Biological vs Conventional Combination Treatment and Work Loss in Early Rheumatoid Arthritis: A Randomized Trial

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**IMPORTANCE** The introduction of biological tumor necrosis factor inhibitors has improved the treatment of rheumatoid arthritis (RA) but at a substantial cost. These drugs have been shown to lead to superior radiological outcomes compared with a combination of conventional disease-modifying antirheumatic drugs over 2 years.

**OBJECTIVE** To investigate whether radiological superiority translates into better work loss outcomes.

**DESIGN, SETTING, AND PARTICIPANTS** Multicenter, 2-arm, parallel, randomized, active-controlled, open-label trial. Patients with early RA (symptom duration <1 year) were recruited from 15 rheumatology clinics in Sweden from October 1, 2002, through December 31, 2005. The study population was restricted to working-age patients (aged <63 years).

**INTERVENTIONS** Patients who did not achieve low disease activity after 3 to 4 months of methotrexate therapy were randomized to receive additional biological treatment with infliximab or conventional combination treatment with sulfasalazine plus hydroxychloroquine.

**MAIN OUTCOMES AND MEASURES** Monthly sick leave and disability pension days 21 months after randomization retrieved from the nationwide Swedish Social Insurance Office register. Main analyses were by intention to treat, including all patients, and adjusted for baseline sick leave and disability pension.

**RESULTS** Of 204 eligible patients, 105 were randomized to biological and 99 to conventional treatment. Seven patients in the biological and 4 in the conventional treatment group never received the study drug, and 72 and 52 patients, respectively, followed the study per protocol for 21 months. The baseline mean (SD) work loss was 17 (13) d/mo (median, 16 d/mo) in both groups (mean difference, 0.6 d/mo; 95% CI, −3.0 to 3.9). The mean changes in work loss at 21 months were −4.9 d/mo in the biological and −6.2 d/mo in the conventional treatment group (adjusted mean difference, 1.6 d/mo; 95% CI, −1.2 to 4.4). Including only patients receiving at least 1 dose of assigned treatment, the adjusted mean difference was 1.5 d/mo (95% CI, −1.5 to 4.4), and in per-protocol analysis the adjusted mean difference was 0.3 d/mo (95% CI, −2.8 to 3.8).

**CONCLUSIONS AND RELEVANCE** The radiological superiority of biological compared with conventional combination therapy did not translate into better work loss outcomes in patients with early RA who had experienced an insufficient response to methotrexate.

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Rheumatoid arthritis (RA) affects approximately 0.6% of Americans and has been estimated to incur annual costs of $1 billion due to work loss. Work loss is highly prevalent already among patients with newly diagnosed RA and is the largest driver of the societal costs associated with the disease. Work disability rates have been suggested to be country specific due to substantial differences in social policy between countries, but a recent review found similar rates in US and northern European studies. The introduction during the last decade of biological drugs, with superior efficacy in treating disease activity compared with nonbiological alternatives, has raised hopes that the ability to work will likewise improve or be preserved with biological treatment, especially in patients with early RA.

In randomized clinical trials including patients with early RA, biological treatment with the tumor necrosis factor (TNF) inhibitors infliximab, adalimumab, and etanercept, in combination with methotrexate, has been shown to be clinically and radiologically superior to methotrexate monotherapy. Based on self-reported work loss, biological therapy also has been shown to result in better work outcomes than methotrexate monotherapy. To our knowledge, however, the effect of biological agents on work loss compared with that of combination disease-modifying antirheumatic drugs (DMARDs) has not been investigated in randomized trials.

To our knowledge, no randomized clinical trial of TNF inhibitors has so far evaluated the effect on work loss using objective outcome data. Such a design can be used to assess whether the superior improvement in measures of disease activity translates into actual changes in work loss, something that is commonly claimed and used as one motivation for the high cost of biological drugs in RA.

In the Swedish Pharmacotherapy (Swefot) study in patients with early RA in whom methotrexate monotherapy had failed, adding infliximab to methotrexate was radiologically superior to adding sulfasalazine plus hydroxychloroquine over 2 years. The aim of the current analysis was to evaluate whether this radiological superiority translated into greater improvement in sick leave and disability pension, assessed on the basis of objective work loss data from the Swedish Social Insurance Agency register.

