# Supplemental Information

## Supplemental Methods

### *A. Biologic Initiation Time Phases, Definitions, and Coding*

Several phases of biologic initiation were predefined in our conceptual model of biologic initiation time (Fig 2). Important beginning and end points of phases of biologic initiation time were determined by chart review of clinical notes, as described in the main text. All phases could potentially overlap. For example, if the laboratory evaluation phase occurred simultaneously to the contemplation phase, this time was accounted for in both phases. All patients were required to have received a biologic for inclusion, although the medication ultimately initiated might have differed from the one initially recommended because of step therapy requirements.

### *B. Cohort Characteristics*

#### *Demographics*

Recorded demographic information at the time of bioloigc recommendation included age, sex, race, zip code, and socioeconomic status, defined as the median income of the zip code as determined by 2018 US Census data.[51] Sex was documented as classified in the medical record and used for legal and/or administrative purposes. Self-identified race, as classified by the child or their family, was recorded as White, Black, Asian American, American Indian or Alaska Native, and other. Race was assessed to determine any differential associations or interactions between prior authorization requirement, insurance type, complicated prior authorization processes, and outcomes and also because of its known role as a risk factor for increased healthcare utilization in IBD.[30] Given that 87.4% of our cohort was recorded as White, race was dichotomized as White or non-White for all analyses because of the low number of individuals in non-White categories.

#### *Year of Recommendation*

Year of biologic medication recommendation was recorded. Infliximab received US Food and Drug Administration approval for pediatric Crohn's disease in 2006 (before study inclusion criteria date of January 1, 2010) and for pediatric ulcerative colitis in 2011. Adalimumab was approved for pediatric Crohn's disease in 2014 and for pediatric ulcerative colitis in 2021. The number of patients who initiated each therapy, before and after approval date, stratified by disease type, was recorded. Two patients with ulcerative colitis received infliximab before 2011, both of whom required a prior authorization ($P = .99$). Four patients with Crohn's disease received adalimumab before 2014, 3 of whom required a prior authorization and one whom did not ($P = .99$) (Supplemental Results E).

#### *IBD Classification*

Each patient's IBD physician was recorded and dichotomized as being an IBD specialist or non-IBD specialist. Physicians were classified as IBD specialists if they were an attending physician who belonged to the IBD center. Anthropometric data included height, weight, BMI, and BMI *z*-score category (normal, mild, moderate, or severe), as determined by using Centers for Disease Control and Prevention growth charts. IBD phenotype data included IBD subtype (Crohn's disease, ulcerative colitis, or IBD unclassified) determined via clinical notes at the time of physician biologic recommendation.[29] IBD distribution and behavior was recorded and classified per Montreal classification.

#### *Medication History*

Medication data included biologic medication initiated, biologic initiation reason, concomitant medications, and prior medications (including responses to prior medications). Biologic medication initiation reason was coded as a categorical variable as follows: (1) nonresponse to prior medication (with subcategories to define nonresponse to prior biologic or immunomodulator or to corticosteroids); (2) intolerance to prior medication; (3) allergy or antibodies to prior biologic medication; (4) changed biologic due to preference of drug route (intravenous versus subcutaneous or intramuscular) for lifestyle reasons, such as age, distance from hospital, or going to college; or (5) no prior medications trialed. In some cases, patients could have multiple biologic medication initiation reasons.

#### *Disease Severity Indicators*

Clinical data included prior IBD-related complications (penetrating complications, such as abscess or fistula; ED visit; hospitalization; or *C difficile* infection) within 30 days prior to physician recommendation, history of any prior IBD-related surgery, and baseline physician's global assessment, when available, closest to and within 30 days of physician recommendation. Baseline biochemical markers (hemoglobin, C-reactive protein, or fecal calprotectin) and physician's global assessment were recorded but not included in any regression or IPTWRA models because of missingness in approximately one-third of patients.

#### *Pre-Biologic Screening*

Pre-biologic screening data closest to and before biologic initiation

included tuberculosis screening (QuantiFERON Gold, Mantoux test, or chest radiograph), hepatitis B virus screening (surface antibody and antigen), and VZV antibody screening (Supplemental Table 6).

