## 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 2 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 2 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 asthma.

**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 2 of 4 and contains results for cohorts 4-7.

**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 short-acting beta-2 agonist (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 2 of 4 (Prevalent Cohorts)**

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

Report 2: In this report, we include users in cohorts 4-7 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 4) Users are included in Cohort 4 if there is at least one day of ACM or FDC-LABA use during the prevalent LABA exposure episode.
Cohort 5) Users are included in Cohort 5 if there is either ACM or FDC-LABA use for at least 50% the duration of the prevalent LABA exposure episode.
Cohort 6) Users are included in Cohort 5 if there is either ACM or FDC-LABA use for at least 75% the duration of the prevalent LABA exposure episode.
Cohort 7) Users are included in Cohort 7 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 4) 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 asthma patients.
Cohort 5) 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 asthma patients.
Cohort 6) 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 asthma patients.
Cohort 7) 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 asthma patients.

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 2 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 - i**ndicator 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 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 | 0.026854 | (0.020788, 0.032921) | <.001 |
| Baseline Trend | -0.000154 | (-0.000385, 0.000078) | 0.191 |
| Level Change (After Intervention 1) | 0.000175 | (-0.006157, 0.006506) | 0.956 |
| Trend Change (After Intervention 1) | 0.000046 | (-0.000242, 0.000335) | 0.751 |
| **Most Parsimonious Final Model Parameters (df = 105)[2,3]** | | | |
| Intercept | 0.026133 | (0.022122, 0.030145) | <.001 |
| Baseline Trend | -0.000121 | (-0.000186, -0.000056) | <.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 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 | 0.024722 | (0.019677, 0.029768) | <.001 |
| Baseline Trend | -0.000148 | (-0.000341, 0.000045) | 0.131 |
| Level Change (After Intervention 1) | -0.001122 | (-0.006375, 0.004132) | 0.673 |
| Trend Change (After Intervention 1) | 0.000047 | (-0.000193, 0.000287) | 0.698 |
| **46-64 (df = 103)[2]** | | | |
| Intercept | 0.031869 | (0.024839, 0.038898) | <.001 |
| Baseline Trend | -0.000214 | (-0.000478, 0.000051) | 0.112 |
| Level Change (After Intervention 1) | -0.001364 | (-0.008252, 0.005525) | 0.695 |
| Trend Change (After Intervention 1) | 0.000115 | (-0.000221, 0.000451) | 0.498 |
| **65+ (df = 103)[2]** | | | |
| Intercept | 0.021938 | (0.015344, 0.028533) | <.001 |
| Baseline Trend | -0.000109 | (-0.000365, 0.000148) | 0.404 |
| Level Change (After Intervention 1) | 0.004840 | (-0.002542, 0.012221) | 0.196 |
| Trend Change (After Intervention 1) | -0.000001 | (-0.000312, 0.000310) | 0.995 |
| **Most Parsimonious Final Model Parameters[3]** | | | |
| **Age Group (Years)** | | | |
| **18-45 (df = 105)[2]** | | | |
| Intercept | 0.024149 | (0.020769, 0.027530) | <.001 |
| Baseline Trend | -0.000132 | (-0.000187, -0.000078) | <.001 |
| **46-64 (df = 105)[2]** | | | |
| Intercept | 0.030295 | (0.025565, 0.035024) | <.001 |
| Baseline Trend | -0.000157 | (-0.000233, -0.000080) | <.001 |
| **65+ (df = 106)[2]** | | | |
| Intercept | 0.019096 | (0.016608, 0.021583) | <.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 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 | 0.025205 | (0.019367, 0.031043) | <.001 |
| Baseline Trend | -0.000136 | (-0.000359, 0.000087) | 0.228 |
| Level Change (After Intervention 1) | 0.000774 | (-0.005323, 0.006870) | 0.802 |
| Trend Change (After Intervention 1) | 0.000028 | (-0.000249, 0.000306) | 0.841 |
| **Male (df = 103)[2]** | | | |
| Intercept | 0.030499 | (0.023881, 0.037116) | <.001 |
| Baseline Trend | -0.000192 | (-0.000445, 0.000061) | 0.134 |
| Level Change (After Intervention 1) | -0.001122 | (-0.008048, 0.005804) | 0.749 |
| Trend Change (After Intervention 1) | 0.000087 | (-0.000227, 0.000402) | 0.582 |
| **Most Parsimonious Final Model Parameters[3]** | | | |
| **Sex** | | | |
| **Female (df = 105)[2]** | | | |
| Intercept | 0.024702 | (0.020809, 0.028596) | <.001 |
| Baseline Trend | -0.000108 | (-0.000171, -0.000045) | 0.001 |
| **Male (df = 105)[2]** | | | |
| Intercept | 0.029306 | (0.024925, 0.033688) | <.001 |
| Baseline Trend | -0.000150 | (-0.000222, -0.000079) | <.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 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 | 0.037851 | (0.030456, 0.045247) | <.001 |
| Baseline Trend | -0.000415 | (-0.000690, -0.000139) | 0.004 |
| Level Change (After Intervention 1) | -0.000743 | (-0.007732, 0.006246) | 0.833 |
| Trend Change (After Intervention 1) | 0.000355 | (0.000001, 0.000709) | 0.050 |
| **American Indian/Alaska Native (df = 103)[2]** | | | |
| Intercept | 0.010445 | (0.006040, 0.014851) | <.001 |
| Baseline Trend | 0.000125 | (-0.000050, 0.000301) | 0.160 |
| Level Change (After Intervention 1) | 0.002503 | (-0.002816, 0.007822) | 0.353 |
| Trend Change (After Intervention 1) | -0.000245 | (-0.000451, -0.000039) | 0.020 |
| **Asian (df = 103)[2]** | | | |
| Intercept | 0.008313 | (0.003625, 0.013000) | <.001 |
| Baseline Trend | 0.000137 | (-0.000044, 0.000318) | 0.138 |
| Level Change (After Intervention 1) | 0.002812 | (-0.002295, 0.007920) | 0.277 |
| Trend Change (After Intervention 1) | -0.000207 | (-0.000429, 0.000015) | 0.067 |
| **Black/African American (df = 103)[2]** | | | |
| Intercept | 0.009976 | (0.004229, 0.015723) | <.001 |
| Baseline Trend | 0.000128 | (-0.000089, 0.000346) | 0.244 |
| Level Change (After Intervention 1) | 0.001811 | (-0.003954, 0.007575) | 0.535 |
| Trend Change (After Intervention 1) | -0.000212 | (-0.000486, 0.000062) | 0.128 |
| **Native Hawaiian/Other Pacific Islander (df = 103)[2]** | | | |
| Intercept | 0.009177 | (0.007271, 0.011084) | <.001 |
| Baseline Trend | 0.000045 | (-0.000031, 0.000122) | 0.244 |
| Level Change (After Intervention 1) | -0.001979 | (-0.004353, 0.000395) | 0.101 |
| Trend Change (After Intervention 1) | -0.000073 | (-0.000162, 0.000015) | 0.103 |
| **White (df = 103)[2]** | | | |
| Intercept | 0.011206 | (0.006017, 0.016395) | <.001 |
| Baseline Trend | 0.000222 | (0.000019, 0.000426) | 0.032 |
| Level Change (After Intervention 1) | 0.000483 | (-0.005419, 0.006384) | 0.871 |
| Trend Change (After Intervention 1) | -0.000347 | (-0.000591, -0.000102) | 0.006 |
| **Most Parsimonious Final Model Parameters[3]** | | | |
| **Race** | | | |
| **Unknown (df = 104)[2]** | | | |
| Intercept | 0.038044 | (0.030869, 0.045220) | <.001 |
| Baseline Trend | -0.000429 | (-0.000669, -0.000190) | <.001 |
| Trend Change (After Intervention 1) | 0.000362 | (0.000016, 0.000709) | 0.041 |

**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 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[3]** | | | |
| **Race** | | | |
| **American Indian/Alaska Native (df = 104)[2]** | | | |
| Intercept | 0.009724 | (0.005445, 0.014004) | <.001 |
| Baseline Trend | 0.000177 | (0.000036, 0.000319) | 0.015 |
| Trend Change (After Intervention 1) | -0.000272 | (-0.000477, -0.000068) | 0.010 |
| **Asian (df = 106)[2]** | | | |
| Intercept | 0.013140 | (0.010909, 0.015371) | <.001 |
| **Black/African American (df = 106)[2]** | | | |
| Intercept | 0.013680 | (0.011226, 0.016135) | <.001 |
| **Native Hawaiian/Other Pacific Islander (df = 105)[2]** | | | |
| Intercept | 0.009871 | (0.009017, 0.010726) | <.001 |
| Trend Change (After Intervention 1) | -0.000046 | (-0.000076, -0.000016) | 0.003 |
| **White (df = 104)[2]** | | | |
| Intercept | 0.011074 | (0.006157, 0.015991) | <.001 |
| Baseline Trend | 0.000232 | (0.000069, 0.000396) | 0.006 |
| Trend Change (After Intervention 1) | -0.000352 | (-0.000587, -0.000116) | 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]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 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 | 0.026401 | (0.020380, 0.032422) | <.001 |
| Baseline Trend | -0.000143 | (-0.000373, 0.000087) | 0.220 |
| Level Change (After Intervention 1) | 0.000144 | (-0.006150, 0.006437) | 0.964 |
| Trend Change (After Intervention 1) | 0.000036 | (-0.000250, 0.000322) | 0.804 |
| **Most Parsimonious Final Model Parameters (df = 105)[2,3]** | | | |
| Intercept | 0.025837 | (0.021853, 0.029822) | <.001 |
| Baseline Trend | -0.000118 | (-0.000182, -0.000053) | <.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 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 | 0.024449 | (0.019415, 0.029484) | <.001 |
| Baseline Trend | -0.000142 | (-0.000334, 0.000050) | 0.146 |
| Level Change (After Intervention 1) | -0.001139 | (-0.006376, 0.004098) | 0.667 |
| Trend Change (After Intervention 1) | 0.000041 | (-0.000198, 0.000281) | 0.734 |
| **46-64 (df = 103)[2]** | | | |
| Intercept | 0.031238 | (0.024296, 0.038180) | <.001 |
| Baseline Trend | -0.000199 | (-0.000460, 0.000062) | 0.134 |
| Level Change (After Intervention 1) | -0.001373 | (-0.008207, 0.005461) | 0.691 |
| Trend Change (After Intervention 1) | 0.000100 | (-0.000231, 0.000432) | 0.549 |
| **65+ (df = 103)[2]** | | | |
| Intercept | 0.021278 | (0.014748, 0.027808) | <.001 |
| Baseline Trend | -0.000093 | (-0.000347, 0.000162) | 0.472 |
| Level Change (After Intervention 1) | 0.004765 | (-0.002557, 0.012087) | 0.200 |
| Trend Change (After Intervention 1) | -0.000016 | (-0.000324, 0.000292) | 0.917 |
| **Most Parsimonious Final Model Parameters[3]** | | | |
| **Age Group (Years)** | | | |
| **18-45 (df = 105)[2]** | | | |
| Intercept | 0.023967 | (0.020592, 0.027342) | <.001 |
| Baseline Trend | -0.000130 | (-0.000185, -0.000076) | <.001 |
| **46-64 (df = 105)[2]** | | | |
| Intercept | 0.029882 | (0.025222, 0.034542) | <.001 |
| Baseline Trend | -0.000152 | (-0.000227, -0.000076) | <.001 |
| **65+ (df = 106)[2]** | | | |
| Intercept | 0.018933 | (0.016486, 0.021380) | <.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 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 | 0.024780 | (0.018981, 0.030580) | <.001 |
| Baseline Trend | -0.000127 | (-0.000348, 0.000095) | 0.260 |
| Level Change (After Intervention 1) | 0.000752 | (-0.005309, 0.006814) | 0.806 |
| Trend Change (After Intervention 1) | 0.000019 | (-0.000257, 0.000294) | 0.893 |
| **Male (df = 103)[2]** | | | |
| Intercept | 0.029977 | (0.023422, 0.036532) | <.001 |
| Baseline Trend | -0.000180 | (-0.000431, 0.000071) | 0.158 |
| Level Change (After Intervention 1) | -0.001177 | (-0.008058, 0.005704) | 0.735 |
| Trend Change (After Intervention 1) | 0.000075 | (-0.000236, 0.000387) | 0.633 |
| **Most Parsimonious Final Model Parameters[3]** | | | |
| **Sex** | | | |
| **Female (df = 105)[2]** | | | |
| Intercept | 0.024422 | (0.020548, 0.028296) | <.001 |
| Baseline Trend | -0.000104 | (-0.000167, -0.000042) | 0.001 |
| **Male (df = 105)[2]** | | | |
| Intercept | 0.028972 | (0.024638, 0.033306) | <.001 |
| Baseline Trend | -0.000146 | (-0.000217, -0.000076) | <.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 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 | 0.037491 | (0.030174, 0.044807) | <.001 |
| Baseline Trend | -0.000406 | (-0.000679, -0.000133) | 0.004 |
| Level Change (After Intervention 1) | -0.000754 | (-0.007696, 0.006187) | 0.830 |
| Trend Change (After Intervention 1) | 0.000346 | (-0.000004, 0.000696) | 0.053 |
| **American Indian/Alaska Native (df = 103)[2]** | | | |
| Intercept | 0.009763 | (0.005323, 0.014204) | <.001 |
| Baseline Trend | 0.000142 | (-0.000035, 0.000319) | 0.114 |
| Level Change (After Intervention 1) | 0.002401 | (-0.002920, 0.007723) | 0.373 |
| Trend Change (After Intervention 1) | -0.000260 | (-0.000468, -0.000053) | 0.015 |
| **Asian (df = 103)[2]** | | | |
| Intercept | 0.007653 | (0.002940, 0.012367) | 0.002 |
| Baseline Trend | 0.000153 | (-0.000029, 0.000335) | 0.098 |
| Level Change (After Intervention 1) | 0.002673 | (-0.002426, 0.007773) | 0.301 |
| Trend Change (After Intervention 1) | -0.000221 | (-0.000445, 0.000002) | 0.052 |
| **Black/African American (df = 103)[2]** | | | |
| Intercept | 0.009426 | (0.003716, 0.015135) | 0.001 |
| Baseline Trend | 0.000141 | (-0.000075, 0.000358) | 0.197 |
| Level Change (After Intervention 1) | 0.001805 | (-0.003947, 0.007558) | 0.535 |
| Trend Change (After Intervention 1) | -0.000225 | (-0.000497, 0.000047) | 0.104 |
| **Native Hawaiian/Other Pacific Islander (df = 103)[2]** | | | |
| Intercept | 0.008899 | (0.006987, 0.010812) | <.001 |
| Baseline Trend | 0.000050 | (-0.000027, 0.000127) | 0.200 |
| Level Change (After Intervention 1) | -0.001929 | (-0.004309, 0.000451) | 0.111 |
| Trend Change (After Intervention 1) | -0.000078 | (-0.000167, 0.000011) | 0.084 |
| **White (df = 103)[2]** | | | |
| Intercept | 0.010522 | (0.005335, 0.015708) | <.001 |
| Baseline Trend | 0.000238 | (0.000036, 0.000441) | 0.022 |
| Level Change (After Intervention 1) | 0.000414 | (-0.005479, 0.006307) | 0.889 |
| Trend Change (After Intervention 1) | -0.000362 | (-0.000606, -0.000117) | 0.004 |
| **Most Parsimonious Final Model Parameters[3]** | | | |
| **Race** | | | |
| **Unknown (df = 104)[2]** | | | |
| Intercept | 0.037688 | (0.030591, 0.044786) | <.001 |
| Baseline Trend | -0.000421 | (-0.000658, -0.000184) | <.001 |
| Trend Change (After Intervention 1) | 0.000354 | (0.000011, 0.000697) | 0.043 |

**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 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[3]** | | | |
| **Race** | | | |
| **American Indian/Alaska Native (df = 104)[2]** | | | |
| Intercept | 0.009079 | (0.004755, 0.013403) | <.001 |
| Baseline Trend | 0.000192 | (0.000048, 0.000335) | 0.009 |
| Trend Change (After Intervention 1) | -0.000286 | (-0.000493, -0.000080) | 0.007 |
| **Asian (df = 104)[2]** | | | |
| Intercept | 0.007030 | (0.002093, 0.011968) | 0.006 |
| Baseline Trend | 0.000204 | (0.000040, 0.000369) | 0.015 |
| Trend Change (After Intervention 1) | -0.000247 | (-0.000484, -0.000009) | 0.042 |
| **Black/African American (df = 106)[2]** | | | |
| Intercept | 0.013556 | (0.011071, 0.016041) | <.001 |
| **Native Hawaiian/Other Pacific Islander (df = 105)[2]** | | | |
| Intercept | 0.009731 | (0.008876, 0.010587) | <.001 |
| Trend Change (After Intervention 1) | -0.000043 | (-0.000073, -0.000014) | 0.005 |
| **White (df = 104)[2]** | | | |
| Intercept | 0.010408 | (0.005495, 0.015322) | <.001 |
| Baseline Trend | 0.000247 | (0.000084, 0.000410) | 0.003 |
| Trend Change (After Intervention 1) | -0.000366 | (-0.000601, -0.000130) | 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]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 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 | 0.026041 | (0.020040, 0.032042) | <.001 |
| Baseline Trend | -0.000134 | (-0.000364, 0.000095) | 0.248 |
| Level Change (After Intervention 1) | 0.000094 | (-0.006178, 0.006366) | 0.976 |
| Trend Change (After Intervention 1) | 0.000028 | (-0.000257, 0.000313) | 0.846 |
| **Most Parsimonious Final Model Parameters (df = 105)[2,3]** | | | |
| Intercept | 0.025603 | (0.021628, 0.029579) | <.001 |
| Baseline Trend | -0.000115 | (-0.000179, -0.000050) | <.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 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 | 0.024228 | (0.019201, 0.029255) | <.001 |
| Baseline Trend | -0.000137 | (-0.000328, 0.000055) | 0.161 |
| Level Change (After Intervention 1) | -0.001160 | (-0.006385, 0.004065) | 0.661 |
| Trend Change (After Intervention 1) | 0.000036 | (-0.000203, 0.000275) | 0.764 |
| **46-64 (df = 103)[2]** | | | |
| Intercept | 0.030774 | (0.023868, 0.037679) | <.001 |
| Baseline Trend | -0.000188 | (-0.000448, 0.000072) | 0.154 |
| Level Change (After Intervention 1) | -0.001416 | (-0.008222, 0.005390) | 0.681 |
| Trend Change (After Intervention 1) | 0.000090 | (-0.000239, 0.000420) | 0.588 |
| **65+ (df = 103)[2]** | | | |
| Intercept | 0.020679 | (0.014173, 0.027186) | <.001 |
| Baseline Trend | -0.000077 | (-0.000330, 0.000177) | 0.549 |
| Level Change (After Intervention 1) | 0.004619 | (-0.002672, 0.011911) | 0.212 |
| Trend Change (After Intervention 1) | -0.000031 | (-0.000338, 0.000276) | 0.843 |
| **Most Parsimonious Final Model Parameters[3]** | | | |
| **Age Group (Years)** | | | |
| **18-45 (df = 105)[2]** | | | |
| Intercept | 0.023821 | (0.020449, 0.027193) | <.001 |
| Baseline Trend | -0.000129 | (-0.000183, -0.000074) | <.001 |
| **46-64 (df = 105)[2]** | | | |
| Intercept | 0.029569 | (0.024939, 0.034200) | <.001 |
| Baseline Trend | -0.000148 | (-0.000223, -0.000073) | <.001 |
| **65+ (df = 106)[2]** | | | |
| Intercept | 0.018798 | (0.016371, 0.021226) | <.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 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 | 0.024416 | (0.018644, 0.030189) | <.001 |
| Baseline Trend | -0.000118 | (-0.000339, 0.000103) | 0.292 |
| Level Change (After Intervention 1) | 0.000705 | (-0.005330, 0.006740) | 0.817 |
| Trend Change (After Intervention 1) | 0.000011 | (-0.000264, 0.000285) | 0.939 |
| **Male (df = 103)[2]** | | | |
| Intercept | 0.029630 | (0.023075, 0.036185) | <.001 |
| Baseline Trend | -0.000172 | (-0.000422, 0.000079) | 0.177 |
| Level Change (After Intervention 1) | -0.001230 | (-0.008102, 0.005642) | 0.723 |
| Trend Change (After Intervention 1) | 0.000068 | (-0.000243, 0.000379) | 0.666 |
| **Most Parsimonious Final Model Parameters[3]** | | | |
| **Sex** | | | |
| **Female (df = 105)[2]** | | | |
| Intercept | 0.024188 | (0.020326, 0.028050) | <.001 |
| Baseline Trend | -0.000102 | (-0.000165, -0.000039) | 0.002 |
| **Male (df = 105)[2]** | | | |
| Intercept | 0.028739 | (0.024404, 0.033073) | <.001 |
| Baseline Trend | -0.000144 | (-0.000214, -0.000073) | <.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 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 | 0.037238 | (0.029958, 0.044519) | <.001 |
| Baseline Trend | -0.000400 | (-0.000672, -0.000128) | 0.004 |
| Level Change (After Intervention 1) | -0.000787 | (-0.007700, 0.006125) | 0.822 |
| Trend Change (After Intervention 1) | 0.000340 | (-0.000008, 0.000689) | 0.056 |
| **American Indian/Alaska Native (df = 103)[2]** | | | |
| Intercept | 0.009433 | (0.004954, 0.013912) | <.001 |
| Baseline Trend | 0.000147 | (-0.000031, 0.000325) | 0.105 |
| Level Change (After Intervention 1) | 0.002418 | (-0.002933, 0.007768) | 0.372 |
| Trend Change (After Intervention 1) | -0.000263 | (-0.000472, -0.000053) | 0.014 |
| **Asian (df = 103)[2]** | | | |
| Intercept | 0.007120 | (0.002382, 0.011857) | 0.004 |
| Baseline Trend | 0.000168 | (-0.000015, 0.000350) | 0.071 |
| Level Change (After Intervention 1) | 0.002489 | (-0.002610, 0.007588) | 0.335 |
| Trend Change (After Intervention 1) | -0.000235 | (-0.000459, -0.000010) | 0.041 |
| **Black/African American (df = 103)[2]** | | | |
| Intercept | 0.008872 | (0.003162, 0.014581) | 0.003 |
| Baseline Trend | 0.000156 | (-0.000060, 0.000372) | 0.156 |
| Level Change (After Intervention 1) | 0.001757 | (-0.003983, 0.007498) | 0.545 |
| Trend Change (After Intervention 1) | -0.000239 | (-0.000512, 0.000033) | 0.084 |
| **Native Hawaiian/Other Pacific Islander (df = 103)[2]** | | | |
| Intercept | 0.008741 | (0.006834, 0.010648) | <.001 |
| Baseline Trend | 0.000052 | (-0.000024, 0.000129) | 0.179 |
| Level Change (After Intervention 1) | -0.001904 | (-0.004278, 0.000469) | 0.115 |
| Trend Change (After Intervention 1) | -0.000080 | (-0.000168, 0.000009) | 0.076 |
| **White (df = 103)[2]** | | | |
| Intercept | 0.009955 | (0.004758, 0.015153) | <.001 |
| Baseline Trend | 0.000252 | (0.000049, 0.000455) | 0.016 |
| Level Change (After Intervention 1) | 0.000341 | (-0.005557, 0.006238) | 0.909 |
| Trend Change (After Intervention 1) | -0.000374 | (-0.000619, -0.000129) | 0.003 |
| **Most Parsimonious Final Model Parameters[3]** | | | |
| **Race** | | | |
| **Unknown (df = 104)[2]** | | | |
| Intercept | 0.037445 | (0.030382, 0.044509) | <.001 |
| Baseline Trend | -0.000416 | (-0.000651, -0.000180) | <.001 |
| Trend Change (After Intervention 1) | 0.000348 | (0.000007, 0.000690) | 0.046 |

**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 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[3]** | | | |
| **Race** | | | |
| **American Indian/Alaska Native (df = 104)[2]** | | | |
| Intercept | 0.008748 | (0.004377, 0.013119) | <.001 |
| Baseline Trend | 0.000197 | (0.000052, 0.000341) | 0.008 |
| Trend Change (After Intervention 1) | -0.000289 | (-0.000498, -0.000080) | 0.007 |
| **Asian (df = 104)[2]** | | | |
| Intercept | 0.006537 | (0.001593, 0.011482) | 0.010 |
| Baseline Trend | 0.000216 | (0.000051, 0.000380) | 0.011 |
| Trend Change (After Intervention 1) | -0.000258 | (-0.000496, -0.000020) | 0.034 |
| **Black/African American (df = 106)[2]** | | | |
| Intercept | 0.013436 | (0.010894, 0.015978) | <.001 |
| **Native Hawaiian/Other Pacific Islander (df = 105)[2]** | | | |
| Intercept | 0.009644 | (0.008790, 0.010498) | <.001 |
| Trend Change (After Intervention 1) | -0.000042 | (-0.000072, -0.000012) | 0.007 |
| **White (df = 104)[2]** | | | |
| Intercept | 0.009862 | (0.004940, 0.014785) | <.001 |
| Baseline Trend | 0.000259 | (0.000095, 0.000422) | 0.002 |
| Trend Change (After Intervention 1) | -0.000377 | (-0.000613, -0.000141) | 0.002 |

[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
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 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 | 0.026506 | (0.020481, 0.032530) | <.001 |
| Baseline Trend | -0.000146 | (-0.000376, 0.000084) | 0.212 |
| Level Change (After Intervention 1) | 0.000141 | (-0.006153, 0.006435) | 0.965 |
| Trend Change (After Intervention 1) | 0.000039 | (-0.000247, 0.000325) | 0.788 |
| **Most Parsimonious Final Model Parameters (df = 105)[2,3]** | | | |
| Intercept | 0.025899 | (0.021913, 0.029884) | <.001 |
| Baseline Trend | -0.000118 | (-0.000183, -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 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 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 | 0.024503 | (0.019487, 0.029520) | <.001 |
| Baseline Trend | -0.000143 | (-0.000334, 0.000049) | 0.143 |
| Level Change (After Intervention 1) | -0.001153 | (-0.006381, 0.004074) | 0.663 |
| Trend Change (After Intervention 1) | 0.000042 | (-0.000196, 0.000281) | 0.727 |
| **46-64 (df = 103)[2]** | | | |
| Intercept | 0.031413 | (0.024453, 0.038373) | <.001 |
| Baseline Trend | -0.000204 | (-0.000466, 0.000058) | 0.125 |
| Level Change (After Intervention 1) | -0.001351 | (-0.008190, 0.005488) | 0.696 |
| Trend Change (After Intervention 1) | 0.000106 | (-0.000227, 0.000438) | 0.529 |
| **65+ (df = 103)[2]** | | | |
| Intercept | 0.021360 | (0.014805, 0.027916) | <.001 |
| Baseline Trend | -0.000094 | (-0.000350, 0.000161) | 0.466 |
| Level Change (After Intervention 1) | 0.004709 | (-0.002631, 0.012049) | 0.206 |
| Trend Change (After Intervention 1) | -0.000014 | (-0.000323, 0.000296) | 0.929 |
| **Most Parsimonious Final Model Parameters[3]** | | | |
| **Age Group (Years)** | | | |
| **18-45 (df = 105)[2]** | | | |
| Intercept | 0.024007 | (0.020645, 0.027369) | <.001 |
| Baseline Trend | -0.000131 | (-0.000185, -0.000076) | <.001 |
| **46-64 (df = 105)[2]** | | | |
| Intercept | 0.029975 | (0.025299, 0.034651) | <.001 |
| Baseline Trend | -0.000153 | (-0.000229, -0.000077) | <.001 |
| **65+ (df = 106)[2]** | | | |
| Intercept | 0.018945 | (0.016488, 0.021402) | <.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 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 | 0.024881 | (0.019079, 0.030683) | <.001 |
| Baseline Trend | -0.000129 | (-0.000351, 0.000092) | 0.250 |
| Level Change (After Intervention 1) | 0.000750 | (-0.005311, 0.006811) | 0.807 |
| Trend Change (After Intervention 1) | 0.000021 | (-0.000254, 0.000297) | 0.877 |
| **Male (df = 103)[2]** | | | |
| Intercept | 0.030093 | (0.023534, 0.036653) | <.001 |
| Baseline Trend | -0.000183 | (-0.000434, 0.000068) | 0.151 |
| Level Change (After Intervention 1) | -0.001181 | (-0.008063, 0.005700) | 0.734 |
| Trend Change (After Intervention 1) | 0.000079 | (-0.000233, 0.000390) | 0.618 |
| **Most Parsimonious Final Model Parameters[3]** | | | |
| **Sex** | | | |
| **Female (df = 105)[2]** | | | |
| Intercept | 0.024482 | (0.020608, 0.028355) | <.001 |
| Baseline Trend | -0.000105 | (-0.000168, -0.000042) | 0.001 |
| **Male (df = 105)[2]** | | | |
| Intercept | 0.029037 | (0.024699, 0.033376) | <.001 |
| Baseline Trend | -0.000147 | (-0.000218, -0.000077) | <.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 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 | 0.037517 | (0.030199, 0.044834) | <.001 |
| Baseline Trend | -0.000406 | (-0.000680, -0.000133) | 0.004 |
| Level Change (After Intervention 1) | -0.000776 | (-0.007716, 0.006163) | 0.825 |
| Trend Change (After Intervention 1) | 0.000347 | (-0.000004, 0.000697) | 0.052 |
| **American Indian/Alaska Native (df = 103)[2]** | | | |
| Intercept | 0.010135 | (0.005651, 0.014619) | <.001 |
| Baseline Trend | 0.000130 | (-0.000048, 0.000309) | 0.151 |
| Level Change (After Intervention 1) | 0.002507 | (-0.002860, 0.007874) | 0.356 |
| Trend Change (After Intervention 1) | -0.000248 | (-0.000458, -0.000039) | 0.021 |
| **Asian (df = 103)[2]** | | | |
| Intercept | 0.007894 | (0.003198, 0.012589) | 0.001 |
| Baseline Trend | 0.000146 | (-0.000035, 0.000328) | 0.112 |
| Level Change (After Intervention 1) | 0.002758 | (-0.002347, 0.007864) | 0.287 |
| Trend Change (After Intervention 1) | -0.000216 | (-0.000438, 0.000006) | 0.057 |
| **Black/African American (df = 103)[2]** | | | |
| Intercept | 0.009717 | (0.003978, 0.015455) | 0.001 |
| Baseline Trend | 0.000134 | (-0.000083, 0.000351) | 0.225 |
| Level Change (After Intervention 1) | 0.001840 | (-0.003916, 0.007596) | 0.528 |
| Trend Change (After Intervention 1) | -0.000217 | (-0.000491, 0.000057) | 0.119 |
| **Native Hawaiian/Other Pacific Islander (df = 103)[2]** | | | |
| Intercept | 0.009150 | (0.007259, 0.011042) | <.001 |
| Baseline Trend | 0.000043 | (-0.000033, 0.000119) | 0.268 |
| Level Change (After Intervention 1) | -0.001864 | (-0.004221, 0.000493) | 0.120 |
| Trend Change (After Intervention 1) | -0.000071 | (-0.000159, 0.000017) | 0.112 |
| **White (df = 103)[2]** | | | |
| Intercept | 0.010739 | (0.005557, 0.015920) | <.001 |
| Baseline Trend | 0.000233 | (0.000030, 0.000435) | 0.025 |
| Level Change (After Intervention 1) | 0.000430 | (-0.005458, 0.006318) | 0.885 |
| Trend Change (After Intervention 1) | -0.000356 | (-0.000600, -0.000112) | 0.005 |
| **Most Parsimonious Final Model Parameters[3]** | | | |
| **Race** | | | |
| **Unknown (df = 104)[2]** | | | |
| Intercept | 0.037719 | (0.030620, 0.044818) | <.001 |
| Baseline Trend | -0.000422 | (-0.000659, -0.000185) | <.001 |
| Trend Change (After Intervention 1) | 0.000355 | (0.000012, 0.000698) | 0.043 |

