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### Reduction in orthopaedic surgery in patients with rheumatoid arthritis: a Norwegian register-based study

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# Reduction in orthopaedic surgery in patients with rheumatoid arthritis: a Norwegian register-based study

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**Objectives:** The disease course of patients with rheumatoid arthritis (RA) has become milder in recent years. In this study we investigated the incidence of orthopaedic surgery in patients with RA.

**Method:** From the Norwegian Arthroplasty Register we selected joint replacement procedures conducted during the years 1994–2012 (n = 11 337), and from the Norwegian Patient Register we obtained data on synovectomies (n = 4782) and arthrodeses (n = 6022) during 1997–2012. Using Poisson regression we analysed the time trends in the incidence of procedures performed.

**Results:** There was a significant decrease in the incidence of arthroplasty surgery (coefficient of –0.050 per year) and synovectomies (coefficient of –0.10) and a declining trend of arthrodeses in patients with RA in the study periods. The greatest reduction was found in procedures involving the wrist and hand.

**Conclusions:** We found a decrease in orthopaedic surgery in patients with RA that continued into the biologic era and throughout the study period. The general increasing trend in the use of synthetic and biological disease-modifying anti-rheumatic drugs (DMARDs) thus coincides with less joint destruction and an improved long-term prognosis of patients with RA.

There has been a growing emphasis on diagnosing and treating rheumatoid arthritis (RA) early and intensively with the aim of preventing disability and reducing mortality, and the disease course has become milder in recent years (1–3). Methotrexate alone or in combination with other disease-modifying anti-rheumatic drugs (DMARDs) has, since its introduction in the late 1970s, assumed a dominant role in the treatment strategy. DMARDs have been shown to prevent joint destruction (4), and methotrexate has been introduced increasingly earlier (5) to achieve adequate disease control. The introduction of biologics in the past decades (1999 in Norway) has further improved the treatment of RA because of their significant impact on disease signs and symptoms as well as their ability to slow radiographic progression of joint damage (6, 7), and has changed the prognosis of patients for whom other treatment modalities are not sufficient.

Joint replacement surgery can be considered an objective proxy for joint destruction, and studying time trends in prosthesis surgery gives valuable information regarding the prognosis of patients with RA. Estimates from

previous years show that 25% of patients with RA would undergo total joint replacement within 22 years of disease onset (8), but the results of some studies now indicate a declining incidence of prosthesis surgery among these patients in recent years (9–14). Jämsen et al found a decline in the annual incidence of joint replacement surgery in Finland in the years 1995–2010 (15), and also showed that in the same time period the number of individuals using synthetic and biological DMARDs was increasing. Their study did not consider arthroplasties in joints distal to the elbow or knee, or arthrodeses or synovectomies. In their cohort study of 992 patients with RA, Kievit et al also found an increasing use of DMARDs in the years 1989–2008, and a trend towards a reduced incidence of orthopaedic rheumatic surgery in 2006–2008 (16).

In 2007 our group published a study describing the reduction in orthopaedic surgery among patients with chronic inflammatory joint diseases in Norway (17). The change in treatment mainly represented by methotrexate is thought to be a major contributor to this reduction (18), although it has been argued that the improved outcome in patients with RA is partly a secular trend (19). In the study from 2007, only patients operated on before the year 2005 were included, and any influence of the introduction of biological agents would be uncertain, as their use was limited and of short

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duration. We now wanted to investigate the incidence of orthopaedic surgery among RA patients from 1994/97 to 2012 to address this matter further.

## Method

The present study considered arthrodeses, synovectomies, and joint replacement procedures in patients with RA. For arthroplasties, procedures in patients with osteoarthritis (OA) were included for comparison.

