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_mpl2p_wp058

Request ID: cder_mpl2p_wp058

Request Description: This report contains the estimates of prevalent utilization of hydrochlorothiazide (HCTZ)-containing diuretics, non HCTZ-containing diuretics, and antihypertensives in the Sentinel Distributed Database (SDD) to understand the impact of labeling changes that were made on August 8, 2020.

Sentinel Routine Querying Module: Cohort Identification and Descriptive Analysis (CIDA) module, version 12.1.0

Data Source: We distributed this query to Merative MarketScan Research Databases on January 10, 2024. The study period included data from January 1, 2017 through December 31, 2022.

Study Design: This query assessed the prevalence of outpatient exposure to HCTZ-containing diuretics, non HCTZ-containing diuretics, and antihypertensives among individuals within the SDD, overall and by calendar year-month. Results were reported overall and stratified by age group; sex; race; and both age group and race. This query is part two of a two-part analysis, where part two contains inclusion or exclusion criteria for history of skin cancer. This report presents the results from the Interrupted time series (ITS) analyses performed using data from cder_mpl2p_wp058_nsdp2_v01. Please refer to the main report for the Appendices.

This was a Type 2 analysis in the Query Request Package (QRP) documentation.

Exposure(s) of Interest: The exposures of interest were any HCTZ-containing product (including HCTZ monotherapy, any HCTZ combination product, HCTZ-angiotensin converting enzyme inhibitor [ACEi] combination product, HCTZ-angiotensin receptor blocker [ARB] combination product, HCTZ-potassium sparing diuretic combination product, HCTZ-beta blocker combination product, HCTZ-ARB-calcium channel blocker [CCB] combination product, HCTZ-direct renin inhibitor combination product, and HCTZ-central alpha 2 agonist combination product), any HCTZ containing product with HCTZ strength < 25 mg, any HCTZ containing product with HCTZ strength ≥ 25 mg, any HCTZ combination product with HCTZ strength < 25 mg, any HCTZ combination product with HCTZ strength ≥ 25 mg, any non HCTZ-containing diuretic (including chlorothiazide, bendroflumethiazide, and thiazide-like diuretics), ACEi, CCB, ARB, beta-blocker, potassium sparing diuretic, and loop diuretic. Additionally, two groups of exposures were defined as denominators for calculating proportions by calendar year-month: limited denominator (any HCTZ-containing product, chlorothiazide, bendroflumethiazide, or thiazide-like diuretic) and full denominator (any HCTZ-containing product, chlorothiazide, bendroflumethiazide, thiazide-like diuretic, or any antihypertensive). All qualifying exposures during the study period were evaluated. The exposures of interest were defined using National Drug Code (NDCs). See Appendix B for generic and brand names of medical products.

Cohort Eligibility Criteria: We identified cohorts which included patients of all ages. The following age groups were defined: 0-40, 41-54, 55-64, 65-74, 75-84, and 85 years of age or greater. No pre-index enrollment requirement was applied.

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. No exposure episode gaps or extensions were considered in the creation of the episode. Dispensings in each cohort were stockpiled with all other exposure-defining dispensings within the cohort, regardless of the original drug class. 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 the Data Partner; or 4) the end of the query period (December 31, 2022).

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 August 8, 2020, which is the date of the HCTZ drug safety communication (DSC)[1] issued by the US Food and Drug Administration (FDA). Numerator and denominator counts used to calculate observed rates were taken to be the number of patients with any duration of the exposure episode during the corresponding month interval. The rate modeled is described below:

Overview for Request: cder_mpl2p_wp058
Cohort 1) The rate used for the interrupted time series (ITS) regression model is the number of patients with use of any HCTZ-containing product among users in the limited denominator cohort. Cohort 2) The rate used for the ITS regression model is the number of patients with use of HCTZ single ingredient among users in the limited denominator cohort. Cohort 3) The rate used for the ITS regression model is the number of patients with use of ACEI + HCTZ combo product among users in the limited denominator cohort. Cohort 4) The rate used for the ITS regression model is the number of patients with use of ARB + HCTZ combo product among users in the limited denominator cohort. Cohort 5) The rate used for the ITS regression model is the number of patients with use of potassium-sparing diuretic + HCTZ combo product among users in the limited denominator cohort. Cohort 6) The rate used for the ITS regression model is the number of patients with use of beta blocker + HCTZ combo product among users in the limited denominator cohort. Cohort 7) The rate used for the ITS regression model is the number of patients with use of ARB + CCB + HCTZ combo product among users in the limited denominator cohort. Cohort 8) The rate used for the ITS regression model is the number of patients with use of direct renin inhibitor + HCTZ combo product among users in the limited denominator cohort. Cohort 9) The rate used for the ITS regression model is the number of patients with use of central alpha 2 agonist + HCTZ combo product among users in the limited denominator cohort. Cohort 10) The rate used for the ITS regression model is the number of patients with use of any HCTZ-containing products among users in the full denominator cohort. Cohort 11) The rate used for the ITS regression model is the number of patients with use of chlorothiazide, bendroflumethiazide or thiazide-like diuretic product among users in the full denominator cohort. Cohort 12) The rate used for the ITS regression model is the number of patients with use of non-HCTZ combination ACEI product among users in the full denominator cohort. Cohort 13) The rate used for the ITS regression model is the number of patients with use of non-HCTZ combination CCB product among users in the full denominator cohort. Cohort 14) The rate used for the ITS regression model is the number of patients with use of non-HCTZ combination potassium-sparing diuretic product among users in the full denominator cohort. Cohort 15) The rate used for the ITS regression model is the number of patients with use of loop diuretic product among users in the full denominator cohort. ITS regression was performed for overall population. We also fitted these same models using an anticipatory and lag period from June 1, 2020 to October 1, 2020 during which observations were not included in the autoregression model. **Please see the Appendices C.1-C.2 for the specifications of parameters used in the analyses for this request.** **Limitations:** Algorithms to define exposures, inclusion, and exclusion criteria are imperfect and may result in misclassification. Therefore, data should be interpreted with this limitation in mind. **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]Drug Safety-related Labeling Changes (SrLC). Fda.gov. Published 2020. https://www.accessdata.fda.gov/scripts/cder/safetylabelingchanges/index.cfm?event=searchdetail.page&DrugNameID=2310

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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).

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

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 1. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ/ACEI Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.175104	(0.170615, 0.179593)	<.001
Baseline trend	-0.000074	(-0.000237, 0.000088)	0.364
Level Change (After Intervention 1)	-0.000999	(-0.005126, 0.003128)	0.631
Trend Change (After Intervention 1)	0.000052	(-0.000327, 0.000432)	0.784
Most Parsimonious Final Model Parameters (df = 71)[2,3]			
Intercept	0.175034	(0.171420, 0.178647)	<.001
Baseline trend	-0.000074	(-0.000160, 0.000011)	0.087

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 2. Absolute and Relative Changes in Proportion of HCTZ/ACEI Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.171688	0.171688
Relative Change (%) at 1 Months after Intervention 1	0.00	(0.00, 0.00)	0.171688	0.171688
Absolute Change at 2 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.171614	0.171614
Relative Change (%) at 2 Months after Intervention 1	0.00	(0.00, 0.00)	0.171614	0.171614
Absolute Change at 3 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.171540	0.171540
Relative Change (%) at 3 Months after Intervention 1	0.00	(0.00, 0.00)	0.171540	0.171540
Absolute Change at 4 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.171465	0.171465
Relative Change (%) at 4 Months after Intervention 1	0.00	(0.00, 0.00)	0.171465	0.171465
Absolute Change at 5 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.171391	0.171391
Relative Change (%) at 5 Months after Intervention 1	0.00	(0.00, 0.00)	0.171391	0.171391
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.171317	0.171317
Relative Change (%) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.171317	0.171317
Absolute Change at 7 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.171242	0.171242
Relative Change (%) at 7 Months after Intervention 1	0.00	(0.00, 0.00)	0.171242	0.171242
Absolute Change at 8 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.171168	0.171168
Relative Change (%) at 8 Months after Intervention 1	0.00	(0.00, 0.00)	0.171168	0.171168
Absolute Change at 9 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.171094	0.171094
Relative Change (%) at 9 Months after Intervention 1	0.00	(0.00, 0.00)	0.171094	0.171094
Absolute Change at 10 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.171019	0.171019
Relative Change (%) at 10 Months after Intervention 1	0.00	(0.00, 0.00)	0.171019	0.171019
Absolute Change at 11 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.170945	0.170945
Relative Change (%) at 11 Months after Intervention 1	0.00	(0.00, 0.00)	0.170945	0.170945
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.170871	0.170871
Relative Change (%) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.170871	0.170871
Absolute Change at 13 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.170796	0.170796
Relative Change (%) at 13 Months after Intervention 1	0.00	(0.00, 0.00)	0.170796	0.170796
Absolute Change at 14 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.170722	0.170722
Relative Change (%) at 14 Months after Intervention 1	0.00	(0.00, 0.00)	0.170722	0.170722
Absolute Change at 15 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.170648	0.170648

