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).

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Overview for Request: cder_mpl2r_wp012, Report 1 of 4 (Incident Cohorts)

Request ID: cder_mpl2r_wp012_nsdp_v01

Request Description: In this request, we estimate the longitudinal trend in incident 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 1 of 4 of the incident cohort reports and focuses on longitudinal rates with the dispensing of single ingredient LABAs (SI-LABAs) as the numerator.

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 incident users of LABAs, consisting of both SI-LABAs and fixed dose combination LABAs (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 1 of 4 and contains results for cohorts 1-3.

Exposures of Interest: We defined exposure of interest as the first qualifying dispensing of any LABA product. New use is defined as having no prior use of any LABA product in the 183 days prior to index date. We defined each exposure and exposure incidence 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 1 of 4 (Incident Cohorts)

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

Report 1: In this report, we include users in cohorts 1-3 if there is SI-LABA use present on dispensing date of incident LABA use. SI-LABA use is 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. SI-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; do not have COPD, cystic fibrosis, bronchiectasis, pulmonary hypertension or embolism, or bronchopulmonary dysplasia in the 365 days prior to and including SI-LABA dispensing date; and do not have asthma in the 365 days prior to SI-LABA dispensing date. Additional differences are detailed below:

Cohort 1) SI-LABA use is not considered if ACM was dispensed on the same day. Asthma is defined as one asthma diagnosis in any care setting.
Cohort 2) SI-LABA use is not considered if in the presence of an ACM dispensing as determined by days supply. Asthma is defined as one asthma diagnosis in an IP or ED care setting or as two diagnoses in an AV or OA care setting. Asthma inclusion is also considered on SI-LABA index date.
Cohort 3) SI-LABA use is not considered if in the presence of an ACM or FDC-LABA dispensing as determined by days supply. Asthma inclusion definition is the same as in Cohort 2.

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 1) The rate used for the ITS regression model is the number of incident SI-LABA users among all incident LABA users in the absence of same-day ACMs as defined using dispensing date only.
Cohort 2) The rate used for the ITS regression model is the number of incident SI-LABA users among all incident LABA users in the absence of same-day ACMs as defined using days supply.
Cohort 3) The rate used for the ITS regression model is the number of incident SI-LABA users among LABA-naive asthma patients in the absence of same-day non-LABA ACMs or FDC-LABA as defined using days supply.

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 specifications of parameters used in the analyses for this request.

Overview for Request: cder_mpl2r_wp012, Report 1 of 4 (Incident 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.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

*all terms may not be used in this report

Table 1a. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing among Incident LABA Users 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	0.075492	(0.070663, 0.080321)	<.001
Baseline Trend	-0.001470	(-0.001656, -0.001284)	<.001
Level Change (After Intervention 1)	0.003403	(-0.001792, 0.008598)	0.197
Trend Change (After Intervention 1)	0.001341	(0.001112, 0.001570)	<.001
Most Parsimonious Final Model Parameters (df = 104)[2,3]			
Intercept	0.074530	(0.069399, 0.079661)	<.001
Baseline Trend	-0.001400	(-0.001571, -0.001229)	<.001
Trend Change (After Intervention 1)	0.001303	(0.001056, 0.001551)	<.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 Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing among Incident LABA Users 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	0.054702	(0.051713, 0.057690)	<.001
Baseline Trend	-0.001104	(-0.001223, -0.000984)	<.001
Level Change (After Intervention 1)	0.002907	(-0.000759, 0.006573)	0.119
Trend Change (After Intervention 1)	0.001011	(0.000872, 0.001150)	<.001
46-64 (df = 103)[2]			
Intercept	0.089931	(0.084192, 0.095671)	<.001
Baseline Trend	-0.001740	(-0.001969, -0.001511)	<.001
Level Change (After Intervention 1)	0.005141	(-0.001782, 0.012065)	0.144
Trend Change (After Intervention 1)	0.001525	(0.001257, 0.001793)	<.001
65+ (df = 103)[2]			
Intercept	0.127850	(0.116347, 0.139353)	<.001
Baseline Trend	-0.002713	(-0.003168, -0.002258)	<.001
Level Change (After Intervention 1)	0.014655	(0.001102, 0.028208)	0.034
Trend Change (After Intervention 1)	0.002374	(0.001834, 0.002915)	<.001
Most Parsimonious Final Model Parameters[3]			
Age Group (Years)			
18-45 (df = 104)[2]			
Intercept	0.053817	(0.050757, 0.056876)	<.001
Baseline Trend	-0.001042	(-0.001143, -0.000941)	<.001
Trend Change (After Intervention 1)	0.000978	(0.000832, 0.001124)	<.001
46-64 (df = 104)[2]			
Intercept	0.087815	(0.080769, 0.094861)	<.001
Baseline Trend	-0.001614	(-0.001848, -0.001379)	<.001
Trend Change (After Intervention 1)	0.001444	(0.001105, 0.001783)	<.001
65+ (df = 103)[2]			
Intercept	0.127850	(0.116347, 0.139353)	<.001
Baseline Trend	-0.002713	(-0.003168, -0.002258)	<.001
Level Change (After Intervention 1)	0.014655	(0.001102, 0.028208)	0.034
Trend Change (After Intervention 1)	0.002374	(0.001834, 0.002915)	<.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 Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing among Incident LABA Users 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	0.078352	(0.073424, 0.083281)	<.001
Baseline Trend	-0.001558	(-0.001751, -0.001365)	<.001
Level Change (After Intervention 1)	0.004942	(-0.000687, 0.010571)	0.085
Trend Change (After Intervention 1)	0.001414	(0.001182, 0.001647)	<.001
Male (df = 103)[2]			
Intercept	0.071167	(0.065536, 0.076797)	<.001
Baseline Trend	-0.001379	(-0.001599, -0.001159)	<.001
Level Change (After Intervention 1)	0.004123	(-0.002263, 0.010509)	0.203
Trend Change (After Intervention 1)	0.001237	(0.000971, 0.001503)	<.001
Most Parsimonious Final Model Parameters[3]			
Sex			
Female (df = 104)[2]			
Intercept	0.076979	(0.071915, 0.082042)	<.001
Baseline Trend	-0.001457	(-0.001625, -0.001289)	<.001
Trend Change (After Intervention 1)	0.001362	(0.001119, 0.001605)	<.001
Male (df = 104)[2]			
Intercept	0.069917	(0.063729, 0.076105)	<.001
Baseline Trend	-0.001290	(-0.001496, -0.001084)	<.001
Trend Change (After Intervention 1)	0.001186	(0.000888, 0.001484)	<.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 Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing among Incident LABA Users 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	0.041609	(0.039114, 0.044105)	<.001
Baseline Trend	-0.000736	(-0.000836, -0.000636)	<.001
Level Change (After Intervention 1)	0.004358	(0.001276, 0.007441)	0.006
Trend Change (After Intervention 1)	0.000595	(0.000479, 0.000711)	<.001
American Indian/Alaska Native (df = 103)[3]			
Intercept	0.279257	(0.230863, 0.327651)	<.001
Baseline Trend	-0.006559	(-0.008520, -0.004598)	<.001
Level Change (After Intervention 1)	0.036002	(-0.025016, 0.097021)	0.245
Trend Change (After Intervention 1)	0.005911	(0.003678, 0.008143)	<.001
Asian (df = 103)[3]			
Intercept	0.224484	(0.207745, 0.241222)	<.001
Baseline Trend	-0.004968	(-0.005647, -0.004290)	<.001
Level Change (After Intervention 1)	0.007149	(-0.013957, 0.028254)	0.503
Trend Change (After Intervention 1)	0.004660	(0.003887, 0.005432)	<.001
Black/African American (df = 103)[2]			
Intercept	0.142885	(0.129122, 0.156648)	<.001
Baseline Trend	-0.003065	(-0.003613, -0.002518)	<.001
Level Change (After Intervention 1)	0.005196	(-0.011341, 0.021732)	0.535
Trend Change (After Intervention 1)	0.002813	(0.002168, 0.003459)	<.001
Native Hawaiian/Other Pacific Islander (df = 103)[3]			
Intercept	0.089055	(0.058689, 0.119421)	<.001
Baseline Trend	-0.000832	(-0.002062, 0.000398)	0.183
Level Change (After Intervention 1)	-0.049108	(-0.087396, -0.010821)	0.012
Trend Change (After Intervention 1)	0.001036	(-0.000365, 0.002437)	0.146
White (df = 103)[2]			
Intercept	0.196747	(0.179495, 0.213999)	<.001
Baseline Trend	-0.004317	(-0.004960, -0.003674)	<.001
Level Change (After Intervention 1)	0.006816	(-0.009442, 0.023074)	0.408
Trend Change (After Intervention 1)	0.004147	(0.003321, 0.004974)	<.001
Most Parsimonious Final Model Parameters[4]			
Race			
Unknown (df = 103)[2]			
Intercept	0.041609	(0.039114, 0.044105)	<.001
Baseline Trend	-0.000736	(-0.000836, -0.000636)	<.001
Level Change (After Intervention 1)	0.004358	(0.001276, 0.007441)	0.006
Trend Change (After Intervention 1)	0.000595	(0.000479, 0.000711)	<.001

Table 1d. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing among Incident LABA Users in the Sentinel Distributed Database (SDD) after June 2, 2010[1], by Race

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Most Parsimonious Final Model Parameters[4]			
Race			
American Indian/Alaska Native (df = 104)[3]			
Intercept	0.268333	(0.223545, 0.313122)	<.001
Baseline Trend	-0.005797	(-0.007274, -0.004319)	<.001
Trend Change (After Intervention 1)	0.005501	(0.003376, 0.007626)	<.001
Asian (df = 104)[3]			
Intercept	0.222315	(0.206892, 0.237737)	<.001
Baseline Trend	-0.004817	(-0.005326, -0.004308)	<.001
Trend Change (After Intervention 1)	0.004578	(0.003847, 0.005310)	<.001
Black/African American (df = 104)[2]			
Intercept	0.141380	(0.124723, 0.158037)	<.001
Baseline Trend	-0.002955	(-0.003509, -0.002401)	<.001
Trend Change (After Intervention 1)	0.002752	(0.001951, 0.003552)	<.001
Native Hawaiian/Other Pacific Islander (df = 105)[3]			
Intercept	0.071168	(0.056247, 0.086090)	<.001
Level Change (After Intervention 1)	-0.059643	(-0.078906, -0.040379)	<.001
White (df = 104)[2]			
Intercept	0.194985	(0.177309, 0.212661)	<.001
Baseline Trend	-0.004181	(-0.004771, -0.003591)	<.001
Trend Change (After Intervention 1)	0.004078	(0.003223, 0.004933)	<.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]Ordinary least squares method is used to obtain the estimates here. The p-value is calculated under the assumption of asymptotic normality.

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

Table 1e. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing among Incident LABA Users 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	0.038376	(0.035820, 0.040931)	<.001
Baseline Trend	-0.000721	(-0.000822, -0.000620)	<.001
Level Change (After Intervention 1)	0.000953	(-0.002067, 0.003973)	0.533
Trend Change (After Intervention 1)	0.000646	(0.000526, 0.000766)	<.001
Most Parsimonious Final Model Parameters (df = 104)[2,3]			
Intercept	0.038036	(0.035035, 0.041036)	<.001
Baseline Trend	-0.000699	(-0.000799, -0.000599)	<.001
Trend Change (After Intervention 1)	0.000634	(0.000490, 0.000778)	<.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 Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing among Incident LABA Users 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	0.029568	(0.027652, 0.031484)	<.001
Baseline Trend	-0.000578	(-0.000655, -0.000500)	<.001
Level Change (After Intervention 1)	0.000708	(-0.001708, 0.003124)	0.562
Trend Change (After Intervention 1)	0.000524	(0.000435, 0.000612)	<.001
46-64 (df = 103)[3]			
Intercept	0.042974	(0.039644, 0.046305)	<.001
Baseline Trend	-0.000791	(-0.000925, -0.000657)	<.001
Level Change (After Intervention 1)	0.001311	(-0.002798, 0.005420)	0.528
Trend Change (After Intervention 1)	0.000678	(0.000523, 0.000833)	<.001
65+ (df = 103)[2]			
Intercept	0.069907	(0.063376, 0.076438)	<.001
Baseline Trend	-0.001460	(-0.001725, -0.001196)	<.001
Level Change (After Intervention 1)	0.005499	(-0.002736, 0.013734)	0.188
Trend Change (After Intervention 1)	0.001302	(0.001000, 0.001603)	<.001
Most Parsimonious Final Model Parameters[4]			
Age Group (Years)			
18-45 (df = 104)[2]			
Intercept	0.029353	(0.027589, 0.031118)	<.001
Baseline Trend	-0.000563	(-0.000621, -0.000504)	<.001
Trend Change (After Intervention 1)	0.000516	(0.000432, 0.000600)	<.001
46-64 (df = 104)[3]			
Intercept	0.042580	(0.039438, 0.045722)	<.001
Baseline Trend	-0.000764	(-0.000868, -0.000660)	<.001
Trend Change (After Intervention 1)	0.000663	(0.000513, 0.000813)	<.001
65+ (df = 104)[2]			
Intercept	0.068239	(0.062183, 0.074295)	<.001
Baseline Trend	-0.001344	(-0.001544, -0.001144)	<.001
Trend Change (After Intervention 1)	0.001239	(0.000952, 0.001526)	<.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]Ordinary least squares method is used to obtain the estimates here. The p-value is calculated under the assumption of asymptotic normality.

[3]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.

[4]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 Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing among Incident LABA Users 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	0.039206	(0.036658, 0.041754)	<.001
Baseline Trend	-0.000750	(-0.000853, -0.000647)	<.001
Level Change (After Intervention 1)	0.001468	(-0.001705, 0.004642)	0.361
Trend Change (After Intervention 1)	0.000670	(0.000552, 0.000788)	<.001
Male (df = 103)[3]			
Intercept	0.039010	(0.036123, 0.041896)	<.001
Baseline Trend	-0.000768	(-0.000885, -0.000651)	<.001
Level Change (After Intervention 1)	0.003076	(-0.000563, 0.006716)	0.097
Trend Change (After Intervention 1)	0.000680	(0.000547, 0.000813)	<.001
Most Parsimonious Final Model Parameters[4]			
Sex			
Female (df = 104)[2]			
Intercept	0.038765	(0.036378, 0.041151)	<.001
Baseline Trend	-0.000719	(-0.000798, -0.000640)	<.001
Trend Change (After Intervention 1)	0.000653	(0.000540, 0.000767)	<.001
Male (df = 104)[2]			
Intercept	0.038225	(0.034928, 0.041521)	<.001
Baseline Trend	-0.000707	(-0.000816, -0.000598)	<.001
Trend Change (After Intervention 1)	0.000649	(0.000492, 0.000806)	<.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]Ordinary least squares method is used to obtain the estimates here. The p-value is calculated under the assumption of asymptotic normality.

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

Table 1h. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing among Incident LABA Users 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	0.024087	(0.022127, 0.026048)	<.001
Baseline Trend	-0.000422	(-0.000501, -0.000343)	<.001
Level Change (After Intervention 1)	0.000926	(-0.001503, 0.003355)	0.451
Trend Change (After Intervention 1)	0.000356	(0.000265, 0.000448)	<.001
American Indian/Alaska Native (df = 103)[3]			
Intercept	0.039352	(0.007540, 0.071165)	0.016
Baseline Trend	-0.000071	(-0.001360, 0.001218)	0.913
Level Change (After Intervention 1)	-0.000696	(-0.040807, 0.039415)	0.973
Trend Change (After Intervention 1)	-0.000622	(-0.002090, 0.000845)	0.402
Asian (df = 103)[2]			
Intercept	0.099833	(0.090095, 0.109570)	<.001
Baseline Trend	-0.002222	(-0.002617, -0.001827)	<.001
Level Change (After Intervention 1)	0.005807	(-0.006507, 0.018122)	0.352
Trend Change (After Intervention 1)	0.002027	(0.001580, 0.002474)	<.001
Black/African American (df = 103)[2]			
Intercept	0.053373	(0.047316, 0.059430)	<.001
Baseline Trend	-0.000846	(-0.001092, -0.000599)	<.001
Level Change (After Intervention 1)	-0.009402	(-0.017109, -0.001695)	0.017
Trend Change (After Intervention 1)	0.000758	(0.000482, 0.001034)	<.001
Native Hawaiian/Other Pacific Islander (df = 103)[3]			
Intercept	0.018350	(-0.004522, 0.041222)	0.115
Baseline Trend	0.000514	(-0.000413, 0.001441)	0.274
Level Change (After Intervention 1)	-0.034071	(-0.062909, -0.005233)	0.021
Trend Change (After Intervention 1)	-0.000399	(-0.001454, 0.000656)	0.455
White (df = 103)[3]			
Intercept	0.084852	(0.079752, 0.089953)	<.001
Baseline Trend	-0.001838	(-0.002044, -0.001631)	<.001
Level Change (After Intervention 1)	0.006119	(-0.000312, 0.012549)	0.062
Trend Change (After Intervention 1)	0.001689	(0.001454, 0.001924)	<.001
Most Parsimonious Final Model Parameters[4]			
Race			
Unknown (df = 104)[2]			
Intercept	0.023802	(0.021945, 0.025658)	<.001
Baseline Trend	-0.000402	(-0.000464, -0.000341)	<.001
Trend Change (After Intervention 1)	0.000346	(0.000257, 0.000434)	<.001
American Indian/Alaska Native (df = 105)[3]			
Intercept	0.037245	(0.024010, 0.050480)	<.001
Trend Change (After Intervention 1)	-0.000731	(-0.001195, -0.000266)	0.002

Table 1h. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing among Incident LABA Users in the Sentinel Distributed Database (SDD) after June 2, 2010[1], by Race

	Beta Estimate	95% Confidence Interval	Approximate P-Value
Most Parsimonious Final Model Parameters[4]			
Race			
Asian (df = 104)[2]			
Intercept	0.098039	(0.089049, 0.107030)	<.001
Baseline Trend	-0.002098	(-0.002394, -0.001802)	<.001
Trend Change (After Intervention 1)	0.001961	(0.001535, 0.002386)	<.001
Black/African American (df = 103)[2]			
Intercept	0.053373	(0.047316, 0.059430)	<.001
Baseline Trend	-0.000846	(-0.001092, -0.000599)	<.001
Level Change (After Intervention 1)	-0.009402	(-0.017109, -0.001695)	0.017
Trend Change (After Intervention 1)	0.000758	(0.000482, 0.001034)	<.001
Native Hawaiian/Other Pacific Islander (df = 105)[3]			
Intercept	0.029400	(0.018203, 0.040598)	<.001
Level Change (After Intervention 1)	-0.019865	(-0.034321, -0.005409)	0.008
White (df = 104)[3]			
Intercept	0.082996	(0.078226, 0.087766)	<.001
Baseline Trend	-0.001708	(-0.001866, -0.001551)	<.001
Trend Change (After Intervention 1)	0.001619	(0.001393, 0.001846)	<.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]Ordinary least squares method is used to obtain the estimates here. The p-value is calculated under the assumption of asymptotic normality.

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

Table 1i. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (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	0.000446	(0.000419, 0.000473)	<.001
Baseline Trend	-0.000008	(-0.000009, -0.000007)	<.001
Level Change (After Intervention 1)	-0.000004	(-0.000036, 0.000029)	0.829
Trend Change (After Intervention 1)	0.000007	(0.000006, 0.000008)	<.001
Most Parsimonious Final Model Parameters (df = 104)[2,3]			
Intercept	0.000447	(0.000422, 0.000472)	<.001
Baseline Trend	-0.000008	(-0.000009, -0.000007)	<.001
Trend Change (After Intervention 1)	0.000007	(0.000006, 0.000008)	<.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 Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (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	0.000326	(0.000307, 0.000346)	<.001
Baseline Trend	-0.000006	(-0.000007, -0.000005)	<.001
Level Change (After Intervention 1)	-0.000006	(-0.000030, 0.000019)	0.638
Trend Change (After Intervention 1)	0.000006	(0.000005, 0.000006)	<.001
46-64 (df = 103)[2]			
Intercept	0.000560	(0.000522, 0.000598)	<.001
Baseline Trend	-0.000010	(-0.000011, -0.000008)	<.001
Level Change (After Intervention 1)	-0.000009	(-0.000058, 0.000039)	0.698
Trend Change (After Intervention 1)	0.000008	(0.000006, 0.000010)	<.001
65+ (df = 103)[3]			
Intercept	0.000608	(0.000559, 0.000657)	<.001
Baseline Trend	-0.000012	(-0.000014, -0.000010)	<.001
Level Change (After Intervention 1)	0.000028	(-0.000034, 0.000090)	0.364
Trend Change (After Intervention 1)	0.000011	(0.000008, 0.000013)	<.001
Most Parsimonious Final Model Parameters[4]			
Age Group (Years)			
18-45 (df = 104)[2]			
Intercept	0.000328	(0.000310, 0.000346)	<.001
Baseline Trend	-0.000006	(-0.000007, -0.000006)	<.001
Trend Change (After Intervention 1)	0.000006	(0.000005, 0.000006)	<.001
46-64 (df = 104)[2]			
Intercept	0.000563	(0.000528, 0.000598)	<.001
Baseline Trend	-0.000010	(-0.000011, -0.000009)	<.001
Trend Change (After Intervention 1)	0.000008	(0.000007, 0.000010)	<.001
65+ (df = 104)[3]			
Intercept	0.000599	(0.000554, 0.000644)	<.001
Baseline Trend	-0.000011	(-0.000013, -0.000010)	<.001
Trend Change (After Intervention 1)	0.000010	(0.000008, 0.000012)	<.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]Ordinary least squares method is used to obtain the estimates here. The p-value is calculated under the assumption of asymptotic normality.

[3]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.

[4]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 Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (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	0.000444	(0.000421, 0.000467)	<.001
Baseline Trend	-0.000008	(-0.000009, -0.000007)	<.001
Level Change (After Intervention 1)	-0.000002	(-0.000031, 0.000027)	0.882
Trend Change (After Intervention 1)	0.000007	(0.000006, 0.000008)	<.001
Male (df = 103)[2]			
Intercept	0.000462	(0.000427, 0.000498)	<.001
Baseline Trend	-0.000009	(-0.000010, -0.000007)	<.001
Level Change (After Intervention 1)	0.000012	(-0.000033, 0.000057)	0.586
Trend Change (After Intervention 1)	0.000008	(0.000006, 0.000009)	<.001
Most Parsimonious Final Model Parameters[3]			
Sex			
Female (df = 104)[2]			
Intercept	0.000444	(0.000423, 0.000466)	<.001
Baseline Trend	-0.000008	(-0.000009, -0.000007)	<.001
Trend Change (After Intervention 1)	0.000007	(0.000006, 0.000008)	<.001
Male (df = 104)[2]			
Intercept	0.000459	(0.000426, 0.000492)	<.001
Baseline Trend	-0.000008	(-0.000010, -0.000007)	<.001
Trend Change (After Intervention 1)	0.000008	(0.000006, 0.000009)	<.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. Ordinary least squares method is used to obtain the estimates here. The p-value is calculated under the assumption of asymptotic normality.