**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 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[3]** | | | |
| **Race** | | | |
| Baseline Trend | 0.000182 | (0.000037, 0.000327) | 0.015 |
| Trend Change (After Intervention 1) | -0.000275 | (-0.000485, -0.000066) | 0.010 |
| **Asian (df = 104)[2]** | | | |
| Intercept | 0.007251 | (0.002327, 0.012175) | 0.004 |
| Baseline Trend | 0.000199 | (0.000035, 0.000363) | 0.018 |
| Trend Change (After Intervention 1) | -0.000242 | (-0.000479, -0.000005) | 0.046 |
| **Black/African American (df = 106)[2]** | | | |
| Intercept | 0.013611 | (0.011134, 0.016088) | <.001 |
| **Native Hawaiian/Other Pacific Islander (df = 105)[2]** | | | |
| Intercept | 0.009805 | (0.008964, 0.010647) | <.001 |
| Trend Change (After Intervention 1) | -0.000045 | (-0.000074, -0.000016) | 0.003 |
| **White (df = 104)[2]** | | | |
| Intercept | 0.010621 | (0.005713, 0.015530) | <.001 |
| Baseline Trend | 0.000241 | (0.000079, 0.000405) | 0.004 |
| Trend Change (After Intervention 1) | -0.000360 | (-0.000595, -0.000125) | 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]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 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) | 0.020322 | 0.020322 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.020322 | 0.020322 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.019596 | 0.019596 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.019596 | 0.019596 |

[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 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) | 0.017794 | 0.017794 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.017794 | 0.017794 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.017000 | 0.017000 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.017000 | 0.017000 |
| **46-64** | | | | |
| Absolute Change at 6 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.022773 | 0.022773 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.022773 | 0.022773 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.021833 | 0.021833 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.021833 | 0.021833 |
| **65+** | | | | |
| Absolute Change at 6 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.019096 | 0.019096 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.019096 | 0.019096 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.019096 | 0.019096 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.019096 | 0.019096 |

[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 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) | 0.019530 | 0.019530 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.019530 | 0.019530 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.018883 | 0.018883 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.018883 | 0.018883 |
| **Male** | | | | |
| Absolute Change at 6 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.022092 | 0.022092 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.022092 | 0.022092 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.021190 | 0.021190 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.021190 | 0.021190 |

[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 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 | 0.002175 | (0.000118, 0.004231) | 0.019611 | 0.017436 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 12.47 | (-3.48, 28.43) | 0.019611 | 0.017436 |
| Absolute Change at 12 Months after Intervention 1 | 0.004349 | (0.000236, 0.008463) | 0.019209 | 0.014860 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 29.27 | (-12.50, 71.04) | 0.019209 | 0.014860 |
| **American Indian/Alaska Native** | | | | |
| Absolute Change at 6 Months after Intervention 1 | -0.001635 | (-0.002847, -0.000423) | 0.016597 | 0.018232 |
| Relative Change (Percent) at 6 Months after Intervention 1 | -8.97 | (-14.07, -3.87) | 0.016597 | 0.018232 |
| Absolute Change at 12 Months after Intervention 1 | -0.003269 | (-0.005694, -0.000845) | 0.016026 | 0.019296 |
| Relative Change (Percent) at 12 Months after Intervention 1 | -16.94 | (-26.05, -7.84) | 0.016026 | 0.019296 |
| **Asian** | | | | |
| Absolute Change at 6 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.013140 | 0.013140 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.013140 | 0.013140 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.013140 | 0.013140 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.013140 | 0.013140 |
| **Black/African American** | | | | |
| Absolute Change at 6 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.013680 | 0.013680 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.013680 | 0.013680 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.013680 | 0.013680 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.013680 | 0.013680 |
| **Native Hawaiian/Other Pacific Islander** | | | | |
| Absolute Change at 6 Months after Intervention 1 | -0.000276 | (-0.000453, -0.000099) | 0.009595 | 0.009871 |
| Relative Change (Percent) at 6 Months after Intervention 1 | -2.79 | (-4.43, -1.15) | 0.009595 | 0.009871 |
| Absolute Change at 12 Months after Intervention 1 | -0.000552 | (-0.000905, -0.000198) | 0.009320 | 0.009871 |
| Relative Change (Percent) at 12 Months after Intervention 1 | -5.59 | (-8.87, -2.31) | 0.009320 | 0.009871 |

**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 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 | -0.002110 | (-0.003507, -0.000712) | 0.020111 | 0.022221 |
| Relative Change (Percent) at 6 Months after Intervention 1 | -9.49 | (-14.23, -4.76) | 0.020111 | 0.022221 |
| Absolute Change at 12 Months after Intervention 1 | -0.004219 | (-0.007015, -0.001424) | 0.019395 | 0.023614 |
| Relative Change (Percent) at 12 Months after Intervention 1 | -17.87 | (-26.26, -9.48) | 0.019395 | 0.023614 |

[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 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) | 0.020194 | 0.020194 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.020194 | 0.020194 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.019488 | 0.019488 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.019488 | 0.019488 |

[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 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) | 0.017715 | 0.017715 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.017715 | 0.017715 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.016933 | 0.016933 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.016933 | 0.016933 |
| **46-64** | | | | |
| Absolute Change at 6 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.022601 | 0.022601 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.022601 | 0.022601 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.021691 | 0.021691 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.021691 | 0.021691 |
| **65+** | | | | |
| Absolute Change at 6 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.018933 | 0.018933 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.018933 | 0.018933 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.018933 | 0.018933 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.018933 | 0.018933 |

[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 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) | 0.019406 | 0.019406 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.019406 | 0.019406 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.018779 | 0.018779 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.018779 | 0.018779 |
| **Male** | | | | |
| Absolute Change at 6 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.021950 | 0.021950 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.021950 | 0.021950 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.021072 | 0.021072 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.021072 | 0.021072 |

[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 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 | 0.002123 | (0.000089, 0.004157) | 0.019604 | 0.017481 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 12.14 | (-3.49, 27.77) | 0.019604 | 0.017481 |
| Absolute Change at 12 Months after Intervention 1 | 0.004245 | (0.000177, 0.008314) | 0.019201 | 0.014955 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 28.39 | (-12.24, 69.01) | 0.019201 | 0.014955 |
| **American Indian/Alaska Native** | | | | |
| Absolute Change at 6 Months after Intervention 1 | -0.001718 | (-0.002944, -0.000493) | 0.016553 | 0.018271 |
| Relative Change (Percent) at 6 Months after Intervention 1 | -9.41 | (-14.48, -4.33) | 0.016553 | 0.018271 |
| Absolute Change at 12 Months after Intervention 1 | -0.003437 | (-0.005888, -0.000986) | 0.015983 | 0.019420 |
| Relative Change (Percent) at 12 Months after Intervention 1 | -17.70 | (-26.69, -8.71) | 0.015983 | 0.019420 |
| **Asian** | | | | |
| Absolute Change at 6 Months after Intervention 1 | -0.001480 | (-0.002892, -0.000069) | 0.015351 | 0.016832 |
| Relative Change (Percent) at 6 Months after Intervention 1 | -8.80 | (-15.24, -2.36) | 0.015351 | 0.016832 |
| Absolute Change at 12 Months after Intervention 1 | -0.002961 | (-0.005784, -0.000138) | 0.015096 | 0.018057 |
| Relative Change (Percent) at 12 Months after Intervention 1 | -16.40 | (-27.81, -4.98) | 0.015096 | 0.018057 |
| **Black/African American** | | | | |
| Absolute Change at 6 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.013556 | 0.013556 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.013556 | 0.013556 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.013556 | 0.013556 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.013556 | 0.013556 |
| **Native Hawaiian/Other Pacific Islander** | | | | |
| Absolute Change at 6 Months after Intervention 1 | -0.000260 | (-0.000437, -0.000083) | 0.009471 | 0.009731 |
| Relative Change (Percent) at 6 Months after Intervention 1 | -2.67 | (-4.35, -1.00) | 0.009471 | 0.009731 |
| Absolute Change at 12 Months after Intervention 1 | -0.000520 | (-0.000875, -0.000166) | 0.009211 | 0.009731 |
| Relative Change (Percent) at 12 Months after Intervention 1 | -5.35 | (-8.69, -2.00) | 0.009211 | 0.009731 |

**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 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 | -0.002195 | (-0.003592, -0.000799) | 0.020064 | 0.022260 |
| Relative Change (Percent) at 6 Months after Intervention 1 | -9.86 | (-14.53, -5.20) | 0.020064 | 0.022260 |
| Absolute Change at 12 Months after Intervention 1 | -0.004391 | (-0.007184, -0.001598) | 0.019350 | 0.023741 |
| Relative Change (Percent) at 12 Months after Intervention 1 | -18.50 | (-26.72, -10.27) | 0.019350 | 0.023741 |

[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 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) | 0.020091 | 0.020091 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.020091 | 0.020091 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.019402 | 0.019402 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.019402 | 0.019402 |

[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 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) | 0.017652 | 0.017652 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.017652 | 0.017652 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.016881 | 0.016881 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.016881 | 0.016881 |
| **46-64** | | | | |
| Absolute Change at 6 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.022465 | 0.022465 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.022465 | 0.022465 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.021577 | 0.021577 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.021577 | 0.021577 |
| **65+** | | | | |
| Absolute Change at 6 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.018798 | 0.018798 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.018798 | 0.018798 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.018798 | 0.018798 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.018798 | 0.018798 |

[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 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) | 0.019304 | 0.019304 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.019304 | 0.019304 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.018694 | 0.018694 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.018694 | 0.018694 |
| **Male** | | | | |
| Absolute Change at 6 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.021846 | 0.021846 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.021846 | 0.021846 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.020984 | 0.020984 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.020984 | 0.020984 |

[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 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 | 0.002090 | (0.000066, 0.004114) | 0.019589 | 0.017499 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 11.94 | (-3.53, 27.41) | 0.019589 | 0.017499 |
| Absolute Change at 12 Months after Intervention 1 | 0.004180 | (0.000131, 0.008229) | 0.019185 | 0.015005 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 27.86 | (-12.18, 67.90) | 0.019185 | 0.015005 |
| **American Indian/Alaska Native** | | | | |
| Absolute Change at 6 Months after Intervention 1 | -0.001734 | (-0.002974, -0.000495) | 0.016446 | 0.018180 |
| Relative Change (Percent) at 6 Months after Intervention 1 | -9.54 | (-14.67, -4.41) | 0.016446 | 0.018180 |
| Absolute Change at 12 Months after Intervention 1 | -0.003469 | (-0.005947, -0.000991) | 0.015891 | 0.019359 |
| Relative Change (Percent) at 12 Months after Intervention 1 | -17.92 | (-26.99, -8.84) | 0.015891 | 0.019359 |
| **Asian** | | | | |
| Absolute Change at 6 Months after Intervention 1 | -0.001550 | (-0.002963, -0.000136) | 0.015336 | 0.016885 |
| Relative Change (Percent) at 6 Months after Intervention 1 | -9.18 | (-15.53, -2.83) | 0.015336 | 0.016885 |
| Absolute Change at 12 Months after Intervention 1 | -0.003099 | (-0.005926, -0.000272) | 0.015079 | 0.018179 |
| Relative Change (Percent) at 12 Months after Intervention 1 | -17.05 | (-28.24, -5.85) | 0.015079 | 0.018179 |
| **Black/African American** | | | | |
| Absolute Change at 6 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.013436 | 0.013436 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.013436 | 0.013436 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.013436 | 0.013436 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.013436 | 0.013436 |
| **Native Hawaiian/Other Pacific Islander** | | | | |
| Absolute Change at 6 Months after Intervention 1 | -0.000250 | (-0.000427, -0.000073) | 0.009394 | 0.009644 |
| Relative Change (Percent) at 6 Months after Intervention 1 | -2.59 | (-4.28, -0.90) | 0.009394 | 0.009644 |
| Absolute Change at 12 Months after Intervention 1 | -0.000500 | (-0.000853, -0.000146) | 0.009144 | 0.009644 |
| Relative Change (Percent) at 12 Months after Intervention 1 | -5.18 | (-8.56, -1.80) | 0.009144 | 0.009644 |

**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 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 | -0.002264 | (-0.003663, -0.000865) | 0.020021 | 0.022285 |
| Relative Change (Percent) at 6 Months after Intervention 1 | -10.16 | (-14.78, -5.54) | 0.020021 | 0.022285 |
| Absolute Change at 12 Months after Intervention 1 | -0.004528 | (-0.007327, -0.001729) | 0.019310 | 0.023838 |
| Relative Change (Percent) at 12 Months after Intervention 1 | -18.99 | (-27.11, -10.88) | 0.019310 | 0.023838 |

[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 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) | 0.020216 | 0.020216 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.020216 | 0.020216 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.019505 | 0.019505 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.019505 | 0.019505 |

[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 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) | 0.017732 | 0.017732 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.017732 | 0.017732 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.016947 | 0.016947 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.016947 | 0.016947 |
| **46-64** | | | | |
| Absolute Change at 6 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.022634 | 0.022634 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.022634 | 0.022634 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.021717 | 0.021717 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.021717 | 0.021717 |
| **65+** | | | | |
| Absolute Change at 6 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.018945 | 0.018945 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.018945 | 0.018945 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.018945 | 0.018945 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.018945 | 0.018945 |

[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 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) | 0.019428 | 0.019428 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.019428 | 0.019428 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.018797 | 0.018797 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.018797 | 0.018797 |
| **Male** | | | | |
| Absolute Change at 6 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.021972 | 0.021972 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.021972 | 0.021972 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.021089 | 0.021089 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.021089 | 0.021089 |

[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 Asthma in the Sentinel Distributed Database (SDD) after June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend, by Race**

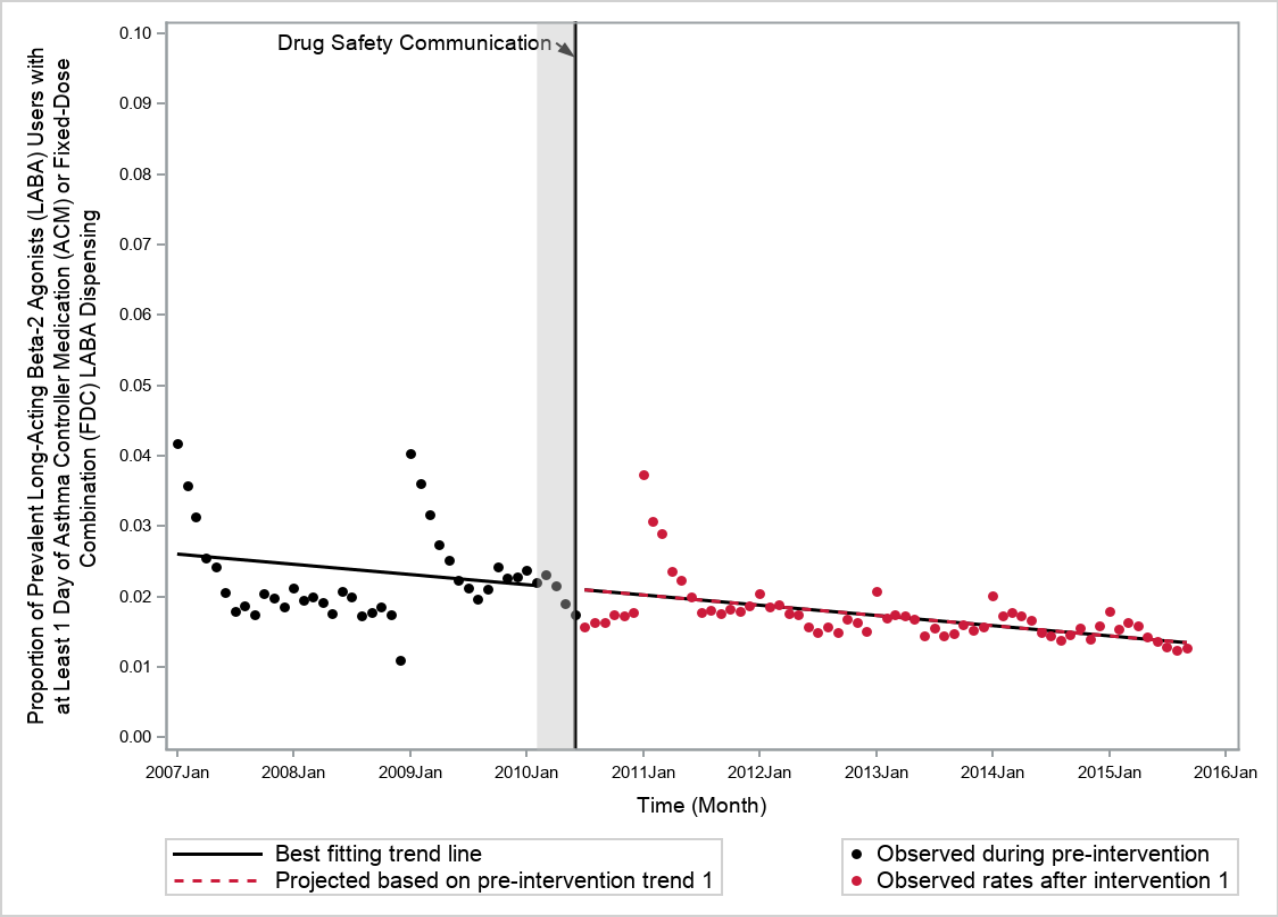
| Outcome Measure | Beta Estimate | 95% Confidence Interval | Predicted Rate (With Intervention) | Extrapolated Rate (Without Intervention) |
|---|---|---|---|---|
| **Race** | | | | |
| **Unknown** | | | | |
| Absolute Change at 6 Months after Intervention 1 | 0.002129 | (0.000094, 0.004164) | 0.019598 | 0.017469 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 12.19 | (-3.47, 27.85) | 0.019598 | 0.017469 |
| Absolute Change at 12 Months after Intervention 1 | 0.004258 | (0.000189, 0.008327) | 0.019195 | 0.014937 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 28.51 | (-12.23, 69.24) | 0.019195 | 0.014937 |
| **American Indian/Alaska Native** | | | | |
| Absolute Change at 6 Months after Intervention 1 | -0.001653 | (-0.002895, -0.000411) | 0.016505 | 0.018158 |
| Relative Change (Percent) at 6 Months after Intervention 1 | -9.10 | (-14.32, -3.88) | 0.016505 | 0.018158 |
| Absolute Change at 12 Months after Intervention 1 | -0.003306 | (-0.005789, -0.000822) | 0.015945 | 0.019250 |
| Relative Change (Percent) at 12 Months after Intervention 1 | -17.17 | (-26.47, -7.87) | 0.015945 | 0.019250 |
| **Asian** | | | | |
| Absolute Change at 6 Months after Intervention 1 | -0.001452 | (-0.002859, -0.000045) | 0.015366 | 0.016818 |
| Relative Change (Percent) at 6 Months after Intervention 1 | -8.63 | (-15.10, -2.17) | 0.015366 | 0.016818 |
| Absolute Change at 12 Months after Intervention 1 | -0.002904 | (-0.005718, -0.000090) | 0.015110 | 0.018014 |
| Relative Change (Percent) at 12 Months after Intervention 1 | -16.12 | (-27.60, -4.64) | 0.015110 | 0.018014 |
| **Black/African American** | | | | |
| Absolute Change at 6 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.013611 | 0.013611 |
| Relative Change (Percent) at 6 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.013611 | 0.013611 |
| Absolute Change at 12 Months after Intervention 1 | 0.000000 | (0.000000, 0.000000) | 0.013611 | 0.013611 |
| Relative Change (Percent) at 12 Months after Intervention 1 | 0.00 | (0.00, 0.00) | 0.013611 | 0.013611 |
| **Native Hawaiian/Other Pacific Islander** | | | | |
| Absolute Change at 6 Months after Intervention 1 | -0.000270 | (-0.000444, -0.000096) | 0.009535 | 0.009805 |
| Relative Change (Percent) at 6 Months after Intervention 1 | -2.76 | (-4.38, -1.13) | 0.009535 | 0.009805 |
| Absolute Change at 12 Months after Intervention 1 | -0.000540 | (-0.000889, -0.000192) | 0.009265 | 0.009805 |
| Relative Change (Percent) at 12 Months after Intervention 1 | -5.51 | (-8.77, -2.25) | 0.009265 | 0.009805 |

**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 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 | -0.002161 | (-0.003556, -0.000765) | 0.020051 | 0.022211 |
| Relative Change (Percent) at 6 Months after Intervention 1 | -9.73 | (-14.42, -5.04) | 0.020051 | 0.022211 |
| Absolute Change at 12 Months after Intervention 1 | -0.004322 | (-0.007112, -0.001531) | 0.019339 | 0.023660 |
| Relative Change (Percent) at 12 Months after Intervention 1 | -18.27 | (-26.55, -9.98) | 0.019339 | 0.023660 |

[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

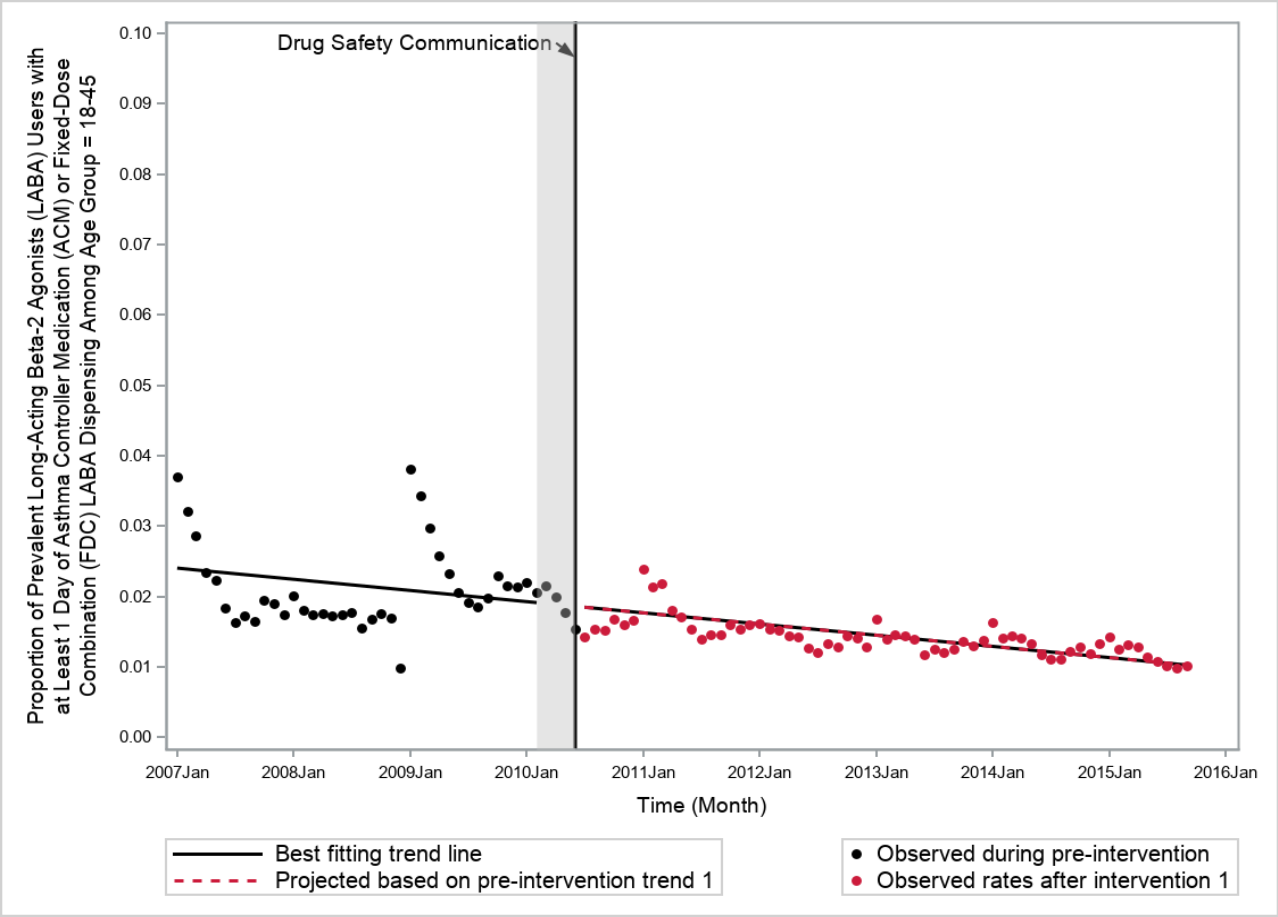
**Figure 1. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2]**




[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).

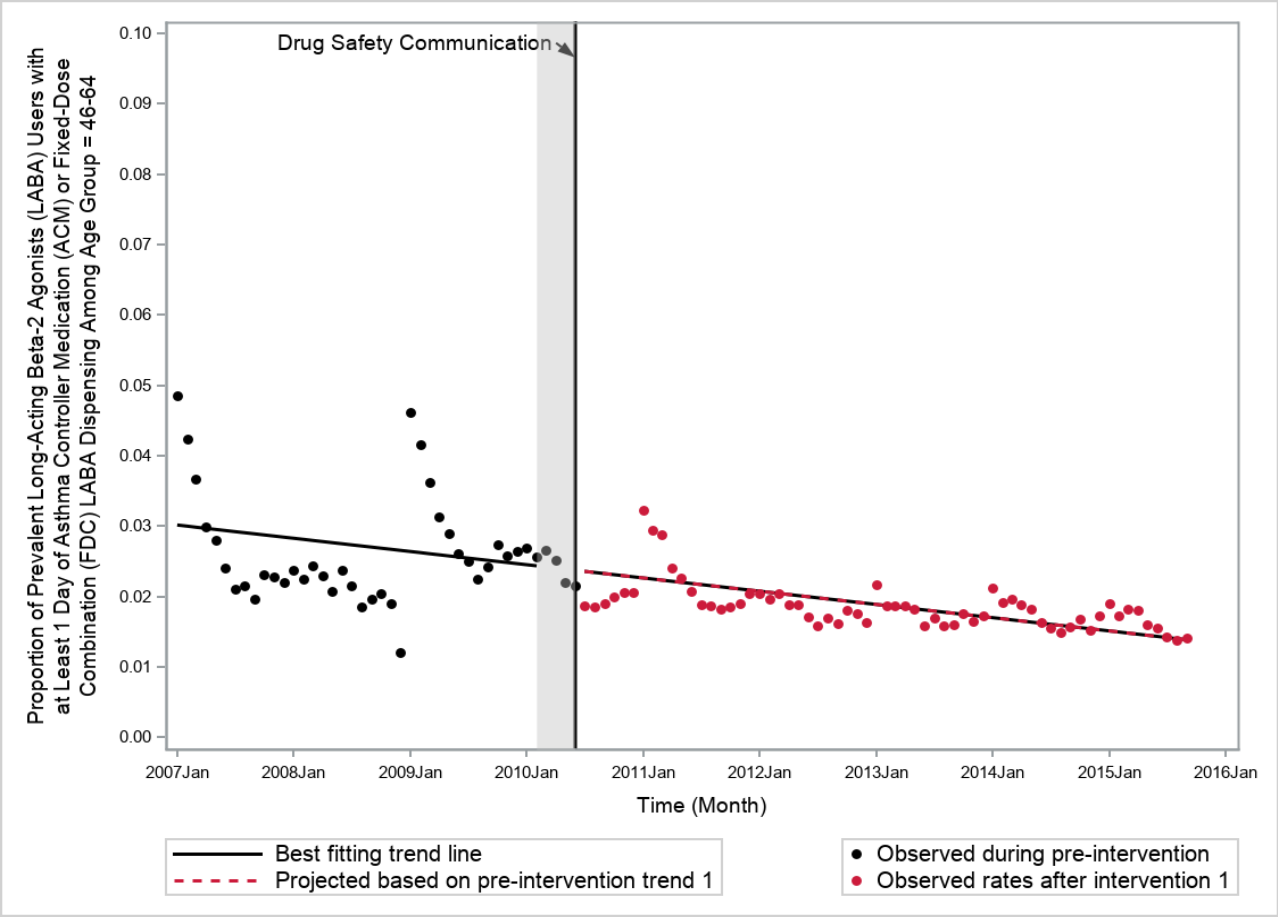
**Figure 2. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Age Group = 18-45**




[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).