### C. Linear Regression Analyses of Biologic Initiation Time

Univariable linear regression was employed to assess the association of all measured covariables with biologic initiation time (Table 2, Supplemental Table 8). Stepwise forward selection was used to construct the multivariable model on the basis of maximal explanation of biologic initiation time variance, as determined by adjusted $R^2$. After the addition of each variable, a partial F statistic was calculated to determine if the variable significantly contributed to the model. The model was considered complete once no additional variables significantly contributed to explained variance. Given the primary aim of explaining the association between prior authorization requirement and biologic initiation time, any collinear variables to our exposure of interest were excluded from the model. This resulted in the prior authorization phase time being excluded from the final model because it was collinear with prior authorization requirement and complicated prior authorization requirement. Insurance type was included in the final model, despite not being a statistically significant variable, to account for any differential effects of insurance type on biologic initiation time. After model specification, regression diagnostics were used to verify assumptions. The final multivariable regression model explaining biologic initiation time was determined to have no significant multicollinearity (maximum variance inflation factor = 1.08), was overall linear, and found no patients with significant leverage or influence.[52] Probability--probability plots as well as the Breusch-Pagan test revealed violations of heteroskedasticity.[53] The Shapiro-Wilk test determined nonnormality of the data in skewness but not kurtosis.[33] To compensate for this, bootstrapped SEs were used.[54] Results were represented as regression coefficients and corresponding 95% CIs. There were complete data for all patients and all variables used in the final multivariable regression model.

### D. Inverse Probability of Treatment Weighted Regression Adjustment Analyses of Healthcare Utilization

Given the relatively low number of adverse event outcomes (13, 27, and 45 at 30, 90, and 180 days, respectively), the binary nature of the primary outcome, and the high number of potentially confounding covariables, propensity score methods were used.

Univariable logistic regression was used to select important demographic, insurance-related, and disease severity–related covariables associated with exposures and/or outcomes of interest for potential inclusion in IPTWRA models to reduce confounding and increase precision of estimates.[38] This approach was used to maximize covariable balance while also maximizing precision of our model.[39] All covariables with complete data and univariable logistic regression $P$ values associated with the outcome at a level of $P \leq .5$ were considered for inclusion into the IPTWRA model. The propensity score was derived from a logistic regression model and computed as the probability of requiring prior authorization conditional on included covariables. After initial model specification, raw SMDs were assessed for baseline covariable balance between exposure groups. The cohort was trimmed (patients excluded) to include only patients with similar propensity scores (common support) to achieve covariable balance between exposure groups. Next, IPTWRA was used to determine average treatment effects of prior authorization requirement on subsequent IBD-related healthcare utilization outcomes and corticosteroid dependence. Covariable balance after IPTWRA was assessed via analysis of absolute SMDs and variance ratios (VRs), with a goal absolute SMD $<0.1$ and a goal VR between 0.8 and 1.2 (Supplemental Table 4).[36] Covariables were respecified until these thresholds were met. Models were specified to include the maximum amount of variables possible while conforming to SMD and VR goals, with preference given to variables with higher association with the outcome of interest to best account for potential confounding and maximize precision of estimates. Results were represented as average treatment effects (described as percentages) and corresponding 95% CIs and $P$ values.

Covariables used in IPTWRA models included age, race, sex, insurance type, socioeconomic status, IBD subtype, BMI $z$-score, medication ordered, concomitant and prior medications, response to prior medications, prior IBD-related complications, and prior surgery. Socioeconomic status was coded as both a continuous variable (median income of patient zip code in thousands of dollars) and a binary variable (median income of patient zip code above or below the 50th percentile). When possible, given SMD and VR goals, the continuous variable was given preference in IPTWRA models but was substituted for the binary form of the variable when covariable balance of the continuous variable was not possible, likely because of collinearity with prior authorization requirement.

Several propensity score analysis strategies for optimal covariable weighting and balance among exposure groups were assessed. These included propensity score matching, nearest-neighbor matching, regression adjustment, inverse probability weighting, IPTWRA, and augmented inverse probability weighting. IPTWRA routinely resulted in the best covariable balance (defined as an absolute SMD <0.1) between patients who did and did not require a prior authorization and was therefore implemented for all analyses. Adequate covariable balance was assessed by using graphical methods, SMDs, and VRs. The balance of covariables in IPTWRA models was confirmed to not violate overlap and overidentification assumptions. IPTWRA analyses were performed by using the *teffects* package in Stata.[40]

Regarding IPTWRA subgroup analyses involving patients with Crohn's disease and patients recommended infliximab, absolute SMD goals were liberalized (<0.25) because of an inability to robustly match covariables among smaller subsets of patients with fewer outcomes within more stringent thresholds.

