Arthritis Care & Research
Vol. 62, No. 2, February 2010, pp 226–234
DOI 10.1002/acr.20072

ORIGINAL ARTICLE

Improvement in Work Place and Household Productivity for Patients With Early Rheumatoid Arthritis Treated With Adalimumab Plus Methotrexate: Work Outcomes and Their Correlations With Clinical and Radiographic Measures From a Randomized Controlled Trial Companion Study

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Objective. **To evaluate household and work place outcomes for patients with rheumatoid arthritis (RA) who were homemakers or employed workers, respectively, and who were treated with adalimumab plus methotrexate versus methotrexate monotherapy. We also determined baseline predictors of household and work place outcomes.**

Methods. **Data were from a health economic companion study to PREMIER, a 2-year, randomized controlled trial of methotrexate-naive patients with early RA (<3 years) who received treatment with adalimumab plus methotrexate, adalimumab, or methotrexate. Absenteeism (number of days missed or unfit to work), presenteeism (self-judgment of the effects of RA on job or household performance), and employment status were collected from self-reports at baseline and varying time points during the study.**

Results. **Household and work place outcomes were generally similar for homemakers and employed workers. Over 2 years, patients who received combination therapy missed approximately half as many days as patients who received methotrexate (17.4 versus 36.9 days for employed workers; 7.9 versus 18.6 days for homemakers). Presenteeism was lower (reflecting better productivity) for combination therapy than methotrexate monotherapy. The likelihood of gaining/retaining employment over 2 years was greater for combination therapy than methotrexate monotherapy (odds ratio 1.530, 95% confidence interval 1.038–2.255; $P = 0.0318$). Baseline radiographic progression was an independent predictor for retaining/gaining employment at 2 years.**

Conclusion. **Compared with methotrexate monotherapy, combination therapy was associated with more positive work outcomes: less absenteeism, less presenteeism, and greater likelihood of gaining/retaining employment. Radiographic progression at baseline was predictive of the ability to retain or gain employment.**

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease that causes significant disability, impacts health-related quality of life, and is a major economic burden (1–5). Many studies have shown RA to be associated with absenteeism (6–8), job loss (6,8–13), and impairment in work productivity (3,6–8). Approximately 20–30% of patients with RA experience permanent work disability dur-

Supported by Abbott Laboratories.

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Dr. van Vollenhoven has received consultant fees, speaking fees, honoraria, and/or research grants (less than $10,000 each) from Abbott Pharmaceuticals, Bristol-Myers Squibb, Centocor, Roche, Wyeth, and Schering-Plough. Drs. Cifaldi, Ray, and Chen own stock and/or hold stock options in Abbott Laboratories. Dr. Weisman has received consultant fees (less than $10,000 each) from Abbott, Centocor, Genentech, Amgen, Rigel, Lilly, Biogen, UCB, and Roche, has served on the consulting/advisory/data safety monitoring boards for Amgen/Wyeth, ARRAY Biopharma, Crescendo Bioscience, Inc., Elan, Lilly, Merck & Co., Inc., Novartis, and UCB, and has received research grants from

ing the first 2–3 years of the disease (4). Although a few studies have described the negative impact of RA on unpaid work (14–16), most studies have emphasized the impact of RA on paid work.

Treatment with a tumor necrosis factor antagonist combined with methotrexate has proven to be effective for improving symptoms of RA in patients with early disease (17–19). In the PREMIER study, a large, 2-year clinical trial that assessed the efficacy and safety of adalimumab alone, methotrexate alone, and adalimumab plus methotrexate combination therapy, treatment with combination therapy was more effective than either monotherapy for improvement in signs and symptoms of RA, physical functioning, health-related quality of life, and radiographic progression (17,20).

The current study reports data from DE032, a companion health economic analysis to PREMIER that was completed in parallel with PREMIER. DE032 evaluated work outcomes over 2 years (during blinded treatment) for patients who were treated with combination adalimumab plus methotrexate therapy or monotherapy (either adalimumab or methotrexate). Our primary objective was to compare work outcomes for patients treated with combination therapy versus methotrexate monotherapy, with emphasis on evaluation of outcomes for both employed workers and homemakers. The study included 3 measures of work outcomes: absenteeism, presenteeism, and employment status. No previous studies of treatment in early RA have included all 3 measures.

Our second objective was to determine which baseline patient or disease characteristics were correlated with work outcomes over 2 years across the treatment groups. A third, related objective was to explore the relationships between baseline radiographic progression and work outcomes. Previous research has demonstrated radiographic damage to be longitudinally associated with physical function and disability (21,22). One study has demonstrated a cross-sectional association between baseline total Sharp score (TSS) and baseline employment (23). However, the independent contribution of radiographic progression to change in work outcomes, such as the ability to gain or retain employment, is less clear. Therefore, we evaluated the relationship between baseline TSS and 3 different work outcomes over 2 years. If radiographic progression at baseline is an independent predictor of work outcomes, it would further support the importance of prevention of radiographic damage in early RA treatment and elevate the importance of radiographic progression in health economic models of early RA.