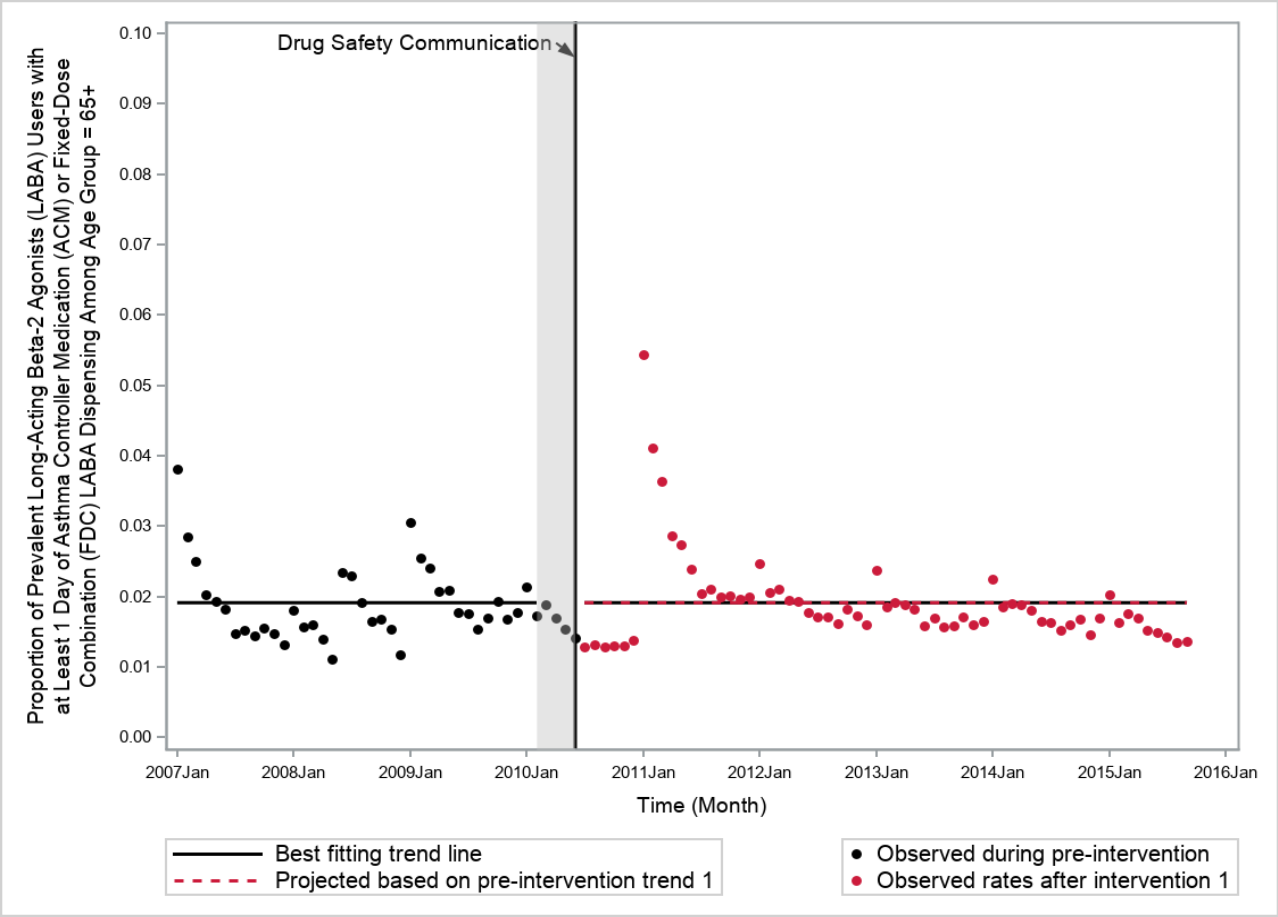
**Figure 3. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Age Group = 46-64**




[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).

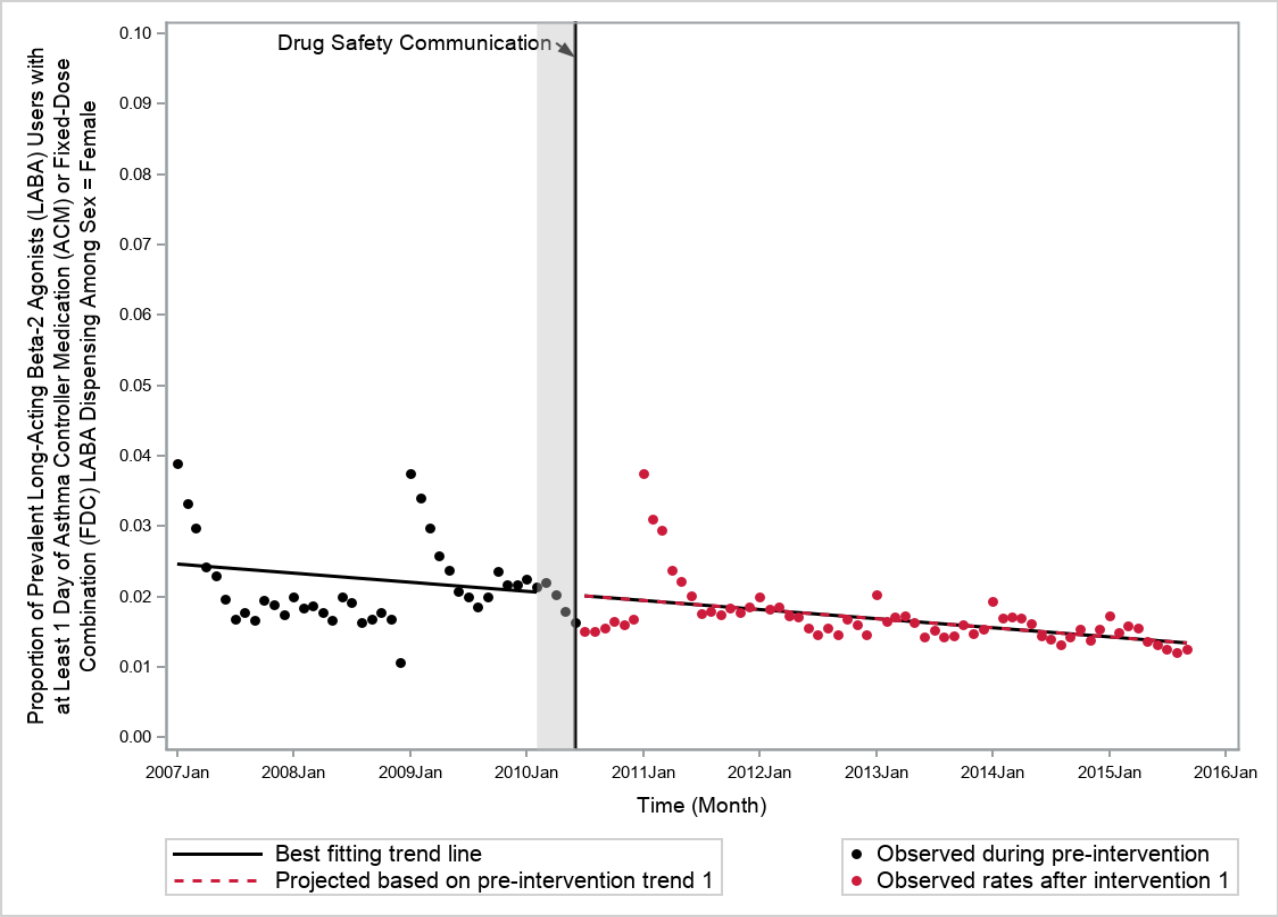
**Figure 4. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Age Group = 65+**




[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).

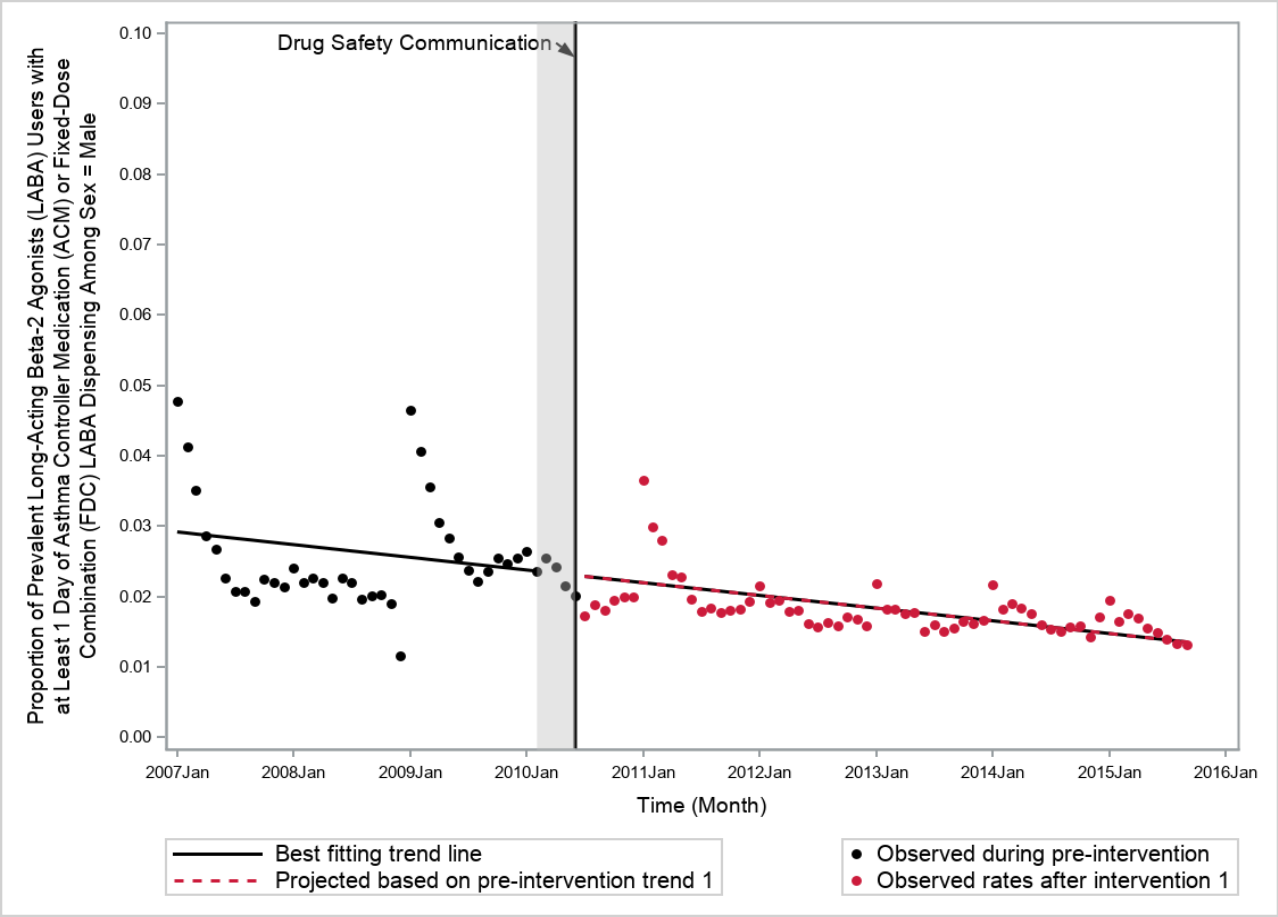
**Figure 5. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Sex = Female**




[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).

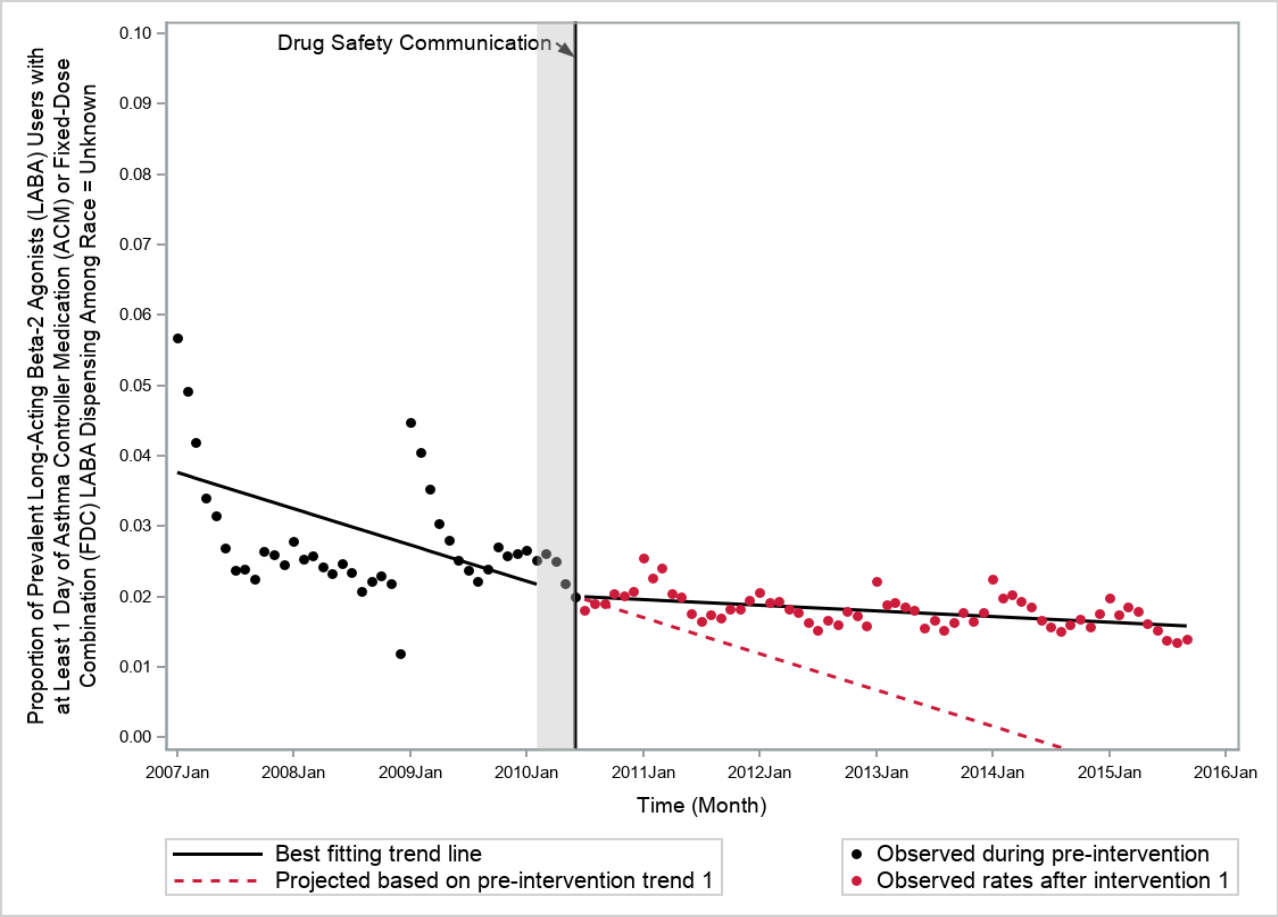
**Figure 6. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Sex = Male**




[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).

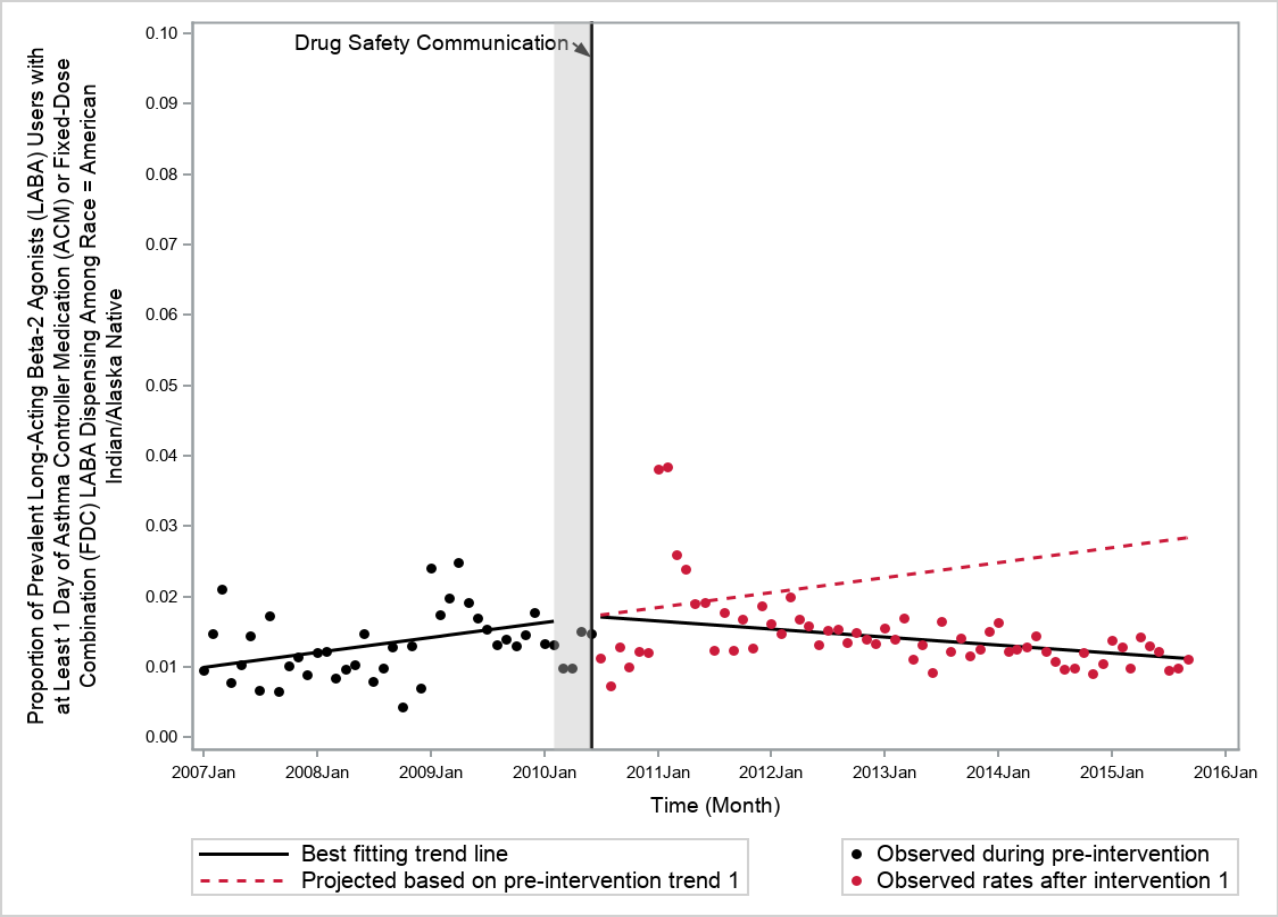
**Figure 7. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = Unknown**




[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).

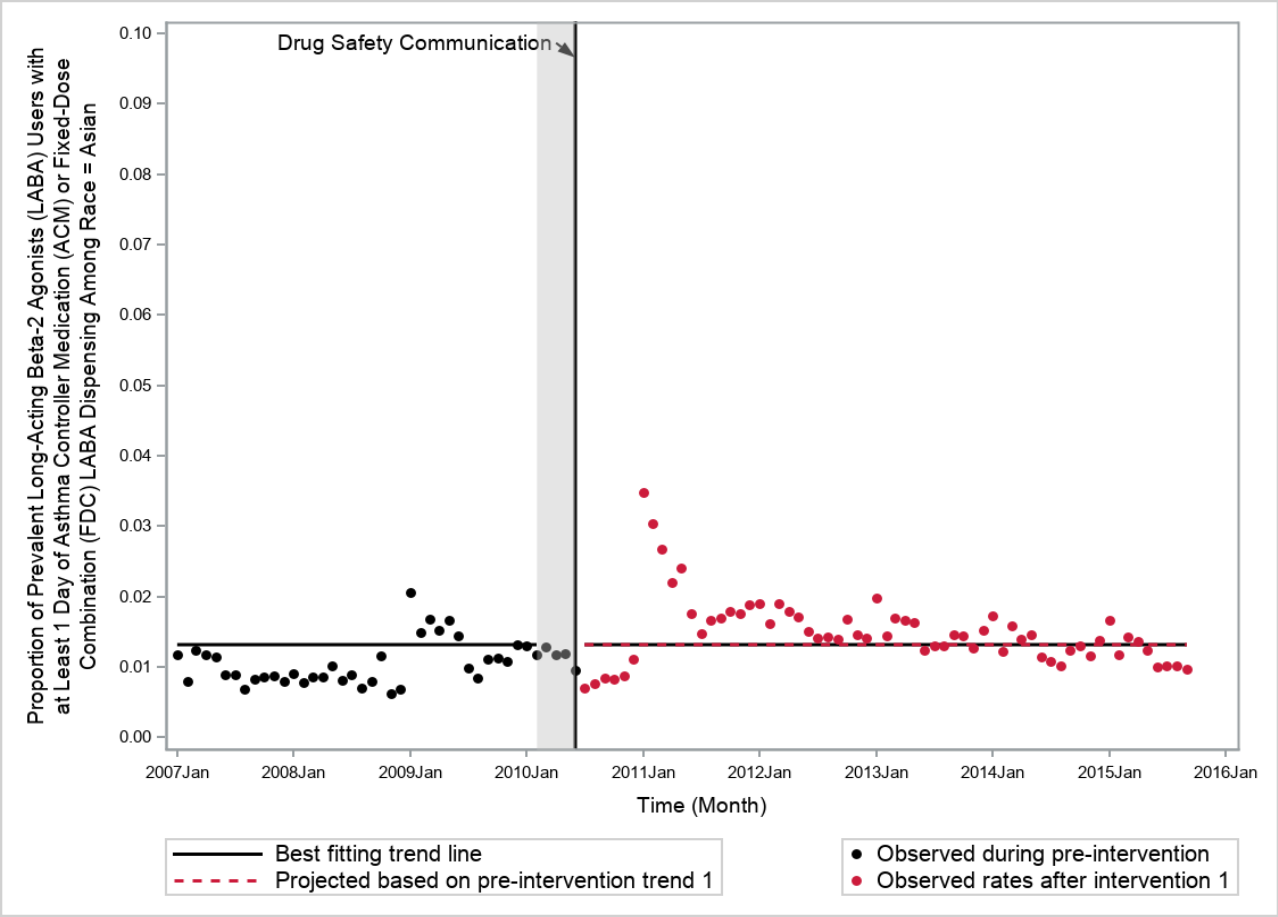
**Figure 8. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = American Indian/Alaska Native**




[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).

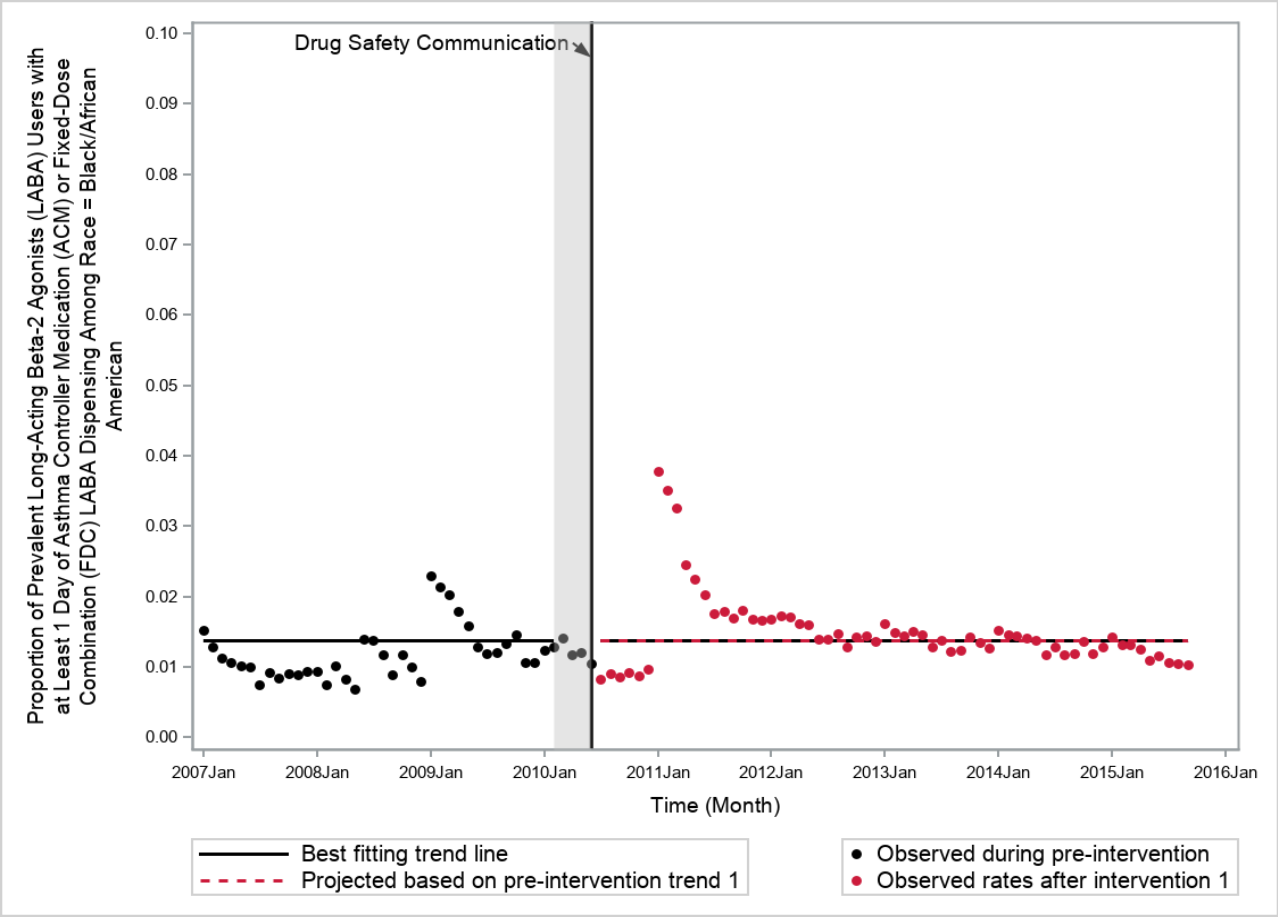
**Figure 9. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = Asian**




[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).

