

# Adherence rates and health care costs in Crohn's disease patients receiving certolizumab pegol with and without home health nurse assistance: results from a retrospective analysis of patient claims and home health nurse data

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**Background:** Patient support programs have a positive effect on adherence to therapy. Certolizumab pegol (CZP) is a tumor necrosis factor antagonist for the treatment of Crohn's disease.

**Objectives:** To assess, using real-world claims data, whether home health nurse assistance had an effect on patients' adherence to CZP and to measure its impact on health care use and costs.

**Methods:** A retrospective analysis of medical and pharmacy claims data from the IQVIA Real-World Data Adjudicated Claims Database was conducted using data from January 1, 2007 through September 30, 2015. CZP patients with Crohn's disease were eligible to receive self-administration instructions from a nurse or nurse-administered CZP injections, or both. These services were provided by CIMplicity®, a home health nurse program sponsored by UCB Pharma. Cohorts were based on patients with and without nurse assistance and were matched based on gender and categorical age. Adherence to CZP was determined using the medication possession ratio (MPR) and proportion of days covered (PDC). A Kaplan–Meier analysis was performed to compare time to discontinuation of CZP between the two cohorts. Multivariate regression analyses were performed, adjusting for additional covariates to compare the effect of CZP with and without nurse assistance on hospitalization and total health care costs.

**Results:** Patients with at least 12 months of continuous enrollment post-index date were evaluated for adherence to CZP (n=276 in each cohort). The mean and median PDC and MPR values were higher with nurse assistance than without. Time to discontinuation was significantly longer in patients who received CZP with nurse assistance than without ( $P=0.0004$ ). Results from the multivariate analyses showed a significant reduction in all-cause hospitalization ( $-55.8\%$ ;  $P=0.0026$ ) and total health care costs ( $-14.3\%$ ;  $P=0.0045$ ) with nurse assistance.

**Conclusion:** This analysis suggests that home health nurse assistance increases adherence to CZP and reduces health care costs in patients with Crohn's disease.

**Keywords:** certolizumab pegol, adherence, cost, nurse assistance, patient support program, Crohn's disease, claims data

## Introduction

Certolizumab pegol (CZP) is a tumor necrosis factor (TNF) alpha antagonist approved for the treatment of moderate-to-severe Crohn's disease refractory to conventional

therapy, in addition to rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. CZP, which is subcutaneously administered, consists of a Fab fragment of a humanized monoclonal antibody that has been PEGylated to remove the Fc portion. It is available in two formulations: a prefilled syringe for self-administration and a lyophilized powder for reconstitution and administration by a health care professional.<sup>1</sup> The efficacy and tolerability of CZP for the treatment of Crohn's disease have been demonstrated in two randomized, placebo-controlled clinical trials, PRECiSE 1<sup>2</sup> and PRECiSE 2,<sup>3</sup> and a 7-year open-label extension study, PRECiSE 3.<sup>4</sup> In developed countries, adherence to therapy for chronic disease states is ~50%.<sup>5</sup> This could have a major impact on patients' quality-of-life and represents a major clinical and economic burden.<sup>5</sup> Furthermore, disrupted or episodic TNF antagonist therapy may lead to antidrug antibody formation and/or reduced effectiveness of therapy.<sup>6</sup> Patient support programs have a positive effect on adherence to therapy in patients with chronic disease.<sup>7</sup> CIMplicity<sup>®</sup> (UCB Pharma, Smyrna, GA, USA), a home health nurse program sponsored by UCB Pharma, provides live nurse support and was available to all patients who were treated with CZP and whose physicians deemed it appropriate. Two options were available to patients in the nurse support program. Patients could receive training on how to self-inject CZP using the prefilled syringe. This usually occurred as part of a one-time visit; however, there were occasions when patients would request a second visit if they were not yet comfortable with self-injection. The second option involved a nurse visiting the patient's home and injecting the patient with the lyophilized powder formulation. These were ongoing visits, once or twice per month, as guided by the physician. Patients were eligible to maintain these visits for as long as they remained on CZP therapy. CZP was administered as instructed in the label (induction phase: 400 mg at weeks 0, 2, and 4; maintenance phase: 400 mg every 4 weeks thereafter) or as guided by the physician.<sup>8</sup> In this analysis, patients who received either of these options (instructions on self-administration by a nurse or nurse-administered injections) are jointly referred to as receiving "home health nurse assistance." Patients who received neither of these options are referred to as being "without nurse assistance." The objective of this analysis, using real-world claims data, was to compare the impact of home health nurse assistance on patients' adherence and persistence with CZP therapy, compared with patients who received no home health nurse assistance, and to measure the impact of the program on health care resource use and costs in this patient population.