Abbott, Amgen, ARRAY Biopharma, Bristol-Myers Squibb, Centocor, Genentech, Human Genome Sciences, MedImmune, Novo Nordisk, Wyeth, XDx, Inc., and UCB.

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Submitted for publication December 23, 2008; accepted in revised form September 21, 2009.

PATIENTS AND METHODS

Design and patients. Details of the methodology of PREMIER have been previously reported (17). PREMIER is a 2-year, multicenter, randomized, double-blind, parallel-group study of patients with early RA (see Supplementary Figure 1, available in the online version of this article at http://www3.interscience.wiley.com/journal/77005015/home). Patients were randomly assigned to treatment with either adalimumab 40 mg subcutaneously every other week plus methotrexate, adalimumab monotherapy (plus placebo), or methotrexate monotherapy (plus placebo injection). Patients were from Europe (54%), North America (40%), or Australia (6%). To have been eligible for the study, patients must have met American College of Rheumatology (formerly the American Rheumatism Association) 1987 revised criteria for RA (24), must have had a disease duration of less than 3 years, must have never received methotrexate therapy, and must have met other predetermined inclusion and exclusion criteria, as previously reported (17). Patients provided separate consents for PREMIER and DE032. All of the patients who had consented to participate in DE032 were included in analyses at baseline.

Assessments. At baseline, demographic characteristics of age, sex, and employment status were collected. Employment status was one of the following: employed, self-employed, homemaker, pensioner/retiree, unemployed, student/trainee/apprentice, or other. Disease-related characteristics that were assessed at baseline included disease duration, 28-joint Disease Activity Score (DAS28), and radiographic measurements (joint space narrowing, joint erosion, and TSS). General health and functional status measures assessed at baseline were the Health Assessment Questionnaire (HAQ), the Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F), and the Short Form 36 (SF-36) Health Survey physical component summary (PCS) and mental component summary (MCS) scores.

Data for the central work-related outcome measures (absenteeism, presenteeism, and employment status) were collected via a patient questionnaire that was completed at baseline and throughout the 2-year study period at weeks 4, 8, 10, 12, 26, 42, 52, 76, and 104. Patients were asked to report the following information.

Absenteeism assessment. Patients who were employed reported the number of days missed at work because of RA in the last 4 weeks (at the baseline visit) or since the last assessment (at all other visits). Homemakers reported the number of days they were "unfit to work at home" because of RA.

Presenteeism assessment. Employed patients reported the degrees to which their normal work performance was affected by RA in the last week, responding on a visual analog scale (VAS) scored from 0 (unaffected) to 100 (completely affected). Homemakers reported the extent to which their household work was affected by using the same VAS. This VAS work measure was specifically designed for use in this study.

Employment status assessment. Patients reported their employment status (employed, self-employed, homemaker, pensioner/retiree, unemployed, student/trainee/apprentice, or other) at baseline and indicated whether there was a change in their status since their last visit. Patients could report more than one category if applicable to their situations.

At baseline, patients were categorized by whether they were employed (identified themselves as employed or self-employed) or not employed (all other categories). Patients were considered to have "favorable employment status" if they remained employed or gained employment during the study and "unfavorable employment status" if they remained unemployed or lost their job.

Patients who identified themselves as homemakers were all considered to be homemakers, regardless of whether they also identified themselves as employed or self-employed. For patients who considered themselves to be both employed and a homemaker, absenteeism and presenteeism were assessed separately for their employed work and their household work.

Statistical analysis. There were 3 parts to the analysis. First, we determined the effect of treatment on work outcomes over 2 years for the combination group versus the methotrexate group and the adalimumab group versus the methotrexate group. Second, we conducted a correlation analysis to examine the associations between the baseline variables and work outcomes. Finally, based on the results of our correlation analyses, which indicated that TSS at baseline was associated with later employment status, we conducted an exploratory analysis to determine the independent predictors for favorable employment status (gaining or retaining employment).

Analysis of treatment group effects. To assess possible treatment group differences at baseline, we compared the adalimumab plus methotrexate group and the adalimumab monotherapy group each with the methotrexate group on demographics and baseline characteristics by using Student's *t*-tests for continuous variables and chi-square tests for categorical variables.

The methotrexate group was the comparator for all treatment group comparisons. The alpha level was 0.05. Analyses of absenteeism and presenteeism included only those patients who were either employed workers or homemakers.