Table 1l. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (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	0.000355	(0.000336, 0.000374)	<.001
Baseline Trend	-0.000006	(-0.000007, -0.000006)	<.001
Level Change (After Intervention 1)	0.000005	(-0.000019, 0.000029)	0.659
Trend Change (After Intervention 1)	0.000006	(0.000005, 0.000006)	<.001
American Indian/Alaska Native (df = 103)[3]			
Intercept	0.000268	(0.000007, 0.000529)	0.044
Baseline Trend	0.000004	(-0.000006, 0.000015)	0.427
Level Change (After Intervention 1)	-0.000227	(-0.000556, 0.000102)	0.175
Trend Change (After Intervention 1)	-0.000008	(-0.000020, 0.000004)	0.175
Asian (df = 103)[2]			
Intercept	0.000674	(0.000622, 0.000726)	<.001
Baseline Trend	-0.000014	(-0.000017, -0.000012)	<.001
Level Change (After Intervention 1)	0.000025	(-0.000040, 0.000091)	0.446
Trend Change (After Intervention 1)	0.000013	(0.000011, 0.000016)	<.001
Black/African American (df = 103)[2]			
Intercept	0.000351	(0.000313, 0.000389)	<.001
Baseline Trend	-0.000004	(-0.000006, -0.000003)	<.001
Level Change (After Intervention 1)	-0.000097	(-0.000146, -0.000049)	<.001
Trend Change (After Intervention 1)	0.000004	(0.000002, 0.000006)	<.001
Native Hawaiian/Other Pacific Islander (df = 103)[3]			
Intercept	0.000125	(-0.000024, 0.000274)	0.099
Baseline Trend	0.000004	(-0.000002, 0.000010)	0.177
Level Change (After Intervention 1)	-0.000247	(-0.000435, -0.000059)	0.011
Trend Change (After Intervention 1)	-0.000004	(-0.000011, 0.000003)	0.246
White (df = 103)[2]			
Intercept	0.000649	(0.000596, 0.000701)	<.001
Baseline Trend	-0.000012	(-0.000015, -0.000010)	<.001
Level Change (After Intervention 1)	0.000013	(-0.000051, 0.000076)	0.694
Trend Change (After Intervention 1)	0.000011	(0.000009, 0.000014)	<.001
Most Parsimonious Final Model Parameters[4]			
Race			
Unknown (df = 104)[2]			
Intercept	0.000353	(0.000336, 0.000371)	<.001
Baseline Trend	-0.000006	(-0.000007, -0.000006)	<.001
Trend Change (After Intervention 1)	0.000005	(0.000005, 0.000006)	<.001

Table 1l. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (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[4]			
Race			
American Indian/Alaska Native (df = 105)[3]			
Intercept	0.000322	(0.000213, 0.000432)	<.001
Trend Change (After Intervention 1)	-0.000006	(-0.000010, -0.000003)	0.001
Asian (df = 104)[2]			
Intercept	0.000666	(0.000618, 0.000714)	<.001
Baseline Trend	-0.000014	(-0.000016, -0.000012)	<.001
Trend Change (After Intervention 1)	0.000013	(0.000011, 0.000015)	<.001
Black/African American (df = 103)[2]			
Intercept	0.000351	(0.000313, 0.000389)	<.001
Baseline Trend	-0.000004	(-0.000006, -0.000003)	<.001
Level Change (After Intervention 1)	-0.000097	(-0.000146, -0.000049)	<.001
Trend Change (After Intervention 1)	0.000004	(0.000002, 0.000006)	<.001
Native Hawaiian/Other Pacific Islander (df = 105)[3]			
Intercept	0.000214	(0.000141, 0.000288)	<.001
Level Change (After Intervention 1)	-0.000159	(-0.000253, -0.000064)	0.001
White (df = 104)[2]			
Intercept	0.000645	(0.000596, 0.000694)	<.001
Baseline Trend	-0.000012	(-0.000014, -0.000011)	<.001
Trend Change (After Intervention 1)	0.000011	(0.000009, 0.000013)	<.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]Ordinary least squares method is used to obtain the estimates here. The p-value is calculated under the assumption of asymptotic normality.

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

Table 2a. Absolute and Relative Changes in Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing among Incident LABA Users 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	0.007820	(0.006353, 0.009286)	0.015170	0.007350
Relative Change (Percent) at 6 Months after Intervention 1	106.40	(24.06, 188.74)	0.015170	0.007350
Absolute Change at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A

[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 Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing among Incident LABA Users after in the Sentinel Distributed Database (SDD) June 2, 2010[1] Compared with Expected Rates Derived from Baseline Trend, by Age Group

Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Age Group (Years)				
18-45				
Absolute Change at 6 Months after Intervention 1	0.005867	(0.005001, 0.006733)	0.009674	0.003807
Relative Change (Percent) at 6 Months after Intervention 1	154.10	(29.89, 278.30)	0.009674	0.003807
Absolute Change at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
46-64				
Absolute Change at 6 Months after Intervention 1	0.008664	(0.006651, 0.010677)	0.019021	0.010356
Relative Change (Percent) at 6 Months after Intervention 1	83.66	(16.74, 150.58)	0.019021	0.010356
Absolute Change at 12 Months after Intervention 1	0.017328	(0.013302, 0.021355)	0.018003	0.000674
Relative Change (Percent) at 12 Months after Intervention 1	2570.66	(-25586.8, 30728.13)	0.018003	0.000674
65+				
Absolute Change at 6 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 6 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A

[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 Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing among Incident LABA Users 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	0.008172	(0.006731, 0.009613)	0.015225	0.007052
Relative Change (Percent) at 6 Months after Intervention 1	115.88	(26.43, 205.32)	0.015225	0.007052
Absolute Change at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Male				
Absolute Change at 6 Months after Intervention 1	0.007115	(0.005340, 0.008889)	0.015105	0.007991
Relative Change (Percent) at 6 Months after Intervention 1	89.04	(8.80, 169.28)	0.015105	0.007991
Absolute Change at 12 Months after Intervention 1	0.014230	(0.010681, 0.017778)	0.014480	0.000250
Relative Change (Percent) at 12 Months after Intervention 1	5692.48	(-141319, 152703.8)	0.014480	0.000250

[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 Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing among Incident LABA Users 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	0.007928	(0.004574, 0.011281)	0.014207	0.006279
Relative Change (Percent) at 6 Months after Intervention 1	126.26	(18.39, 234.12)	0.014207	0.006279
Absolute Change at 12 Months after Intervention 1	0.011497	(0.007763, 0.015231)	0.013360	0.001863
Relative Change (Percent) at 12 Months after Intervention 1	617.19	(-717.51, 1951.89)	0.013360	0.001863
American Indian/Alaska Native				
Absolute Change at 6 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 6 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Asian				
Absolute Change at 6 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 6 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Black/African American				
Absolute Change at 6 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 6 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Native Hawaiian/Other Pacific Islander				
Absolute Change at 6 Months after Intervention 1	-0.059643	(-0.078684, -0.040601)	0.011526	0.071168
Relative Change (Percent) at 6 Months after Intervention 1	-83.81	(-101.06, -66.55)	0.011526	0.071168
Absolute Change at 12 Months after Intervention 1	-0.059643	(-0.078684, -0.040601)	0.011526	0.071168
Relative Change (Percent) at 12 Months after Intervention 1	-83.81	(-101.06, -66.55)	0.011526	0.071168

Table 2d. Absolute and Relative Changes in Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing among Incident LABA Users 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	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 6 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A

[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 Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing among Incident LABA Users 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	0.003802	(0.002946, 0.004658)	0.008290	0.004488
Relative Change (Percent) at 6 Months after Intervention 1	84.73	(18.49, 150.96)	0.008290	0.004488
Absolute Change at 12 Months after Intervention 1	0.007604	(0.005891, 0.009317)	0.007898	0.000294
Relative Change (Percent) at 12 Months after Intervention 1	2586.56	(-25016.0, 30189.12)	0.007898	0.000294

[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 Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing among Incident LABA Users 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	0.003094	(0.002598, 0.003591)	0.005446	0.002352
Relative Change (Percent) at 6 Months after Intervention 1	131.59	(31.08, 232.10)	0.005446	0.002352
Absolute Change at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
46-64				
Absolute Change at 6 Months after Intervention 1	0.003976	(0.003088, 0.004864)	0.009907	0.005931
Relative Change (Percent) at 6 Months after Intervention 1	67.04	(23.44, 110.64)	0.009907	0.005931
Absolute Change at 12 Months after Intervention 1	0.007952	(0.006175, 0.009729)	0.009302	0.001350
Relative Change (Percent) at 12 Months after Intervention 1	589.24	(-908.05, 2086.52)	0.009302	0.001350
65+				
Absolute Change at 6 Months after Intervention 1	0.007434	(0.005730, 0.009138)	0.011177	0.003743
Relative Change (Percent) at 6 Months after Intervention 1	198.62	(-106.74, 503.98)	0.011177	0.003743
Absolute Change at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A

[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 Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing among Incident LABA Users 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	0.003921	(0.003247, 0.004594)	0.008184	0.004263
Relative Change (Percent) at 6 Months after Intervention 1	91.97	(34.71, 149.23)	0.008184	0.004263
Absolute Change at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Male				
Absolute Change at 6 Months after Intervention 1	0.003895	(0.002962, 0.004827)	0.008196	0.004301
Relative Change (Percent) at 6 Months after Intervention 1	90.54	(12.62, 168.46)	0.008196	0.004301
Absolute Change at 12 Months after Intervention 1	0.007789	(0.005925, 0.009654)	0.007850	0.000061
Relative Change (Percent) at 12 Months after Intervention 1	12799.10	(-683857, 709455.5)	0.007850	0.000061

[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 Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing among Incident LABA Users 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	0.002074	(0.001550, 0.002599)	0.006575	0.004501
Relative Change (Percent) at 6 Months after Intervention 1	46.09	(19.31, 72.87)	0.006575	0.004501
Absolute Change at 12 Months after Intervention 1	0.004149	(0.003100, 0.005197)	0.006237	0.002088
Relative Change (Percent) at 12 Months after Intervention 1	198.68	(-25.40, 422.77)	0.006237	0.002088
American Indian/Alaska Native				
Absolute Change at 6 Months after Intervention 1	-0.004383	(-0.007137, -0.001630)	0.032861	0.037245
Relative Change (Percent) at 6 Months after Intervention 1	-11.77	(-17.30, -6.24)	0.032861	0.037245
Absolute Change at 12 Months after Intervention 1	-0.008767	(-0.014273, -0.003260)	0.028478	0.037245
Relative Change (Percent) at 12 Months after Intervention 1	-23.54	(-34.60, -12.48)	0.028478	0.037245
Asian				
Absolute Change at 6 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 6 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Black/African American				
Absolute Change at 6 Months after Intervention 1	-0.004854	(-0.013166, 0.003458)	0.007920	0.012774
Relative Change (Percent) at 6 Months after Intervention 1	-38.00	(-85.96, 9.96)	0.007920	0.012774
Absolute Change at 12 Months after Intervention 1	-0.000306	(-0.009546, 0.008933)	0.007393	0.007699
Relative Change (Percent) at 12 Months after Intervention 1	-3.98	(-119.97, 112.02)	0.007393	0.007699
Native Hawaiian/Other Pacific Islander				
Absolute Change at 6 Months after Intervention 1	-0.019865	(-0.034154, -0.005575)	0.009535	0.029400
Relative Change (Percent) at 6 Months after Intervention 1	-67.57	(-100.64, -34.49)	0.009535	0.029400
Absolute Change at 12 Months after Intervention 1	-0.019865	(-0.034154, -0.005575)	0.009535	0.029400
Relative Change (Percent) at 12 Months after Intervention 1	-67.57	(-100.64, -34.49)	0.009535	0.029400

Table 2h. Absolute and Relative Changes in Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing among Incident LABA Users 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	0.009715	(0.008373, 0.011057)	0.010714	0.000999
Relative Change (Percent) at 6 Months after Intervention 1	972.38	(-2954.18, 4898.94)	0.010714	0.000999
Absolute Change at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A

[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 Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (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	0.000043	(0.000036, 0.000050)	0.000097	0.000054
Relative Change (Percent) at 6 Months after Intervention 1	80.01	(37.26, 122.77)	0.000097	0.000054
Absolute Change at 12 Months after Intervention 1	0.000086	(0.000072, 0.000100)	0.000091	0.000005
Relative Change (Percent) at 12 Months after Intervention 1	1823.53	(-8019.36, 11666.43)	0.000091	0.000005

[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 Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (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	0.000033	(0.000028, 0.000039)	0.000059	0.000026
Relative Change (Percent) at 6 Months after Intervention 1	129.52	(37.98, 221.07)	0.000059	0.000026
Absolute Change at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
46-64				
Absolute Change at 6 Months after Intervention 1	0.000050	(0.000040, 0.000060)	0.000133	0.000083
Relative Change (Percent) at 6 Months after Intervention 1	60.33	(27.99, 92.67)	0.000133	0.000083
Absolute Change at 12 Months after Intervention 1	0.000100	(0.000080, 0.000120)	0.000123	0.000023
Relative Change (Percent) at 12 Months after Intervention 1	438.81	(-315.49, 1193.10)	0.000123	0.000023
65+				
Absolute Change at 6 Months after Intervention 1	0.000062	(0.000049, 0.000074)	0.000117	0.000055
Relative Change (Percent) at 6 Months after Intervention 1	111.71	(15.63, 207.79)	0.000117	0.000055
Absolute Change at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A

[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 Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (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	0.000043	(0.000037, 0.000049)	0.000097	0.000054
Relative Change (Percent) at 6 Months after Intervention 1	78.62	(42.95, 114.29)	0.000097	0.000054
Absolute Change at 12 Months after Intervention 1	0.000085	(0.000073, 0.000097)	0.000091	0.000005
Relative Change (Percent) at 12 Months after Intervention 1	1570.92	(-4732.82, 7874.65)	0.000091	0.000005
Male				
Absolute Change at 6 Months after Intervention 1	0.000045	(0.000036, 0.000055)	0.000096	0.000051
Relative Change (Percent) at 6 Months after Intervention 1	88.52	(25.21, 151.83)	0.000096	0.000051
Absolute Change at 12 Months after Intervention 1	0.000091	(0.000072, 0.000109)	0.000091	0.000000
Relative Change (Percent) at 12 Months after Intervention 1	38145.90	(-5174015, 5250307)	0.000091	0.000000

[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 Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (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

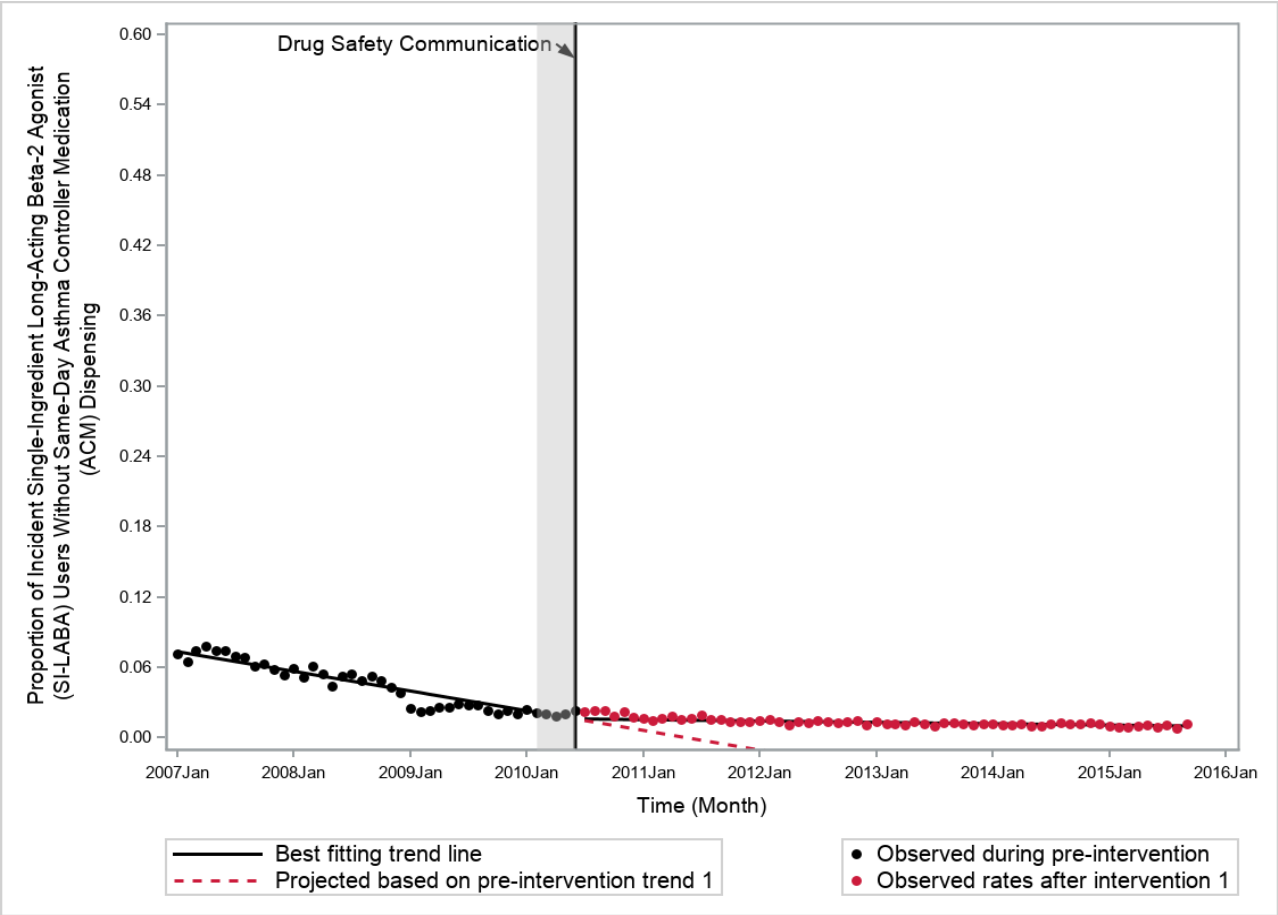
Outcome Measure	Beta Estimate	95% Confidence Interval	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Race				
Unknown				
Absolute Change at 6 Months after Intervention 1	0.000033	(0.000028, 0.000038)	0.000082	0.000049
Relative Change (Percent) at 6 Months after Intervention 1	67.51	(38.69, 96.32)	0.000082	0.000049
Absolute Change at 12 Months after Intervention 1	0.000066	(0.000056, 0.000076)	0.000077	0.000011
Relative Change (Percent) at 12 Months after Intervention 1	615.08	(-446.26, 1676.42)	0.000077	0.000011
American Indian/Alaska Native				
Absolute Change at 6 Months after Intervention 1	-0.000039	(-0.000061, -0.000016)	0.000283	0.000322
Relative Change (Percent) at 6 Months after Intervention 1	-12.01	(-17.29, -6.73)	0.000283	0.000322
Absolute Change at 12 Months after Intervention 1	-0.000077	(-0.000123, -0.000032)	0.000245	0.000322
Relative Change (Percent) at 12 Months after Intervention 1	-24.03	(-34.58, -13.47)	0.000245	0.000322
Asian				
Absolute Change at 6 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 6 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Black/African American				
Absolute Change at 6 Months after Intervention 1	-0.000075	(-0.000127, -0.000022)	0.000067	0.000142
Relative Change (Percent) at 6 Months after Intervention 1	-52.64	(-76.64, -28.65)	0.000067	0.000142
Absolute Change at 12 Months after Intervention 1	-0.000052	(-0.000110, 0.000006)	0.000063	0.000115
Relative Change (Percent) at 12 Months after Intervention 1	-45.12	(-77.29, -12.96)	0.000063	0.000115
Native Hawaiian/Other Pacific Islander				
Absolute Change at 6 Months after Intervention 1	-0.000159	(-0.000252, -0.000065)	0.000056	0.000214
Relative Change (Percent) at 6 Months after Intervention 1	-74.06	(-102.99, -45.13)	0.000056	0.000214
Absolute Change at 12 Months after Intervention 1	-0.000159	(-0.000252, -0.000065)	0.000056	0.000214
Relative Change (Percent) at 12 Months after Intervention 1	-74.06	(-102.99, -45.13)	0.000056	0.000214

Table 2l. Absolute and Relative Changes in Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (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	0.000065	(0.000051, 0.000079)	0.000123	0.000058
Relative Change (Percent) at 6 Months after Intervention 1	112.31	(9.52, 215.09)	0.000123	0.000058
Absolute Change at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (Percent) at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A

[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.

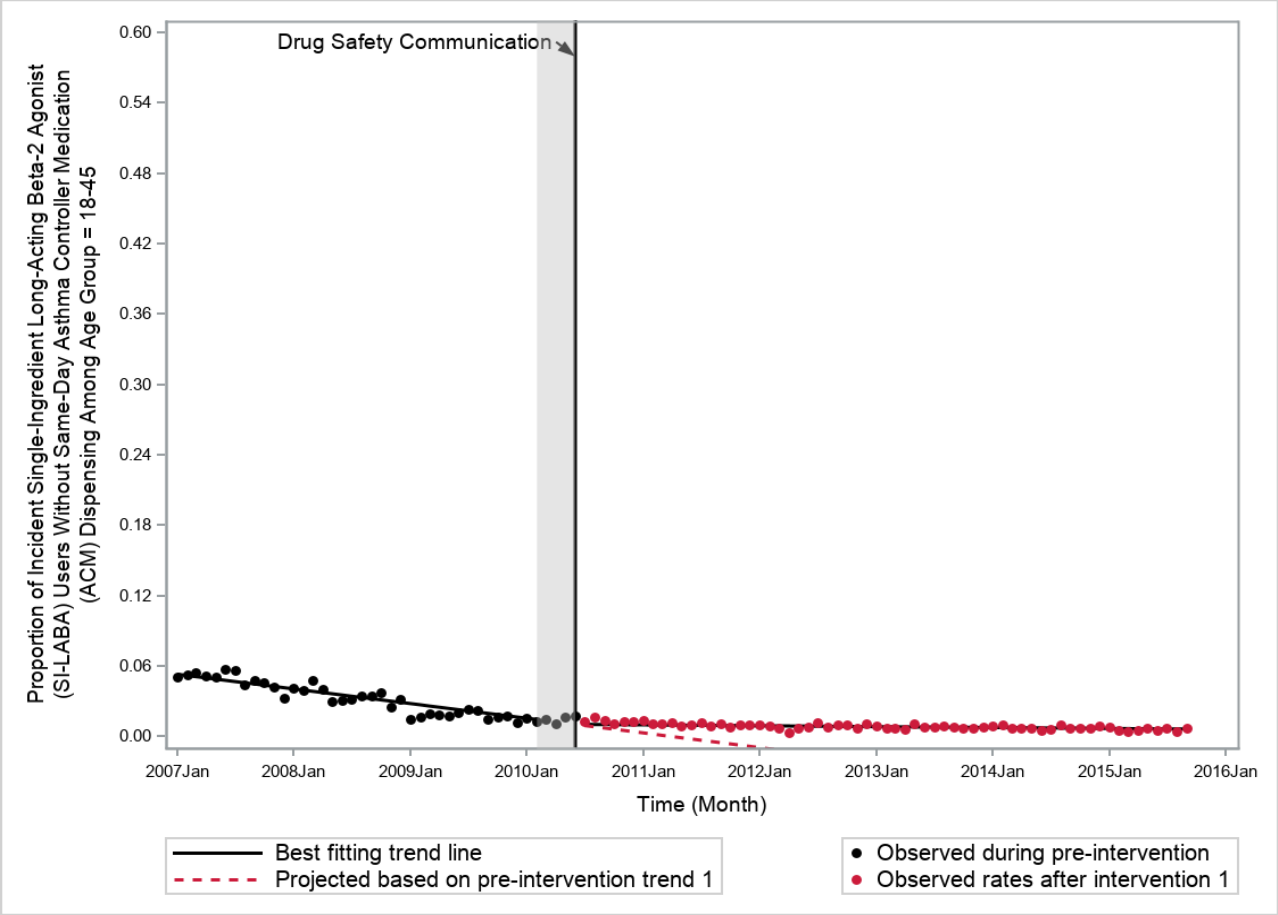
Figure 1. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2]



[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).