## Methods

### Study design and data sources

A retrospective analysis of patient medical and pharmacy claims data from the IQVIA (formerly QuintilesIMS) Real-World Data Adjudicated Claims Database (formerly known as PharMetrics Plus) was conducted using data from January 1, 2007 through September 30, 2015. This database comprises adjudicated claims for more than 150 million unique members across the United States, with a diverse representation of geography, employers, payers, providers, and therapy areas. Data from the home health nurse program on patient enrollment and referrals were linked to the IQVIA Real-World Data Adjudicated Claims Database using patient encryption software that created a de-identified, Health Insurance Portability and Accountability Act (HIPAA)-compliant patient identifier. The unique patient identifier allowed patients enrolled in the nurse assistance program to be anonymously identified and linked to the IQVIA Real-World Data Adjudicated Claims Database. No Institutional Review Board review was required for this retrospective cohort analysis, which used HIPAA-compliant, de-identified patient data.

### Study population

Eligible patients enrolled in the home health program between January 1, 2008 and September 30, 2014 were required to be newly treated (defined as patients without a CZP medical or pharmacy claim in the 12-month period prior to the index date [defined as the first dose of CZP]) with CZP within 60 days before or after enrollment into the program; have a diagnosis of Crohn's disease between the index date and the 12-month pre-index period; and be continuously enrolled in a health plan for 12 months prior to the index date and for  $\geq 60$  days after the index date. Patients were excluded if they had a medical claim for rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis (using International Classification of Diseases, Version 9, Clinical Modification codes) in the pre-index period. Exact matching was performed based on patients' gender and categorical age, with a 1:1 ratio of patients with or without nurse assistance.

### Adherence and persistence

Descriptive study outcomes included adherence and persistence measures in patients with at least 12 months of continuous enrollment in a health plan (ie, with both medical and pharmacy coverage) post-index date. For this analysis, adherence to CZP treatment was determined using the medication possession ratio (MPR) and proportion of days covered (PDC). MPR was defined as the total supply of the

prescription ( $\leq 360$  days) during the study period divided by a fixed observation period (360 days); the time period of 360 days was chosen to avoid having to account for different number of days in a month and leap years. PDC was defined as the total number of days supplied with the medication during the follow-up period divided by the total number of days in the fixed follow-up period (which was 360 days for patients in both cohorts). Adherence was defined as either an MPR or a PDC value of  $\geq 80\%$ . Persistence was defined as the continuous duration of therapy from initiation of CZP treatment to discontinuation of therapy (defined as having a gap of  $\geq 45$  days between end of supply and the next fill).

### Time to treatment discontinuation

A Kaplan–Meier survival analysis with a variable follow-up period was performed to compare time to discontinuation of CZP treatment between patients who received nurse assistance versus those who did not receive assistance. In this survival analysis, patients were censored at time of discontinuation, at disenrollment, or at end of study (whichever occurred first).

### Hospitalization and total health care costs

All-cause hospitalization and total health care costs (both medical and pharmacy costs) were evaluated in patients with 12 months of continuous enrollment in a health plan post-index date. All costs were based on the allowed amount (ie, the contracted reimbursable amount that the health plan agreed to pay to service providers).

### Multivariate regression analyses

In addition to the descriptive analyses, multivariate regression analyses were also performed using a generalized linear model with log link and gamma distribution, adjusting for additional covariates to compare the effect of CZP therapy with and without nurse assistance on costs related to all-cause hospitalization and total health care costs. This model was selected because it accounts for high positive skewness common in health care cost data and provides more precise estimates of the population mean.<sup>9–11</sup> The following baseline covariates were evaluated, in combination with CZP, for their impact on hospitalization and total health care costs: plan type (other vs preferred provider organization); payer type (other vs commercial); comorbid conditions observed during the 12-month pre-index period (ie, atherosclerotic cardiovascular disease, asthma, chronic obstructive pulmonary disease, cancer, hypertension, and diabetes; yes vs no); medication history based on pharmacy claims for oral and injectable drugs and

medical claims for injectable drugs (ie, corticosteroids, TNF antagonists, methotrexate, thiopurines, and anti-anxiety medication; yes vs no); number of prior hospitalizations; and history of surgery related to Crohn's disease based on the 12-month pre-index period (yes vs no).

