year with the expected remaining time in the workforce for different age groups. A simplified calculation was used, assuming that age of retirement was 64 years the entire period. As the mean age for DP in RA patients was 53 years, 11 years of production were lost. The incidence approach makes discounting appropriate, and for each age group the remaining time until 64 years of age was discounted by 3%, thus reducing from 11 to 8.7 years. DP can be part time, and on average, RA patients reduced their working capacity by ~65%, giving the equivalent of 5.7 years of full-time work. The value of a lost full-time year was calculated using an average annual cost of a full-time worker in 2009 and was ~SEK 500 000 (€52 404), including taxes and other fees [21]. The same cost was used for the entire period. The average exchange rate in 2010 was €1 = 9.5413 SEK.

Statistics

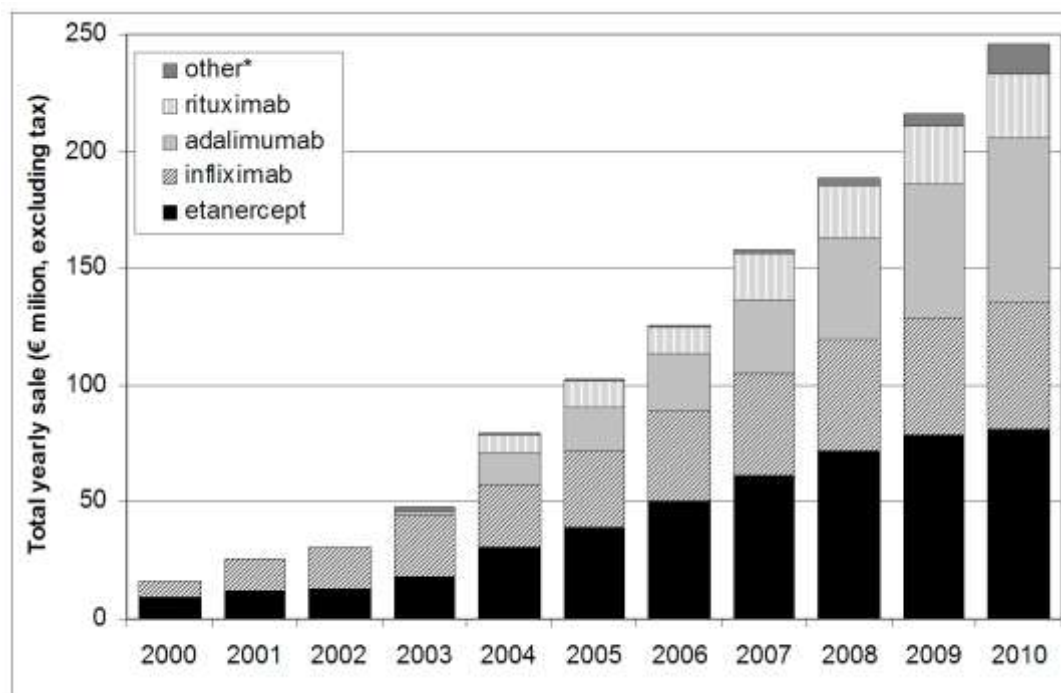
Annual incidence rates of DP were calculated for each year. Calculations were performed for the total group and for men and women separately and also for different age groups. Data on age distribution and birth rates in the population were obtained from the governmental database Statistics Sweden [22]. Data are presented with frequencies and descriptive statistics. Linear regression models were performed analysing trends over time and associations between DP due to RA and DP due to all diagnoses. A $P < 0.05$ was considered statistically significant. All analyses were performed using PASW version 18.0. (SPSS, Chicago, IL, USA).

Results

Drugs

Prior to the biologic era, drug costs for RA patients were rather low. In 1997, the total cost of medication for RA patients in Sweden was €11.9 million, of which ~€6.7 million were costs for DMARDs [http://apotekensservice.se/om_statistik/ (2007–10) and personal communication for older data]. Biologic drugs were introduced around the year 2000 and costs of biologics in Sweden during the first year amounted to €18 million. During the following decade, prescription of biologics increased substantially, and in 2010, costs for biologic drugs in Sweden amounted to almost €250 million [23] (Fig. 1).

