

Impact of Medication Adherence on Healthcare Resource Utilization, Work Loss, and Associated Costs in a Privately Insured Employed Population Treated With Adalimumab in the United States

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Objective: The aim of this study was to evaluate the impact of adherence to adalimumab on all-cause work loss, healthcare resource utilization (HRU), and direct medical and indirect costs over 2 years using real-world data. **Methods:** This was a retrospective cohort study using a large, United States administrative claims database. Adult patients treated with adalimumab were grouped into adherent and non-adherent cohorts and followed for up to 2 years. Outcomes were compared between cohorts. **Results:** Over 2 years, adherent patients had \$10,214 lower per patient medical and indirect costs compared to non-adherent patients, resulting from lower HRU, fewer days of absenteeism, and lower rates of work loss events. **Conclusion:** Patient and societal benefits of adherence to adalimumab are significant over 2 years. These findings highlight the importance of policies aimed at improving adherence to self-administered medications.

Keywords: adalimumab, autoimmune disorders, healthcare costs, healthcare resource utilization, medication adherence, work loss

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Ethical considerations and disclosure: The data used in this study were de-identified and complied with the patient confidentiality requirements of the Health Insurance Portability and Accountability Act and the Declaration of Helsinki. Thus, no institutional review board approval was required.

Manish Mittal and Manan Shah are employees of AbbVie, Inc. and own stock/stock options. Min Yang, Wei Gao, and Christopher Carley are employees of Analysis Group Inc., which has received consultancy fees from AbbVie, Inc. Bruce Sherman declares no conflicts of interest with respect to the research, authorship, and/or publication of this article.

Specific author contributions: All authors participated in the design of the study and contributed to the manuscript development. Data were collected by Analysis Group, Inc. (Min Yang, Wei Gao, and Christopher Carley) and analyzed and interpreted in collaboration with all other authors. Manuscript drafts were prepared by the authors with editorial assistance from a professional medical writer ultimately paid by the sponsor, AbbVie, Inc. All the authors vouch for the accuracy and completeness of the data reported and the adherence of the study to the protocol, and all the authors made the decision to submit the manuscript for publication.

Clinical significance: Findings from this study highlight that interventions aimed at improving adherence to self-administered medications can significantly benefit the lives of the patients and their families, as well as society as a whole.

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Medication adherence is critical to realizing the full benefits of a pharmaceutical therapy. However, poor adherence remains common in self-administered prescription medications. Research has found that approximately 50% of prescriptions are not taken as instructed,^{1,2} resulting in a substantial burden to patients and to society as a whole. Hundreds of billions of dollars in costs are attributed to medication non-adherence annually in the United States (US).^{1,3} A 2012 systematic literature review conducted by the Agency for Healthcare Research and Quality (AHRQ) on the impact of adherence to self-administered medications found that improvement in adherence resulted in improvement in clinical outcomes for a number of chronic conditions.⁴ Another systematic literature review, in 2017, further confirmed the substantial medical cost burden due to medication non-adherence across multiple clinical conditions, with direct all-cause costs of non-adherence ranging from \$1037 to \$53,793 (2015 US dollars [USD]) per patient per year.⁵ Evidence for the economic impact of non-adherence in autoimmune conditions is currently limited. However, such impact should not be underestimated. Autoimmune conditions often affect the working age population and impair patients' ability to work and perform regular activities.⁶ This has been shown to interfere with productivity and harm career trajectory and salary growth rates in the workplace.⁷⁻⁹

Adalimumab, a tumor necrosis factor-alpha (TNF) inhibitor agent, has been approved by the US Food and Drug Administration (FDA) for the treatment of 10 autoimmune indications, including rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, plaque psoriasis, ankylosing spondylitis, adult and pediatric Crohn's disease, ulcerative colitis, hidradenitis suppurativa, and uveitis.¹⁰ Along with other anti-TNF agents, these therapies have altered the treatment landscape and clinical management of these chronic autoimmune conditions, improved patient outcomes through enhanced quality of life, improved productivity,¹¹⁻¹⁴ and improved ability to work.¹⁵⁻¹⁸

However, one-third of patients treated with anti-TNF therapies, and as many as 83% of young adults, are not adherent to their medication and may not be receiving the full benefit of these therapies.^{19,20} For example, non-adherence has been found to be associated with loss of response to anti-TNF therapy and higher disease activity.²¹ This study quantified the value of adherence to adalimumab in regards to all-cause healthcare resource utilization (HRU), work loss (ie, leaves of absence, short-term disability, and absenteeism days), direct medical costs, and indirect costs among employed adult patients in the US treated with adalimumab for an FDA-approved indication over a 2-year timeframe.