Methods

The Swefot trial has been described in more detail elsewhere. Briefly, adult patients (aged ≥18 years) with a diagnosis of early RA (symptom duration <1 year) were recruited from 15 rheumatology units in Sweden from October 1, 2002, through December 31, 2005. The key inclusion criteria were (1) RA diagnosed according to revised American College of Rheumatology criteria; (2) no previous treatment with DMARDs; (3) no oral or stable glucocorticoid therapy for at least 4 weeks, using at most 10 mg/d prednisolone (or equivalent); and (4) a disease-activity score based on a 28-joint count disease activity score (DAS28) of more than 3.2.

Procedures

Run-in Period

At inclusion, all patients were prescribed methotrexate (2.5-mg tablets) to be taken every week at an initial dose of 10 mg. This dose was increased every 2 weeks by 5-mg increments to 20 mg/wk. In addition, folic acid supplements were prescribed to all patients in tablets of 5 mg to be taken 1 to 6 times a week but not on the day of methotrexate intake.

Randomization

The DAS28 was assessed at a follow-up visit after the 3- to 4-month run-in period. If the score was 3.2 or less, patients continued treatment with methotrexate and did not participate further in the trial. Patients who did not achieve low disease activity during the run-in phase were randomized to receive additional treatment with 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 (1000 mg twice daily, given orally) and hydroxychloroquine (400 mg/d, 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. We did not use stratification or blocking. Physicians and patients were aware of the treatment allocation (addition of 2 oral drugs vs 1 infusion).

Treatment Adjustments

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

Follow-up

The included patients were scheduled for a visit at the rheumatology clinic at run-in, randomization, and 3, 6, 9, 15, and 21 months after randomization. Patients could discontinue the assigned treatment at any time for lack of effectiveness or adverse effects or by their own choice.

Study Population

The current analysis of the Swefot trial population included only patients with early RA of working age (<63 years) at randomization.

Study Outcome

The primary outcome of the Swefot study was achievement of a good response according to European League Against Rheumatism criteria, and these results have been reported elsewhere.
The current study analyzed work loss change measured as monthly days with sick leave and disability pension compensation (maximum, 30 d/mo). Secondary analyses of health economic outcomes were prespecified. We used the time at randomization, that is, the start of biological or conventional combination treatment, as the baseline. Complete outcome data on sick leave and disability pensions for all participants and time points were retrieved from the Swedish Social Insurance Agency.

**General Population Control Cohort**

General population controls were identified from the Swedish Register of the Total Population by sampling 5 sex-, age-, education-, and county-matched controls per patient with RA. Thus, the control cohort included for comparison 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 patient with RA in the trial.

**Statistical Analysis**

The initial trial protocol of the Swefot study was designed to detect a difference of 15% in treatment response as measured by the DAS28, with a statistical power of 90% (α = .05). With the assumption that 67% of all the included patients would undergo random allocation, a total of 600 patients would be needed, resulting in a random allocation of 200 patients to each treatment arm. For different reasons, mainly owing to slower recruitment than anticipated, the Swefot trial closed after enrollment of 487 patients. To detect a difference of 15% in primary outcome between treatment arms, with fewer patients in each arm, the statistical power would be reduced to about 75% (α = .05).

Data were analyzed in all patients who had undergone random allocation and were younger than 63 years (intention-to-treat analysis; complete outcome data are available from the register linkage). A few patients never received their allocated treatment. These patients were removed in a modified intention-to-treat analysis.

Between-group differences with 95% CIs in the nonnormally distributed study outcome were estimated using bias-corrected and accelerated nonparametric bootstrapping (at 12, 6, 3, and 0 months before randomization), with 1000 replications the size of the original study. Differences between treatment arms at 12 and 21 months after randomization were analyzed by analysis of covariance, with adjustment for days of work loss during the month before randomization. The same analysis was repeated for the modified intention-to-treat population and patients completing 1 and/or 2 years according to the protocol (per-protocol analysis).

To compare baseline mean days of sick leave and disability pension between sex and smoking status categories, we used t tests, and to compare age, educational level, and health assessment questionnaire categories, we used 1-way analysis of variance. We used χ2 tests to compare categories of sick leave and disability pension between treatment arms and Kaplan-Meier curves and Cox proportional hazards regression to assess between-group differences in time on assigned treatment (eFigure 1 in Supplement).