Table 2. Absolute and Relative Changes in Proportion of HCTZ/ACEI Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Relative Change (%) at 15 Months after Intervention 1	0.00	(0.00, 0.00)	0.170648	0.170648
Absolute Change at 16 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.170573	0.170573
Relative Change (%) at 16 Months after Intervention 1	0.00	(0.00, 0.00)	0.170573	0.170573
Absolute Change at 17 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.170499	0.170499
Relative Change (%) at 17 Months after Intervention 1	0.00	(0.00, 0.00)	0.170499	0.170499
Absolute Change at 18 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.170425	0.170425
Relative Change (%) at 18 Months after Intervention 1	0.00	(0.00, 0.00)	0.170425	0.170425
Absolute Change at 19 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.170350	0.170350
Relative Change (%) at 19 Months after Intervention 1	0.00	(0.00, 0.00)	0.170350	0.170350
Absolute Change at 20 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.170276	0.170276
Relative Change (%) at 20 Months after Intervention 1	0.00	(0.00, 0.00)	0.170276	0.170276
Absolute Change at 21 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.170202	0.170202
Relative Change (%) at 21 Months after Intervention 1	0.00	(0.00, 0.00)	0.170202	0.170202
Absolute Change at 22 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.170127	0.170127
Relative Change (%) at 22 Months after Intervention 1	0.00	(0.00, 0.00)	0.170127	0.170127
Absolute Change at 23 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.170053	0.170053
Relative Change (%) at 23 Months after Intervention 1	0.00	(0.00, 0.00)	0.170053	0.170053
Absolute Change at 24 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.169979	0.169979
Relative Change (%) at 24 Months after Intervention 1	0.00	(0.00, 0.00)	0.169979	0.169979
Absolute Change at 25 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.169904	0.169904
Relative Change (%) at 25 Months after Intervention 1	0.00	(0.00, 0.00)	0.169904	0.169904
Absolute Change at 26 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.169830	0.169830
Relative Change (%) at 26 Months after Intervention 1	0.00	(0.00, 0.00)	0.169830	0.169830
Absolute Change at 27 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.169756	0.169756
Absolute Change at 27 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.169756	0.169756
Relative Change (%) at 27 Months after Intervention 1	0.00	(0.00, 0.00)	0.169756	0.169756
Relative Change (%) at 27 Months after Intervention 1	0.00	(0.00, 0.00)	0.169756	0.169756

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 3. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ/ARB/CCB Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.008333	(0.008100, 0.008567)	<.001
Baseline trend	-0.000023	(-0.000032, -0.000014)	<.001
Level Change (After Intervention 1)	0.000101	(-0.000263, 0.000464)	0.582
Trend Change (After Intervention 1)	-0.000074	(-0.000096, -0.000051)	<.001
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.008316	(0.008092, 0.008541)	<.001
Baseline trend	-0.000022	(-0.000030, -0.000014)	<.001
Trend Change (After Intervention 1)	-0.000071	(-0.000091, -0.000050)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 4. Absolute and Relative Changes in Proportion of HCTZ/ARB/CCB Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	-0.000071	(-0.000091, -0.000050)	0.007255	0.007326
Relative Change (%) at 1 Months after Intervention 1	-0.96	(-1.22, -0.70)	0.007255	0.007326
Absolute Change at 2 Months after Intervention 1	-0.000141	(-0.000182, -0.000100)	0.007163	0.007304
Relative Change (%) at 2 Months after Intervention 1	-1.93	(-2.45, -1.41)	0.007163	0.007304
Absolute Change at 3 Months after Intervention 1	-0.000212	(-0.000273, -0.000150)	0.007070	0.007282
Relative Change (%) at 3 Months after Intervention 1	-2.90	(-3.68, -2.13)	0.007070	0.007282
Absolute Change at 4 Months after Intervention 1	-0.000282	(-0.000364, -0.000200)	0.006978	0.007260
Relative Change (%) at 4 Months after Intervention 1	-3.88	(-4.92, -2.85)	0.006978	0.007260
Absolute Change at 5 Months after Intervention 1	-0.000353	(-0.000455, -0.000250)	0.006885	0.007238
Relative Change (%) at 5 Months after Intervention 1	-4.87	(-6.16, -3.58)	0.006885	0.007238
Absolute Change at 6 Months after Intervention 1	-0.000423	(-0.000546, -0.000301)	0.006793	0.007216
Relative Change (%) at 6 Months after Intervention 1	-5.86	(-7.41, -4.31)	0.006793	0.007216
Absolute Change at 7 Months after Intervention 1	-0.000494	(-0.000636, -0.000351)	0.006700	0.007194
Relative Change (%) at 7 Months after Intervention 1	-6.86	(-8.67, -5.05)	0.006700	0.007194
Absolute Change at 8 Months after Intervention 1	-0.000564	(-0.000727, -0.000401)	0.006608	0.007172
Relative Change (%) at 8 Months after Intervention 1	-7.86	(-9.93, -5.80)	0.006608	0.007172
Absolute Change at 9 Months after Intervention 1	-0.000635	(-0.000818, -0.000451)	0.006515	0.007150
Relative Change (%) at 9 Months after Intervention 1	-8.87	(-11.19, -6.56)	0.006515	0.007150
Absolute Change at 10 Months after Intervention 1	-0.000705	(-0.000909, -0.000501)	0.006423	0.007128
Relative Change (%) at 10 Months after Intervention 1	-9.89	(-12.47, -7.32)	0.006423	0.007128
Absolute Change at 11 Months after Intervention 1	-0.000776	(-0.001000, -0.000551)	0.006330	0.007106
Relative Change (%) at 11 Months after Intervention 1	-10.91	(-13.74, -8.08)	0.006330	0.007106
Absolute Change at 12 Months after Intervention 1	-0.000846	(-0.001091, -0.000601)	0.006238	0.007084
Relative Change (%) at 12 Months after Intervention 1	-11.94	(-15.03, -8.86)	0.006238	0.007084
Absolute Change at 13 Months after Intervention 1	-0.000917	(-0.001182, -0.000651)	0.006145	0.007062
Relative Change (%) at 13 Months after Intervention 1	-12.98	(-16.32, -9.64)	0.006145	0.007062
Absolute Change at 14 Months after Intervention 1	-0.000987	(-0.001273, -0.000701)	0.006053	0.007040
Relative Change (%) at 14 Months after Intervention 1	-14.02	(-17.62, -10.43)	0.006053	0.007040
Absolute Change at 15 Months after Intervention 1	-0.001058	(-0.001364, -0.000751)	0.005960	0.007018
Relative Change (%) at 15 Months after Intervention 1	-15.07	(-18.92, -11.22)	0.005960	0.007018
Absolute Change at 16 Months after Intervention 1	-0.001128	(-0.001455, -0.000801)	0.005868	0.006996
Relative Change (%) at 16 Months after Intervention 1	-16.12	(-20.23, -12.02)	0.005868	0.006996

Table 4. Absolute and Relative Changes in Proportion of HCTZ/ARB/CCB Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 17 Months after Intervention 1	-0.001199	(-0.001546, -0.000851)	0.005775	0.006974
Relative Change (%) at 17 Months after Intervention 1	-17.19	(-21.54, -12.83)	0.005775	0.006974
Absolute Change at 18 Months after Intervention 1	-0.001269	(-0.001637, -0.000902)	0.005682	0.006952
Relative Change (%) at 18 Months after Intervention 1	-18.26	(-22.86, -13.65)	0.005682	0.006952
Absolute Change at 19 Months after Intervention 1	-0.001340	(-0.001727, -0.000952)	0.005590	0.006930
Relative Change (%) at 19 Months after Intervention 1	-19.33	(-24.19, -14.47)	0.005590	0.006930
Absolute Change at 20 Months after Intervention 1	-0.001410	(-0.001818, -0.001002)	0.005497	0.006908
Relative Change (%) at 20 Months after Intervention 1	-20.41	(-25.53, -15.30)	0.005497	0.006908
Absolute Change at 21 Months after Intervention 1	-0.001481	(-0.001909, -0.001052)	0.005405	0.006885
Relative Change (%) at 21 Months after Intervention 1	-21.50	(-26.87, -16.14)	0.005405	0.006885
Absolute Change at 22 Months after Intervention 1	-0.001551	(-0.002000, -0.001102)	0.005312	0.006863
Relative Change (%) at 22 Months after Intervention 1	-22.60	(-28.21, -16.98)	0.005312	0.006863
Absolute Change at 23 Months after Intervention 1	-0.001622	(-0.002091, -0.001152)	0.005220	0.006841
Relative Change (%) at 23 Months after Intervention 1	-23.70	(-29.57, -17.84)	0.005220	0.006841
Absolute Change at 24 Months after Intervention 1	-0.001692	(-0.002182, -0.001202)	0.005127	0.006819
Relative Change (%) at 24 Months after Intervention 1	-24.81	(-30.93, -18.70)	0.005127	0.006819
Absolute Change at 25 Months after Intervention 1	-0.001763	(-0.002273, -0.001252)	0.005035	0.006797
Relative Change (%) at 25 Months after Intervention 1	-25.93	(-32.29, -19.57)	0.005035	0.006797
Absolute Change at 26 Months after Intervention 1	-0.001833	(-0.002364, -0.001302)	0.004942	0.006775
Relative Change (%) at 26 Months after Intervention 1	-27.05	(-33.66, -20.44)	0.004942	0.006775
Absolute Change at 27 Months after Intervention 1	-0.001904	(-0.002455, -0.001352)	0.004850	0.006753
Absolute Change at 27 Months after Intervention 1	-0.001904	(-0.002455, -0.001352)	0.004850	0.006753
Relative Change (%) at 27 Months after Intervention 1	-28.19	(-35.04, -21.33)	0.004850	0.006753
Relative Change (%) at 27 Months after Intervention 1	-28.19	(-35.04, -21.33)	0.004850	0.006753