METHODS

Data Source

This study used medical, pharmacy, and work loss data from the OptumHealth Reporting and Insights database, covering the first quarter (Q1) of 2007 to Q1 2017. This large-scale US employer

database includes approximately 20 million individuals, primarily adults aged under 65 years enrolled in commercial insurance from 84 self-insured Fortune 500 companies. The data represent a nationwide distribution across the US and a broad range of job classifications covering healthcare, manufacturing, service, technology, retail, and public sector industries. Medical and drug claims were available for all beneficiaries. Measures of work loss, including disability claims, were available for patients from 44 of the 84 companies. The data were de-identified and complied with the patient confidentiality requirements of the Health Insurance Portability and Accountability Act and the Declaration of Helsinki. Thus, no institutional review board approval was required for this study.

Sample Selection and Study Design

Actively employed adults (18 to 64 years old) were eligible for inclusion if they had at least two of the same diagnosis claims on separate dates for any adalimumab-approved indication (diagnosis codes listed in Supplemental Table 1, <http://links.lww.com/JOM/A979>). In addition, patients were required to have initiated adalimumab following a diagnosis of the condition, have enrollment in a healthcare plan for at least 6 months before the index date (first adalimumab claim) and at least 12 months after the index date, and have at least one additional claim for adalimumab in the first year following the index date. Patients from employers that contributed work loss information to the database were included in a subset of the sample used for work loss and indirect cost estimations.

Patients were followed after the index date for a minimum of 1 year and up to the earliest of health plan disenrollment, end of data availability, or 2 years following the index date. Figure 1 illustrates the longitudinal cohort study design. During the first year of follow-up, medication adherence to adalimumab was estimated using the proportion of days covered (PDC) over the 12 months following the index date. The PDC was determined by summing the number of days covered by the reported days supply of adalimumab claims divided by 365 days. Patients were grouped into adherent and non-adherent cohorts based on a commonly used PDC cutoff of 80%.²² Medication use was identified by the National Drug Code or Healthcare Common Procedural Coding System code (codes listed in Supplemental Table 2, <http://links.lww.com/JOM/A979>).

Outcomes

The outcomes evaluated in the study included annual HRU, direct medical healthcare costs, work loss, indirect costs, and total (direct and indirect) costs. All outcomes were summarized and compared between the adherent and non-adherent cohorts over each year of the study period. Outcomes in year 2 were evaluated among patients with continuous enrollment for at least the entire second year. A sensitivity analysis was conducted among patients with continuous enrollment for at least the first 3 months of year 2 and outcomes were extrapolated to a full year.

For HRU outcomes, the proportions of patients with all-cause inpatient admissions, emergency department (ED) visits, and composite hospital visits (inpatient and ED) were reported. Other services (eg, outpatient visits) were reported at baseline and were included in the estimation of direct medical costs. Direct medical costs were calculated from a societal perspective as the annual sum of patient out-of-pocket costs and the amount covered by both primary and secondary insurance for inpatient, ED, outpatient, home health aide, and other medical services (eg, rehabilitation centers, independent labs, hospice and nursing facilities, birthing centers). Medical costs were adjusted to 2020 USD values using the medical care component of the Consumer Price Index.²³

The analyses on work loss and indirect costs were conducted among patients whose employers reported disability claims. Work loss outcomes reported in this study included leaves of absence, short-term disability, and disability or medically-related absenteeism days (eg, an office visit or a hospitalization event that occurred during weekdays). Indirect costs were imputed based on the individual employee's daily wage (calculated using observed annual income) multiplied by the total days of disability or medical-related work loss.^{24,25} Each hospitalization day, emergency visit, and day on short-term or long-term disability accounted for a full day of work loss, while each outpatient visit (including home health aide) or other medical visit accounted for half a day of work loss. To account for the mandatory waiting period before disability benefits began, a 5-day sick/waiting period was assumed to precede all disability claims. Leaves of absence were not included in the calculation of indirect costs due to lack of available data on start and end dates. Wages were inflated to 2020 USD values using the overall Consumer Price Index.²³

Statistical Analyses

Descriptive statistics were reported by adherence cohort for patient characteristics (eg, age, sex, region, index year, key autoimmune conditions, prior use of biologics, Charlson Comorbidity Index [CCI]²⁶), HRU, medical costs, and work loss events measured during the 6-month baseline period. Statistical comparisons used *t* tests for continuous variables and chi-squared tests for binary and categorical variables.