## Supplemental Results

### *A. Biologic Initiation Time and Phase Lengths Stratified by Prior Authorization Requirement*

The median lengths and IQRs of biologic initiation time and phase lengths of the cohort overall, as well as stratified by prior authorization, are presented in Supplemental Table 7. In the right column are univariable regression coefficients describing the association of prior authorization requirement with biologic initiation time and phase lengths. Prior authorization requirement was associated with a significantly longer prior authorization phase (12.6 [95% CI 9.0 to 16.1]), a shorter scheduling and processing phase (−3.5 [95% CI −6.9 to −0.1]), and an overall longer biologic initiation time (9.2 [95% CI 3.7 to 14.7]). All other associations between prior authorization requirement and biologic initiation time and phase lengths were not statistically significant. The median contemplative, laboratory evaluation, and administrative phases were all 0 days. This was due to (1) the majority of patients making their decisions to initiate biologics on the day of recommendation; (2) the majority of patients having had laboratory evaluation completed by time of decision, possibly to expedite non–prior authorization phases under provider control; and (3) the time from decision and laboratory evaluation to prior authorization initiation being 0 days.

### *B. Univariable Relationships Between Prior Authorization, Covariables, and Biologic Initiation Time Phases*

Measured covariables significantly correlated to specific phases of biologic initiation time are presented in Fig 3. These associations included clinic messages (contemplative phase); nonimmunity to VZV and initiation of infliximab (laboratory evaluation phase); prior authorization requirement, complicated prior authorization requirement, private insurance, and prior biologic exposure (prior authorization phase); and increasing year of biologic recommendation, lifestyle-related medication change reason, and initiation of adalimumab (scheduling and processing phase). Other covariables were associated with shortened biologic initiation time phases, including receiving care from an IBD specialist (contemplative phase); prior biologic exposure (laboratory evaluation phase); private insurance (administrative phase); initiation of infliximab and enteral supplement use (prior authorization phase); and nonresponse to corticosteroids and initiation of infliximab (scheduling and processing phase). These were exploratory analyses and not corrected for multiple testing.

### *C. Subgroup Analysis: IBD Subtype*

Exploratory subgroup analyses investigating the association of IBD subtype with outcomes of interest demonstrated that IBD subtype was not associated with biologic initiation time in univariable or multivariable analyses. Subgroup analysis exclusively examining patients with Crohn's disease ($n = 148$) adjusting for disease behavior and location yielded IPTWRA results similar to primary analyses. Prior authorization requirement was associated with increased adverse events at both 30 (8.4%; 95% CI 2.0 to 14.8) and 180 days (11.6%; 95% CI 1.8 to 21.5) (Supplemental Table 11). Because of collinearity, insurance type and socioeconomic status were not able to be adjusted for in Crohn's disease–specific subgroup analyses. Similar subgroup analyses in patients with ulcerative colitis were not possible because of the smaller sample size ($n = 32$).

### *D. Subgroup Analysis: Anti-TNF-α Subtypes*

Exploratory subgroup analyses examining the association of the initiation of specific anti-TNF-α medications with biologic initiation time demonstrated on univariable analyses that infliximab initiation was associated with a 9-day decrease in biologic initiation time (95% CI −13.8 to −4.2) compared with initiation of any other biologics (Supplemental Table 8). Conversely, adalimumab initiation was associated with an 8.8-day increase in biologic initiation time (95% CI 3.6 to 14.0) compared

with initiation of any other biologics. These associations were nonsignificant on multivariable analysis. Subgroup analysis examining the associations of prior authorization requirement with adverse events exclusively in patients initiating infliximab demonstrated that prior authorization requirement was significantly associated with adverse events at both 90 days (12.1%; 95% CI 1.8 to 22.3) and 180 days (15.6%; 95% CI 2.0 to 29.1) (Supplemental Table 12) but not 30 days. Similar to patients with ulcerative colitis, sensitivity analyses examining patients recommended adalimumab could not be completed because of the small sample size, and insurance type and socioeconomic status could not be adjusted for.

### *E. Year of Approval*

Two patients with ulcerative colitis received infliximab before US Food and Drug Administration approval in 2011, both of whom required a prior authorization ($P = .99$). Four patients with Crohn disease received adalimumab before US Food and Drug Administration approval in 2014, 3 of whom required a prior authorization and one whom did not ($P = .99$).