### Statistical analyses

For the descriptive part of the analysis, categorical measures were expressed as frequency (number of cases [n]) and percentages (%) for each cohort. For continuous variables, findings were presented as the mean, standard deviation (SD), median, and minimum–maximum. Time to discontinuation of treatment between the cohorts was compared using Kaplan–Meier survival curves. All analyses were based on observed data. An independent two-sample *t*-test was used to compare sample means, a Wilcoxon rank sum test to compare medians for continuous variables, and a chi-square test to compare proportions. All tests were conducted assuming a two-tailed test of significance and an alpha level set a priori at 0.05.

For the multivariate analyses, generalized linear models were used to assess the marginal effect of CZP with nurse assistance on costs related to hospitalization, emergency department visits, pharmacy, and total costs compared with the effect of control scenarios (ie, CZP without nurse assistance). Models were run in matched cohorts and adjusted for baseline demographic and clinical covariates as potential confounders.

## Results

### Baseline demographics

The unmatched population consisted of a total of 1,006 patients ( $n=420$  in the cohort with nurse assistance vs  $n=586$  in the cohort without nurse assistance). After matching, each cohort consisted of  $n=417$  patients, with baseline variables being similar between the cohorts (Table 1). In the matched population, the mean (SD) continuous age in the cohort with nurse assistance was 39.1 (12.0) years versus 38.9 (12.4) years in the cohort without nurse assistance ( $P=0.8290$ ). Approximately half of patients in each cohort had a history of previous use of a TNF antagonist (49.9% in the cohort with nurse assistance vs 54.4% in the cohort without nurse assistance). A high proportion of patients in the matched population had previously undergone one or more surgeries related to Crohn's disease (72.7% of those with nurse assistance vs 68.3% without;  $P=0.1717$ ).

### Adherence and persistence

Patients with 12 months of post-index continuous enrollment in a health plan ( $n=552$ ;  $n=276$  in each of the two cohorts)

**Table 1** Baseline demographics and clinical characteristics of the matched population<sup>a</sup>

Characteristics	CZP with nurse assistance (n=417)	CZP without nurse assistance (n=417)	P-value
Age (continuous), mean (SD), years	39.1 (12.0)	38.9 (12.4)	0.8290
Gender, n (%)			
Female	232 (55.6)	232 (55.6)	1.0000
Male	185 (44.4)	185 (44.4)	1.0000
Payer type, n (%)			
Commercial	228 (54.7)	238 (57.1)	0.2558
Self-insured	187 (44.8)	173 (41.5)	
Medicaid	2 (0.5)	6 (1.4)	
Charlson comorbidity index <sup>b</sup> , mean (SD)	0.46 (0.99)	0.40 (0.77)	0.3114
Medication history, n (%)			
Corticosteroids	312 (74.8)	317 (76.0)	0.6876
TNF antagonists	208 (49.9)	227 (54.4)	0.1878
Monoclonal antibodies	2 (0.5)	1 (0.2)	0.5630
Methotrexate	14 (3.4)	24 (5.8)	0.0968
Thiopurines	149 (35.7)	137 (32.9)	0.3814
Anti-anxiety medication	145 (34.8)	136 (32.6)	0.5097
Antidepressants	127 (30.5)	120 (28.8)	0.5955
Hospitalizations, mean (SD)	0.57 (1.07)	0.57 (1.19)	0.9755
History of CD-related surgery, n (%)			
≥1 surgery	303 (72.7)	285 (68.3)	0.1717

**Notes:** <sup>a</sup>Exact matching was performed using gender and categorical age, with a 1:1 ratio of cases to controls. <sup>b</sup>Dartmouth–Manitoba adaptation of the Charlson comorbidity index.<sup>26</sup>

**Abbreviations:** CD, Crohn's disease; CZP, certolizumab pegol; SD, standard deviation; TNF, tumor necrosis factor.

were evaluated for adherence and persistence to CZP therapy. The mean and median PDC values were higher with nurse assistance than without nurse assistance (Table 2; Figure 1). A higher percentage of patients with nurse assistance had a PDC value  $\geq 80\%$  than patients without nurse assistance (40.2% vs 33.7%;  $P=0.1125$ ), though this trend was not statistically significant. Similarly, both the mean and median MPR values were higher in the nurse assistance cohort than in the cohort without nurse assistance (Table 2; Figure 1). A higher percentage of patients who received nurse assistance