All of the work outcomes were analyzed over 2 years. Because more patients discontinued the study in the monotherapy arms than in the combination therapy arm, an adjustment for duration in the study was included in all analyses of treatment effects. In the analysis models for cumulative variables, an adjustment was made for duration of a patient's participation in the study. For repeated-measurement variables, a mixed model was applied to address the issue of missing data.

Absenteeism analysis. For each patient, the cumulative number of missed work days (for employed workers) or days unfit to work (for homemakers) at each visit was calculated. Because the high incidence of zero values for reports of missed days leads to biased estimates of means, the observed absenteeism values were analyzed within a Zero-inflated Poisson (ZIP) model. A 2-step procedure was applied in the ZIP model to account for the excessive zero values in absenteeism. The ZIP model estimated the number of missed days for 6-month intervals while accounting for the probability of missing work and the number of missed days for those who missed work. The ZIP model included an adjustment for duration in the study and was used to estimate the effect of treatment group on absenteeism within each group of workers (employed workers and homemakers). Separate models analyzed combination versus methotrexate therapy and adalimumab versus methotrexate therapy.

Presenteeism analysis. Mean VAS work scores were calculated during the 2-year study period for both employed workers and homemakers. A mixed model with a random-intercept approach was used to evaluate the effects of treatment group on presenteeism, with adjustment for baseline VAS work scores. Least square means from the mixed model were compared at each visit in separate analyses for combination versus methotrexate therapy and adalimumab versus methotrexate therapy.

Employment status analysis. Each patient's employment status over the 2-year study was coded as either favorable (gained or retained employment) or unfavorable (remained unemployed or lost a job). We first analyzed the effect of treatment group on employment status by using a simple logistic regression model to compare the odds of favorable employment status in the combination therapy and methotrexate groups. Based on the analysis for treatment group differences, in which patients in the methotrexate group had greater TSS than those for either adalimumab group, we conducted a multivariate analysis between the 3 treatment groups that controlled for treatment group, time on treatment, TSS, and other baseline variables identified through a stepwise selection procedure.

Correlations between baseline variables and work outcomes. Correlation analyses were conducted to examine the association between baseline variables and presenteeism (VAS work score at the patient's last visit), absenteeism (missed work or not during 2 years), and employment status (favorable or unfavorable over 2 years). For presenteeism, the correlations were measured with Pearson's correlation coefficients. For the binary outcomes of absenteeism and employment status, univariate logistic models were used. Only employed patients were included in the analyses of presenteeism and absenteeism. All of the patients were included in the analysis of employment status.

Additional exploratory analysis. Based on the findings of the univariate correlation analyses, we pooled the treatment groups and further evaluated the relationship between baseline radiographic score (TSS) and employment status, independent of treatment effect, by using the multivariate regression model discussed above.

Table 1. Baseline demographics and disease characteristics*

	MTX (n = 214)	Adalimumab + MTX (n = 219)	*P* vs. MTX†	Adalimumab (n = 231)	*P* vs. MTX†
Age, years	52.2 ± 13.1	51.4 ± 13.7	0.5498	51.5 ± 13.0	0.5896
Men, no. (%)	56 (26.2)	62 (28.3)	0.6167	49 (21.2)	0.2186
Race (white), no. (%)	202 (94.4)	205 (93.6)	0.7310	216 (93.5)	0.6957
Disease duration, years since diagnosis	0.8 ± 0.9	0.8 ± 0.8	0.3899	0.7 ± 0.8	0.1262
Prior DMARDs, no. (%)	64 (29.9)	71 (32.4)	0.5724	72 (31.2)	0.7727
Swollen joint count (range 0–66)	22.8 ± 12.3	21.7 ± 11.6	0.3496	22.1 ± 10.9	0.5348
Tender joint count (range 0–68)	32.1 ± 14.3	31.3 ± 14.7	0.5504	31.7 ± 13.3	0.7201
HAQ score	1.5 ± 0.7	1.5 ± 0.7	0.9784	1.6 ± 0.6	0.0209
DAS28 score	6.4 ± 0.9	6.3 ± 0.9	0.6373	6.3 ± 0.9	0.8727
Joint erosion score	13.7 ± 13.3	10.8 ± 12.4	0.0224	10.9 ± 10.9	0.0164
Joint space narrowing score	8.3 ± 10.6	7.0 ± 9.0	0.1725	6.7 ± 7.9	0.0691
Total Sharp score	22.0 ± 21.8	17.8 ± 19.7	0.0392	17.5 ± 17.4	0.0191
Employed workers, no. (%)‡	110 (51.4)	130 (59.4)	n/a	125 (54.1)	n/a
Absenteeism (missed days)	5.2 ± 8.7	4.2 ± 7.6	0.3554	4.1 ± 7.6	0.3155
Presenteeism (VAS work score)	52.3 ± 30.4	51.1 ± 33.0	0.7692	53.7 ± 30.6	0.7233
Homemakers, no. (%)‡	84 (39.3)	80 (36.5)	n/a	86 (37.2)	n/a
Absenteeism (missed days)	5.6 ± 9.3	6.4 ± 9.6	0.5376	6.9 ± 9.7	0.3406
Presenteeism (VAS work score)	55.2 ± 27.5	59.0 ± 28.7	0.3872	64.4 ± 24.5	0.0197

