Infliximab Versus Conventional Combination Treatment and Seven-Year Work Loss in Early Rheumatoid Arthritis: Results of a Randomized Swedish Trial

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Objective. To compare long-term work loss in methotrexate-refractory early rheumatoid arthritis (RA) patients randomized to the addition of infliximab or conventional combination treatment.

Methods. This study was a multicenter, 2-arm, parallel, randomized, active-controlled, open-label trial. RA patients with <1-year symptom duration were recruited from 15 rheumatology clinics in Sweden between 2002–2005. Patients who did not achieve low disease activity after 3–4 months of methotrexate therapy were randomized to the addition of infliximab or conventional combination treatment with sulfasalazine plus hydroxychloroquine. Yearly sick leave and disability pension days >7 years after randomization were retrieved from nationwide registers kept by the Swedish Social Insurance Agency.

Results. Of 210 working-age patients, 109 were randomized to infliximab (mean age 48.4 years, 73% women) and 101 to conventional therapy (mean age 48.7 years, 77% women). The year before randomization, the mean number of annual work days lost was 127 in the infliximab arm and 118 in the conventional treatment group (mean difference 9 [95% CI 23, 39]). Compared to the year before randomization, the mean changes at 7 years were −25 days in the infliximab and −26 days in the conventional treatment group (adjusted mean difference 10 [95% CI 25, 46]). The cumulative mean for work-loss days was 846 in the infliximab group and 701 in the conventional treatment group (adjusted mean difference 104 [95% CI 56, 284]).

Conclusion. Long-term work loss improved significantly in early RA patients randomized to infliximab plus methotrexate or conventional combination therapy. No difference was detected between strategies, and the level of work-loss days remained twice that observed in the general population.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic disease characterized by systemic inflammation and joint destruction. An estimated 0.6% and 41 per 100,000 Americans per year are affected by RA (1,2). Over the last 2 decades, many new antirheumatic drugs have been introduced, and together with treat-to-target strategies, the attitude has changed from reactive to preventive therapies aiming for remission and improved work ability. However, with the destructive nature of the disease, work disability is still highly prevalent among RA patients, already in the first

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Significance & Innovations

- In methotrexate-refractory early rheumatoid arthritis (RA), work loss improved significantly over 7 years in patients treated with a strategy starting with the addition of infliximab or conventional combination therapy to methotrexate.
- No difference in work-loss days over 7 years between patients randomly allocated to infliximab plus methotrexate or conventional combination therapy could be detected, and any long-term persisting effect of the small but statistically significant radiologic difference at 2 years favoring the infliximab treatment strategy did not translate into better work-loss outcomes.
- Based on the long-term work-loss findings from the Swedish Pharmacotherapy (SWEFOT) trial, and when taking into account the substantially higher cost of biologic agents, an attempt using a strategy with a combination of conventional disease-modifying antirheumatic drugs appears imperative before starting infliximab treatment in methotrexate-refractory early RA.
- Nonrandomized patients who had a favorable response to methotrexate monotherapy reduced their work-loss days to the same level as the general population within a year after treatment start.

years after disease onset (3–6). Work loss has been reported to be the largest driver of societal costs in RA (7,8) and has been estimated to incur annual costs of $11 billion (56% of total RA costs) in the US (9).

Biologic tumor necrosis factor (TNF) inhibitors have shown superior efficacy regarding disease activity suppression compared to nonbiologic single disease-modifying antirheumatic drug (DMARD) alternatives (10), and some studies, when using a single DMARD comparator, suggest that the high costs of biologic agents will be offset by improvements in work loss, especially in patients with early RA (11–15). However, already at the beginning of the biologic agent era, the randomized Finnish Rheumatoid Arthritis Combination Therapy Trial also reported a strategy of initial combination of conventional DMARDs to result in superior disease activity and work-loss outcomes as compared to a single DMARD regimen in early RA (16,17). Furthermore, as summarized in a recent review (18), the available randomized trials of biologic agent versus combination DMARD strategies in early RA report no differences in clinical outcomes and no or small differences in radiologic outcomes (19,20). Rather than using single DMARD comparators, it thus appears clinically more relevant to compare a biologic agent combination alternative to a combination of conventional DMARDs in studies of work loss.