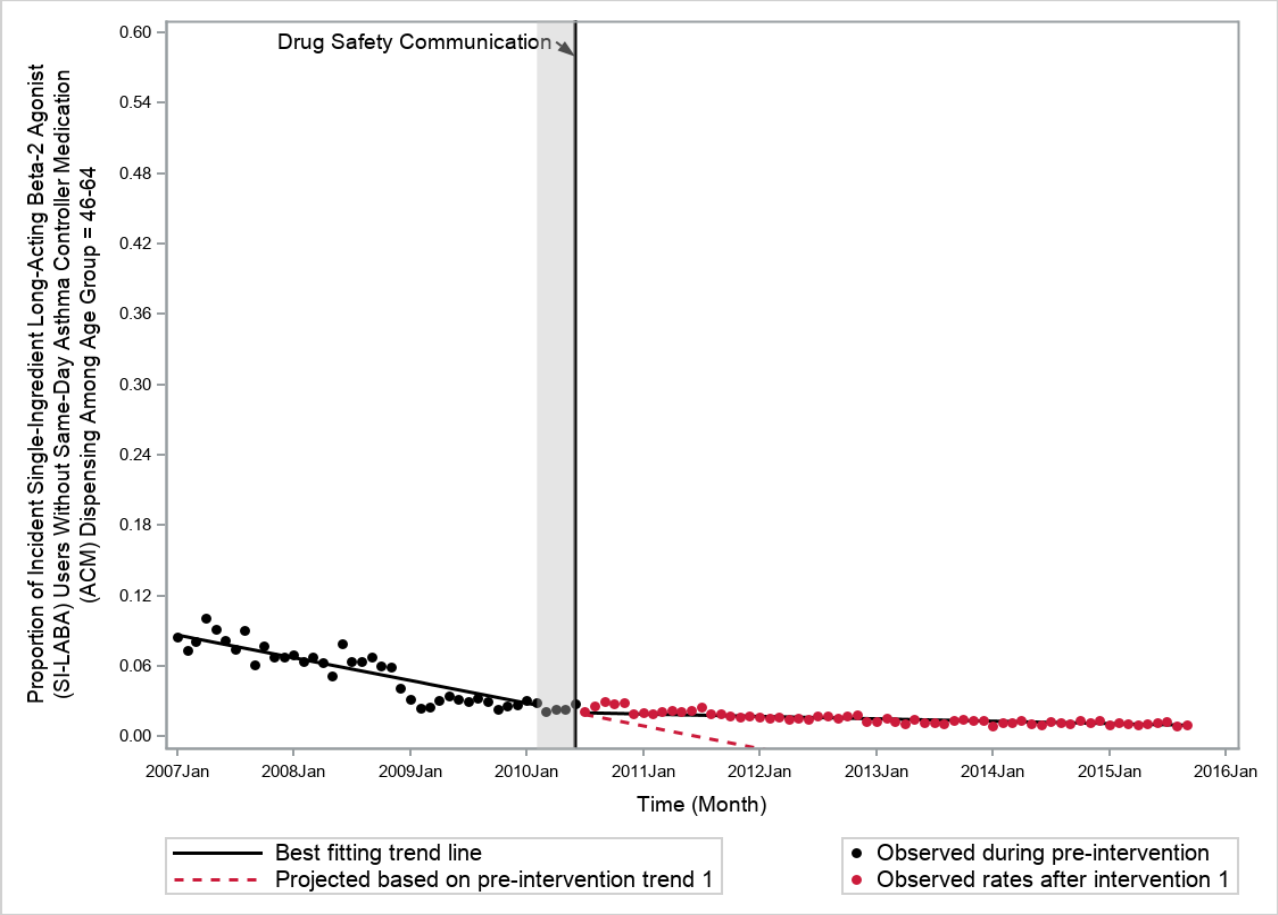
Figure 2. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2], where Age Group = 18-45



[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).

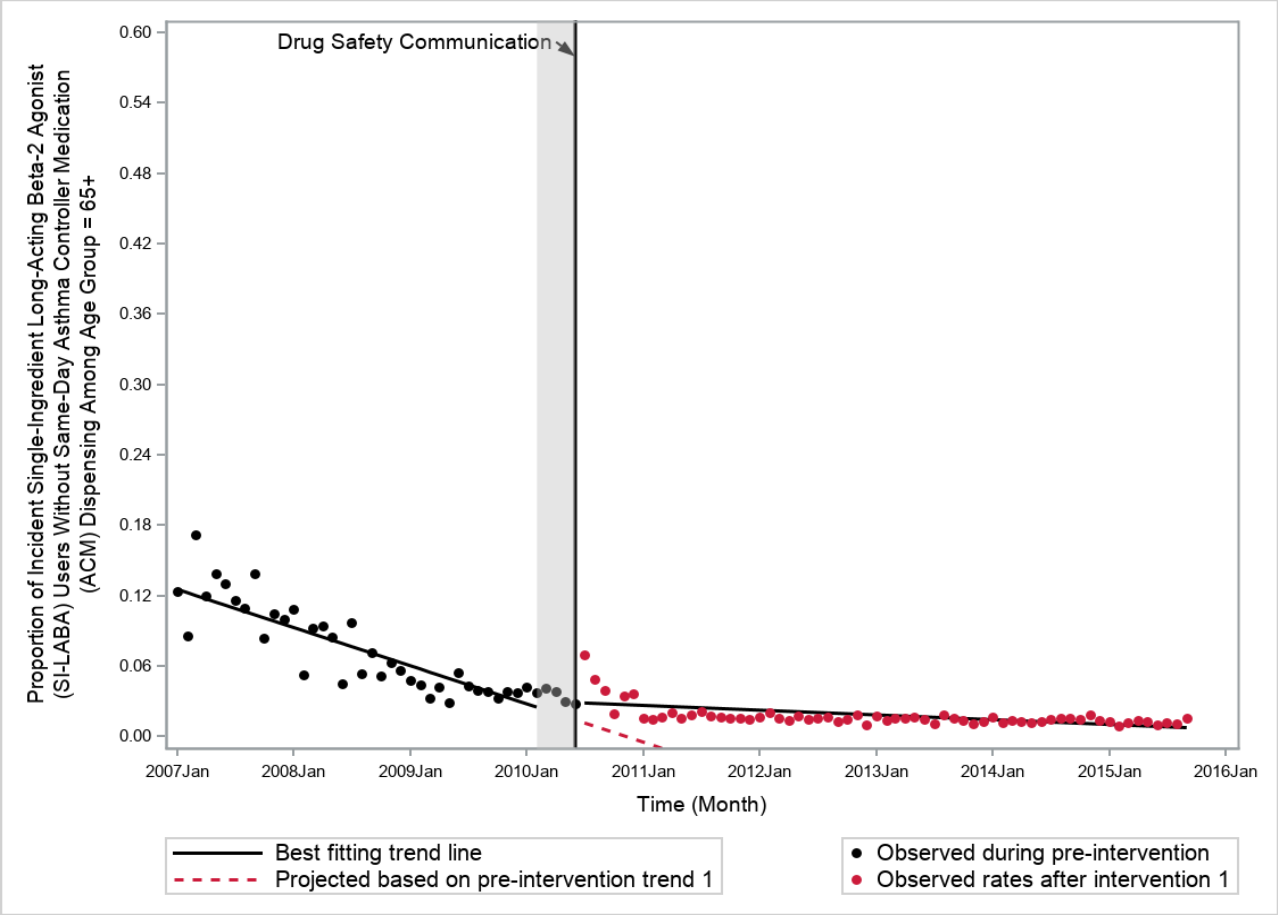
Figure 3. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2], where Age Group = 46-64



[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).

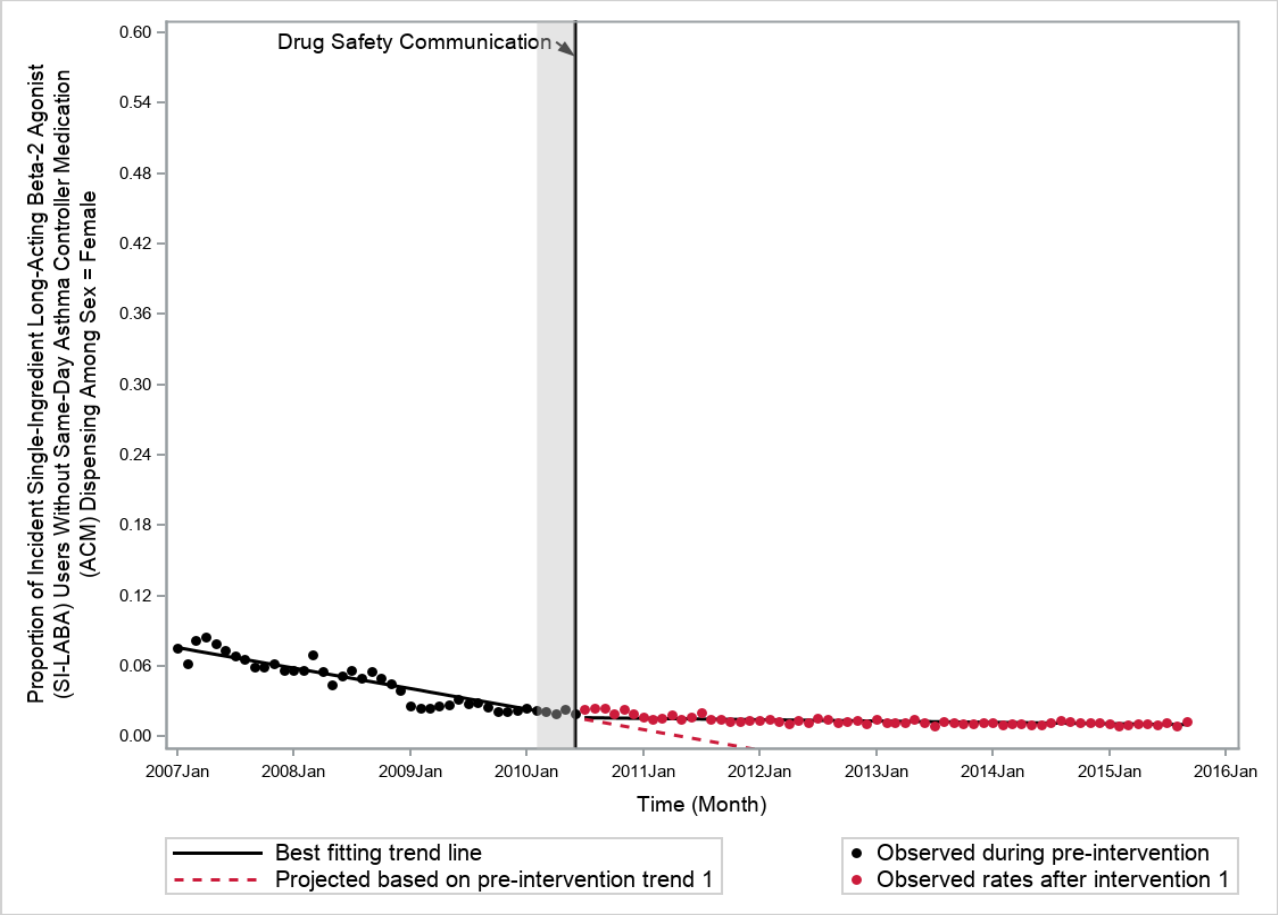
Figure 4. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2], where Age Group = 65+



[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).

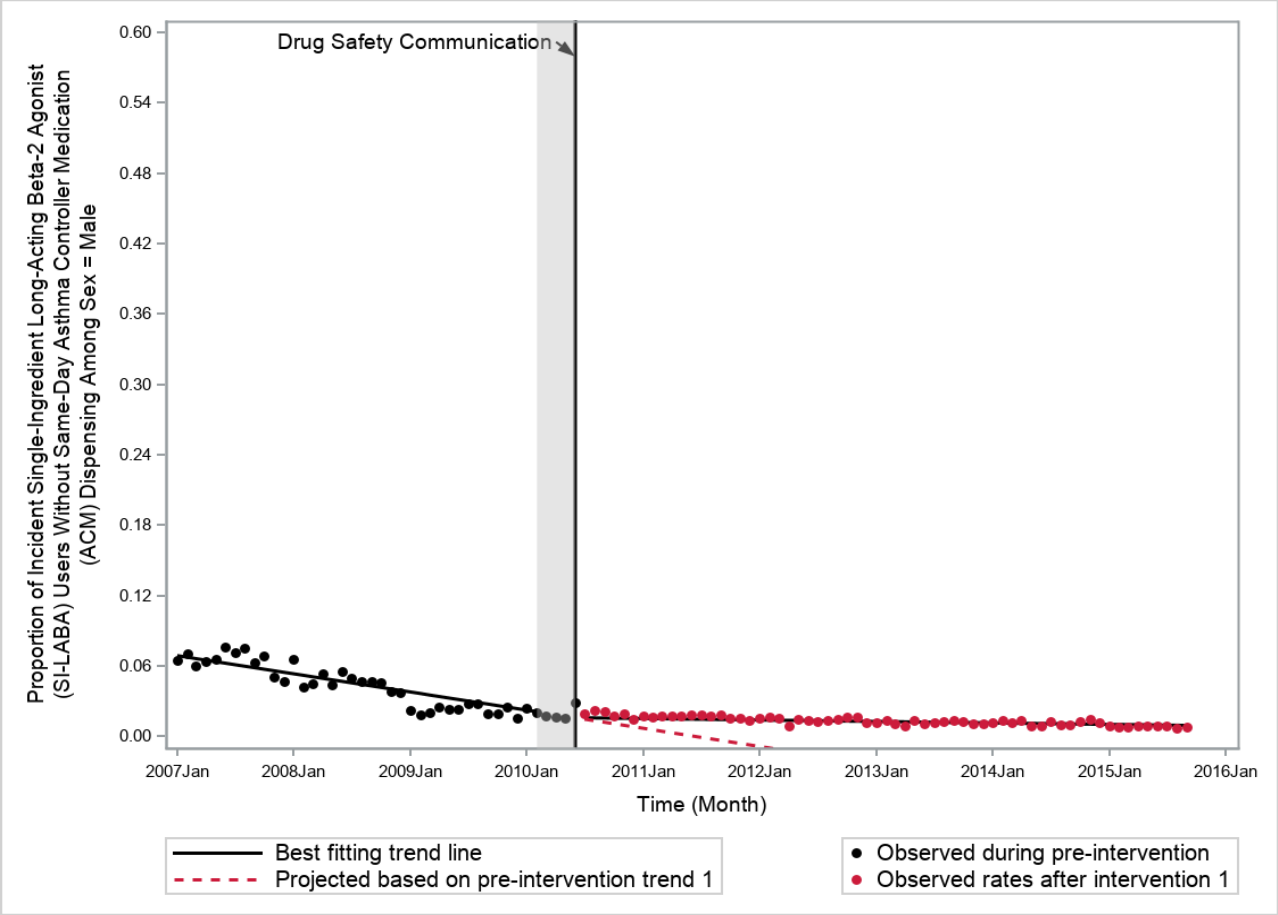
Figure 5. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2], where Sex = Female



[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).

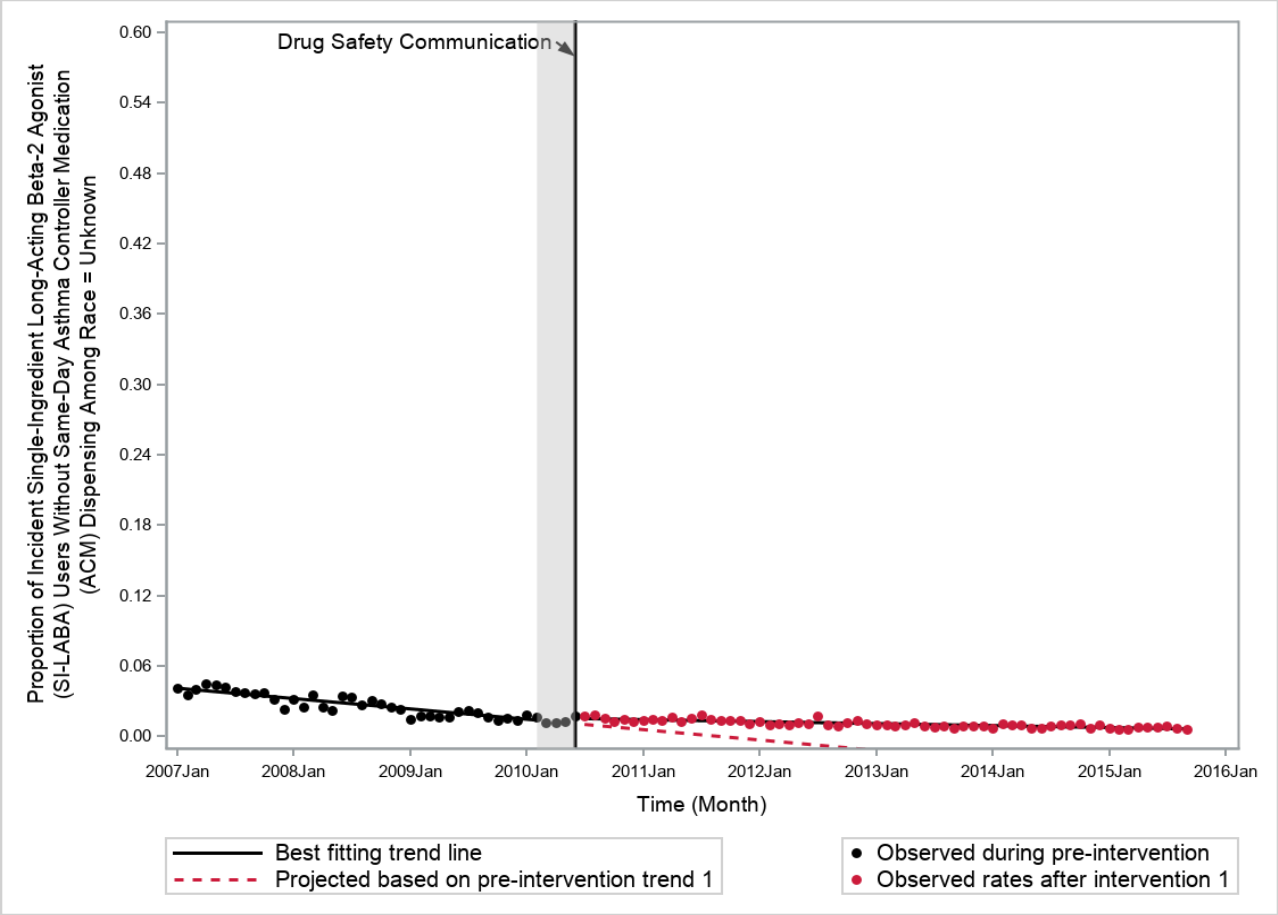
Figure 6. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2], where Sex = Male



[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).

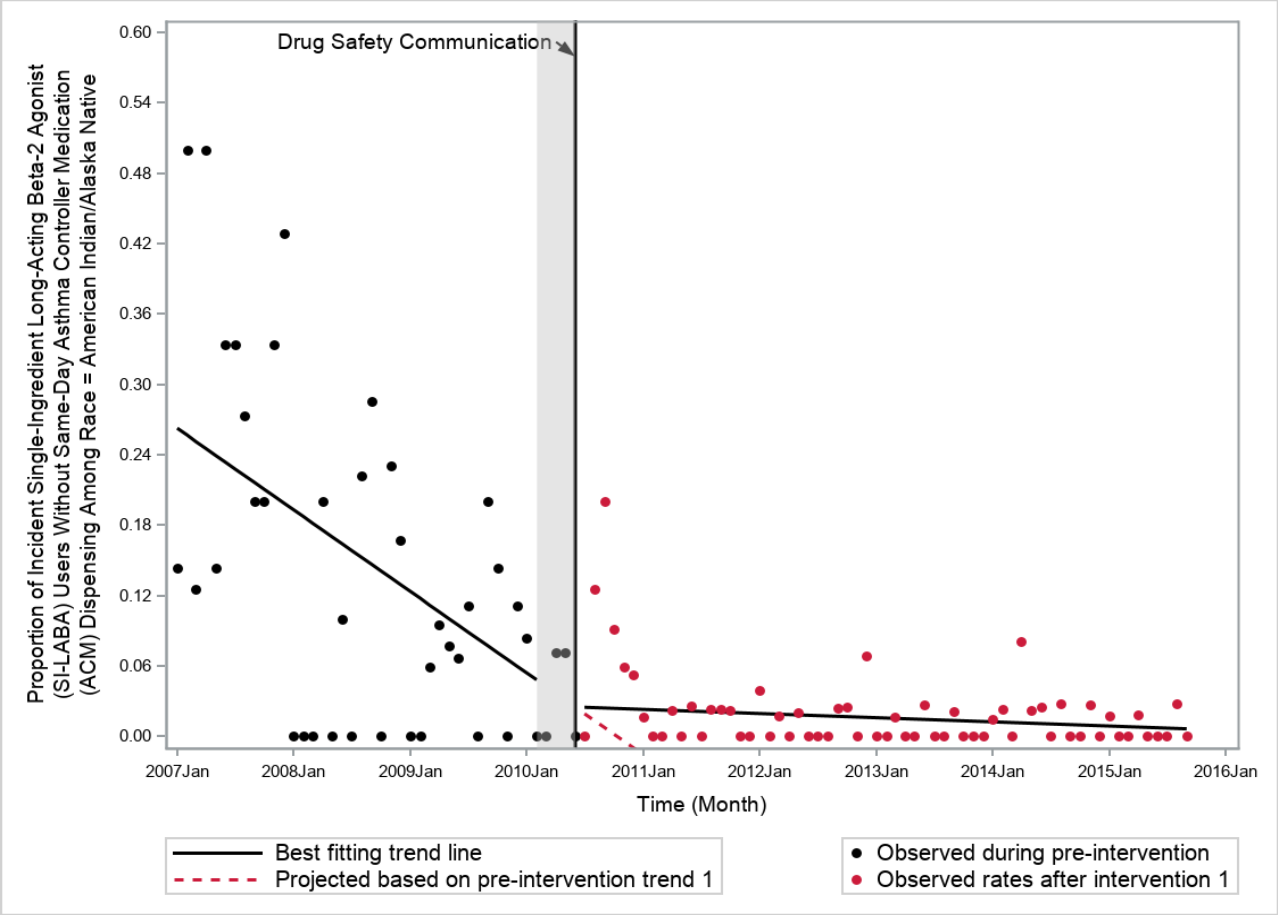
Figure 7. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2], where Race = Unknown



[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).

