Disclaimer

The following report(s) provides findings from an FDA-initiated query using Sentinel. While Sentinel queries may be undertaken to assess potential medical product safety risks, they may also be initiated for various other reasons. Some examples include determining a rate or count of an identified health outcome of interest, examining medical product use, exploring the feasibility of future, more detailed analyses within Sentinel, and seeking to better understand Sentinel capabilities.

Data obtained through Sentinel are intended to complement other types of evidence such as preclinical studies, clinical trials, postmarket studies, and adverse event reports, all of which are used by FDA to inform regulatory decisions regarding medical product safety. The information contained in this report is provided as part of FDA's commitment to place knowledge acquired from Sentinel in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Sentinel queries will continue to be communicated through existing channels.

FDA wants to emphasize that the fact that FDA has initiated a query involving a medical product and is reporting findings related to that query does not mean that FDA is suggesting health care practitioners should change their prescribing practices for the medical product or that patients taking the medical product should stop using it. Patients who have questions about the use of an identified medical product should contact their health care practitioners.

The following report contains a description of the request, request specifications, and results from the modular program run(s).

If you are using a web page screen reader and are unable to access this document, please contact the Sentinel Operations Center for assistance at info@sentinelsystem.org.

Overview for Request: cder_mpl2r_wp012, Report 3 of 4 (Prevalent Cohorts)

Request ID: cder_mpl2r_wp012_nsdp_v01

Request Description: In this request, we estimate the longitudinal trend in prevalent use of long-acting beta-2 agonist (LABA) with and without a long-term asthma controller medication (ACM) among asthma patients in the Sentinel Distributed Database (SDD). This is report 3 of 4 of the prevalent cohort reports and focuses on longitudinal rates of LABA users in the presence of ACM or fixed dose combination LABAs (FDC-LABA) dispensings among LABA-naive patients with poorly-controlled asthma. This definition of poorly-controlled asthma requires three instances of short-acting beta-2 agonist (SABA) canisters in the baseline period.

Sentinel Routine Querying Module: Cohort Identification and Descriptive Analysis (CIDA) tool, version 9.3.1

Data Source: We distributed this request on April 6, 2020 and queried data from January 1, 2006 through September 30, 2015 in 16 Data Partners contributing to the SDD. See Appendix A for a list of the latest dates of available data for each Data Partner.

Study Design: We followed prevalent users of LABAs, consisting of both single ingredient LABAs (SI-LABAs) and FDC-LABAs, on their exposed time until censoring criteria are met. We created fifteen cohorts consisting of these LABA users who also had overlapping days supply and/or dispensing date with either SI-LABA or non-LABA ACM episodes. Non-LABA ACM (referred to as simply "ACM" below) are defined as inhaled corticosteroids (ICS), leukotriene modifiers, chromones, oral systemic corticosteroids, immunomodulators, and methylxanthines. We calculated rates based off counts from these cohorts. These rates are then used to create an interrupted time series (ITS) regression model. This is report 3 of 4 and contains results for cohorts 8-11.

Exposures of Interest: We defined exposure of interest as the first qualifying dispensing of any LABA product. We defined each exposure using National Drug Codes (NDCs) observed in the outpatient pharmacy dispensings. Please see Appendix B for a list of generic and brand names of medical products used to define exposures.

Inclusion and Exclusion Criteria: All cohorts required exclusion of chronic obstructive pulmonary disease (COPD), cystic fibrosis, bronchiectasis, pulmonary hypertension or embolism, or bronchopulmonary dysplasia in the 365 days prior to and including index date. Additionally, all cohorts required inclusion of an asthma diagnosis. Cohorts 8-15 also required fulfillment of the poorly controlled asthma inclusion criteria. For cohort 1 only, asthma is defined as one asthma diagnosis in the 365 days prior to index date in any care setting. Otherwise, asthma is defined as either one asthma diagnosis in either an inpatient (IP) or emergency department (ED) care setting, or two instances of asthma diagnosis in either an ambulatory visit (AV) or other ambulatory (OA) care setting in the 365 days prior to or including index date. An individual is considered to have poorly controlled asthma if any of the following inclusion criteria are fulfilled:

1) One instance of ICS or leukotriene modifiers in the 90 days prior to index date
2) One instance of asthma diagnosis in the 90 days prior to index date in either IP or ED care setting
3) Two instances of oral corticosteroids with dispensings of 21 days supply or smaller in the 90 days prior to index date
4) (for cohorts 8-11 only) Three instances of SABA canisters dispensed in the 183 days prior to index date

We defined all inclusion and exclusion criteria using NDCs or International Classification of Diseases, Ninth Revision (ICD-9-CM) diagnosis codes. Please refer to Appendix C for a list of diagnosis codes and Appendix D for a list of generic and brand names of medical products used to define inclusion and exclusion criteria.

Overview for Request: cder_mpl2r_wp012, Report 3 of 4 (Prevalent Cohorts)

Overlap Criteria: Only users who fulfill overlap criteria specified below enter the cohorts.

Report 3: In this report, we include users in cohorts 8-11 if there is ACM use or FDC-LABA use present during prevalent LABA use. ACM and FDC-LABA use are defined as any valid exposure episode during the query period, where episodes are created with an episode gap that is 25% of the days supply of the previous dispensing. FDC-LABA use must be preceded by continuous enrollment in medical and prescription drug insurance plans for at least 365 days prior to dispensing date, during which gaps in coverage of up to 45 days were allowed; and do not have chronic obstructive pulmonary disease (COPD), cystic fibrosis, bronchiectasis, pulmonary hypertension or embolism, or bronchopulmonary dysplasia in the 365 days prior to and including FDC-LABA dispensing date. Additional differences are detailed below:

Cohort 8) Users are included in Cohort 8 if there is at least one day of ACM or FDC-LABA use during the prevalent LABA exposure episode.
Cohort 9) Users are included in Cohort 9 if there is either ACM or FDC-LABA use for at least 50% the duration of the prevalent LABA exposure episode.
Cohort 10) Users are included in Cohort 10 if there is either ACM or FDC-LABA use for at least 75% the duration of the prevalent LABA exposure episode.
Cohort 11) Users are included in Cohort 11 if there is either ACM or FDC-LABA use on prevalent LABA dispensing date.

Follow-Up Time: We determined follow-up time based on the length of exposure episodes, which was defined using days supply information recorded in the outpatient pharmacy dispensings to create any period of continuous exposure. We considered an exposure episode continuous if gaps in days covered by days supply were less than 25% of the previous dispensing's days supply. This query analyzed only the first valid exposure episode per eligible member. Follow-up began on the index date and continued until the last day of supply of the last dispensing, or until the first occurrence of any of the following: 1) disenrollment; 2) death; 3) the end date of the data provided by each Data Partner; or 4) the end of the query period (September 30, 2015).

Analysis: We fitted an autoregression piecewise linear model describing the change of an observed rate over exposure time in months with an autoregression lag of 12 months and an intervention date on June 2, 2010, which is the date of the LABA drug safety communication (DSC)[1] issued by the US Food and Drug Administration (FDA). When determining the number of users in any given month for rate calculation purposes, exposure episode follow-up time is truncated on intervention date. The rate modeled is described below:

Cohort 8) The rate used for the ITS regression model is the number of prevalent LABA users with at least one day of overlapping ACM or FDC-LABA use among LABA-naive poorly-controlled asthma patients, defined with SABA canisters.
Cohort 9) The rate used for the ITS regression model is the number of prevalent LABA users with at least 50% adherence to ACM or FDC-LABA use among LABA-naive poorly-controlled asthma patients, defined with SABA canisters.
Cohort 10) The rate used for the ITS regression model is the number of prevalent LABA users with at least 75% adherence to ACM or FDC-LABA use among LABA-naive poorly-controlled asthma patients, defined with SABA canisters.
Cohort 11) The rate used for the ITS regression model is the number of prevalent LABA users with same-day ACM or FDC-LABA dispensing among LABA-naive poorly-controlled asthma patients, defined with SABA canisters.

ITS regression is performed for overall population and in subgroups defined by: age groups (18-45, 46-64, 65+ years), sex (male, female), and race (American Indian or Alaskan native, Asian, black or African American, native Hawaiian or other Pacific islander, white, or unknown).

Limitations: 1) As with all observational studies, this evaluation is limited in its ability to control for all sources of potential bias. 2) Algorithms to define exposures, inclusion and exclusion criteria, and covariates are imperfect and may be misclassified. Therefore, data should be interpreted with this limitation in mind. 3.) Race data may not completely captured at individual Data Partner. 4.) Piecewise linear regression models were used for the ITS analysis. Seasonality in data was not factored into adjustment.

Please see Appendix E for the parameter specifications used in the analyses.

Overview for Request: cder_mpl2r_wp012, Report 3 of 4 (Prevalent Cohorts)
Notes: Please contact the Sentinel Operations Center (info@sentinelsystem.org) for questions and to provide comments/suggestions for future enhancements to this document. For more information on Sentinel's routine querying modules, please refer to the documentation (https://dev.sentinelsystem.org/projects/SENTINEL/repos/sentinel-routine-querying-tool-documentation/browse).

[1]Food and Drug Administration (FDA). 2010 Drug Safety Communications. Available from: https://www.fda.gov/drugs/drug-safety-and-availability/2010-drug-safety-communications. Last updated March 8, 2016. Accessed May 7, 2020.

Sentinel

Table of Contents

Table of Contents

Table of Contents

Table of Contents

Table of Contents

Table of Contents

Table of Contents

Glossary of Terms for Analyses Using
Cohort Identification and Descriptive Analysis (CIDA) Module*

Amount Supplied - number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing.

Blackout Period - number of days at the beginning of a treatment episode that events are to be ignored. If an event occurs during the blackout period, the episode is excluded.

Care Setting - type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible care settings include: Inpatient Hospital Stay (IP), Non-Acute Institutional Stay (IS), Emergency Department (ED), Ambulatory Visit (AV), and Other Ambulatory Visit (OA). For laboratory results, possible care settings include: Emergency Department (E), Home (H), Inpatient (I), Outpatient (O), or Unknown or Missing (U). The Care Setting, along with the Principal Diagnosis Indicator (PDX), forms the Care Setting/PDX parameter.

- **Ambulatory Visit (AV) -** includes visits at outpatient clinics, same-day surgeries, urgent care visits, and other same-day ambulatory hospital encounters, but excludes emergency department encounters.
- **Emergency Department (ED) -** includes ED encounters that become inpatient stays (in which case inpatient stays would be a separate encounter). Excludes urgent care visits.
- **Inpatient Hospital Stay (IP) -** includes all inpatient stays, same-day hospital discharges, hospital transfers, and acute hospital care where the discharge is after the admission date.
- **Non-Acute Institutional Stay (IS) -** includes hospice, skilled nursing facility (SNF), rehab center, nursing home, residential, overnight non-hospital dialysis and other non-hospital stays.
- **Other Ambulatory Visit (OA) -** includes other non overnight AV encounters such as hospice visits, home health visits, skilled nursing facility visits, other non-hospital visits, as well as telemedicine, telephone and email consultations.

Charlson/Elixhauser Combined Comorbidity Score - calculated based on comorbidities observed during a requester-defined window around the exposure episode start date (e.g., in the 183 days prior to index).

Code Days - the minimum number of times the diagnosis must be found during the evaluation period in order to fulfill the algorithm to identify the corresponding patient characteristic.

Cohort Definition (drug/exposure) - indicates how the cohort will be defined: 01: Cohort includes only the first valid treatment episode during the query period; 02: Cohort includes all valid treatment episodes during the query period; 03: Cohort includes all valid treatment episodes during the query period until an event occurs.

Computed Start Marketing Date - represents the first observed dispensing date among all valid users within a GROUP (scenario) within each Data Partner site.

Days Supplied - number of days supplied for all dispensings in qualifying treatment episodes.

Eligible Members - number of members eligible for an incident treatment episode (defined by the drug/exposure and event washout periods) with drug and medical coverage during the query period.

Enrollment Gap - number of days allowed between two consecutive enrollment periods without breaking a “continuously enrolled” sequence.

Episodes - treatment episodes; length of episode is determined by days supplied in one dispensing or consecutive dispensings bridged by the episode gap.

Episode Gap - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the same treatment episode.

Event Deduplication - specifies how events are counted by the Modular Program (MP) algorithm: 0: Counts all occurrences of a health outcome of interest (HOI) during an exposure episode; 1: de-duplicates occurrences of the same HOI code and code type on the same day; 2: de-duplicates occurrences of the same HOI group on the same day (e.g., de-duplicates at the group level).

Exposure Episode Length - number of days after exposure initiation that is considered "exposed time."

Exposure Extension Period - number of days post treatment period in which the outcomes/events are counted for a treatment episode. Extensions are added after any episode gaps have been bridged.

Lookback Period - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).

Maximum Episode Duration - truncates exposure episodes after a requester-specified number of exposed days. Applied after any gaps are bridged and extension days added to the length of the exposure episode.

Member-Years - sum of all days of enrollment with medical and drug coverage in the query period preceded by an exposure washout period all divided by 365.25.

Minimum Days Supplied - specifies a minimum number of days in length of the days supplied for the episode to be considered.

Minimum Episode Duration - specifies a minimum number of days in length of the episode for it to be considered. Applied after any gaps are bridged and extension days added to the length of the exposure episode.

Monitoring Period - used to define time periods of interest for both sequential analysis and simple cohort characterization requests.

Principal Diagnosis (PDX) - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. 'P' = principal diagnosis, 'S' = secondary diagnosis, 'X' = unspecified diagnosis, '.' = blank. Along with the Care Setting values, forms the Caresetting/PDX parameter.

Query Period - period in which the modular program looks for exposures and outcomes of interest.

Switch Evaluation Step Value - value used to differentiate evaluation step. Each switch pattern can support up to 2 evaluation steps (0 = switch pattern evaluation start; 1 = first evaluation; 2 = second evaluation).

Switch Gap Inclusion Indicator - indicator for whether gaps in treatment episodes that are included in a switch episode will be counted as part of the switch episode duration.

Switch Pattern Cohort Inclusion Date - indicates which date to use for inclusion into the switch pattern cohort of interest as well as optionally as the index date of the treatment episode initiating the switch pattern. Valid options are the product approval date, product marketing date, other requester defined date, or computed start marketing date.

Switch Pattern Cohort Inclusion Strategy - indicates how the switch pattern cohort inclusion date will be used: 01: used only as a switch cohort entry date. First treatment episode dispensing date is used as index for computing time to first switch; 02: used as switch cohort entry date and as initial switch step index date for computing time to first switch.

Treatment Episode Truncation Indicator - indicates whether the exposure episode will be truncated at the occurrence of a requester-specified code.

Washout Period (drug/exposure) - number of days a user is required to have no evidence of prior exposure (drug dispensing/procedure) and continuous drug and medical coverage prior to an incident treatment episode.

Washout Period (event/outcome) - number of days a user is required to have no evidence of a prior event (procedure/diagnosis) and continuous drug and medical coverage prior to an incident treatment episode.

Years at Risk - number of days supplied plus any episode gaps and exposure extension periods all divided by 365.25.

*all terms may not be used in this report

Table 1a. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1]

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Initial Model Parameters (df = 103)[2]			
Intercept	0.032153	(0.026352, 0.037955)	<.001
Baseline Trend	-0.000142	(-0.000365, 0.000081)	0.210
Level Change (After Intervention 1)	-0.000078	(-0.006318, 0.006163)	0.980
Trend Change (After Intervention 1)	0.000025	(-0.000250, 0.000300)	0.857
Most Parsimonious Final Model Parameters (df = 105)[2,3]			
Intercept	0.031779	(0.027964, 0.035593)	<.001
Baseline Trend	-0.000127	(-0.000189, -0.000065)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

[2]df = degrees of freedom. Maximum likelihood estimation method is used to obtain the estimates here. Maximum likelihood estimation method adjusts for autocorrelation. The p-value is calculated under the assumption of asymptotic normality.

[3]Most parsimonious final model parameters were selected from initial model parameters using backwards selection with a cutoff of 0.05

Table 1b. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1], by Age Group

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Initial Model Parameters			
Age Group (Years)			
18-45 (df = 103)[2]			
Intercept	0.030714	(0.025475, 0.035953)	<.001
Baseline Trend	-0.000143	(-0.000345, 0.000058)	0.161
Level Change (After Intervention 1)	-0.001028	(-0.006638, 0.004582)	0.717
Trend Change (After Intervention 1)	0.000019	(-0.000229, 0.000268)	0.879
46-64 (df = 103)[2]			
Intercept	0.036442	(0.030208, 0.042676)	<.001
Baseline Trend	-0.000178	(-0.000417, 0.000061)	0.142
Level Change (After Intervention 1)	-0.001261	(-0.007851, 0.005329)	0.705
Trend Change (After Intervention 1)	0.000064	(-0.000232, 0.000360)	0.671
65+ (df = 103)[2]			
Intercept	0.024281	(0.018497, 0.030065)	<.001
Baseline Trend	-0.000069	(-0.000296, 0.000159)	0.551
Level Change (After Intervention 1)	0.004412	(-0.002279, 0.011104)	0.194
Trend Change (After Intervention 1)	-0.000019	(-0.000291, 0.000253)	0.890
Most Parsimonious Final Model Parameters[3]			
Age Group (Years)			
18-45 (df = 105)[2]			
Intercept	0.030544	(0.027071, 0.034016)	<.001
Baseline Trend	-0.000145	(-0.000201, -0.000088)	<.001
46-64 (df = 105)[2]			
Intercept	0.035621	(0.031505, 0.039737)	<.001
Baseline Trend	-0.000154	(-0.000221, -0.000087)	<.001
65+ (df = 106)[2]			
Intercept	0.022934	(0.020859, 0.025010)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

[2]df = degrees of freedom. Maximum likelihood estimation method is used to obtain the estimates here. Maximum likelihood estimation method adjusts for autocorrelation. The p-value is calculated under the assumption of asymptotic normality.

[3]Most parsimonious final model parameters were selected from initial model parameters using backwards selection with a cutoff of 0.05

Table 1c. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1], by Sex

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Initial Model Parameters			
Sex			
Female (df = 103)[2]			
Intercept	0.030423	(0.024800, 0.036046)	<.001
Baseline Trend	-0.000122	(-0.000338, 0.000095)	0.267
Level Change (After Intervention 1)	0.000294	(-0.005759, 0.006348)	0.923
Trend Change (After Intervention 1)	0.000008	(-0.000259, 0.000274)	0.954
Male (df = 103)[2]			
Intercept	0.035986	(0.029764, 0.042208)	<.001
Baseline Trend	-0.000185	(-0.000425, 0.000056)	0.130
Level Change (After Intervention 1)	-0.000917	(-0.007686, 0.005853)	0.789
Trend Change (After Intervention 1)	0.000062	(-0.000232, 0.000357)	0.676
Most Parsimonious Final Model Parameters[3]			
Sex			
Female (df = 105)[2]			
Intercept	0.030276	(0.026555, 0.033997)	<.001
Baseline Trend	-0.000113	(-0.000173, -0.000052)	<.001
Male (df = 105)[2]			
Intercept	0.035144	(0.031058, 0.039231)	<.001
Baseline Trend	-0.000156	(-0.000223, -0.000090)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

[2]df = degrees of freedom. Maximum likelihood estimation method is used to obtain the estimates here. Maximum likelihood estimation method adjusts for autocorrelation. The p-value is calculated under the assumption of asymptotic normality.

[3]Most parsimonious final model parameters were selected from initial model parameters using backwards selection with a cutoff of 0.05

Table 1d. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1], by Race

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Initial Model Parameters			
Race			
Unknown (df = 103)[2]			
Intercept	0.044702	(0.038146, 0.051258)	<.001
Baseline Trend	-0.000397	(-0.000648, -0.000146)	0.002
Level Change (After Intervention 1)	-0.001148	(-0.008052, 0.005756)	0.742
Trend Change (After Intervention 1)	0.000313	(0.000001, 0.000624)	0.049
American Indian/Alaska Native (df = 103)[2]			
Intercept	0.014565	(0.008962, 0.020168)	<.001
Baseline Trend	0.000105	(-0.000119, 0.000329)	0.354
Level Change (After Intervention 1)	0.003455	(-0.003354, 0.010263)	0.317
Trend Change (After Intervention 1)	-0.000207	(-0.000469, 0.000054)	0.119
Asian (df = 103)[2]			
Intercept	0.012254	(0.007543, 0.016966)	<.001
Baseline Trend	0.000100	(-0.000084, 0.000285)	0.283
Level Change (After Intervention 1)	0.004336	(-0.001060, 0.009732)	0.114
Trend Change (After Intervention 1)	-0.000153	(-0.000375, 0.000069)	0.174
Black/African American (df = 103)[2]			
Intercept	0.014950	(0.008498, 0.021401)	<.001
Baseline Trend	0.000122	(-0.000123, 0.000368)	0.326
Level Change (After Intervention 1)	0.002907	(-0.003727, 0.009541)	0.387
Trend Change (After Intervention 1)	-0.000212	(-0.000519, 0.000095)	0.175
Native Hawaiian/Other Pacific Islander (df = 103)[3]			
Intercept	0.014250	(0.011828, 0.016672)	<.001
Baseline Trend	0.000018	(-0.000080, 0.000117)	0.711
Level Change (After Intervention 1)	-0.002405	(-0.005459, 0.000649)	0.122
Trend Change (After Intervention 1)	-0.000049	(-0.000161, 0.000063)	0.388
White (df = 103)[2]			
Intercept	0.015595	(0.010568, 0.020621)	<.001
Baseline Trend	0.000200	(0.000003, 0.000397)	0.047
Level Change (After Intervention 1)	0.000833	(-0.004884, 0.006550)	0.773
Trend Change (After Intervention 1)	-0.000308	(-0.000545, -0.000072)	0.011
Most Parsimonious Final Model Parameters[4]			
Race			
Unknown (df = 104)[2]			
Intercept	0.045027	(0.038723, 0.051331)	<.001
Baseline Trend	-0.000420	(-0.000630, -0.000210)	<.001
Trend Change (After Intervention 1)	0.000325	(0.000022, 0.000629)	0.036

Table 1d. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1], by Race

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Most Parsimonious Final Model Parameters[4]			
Race			
American Indian/Alaska Native (df = 106)[2]			
Intercept	0.018177	(0.016123, 0.020231)	<.001
Asian (df = 105)[2]			
Intercept	0.014441	(0.011927, 0.016955)	<.001
Level Change (After Intervention 1)	0.004594	(0.001413, 0.007776)	0.005
Black/African American (df = 106)[2]			
Intercept	0.018991	(0.016214, 0.021767)	<.001
Native Hawaiian/Other Pacific Islander (df = 105)[3]			
Intercept	0.014645	(0.013459, 0.015831)	<.001
Level Change (After Intervention 1)	-0.003004	(-0.004535, -0.001473)	<.001
White (df = 104)[2]			
Intercept	0.015370	(0.010603, 0.020138)	<.001
Baseline Trend	0.000217	(0.000058, 0.000375)	0.008
Trend Change (After Intervention 1)	-0.000317	(-0.000546, -0.000088)	0.007

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

[2]df = degrees of freedom. Maximum likelihood estimation method is used to obtain the estimates here. Maximum likelihood estimation method adjusts for autocorrelation. The p-value is calculated under the assumption of asymptotic normality.

[3]Ordinary least squares method is used to obtain the estimates here. The p-value is calculated under the assumption of asymptotic normality.

[4]Most parsimonious final model parameters were selected from initial model parameters using backwards selection with a cutoff of 0.05
Race data may not be completely populated at all Data Partners; therefore, data about race may be incomplete

Table 1e. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1]

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Initial Model Parameters (df = 103)[2]			
Intercept	0.031344	(0.025612, 0.037077)	<.001
Baseline Trend	-0.000124	(-0.000345, 0.000097)	0.268
Level Change (After Intervention 1)	-0.000111	(-0.006290, 0.006068)	0.972
Trend Change (After Intervention 1)	0.000008	(-0.000264, 0.000279)	0.955
Most Parsimonious Final Model Parameters (df = 105)[2,3]			
Intercept	0.031236	(0.027456, 0.035016)	<.001
Baseline Trend	-0.000120	(-0.000182, -0.000059)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

[2]df = degrees of freedom. Maximum likelihood estimation method is used to obtain the estimates here. Maximum likelihood estimation method adjusts for autocorrelation. The p-value is calculated under the assumption of asymptotic normality.

[3]Most parsimonious final model parameters were selected from initial model parameters using backwards selection with a cutoff of 0.05

Table 1f. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1], by Age Group

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Initial Model Parameters			
Age Group (Years)			
18-45 (df = 103)[2]			
Intercept	0.030207	(0.024997, 0.035417)	<.001
Baseline Trend	-0.000132	(-0.000333, 0.000068)	0.193
Level Change (After Intervention 1)	-0.001034	(-0.006607, 0.004538)	0.714
Trend Change (After Intervention 1)	0.000009	(-0.000239, 0.000256)	0.946
46-64 (df = 103)[2]			
Intercept	0.035434	(0.029291, 0.041577)	<.001
Baseline Trend	-0.000156	(-0.000392, 0.000080)	0.192
Level Change (After Intervention 1)	-0.001262	(-0.007780, 0.005255)	0.702
Trend Change (After Intervention 1)	0.000042	(-0.000250, 0.000333)	0.776
65+ (df = 103)[2]			
Intercept	0.023049	(0.017357, 0.028741)	<.001
Baseline Trend	-0.000039	(-0.000263, 0.000185)	0.728
Level Change (After Intervention 1)	0.004270	(-0.002330, 0.010870)	0.202
Trend Change (After Intervention 1)	-0.000046	(-0.000314, 0.000221)	0.732
Most Parsimonious Final Model Parameters[3]			
Age Group (Years)			
18-45 (df = 105)[2]			
Intercept	0.030197	(0.026736, 0.033658)	<.001
Baseline Trend	-0.000141	(-0.000197, -0.000084)	<.001
46-64 (df = 105)[2]			
Intercept	0.034938	(0.030882, 0.038995)	<.001
Baseline Trend	-0.000146	(-0.000212, -0.000080)	<.001
65+ (df = 106)[2]			
Intercept	0.022636	(0.020591, 0.024681)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

[2]df = degrees of freedom. Maximum likelihood estimation method is used to obtain the estimates here. Maximum likelihood estimation method adjusts for autocorrelation. The p-value is calculated under the assumption of asymptotic normality.

[3]Most parsimonious final model parameters were selected from initial model parameters using backwards selection with a cutoff of 0.05

Table 1g. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1], by Sex

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Initial Model Parameters			
Sex			
Female (df = 103)[2]			
Intercept	0.029659	(0.024096, 0.035222)	<.001
Baseline Trend	-0.000105	(-0.000319, 0.000109)	0.334
Level Change (After Intervention 1)	0.000272	(-0.005725, 0.006270)	0.928
Trend Change (After Intervention 1)	-0.000008	(-0.000272, 0.000255)	0.950
Male (df = 103)[2]			
Intercept	0.035073	(0.028940, 0.041207)	<.001
Baseline Trend	-0.000164	(-0.000401, 0.000073)	0.174
Level Change (After Intervention 1)	-0.000986	(-0.007679, 0.005707)	0.771
Trend Change (After Intervention 1)	0.000043	(-0.000248, 0.000333)	0.771
Most Parsimonious Final Model Parameters[3]			
Sex			
Female (df = 105)[2]			
Intercept	0.029761	(0.026064, 0.033458)	<.001
Baseline Trend	-0.000107	(-0.000167, -0.000047)	<.001
Male (df = 105)[2]			
Intercept	0.034537	(0.030509, 0.038566)	<.001
Baseline Trend	-0.000149	(-0.000215, -0.000084)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

[2]df = degrees of freedom. Maximum likelihood estimation method is used to obtain the estimates here. Maximum likelihood estimation method adjusts for autocorrelation. The p-value is calculated under the assumption of asymptotic normality.

[3]Most parsimonious final model parameters were selected from initial model parameters using backwards selection with a cutoff of 0.05

Table 1h. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1], by Race

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Initial Model Parameters			
Race			
Unknown (df = 103)[2]			
Intercept	0.044093	(0.037663, 0.050524)	<.001
Baseline Trend	-0.000383	(-0.000629, -0.000136)	0.003
Level Change (After Intervention 1)	-0.001162	(-0.007970, 0.005646)	0.736
Trend Change (After Intervention 1)	0.000299	(-0.000006, 0.000604)	0.055
American Indian/Alaska Native (df = 103)[2]			
Intercept	0.013458	(0.008876, 0.018040)	<.001
Baseline Trend	0.000117	(-0.000069, 0.000302)	0.214
Level Change (After Intervention 1)	0.004391	(-0.001314, 0.010096)	0.130
Trend Change (After Intervention 1)	-0.000226	(-0.000437, -0.000014)	0.037
Asian (df = 103)[2]			
Intercept	0.011271	(0.006509, 0.016034)	<.001
Baseline Trend	0.000123	(-0.000064, 0.000309)	0.194
Level Change (After Intervention 1)	0.004176	(-0.001246, 0.009598)	0.130
Trend Change (After Intervention 1)	-0.000172	(-0.000396, 0.000053)	0.132
Black/African American (df = 103)[2]			
Intercept	0.013745	(0.007328, 0.020162)	<.001
Baseline Trend	0.000153	(-0.000092, 0.000397)	0.218
Level Change (After Intervention 1)	0.002787	(-0.003823, 0.009396)	0.405
Trend Change (After Intervention 1)	-0.000242	(-0.000547, 0.000063)	0.119
Native Hawaiian/Other Pacific Islander (df = 103)[3]			
Intercept	0.013896	(0.011444, 0.016349)	<.001
Baseline Trend	0.000022	(-0.000078, 0.000121)	0.668
Level Change (After Intervention 1)	-0.002266	(-0.005358, 0.000826)	0.149
Trend Change (After Intervention 1)	-0.000052	(-0.000165, 0.000061)	0.367
White (df = 103)[2]			
Intercept	0.014433	(0.009399, 0.019467)	<.001
Baseline Trend	0.000226	(0.000029, 0.000423)	0.025
Level Change (After Intervention 1)	0.000760	(-0.004950, 0.006471)	0.792
Trend Change (After Intervention 1)	-0.000332	(-0.000569, -0.000095)	0.007
Most Parsimonious Final Model Parameters[4]			
Race			
Unknown (df = 104)[2]			
Intercept	0.044426	(0.038244, 0.050608)	<.001
Baseline Trend	-0.000407	(-0.000613, -0.000201)	<.001
Trend Change (After Intervention 1)	0.000312	(0.000014, 0.000609)	0.040

Table 1h. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1], by Race

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Most Parsimonious Final Model Parameters[4]			
Race			
American Indian/Alaska Native (df = 106)[2]			
Intercept	0.017901	(0.015790, 0.020012)	<.001
Asian (df = 105)[2]			
Intercept	0.013965	(0.011414, 0.016516)	<.001
Level Change (After Intervention 1)	0.004956	(0.001732, 0.008181)	0.003
Black/African American (df = 106)[2]			
Intercept	0.018729	(0.015865, 0.021594)	<.001
Native Hawaiian/Other Pacific Islander (df = 105)[3]			
Intercept	0.014361	(0.013160, 0.015561)	<.001
Level Change (After Intervention 1)	-0.002787	(-0.004337, -0.001238)	<.001
White (df = 104)[2]			
Intercept	0.014226	(0.009445, 0.019008)	<.001
Baseline Trend	0.000241	(0.000083, 0.000400)	0.003
Trend Change (After Intervention 1)	-0.000340	(-0.000570, -0.000111)	0.004

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

[2]df = degrees of freedom. Maximum likelihood estimation method is used to obtain the estimates here. Maximum likelihood estimation method adjusts for autocorrelation. The p-value is calculated under the assumption of asymptotic normality.

[3]Ordinary least squares method is used to obtain the estimates here. The p-value is calculated under the assumption of asymptotic normality.

[4]Most parsimonious final model parameters were selected from initial model parameters using backwards selection with a cutoff of 0.05
Race data may not be completely populated at all Data Partners; therefore, data about race may be incomplete

Table 1i. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1]

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Initial Model Parameters (df = 103)[2]			
Intercept	0.030641	(0.024954, 0.036328)	<.001
Baseline Trend	-0.000108	(-0.000327, 0.000112)	0.332
Level Change (After Intervention 1)	-0.000209	(-0.006339, 0.005921)	0.946
Trend Change (After Intervention 1)	-0.000007	(-0.000276, 0.000263)	0.960
Most Parsimonious Final Model Parameters (df = 105)[2,3]			
Intercept	0.030768	(0.027005, 0.034532)	<.001
Baseline Trend	-0.000115	(-0.000176, -0.000054)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

[2]df = degrees of freedom. Maximum likelihood estimation method is used to obtain the estimates here. Maximum likelihood estimation method adjusts for autocorrelation. The p-value is calculated under the assumption of asymptotic normality.

[3]Most parsimonious final model parameters were selected from initial model parameters using backwards selection with a cutoff of 0.05

Table 1j. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1], by Age Group

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Initial Model Parameters			
Age Group (Years)			
18-45 (df = 103)[2]			
Intercept	0.029734	(0.024564, 0.034904)	<.001
Baseline Trend	-0.000121	(-0.000320, 0.000078)	0.230
Level Change (After Intervention 1)	-0.001084	(-0.006617, 0.004449)	0.698
Trend Change (After Intervention 1)	-0.000002	(-0.000247, 0.000243)	0.986
46-64 (df = 103)[2]			
Intercept	0.034582	(0.028496, 0.040669)	<.001
Baseline Trend	-0.000137	(-0.000371, 0.000096)	0.247
Level Change (After Intervention 1)	-0.001347	(-0.007810, 0.005116)	0.680
Trend Change (After Intervention 1)	0.000025	(-0.000264, 0.000314)	0.863
65+ (df = 103)[2]			
Intercept	0.021953	(0.016292, 0.027613)	<.001
Baseline Trend	-0.000011	(-0.000234, 0.000211)	0.919
Level Change (After Intervention 1)	0.004001	(-0.002555, 0.010557)	0.229
Trend Change (After Intervention 1)	-0.000071	(-0.000337, 0.000195)	0.598
Most Parsimonious Final Model Parameters[3]			
Age Group (Years)			
18-45 (df = 105)[2]			
Intercept	0.029892	(0.026449, 0.033335)	<.001
Baseline Trend	-0.000137	(-0.000193, -0.000081)	<.001
46-64 (df = 105)[2]			
Intercept	0.034350	(0.030324, 0.038376)	<.001
Baseline Trend	-0.000139	(-0.000204, -0.000073)	<.001
65+ (df = 106)[2]			
Intercept	0.022375	(0.020328, 0.024421)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

[2]df = degrees of freedom. Maximum likelihood estimation method is used to obtain the estimates here. Maximum likelihood estimation method adjusts for autocorrelation. The p-value is calculated under the assumption of asymptotic normality.