**SUPPLEMENTAL TABLE 4** Raw and Weighted Absolute Standardized Mean Differences for IPTWRA Models

| | Raw Standardized Mean Difference | Weighted Standardized Mean Difference |
|---|---|---|
| Healthcare utilization within 30 d | | |
| Insurance type (private, versus public) | 0.52 | 0.06 |
| Sex (female, versus male) | 0.15 | 0.01 |
| Race (White, versus Non-White) | 0.45 | 0.03 |
| Socioeconomic status (>50th percentile, versus <50th percentile) | 0.04 | 0.06 |
| BMI *z*-score | | |
| Normal (>−1) | Reference | Reference |
| Mild malnutrition (−2 to −1) | 0.14 | 0.08 |
| Moderate-severe malnutrition (<−2) | 0.18 | 0.04 |
| Emergency department visit (prior 30 d) | 0.07 | 0.00 |
| Prior surgery | 0.00 | 0.03 |
| No. prior biologics | 0.08 | 0.01 |
| Prior immunomodulator | 0.09 | 0.02 |
| No response to biologic or immunomodulator | 0.11 | 0.06 |
| Concomitant antibiotics | 0.05 | 0.03 |
| Concomitant corticosteroids | 0.20 | 0.06 |
| Healthcare utilization within 90 d | | |
| Insurance type (private, versus public) | 0.75 | 0.07 |
| Race (White, versus Non-White) | 0.75 | 0.07 |
| Socioeconomic status (thousands of dollars) | 0.12 | 0.06 |
| Any complication (prior 30 d) | 0.14 | 0.09 |
| Prior IBD-related surgery | 0.04 | 0.02 |
| Prior biologic | 0.31 | 0.06 |
| No response to corticosteroids | 0.20 | 0.06 |
| Concomitant antibiotic | 0.04 | 0.07 |
| Concomitant corticosteroid | 0.28 | 0.09 |
| Concomitant biologic | 0.34 | 0.00 |
| No concomitant medications | 0.11 | 0.00 |
| Healthcare utilization within 180 d | | |
| Insurance type (private, versus public) | 0.60 | 0.05 |
| Race (White, versus Non-White) | 0.52 | 0.00 |
| IBD subtype | | |
| Crohn's disease | Reference | Reference |
| Ulcerative colitis or IBD-undetermined | 0.18 | 0.04 |
| Any complication (prior 30 d) | 0.06 | 0.07 |
| Prior IBD-related surgery | 0.06 | 0.05 |
| No. prior biologics | 0.13 | 0.08 |
| Prior immunomodulator | 0.09 | 0.07 |
| Concomitant antibiotics | 0.09 | 0.10 |
| Concomitant corticosteroid | 0.13 | 0.01 |
| Biologic initiation reason: nonresponse | 0.03 | 0.03 |
| Biologic initiation reason: no prior medications | 0.05 | 0.09 |
| Corticosteroid dependence at 90 d | | |
| Age, y | 0.01 | 0.06 |
| Race (White, versus Non-White) | 0.42 | 0.02 |
| IBD subtype | | |
| Crohn's disease | Reference | Reference |
| Ulcerative colitis or IBD-undetermined | 0.17 | 0.01 |
| BMI *z*-score | | |
| Normal (>−1) | Reference | Reference |
| Mild malnutrition (−2 to −1) | 0.08 | 0.00 |
| Moderate-severe malnutrition (<−2) | 0.12 | 0.03 |
| Hospitalization (prior 30 d) | 0.08 | 0.02 |
| Prior biologic | 0.29 | 0.08 |
| Prior immunomodulator | 0.17 | 0.08 |
| No prior biologic or immunomodulator | 0.35 | 0.01 |
| Concomitant 5-aminosalicylic acid | 0.19 | 0.00 |
| Concomitant antibiotics | 0.05 | 0.11 |

**SUPPLEMENTAL TABLE 4** Continued

| | Raw Standardized Mean Difference | Weighted Standardized Mean Difference |
|---|---|---|
| Concomitant corticosteroid | 0.06 | 0.09 |
| Steroids initiated at time of recommendation | 0.21 | 0.06 |
| No concomitant medications | 0.19 | 0.02 |
| No response to biologic or immunomodulator | 0.21 | 0.05 |
| No response to corticosteroids | 0.13 | 0.03 |

Raw and weighted absolute standardized mean differences for variables included in inverse probability of treatment-weighted regression adjustment models assessing the average treatment effect of prior authorization requirement on likelihood of healthcare utilization (hospitalization, surgery, or ED visit) at 30 d, 90 d, and 180 d, and on corticosteroid dependence at 90 d, of physician recommendation of biologic medication. Goal absolute SMD $< 0.1$.