* Values are the mean ± SD unless otherwise indicated. MTX = methotrexate; DMARDs = disease-modifying antirheumatic drugs; HAQ = Health Assessment Questionnaire; DAS28 = 28-joint Disease Activity Score; n/a = not applicable; VAS = visual analog scale.
† *P* values are from a Student's *t*-test for continuous variables and a chi-square test for categorical variables for difference from the MTX group.
‡ The categories of employed workers and homemakers are not mutually exclusive. Baseline absenteeism and presenteeism for employed workers and homemakers are reported for the 4 weeks prior to the first study visit.

RESULTS

Of the 799 patients enrolled in PREMIER, 664 (83%) gave consent to participate in DE032 (n = 219 adalimumab plus methotrexate, n = 214 methotrexate, n = 231 adalimumab). At year 2, more patients in the combination therapy group than in the monotherapy groups had completed the study (76% adalimumab plus methotrexate, 61% adalimumab, 66% methotrexate). These completion rates were very similar to those reported for the larger study population of PREMIER (17).

Demographics and baseline characteristics. Demographics and baseline clinical characteristics for DE032 patients were similar to those of the population in PREMIER (17). Overall, 74.8% of patients in the sample were women and 93.8% were white. They had a mean age of 51.7 years (range 18–82 years), and their mean disease duration was <1 year. At baseline, 55% of the patients were employed, 37.7% were homemakers, 23.2% were pensioners/retirees, 8.9% were unemployed, 1.4% were students/trainees/apprentices, and 2.6% were other. Of the homemakers and employed workers, 92.4% and 71.8%, respectively, were women.

Combination therapy versus methotrexate. Baseline characteristics were similar for the combination therapy group and the methotrexate monotherapy group, except that the combination group had lower baseline TSS and erosion scores than the methotrexate group. The percentage of employed patients in the combination therapy group (n = 130 [59.4%]) did not differ significantly from the percentage in the methotrexate group (n = 110 [51.4%]). Likewise, the percentage of homemakers in the combination therapy group (n = 80 [36.5%]) did not differ from the percentage in the methotrexate group (n = 84 [39.3%]). The percentages of patients who identified themselves as both employed workers and homemakers were similar in the combination therapy (n = 33 [15.1%]) and methotrexate (n = 35 [16.4%]) groups. Within both the employed worker and homemaker groups, the combination therapy and methotrexate groups did not differ in baseline absenteeism or presenteeism (Table 1).

Adalimumab versus methotrexate. The adalimumab group had a slightly greater baseline mean HAQ score (*P* = 0.0209), but lower TSS (*P* = 0.0191) and erosion (*P* = 0.0164) scores than did the methotrexate group. The percentages of employed patients (n = 125 [54.1%]) and homemakers (n = 86 [37.2%]) in the adalimumab group were similar to the percentages in the methotrexate group. The percentage of patients who identified themselves as both employed workers and homemakers in the adalimumab group (n = 35 [15.2%]) was similar to the percentage in the methotrexate group. For employed workers, baseline absenteeism and presenteeism scores were similar in each monotherapy group. For homemakers, baseline absenteeism was similar for the monotherapy groups, but the baseline presenteeism score was greater for the adalimumab group than for the methotrexate group (adalimumab mean 64.4 and methotrexate mean 55.2; *P* = 0.0197).

Treatment effects on work outcomes: combination therapy versus methotrexate. *Absenteeism.* Based on the ZIP model estimates over 2 years for employed workers, the estimated incidence rate per day for missed work was