In the follow-up period, descriptive statistics were reported by adherence cohort for the outcomes described above over each year of follow-up. Statistical tests for each outcome of interest were performed using a generalized linear model adjusting for age, sex, CCI, baseline income (as reported by employers), other biologic medication use (during baseline and in the concurrent year of follow-up), and adalimumab intended therapeutic area. For binary outcomes (HRU and work loss events), a logit-link function and binomial distribution were used. For count outcomes (days of work loss from disability and medical absence), a log-link function and

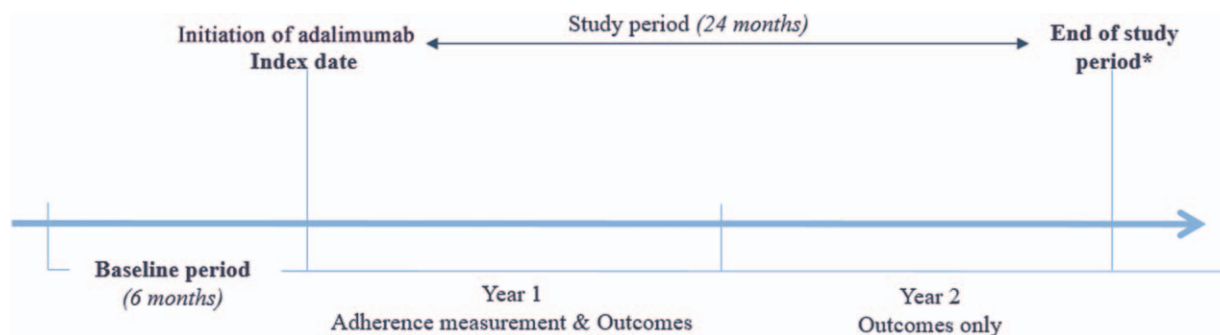


FIGURE 1. Study design. Note: (*) In the post-index study period, patients were followed until disenrollment or the end of the study period, whichever came first.

negative binomial distribution were used. For continuous cost outcomes, a log-link function and gamma distribution were used.

A *P*-value of 0.05 was used to determine statistical significance. All analyses were performed using SAS Enterprise Guide Version 7.1 (SAS Institute, Cary, NC).

RESULTS

Study Population

The sample selection process is illustrated in Figure 2. Of 215,713 patients identified as having a condition of interest, 12,096 were treated with adalimumab. In total, 2159 employed patients met the remaining sample selection criteria and were included in the analyses of HRU and direct costs. Of these patients, 1517 were from employers who reported data on disability claims and were included in the analyses of work loss and indirect costs. The distribution of therapeutic area use among all patients was 42.9% (*n* = 926) for rheumatology, 32.7% (*n* = 707) for dermatology, 23.3% (*n* = 504) for gastroenterology, and 1.0% (*n* = 22) for ophthalmology; among patients with disability data, the distribution was comparable: 42.5% (*n* = 644), 33.0% (*n* = 500), 23.7% (*n* = 359), and 0.9% (*n* = 14), respectively. In year 2, 1453 patients with full enrollment were included for analysis.

Patient baseline characteristics are shown in Table 1. Of the total patient cohort (*N* = 2159), 1011 (46.8%) were classified into the adherent (PDC ≥ 80%) cohort and the remaining 1148 (53.2%) into the non-adherent (PDC < 80%) cohort based on PDC during year 1. The mean age of adherent patients at index date was slightly higher than that of non-adherent patients (mean [SD]: 46.1 [10.5] vs

44.2 [10.3] years, respectively; *P* < 0.001), and the adherent cohort had a higher proportion of males (58.7% vs 52.2%; *P* = 0.003). The distribution of intended therapeutic area use for patients in the adherent versus non-adherent cohorts was 28.3% vs 36.7% dermatology (*P* < 0.001), 27.9% vs 19.3% gastroenterology (*P* < 0.001), 42.7% vs 43.0% rheumatology (*P* = 0.888), and 1.1% vs 1.0% ophthalmology (*P* = 0.764), respectively. Mean CCI, prior use of biologics, annual salary, HRU, work loss, and direct and indirect costs were comparable between cohorts during the baseline period.

Healthcare Resource Utilization

During the study period, the proportion of adherent patients with any composite hospital visit was significantly lower than that of the non-adherent patients in both year 1 (29.4% vs 39.8%, *P* < 0.001) and year 2 (29.7% vs 37.9%, *P* < 0.001) (Table 2). Specifically, in year 1, adherent patients had significantly lower rates of inpatient visits (10.0% vs 14.4%, *P* < 0.001) and ED visits (24.6% vs 32.1%, *P* = 0.002) compared with non-adherent patients. In year 2, adherent patients had significantly lower rates of inpatient visits (10.8% vs 13.4%, *P* = 0.015) and ED visits (23.0% vs 30.4%, *P* < 0.001) relative to patients in the non-adherence cohort.