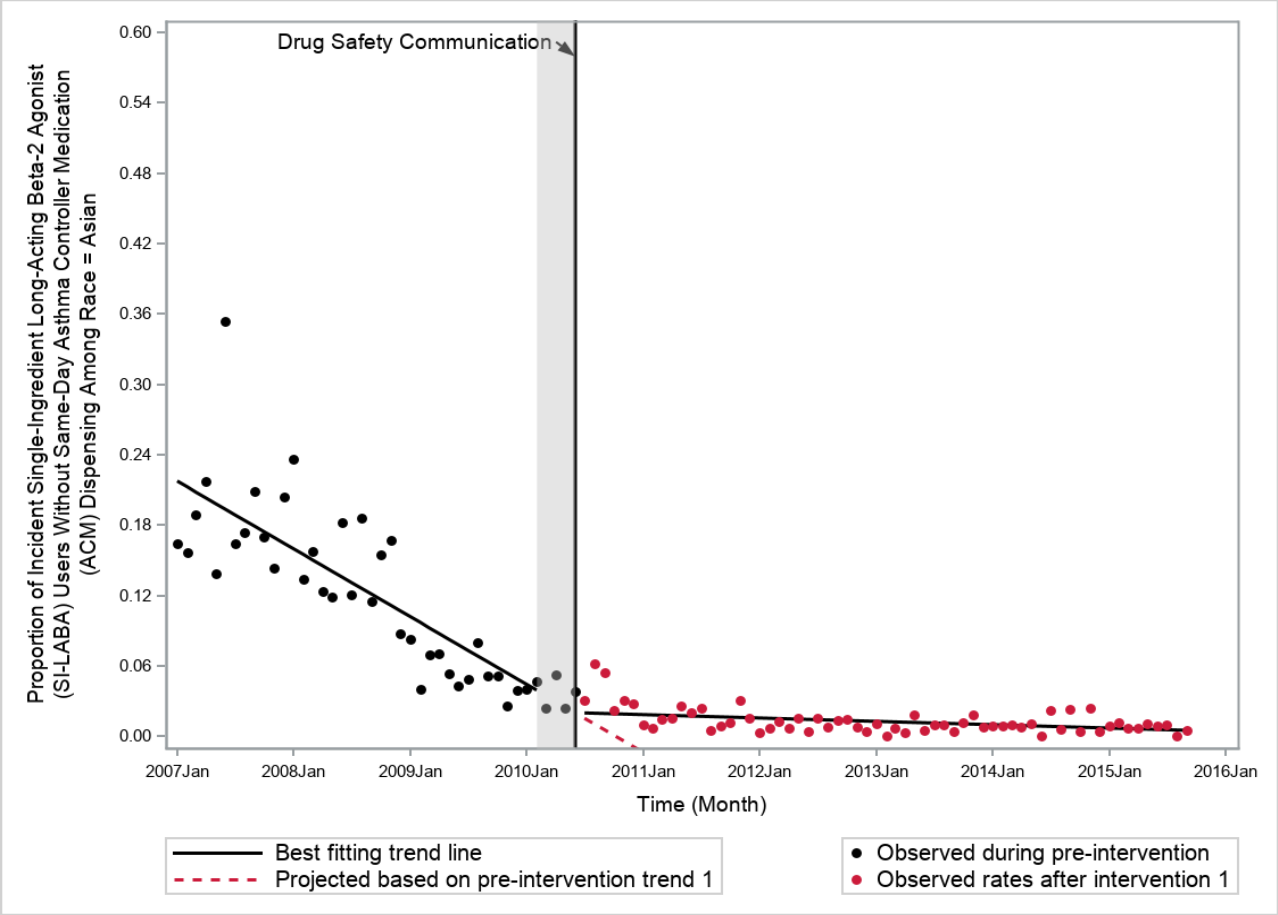
Figure 8. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2], where Race = American Indian/Alaska Native



[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).

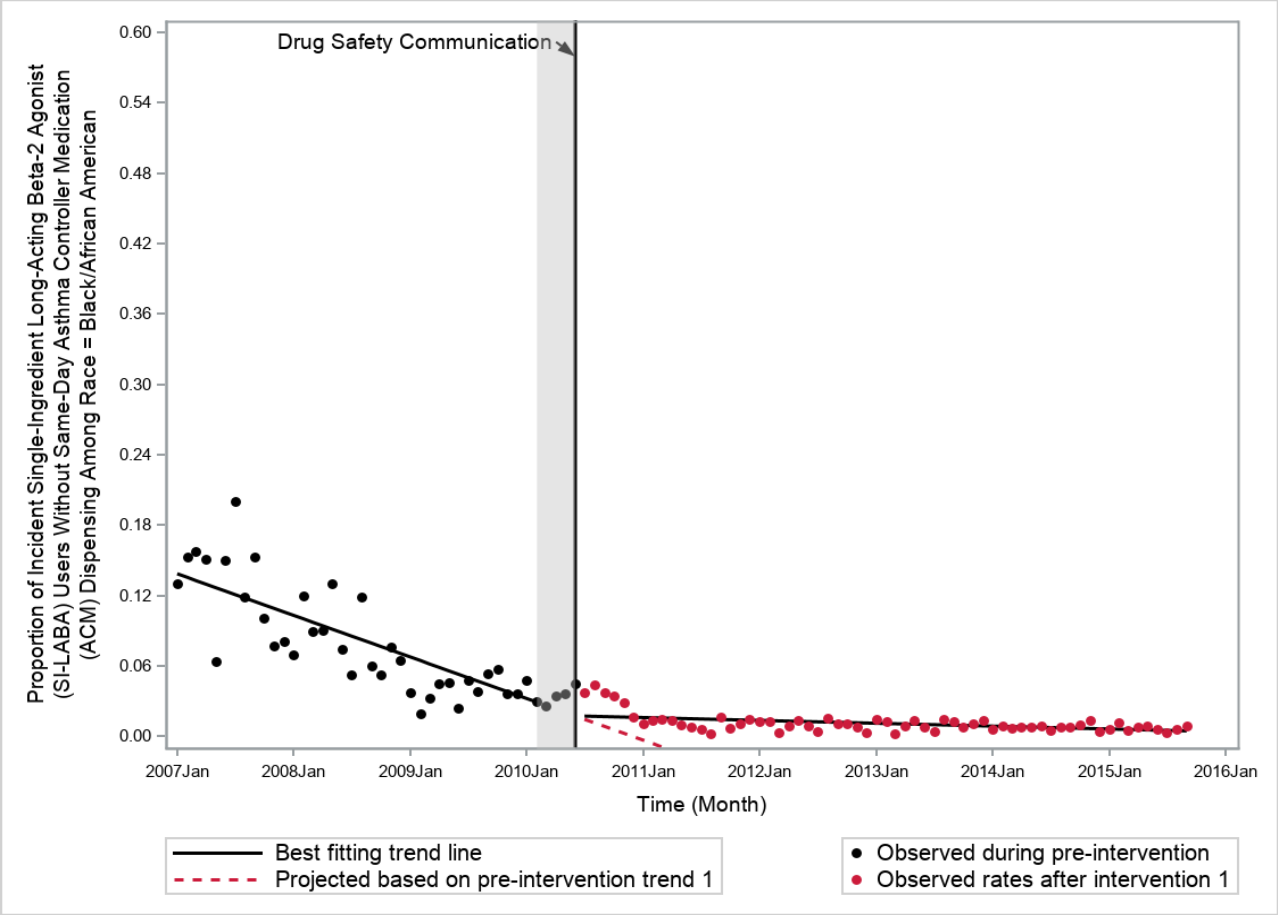
Figure 9. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2], where Race = Asian



[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).

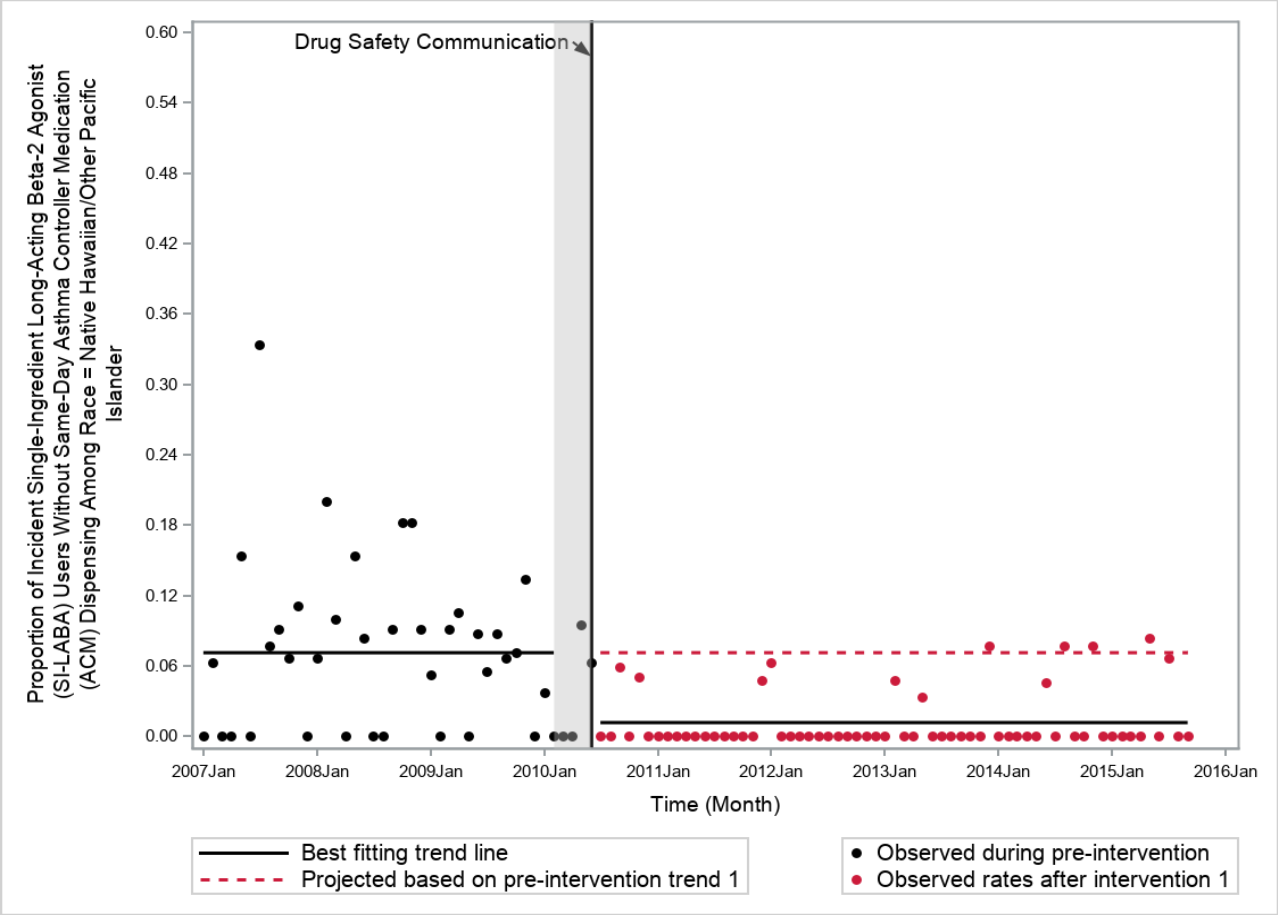
Figure 10. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2], where Race = Black/African American



[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).

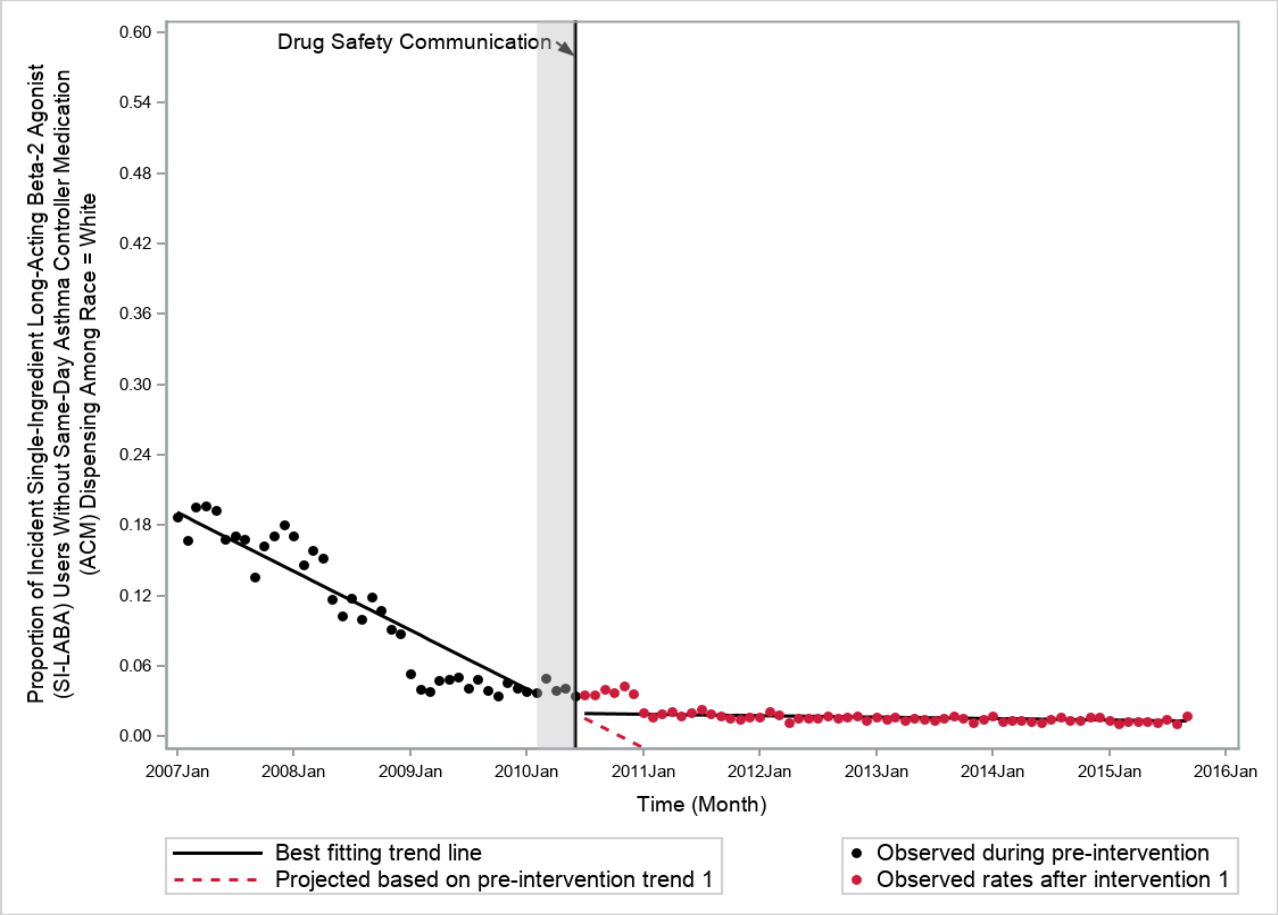
Figure 11. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2], where Race = Native Hawaiian/Other Pacific Islander



[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).

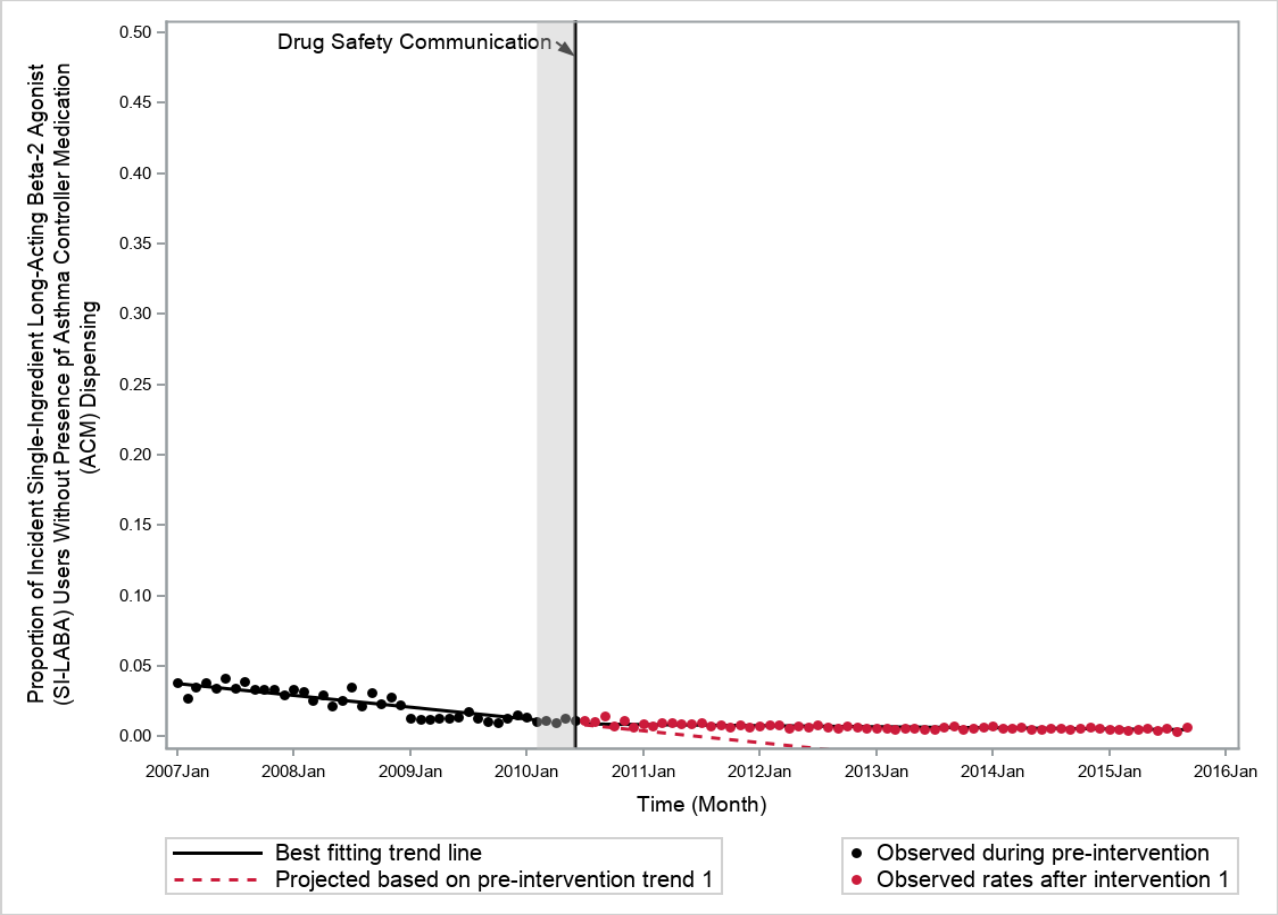
Figure 12. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Same-Day Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2], where Race = White



[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 Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2,3]

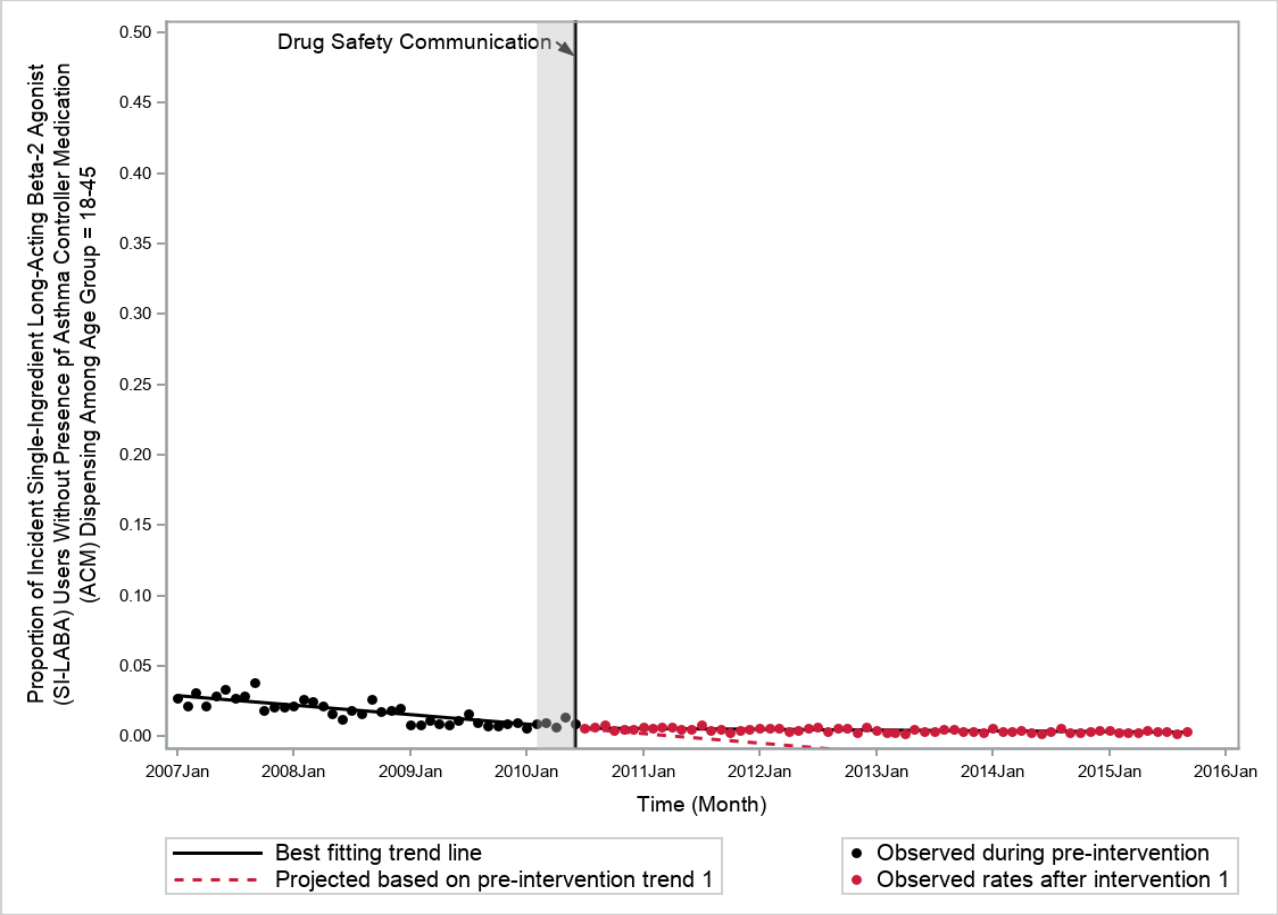


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 14. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2,3], where Age Group = 18-45

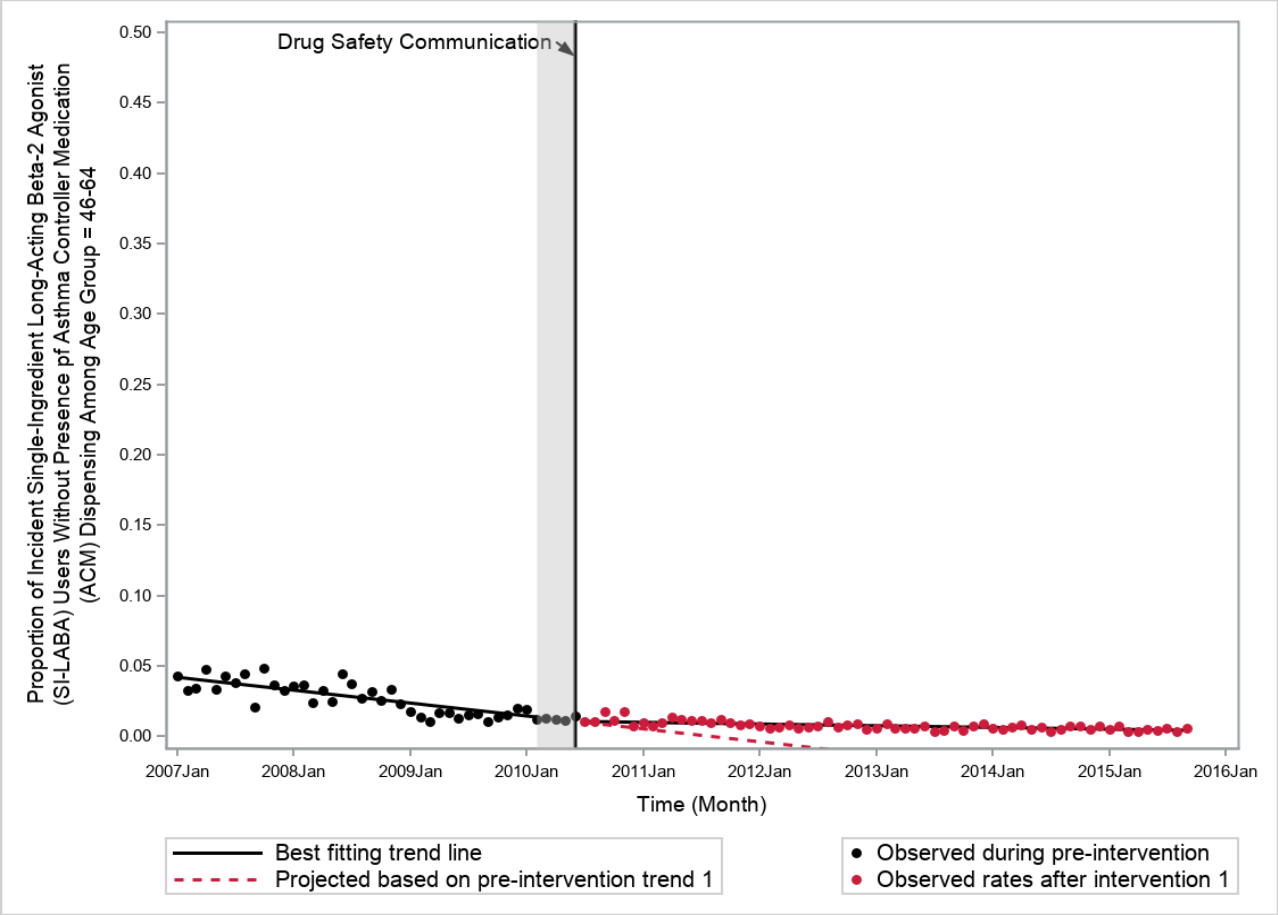


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 15. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2,3], where Age Group = 46-64