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 5. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ/ARB Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.291543	(0.271287, 0.311798)	<.001
Baseline trend	-0.001515	(-0.002238, -0.000791)	<.001
Level Change (After Intervention 1)	-0.000933	(-0.004833, 0.002967)	0.635
Trend Change (After Intervention 1)	0.001475	(-0.000295, 0.003244)	0.101
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.290844	(0.270967, 0.310722)	<.001
Baseline trend	-0.001510	(-0.002212, -0.000807)	<.001
Trend Change (After Intervention 1)	0.001467	(-0.000182, 0.003115)	0.081

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 6. Absolute and Relative Changes in Proportion of HCTZ/ARB Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.001467	(-0.000216, 0.003149)	0.224382	0.222915
Relative Change (%) at 1 Months after Intervention 1	0.66	(-0.14, 1.46)	0.224382	0.222915
Absolute Change at 2 Months after Intervention 1	0.002933	(-0.000433, 0.006299)	0.224339	0.221406
Relative Change (%) at 2 Months after Intervention 1	1.32	(-0.29, 2.94)	0.224339	0.221406
Absolute Change at 3 Months after Intervention 1	0.004400	(-0.000649, 0.009448)	0.224296	0.219896
Relative Change (%) at 3 Months after Intervention 1	2.00	(-0.45, 4.45)	0.224296	0.219896
Absolute Change at 4 Months after Intervention 1	0.005866	(-0.000866, 0.012598)	0.224253	0.218387
Relative Change (%) at 4 Months after Intervention 1	2.69	(-0.61, 5.99)	0.224253	0.218387
Absolute Change at 5 Months after Intervention 1	0.007333	(-0.001082, 0.015747)	0.224210	0.216877
Relative Change (%) at 5 Months after Intervention 1	3.38	(-0.79, 7.55)	0.224210	0.216877
Absolute Change at 6 Months after Intervention 1	0.008799	(-0.001298, 0.018897)	0.224167	0.215368
Relative Change (%) at 6 Months after Intervention 1	4.09	(-0.96, 9.13)	0.224167	0.215368
Absolute Change at 7 Months after Intervention 1	0.010266	(-0.001515, 0.022046)	0.224124	0.213858
Relative Change (%) at 7 Months after Intervention 1	4.80	(-1.15, 10.75)	0.224124	0.213858
Absolute Change at 8 Months after Intervention 1	0.011732	(-0.001731, 0.025196)	0.224081	0.212349
Relative Change (%) at 8 Months after Intervention 1	5.53	(-1.34, 12.39)	0.224081	0.212349
Absolute Change at 9 Months after Intervention 1	0.013199	(-0.001947, 0.028345)	0.224038	0.210839
Relative Change (%) at 9 Months after Intervention 1	6.26	(-1.54, 14.06)	0.224038	0.210839
Absolute Change at 10 Months after Intervention 1	0.014666	(-0.002164, 0.031495)	0.223995	0.209330
Relative Change (%) at 10 Months after Intervention 1	7.01	(-1.75, 15.76)	0.223995	0.209330
Absolute Change at 11 Months after Intervention 1	0.016132	(-0.002380, 0.034644)	0.223952	0.207820
Relative Change (%) at 11 Months after Intervention 1	7.76	(-1.96, 17.49)	0.223952	0.207820
Absolute Change at 12 Months after Intervention 1	0.017599	(-0.002597, 0.037794)	0.223909	0.206311
Relative Change (%) at 12 Months after Intervention 1	8.53	(-2.19, 19.25)	0.223909	0.206311
Absolute Change at 13 Months after Intervention 1	0.019065	(-0.002813, 0.040943)	0.223866	0.204801
Relative Change (%) at 13 Months after Intervention 1	9.31	(-2.42, 21.04)	0.223866	0.204801
Absolute Change at 14 Months after Intervention 1	0.020532	(-0.003029, 0.044093)	0.223823	0.203292
Relative Change (%) at 14 Months after Intervention 1	10.10	(-2.67, 22.87)	0.223823	0.203292
Absolute Change at 15 Months after Intervention 1	0.021998	(-0.003246, 0.047242)	0.223780	0.201782
Relative Change (%) at 15 Months after Intervention 1	10.90	(-2.92, 24.73)	0.223780	0.201782

Table 6. Absolute and Relative Changes in Proportion of HCTZ/ARB Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 16 Months after Intervention 1	0.023465	(-0.003462, 0.050392)	0.223737	0.200273
Relative Change (%) at 16 Months after Intervention 1	11.72	(-3.19, 26.62)	0.223737	0.200273
Absolute Change at 17 Months after Intervention 1	0.024931	(-0.003678, 0.053541)	0.223695	0.198763
Relative Change (%) at 17 Months after Intervention 1	12.54	(-3.46, 28.55)	0.223695	0.198763
Absolute Change at 18 Months after Intervention 1	0.026398	(-0.003895, 0.056691)	0.223652	0.197254
Relative Change (%) at 18 Months after Intervention 1	13.38	(-3.75, 30.51)	0.223652	0.197254
Absolute Change at 19 Months after Intervention 1	0.027865	(-0.004111, 0.059840)	0.223609	0.195744
Relative Change (%) at 19 Months after Intervention 1	14.24	(-4.04, 32.51)	0.223609	0.195744
Absolute Change at 20 Months after Intervention 1	0.029331	(-0.004328, 0.062990)	0.223566	0.194234
Relative Change (%) at 20 Months after Intervention 1	15.10	(-4.35, 34.55)	0.223566	0.194234
Absolute Change at 21 Months after Intervention 1	0.030798	(-0.004544, 0.066139)	0.223523	0.192725
Relative Change (%) at 21 Months after Intervention 1	15.98	(-4.67, 36.63)	0.223523	0.192725
Absolute Change at 22 Months after Intervention 1	0.032264	(-0.004760, 0.069289)	0.223480	0.191215
Relative Change (%) at 22 Months after Intervention 1	16.87	(-5.01, 38.75)	0.223480	0.191215
Absolute Change at 23 Months after Intervention 1	0.033731	(-0.004977, 0.072438)	0.223437	0.189706
Relative Change (%) at 23 Months after Intervention 1	17.78	(-5.35, 40.91)	0.223437	0.189706
Absolute Change at 24 Months after Intervention 1	0.035197	(-0.005193, 0.075588)	0.223394	0.188196
Relative Change (%) at 24 Months after Intervention 1	18.70	(-5.71, 43.12)	0.223394	0.188196
Absolute Change at 25 Months after Intervention 1	0.036664	(-0.005410, 0.078737)	0.223351	0.186687
Relative Change (%) at 25 Months after Intervention 1	19.64	(-6.09, 45.37)	0.223351	0.186687
Absolute Change at 26 Months after Intervention 1	0.038130	(-0.005626, 0.081887)	0.223308	0.185177
Relative Change (%) at 26 Months after Intervention 1	20.59	(-6.48, 47.66)	0.223308	0.185177
Absolute Change at 27 Months after Intervention 1	0.039597	(-0.005842, 0.085036)	0.223265	0.183668
Absolute Change at 27 Months after Intervention 1	0.039597	(-0.005842, 0.085036)	0.223265	0.183668
Relative Change (%) at 27 Months after Intervention 1	21.56	(-6.88, 50.00)	0.223265	0.183668
Relative Change (%) at 27 Months after Intervention 1	21.56	(-6.88, 50.00)	0.223265	0.183668