**SUPPLEMENTAL TABLE 5** Cohort Insurance Characteristics

| | Total ($N = 190$) | Public Insurance ($n = 54$) | Private Insurance ($n = 136$) | *P* |
|---|---|---|---|---|
| Public insurance type, *n* (%) | | | | |
| Medicaid | — | 33 (61) | — | — |
| Tricare | — | 14 (26) | — | — |
| Child Health Plan Plus | — | 7 (13) | — | — |
| Private insurance group, *n* (%) | | | | |
| Aetna | — | — | 11 (8) | — |
| Anthem | — | — | 33 (24) | — |
| Cigna | — | — | 30 (22) | — |
| Kaiser | — | — | 15 (11) | — |
| United | — | — | 38 (28) | — |
| Other | — | — | 9 (7) | — |
| Prior authorization required, *n* (%) | 141 (74) | 28 (52) | 113 (83) | <.001 |
| Complicated prior authorization process, *n* (%) | 25 (13) | 3 (6) | 22 (16) | .06 |
| Step therapy, *n* (%) | | | | |
| Requested | 7 (4) | 2 (4) | 5 (4) | >.99 |
| Required | 4 (2) | 0 | 4 (3) | .58 |
| Letter of appeal | 12 (6) | 2 (4) | 10 (7) | .51 |
| Peer-to-peer meeting | 11 (6) | 1 (2) | 10 (7) | .18 |

Cohort summary statistics of insurance providers, prior authorization requirements, and complicated prior authorization requirements stratified by insurance type. Step therapy required indicates that step therapy was requested by the insurance company and the physician was required to alter the initial physician-recommended therapy to therapy requested by insurance company. Percentages represent the number of outcomes per total exposed in strata. —, not applicable.

**SUPPLEMENTAL TABLE 6** Pre-Biologic Screening Evaluation

| | Total ($N$ = 190) | Prior Authorization Required ($n$ = 141) | No Prior Authorization Required ($n$ = 49) | $P$ |
|---|---|---|---|---|
| QuantiFERON Gold result | | | | .42 |
| Negative | 122 (64) | 88 (62) | 34 (69) | — |
| Indeterminate | 21 (11) | 18 (13) | 3 (6) | — |
| Positive | 0 | — | 0 | — |
| Not done | 47 (25) | 35 (25) | 12 (25) | — |
| Alternative tuberculosis screening test | | | | .81 |
| Purified protein derivative | 34 (18) | 26 (18) | 8 (16) | — |
| Chest radiograph | 19 (10) | 15 (11) | 4 (8) | — |
| Repeat QuantiFERON Gold | 2 (1) | 1 (1) | 1 (2) | — |
| None | 135 (71) | 99 (70) | 36 (74) | — |
| Hepatitis B virus surface antigen | | | | .01 |
| Reactive | 2 (1) | 0 | 2 (4) | — |
| Nonreactive | 151 (80) | 109 (77) | 42 (86) | — |
| Not done | 37 (20) | 32 (23) | 5 (10) | — |
| Hepatitis B virus surface antibody | | | | .14 |
| Nonreactive | 99 (52) | 75 (53) | 24 (49) | — |
| Reactive | 52 (27) | 33 (77) | 19 (39) | — |
| Equivocal | 6 (3) | 5 (4) | 1 (2) | — |
| Not done | 33 (17) | 28 (20) | 5 (10) | — |
| VZV IgG | | | | .96 |
| Positive | 95 (50) | 70 (50) | 25 (51) | — |
| Negative | 53 (28) | 39 (28) | 14 (29) | — |
| Equivocal | 6 (3) | 5 (4) | 1 (2) | — |
| Not done | 36 (19) | 27 (19) | 9 (18) | — |
| VZV vaccination before biologic initiation | | | | .23 |
| Yes | 148 (78) | 113 (80) | 35 (71) | — |
| No | 42 (22) | 28 (20) | 14 (29) | — |

—, not applicable.