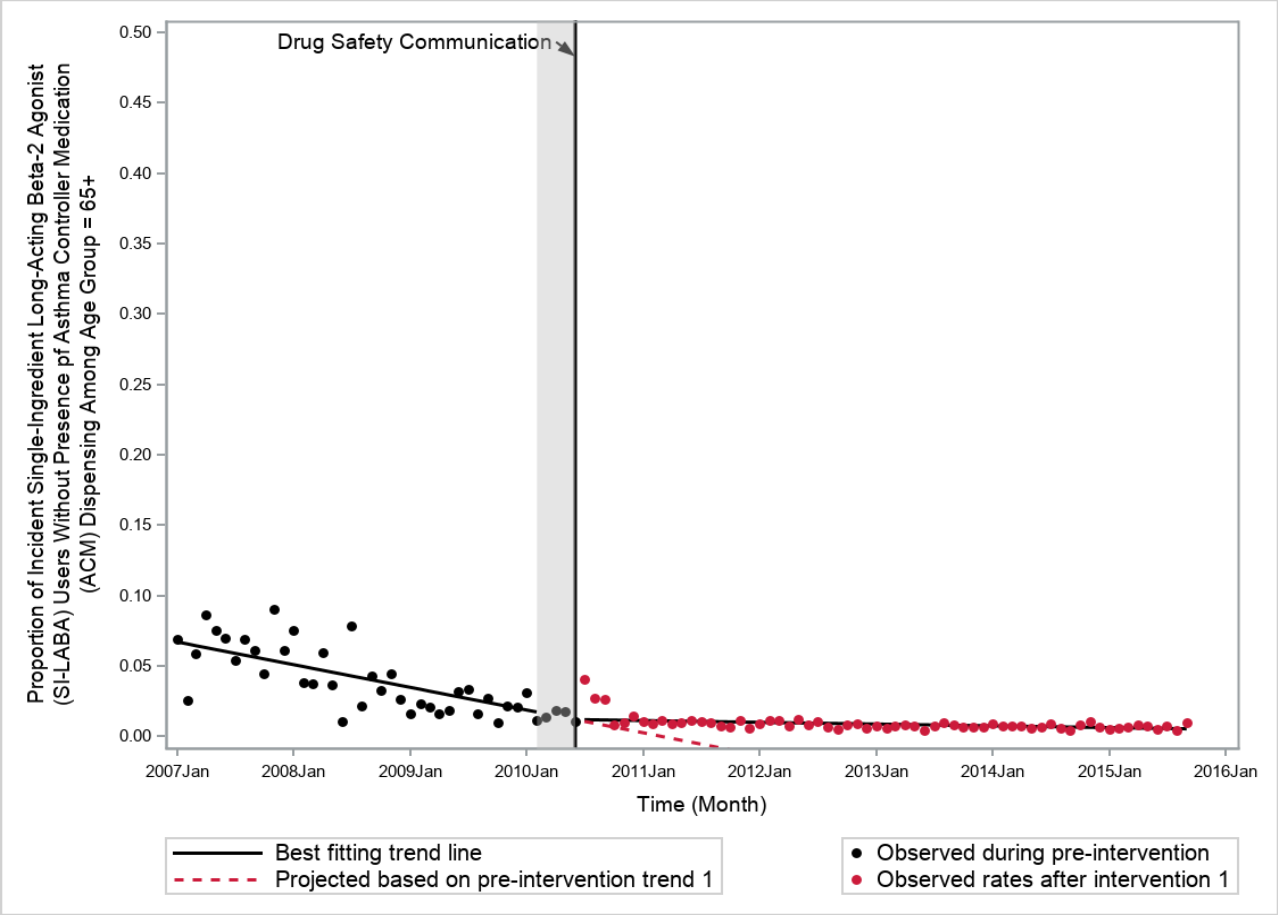


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 16. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2,3], where Age Group = 65+

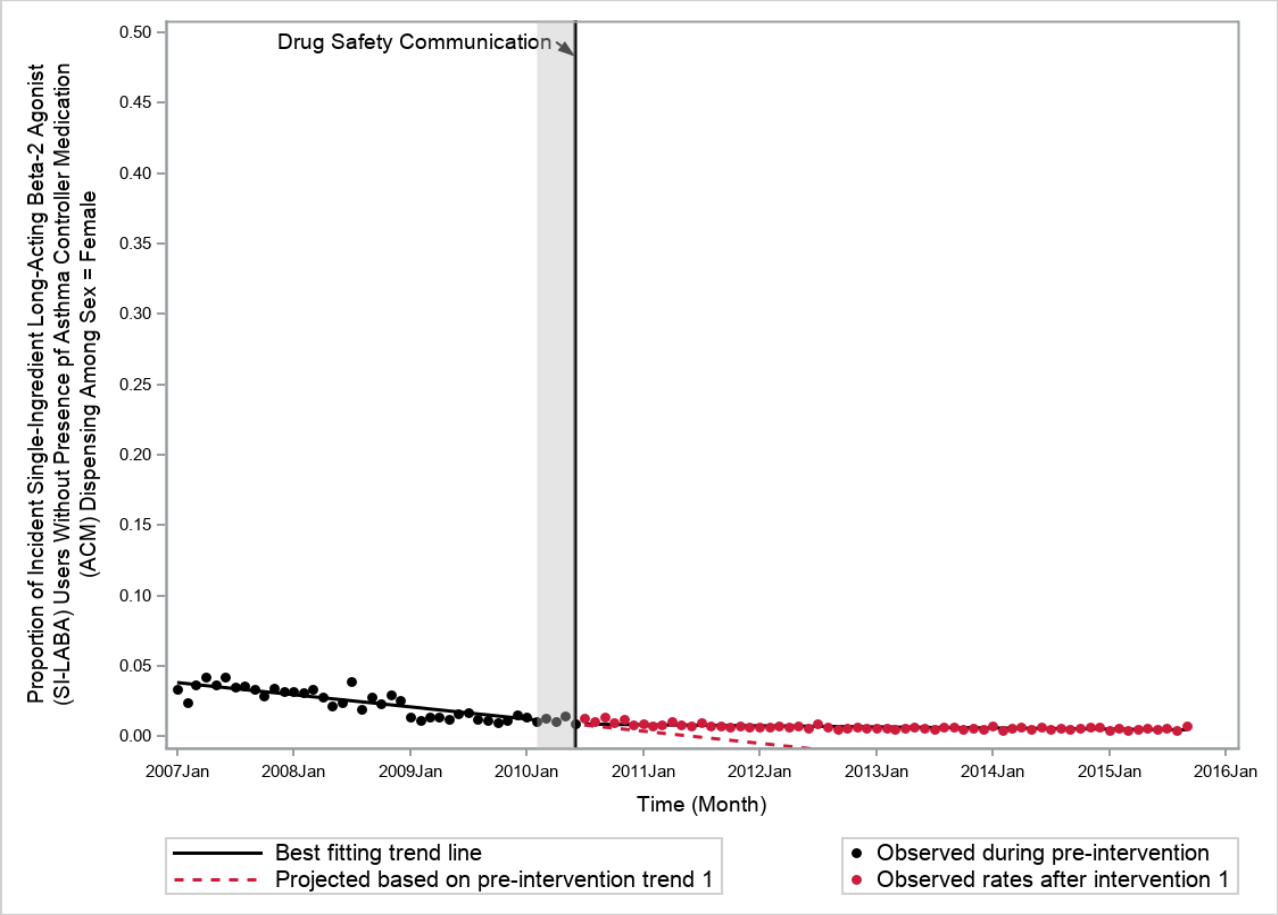


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 17. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2,3], where Sex = Female

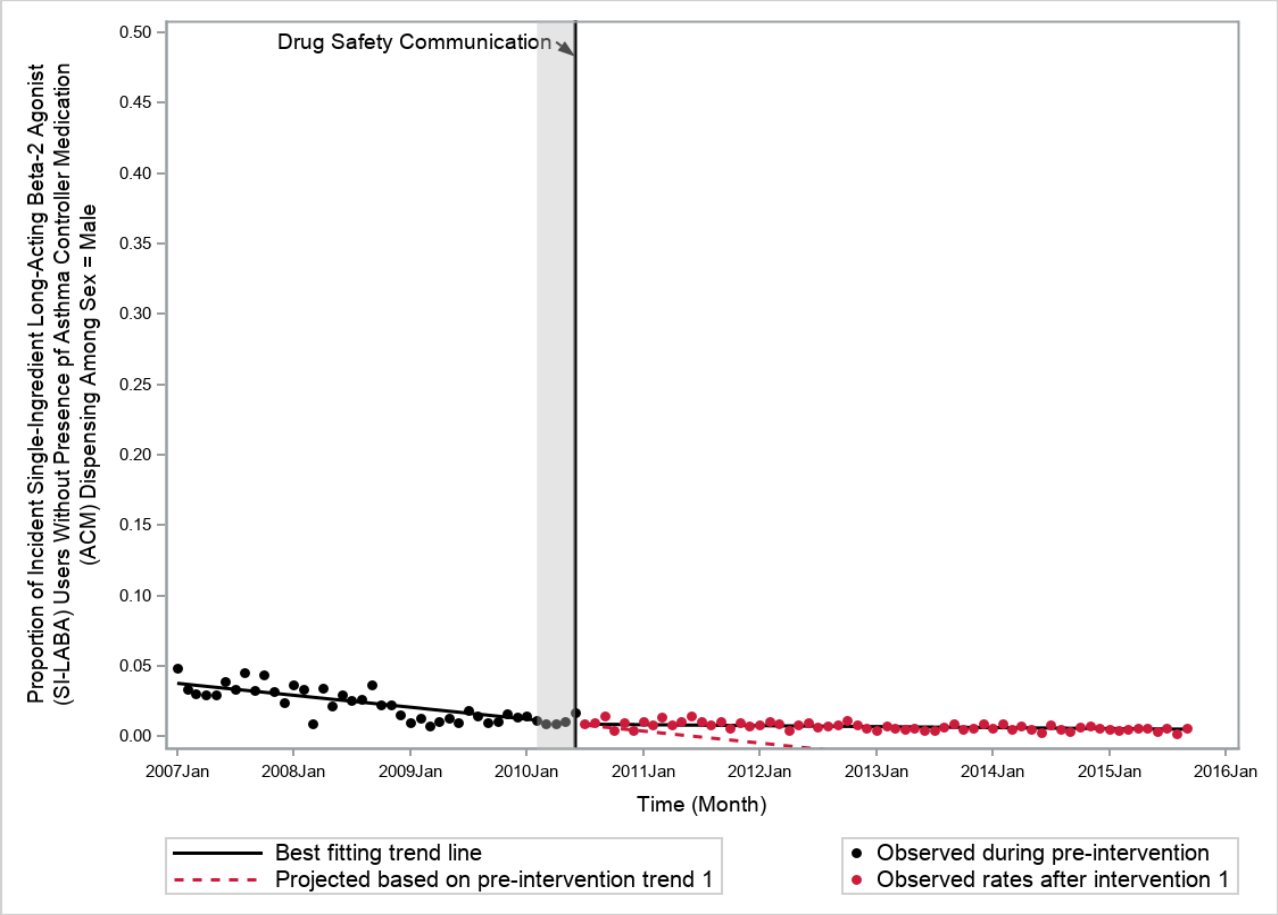


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 18. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2,3], where Sex = Male

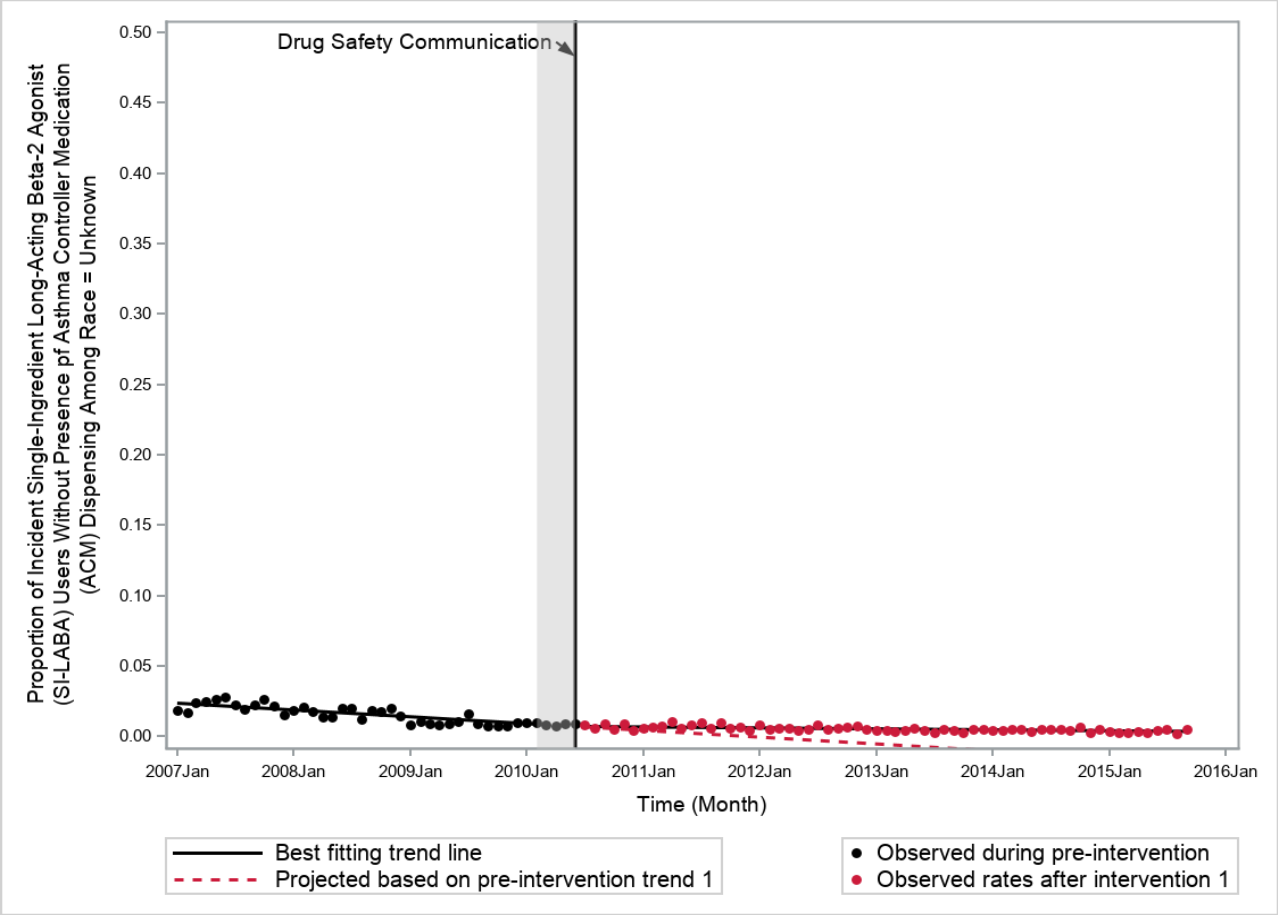


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 19. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2,3], where Race = Unknown

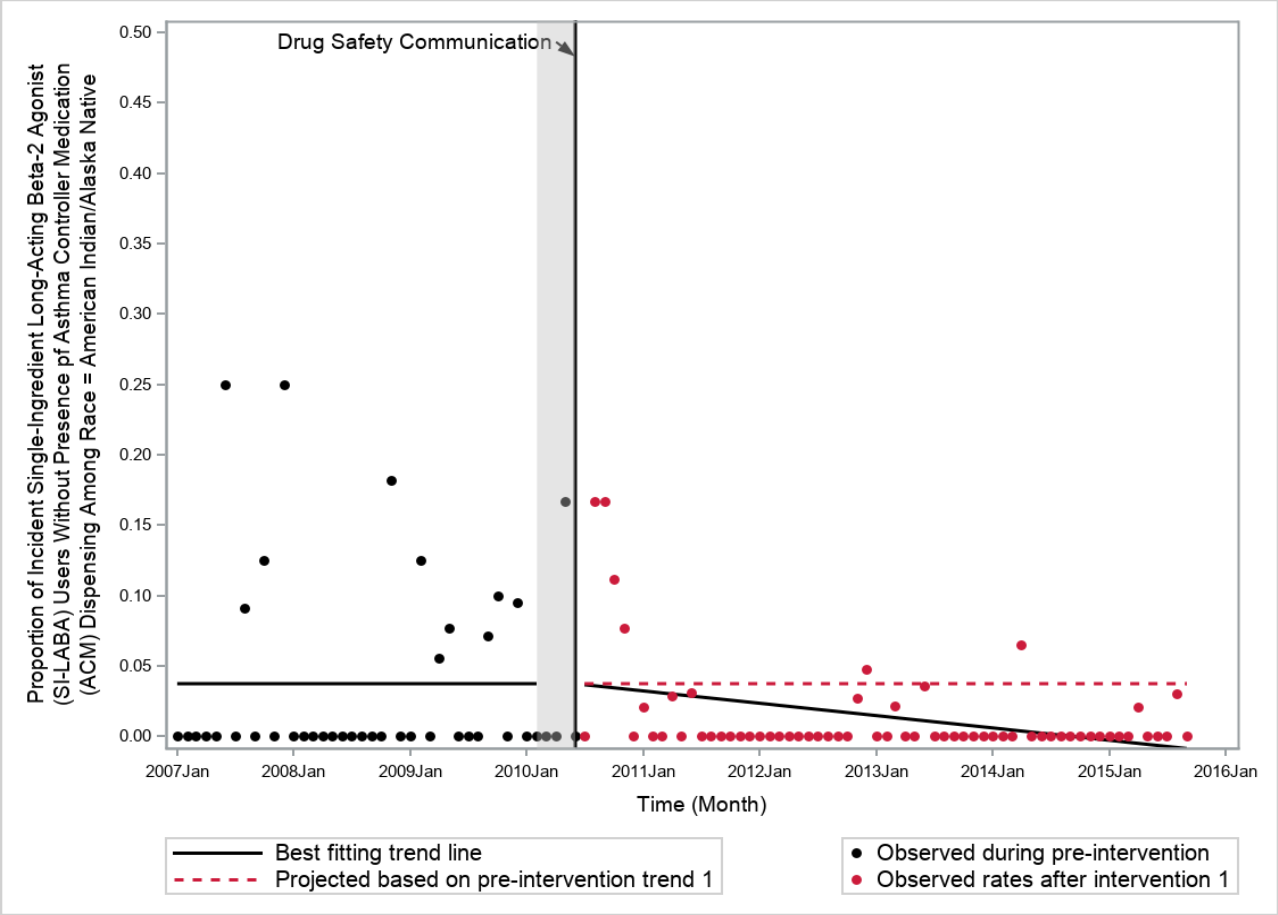


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 20. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2,3], where Race = American Indian/Alaska Native

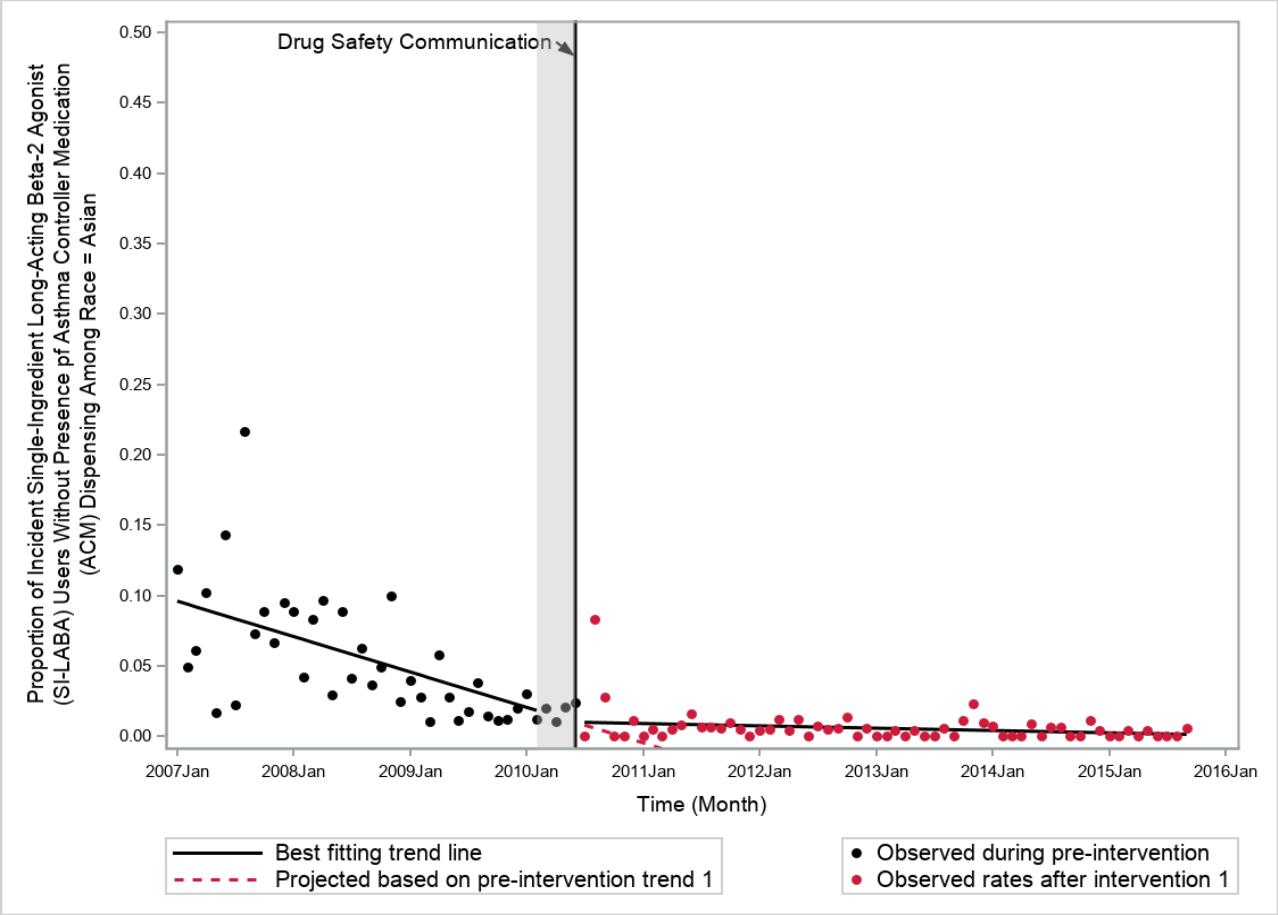


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 21. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2,3], where Race = Asian