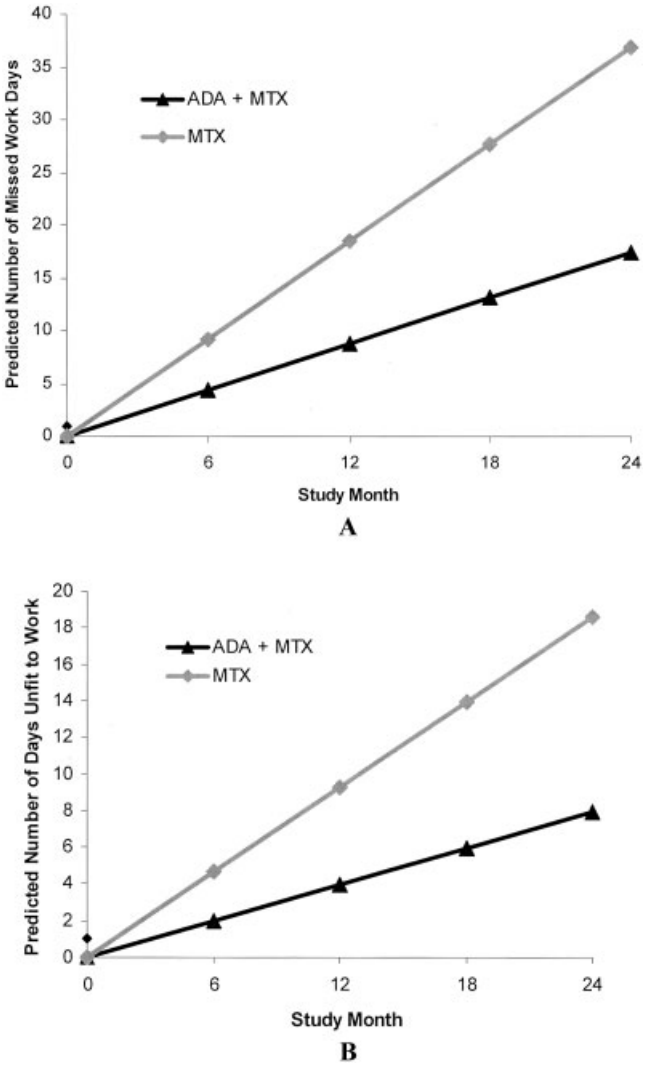

Figure 1. **A**, Absenteeism for employed workers: predicted mean cumulative number of missed work days caused by RA. Data are from a Zero-inflated Poisson model. Includes all of the patients who ever reported being employed or self-employed at each visit. **B**, Absenteeism for homemakers: predicted mean cumulative number of missed work days caused by RA. Data are from a Zero-inflated Poisson model. Includes all of the patients who ever reported being a homemaker at each visit. ADA = adalimumab; MTX = methotrexate.

0.0239 (SE 0.00282) for the adalimumab plus methotrexate group and 0.0506 (SE 0.00553) for the methotrexate monotherapy group. Accordingly, the estimated mean number of missed work days for the combination therapy group was approximately half that of the methotrexate monotherapy group (17.4 versus 36.9 missed days; $P < 0.0001$) over 2 years (Figure 1A). Similarly, for homemakers, the incidence rate for missed work (i.e., being unfit to perform household duties) per day was 0.0108 (SE 0.00187) for the combination therapy group and 0.0254 (SE 0.00340) for the methotrexate group. Homemakers in the adalimumab plus methotrexate group missed approximately half as many days over 2 years as the methotrexate monotherapy group (7.9 versus 18.6 missed days; $P < 0.0001$) (Figure 1B).

Presenteeism. For both employed workers and homemakers, the combination therapy and methotrexate groups demonstrated improvements in presenteeism during the study (i.e., decreasing VAS work scores after baseline), with the greatest improvements occurring in the first few months of the study (Figures 2A and B). For employed workers (Figure 2A), mean VAS work scores were lower (indicating better productivity) for the adalimumab plus methotrexate group than the methotrexate monotherapy group during the 2-year study, with differences between the 2 groups' mean VAS scores ranging from 7.2 to 15.7 across visits ($P < 0.05$ for all visits). For homemakers (Figure 2B), mean VAS work scores were lower (indicating better productivity) for the adalimumab plus methotrexate group than the methotrexate monotherapy group during the 2-year study, with differences between the 2 groups'

