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Adalimumab, etanercept, and infliximab utilization patterns and drug costs among rheumatoid arthritis patients

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Abstract**Objectives:**

To evaluate the utilization patterns of the anti-tumor necrosis factor (anti-TNF) agents Humira (adalimumab), Enbrel (etanercept), and Remicade (infliximab) in patients with rheumatoid arthritis (RA) and compare medication costs during the first year of treatment. (Humira is a registered trademark of Abbott Laboratories, IL; Enbrel is a registered trademark of Immunex Corporation, CA; and Remicade is a registered trademark of Janssen Biotech, Inc., PA).

Methods:

This retrospective analysis of medical and pharmacy claims included patients who were aged ≥ 18 years, had ≥ 2 RA diagnosis codes, and had ≥ 365 days of persistence with the index anti-TNF. Patients excluded had claims for anti-TNF agents within 6 months before the index date. Refill patterns for adalimumab and etanercept, number of infliximab infusions, time between infusions, and dose per infusion were analyzed for 12 months. Direct anti-TNF medication costs were compared among anti-TNFs for the initial treatment year.

Results:

Infliximab-treated patients ($n = 457$) were significantly older than adalimumab- ($n = 337$) or etanercept-treated patients ($n = 902$). Time between refills was longer than recommended for 28% and 30% of adalimumab and etanercept refill periods, respectively. Potential cumulative time without therapy was 33 days for adalimumab and 43 days for etanercept. Statistically significant differences in mean per-patient anti-TNF medication costs for the first year were reported for adalimumab, etanercept, and infliximab (\$14,991, \$13,361, and \$18,139, respectively; $p < 0.0001$); however, a cost assessment using labeled dosing of the anti-TNF agents with optimal treatment compliance yielded comparable annual medication costs.

Limitations:

This analysis only evaluated utilization patterns for selected anti-TNF agents and was not inclusive of other medications that patients may have been using for RA. Absolute patient adherence could not be assessed due to lack of information on how patients were self-administering adalimumab and etanercept or if samples of the agents were made available.

Conclusions:

This study identified gaps in patients' refills compared with prescriber recommendations. The infliximab-treated group had infusion patterns consistent with prescribing information. Potential clinical and economic implications of dose attenuation with adalimumab and etanercept should be explored further.

Introduction

Tumor necrosis factor inhibitors (anti-TNFs) are biologic agents used in treating rheumatoid arthritis (RA). Humira (adalimumab) and Enbrel (etanercept) are subcutaneously injected anti-TNFs, which may be self-administered, with prescribing recommendations for biweekly or weekly administration (adalimumab: 40 mg every other week with concomitant methotrexate, with potential dose frequency increase to 40 mg/week without concomitant methotrexate; etanercept: 50 mg/week with or without concomitant methotrexate)^{1,2}. Infliximab is a weight-based anti-TNF approved for use with concomitant methotrexate in RA. (Humira is a registered trademark of Abbott Laboratories, IL; Enbrel is a registered trademark of Immunex Corporation, CA; and Remicade is a registered trademark of Janssen Biotech, Inc., PA). Infliximab is administered via intravenous infusion at weeks 0, 2, and 6 and every 8 weeks thereafter³. Induction dosing for RA is recommended at 3 mg/kg with a potential dose increase to 10 mg/kg or dosing every 4 weeks, during the maintenance period, to optimize patient response. To date, there have not been any published head-to-head anti-TNF studies demonstrating superiority in clinical efficacy or effectiveness among adalimumab, etanercept, or infliximab in RA. A United States (US)-based systematic review concluded that there is insufficient evidence to determine which anti-TNF regimen should be preferred in first-line treatment of RA⁴. Given this insight, variable dosing and patient adherence may contribute to any differences in observed clinical effectiveness and economic outcomes.