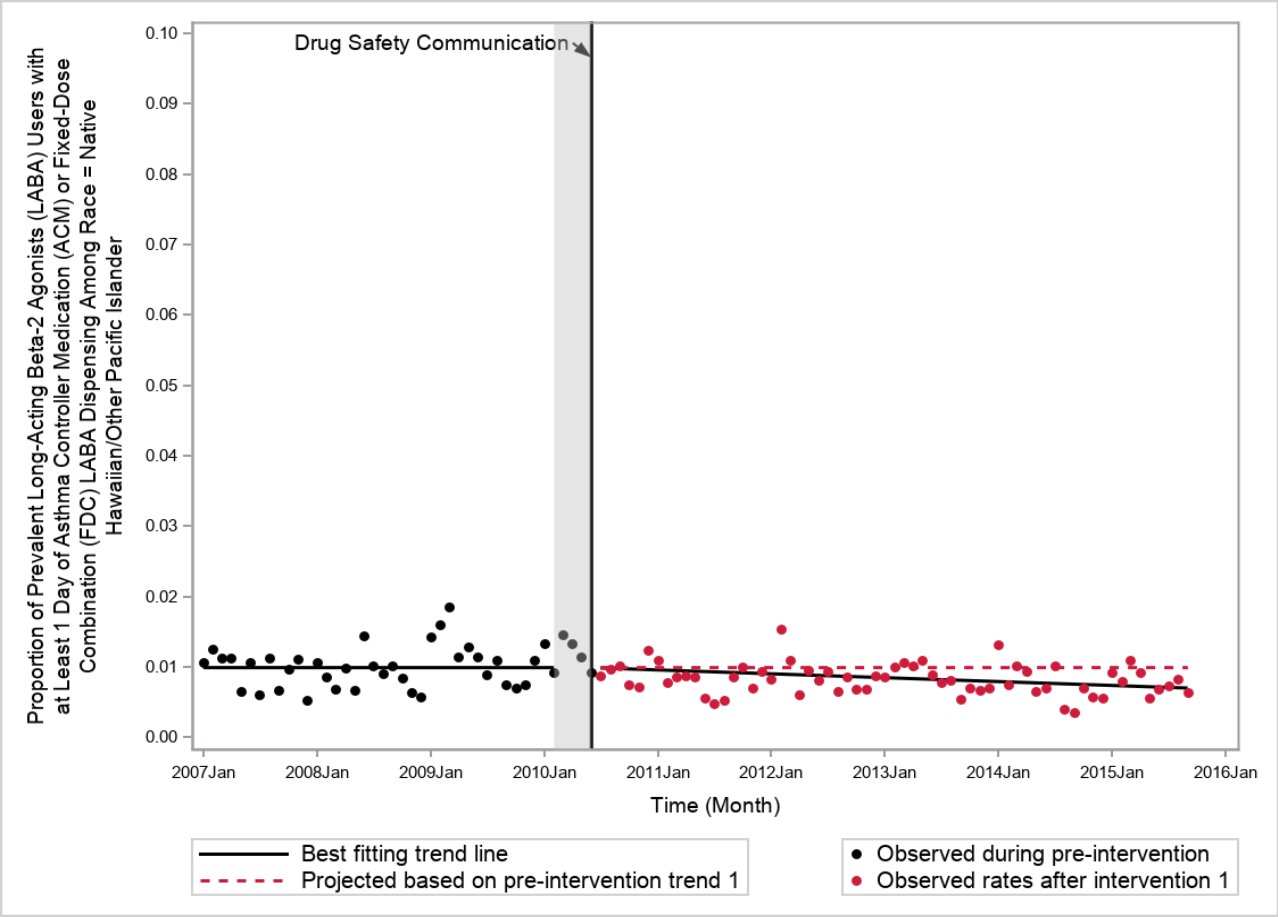
**Figure 10. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = Black/African American**




[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).

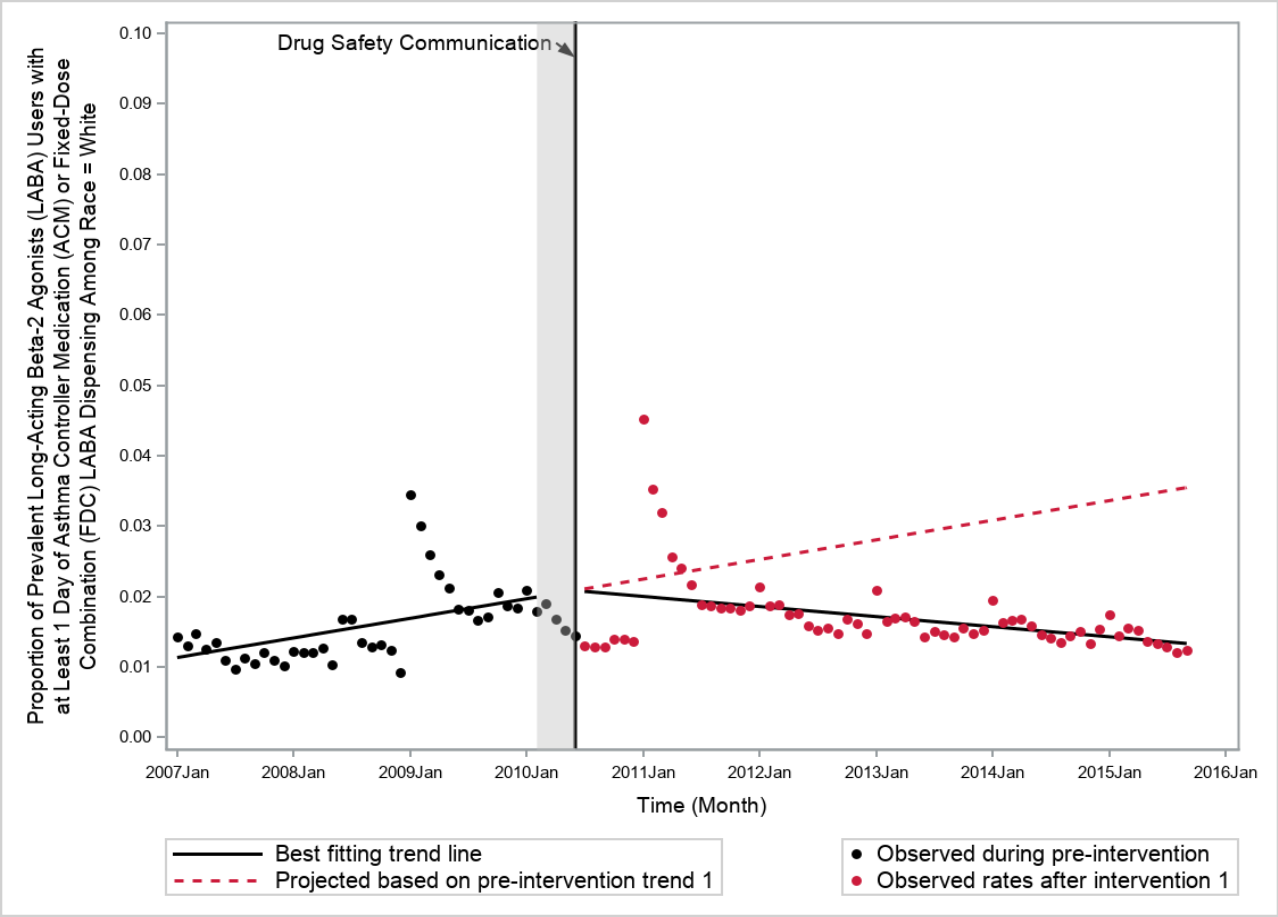
**Figure 11. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = Native Hawaiian/Other Pacific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

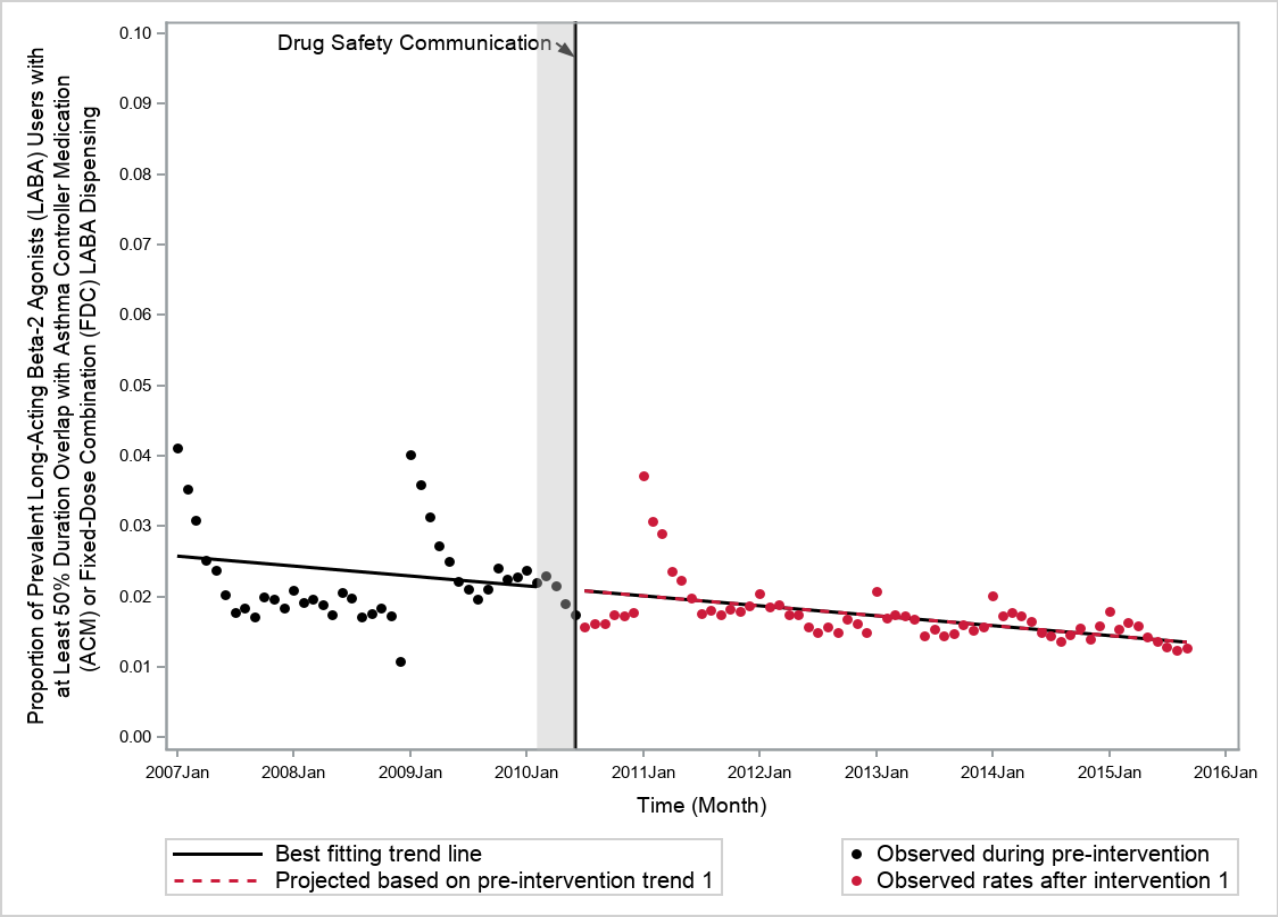
**Figure 12. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 1 Day of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = White**




[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).

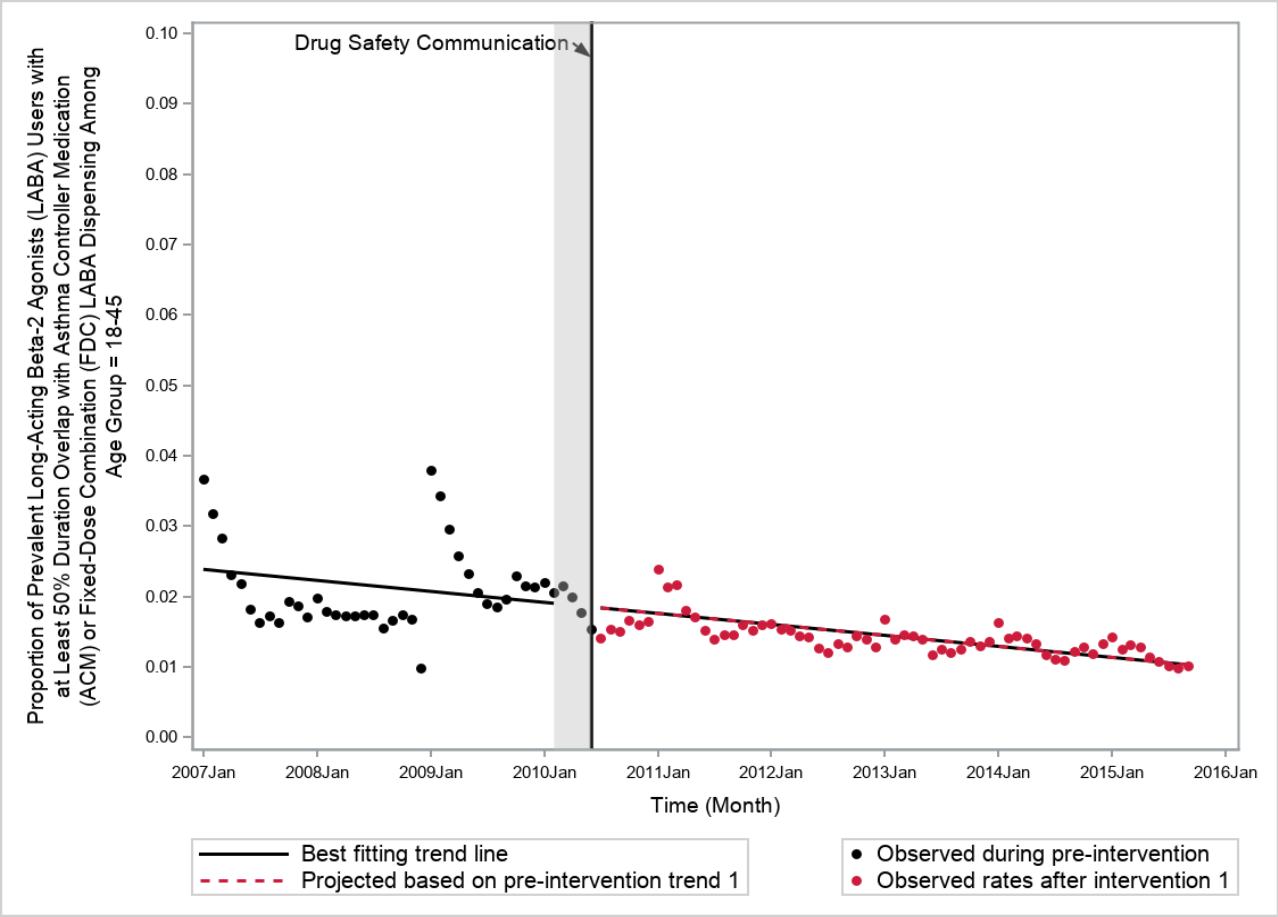
**Figure 13. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2]**




[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).

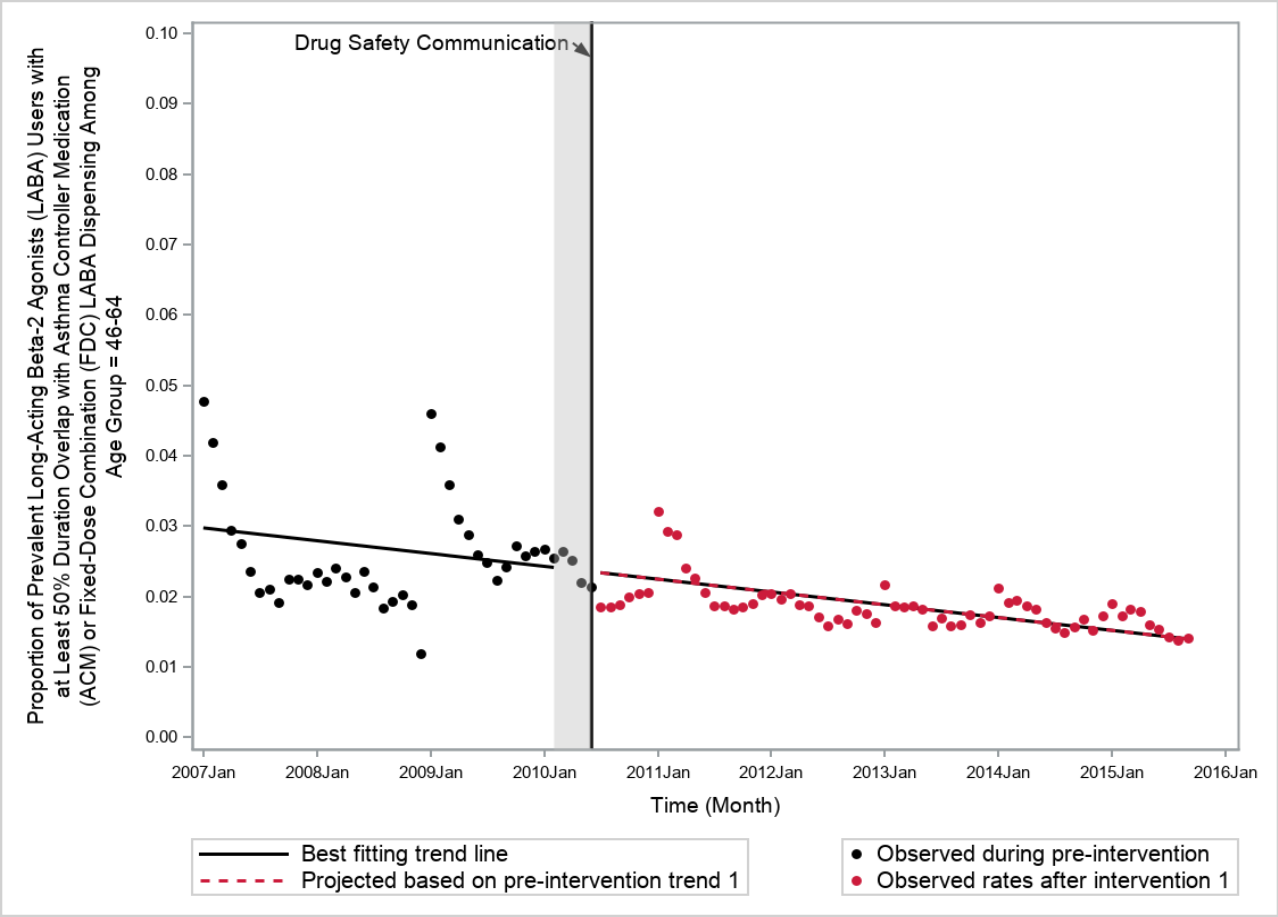
**Figure 14. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Age Group = 18-45**




[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).

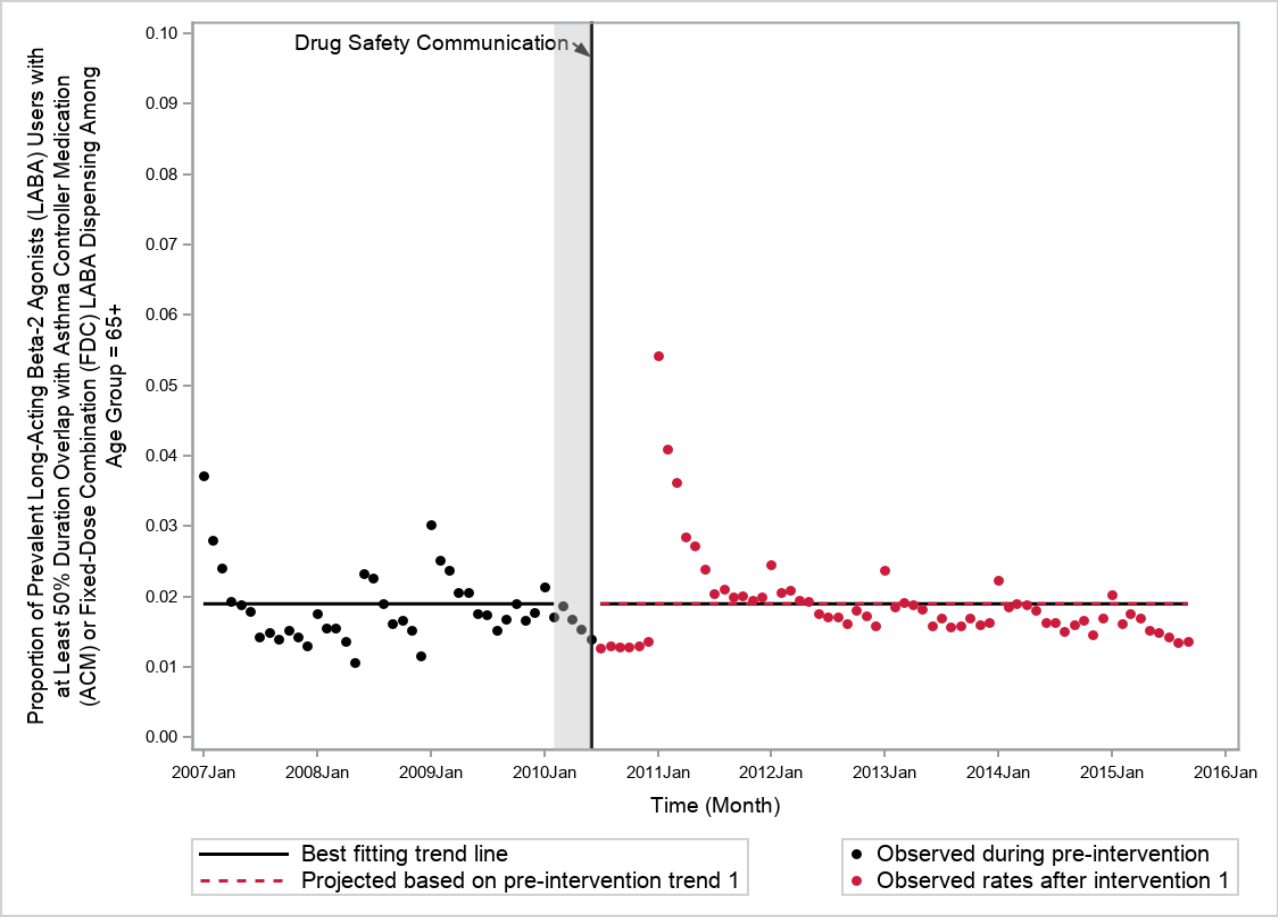
**Figure 15. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Age Group = 46-64**




[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).

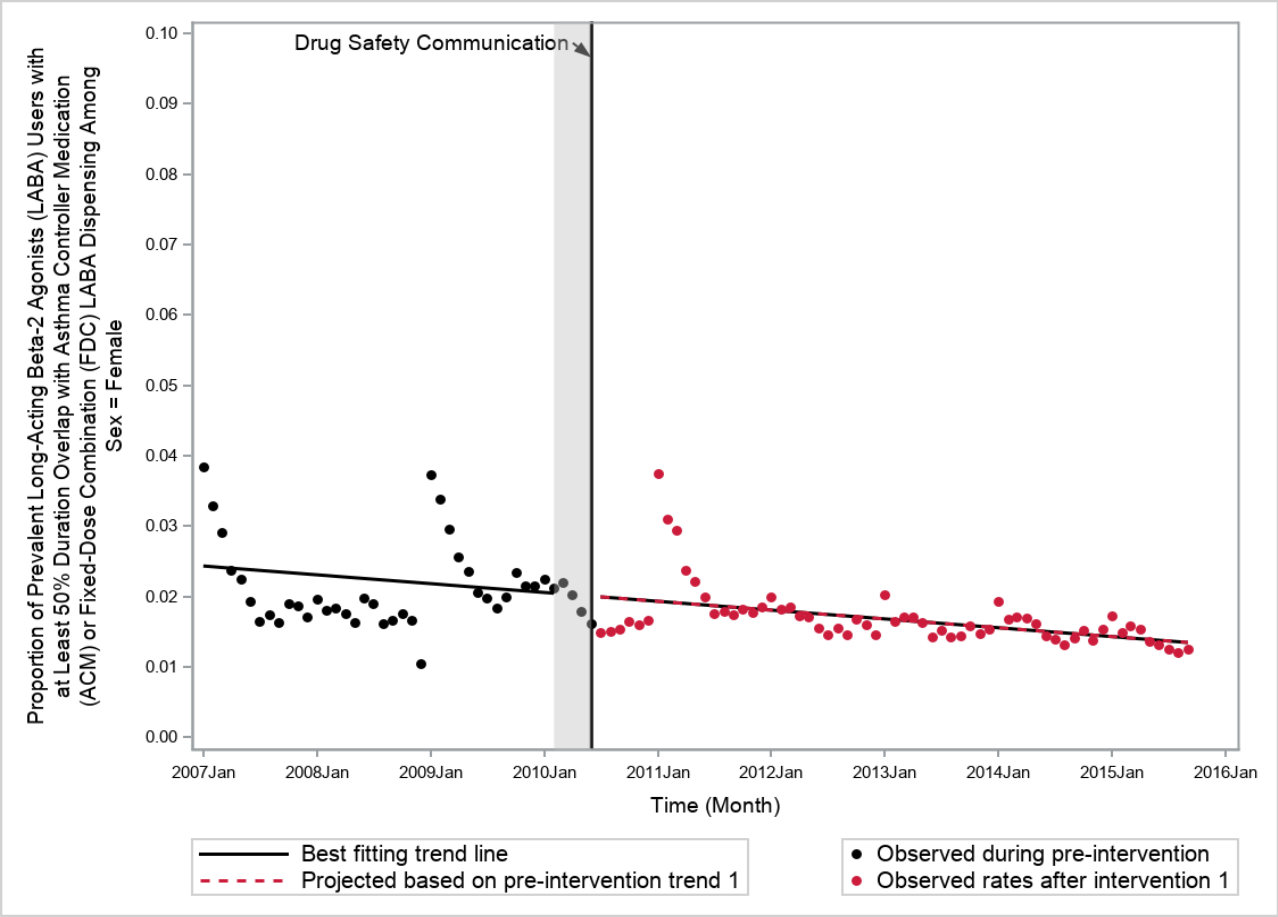
**Figure 16. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Age Group = 65+**




[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).

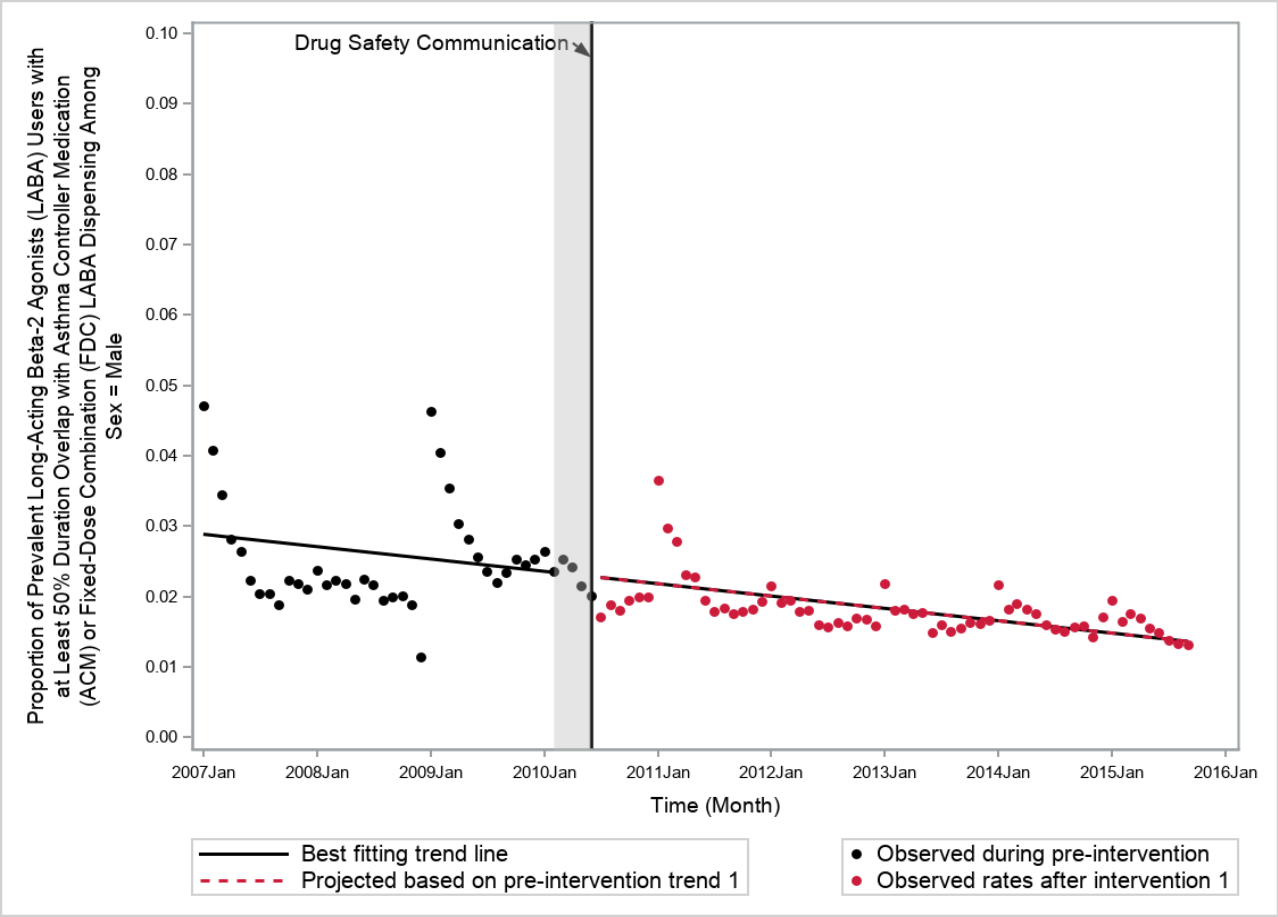
**Figure 17. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Sex = Female**




[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).