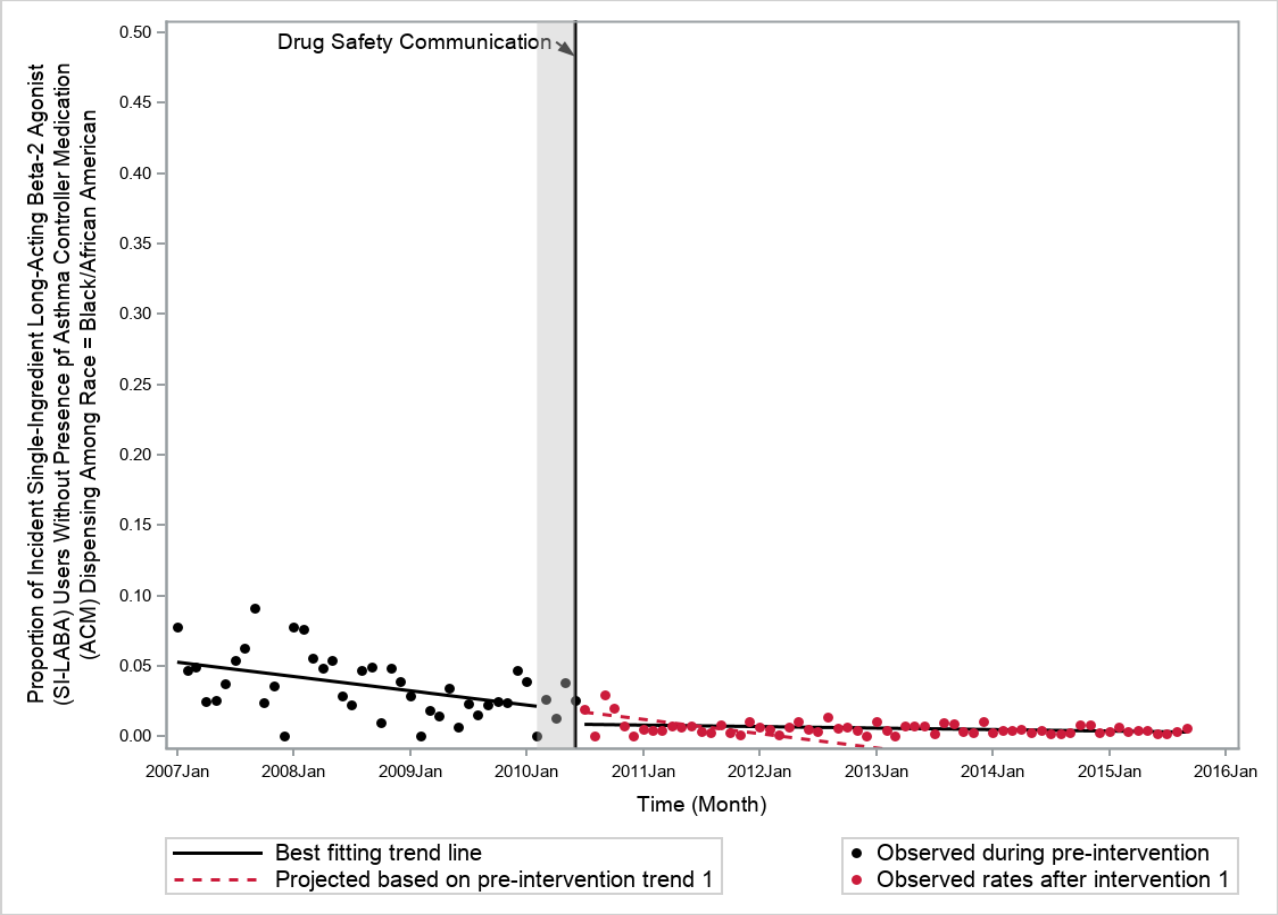


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 22. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2,3], where Race = Black/African American

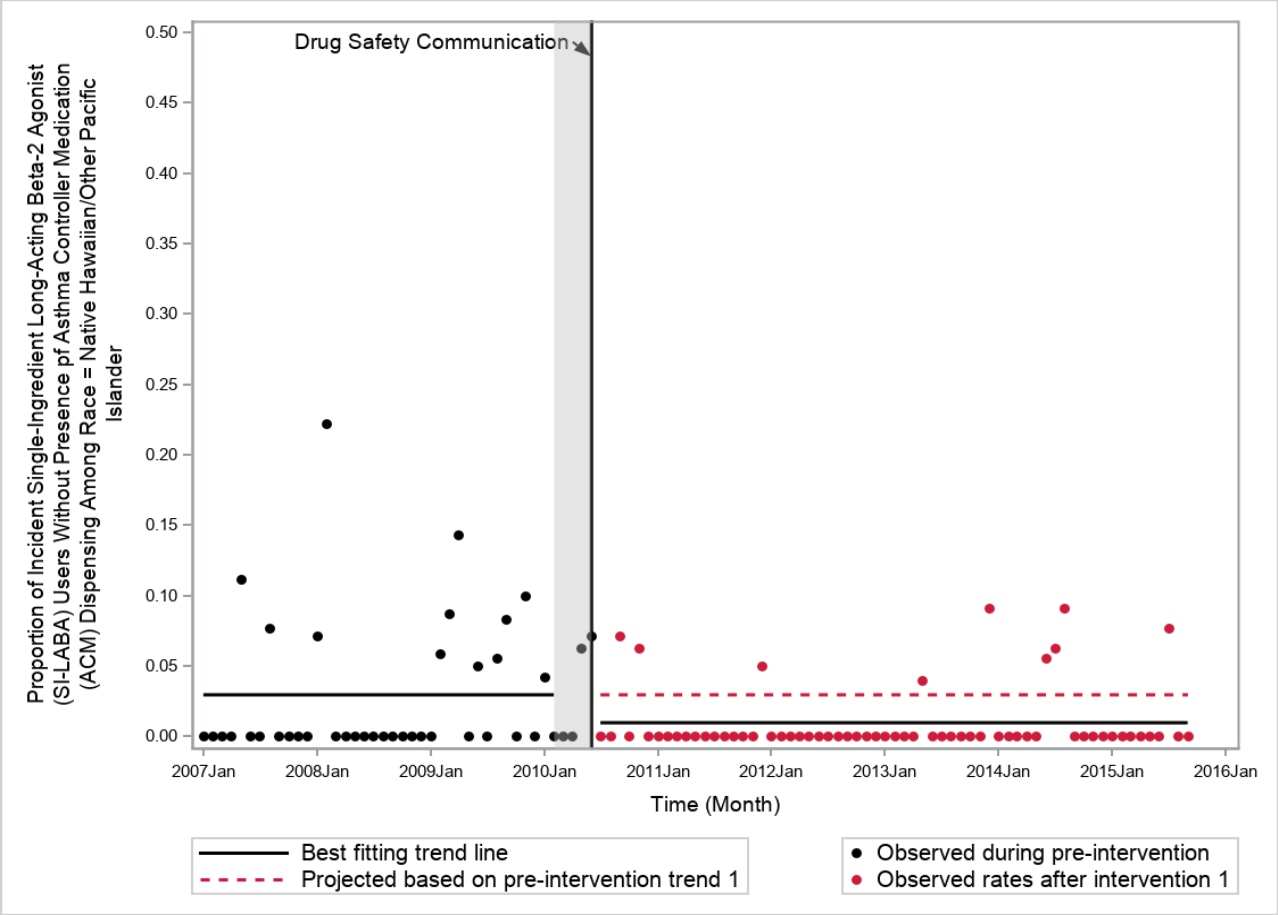


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 23. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2,3], where Race = Native Hawaiian/Other Pacific Islander

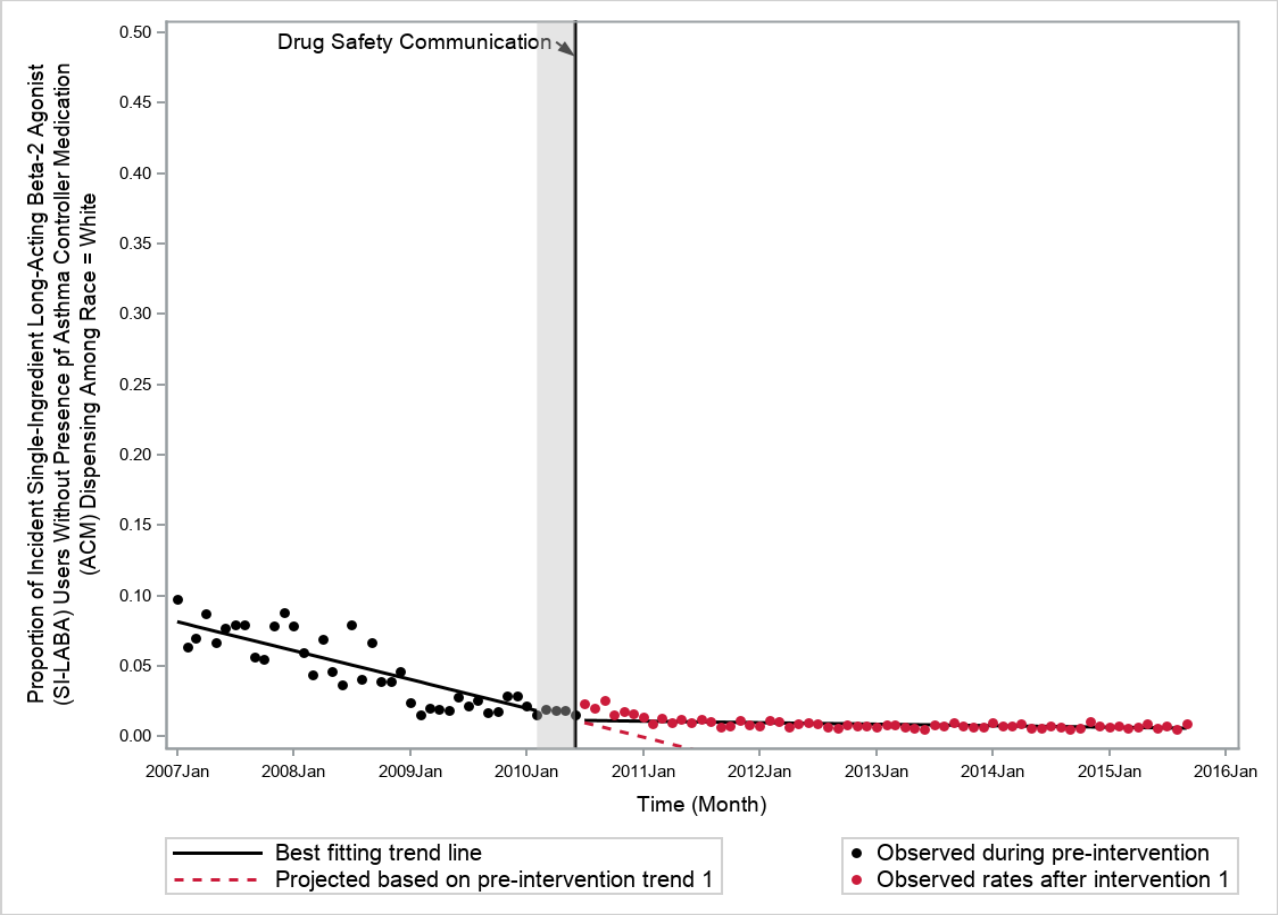


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 24. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) Dispensing Among Incident LABA Users Before and After June 2, 2010[1,2,3], where Race = White

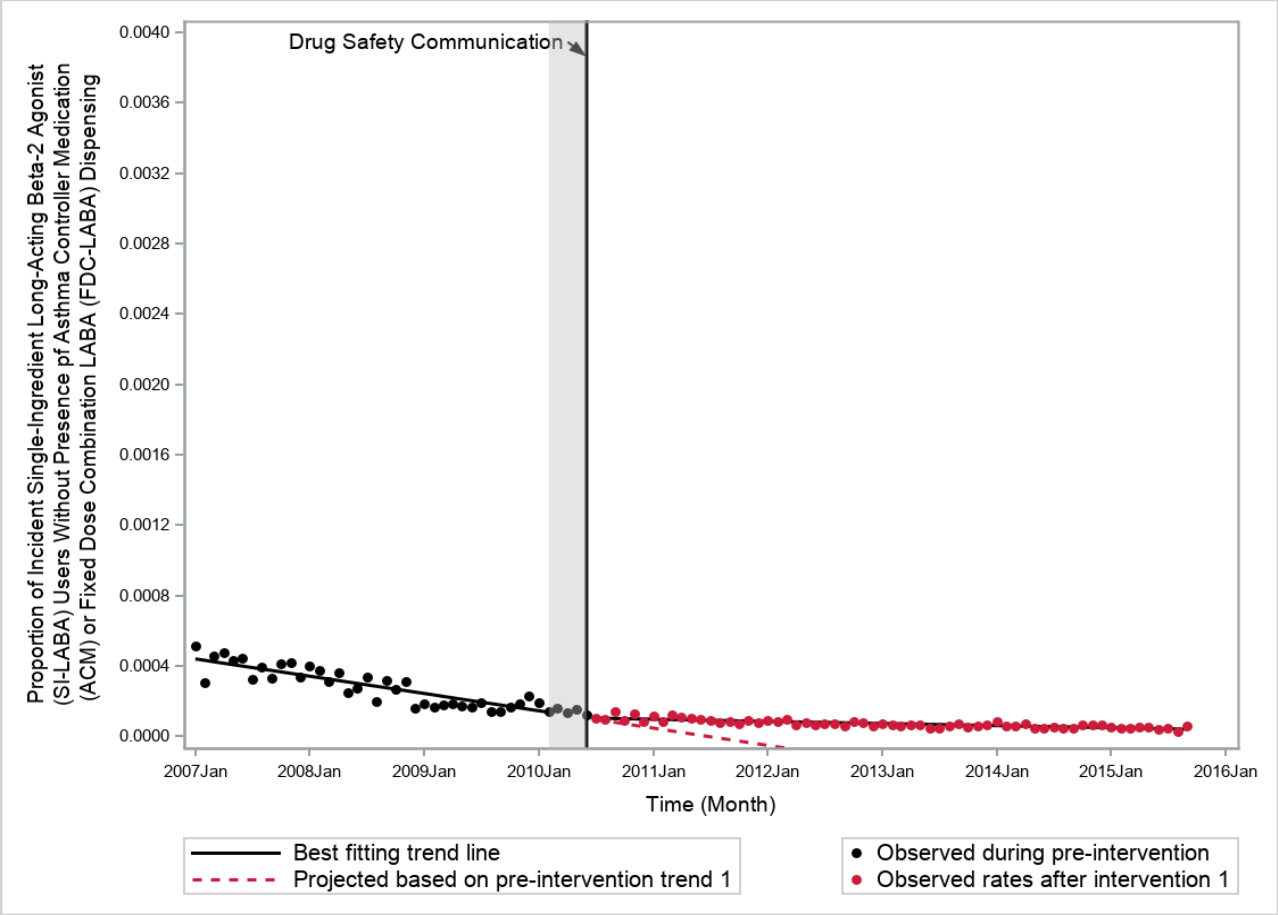


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 25. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (FDC-LABA) Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2,3]

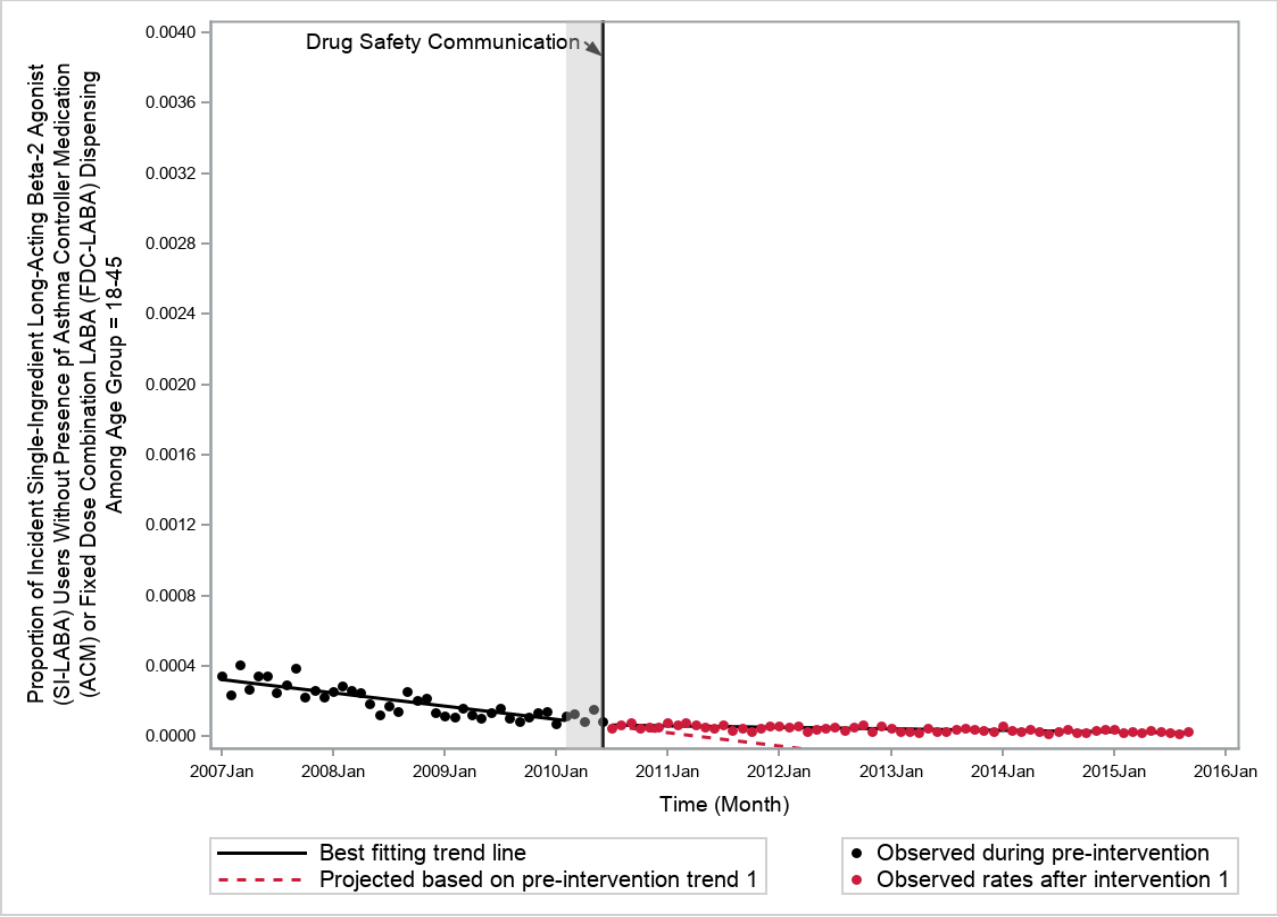


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 26. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (FDC-LABA) Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2,3], where Age Group = 18-45

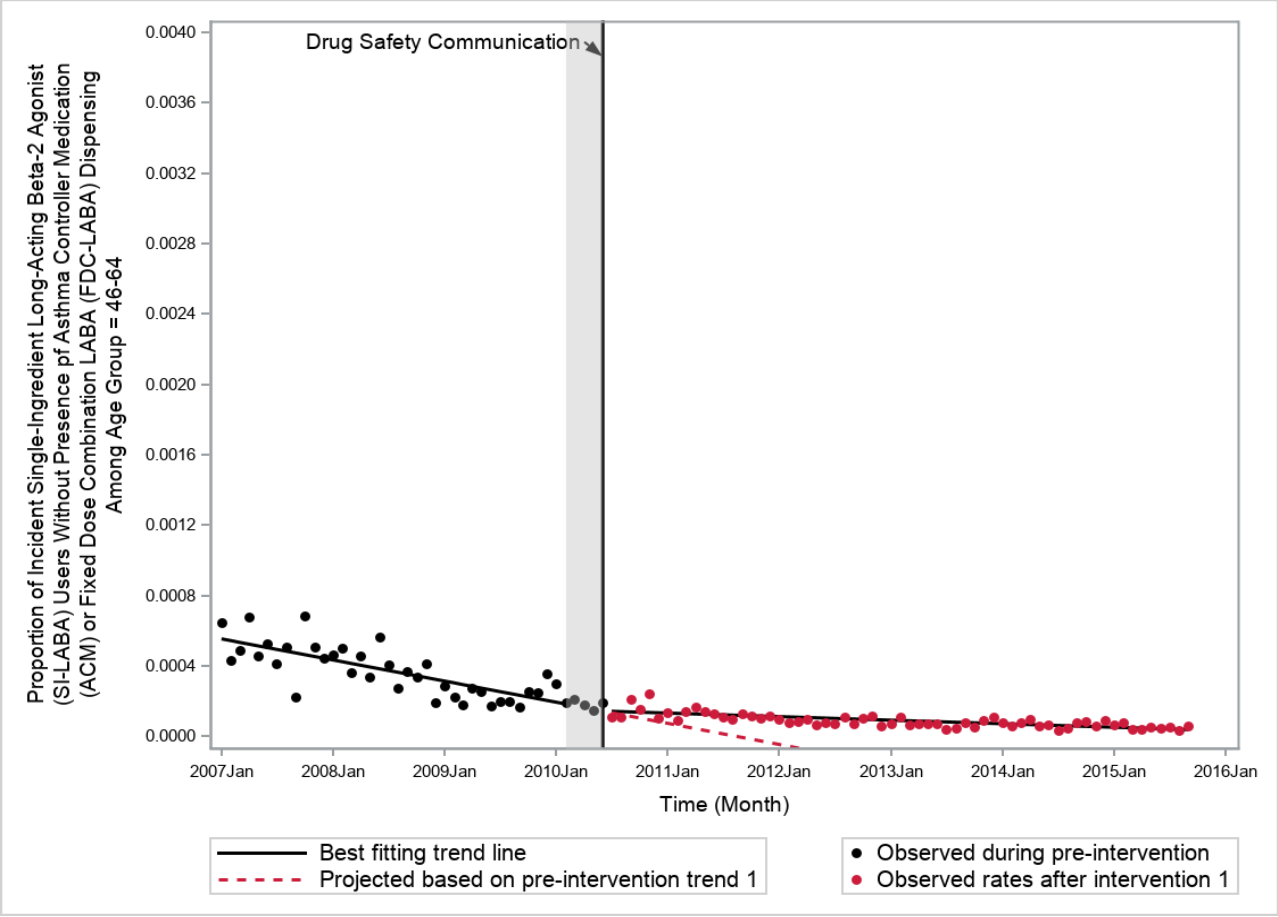


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 27. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (FDC-LABA) Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2,3], where Age Group = 46-64