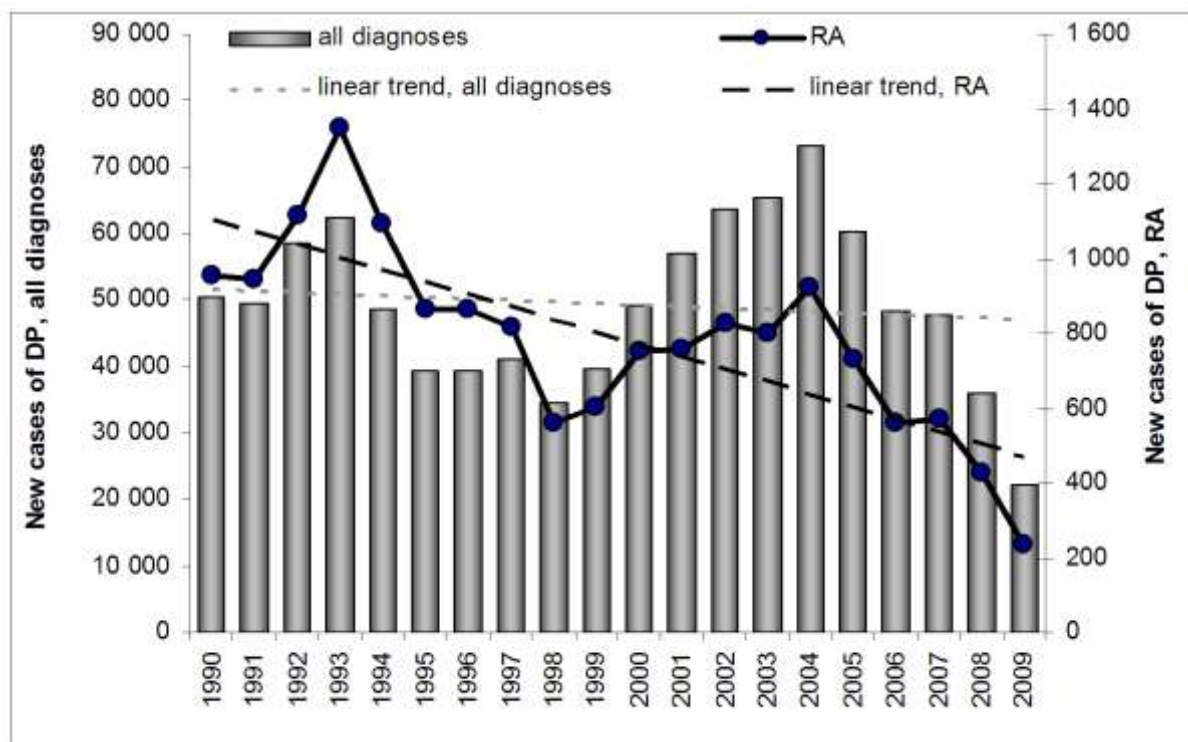
Fig. 1. Sales of biologic drugs in Sweden during the years 2000–10, all diagnoses. Others include anakinra, abatacept, certolizumab, golimumab and tocilizumab.



DPs in patients with RA vs patients with all diagnoses

The levels of new DPs due to RA and the levels of new DPs due to all diagnoses in the general population followed each other quite closely from 1990 to 2010 (Fig. 2). Between 1990 and 1993, there was a general increase in new cases of DP in patients with RA as well as in patients with other diagnoses. During this period, the gross national product (GNP) in Sweden decreased and there was a strong negative correlation between GNP and DP. During these years Sweden had a generous policy for allowing DP. In 1993–98, the GNP increased, and this led to a decrease in DPs. Access to DPs also became more restricted during these years. Between 1998 and 2004, GNP decreased again and was followed by an increase in DPs. During this period, the regulations were eased and a substantial number of older patients and patients on long-term sick leave were granted DP. The total incidence of DP reached its maximum in 2004, and thereafter decreased substantially.

Fig. 2. Number of patients with new DPs due to RA and due to all diagnoses and linear trends over time for RA and for all diagnoses, 1990–2010.



The number of new DPs fluctuated over time in slow cycles, with a high peak late in the period. A simple linear regression between the total number of new DPs and time does not show a significant linear trend (unstandardized β -coefficient = -231 , $R^2 = 0.012$, $P = 0.65$). The number of new DPs due to RA showed a more apparent decrease, despite several small peaks, and the negative trend over time is significant (unstandardized β -coefficient = -33 , $R^2 = 0.59$, $P < 0.001$).

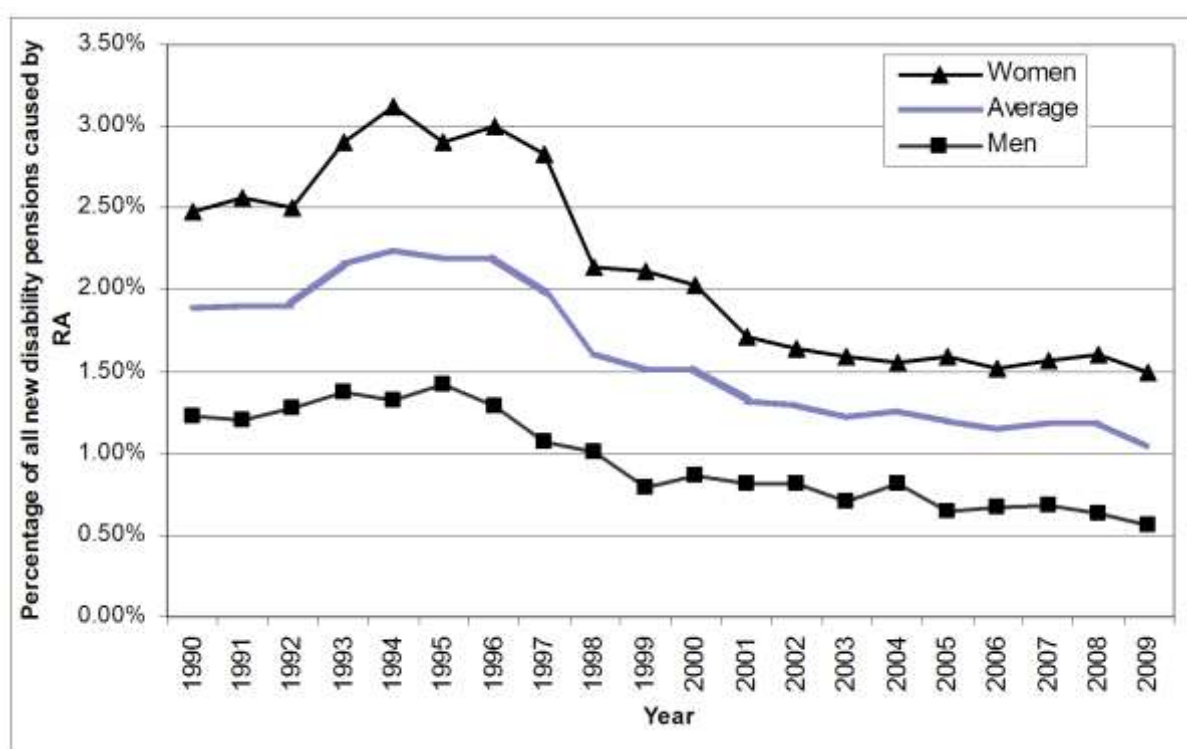
The number of patients obtaining DP due to RA was 957 in 1990 and increased by 41% to 1348 in 2003. DPs in patients with all diagnoses also increased, but only by 24%. A substantial decrease in DPs was seen over the following 5 years, with a larger decrease for RA patients compared with DPs in patients with all diagnoses. The total decrease in DPs between 1990 and 1998 was 42% for RA patients compared with 32% for patients with all diagnoses. Between 1998 and 2004, DPs for RA patients increased by 65%, while the increase due to all diagnoses was 112%. A relatively large proportion of this increase in the general population was, however, attributable to patients with psychiatric diagnoses. There was a general increase in DPs due to psychiatric diagnoses in Sweden during this period. In the early 1990s, psychiatric diagnoses made up $\sim 15\%$ of all DPs but increased to $\sim 33\%$ of total DPs in 2004. The total decrease in DP between 1998 and 2009 was, however, larger for RA patients than for patients with all diagnoses, 58 vs 35% (Table 1).

