

Impact of Targeted Therapy on Healthcare Resource Utilization Among Patients with Atopic Dermatitis

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Abstract

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Background: Atopic dermatitis (AD), the most prevalent inflammatory dermatologic condition, manifests as dry skin, erythema, and rashes. Although there have been many approvals of targeted therapies, no studies have quantified their impact on healthcare resource utilization (HCRU) and related costs among patients diagnosed with AD.

Objective: To assess the impact of targeted therapy on intensive HCRU (inpatient and emergency department [ED] visits) and costs between those who have and have not been prescribed a targeted therapy among patients with AD in the US.

Methods: Retrospective cohort study using MarketScan Commercial claims database. Subjects with AD who were prescribed and not prescribed a targeted therapy between January 1st, 2017 and December 31st, 2022 were identified. A difference-in-differences analysis was used to assess the effect of targeted therapy on HCRU and costs among AD patients. The study period was from January 1st, 2012, through December 31st, 2023.

Results: We identified 157,966 individuals with AD, 148,646 of whom were not treated with a targeted therapy, while 9,320 received such treatment. Those who were prescribed a targeted therapy led to a 0.016 (95% CI: -0.021, -0.010; p-value < 0.01) decrease in the average proportion of inpatient visits and 0.017 (95% CI: -0.025, -0.008; p-value < 0.01) decrease in the average proportion of ED visits compared to those not on a targeted therapy.

On average, targeted therapy was associated with an increase of \$25,219 (95% CI: 24,759, 25,679; p-value < 0.01) in total cost and \$26,061 (95% CI: 25,734, 26,387; p-value < 0.01) in drug cost, along with a \$909 (95% CI: -1,106, -711; p-value < 0.01) decrease in outpatient cost and a \$251 (95% CI: -382, -119; p-value < 0.01) decrease in inpatient cost compared to those not on a targeted therapy.

Conclusion: We found a significant decrease in the average proportion of AD patients requiring inpatient or ED visits when treated with targeted therapy compared to those not on such therapy, suggesting that the targeted therapies may be effective in reducing intensive healthcare resource use. Further research should be conducted to understand how adherence to targeted therapy and treatment history can impact HCRU and cost.

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1. Introduction

Atopic dermatitis (AD) is the most prevalent inflammatory dermatologic disorder, affecting approximately 10% to 30% of children and 2% to 10% of adults.¹ Its common manifestations include pruritus, dry skin, rashes, and erythema.¹ If left untreated, AD significantly impacts patients' quality of life, leading to sleep disturbances, decreased productivity at school or work, and adverse effects on mental health.² The chronic nature and increasing prevalence of AD contribute to a substantial economic burden in the United States (US). In 2015, the estimated annual cost of AD in the US amounted to approximately \$5.3 billion.³ Furthermore, a study revealed a notable rise in total emergency department costs from \$265 million in 2006 to \$642 million in 2012.⁴

Until 2017, the primary systemic treatment option for moderate-to-severe AD were conventional immunosuppressants.⁵ Significant progress has been made since then with the FDA approval of biologics and small molecules such as dupixent, upadacitinib, and tralokinumab for treating more severe forms of AD.⁶ While the pivotal trials for these medications primarily emphasized improvement in disease severity through their primary endpoints, they also highlighted the limited research on other outcomes that are typically associated with higher costs, such as intensive HCRU including inpatient and ED visits, particularly in the real-world setting.^{7,8} Assessing the broader impact of targeted therapy on clinical outcomes and intensive all-cause HCRU is critical to understand the real-world impact of the new AD therapy and its economic implications.

Hence, in this study, we aim to investigate the impact of targeted therapy on intensive all-cause HCRU and costs among individuals who are diagnosed with AD.

2.Methods

2.1 Study Design and Data Sources

We conducted an observational retrospective cohort study using the Merative[®] MarketScan[®] commercial database, specifically the Commercial Claims and Encounters (CCAE) database, from January 1st, 2012, through December 31st, 2023. This database contains medical and drug claims data for approximately 300 million individuals, including their spouses and dependents, who are enrolled in over 350 employer-sponsored private health insurance plans.⁹ These plans are offered by more than 40 different health insurance providers.⁹

2.2 Study Population

We identified patients with AD by having at least 1 inpatient or 2 outpatient AD diagnosis in any billing position during the enrollment period, from January 1st, 2017, through December 31st, 2022 ([Figure 7.1](#)).¹⁰ The International Classification of Diseases, Tenth Revision (ICD-10-CM) diagnosis codes of L20.% were used to identify those with AD, where “%” acts as a wildcard to specify different subcategories of the condition.

We defined the treatment group as individuals diagnosed with AD and prescribed a targeted therapy (defined below) during the enrollment period. Controls are those diagnosed with AD but not prescribed a targeted therapy. A targeted therapy is defined as an advanced therapy used to treat moderate-severe forms of AD including abrocitinib, baricitinib, dupilumab, tralokinumab, and upadacitinib that was FDA approved starting from 2017 ([App. A](#)).¹¹ The index date for the treated group is defined as the date of first prescription of a targeted therapy. The control group’s index date will be 1 year after their continuous enrollment begins during the study period to ensure comparable follow-up duration with the treated group. The enrollment period was implemented to allow for a minimum of 1 year of follow-up before and after the index date.

Patients were required to meet the following additional inclusion criteria: (1) ≥ 18 years old for the entire study period and (2) continuous insurance enrollment for ≥ 12 months prior to and after the index date for a minimum total of 24 months within the study

period. For patients who have > 1 continuous enrollment period that satisfy the inclusion criteria, we kept only the first instance.