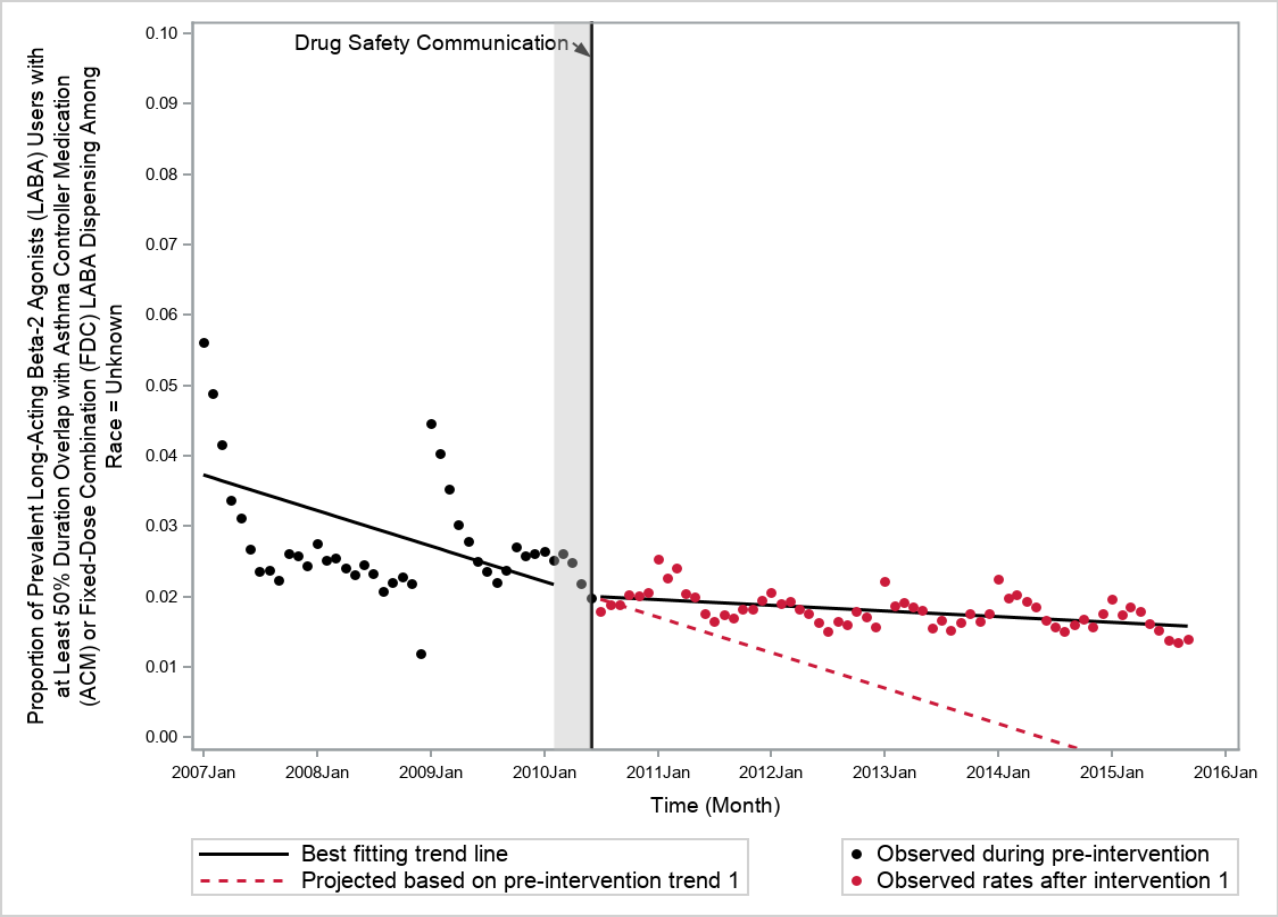
**Figure 18. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Sex = Male**




[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).

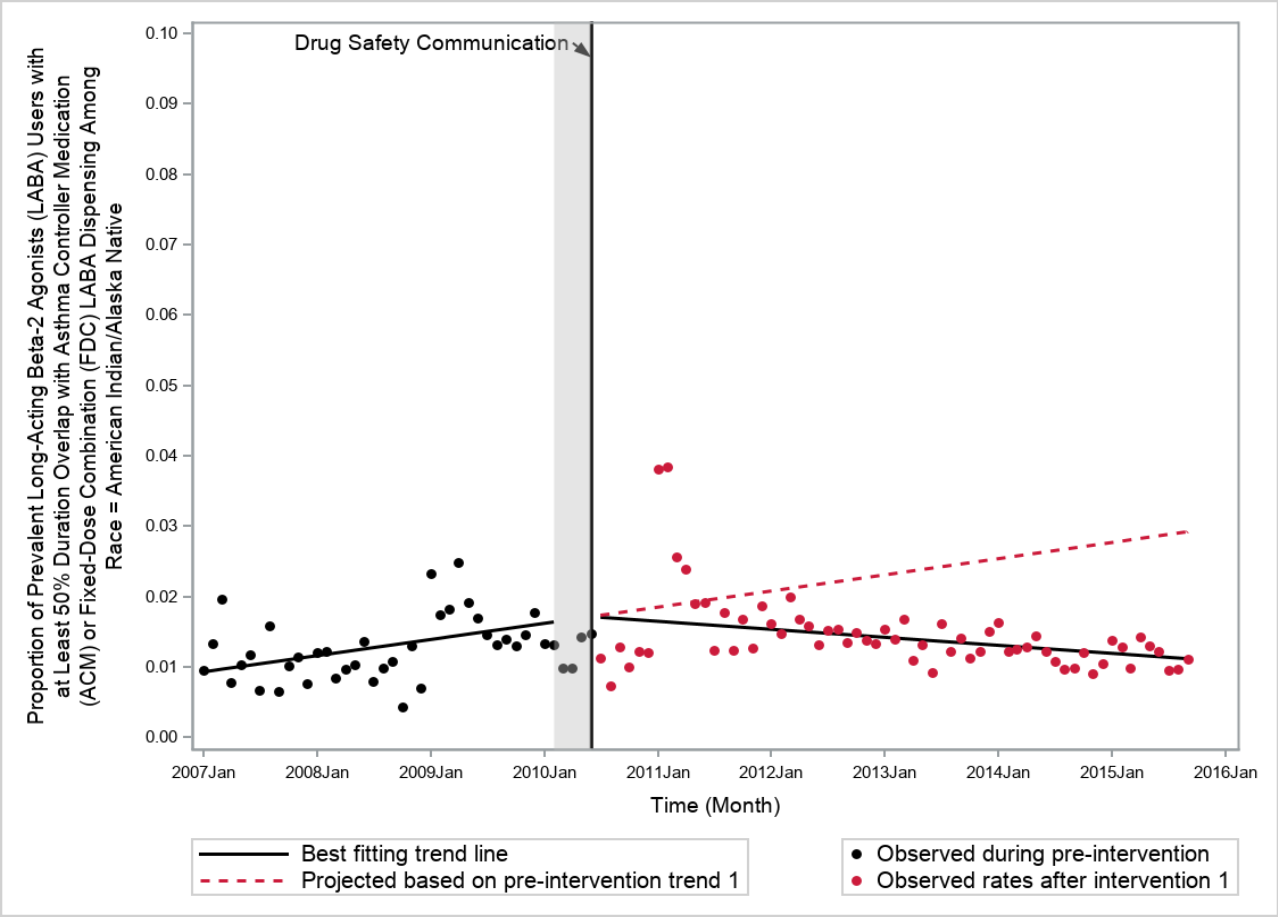
**Figure 19. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = Unknown**




[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).

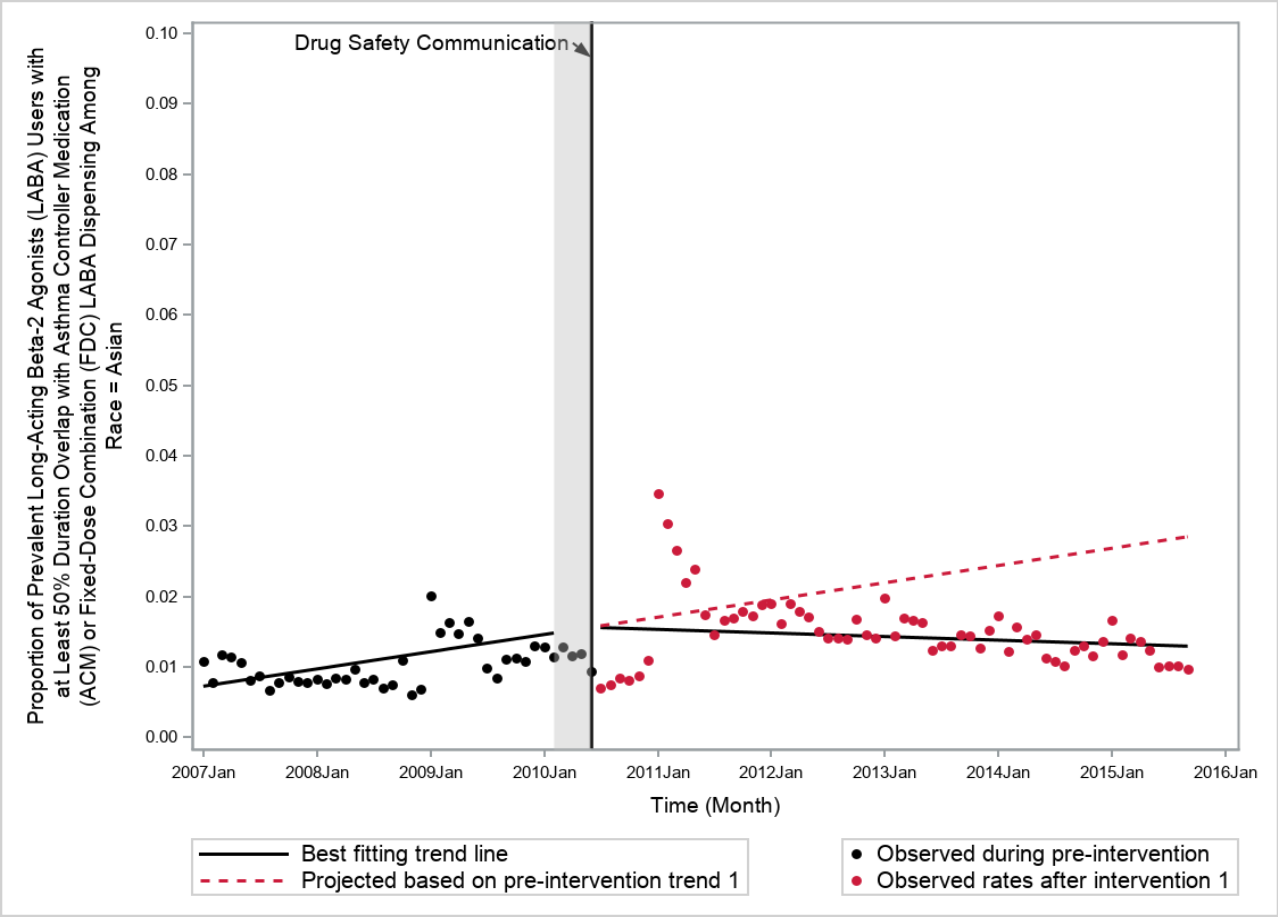
**Figure 20. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = American Indian/Alaska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

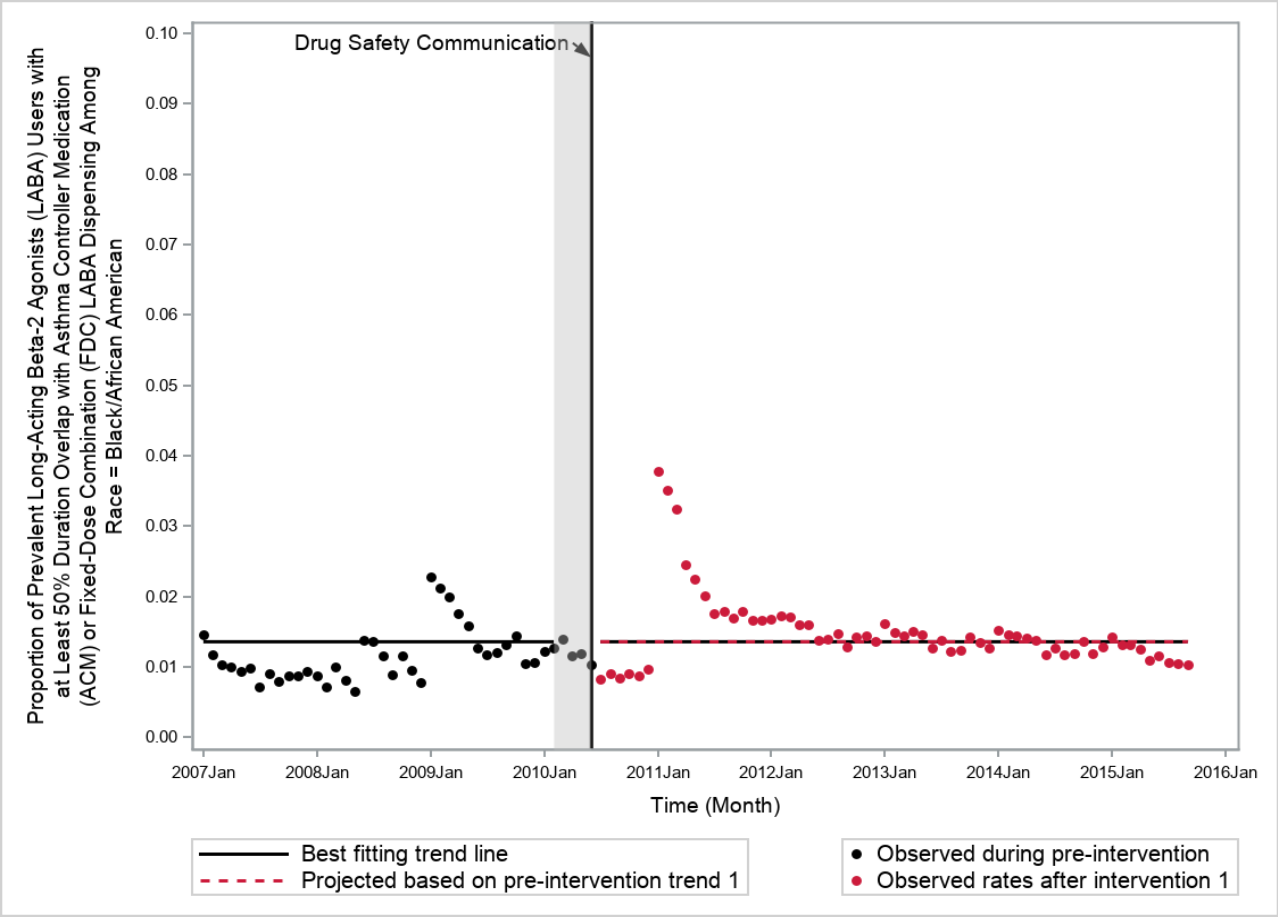
**Figure 21. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = Asian**




[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).

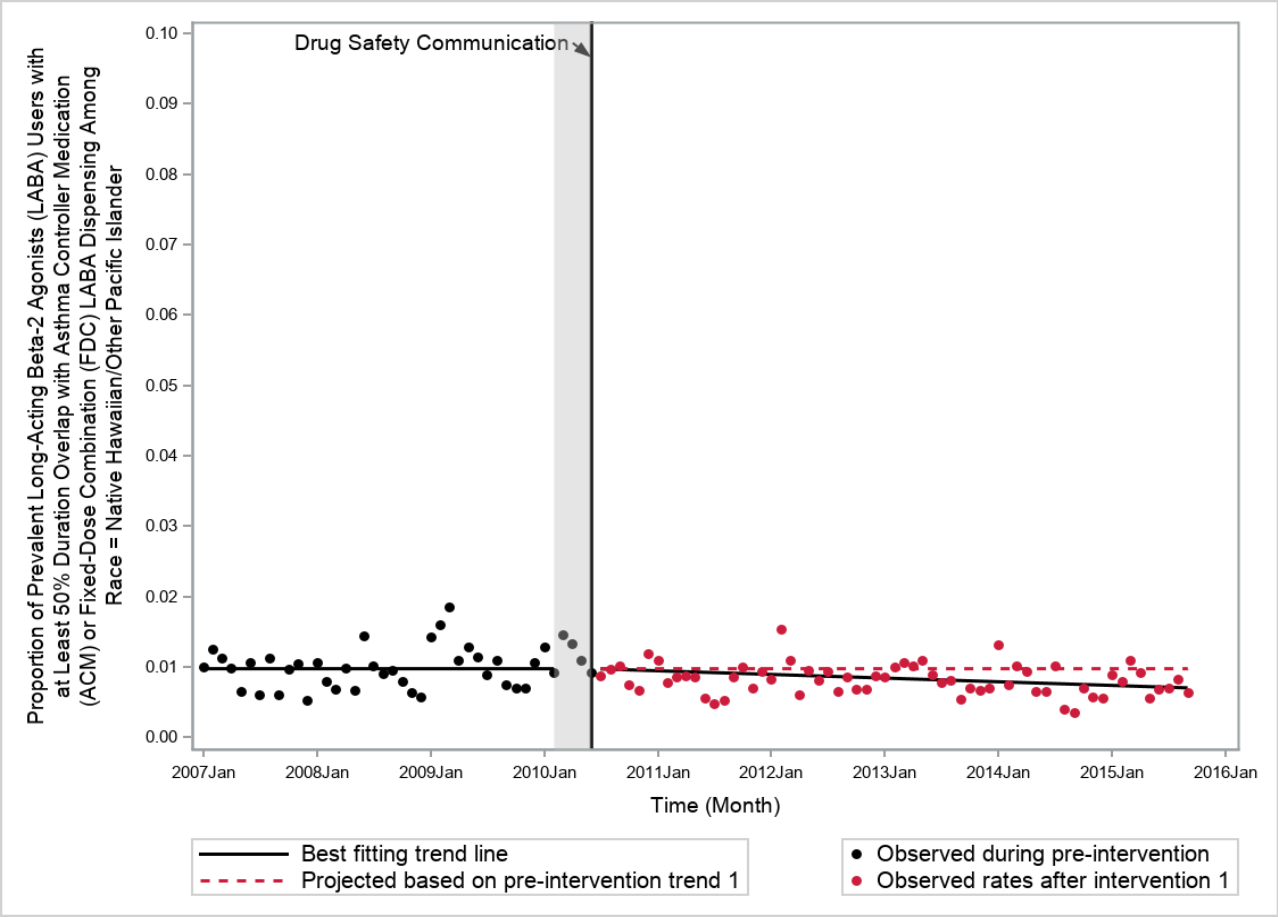
**Figure 22. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = Black/African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

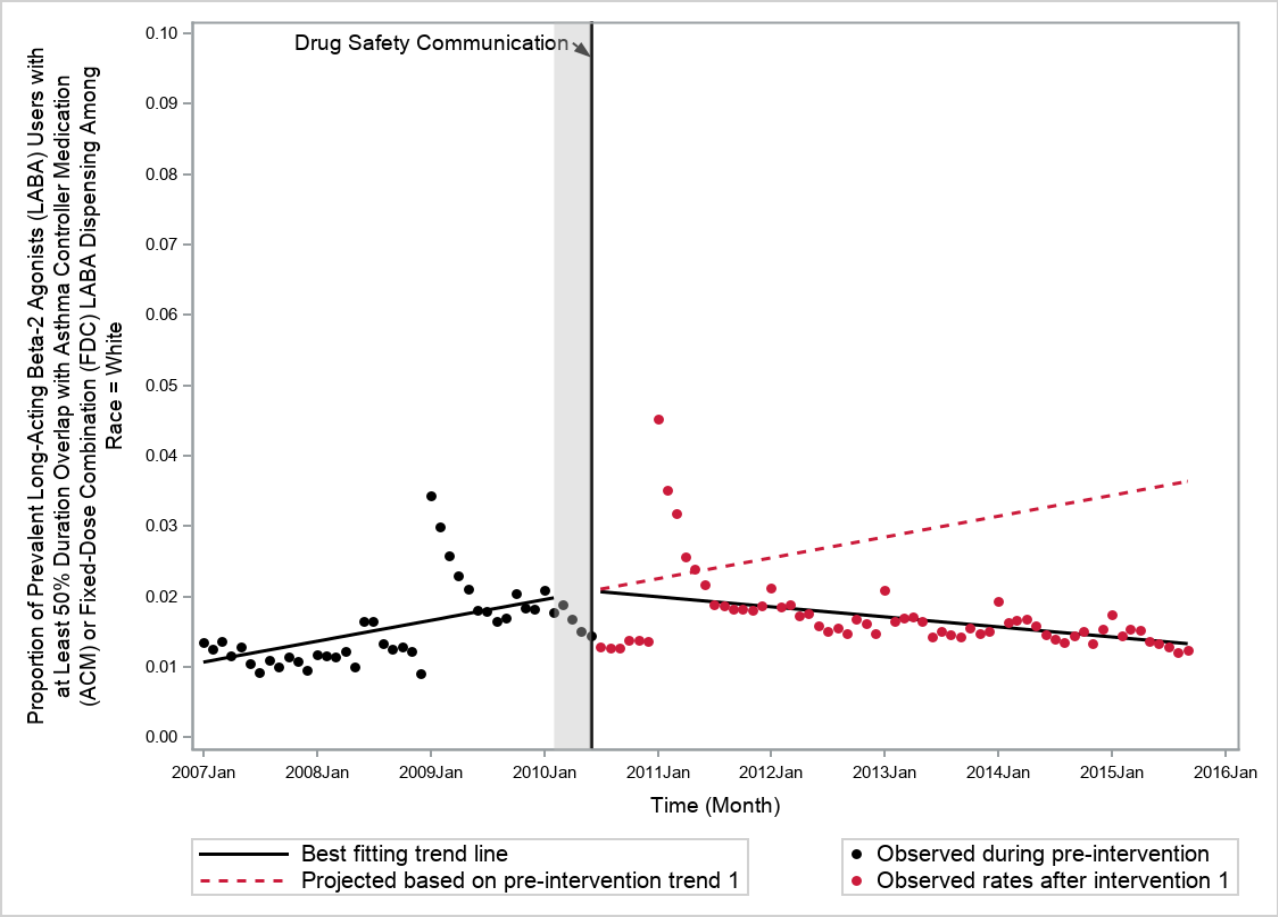
**Figure 23. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = Native Hawaiian/Other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

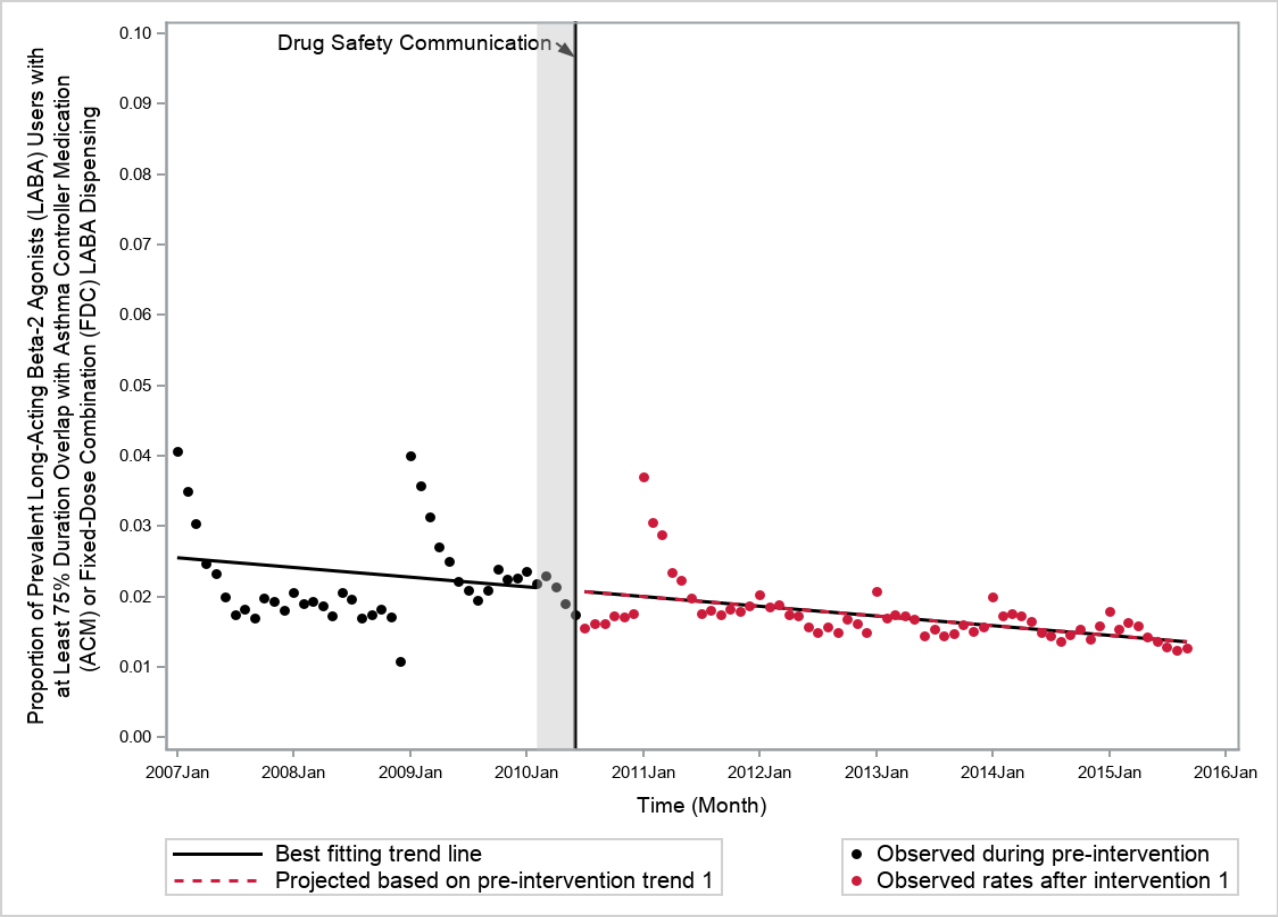
**Figure 24. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 50% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = White**




[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).

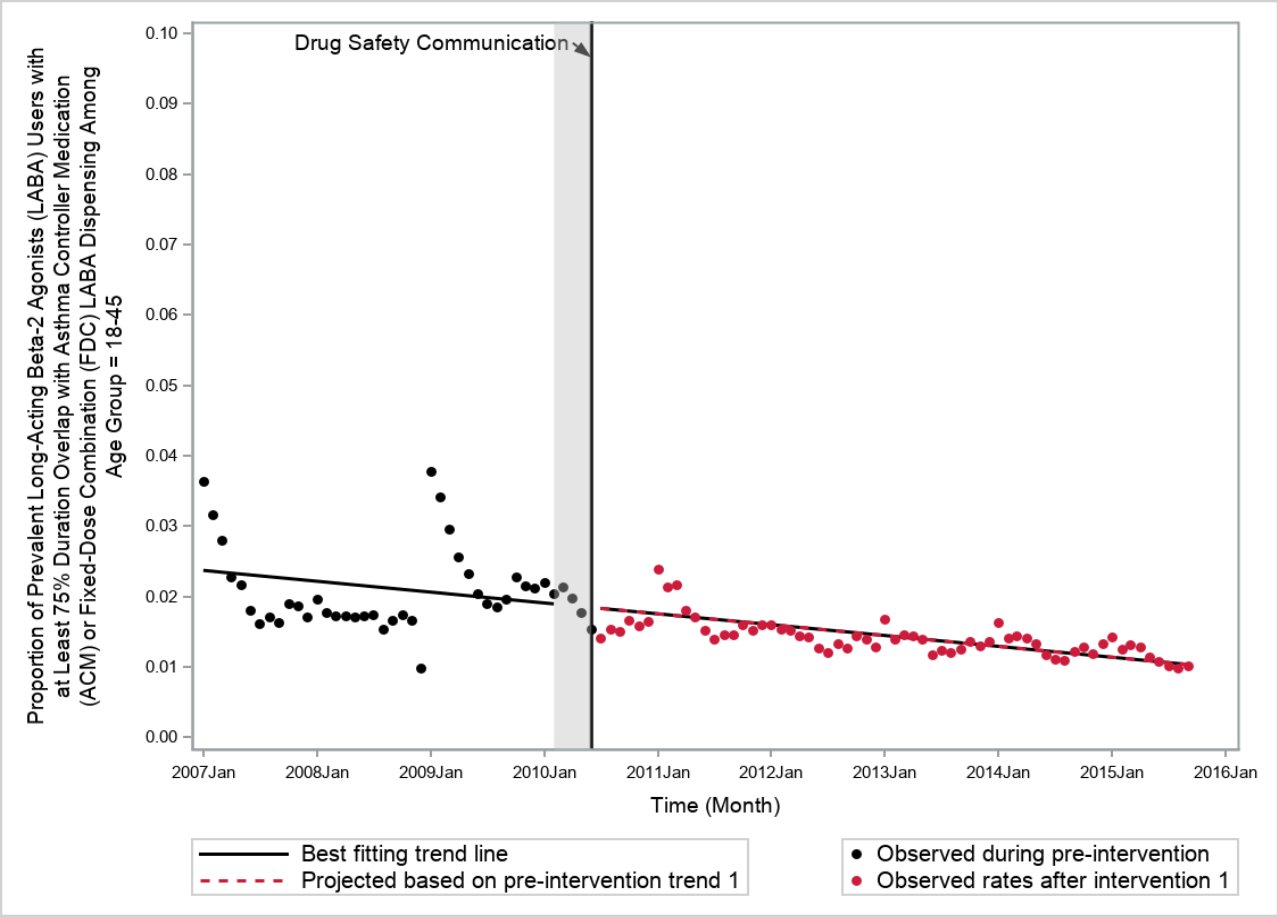
**Figure 25. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2]**




[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).