Table 1. Number of new DPs due to RA and to all diagnoses 1990 2009 and changes between years (%)

Years	new DP (n)		new DP (n)	
	RA-patients	change (%)	all diagnoses	change (%)
1990 - 1993	957 → 1348	+41	50 500 → 62 500	+24
1993 - 1998	1348 → 558	-59	62 500 → 34 500	-45
1998 - 2004	558 → 923	+65	34 500 → 73 000	+112
2004 - 2009	923 → 230	-75	73 000 → 22 000	-70

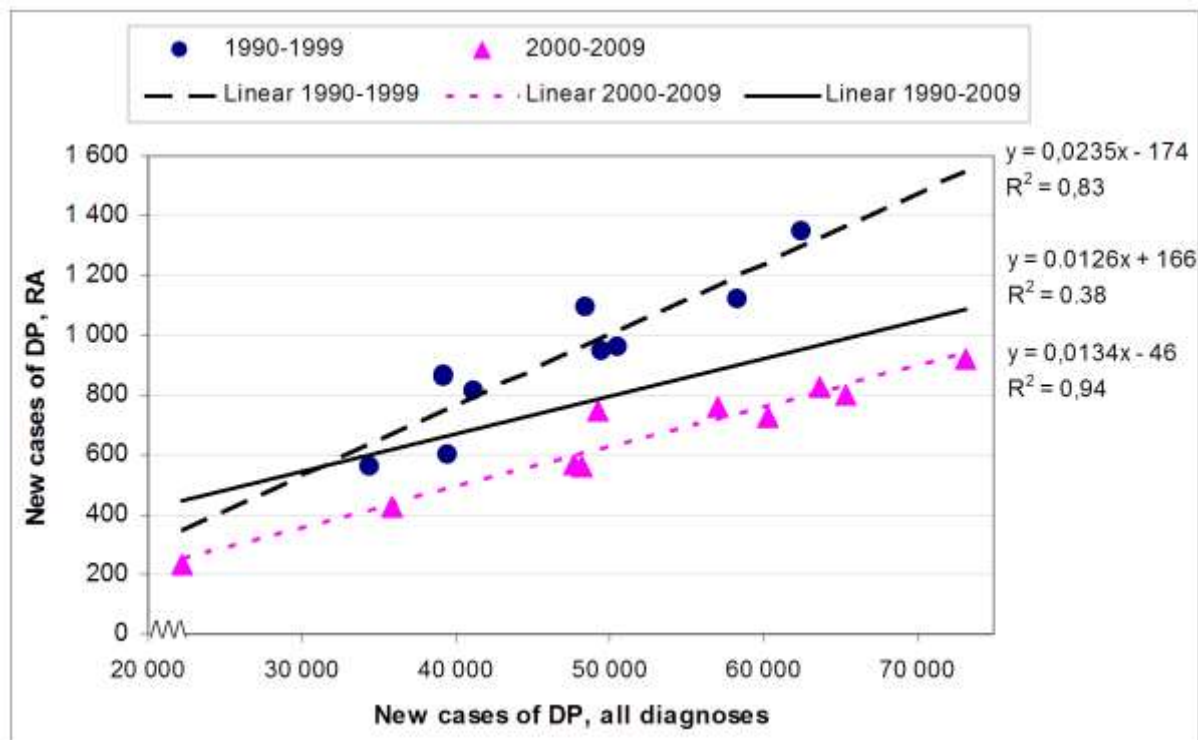
The number of new DPs caused by RA is dependent on several factors, such as the effects of treatment and incidence of the disease, but also on secular trends in society due to changing political policies over time. Since policies are likely to affect patients with RA as well as patients with other diagnoses, the proportion of DPs due to RA out of total number of DPs due to all diagnoses was calculated for each year. In 1990, the proportion of DPs caused by RA was 1.9% of the total DPs. The percentage for men was 1.2% and for women 2.5%. In 1992, there was an increase in RA-related pensions compared with all diagnoses, followed by a similar decrease in 1996. After 1997, however, the proportion of DPs caused by RA out of the total DPs decreased from 2% in 1997 to 1% in 2009 (Fig. 3).