Observational studies have compared economic differences among anti-TNFs and specifically evaluated infliximab dosing. Comparative cost analyses have reported annual infliximab treatment costs in patients with RA to be significantly higher than those of adalimumab or etanercept, with an estimate as high as 55% more costly^{5–9}. Health plan dosing studies have reported patients treated with infliximab receiving induction and maintenance doses consistent with dosages recommended by the US Food and Drug Administration (FDA)^{10–14}. A retrospective chart review of infliximab use in a large western US managed care organization found average infliximab induction and maintenance doses of 3.5 ± 0.6 mg/kg and 4.2 ± 1.4 mg/kg, respectively¹⁰. Braid *et al.*¹¹ examined Medicare claims data from 2001–2003, reporting that the average infliximab utilization was 366.7 mg and a mean of 7.1 infusions/year; 78% of all infliximab utilization was <400 mg. A separate study of patients with RA treated in 16 rheumatology clinics between 1999 and 2002 showed mean induction and maintenance doses of 3.38 mg/kg vs 4.51 mg/kg ($p < 0.001$)¹². Additionally, analysis of managed care data has reported an infliximab adherence rate of 80.9%¹⁵.

The literature is limited regarding adherence evaluations in patients with RA who are prescribed adalimumab or etanercept. A systematic literature review of adherence with biologics in RA highlighted 4 studies reporting adalimumab or etanercept adherence rates in US data sources ranging from 52–85% (with 41–51% of patients achieving a medication possession ratio $\geq 80\%$)^{15,16}. These data reveal variable adherence rates for adalimumab and etanercept and signal potential patient compliance challenges, as evidenced by nearly one-half of patients having medication possession ratios <80%. Evaluating refill patterns for adalimumab and etanercept provides a different discernment of adherence. This retrospective analysis evaluated refill patterns for adalimumab and etanercept as well as dosing and infusion patterns for infliximab, and it compared anti-TNF costs in patients with RA persistently treated during the first year of therapy.

Patients and methods

Sample selection

Medical and pharmacy claims from January 1, 2000, to December 31, 2006, were obtained from the PharMetrics LifeLink Health Plan Database¹⁷, a national commercial database with claims from >80 health plans. The first claim for the anti-TNF agent served as the index date for each patient. Patients included in the analysis were aged ≥ 18 years, were continuously enrolled in a health plan for 6 months pre-index and 12 months post-index, had ≥ 2 *International Classification of Diseases, Ninth Edition, Clinical Modification* (ICD-9-CM) diagnosis codes (714.xx) for RA during the pre-index period, had no pre-index biologics (i.e., infliximab, etanercept, adalimumab, abatacept, or rituximab), and had ≥ 365 days of persistence (i.e., number of days between the first and last claims for index anti-TNF agent). Exclusion criteria included: a diagnosis of ankylosing spondylitis, psoriatic arthritis, psoriasis, Crohn's disease, or ulcerative colitis at any time; post-index anti-TNF switching; or an abatacept or rituximab claim at any time. Data were assessed for the first year of persistent treatment. Baseline demographics and RA disease severity were reported. Pharmacy refill patterns, infusion patterns, and anti-TNF medication costs were evaluated for the 12-month post-index period.

Comorbidity and RA disease severity

Comorbidities were measured using the Charlson Comorbidity Index (CCI)¹⁸, a weighted index that allows for prospective comorbidity and mortality risk classification in longitudinal studies. As the CCI score increases, a patient's risk of comorbid mortality increases. Disease severity was measured using MedStat disease

staging¹⁹, which employs ICD-9-CM codes to classify patients with a particular disease who require similar treatment and have similar expected outcomes. Disease severity was classified using a 5-point scale (Stage 0 = no complications, Stage 1 = specific disease with no complications, Stage 2 = specific disease with local complications, Stage 3 = specific disease with multiple sites of systemic complications, Stage 4 = death). The MedStat methodology uses a cumulative approach; for example, stage 1.01 for RA is based on ICD-9-CM codes 714.0, 714.2, and 714.4, which correspond to the American College of Rheumatology diagnostic criteria of a history of morning stiffness and 1 of the following: 3 joints with swelling or effusion, swelling or effusion of the hand or wrist joints, symmetrical bilateral joint swelling, subcutaneous nodules, RA (as evidenced by radiograph of any joint), or rheumatoid factor titer of 1:160. In addition, to have a disease stage of 3.0, a patient must have been previously classified as stage 2.0. Once an individual meets the criteria for a particular stage, he or she cannot revert to a lesser stage. This methodology has been used to compare disease severity in retrospective analyses when detailed clinical outcome data were unavailable²⁰.