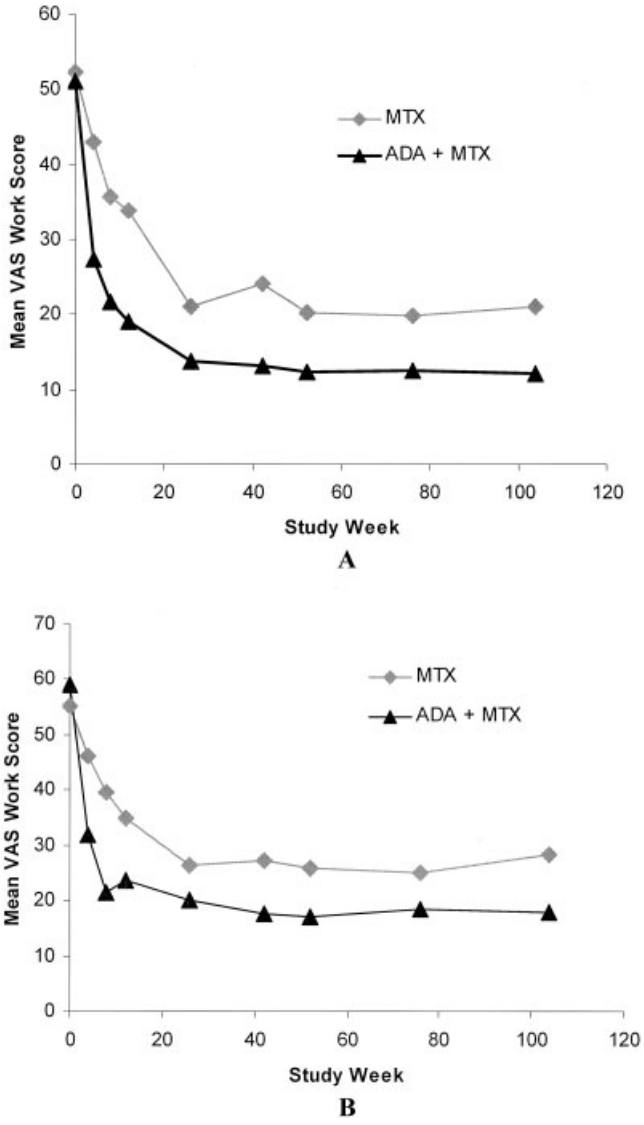

Figure 2. **A**, Presenteeism for employed workers: least squares mean visual analog scale (VAS) work scores over the 2-year study period. Lower scores indicate better work performance. **B**, Presenteeism for homemakers: least squares mean VAS work scores over the 2-year study period. Lower scores indicate better work performance. MTX = methotrexate; ADA = adalimumab.

Table 2. Association between baseline variables and work outcomes during the study*

Variable	Presenteeism†		Missed work‡		Favorable employment status§	
	Pearson's *r*	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
HAQ score	0.32	< 0.0001	2.083 (1.495–2.903)	< 0.0001	0.482 (0.375–0.619)	< 0.0001
SF-36 PCS score	−0.21	< 0.0001	0.950 (0.925–0.975)	< 0.001	1.031 (1.010–1.052)	< 0.01
SF-36 MCS score	−0.19	< 0.001	0.955 (0.938–0.973)	< 0.0001	1.016 (1.002–1.029)	< 0.05
Age, years	0.12	< 0.025	1.011 (0.992–1.030)	NS	0.932 (0.918–0.9845)	< 0.0001
Sex (female vs. male)	n/a	n/a	1.066 (0.682–1.668)	NS	0.617 (0.429–0.889)	< 0.01
Total Sharp score	0.03	NS	0.994 (0.981–1.007)	NS	0.980 (0.971–0.989)	< 0.0001
Joint space narrowing score	0.03	NS	0.984 (0.956–1.013)	NS	0.954 (0.935–0.975)	< 0.0001
Joint erosion score	0.03	NS	0.994 (0.974–1.013)	NS	0.974 (0.961–0.988)	< 0.001
DAS28 score	0.22	< 0.0001	1.326 (1.058–1.661)	< 0.05	0.868 (0.730–1.032)	NS
Disease duration	−0.03	NS	0.748 (0.571–0.980)	< 0.05	0.908 (0.749–1.101)	NS
FACIT-F	−0.20	< 0.0001	0.953 (0.935–0.971)	< 0.0001	1.005 (0.992–1.019)	NS

* OR = odds ratio; 95% CI = 95% confidence interval; HAQ = Health Assessment Questionnaire; SF-36 = Short Form 36 Health Survey; PCS = physical component summary; MCS = mental component summary; NS = not significant; n/a = not applicable; DAS28 = 28-joint Disease Activity Score; FACIT-F = Functional Assessment of Chronic Illness Therapy–Fatigue.
† Data are from Pearson's correlation coefficients between visual analog scale presenteeism and baseline variables.
‡ Data are from a logistic analysis of correlation of baseline variables to missed work (yes or no) over 2 years.
§ Data are from a logistic analysis of correlation of baseline variables with employment status (gained/retained or lost/not gained).

mean VAS scores ranging from 6.3 to 18.0 ($P < 0.05$ at all but 2 visits).

Employment status. The percentages of patients who retained or gained employment over the 2 years of the study were 57.6% (121 of 210) for the combination therapy group and 47.6% (100 of 210) for the methotrexate group. Based on the logistic model controlling for duration, patients treated with combination therapy were more likely to retain or gain employment than were those who received methotrexate alone (odds ratio [OR] 1.530, 95% confidence interval [95% CI] 1.038–2.255). After pooling the treatment groups, adjusting for treatment, time on treatment, baseline TSS, and other variables selected through a stepwise selection procedure (age, sex, and HAQ), we determined that the OR for treatment with adalimumab combination therapy changed from 1.530 to 1.554 (95% CI 1.004–2.405; $P = 0.0479$).