Fig. 3. The proportion of new DPs due to RA out of total DPs due to all diagnoses.



The linear associations between new DPs due to RA and new DPs due to all diagnoses are significant. The regression model including the total period gives an adjusted $R^2 = 0.38$ ($P = 0.004$). When 1990–99 and 2000–09 were analysed separately, the regression models showed even stronger associations, with extremely high R^2 -values ($P < 0.0001$) (Fig. 4).

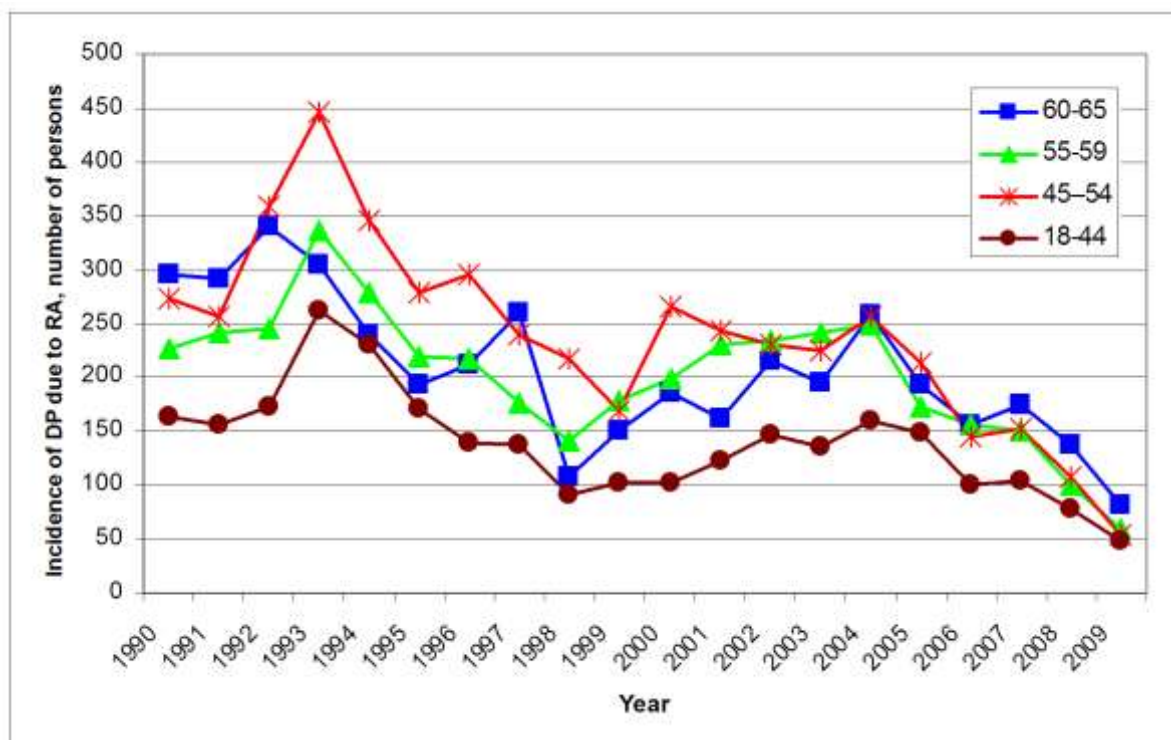
Fig. 4. Annual number of new DPs due to RA vs all diagnoses and linear regressions for the periods 1990–99, 2000–09 and the total period 1990–2009.



Age

The true annual incidence of RA is not known, but RA is age dependent and peak rates for newly diagnosed patients with RA are in the age group between 55 and 59 years. This is also a common age of early retirement due to RA. In 1990, 54% of patients receiving DPs were between 55 and 65 years old, and this proportion increased to 61% in 2009. Birth rates were high in Sweden during 1943–49, and the number of persons between 55 and 65 years of age increased by 12%, from 840 000 in 1990 to 940 000 in 1998, and by another 28%, to 1 200 000, in 2009, indicating a possible increase in new RA patients during this period. The incidence of DP in four different age groups (approximately of the same size) is shown in Fig. 5. The development is rather similar in all groups. After 1993, the number of DPs decreased in all age groups, even in ages >55 years, where the number of DPs might be expected to increase due to the increasing population in this age group (Fig. 5).

Fig. 5. Number of new DPs due to RA in different age groups. Age spans are of different widths, but of approximately the same size.



The decrease in DPs due to RA in different age groups becomes even clearer when examining DPs/100 000 inhabitants in different age groups. Between 1990 and 2009 this number decreased by 80% in all age groups except the youngest, where the decrease was 70% (Fig. 6).

Fig. 6. Number of new DPs due to RA/100 000 inhabitants in different age groups.