2.3 Study Outcomes

The primary outcomes of interest were two indicators for severe AD: (1) all-cause inpatient visits and (2) all-cause ED visits in a given year. The secondary outcomes of interest were the all-cause total, drug, inpatient, and outpatient costs each year. Total cost was defined as the sum of inpatient, outpatient, and drug costs. All costs were adjusted using the medical care component of the consumer price index to reflect values in 2023 dollars.¹²

2.4 Statistical Analysis

We summarized the baseline patient characteristics using mean and standard deviation (SD) for continuous variables and percentages for categorical variables. These include patient's sex, age, geographic region, and targeted therapy prescribed assessed on index date. The Charlson Comorbidity Index (CCI) was calculated using comorbidity, an R package, which uses ICD-10 diagnosis codes on medical claims collected during the 12-month pre-index period.^{13–16} We assessed the differences in baseline characteristics between the two groups by using the Mann Whitney test for age and chi-square test for sex, region, and CCI.

We employed difference-in-differences (DiD) analysis to estimate the effect of targeted therapy on HCRU outcomes due to its ability to control for all unobserved time-invariant confounders and all time-varying confounders common to both treatment and control groups. We compared changes in outcomes before and after the prescription of the first targeted therapy between the treatment and control groups.

[Appendix B](#) shows the full DiD regression model. In the equation, the coefficient of interest (the DiD estimator) was the coefficient on an interaction term between the treatment group indicator and the post-period indicator. The DiD estimator for the primary outcomes were estimated as the difference in the change in the average proportion of all-cause inpatient or ED visits between the periods before and after the index date, and between those who did and did not receive a prescription of a targeted

therapy. Cost outcome estimators were calculated similarly, covering total costs, inpatient costs, outpatient costs, and drug costs. Negative costs were set to \$0, and all cost values were winsorized to the 99th percentile to mitigate the influence of outliers. We restricted the number of person-years per subject to a maximum of 6 years before the index date and 4 years after.

We adjusted for person indicators, calendar year-month indicators and time-varying comorbidities using the CCI. Including these indicators in the model allows us to control for individual-level time-invariant confounders and systemic changes over time common to everyone such as changes in healthcare practices or seasonality in disease progression. Standard errors were clustered at the individual patient level.

In DiD method, the parallel trends assumption posits that in the absence of treatment, the treated and control groups would have followed similar trends over time. We investigated the parallel trends assumption of our study through visual inspection of the mean outcomes for both groups graphed over time.

All the statistical analyses results were performed using R Statistical Software (v4.2.2; R Core Team 2024).

3. Results

3.1 Baseline Characteristics

We identified a total of 157,966 individuals diagnosed with AD in the MarketScan database between January 1, 2017, and December 31, 2022, who met the eligibility criteria. These included 148,646 controls and 9,320 individuals treated with targeted therapy ([Figure 7.2](#)), 99% of whom were prescribed dupilumab ([Table 6.1](#)). In total, we observed 796,254 person-years, where the control group contributed more person-years across all the years included in the analysis compared to the treated group ([App. C](#)).

The mean [SD] age at baseline was 41.1 [13.6] years for the treated group and 41.6 [14.1] years for the controls, with a statistically significant difference likely due to large sample size ($p = 0.008$) ([Table 6.1](#)). The treated group had a higher proportion of males

than controls (42% vs. 34%, $p < 0.001$). The treated group had more individuals from the south, while the control group had more from the northeast and west ($p < 0.001$). The control group had a higher proportion of individuals with a CCI score of 0 (46% vs. 57%) and a lower proportion with a CCI score of ≥ 3 (13% vs 10%, p -value < 0.001).

3.2 Primary Outcomes

The parallel trends graph ([App. D](#)) for both inpatient ([Panel A](#)) and ED ([Panel B](#)) visits generally support the assumption of parallel trends. The ED visit graph shows a stronger adherence to the assumption compared to the graph for the inpatient visit, which exhibits some noise in the pre-period.

Among AD patients, being prescribed a targeted therapy led to an additional 1.6 percentage point (95% CI: -0.021, -0.010; p -value < 0.01) decrease in the average proportion of inpatient visits and 1.7 percentage point (95% CI: -0.025, -0.008; p -value < 0.01) decrease in the average proportion of ED visits between pre- and post-period compared to those not on a targeted therapy ([Table 6.2](#)).

3.3 Secondary Outcomes

The parallel trends graph for the secondary outcomes ([App. E](#)), including total cost ([Panel A](#)), drug cost ([Panel B](#)), outpatient cost ([Panel C](#)), and inpatient cost ([Panel D](#)), clearly shows a violation of the parallel trend assumption. Therefore, we can only infer an association between the use of targeted therapy and cost, rather than a causal relationship.

On average, targeted therapy was associated with a \$25,219 (95% CI: 24,759, 25,679; p -value < 0.01) increase in total cost and \$26,061 (95% CI: 25,734, 26,387; p -value < 0.01) increase in drug cost compared to those not on a targeted therapy.

Targeted therapy was also associated with an additional \$909 (95% CI: -1,106, -711; p -value < 0.01) decrease in mean outpatient cost and \$251 (95% CI: -382, -119; p -value < 0.01) decrease in inpatient cost when compared to those not on a targeted therapy ([Table 6.3](#)).