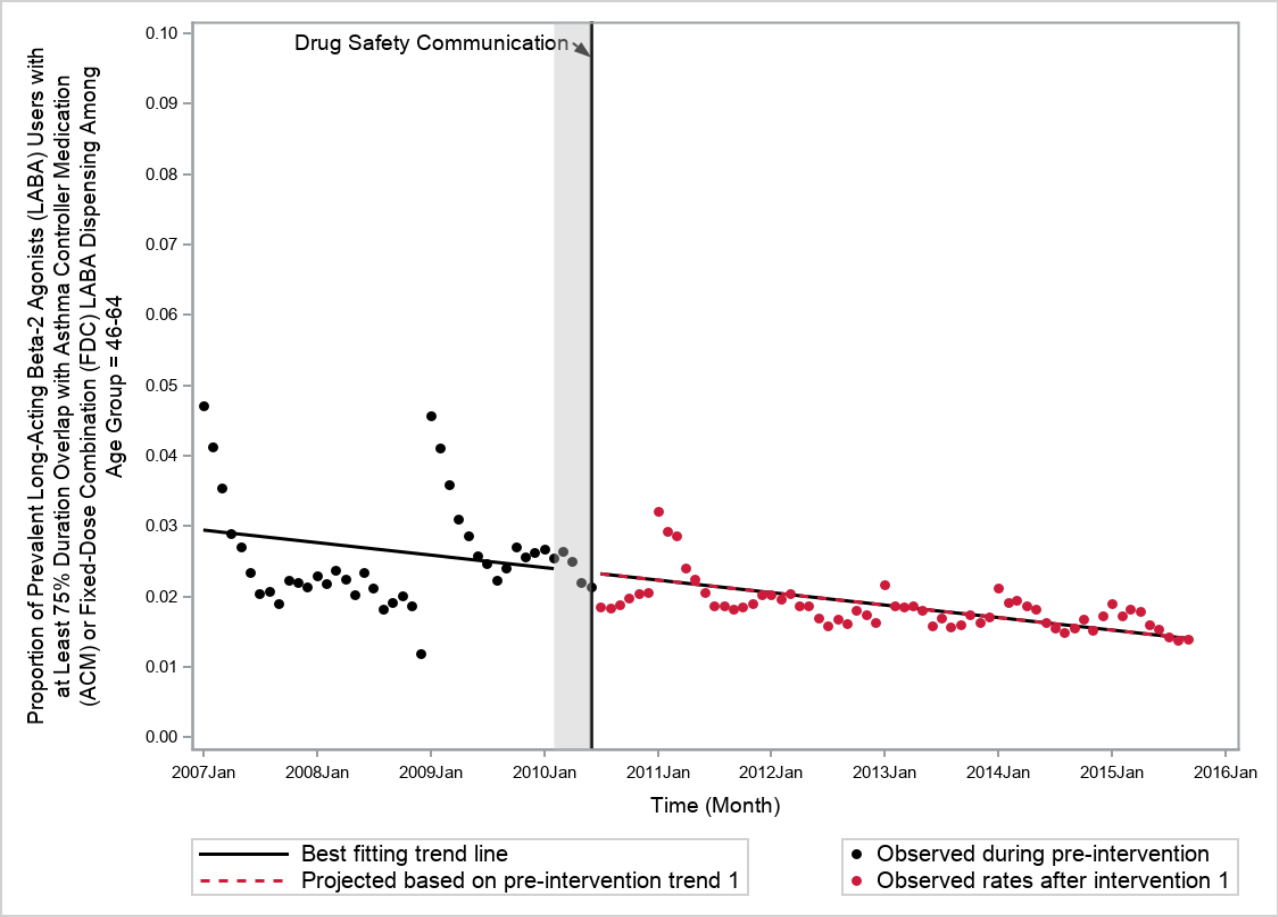
**Figure 26. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Age Group = 18-45**




[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).

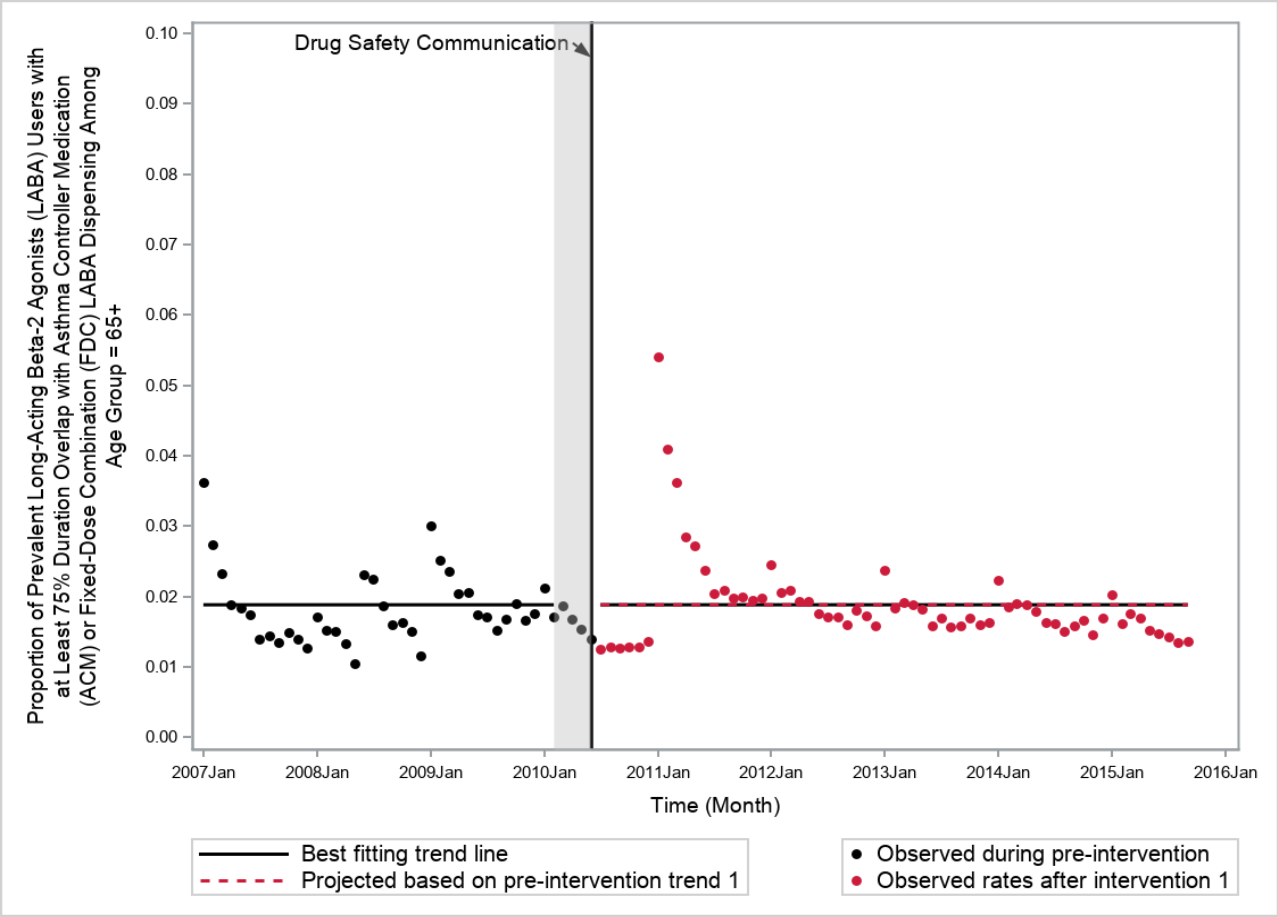
**Figure 27. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Age Group = 46-64**




[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).

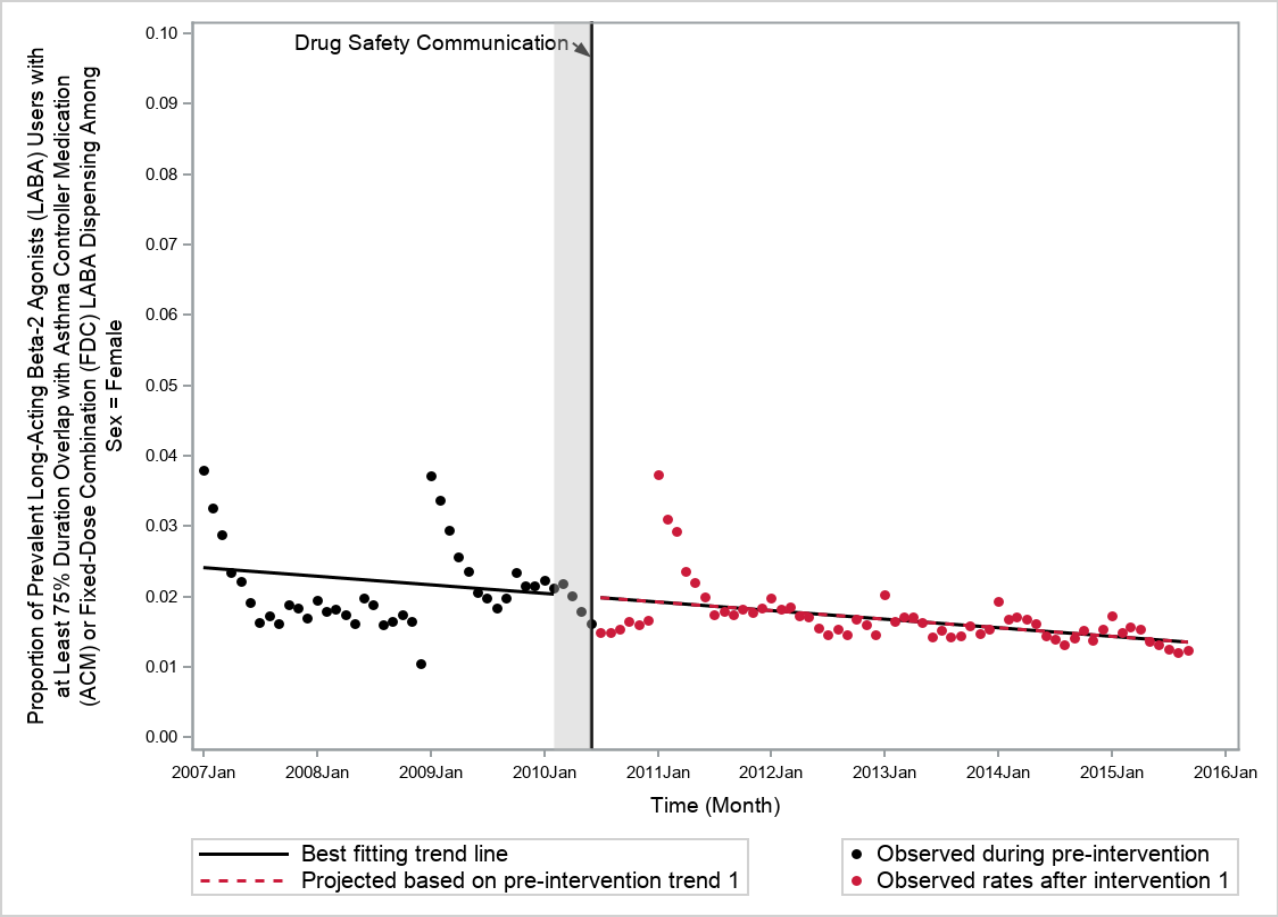
**Figure 28. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Age Group = 65+**




[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).

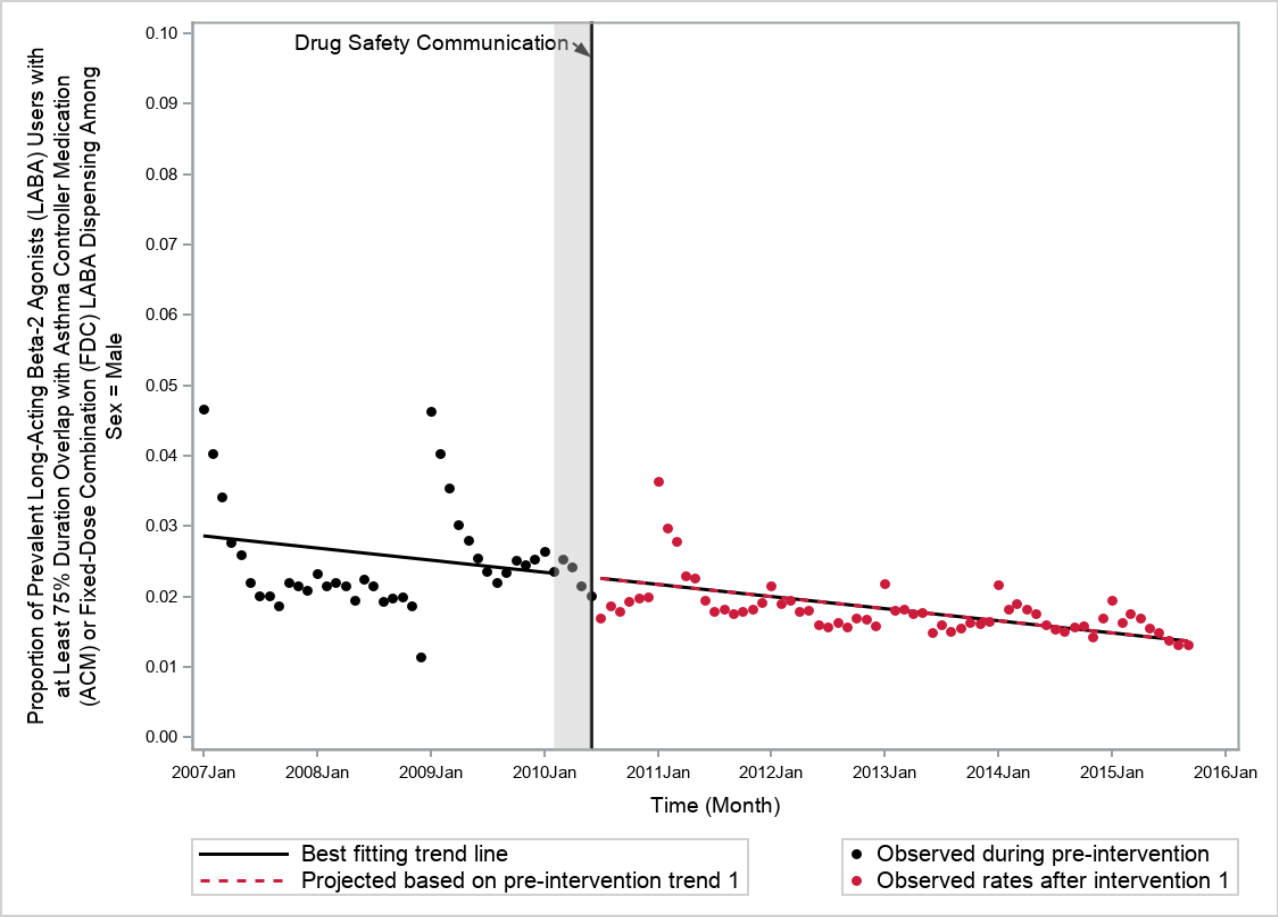
**Figure 29. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Sex = Female**




[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).

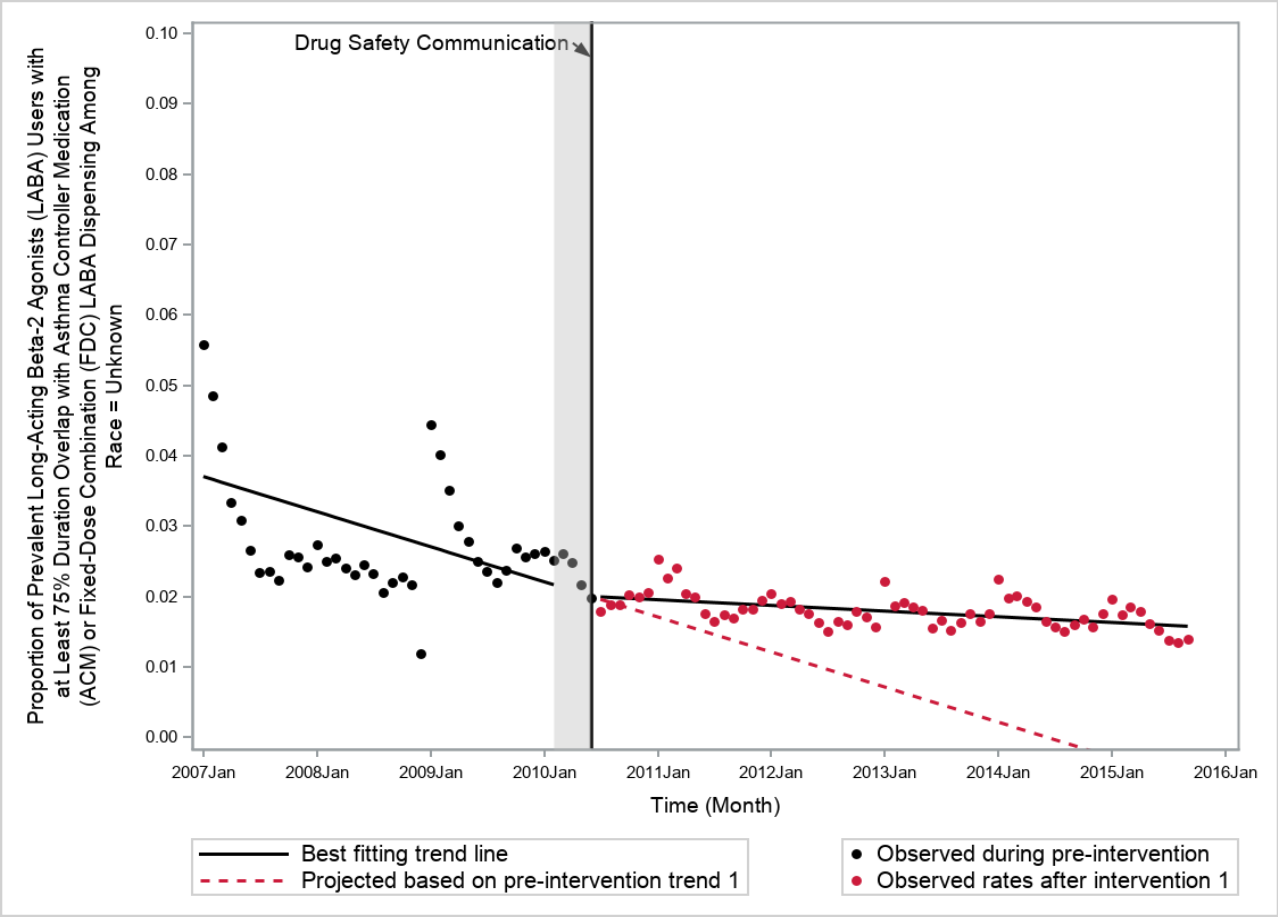
**Figure 30. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Sex = Male**




[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).

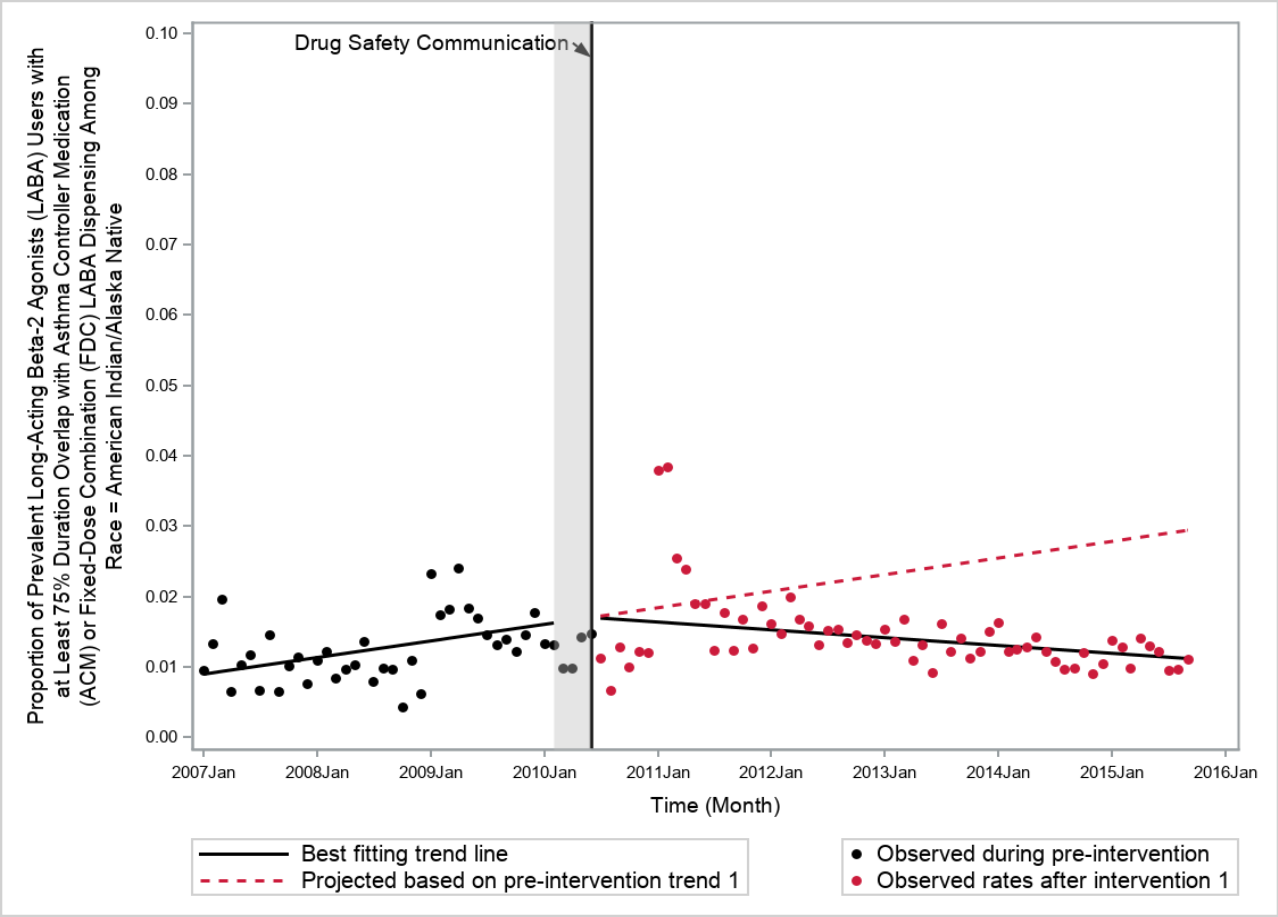
**Figure 31. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = Unknown**




[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).

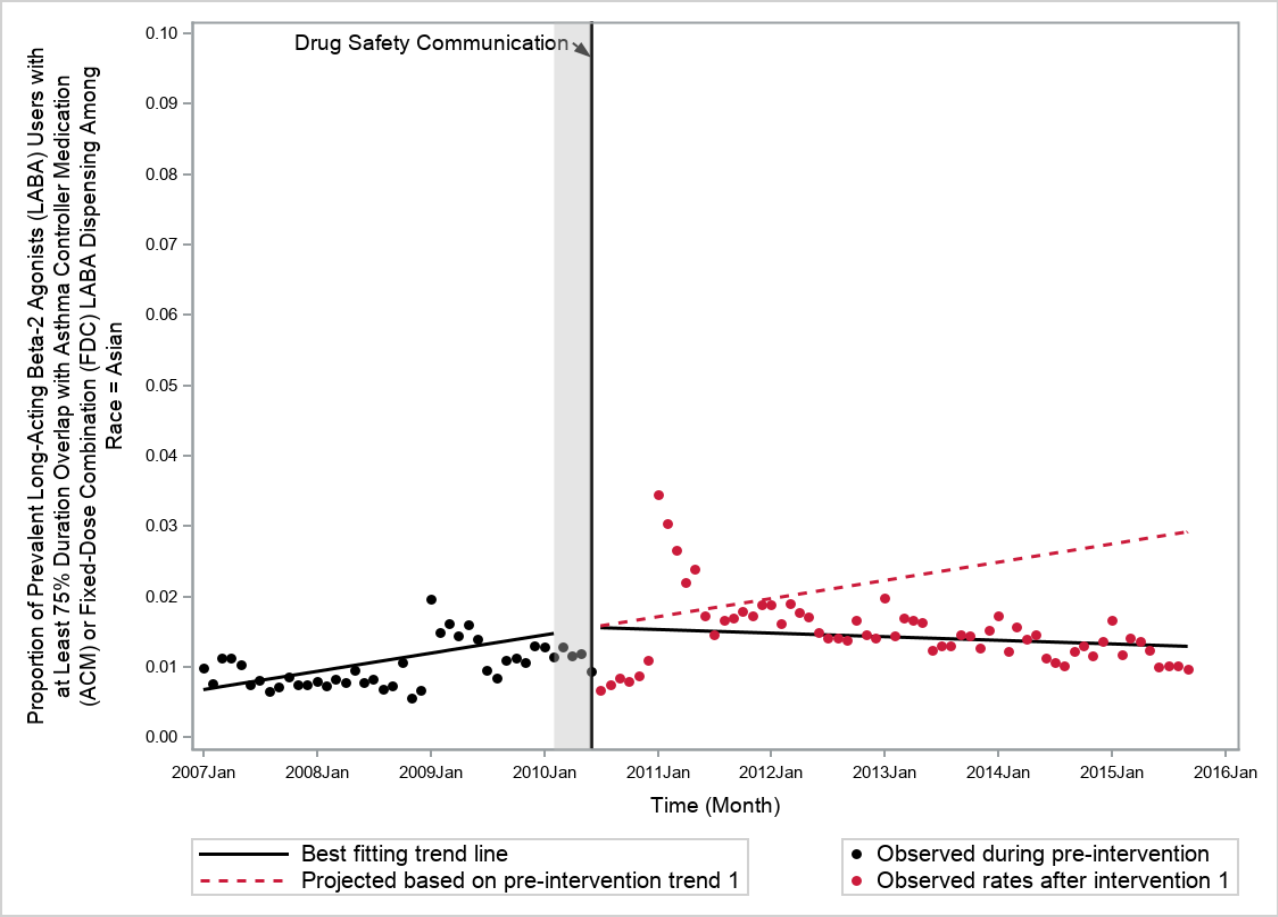
**Figure 32. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = American Indian/Alaska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

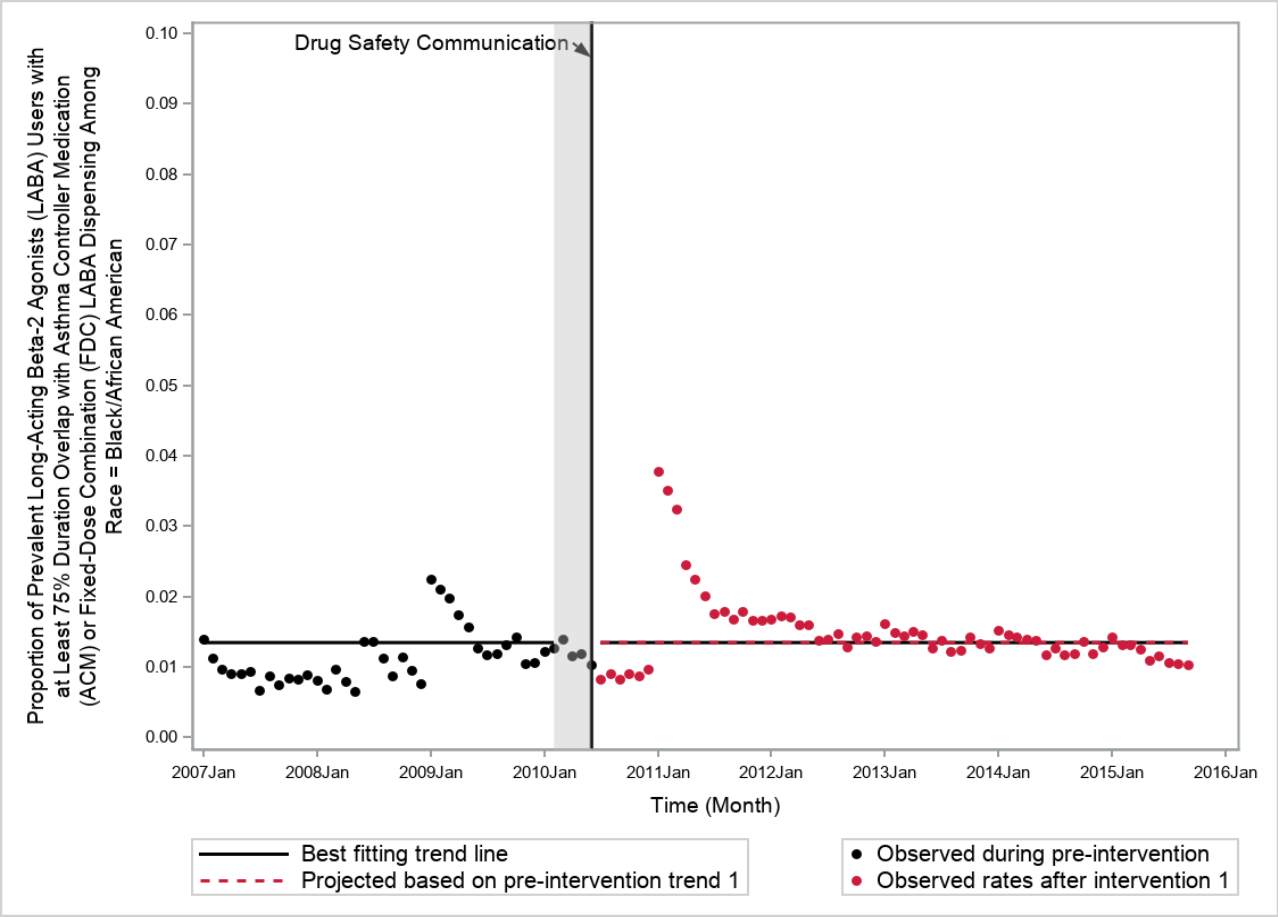
**Figure 33. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = Asian**




[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).