Treatment effects on work outcomes: adalimumab versus methotrexate. *Absenteeism.* Similar to the result for the combination therapy group, the ZIP model estimated that employed workers in the adalimumab monotherapy group had a missed work incidence rate per day of 0.0257 (SE 0.00262). The adalimumab group missed approximately half as many estimated days as the methotrexate monotherapy group over 2 years (18.7 versus 36.9 missed days; $P < 0.0001$). For homemakers, the estimated missed work incidence rate per day for the adalimumab monotherapy group was 0.0362 (SE 0.00377). Accordingly, the predicted number of missed days over 2 years was significantly greater for the adalimumab group than for the methotrexate group (26.4 versus 18.6 missed days; $P = 0.004$).

Presenteeism. For both employed workers and homemakers, improvements in presenteeism for the 2 monotherapy groups were not significantly different at most visits during the study.

Employment status. The percentages of patients who achieved a favorable employment status over the 2 years of the study were 51.8% (116 of 224) for the adalimumab group and 47.6% (100 of 210) for the methotrexate group. Based on the logistic model controlling for duration, the difference between the monotherapy groups was not statistically significant (OR 1.185, 95% CI 0.812–1.728; $P = 0.3789$). After pooling the treatment groups, adjusting for treatment group, time on treatment, baseline TSS, and other variables identified through a stepwise selection procedure (age, sex, and HAQ), we found that the results for adalimumab monotherapy were still not statistically significant for favorable employment status (OR 1.285, 95% CI 0.837–1.972).

Correlations between baseline variables and work outcomes across treatment groups. The HAQ, SF-36 PCS, and SF-36 MCS were statistically significant correlates of all 3 work outcomes (Table 2). The DAS28, disease duration, and fatigue (FACIT-F score) were correlated with absenteeism and presenteeism but not employment status. Age was correlated with presenteeism and with employment status. TSS was correlated with employment status but not absenteeism or presenteeism.

Additional exploratory analysis. To further explore the relationship between baseline TSS and employment status across the treatment groups, we performed a multivariate regression analysis that included the baseline variables correlated with favorable employment status (Table 3). In this analysis, a 10-point increase in baseline TSS was associated with a 9.6% decrease in the odds of achieving favorable employment status ($P < 0.05$) (Figure 3).

DISCUSSION

In this 2-year, prospective study of patients with early RA, patients who received combination therapy with adalimumab plus methotrexate demonstrated greater improvements than patients who received methotrexate mono-

Table 3. Relationship between selected baseline variables and favorable employment status*

Variable	Odds ratio (95% CI)	*P*
Age, years	0.936 (0.921–0.950)	< 0.0001
Sex (female vs. male)	0.548 (0.361–0.831)	< 0.01
Health Assessment Questionnaire	0.608 (0.460–0.803)	< 0.01
Adalimumab + MTX vs. MTX	1.554 (1.004–2.405)	< 0.05
Adalimumab vs. MTX	1.285 (0.837–1.972)	NS
Dosing duration	1.0 (0.999–1.001)	NS
Total Sharp score (10 points)	0.904 (0.818–0.998)	< 0.05

* Data are from a multivariate logistic regression model of employment status with baseline scores as predictor variables. 95% CI = 95% confidence interval; MTX = methotrexate; NS = not significant.

therapy in all 3 work outcomes that were measured: days missed or unfit to work, disruption in work due to RA, and ability to gain or retain employment. These data provide additional evidence of the superiority of combination treatment, which is known to lead to greater improvements in signs and symptoms of RA, functional disability, health-related quality of life, and slowing of radiographic progression than methotrexate alone (17,20). The findings complement recent studies with smaller populations and shorter study durations in which patients who received combination treatment had better work outcomes than patients who received methotrexate alone (25,26).

The patterns of work outcomes for employed workers and homemakers were very similar in this study; combination treatment was superior to methotrexate for both absenteeism and presenteeism. The current data add to the literature by demonstrating the positive impact of RA treatment on the functioning of homemakers, who are

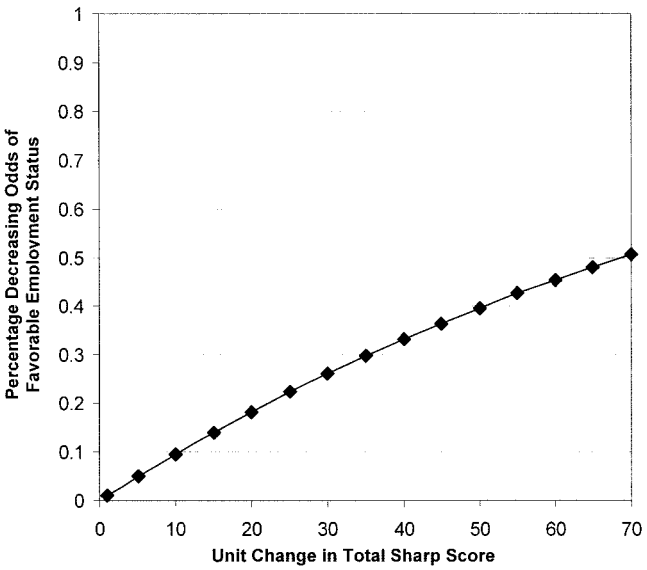

Figure 3. Relationship between unit change in total Sharp score and decreasing odds of favorable employment status.

mostly women and who may find that RA impacts their performance in important parental, caretaker, household, social, and community roles (14,15).