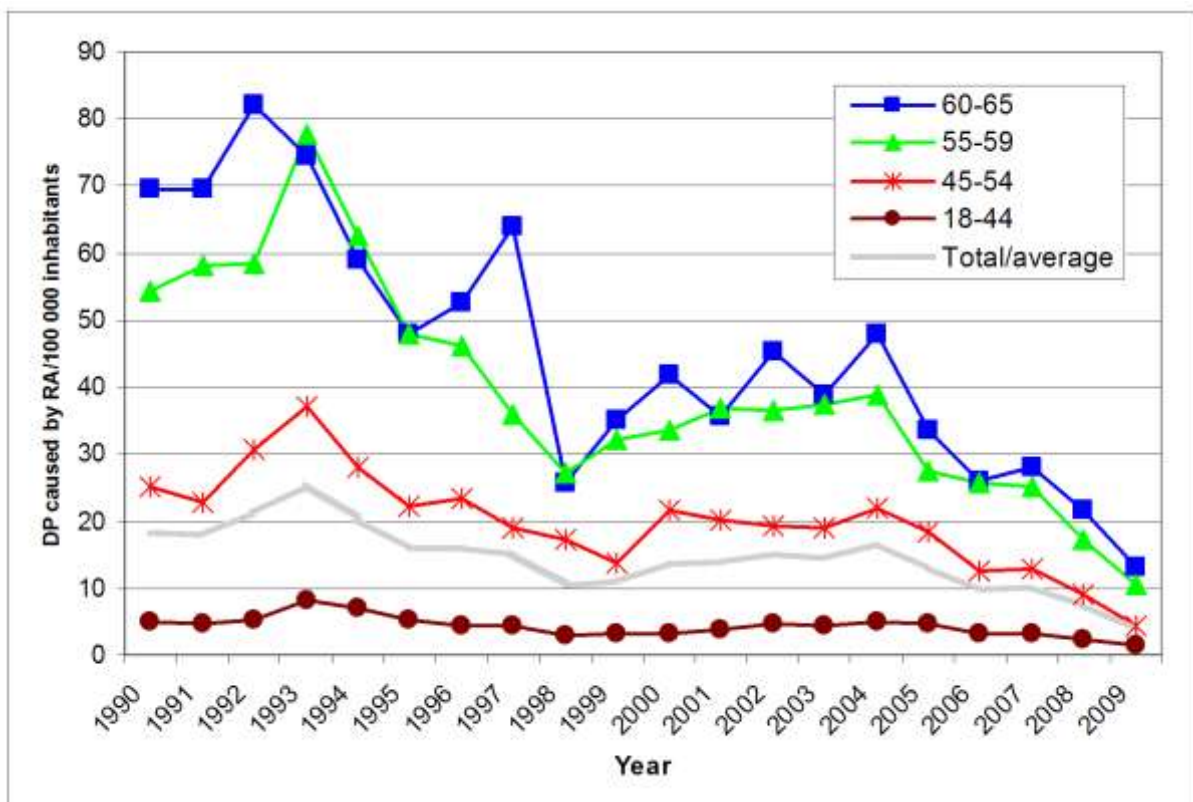
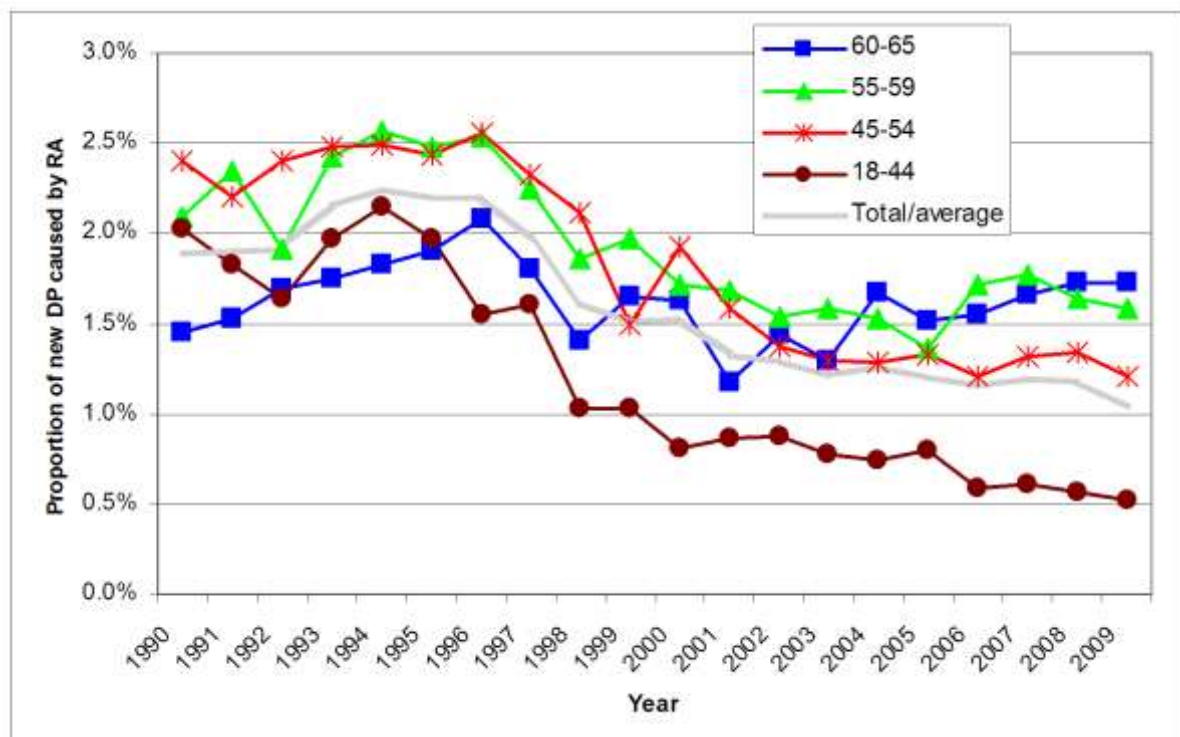


Fig. 7 shows the proportion of all new DPs caused by RA in different age groups (like Fig. 3, but with age). For ages 60–65 years the proportion is relatively stable or even increasing, while all other groups show decreasing proportions and this is most pronounced in the group younger than 45 years of age.

Fig. 7. DPs caused by RA. Proportion of all new DPs in different age groups.