Table 7. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ/BB Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.026667	(0.026252, 0.027083)	<.001
Baseline trend	-0.000070	(-0.000086, -0.000055)	<.001
Level Change (After Intervention 1)	0.000945	(0.000371, 0.001520)	0.002
Trend Change (After Intervention 1)	0.000013	(-0.000025, 0.000051)	0.510
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.026619	(0.026257, 0.026982)	<.001
Baseline trend	-0.000068	(-0.000081, -0.000055)	<.001
Level Change (After Intervention 1)	0.001054	(0.000533, 0.001575)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 8. Absolute and Relative Changes in Proportion of HCTZ/BB Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.001054	(0.000496,	0.024606	0.023553
Relative Change (%) at 1 Months after Intervention 1	4.47	(2.05, 6.90)	0.024606	0.023553
Absolute Change at 2 Months after Intervention 1	0.001054	(0.000496,	0.024538	0.023485
Relative Change (%) at 2 Months after Intervention 1	4.49	(2.05, 6.92)	0.024538	0.023485
Absolute Change at 3 Months after Intervention 1	0.001054	(0.000496,	0.024470	0.023416
Relative Change (%) at 3 Months after Intervention 1	4.50	(2.06, 6.94)	0.024470	0.023416
Absolute Change at 4 Months after Intervention 1	0.001054	(0.000496,	0.024402	0.023348
Relative Change (%) at 4 Months after Intervention 1	4.51	(2.06, 6.96)	0.024402	0.023348
Absolute Change at 5 Months after Intervention 1	0.001054	(0.000496,	0.024334	0.023280
Relative Change (%) at 5 Months after Intervention 1	4.53	(2.06, 6.99)	0.024334	0.023280
Absolute Change at 6 Months after Intervention 1	0.001054	(0.000496,	0.024265	0.023212
Relative Change (%) at 6 Months after Intervention 1	4.54	(2.07, 7.01)	0.024265	0.023212
Absolute Change at 7 Months after Intervention 1	0.001054	(0.000496,	0.024197	0.023144
Relative Change (%) at 7 Months after Intervention 1	4.55	(2.07, 7.03)	0.024197	0.023144
Absolute Change at 8 Months after Intervention 1	0.001054	(0.000496,	0.024129	0.023076
Relative Change (%) at 8 Months after Intervention 1	4.57	(2.07, 7.06)	0.024129	0.023076
Absolute Change at 9 Months after Intervention 1	0.001054	(0.000496,	0.024061	0.023007
Relative Change (%) at 9 Months after Intervention 1	4.58	(2.08, 7.08)	0.024061	0.023007
Absolute Change at 10 Months after Intervention 1	0.001054	(0.000496,	0.023993	0.022939
Relative Change (%) at 10 Months after Intervention 1	4.59	(2.08, 7.10)	0.023993	0.022939
Absolute Change at 11 Months after Intervention 1	0.001054	(0.000496,	0.023925	0.022871
Relative Change (%) at 11 Months after Intervention 1	4.61	(2.09, 7.13)	0.023925	0.022871
Absolute Change at 12 Months after Intervention 1	0.001054	(0.000496,	0.023857	0.022803
Relative Change (%) at 12 Months after Intervention 1	4.62	(2.09, 7.15)	0.023857	0.022803
Absolute Change at 13 Months after Intervention 1	0.001054	(0.000496,	0.023788	0.022735
Relative Change (%) at 13 Months after Intervention 1	4.63	(2.09, 7.17)	0.023788	0.022735
Absolute Change at 14 Months after Intervention 1	0.001054	(0.000496,	0.023720	0.022667
Relative Change (%) at 14 Months after Intervention 1	4.65	(2.10, 7.20)	0.023720	0.022667
Absolute Change at 15 Months after Intervention 1	0.001054	(0.000496,	0.023652	0.022599
Relative Change (%) at 15 Months after Intervention 1	4.66	(2.10, 7.22)	0.023652	0.022599
Absolute Change at 16 Months after Intervention 1	0.001054	(0.000496,	0.023584	0.022530
Relative Change (%) at 16 Months after Intervention 1	4.68	(2.10, 7.25)	0.023584	0.022530

Table 8. Absolute and Relative Changes in Proportion of HCTZ/BB Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 17 Months after Intervention 1	0.001054	(0.000496,	0.023516	0.022462
Relative Change (%) at 17 Months after Intervention 1	4.69	(2.11, 7.27)	0.023516	0.022462
Absolute Change at 18 Months after Intervention 1	0.001054	(0.000496,	0.023448	0.022394
Relative Change (%) at 18 Months after Intervention 1	4.70	(2.11, 7.30)	0.023448	0.022394
Absolute Change at 19 Months after Intervention 1	0.001054	(0.000496,	0.023380	0.022326
Relative Change (%) at 19 Months after Intervention 1	4.72	(2.12, 7.32)	0.023380	0.022326
Absolute Change at 20 Months after Intervention 1	0.001054	(0.000496,	0.023311	0.022258
Relative Change (%) at 20 Months after Intervention 1	4.73	(2.12, 7.35)	0.023311	0.022258
Absolute Change at 21 Months after Intervention 1	0.001054	(0.000496,	0.023243	0.022190
Relative Change (%) at 21 Months after Intervention 1	4.75	(2.12, 7.37)	0.023243	0.022190
Absolute Change at 22 Months after Intervention 1	0.001054	(0.000496,	0.023175	0.022122
Relative Change (%) at 22 Months after Intervention 1	4.76	(2.13, 7.40)	0.023175	0.022122
Absolute Change at 23 Months after Intervention 1	0.001054	(0.000496,	0.023107	0.022053
Relative Change (%) at 23 Months after Intervention 1	4.78	(2.13, 7.42)	0.023107	0.022053
Absolute Change at 24 Months after Intervention 1	0.001054	(0.000496,	0.023039	0.021985
Relative Change (%) at 24 Months after Intervention 1	4.79	(2.14, 7.45)	0.023039	0.021985
Absolute Change at 25 Months after Intervention 1	0.001054	(0.000496,	0.022971	0.021917
Relative Change (%) at 25 Months after Intervention 1	4.81	(2.14, 7.47)	0.022971	0.021917
Absolute Change at 26 Months after Intervention 1	0.001054	(0.000496,	0.022902	0.021849
Relative Change (%) at 26 Months after Intervention 1	4.82	(2.14, 7.50)	0.022902	0.021849
Absolute Change at 27 Months after Intervention 1	0.001054	(0.000496,	0.022834	0.021781
Absolute Change at 27 Months after Intervention 1	0.001054	(0.000496,	0.022834	0.021781
Relative Change (%) at 27 Months after Intervention 1	4.84	(2.15, 7.53)	0.022834	0.021781
Relative Change (%) at 27 Months after Intervention 1	4.84	(2.15, 7.53)	0.022834	0.021781

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 9. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ/Central Alpha-2 Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.000060	(0.000042, 0.000078)	<.001
Baseline trend	-0.000002	(-0.000002, -0.000001)	<.001
Level Change (After Intervention 1)	-0.000000	(-0.000008, 0.000008)	0.947
Trend Change (After Intervention 1)	0.000002	(0.000001, 0.000004)	0.004
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.000060	(0.000042, 0.000078)	<.001
Baseline trend	-0.000002	(-0.000002, -0.000001)	<.001
Trend Change (After Intervention 1)	0.000002	(0.000001, 0.000004)	0.003

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 10. Absolute and Relative Changes in Proportion of HCTZ/Central Alpha-2 Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 1 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 2 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 2 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 3 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 3 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 4 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 4 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 5 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 5 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 6 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 6 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 7 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 7 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 8 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 8 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 9 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 9 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 10 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 10 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 11 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 11 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 (%) at 12 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 13 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 13 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 14 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 14 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 15 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 15 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 16 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 16 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 17 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A

Table 10. Absolute and Relative Changes in Proportion of HCTZ/Central Alpha-2 Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Relative Change (%) at 17 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 18 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 18 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 19 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 19 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 20 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 20 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 21 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 21 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 22 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 22 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 23 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 23 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 24 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 24 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 25 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 25 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 26 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 26 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 27 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 27 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 27 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 27 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 August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 11. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ-Containing Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.283324	(0.280460, 0.286189)	<.001
Baseline trend	-0.000855	(-0.000961, -0.000749)	<.001
Level Change (After Intervention 1)	0.001713	(-0.001594, 0.005020)	0.305
Trend Change (After Intervention 1)	0.000314	(0.000060, 0.000567)	0.016
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.282865	(0.278821, 0.286910)	<.001
Baseline trend	-0.000825	(-0.000966, -0.000683)	<.001
Trend Change (After Intervention 1)	0.000297	(-0.000036, 0.000631)	0.080

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 12. Absolute and Relative Changes in Proportion of HCTZ-Containing Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000297	(-0.000042, 0.000637)	0.246055	0.245758
Relative Change (%) at 1 Months after Intervention 1	0.12	(-0.02, 0.26)	0.246055	0.245758
Absolute Change at 2 Months after Intervention 1	0.000595	(-0.000084, 0.001273)	0.245528	0.244933
Relative Change (%) at 2 Months after Intervention 1	0.24	(-0.04, 0.52)	0.245528	0.244933
Absolute Change at 3 Months after Intervention 1	0.000892	(-0.000126, 0.001910)	0.245000	0.244108
Relative Change (%) at 3 Months after Intervention 1	0.37	(-0.06, 0.79)	0.245000	0.244108
Absolute Change at 4 Months after Intervention 1	0.001189	(-0.000168, 0.002547)	0.244473	0.243284
Relative Change (%) at 4 Months after Intervention 1	0.49	(-0.08, 1.05)	0.244473	0.243284
Absolute Change at 5 Months after Intervention 1	0.001487	(-0.000210, 0.003183)	0.243946	0.242459
Relative Change (%) at 5 Months after Intervention 1	0.61	(-0.10, 1.32)	0.243946	0.242459
Absolute Change at 6 Months after Intervention 1	0.001784	(-0.000253, 0.003820)	0.243418	0.241635
Relative Change (%) at 6 Months after Intervention 1	0.74	(-0.12, 1.59)	0.243418	0.241635
Absolute Change at 7 Months after Intervention 1	0.002081	(-0.000295, 0.004457)	0.242891	0.240810
Relative Change (%) at 7 Months after Intervention 1	0.86	(-0.14, 1.86)	0.242891	0.240810
Absolute Change at 8 Months after Intervention 1	0.002378	(-0.000337, 0.005094)	0.242364	0.239985
Relative Change (%) at 8 Months after Intervention 1	0.99	(-0.16, 2.14)	0.242364	0.239985
Absolute Change at 9 Months after Intervention 1	0.002676	(-0.000379, 0.005730)	0.241837	0.239161
Relative Change (%) at 9 Months after Intervention 1	1.12	(-0.18, 2.41)	0.241837	0.239161
Absolute Change at 10 Months after Intervention 1	0.002973	(-0.000421, 0.006367)	0.241309	0.238336
Relative Change (%) at 10 Months after Intervention 1	1.25	(-0.20, 2.69)	0.241309	0.238336
Absolute Change at 11 Months after Intervention 1	0.003270	(-0.000463, 0.007004)	0.240782	0.237512
Relative Change (%) at 11 Months after Intervention 1	1.38	(-0.22, 2.97)	0.240782	0.237512
Absolute Change at 12 Months after Intervention 1	0.003568	(-0.000505, 0.007640)	0.240255	0.236687
Relative Change (%) at 12 Months after Intervention 1	1.51	(-0.24, 3.26)	0.240255	0.236687
Absolute Change at 13 Months after Intervention 1	0.003865	(-0.000547, 0.008277)	0.239727	0.235862
Relative Change (%) at 13 Months after Intervention 1	1.64	(-0.26, 3.54)	0.239727	0.235862
Absolute Change at 14 Months after Intervention 1	0.004162	(-0.000589, 0.008914)	0.239200	0.235038
Relative Change (%) at 14 Months after Intervention 1	1.77	(-0.29, 3.83)	0.239200	0.235038
Absolute Change at 15 Months after Intervention 1	0.004460	(-0.000631, 0.009550)	0.238673	0.234213
Relative Change (%) at 15 Months after Intervention 1	1.90	(-0.31, 4.12)	0.238673	0.234213
Absolute Change at 16 Months after Intervention 1	0.004757	(-0.000673, 0.010187)	0.238145	0.233389
Relative Change (%) at 16 Months after Intervention 1	2.04	(-0.33, 4.41)	0.238145	0.233389
Absolute Change at 17 Months after Intervention 1	0.005054	(-0.000715, 0.010824)	0.237618	0.232564