[3]Most parsimonious final model parameters were selected from initial model parameters using backwards selection with a cutoff of 0.05

Table 1k. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1], by Sex

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Initial Model Parameters			
Sex			
Female (df = 103)[2]			
Intercept	0.028977	(0.023467, 0.034487)	<.001
Baseline Trend	-0.000089	(-0.000302, 0.000123)	0.407
Level Change (After Intervention 1)	0.000186	(-0.005756, 0.006128)	0.951
Trend Change (After Intervention 1)	-0.000023	(-0.000284, 0.000238)	0.863
Male (df = 103)[2]			
Intercept	0.034331	(0.028217, 0.040445)	<.001
Baseline Trend	-0.000147	(-0.000383, 0.000090)	0.221
Level Change (After Intervention 1)	-0.001107	(-0.007770, 0.005556)	0.742
Trend Change (After Intervention 1)	0.000027	(-0.000262, 0.000317)	0.851
Most Parsimonious Final Model Parameters[3]			
Sex			
Female (df = 105)[2]			
Intercept	0.029308	(0.025631, 0.032986)	<.001
Baseline Trend	-0.000102	(-0.000162, -0.000042)	0.001
Male (df = 105)[2]			
Intercept	0.034039	(0.030014, 0.038063)	<.001
Baseline Trend	-0.000143	(-0.000209, -0.000078)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

[2]df = degrees of freedom. Maximum likelihood estimation method is used to obtain the estimates here. Maximum likelihood estimation method adjusts for autocorrelation. The p-value is calculated under the assumption of asymptotic normality.

[3]Most parsimonious final model parameters were selected from initial model parameters using backwards selection with a cutoff of 0.05

Table 1l. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1], by Race

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Initial Model Parameters			
Race			
Unknown (df = 103)[2]			
Intercept	0.043537	(0.037199, 0.049875)	<.001
Baseline Trend	-0.000369	(-0.000612, -0.000126)	0.003
Level Change (After Intervention 1)	-0.001250	(-0.007978, 0.005479)	0.713
Trend Change (After Intervention 1)	0.000286	(-0.000014, 0.000587)	0.062
American Indian/Alaska Native (df = 103)[2]			
Intercept	0.012755	(0.008072, 0.017437)	<.001
Baseline Trend	0.000129	(-0.000060, 0.000317)	0.180
Level Change (After Intervention 1)	0.004378	(-0.001430, 0.010186)	0.138
Trend Change (After Intervention 1)	-0.000234	(-0.000450, -0.000018)	0.034
Asian (df = 103)[2]			
Intercept	0.010396	(0.005590, 0.015202)	<.001
Baseline Trend	0.000146	(-0.000042, 0.000334)	0.127
Level Change (After Intervention 1)	0.003912	(-0.001541, 0.009366)	0.158
Trend Change (After Intervention 1)	-0.000191	(-0.000418, 0.000035)	0.097
Black/African American (df = 103)[2]			
Intercept	0.012832	(0.006397, 0.019267)	<.001
Baseline Trend	0.000175	(-0.000069, 0.000420)	0.158
Level Change (After Intervention 1)	0.002703	(-0.003892, 0.009298)	0.418
Trend Change (After Intervention 1)	-0.000264	(-0.000571, 0.000042)	0.090
Native Hawaiian/Other Pacific Islander (df = 103)[3]			
Intercept	0.013555	(0.011106, 0.016004)	<.001
Baseline Trend	0.000028	(-0.000071, 0.000127)	0.579
Level Change (After Intervention 1)	-0.002188	(-0.005276, 0.000900)	0.163
Trend Change (After Intervention 1)	-0.000058	(-0.000171, 0.000055)	0.308
White (df = 103)[2]			
Intercept	0.013457	(0.008420, 0.018494)	<.001
Baseline Trend	0.000248	(0.000051, 0.000445)	0.014
Level Change (After Intervention 1)	0.000655	(-0.005051, 0.006360)	0.820
Trend Change (After Intervention 1)	-0.000352	(-0.000589, -0.000114)	0.004
Most Parsimonious Final Model Parameters[4]			
Race			
Unknown (df = 104)[2]			
Intercept	0.043896	(0.037799, 0.049993)	<.001
Baseline Trend	-0.000395	(-0.000598, -0.000192)	<.001
Trend Change (After Intervention 1)	0.000300	(0.000007, 0.000594)	0.045

Table 1l. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1], by Race

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Most Parsimonious Final Model Parameters[4]			
Race			
American Indian/Alaska Native (df = 104)[2]			
Intercept	0.015552	(0.013236, 0.017867)	<.001
Level Change (After Intervention 1)	0.006932	(0.002486, 0.011378)	0.003
Trend Change (After Intervention 1)	-0.000104	(-0.000208, -0.000000)	0.050
Asian (df = 105)[2]			
Intercept	0.012892	(0.008843, 0.016941)	<.001
Baseline Trend	0.000072	(0.000006, 0.000137)	0.033
Black/African American (df = 106)[2]			
Intercept	0.018518	(0.015542, 0.021494)	<.001
Native Hawaiian/Other Pacific Islander (df = 105)[3]			
Intercept	0.014154	(0.012954, 0.015354)	<.001
Level Change (After Intervention 1)	-0.002595	(-0.004144, -0.001046)	0.001
White (df = 104)[2]			
Intercept	0.013279	(0.008496, 0.018061)	<.001
Baseline Trend	0.000261	(0.000102, 0.000420)	0.002
Trend Change (After Intervention 1)	-0.000358	(-0.000588, -0.000129)	0.003

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

[2]df = degrees of freedom. Maximum likelihood estimation method is used to obtain the estimates here. Maximum likelihood estimation method adjusts for autocorrelation. The p-value is calculated under the assumption of asymptotic normality.

[3]Ordinary least squares method is used to obtain the estimates here. The p-value is calculated under the assumption of asymptotic normality.

[4]Most parsimonious final model parameters were selected from initial model parameters using backwards selection with a cutoff of 0.05
Race data may not be completely populated at all Data Partners; therefore, data about race may be incomplete

Table 1m. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1]

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Initial Model Parameters (df = 103)[2]			
Intercept	0.031545	(0.025816, 0.037274)	<.001
Baseline Trend	-0.000128	(-0.000349, 0.000092)	0.252
Level Change (After Intervention 1)	-0.000144	(-0.006320, 0.006033)	0.963
Trend Change (After Intervention 1)	0.000013	(-0.000259, 0.000284)	0.927
Most Parsimonious Final Model Parameters (df = 105)[2,3]			
Intercept	0.031365	(0.027593, 0.035138)	<.001
Baseline Trend	-0.000122	(-0.000183, -0.000061)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

[2]df = degrees of freedom. Maximum likelihood estimation method is used to obtain the estimates here. Maximum likelihood estimation method adjusts for autocorrelation. The p-value is calculated under the assumption of asymptotic normality.

[3]Most parsimonious final model parameters were selected from initial model parameters using backwards selection with a cutoff of 0.05

Table 1n. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1], by Age Group

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Initial Model Parameters			
Age Group (Years)			
18-45 (df = 103)[2]			
Intercept	0.030326	(0.025138, 0.035515)	<.001
Baseline Trend	-0.000134	(-0.000334, 0.000065)	0.185
Level Change (After Intervention 1)	-0.001080	(-0.006643, 0.004483)	0.701
Trend Change (After Intervention 1)	0.000011	(-0.000235, 0.000257)	0.932
46-64 (df = 103)[2]			
Intercept	0.035704	(0.029573, 0.041834)	<.001
Baseline Trend	-0.000163	(-0.000398, 0.000072)	0.172
Level Change (After Intervention 1)	-0.001264	(-0.007771, 0.005243)	0.701
Trend Change (After Intervention 1)	0.000049	(-0.000242, 0.000340)	0.737
65+ (df = 103)[2]			
Intercept	0.023273	(0.017553, 0.028992)	<.001
Baseline Trend	-0.000044	(-0.000269, 0.000181)	0.701
Level Change (After Intervention 1)	0.004185	(-0.002442, 0.010813)	0.213
Trend Change (After Intervention 1)	-0.000041	(-0.000310, 0.000228)	0.763
Most Parsimonious Final Model Parameters[3]			
Age Group (Years)			
18-45 (df = 105)[2]			
Intercept	0.030289	(0.026845, 0.033732)	<.001
Baseline Trend	-0.000142	(-0.000198, -0.000086)	<.001
46-64 (df = 105)[2]			
Intercept	0.035097	(0.031052, 0.039142)	<.001
Baseline Trend	-0.000148	(-0.000213, -0.000082)	<.001
65+ (df = 106)[2]			
Intercept	0.022682	(0.020633, 0.024732)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

[2]df = degrees of freedom. Maximum likelihood estimation method is used to obtain the estimates here. Maximum likelihood estimation method adjusts for autocorrelation. The p-value is calculated under the assumption of asymptotic normality.

[3]Most parsimonious final model parameters were selected from initial model parameters using backwards selection with a cutoff of 0.05

Table 1o. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1], by Sex

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Initial Model Parameters			
Sex			
Female (df = 103)[2]			
Intercept	0.029877	(0.024312, 0.035441)	<.001
Baseline Trend	-0.000110	(-0.000324, 0.000105)	0.312
Level Change (After Intervention 1)	0.000247	(-0.005748, 0.006242)	0.935
Trend Change (After Intervention 1)	-0.000003	(-0.000267, 0.000260)	0.981
Male (df = 103)[2]			
Intercept	0.035236	(0.029117, 0.041355)	<.001
Baseline Trend	-0.000167	(-0.000404, 0.000069)	0.164
Level Change (After Intervention 1)	-0.001040	(-0.007726, 0.005647)	0.758
Trend Change (After Intervention 1)	0.000047	(-0.000243, 0.000336)	0.749
Most Parsimonious Final Model Parameters[3]			
Sex			
Female (df = 105)[2]			
Intercept	0.029902	(0.026211, 0.033593)	<.001
Baseline Trend	-0.000109	(-0.000169, -0.000049)	<.001
Male (df = 105)[2]			
Intercept	0.034642	(0.030625, 0.038658)	<.001
Baseline Trend	-0.000150	(-0.000216, -0.000085)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

[2]df = degrees of freedom. Maximum likelihood estimation method is used to obtain the estimates here. Maximum likelihood estimation method adjusts for autocorrelation. The p-value is calculated under the assumption of asymptotic normality.

[3]Most parsimonious final model parameters were selected from initial model parameters using backwards selection with a cutoff of 0.05

Table 1p. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1], by Race

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Initial Model Parameters			
Race			
Unknown (df = 103)[2]			
Intercept	0.044130	(0.037701, 0.050558)	<.001
Baseline Trend	-0.000383	(-0.000629, -0.000136)	0.003
Level Change (After Intervention 1)	-0.001235	(-0.008040, 0.005570)	0.720
Trend Change (After Intervention 1)	0.000300	(-0.000006, 0.000605)	0.054
American Indian/Alaska Native (df = 103)[2]			
Intercept	0.013900	(0.009148, 0.018652)	<.001
Baseline Trend	0.000107	(-0.000085, 0.000298)	0.273
Level Change (After Intervention 1)	0.004356	(-0.001551, 0.010263)	0.147
Trend Change (After Intervention 1)	-0.000216	(-0.000435, 0.000004)	0.054
Asian (df = 103)[2]			
Intercept	0.011739	(0.007023, 0.016456)	<.001
Baseline Trend	0.000111	(-0.000074, 0.000296)	0.238
Level Change (After Intervention 1)	0.004274	(-0.001138, 0.009687)	0.120
Trend Change (After Intervention 1)	-0.000161	(-0.000383, 0.000061)	0.154
Black/African American (df = 103)[2]			
Intercept	0.014459	(0.007997, 0.020921)	<.001
Baseline Trend	0.000132	(-0.000113, 0.000378)	0.288
Level Change (After Intervention 1)	0.002931	(-0.003689, 0.009552)	0.382
Trend Change (After Intervention 1)	-0.000221	(-0.000529, 0.000086)	0.157
Native Hawaiian/Other Pacific Islander (df = 103)[3]			
Intercept	0.014143	(0.011682, 0.016604)	<.001
Baseline Trend	0.000018	(-0.000082, 0.000118)	0.718
Level Change (After Intervention 1)	-0.002264	(-0.005367, 0.000839)	0.151
Trend Change (After Intervention 1)	-0.000050	(-0.000164, 0.000063)	0.382
White (df = 103)[2]			
Intercept	0.014821	(0.009808, 0.019834)	<.001
Baseline Trend	0.000216	(0.000020, 0.000413)	0.031
Level Change (After Intervention 1)	0.000766	(-0.004929, 0.006462)	0.790
Trend Change (After Intervention 1)	-0.000323	(-0.000559, -0.000086)	0.008
Most Parsimonious Final Model Parameters[4]			
Race			
Unknown (df = 104)[2]			
Intercept	0.044481	(0.038300, 0.050661)	<.001
Baseline Trend	-0.000408	(-0.000614, -0.000202)	<.001
Trend Change (After Intervention 1)	0.000313	(0.000016, 0.000611)	0.039

Table 1p. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1], by Race

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Most Parsimonious Final Model Parameters[4]			
Race			
American Indian/Alaska Native (df = 106)[2]			
Intercept	0.017999	(0.015838, 0.020159)	<.001
Asian (df = 105)[2]			
Intercept	0.014157	(0.011644, 0.016669)	<.001
Level Change (After Intervention 1)	0.004809	(0.001627, 0.007991)	0.003
Black/African American (df = 106)[2]			
Intercept	0.018858	(0.016021, 0.021696)	<.001
Native Hawaiian/Other Pacific Islander (df = 105)[3]			
Intercept	0.014535	(0.013329, 0.015740)	<.001
Level Change (After Intervention 1)	-0.002917	(-0.004473, -0.001361)	<.001
White (df = 104)[2]			
Intercept	0.014612	(0.009851, 0.019374)	<.001
Baseline Trend	0.000232	(0.000074, 0.000390)	0.004
Trend Change (After Intervention 1)	-0.000331	(-0.000559, -0.000102)	0.005

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

[2]df = degrees of freedom. Maximum likelihood estimation method is used to obtain the estimates here. Maximum likelihood estimation method adjusts for autocorrelation. The p-value is calculated under the assumption of asymptotic normality.

[3]Ordinary least squares method is used to obtain the estimates here. The p-value is calculated under the assumption of asymptotic normality.

[4]Most parsimonious final model parameters were selected from initial model parameters using backwards selection with a cutoff of 0.05
Race data may not be completely populated at all Data Partners; therefore, data about race may be incomplete

Table 2a. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.025701	0.025701
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.025701	0.025701
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.024941	0.024941
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.024941	0.024941

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

Table 2b. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend, by Age Group

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Age Group (Years)				
18-45				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.023596	0.023596
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.023596	0.023596
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.022727	0.022727
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.022727	0.022727
46-64				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.028245	0.028245
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.028245	0.028245
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.027323	0.027323
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.027323	0.027323
65+				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.022934	0.022934
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.022934	0.022934
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.022934	0.022934
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.022934	0.022934

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

Table 2c. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend, by Sex

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Sex				
Female				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.024856	0.024856
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.024856	0.024856
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.024178	0.024178
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.024178	0.024178
Male				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.027641	0.027641
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.027641	0.027641
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.026703	0.026703
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.026703	0.026703

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

Table 2d. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend, by Race

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Race				
Unknown				
Absolute Change at 6 Months after Intervention 1	0.001951	(0.000152, 0.003750)	0.026809	0.024858
Relative Change (Percent) at 6 Months after Intervention 1	7.85	(-0.97, 16.66)	0.026809	0.024858
Absolute Change at 12 Months after Intervention 1	0.003901	(0.000304, 0.007499)	0.026238	0.022337
Relative Change (Percent) at 12 Months after Intervention 1	17.47	(-3.46, 38.39)	0.026238	0.022337
American Indian/Alaska Native				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.018177	0.018177
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.018177	0.018177
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.018177	0.018177
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.018177	0.018177
Asian				
Absolute Change at 6 Months after Intervention 1	0.004594	(0.001441, 0.007747)	0.019035	0.014441
Relative Change (Percent) at 6 Months after Intervention 1	31.81	(5.59, 58.04)	0.019035	0.014441
Absolute Change at 12 Months after Intervention 1	0.004594	(0.001441, 0.007747)	0.019035	0.014441
Relative Change (Percent) at 12 Months after Intervention 1	31.81	(5.59, 58.04)	0.019035	0.014441
Black/African American				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.018991	0.018991
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.018991	0.018991
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.018991	0.018991
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.018991	0.018991
Native Hawaiian/Other Pacific Islander				
Absolute Change at 6 Months after Intervention 1	-0.003004	(-0.004517, -0.001490)	0.011642	0.014645
Relative Change (Percent) at 6 Months after Intervention 1	-20.51	(-29.63, -11.39)	0.011642	0.014645
Absolute Change at 12 Months after Intervention 1	-0.003004	(-0.004517, -0.001490)	0.011642	0.014645
Relative Change (Percent) at 12 Months after Intervention 1	-20.51	(-29.63, -11.39)	0.011642	0.014645

Table 2d. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend, by Race

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Race				
White				
Absolute Change at 6 Months after Intervention 1	-0.001902	(-0.003257, -0.000546)	0.023868	0.025770
Relative Change (Percent) at 6 Months after Intervention 1	-7.38	(-11.62, -3.14)	0.023868	0.025770
Absolute Change at 12 Months after Intervention 1	-0.003803	(-0.006514, -0.001093)	0.023266	0.027070
Relative Change (Percent) at 12 Months after Intervention 1	-14.05	(-21.75, -6.35)	0.023266	0.027070

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.
Race data may not be completely populated at all Data Partners; therefore, data about race may be incomplete

Table 2e. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.025463	0.025463
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.025463	0.025463
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.024741	0.024741
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.024741	0.024741

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

Table 2f. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma after in the Sentinel Distributed Database (SDD) June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend, by Age Group

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Age Group (Years)				
18-45				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.023444	0.023444
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.023444	0.023444
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.022600	0.022600
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.022600	0.022600
46-64				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.027951	0.027951
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.027951	0.027951
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.027078	0.027078
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.027078	0.027078
65+				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.022636	0.022636
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.022636	0.022636
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.022636	0.022636
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.022636	0.022636

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

Table 2g. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend, by Sex

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Sex				
Female				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.024629	0.024629
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.024629	0.024629
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.023987	0.023987
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.023987	0.023987
Male				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.027377	0.027377
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.027377	0.027377
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.026483	0.026483
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.026483	0.026483

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

Table 2h. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend, by Race

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Race				
Unknown				
Absolute Change at 6 Months after Intervention 1	0.001870	(0.000106, 0.003634)	0.026770	0.024900
Relative Change (Percent) at 6 Months after Intervention 1	7.51	(-1.05, 16.07)	0.026770	0.024900
Absolute Change at 12 Months after Intervention 1	0.003740	(0.000213, 0.007268)	0.026200	0.022460
Relative Change (Percent) at 12 Months after Intervention 1	16.65	(-3.53, 36.84)	0.026200	0.022460
American Indian/Alaska Native				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.017901	0.017901
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.017901	0.017901
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.017901	0.017901
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.017901	0.017901
Asian				
Absolute Change at 6 Months after Intervention 1	0.004956	(0.001756, 0.008156)	0.018921	0.013965
Relative Change (Percent) at 6 Months after Intervention 1	35.49	(7.41, 63.57)	0.018921	0.013965
Absolute Change at 12 Months after Intervention 1	0.004956	(0.001756, 0.008156)	0.018921	0.013965
Relative Change (Percent) at 12 Months after Intervention 1	35.49	(7.41, 63.57)	0.018921	0.013965
Black/African American				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.018729	0.018729
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.018729	0.018729
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.018729	0.018729
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.018729	0.018729
Native Hawaiian/Other Pacific Islander				
Absolute Change at 6 Months after Intervention 1	-0.002787	(-0.004320, -0.001255)	0.011573	0.014361
Relative Change (Percent) at 6 Months after Intervention 1	-19.41	(-28.89, -9.93)	0.011573	0.014361
Absolute Change at 12 Months after Intervention 1	-0.002787	(-0.004320, -0.001255)	0.011573	0.014361
Relative Change (Percent) at 12 Months after Intervention 1	-19.41	(-28.89, -9.93)	0.011573	0.014361

Table 2h. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend, by Race

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Race				
White				
Absolute Change at 6 Months after Intervention 1	-0.002042	(-0.003401, -0.000682)	0.023765	0.025807
Relative Change (Percent) at 6 Months after Intervention 1	-7.91	(-12.08, -3.74)	0.023765	0.025807
Absolute Change at 12 Months after Intervention 1	-0.004083	(-0.006802, -0.001365)	0.023171	0.027255
Relative Change (Percent) at 12 Months after Intervention 1	-14.98	(-22.50, -7.46)	0.023171	0.027255

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.
Race data may not be completely populated at all Data Partners; therefore, data about race may be incomplete

Table 2i. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.025254	0.025254
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.025254	0.025254
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.024565	0.024565
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.024565	0.024565

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

Table 2j. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend, by Age Group

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Age Group (Years)				
18-45				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.023313	0.023313
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.023313	0.023313
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.022491	0.022491
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.022491	0.022491
46-64				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.027690	0.027690
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.027690	0.027690
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.026858	0.026858
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.026858	0.026858
65+				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.022375	0.022375
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.022375	0.022375
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.022375	0.022375
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.022375	0.022375

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

Table 2k. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend, by Sex

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Sex				
Female				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.024427	0.024427
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.024427	0.024427
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.023817	0.023817
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.023817	0.023817
Male				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.027153	0.027153
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.027153	0.027153
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.026293	0.026293
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.026293	0.026293

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

Table 2l. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend, by Race

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Race				
Unknown				
Absolute Change at 6 Months after Intervention 1	0.001801	(0.000062, 0.003541)	0.026728	0.024927
Relative Change (Percent) at 6 Months after Intervention 1	7.23	(-1.15, 15.60)	0.026728	0.024927
Absolute Change at 12 Months after Intervention 1	0.003603	(0.000124, 0.007081)	0.026159	0.022556
Relative Change (Percent) at 12 Months after Intervention 1	15.97	(-3.66, 35.61)	0.026159	0.022556
American Indian/Alaska Native				
Absolute Change at 6 Months after Intervention 1	0.006307	(0.002331, 0.010284)	0.021859	0.015552
Relative Change (Percent) at 6 Months after Intervention 1	40.56	(11.15, 69.96)	0.021859	0.015552
Absolute Change at 12 Months after Intervention 1	0.005683	(0.002089, 0.009276)	0.021235	0.015552
Relative Change (Percent) at 12 Months after Intervention 1	36.54	(9.69, 63.39)	0.021235	0.015552
Asian				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.016327	0.016327
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.016327	0.016327
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.016756	0.016756
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.016756	0.016756
Black/African American				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.018518	0.018518
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.018518	0.018518
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.018518	0.018518
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.018518	0.018518
Native Hawaiian/Other Pacific Islander				
Absolute Change at 6 Months after Intervention 1	-0.002595	(-0.004126, -0.001064)	0.011558	0.014154
Relative Change (Percent) at 6 Months after Intervention 1	-18.34	(-28.01, -8.66)	0.011558	0.014154
Absolute Change at 12 Months after Intervention 1	-0.002595	(-0.004126, -0.001064)	0.011558	0.014154
Relative Change (Percent) at 12 Months after Intervention 1	-18.34	(-28.01, -8.66)	0.011558	0.014154

Table 2l. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend, by Race

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Race				
White				
Absolute Change at 6 Months after Intervention 1	-0.002151	(-0.003510, -0.000791)	0.023656	0.025806
Relative Change (Percent) at 6 Months after Intervention 1	-8.33	(-12.45, -4.22)	0.023656	0.025806
Absolute Change at 12 Months after Intervention 1	-0.004301	(-0.007020, -0.001582)	0.023071	0.027372
Relative Change (Percent) at 12 Months after Intervention 1	-15.71	(-23.09, -8.34)	0.023071	0.027372

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.
Race data may not be completely populated at all Data Partners; therefore, data about race may be incomplete

Table 2m. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.025514	0.025514
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.025514	0.025514
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.024783	0.024783
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.024783	0.024783

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

Table 2n. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend, by Age Group

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Age Group (Years)				
18-45				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.023484	0.023484
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.023484	0.023484
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.022634	0.022634
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.022634	0.022634
46-64				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.028014	0.028014
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.028014	0.028014
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.027128	0.027128
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.027128	0.027128
65+				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.022682	0.022682
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.022682	0.022682
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.022682	0.022682
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.022682	0.022682

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

Table 2o. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend, by Sex

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Sex				
Female				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.024685	0.024685
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.024685	0.024685
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.024033	0.024033
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.024033	0.024033
Male				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.027418	0.027418
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.027418	0.027418
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.026515	0.026515
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.026515	0.026515

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.

Table 2p. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend, by Race

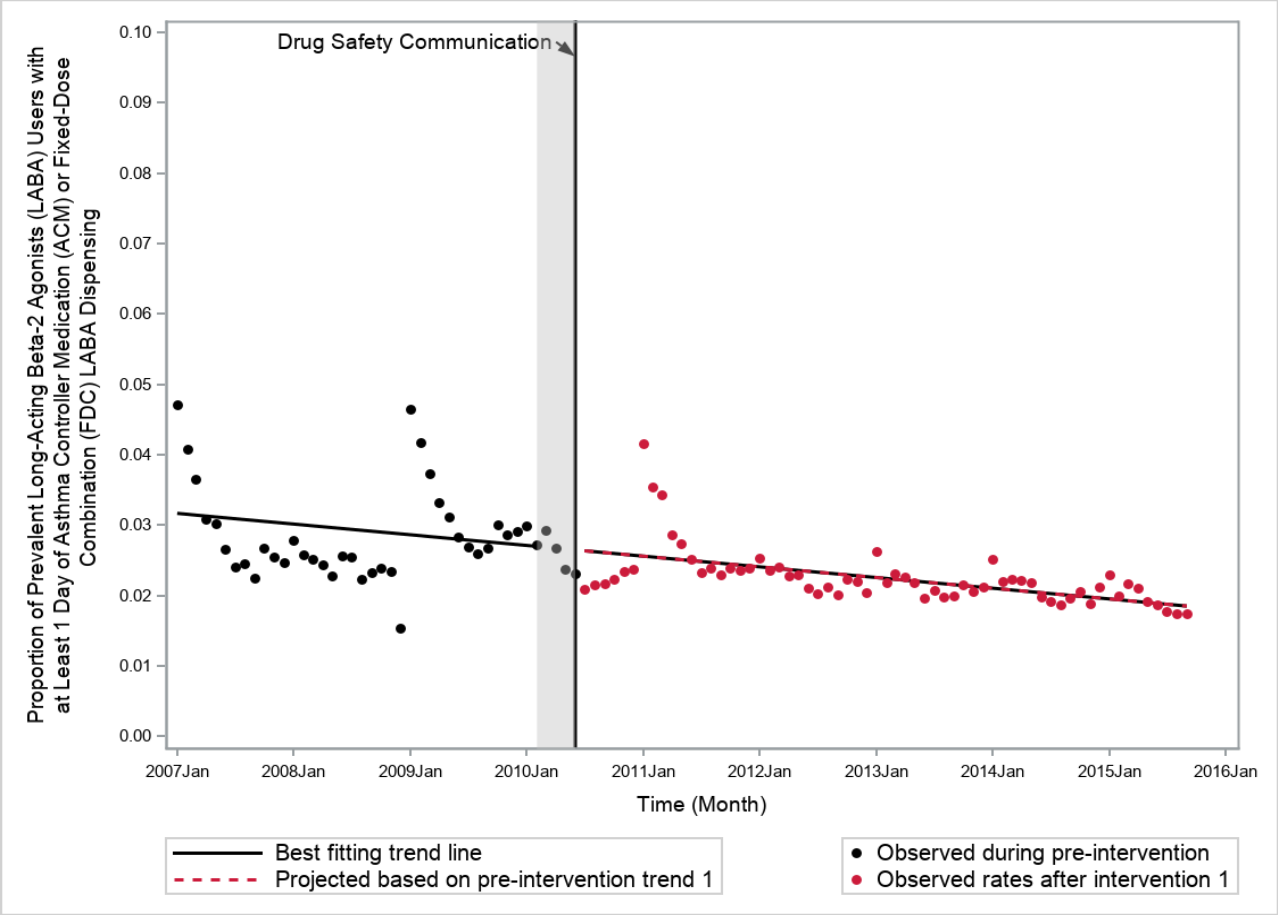
Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Race				
Unknown				
Absolute Change at 6 Months after Intervention 1	0.001879	(0.000115, 0.003642)	0.026770	0.024891
Relative Change (Percent) at 6 Months after Intervention 1	7.55	(-1.02, 16.11)	0.026770	0.024891
Absolute Change at 12 Months after Intervention 1	0.003757	(0.000230, 0.007284)	0.026200	0.022442
Relative Change (Percent) at 12 Months after Intervention 1	16.74	(-3.48, 36.96)	0.026200	0.022442
American Indian/Alaska Native				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.017999	0.017999
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.017999	0.017999
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.017999	0.017999
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.017999	0.017999
Asian				
Absolute Change at 6 Months after Intervention 1	0.004809	(0.001654, 0.007964)	0.018966	0.014157
Relative Change (Percent) at 6 Months after Intervention 1	33.97	(6.88, 61.05)	0.018966	0.014157
Absolute Change at 12 Months after Intervention 1	0.004809	(0.001654, 0.007964)	0.018966	0.014157
Relative Change (Percent) at 12 Months after Intervention 1	33.97	(6.88, 61.05)	0.018966	0.014157
Black/African American				
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.018858	0.018858
Relative Change (Percent) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.018858	0.018858
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.018858	0.018858
Relative Change (Percent) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.018858	0.018858
Native Hawaiian/Other Pacific Islander				
Absolute Change at 6 Months after Intervention 1	-0.002917	(-0.004455, -0.001378)	0.011618	0.014535
Relative Change (Percent) at 6 Months after Intervention 1	-20.07	(-29.43, -10.70)	0.011618	0.014535
Absolute Change at 12 Months after Intervention 1	-0.002917	(-0.004455, -0.001378)	0.011618	0.014535
Relative Change (Percent) at 12 Months after Intervention 1	-20.07	(-29.43, -10.70)	0.011618	0.014535

Table 2p. Absolute and Relative Changes in Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing among LABA-Naive Patients with Poorly Controlled Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend, by Race

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Race				
White				
Absolute Change at 6 Months after Intervention 1	-0.001984	(-0.003337, -0.000630)	0.023760	0.025744
Relative Change (Percent) at 6 Months after Intervention 1	-7.71	(-11.90, -3.51)	0.023760	0.025744
Absolute Change at 12 Months after Intervention 1	-0.003968	(-0.006675, -0.001260)	0.023167	0.027135
Relative Change (Percent) at 12 Months after Intervention 1	-14.62	(-22.20, -7.04)	0.023167	0.027135

[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model. An anticipatory period starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the intervention was implemented.
Race data may not be completely populated at all Data Partners; therefore, data about race may be incomplete

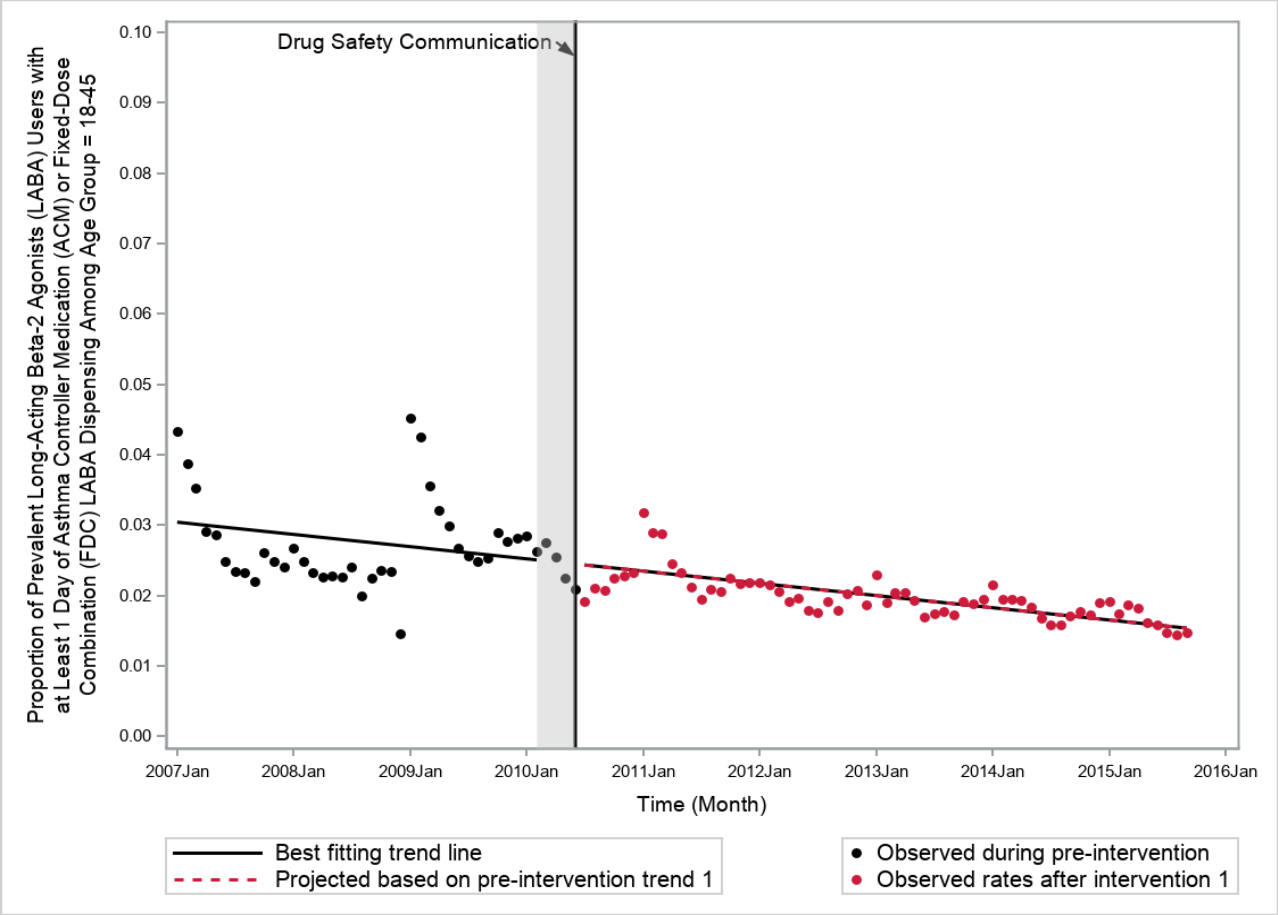
Figure 1. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2]