Most patients receiving a primary joint arthroplasty in Norway from 1994 until today are registered in the Norwegian Arthroplasty Register. Registration is carried out by the operating surgeon, and although not compulsory, there is a very high degree of registration completeness for the most frequently replaced joints (hip 97%, knee 95%) (20), and a somewhat lower degree for the less common operations (ankle 82%, wrist 52%) (21). Data concerning the diagnosis were derived from the inclusion form on which both OA and RA are separate options. When more than one diagnosis was recorded, we determined RA to overrate OA, and each joint was considered a separate case, also when concerned with joints of the hands and feet. In patients with RA, an average of 3.3 finger joints and 1.3 toe joints were replaced per patient, whereas multiple joint replacements were less common among patients with OA, with an average per patient of 1.2 finger joints and 1.0 toe joints.

The Norwegian Patient Register was established in 1997, and receives information from the hospitals' electronic administrative patient records. Using ICD-9 and ICD-10, patients with RA were identified and information regarding all synovectomies and arthrodeses in these patients could be extracted. The location of a synovectomy or an arthrodesis was given in the surgical procedure code, and unlike the arthroplasty register, where each joint is registered separately, procedures of the ankle and foot were grouped together, as were procedures of the wrist and hand. As for

arthroplasties, each procedure was considered a separate case.

## Statistical analysis

Descriptive statistics were used for presentation of the patient characteristics. For the analysis of age, the Student's t-test was used, while  $\chi^2$  were used when analysing gender distribution. We analysed trends in the annual incidence, that is the number of operated joints per 100 000 inhabitants in respective years, as we did not have reliable figures for the number of Norwegian patients with RA. Some analyses were also performed in different age categories (0–49, 50–59, 60–69, 70–79, and > 80 years). Population figures were obtained from Statistics Norway (available at [www.ssb.no/english](http://www.ssb.no/english)).

Poisson regression analysis was used to analyse trends in the incidence of the different procedures and in the different patient subgroups. The significance level was set to 5%.

Statistical analyses were performed in SPSS version 22, 2013 and the statistical program R version 3.0.2 (25 September 2013).

## Results

In the study period 1994–2012, 11 337 joint replacement procedures were performed in 6394 patients with RA whereas 135 109 procedures were performed in 106 008 patients with OA. In the years 1997–2012, 4782 synovectomies and 6022 arthrodeses were performed in patients suffering from RA.

### Age and sex at surgery

For arthroplasty procedures, the mean age at surgery was significantly lower among patients with RA (63 years) than among patients with OA (70 years) ( $p < 0.001$ ). There were more women than men in

Table 1. Number of procedures and age at surgery of different joints in patients with rheumatoid arthritis (RA).

	Joint replacement		Arthrodesis		Synovectomy	
	n	Age (years)	n	Age (years)	n	Age (years)
Shoulder	855	64 (13)	12	61 (12)	433	58 (14)
Elbow	609	62 (13)	16	63 (11)	379	55 (14)
Wrist/carpus/finger*	134/99/2619	55 (13)/62 (14)/61 (12)	2191	61 (12)	1867	57 (14)
Hip	3045	64 (14)	21	74 (11)	14	52 (17)
Knee	2925	66 (12)	30	61 (16)	1133	52 (17)
Ankle/foot*	246/805	58 (14)/61 (12)	3743	62 (12)	948	54 (14)
Total†	11 337	63 (13)	6022	62 (12)	4782	55 (15)
Women/men	9330/2007		4983/1039		3546/1236	

Age given as mean (standard deviation).

\*For the joint replacements, separate numbers for ankle and toes as well as wrist, carpus, and fingers were registered, whereas these were grouped together for arthrodeses and synovectomies.

†Some reports did not specify which joint was operated on, hence the total number may be larger than the sum.