4. Discussion

We conducted a retrospective cohort study using MarketScan claims data to quantify the causal effects of targeted therapy on intensive HCRU and costs among those diagnosed with AD. On average, targeted therapy led to a 1.6 percentage point decrease in proportion of inpatient visits and 1.7 percentage point decrease in the proportion of ED visits compared to those not on a targeted therapy. In relative terms, targeted therapy resulted in a 23% reduction in inpatient visits and a 10% reduction in ED visits compared to the control mean of the study period. Targeted therapies have been demonstrated to improve symptoms associated with AD such as skin clearance, reduction in itchiness, and decreased frequency of flares. The resulting improvement in symptom management can lead to a decreased likelihood of requiring an ED or inpatient visit. Numerous studies have also shown that targeted therapy can effectively manage AD symptoms which can lead to a significant improvement in a patient's quality of life by enhancing sleep patterns and reducing anxiety and depression, perhaps further reducing the likelihood of related hospitalizations and ED visits.^{17,18}

Targeted therapy was associated with an additional \$25,219 increase in mean total costs and \$26,061 increase in mean drug costs, while also contributing to an additional \$909 decrease in mean outpatient costs and \$251 decrease in mean inpatient costs. Despite a decrease in intensive HCRU, there was a significant rise in total costs, mainly driven by higher drug costs likely due to the high prices of targeted therapies. A recent study in 2021 further highlighted the substantial cost of targeted therapies, revealing out of an average of \$2,381 spent on all-cause healthcare spending for adults with AD, \$1,997 (84%) was attributed to outpatient pharmacy claims, with 72% of that amount being spent on targeted therapies.¹⁹ Compared to the control mean of the study period, targeted therapy was associated with a 280% increase in mean total cost, 1,123% increase in mean drug costs. However, there was a reduction in mean outpatient and inpatient costs, 17.8% and 24%, respectively. These outcomes illustrate the real-world impact of targeted therapy in reducing intensive HCRU, though they are accompanied by increased cost.

To our knowledge, this is the first real-world study to investigate the impact of targeted therapy on HCRU and cost among individuals diagnosed with AD. The reduction in inpatient and ED visits follows in line with the reduction in outpatient and inpatient costs. If we extrapolate these results to Kwa's study on the financial burden of ED visits on AD, a 10% reduction in ED visits could translate to a reduction in total ED cost of approximately \$64 million in 2012 dollars.⁴ These results may be utilized in future models that evaluate the true value of targeted therapy in treating AD patients. It is essential to acknowledge that although our study reflects the current treatment landscape for moderate-severe AD, dupilumab made up most of the targeted therapy population.

The findings from this study should be interpreted with caution for certain limitations. This study assessed the impact of targeted therapy on AD patients with employer-sponsored private health insurance. Consequently, the results may not be generalizable to the broader population, specifically to those not on an employer sponsored insurance plan, such as those on Medicare. Additionally, we did not capture patient variability in therapy duration due to switches and discontinuations for adverse events or effectiveness issues. Relatedly, the study's shortened timeframe may not accurately capture the long-term impacts of targeted therapy on intensive HCRU and cost.

5. Conclusion

AD patients who were prescribed a targeted therapy were found to have a significantly lower probability of visiting the ED or having an inpatient admission compared to those not on a targeted therapy. Correspondingly, the prescription of a targeted therapy was associated with a reduction in the mean outpatient and inpatient costs, but an increase in the mean total and drug costs. The result of this analysis showcases the beneficial impact of targeted therapy, but at a cost. Further studies should be conducted to assess the AD population at a more granular level to better understand the effects of targeted therapy in the population.

6. Tables

6.1 Baseline Characteristics

Characteristic	Treated, N = 9,320	Untreated, N = 148,646	p-value[†]
Age - mean (SD)	41.13 (14.14)	41.58 (13.57)	0.008
Male - n (%)	3,912 (42%)	51,165 (34%)	<0.001
Region - n (%)			<0.001
Northeast	1,185 (13%)	24,023 (16%)	
North Central	1,232 (13%)	20,012 (13%)	
South	3,803 (41%)	56,079 (38%)	
West	959 (10%)	19,008 (13%)	
Unknown	2,141 (23%)	29,524 (20%)	
Comorbidity Index - n (%)			<0.001
0	4,258 (46%)	85,301 (57%)	
1	3,027 (32%)	34,951 (24%)	
2	833 (8.9%)	13,593 (9.1%)	
≥3	1,202 (13%)	14,801 (10.0%)	
Targeted Therapy - n (%)			
abrocitinib	-	-	
baricitinib	8 (<0.1%)	-	
dupilumab	9,247 (99%)	-	
tralokinumab	1 (<0.1%)	-	
upadacitinib	64 (0.7%)	-	
no treatment	-	148,646 (100%)	

[†] Wilcoxon rank sum test; Pearson's Chi-squared test

6.2 Impact of Targeted Therapy on HCRU

Impact of Targeted Therapy on HCRU		
	<i>Dependent variable:</i>	
	Inpatient Visit (1)	ED Visit (2)
Treatment Effect	-0.016*** (-0.021, -0.010)	-0.017*** (-0.025, -0.008)
Control Mean	0.069	0.166
n (person-years)	796254	796254

Note: * p<0.1; ** p<0.05; *** p<0.01

Notes: Each column reports results from a separate linear regression that controls for person-indicators, calendar year-month, and CCI. Coefficients on the interaction between an indicator for the treatment group and an indicator for the post period are reported, with 95% confidence intervals in parentheses. Standard errors are clustered at the individual patient level. *p<0.1; **p<0.05; ***p<0.01.

6.3 Impact of Targeted Therapy on Costs

Impact of Targeted Therapy on Cost				
	<i>Dependent variable:</i>			
	Total Cost (1)	Drug Cost (2)	Outpatient Cost (3)	Inpatient Cost (4)
Treatment Effect	25,219.290*** (24,759.230, 25,679.340)	26,061.260*** (25,734.560, 26,387.960)	-909.245*** (-1,106.970, -711.520)	-251.006*** (-382.273, -119.739)
Control Mean	9012.696	2318.823	5097.342	1026.238
n (person-years)	796254	796254	796254	796254