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

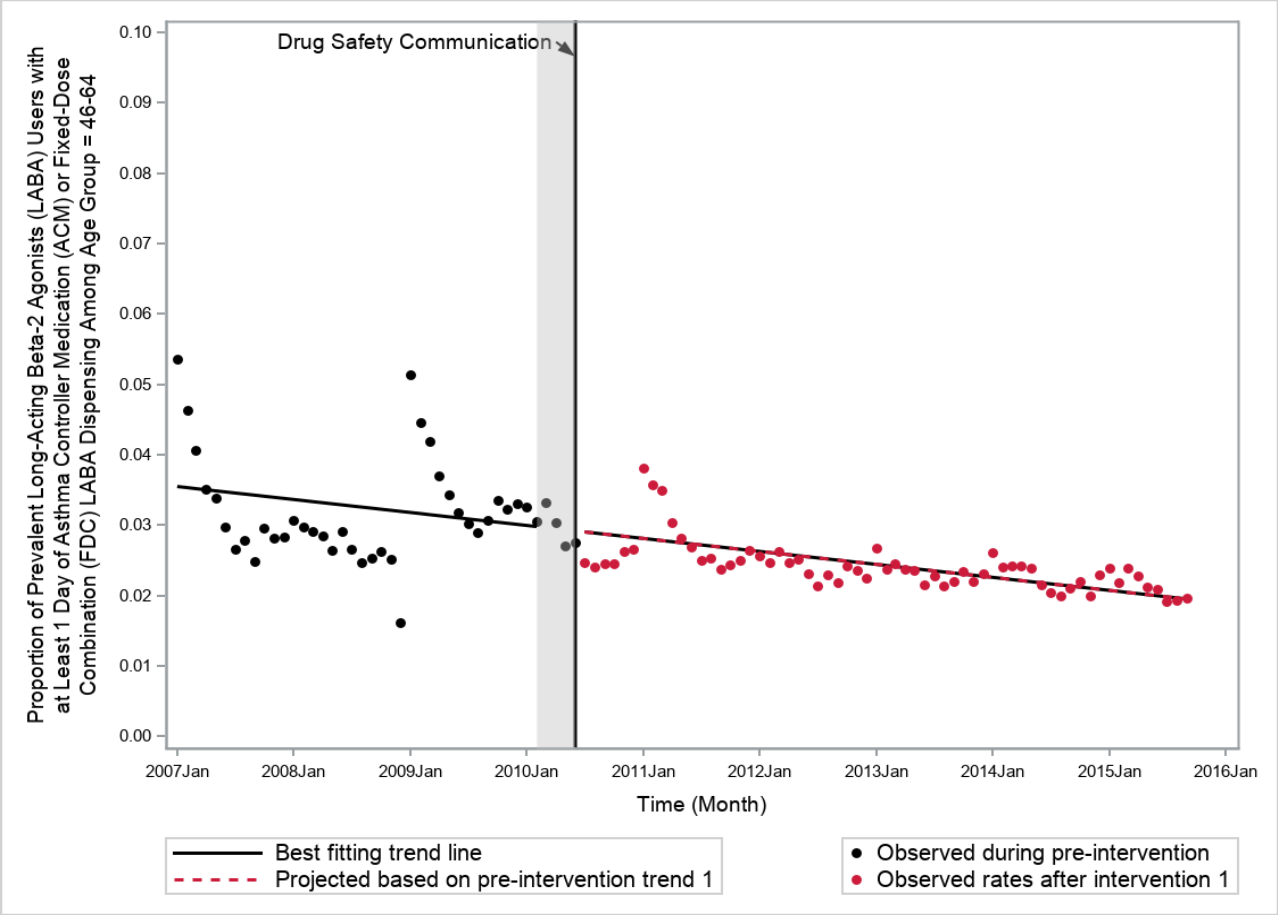
Figure 2. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Age Group = 18-45



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

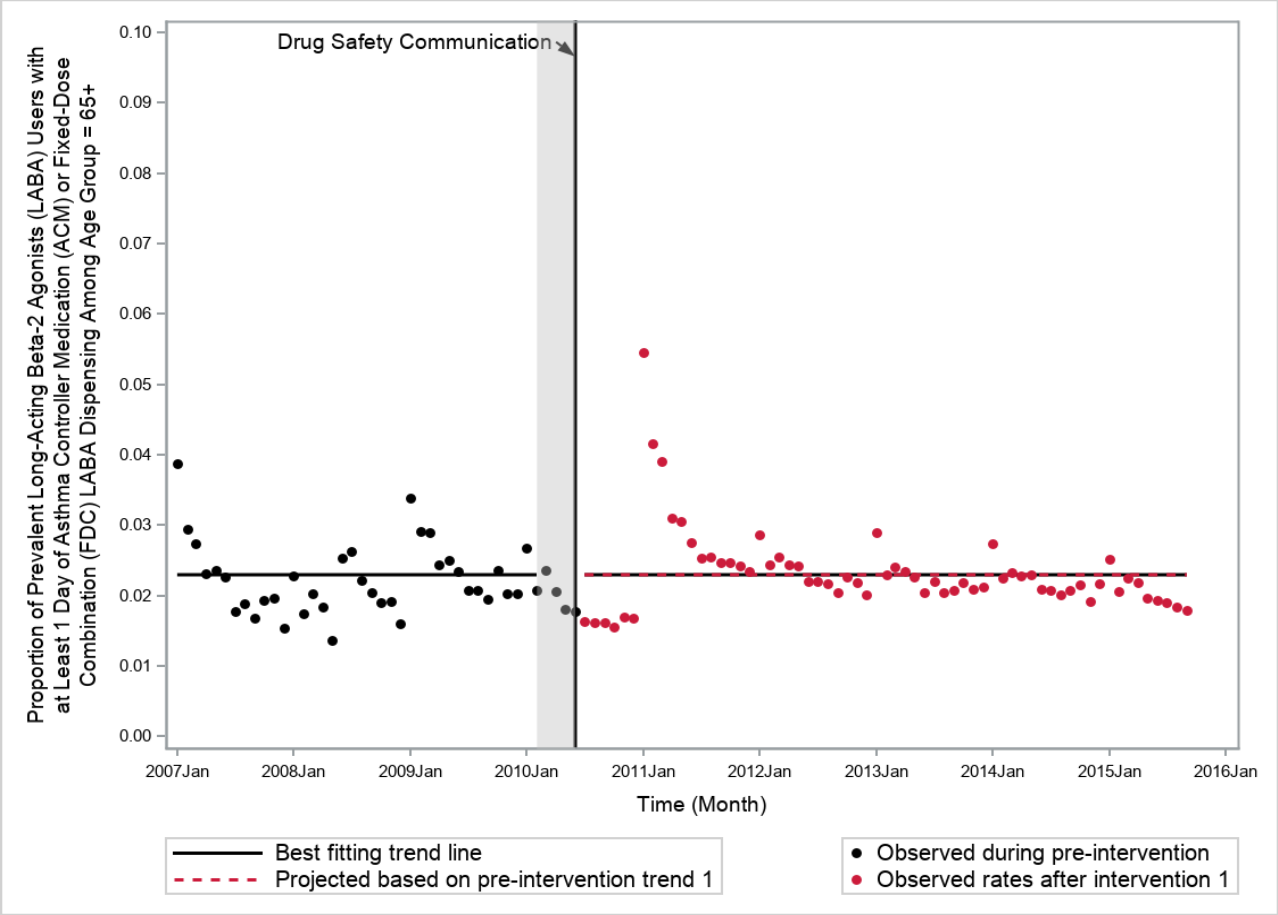
Figure 3. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Age Group = 46-64



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

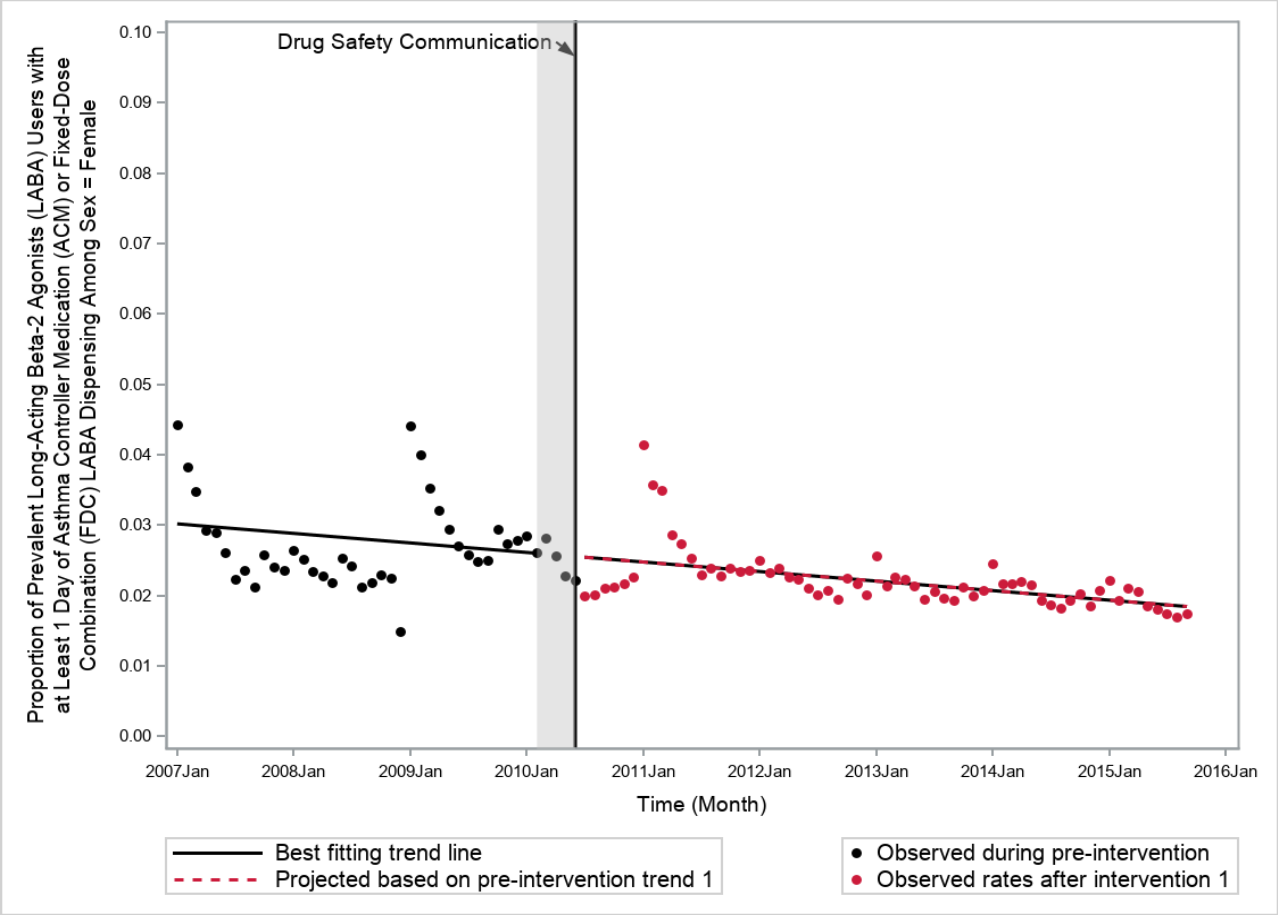
Figure 4. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Age Group = 65+



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

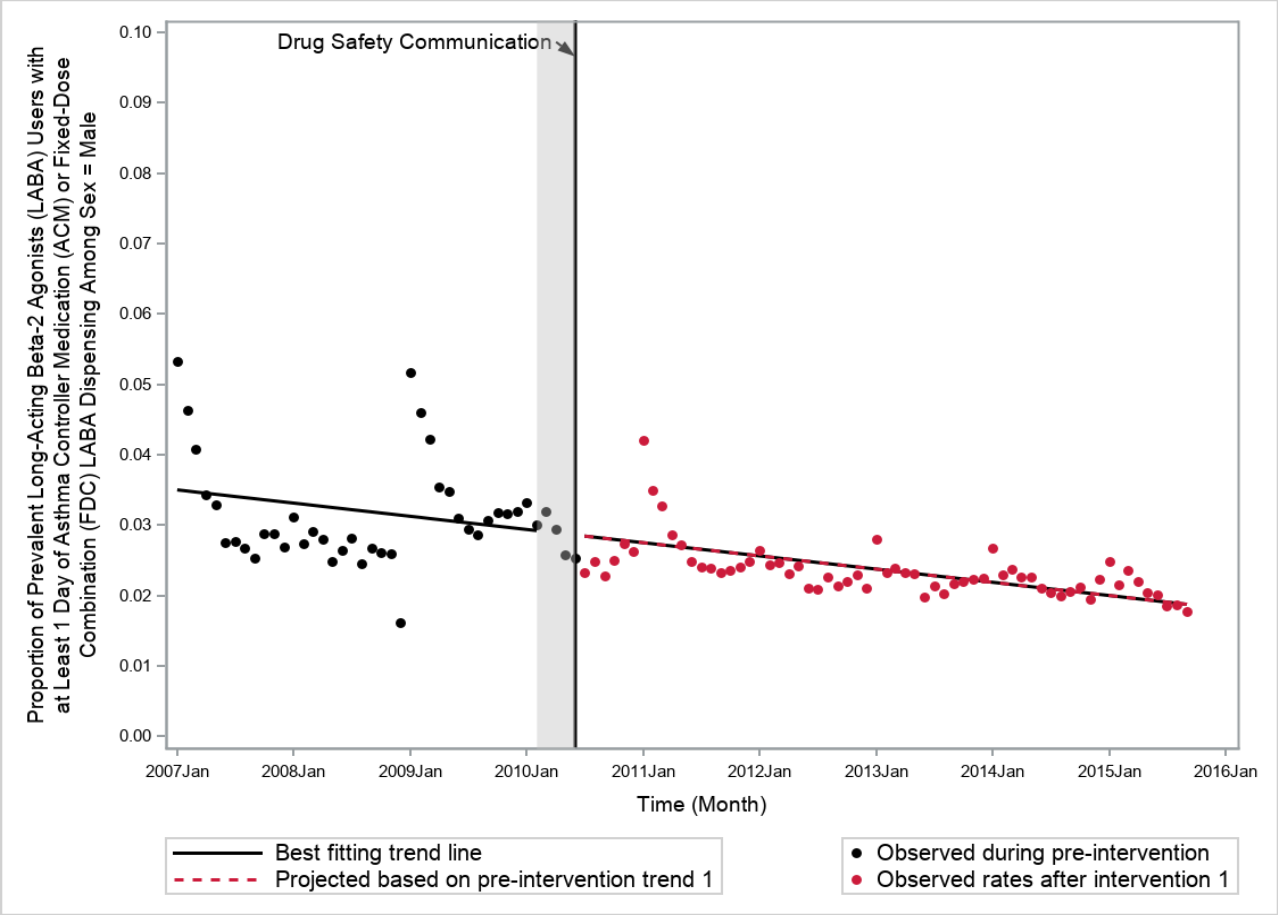
Figure 5. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Sex = Female



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

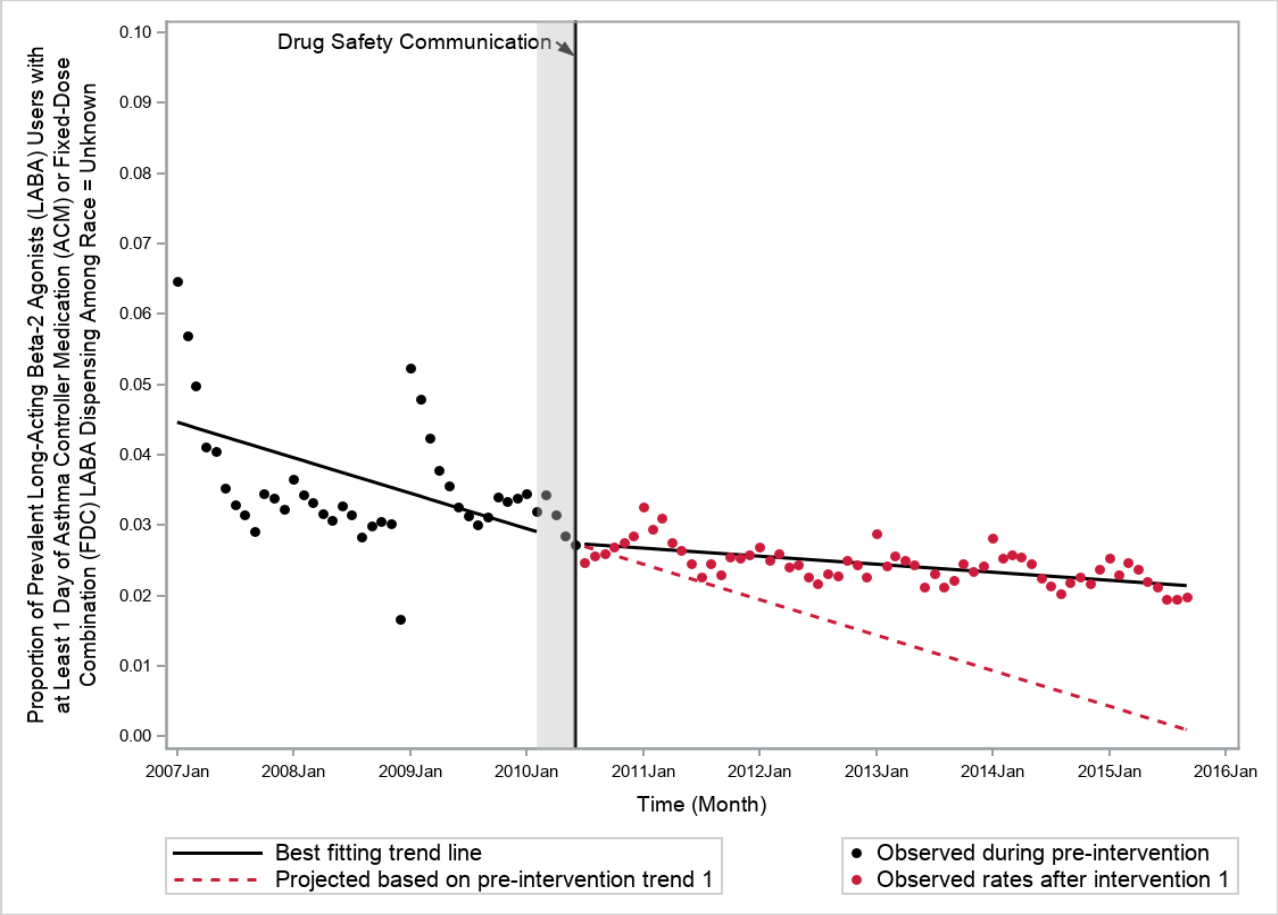
Figure 6. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Sex = Male



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

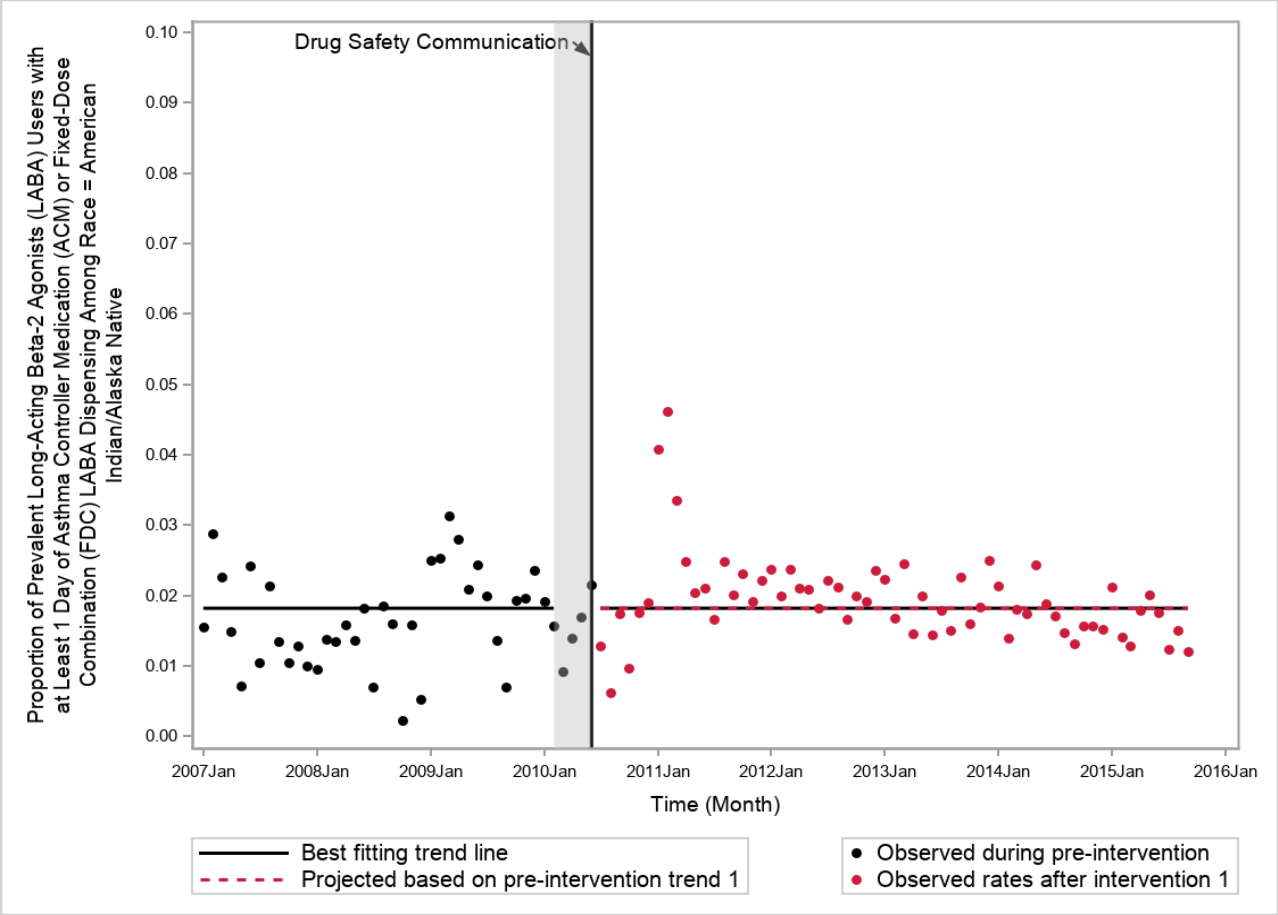
Figure 7. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = Unknown



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

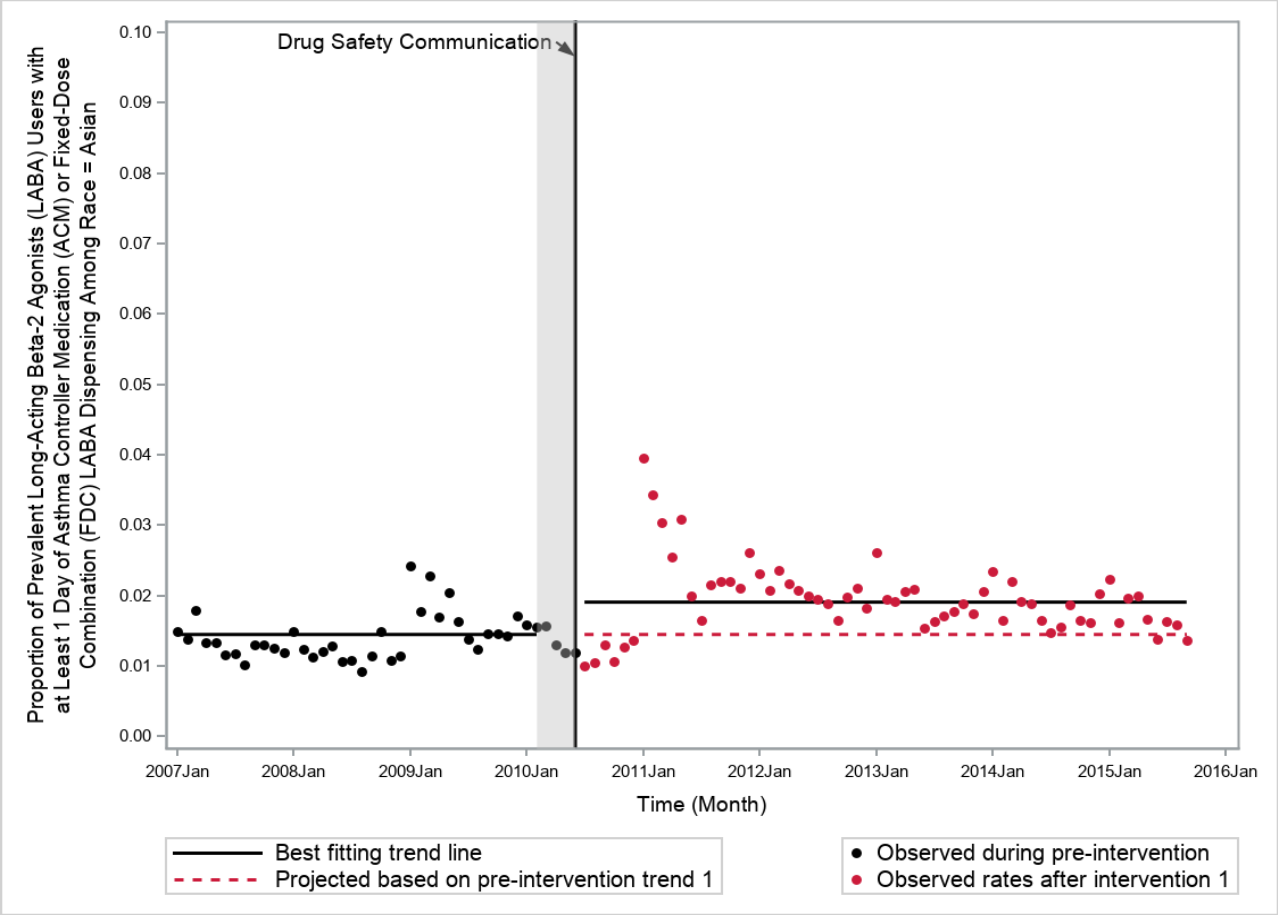
Figure 8. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = American Indian/Alaska Native



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

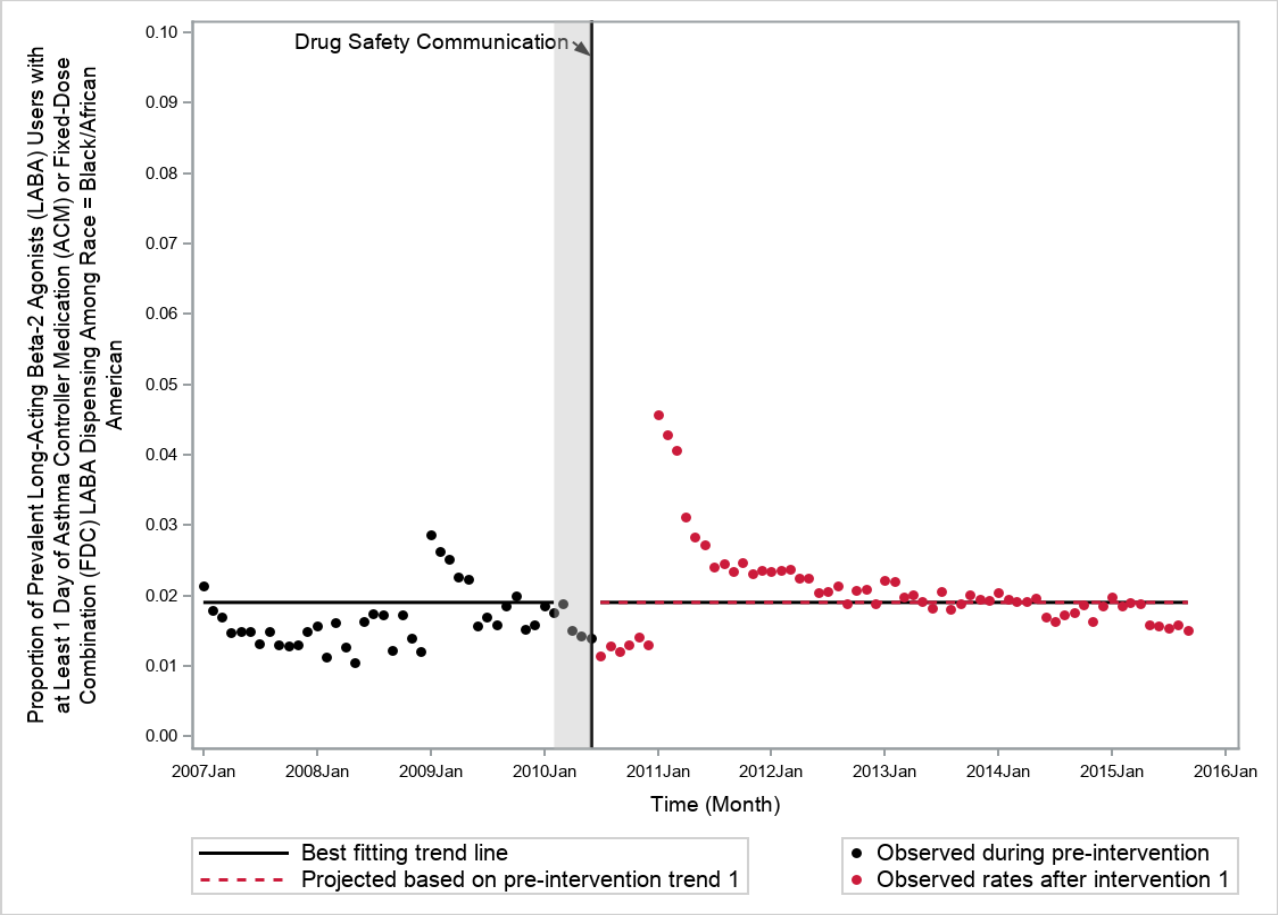
Figure 9. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = Asian



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

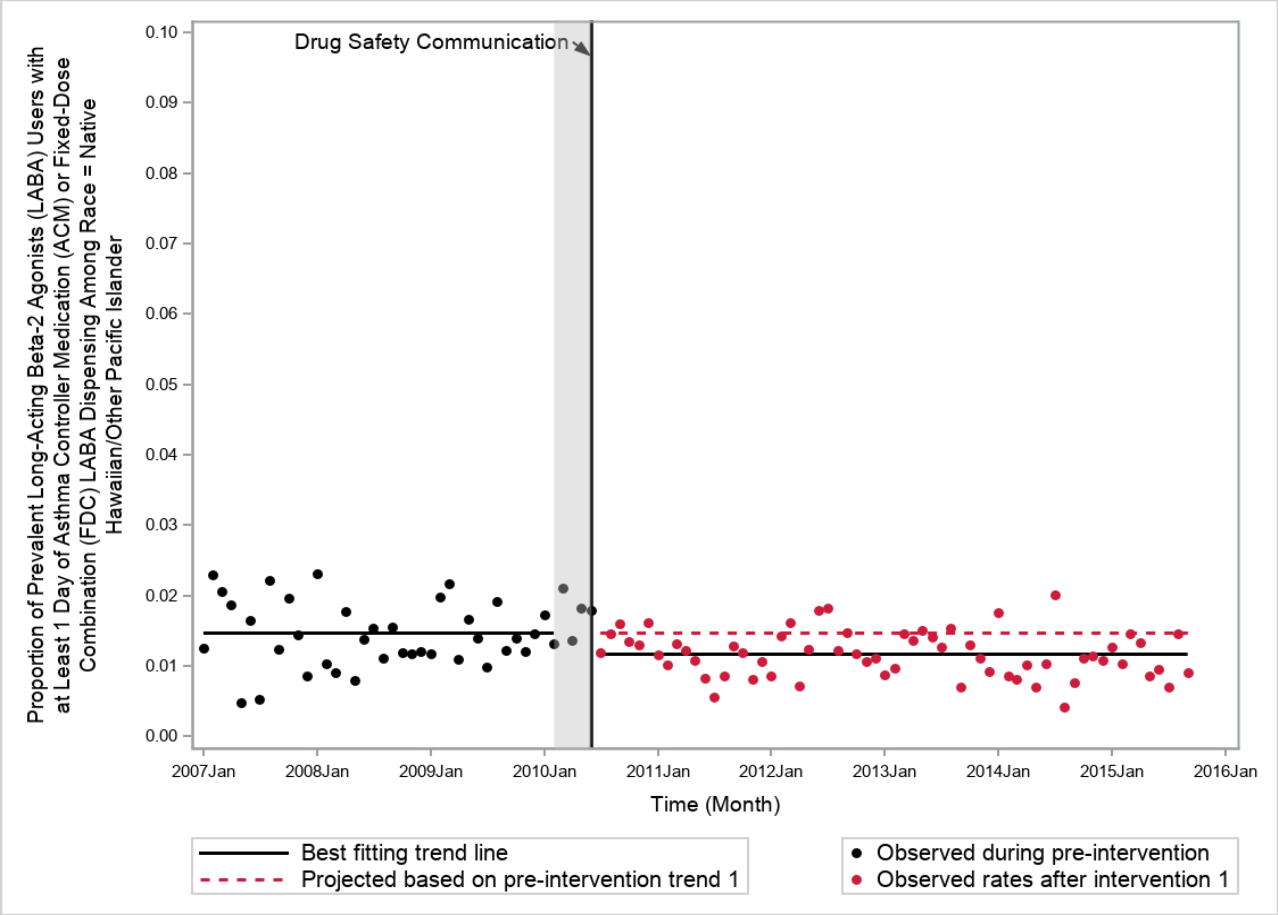
Figure 10. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = Black/African American