Adalimumab and etanercept pharmacy refill measures

Adalimumab and etanercept pharmacy refills were assessed by capturing mean number of treatment days authorized by the prescriber and submitted on the pharmacy claim in the days supply field and by performing a prescription gap analysis calculation of the length of time between the initial and subsequent fill service dates. The sum of the difference between the actual time to refill and the prescriber-authorized days supply was used to calculate the gaps (or potential cumulative time without therapy).

Formula for prescription gap analysis

$$\begin{aligned} & \Sigma(\text{Actual time to refill}_x \\ & \quad - \text{Prescriber-authorized days supply for refill}_{x-1}) \\ & = \text{Number of days without drug for first year} \end{aligned}$$

Mean and median numbers of adalimumab and etanercept prescription fills per patient for the first year were also examined. Percentages of patients refilling adalimumab or etanercept prescriptions during the first year were graphically displayed.

Infliximab infusions and dosing measures

Infliximab infusions were evaluated by calculating mean number of days between infusions billed using Healthcare Common Procedure Coding System code J1745. Mean

number of infusions by treatment period was reported. A proxy formula was used to estimate infliximab dose at each infusion, because neither doses nor units were recorded on the procedure claims. Infliximab doses were calculated by dividing the health plan's allowed amount for each claim by the wholesale acquisition cost for a 100-mg vial during the year of claim payment. The health plan's allowed amount on each claim included the total amount paid by the plan and the patient. The health plan's allowed amount was used because it represents the full cost of infliximab billed to the plan and will not overinflate costs to the same degree as charged amounts²¹. The allowed amount, however, does not represent the costs that a health plan reimbursed for infliximab, as that information is typically not publicly available. Only patients with complete claim information (i.e., no negative or null value in the allowed amount field) were included in the dosing analysis. Results for infliximab infusions and doses were reported for induction (index to day 56), maintenance (day 57 to day 365), and the first year overall (index to day 365).

Direct anti-TNF medication cost assessments

Inflation-adjusted plan-paid anti-TNF medication costs were reported for the first year. Adalimumab and etanercept direct medication costs included costs on pharmacy claims. Infliximab direct medication costs included drug costs and any administration/infusion fees submitted on the same medical claim. A secondary cost analysis was conducted by calculating annual costs for each anti-TNF based on expected cumulative utilization for 1 year of persistent treatment (using dosing within the FDA-approved prescribing information and assuming 100% treatment adherence). Adalimumab cost calculations were based on a dosage of 40 mg every other week¹. Etanercept cost calculations were based on a dosage of 50 mg once weekly². Infliximab cost calculations were based on initial doses of 3 mg/kg administered intravenously at weeks 0, 2, and 6 and every 8 weeks thereafter, with a dose increase to 5 mg/kg (every 8 weeks) after 6 months²². The cost of the entire infliximab vial and administration costs were accounted for in calculations.

Statistical analyses

Pairwise comparisons were used to assess differences in baseline characteristics using *t* tests (generalized linear models). Differences in costs were tested using Wilcoxon rank sum tests. Statistical significance was defined as a 2-sided α -level of ≤ 0.05 . All statistical analyses were performed using SAS release 9.1.3 (SAS Institute, Inc., Cary, NC).

Table 1. Patient clinical and demographic characteristics.

	All patients (n = 1696)	Adalimumab (n = 337)	Etanercept (n = 902)	Infliximab (n = 457)	p-value (infliximab vs adalimumab)	p-value (infliximab vs etanercept)
Mean age, years	49.90	49.20	48.84	52.50	<0.0001	<0.0001
Women, %	76.06	75.37	77.45	73.74	>0.05	>0.05
Mean CCI	2.24	2.18	2.21	2.35	0.2204	0.1981
RA Disease Staging ^a	1.50	1.48	1.46	1.57	0.0739	0.008

^aMedstat Disease Staging (Stage 0 = no complications, Stage 1 = specific disease with no complications, Stage 2 = specific disease with local complications, Stage 3 = specific disease with multiple sites of systemic complications, Stage 4 = death). CCI, Charlson Comorbidity Index; RA, rheumatoid arthritis.