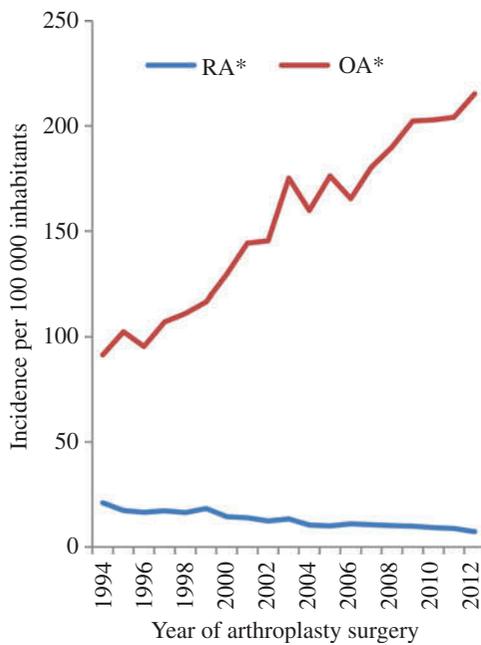


Figure 1. Incidence of arthroplasty surgery in patients with rheumatoid arthritis (RA) vs. osteoarthritis (OA). \* $p < 0.001$ .

both groups but the female count among RA patients (82%) was higher ( $p < 0.001$ ) than among OA patients (68%). RA patients were younger (55 years) at synovectomy than at arthrodesis (62 years), and oldest at

prosthesis surgery (63 years). We found that 74% of synovectomies and 83% of arthrodeses were performed in women. Age at surgery for each separate joint is shown in Table 1.

Distribution of procedures in different joints

Fingers, knees, and hips comprised the bulk of replaced joints, whereas arthrodeses above all were performed in the wrist/hand and ankle/foot. Synovectomies were infrequent in the hip, but otherwise performed in all joints, and most commonly in the wrist/hand. The total spread is presented in Table 1.

Arthroplasties

The incidence of prosthesis surgery in RA patients declined during the entire study period, with a coefficient of  $-0.050$  ( $p < 0.001$ ), whereas the incidence in OA patients increased significantly with a coefficient of  $0.047$  ( $p < 0.001$ ) (Figure 1).

We also found that the mean age at surgery in patients with RA was significantly ( $p < 0.001$ ) higher in 2012 (66 years) than in 1994 (62 years). Among patients with OA, the mean age at surgery in 2012 was somewhat lower than in 1994 (69 years vs. 71 years,  $p < 0.001$ ). The reduction in arthroplasty surgery among RA patients