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

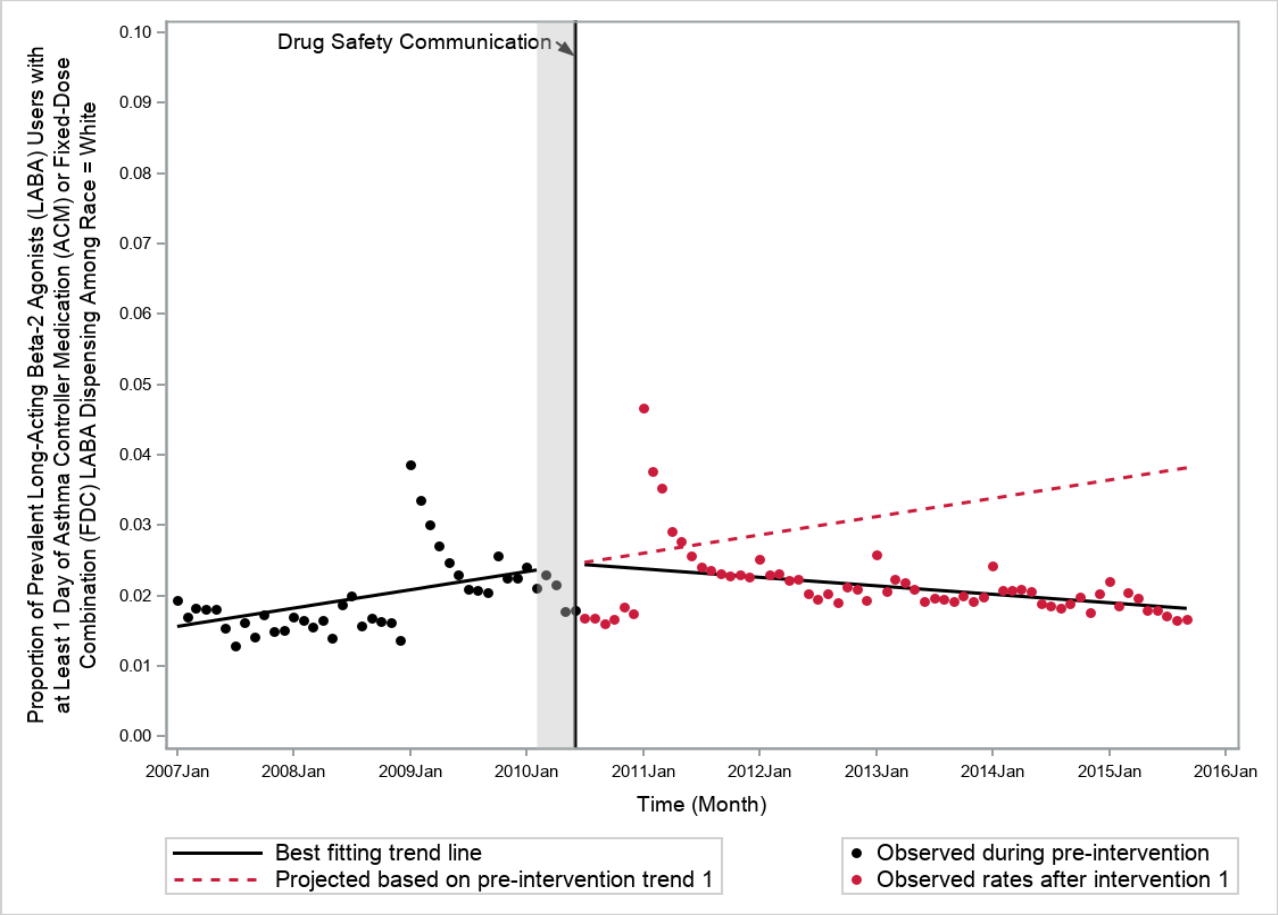
Figure 11. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = Native Hawaiian/Other Pacific Islander



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

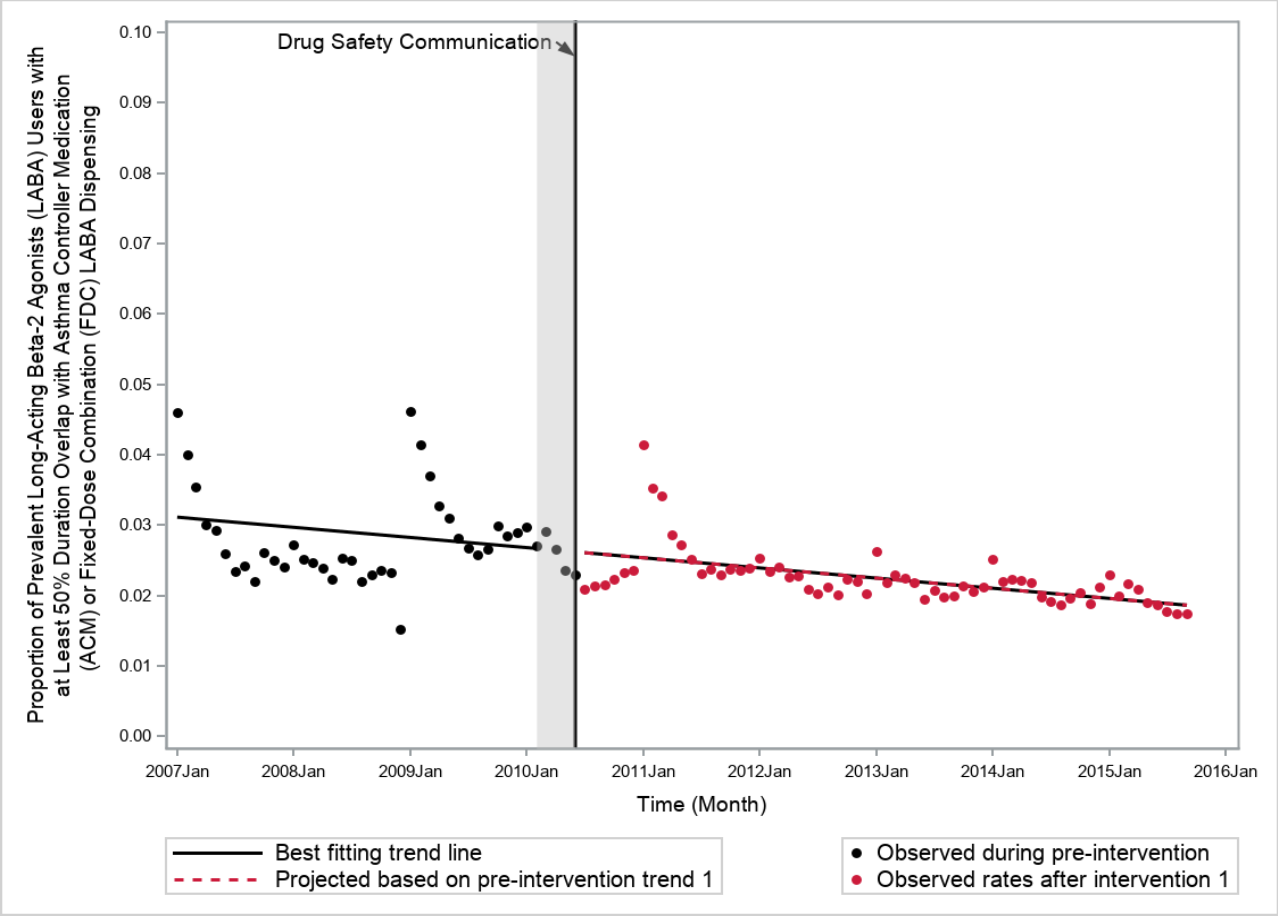
Figure 12. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = White



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

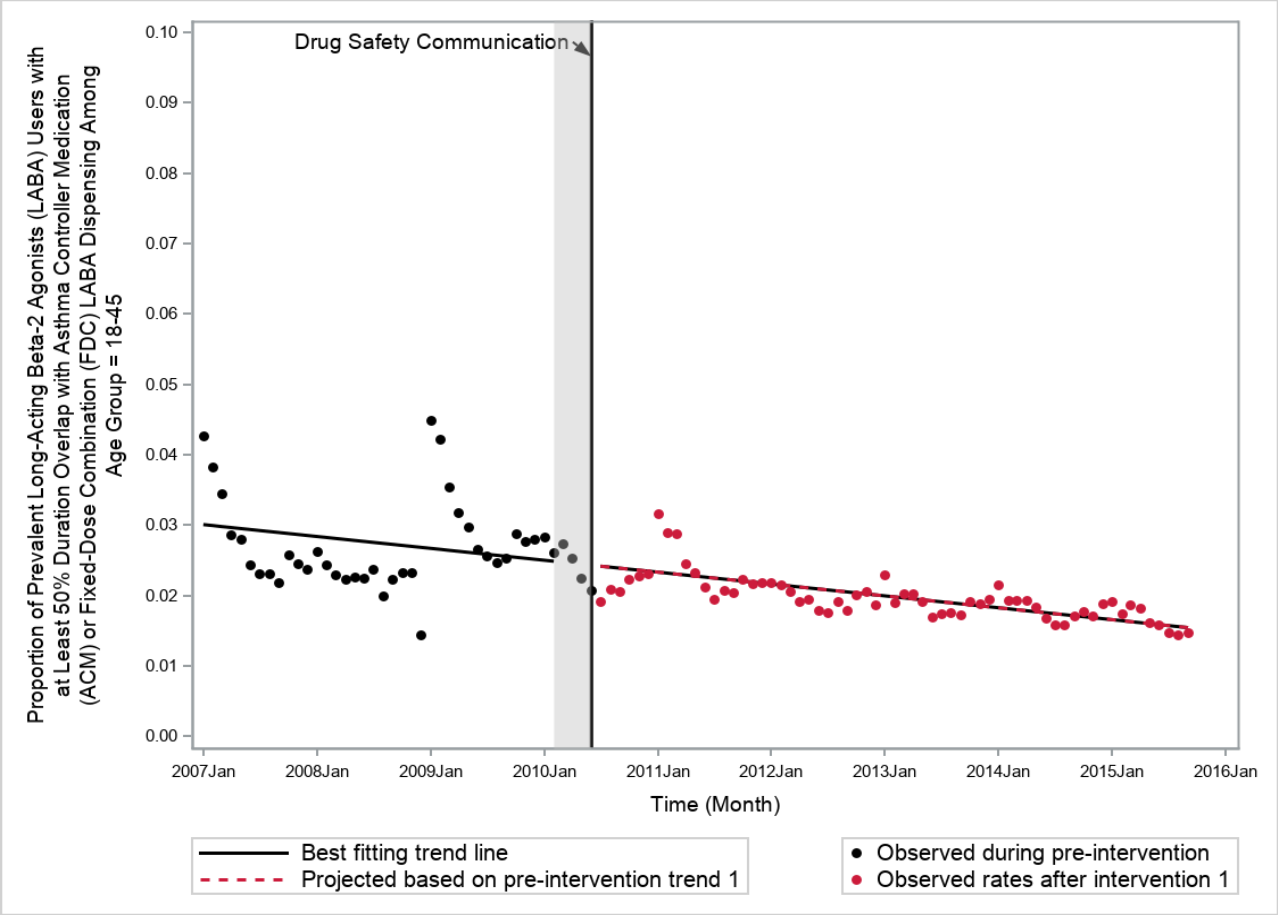
Figure 13. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2]



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

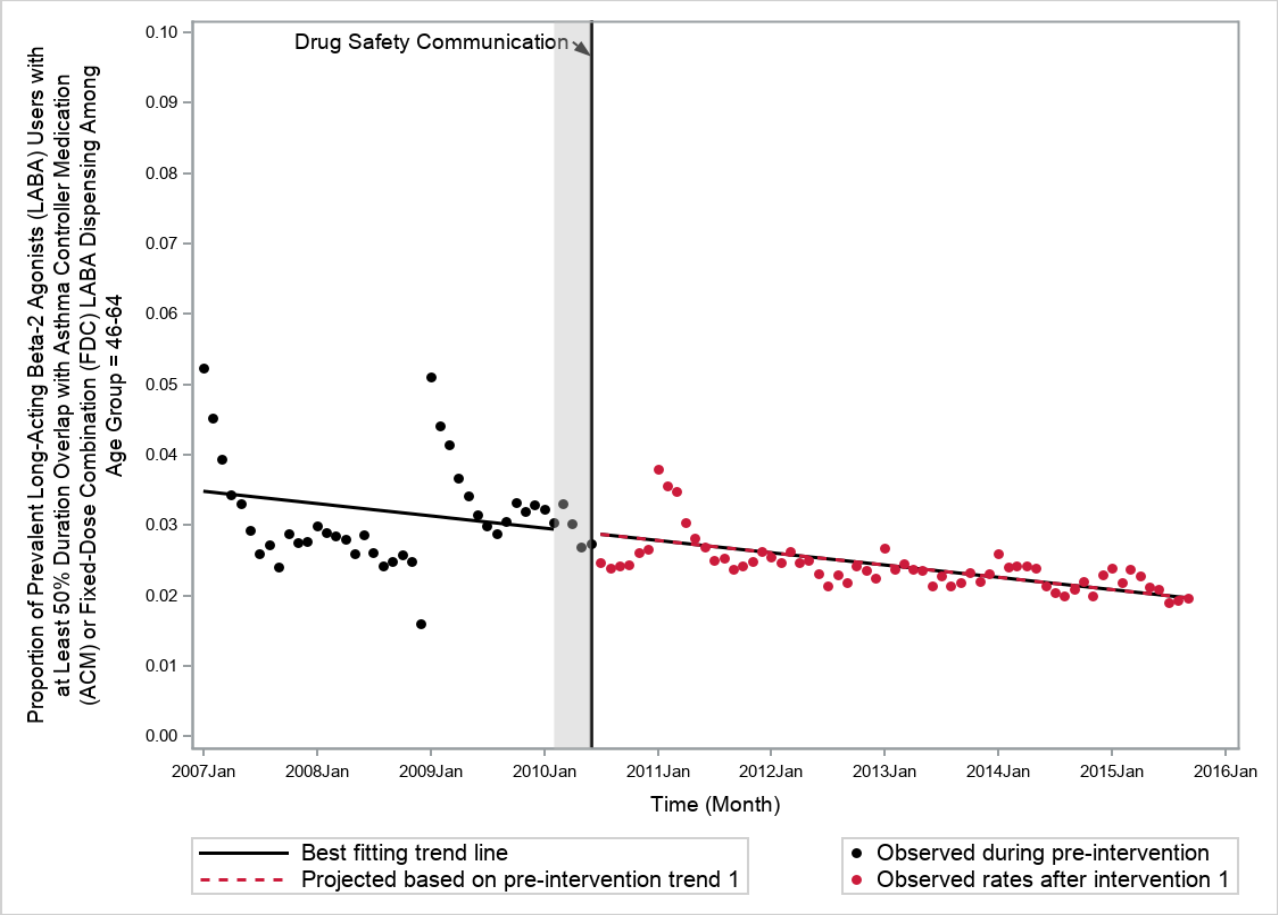
Figure 14. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Age Group = 18-45



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

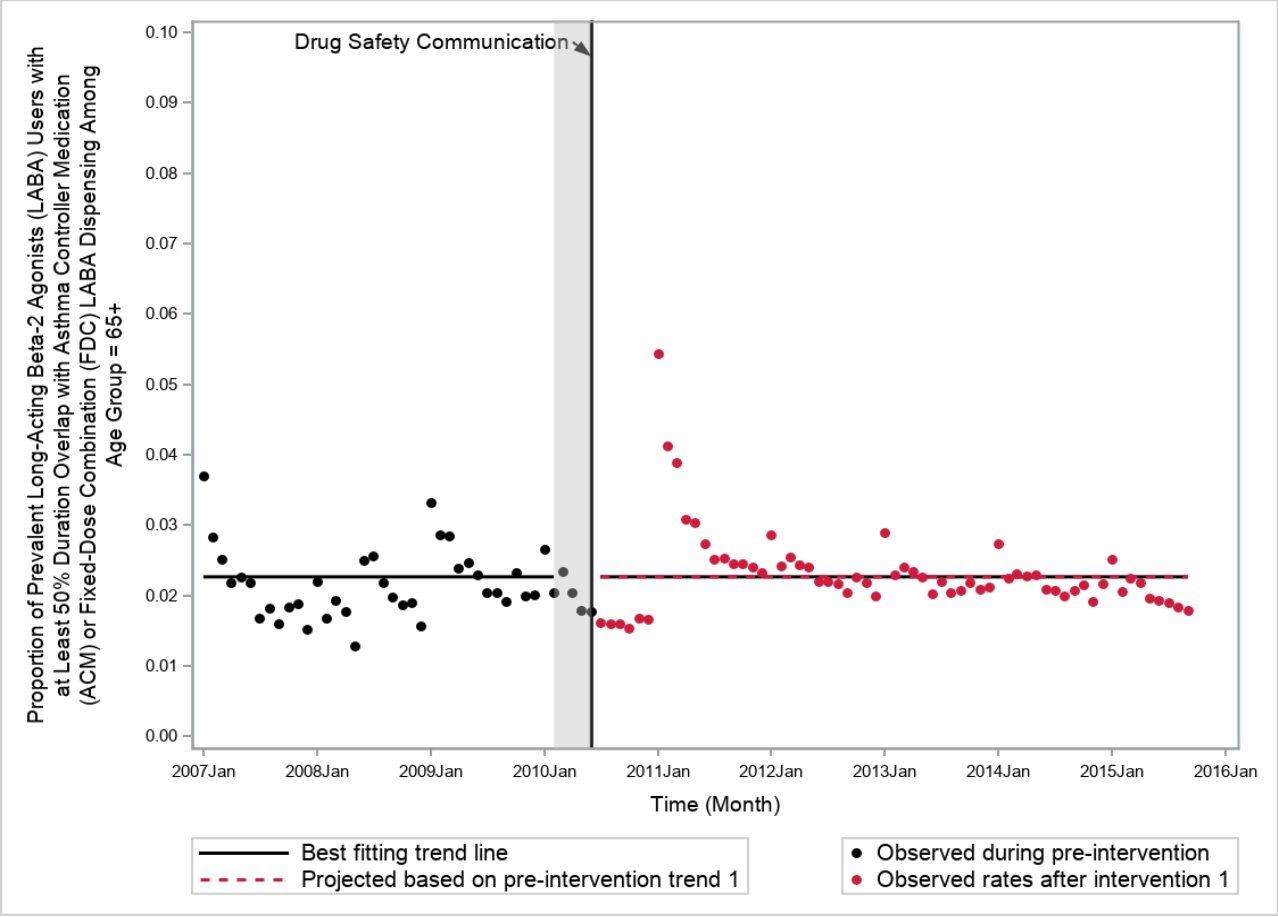
Figure 15. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Age Group = 46-64



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

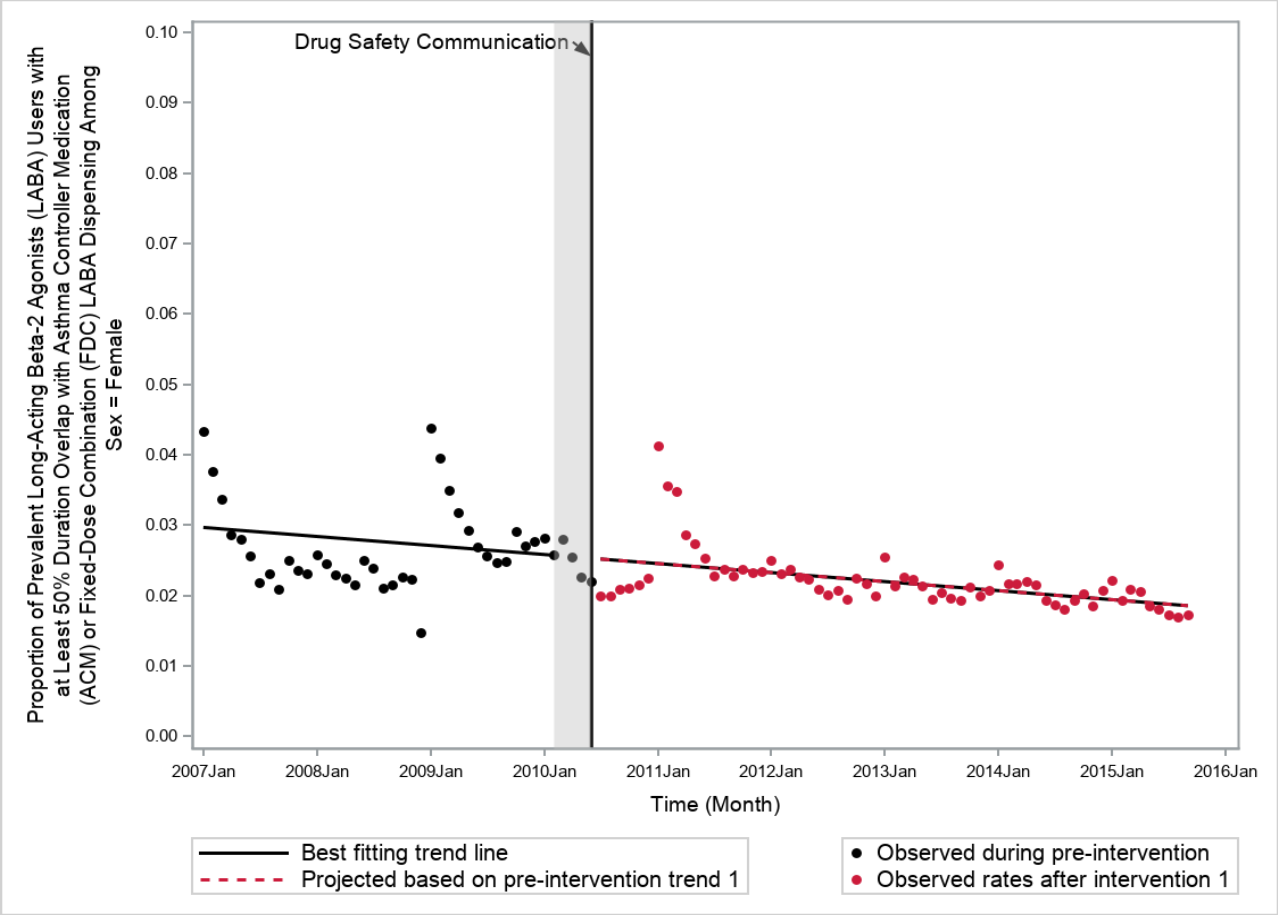
Figure 16. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Age Group = 65+



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

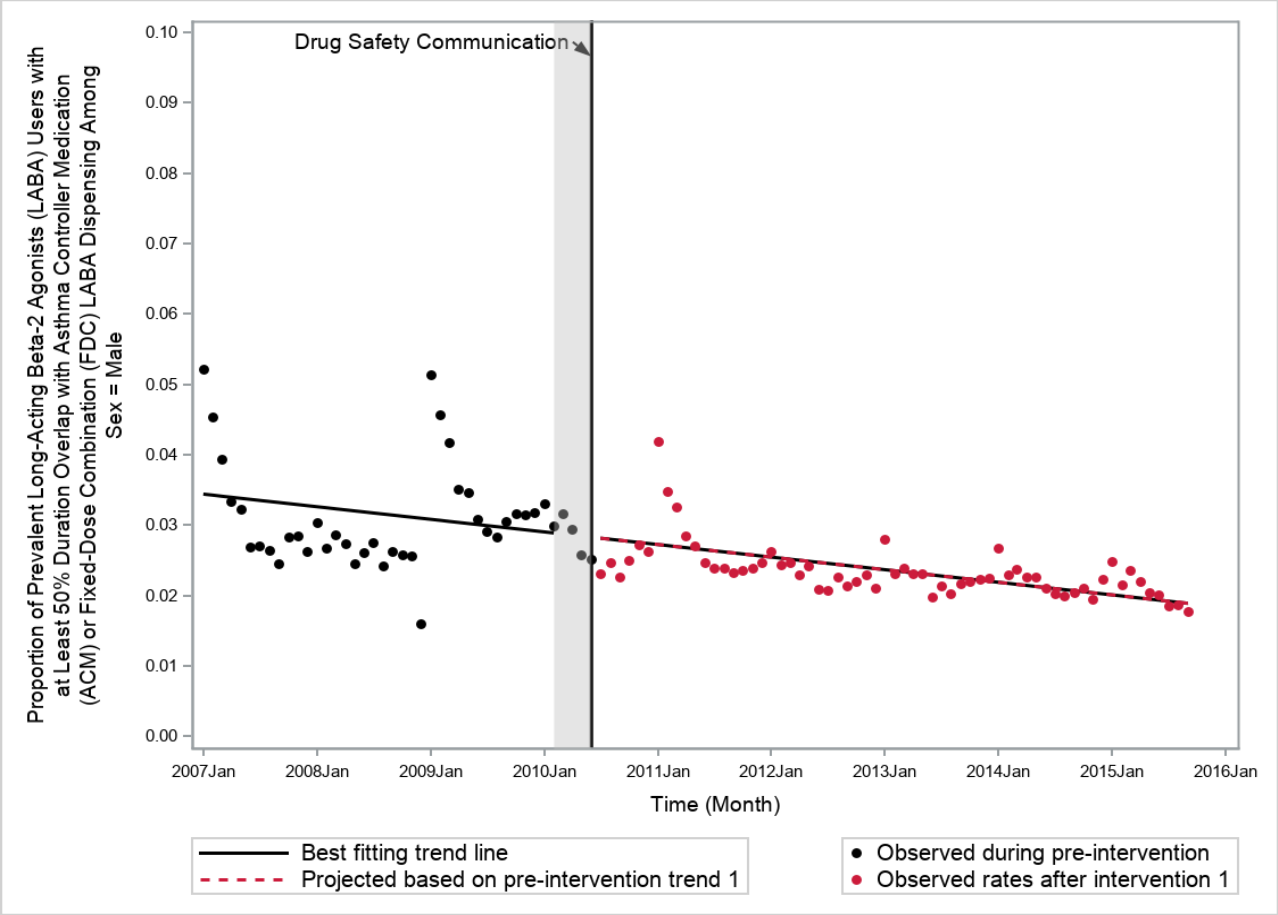
Figure 17. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Sex = Female



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

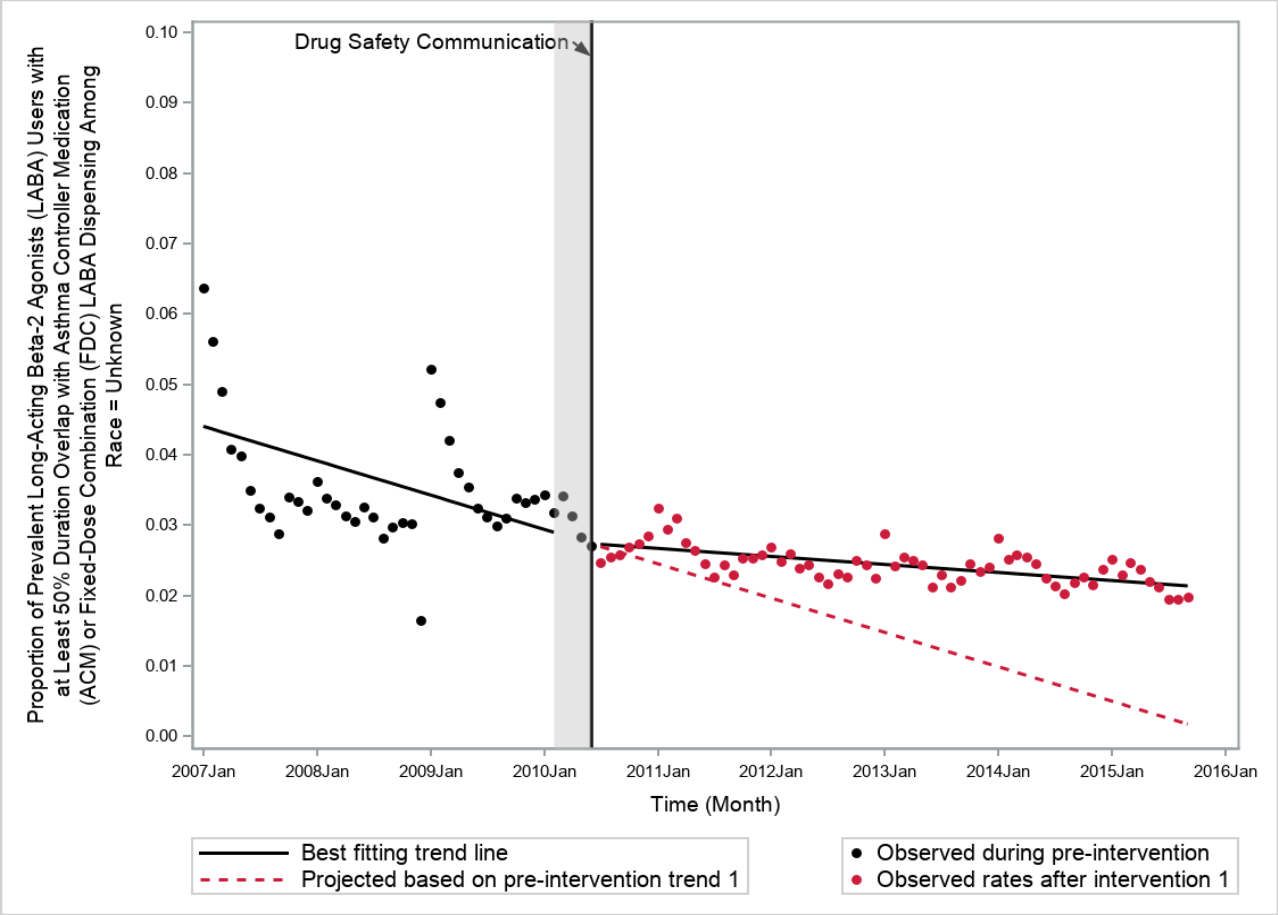
Figure 18. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Sex = Male



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

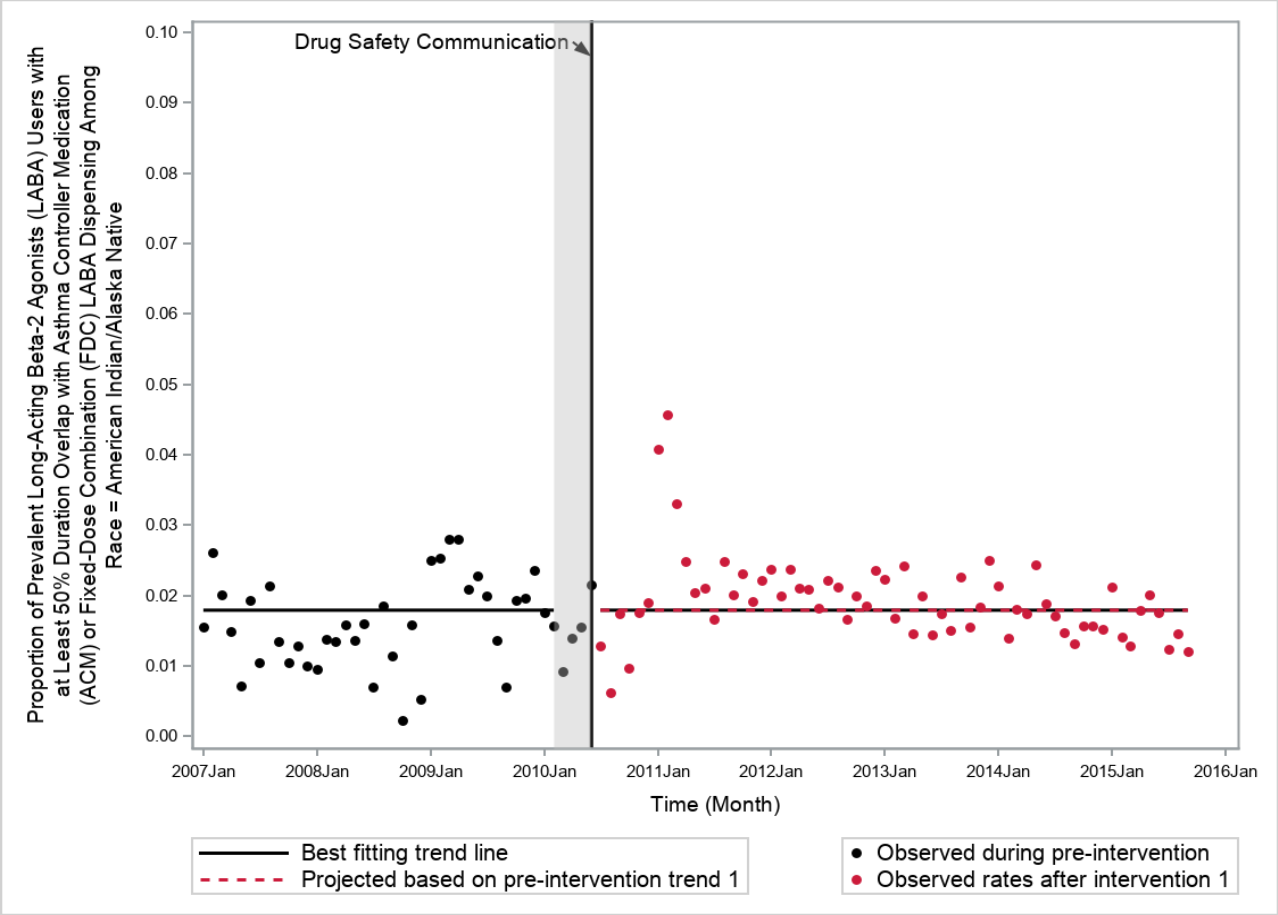
Figure 19. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = Unknown