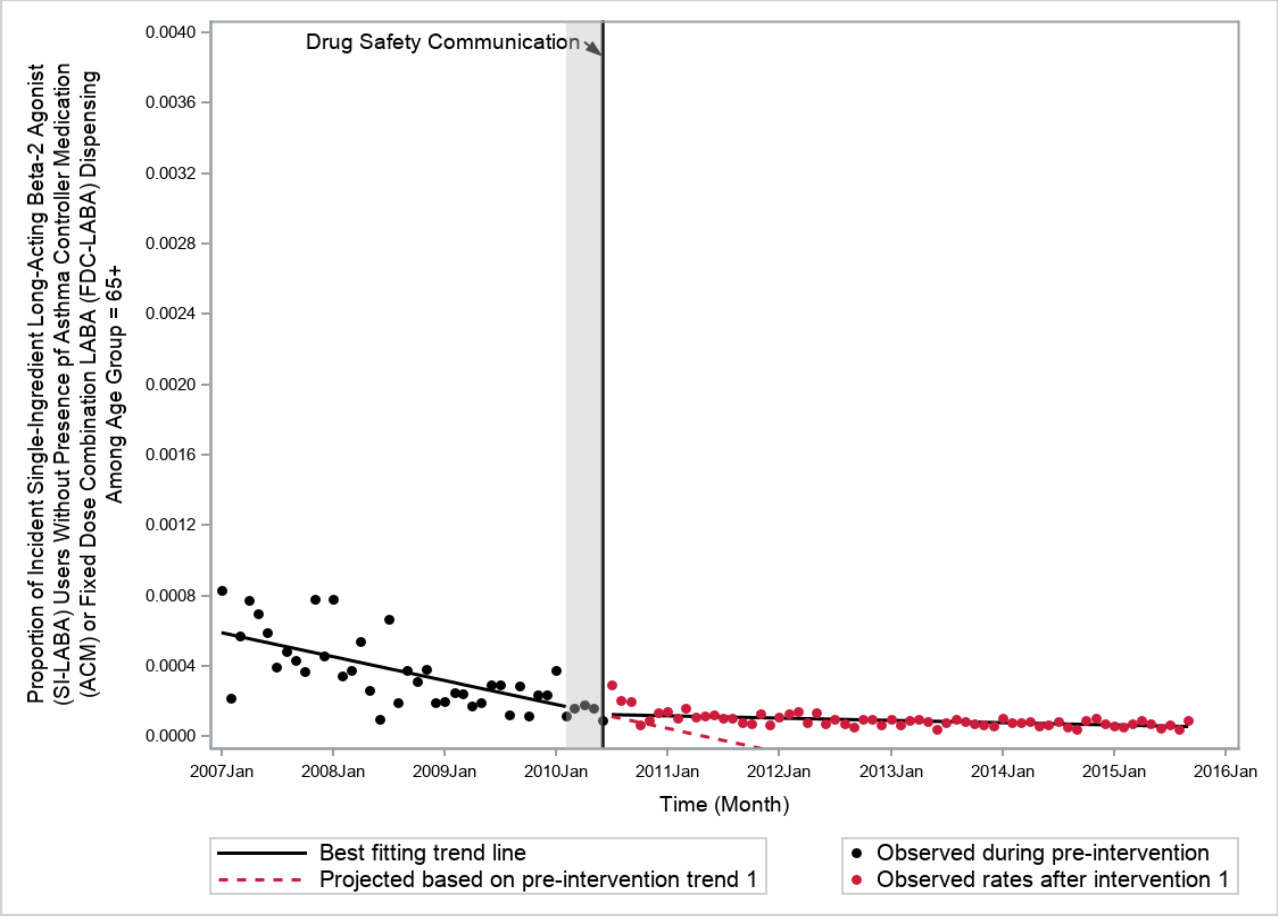


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 28. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (FDC-LABA) Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2,3], where Age Group = 65+

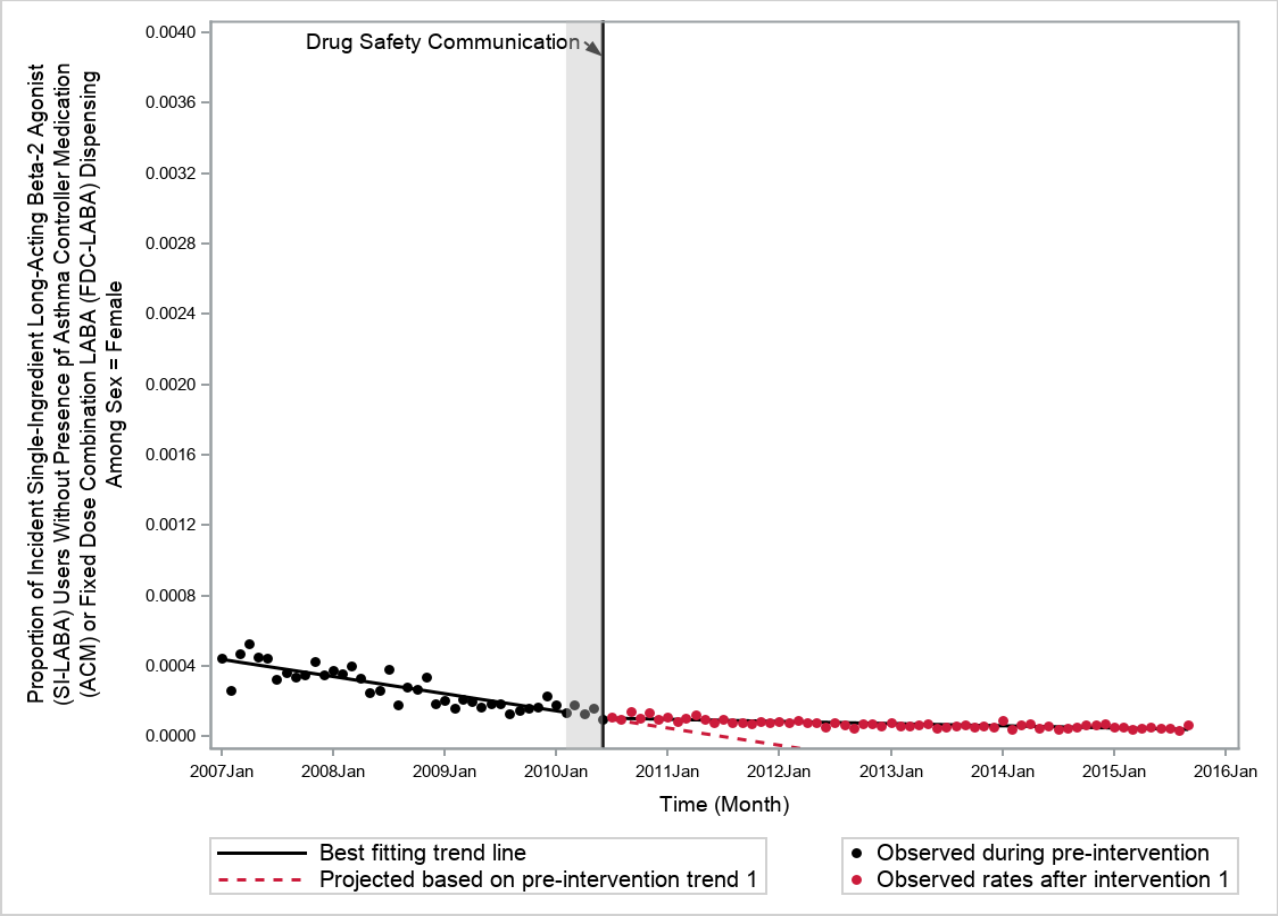


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 29. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (FDC-LABA) Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2,3], where Sex = Female

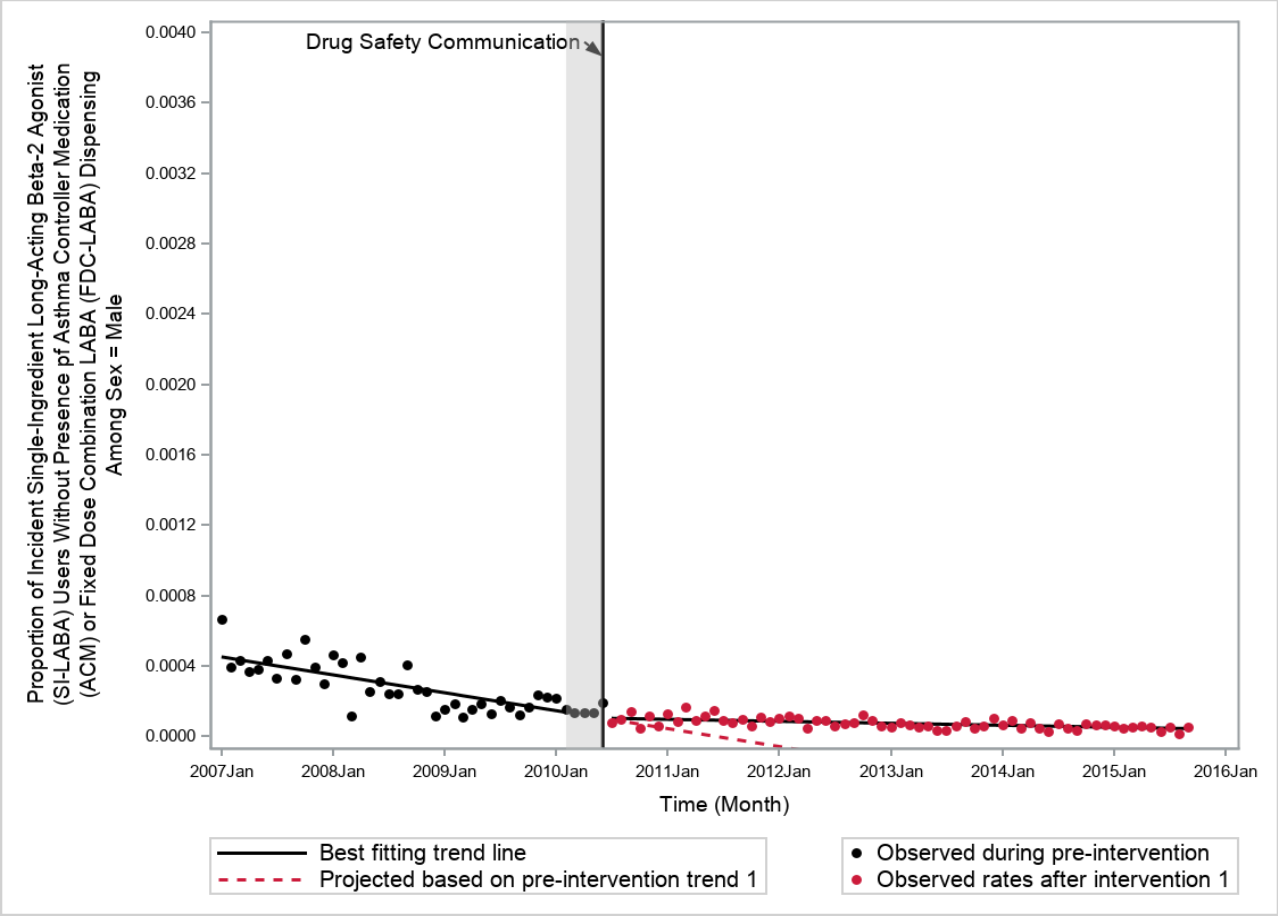


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 30. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (FDC-LABA) Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2,3], where Sex = Male

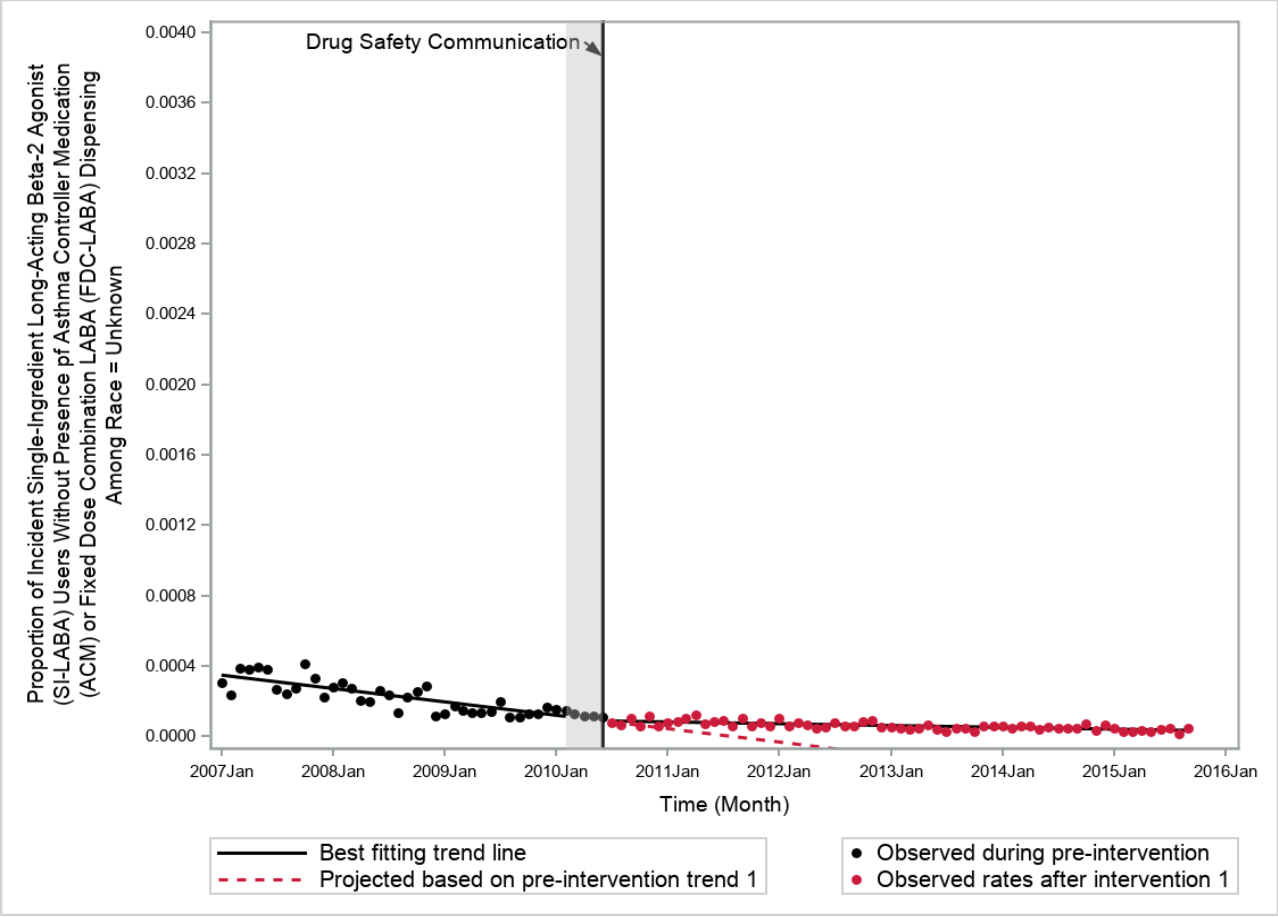


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 31. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (FDC-LABA) Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2,3], where Race = Unknown

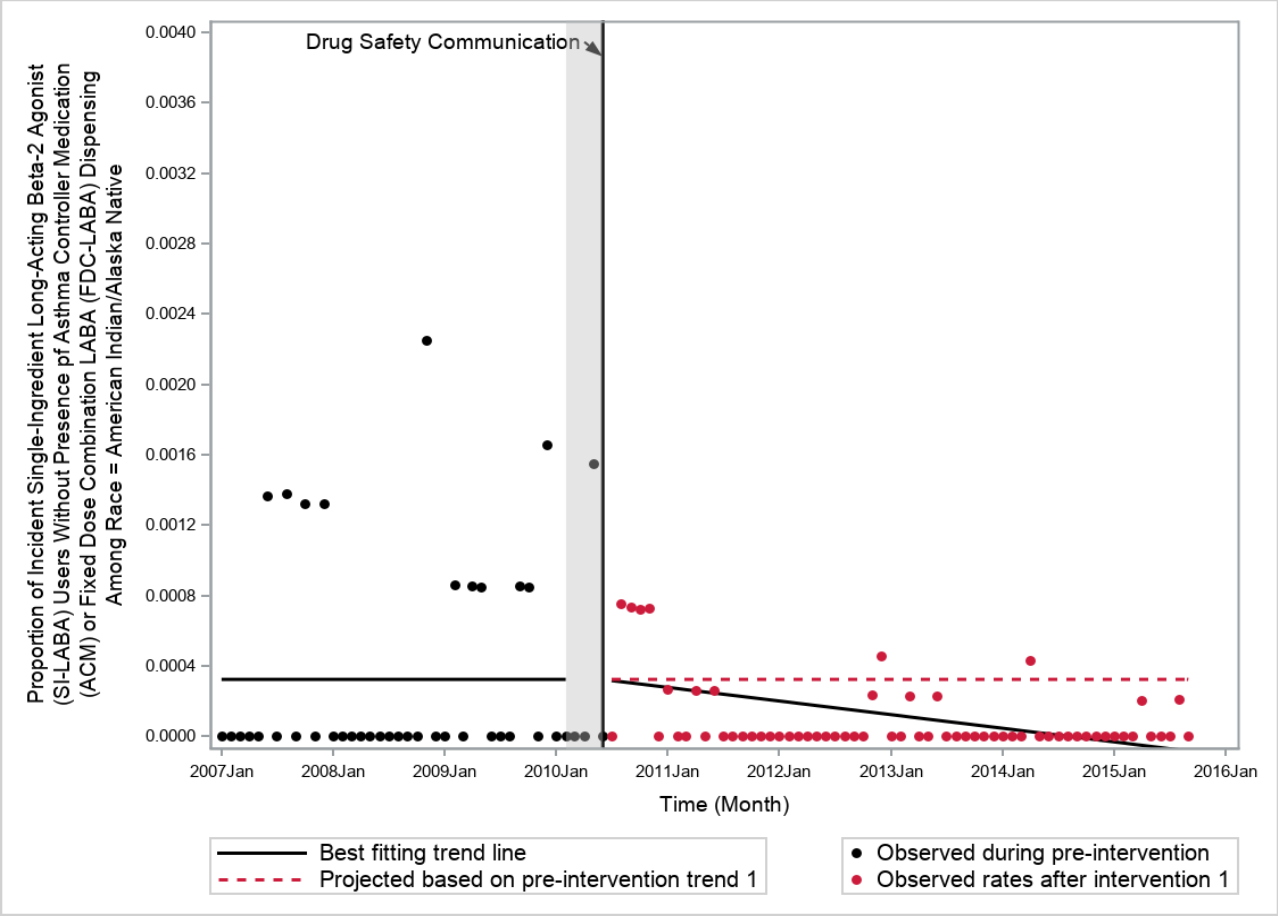


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 32. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (FDC-LABA) Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2,3], where Race = American Indian/Alaska Native

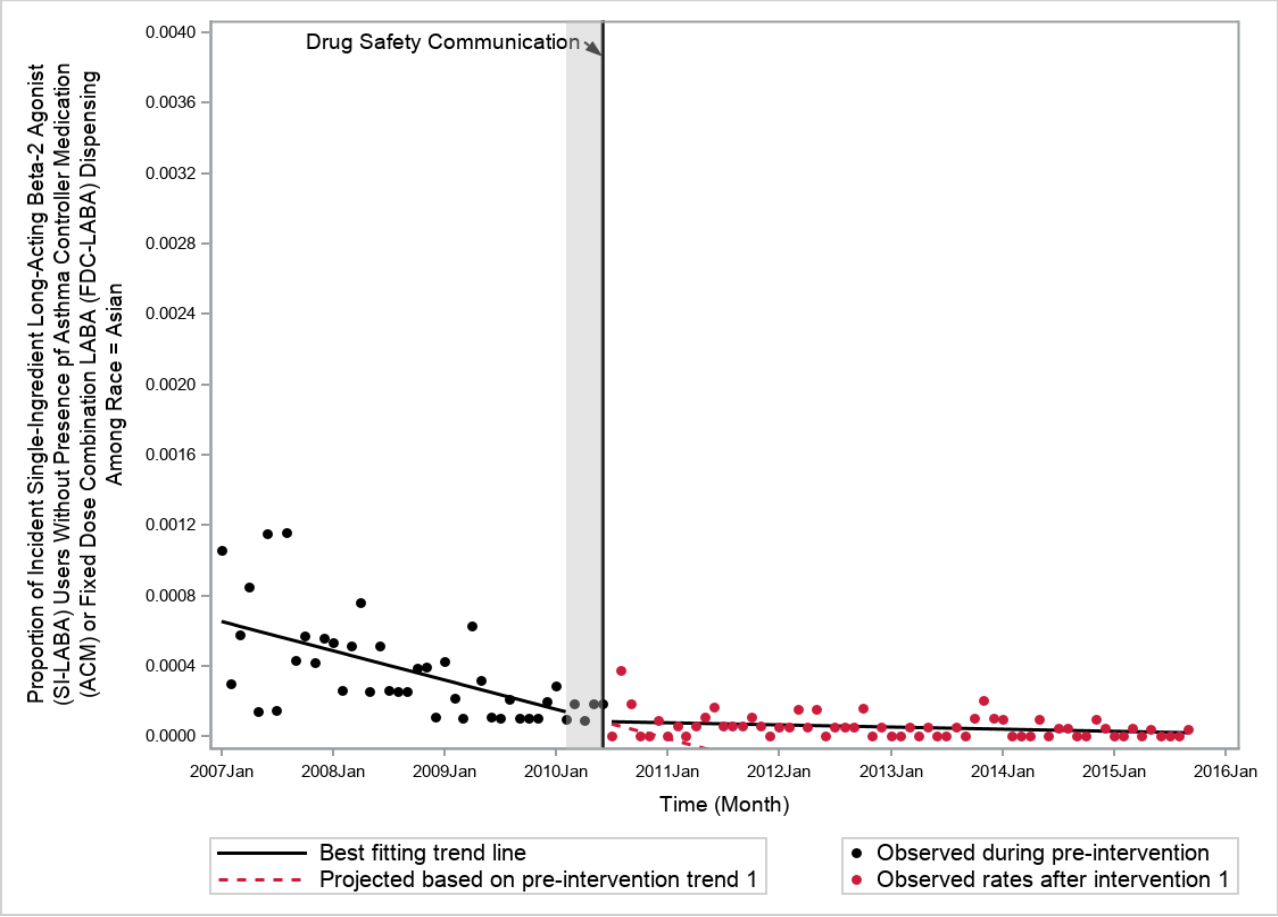


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 33. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (FDC-LABA) Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2,3], where Race = Asian

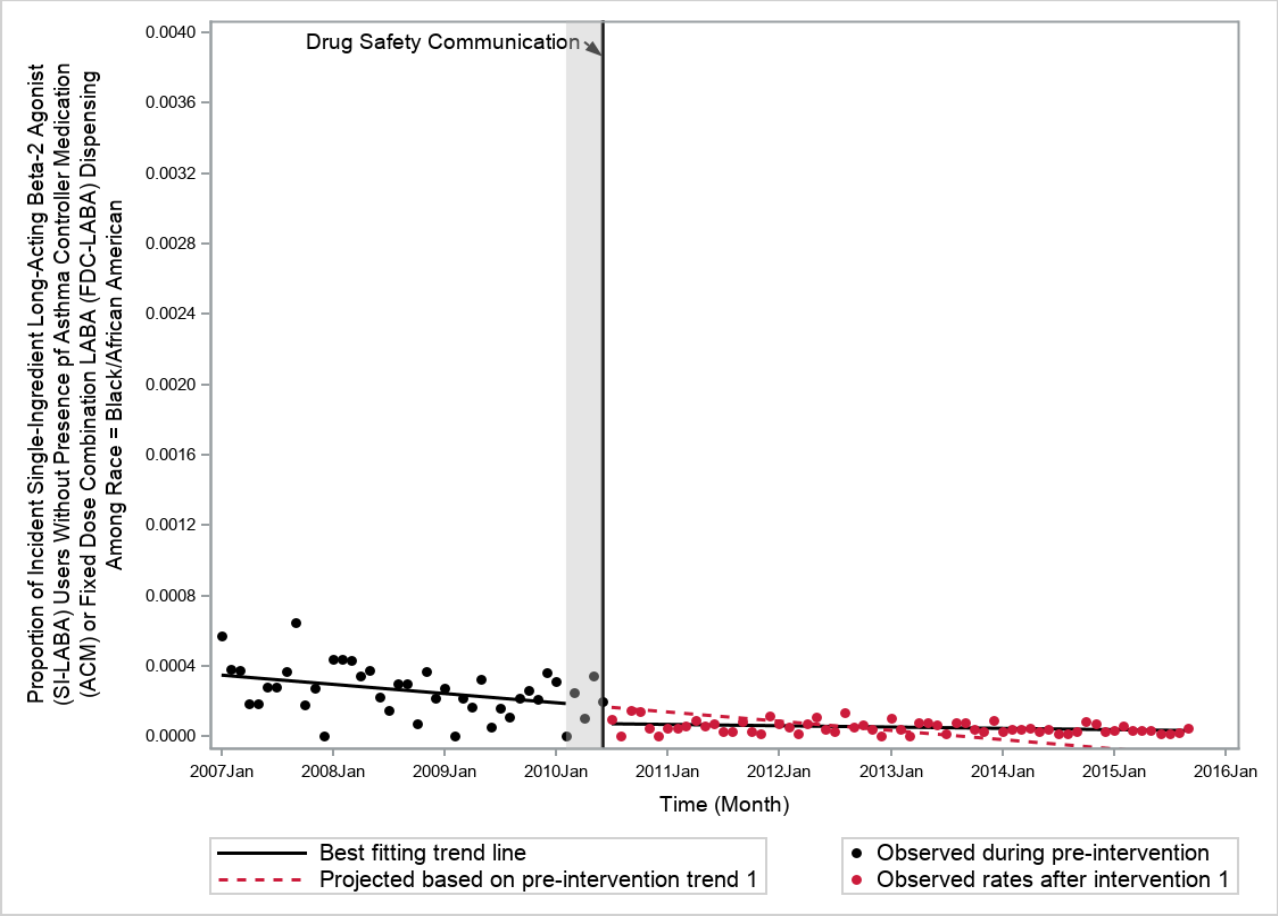


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 34. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (FDC-LABA) Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2,3], where Race = Black/African American