Data were analyzed with SAS software (version 9.2; SAS Institute Inc). Reported P values are 2-sided, and differences were considered statistically significant at P < .05. For estimates generated by nonparametric bootstrapping, no P values are provided.

**Results**

A total of 493 patients were recruited from October 1, 2002, through December 31, 2005, with 487 patients enrolled in the study. Of 258 patients undergoing random allocation, 204 were younger than 63 years, of whom 105 were randomized to biological and 99 to conventional treatment (eFigure 2 in Supplement). Seven patients in the biological and 4 in the conventional treatment group never received the study drug. The baseline characteristics of randomized patients younger than 63 years were similar between the treatment groups (Table 1).

**Table 1. Characteristics of Randomized Patients**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Biological (n = 105)</th>
<th>Conventional (n = 99)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex, No. (%)</td>
<td>77 (73)</td>
<td>76 (77)</td>
</tr>
<tr>
<td>Rheumatoid factor positive, No. (%)</td>
<td>76 (72)</td>
<td>67 (68)</td>
</tr>
<tr>
<td>Age, mean (SD) [range], y</td>
<td>47.6 (10.9) [19-63]</td>
<td>48.2 (11.5) [19-63]</td>
</tr>
<tr>
<td>Symptom duration, mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At run-in</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>7.2 (3.5)</td>
<td>6.7 (3.1)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>6.7 (4.8-9.5)</td>
<td>5.9 (4.4-8.7)</td>
</tr>
<tr>
<td>At randomization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>10.5 (3.5)</td>
<td>10.0 (3.1)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>10.2 (8.1-12.7)</td>
<td>9.3 (7.5-12.2)</td>
</tr>
<tr>
<td>DAS28, mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At run-in</td>
<td>5.8 (0.9)</td>
<td>6.0 (1.0)</td>
</tr>
<tr>
<td>At randomization</td>
<td>4.9 (1.0)</td>
<td>4.8 (1.0)</td>
</tr>
<tr>
<td>Health assessment questionnaire, mean (SD)&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At run-in</td>
<td>1.2 (0.6)</td>
<td>1.3 (0.6)</td>
</tr>
<tr>
<td>At randomization</td>
<td>0.9 (0.5)</td>
<td>1.0 (0.5)</td>
</tr>
<tr>
<td>Educational level, No. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤9 y</td>
<td>13 (12)</td>
<td>16 (16)</td>
</tr>
<tr>
<td>10-12 y</td>
<td>65 (62)</td>
<td>55 (56)</td>
</tr>
<tr>
<td>&gt;12 y</td>
<td>27 (26)</td>
<td>28 (28)</td>
</tr>
<tr>
<td>Status as smoker&lt;sup&gt;b&lt;/sup&gt;</td>
<td>30 (30)</td>
<td>23 (23)</td>
</tr>
</tbody>
</table>

Abbreviations: DAS28, 28-joint count disease activity score; IQR, interquartile range.

<sup>a</sup> Balanced treatment included infliximab plus methotrexate; conventional treatment, sulfasalazine and hydroxychloroquine plus methotrexate.

<sup>b</sup> The health assessment questionnaire is a standardized measure of self-reported disability (functional status); this information was missing for 4 patients in the biological and 2 in the conventional treatment group.

<sup>c</sup> Information on smoking status was missing for 5 patients in the biological and 1 in the conventional treatment group.
Sick Leave and Disability Pension Before Randomization

At randomization, the mean (SD) overall number of days on sick leave and disability pension was 17 (13) d/mo in both treatment groups (Figure 1). Greater work loss was seen with older age (aged 19-44 years, 14 d/mo; 45-54 years, 18 d/mo; ≥55 years, 19 d/mo; \( P = .048 \)) and health assessment questionnaire category (<1.0, 13 d/mo; 1.0-1.49, 21 d/mo; ≥1.5, 26 d/mo; \( P < .001 \)), as well as with lower educational level (≤9 years, 21 d/mo; 10-12 years, 17 d/mo; >12 years, 14 d/mo; \( P = .04 \)) and in smokers (smokers, 21 d/mo; nonsmokers: 15 d/mo; \( P = .007 \)).