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

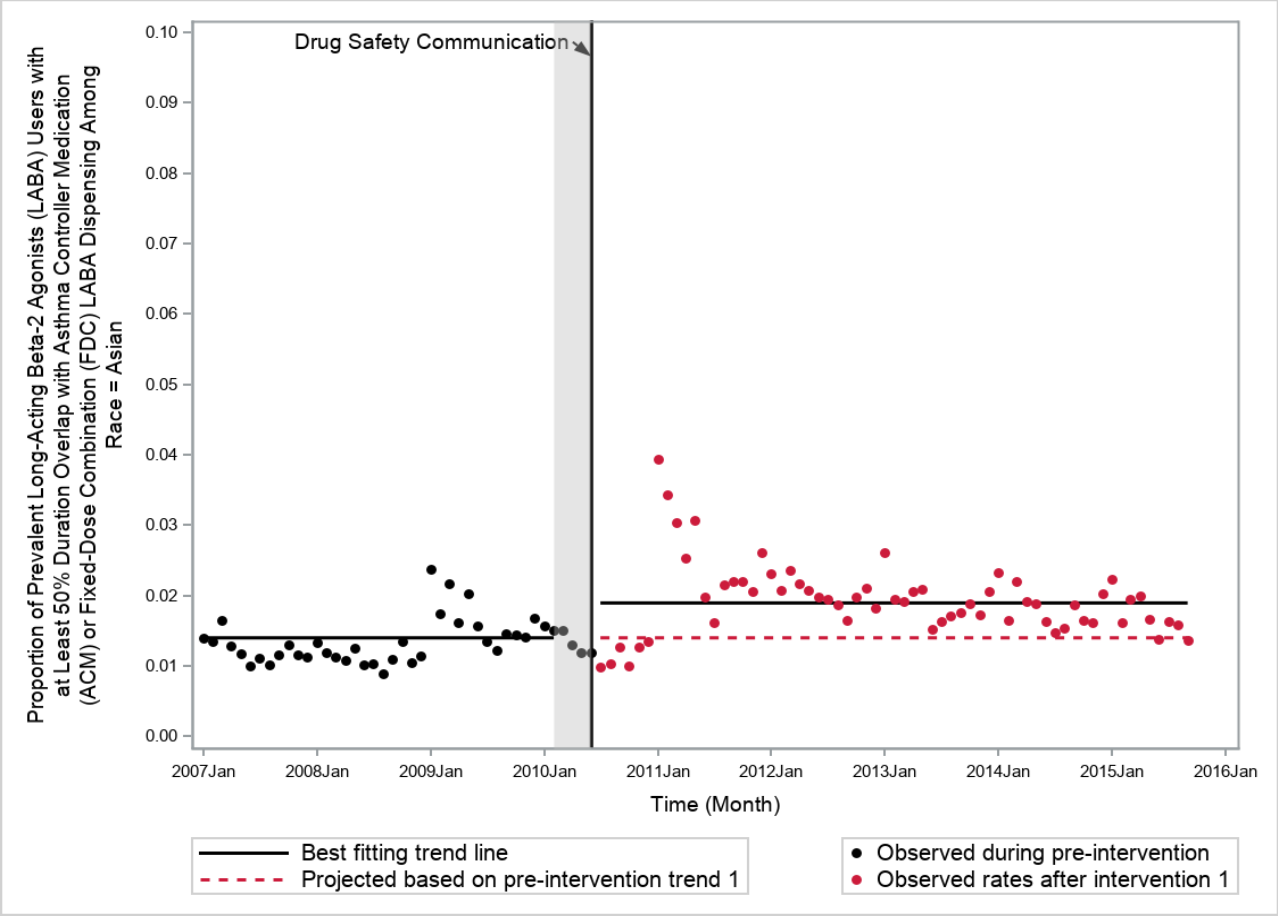
Figure 20. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = American Indian/Alaska Native



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

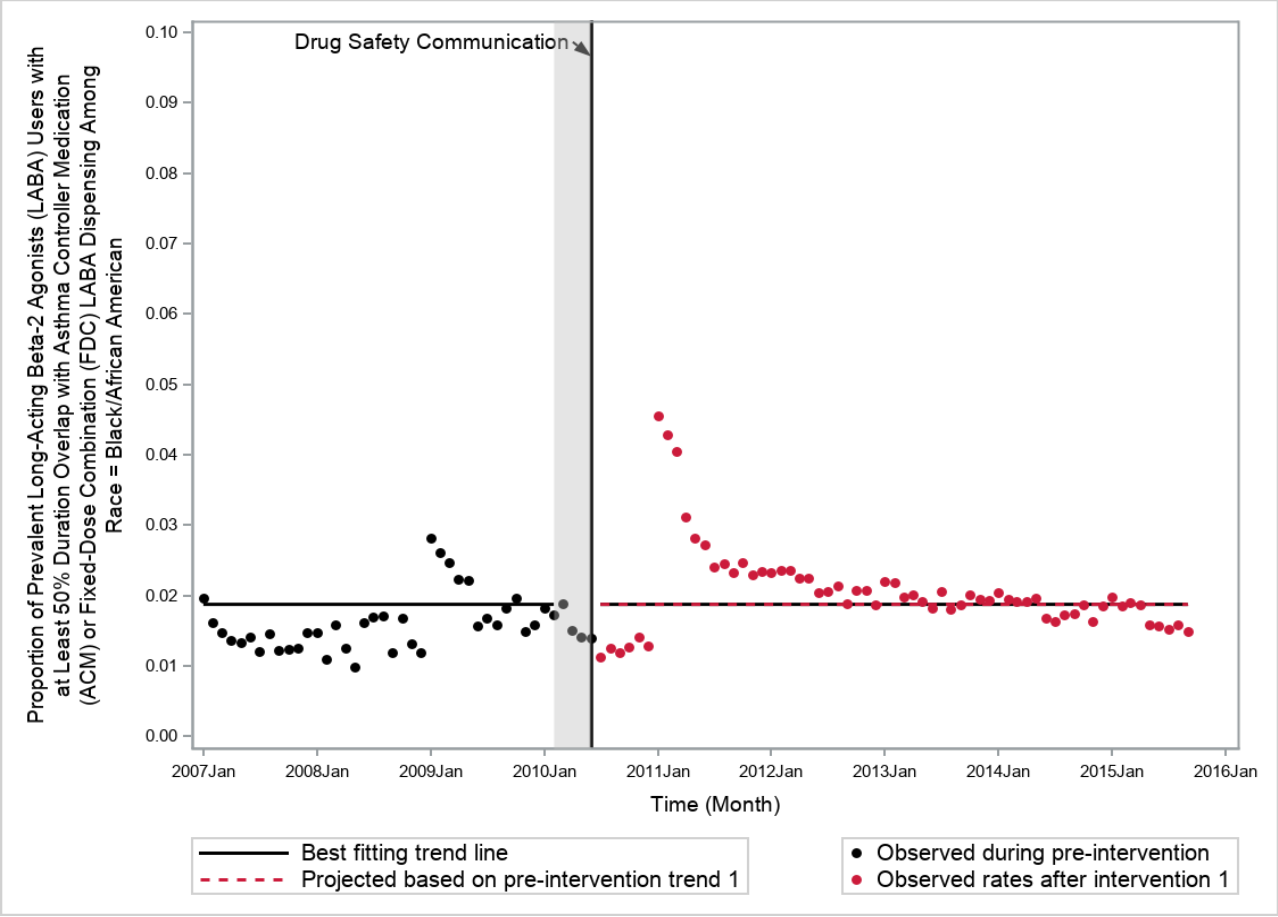
Figure 21. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = Asian



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

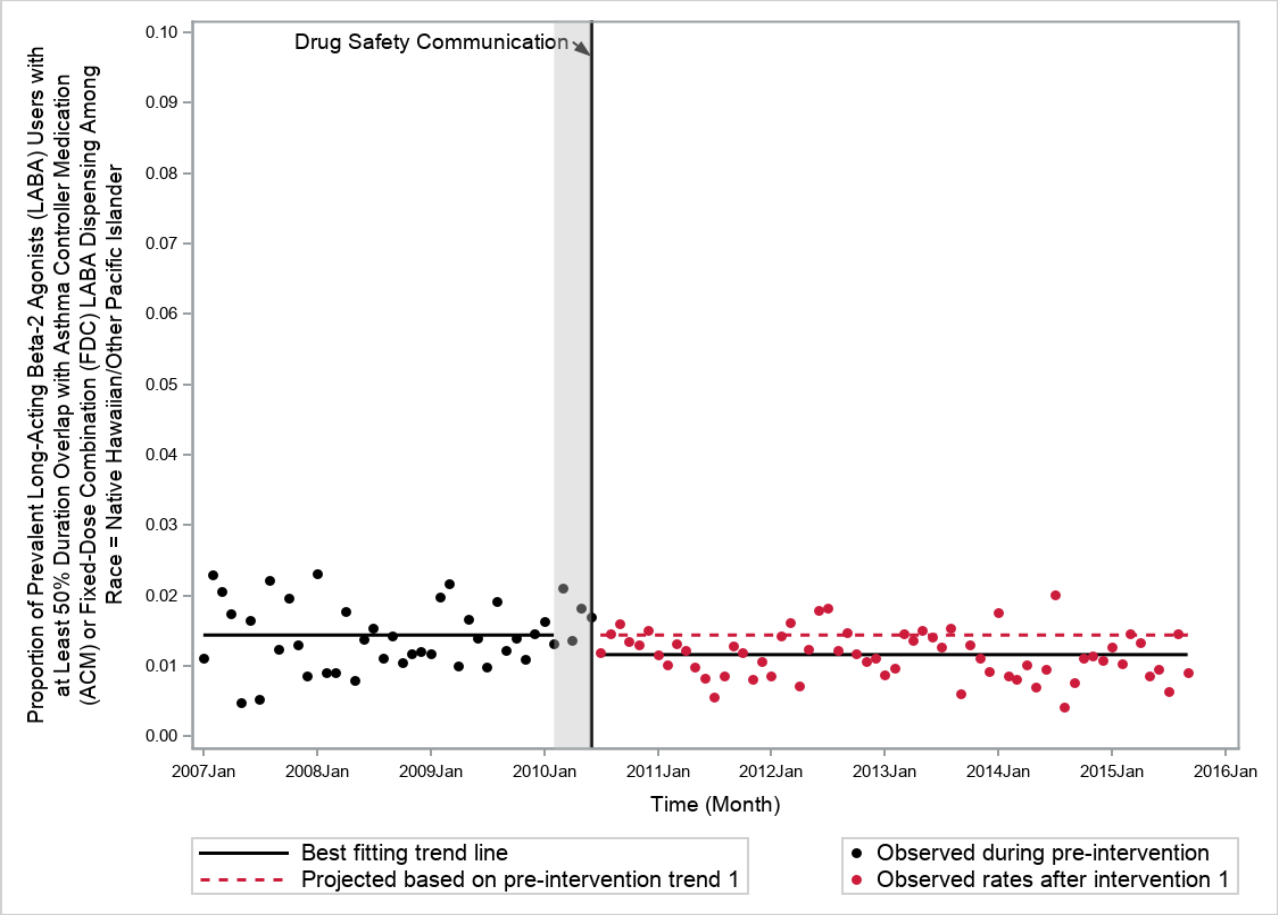
Figure 22. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = Black/African American



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

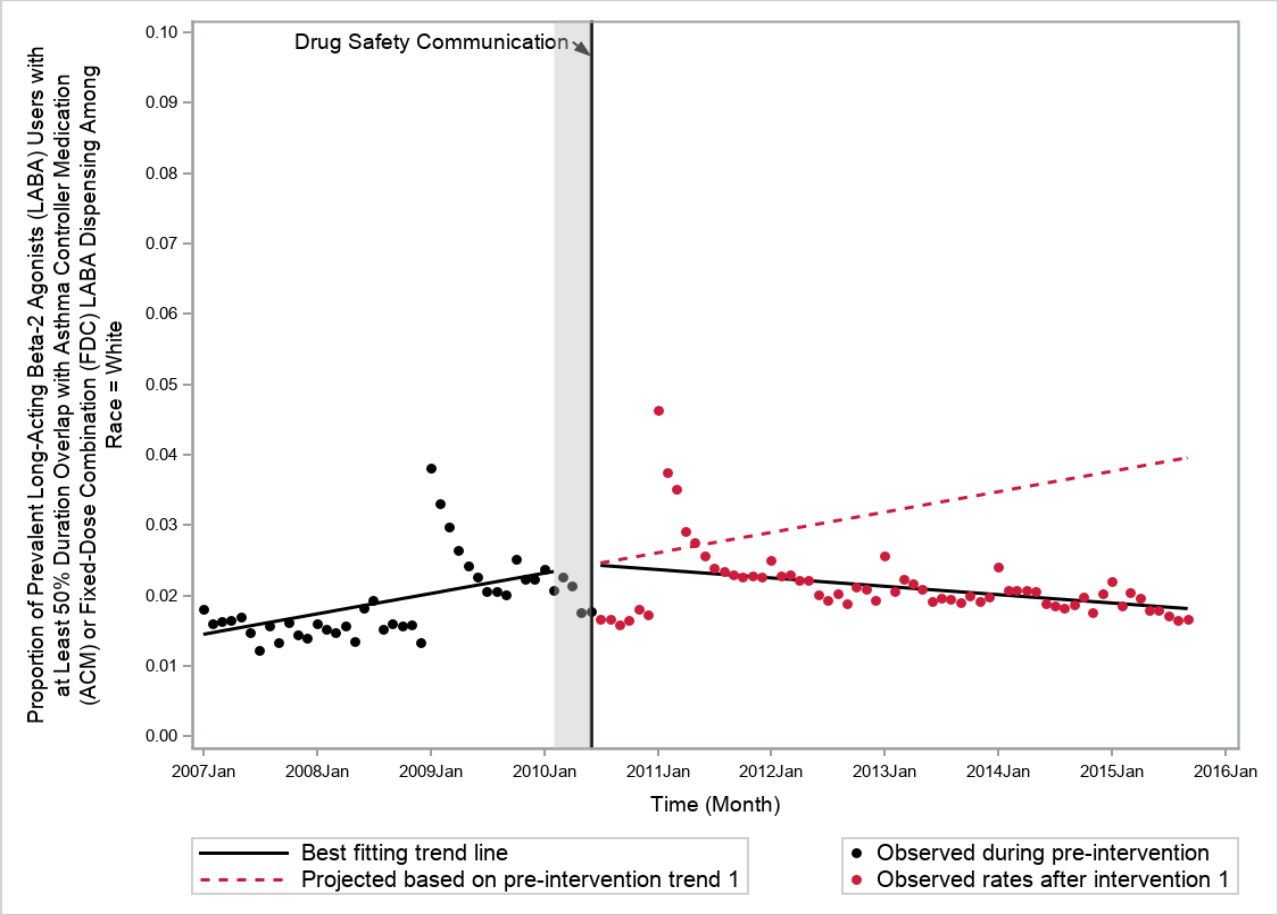
Figure 23. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = Native Hawaiian/Other Pacific Islander



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

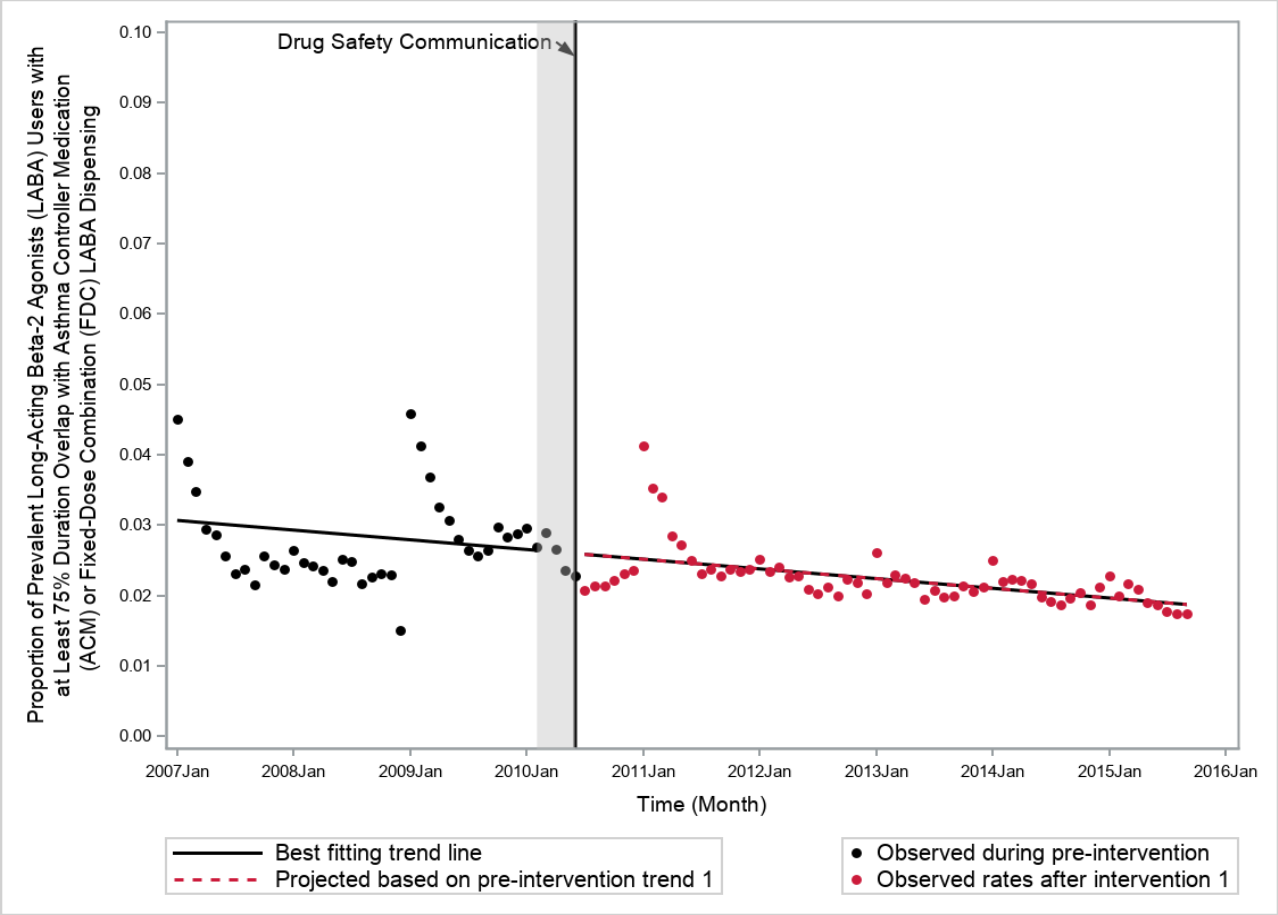
Figure 24. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = White



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

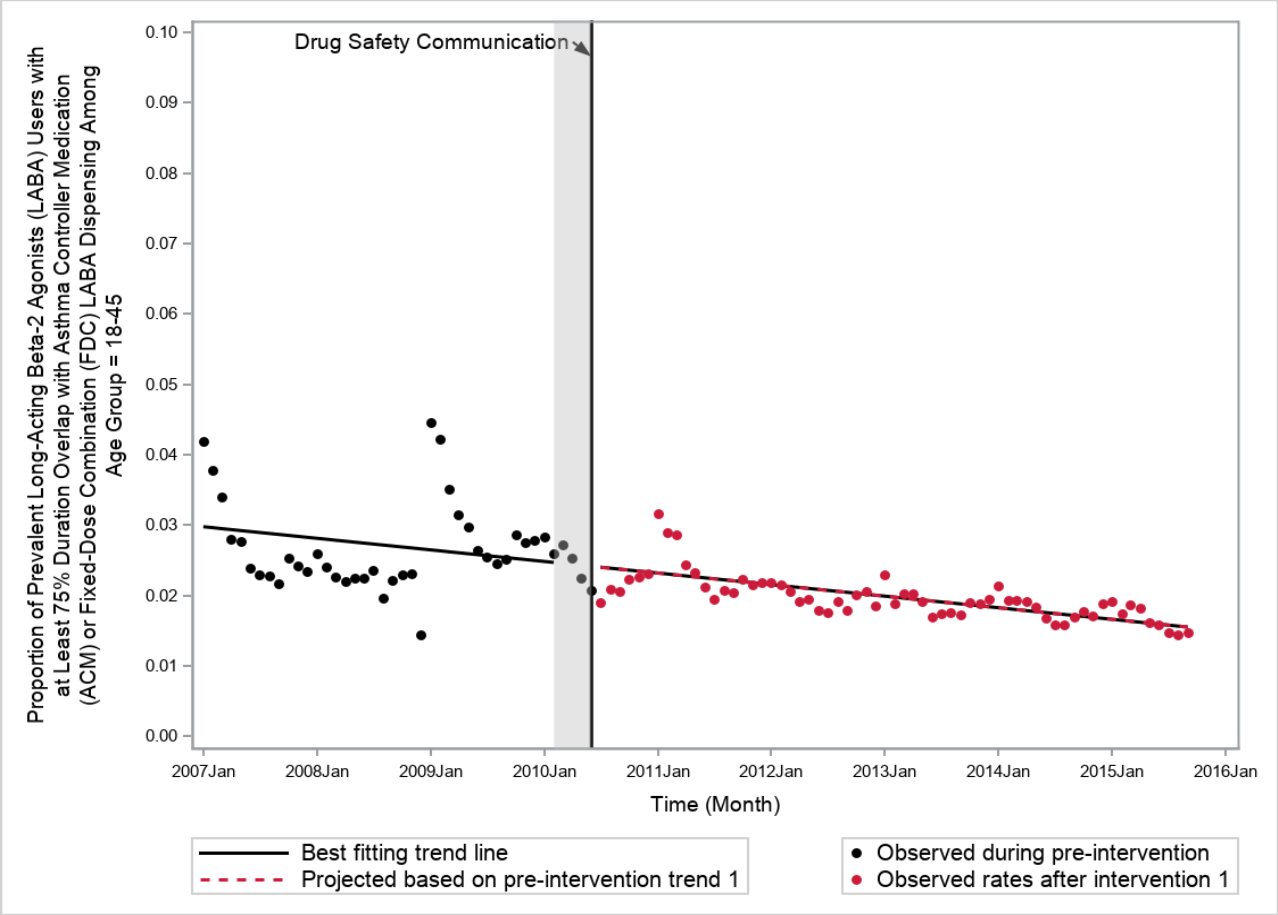
Figure 25. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2]



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

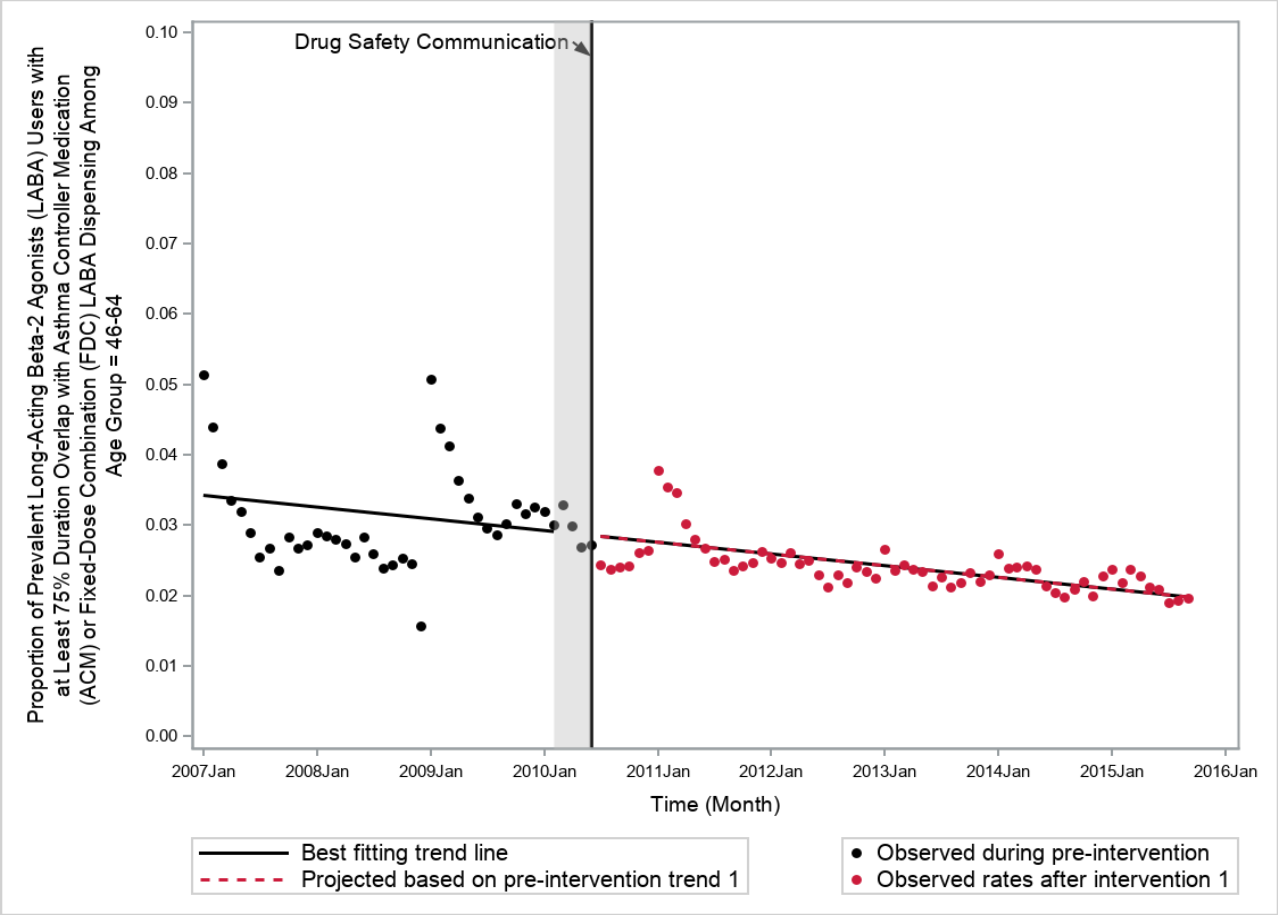
Figure 26. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Age Group = 18-45



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

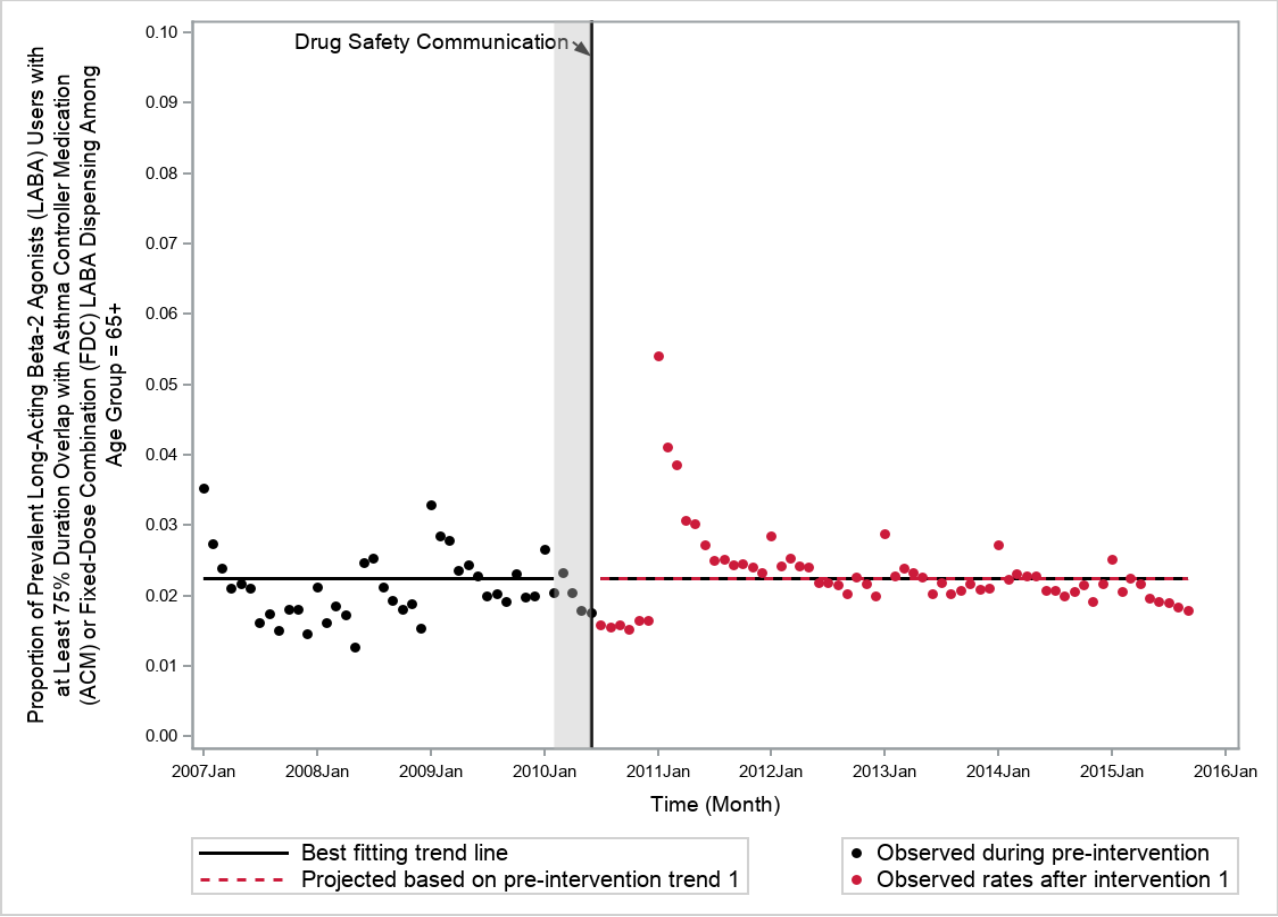
Figure 27. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Age Group = 46-64



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

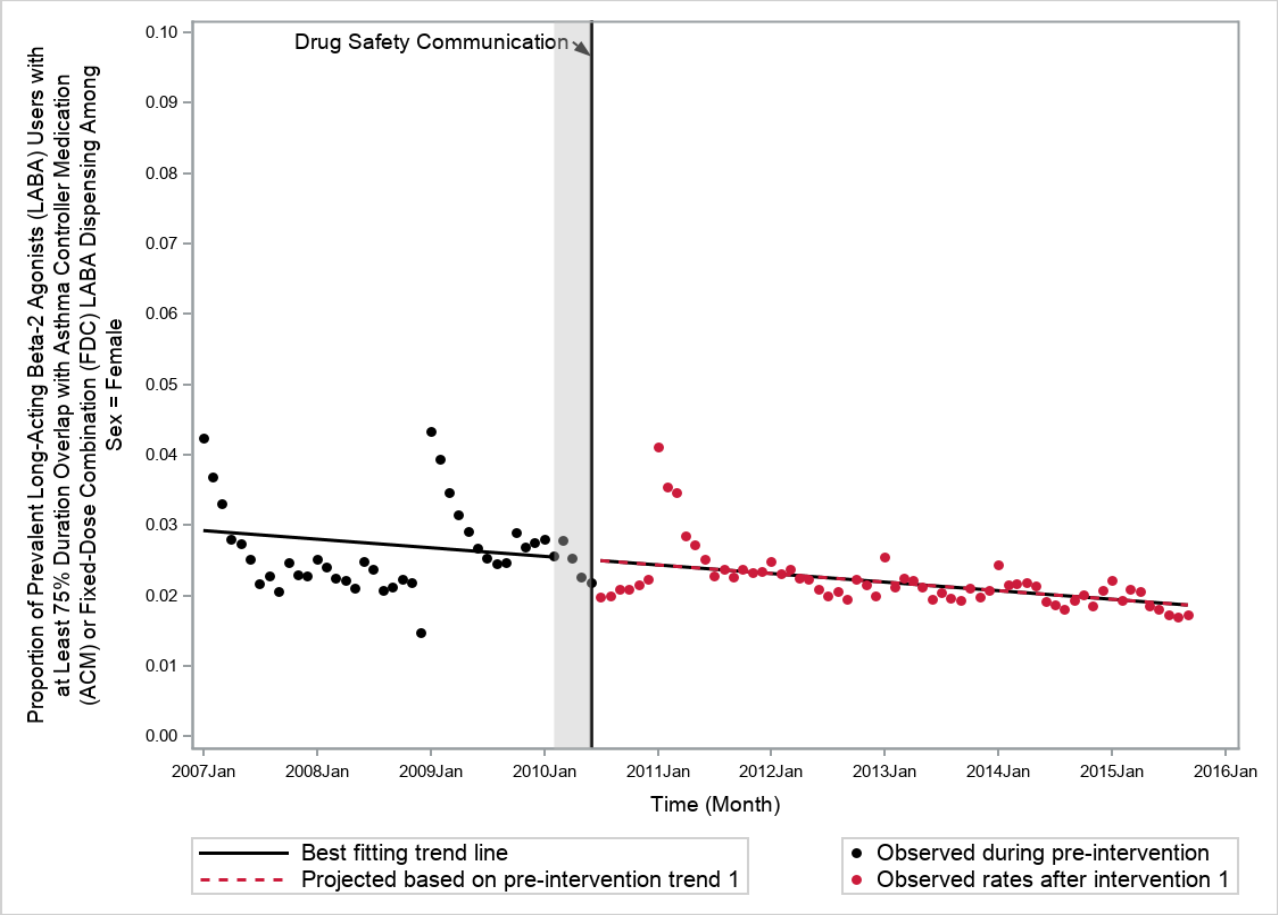
Figure 28. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Age Group = 65+