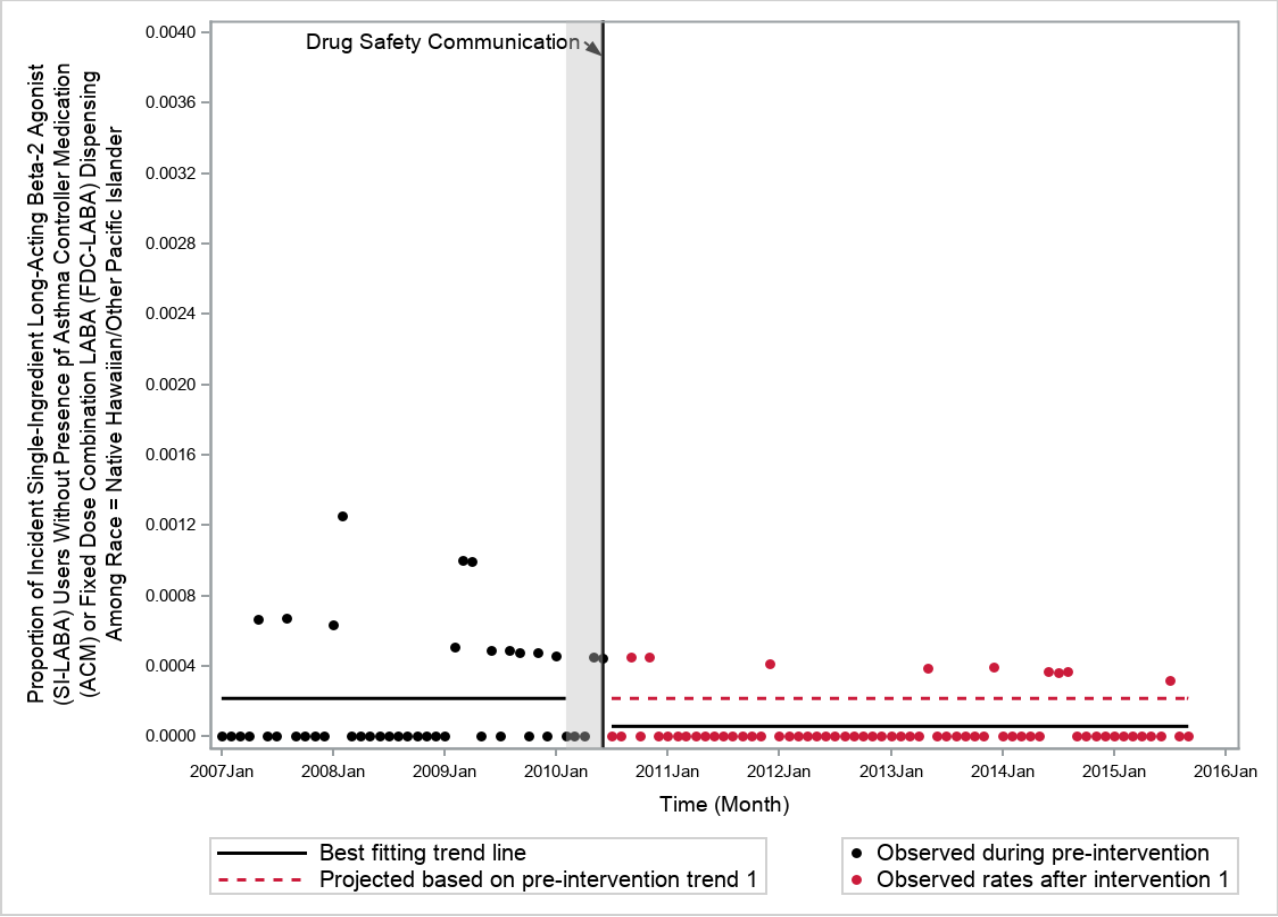


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 35. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (FDC-LABA) Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2,3], where Race = Native Hawaiian/Other Pacific Islander

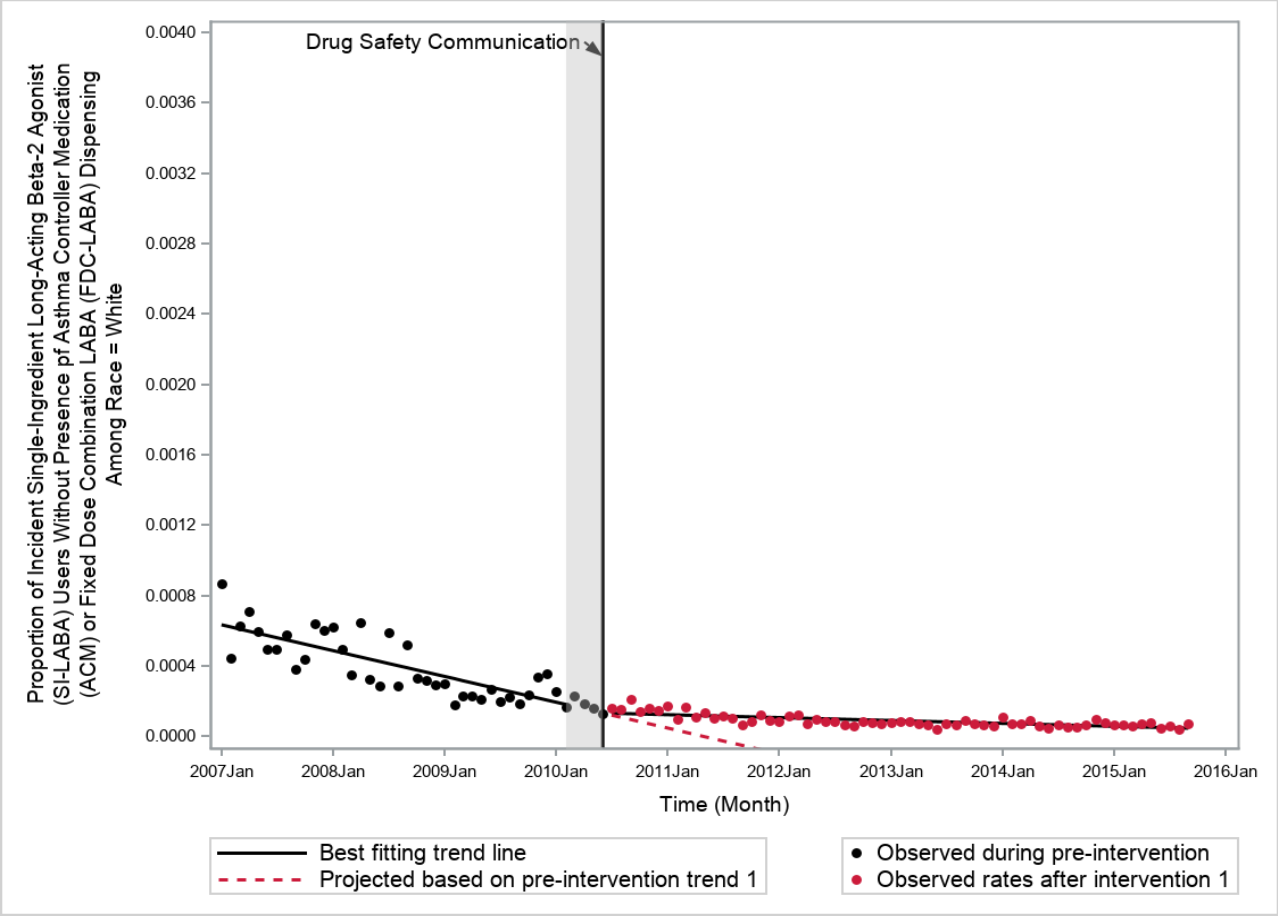


[1]The ITS model is performed with rounding to the nearest subsequent month for June 2, 2010 as the start of drug safety communication. Data from January 1, 2007 to September 30, 2015 is used to create the model.

[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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

Figure 36. Proportion of Incident Single-Ingredient Long-Acting Beta-2 Agonist (SI-LABA) Users Without Presence of Asthma Controller Medication (ACM) or Fixed Dose Combination LABA (FDC-LABA) Dispensing Among LABA-Naive Patients with Asthma Before and After June 2, 2010[1,2,3], 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).

[3]SI-LABA use is only considered if in the absence of ACM dispensing as determined by days supply on SI-LABA dispensing date.

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 Agonists (LABAs) 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 Agonists (LABAs) 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 Agonists (LABAs) and Other non-LABA Asthma Controller Medication (ACM) in this Request

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

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

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

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

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

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

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

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

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

Appendix E. Specifications Defining Parameters for this Request

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

Query Period: January 01, 2006 - September 30, 2015
Coverage Requirement: Medical & Drug Coverage
Pre-Index Enrollment Requirement: See below
Post-Index Enrollment Requirement: N/A
Enrollment Gap: 45 days
Age Groups: 18-45, 46-64, 65+ years
Sex Groups: Male, female
Stratifications: Age group, sex, race, ethnicity, Census Bureau regions
Censor Output Categorization: 0-30, 31-60, 61-90, 91-120, 121-183, 184-365, 366-730, 730+ 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

		Cohort 1	
		Recommendation 1 Paper Replication	
		Scenario 1	Scenario 2
ITS Analysis Groups	**Group Name**	**grp1_rep_laba**	**grp1_rep_silaba**
	ITS Group	**Primary**	**Secondary**
	Rate Denominator Definition	All incident LABA users	N/A
	Rate Denominator	Number of patients	N/A
	Rate Numerator Definition	N/A	Incident SI-LABA users
	Rate Numerator	N/A	Number of adherent patients
	Pre-Index Enrollment Requirement	365 days	365 days

Appendix E. Specifications Defining Parameters for this Request

		Cohort 1	
		Recommendation 1 Paper Replication	
		Scenario 1	Scenario 2
Drug/Exposure	**Exposure**	All LABA products (Single-ingredient (SI) OR fixed-dose combination (FDC))	Single-ingredient long-acting beta-2 agonist (SI-LABA)
	Care Setting	N/A	N/A
	Incident with Respect to	All LABA products (SI or FDC)	
	Washout	183 days	0 days
	Exposure Episode Truncation Criteria	*Death *Data Partner (DP) end date *Query end date	*Death *DP end date *Query end date
	Cohort Definition	Only the first valid treatment episode during the query period (01)	Cohort includes all valid exposure episodes during the query period (02)
	Prevalent Cohort Creation?	Yes	N/A
	Exposure Episode Gap	25% previous days' supply	25% previous days' supply
	Exposure Extension Period	0 days	0 days
	Minimum Episode Duration	1 day	1 day
	Minimum Days Supplied	1 day	1 day
	Intention-to-Treat Days	N/A	N/A
Inclusion/Exclusion Criteria	**Conditions**	*Chronic obstructive pulmonary disease (COPD) *Cystic fibrosis *Bronchiectasis *Pulmonary hypertension or embolism *Bronchopulmonary dysplasia *Congestive heart failure	*Chronic obstructive pulmonary disease (COPD) *Cystic fibrosis *Bronchiectasis *Pulmonary hypertension or embolism *Bronchopulmonary dysplasia *Congestive heart failure
	Include or Exclude	Exclusion	Exclusion
	Care Setting/Principal Diagnosis (PDX)	Any	Any
	Lookback Period	(-365, 0) days	(-365, 0) days
	Number of Code Occurrences	1 instance	1 instance

Appendix E. Specifications Defining Parameters for this Request

		Cohort 1	
		Recommendation 1 Paper Replication	
		Scenario 1	Scenario 2
Inclusion /Exclusion Criteria	**Conditions**	Asthma (493.xx)	Asthma (493.xx)
	Include or Exclude	Inclusion	Inclusion
	Care Setting/PDX	Any	Any
	Lookback Period	(-365, -1) days	(-365, -1) days
	Number of Code Occurrences	1 instance	1 instance
Inclusion /Exclusion Criteria	**Conditions**		Non-LABA asthma controller medication (ICS, leukotriene modifier, chromones, oral systemic corticosteroids, immunomodulators, and methylxanthines) (lookback period: dispensing date)
	Include or Exclude		Exclusion
	Care Setting/PDX		N/A
	Lookback Period		(0, 0) days
	Number of Code Occurrences		1 instance
Stockpiling	**Same Day Dispensing (Days Supplied)**	Sum	Sum
	Same Day Dispensing (Amount Supplied)	Sum	Sum
	Range of Allowable Days Supplied	N/A	N/A
	Range of Allowable Amount Supplied	N/A	N/A
	Overlap Percentage Processing	Default	Default
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	

Appendix E. Specifications Defining Parameters for this Request

		Cohort 1	
		Recommendation 1 Paper Replication	
		Scenario 1	Scenario 2
Adherence	**Adherence Name**	**Incident SI-LABA Users**	
	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	
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 FDC All LABA non-LABA ACM	
	Care Setting/PDX	N/A	
	Covariate Evaluation Window	(-183, -1) days	

Appendix E. Specifications Defining Parameters for this Request

		Cohort 1	
		Recommendation 1 Paper Replication	
		Scenario 1	Scenario 2
Baseline Covariates	**Covariates**	non-LABA ACM	
	Care Setting/PDX	N/A	
	Covariate Evaluation Window	(-365, -184) days	
Baseline Covariates	**Covariates**	SI-LABA FDC All LABA non-LABA ACM	
	Care Setting/PDX	N/A	
	Covariate Evaluation Window	(0, 0) days	
Utilization/ Comorbidity Score	**Comorbidity Score Evaluation Window**	(-365, 0) days	
	Medical Utilization Evaluation Window	(-365, 0) days	
	Medical Utilization Care Setting	IP, IS, AV, OA, ED	
	Drug Utilization Evaluation Window	(-365, 0) days	

		Cohort 2	
		Recommendation 1 Paper Replication, Days Supply and Asthma Definition	
		Scenario 3	Scenario 4
ITS Analysis Groups	**Group Name**	**grp234_asthma_laba**	**grp2_silaba_siinc**
	ITS Group	**Primary**	**Secondary**
	Rate Denominator Definition	All incident LABA users	N/A
	Rate Denominator	Number of patients	N/A
	Rate Numerator Definition	N/A	Incident SI-LABA users
	Rate Numerator	N/A	Number of adherent patients
	Pre-Index Enrollment Requirement	365 days	365 days

Appendix E. Specifications Defining Parameters for this Request

		Cohort 2	
		Recommendation 1 Paper Replication, Days Supply and Asthma Definition	
		Scenario 3	Scenario 4
Drug/Exposure	**Exposure**	All LABA products (SI or FDC)	SI-LABA
	Care Setting	N/A	N/A
	Incident with Respect to	All LABA products (SI or FDC)	
	Washout	183 days	0 days
	Exposure Episode Truncation Criteria	*Death *DP end date *Query end date	*Death *DP end date *Query end date
	Cohort Definition	Only the first valid treatment episode during the query period (01)	Cohort includes all valid exposure episodes during the query period (02)
	Prevalent Cohort Creation?	Yes	N/A
	Exposure Episode Gap	25% previous days' supply	25% previous days' supply
	Exposure Extension Period	0 days	0 days
	Minimum Episode Duration	1 day	1 day
	Minimum Days Supplied	1 day	1 day
	Intention-to-Treat Days	N/A	N/A
Inclusion/Exclusion Criteria	**Conditions**	*COPD *Cystic fibrosis *Bronchiectasis *Pulmonary hypertension or embolism *Bronchopulmonary dysplasia *Congestive heart failure	*COPD *Cystic fibrosis *Bronchiectasis *Pulmonary hypertension or embolism *Bronchopulmonary dysplasia *Congestive heart failure
	Include or Exclude	Exclusion	Exclusion
	Care Setting/PDX	Any	Any
	Lookback Period	(-365, 0) days	(-365, 0) days
	Number of Code Occurrences	1 instance	1 instance

Appendix E. Specifications Defining Parameters for this Request

		Cohort 2	
		Recommendation 1 Paper Replication, Days Supply and Asthma Definition	
		Scenario 3	Scenario 4
Inclusion/Exclusion Criteria	**Conditions**	Asthma (493.xx)	Asthma (493.xx)
	Include or Exclude	Inclusion	Inclusion
	Care Setting/PDX	IP*, ED*, AV*, OA*	IP*, ED*, AV*, OA*
	Lookback Period	(-365, 0) days	(-365, 0) days
	Number of Code Occurrences	1 instance if (IP*, ED*) 2 instances if (AV*, OA*)	1 instance if (IP*, ED*) 2 instances if (AV*, OA*)
Inclusion/Exclusion Criteria	**Conditions**		Non-LABA asthma controller medication (ICS, leukotriene modifier, chromones, oral systemic corticosteroids, immunomodulators, and methylxanthines) (lookback period: days supply)
	Include or Exclude		Exclusion
	Care Setting/PDX		N/A
	Lookback Period		(0, 0) days
	Number of Code Occurrences		1 instance
Stockpiling	**Same Day Dispensing (Days Supplied)**	Sum	Sum
	Same Day Dispensing (Amount Supplied)	Sum	Sum
	Range of Allowable Days Supplied	N/A	N/A
	Range of Allowable Amount Supplied	N/A	N/A
	Overlap Percentage Processing	Default	Default
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	

Appendix E. Specifications Defining Parameters for this Request

		Cohort 2	
		Recommendation 1 Paper Replication, Days Supply and Asthma Definition	
		Scenario 3	Scenario 4
Adherence	**Adherence Name**	**Incident SI-LABA Users (Sensitivity Analysis)**	
	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	
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	
	Continuous Enrollment Required?	No	
Baseline Covariates	**Covariates**	SI-LABA	
	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	

Appendix E. Specifications Defining Parameters for this Request

		Cohort 2 Recommendation 1 Paper Replication, Days Supply and Asthma Definition	
		Scenario 3	**Scenario 4**
Baseline Covariates	**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	

		Cohort 3 Recommendation 1 SI-LABA Only	
		Scenario 3	**Scenario 5**
ITS Analysis Groups	**Group Name**	**grp234_asthma_laba**	**grp3_silaba_allinc**
	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 SI-LABA users with no same-day use of any non-LABA ACM OR FDC**
	Rate Numerator	N/A	Number of adherent patients
	Pre-Index Enrollment Requirement	365 days	365 days
Drug/ Exposure	**Exposure**	All LABA products (SI or FDC)	SI-LABA
	Care Setting	N/A	N/A
	Incident with Respect to	All LABA products (SI or FDC)	
	Washout	183 days	0 days

Appendix E. Specifications Defining Parameters for this Request

		Cohort 3	
		Recommendation 1 SI-LABA Only	
		Scenario 3	Scenario 5
Drug/ Exposure	**Exposure Episode Truncation Criteria**	*Death *DP end date *Query end date	*Death *DP end date *Query end date
	Cohort Definition	Only the first valid treatment episode during the query period (01)	Cohort includes all valid exposure episodes during the query period (02)
	Prevalent Cohort Creation?	Yes	N/A
	Exposure Episode Gap	25% previous days' supply	25% previous days' supply
	Exposure Extension Period	0 days	0 days
	Minimum Episode Duration	1 day	1 day
	Minimum Days Supplied	1 day	1 day
	Intention-to-Treat Days	N/A	N/A
Inclusion/Exclusion Criteria	**Conditions**	*Chronic obstructive pulmonary disease (COPD) *Cystic fibrosis *Bronchiectasis *Pulmonary hypertension or embolism *Bronchopulmonary dysplasia *Congestive heart failure	*Chronic obstructive pulmonary disease (COPD) *Cystic fibrosis *Bronchiectasis *Pulmonary hypertension or embolism *Bronchopulmonary dysplasia *Congestive heart failure
	Include or Exclude	Exclusion	Exclusion
	Care Setting/PDX	Any	Any
	Lookback Period	(-365, 0) days	(-365, 0) days
	Number of Code Occurrences	1 instance	1 instance
Inclusion/Exclusion Criteria	**Conditions**	Asthma (493.xx)	Asthma (493.xx)
	Include or Exclude	Inclusion	Inclusion
	Care Setting/PDX	**IP*, ED*, AV*, OA***	**IP*, ED*, AV*, OA***
	Lookback Period	**(-365, 0) days**	**(-365, 0) days**
	Number of Code Occurrences	**1 instance if (IP*, ED*) 2 instances if (AV*, OA*)**	**1 instance if (IP*, ED*) 2 instances if (AV*, OA*)**

Appendix E. Specifications Defining Parameters for this Request

		Cohort 3	
		Recommendation 1 SI-LABA Only	
		Scenario 3	Scenario 5
Inclusion/Exclusion Criteria	**Conditions**		Non-LABA asthma controller medication (ICS, leukotriene modifier, chromones, oral systemic corticosteroids, immunomodulators, and methylxanthines) OR **(FDC)** **(lookback period: days supply)**
	Include or Exclude		Exclusion
	Care Setting/PDX		Any
	Lookback Period		(0, 0) days
	Number of Code Occurrences		1 instance
Stockpiling	**Same Day Dispensing (Days Supplied)**	Sum	Sum
	Same Day Dispensing (Amount Supplied)	Sum	Sum
	Range of Allowable Days Supplied	N/A	N/A
	Range of Allowable Amount Supplied	N/A	N/A
	Overlap Percentage Processing	Default	Default
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 SI-LABA-only Users**	
	Minimum/Maximum Episode Length or Overlap Time (Overlap)	1 day minimum	
	Minimum/Maximum Secondary Episode Count (Multiple Events)	N/A	

Appendix E. Specifications Defining Parameters for this Request

		Cohort 3	
		Recommendation 1 SI-LABA Only	
		Scenario 3	Scenario 5
Adherence	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	
Baseline Covariates	Covariates	SI-LABA FDC All LABA non-LABA ACM	
	Care Setting/PDX	N/A	
	Covariate Evaluation Window	(-183, -1) days	
	Covariates	non-LABA ACM	
	Care Setting/PDX	N/A	
	Covariate Evaluation Window	(-365, -184) days	

Appendix E. Specifications Defining Parameters for this Request

		Cohort 3	
		Recommendation 1 SI-LABA Only	
		Scenario 3	Scenario 5
Baseline Covariates	**Covariates**	SI-LABA FDC All LABA non-LABA ACM	
	Care Setting/PDX	N/A	
	Covariate Evaluation Window	(0, 0) days	
Utilization/ Comorbidity Score	**Comorbidity Score Evaluation Window**	(-365, 0) days	
	Medical Utilization Evaluation Window	(-365, 0) days	
	Medical Utilization Care Setting	IP, IS, AV, OA, ED	
	Drug Utilization Evaluation Window	(-365, 0) days	