Work Loss

Compared to non-adherent patients, adherent patients had significantly lower rates of leave of absence (5.1% vs 10.6%, *P* < 0.001) and short-term disability events (2.3% vs 6.0%, *P* < 0.001) in year 1 following initiation of adalimumab (Table 3). The adherent cohort also had a significantly lower rate of leave of absence events (4.9% vs 10.0%, *P* = 0.003) and short-

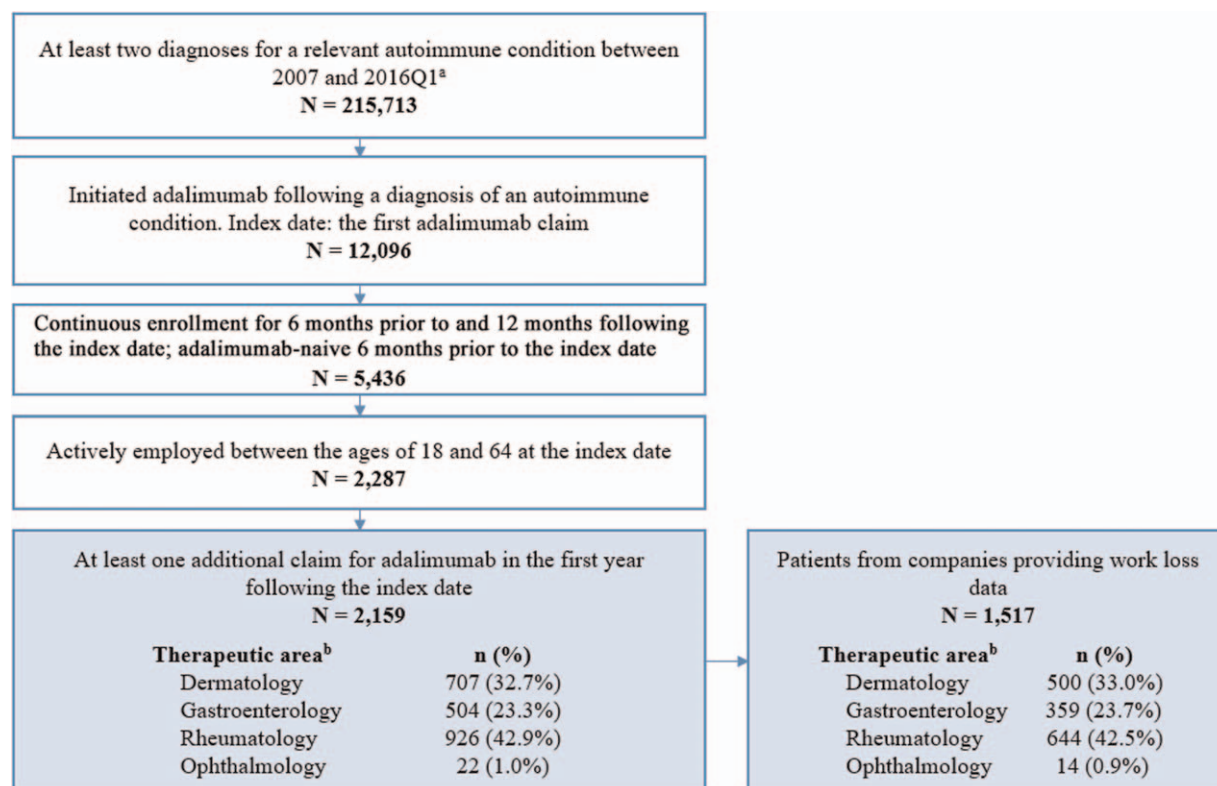


FIGURE 2. Sample selection. ICD-9 (10)-CM, International Classification of Diseases – Ninth (Tenth) edition – Clinical Modification; Q1, first quarter. *Notes:* (^a) Diagnoses were identified by ICD-9-CM or ICD-10-CM codes listed as either the primary or secondary diagnosis code in the medical claims database; (^b) For patients with multiple indications, index therapeutic area was assigned according to the most recent diagnosis prior to the index date.