Loss of productivity and biologic drugs

The average age at the time point of DP due to RA was relatively stable, ~53 years of age throughout the entire period, resulting in an average of 5.7 discounted years of lost productivity. Accordingly, the value of lost production due to DP for an average RA patient was SEK 2.8 million (€298 000). If the entire gain in terms of reduced DP due to RA from year 2000 is assumed to be related to treatment with biologic drugs, the reduced costs corresponding to the decrease in DP, SEK 1465 million (€154 million), would offset a considerable part of the costs for biologic drugs, SEK 2115 million (€222 million). This is, however, rather unlikely, since DPs for all diagnoses decreased by 55% between 2000 and 2009, suggesting that a similar decrease would also have been the case in RA patients, regardless of biologic drugs. The decrease in DPs in RA patients was, however, 69%. Assuming the additional 14% is due to biologic treatment, this could be valued by calculating 14% of patients in year 2000, corresponding to 106 patients, and that is equivalent to a reduced cost of SEK 300 million (€31 million).

Discussion

The incidence of DPs in Sweden due to RA has decreased substantially over recent years. The decreasing incidence of permanent work disability coincides with a trend towards earlier and more aggressive treatment with DMARDs and with the introduction of biologic drugs. A similar declining incidence of permanent work disability was, however, simultaneously seen in patients with all diagnoses in the general population.

Previous studies have reported that work disability rates have been significantly higher among RA patients compared with work disability rates in the general population, and also that women have been more likely than men to become work disabled [8, 11, 24]. A Dutch study reported that 37% of RA patients <65 years of age were work disabled, compared with 9% in the general Dutch population [11]. Barrett et al. [8] reported that RA patients were 32 times more likely to stop working compared with their healthy controls. In the USA, labour force participation was 20% lower in men with arthritis and 25% lower in women with arthritis compared with men and women without arthritis [25]. In a recent report from a Swedish RA cohort, 46% of the RA patients were on DP in 2007, compared with 19% of the general population. Women were more likely to become work disabled, as were older patients and those with low educational level [26].

The decrease in DP in RA patients may reflect the new treatment strategies with biologic agents, but, in fact, a substantial decrease in DP was seen prior to introduction of biologics, suggesting apparent effects of the early and more aggressive use of conventional DMARDs and escalation of treatment with DMARDs in various combinations. The biologic agents have proved clinically effective, but data on the effect on working capacity after anti-TNF treatment are conflicting [27–32]. Some studies have reported increased employability in patients treated with biologic agents, but similar improvements have been reported in patients who were treated with conventional DMARDs [27, 31, 33, 34]. Wolfe et al. [29] did not find that anti-TNF treatment was associated with any reduction in work disability, and in a recent Swedish report, sick leave decreased in RA patients after starting anti-TNF therapy, but the rate of DPs continued to increase [32]. In the Quantitative Patient Questionnaires in Standard Monitoring of Patients with Rheumatoid Arthritis (QUEST-RA) study, there was no significant effect on working capacity in patients taking biologic agents [35]. This might reflect that in patients with long-standing disease, joint damage is associated with irreversible disability and improvements are limited [36]. Many patients have also become work disabled early after diagnosis, and once DPs have been granted there is limited success in returning to work, despite good response to biologic therapy [35, 37, 38].

The decreasing incidence of DP may, however, also be due to secular trends in society due to new political policies as well as demographic changes in age structure in the general population over recent decades. The policy regarding DPs in Sweden has changed during the recent decade and the possibility of obtaining early retirement has become more limited, and this has led to an increase in workforce participation. The levels of remuneration have fluctuated over the years depending on changes in the social security system, and this has also influenced employment rates. With increasing unemployment rates, patients may also be more anxious to keep their jobs. However, the possible effects of the prevailing political and economic conditions over the years might not affect RA patients in the same way as patients with all diagnoses.

Demographic changes in age structure, educational level, labour market and working conditions also affect levels of DP. Female sex, old age and demanding physical work have been associated with a loss of working capacity in RA patients [2, 9, 10, 12, 26, 39]. A substantial number of manual physically demanding jobs have disappeared in recent years, and this may have increased the possibility for RA patients to maintain working capacity in more sedentary work. The level of education is strongly associated with employability, and the educational level has increased over the years. This may also enable RA patients to maintain employability in more suitable jobs [2, 7, 13]. A recent report from Germany showed

that there was a tendency towards higher workforce participation in RA patients, but, as in the present study, this was also seen in the general population [40].

If changes in the number of DPs are caused by the effects of prevailing political economic conditions, the level of RA-related pensions would be expected to constitute a stable proportion of total pensions due to all diagnoses. The proportional decrease of new DPs over the past 20 years was, however, larger for RA patients than for patients with all diagnoses. The proportion of new DPs due to RA out of the total DPs due to all diagnoses decreased from 2% in 1997 to 1% in 2009. Recent data from Sweden also indicate that the incidence of primary total hip arthroplasties in patients with RA decreased substantially after 2001 [41]. Similar decreasing trends are observed in RA-related surgical interventions of upper limbs [42]. Some of these improvements may, however, be late effects of the more aggressive DMARD treatment prior to the biologic era.

The various structures of health-care systems in different countries make comparisons between studies difficult. Work disability rates have generally been higher in European countries compared with those in the USA, possibly due to different social security systems with more limited access to welfare facilities in the USA. Generous compensations may also be a possible incentive to withdraw from the labour market. In recent years, however, access to social security benefits in many European countries has become more restricted, so this difference between countries will probably diminish. The use of biologics also differs between countries. Different national guidelines for treatment of patients may limit access to treatment in some countries [43]. There are no formal restrictions for prescription of biologic drugs in Sweden and drug costs are almost entirely subsidized by society. Swedish guidelines recommend that biologics should be available for patients with high disease activity who have failed to respond to at least one prior DMARD treatment, usually MTX, and the use of biologic drugs in Sweden is among the highest in Europe [44].