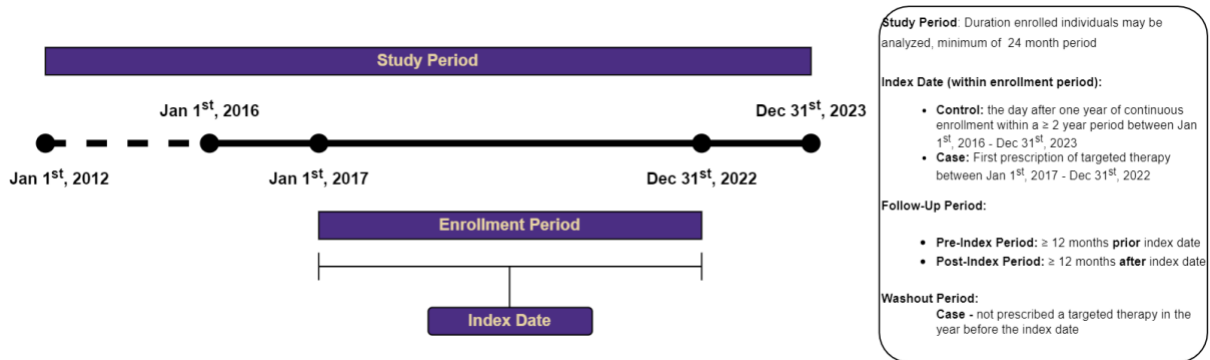
Note: Cost were winsorized at the 99th percentile * p<0.1; ** p<0.05; *** p<0.01

Notes: Each column reports results from a separate linear regression that controls for person-indicators, calendar year-month, and CCI. All costs were winsorized at the 99th percentile.

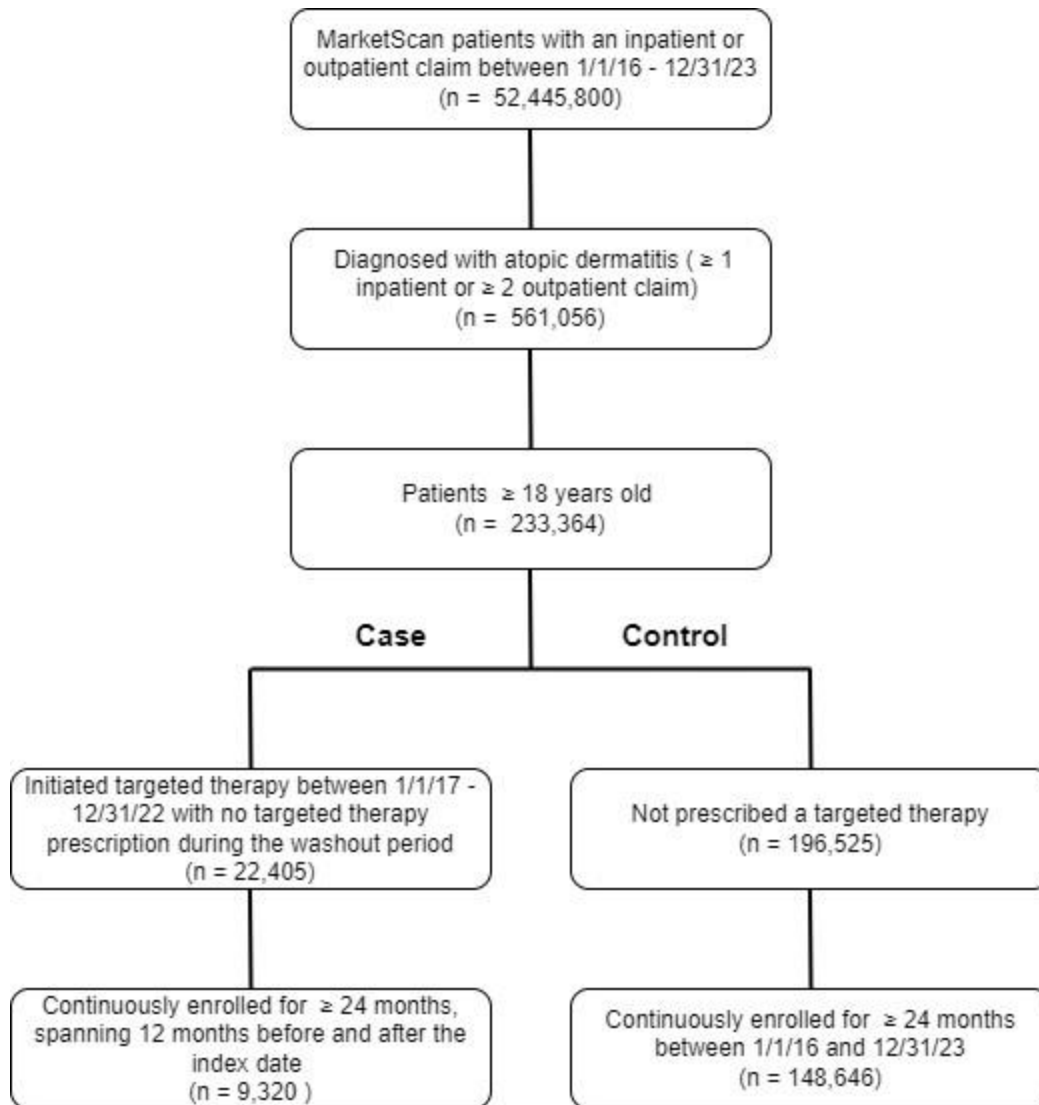
Coefficients on the interaction between an indicator for the treatment group and an indicator for the post period are reported, with 95% confidence intervals in parentheses. Standard errors are clustered at the individual patient level. * $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$.