**SUPPLEMENTAL TABLE 7** Biologic Initiation Time and Phase Lengths Stratified by Prior Authorization Requirement

| Prior Authorization Requirement | Total ($N$ = 190) | Prior Authorization Required ($n$ = 141) | No Prior Authorization Required ($n$ = 49) | Univariable Linear Regression β Coefficient[a] (95% CI) |
|---|---|---|---|---|
| Contemplative phase, d | 0 (0–0) | 0 (0–1) | 0 (0–0) | 1.3 (−0.7 to 3.4) |
| Laboratory evaluation phase, d | 0 (0–4) | 0 (0–4) | 0 (0–3) | 1.6 (−0.9 to 4.1) |
| Administrative phase, d | 0 (0–0) | 0 (0–0) | 0 (0–0) | −1.1 (−2.6 to 0.4) |
| Prior authorization phase, d | 6 (0–14) | 8 (5–16) | 0 (0–0) | 12.6 (9.0 to 16.1) |
| Scheduling and processing phase, d | 10.5 (5–17) | 9 (4–16) | 11 (9–21) | −3.5 (−6.9 to −0.1) |
| Biologic initiation time, d | 21 (13–35) | 25 (16–38) | 13 (9–28) | 9.2 (3.7 to 14.7) |

Biologic initiation time and phases of biologic initiation time lengths, in median (IQR), stratified by prior authorization requirement, along with univariable linear regression coefficients of the associations of prior authorization requirement with biologic initiation time and biologic initiation time phases. The median contemplative, laboratory evaluation, and administrative phases were all 0 d. This was due to (1) the majority of patients making their decisions to initiate biologics on the day of recommendation; (2) the majority of patients having had laboratory evaluation completed by the time of decision, possibly to expedite non–prior authorization phases under provider control; and (3) the time from decision and laboratory evaluation to prior authorization initiation being 0 d. Values other than univariable linear regression coefficients represent median (IQR).

[a] Univariable regression coefficients represent change in biologic initiation time or biologic initiation time phase length, in days, associated with prior authorization requirement.

**SUPPLEMENTAL TABLE 8** Univariable and Multivariable Linear Regression Analyses of Biologic Initiation Time

| | Univariable Linear Regression β Coefficient[a] (95% CI), d | Multivariable Linear Regression β Coefficient[a] (95% CI), d |
|---|---|---|
| Prior authorization | | |
| Not required | Reference | Reference |
| Required, uncomplicated | 7.2 (1.7 to 12.7) | 10.2 (8.2 to 12.3) |
| Required, complicated | 18.5 (10.5 to 26.4) | 24.6 (16.4 to 32.8) |
| Insurance type (private) | 2.9 (−2.5 to 8.4) | −0.4 (−3.4 to 2.6) |
| Age, y | 0.1 (−0.8 to 0.9) | — |
| Female sex (reference: male sex) | −3.5 (−8.4 to 1.4) | — |
| White race (reference: non-White) | 5.2 (−2.2 to 12.5) | — |
| Year of recommendation | 1.07 (0.1 to 2.0) | — |
| IBD specialist | −2.3 (−7.4 to 2.8) | — |
| IBD subtype | | |
| Crohn's disease | Reference | — |
| Ulcerative colitis | 0.8 (−5.8 to 7.5) | — |
| IBD unclassified | −1.7 (−12.8 to 9.4) | — |
| BMI *z*-score | | |
| Normal | Reference | — |
| Mild malnutrition | −2.9 (−8.7 to 2.9) | — |
| Moderate malnutrition | −2.8 (−11.1 to 5.5) | — |
| Severe malnutrition | −3.2 (−14.5 to 8.0) | — |
| Medication | | |
| Infliximab | −9.0 (−13.8 to −4.2) | — |
| Adalimumab | 8.8 (3.6 to 14.0) | — |
| Certolizumab | 7.1 (−7.0 to 21.1) | — |
| Vedolizumab | −0.5 (−10.2 to 9.3) | — |
| Ustekinumab | 5.7 (−8.4 to 19.8) | — |
| Biologic initiation reason | | |
| Nonresponse | −2.5 (−8.3 to 3.2) | — |
| Intolerance | 6.4 (−4.1 to 16.9) | — |
| Antibodies or allergy | 3.2 (−6.6 to 12.9) | — |
| Lifestyle | 20.5 (3.5 to 37.4) | — |
| No prior medications | −4.8 (−11.9 to 2.2) | — |
| Concomitant therapies | | |
| 5-Aminosalicylic acid | 1.3 (−4.1 to 6.6) | — |
| Antibiotic | −1.0 (−8.3 to 6.3) | — |
| Corticosteroid | −4.4 (−9.6 to 0.8) | — |
| Budesonide | −2.7 (−10.1 to 4.7) | — |
| Immunomodulator | 3.1 (−1.8 to 8.1) | — |
| Biologic | −0.9 (−7.2 to 5.3) | — |
| Enteral supplement | −5.1 (−11.5 to 1.3) | — |
| Biologic initiation time phase | | |
| Contemplative | 0.9 (0.5 to 1.2) | 0.9 (0.7 to 1.2) |
| Laboratory evaluation | 0.3 (0.0 to 0.6) | — |
| Administrative | 0.8 (0.3 to 1.3) | 0.9 (0.7 to 1.2) |
| Prior authorization | 0.9 (0.8 to 1.1) | — |
| Scheduling and processing | 0.9 (0.7 to 1.1) | 1.1 (0.9 to 1.2) |
| Complication 30 d before recommendation | | |
| Abscess[b] | 1.3 (−7.0 to 9.5) | — |
| Emergency department visit | 1.6 (−5.6 to 8.7) | — |
| Hospitalization | −1.2 (−8.5 to 6.1) | — |
| *C difficile* infection[c] | −11.1 (−23.2 to 1.1) | — |
| Any complication | −1.8 (−7.4 to 3.8) | — |
| Prior surgery | 3.3 (−6.1 to 12.8) | — |
| Prior therapies | | |
| Biologic | 3.5 (−2.2 to 9.1) | — |
| Immunomodulator | 3.9 (−1.0 to 8.8) | — |
| No prior biologic or immunomodulator | −4.8 (−9.9 to 0.3) | — |