The randomized Swedish Pharmacotherapy (SWEFOT) trial was an investigator-initiated study aiming to compare the TNF inhibitor infliximab, in addition to methotrexate (MTX), to a combination of conventional DMARDs in early RA patients with insufficient response to MTX. From the 2-year results of this trial, we previously reported a small but statistically significant difference in radiographic outcomes favoring the infliximab group, while disease activity, quality of life, and work loss improved similarly in both treatment arms (21–24). To the best of our knowledge, no randomized controlled trial has so far evaluated the long-term effect of a biologic drug on work loss compared to combination DMARDs. While work loss may be more inert to treatment than clinical and radiologic outcomes, long-term data are important, although they are likely to include challenges with low drug adherence several years after treatment allocation.

In addition to the head-to-head comparison, work-loss outcomes in the nonrandomized patients who had a favorable response to MTX in the SWEFOT trial may add important data to the ongoing discussion of any potential treatment window and whether to use an initial aggressive treatment strategy or a step-up approach (25,26). Excellent clinical outcomes have previously been reported in this patient group (27,28), but no study has investigated work-loss outcomes in initial MTX responders in early RA.

The aim of this study was to compare the long-term and objectively assessed sick leave and disability pension in MTX-refractory early RA patients randomized to infliximab plus MTX or conventional combination therapy, who after the 2-year trial period were treated according to best practice. A secondary aim was to evaluate work loss in the nonrandomized MTX responders in comparison with the general population.

PATIENTS AND METHODS

The SWEFOT trial has been described previously in more detail (29). Briefly, adult patients (ages >18 years) diagnosed with early RA (<1-year symptom duration) were recruited from 15 rheumatology units in Sweden between 2002 and 2005. Key inclusion criteria were RA according to the revised American College of Rheumatology criteria (30); no previous DMARD use; no oral, or stable, glucocorticoid therapy for at least 4 weeks; and a Disease Activity Score based on 28-joint count (DAS28) of >3.2 (31).

Procedures. Run-in period and randomization. At inclusion, all patients were prescribed MTX monotherapy (2.5-mg tablets), with an initial dose of 10 mg weekly, increased every 2 weeks by 5-mg increments to 20 mg a week. DAS28 was assessed at a followup visit after the 3 to 4-month run-in period. If the score was ≤3.2 (low disease activity), patients continued treatment with MTX and did not participate further in the trial. Patients who did not achieve low disease activity during the run-in phase were randomized to the addition of either infliximab (3 mg/kg body weight, rounded up to the nearest 100-mg increment, given intravenously at weeks 0, 2, and 6, and every 8 weeks thereafter) or conventional combination therapy with sulfasalazine (1,000 mg twice daily, given orally) and hydroxychloroquine (400 mg daily, given orally).

The computer-generated random list for treatment allocation was kept at the study center. The statistician who prepared the list had no further role in the study. When a patient at the 3-month visit was judged to be eligible for randomization, the investigator contacted the central study
coordinator by telephone and requested randomization. Stratification or blocking was not used in the randomization process, and both doctors and patients were aware of the treatment allocation (addition of 2 oral drugs versus 1 infusion).

Treatment adjustments. In the trial protocol, dose and frequency adjustments were permitted for sulfasalazine plus hydroxychloroquine, but only frequency changes for infliximab. Sulfasalazine plus hydroxychloroquine could be discontinued and replaced by cyclosporin A (2.5 mg/kg daily in divided doses; increase allowed to 5 mg/kg daily), and infliximab could be discontinued and replaced by etanercept (50 mg weekly).

Followup and study population. In the present study, patients were followed for 7 years. During the first 2-year trial period, included patients were scheduled for a visit at the rheumatology clinic at 7 different time points. From years 3 through 7, data on treatment were collected from the Swedish Rheumatology Quality Register (32), for both the randomized and the nonrandomized patients. Randomized patients could discontinue the assigned treatment at any time for lack of effectiveness, side effects, or by own choice. Treatment was decided by the responsible rheumatologist in case of discontinuation and after the 2-year trial period, as well as after the run-in period in nonrandomized patients who had a favorable response to MTX. The current analysis of the SWEFOT trial population included only early RA patients of working age (<64 years) at randomization.