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

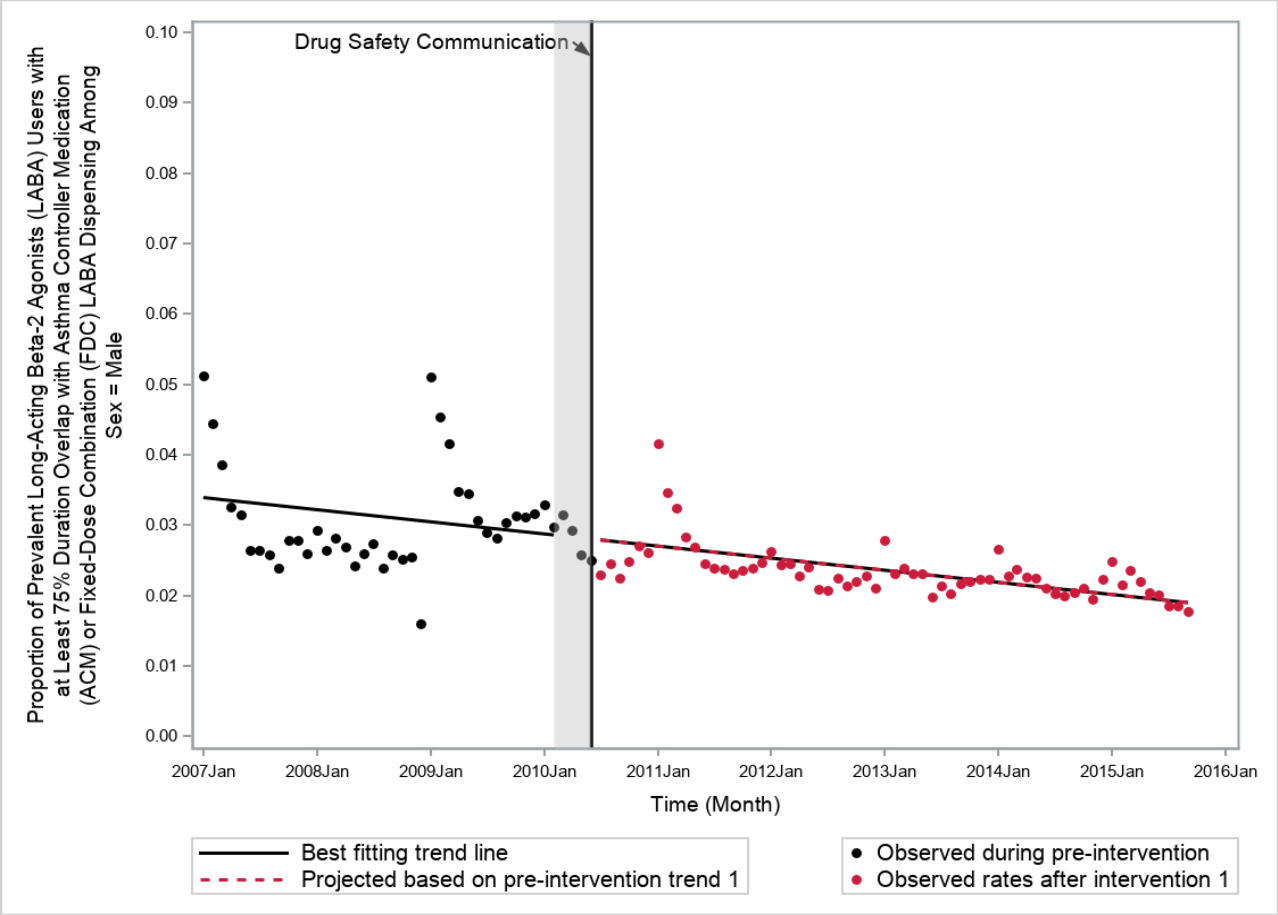
Figure 29. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Sex = Female



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

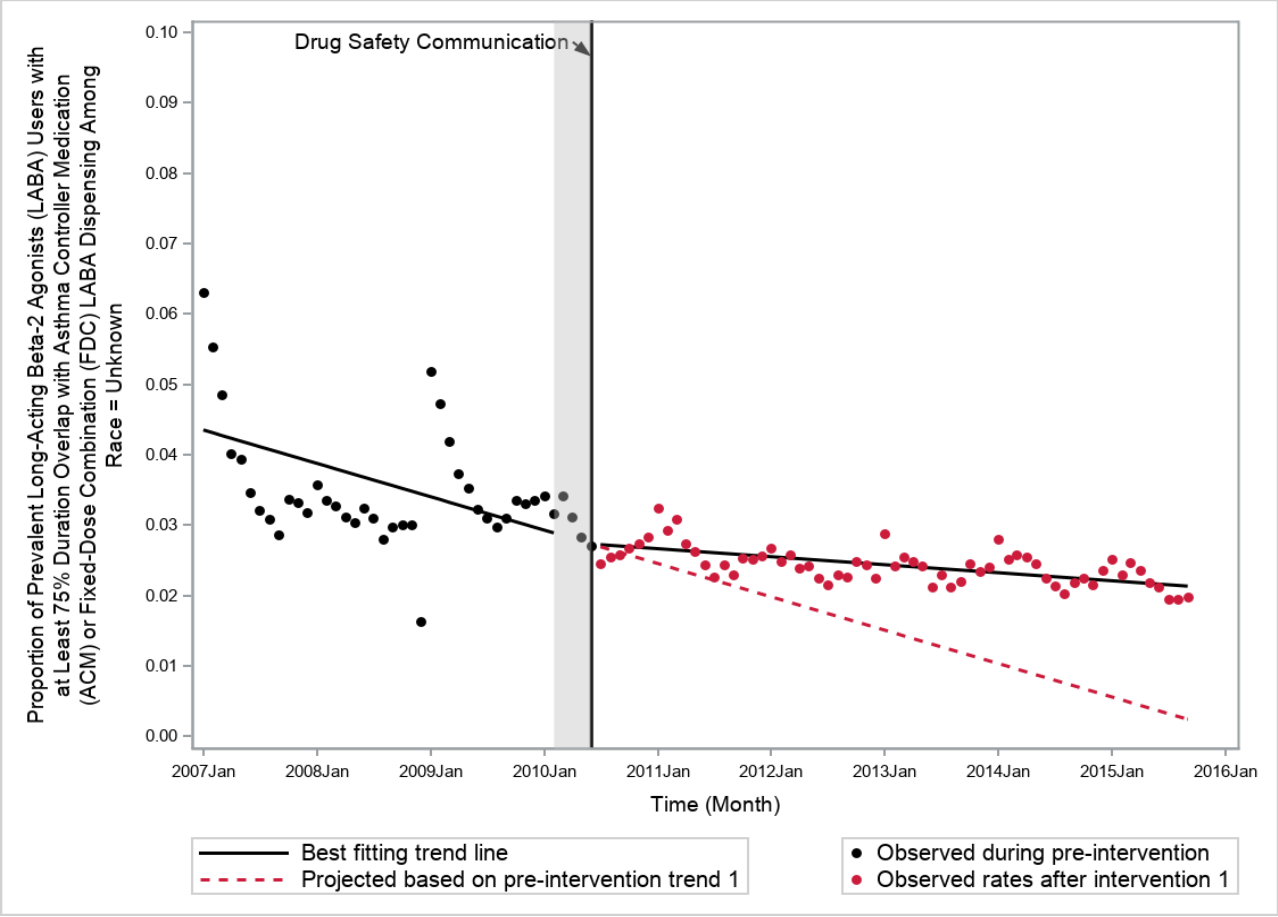
Figure 30. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Sex = Male



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

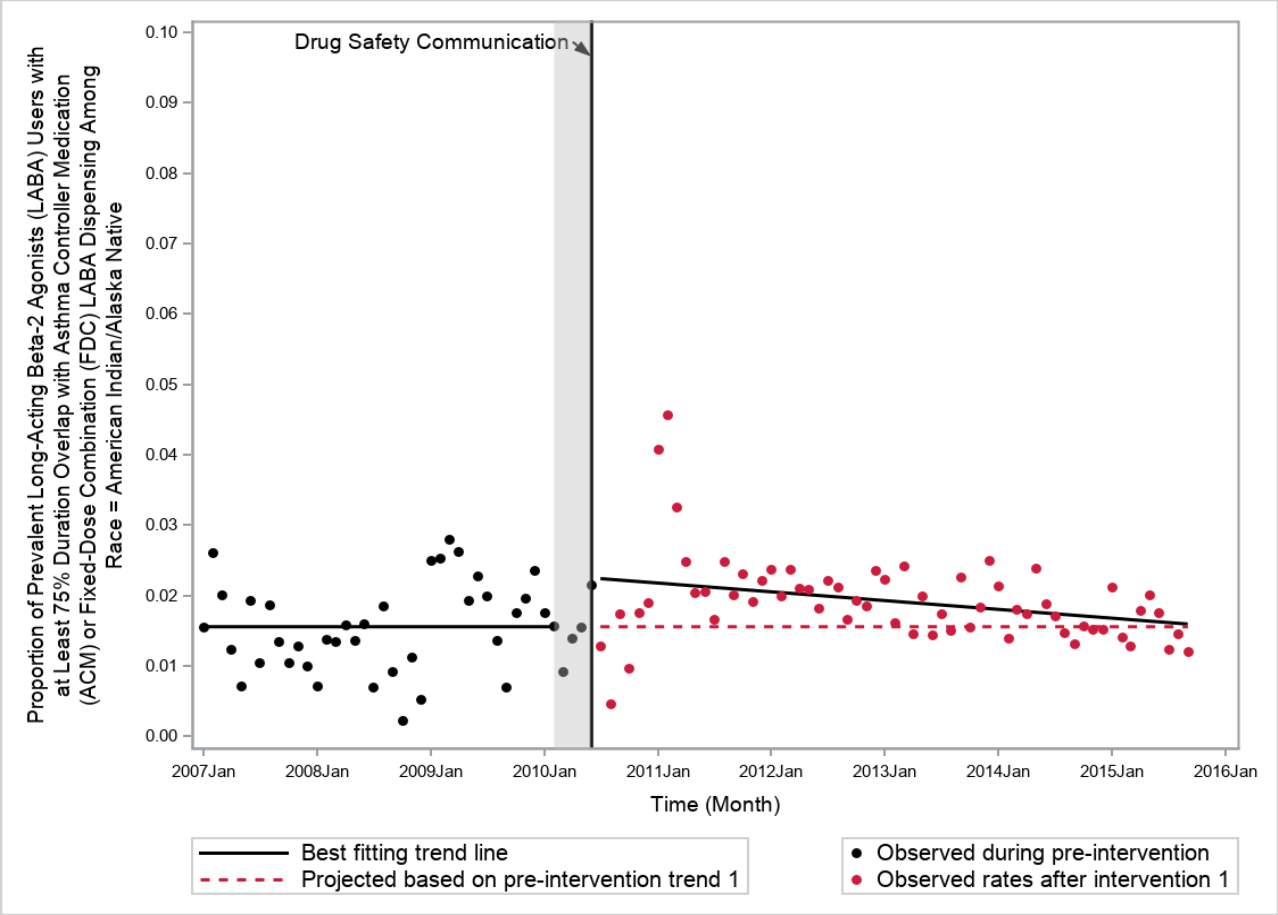
Figure 31. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = Unknown



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

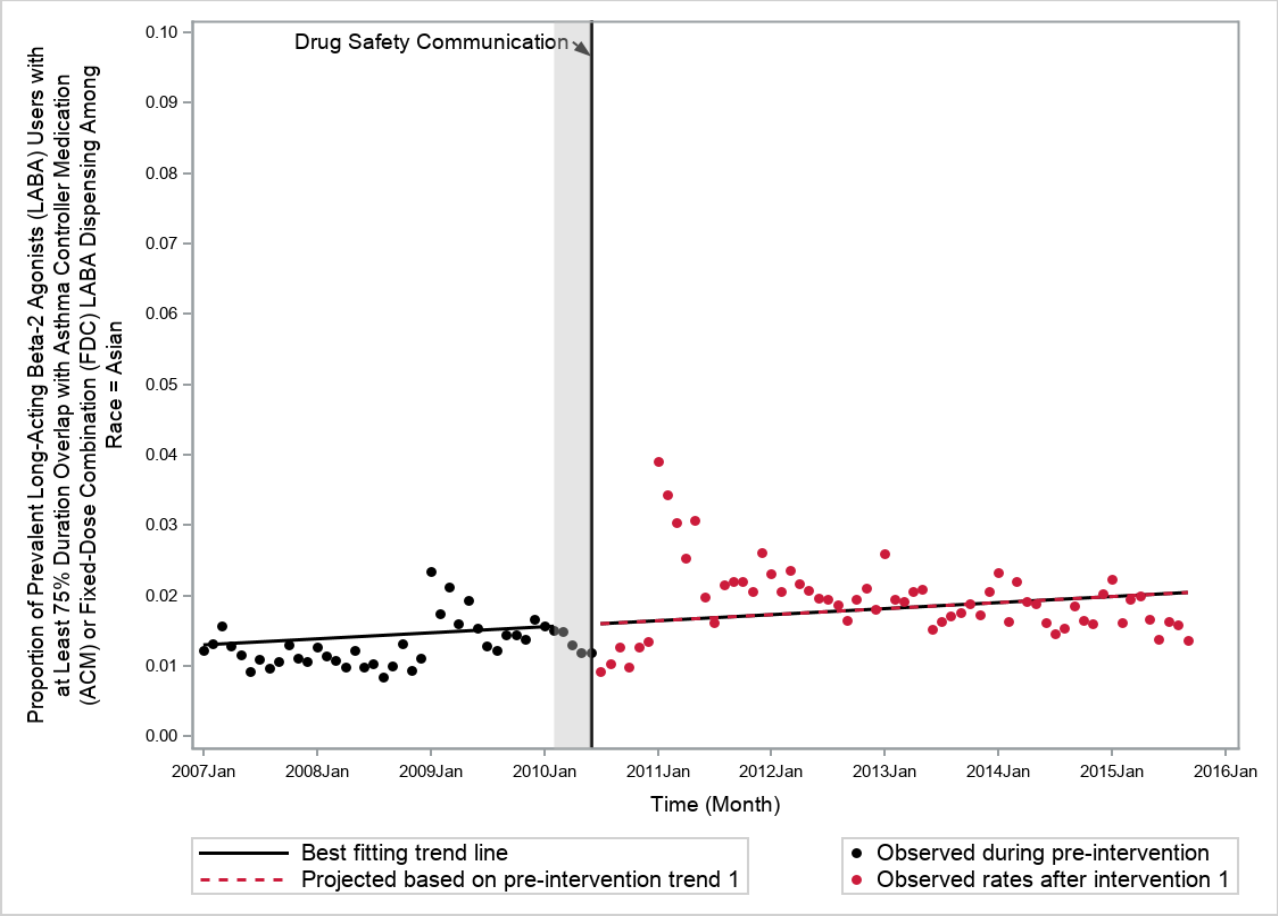
Figure 32. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = American Indian/Alaska Native



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

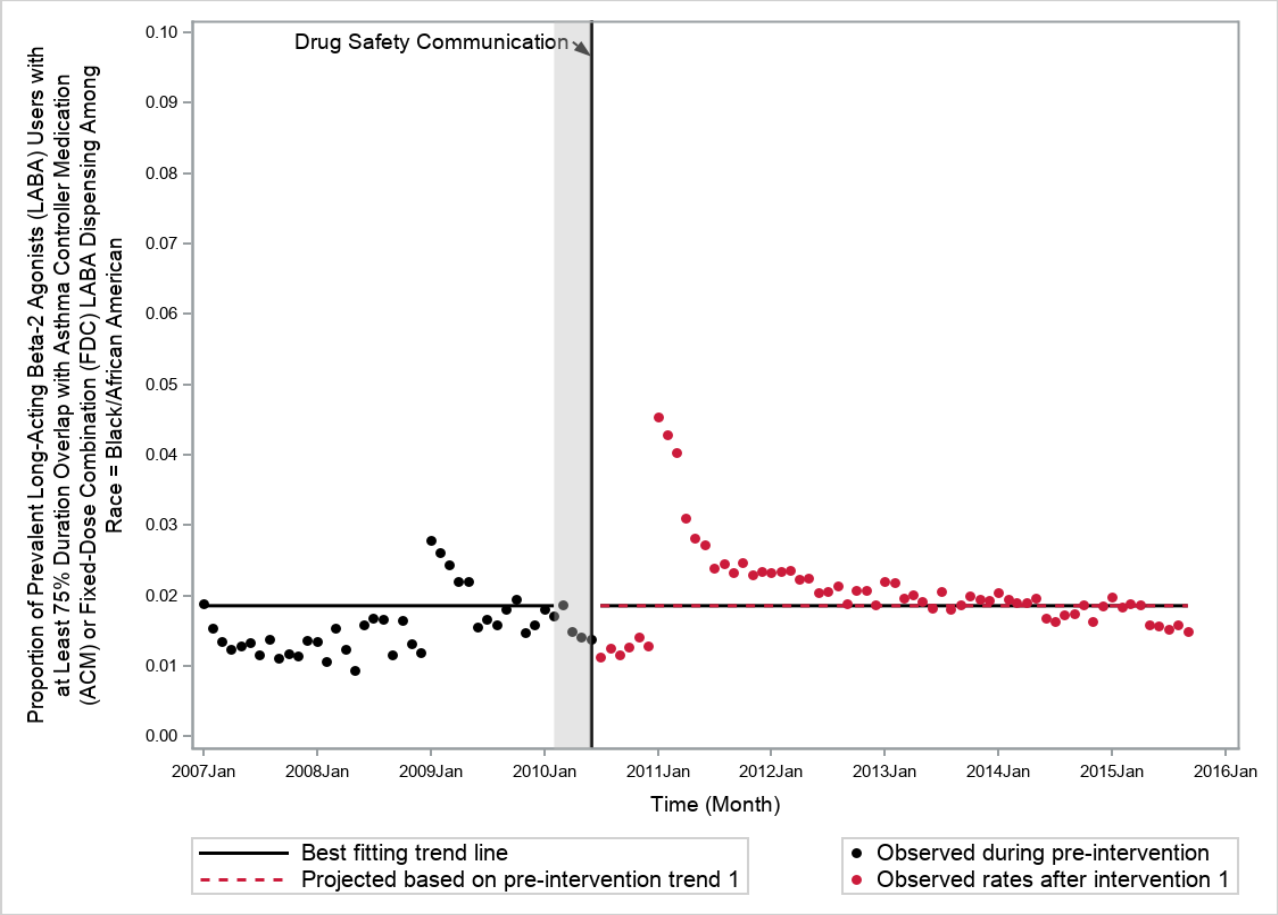
Figure 33. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = Asian



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

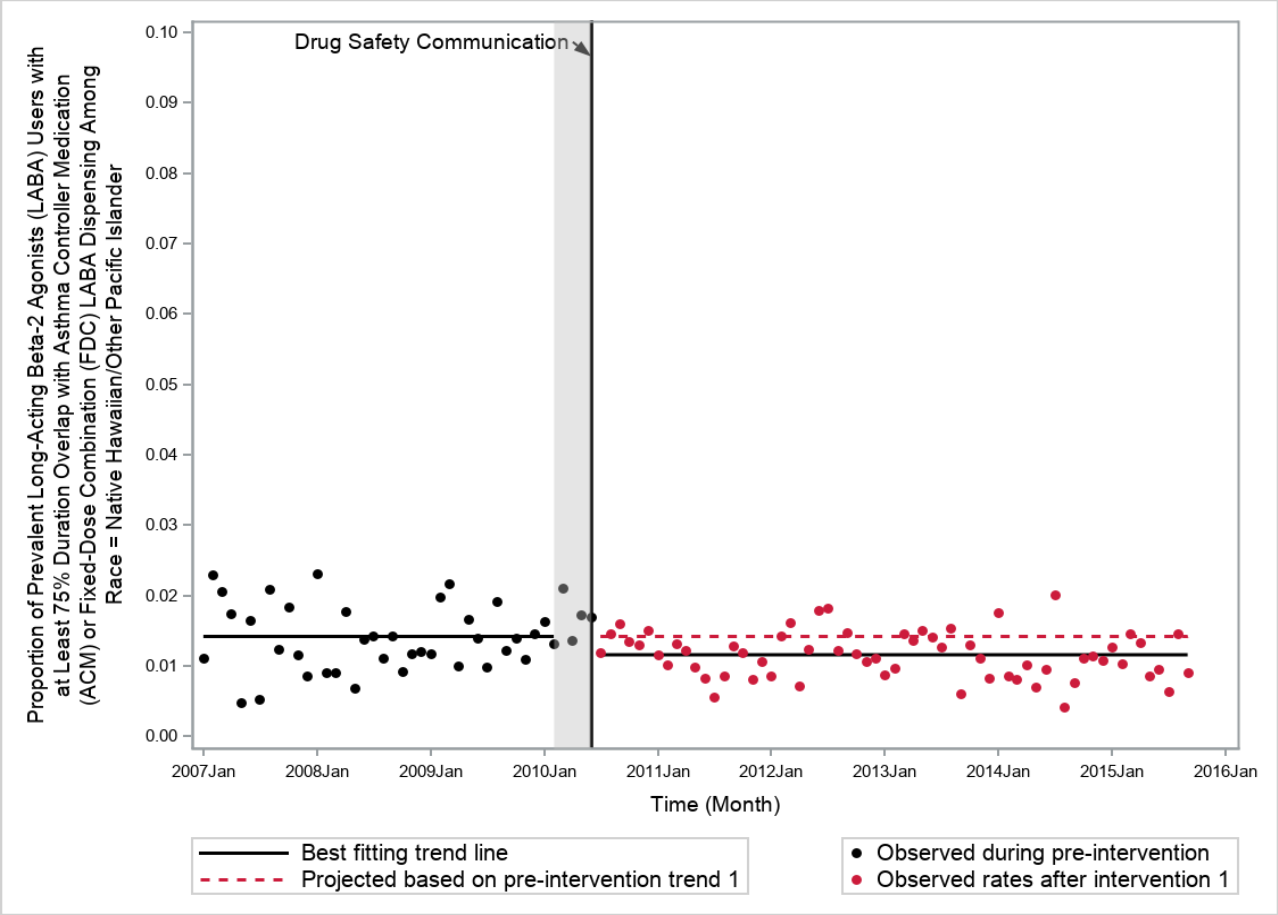
Figure 34. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = Black/African American



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

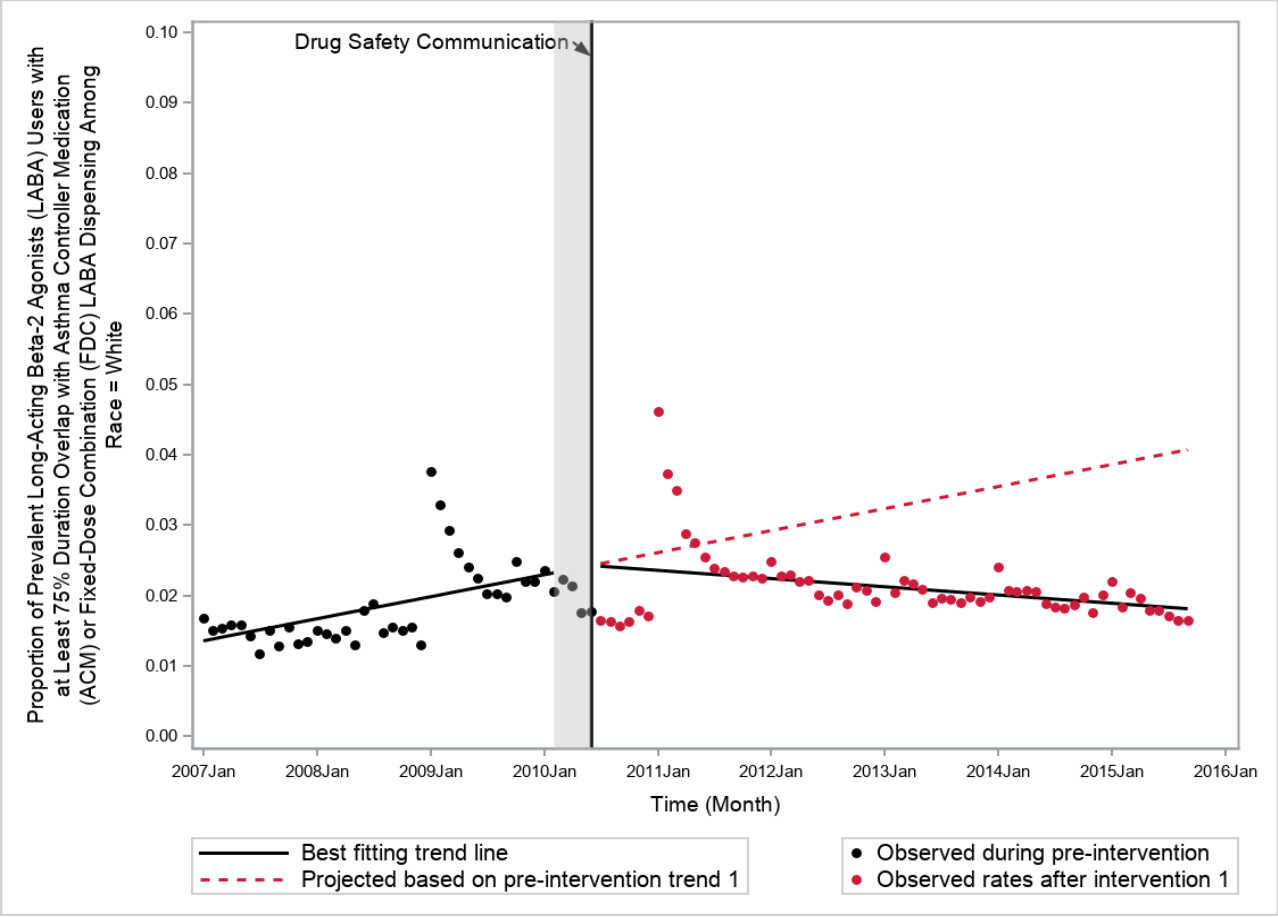
Figure 35. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = Native Hawaiian/Other Pacific Islander



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

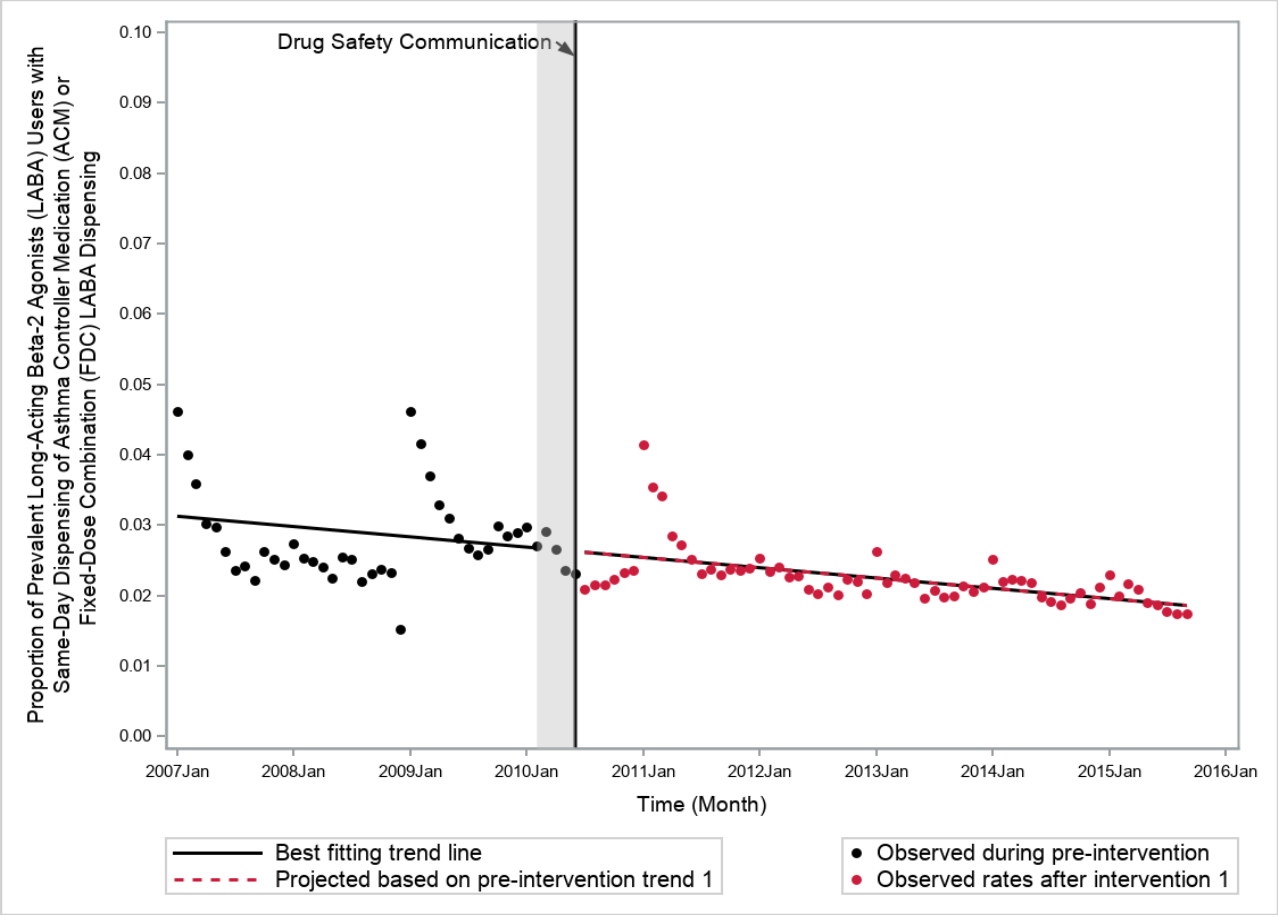
Figure 36. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = White



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

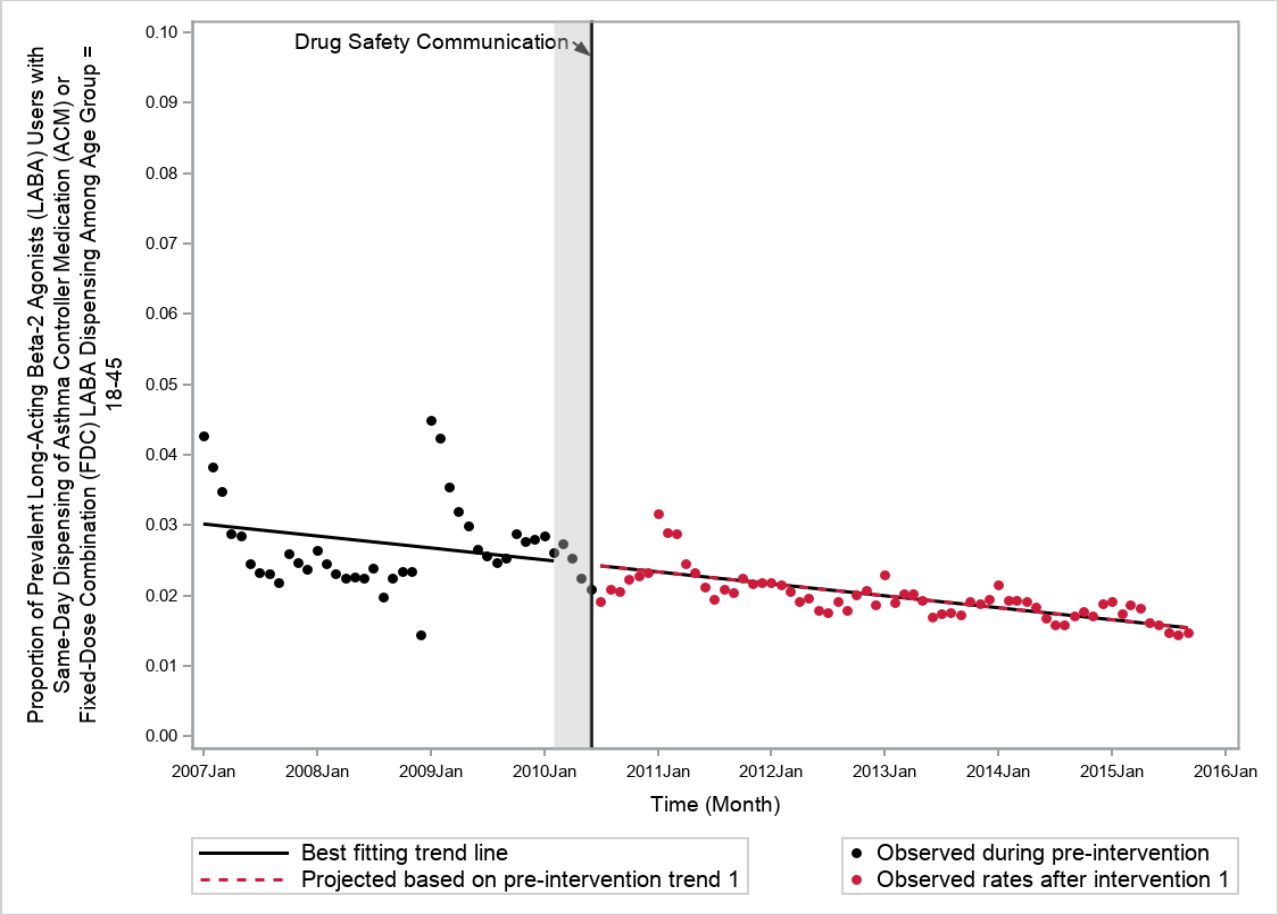
Figure 37. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2]



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

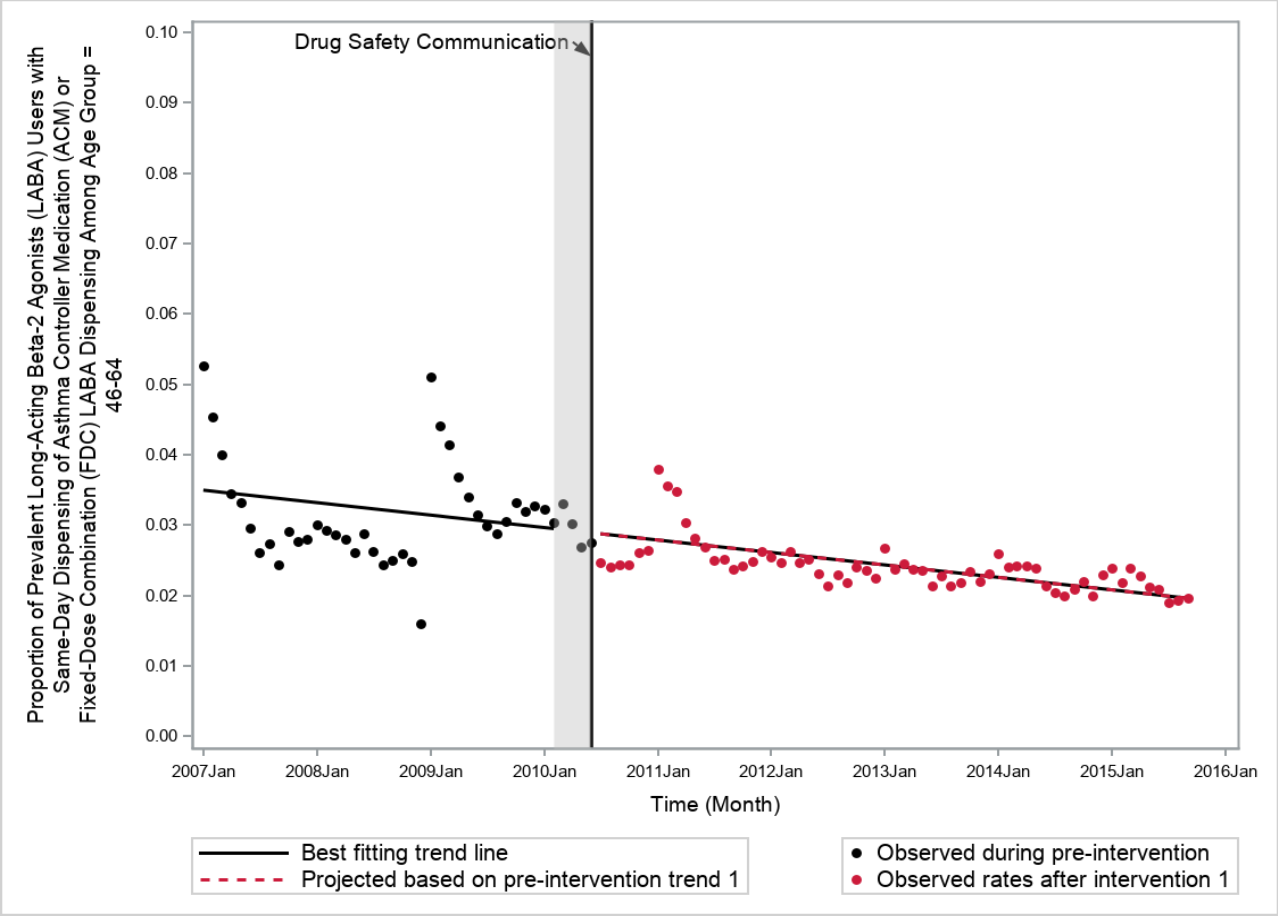
Figure 38. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Age Group = 18-45