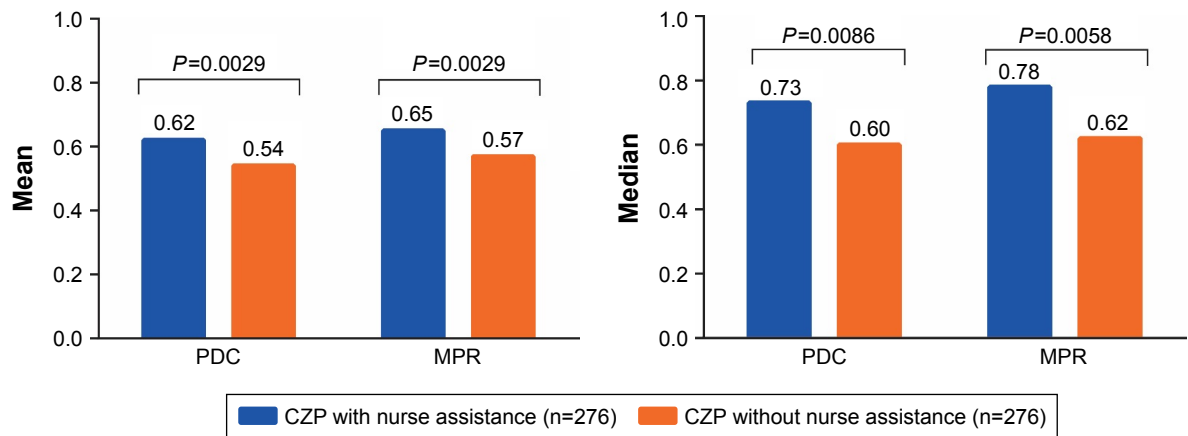
had an MPR  $\geq 80\%$  than those in the cohort without nurse assistance (45.3% vs 37.3%;  $P=0.0572$ ), though this trend was not statistically significant.

Mean (SD) duration of persistence with treatment was significantly higher in patients with nurse assistance than in those without (240.8  $\pm$  132.9] days vs 215.6  $\pm$  139.4] days;  $P=0.0304$ ; Table 2). The percentage of patients who were persistent with treatment was significantly higher in patients with nurse assistance than in those without (50.4% vs 42.0%;  $P=0.0496$ ; Table 2).

**Table 2** Adherence and persistence with certolizumab pegol therapy with and without nurse assistance

Compliance parameter	CZP with nurse assistance (n=276)	CZP without nurse assistance (n=276)	P-value
PDC			
Mean (SD)	0.62 (0.29)	0.54 (0.32)	0.0029
Median (min–max)	0.73 (0.04–1.00)	0.60 (0.04–1.00)	0.0086
MPR			
Mean (SD)	0.65 (0.30)	0.57 (0.33)	0.0029
Median (min–max)	0.78 (0.04–1.00)	0.62 (0.04–1.00)	0.0058
Adherence to treatment, n (%)			
Patients with PDC $\geq 80\%$	111 (40.2)	93 (33.7)	0.1125
Patients with MPR $\geq 80\%$	125 (45.3)	103 (37.3)	0.0572
Persistence with treatment, n (%)	139 (50.4)	116 (42.0)	0.0496
Duration of persistence (days)			
Mean (SD)	240.8 (132.9)	215.6 (139.4)	0.0304
Median (min–max)	360 (14–360)	223.5 (14–360)	0.0200

**Abbreviations:** CZP, certolizumab pegol; max, maximum; min, minimum; MPR, medication possession ratio; PDC, proportion of days covered; SD, standard deviation.



**Figure 1** Adherence to CZP therapy using the PDC and MPR measures with and without nurse assistance.  
**Abbreviations:** CZP, certolizumab pegol; MPR, medication possession ratio; PDC, proportion of days covered.