TABLE 1. Baseline Characteristics

	Adherent Cohort (N = 1011)	Non-Adherent Cohort (N = 1148)	P
Demographic characteristics			
Age at index date (years), mean ± SD	46.1 ± 10.5	44.2 ± 10.3	<0.001*
Male, n (%)	593 (58.7%)	599 (52.2%)	0.003*
Region, n (%)			0.089
Northeast	158 (15.6%)	176 (15.3%)	
Midwest	301 (29.8%)	285 (24.8%)	
South	384 (38.0%)	485 (42.2%)	
West	160 (15.8%)	189 (16.5%)	
Unknown	8 (0.8%)	13 (1.1%)	
Financial status			
Annual salary (2020 \$USD), mean ± SD	78,698.7 ± 68,294.1	75,050.5 ± 63,744.0	0.201
Industry type, n (%)			0.139
Healthcare	79 (7.8%)	114 (9.9%)	
Manufacturing	112 (11.1%)	96 (8.4%)	
Public sector	29 (2.9%)	36 (3.1%)	
Retail	159 (15.7%)	207 (18.0%)	
Service ⁵	169 (16.7%)	180 (15.7%)	
Technology	78 (7.7%)	120 (10.5%)	
Transportation	340 (33.6%)	344 (30.0%)	
Other	45 (4.5%)	51 (4.4%)	
Disease characteristics, n (%)			
Therapeutic area			
Dermatology	286 (28.3%)	421 (36.7%)	<0.001*
Gastroenterology	282 (27.9%)	222 (19.3%)	<0.001*
Rheumatology	432 (42.7%)	494 (43.0%)	0.888
Ophthalmology	11 (1.1%)	11 (1.0%)	0.764
Year of index date, n (%)			
2007–2008	141 (13.9%)	153 (13.3%)	0.676
2009–2010	230 (22.7%)	302 (26.3%)	0.056
2011–2012	295 (29.2%)	287 (25.0%)	0.029*
2013–2014	227 (22.5%)	268 (23.3%)	0.623
2015–2016	118 (11.7%)	138 (12.0%)	0.802
Prior use of biologics	210 (20.8%)	243 (21.2%)	0.822
Charlson Comorbidity Index, mean ± SD	0.5 ± 0.8	0.5 ± 0.7	0.748
Charlson Comorbidity Index Group, n (%)			0.706
0	655 (64.8%)	734 (63.9%)	
1–2	335 (33.1%)	389 (33.9%)	
3–4	17 (1.7%)	23 (2.0%)	
5+	4 (0.2%)	2 (0.1%)	
HRU, n (%)			
Emergency	173 (17.1%)	205 (17.9%)	0.649
Inpatient	81 (8.0%)	94 (8.2%)	0.881
Outpatient	1001 (99.0%)	1138 (99.1%)	0.775
Home health aid	62 (6.1%)	67 (5.8%)	0.772
Work loss events, n (%)			
Leave of absence	19 (2.7%)	35 (4.3%)	0.096
Short-term disability	17 (2.4%)	15 (1.8%)	0.432
Direct medical costs (2020 \$USD), mean ± SD	6983.7 ± 12,348.4	7395.9 ± 16,744.3	0.512
Indirect costs (2020 \$USD), mean ± SD	(N = 702)	(N = 815)	
Medical	1175.1 ± 1,869.0	1157.9 ± 2,357.0	0.850
Disability	115.9 ± 1,181.7	116.7 ± 1,153.9	0.955

HRU, healthcare resource utilization; SD, standard deviation; USD, United States dollars.

*Statistically significant at $P < 0.05$.

term disability events (2.5% vs 5.1%, $P = 0.026$) versus the non-adherent cohort in year 2. In addition, on average, adherent patients had significantly fewer total days of work loss due to medical absence than non-adherent patients in both years (year 1: 8.8 [SD: 9.1] vs 10.3 [10.5] days, $P = 0.014$; year 2: 8.8 [9.6] vs 10.5 [12.5] days, $P < 0.001$).

Direct and Indirect Healthcare Costs

Patients in the adherent cohort had significantly lower direct medical costs (year 1: difference = $-\$5696$; year 2: $-\$3581$, both $P < 0.001$), indirect costs (year 1: $-\$891$, $P < 0.001$; year 2: $-\$46$,

$P < 0.001$), and total combined medical and indirect costs (year 1: $-\$6586$; year 2: $-\$3627$, both $P < 0.001$) compared with patients in the non-adherent cohort (Fig. 3). Specifically, in year 1, the adherent cohort had per patient per year (PPPY) direct medical costs of $\$9160$ (SD: $\$19,435$), indirect costs of $\$2115$ ($\$4481$), and total costs of $\$11,274$ ($\$21,285$); PPPY costs for the non-adherent group were $\$14,855$ ($\$38,170$), $\$3005$ ($\$7846$), and $\$17,861$ ($\$41,564$), respectively. In year 2, the adherent cohort had PPPY direct medical costs of $\$13,236$ (SD: $\$30,903$), indirect costs of $\$2580$ ($\$6649$), and total costs of $\$15,816$ ($\$34,021$); PPPY costs for the non-adherent group were $\$16,817$ ($\$56,381$), $\$2626$ ($\$5529$), and $\$19,443$ ($\$58,036$),