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

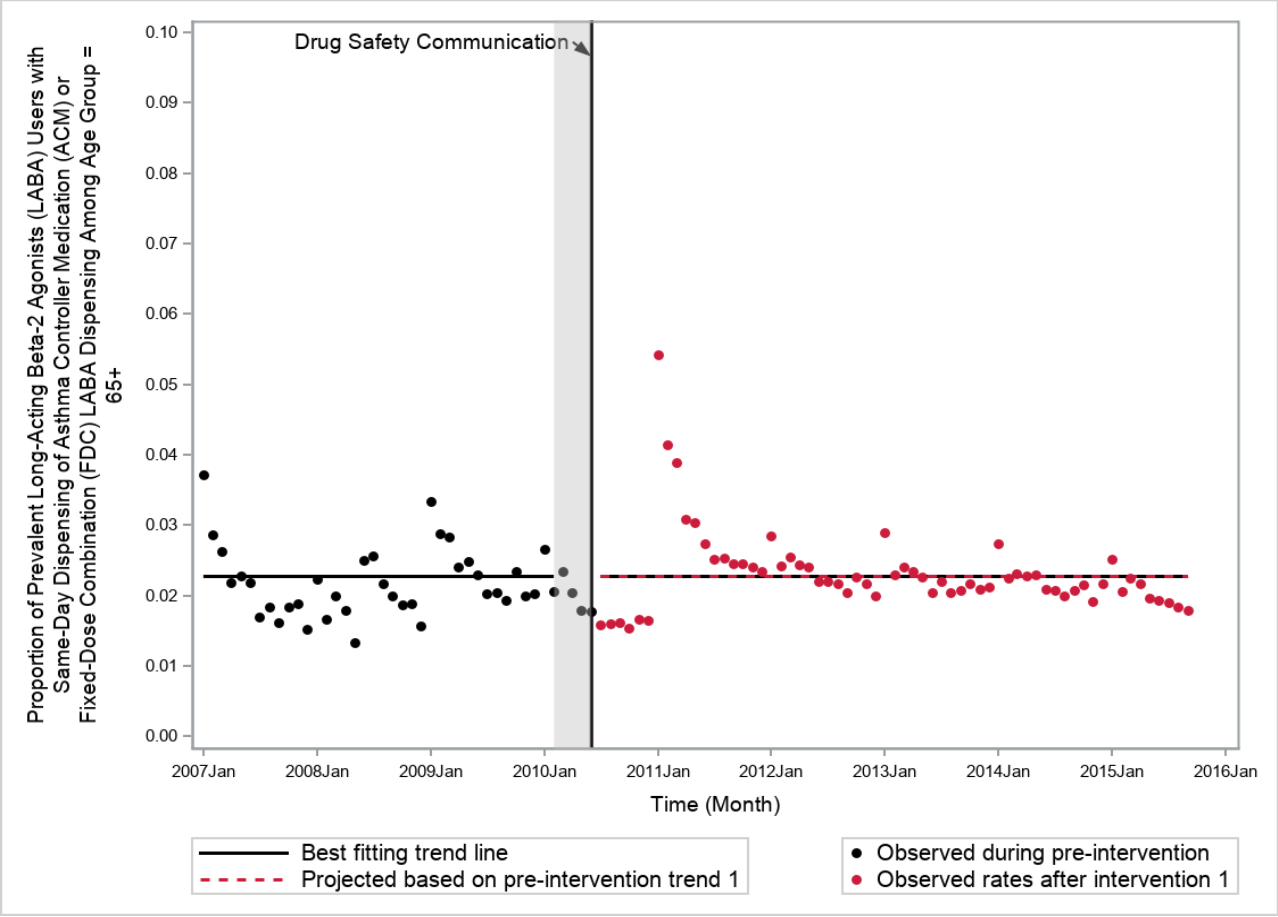
Figure 39. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Age Group = 46-64



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

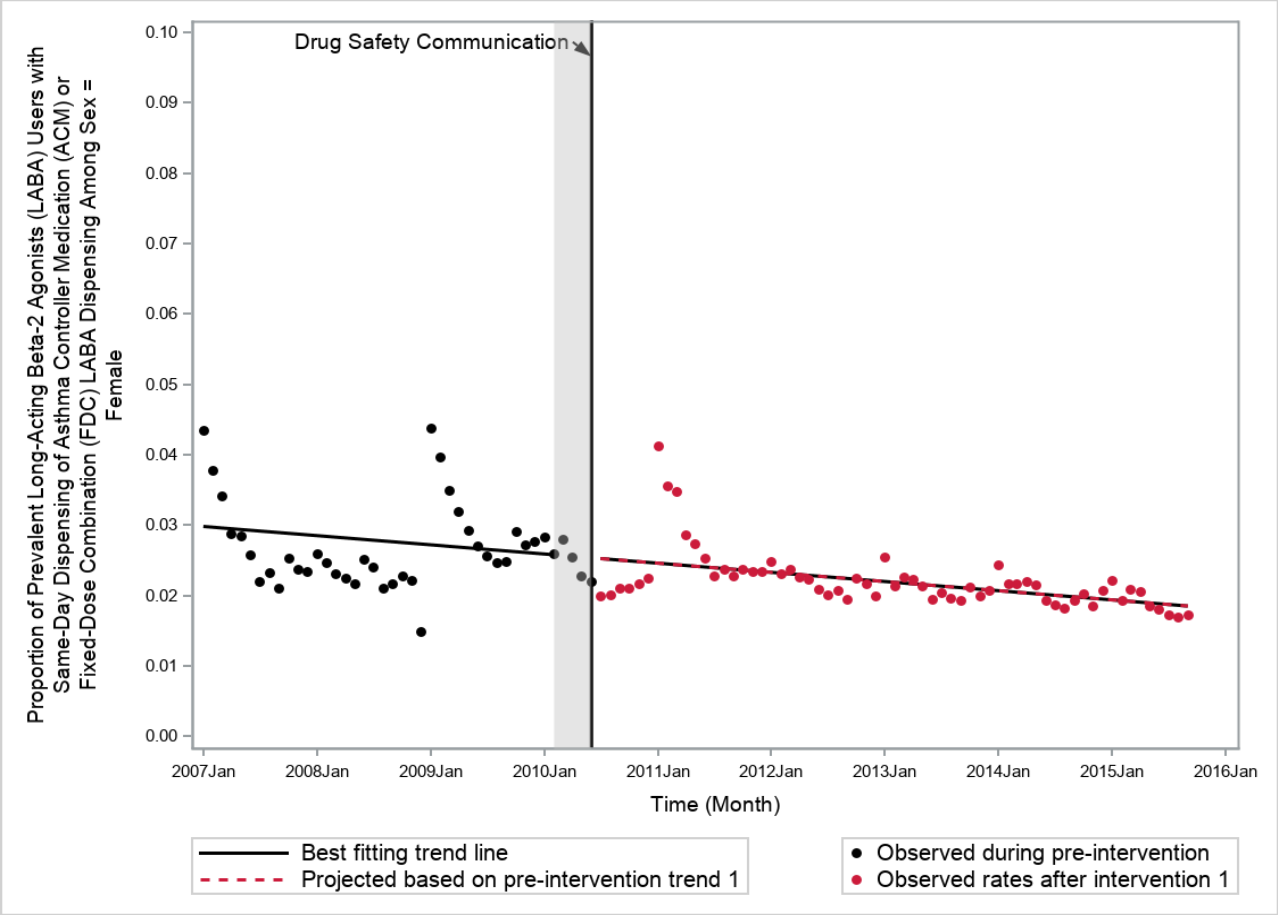
Figure 40. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Age Group = 65+



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

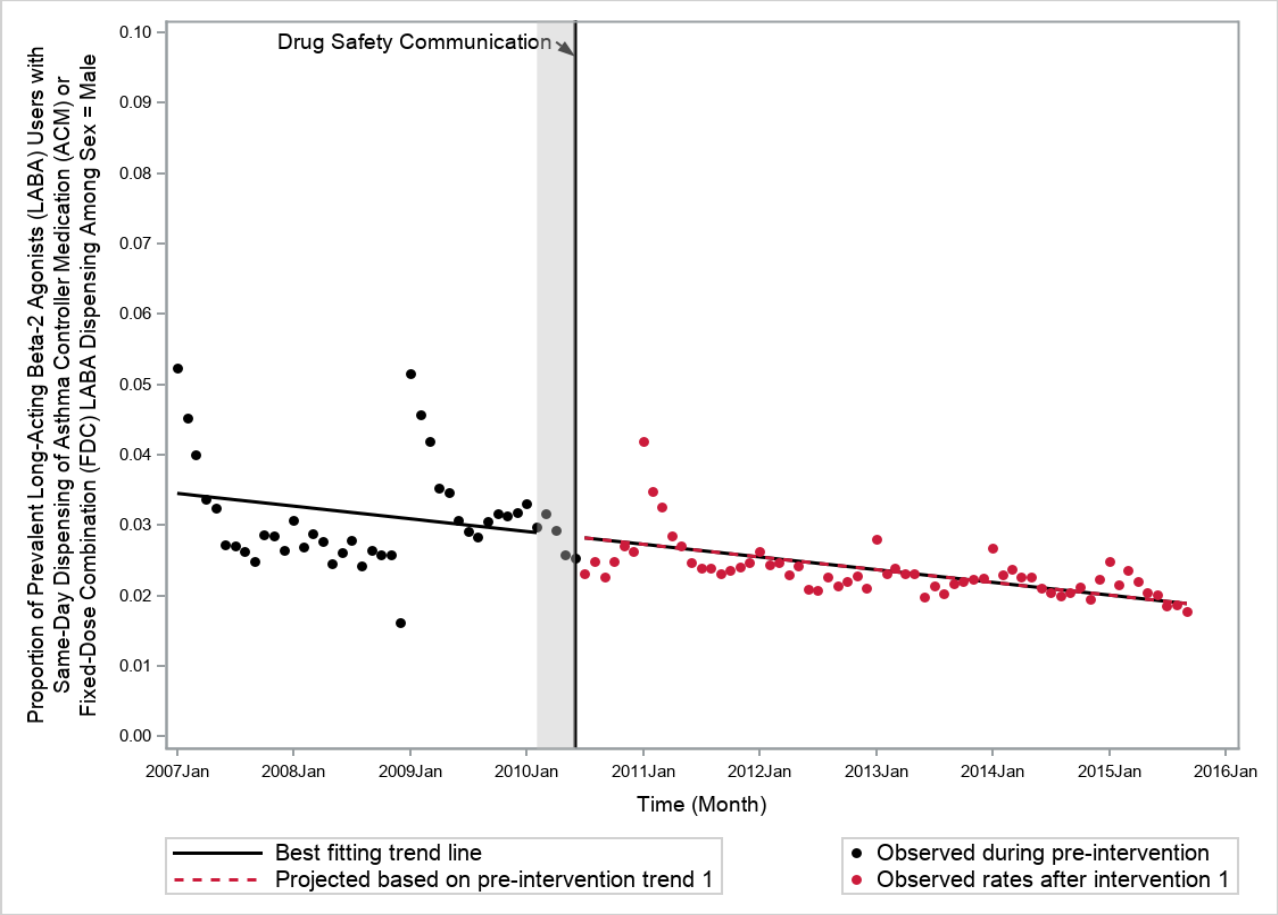
Figure 41. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Sex = Female



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

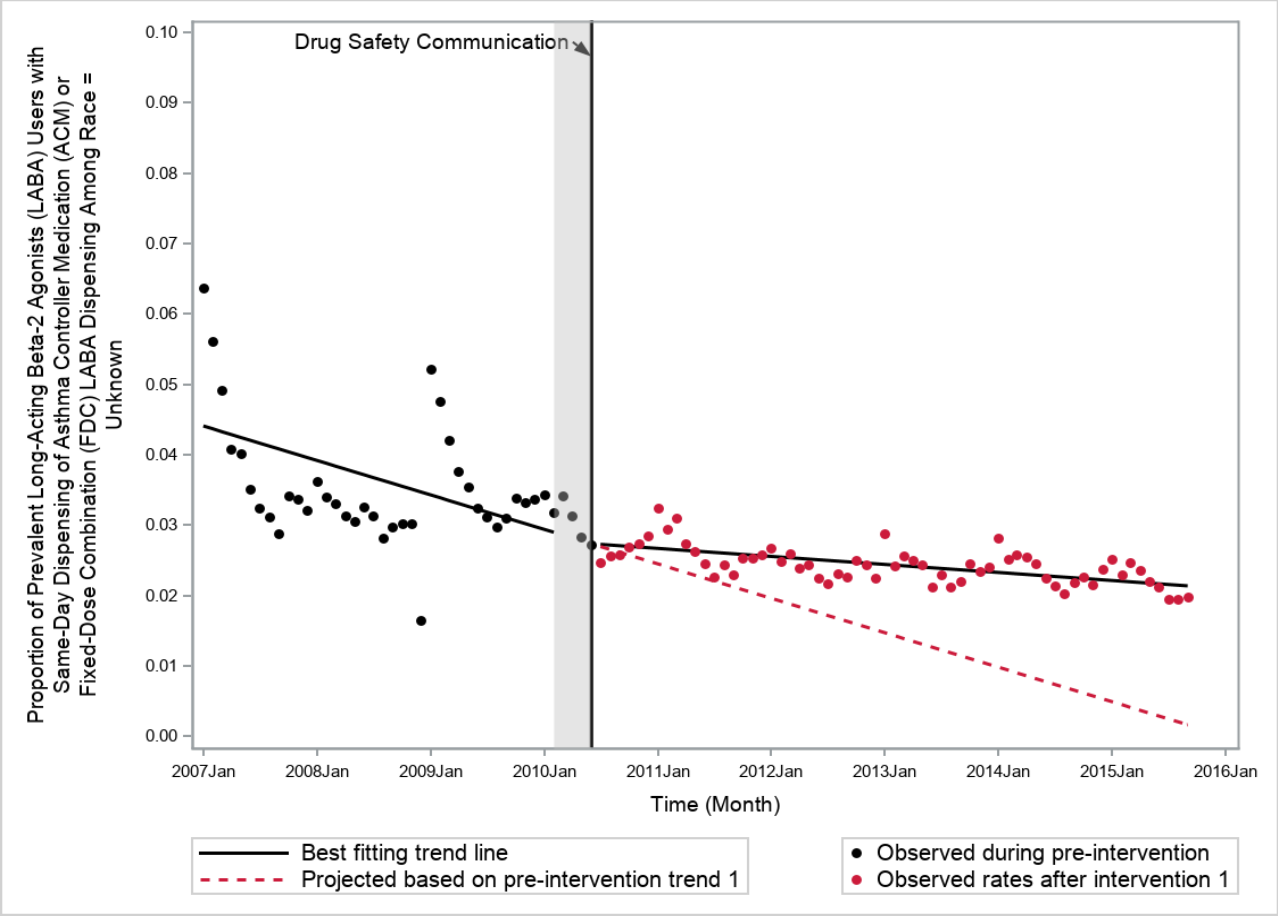
Figure 42. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Sex = Male



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

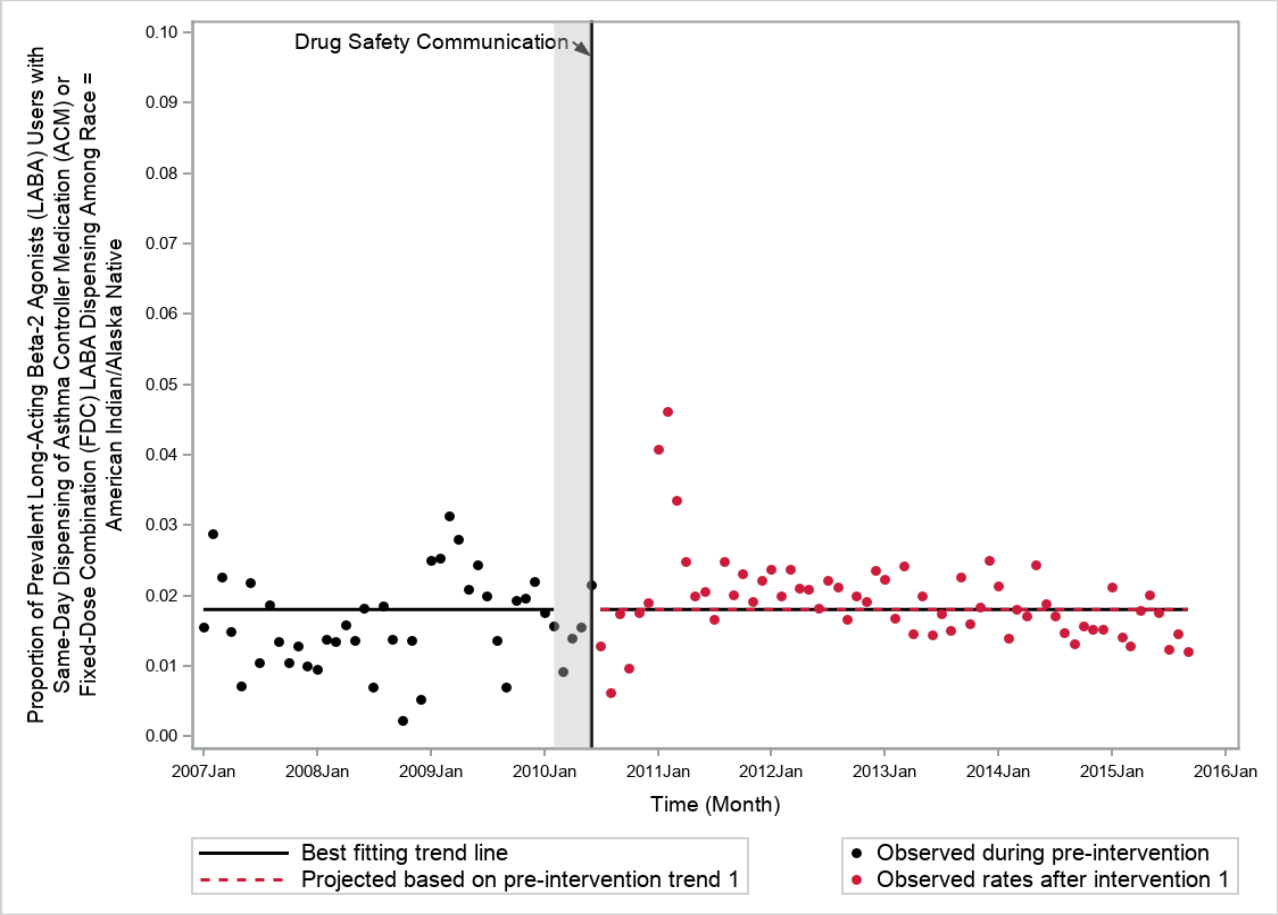
Figure 43. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = Unknown



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

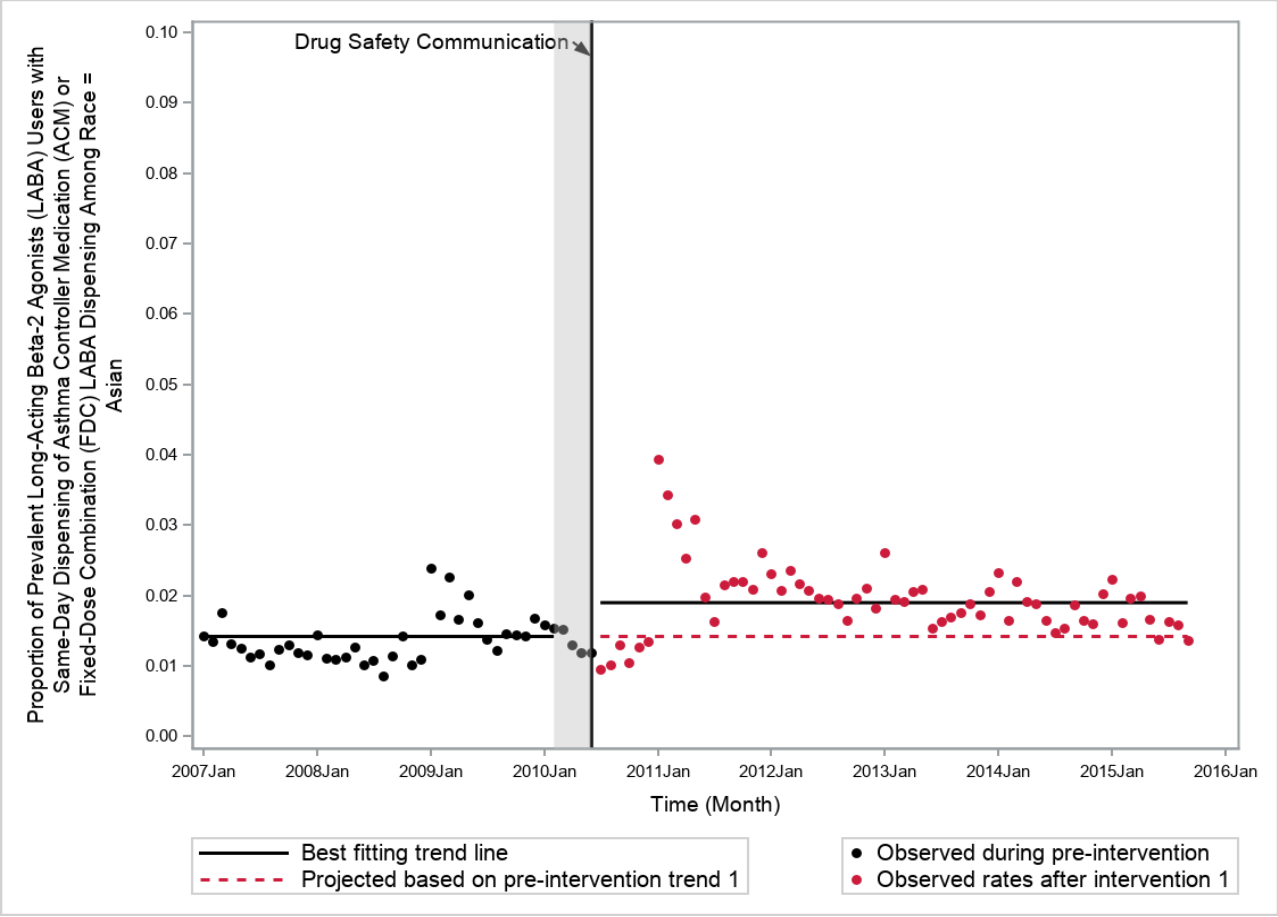
Figure 44. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = American Indian/Alaska Native



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

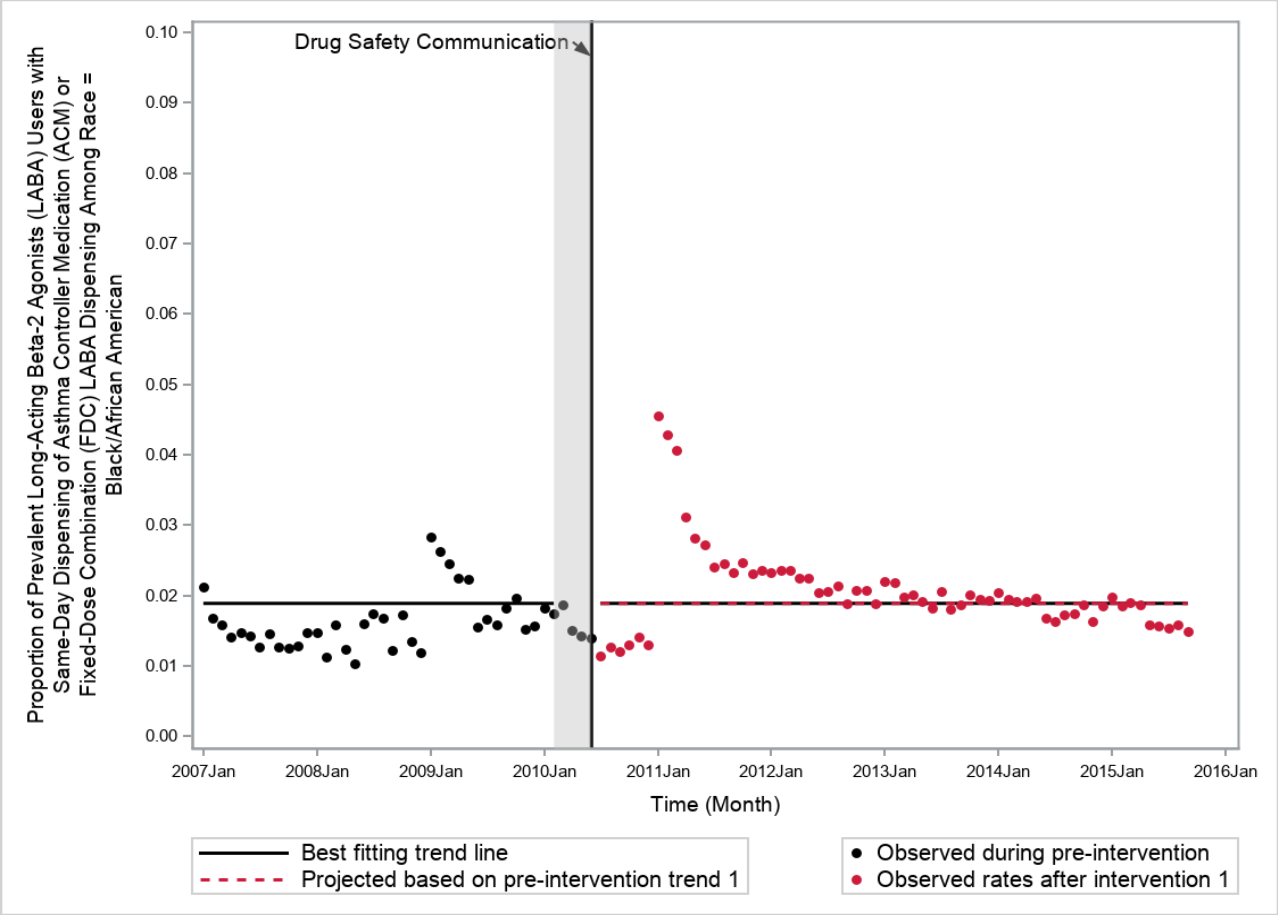
Figure 45. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = Asian



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

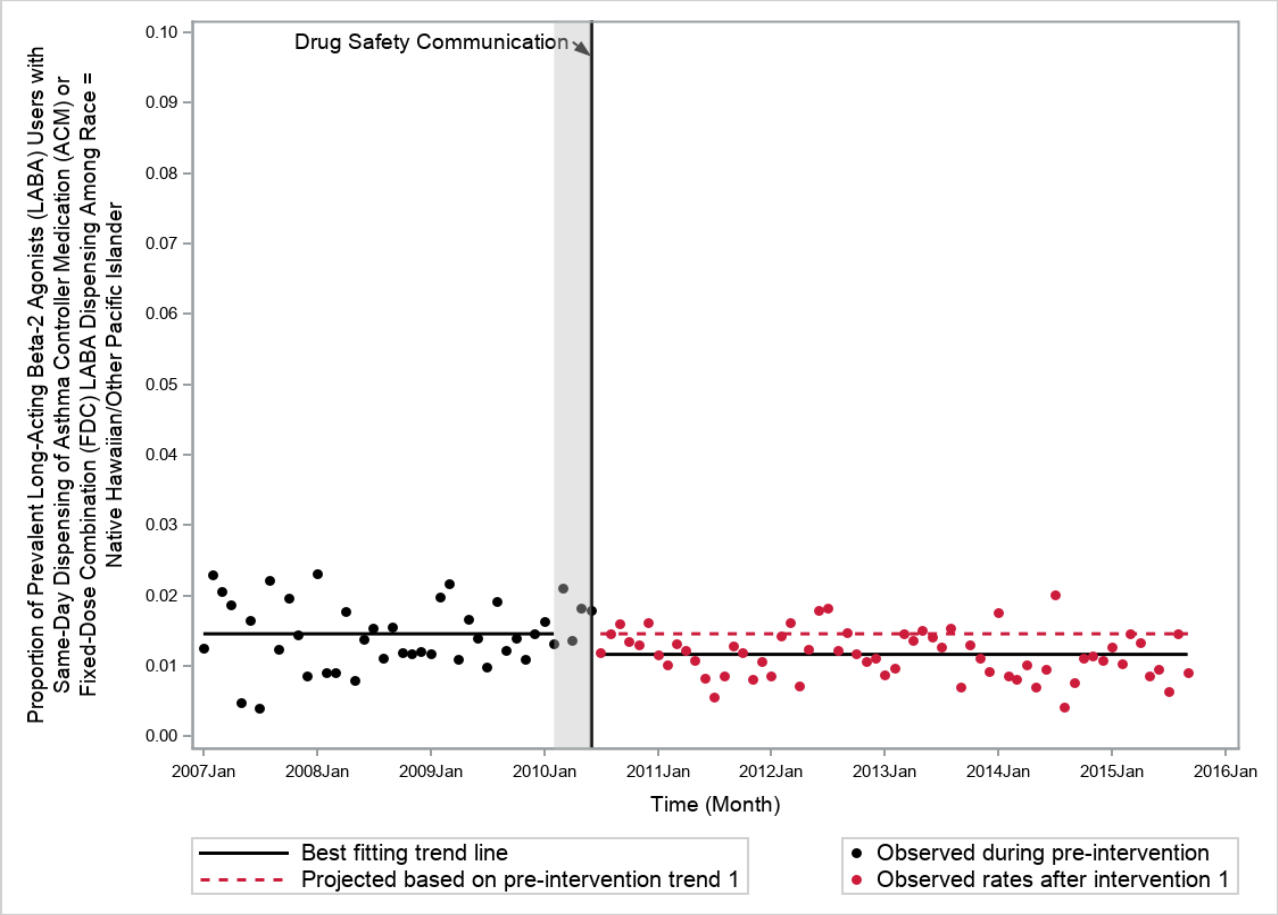
Figure 46. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = Black/African American



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

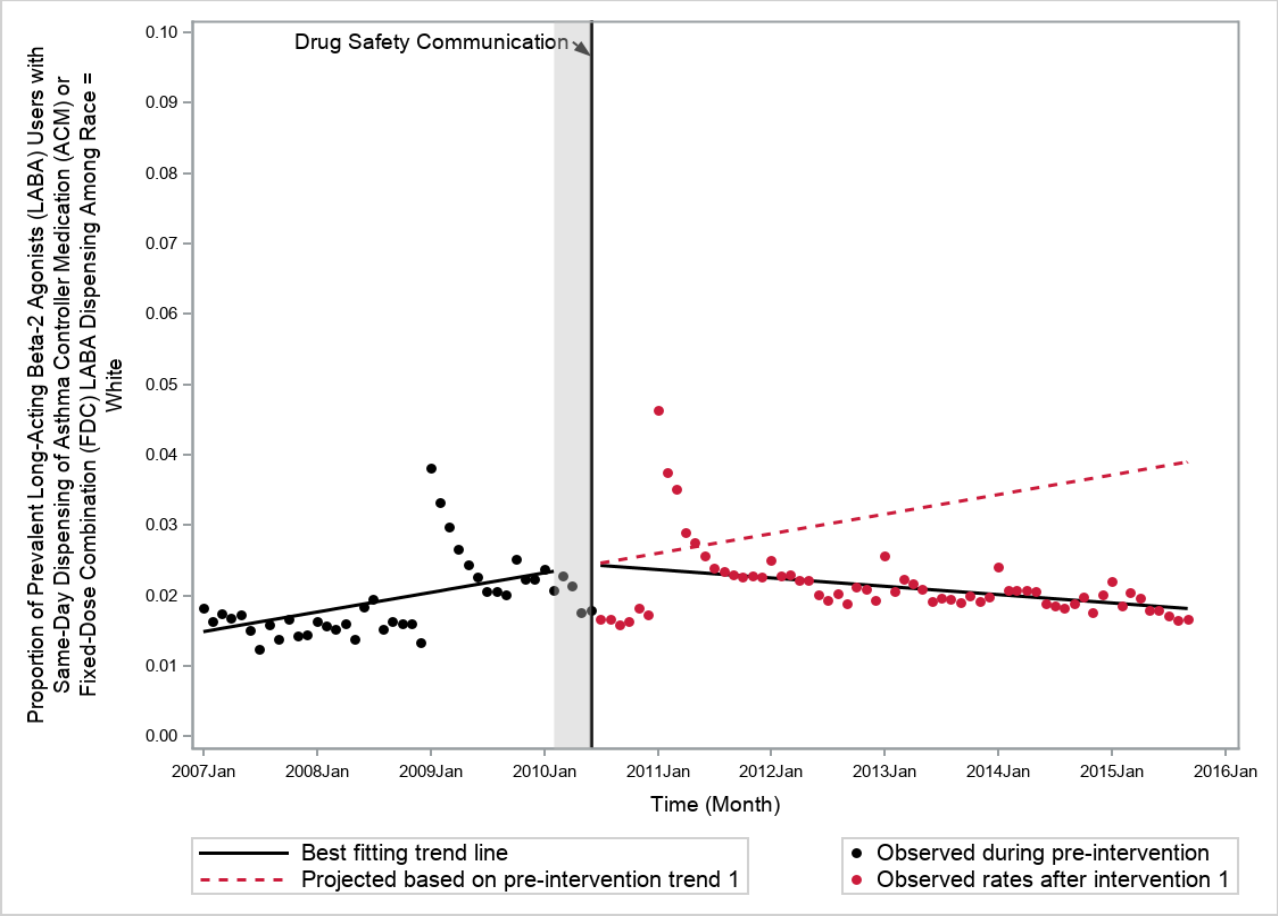
Figure 47. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = Native Hawaiian/Other Pacific Islander



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

Figure 48. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Poorly Controlled Asthma Before and After June 2, 2010[1,2], where Race = White



[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[2]The gray box indicates the timing of the anticipatory period, starting from February 2, 2010 (rounded to the nearest subsequent month) up to the month prior to the first intervention (June 2, 2010).