To conclude, the incidence of DP in RA patients has declined in recent years, and this may reflect new treatment strategies with biologics. However, a similar decrease in DPs has been simultaneously seen in the general population. During recent decades, the labour market has changed and RA patients may maintain employability in more sedentary work instead of manual jobs. Educational level is also associated with employability, and the level of education has increased over the years, especially in younger ages, and this may also affect DPs. Prevailing political and economic conditions have a large impact on the labour market and permanent work disability, but may possibly affect patients with various diagnoses in different ways. The strong association between DPs due to RA and DPs due to all diagnoses suggests that all DPs are strongly determined by similar external factors such as changing policies and unemployment rates, and the possible treatment effects may be obscured by this. The present data indicate a need for further investigations, taking important external confounding factors into account.

Key messages:

- Incidence of DP due to RA has decreased since the introduction of biologic drugs.
- DP due to RA is largely determined by societal factors.
- External factors must be considered when evaluating the effects of biologic drugs on work disability.

Acknowledgements

Funding: This work was supported by the County Council in Östergötland, the Swedish Rheumatism Association, The Medical Research County Council of South-East Sweden (FORSS) and the Eugenia-Norrbacka Foundation.

Disclosure statement: The authors have declared no conflicts of interest.

References

1. Lapsley HM, March LM, Tribe KL, Cross MJ, Courtenay BG, Brooks PM. Living with rheumatoid arthritis: Expenditures, health status, and social impact on patients. *Ann Rheum Dis* 2002;61:818-21.
2. Hallert E, Husberg M, Jonsson D, Skogh T. Rheumatoid arthritis is already expensive during the first year of the disease (the Swedish TIRA project). *Rheumatology (Oxford)* 2004;43:1374-82.
3. Franke LC, Ament AJ, van de Laar MA, Boonen A, Severens JL. Cost-of-illness of rheumatoid arthritis and ankylosing spondylitis. *Clin Exp Rheumatol* 2009;27:S118-23.
4. Jantti J, Aho K, Kaarela K, Kautiainen H. Work disability in an inception cohort of patients with seropositive rheumatoid arthritis: A 20 year study. *Rheumatology (Oxford)* 1999;38:1138-41.
5. Newhall-Perry K, Law NJ, Ramos B, et al. Direct and indirect costs associated with the onset of seropositive rheumatoid arthritis. Western consortium of practicing rheumatologists. *J Rheumatol* 2000;27:1156-63.
6. Hallert E, Husberg M, Skogh T. Costs and course of disease and function in early rheumatoid arthritis: A 3-year follow-up (the Swedish TIRA project). *Rheumatology (Oxford)* 2006;45:325-31.
7. Doeglas D, Suurmeijer T, Krol B, Sanderman R, van Leeuwen M, van Rijswijk M. Work disability in early rheumatoid arthritis. *Ann Rheum Dis* 1995;54:455-60.
8. Barrett EM, Scott DG, Wiles NJ, Symmons DP. The impact of rheumatoid arthritis on employment status in the early years of disease: A UK community-based study. *Rheumatology (Oxford)* 2000;39:1403-9.
9. Sokka T. Work disability in early rheumatoid arthritis. *Clin Exp Rheumatol* 2003;21:S71-4.
10. Reisine S, McQuillan J, Fifield J. Predictors of work disability in rheumatoid arthritis patients. A five-year followup. *Arthritis Rheum* 1995;38:1630-7.
11. van Jaarsveld CH, Jacobs JW, Schrijvers AJ, van Albada-Kuipers GA, Hofman DM, Bijlsma JW. Effects of rheumatoid arthritis on employment and social participation during the first years of disease in The Netherlands. *Br J Rheumatol* 1998;37:848-53.

12. Young A, Dixey J, Kulinskaya E, et al. Which patients stop working because of rheumatoid arthritis? Results of five years' follow up in 732 patients from the Early RA study (ERAS). *Ann Rheum Dis* 2002;61:335-40.
13. Eberhardt K, Larsson BM, Nived K, Lindqvist E. Work disability in rheumatoid arthritis--development over 15 years and evaluation of predictive factors over time. *J Rheumatol* 2007;34:481-7.
14. Fries JF. Current treatment paradigms in rheumatoid arthritis. *Rheumatology (Oxford)* 2000;39 Suppl 1:30-5.
15. Michaud K, Messer J, Choi HK, Wolfe F. Direct medical costs and their predictors in patients with rheumatoid arthritis: A three-year study of 7,527 patients. *Arthritis Rheum* 2003;48:2750-62.
16. Kavanaugh A. Economic consequences of established rheumatoid arthritis and its treatment. *Best Pract Res Clin Rheumatol* 2007;21:929-42.
17. Gulfe A, Kristensen LE, Saxne T, Jacobsson LT, Petersson IF, Geborek P. Rapid and sustained health utility gain in anti-tumour necrosis factor-treated inflammatory arthritis: Observational data during 7 years in southern Sweden. *Ann Rheum Dis* 2010;69:352-7.
18. National Social Insurance Register. Riksförsäkringsverket. [socialförsäkring] [in Swedish]. 1990–97.
19. <http://statistik.forsakringskassan.se/portal/page/portal/intstat/bof/statpub> 1998-2006 (15 June 2011, date last accessed)
20. Eurostat. <http://ec.europa.eu/eurostat/> (15 June 2011, date last accessed).
21. Svenskt näringsliv. www.svensktnaringsliv.se (15 June 2011, date last accessed).
22. Statistics Sweden. www.scb.se (15 June 2011, date last accessed).
23. Jonsson D, Husberg M. Socioeconomic costs of rheumatic diseases. Implications for technology assessment. *Int J Technol Assess Health Care* 2000;16:1193-200.
24. Odegard S, Finset A, Kvien TK, Mowinckel P, Uhlig T. Work disability in rheumatoid arthritis is predicted by physical and psychological health status: A 7-year study from the Oslo RA register. *Scand J Rheumatol* 2005;34:441-7.
25. Yelin E. Arthritis. The cumulative impact of a common chronic condition. *Arthritis Rheum* 1992;35:489-97.
26. Neovius M, Simard JF, Askling J. How large are the productivity losses in contemporary patients with RA, and how soon in relation to diagnosis do they develop? *Ann Rheum Dis* 2011;70:1010-5.
27. Smolen JS, Han C, van der Heijde D, et al. Infliximab treatment maintains employability in patients with early rheumatoid arthritis. *Arthritis Rheum* 2006;54:716-22.