Table 12. Absolute and Relative Changes in Proportion of HCTZ-Containing Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Relative Change (%) at 17 Months after Intervention 1	2.17	(-0.35, 4.70)	0.237618	0.232564
Absolute Change at 18 Months after Intervention 1	0.005351	(-0.000758, 0.011460)	0.237091	0.231739
Relative Change (%) at 18 Months after Intervention 1	2.31	(-0.38, 5.00)	0.237091	0.231739
Absolute Change at 19 Months after Intervention 1	0.005649	(-0.000800, 0.012097)	0.236564	0.230915
Relative Change (%) at 19 Months after Intervention 1	2.45	(-0.40, 5.29)	0.236564	0.230915
Absolute Change at 20 Months after Intervention 1	0.005946	(-0.000842, 0.012734)	0.236036	0.230090
Relative Change (%) at 20 Months after Intervention 1	2.58	(-0.43, 5.59)	0.236036	0.230090
Absolute Change at 21 Months after Intervention 1	0.006243	(-0.000884, 0.013370)	0.235509	0.229266
Relative Change (%) at 21 Months after Intervention 1	2.72	(-0.45, 5.90)	0.235509	0.229266
Absolute Change at 22 Months after Intervention 1	0.006541	(-0.000926, 0.014007)	0.234982	0.228441
Relative Change (%) at 22 Months after Intervention 1	2.86	(-0.47, 6.20)	0.234982	0.228441
Absolute Change at 23 Months after Intervention 1	0.006838	(-0.000968, 0.014644)	0.234454	0.227616
Relative Change (%) at 23 Months after Intervention 1	3.00	(-0.50, 6.51)	0.234454	0.227616
Absolute Change at 24 Months after Intervention 1	0.007135	(-0.001010, 0.015281)	0.233927	0.226792
Relative Change (%) at 24 Months after Intervention 1	3.15	(-0.52, 6.82)	0.233927	0.226792
Absolute Change at 25 Months after Intervention 1	0.007433	(-0.001052, 0.015917)	0.233400	0.225967
Relative Change (%) at 25 Months after Intervention 1	3.29	(-0.55, 7.13)	0.233400	0.225967
Absolute Change at 26 Months after Intervention 1	0.007730	(-0.001094, 0.016554)	0.232872	0.225143
Relative Change (%) at 26 Months after Intervention 1	3.43	(-0.58, 7.44)	0.232872	0.225143
Absolute Change at 27 Months after Intervention 1	0.008027	(-0.001136, 0.017191)	0.232345	0.224318
Absolute Change at 27 Months after Intervention 1	0.008027	(-0.001136, 0.017191)	0.232345	0.224318
Relative Change (%) at 27 Months after Intervention 1	3.58	(-0.60, 7.76)	0.232345	0.224318
Relative Change (%) at 27 Months after Intervention 1	3.58	(-0.60, 7.76)	0.232345	0.224318

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 13. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ-Containing Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.945812	(0.945123, 0.946502)	<.001
Baseline trend	-0.000369	(-0.000396, -0.000343)	<.001
Level Change (After Intervention 1)	0.000193	(-0.000970, 0.001356)	0.742
Trend Change (After Intervention 1)	0.000121	(0.000052, 0.000190)	<.001
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.945777	(0.945134, 0.946420)	<.001
Baseline trend	-0.000367	(-0.000390, -0.000345)	<.001
Trend Change (After Intervention 1)	0.000127	(0.000067, 0.000186)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 14. Absolute and Relative Changes in Proportion of HCTZ-Containing Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000127	(0.000068, 0.000186)	0.929376	0.929249
Relative Change (%) at 1 Months after Intervention 1	0.01	(0.01, 0.02)	0.929376	0.929249
Absolute Change at 2 Months after Intervention 1	0.000254	(0.000135, 0.000372)	0.929136	0.928882
Relative Change (%) at 2 Months after Intervention 1	0.03	(0.01, 0.04)	0.929136	0.928882
Absolute Change at 3 Months after Intervention 1	0.000380	(0.000203, 0.000558)	0.928895	0.928515
Relative Change (%) at 3 Months after Intervention 1	0.04	(0.02, 0.06)	0.928895	0.928515
Absolute Change at 4 Months after Intervention 1	0.000507	(0.000270, 0.000744)	0.928655	0.928147
Relative Change (%) at 4 Months after Intervention 1	0.05	(0.03, 0.08)	0.928655	0.928147
Absolute Change at 5 Months after Intervention 1	0.000634	(0.000338, 0.000930)	0.928414	0.927780
Relative Change (%) at 5 Months after Intervention 1	0.07	(0.04, 0.10)	0.928414	0.927780
Absolute Change at 6 Months after Intervention 1	0.000761	(0.000405, 0.001117)	0.928174	0.927413
Relative Change (%) at 6 Months after Intervention 1	0.08	(0.04, 0.12)	0.928174	0.927413
Absolute Change at 7 Months after Intervention 1	0.000888	(0.000473, 0.001303)	0.927933	0.927046
Relative Change (%) at 7 Months after Intervention 1	0.10	(0.05, 0.14)	0.927933	0.927046
Absolute Change at 8 Months after Intervention 1	0.001015	(0.000540, 0.001489)	0.927693	0.926678
Relative Change (%) at 8 Months after Intervention 1	0.11	(0.06, 0.16)	0.927693	0.926678
Absolute Change at 9 Months after Intervention 1	0.001141	(0.000608, 0.001675)	0.927453	0.926311
Relative Change (%) at 9 Months after Intervention 1	0.12	(0.07, 0.18)	0.927453	0.926311
Absolute Change at 10 Months after Intervention 1	0.001268	(0.000676, 0.001861)	0.927212	0.925944
Relative Change (%) at 10 Months after Intervention 1	0.14	(0.07, 0.20)	0.927212	0.925944
Absolute Change at 11 Months after Intervention 1	0.001395	(0.000743, 0.002047)	0.926972	0.925577
Relative Change (%) at 11 Months after Intervention 1	0.15	(0.08, 0.22)	0.926972	0.925577
Absolute Change at 12 Months after Intervention 1	0.001522	(0.000811, 0.002233)	0.926731	0.925209
Relative Change (%) at 12 Months after Intervention 1	0.16	(0.09, 0.24)	0.926731	0.925209
Absolute Change at 13 Months after Intervention 1	0.001649	(0.000878, 0.002419)	0.926491	0.924842
Relative Change (%) at 13 Months after Intervention 1	0.18	(0.09, 0.26)	0.926491	0.924842
Absolute Change at 14 Months after Intervention 1	0.001776	(0.000946, 0.002605)	0.926250	0.924475
Relative Change (%) at 14 Months after Intervention 1	0.19	(0.10, 0.28)	0.926250	0.924475
Absolute Change at 15 Months after Intervention 1	0.001902	(0.001013, 0.002791)	0.926010	0.924107
Relative Change (%) at 15 Months after Intervention 1	0.21	(0.11, 0.30)	0.926010	0.924107
Absolute Change at 16 Months after Intervention 1	0.002029	(0.001081, 0.002977)	0.925769	0.923740
Relative Change (%) at 16 Months after Intervention 1	0.22	(0.12, 0.32)	0.925769	0.923740
Absolute Change at 17 Months after Intervention 1	0.002156	(0.001149, 0.003164)	0.925529	0.923373