Appendix A. Start and End Dates for Each Data Partner (DP) up to Request Distribution Date (April 6, 2020)

DP ID	Start Date[1]	End Date[1]
DP01	1/1/2004	8/31/2019
DP02	1/1/2008	3/31/2019
DP03	1/1/2000	7/31/2019
DP04	1/1/2006	6/30/2019
DP05	1/1/2000	4/30/2019
DP06	1/1/2000	2/28/2019
DP07	1/1/2000	6/30/2019
DP08	1/1/2000	3/31/2019
DP09	1/1/2000	1/31/2019
DP10	1/1/2010	6/30/2019
DP11	1/1/2012	6/30/2018
DP12	1/1/2008	9/30/2019
DP13	1/1/2005	7/31/2018
DP14	1/1/2000	12/31/2017
DP15	1/1/2000	4/30/2018
DP16	6/1/2007	7/31/2019

[1]The start and end dates are based on the minimum and maximum dates within each DP. The month with the maximum date must have at least 80% of the number of records in the previous month.

Appendix B. List of Generic and Brand Names of Medical Products Used to Define Single Ingredient (SI) and Fixed Dose Combination (FDC) Long-Acting Beta-2 Agonist (LABA)s and Other non-LABA Asthma Controller Medication (ACM) in this Request

Generic Name	Brand Name
SI-LABA	
formoterol fumarate	Foradil Aerolizer
salmeterol xinafoate	Serevent
salmeterol xinafoate	Serevent Diskus
FDC-LABA	
budesonide/formoterol fumarate	Symbicort
fluticasone furoate/umeclidinium bromide/vilanterol trifenat	Trelegy Ellipta
fluticasone furoate/vilanterol trifenatate	Breo Ellipta
fluticasone propionate/salmeterol xinafoate	AirDuo RespiClick
fluticasone propionate/salmeterol xinafoate	fluticasone propion-salmeterol
fluticasone propionate/salmeterol xinafoate	Advair Diskus
fluticasone propionate/salmeterol xinafoate	Wixela Inhub
fluticasone propionate/salmeterol xinafoate	Advair HFA
mometasone furoate/formoterol fumarate	Dulera
Inhaled Corticosteroids	
beclomethasone dipropionate	Qvar
beclomethasone dipropionate	Qvar RediHaler
budesonide	Pulmicort Flexhaler
budesonide	Pulmicort Turbuhaler
ciclesonide	Alvesco
flunisolide	Aerobid
flunisolide	Aerospan
flunisolide/menthol	Aerobid-M
fluticasone furoate	Arnuity Ellipta
fluticasone propionate	Flovent
fluticasone propionate	ArmonAir RespiClick
fluticasone propionate	Flovent Diskus
fluticasone propionate	Flovent HFA
mometasone furoate	Asmanex Twisthaler
mometasone furoate	Asmanex HFA
triamcinolone acetonide	Azmacort
Leukotriene Modifiers	
montelukast sodium	montelukast
montelukast sodium	Singulair
zafirlukast	Accolate
zafirlukast	zafirlukast
zileuton	Zyflo
zileuton	zileuton
zileuton	Zyflo CR

Appendix B. List of Generic and Brand Names of Medical Products Used to Define Single Ingredient (SI) and Fixed Dose Combination (FDC) Long-Acting Beta-2 Agonist (LABA)s and Other non-LABA Asthma Controller Medication (ACM) in this Request

Generic Name	Brand Name
Chromones	
cromolyn sodium	Intal
cromolyn sodium	Intal 112
cromolyn sodium	Intal 200
nedocromil sodium	Tilade
Oral Corticosteroids	
cortisone acetate	cortisone
dexamethasone	Dexamethasone Intensol
dexamethasone	Baycadron
dexamethasone	Decadron
dexamethasone	dexamethasone
dexamethasone	DexPak 10 day
dexamethasone	DexPak 13 Day
dexamethasone	DexPak 6 Day
dexamethasone	Dxevo
dexamethasone	HiDex
dexamethasone	LoCort
dexamethasone	TaperDex
dexamethasone	Zema-Pak
dexamethasone	ZoDex
dexamethasone	ZonaCort
methylprednisolone	Medrol
methylprednisolone	methylprednisolone
methylprednisolone	Medrol (Pak)
methylprednisolone	Meprolone Unipak
methylprednisolone	Methylpred
methylprednisolone	Methylpred DP
prednisolone	prednisolone
prednisolone	Prelone
prednisolone	Millipred
prednisolone	Millipred DP
prednisolone acetate	Flo-Pred
prednisolone sodium phosphate	Millipred
prednisolone sodium phosphate	prednisolone sodium phosphate
prednisolone sodium phosphate	Orapred
prednisolone sodium phosphate	Veripred 20
prednisolone sodium phosphate	Bubbli-Pred
prednisolone sodium phosphate	Pediapred
prednisolone sodium phosphate	Orapred ODT
Prednisolone Sodium Phosphate/Peak Flow Meter	Asmalpred
Prednisolone Sodium Phosphate/Peak Flow Meter	Asmalpred Plus
prednisone	Prednisone Intensol

Appendix B. List of Generic and Brand Names of Medical Products Used to Define Single Ingredient (SI) and Fixed Dose Combination (FDC) Long-Acting Beta-2 Agonist (LABA)s and Other non-LABA Asthma Controller Medication (ACM) in this Request

Generic Name	Brand Name
prednisone	prednisone
prednisone	Deltasone
prednisone	Rayos
prednisone	Sterapred DS
prednisone	Sterapred
Immunomodulators	
benralizumab	Fasenra
dupilumab	Dupixent
mepolizumab	Nucala
omalizumab	Xolair
reslizumab	Cinqair
Methylxanthines	
aminophylline	aminophylline
dyphylline	Dylix
dyphylline	Lufyllin
theophylline anhydrous	Slo-Bid Gyrocaps
theophylline anhydrous	TheoCap
theophylline anhydrous	theophylline
theophylline anhydrous	Theo-24
theophylline anhydrous	Elixophyllin
theophylline anhydrous	Quibron-T
theophylline anhydrous	Uniphyl
theophylline anhydrous	Theochron
theophylline anhydrous	Quibron-T/SR

Appendix C. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Diagnosis Codes Used to Define Inclusion and Exclusion Criteria in this Request

Code	Description	Code Category	Code Type
	Asthma		
493	Asthma	Diagnosis	ICD-9-CM
493.0	Extrinsic asthma	Diagnosis	ICD-9-CM
493.00	Extrinsic asthma, unspecified	Diagnosis	ICD-9-CM
493.01	Extrinsic asthma with status asthmaticus	Diagnosis	ICD-9-CM
493.02	Extrinsic asthma, with (acute) exacerbation	Diagnosis	ICD-9-CM
493.1	Intrinsic asthma	Diagnosis	ICD-9-CM
493.10	Intrinsic asthma, unspecified	Diagnosis	ICD-9-CM
493.11	Intrinsic asthma with status asthmaticus	Diagnosis	ICD-9-CM
493.12	Intrinsic asthma, with (acute) exacerbation	Diagnosis	ICD-9-CM
493.2	Chronic obstructive asthma	Diagnosis	ICD-9-CM
493.20	Chronic obstructive asthma, unspecified	Diagnosis	ICD-9-CM
493.21	Chronic obstructive asthma with status asthmaticus	Diagnosis	ICD-9-CM
493.22	Chronic obstructive asthma, with (acute) exacerbation	Diagnosis	ICD-9-CM
493.8	Other forms of asthma	Diagnosis	ICD-9-CM
493.81	Exercise induced bronchospasm	Diagnosis	ICD-9-CM
493.82	Cough variant asthma	Diagnosis	ICD-9-CM
493.9	Unspecified asthma	Diagnosis	ICD-9-CM
493.90	Asthma, unspecified, unspecified status	Diagnosis	ICD-9-CM
493.91	Asthma, unspecified with status asthmaticus	Diagnosis	ICD-9-CM
493.92	Asthma, unspecified, with (acute) exacerbation	Diagnosis	ICD-9-CM
	Chronic Obstructive Pulmonary Disease (COPD)		
490	Bronchitis, not specified as acute or chronic	Diagnosis	ICD-9-CM
491	Chronic bronchitis	Diagnosis	ICD-9-CM
491.0	Simple chronic bronchitis	Diagnosis	ICD-9-CM
491.1	Mucopurulent chronic bronchitis	Diagnosis	ICD-9-CM
491.2	Obstructive chronic bronchitis	Diagnosis	ICD-9-CM
491.20	Obstructive chronic bronchitis, without exacerbation	Diagnosis	ICD-9-CM
491.21	Obstructive chronic bronchitis, with (acute) exacerbation	Diagnosis	ICD-9-CM
491.22	Obstructive chronic bronchitis with acute bronchitis	Diagnosis	ICD-9-CM
491.8	Other chronic bronchitis	Diagnosis	ICD-9-CM
491.9	Unspecified chronic bronchitis	Diagnosis	ICD-9-CM
492	Emphysema	Diagnosis	ICD-9-CM
492.0	Emphysematous bleb	Diagnosis	ICD-9-CM
492.8	Other emphysema	Diagnosis	ICD-9-CM
493.2	Chronic obstructive asthma	Diagnosis	ICD-9-CM
493.20	Chronic obstructive asthma, unspecified	Diagnosis	ICD-9-CM
493.21	Chronic obstructive asthma with status asthmaticus	Diagnosis	ICD-9-CM
493.22	Chronic obstructive asthma, with (acute) exacerbation	Diagnosis	ICD-9-CM
496	Chronic airway obstruction, not elsewhere classified	Diagnosis	ICD-9-CM

Appendix C. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Diagnosis Codes Used to Define Inclusion and Exclusion Criteria in this Request

Code	Description	Code Category	Code Type
	Cystic Fibrosis		
277.0	Cystic fibrosis	Diagnosis	ICD-9-CM
277.00	Cystic fibrosis without mention of meconium ileus	Diagnosis	ICD-9-CM
277.01	Cystic fibrosis with meconium ileus	Diagnosis	ICD-9-CM
277.02	Cystic fibrosis with pulmonary manifestations	Diagnosis	ICD-9-CM
277.03	Cystic fibrosis with gastrointestinal manifestations	Diagnosis	ICD-9-CM
277.09	Cystic fibrosis with other manifestations	Diagnosis	ICD-9-CM
	Bronchiectasis		
494	Bronchiectasis	Diagnosis	ICD-9-CM
494.0	Bronchiectasis without acute exacerbation	Diagnosis	ICD-9-CM
494.1	Bronchiectasis with acute exacerbation	Diagnosis	ICD-9-CM
	Pulmonary Hypertension or Embolism		
415.1	Pulmonary embolism and infarction	Diagnosis	ICD-9-CM
415.11	Iatrogenic pulmonary embolism and infarction	Diagnosis	ICD-9-CM
415.12	Septic pulmonary embolism	Diagnosis	ICD-9-CM
415.13	Saddle embolus of pulmonary artery	Diagnosis	ICD-9-CM
415.19	Other pulmonary embolism and infarction	Diagnosis	ICD-9-CM
416.0	Primary pulmonary hypertension	Diagnosis	ICD-9-CM
	Bronchopulmonary Dysplasia		
770.7	Chronic respiratory disease arising in the perinatal period	Diagnosis	ICD-9-CM
	Congestive Heart Failure		
428	Heart failure	Diagnosis	ICD-9-CM
428.0	Congestive heart failure, unspecified	Diagnosis	ICD-9-CM
428.1	Left heart failure	Diagnosis	ICD-9-CM
428.2	Systolic heart failure	Diagnosis	ICD-9-CM
428.20	Unspecified systolic heart failure	Diagnosis	ICD-9-CM
428.21	Acute systolic heart failure	Diagnosis	ICD-9-CM
428.22	Chronic systolic heart failure	Diagnosis	ICD-9-CM
428.23	Acute on chronic systolic heart failure	Diagnosis	ICD-9-CM
428.3	Diastolic heart failure	Diagnosis	ICD-9-CM
428.30	Unspecified diastolic heart failure	Diagnosis	ICD-9-CM
428.31	Acute diastolic heart failure	Diagnosis	ICD-9-CM
428.32	Chronic diastolic heart failure	Diagnosis	ICD-9-CM
428.33	Acute on chronic diastolic heart failure	Diagnosis	ICD-9-CM
428.4	Combined systolic and diastolic heart failure	Diagnosis	ICD-9-CM
428.40	Unspecified combined systolic and diastolic heart failure	Diagnosis	ICD-9-CM
428.41	Acute combined systolic and diastolic heart failure	Diagnosis	ICD-9-CM
428.42	Chronic combined systolic and diastolic heart failure	Diagnosis	ICD-9-CM
428.43	Acute on chronic combined systolic and diastolic heart failure	Diagnosis	ICD-9-CM
428.9	Unspecified heart failure	Diagnosis	ICD-9-CM

Appendix D. List of Generic and Brand Names of Medical Products Used to Define Poorly Controlled Asthma in this Request

Generic Name	Brand Name
Inhaled Corticosteroids	
beclomethasone dipropionate	Qvar
beclomethasone dipropionate	Qvar RediHaler
budesonide	Pulmicort Flexhaler
budesonide	Pulmicort Turbuhaler
ciclesonide	Alvesco
flunisolide	Aerobid
flunisolide	Aerospan
flunisolide/menthol	Aerobid-M
fluticasone furoate	Arnuity Ellipta
fluticasone propionate	Flovent
fluticasone propionate	ArmonAir RespiClick
fluticasone propionate	Flovent Diskus
fluticasone propionate	Flovent HFA
mometasone furoate	Asmanex Twisthaler
mometasone furoate	Asmanex HFA
triamcinolone acetonide	Azmacort
Leukotriene Modifiers	
montelukast sodium	montelukast
montelukast sodium	Singulair
zafirlukast	Accolate
zafirlukast	zafirlukast
zileuton	Zyflo
zileuton	zileuton
zileuton	Zyflo CR
Oral Corticosteroids	
cortisone acetate	cortisone
dexamethasone	Dexamethasone Intensol
dexamethasone	Baycadron
dexamethasone	Decadron
dexamethasone	dexamethasone
dexamethasone	DexPak 10 day
dexamethasone	DexPak 13 Day
dexamethasone	DexPak 6 Day
dexamethasone	Dxevo
dexamethasone	HiDex
dexamethasone	LoCort
dexamethasone	TaperDex
dexamethasone	Zema-Pak
dexamethasone	ZoDex
dexamethasone	ZonaCort
methylprednisolone	Medrol
methylprednisolone	methylprednisolone
methylprednisolone	Medrol (Pak)

Appendix D. List of Generic and Brand Names of Medical Products Used to Define Poorly Controlled Asthma in this Request

Generic Name	Brand Name
methylprednisolone	Meprolone Unipak
methylprednisolone	Methylpred
methylprednisolone	Methylpred DP
prednisolone	prednisolone
prednisolone	Prelone
prednisolone	Millipred
prednisolone	Millipred DP
prednisolone acetate	Flo-Pred
prednisolone sodium phosphate	Millipred
prednisolone sodium phosphate	prednisolone sodium phosphate
prednisolone sodium phosphate	Orapred
prednisolone sodium phosphate	Veripred 20
prednisolone sodium phosphate	Bubbli-Pred
prednisolone sodium phosphate	Pediapred
prednisolone sodium phosphate	Orapred ODT
Prednisolone Sodium Phosphate/Peak Flow Meter	Asmalpred
Prednisolone Sodium Phosphate/Peak Flow Meter	Asmalpred Plus
prednisone	Prednisone Intensol
prednisone	prednisone
prednisone	Deltasone
prednisone	Rayos
prednisone	Sterapred DS
prednisone	Sterapred
Short-Acting Beta-2 Agonists (SABA)	
albuterol	albuterol
albuterol	albuterol (refill)
albuterol	Proventil
albuterol	Proventil (Refill)
albuterol	Ventolin
albuterol sulfate	ProAir RespiClick
albuterol sulfate	albuterol sulfate
albuterol sulfate	ProAir HFA
albuterol sulfate	Proventil HFA
albuterol sulfate	Ventolin HFA
levalbuterol tartrate	levalbuterol tartrate
levalbuterol tartrate	Xopenex HFA
metaproterenol sulfate	Alupent
pirbuterol acetate	Maxair Autohaler

Appendix E. Specifications Defining Parameters for this Request

This request executed the Cohort Identification and Descriptive Analysis (CIDA) tool, version 9.3.1, to estimate incident use of long-acting beta-2 agonist (LABA) with and without a long-term asthma controller medication (ACM) among asthma patients before and after drug safety communications (DSCs) issued on June 2, 2010 in the Sentinel Distributed Database (SDD). The purpose of the request is to test the newly added functionality for interrupted time series (ITS) analysis, which creates regression models of rates over time after truncating follow-up time at a pre-specified intervention date.

Query Period: January 01, 2006 - September 30, 2015
Coverage Requirement: Medical & Drug Coverage
Pre-Index Enrollment Requirement: See below
Post-Index Enrollment Requirement: N/A
Enrollment Gap: 45 days
Age Groups: 18-45, 46-64, 65+ years
Sex Groups: Male, female
Stratifications: Age group, sex, race, ethnicity, Census Bureau regions
Censor Output Categorization: 0-30, 31-60, 61-90, 91-120, 121-183, 184-365, 366-730, 730+
Restrictions: N/A
Envelope Macro: No reclassification
Features: Interrupted time series (ITS) analysis, distribution of index-defining codes, multiple events/overlap, censoring output
Freeze Data: Yes

		Cohorts 8-10 Recommendation 2 Poorly controlled LABA		
		Scenario 8	**Scenario 6**	**Scenario 7**
ITS Analysis Groups	**Group Name**	**grp5_pcasthma**	**grp456_acm2**	**grp456_fdc2**
	ITS Group	**Primary**	**Secondary**	
	Rate Denominator Definition	**Poorly controlled asthma patients**	N/A	
	Rate Denominator	**Number of eligible members**	N/A	
	Rate Numerator Definition	N/A	**Incident LABA users concurrent with ACM use**	
	Rate Numerator	N/A	Number of adherent patients	
	Pre-Index Enrollment Requirement	365 days	0 days	365 days

Appendix E. Specifications Defining Parameters for this Request

		Cohorts 8-10 Recommendation 2 Poorly controlled LABA		
		Scenario 8	**Scenario 6**	**Scenario 7**
Drug/Exposure	**Exposure**	All LABA products (Single-ingredient (SI) OR fixed-dose combination (FDC))	Non-LABA asthma controller medication (ACM) (ICS, leukotriene modifier, chromones, oral systemic corticosteroids, immunomodulators, and methylxanthines)	FDC LABA
	Care Setting	N/A	N/A	N/A
	Incident with Respect To	All LABA products (SI or FDC)		
	Washout	183 days	0 days	0 days
	Exposure Episode Truncation Criteria	*Death *Data Partner (DP) end date *Query end date	*Death *DP end date *Query end date	*Death *DP end date *Query end date
	Cohort Definition	Only the first valid treatment episode during the query period (01)	Cohort includes all valid exposure episodes during the query period (02)	Cohort includes all valid exposure episodes during the query period (02)
	Prevalent Cohort Creation?	Yes	N/A	N/A
	Exposure Episode Gap	25% previous days' supply	25% previous days' supply	25% previous days' supply
	Exposure Extension Period	0 days	0 days	0 days
	Minimum Episode Duration	1 day	1 day	1 day
	Minimum Days Supplied	1 day	1 day	1 day
	Intention-to-Treat Days	N/A	N/A	N/A
Inclusion/Exclusion Criteria	**Conditions**	*Chronic obstructive pulmonary disease (COPD) *Cystic fibrosis *Bronchiectasis *Pulmonary hypertension or embolism *Bronchopulmonary dysplasia *Congestive heart failure		*COPD *Cystic fibrosis *Bronchiectasis *Pulmonary hypertension or embolism *Bronchopulmonary dysplasia *Congestive heart failure
	Include or Exclude	Exclusion		Exclusion
	Care Setting/Principal Diagnosis (PDX)	Any		Any
	Lookback Period	(-365, 0) days		(-365, 0) days
	Number of Code Occurrences	1 instance		1 instance

Appendix E. Specifications Defining Parameters for this Request

		Cohorts 8-10 Recommendation 2 Poorly controlled LABA		
		Scenario 8	**Scenario 6**	**Scenario 7**
Inclusion/Exclusion Criteria	**Conditions**	Asthma (493.xx)		
	Include or Exclude	Inclusion		
	Care Setting/PDX	IP*, ED*, AV*, OA*		
	Lookback Period	(-365, 0) days		
	Number of Code Occurrences	1 instance if (IP*, ED*) 2 instances if (AV*, OA*)		
Inclusion/Exclusion Criteria	**Conditions**	**Poorly controlled asthma (ICS or LM dispensing) (lookback period: days supply)**		
	Include or Exclude	**Inclusion**		
	Care Setting/PDX	**N/A**		
	Lookback Period	**(-90, -1) days**		
	Number of Code Occurrences	**1 instance**		
		OR		
Inclusion/Exclusion Criteria	**Conditions**	**Poorly controlled asthma (asthma (493.xx))**		
	Include or Exclude	**Inclusion**		
	Care Setting/PDX	**IP*, ED***		
	Lookback Period	**(-90, -1) days**		
	Number of Code Occurrences	**1 instance**		
		OR		
Inclusion/Exclusion Criteria	**Conditions**	**Poorly controlled asthma (oral corticosteroids dispensing of 21 days' supply or smaller) (combo) (lookback period: days supply)**		
	Include or Exclude	**Inclusion**		
	Care Setting/PDX	**N/A**		
	Lookback Period	**(-90, -1)**		
	Number of Code Occurrences	**2 instances**		

Appendix E. Specifications Defining Parameters for this Request

		Cohorts 8-10 Recommendation 2 Poorly controlled LABA		
		Scenario 8	**Scenario 6**	**Scenario 7**
		OR		
Inclusion/Exclusion Criteria	**Conditions**	**Poorly controlled asthma (SABA canisters) (lookback period: dispensing date)**		
	Include or Exclude	**Inclusion**		
	Care Setting/PDX	**N/A**		
	Lookback Period	**(-183, -1) days**		
	Number of Code Occurrences	**3 instances**		
Stockpiling	**Same Day Dispensing (Days Supplied)**	Sum	Sum	Sum
	Same Day Dispensing (Amount Supplied)	Sum	Sum	Sum
	Range of Allowable Days Supplied	N/A	N/A	N/A
	Range of Allowable Amount Supplied	N/A	N/A	N/A
	Overlap Percentage Processing	Default	Default	Default
Multiple Events / Overlap	**Multiple Events or Overlap?**	Overlap (**M78_pc_laba)**		
	Group Identifier	Primary	Secondary	
	Observation Window Around Primary Episode	(Index date, episode end)		
	Secondary Episode to Use for Time Metrics	N/A		
	Minimum Cutoff to be Considered Adherent	1 day		
	Categories for Overlap Metrics	0-<25 25-<50 50-<75 >=75 =100%		
	Primary Episode Categories	0-30 31-60 61-90 91-120 121-183 184-365 366-730 731+		
Adherence	**Adherence Name**	**Incident LABA Users 50% concurrent with ACM Use (M78_pc_laba_50)**		
	Minimum/Maximum Episode Length or Overlap Time (Overlap)	50% minimum		
	Minimum/Maximum Secondary Episode Count (Multiple Events)	N/A		

Appendix E. Specifications Defining Parameters for this Request

		Cohorts 8-10		
		Recommendation 2 Poorly controlled LABA		
		Scenario 8	Scenario 6	Scenario 7
Adherence	Minimum/Maximum Secondary Episode Gap (Multiple Events)	N/A		
	Minimum/Maximum Time to Secondary Episode Count (Multiple Events)	N/A		
Adherence	Adherence Name	Incident LABA Users 75% concurrent with ACM Use (M78_pc_laba_75)		
	Minimum/Maximum Episode Length or Overlap Time (Overlap)	75% minimum		
	Minimum/Maximum Secondary Episode Count (Multiple Events)	N/A		
	Minimum/Maximum Secondary Episode Gap (Multiple Events)	N/A		
	Minimum/Maximum Time to Secondary Episode Count (Multiple Events)	N/A		
ITS Analysis	Data Range Start, End	Full query period		
	Anticipatory Date 1 Start	February 2010		
	Intervention Date 1	June 2010		
	Anticipatory Date 2 Start	N/A		
	Intervention Date 2	N/A		
	Interval Length	Month		
	P-Value	0.05		
	Autoregression Lag	12 months		
	Autoregression Model Parameter Cutoff	0.2		
	Time Points at Which to Report Difference Metrics	January 2011, June 2011, January 2012, June 2012		
	Continuous Enrollment Required?	No		

Appendix E. Specifications Defining Parameters for this Request

		Cohorts 8-10		
		Recommendation 2 Poorly controlled LABA		
		Scenario 8	Scenario 6	Scenario 7
Baseline Covariates	**Covariates**	SI-LABA FDC All LABA non-LABA ACM		
	Care Setting/PDX	N/A		
	Covariate Evaluation Window	(-183, -1) days		
Baseline Covariates	**Covariates**	non-LABA ACM		
	Care Setting/PDX	N/A		
	Covariate Evaluation Window	(-365, -184) days		
Baseline Covariates	**Covariates**	SI-LABA FDC All LABA non-LABA ACM		
	Care Setting/PDX	N/A		
	Covariate Evaluation Window	(0, 0) days		
Utilization/ Comorbidity Score	**Comorbidity Score Evaluation Window**	(-365, 0) days		
	Medical Utilization Evaluation Window	(-365, 0) days		
	Medical Utilization Care Setting	IP, IS, AV, OA, ED		
	Drug Utilization Evaluation Window	(-365, 0) days		

Appendix E. Specifications Defining Parameters for this Request

		Cohort 11		
		Recommendation 2 Poorly controlled LABA, SI-LABA in ACM presence (Measures 11, 12)		
		Scenario 8	**Scenario 6**	**Scenario 7**
ITS Analysis Groups	**Group Name**	**grp5_pcasthma**	**grp456_acm2**	**grp456_fdc2**
	ITS Group	**Primary**	**Secondary**	
	Rate Denominator Definition	**Poorly controlled asthma patients**	N/A	
	Rate Denominator	**Number of eligible members**	N/A	
	Rate Numerator Definition	N/A	**Incident LABA users concurrent with ACM use**	
	Rate Numerator	N/A	Number of adherent patients	
	Pre-Index Enrollment Requirement	365 days	0 days	365 days
Drug/Exposure	**Exposure**	All LABA products (SI or FDC)	Non-LABA ACM (ICS, leukotriene modifier, chromones, oral systemic corticosteroids, immunomodulators, and methylxanthines)	FDC LABA
	Care Setting	N/A	N/A	N/A
	Incident with Respect To	All LABA products (SI or FDC)		
	Washout	183 days	0 days	0 days
	Exposure Episode Truncation Criteria	*Death *DP end date *Query end date	*Death *DP end date *Query end date	*Death *DP end date *Query end date
	Cohort Definition	Only the first valid treatment episode during the query period (01)	Cohort includes all valid exposure episodes during the query period (02)	Cohort includes all valid exposure episodes during the query period (02)
	Prevalent Cohort Creation?	Yes	N/A	N/A
	Exposure Episode Gap	25% previous days' supply	25% previous days' supply	25% previous days' supply
	Exposure Extension Period	0 days	0 days	0 days
	Minimum Episode Duration	1 day	1 day	1 day
	Minimum Days Supplied	1 day	1 day	1 day
	Intention-to-Treat Days	N/A	N/A	N/A

Appendix E. Specifications Defining Parameters for this Request

		Cohort 11		
		Recommendation 2 Poorly controlled LABA, SI-LABA in ACM presence (Measures 11, 12)		
		Scenario 8	**Scenario 6**	**Scenario 7**
Inclusion/Exclusion Criteria	**Conditions**	*COPD *Cystic fibrosis *Bronchiectasis *Pulmonary hypertension or embolism *Bronchopulmonary dysplasia *Congestive heart failure		*COPD *Cystic fibrosis *Bronchiectasis *Pulmonary hypertension or embolism *Bronchopulmonary dysplasia *Congestive heart failure
	Include or Exclude	Exclusion		Exclusion
	Care Setting/PDX	Any		Any
	Lookback Period	(-365, 0) days		(-365, 0) days
	Number of Code Occurrences	1 instance		1 instance
Inclusion/ Exclusion Criteria	**Conditions**	Asthma (493.xx)		
	Include or Exclude	Inclusion		
	Care Setting/PDX	IP*, ED*, AV*, OA*		
	Lookback Period	(-365, 0) days		
	Number of Code Occurrences	1 instance if (IP*, ED*) 2 instances if (AV*, OA*)		
Inclusion/ Exclusion Criteria	**Conditions**	**Poorly controlled asthma (ICS or LM dispensing) (lookback period: days supply)**		
	Include or Exclude	**Inclusion**		
	Care Setting/PDX	**N/A**		
	Lookback Period	**(-90, -1) days**		
	Number of Code Occurrences	**1 instance**		
		OR		
Inclusion/ Exclusion Criteria	**Conditions**	**Poorly controlled asthma (asthma (493.xx))**		
	Include or Exclude	**Inclusion**		

Appendix E. Specifications Defining Parameters for this Request

		Cohort 11		
		Recommendation 2 Poorly controlled LABA, SI-LABA in ACM presence (Measures 11, 12)		
		Scenario 8	Scenario 6	Scenario 7
Inclusion/ Exclusion Criteria	Care Setting/PDX	IP*, ED*		
	Lookback Period	(-90, -1) days		
	Number of Code Occurrences	1 instance		
	OR			
Inclusion/ Exclusion Criteria	Conditions	Poorly controlled asthma (oral corticosteroids dispensing of 21 days' supply or smaller) (combo) (lookback period: days supply)		
	Include or Exclude	Inclusion		
	Care Setting/PDX	N/A		
	Lookback Period	(-90, -1) days		
	Number of Code Occurrences	2 instances		
	OR			
Inclusion/ Exclusion Criteria	Conditions	Poorly controlled asthma (SABA canisters) (lookback period: dispensing date)		
	Include or Exclude	Inclusion		
	Care Setting/PDX	N/A		
	Lookback Period	(-183, -1) days		
	Number of Code Occurrences	3 instances		
Stockpiling	Same Day Dispensing (Days Supplied)	Sum	Sum	Sum
	Same Day Dispensing (Amount Supplied)	Sum	Sum	Sum
	Range of Allowable Days Supplied	N/A	N/A	N/A
	Range of Allowable Amount Supplied	N/A	N/A	N/A
	Overlap Percentage Processing	Default	Default	Default
Multiple Events / Overlap	Multiple Events or Overlap?	Overlap		
	Group Identifier	Primary	Secondary	
	Observation Window Around Primary Episode	(Index date, index date)		

Appendix E. Specifications Defining Parameters for this Request

		Cohort 11		
		Recommendation 2 Poorly controlled LABA, SI-LABA in ACM presence (Measures 11, 12)		
		Scenario 8	Scenario 6	Scenario 7
Multiple Events /Overlap	Secondary Episode to Use for Time Metrics	N/A		
	Minimum Cutoff to be Considered Adherent	N/A		
	Categories for Overlap Metrics	N/A		
	Primary Episode Categories	N/A		
Adherence	Adherence Name	Incident LABA Users, SI-LABA in ACM presence (M1112_pc_laba2)		
	Minimum/Maximum Episode Length or Overlap Time (Overlap)	1 day minimum		
	Minimum/Maximum Secondary Episode Count (Multiple Events)	N/A		
	Minimum/Maximum Secondary Episode Gap (Multiple Events)	N/A		
	Minimum/Maximum Time to Secondary Episode Count (Multiple Events)	N/A		
Adherence	Adherence Name	N/A		
	Minimum/Maximum Episode Length or Overlap Time (Overlap)	N/A		
	Minimum/Maximum Secondary Episode Count (Multiple Events)	N/A		
	Minimum/Maximum Secondary Episode Gap (Multiple Events)	N/A		
	Minimum/Maximum Time to Secondary Episode Count (Multiple Events)	N/A		
ITS Analysis	Data Range Start, End	Full query period		
	Anticipatory Date 1 Start	February 2010		
	Intervention Date 1	June 2010		
	Anticipatory Date 2 Start	N/A		

Appendix E. Specifications Defining Parameters for this Request

		Cohort 11		
		Recommendation 2 Poorly controlled LABA, SI-LABA in ACM presence (Measures 11, 12)		
		Scenario 8	Scenario 6	Scenario 7
ITS Analysis	**Intervention Date 2**	N/A		
	Interval Length	Month		
	P-Value	0.05		
	Autoregression Lag	12 months		
	Autoregression Model Parameter Cutoff	0.2		
	Time Points at Which to Report Difference Metrics	January 2011, June 2011, January 2012, June 2012		
	Continuous Enrollment Required?	No		
Baseline Covariates	**Covariates**	SI-LABA FDC All LABA non-LABA ACM		
	Care Setting/PDX	N/A		
	Covariate Evaluation Window	(-183, -1) days		
	Covariates	non-LABA ACM		
	Care Setting/PDX	N/A		
	Covariate Evaluation Window	(-365, -184)		
	Covariates	SI-LABA FDC All LABA non-LABA ACM		
	Care Setting/PDX	N/A		
	Covariate Evaluation Window	(0, 0)		
Utilization/ Comorbidity Score	**Comorbidity Score Evaluation Window**	(-365, 0) days		
	Medical Utilization Evaluation Window	(-365, 0) days		
	Medical Utilization Care Setting	IP, IS, AV, OA, ED		
	Drug Utilization Evaluation Window	(-365, 0) days		