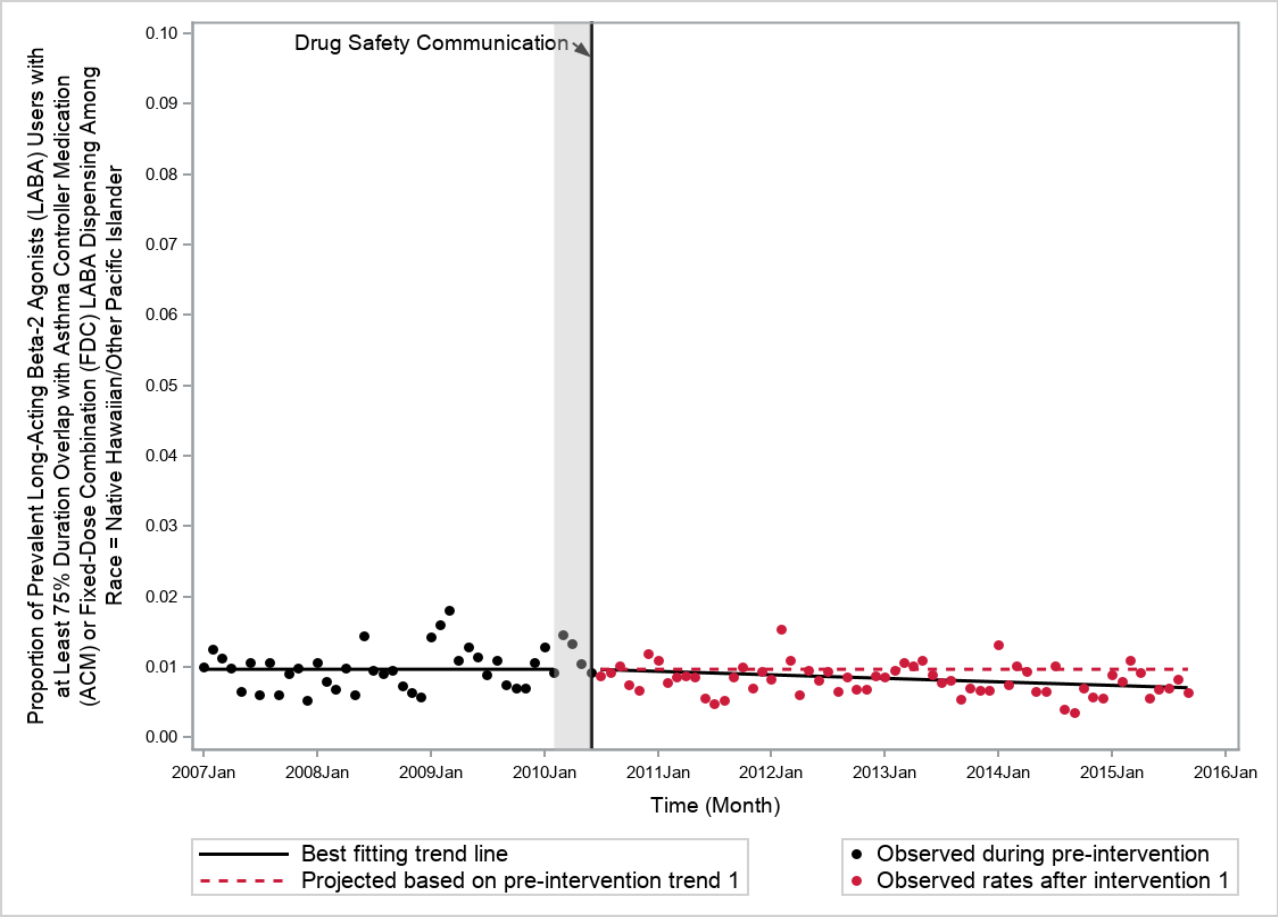
**Figure 34. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = Black/African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

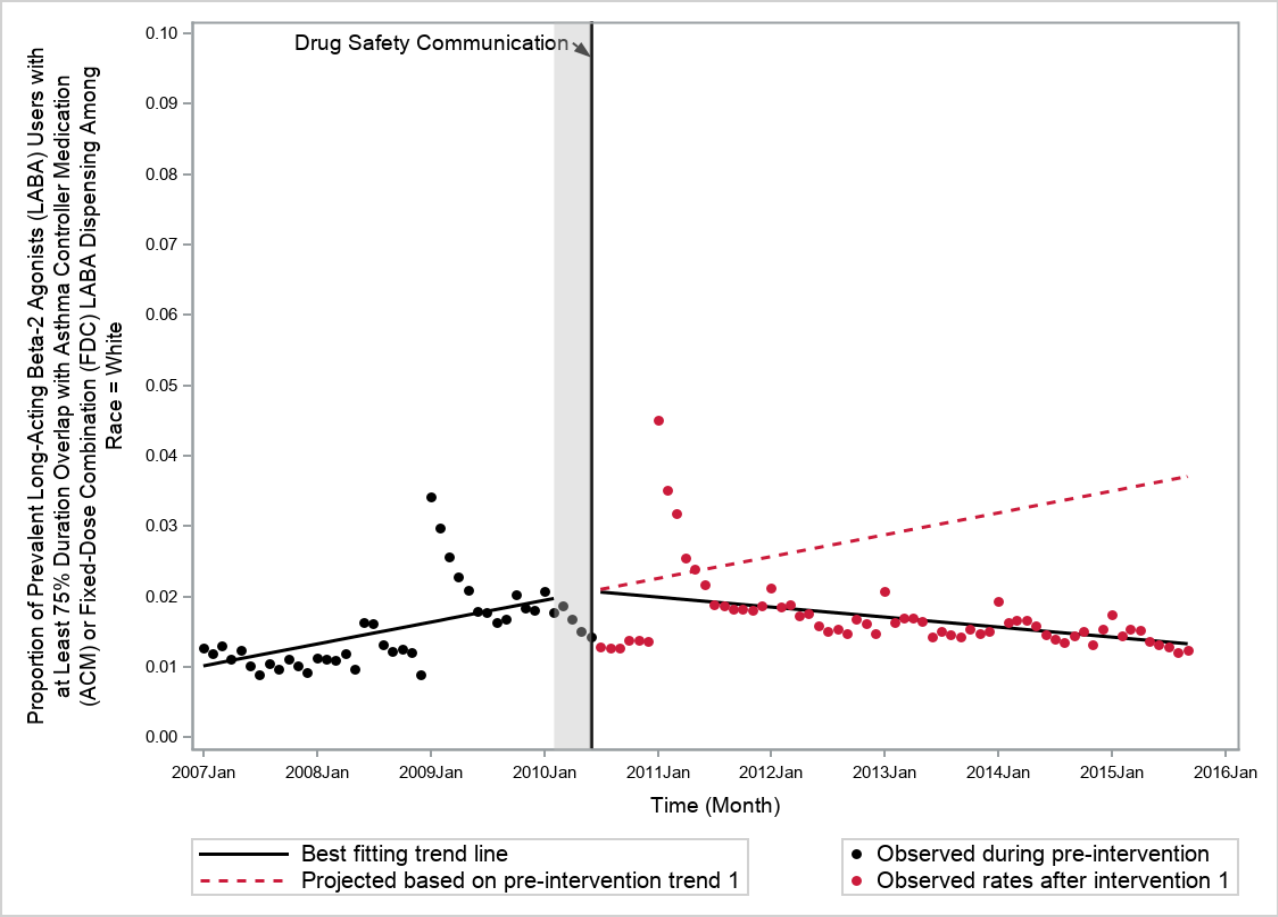
**Figure 35. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = Native Hawaiian/Other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

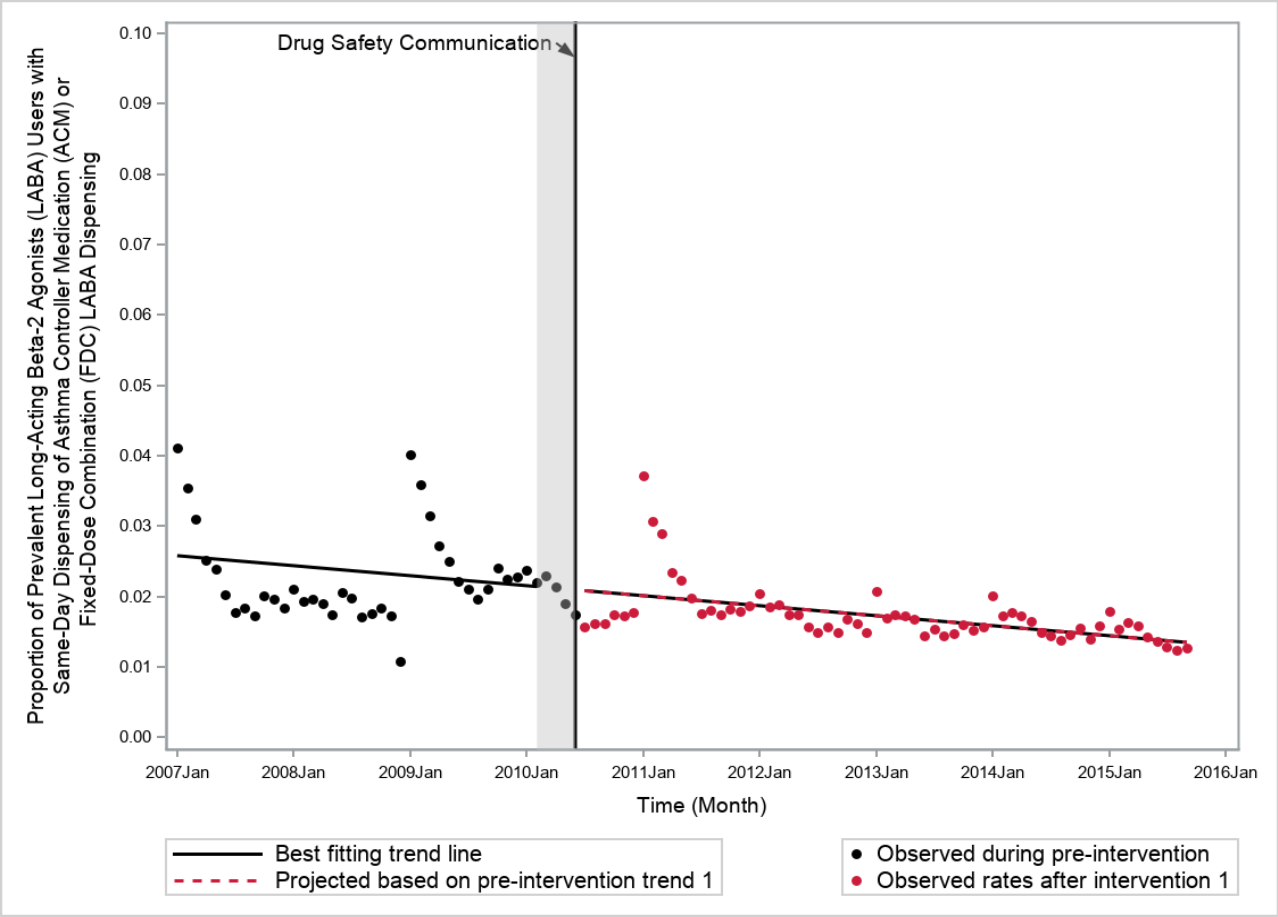
**Figure 36. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with at Least 75% Duration Overlap with Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = White**




[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).

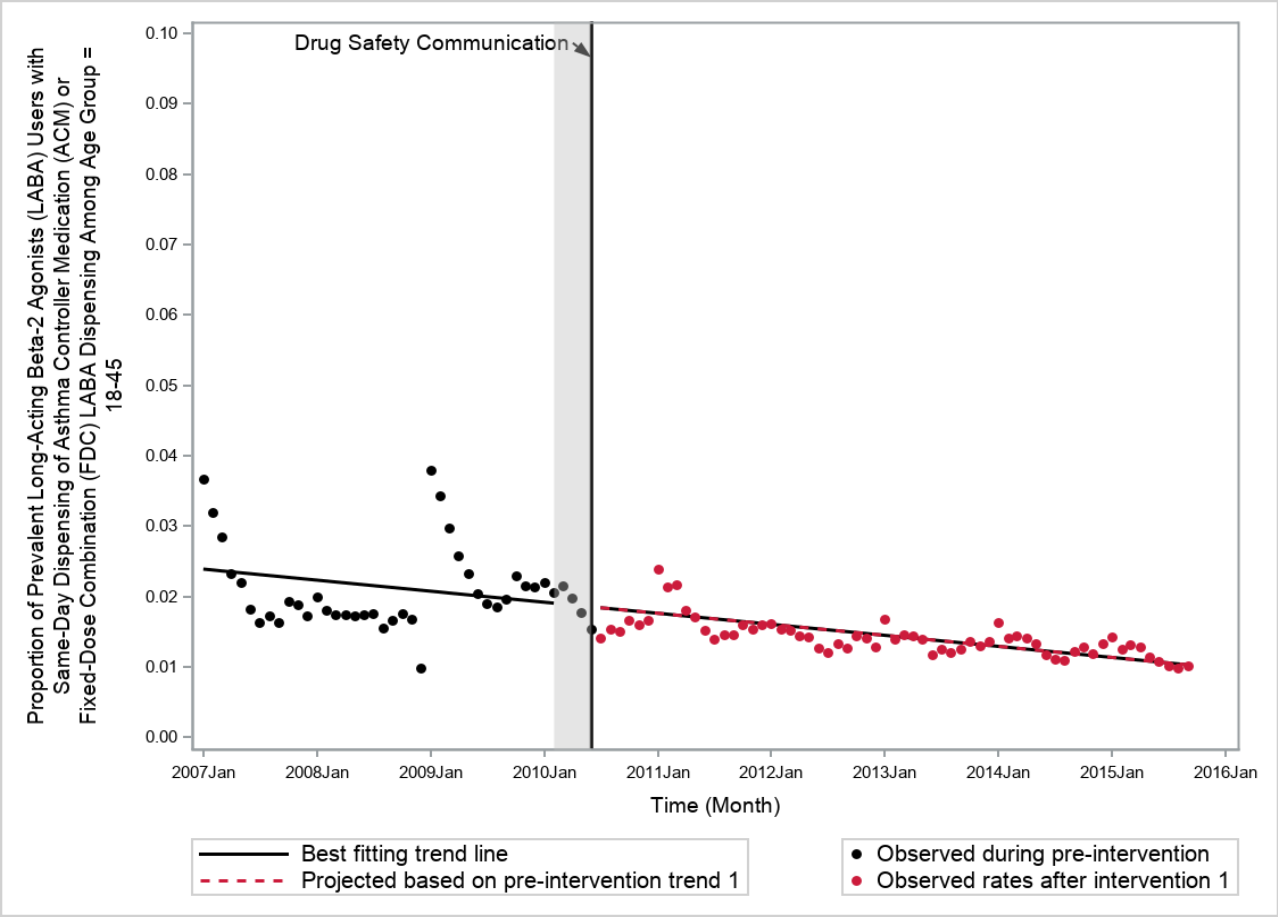
**Figure 37. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2]**




[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).

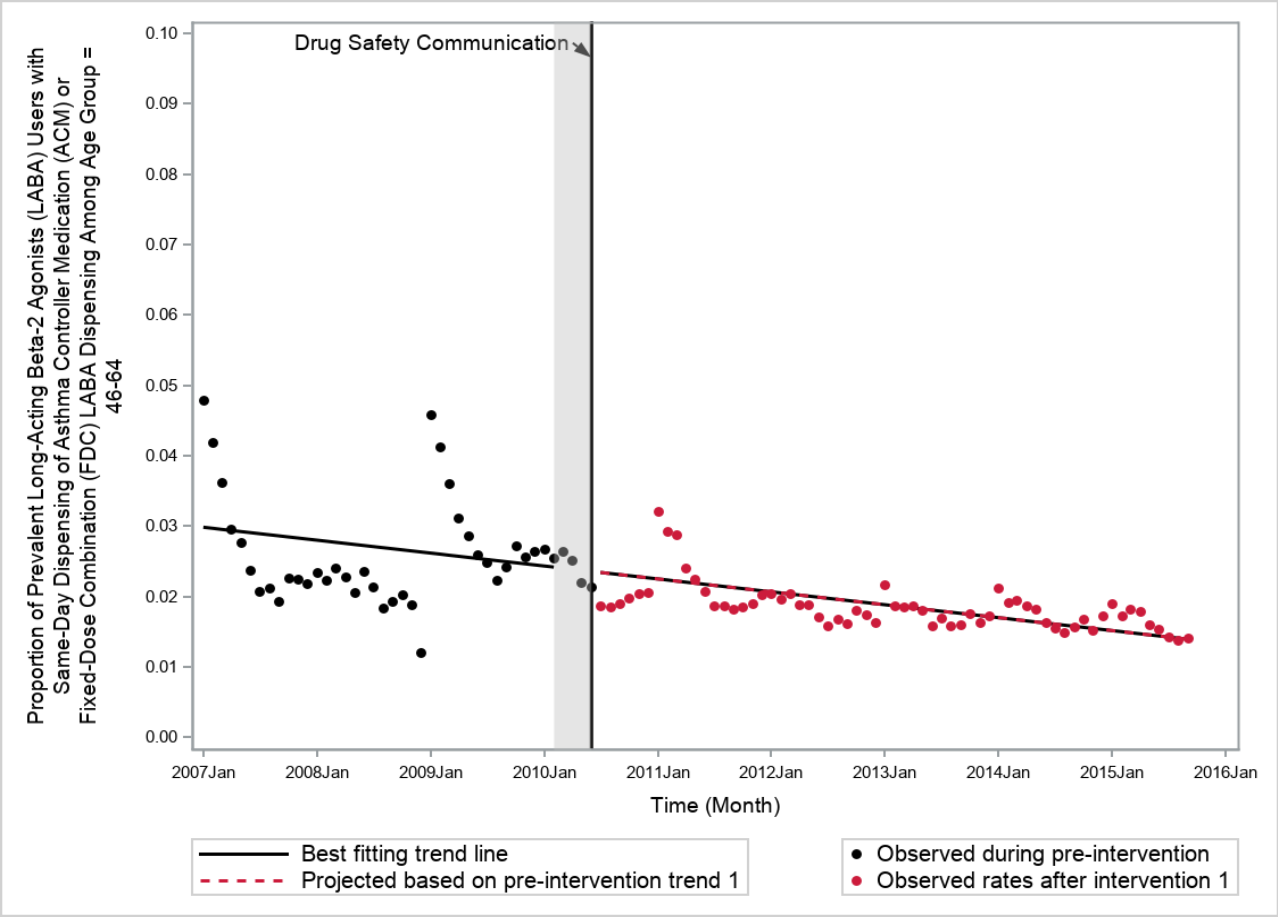
**Figure 38. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Age Group = 18-45**




[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).

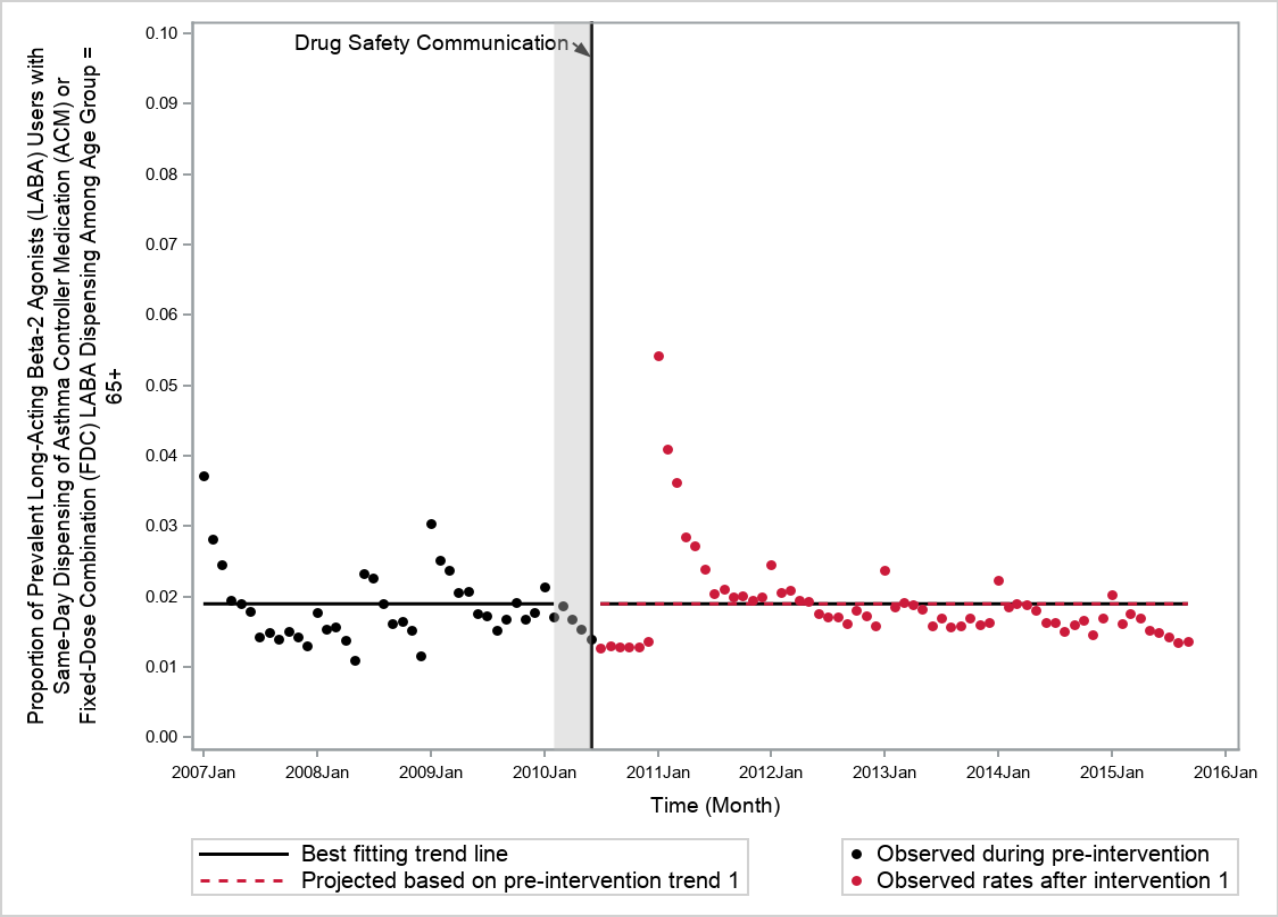
**Figure 39. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Age Group = 46-64**




[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).

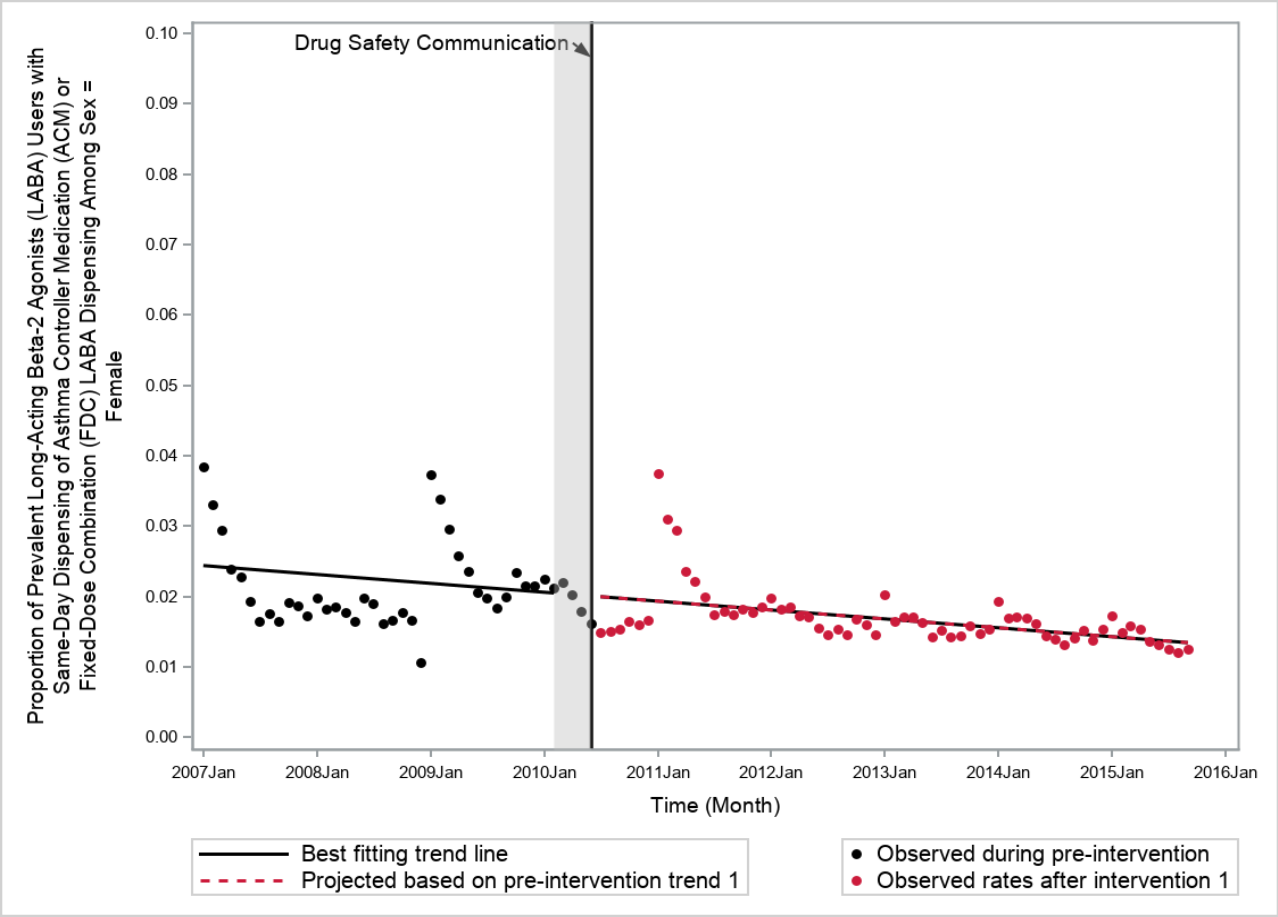
**Figure 40. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Age Group = 65+**




[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).

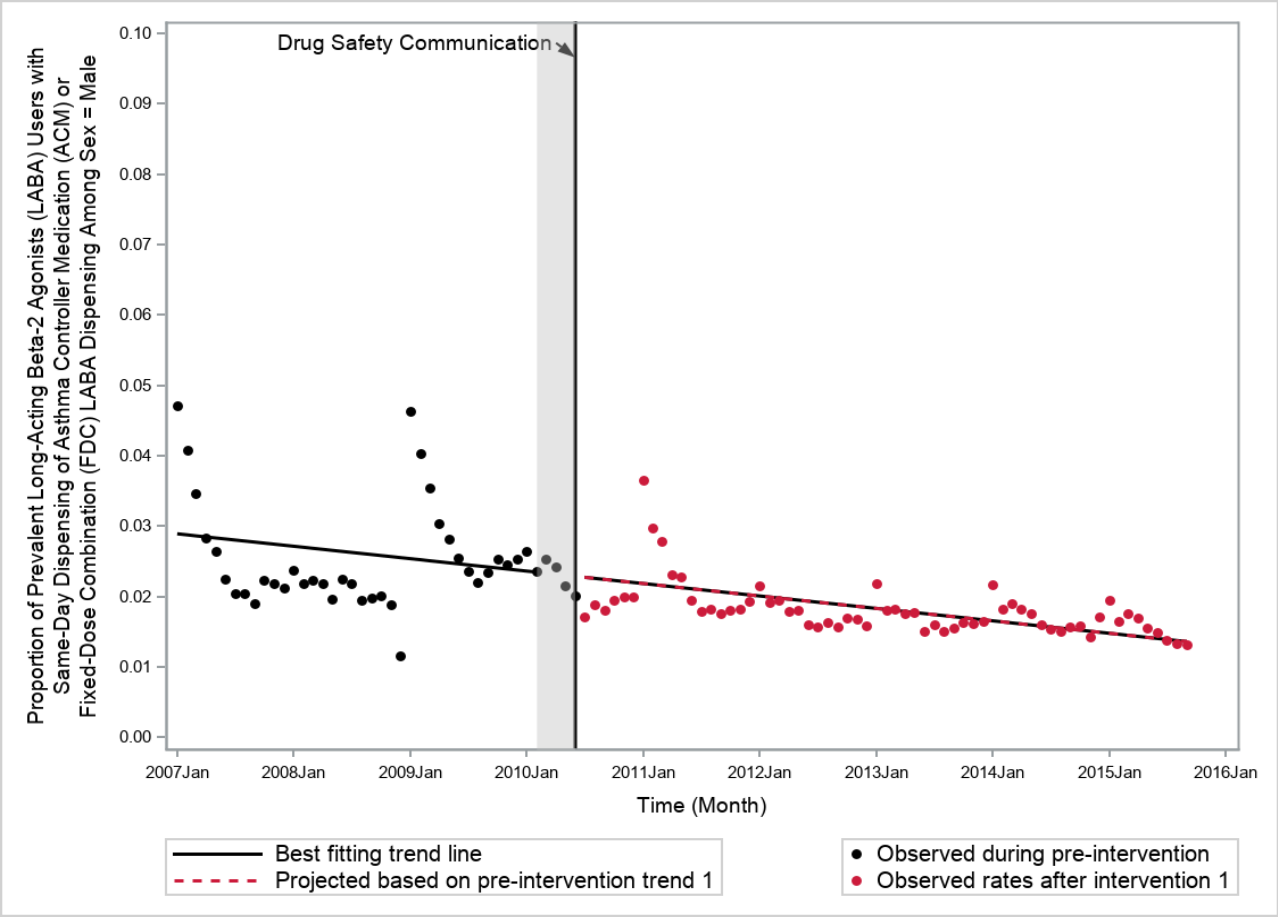
**Figure 41. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Sex = Female**




[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).