7. Figures

7.1 Study Design



7.2 Cohort Selection and Attrition Diagram



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9. Appendices

9.1 Appendix A – Drug ICD-10 Codes

Drug	ICD-10 Codes
Abrocitinib	00069023530, 00069043530, 00069033530, 63539023614, 63539033614, 63539043614
Baricitinib	00002418230, 00002418261, 00002447930, 00002473230, 00002447961
Dupilumab	00024591401, 00024591502, 00024591500, 00024591601, 00024591801, 00024591901, 00024591902, 00024591900, 00024591920, 00024591100, 00024591101, 00024591102, 00024591120, 00024591400, 00024591402, 00024591420, 00024591501, 00024591520, 00024591800, 00024591802, 00024591820
Tralokinumab	50222034602, 50222034604, 50222034601, 50222034622, 50222034691, 50222034692
Upadacitinib	00074230630, 00074104328, 00074231030, 00074104314, 00074230670, 00074231020

9.2 Appendix B – Regression Model

$$Y_{it} = \beta_0 + \beta_1 post_t + \beta_2 treated_i * post_t + \beta_3 calyear_t * month_t + \beta_4 CCI_{it} + \alpha person_i + \delta calyear_t + \theta month_t + \varepsilon_{it}$$

Y_{it} : outcome of interest (ED visit, inpatient visit, and total cost)

B_1 : coefficient on an indicator for if the year falls after index date

$Treated_i$: indicator for the treated group

B_2 : the DiD coefficient of interest

B_3 : coefficient of interaction between calendar year and quarter

B_4 : coefficient for Charlson Comorbidity Index (time varying)

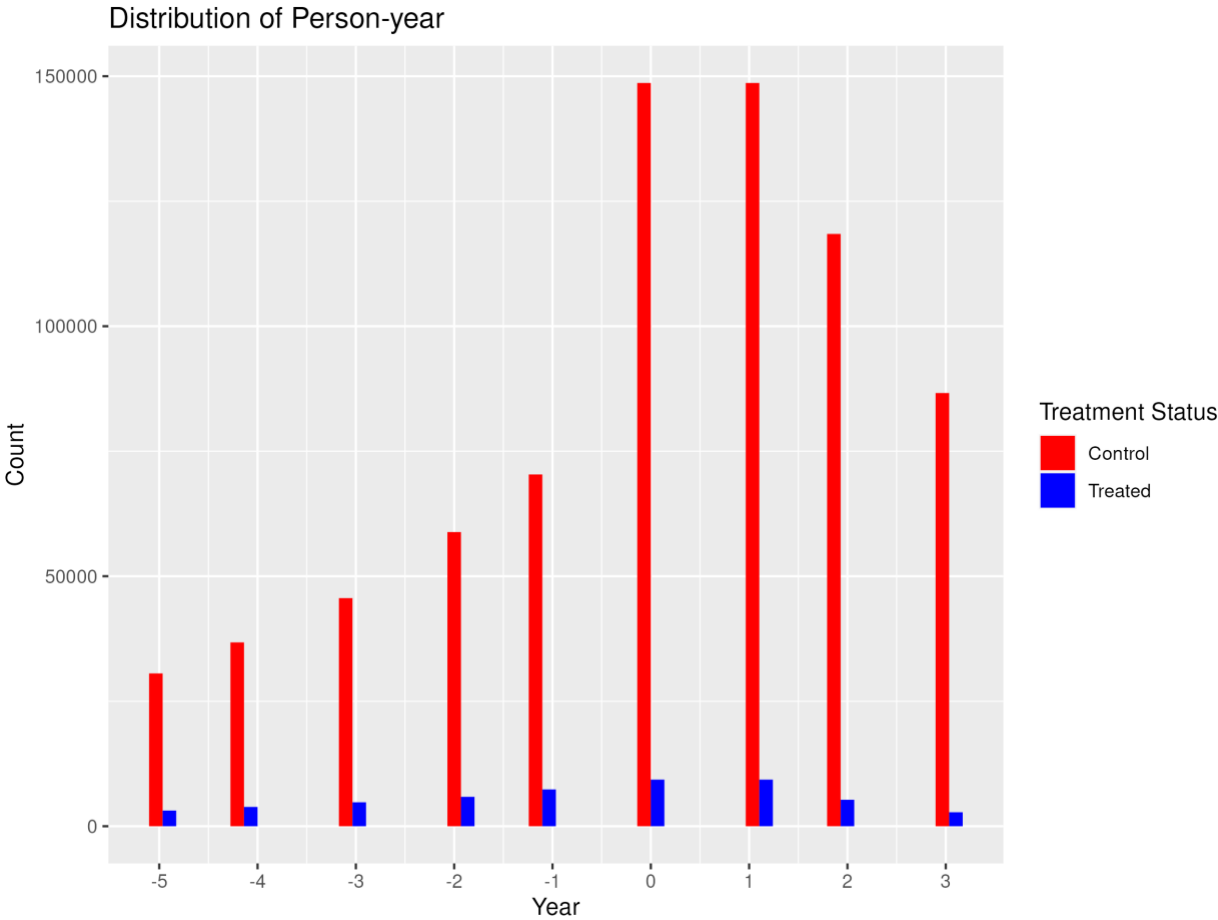
α : coefficient on an indicator for individual, I