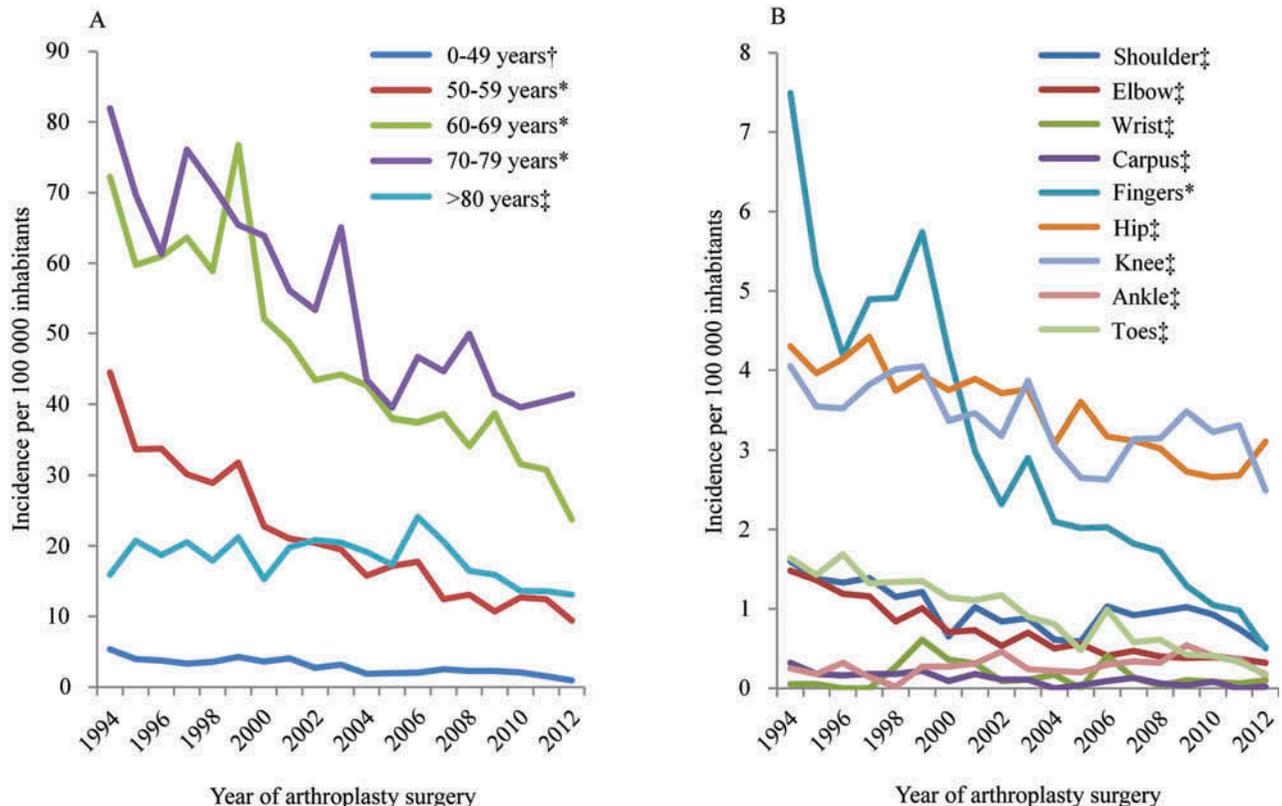


Figure 2. Joint replacement surgery (A) in different age groups and (B) in different joints in patients with rheumatoid arthritis (RA). \* $p < 0.001$ , † $p < 0.05$ , ‡ $p > 0.05$ .

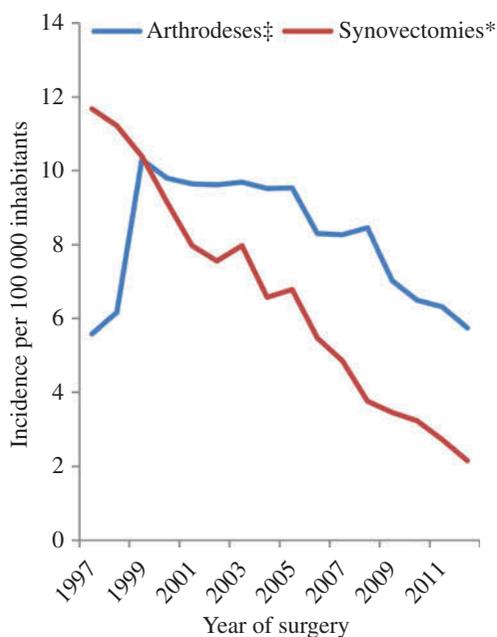
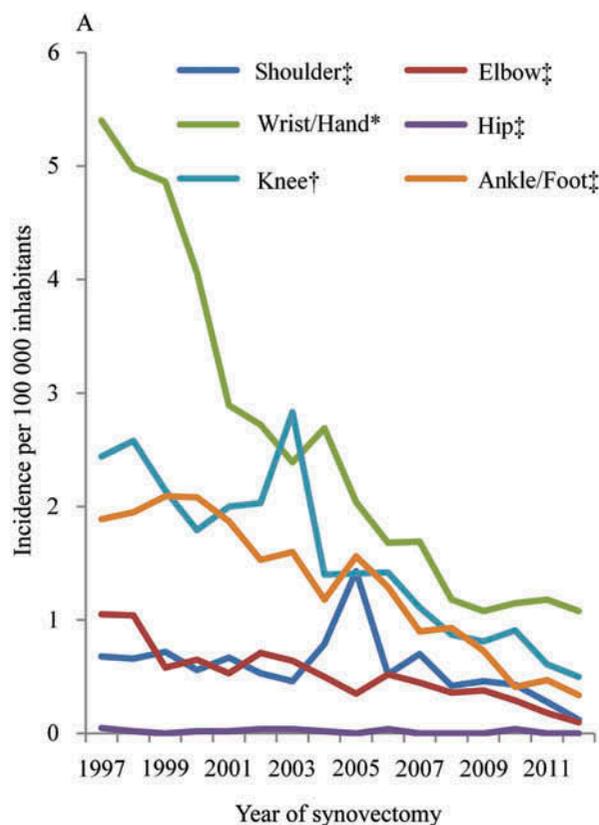