28. Laas K, Peltomaa R, Kautiainen H, Puolakka K, Leirisalo-Repo M. Pharmacoeconomic study of patients with chronic inflammatory joint disease before and during infliximab treatment. *Ann Rheum Dis* 2006;65:924-8.
29. Wolfe F, Allaire S, Michaud K. The prevalence and incidence of work disability in rheumatoid arthritis, and the effect of anti-tumor necrosis factor on work disability. *J Rheumatol* 2007;34:2211-7.
30. Allaire S, Wolfe F, Niu J, Zhang Y, Zhang B, LaValley M. Evaluation of the effect of anti-tumor necrosis factor agent use on rheumatoid arthritis work disability: The jury is still out. *Arthritis Rheum* 2008;59:1082-9.
31. Halpern MT, Cifaldi MA, Kvien TK. Impact of adalimumab on work participation in rheumatoid arthritis: Comparison of an open-label extension study and a registry-based control group. *Ann Rheum Dis* 2009;68:930-7.
32. Olofsson T, Englund M, Saxne T, et al. Decrease in sick leave among patients with rheumatoid arthritis in the first 12 months after start of treatment with tumour necrosis factor antagonists: A population-based controlled cohort study. *Ann Rheum Dis* 2010;69:2131-6.
33. Zirkzee EJ, Sneep AC, de Buck PD, et al. Sick leave and work disability in patients with early arthritis. *Clin Rheumatol* 2008;27:11-9.
34. Puolakka K, Kautiainen H, Mottonen T, et al. Impact of initial aggressive drug treatment with a combination of disease-modifying antirheumatic drugs on the development of work disability in early rheumatoid arthritis: A five-year randomized followup trial. *Arthritis Rheum* 2004;50:55-62.
35. Sokka T, Kautiainen H, Pincus T, et al. Work disability remains a major problem in rheumatoid arthritis in the 2000s: Data from 32 countries in the QUEST-RA study. *Arthritis Res Ther* 2010;12:R42.
36. Aletaha D, Strand V, Smolen JS, Ward MM. Treatment-related improvement in physical function varies with duration of rheumatoid arthritis: A pooled analysis of clinical trial results. *Ann Rheum Dis* 2008;67:238-43.
37. Han C, Smolen J, Kavanaugh A, St Clair EW, Baker D, Bala M. Comparison of employability outcomes among patients with early or long-standing rheumatoid arthritis. *Arthritis Rheum* 2008;59:510-4.
38. Hallert E, Husberg M, Skogh T. 28-joint count disease activity score at 3 months after diagnosis of early rheumatoid arthritis is strongly associated with direct and indirect costs over the following 4 years: The Swedish TIRA project. *Rheumatology (Oxford)* 2011;50:117-23.
39. Wallenius M, Skomsvoll JF, Koldingsnes W, et al. Comparison of work disability and health-related quality of life between males and females with rheumatoid arthritis below the age of 45 years. *Scand J Rheumatol* 2009;38:178-83.
40. Ziegler S, Huscher D, Karberg K, Krause A, Wassenberg S, Zink A. Trends in treatment and outcomes of rheumatoid arthritis in germany 1997-2007: Results from the National

Database of the German Collaborative Arthritis Centres. *Ann Rheum Dis* 2010;69:1803-8.

41. Hekmat K, Jacobsson L, Nilsson JA, et al. Decrease in the incidence of total hip arthroplasties in patients with rheumatoid arthritis - results from a well defined population in south Sweden. *Arthritis Res Ther* 2011;13(2):R67. [Epub ahead of print].
42. Weiss RJ, Ehlin A, Montgomery SM, Wick MC, Stark A, Wretenberg P. Decrease of RA-related orthopaedic surgery of the upper limbs between 1998 and 2004: data from 54,579 Swedish RA inpatients. *Rheumatology (Oxford)* 2008;47(4):491-4.
43. Hyrich KL, Watson KD, Lunt M, Symmons DP. Changes in disease characteristics and response rates among patients in the united kingdom starting anti-tumour necrosis factor therapy for rheumatoid arthritis between 2001 and 2008. *Rheumatology (Oxford)* 2011;50:117-23.
44. Lundkvist J, Kastang F, Kobelt G. The burden of rheumatoid arthritis and access to treatment: Health burden and costs. *Eur J Health Econ* 2008;8 Suppl 2:S49-60.