Approximately 1 year before randomization, the overall mean monthly days of sick leave and disability pension started to increase from the same level as in the matched general population controls (5 vs 5 d/mo; mean difference, −0.5; 95% CI, −1.9 to 1.3) (Figure 2) and increased rapidly to 11 d/mo at 6 months before randomization (mean difference, 5.8; 95% CI, 4.1-7.9).

The mean number of days peaked at the start of the run-in phase in the (future) biological and conventional treatment groups at 20 and 18 d/mo, respectively (mean difference, 1.6; 95% CI, −1.9 to 5.1), and decreased during the run-in period to 17 d/mo in both groups (mean difference, 0.6; 95% CI, −3.0 to 3.9) (Figure 2).

Sick Leave and Disability Pension After Randomization

Mean Development

At 12 months after randomization, the mean number of days lost had decreased to 13 d/mo in both biological (change, −4.1) and conventional (change, −4.0) treatment groups (adjusted mean difference, 0.1; 95% CI, −2.7 to 3.3) (Table 2). Corresponding means at 21 months were 12 d/mo (change, −4.9) and 10 d/mo (change, −6.2), resulting in an adjusted mean difference of 1.6 d/mo (95% CI, −1.2 to 4.4) (Table 2).
At 12 months after randomization, the median number of work days lost had decreased in both groups from 16 to 8 d/mo and was stable thereafter until 21 months in the conventional treatment group, at which point it was 13 d/mo in the biological treatment group (Figure 3).

Table 2. Change From Baseline in Days on Sick Leave and Disability Pension 12 and 21 Months After Randomization

<table>
<thead>
<tr>
<th>Method of Analysis a</th>
<th>Patients, No.</th>
<th>Work Loss, Mean (SD), d/mo</th>
<th>Change vs Baseline (SE), d/mo</th>
<th>Adjusted Difference (95% CI), d/mo b</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 mo After Randomization</td>
<td>Intention to treat 204 13 (13) 13 (13)</td>
<td>−4.1 (1.2)</td>
<td>−4.0 (1.1)</td>
<td>0.1 (−2.7 to 3.3)</td>
</tr>
<tr>
<td>Modified intention to treat 193 13 (13) 13 (13)</td>
<td>−4.4 (1.2)</td>
<td>−3.9 (1.1)</td>
<td>−0.2 (−3.2 to 2.7)</td>
<td></td>
</tr>
<tr>
<td>Per protocol 140 12 (13) 12 (13)</td>
<td>−4.3 (1.3)</td>
<td>−5.0 (1.3)</td>
<td>0.5 (−2.8 to 3.7)</td>
<td></td>
</tr>
<tr>
<td>21 mo After Randomization</td>
<td>Intention to treat 204 12 (13) 10 (12)</td>
<td>−4.9 (1.2)</td>
<td>−6.2 (1.0)</td>
<td>1.6 (−1.2 to 4.4)</td>
</tr>
<tr>
<td>Modified intention to treat 193 13 (12) 11 (12)</td>
<td>−5.1 (1.3)</td>
<td>−6.2 (1.1)</td>
<td>1.5 (−1.5 to 4.4)</td>
<td></td>
</tr>
<tr>
<td>Per protocol 124 11 (12) 11 (12)</td>
<td>−6.1 (1.4)</td>
<td>−6.8 (1.2)</td>
<td>0.3 (−2.8 to 3.8)</td>
<td></td>
</tr>
</tbody>
</table>

* The intention-to-treat analysis included all randomized patients of working age; the modified intention-to-treat analysis, all randomized patients of working age who received ≥1 dose of the study drug.

b Biological treatment included infliximab plus methotrexate; conventional treatment, sulfasalazine and hydroxychloroquine plus methotrexate.

c Adjusted for baseline observation (WorkDaysLost 12mo/21mo = α + β1 · group + β2 · WorkDaysLost baseline + ε). Confidence intervals were estimated by using nonparametric bootstrapping.
From randomization to 21 months, the proportion with no registered work loss increased from 27% to 42% ($P < .001$) in the biological treatment group and from 32% to 47% ($P < .001$) in the conventional treatment group, with no between-group difference ($P = .42$). The corresponding numbers for patients with full-time sick leave and disability pension decreased from 33% to 24% in the biological treatment group ($P = .001$) and from 41% to 20% ($P < .001$) in the conventional treatment group, with no between-group difference ($P = .54$).