δ : coefficient on an indicator for year, t

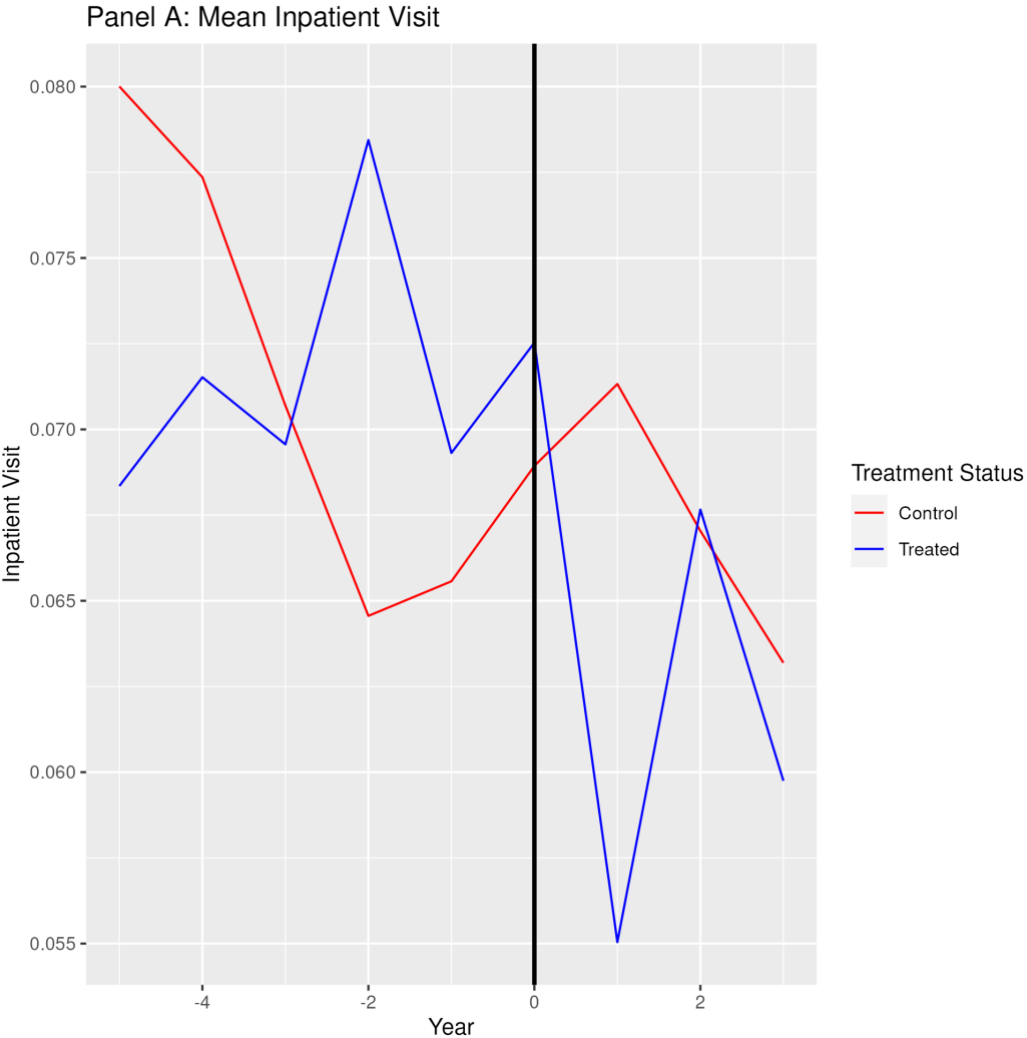
θ : coefficient on an indicator for month

ε_{it} : the error term clustered at the individual level

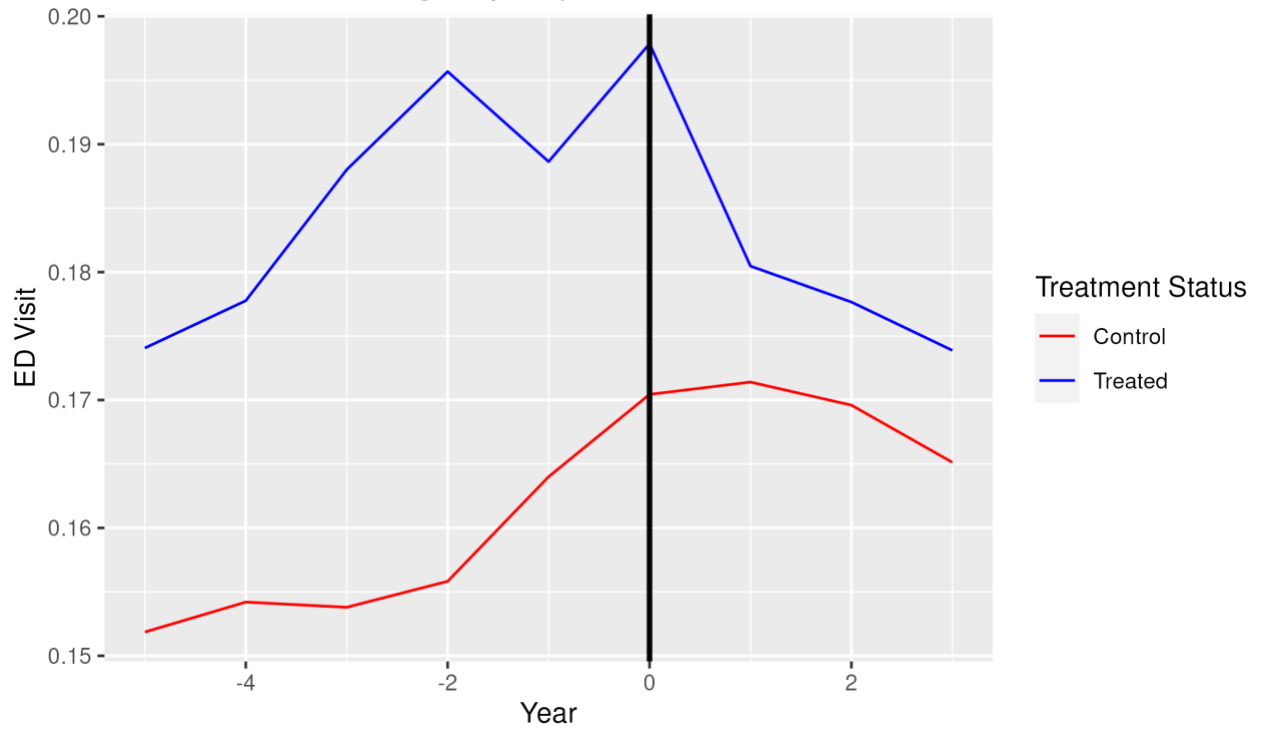
9.3 Appendix C – Distribution of Person-years