Table 14. Absolute and Relative Changes in Proportion of HCTZ-Containing Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Relative Change (%) at 17 Months after Intervention 1	0.23	(0.12, 0.34)	0.925529	0.923373
Absolute Change at 18 Months after Intervention 1	0.002283	(0.001216, 0.003350)	0.925288	0.923006
Relative Change (%) at 18 Months after Intervention 1	0.25	(0.13, 0.36)	0.925288	0.923006
Absolute Change at 19 Months after Intervention 1	0.002410	(0.001284, 0.003536)	0.925048	0.922638
Relative Change (%) at 19 Months after Intervention 1	0.26	(0.14, 0.38)	0.925048	0.922638
Absolute Change at 20 Months after Intervention 1	0.002537	(0.001351, 0.003722)	0.924808	0.922271
Relative Change (%) at 20 Months after Intervention 1	0.28	(0.15, 0.40)	0.924808	0.922271
Absolute Change at 21 Months after Intervention 1	0.002663	(0.001419, 0.003908)	0.924567	0.921904
Relative Change (%) at 21 Months after Intervention 1	0.29	(0.15, 0.42)	0.924567	0.921904
Absolute Change at 22 Months after Intervention 1	0.002790	(0.001486, 0.004094)	0.924327	0.921536
Relative Change (%) at 22 Months after Intervention 1	0.30	(0.16, 0.44)	0.924327	0.921536
Absolute Change at 23 Months after Intervention 1	0.002917	(0.001554, 0.004280)	0.924086	0.921169
Relative Change (%) at 23 Months after Intervention 1	0.32	(0.17, 0.46)	0.924086	0.921169
Absolute Change at 24 Months after Intervention 1	0.003044	(0.001621, 0.004466)	0.923846	0.920802
Relative Change (%) at 24 Months after Intervention 1	0.33	(0.18, 0.49)	0.923846	0.920802
Absolute Change at 25 Months after Intervention 1	0.003171	(0.001689, 0.004652)	0.923605	0.920435
Relative Change (%) at 25 Months after Intervention 1	0.34	(0.18, 0.51)	0.923605	0.920435
Absolute Change at 26 Months after Intervention 1	0.003298	(0.001757, 0.004838)	0.923365	0.920067
Relative Change (%) at 26 Months after Intervention 1	0.36	(0.19, 0.53)	0.923365	0.920067
Absolute Change at 27 Months after Intervention 1	0.003424	(0.001824, 0.005024)	0.923124	0.919700
Absolute Change at 27 Months after Intervention 1	0.003424	(0.001824, 0.005024)	0.923124	0.919700
Relative Change (%) at 27 Months after Intervention 1	0.37	(0.20, 0.55)	0.923124	0.919700
Relative Change (%) at 27 Months after Intervention 1	0.37	(0.20, 0.55)	0.923124	0.919700

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 15. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ/Direct Renin Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.000602	(0.000532, 0.000672)	<.001
Baseline trend	-0.000007	(-0.000010, -0.000005)	<.001
Level Change (After Intervention 1)	-0.000013	(-0.000081, 0.000056)	0.715
Trend Change (After Intervention 1)	0.000000	(-0.000006, 0.000006)	0.934
Most Parsimonious Final Model Parameters (df = 71)[2,3]			
Intercept	0.000604	(0.000546, 0.000662)	<.001
Baseline trend	-0.000008	(-0.000009, -0.000006)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 16. Absolute and Relative Changes in Proportion of HCTZ/Direct Renin Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000000	(0.000000,	0.000263	0.000263
Relative Change (%) at 1 Months after Intervention 1	0.00	(0.00, 0.00)	0.000263	0.000263
Absolute Change at 2 Months after Intervention 1	0.000000	(0.000000,	0.000255	0.000255
Relative Change (%) at 2 Months after Intervention 1	0.00	(0.00, 0.00)	0.000255	0.000255
Absolute Change at 3 Months after Intervention 1	0.000000	(0.000000,	0.000248	0.000248
Relative Change (%) at 3 Months after Intervention 1	0.00	(0.00, 0.00)	0.000248	0.000248
Absolute Change at 4 Months after Intervention 1	0.000000	(0.000000,	0.000240	0.000240
Relative Change (%) at 4 Months after Intervention 1	0.00	(0.00, 0.00)	0.000240	0.000240
Absolute Change at 5 Months after Intervention 1	0.000000	(0.000000,	0.000232	0.000232
Relative Change (%) at 5 Months after Intervention 1	0.00	(0.00, 0.00)	0.000232	0.000232
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000,	0.000225	0.000225
Relative Change (%) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.000225	0.000225
Absolute Change at 7 Months after Intervention 1	0.000000	(0.000000,	0.000217	0.000217
Relative Change (%) at 7 Months after Intervention 1	0.00	(0.00, 0.00)	0.000217	0.000217
Absolute Change at 8 Months after Intervention 1	0.000000	(0.000000,	0.000210	0.000210
Relative Change (%) at 8 Months after Intervention 1	0.00	(0.00, 0.00)	0.000210	0.000210
Absolute Change at 9 Months after Intervention 1	0.000000	(0.000000,	0.000202	0.000202
Relative Change (%) at 9 Months after Intervention 1	0.00	(0.00, 0.00)	0.000202	0.000202
Absolute Change at 10 Months after Intervention 1	0.000000	(0.000000,	0.000194	0.000194
Relative Change (%) at 10 Months after Intervention 1	0.00	(0.00, 0.00)	0.000194	0.000194
Absolute Change at 11 Months after Intervention 1	0.000000	(0.000000,	0.000187	0.000187
Relative Change (%) at 11 Months after Intervention 1	0.00	(0.00, 0.00)	0.000187	0.000187
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000,	0.000179	0.000179
Relative Change (%) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.000179	0.000179
Absolute Change at 13 Months after Intervention 1	0.000000	(0.000000,	0.000172	0.000172
Relative Change (%) at 13 Months after Intervention 1	0.00	(0.00, 0.00)	0.000172	0.000172
Absolute Change at 14 Months after Intervention 1	0.000000	(0.000000,	0.000164	0.000164
Relative Change (%) at 14 Months after Intervention 1	0.00	(0.00, 0.00)	0.000164	0.000164
Absolute Change at 15 Months after Intervention 1	0.000000	(0.000000,	0.000157	0.000157
Relative Change (%) at 15 Months after Intervention 1	0.00	(0.00, 0.00)	0.000157	0.000157
Absolute Change at 16 Months after Intervention 1	0.000000	(0.000000,	0.000149	0.000149
Relative Change (%) at 16 Months after Intervention 1	0.00	(0.00, 0.00)	0.000149	0.000149

Table 16. Absolute and Relative Changes in Proportion of HCTZ/Direct Renin Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 17 Months after Intervention 1	0.000000	(0.000000,	0.000141	0.000141
Relative Change (%) at 17 Months after Intervention 1	0.00	(0.00, 0.00)	0.000141	0.000141
Absolute Change at 18 Months after Intervention 1	0.000000	(0.000000,	0.000134	0.000134
Relative Change (%) at 18 Months after Intervention 1	0.00	(0.00, 0.00)	0.000134	0.000134
Absolute Change at 19 Months after Intervention 1	0.000000	(0.000000,	0.000126	0.000126
Relative Change (%) at 19 Months after Intervention 1	0.00	(0.00, 0.00)	0.000126	0.000126
Absolute Change at 20 Months after Intervention 1	0.000000	(0.000000,	0.000119	0.000119
Relative Change (%) at 20 Months after Intervention 1	0.00	(0.00, 0.00)	0.000119	0.000119
Absolute Change at 21 Months after Intervention 1	0.000000	(0.000000,	0.000111	0.000111
Relative Change (%) at 21 Months after Intervention 1	0.00	(0.00, 0.00)	0.000111	0.000111
Absolute Change at 22 Months after Intervention 1	0.000000	(0.000000,	0.000103	0.000103
Relative Change (%) at 22 Months after Intervention 1	0.00	(0.00, 0.00)	0.000103	0.000103
Absolute Change at 23 Months after Intervention 1	0.000000	(0.000000,	0.000096	0.000096
Relative Change (%) at 23 Months after Intervention 1	0.00	(0.00, 0.00)	0.000096	0.000096
Absolute Change at 24 Months after Intervention 1	0.000000	(0.000000,	0.000088	0.000088
Relative Change (%) at 24 Months after Intervention 1	0.00	(0.00, 0.00)	0.000088	0.000088
Absolute Change at 25 Months after Intervention 1	0.000000	(0.000000,	0.000081	0.000081
Relative Change (%) at 25 Months after Intervention 1	0.00	(0.00, 0.00)	0.000081	0.000081
Absolute Change at 26 Months after Intervention 1	0.000000	(0.000000,	0.000073	0.000073
Relative Change (%) at 26 Months after Intervention 1	0.00	(0.00, 0.00)	0.000073	0.000073
Absolute Change at 27 Months after Intervention 1	0.000000	(0.000000,	0.000065	0.000065
Absolute Change at 27 Months after Intervention 1	0.000000	(0.000000,	0.000065	0.000065
Relative Change (%) at 27 Months after Intervention 1	0.00	(0.00, 0.00)	0.000065	0.000065
Relative Change (%) at 27 Months after Intervention 1	0.00	(0.00, 0.00)	0.000065	0.000065

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 17. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ Single Ingredient Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.329436	(0.310100, 0.348772)	<.001
Baseline trend	0.001965	(0.001281, 0.002649)	<.001
Level Change (After Intervention 1)	0.000841	(-0.005164, 0.006847)	0.781
Trend Change (After Intervention 1)	-0.002310	(-0.003965, -0.000654)	0.007
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.329504	(0.310251, 0.348758)	<.001
Baseline trend	0.001964	(0.001283, 0.002645)	<.001
Trend Change (After Intervention 1)	-0.002264	(-0.003880, -0.000649)	0.007