Table 2. Pharmacy refill patterns for adalimumab and etanercept.

	Adalimumab (n = 337)	Etanercept (n = 902)
Mean No. of prescriber-authorized days	34	32
Mean (SD) time between refills, days		
Fill 1 to Refill 2	46 (47)	45 (48)
Refill 2 to Refill 3	42 (31)	40 (30)
Refill 3 to Refill 4	39 (23)	38 (25)
Refill 4 to Refill 5	41 (26)	39 (25)
Refill 5 to Refill 6	35 (19)	36 (22)
Refill 6 to Refill 7	33 (13)	35 (18)
Refill 7 to Refill 8	34 (16)	33 (14)
Refill 8 to Refill 9	33 (13)	32 (14)
Refill 9 to Refill 10	31 (8)	31 (11)
Refill 10 to Refill 11	31 (11)	31 (10)
Refill 11 to Refill 12	29 (7)	29 (9)

SD, standard deviation.

Results

Demographic and clinical characteristics of RA patient sample

Data from 1696 patients with RA (adalimumab = 337, etanercept = 902, infliximab = 457) were included. The mean age overall was 49.9 years; 76% of patients were women. Infliximab-treated patients were significantly older than adalimumab- or etanercept-treated patients (52.5, 49.2, and 48.8 years, respectively; both comparisons, $p < 0.0001$). Infliximab-treated patients had statistically higher RA disease staging compared with their etanercept-treated counterparts (1.57 vs 1.46, respectively; $p = 0.008$), but no difference was found when compared with adalimumab ($p = 0.0739$). No significant differences were noted among mean CCI scores (Table 1).

Adalimumab and etanercept pharmacy refill measures

Among patients who received adalimumab, mean number of prescriber-authorized treatment days on adalimumab

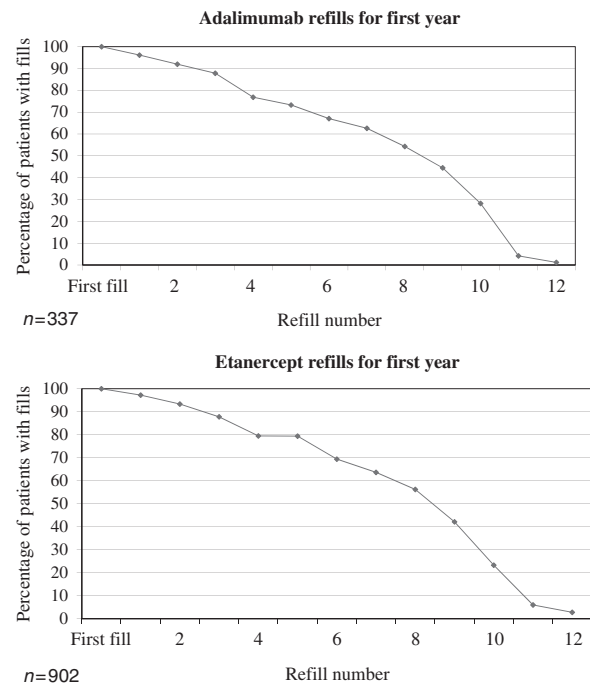


Figure 1. Pharmacy refill patterns for adalimumab and etanercept during the first year of treatment.

pharmacy claims was 34 days. Of etanercept users, mean number of prescriber-authorized treatment days on etanercept pharmacy claims was 32 days. Actual time between prescription refills was longer than expected, based on the prescriber-authorized days supply, for 28% of all adalimumab refill periods and 30% of all etanercept refill periods (Table 2).