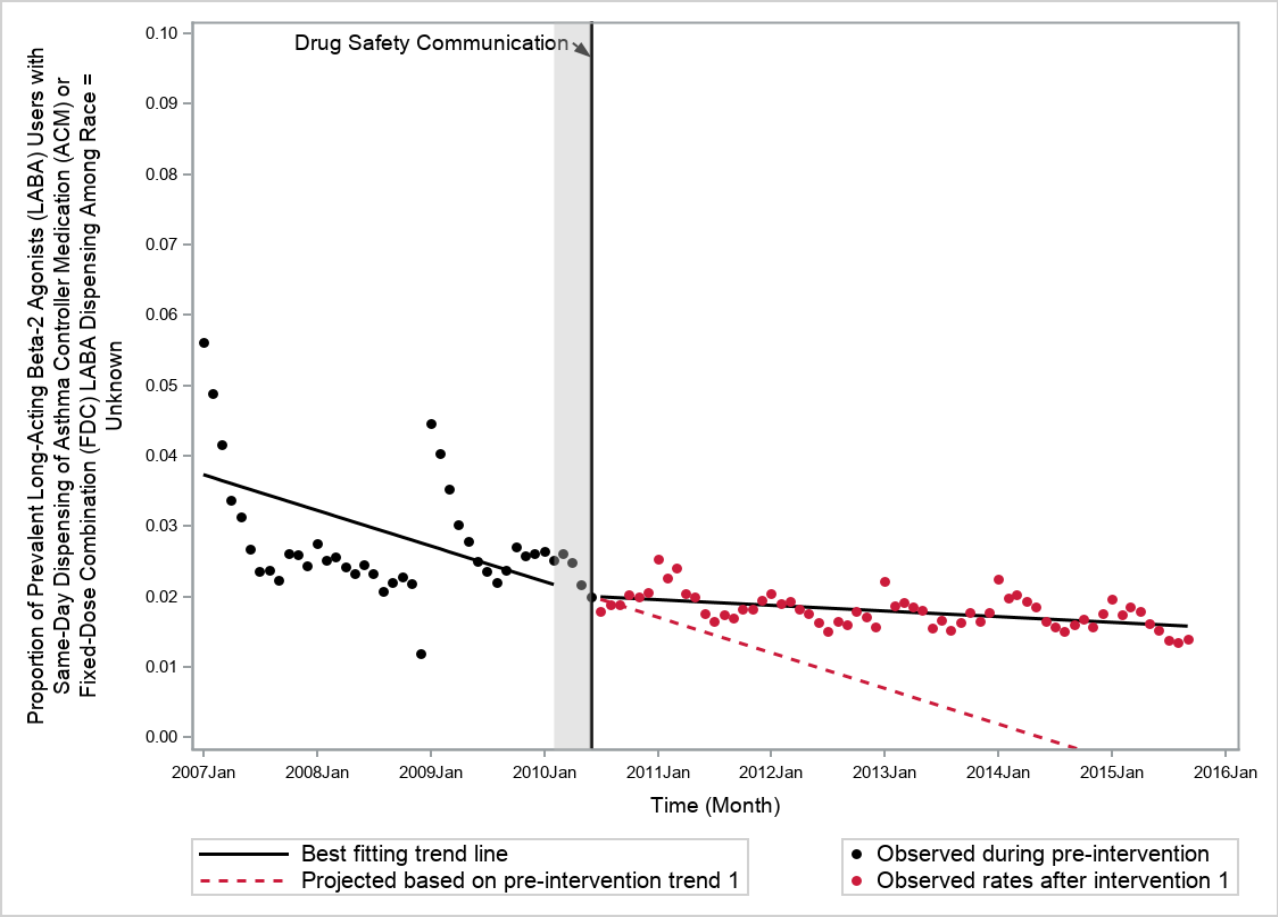
**Figure 42. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Sex = Male**




[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).

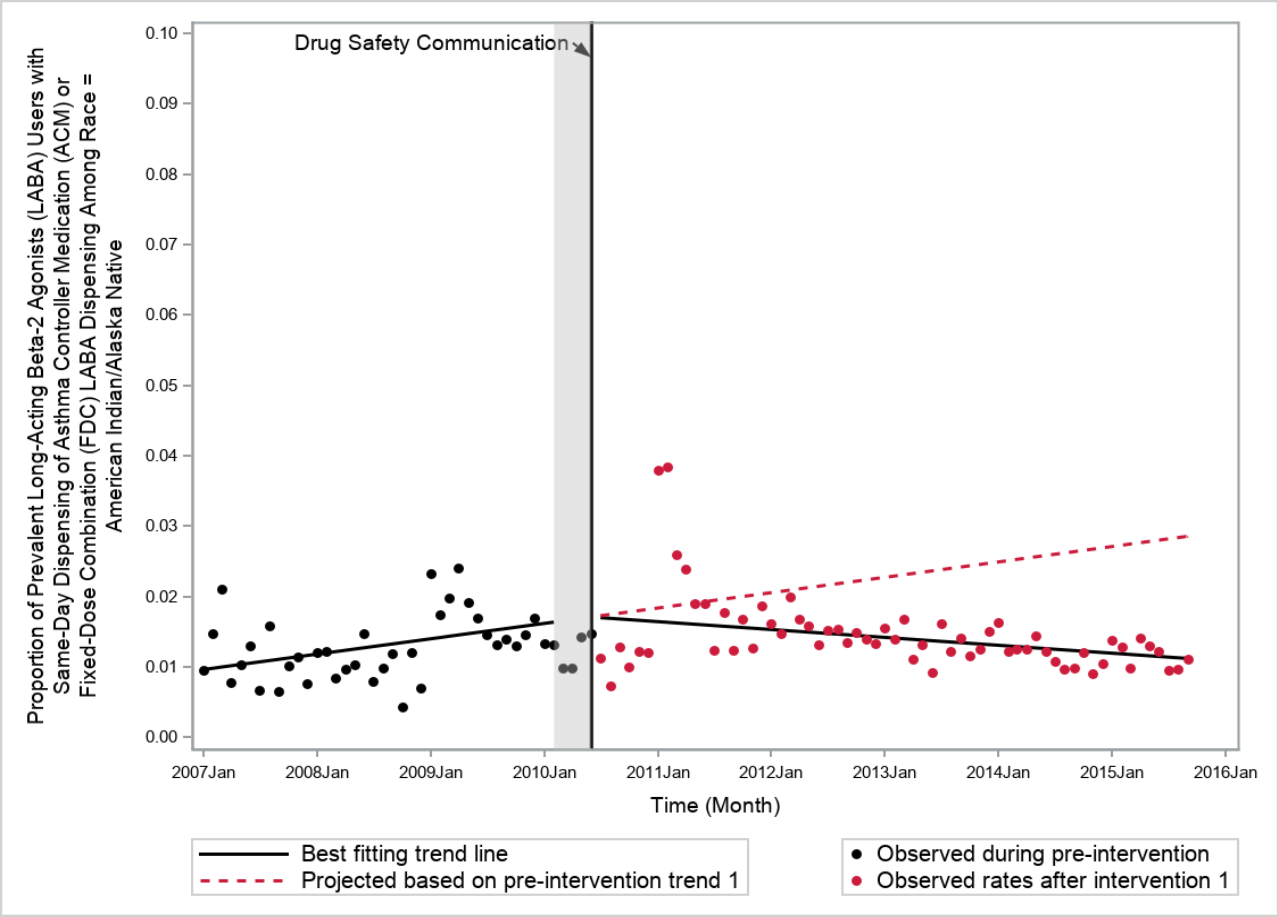
**Figure 43. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = Unknown**




[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).

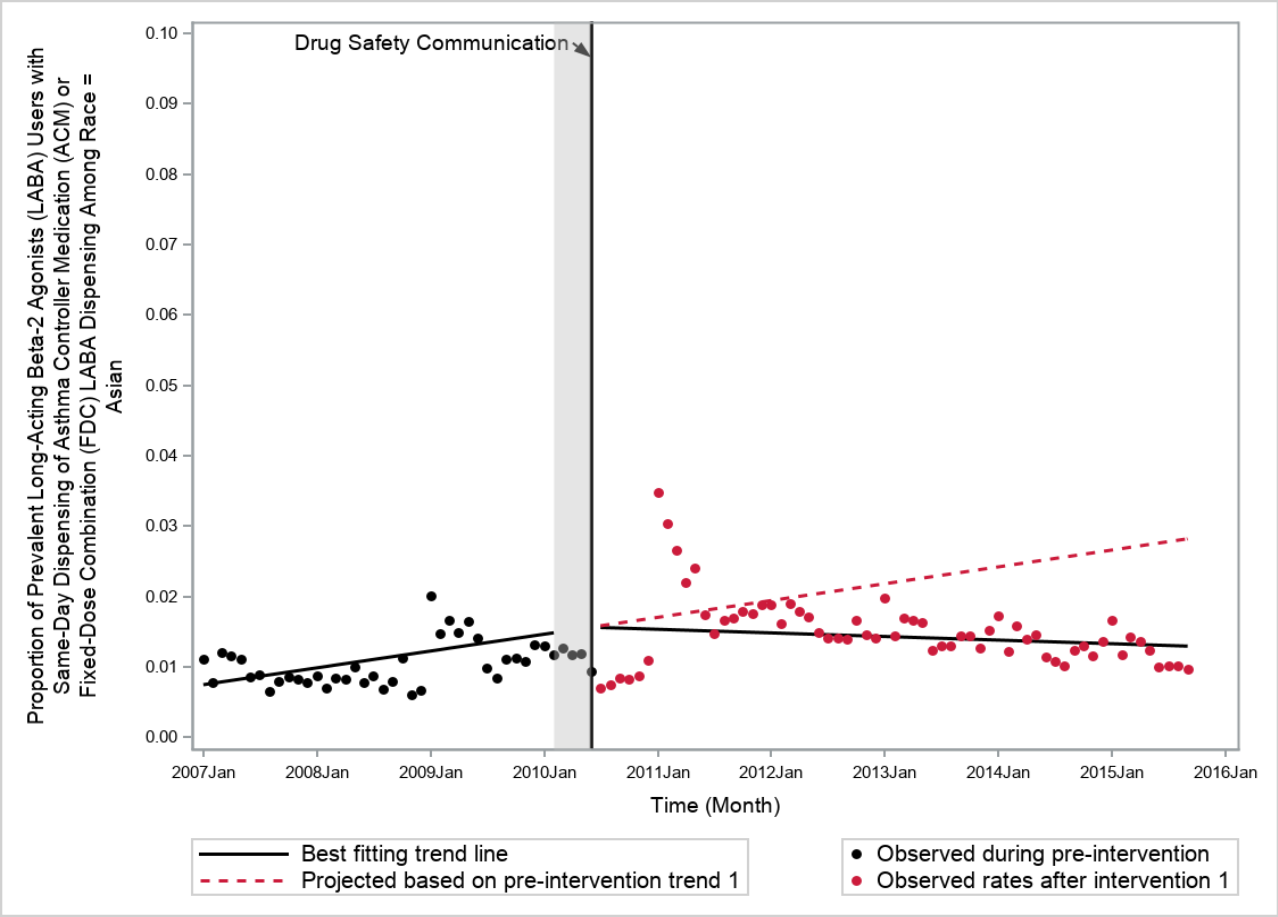
**Figure 44. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = American Indian/Alaska Native**




[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).

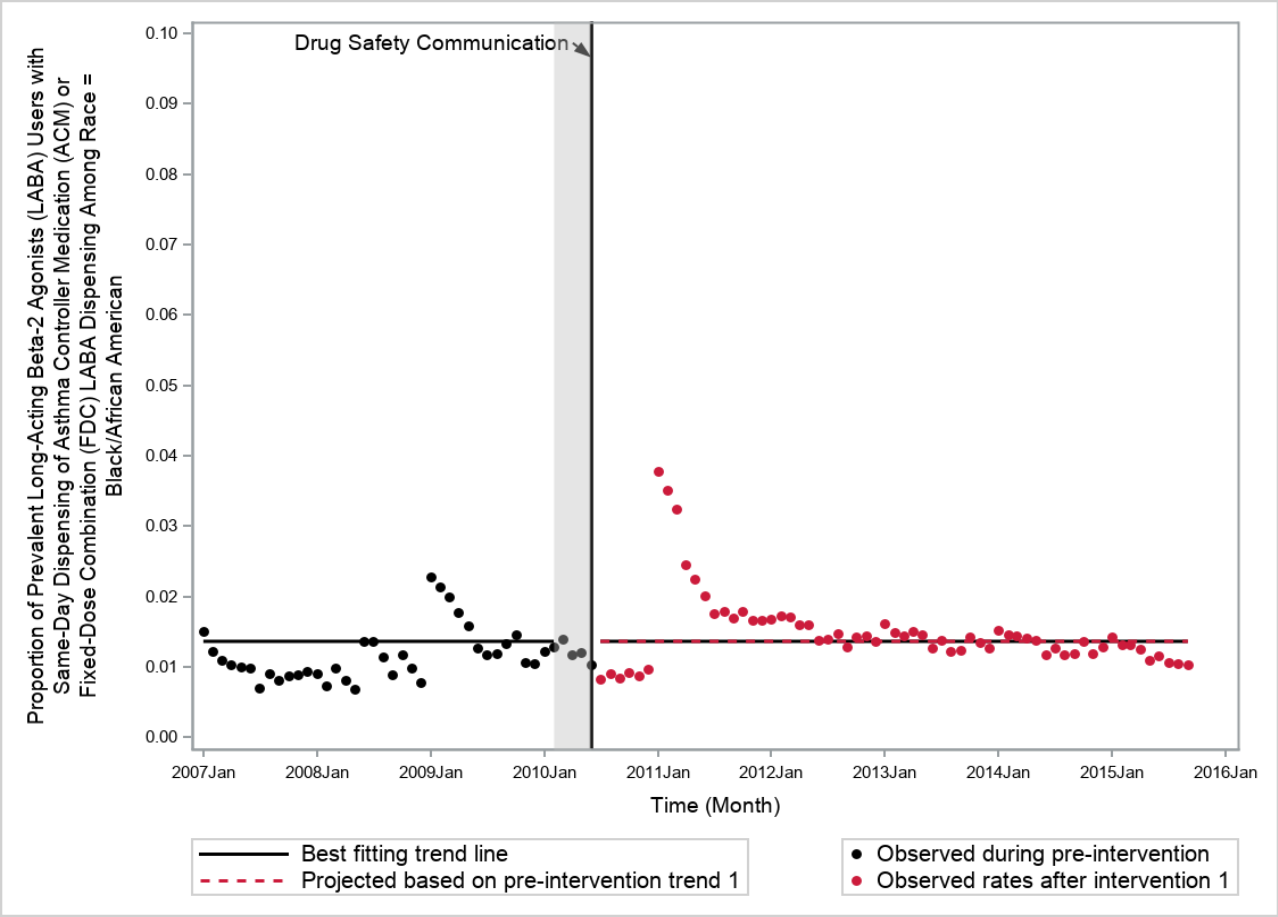
**Figure 45. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = Asian**




[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).

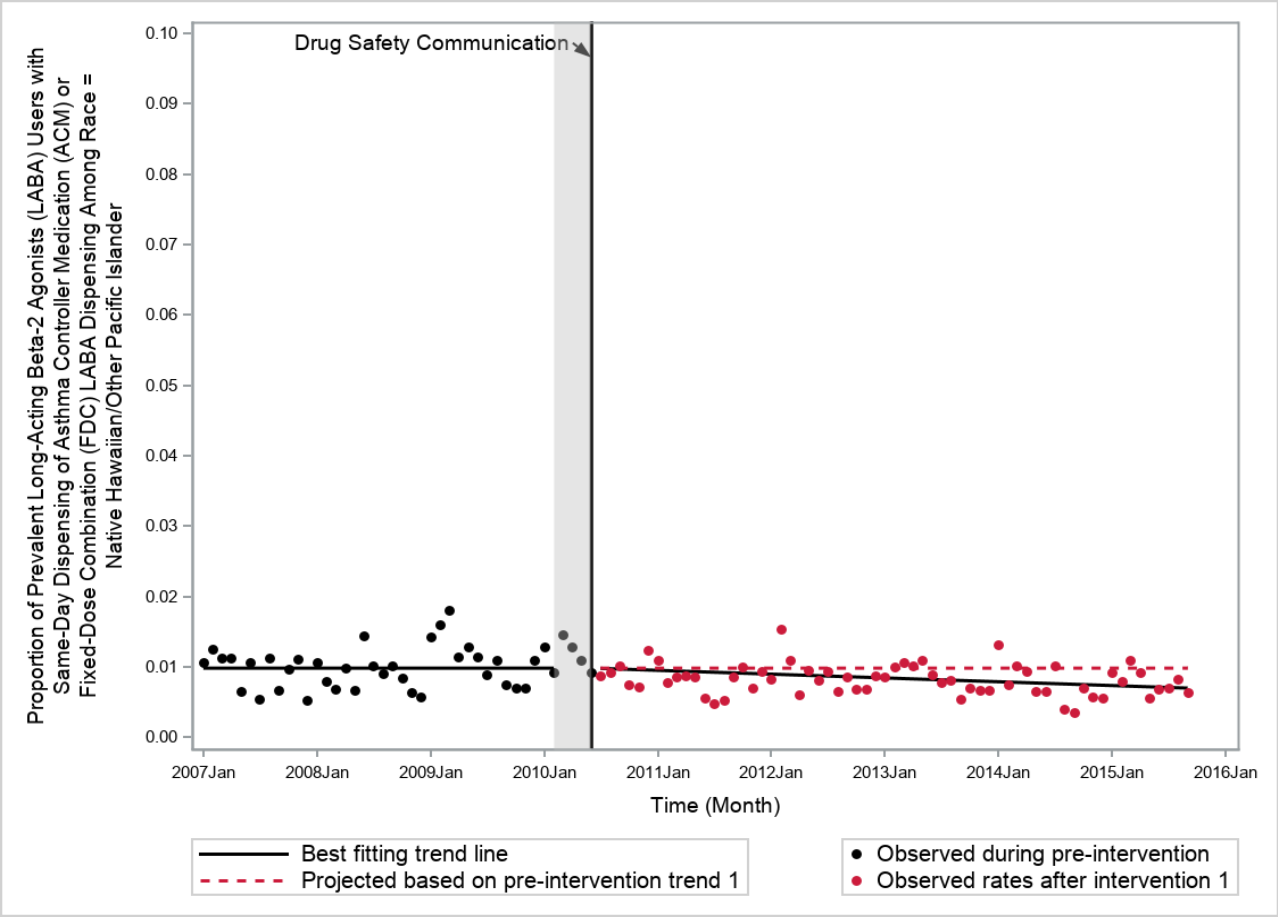
**Figure 46. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = Black/African American**




[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).

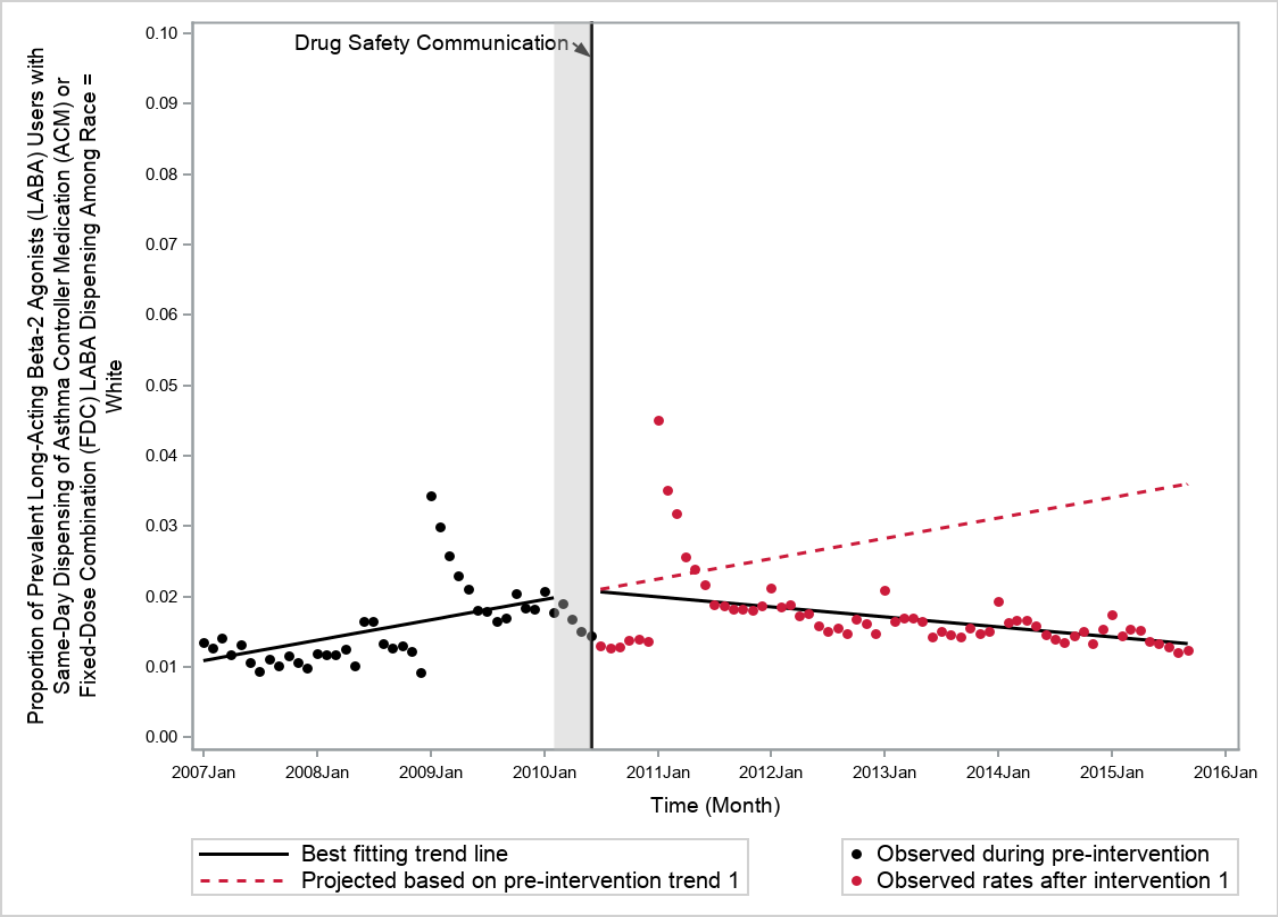
**Figure 47. Proportion of Prevalent Long-Acting Beta-2 Agonists (LABA) Users with Same-Day Dispensing of Asthma Controller Medication (ACM) or Fixed-Dose Combination (FDC) LABA Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2], where Race = Native Hawaiian/Other Pacific 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 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 |
| | **Cystic Fibrosis** | | |
| 277.0 | Cystic fibrosis | Diagnosis | ICD-9-CM |
| 277.00 | Cystic fibrosis without mention of meconium ileus | 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 |
|---|---|---|---|
| 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+ days
**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 4-6 | | |
|---|---|---|---|---|
| | | Recommendation 1<br>All LABA with ACM | | |
| | | Scenario 3 | Scenario 6 | Scenario 7 |
| ITS Analysis Groups | **Group Name** | **grp234_asthma_laba** | **grp456_acm2** | **grp456_fdc2** |
| | **ITS Group** | **Primary** | **Secondary** | |
| | **Rate Denominator Definition** | LABA-naïve 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 4-6 | | |
|---|---|---|---|---|
| | | Recommendation 1<br>All LABA with ACM | | |
| | | Scenario 3 | 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<br>*Data Partner (DP) end date<br>*Query end date | *Death<br>*DP end date<br>*Query end date | *Death<br>*DP end date<br>*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)<br>*Cystic fibrosis<br>*Bronchiectasis<br>*Pulmonary hypertension or embolism<br>*Bronchopulmonary dysplasia<br>*Congestive heart failure | | *COPD<br>*Cystic fibrosis<br>*Bronchiectasis<br>*Pulmonary hypertension or embolism<br>*Bronchopulmonary dysplasia<br>*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 4-6 | | |
|---|---|---|---|---|
| | | Recommendation 1<br>All LABA with ACM | | |
| | | Scenario 3 | 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*)<br>2 instances if (AV*, OA*) | | |
| Inclusion/ Exclusion Criteria | **Conditions** | | | |
| | **Include or Exclude** | | | |
| | **Care Setting/PDX** | | | |
| | **Lookback Period** | | | |
| | **Number of Code Occurrences** | | | |
| 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, 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+ | | |

**Appendix E. Specifications Defining Parameters for this Request**

| | | Cohorts 4-6 | | |
|---|---|---|---|---|
| | | Recommendation 1<br>All LABA with ACM | | |
| | | Scenario 3 | Scenario 6 | Scenario 7 |
| Adherence | **Adherence Name** | **Incident LABA Users 50% concurrent with ACM Use (M34_laba_50)** | | |
| | **Minimum/Maximum Episode Length or Overlap Time (Overlap)** | 50% 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** | **Incident LABA Users 75% concurrent with ACM Use (M34_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 4-6 | | |
|---|---|---|---|---|
| | | Recommendation 1<br>All LABA with ACM | | |
| | | Scenario 3 | Scenario 6 | Scenario 7 |
| Baseline Covariates | **Covariates** | SI-LABA<br>FDC<br>All LABA<br>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) days | | |
| | | | | |
| | **Covariates** | SI-LABA<br>FDC<br>All LABA<br>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 7 | | |
|---|---|---|---|---|
| | | Recommendation 1<br>All LABA with ACM, SI-LABA in ACM presence | | |
| | | Scenario 3 | Scenario 6 | Scenario 7 |
| ITS Analysis Groups | **Group Name** | **grp234_asthma_laba** | **grp456_acm2** | **grp456_fdc2** |
| | **ITS Group** | **Primary** | **Secondary** | |
| | **Rate Denominator Definition** | LABA-naïve 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<br>*DP end date<br>*Query end date | *Death<br>*DP end date<br>*Query end date | *Death<br>*DP end date<br>*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 7 | | |
|---|---|---|---|---|
| | | Recommendation 1<br>All LABA with ACM, SI-LABA in ACM presence | | |
| | | **Scenario 3** | **Scenario 6** | **Scenario 7** |
| Inclusion/Exclusion Criteria | **Conditions** | *COPD<br>*Cystic fibrosis<br>*Bronchiectasis<br>*Pulmonary hypertension or embolism<br>*Bronchopulmonary dysplasia<br>*Congestive heart failure | | *COPD<br>*Cystic fibrosis<br>*Bronchiectasis<br>*Pulmonary hypertension or embolism<br>*Bronchopulmonary dysplasia<br>*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 |
| 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*)<br>2 instances if (AV*, OA*) | | |
| Inclusion/ Exclusion Criteria | **Conditions** | | | |
| | **Include or Exclude** | | | |
| | **Care Setting/PDX** | | | |
| | **Lookback Period** | | | |
| | **Number of Code Occurrences** | | | |
| 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 |

**Appendix E. Specifications Defining Parameters for this Request**

| | | Cohort 7 | | |
|---|---|---|---|---|
| | | Recommendation 1<br>All LABA with ACM, SI-LABA in ACM presence | | |
| | | Scenario 3 | Scenario 6 | Scenario 7 |
| Multiple Events / Overlap | **Multiple Events or Overlap?** | Overlap | | |
| | **Group Identifier** | Primary | Secondary | |
| | **Observation Window Around Primary Episode** | (Index date, index date) | | |
| | **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 (M56_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 | | |

**Appendix E. Specifications Defining Parameters for this Request**

| | | Cohort 7 | | |
|---|---|---|---|---|
| | | Recommendation 1<br>All LABA with ACM, SI-LABA in ACM presence | | |
| | | Scenario 3 | Scenario 6 | Scenario 7 |
| 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 | | |
| Baseline Covariates | **Covariates** | SI-LABA<br>FDC<br>All LABA<br>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) days | | |
| | **Covariates** | SI-LABA | | |
| | **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 | | |