A large percentage of the costs associated with RA are attributable to work disability, and the current study provides valuable information that could inform future cost-effectiveness analyses of biologics in the treatment of RA. The patients in this study had early, aggressive RA that negatively affected physical function and caused work disruption. To adapt to the reality of decreasing physical function, patients might be expected to change jobs, change occupations, or reduce work hours (5,27). The data reported here suggest that early interventions that prevent radiographic damage will increase the probability that a patient will be able to maintain or gain employment. Patients with longer-term disease are more likely to have irreversible function loss (28), but early, aggressive intervention has already been shown to prevent irreversible function loss (29,30) and to increase work capacity (11,31). Limiting the loss of function through early treatment may be especially important for older adults with RA, for whom work disability may be financially devastating (32). Enabling adults to remain in the work force longer is therefore an important goal of RA treatment.

Some research suggests that work disability in RA is more closely associated with demographic and functional status variables than with physiologic measures such as radiographic scores (33–35). In the current study, the 3 work outcomes had different patterns of association with baseline characteristics. The HAQ and the physical and mental health components of the SF-36 were related to all of the work outcome measures. RA disease activity and fatigue were related to presenteeism and absenteeism but not to employment status. Age was also most closely related to change in employment status. Interestingly, radiographic measures of disease at baseline (joint space narrowing, joint erosion, and TSS) were all related to employment status but not to the immediate measures of work disruption (absenteeism and presenteeism).

The current study had several strengths that make it an important addition to the literature on health economic outcomes in patients with RA. This was a large, international study of patients with early, erosive RA, using well-controlled procedures in a double-blind, active-comparator study design. To our knowledge, this was the first such study in early RA, as well as the first to demonstrate the impact of treatment on all 3 important measures of work performance: absenteeism, presenteeism, and employment status. The study also included evaluation of both household work and paid work.

There are several limitations of the work outcome measures used in the study. The measure of presenteeism VAS was conceptually similar to measures that have been used previously (36,37), but it has not been externally validated. It is possible that the presenteeism measure had some overlap with the measure of absenteeism because patients were not specifically asked to exclude their missed days when they reported the extent to which their work productivity was affected by RA. The questions eliciting judgments of missed work days were also somewhat different for the employed workers (how many work days were

missed) and homemakers (how many days they were unfit to work). Both the presenteeism and absenteeism data were derived from patient reports that were not independently verified and, therefore, might have been subject to recall bias. Regarding the measurement of employment status, patients were classified as unemployed whether they considered themselves to be unemployed/retired because of RA or some other reason. Because the reasons for unemployment may be complicated, and it is possible that patients who are retired might return to work after receiving adequate treatment, we chose to include all of the patients in the analysis. A final limitation of the study is that the completion rates were less for the monotherapy groups (61% for adalimumab and 66% for methotrexate) than for the combination therapy group (76%). However, these completion rates were similar to those reported for the full PREMIER study (17).

Employed workers and homemakers with early RA who were treated with adalimumab plus methotrexate combination therapy missed fewer days of work and were more productive than patients treated with methotrexate alone. The ability to retain or gain employment was also more likely in patients treated with combination therapy than methotrexate alone.

These data have implications for cost-effectiveness models of RA therapy. Baseline radiographic progression was an independent predictor of employment status, suggesting that early treatments aimed at reducing radiographic progression might lead to more favorable employment status. When considering treatment options, physicians should factor in the costs associated with poor work outcomes and radiographic progression.

ACKNOWLEDGMENTS

We wish to thank Ellen Stoltzfus, PhD, of JK Associates, and Michael A. Nissen, ELS, of Abbott Laboratories, for their editorial support in the development and revision of this manuscript.

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. Cifaldi 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.

Study conception and design. Van Vollenhoven, Cifaldi, Ray, Chen, Weisman.

Acquisition of data. Van Vollenhoven, Cifaldi, Ray, Chen, Weisman.

Analysis and interpretation of data. Van Vollenhoven, Cifaldi, Ray, Chen, Weisman.

ROLE OF THE STUDY SPONSOR

Abbott Laboratories funded the PREMIER trial and its DE032 companion study. Abbott staff led the design, data collection, and data analysis for the DE032 study results reported here. In addition, Abbott provided and funded writing and publications management support through a medical writing organization and Abbott staff member. The decision to publish this article was the joint decision of all authors, including those who are Abbott employees.

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