Linear regression analyses assessing phase lengths and baseline characteristics with biologic initiation time. The final multivariable model (right column) included prior authorization requirement, insurance type, complicated prior authorization process, contemplative phase, administrative phase, and scheduling and processing phase. Variables not included in the multivariable model (—) were either nonsignificant in the multivariable analysis or, in the case of prior authorization phase length, collinear with the exposure of interest and therefore excluded from the final model (see Supplemental Methods C). Bootstrapped SEs were used to calculate 95% CIs for the multivariable model. —, not applicable.

[a] Regression coefficients represent change in biologic initiation time in days for every 1-unit change of continuous variables.

[b] Abscess diagnosis is based on clinical and/or imaging diagnosis in prior 30 d to medication recommendation.

[c] *C difficile* diagnosis is based on clinical symptoms and a positive stool polymerase chain reaction assay result.

**SUPPLEMENTAL TABLE 9** Cohort Summary Statistics of IBD-Related Healthcare Utilization Outcomes

| Outcome Type | Total ($N$ = 190), $n$ (%) | Prior Authorization Required ($n$ = 141), $n$ (%) | No Prior Authorization Required ($n$ = 49), $n$ (%) | $P$ |
|---|---|---|---|---|
| Any hospitalization, surgery, or emergency department visit | | | | |
| 30 d | 13 (7) | 9 (6) | 4 (8) | .44 |
| 90 d | 27 (14) | 19 (14) | 8 (16) | .39 |
| 180 d | 45 (24) | 35 (25) | 10 (20) | .34 |
| Hospitalization | | | | |
| 30 d | 9 (5) | 7 (5) | 2 (4) | .58 |
| 90 d | 19 (10) | 12 (9) | 7 (14) | .19 |
| 180 d | 36 (19) | 29 (21) | 7 (14) | .23 |
| Surgery | | | | |
| 30 d | 2 (1) | 1 (1) | 1 (2) | .45 |
| 90 d | 7 (4) | 4 (3) | 3 (6) | .26 |
| 180 d | 14 (7) | 10 (7) | 4 (8) | .51 |
| Emergency department visit | | | | |
| 30 d | 12 (6) | 8 (6) | 4 (8) | .37 |
| 90 d | 22 (12) | 16 (11) | 6 (12) | .52 |
| 180 d | 35 (18) | 27 (19) | 8 (16) | .42 |
| Corticosteroid dependence | | | | |
| 90 d | 48 (25) | 41 (29) | 7 (14) | .03 |

IBD-related healthcare utilization outcomes stratified by prior authorization requirement. Outcomes included any hospitalization, surgery, or ED visit; hospitalizations; surgeries; ED visits; and corticosteroid dependence. For each time point, patients were documented as having each type of healthcare utilization outcome but could only be counted once for the combined primary outcome. For example, if a patient had a surgery and a hospitalization, they would be counted for both outcome types but only once for the composite outcome (any hospitalization, surgery, or ED visit). Thus, the sum of individual outcome types at each time point is greater than the combined primary outcome. Percentages represent the number of outcomes per total exposed in strata.