Figure 3. Incidence of arthrodeses and synovectomies in patients with rheumatoid arthritis (RA). \* $p < 0.001$ , † $p > 0.05$ .

was steepest among patients between 50 and 59 years of age (coefficient of  $-0.079$ ,  $p < 0.001$ ) but significant in all age groups below 80 (0–49 years:  $-0.059$ ,  $p < 0.05$ ;



60–69 years:  $-0.051$ ,  $p < 0.001$ ; and 70–79 years:  $-0.040$ ,  $p < 0.001$ ). For patients aged  $> 80$  years, the reduction coefficient of  $-0.013$  was not significant (Figure 2A).

In Figure 2B the incidence of prosthesis surgery in each joint is presented separately, showing that while finger prostheses were previously the most frequently performed, their incidence has declined markedly from 7.5 to 0.5 per 100 000 inhabitants with a coefficient of  $-0.11$  ( $p < 0.001$ ). The reduced number of toe joint prostheses was borderline significant ( $p = 0.057$ ), while the evident declining trends for shoulder, elbow, and hip were not statistically significant.

### Synovectomies

The incidence of synovectomies declined markedly ( $p < 0.001$ ) during the entire study period from 11.7 per 100 000 inhabitants in 1997 to 2.2 per 100 000 inhabitants in 2012 (Figure 3).

Synovectomies of the wrist and hand had the greatest reduction from 5.4 to 1.1 procedures per 100 000 inhabitants (coefficient of  $-0.12$ ,  $p < 0.001$ ) but the coefficient was also negative for all other joints but the hip, and significant in knee joints ( $p < 0.05$ ), and borderline

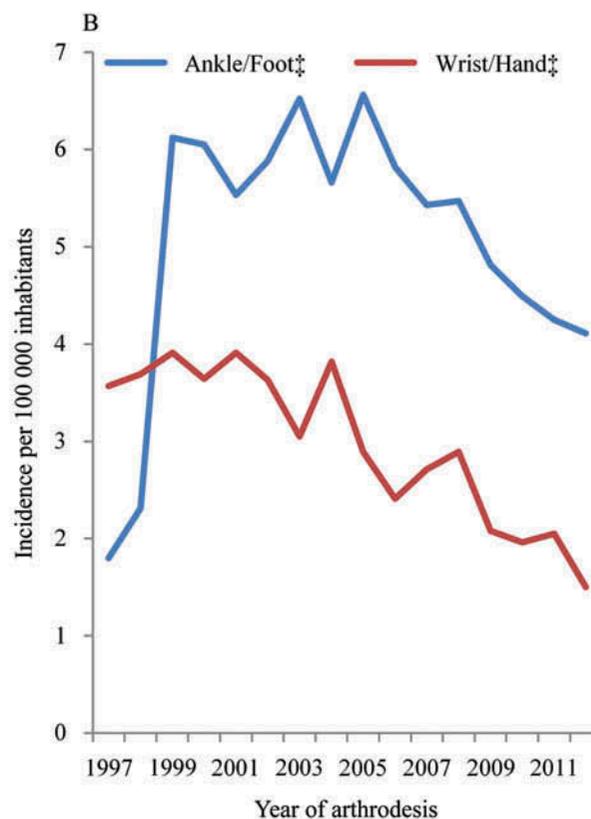


Figure 4. (A) Synovectomies and (B) arthrodeses for different joints in patients with rheumatoid arthritis (RA). The incidences of arthrodeses performed in the shoulder, elbow, hip, and knee were so low that they were excluded from the figure. Absolute numbers can be found in Table 1. \* $p < 0.001$ , † $p < 0.05$ , ‡ $p > 0.05$ .

significant in ankle/foot joints ( $p = 0.052$ ) (Figure 4A). The decrease was most evident (coefficient of  $-0.14$ ,  $p = 0.001$ ) among the youngest patients (age  $< 50$  years) but also statistically significant ( $p < 0.05$ ) in patients aged 50–59 years.