Study outcome. The primary outcome of the SWEFOT study was achievement of a good response according to the European League Against Rheumatism criteria and has been reported elsewhere (29). The current study analyzed work-loss change, measured as accumulated days over 7 years of followup, yearly days, and days per quarter, with sick leave and disability pension compensation (maximum 360 days per year and maximum 90 days per quarter). During the study period, sick leave episodes >14 days were generally not included (compensated by the employer), and for longer periods of absence due to illness, disability pension was granted by the Social Insurance Agency for individuals who were considered to have a persistent reduction of work ability with at least 25% due to illness. Secondary analyses of health economic outcomes were prespecified in the trial protocol. We used time at randomization, i.e., the start of biologic agent or conventional combination treatment, as baseline. To simplify comparisons to the randomized patients, for the nonrandomized MTX responders we used the end date of the run-in period as baseline. Complete outcome data on a daily basis were available for all participants and time points, retrieved from the Swedish Social Insurance Agency, until emigration, death, their 65th birthday, or the end of followup.

General population comparator cohort. General population comparators were identified from the Swedish Register of the Total Population by sampling 5 sex-, age-, education-, and county-matched comparators per RA patient in the nonrandomized MTX responders. Thus, the comparator cohort were Swedish residents without RA at the matching date, and each individual in this comparison cohort was assigned the same index date as the corresponding RA patient.
For different reasons, mainly due to slower recruitment than anticipated, the initial design of 600 patients with the possibility to detect a difference of 15% in treatment response, measured by DAS28, at a statistical power of 90% ($\alpha = 0.05$), the SWEFOT trial closed after enrollment of 487 patients (29). To detect the same difference of 15%, the statistical power would be reduced to approximately 75% ($\alpha = 0.05$).

All working-age patients who had undergone random allocation were analyzed using an intention-to-treat approach. A few patients never received their allocated treatment, and in this study, patients with 1 year into their allocated treatment were removed in a modified intention-to-treat analysis (Figure 1). Finally, with very few patients staying on their allocated treatment for the complete 7 years of followup, we created a modified per-protocol group. Patients allocated to infliximab plus MTX and who were treated with any biologic agents during the complete 7 years of followup, with $\leq 90$ days between stop and start date of any next biologic drug (for those who switched drugs), were included. For the participants allocated to conventional treatment, we included all patients who were not treated with any biologic agents during the complete 7 years of followup.

### Table 1. Characteristics of study subjects and general population comparators*

| Variable | Infliximab treatment (n = 109) | Conventional treatment (n = 101) | MTX responders (n = 91) | General population (n = 455) |
|----------|--------------------------------|---------------------------------|------------------------|-----------------------------|
| Women, no. (%) | 80 (73) | 78 (77) | 58 (64) | 290 (64) |
| Age (range 19–64), years | 48.4 ± 11.1 | 48.7 ± 11.6 | 49.8 ± 12.2 | 49.8 ± 12.1 |
| Rheumatoid factor positive, no. (%) | 78 (72) | 69 (68) | 71 (78) | – |
| Smoking, no. (%)$^\dagger$ | 31 (28) | 24 (24) | 18 (20) | – |
| Symptom duration, months | | | | |
| At run-in | 7.0 ± 3.5 | 6.6 ± 3.1 | 6.4 ± 3.1 | – |
| At start of followup$^\ddagger$ | 10.4 ± 3.4 | 10.0 ± 3.2 | 9.6 ± 3.1 | – |
| DAS28 | | | | |
| At run-in | 5.8 ± 0.9 | 6.0 ± 1.0 | 5.2 ± 0.9 | – |
| At start of followup$^\ddagger$ | 4.9 ± 1.0 | 4.8 ± 1.0 | 2.4 ± 0.7 | – |
| HAQ | | | | |
| At run-in | 1.2 ± 0.6 | 1.3 ± 0.6 | 1.0 ± 0.5 | – |
| At start of followup$^\ddagger$ | 0.9 ± 0.5 | 1.0 ± 0.5 | 0.3 ± 0.4 | – |
| Education level, no. (%) | | | | |
| ≤ 9 years | 14 (13) | 17 (17) | 19 (21) | 95 (21) |
| 10–12 years | 68 (62) | 56 (55) | 44 (48) | 220 (48) |
| > 12 years | 27 (25) | 28 (28) | 28 (31) | 140 (31) |
| Work loss 1 year before start of followup$^\ddagger$ | | | | |
| Total days | 126.8 ± 112.9 | 117.9 ± 112.0 | 73.8 ± 103.8 | 61.9 ± 121.7 |
| Sick leave days | 104.3 ± 98.4 | 82.5 ± 86.6 | 51.1 ± 73.8 | 17.1 ± 56.2 |
| Disability pension days | 22.4 ± 75.2 | 35.3 ± 98.3 | 22.7 ± 84.4 | 44.8 ± 111.0 |
| Unemployment and income, no. (%)$^\S$ | | | | |
| Any compensated days | 11 (10) | 10 (10) | 9 (10) | 39 (9) |
| Any income from paid work | 97 (89) | 83 (82) | 79 (87) | 357 (78) |