TABLE 2. HRU Events Over the Follow-up Period by PDC

	Year 1			Year 2		
	Adherent Cohort (N = 1011)	Non-Adherent Cohort (N = 1148)	P	Adherent Cohort (N = 679)	Non-Adherent Cohort (N = 774)	P
HRU, N (%)						
All hospital visits	297 (29.4%)	457 (39.8%)	<0.001*	202 (29.7%)	293 (37.9%)	<0.001*
Emergency	249 (24.6%)	368 (32.1%)	0.002*	156 (23.0%)	235 (30.4%)	<0.001*
Inpatient	101 (10.0%)	165 (14.4%)	<0.001*	73 (10.8%)	104 (13.4%)	0.015*

HRU, healthcare resource utilization; PDC, proportion of days covered.
*Statistically significant at $P < 0.05$.

respectively. Over 2 years of follow-up, patients adherent to adalimumab incurred per patient medical costs that were \$10,214 lower than those of non-adherent patients.

Sensitivity Analysis

When broadening year 2 analyses to patients who had continuous healthcare plan enrollment for at least 3 months and extrapolating outcomes to a full year, 1958 patients (adherent cohort: $n = 922$; non-adherent cohort: $n = 774$) were included in the analyses of HRU and direct costs. Of these patients, 1392 (adherent cohort: $n = 650$; non-adherent cohort: $n = 743$) were from employers who reported data on disability claims and were included in the analyses of work loss and indirect costs.

The findings from the sensitivity analysis were consistent with the main analysis. Specifically, adherent patients had significantly lower rates of composite hospital visits (27.7% vs 34.4%, $P < 0.001$) and ED visits (21.5% vs 27.3%, $P < 0.001$), and numerically lower rates of inpatient visits (10.3% vs 12.3%, $P = 0.079$) than non-adherent patients. Adherent patients also had significantly lower rates of leaves of absence (5.4% vs 9.6%, $P = 0.016$) and numerically lower rates of short-term disability (2.6% vs 4.7%, $P = 0.052$) in year 2. Patients in the adherent cohort had significantly fewer total days of work loss due to medical absence relative to non-adherent patients (8.8 [SD: 10.1] vs 10.3 [12.6] days, $P = 0.001$). Finally, year 2 direct and indirect costs were also lower for patients in the adherent cohort compared to the non-adherent cohort in this analysis (direct: $-\$3715$; indirect: $-\$449$; combined medical and indirect: $-\$4164$).

DISCUSSION

Non-adherence to self-administered prescription medication is prevalent in the US, imposing a large economic burden on both patients and the US healthcare system.³ Drawing on data from a geographically diverse claims database of many large employers in the US, this study assessed the impact of adalimumab adherence on HRU and associated direct medical costs, work loss, and indirect costs among employed patients receiving adalimumab for one of its FDA-approved indications. Patients were grouped into adherent and non-adherent cohorts (PDC $\geq 80\%$ and $< 80\%$, respectively) and followed for up to 2 years after adalimumab initiation, allowing for an assessment of how adherence to adalimumab affected patients' real-world outcomes over time. The results indicated that patients with higher adherence to adalimumab had significantly lower medical costs and rates of hospital visits over 2 years compared to patients with low adherence, as well as significantly lower risk of work loss due to common types of absenteeism (ie, short-term disability and leave of absence). These results highlight the important role medication adherence plays in realizing the full benefits of therapy. Moreover, these results emphasize the significance of medication adherence in reducing the economic burden to payers and employers. This is consistent with the systematic literature reviews conducted by the AHRQ and by Cutler et al,^{4,5} and provides new evidence from the perspective of patients with autoimmune conditions.

This study builds off previous real-world studies investigating the association between medication adherence and all-cause work loss outcomes, including indirect costs due to absenteeism.^{27,28} The

TABLE 3. Work Loss during the Follow-Up Period

	Year 1			Year 2		
	Adherent Cohort (N = 702)	Non-Adherent Cohort (N = 815)	P	Adherent Cohort (N = 485)	Non-Adherent Cohort (N = 551)	P
Work loss (any), N (%)						
Leave of absence	36 (5.1%)	86 (10.6%)	<0.001*	24 (4.9%)	55 (10.0%)	0.003*
Short-term disability	16 (2.3%)	49 (6.0%)	<0.001*	12 (2.5%)	28 (5.1%)	0.026*
Work loss days, mean \pm SD						
Short-term disability (all patients)	1.6 \pm 14.0	4.5 \pm 24.9	0.068	1.5 \pm 15.2	4.0 \pm 26.5	0.074
Absence due to medical services (all patients)	8.8 \pm 9.1	10.3 \pm 10.5	0.014*	8.8 \pm 9.6	10.5 \pm 12.5	<0.001*
Short-term disability (patients with ≥ 1 event)	68.3 \pm 65.4	76.8 \pm 71.3	0.667	61.1 \pm 78.8	82.0 \pm 90.7	0.885
Absence due to medical services (patients with ≥ 1 absence)	8.8 \pm 9.1	10.4 \pm 10.5	0.006*	8.8 \pm 9.6	10.6 \pm 12.5	<0.001*

SD, standard deviation.
* $P < 0.05$.