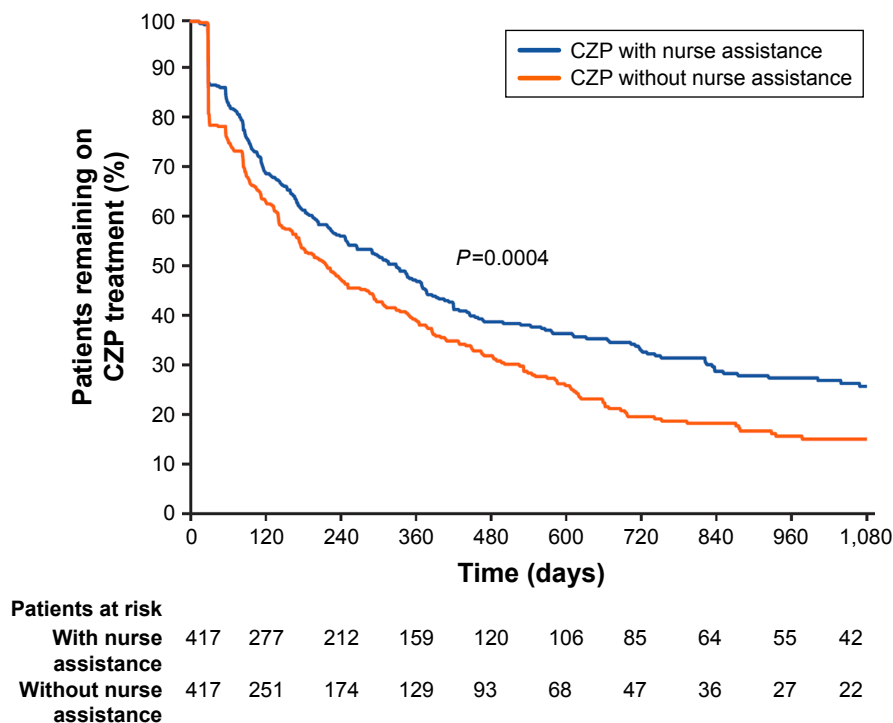
### Time to discontinuation

Results from the Kaplan–Meier analysis revealed that time to discontinuation of treatment was significantly longer in patients who received CZP with nurse assistance than those without over a 3-year period ( $P=0.0004$ ; Figure 2).

### Hospitalization and total health care costs

Patients were also evaluated for the cost of hospitalization and total health care costs. Among all patients, the mean

hospitalization cost per patient with nurse assistance was US\$5,538 lower compared with patients without nurse assistance (Table 3). As the majority of patients did not experience hospitalization during follow-up, the median costs were US\$0 for both cohorts among these patients. Among patients with at least one hospitalization, the mean hospitalization cost per patient for those with nurse assistance was US\$4,174 lower than for those without nurse assistance, with the median cost of hospitalization per patient being US\$3,552 lower with



**Figure 2** Kaplan–Meier curves comparing time to discontinuation of treatment.  
**Note:** Data are presented up to 3 years of follow-up; patients were censored at the end of the 3 years.  
**Abbreviation:** CZP, certolizumab pegol.

**Table 3** The effect of nurse assistance on hospitalizations and total health care costs

Outcome measure	CZP with nurse assistance (n=276)	CZP without nurse assistance (n=276)
Total hospitalizations	151	203
Hospitalizations per patient		
Mean (SD)	0.55 (1.2)	0.74 (1.3)
Median	0.00	0.00
Min, max	0.00, 10.0	0.00, 10.0
Total cost of hospitalizations (US\$)	2,776,751	4,305,173
Cost per patient (US\$)		
Mean (SD)	10,060.69 (43,935.1)	15,598.45 (43,650.0)
Median	0.00	0.00
Min, max	0.00, 646,048.41	0.00, 603,299.28
Patients with at least one hospitalization	77 (27.9)	107 (38.8)
Hospitalization per patient		
Mean (SD)	1.96 (1.6)	1.90 (1.5)
Median	1.00	1.00
Min, max	1.00, 10.00	1.00, 10.00
Length of stay		
Mean (SD)	11.70 (17.5)	10.95 (13.2)
Median	6.00	7.00
Min, max	1.00, 127.00	2.00, 95.00
Total cost of hospitalizations per patient (US\$)		
Mean (SD)	36,061.70 (77,683.00)	40,235.26 (62,788.80)
Median	21,448.79	25,001.22
Min, max	540.35, 646,048.41	2,618.98, 603,299.28
Total health care cost (US\$)	14,716,874.59	17,147,109.00
Total health care cost per patient (US\$)		
Mean (SD)	53,322.01 (56,509.47)	62,127.21 (75,439.05)
Median	40,929.39	44,445.47
Min, max	6,346.47, 746,142.94	1,824.45, 863,539.00

**Abbreviations:** CZP, certolizumab pegol; max, maximum; min, minimum; SD, standard deviation.

nurse assistance than without (Table 3). The median total health care cost per patient with nurse assistance was also lower (US\$40,929 vs US\$44,445; Table 3).