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 18. Absolute and Relative Changes in Proportion of HCTZ Single Ingredient Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	-0.002264	(-0.003856, -	0.415630	0.417894
Relative Change (%) at 1 Months after Intervention 1	-0.54	(-0.90, -0.18)	0.415630	0.417894
Absolute Change at 2 Months after Intervention 1	-0.004529	(-0.007713, -	0.415330	0.419858
Relative Change (%) at 2 Months after Intervention 1	-1.08	(-1.80, -0.36)	0.415330	0.419858
Absolute Change at 3 Months after Intervention 1	-0.006793	(-0.011569, -	0.415030	0.421823
Relative Change (%) at 3 Months after Intervention 1	-1.61	(-2.68, -0.54)	0.415030	0.421823
Absolute Change at 4 Months after Intervention 1	-0.009057	(-0.015426, -	0.414730	0.423787
Relative Change (%) at 4 Months after Intervention 1	-2.14	(-3.56, -0.72)	0.414730	0.423787
Absolute Change at 5 Months after Intervention 1	-0.011322	(-0.019282, -	0.414429	0.425751
Relative Change (%) at 5 Months after Intervention 1	-2.66	(-4.42, -0.89)	0.414429	0.425751
Absolute Change at 6 Months after Intervention 1	-0.013586	(-0.023139, -	0.414129	0.427715
Relative Change (%) at 6 Months after Intervention 1	-3.18	(-5.28, -1.07)	0.414129	0.427715
Absolute Change at 7 Months after Intervention 1	-0.015850	(-0.026995, -	0.413829	0.429680
Relative Change (%) at 7 Months after Intervention 1	-3.69	(-6.13, -1.25)	0.413829	0.429680
Absolute Change at 8 Months after Intervention 1	-0.018115	(-0.030851, -	0.413529	0.431644
Relative Change (%) at 8 Months after Intervention 1	-4.20	(-6.97, -1.43)	0.413529	0.431644
Absolute Change at 9 Months after Intervention 1	-0.020379	(-0.034708, -	0.413229	0.433608
Relative Change (%) at 9 Months after Intervention 1	-4.70	(-7.80, -1.60)	0.413229	0.433608
Absolute Change at 10 Months after Intervention 1	-0.022644	(-0.038564, -	0.412929	0.435572
Relative Change (%) at 10 Months after Intervention 1	-5.20	(-8.62, -1.78)	0.412929	0.435572
Absolute Change at 11 Months after Intervention 1	-0.024908	(-0.042421, -	0.412629	0.437536
Relative Change (%) at 11 Months after Intervention 1	-5.69	(-9.43, -1.95)	0.412629	0.437536
Absolute Change at 12 Months after Intervention 1	-0.027172	(-0.046277, -	0.412328	0.439501
Relative Change (%) at 12 Months after Intervention 1	-6.18	(-10.24, -2.13)	0.412328	0.439501
Absolute Change at 13 Months after Intervention 1	-0.029437	(-0.050134, -	0.412028	0.441465
Relative Change (%) at 13 Months after Intervention 1	-6.67	(-11.04, -2.30)	0.412028	0.441465
Absolute Change at 14 Months after Intervention 1	-0.031701	(-0.053990, -	0.411728	0.443429
Relative Change (%) at 14 Months after Intervention 1	-7.15	(-11.82, -2.47)	0.411728	0.443429
Absolute Change at 15 Months after Intervention 1	-0.033965	(-0.057846, -	0.411428	0.445393
Relative Change (%) at 15 Months after Intervention 1	-7.63	(-12.61, -2.65)	0.411428	0.445393
Absolute Change at 16 Months after Intervention 1	-0.036230	(-0.061703, -	0.411128	0.447358
Relative Change (%) at 16 Months after Intervention 1	-8.10	(-13.38, -2.82)	0.411128	0.447358

Table 18. Absolute and Relative Changes in Proportion of HCTZ Single Ingredient Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 17 Months after Intervention 1	-0.038494	(-0.065559, -	0.410828	0.449322
Relative Change (%) at 17 Months after Intervention 1	-8.57	(-14.14, -2.99)	0.410828	0.449322
Absolute Change at 18 Months after Intervention 1	-0.040758	(-0.069416, -	0.410528	0.451286
Relative Change (%) at 18 Months after Intervention 1	-9.03	(-14.90, -3.16)	0.410528	0.451286
Absolute Change at 19 Months after Intervention 1	-0.043023	(-0.073272, -	0.410228	0.453250
Relative Change (%) at 19 Months after Intervention 1	-9.49	(-15.65, -3.33)	0.410228	0.453250
Absolute Change at 20 Months after Intervention 1	-0.045287	(-0.077129, -	0.409927	0.455214
Relative Change (%) at 20 Months after Intervention 1	-9.95	(-16.40, -3.50)	0.409927	0.455214
Absolute Change at 21 Months after Intervention 1	-0.047551	(-0.080985, -	0.409627	0.457179
Relative Change (%) at 21 Months after Intervention 1	-10.40	(-17.13, -3.67)	0.409627	0.457179
Absolute Change at 22 Months after Intervention 1	-0.049816	(-0.084841, -	0.409327	0.459143
Relative Change (%) at 22 Months after Intervention 1	-10.85	(-17.86, -3.84)	0.409327	0.459143
Absolute Change at 23 Months after Intervention 1	-0.052080	(-0.088698, -	0.409027	0.461107
Relative Change (%) at 23 Months after Intervention 1	-11.29	(-18.58, -4.01)	0.409027	0.461107
Absolute Change at 24 Months after Intervention 1	-0.054344	(-0.092554, -	0.408727	0.463071
Relative Change (%) at 24 Months after Intervention 1	-11.74	(-19.30, -4.17)	0.408727	0.463071
Absolute Change at 25 Months after Intervention 1	-0.056609	(-0.096411, -	0.408427	0.465035
Relative Change (%) at 25 Months after Intervention 1	-12.17	(-20.01, -4.34)	0.408427	0.465035
Absolute Change at 26 Months after Intervention 1	-0.058873	(-0.100267, -	0.408127	0.467000
Relative Change (%) at 26 Months after Intervention 1	-12.61	(-20.71, -4.51)	0.408127	0.467000
Absolute Change at 27 Months after Intervention 1	-0.061137	(-0.104124, -	0.407826	0.468964
Absolute Change at 27 Months after Intervention 1	-0.061137	(-0.104124, -	0.407826	0.468964
Relative Change (%) at 27 Months after Intervention 1	-13.04	(-21.40, -4.67)	0.407826	0.468964
Relative Change (%) at 27 Months after Intervention 1	-13.04	(-21.40, -4.67)	0.407826	0.468964

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 19. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ/Potassium-Sparing Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.122292	(0.119303, 0.125282)	<.001
Baseline trend	-0.000463	(-0.000569, -0.000358)	<.001
Level Change (After Intervention 1)	0.000797	(-0.000774, 0.002369)	0.315
Trend Change (After Intervention 1)	0.000329	(0.000078, 0.000580)	0.011
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.122463	(0.118790, 0.126137)	<.001
Baseline trend	-0.000451	(-0.000574, -0.000328)	<.001
Trend Change (After Intervention 1)	0.000300	(0.000030, 0.000570)	0.030

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 20. Absolute and Relative Changes in Proportion of HCTZ/Potassium-Sparing Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000300	(-0.000011, 0.000610)	0.102467	0.102167
Relative Change (%) at 1 Months after Intervention 1	0.29	(-0.02, 0.61)	0.102467	0.102167
Absolute Change at 2 Months after Intervention 1	0.000600	(-0.000021, 0.001221)	0.102316	0.101716
Relative Change (%) at 2 Months after Intervention 1	0.59	(-0.04, 1.22)	0.102316	0.101716
Absolute Change at 3 Months after Intervention 1	0.000899	(-0.000032, 0.001831)	0.102165	0.101265
Relative Change (%) at 3 Months after Intervention 1	0.89	(-0.06, 1.84)	0.102165	0.101265
Absolute Change at 4 Months after Intervention 1	0.001199	(-0.000043, 0.002441)	0.102013	0.100814
Relative Change (%) at 4 Months after Intervention 1	1.19	(-0.08, 2.46)	0.102013	0.100814
Absolute Change at 5 Months after Intervention 1	0.001499	(-0.000053, 0.003051)	0.101862	0.100363
Relative Change (%) at 5 Months after Intervention 1	1.49	(-0.11, 3.10)	0.101862	0.100363
Absolute Change at 6 Months after Intervention 1	0.001799	(-0.000064, 0.003662)	0.101711	0.099912
Relative Change (%) at 6 Months after Intervention 1	1.80	(-0.13, 3.73)	0.101711	0.099912
Absolute Change at 7 Months after Intervention 1	0.002099	(-0.000074, 0.004272)	0.101560	0.099461
Relative Change (%) at 7 Months after Intervention 1	2.11	(-0.16, 4.38)	0.101560	0.099461
Absolute Change at 8 Months after Intervention 1	0.002399	(-0.000085, 0.004882)	0.101409	0.099010
Relative Change (%) at 8 Months after Intervention 1	2.42	(-0.19, 5.03)	0.101409	0.099010
Absolute Change at 9 Months after Intervention 1	0.002698	(-0.000096, 0.005492)	0.101257	0.098559
Relative Change (%) at 9 Months after Intervention 1	2.74	(-0.21, 5.69)	0.101257	0.098559
Absolute Change at 10 Months after Intervention 1	0.002998	(-0.000106, 0.006103)	0.101106	0.098108
Relative Change (%) at 10 Months after Intervention 1	3.06	(-0.24, 6.35)	0.101106	0.098108
Absolute Change at 11 Months after Intervention 1	0.003298	(-0.000117, 0.006713)	0.100955	0.097657
Relative Change (%) at 11 Months after Intervention 1	3.38	(-0.27, 7.03)	0.100955	0.097657
Absolute Change at 12 Months after Intervention 1	0.003598	(-0.000128, 0.007323)	0.100804	0.097206
Relative Change (%) at 12 Months after Intervention 1	3.70	(-0.30, 7.71)	0.100804	0.097206
Absolute Change at 13 Months after Intervention 1	0.003898	(-0.000138, 0.007934)	0.100653	0.096755
Relative Change (%) at 13 Months after Intervention 1	4.03	(-0.34, 8.39)	0.100653	0.096755
Absolute Change at 14 Months after Intervention 1	0.004198	(-0.000149, 0.008544)	0.100501	0.096304
Relative Change (%) at 14 Months after Intervention 1	4.36	(-0.37, 9.09)	0.100501	0.096304
Absolute Change at 15 Months after Intervention 1	0.004497	(-0.000159, 0.009154)	0.100350	0.095853
Relative Change (%) at 15 Months after Intervention 1	4.69	(-0.40, 9.79)	0.100350	0.095853
Absolute Change at 16 Months after Intervention 1	0.004797	(-0.000170, 0.009764)	0.100199	0.095402
Relative Change (%) at 16 Months after Intervention 1	5.03	(-0.44, 10.50)	0.100199	0.095402