* Values are mean ± SD unless indicated otherwise. Infliximab treatment: infliximab plus methotrexate (MTX). Conventional treatment: sulfasalazine and hydroxychloroquine plus MTX. DAS28 = 28-joint count disease activity score; HAQ = Health Assessment Questionnaire.

$^\dagger$ Missing data on smoking for 5 patients in the infliximab group, 1 patient in the conventional treatment group, and 18 (20%) among the MTX responders.

$^\ddagger$ Day of randomization for randomized patients, end date of the run-in period for MTX responders as well as for their matched general population comparators.

$^\S$ From paid work the calendar year before start of followup.
Table 2. Change from baseline in annual days on sick leave and disability pension 7 years after randomization between infliximab and conventional treatment*  

| Method                        | No. | Baseline | 7 years | Change vs. baseline (SE) | Adjusted difference (95% CI)† |
|-------------------------------|-----|----------|---------|-------------------------|-----------------------------|
|                               | infliximab/ | Infl iximab | Conventional | Infl iximab | Conventional | Infliximab | Conventional | Infliximab | Conventional | Infliximab | Conventional | Infliximab | Conventional | Infliximab | Conventional | Infliximab | Conventional | Infliximab | Conventional |
| Main analysis                 |     |          |         |                          |                             |
| Intention-to-treat            | 82/75 | 131 ± 114 | 107 ± 108 | 107 ± 132 | 81 ± 126 | -25 (13) | -26 (12) | 10 (-25, 46) |
| Alternative analyses          |     |          |         |                          |                             |
| Modified intention-to-treat‡ | 65/42 | 129 ± 115 | 103 ± 103 | 95 ± 122 | 90 ± 135 | -34 (16) | -14 (16) | -10 (-55, 38) |
| Modified per-protocol         | 32/27 | 125 ± 113 | 112 ± 105 | 108 ± 137 | 94 ± 152 | -18 (23) | -18 (26) | 5 (-58, 80) |
* Values are mean ± SD unless indicated otherwise. Intention-to-treat analysis included all randomized patients of working age. Modified intention-to-treat analysis included all randomized patients of working age who completed 1 year according to protocol. Modified per-protocol analysis included all randomized patients of working age who were treated with any biologic drug (for patients allocated to the infliximab group), and patients who did not receive any biologic drug (in the conventional treatment group), and patients who did not receive any biologic drug (in the conventional treatment group) for the complete 7 years of followup period. Infliximab treatment: infliximab plus methotrexate. Conventional treatment: sulfasalazine and hydroxychloroquine plus methotrexate. † Adjusted for work-loss days the year before randomization (WorkDaysLost7y = α + β1 × group + β2 × WorkDaysLostbaseline + c). Confidence intervals were estimated using nonparametric bootstrapping.
‡ ≥1 year on allocated drug.

RESULTS

A total of 493 patients were recruited from October 2002 to December 2005, with 487 patients enrolled in the study (29). Of 258 patients undergoing random allocation, 210 were ages <64 years, of whom 109 were randomized to biologic agent treatment and 101 to conventional treatment (Figure 1). The baseline characteristics of randomized patients ages <64 years were similar between the treatment groups (Table 1).