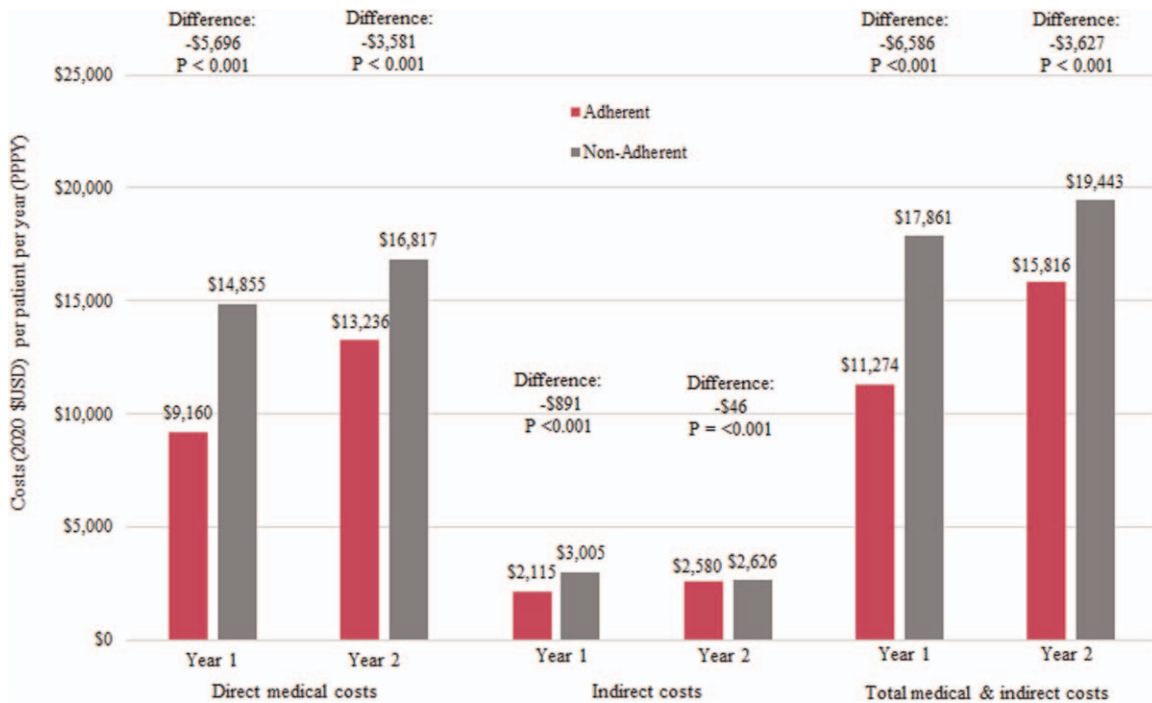


FIGURE 3. Healthcare costs among patients with high versus low adherence to adalimumab. PPPY, per patient per year; USD, United States dollars.

estimated all-cause work loss and indirect costs in this study may represent a conservative estimate of the true impact. Several other studies have shown that presenteeism (impairment while working) may contribute more to work productivity losses than absenteeism among patients with chronic conditions, including autoimmune disorders.²⁹ Li et al reported that reduced performance at work was the leading cause of productivity loss (compared to stopping work or changing jobs) among patients with arthritis.³⁰ Another administrative claims study found that presenteeism costs accounted for up to 77% of total medical and productivity losses for any reason among patients with arthritis; similar ranges were observed for other chronic conditions.³¹ This evidence suggests that, while the costs reported here due to absenteeism associated with non-adherence are substantial (\$937 more in indirect costs versus adherent patients over 2 years), we may be underestimating the full range of indirect costs resulting from non-adherence.

Our results also highlight the importance of policies and interventions that aim to improve medication adherence, thereby reducing burden on patients and employers alike. For many patients with chronic conditions, the growing trend of copay accumulator adjustment programs (CAAPs), which restrict pharmaceutical manufacturer–patient assistance dollar subsidies from being credited towards deductibles and out-of-pocket maximums, may have significant implications on drug accessibility. One recent study found that, in association with higher out-of-pocket spending, patients receiving specialty autoimmune drugs had significantly lower adherence and higher risk of discontinuation following implementation of CAAPs.³² Such a trend could have major implications on the burden placed on patients and the broader healthcare system. CAAPs and other programs affecting patient copay support should be evaluated in light of the present results and those of other studies that have assessed outcomes associated with treatment access or adherence.