**SUPPLEMENTAL TABLE 10** IPTWRA Analyses of Prior Authorization Requirement on IBD-Related Healthcare Utilization Stratified by Individual Outcome Type

| | | | Prior Authorization Required | | No Prior Authorization Required | | | |
|---|---|---|---|---|---|---|---|---|
| Outcome | Time Frame, d | $n$[a] | Outcome Present | No Outcome Present | Outcome Present | No Outcome Present | Average Treatment Effect,[b] % (95% CI) | $P$ |
| ED visit | 180 | 167 | 25 | 101 | 5 | 35 | 8.3 (−1.4 to 17.9) | .09 |
| Hospitalization | 180 | 167 | 26 | 100 | 4 | 37 | 12.6 (3.8 to 21.3) | .005 |
| Surgery | 180 | 167 | 10 | 116 | 1 | 40 | 6.5 (1.0 to 12.1) | .02 |

Average treatment effects of prior authorization requirement on IBD-related healthcare utilization within 30, 90, and 180 d of physician biologic recommendation stratified by individual healthcare utilization outcome type.

[a] $n$ represents the No. patients remaining in each exposure group after patients outside common support were dropped.

[b] Average treatment effect represents change in likelihood of healthcare utilization attributable to the exposure after covariable adjustment.

**SUPPLEMENTAL TABLE 11** IPTWRA Analyses of Prior Authorization Requirement on IBD-Related Healthcare Utilization Among Patients With Crohn's Disease

| | | Prior Authorization Required | | No Prior Authorization Required | | | |
|---|---|---|---|---|---|---|---|
| Time Frame, d | $n$[a] | Outcome Present[b] | No Outcome Present | Outcome Present | No Outcome Present | Average Treatment Effect,[c] % (95% CI) | $P$ |
| 30 | 134 | 6 | 99 | 1 | 28 | 8.4 (2.0 to 14.8) | .01 |
| 90 | 137 | 11 | 96 | 3 | 27 | 3.6 (−2.6 to 9.8) | .25 |
| 180 | 131 | 17 | 77 | 6 | 31 | 11.6 (1.8 to 21.5) | .02 |

Average treatment effects of prior authorization requirement on IBD-related healthcare utilization within 30, 90, and 180 d of physician biologic recommendation for patients with IBD subtype Crohn's disease.

[a] $n$ represents the number of patients remaining after patients outside of common support were dropped.

[b] Combined outcome of hospitalization, surgery, or ED visit.

[c] Average treatment effect represents change in likelihood of outcome attributable to the exposure after covariable adjustment.

**SUPPLEMENTAL TABLE 12** IPTWRA Analyses of Prior Authorization Requirement on IBD-Related Healthcare Utilization Among Patients Recommended Infliximab

| | | Prior Authorization Required | | No Prior Authorization Required | | | |
|---|---|---|---|---|---|---|---|
| Time Frame, d | *n*[a] | Outcome Present[b] | No Outcome Present | Outcome Present | No Outcome Present | Average Treatment Effect,[c] % (95% CI) | *P* |
| 30 | 96 | 5 | 64 | 1 | 26 | 4.6 (−2.4 to 11.7) | .20 |
| 90 | 96 | 12 | 57 | 1 | 26 | 12.1 (1.8 to 22.3) | .02 |
| 180 | 99 | 17 | 51 | 4 | 27 | 15.6 (2.0 to 29.1) | .02 |

Average treatment effects of prior authorization requirement on IBD-related healthcare utilization within 30, 90, and 180 d of physician biologic recommendation for patients recommended infliximab.

[a] *n* represents the number of patients remaining after patients outside of common support were dropped.

[b] Combined outcome of hospitalization, surgery, or ED visit.

[c] Average treatment effect represents change in likelihood of outcome attributable to the exposure after covariable adjustment.

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