Sick leave and disability pension before randomization. The mean days on sick leave and disability pension in the intention-to-treat analysis the year before randomization was 127 (median 112) in the infliximab arm and 118 (median 105) in the conventional treatment group (mean difference 9 [95% CI –23, 39]). The corresponding mean among the patients who completed 7 years of followup in the intention-to-treat analysis was 131 (n = 82, median 110) in the infliximab group and 107 (n = 75, median 92) in the conventional treatment group (mean difference 24 [95% CI –11, 59]) (Table 2). The mean number of days peaked at the run-in phase in both the future infliximab and conventional treatment groups, with 54 and 51 days per quarter, respectively (mean difference 3 [95% CI –7, 12]) (Figure 3), with almost all additional days due to sick leave in both treatment groups. The proportion of patients who had any sick leave or disability pension days the quarter before randomization was 77% (n = 84) in the infliximab and 74% (n = 75) in the conventional treatment group (P = 0.64), while patients who had full-time disability pension (90 days of 90) were 3 (3%) and 7 (7%) in the infliximab and the conventional treatment groups, respectively (P = 0.16) (Supplementary Figures 1–4, available on the Arthritis Care & Research web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.22899/abstract).

Nonrandomized MTX responders versus matched general population. At 10–12 months before the end of run-in, the overall mean days per quarter of sick leave and disability pension in the nonrandomized group started to increase from a statistically nonsignificant lower level as compared to the general population comparators (10 versus 17 days per quarter, respectively; mean difference –7 [95% CI –12, 0]), and increased to 29 days per quarter during the run-in period (mean difference 13 [95% CI 6, 22]) (Figure 3 and Supplementary Figures 5 and 6, available on the Arthritis Care & Research web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.22899/abstract).

Sick leave and disability pension after randomization. The mean cumulative work-loss days over 7 years in patients <64 years at randomization was 846 in the infliximab group...
and 701 in the conventional treatment group (n = 101, adjusted mean difference 104 [95% CI 2256, 284]) (Figure 4). At 7 years after randomization, mean days per year had decreased to 107 (mean change 225 days) in the infliximab group and to 81 (mean change 226 days) in the conventional treatment group (adjusted mean difference 10, favoring conventional treatment [95% CI 225, 46]) (Table 2).

The corresponding mean days per quarter of sick leave and disability pension at 82–84 months after randomization, when compared to 1–3 months before randomization, was 28 (mean change 227 days) and 20 (mean change 228 days) in the infliximab and the conventional treatment group, respectively (adjusted mean difference 5, favoring conventional treatment [95% CI 25, 15]) (Figure 3). The proportion of patients who had any sick leave or disability pension days at 82–84 months after randomization was 46% (n = 38) in the infliximab arm and 35% (n = 26) in the conventional treatment arm (P = 0.14), while the proportion of patients on full-time disability pension was 15% (n = 12) and 13% (n = 10) in the infliximab and the conventional treatment groups, respectively (P = 0.81) (Supplementary Figures 2 and 4, available on the Arthritis Care & Research web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.22899/abstract). We also analyzed the adjusted mean differences between the infliximab and the conventional treatment groups in the other 27 quarters during followup and could not detect any statistically significant difference in any of the 3-month periods (Figure 3).

Nonrandomized MTX responders versus matched general population within 1 year. The nonrandomized patients decreased their sick leave and disability pension days per quarter to the same level as the general population comparators within 1 year after inclusion in the trial (16 days in the nonrandomized group versus 16 days in the general population, mean difference 21 [95% CI 27, 7]) (Figure 3 and Supplementary Figures 5 and 6, available on the Arthritis Care & Research web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.22899/abstract).

Alternative analyses. Modified intention-to-treat analysis. Of the 210 randomized patients, 65 (60%) who were randomized to infliximab and 42 (42%) to conventional treatment remained >1 year on the per-protocol treatment to
which they were initially allocated. While no difference could be detected between the treatment arms, a numerically greater decrease in sick leave and disability pension days per year was observed in the infliximab group (−34 in the infliximab versus −14 in the conventional group, adjusted mean difference −10 [95% CI −55, 38]) (Table 2).

**Modified per-protocol analysis.** Of the 109 patients randomly allocated to infliximab, 32 (29%) were treated with any biologic drug during the complete 7 years of followup. Of the 101 patients randomized to conventional treatment, we identified 27 patients (27%) who were not treated with any biologic drug during the followup period (Figure 2). In this patient group, as compared to the main analysis findings, we found a similar point estimate of the adjusted mean difference between the treatment arms (Table 2).