Results from the multivariate regression analysis revealed a significant reduction in all-cause hospitalization costs (−55.8%;  $P=0.0026$ ; Table 4) and total health care costs (−14.3%;  $P=0.0045$ ; Table 5) with nurse assistance. This analysis also revealed a significant increase in total health care costs with previous use of other TNF antagonists (27.9%;  $P<0.0001$ ) and concomitant diabetes (43.9%;  $P=0.0119$ ; Table 5). Furthermore, previous use of anti-anxiety medication was also significantly associated with increased all-cause hospitalization costs (92.3%;  $P=0.0344$ ; Table 4) and total health care costs (24.7%;  $P=0.0002$ ; Table 5).

## Discussion

Our findings show that patients who received CZP with the assistance of a home health nurse for the treatment of their Crohn's disease had better adherence and persistence with CZP, and remained on treatment significantly longer

over a 3-year period than patients without nurse assistance ( $P=0.0004$ ).

Nonadherence to TNF antagonist therapy in patients with inflammatory bowel disease (IBD) is a serious problem. According to the World Health Organization, adherence to treatment is the primary determinant to the success of a medical treatment, with poor adherence resulting in reduced effectiveness of therapy.<sup>5</sup> Reasons why patients fail to adhere to their prescribed treatment are many and may include patients' inability to self-administer their treatment.<sup>12</sup> Supplementary care may facilitate improved adherence to treatment and thereby reduce costs.

The home health nurse program was designed to assist patients with the administration of their subcutaneously administered CZP injections, either by providing instructions on self-administration or by nurse-administered injections. In this analysis, the adherence rate to CZP therapy without nurse assistance was 33.7%, and in the cohort with nurse assistance it was 40.2%. Persistence in the cohort without nurse assistance was 42.0% and persistence in the cohort with

**Table 4** Multivariate regression analysis evaluating the impact of certolizumab pegol in combination with other covariates on hospitalization costs

Variable	Parameter coefficient	Exp (coefficient)	% change reduction/increase	Standard error	P-value
<b>CZP with nurse assistance (ref: without)</b>	-0.817	0.442	-55.8	0.272	0.0026
Plan type (other vs PPO)	0.414	1.513	51.3	0.417	0.3211
Payer type (other vs commercial)	0.418	1.519	51.9	0.288	0.1461
Geographic region (ref: South)					
Northeast	-0.160	0.852	-14.8	0.376	0.6704
Midwest	0.285	1.329	32.9	0.335	0.3956
West	-0.896	0.408	-59.2	0.717	0.2114
Comorbid condition (yes vs no)					
ASCVD	-0.416	0.660	-34.0	0.609	0.4949
Asthma	-0.330	0.719	-28.1	0.498	0.5079
COPD	0.366	1.442	44.2	0.770	0.6343
Cancer	0.145	1.157	15.7	0.434	0.7374
Hypertension	-0.186	0.830	-17.0	0.433	0.6675
Diabetes	1.089	2.970	197.0	0.851	0.2005
Medication history (yes vs no)					
Corticosteroids	0.336	1.400	40.0	0.332	0.3106
TNF antagonists	0.436	1.546	54.6	0.274	0.1113
Methotrexate	0.423	1.526	52.6	0.745	0.5702
Thiopurines	-0.168	0.846	-15.4	0.308	0.5860
Anti-anxiety medication	0.654	1.923	92.3	0.309	0.0344
Number of prior hospitalizations	0.371	1.450	45.0	0.137	0.0067
History of surgery (yes vs no)					
Patients with $\geq 1$ surgery	-0.232	0.793	20.7	0.299	0.4373

**Abbreviations:** ASCVD, atherosclerotic cardiovascular disease; COPD, chronic obstructive pulmonary disease; CZP, certolizumab pegol; Exp, exponentiated; PPO, preferred provider organization; ref, reference; TNF, tumor necrosis factor.