### Arthrodeses

There was an increase in arthrodeses of the ankle and foot from 1997 to 1999 (Figure 4B) causing the total number of arthrodeses to increase in these years. The incidence has since been declining from 10.3 to 5.7 procedures per 100 000 inhabitants (coefficient of  $-0.042$ ,  $p = 0.067$ ) (Figure 3). When performing subgroup analyses for each joint, no significant changes were found, but for the subgroup of wrist and hand the incidence declined with a coefficient of  $-0.05$  ( $p = 0.11$ ) during the entire study period from 1997 to 2012. No decrease was seen in the eldest patient group ( $\geq 80$  years), and for the other age groups the decline was not statistically significant.

### Discussion

This study's main finding was a significant decrease in joint replacement surgery and synovectomies in Norwegian patients with RA in the time period 1994/97–2012. There was an increasing number of arthrodeses of the ankle and foot during the first 2 years from 1997 to 1999, and although the reduction in arthrodeses since 1999 was not statistically significant, there was a strong declining trend ( $p = 0.067$ ).

The decreasing number of joint replacements contradicts the general increase in prosthesis surgery as seen in patients with OA. Reasons for the increasing number of arthroplasties for OA in recent years may be the increased proportion of elderly or overweight persons in the population, and a greater acceptance in general for operating on patients of advanced age and with co-morbidities. Increasing surgical capacity might also be a contributory factor. These factors should also affect the use of prosthesis surgery in patients with RA, which is nevertheless diminishing.

Studies of other cohorts have shown a similar decrease in the number of joint replacements (15–17), and the study of this large volume of material from the Norwegian Arthroplasty Register confirms that the trend continues into the era of biologics. When performing subgroup analyses, the decrease is not evident among patients above the age of 80. In addition to the increased acceptance for operating on elderly patients, an explanation for this may be that joint destruction in this age group had, to a greater extent, already occurred before the improvement in treatment of patients with RA. For arthroplasty surgery there is a significant decrease in the incidence of procedures in patients below 80 years of age. Although there is a negative coefficient in these age

groups for the other procedures, the decline is statistically significant only in patients below 60 years of age for synovectomies, and for no age groups with regard to arthrodeses, probably because of the reduced number of study subjects obtained when dividing the groups.

In a review conducted in 2004, Uhlig and Kvien reported that the incidence of RA had generally declined in recent decades (22). Although this might also reflect changing methodology in classification, a true reduced incidence of RA would be expected to affect the incidence of rheumatic orthopaedic surgery. However, as this decline was found to have occurred mainly in the 1970s and early 1980s, it is unlikely to explain all of the steadily continuing decrease in surgical procedures.

We also found a significant increase in mean age at prosthesis surgery in patients with RA from 62 years in 1994 to 66 years in 2012. This might indicate that patients suffer from their disease for longer before needing joint replacement, probably because of better arthritis control inhibiting joint destruction or because of reduced inflammation resulting in less pain and improved function in a destructed joint. It can also be explained by epidemiological changes towards an older population causing the age at onset of RA to increase (19), or by our finding that the decrease in the number of procedures is not evident among the eldest patients.

Hand function is of utmost importance, and while finger joints, followed by hips and knees, were previously the most frequently replaced, these procedures have seen the greatest reduction, with an incidence of 0.5 per 100 000 inhabitants in 2012 compared to 7.5 per 100 000 inhabitants in 1994. The incidence of synovectomies and arthrodeses in the wrist and hand also declined markedly. In a recent study by Nikiphorou et al on an inception cohort of RA patients in the UK, a similarly decreased incidence of intermediate surgery (joint replacements of hands and feet as well as synovectomies and arthrodeses) was found whereas major surgery (joint replacements of the hip, knee, shoulder, and elbow) remained constant (23). The authors discuss whether this could be attributed to a different mechanism and/or a different response to treatment in larger joints. Another probable explanation discussed is that the population is ageing, with the consequent increased prevalence of OA. Increased body weight among RA patients as well as among the general population might also be relevant. The relationship between body weight and joint destruction is complex, but Shourt et al found an increased incidence of joint surgery, and particularly knee surgery, in obese RA patients (24). Our data similarly provided no evidence for a decrease in knee joint replacements.