**DISCUSSION**

In this study we investigated work loss by comparing 2 treatments strategies, rather than 2 specific drug regimens, over 7 years in real world clinical practice, and observed that work loss in MTX-refractory early RA patients improved significantly, with the largest improvement during the first 3 years. However, no difference, per quarter or cumulatively, between patients randomly allocated to infliximab plus MTX or conventional combination therapy could be detected. Nonrandomized patients who responded sufficiently to the initial MTX therapy (Figure 1), had fewer work-loss days already before the run-in phase of the trial, as compared to the future randomized patients, and reduced their work-loss days to the same level as the general population within 1 year after start of MTX treatment.

The results in this study are in line with the 2-year findings from the SWEFOT trial, where a substantial and similar improvement was found in sick leave and disability pension days in both treatment arms at 21 months after randomization (21). Five other recent randomized, controlled trials have compared a biologic agent treatment strategy to a combination of nonbiologic DMARDs. The TEAR (US), BeSt (The Netherlands), and the NEO-RACo trials (Finland) contrasted these treatment alternatives in early RA patients (19,20,36), and found no difference in disease activity, and no or a small difference in radiographic progression. In established RA, randomized trials from the US (RACAT) and the UK (TACIT) have shown that a combination of DMARDs was noninferior to a biologic agent strategy in combination with MTX regarding disease activity, radiographic progression, and health assessment questionnaire scores (37,38).

These findings are consistent with the results from the SWEFOT study. However, none of these other trials have so far published data on work loss. In contrast, several studies have reported superior work-loss improvements in early RA patients randomized to receive an initial biologic agent in combination with MTX, when compared to initial MTX monotherapy (11–15). Based on the short-term and long-term findings of work loss from the SWEFOT trial, and when taking into account the substantially higher cost of biologic agents, an attempt using a strategy with a combination of conventional DMARDs appears imperative before starting infliximab treatment in MTX-refractory early RA.

With respect to the nonrandomized patients who responded favorably to MTX, their work-loss days were at a similar level as the general population comparators within a year after MTX initiation. While immediate initiation of aggressive therapy may be warranted in some patients, a strategy starting with MTX results in approximately one-third of patients achieving low disease activity or remission within a year (27,29,36). Patients who had an insufficient response to MTX and were randomized to a more aggressive treatment alternative increased their work-loss days from the same level as the general population 1 year before randomization, and remained at around twice as high as the general population 7 years after randomization. This persisting gap highlights, also when using long-term work loss as an outcome, the need for earlier diagnosis and a method to discriminate between patients who will have a favorable or insufficient MTX response.

In addition, adjustments in the working environment may also be considered to halt the reduction of work ability. Although work place adjustments are likely to imply an additional cost, as long as unmet needs of earlier diagnosis and prediction of response to MTX exist, adjustments for individuals’ needs may be an important intervention for the benefit of both personal finances and self-esteem, as well as to reduce the gap of work-loss days to the general population.

Via linkage to nationwide registers of work-loss compensation at the Social Insurance Agency, we had access to objectively assessed data on sick leave and disability pension on a daily basis, both before the trial and to more than 7 years after the trial began, for all patients who were initially enrolled in the SWEFOT trial, as well as for general population comparators. While work loss may be more inert to treatment than clinical outcomes, the access to long-term data is important.

The main limitation of the SWEFOT trial was that both patients and physicians were aware of the treatment allocation. Blinding assessment of disease activity was considered in the trial design, but was deemed unfeasible due to limited personnel resources at smaller participating units. Although work loss was objectively assessed using registers, the allocated treatment may have influenced the expectations of work ability from both patients and their rheumatologists.

A limitation for the analysis of quarterly work loss at 7 years was the small sample of randomized working-age patients at 7 years of followup (turning 65 years was by far the most common reason why patients were removed from the analysis). A small sample, in addition to the power calculation in the trial design of detecting between-group difference in disease activity and not work loss, increases the risk of type II errors. However, in the analysis of accumulated work-loss days, all randomized patients ages ≤64 years were included.

Work loss over 7 years improved significantly in MTX-refractory early RA patients randomly allocated to either of 2 treatment strategies, starting with infliximab plus MTX or conventional combination therapy. However, no difference between the 2 strategies could be detected. Patients who responded favorably to MTX monotherapy reduced their work-loss days to the same level as the
general population within a year after MTX initiation, while randomized patients remained at a level twice that in the general population, indicating the need for more effective treatments and more attention to improve work participation in RA.

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AUTHOR CONTRIBUTIONS
All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Eriksson had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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