**Table 5** Multivariate regression analysis evaluating the impact of certolizumab pegol in combination with other covariates on total health care costs

Variable	Parameter coefficient	Exp (coefficient)	% change reduction/increase	Standard error	P-value
<b>CZP with nurse activity (ref: without)</b>	-0.154	0.857	-14.3	0.054	0.0045
Plan type (other vs PPO)	0.051	1.053	5.3	0.085	0.5443
Payer type (other vs commercial)	0.059	1.061	6.1	0.056	0.2884
Geographic region (ref: South)					
Northeast	-0.085	0.919	-8.1	0.074	0.2508
Midwest	0.141	1.152	15.2	0.067	0.0347
West	0.077	1.080	8.0	0.143	0.5909
Comorbid condition (yes vs no)					
ASCVD	0.152	1.164	16.4	0.110	0.1699
Asthma	-0.083	0.921	-7.9	0.099	0.4040
COPD	0.069	1.072	7.2	0.155	0.6559
Cancer	0.095	1.100	10.0	0.083	0.2536
Hypertension	-0.126	0.881	-11.9	0.078	0.1055
Diabetes	0.364	1.439	43.9	0.145	0.0119
Medication history (yes vs no)					
Corticosteroids	0.031	1.031	3.1	0.065	0.6382
TNF antagonists	0.246	1.279	27.9	0.055	<0.0001
Methotrexate	0.014	1.014	1.4	0.140	0.9191
Thiopurines	-0.095	0.910	-9.0	0.058	0.0995
Anti-anxiety medication	0.221	1.247	24.7	0.060	0.0002
Number of prior hospitalizations	0.109	1.116	11.6	0.025	<0.0001
History of surgery (yes vs no)					
Patients with $\geq 1$ surgery	-0.037	0.964	-3.6	0.061	0.5447

**Abbreviations:** ASCVD, atherosclerotic cardiovascular disease; COPD, chronic obstructive pulmonary disease; CZP, certolizumab pegol; Exp, exponentiated; PPO, preferred provider organization; ref, reference; TNF, tumor necrosis factor.

nurse assistance was 50.4%. It is difficult to compare these rates with the adherence rates reported for other TNF antagonists (notably infliximab [Remicade®; Janssen Biotech, Inc, Titusville, NJ, USA] and adalimumab [Humira®; AbbVie, North Chicago, IL, USA]) in the literature, as the latter rates vary widely (from 37% to 96.0%).<sup>13–15</sup> This is most likely a result of the different definitions of adherence, different modes of drug administration, and importantly, shorter study durations (12–20 months rather than 3 years, as reported in this study). Furthermore, the setting is likely to play a role: in a single-institution, tightly managed IBD infusion center, the nonadherence rate for infliximab was 34.3% at 1 year,<sup>13</sup> whereas a higher nonadherence rate of 50% was reported for infliximab, based on claims data from five local health units.<sup>15</sup> Finally, it should be noted that infliximab was used as first-line therapy in the cited studies,<sup>13–15</sup> whereas certolizumab pegol is used as second- or third-line therapy in clinical practice, which is likely to affect the adherence rate.

Another factor that may affect adherence and/or persistence is changing insurance providers over time, for example, as a result of changing employment, with either intermittent loss of medication coverage, loss of medication coverage in the new insurance plan, or inability to obtain new insurance altogether.<sup>16</sup> Because gaps in insurance coverage may influence patients' follow-up, which in turn affects adherence/persistence, our analysis used a fixed follow-up period to evaluate adherence/persistence outcome measures. In this study, approximately one-third of patients were without continuous enrollment in a health plan over 12 months and could not be evaluated for these outcome measures.

The economic burden of Crohn's disease on health care systems is considerable.<sup>17</sup> The majority of patients with Crohn's disease undergo surgery at some stage in their lives; in a study of 615 patients newly diagnosed with Crohn's disease, 74% had undergone surgery after a 7-year follow-up period.<sup>18</sup> Disease remission due to TNF antagonist therapy led to reductions in hospitalizations and surgeries related to Crohn's disease.<sup>19</sup> The longer patients remained in remission, the lower the rates of hospitalizations and surgeries related to Crohn's disease ( $P < 0.01$  and  $P < 0.05$ , respectively).<sup>19</sup> Results of a recent systematic review and meta-analysis revealed that TNF antagonists significantly reduced hospitalization (odds ratio [OR]: 0.46, 95% confidence interval [CI]: 0.36–0.60) and surgery (OR: 0.23, 95% CI: 0.13–0.42) compared with placebo.<sup>20</sup> Furthermore, a systematic review evaluating patient support programs across 64 studies identified a trend toward a reduction in hospitalization when patient support programs were available.<sup>7</sup> This analysis suggests that administration of

CZP with home health nurse assistance leads to significant reductions in hospitalization and total health care costs, as compared with simply prescribing CZP.