9.4 Appendix D – Parallel Trend Graph of Primary Outcomes

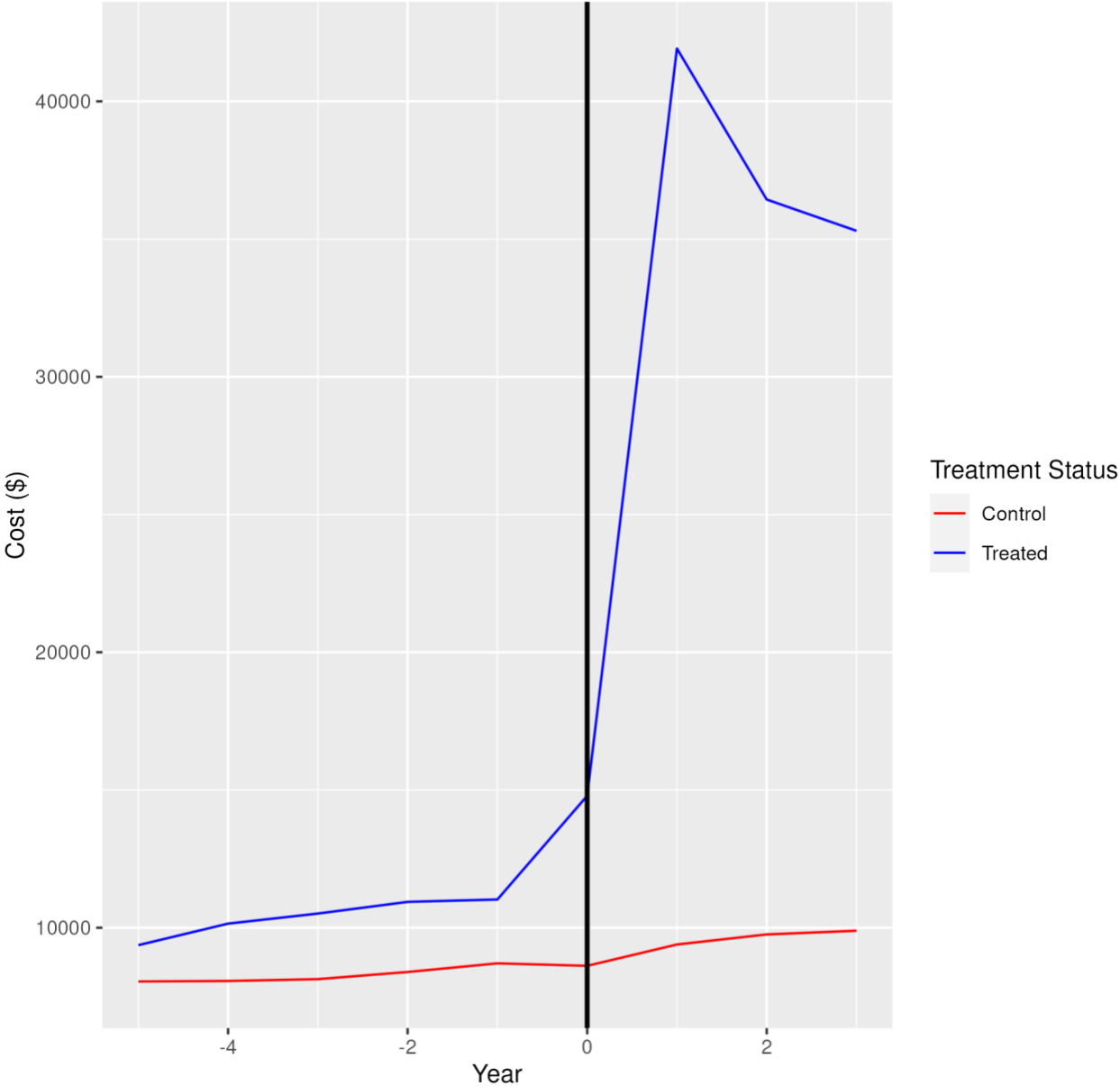


Panel B: Mean Emergency Department Visit

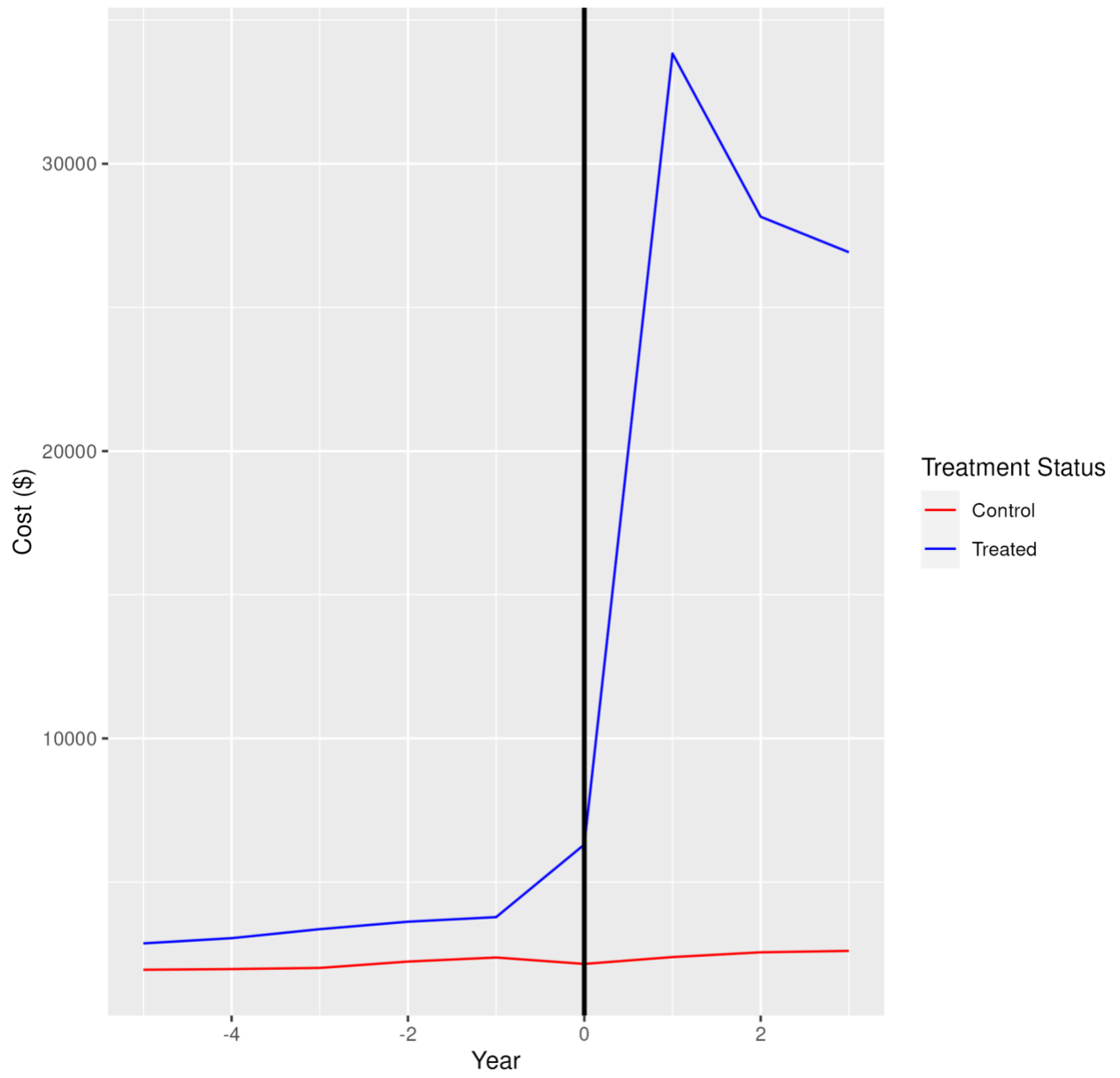