Documented good results for new reverse prostheses of shoulder joints might have made surgeons more eager to perform this procedure, and rheumatologists more prone to recommend surgery to their patients. However, prosthesis of the elbow is a typical RA procedure, and although not strictly statistically significant ( $p = 0.096$ ), there is a

declining trend for this procedure, with a coefficient of  $-0.09$  that equals the trend for toe joint prostheses. Thus, in our study as well as that of Nikiphorou et al, the most RA-specific procedures declined the most, indicating a true change in prognosis for RA patients.

The finding of arthrodesis procedures increasing from 1997 to 1999 before declining might be related to the temporary dip in ankle replacements in Norway in 1997 and 1998 (25). In 1997/98 the Norwegian Thompson Parkridge Richards (TPR) ankle prosthesis, the most popular ankle prosthesis in Norway, stopped being produced, and more patients may in these years have had an arthrodesis performed instead. Using orthopaedic surgery as a surrogate marker for joint destruction, our results are consistent with other studies finding reduced progression in radiographic damage and functional disability (18).

The incidence of orthopaedic surgery was calculated from two large registers, and as with all register studies, some miscoding must be expected. Nevertheless, there is no reason to believe that the degree of perfection should have changed during the study period, or that the completeness of the data should have deteriorated. For arthroplasties of the hip and knee, the data completeness was confirmed to be steadily high for the years 2008–2012 in the 2014 annual report from the Norwegian Arthroplasty Register (20), compared to the years 1999–2002 (21). The data completeness of the more uncommon arthroplasty procedures such as the ankle (82%) and wrist (52%) have not been reported since 2006, and might have improved in later years following greater awareness among surgeons. If so, that would make a declining incidence less evident.

RA has become a more benign disease in later years (1, 16), and this has been postulated to be partly a secular trend (19). By contrast, Finckh et al found that, when adjusting for DMARD use, steroid use, and baseline predictors, the improvement in patient outcome was attributable to more effective anti-rheumatic treatment (18). As the decline in orthopaedic surgery in patients with RA is already evident from 1994, before the introduction of biological agents, it is probably mainly attributable to the introduction of methotrexate in the treatment of this inflammatory disease (26). Tumour necrosis factor (TNF)- $\alpha$  inhibitors has been shown to prevent joint destruction and radiographic damage, and their use should thereby induce a reduction in the need for orthopaedic surgery among patients with RA. Theoretically, we would expect that at some point after the introduction of methotrexate, the incidence of joint replacement surgery should stabilize at a new level, and that a further decrease would be attributable to the introduction of TNF- $\alpha$  inhibitors, but it is difficult to predict when this would occur, especially as RA is now being treated earlier and more aggressively with higher doses of methotrexate (27). It is also among this study's limitations that we can only report the general use of orthopaedic surgery in

Norway, and therefore cannot analyse outcomes of individual patients receiving different treatment, and further studies are required to more specifically evaluate what impact biological treatment has had on the need for rheumatic orthopaedic surgery. As rheumatic surgery is a late outcome of RA, a time delay between change in treatment and change in incidence must be expected. Later studies might give results with higher significance.

## Conclusions

The reduction in rheumatic surgery reported by a few previous authors is confirmed in this analysis of a large amount of material from the Norwegian Arthroplasty Register and the Norwegian Patient Register. The trend seen in earlier time periods is found to continue into the biologic era and throughout the study period from 1994/97 to 2012. The general increasing trend in the use of synthetic and biologic DMARDs thus coincides with less joint destruction and an improved long-term prognosis of patients with RA.

## Acknowledgements

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