In response to low levels of medication adherence, over the past two decades, health systems, insurers, and drug manufacturers

have offered patient support programs (PSPs) aimed at improving health engagement and self-management of medications.³³ These programs provide patients with face-to-face interactions with medical professionals, training programs, support in navigating the insurance and financial assistance processes, provision of materials to keep medications at required temperatures for travel, or reminders to take medications through phone, text, or e-mail.^{34–36} Participation in PSPs has been shown to be successful in improving medication adherence to treatment while also lowering the economic burden to patients, health systems, and society.^{36,37} A Canadian PSP aimed at improving adherence to adalimumab found that nurse-provided care coach calls were particularly effective in preventing failure to initiate therapy.³⁵ Another US study found that the odds of treatment abandonment were up to 70% lower for patients who participated in a PSP.³⁸ The present results noting significantly higher HRU, medical costs, and work loss among patients with suboptimal adherence to adalimumab further underscore the value of such programs.

This study is novel in evaluating the impact of adherence to adalimumab on indirect costs and work loss outcomes, generating real-world evidence using a large-scale, nationally representative employer claims database over a 2-year timeframe. In addition, this study benefits from several other strengths. First, the data used in this study represent a nationwide distribution across the US and a broad range of job classifications and industries. Second, this study explored the association of adherence to adalimumab with outcomes of interest over time. By examining outcomes in years 1 and 2 (for a subset of patients) following the initiation of adalimumab, the potential lag in the effect of adherence on outcomes could be accounted for. Moreover, examining outcomes in year 2 as a function of adherence in year 1 eliminated the possibility of reverse causality (ie, work loss or healthcare utilization driving differential adherence rates). Finally, the models in this study adjusted for key covariates, including demographics, medication use, and

comorbidities. This approach minimized omitted variable bias to the extent observable in the data.

A limitation of the present study is that the results were estimated from claims data for privately insured employees aged 18 to 64 years in the US and, therefore, may not be generalizable to the population of all patients with an indicated autoimmune condition or those covered by Medicare or Medicaid, those not employed, or those employed by small and medium-sized companies. Given the magnitude of the findings among patients with autoimmune conditions treated with adalimumab, further research assessing other treatments and in additional disease areas is warranted. The results are also subject to any errors in the administrative claims, such as inaccurate or incomplete reporting. However, by restricting the sample to actively employed patients, potential missing claims may be minimized and, thus, provide a more accurate cost estimation for adult employees. Furthermore, the patient adherence cohort was created using observable adherence data over the first year following adalimumab initiation. While our study uses prescription fill data to approximate adherence rate, the true adherence to filled prescriptions may not be observed in the data. It should be recognized as well that adherence may change during the second year or patients may discontinue treatment, either of which could have a concurrent impact on second year outcomes. Similarly, patients may have initiated other biologic therapies at any point during the study period. To account for this, observed use of other biologics in each concurrent follow-up year was adjusted for in the models. Moreover, because of the lack of documentation in the database regarding days associated with leave of absence, the potential indirect cost associated with leave of absence was not calculable, resulting in potential underestimation of the indirect costs from the patient perspective. This study also did not account for presenteeism or the cost of workforce disruptions related to disability, which may include administrative and training expenses for replacement workers. Moreover, summary plan descriptions were not available for each company that reported disability claims. Our study therefore used commonly used assumptions such as a 5-day waiting period and a consistent payment rate (for example, across length employee length of tenure or number of days absent in a year) for all patients. Inclusion of precise policy details would have allowed for a more precise estimate of employer costs. This study also did not include pharmaceutical costs due to the criteria that everyone be treated with adalimumab. However, adherence versus non-adherence may be associated with differential pharmaceutical spending for other treatments, including other biologics as well as adalimumab itself. Finally, the results may be confounded by unmeasured covariates, although by adjusting the models for key covariates, this risk of bias was minimized as much as was feasible. All associations should be interpreted in light of these limitations and possible confounders.

CONCLUSIONS

This study examined the impact of medication adherence to adalimumab on HRU, medical costs, work loss, and indirect costs among employed US patients over a 2-year period. The results confirmed that higher adherence was positively associated with fewer hospital visits (ie, ED visits and hospitalization) and lower medical service costs over a 2-year time period, and was associated with a significantly lower risk of work loss events due to leave of absence and short-term disability. As a result, employed patients with high adherence incurred significantly lower indirect costs due to medical- and disability-related absenteeism. These findings further highlight that interventions aimed at improving adherence to self-administered medications can significantly impact the lives of patients and their families, as well as society as a whole.

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