9.5 Appendix E – Parallel Trend Graph of Secondary Outcomes

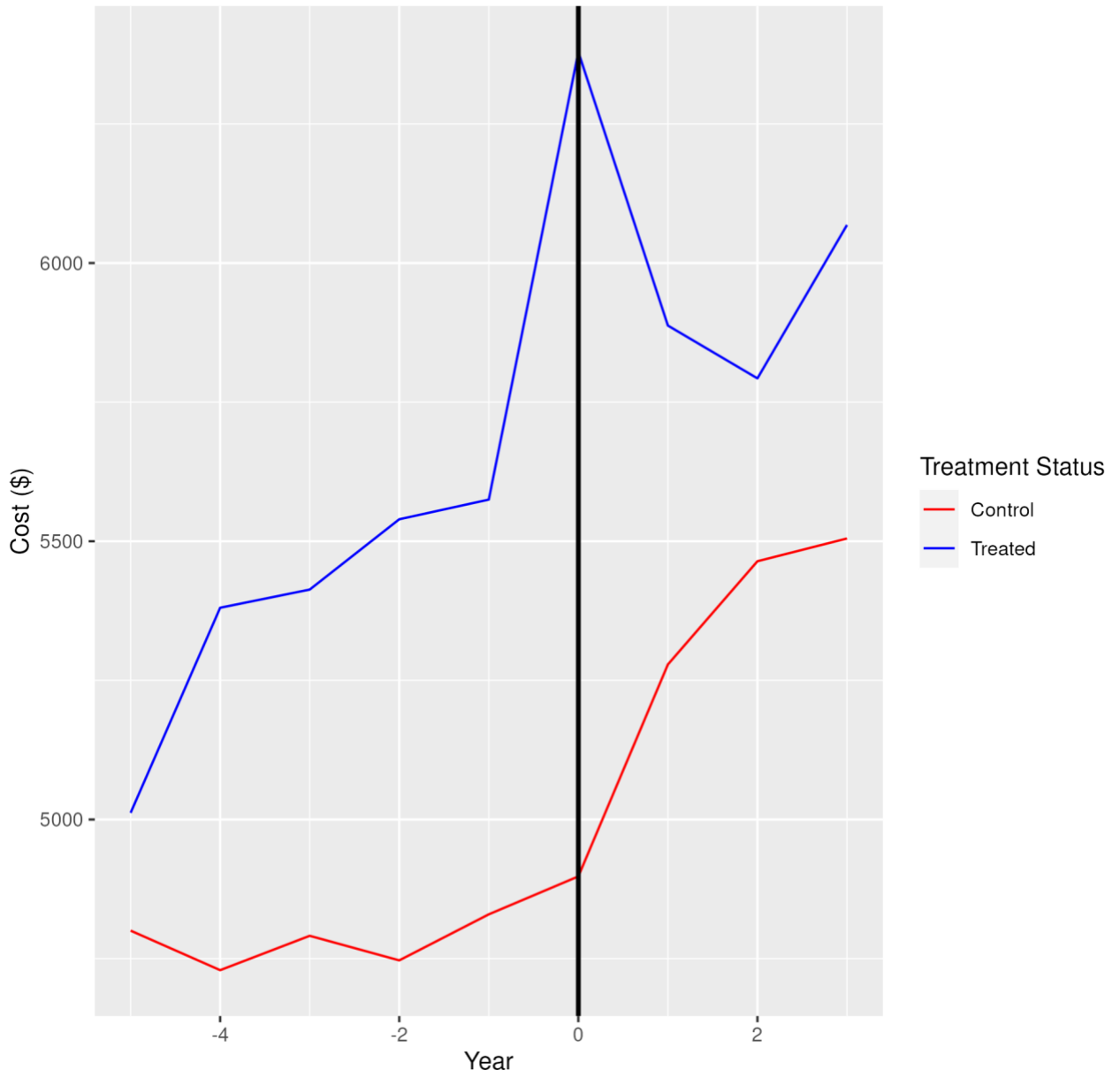
Panel A: Mean Total Cost



Panel B: Mean Drug Cost



Panel C: Mean Outpatient Cost



Panel D: Mean Inpatient Cost