Gap analyses revealed that the potential cumulative time without therapy was 33 days for adalimumab and 43 days for etanercept within the 12-month post-index period. The mean (standard deviation [SD])/median number of pharmacy fills per patient for the first year were 9.97 (SD 3.79)/11 for adalimumab and 9.77 (SD 3.81)/11 for etanercept. The percentage of patients continuing to refill adalimumab and etanercept prescriptions decreased during the first year (Figure 1).

Infliximab infusions and dosing

The majority of infliximab-treated patients (98.5%; $n=450$) received no more than 8 infusions during the first year of treatment. The mean (SD)/median numbers of infusions were 2.71 (SD 0.61)/3, 5.15 (SD 1.28)/5, and 7.86 (SD 1.48)/8 for the induction, maintenance, and first-year periods, respectively. The mean times between induction infusions were as follows: 1st and 2nd = 19 days; 2nd and 3rd = 29 days. The mean times between maintenance infusions spanned 52 to 57 days (Table 3).

A subset of 425 evaluable infliximab-treated patients with complete claim information was included in the dosing analysis. Calculated mean (SD)/median infliximab doses per infusion were 397 (SD 164) mg/370 mg, 455 (SD 193) mg/405 mg, and 437 (SD 168) mg/397 mg for induction, maintenance, and first-year periods, respectively.

Direct anti-TNF medication cost assessments

Significant differences in mean and median direct anti-TNF medication costs existed among the treatment groups. Mean (SD) anti-TNF medication costs for the first year were \$14,991 (SD \$9396), \$13,361 (SD \$9182), and \$18,139 (SD \$9958) for adalimumab,

etanercept, and infliximab, respectively ($p<0.0001$). Median annual anti-TNF medication costs were \$14,979, \$14,225, and \$17,012 for adalimumab, etanercept, and infliximab, respectively ($p<0.0001$). A post hoc analysis of the distribution of cost data for each of the anti-TNFs showed no differences in how the cost data were skewed among the agents. A secondary cost assessment showed that estimated annual costs of adalimumab, etanercept, and infliximab were comparable, even when accounting for administration costs (\$18,886, \$20,190, and \$18,533, respectively), if the anti-TNFs were used according to the prescribing instructions (Table 4).

Discussion

This study was conducted to investigate adalimumab, etanercept, and infliximab utilization patterns while also comparing medication costs in RA. The strengths of this study included: exclusion of patients with other conditions for which the anti-TNFs are indicated and may have different recommended dosing as a confounder of the results, selection of patients with RA newly starting the anti-TNF, and inclusion of patients maintaining persistence on the initiated anti-TNF without switching to another anti-TNF.

Results revealed insights regarding real-world use of these drugs. Although higher treatment costs were associated with infliximab, this may have been influenced by observed differences in patient populations, including disease severity. Examining costs of persistent treatment (with 100% treatment adherence) according to labeled dosing, however, revealed minute numerical differences in costs of all 3 anti-TNF agents. The difference between infliximab's mean observed cost and expected annual cost, when dosed within prescribing guidelines, was $-\$394$. Differences between mean observed costs and expected annual costs, relative to labeled dosing, for adalimumab and etanercept were approximately 10 to 17 times that

Table 3. Time intervals between infliximab infusions ($n=457$).

	Mean length of time (days)
<i>Induction period</i>	
1st to 2nd infusion	19
2nd to 3rd infusion	29
<i>Maintenance period</i>	
3rd to 4th infusion	56
4th to 5th infusion	57
5th to 6th infusion	55
6th to 7th infusion	52
7th to 8th infusion	53

Table 4. Annual cumulative anti-TNF cost considerations using doses within the United States FDA-approved prescribing information (first year of persistent treatment).

	Dosing	Cumulative dose	Cumulative number of syringes/vials	Labeled anti-TNF costs ^a
Adalimumab	40 mg every 2 weeks	1040 mg	26	\$18,886
Etanercept	50 mg once weekly	2600 mg	52	\$20,190
Infliximab	(3 mg/kg ^b , then 5 mg/kg ^b after 6 months, + MTX)	N/A	27	\$16,933 + (8 infusions at \$200 ^c = \$1600) Total cost = \$18,533

^aCosts based on June 2009 WAC: adalimumab \$726.40 per 40 mg syringe; etanercept \$388.26 per 50 mg syringe; infliximab \$627.14 per 100 mg vial.