### Alternative Analyses

**Modified Intention-to-Treat Analysis**

An analysis including only patients receiving at least 1 dose of biological (98 patients [93%]) or conventional treatment (95 patients [96%]) showed differences similar to those in the main analysis (Table 2).

**Per-Protocol Analysis**

Of the 204 randomized patients, 81 (77%) of those randomized to biological and 59 (60%) randomized to conventional treatment continued in the study according to the protocol for at least 1 year ($P = .007$), with 72 (69%) and 52 (53%), respectively, for 2 years ($P = .02$) (eFigure 2 in Supplement). Adjusted mean differences in the per-protocol analysis were similar to the main analysis findings at 12 months but smaller at 21 months after randomization (Table 2).

### Discussion

Over 21 months, work loss improved significantly in working-age patients with early RA with an insufficient response to methotrexate who were randomized to biological or conventional treatment. However, no between-group difference could be detected. Compared with the level in the general population, patients with early RA had 3 times greater sick leave and disability pension at randomization. At 21 months, this difference had been reduced to double that in the general population, with most of the reduction already present at 6 months.

Studies of biological treatment and self-reported work loss have found a stronger effect when treatment is initiated early in the disease course. A recent review identified 4 randomized clinical trials with self-reported work loss in patients with early RA, comparing methotrexate as monotherapy and in combination with TNF inhibitor therapy. All studies found a significant improvement in self-reported work loss favoring TNF inhibitor therapy. None of them compared the effects of biological treatment with combination DMARDs, analyzed findings in patients with early RA with methotrexate failure (as in our trial), or used objectively assessed outcome data. These circumstances, together with different approaches to assess work loss and different follow-up periods, complicate comparisons between these studies and ours.

The likelihood of returning to work once having been unable to work for a longer period (eg, >6 months) is low. None of the 21 patients with part- or full-time disability pension at baseline in this study returned to full-time work; rather, their work loss remained the same or increased. A longer period of sick leave may also reduce the probability of returning to work despite better disease activity control (ie, less structural bone and joint damage, as documented at 9 months) and radiological progression (as documented at 21 months). The work loss outcome may therefore be more inert to treatment than clinical and radiological outcomes. However, we did observe large improvements in work loss in both treatment arms. In addition, using work loss as an outcome may involve other important explanatory variables, such as physical job demand, patient choice, working environment, financial situation, and coping ability.

The number of lost work days in our early RA cohort started from the level of the general population 1 year before randomization. With most patients experiencing increasing work loss closer to RA diagnosis, the potential for reducing this newly experienced work loss may be higher than in individuals with established RA already granted disability pensions. We found significant overall improvements during both the methotrexate run-in and randomized phases, but the level remained double that in the general population after 21 months. The work loss improvement during the run-in phase occurred despite the fact that randomized patients were not regarded as methotrexate responders (ie, they did not achieve low disease activity, defined as a DAS28 <3.2). However, the improvement during the run-in phase was much greater in the nonrandomized patients, most of whom had a favorable DAS28 response at 3 months (eFigure 3 in Supplement).

The introduction of biological agents has enabled better control of disease activity. This may have resulted in an attitude change regarding attainable outcomes with antirheumatic therapy, including clinical indicators and work loss. In the era before biological treatment, the general notion was that disease activity and work loss would only increase after diagnosis. Today, treatment goals are more ambitious, aiming for remission and diminished work loss. Indeed, in most disease areas and in the general population, work loss increases with age. In the Swefot trial, aggressive treatment effectively reversed this development and from the time of run-in, monthly work days lost decreased in the biological and conventional treatment groups from 20 to 12 days and from 18 to 10 days, respectively. This result is remarkable considering the selected study population of patients with methotrexate treatment failure.

The finding that work loss improvement was greater in methotrexate responders than in the nonresponders was expected (eFigure 3 in Supplement). However, it calls into question a key assumption underlying the Swefot design, namely, that it is acceptable to delay 3 to 4 months before starting more aggressive therapy than methotrexate monotherapy. The immediate initiation of more intensive therapy, whether conventional DMARDs, addition of glucocorticoids or even biological agents, may be warranted in certain patients, but we could not investigate this question with the current design.