Our multivariate regression analysis identified diabetes and use of anti-anxiety medication as factors that were shown to significantly increase total health care costs. This is supported by findings from a large United States patient claims database study that identified an association between higher health plan-covered costs and the presence of comorbid conditions (including diabetes and a psychiatric diagnosis) in patients with Crohn's disease.<sup>20</sup> This could suggest that assistance by a home health nurse with CZP administration may be a particularly valuable approach in patients with Crohn's disease who have comorbid conditions, notably anxiety (which is common in patients with IBD).<sup>21–23</sup> A number of studies have reported a link between anxiety and increased IBD-related hospitalizations or surgery, thus affecting health care costs.<sup>24,25</sup> It should be noted that use of antidepressants was not evaluated in our multivariate analysis because of the observed collinearity between antidepressant and anti-anxiety medication use during a previously conducted bivariate analysis (data not shown), so no direct conclusions can be drawn from our analysis with regard to whether antidepressant use is significantly associated with total health care costs and/or hospitalization costs. Conducting subgroup analyses to investigate whether the home health nurse program was of particular benefit in patients with anxiety or other comorbid disease was not possible in our analysis, primarily because of low sample sizes of the subset of patients and a lack of power to detect significant differences. Larger studies are warranted to investigate this further.

Total health care costs were also significantly increased in patients with a history of TNF antagonist use, presumably because these patients had Crohn's disease that was more difficult to treat, resulting in increased use of health care resources over time.

## Limitations

Limitations of this study include those that apply to any observational study, notably the absence of a randomization process, and a self-selection bias arising from patients participating in the program potentially having other characteristics than those in non-participating patients, that is, characteristics that may affect their adherence/persistence and/or use of health care resources (eg, a greater interest in improving their health). Another limitation that is common for studies utilizing a claims database is the absence of clinical severity or patient-reported outcomes, which could



not be derived from health insurance claims in our analysis. However, we mitigated this limitation by including covariates (comorbid conditions, medication history, number of prior hospitalizations, and history of surgery) in the multiple regression analysis to adjust for baseline disease severity between the two cohorts.

## Conclusion

There have been few published studies that evaluate nurse support and its impact on compliance measures and health care costs. This analysis is the first of its kind in assessing CZP use in a community setting comparable to the experience of many patients in clinical practice. It suggests that home health nurse assistance increases adherence to and/or persistence in CZP therapy. Patients receiving nurse assistance remain on CZP treatment significantly longer than those without it. The home health nurse program provides important, consistent, scheduled induction and maintenance dosing. Our findings suggest that home health nurse assistance is associated with significant reductions in hospitalization costs and total health care costs compared with CZP therapy without nurse assistance, thereby potentially reducing the economic burden of Crohn's disease.

## Acknowledgments

This study was sponsored by UCB Pharma. The authors thank the patients and their caregivers who participated in this study, and Fiona Nitsche, PhD, CMPP, of Evidence Scientific Solutions for editorial assistance, which was funded by UCB Pharma. An abstract of this paper was presented at the 29th AMCP Managed Care & Specialty Pharmacy Annual Meeting 2017 as a poster presentation with interim findings. The poster's abstract was published in a "Meeting Abstracts" supplement in the *Journal of Managed Care & Specialty Pharmacy*. 2017;23(3-a Suppl):S82 (abstract K6). DOI: <https://doi.org/10.18553/jmcp.2017.23.3-a.s1>. A second abstract of this paper was presented at the Crohn's & Colitis Foundation of America – Advances in Inflammatory Bowel Diseases Annual Meeting 2016 as a poster presentation with interim findings. The poster's abstract was published in *Inflammatory Bowel Diseases*. 2017;23:S26 (abstract P-065). Available from: <http://journals.lww.com/ibdjournal/pages/contributorindex.aspx?filter=J&year=2017&issue=02001>.

## Author contributions

SJ, DCW, RL, CB, AS, and DAS contributed to the study concept and design. Data were collated by SJ, CB, and AS.

All authors contributed toward data analysis, drafting and critically revising the paper and agree to be accountable for all aspects of the work.

## Disclosure

Douglas C Wolf reports grants, personal fees, and nonfinancial support from the study sponsor outside the submitted work; Srihari Jaganathan was an employee of the study sponsor during the conduct of the study. Chakkarin Burudpakdee and Arpamas Seetasith were contracted by the study sponsor to conduct this study. Robert Low, Edward Lee, Jay Gucky, and Mohamed Yassine were employees of the study sponsor during the study. David A Schwartz reports grants and personal fees from the study sponsor outside of the submitted work. The authors report no other conflicts of interest in this work.

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