^bAssumes 70 kg patient.

^c2009 Medicare Coding and Payment for Drug Administration Services under the Physician Fee Schedule: Non-Facility or Office-based Rates 96413 (1st hour) at \$162.50 and 96415 (each additional hour) at \$37.55.

FDA, Food and Drug Administration; MTX, methotrexate; N/A, not applicable; TNF, tumor necrosis factor; WAC, wholesale acquisition cost.

observed for infliximab (−\$3895 and −\$6829, respectively). Given the assumed patient weight in the modeled expected annual cost calculation for infliximab, these differences would be reduced if the assumed patient weight increased.

Although mean age and female predominance in the overall study population were consistent with published clinical trial and observational studies of patients with RA^{5–10,12,13,23,24}, other differences in patient types were observed. Infliximab-treated patients were significantly older than adalimumab- and etanercept-treated patients and had a higher RA disease stage compared with etanercept, indicative of a more complex disease profile. Similar demographic and clinical differences among patients with RA receiving anti-TNF agents have been reported elsewhere^{23,24}. Additionally, it has been reported that infliximab-treated patients may present with statistically higher medical and pharmacy costs at baseline compared with patients treated with etanercept²³. These differences may drive utilization of healthcare services and total costs, in addition to drug costs, and should be considered in future comparative analyses^{25,26}.

Infliximab infusions and dosing results reported real-world utilization consistent with prescribing information; patients appeared to receive infliximab according to the FDA-recommended schedule of weeks 0, 2, and 6 and every 8 weeks thereafter. Dose increases and more frequent administrations are also supported by the FDA-approved prescribing information and have been proven to have an associated clinical benefit^{1,27–32}. This current analysis suggests that while there was a dose increase from induction to maintenance, the increase was modest. Infliximab dose increases have been cited in the literature as occurring frequently within managed care and having an association with increased costs^{33,34}; however, researchers recently hypothesized that dose increases within the FDA-recommended range and/or physician administration may be associated with significantly longer treatment persistence when compared with adalimumab and etanercept²⁴. Another study reported that a smaller proportion of patients receiving infliximab discontinued therapy compared with patients on etanercept²³.

Furthermore, persistency with anti-TNF agents has a directly proportional effect on pharmacy costs and an inversely proportional effect on non-pharmacy costs³⁵. In a study of 1242 patients with RA receiving infliximab, etanercept, or adalimumab, pharmacy costs were higher, and all other non-pharmacy costs (e.g., inpatient, outpatient, labs) were lower in patients with ≥80% treatment persistency compared with patients with <80% treatment persistency. Investigators also found that patients receiving infliximab had significantly higher persistence than patients receiving adalimumab or etanercept³⁵.

The current analysis was conservative, as persistency was normalized (as an inclusion criterion) across treatment groups. Despite this persistency requirement, there was variance in the refill patterns for adalimumab and etanercept. Approximately one-third of actual pharmacy fills had a longer time to patient refill. Because of this discrepancy between the prescriber recommendation and the patients' refill behavior, some adalimumab-treated patients may have had an approximate cumulative time of 5 weeks without medication over the course of the first year of treatment; some etanercept-treated patients may have had an approximate cumulative time of 6 weeks without medication. These refill patterns may signal questionable adherence behavior, contributing to underutilization of adalimumab and etanercept, and require further investigation.