Our analysis showed that early and aggressive treatment in methotrexate-resistant patients not only stops the trend of increasing work loss days, as in patients with mainly established RA, but partly reverses it. However, we did not find any difference between treatment arms, indicating that the significantly improved disease control associated with infliximab treatment over a 1-year period and the better radiological results after 2 years did not translate into less work loss.
The substantially higher cost of infliximab relative to conventional treatment needs to be weighed against the greater incidence of short-term adverse events leading to discontinuation of conventional treatment (Table 2 in Supplement).20 With respect to work loss, our results indicate that before starting biological therapy in methotrexate-resistant patients with early RA, other intensive treatment regimens may be considered. Furthermore, work loss could be valuable to add as an outcome in the clinical assessment in addition to standard clinical measures in working-age patients. Work loss is often important for patients, and being unable to work affects personal finances and self-esteem.

Strengths of this study include the objective register data on work loss instead of self-reported work loss, as used in previous trials of biological vs mono-DMArD therapy.28 The data were available on a daily basis for every patient at all time points, as well as for patients discontinuing the trial and general population controls. The register data also enabled analysis of work loss before the trial began, showing that enrolled patients did not differ from the general population 1 year before randomization.

A limitation of our study was that patients and physicians were aware of the treatment allocation because infliximab is given as an infusion and conventional combination treatment is given orally. Inconsequently, patients may have been more willing to abandon conventional treatment in favor of biological treatment, or physicians may have made assessments with a subconscious bias. The use of blinded assessors in the trial was considered but was deemed unfeasible owing to limited personnel at smaller participating units. The work loss outcome, however, was assessed not by assessors in the trial but through registers.

Another potential limitation was the restriction to working-age patients, which may have affected the random allocation. As in the patient cohort of the Swefort trial, used for analysis of the primary outcome,20 baseline characteristics were similar between arms.

In conclusion, treatment including a biological agent was not superior to conventional treatment in terms of effect on work loss over a 21-month period in patients with early RA with methotrexate treatment failure. Although a substantial improvement in work loss was achieved in both arms, the persisting gap relative to the general population indicates a need for more effective treatment strategies and earlier diagnosis of RA.

REFERENCES


ARTICLE INFORMATION

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Author Contributions: Mr Eriksson and Dr Neovius had full access to all the data in the study and take responsibility for the accuracy of the data analysis. Study concept and design: All authors. Acquisition of data: Eriksson, Neovius, Bratt, van Vollenhoven, Geborek, Ernestam. Analysis and interpretation of data: Eriksson, Neovius, van Vollenhoven, Ernestam. Drafting of the manuscript: Eriksson, Neovius. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: Eriksson, van Vollenhoven, Geborek. Obtained funding: van Vollenhoven. Administrative, technical, and material support: Neovius, Bratt, Petersson, van Vollenhoven, Ernestam. Study supervision: Neovius, van Vollenhoven, Geborek.

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Previous Presentation: This study was presented in part at the American College of Rheumatology annual conference; November 6, 2011; Chicago, Illinois.

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S71-S74.
Not Better but Quite Good
Effects on Work Loss of Combination Treatment for Rheumatoid Arthritis With and Without Biological Agents

Edward Yelin, PhD

Treatments for rheumatoid arthritis (RA) are far more effective now than even 2 or 3 decades ago. The use of disease-modifying antirheumatic drugs (DMARDs), both conventional and biological, is largely responsible for this improvement, especially when treatment is initiated soon after disease onset. In populations with good access to experienced providers, extra-articular manifestations and joints with profound deformities are becoming less common, if not rare, and the goal has shifted to the induction and maintenance of low disease activity states from the more limited aim of slowing symptomatic and functional decline.

For individuals with RA, expectations of limited symptoms and almost unlimited capacity to maintain activities now seem possible. For society, the improvements in treatment put within reach the goal of limiting the costs associated with RA. To achieve that goal, however, requires reducing the prevalence of work loss, the single largest cost category in RA. A related question is whether the considerable expenditure required for biological agents is offset by reduced work loss costs, let alone whether the agents can “pay” for themselves, reducing disability payments by more than the agents cost, at an annual average of $20 000. (Clearly, they have other benefits that must be incorporated in any cost calculations.)

In this issue of JAMA Internal Medicine, Eriksson and colleagues have taken advantage of a well-done clinical trial in patients with early RA, comparing conventional DMARD treatment with or without the addition of biological agents, to study the effects on work loss. The results of the original clinical trial showed that combination treatments including bio-

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