Lastly, plan-paid medication costs were significantly different for adalimumab, etanercept, and infliximab, with infliximab associated with higher costs. While the observed cost differences are consistent with other studies^{4–7,9,33,35–37}, this analysis attempted to address cost in the context of treatment adherence. Our evaluation of costs in the context of observed treatment adherence is a methodological approach distinctive from that of a recent analysis using the same database. Schabert *et al.*⁹ also used the PharMetrics LifeLink Health Plan Database¹⁷ to calculate annual treatment costs of adalimumab, etanercept, and infliximab. In their analysis, the yearly observed treatment costs in RA were \$17,700, \$14,314, and \$20,390 for adalimumab, etanercept, and infliximab, respectively. The authors attributed the higher observed costs of adalimumab and infliximab to potential dose increases but did not include evidence of observed dose increases in the analysis nor consider reduced treatment adherence as a potential driver of lower observed costs. Cost differences in this current study may be associated with differences in observed utilization patterns – more specifically, inconsistent adalimumab and etanercept refill behavior and consistent infliximab administrations during the first year. Health plans may have been paying less for adalimumab and etanercept prescriptions, but patients may have been using them in a manner inconsistent with prescribing information.

As reported in Table 4, 1-year anti-TNF agent cost considerations are comparable when administered and taken by the patient according to prescribing information. Similar findings of comparable cost, in the context of optimal dosing and adherence, have been reported by the Agency for Healthcare Research and Quality³⁸. Previous adherence research with the anti-TNF agents has shown that patient adherence among Medicare or commercial enrollees with RA is higher with infliximab than with etanercept²². Lower treatment adherence could put the patient at risk for inadequate control of RA symptoms

and disease activity and could influence the use and cost of outpatient and inpatient services. Future research should be directed to exploring the impact of inconsistent refill behavior on clinical outcomes and total payer costs, including medical and pharmacy, rather than focusing on only pharmacy costs.

Limitations

Several limitations exist within this analysis. This study was limited to the first year of anti-TNF treatment, partly due to the study-defined persistence requirement. This represents a unique method in contrast to other observational studies^{5–13}. Given that patients with RA may be treated for variable time periods with the selected index anti-TNF agent, the 1-year persistence requirement for the index anti-TNF agent provided a more informative comparison of initial utilization patterns. This persistency requirement, however, excluded individuals who discontinued treatment or switched treatments.

Limiting results to a 1-year time frame prohibits any conclusions regarding infusion and refill patterns beyond the first year of anti-TNF therapy. Other disease severity measures and comorbidity instruments, such as the Index of Coexistent Diseases and the RA Duke Severity of Illness Checklist, have greater specificity for predicting health outcomes and costs in RA^{39,40} but were not feasible for use in a claims-based analysis. This study was conducted by analyzing claims retrospectively from an administrative database lacking clinical measures, reasons for patients refilling later than expected, or indicators of patient death.

This analysis was limited in scope, as it evaluated utilization patterns only for selected anti-TNF agents and did not include other concomitant medications that patients may have been using for RA. The perspective of this analysis was also limited to that of the health plan's pharmacy budget perspective and, therefore, did not include other costs relevant from a patient perspective (e.g., co-payments, co-insurance, time and costs associated with travel). Future analyses may want to incorporate these types of direct and indirect costs to estimate the total cost of care for anti-TNFs.

Lastly, absolute patient adherence could not be assessed because we did not have information on how patients were self-administering adalimumab and etanercept or if samples of the agents were made available. This analysis was limited to a refill pattern assessment, which provided a window into theoretical patient adherence, with potential drug on-hand as an intermediary measure. The measurement of absolute patient adherence with the self-administered anti-TNF agents, accounting for all possible means of patients acquiring the drug, is a warranted area of research.

Conclusions

This observational study reported differing RA patient populations based on index anti-TNF agents. Refill patterns for adalimumab and etanercept revealed gaps in the time that patients refilled compared to prescriber recommendations; however, infliximab infusion patterns were consistent with prescribing information. Future comparative effectiveness and economic research of anti-TNF agents should adjust for differences in baseline characteristics and observed compliance with prescriber recommendations. Potential clinical and economic implications of dose attenuation with adalimumab and etanercept should be explored further.

Transparency

Declaration of funding

This study was funded by Janssen Scientific Affairs, LLC, Horsham, PA.

Declaration of financial relationships

CTC and RSM have disclosed that they are employees of Janssen Scientific Affairs, LLC. AKC has disclosed that he has no relevant financial relationship to declare.

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