Table 20. Absolute and Relative Changes in Proportion of HCTZ/Potassium-Sparing Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 17 Months after Intervention 1	0.005097	(-0.000181, 0.010375)	0.100048	0.094951
Relative Change (%) at 17 Months after Intervention 1	5.37	(-0.48, 11.21)	0.100048	0.094951
Absolute Change at 18 Months after Intervention 1	0.005397	(-0.000191, 0.010985)	0.099897	0.094500
Relative Change (%) at 18 Months after Intervention 1	5.71	(-0.52, 11.94)	0.099897	0.094500
Absolute Change at 19 Months after Intervention 1	0.005697	(-0.000202, 0.011595)	0.099745	0.094049
Relative Change (%) at 19 Months after Intervention 1	6.06	(-0.56, 12.67)	0.099745	0.094049
Absolute Change at 20 Months after Intervention 1	0.005996	(-0.000213, 0.012206)	0.099594	0.093598
Relative Change (%) at 20 Months after Intervention 1	6.41	(-0.60, 13.41)	0.099594	0.093598
Absolute Change at 21 Months after Intervention 1	0.006296	(-0.000223, 0.012816)	0.099443	0.093147
Relative Change (%) at 21 Months after Intervention 1	6.76	(-0.64, 14.16)	0.099443	0.093147
Absolute Change at 22 Months after Intervention 1	0.006596	(-0.000234, 0.013426)	0.099292	0.092696
Relative Change (%) at 22 Months after Intervention 1	7.12	(-0.69, 14.92)	0.099292	0.092696
Absolute Change at 23 Months after Intervention 1	0.006896	(-0.000244, 0.014036)	0.099141	0.092245
Relative Change (%) at 23 Months after Intervention 1	7.48	(-0.73, 15.68)	0.099141	0.092245
Absolute Change at 24 Months after Intervention 1	0.007196	(-0.000255, 0.014647)	0.098989	0.091794
Relative Change (%) at 24 Months after Intervention 1	7.84	(-0.78, 16.46)	0.098989	0.091794
Absolute Change at 25 Months after Intervention 1	0.007496	(-0.000266, 0.015257)	0.098838	0.091343
Relative Change (%) at 25 Months after Intervention 1	8.21	(-0.83, 17.24)	0.098838	0.091343
Absolute Change at 26 Months after Intervention 1	0.007795	(-0.000276, 0.015867)	0.098687	0.090892
Relative Change (%) at 26 Months after Intervention 1	8.58	(-0.88, 18.03)	0.098687	0.090892
Absolute Change at 27 Months after Intervention 1	0.008095	(-0.000287, 0.016477)	0.098536	0.090440
Absolute Change at 27 Months after Intervention 1	0.008095	(-0.000287, 0.016477)	0.098536	0.090440
Relative Change (%) at 27 Months after Intervention 1	8.95	(-0.93, 18.83)	0.098536	0.090440
Relative Change (%) at 27 Months after Intervention 1	8.95	(-0.93, 18.83)	0.098536	0.090440

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 21. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of ACEI Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.301604	(0.295785, 0.307423)	<.001
Baseline trend	-0.000629	(-0.000826, -0.000432)	<.001
Level Change (After Intervention 1)	0.003527	(-0.000451, 0.007506)	0.082
Trend Change (After Intervention 1)	0.000377	(-0.000057, 0.000810)	0.088
Most Parsimonious Final Model Parameters (df = 69)[2,3]			
Intercept	0.301604	(0.295785, 0.307423)	<.001
Baseline trend	-0.000629	(-0.000826, -0.000432)	<.001
Level Change (After Intervention 1)	0.003527	(-0.000451, 0.007506)	0.082
Trend Change (After Intervention 1)	0.000377	(-0.000057, 0.000810)	0.088

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 22. Absolute and Relative Changes in Proportion of ACEI Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.003904	(-0.000790, 0.008598)	0.277225	0.273321
Relative Change (%) at 1 Months after Intervention 1	1.43	(-0.30, 3.16)	0.277225	0.273321
Absolute Change at 2 Months after Intervention 1	0.004280	(-0.000480, 0.009040)	0.276973	0.272693
Relative Change (%) at 2 Months after Intervention 1	1.57	(-0.20, 3.34)	0.276973	0.272693
Absolute Change at 3 Months after Intervention 1	0.004657	(-0.000268, 0.009583)	0.276721	0.272064
Relative Change (%) at 3 Months after Intervention 1	1.71	(-0.13, 3.55)	0.276721	0.272064
Absolute Change at 4 Months after Intervention 1	0.005034	(-0.000148, 0.010215)	0.276469	0.271436
Relative Change (%) at 4 Months after Intervention 1	1.85	(-0.09, 3.80)	0.276469	0.271436
Absolute Change at 5 Months after Intervention 1	0.005410	(-0.000104, 0.010925)	0.276218	0.270807
Relative Change (%) at 5 Months after Intervention 1	2.00	(-0.08, 4.08)	0.276218	0.270807
Absolute Change at 6 Months after Intervention 1	0.005787	(-0.000126, 0.011700)	0.275966	0.270179
Relative Change (%) at 6 Months after Intervention 1	2.14	(-0.10, 4.38)	0.275966	0.270179
Absolute Change at 7 Months after Intervention 1	0.006164	(-0.000200, 0.012527)	0.275714	0.269550
Relative Change (%) at 7 Months after Intervention 1	2.29	(-0.14, 4.71)	0.275714	0.269550
Absolute Change at 8 Months after Intervention 1	0.006540	(-0.000316, 0.013396)	0.275462	0.268922
Relative Change (%) at 8 Months after Intervention 1	2.43	(-0.19, 5.05)	0.275462	0.268922
Absolute Change at 9 Months after Intervention 1	0.006917	(-0.000465, 0.014299)	0.275210	0.268293
Relative Change (%) at 9 Months after Intervention 1	2.58	(-0.25, 5.41)	0.275210	0.268293
Absolute Change at 10 Months after Intervention 1	0.007294	(-0.000642, 0.015229)	0.274958	0.267665
Relative Change (%) at 10 Months after Intervention 1	2.72	(-0.33, 5.78)	0.274958	0.267665
Absolute Change at 11 Months after Intervention 1	0.007670	(-0.000841, 0.016181)	0.274706	0.267036
Relative Change (%) at 11 Months after Intervention 1	2.87	(-0.41, 6.15)	0.274706	0.267036
Absolute Change at 12 Months after Intervention 1	0.008047	(-0.001057, 0.017150)	0.274454	0.266408
Relative Change (%) at 12 Months after Intervention 1	3.02	(-0.50, 6.54)	0.274454	0.266408
Absolute Change at 13 Months after Intervention 1	0.008423	(-0.001287, 0.018134)	0.274203	0.265779
Relative Change (%) at 13 Months after Intervention 1	3.17	(-0.60, 6.94)	0.274203	0.265779
Absolute Change at 14 Months after Intervention 1	0.008800	(-0.001529, 0.019129)	0.273951	0.265151
Relative Change (%) at 14 Months after Intervention 1	3.32	(-0.70, 7.34)	0.273951	0.265151
Absolute Change at 15 Months after Intervention 1	0.009177	(-0.001782, 0.020135)	0.273699	0.264522
Relative Change (%) at 15 Months after Intervention 1	3.47	(-0.80, 7.74)	0.273699	0.264522
Absolute Change at 16 Months after Intervention 1	0.009553	(-0.002042, 0.021149)	0.273447	0.263894
Relative Change (%) at 16 Months after Intervention 1	3.62	(-0.91, 8.15)	0.273447	0.263894

Table 22. Absolute and Relative Changes in Proportion of ACEI Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 17 Months after Intervention 1	0.009930	(-0.002309, 0.022169)	0.273195	0.263265
Relative Change (%) at 17 Months after Intervention 1	3.77	(-1.03, 8.57)	0.273195	0.263265
Absolute Change at 18 Months after Intervention 1	0.010307	(-0.002583, 0.023196)	0.272943	0.262637
Relative Change (%) at 18 Months after Intervention 1	3.92	(-1.14, 8.99)	0.272943	0.262637
Absolute Change at 19 Months after Intervention 1	0.010683	(-0.002861, 0.024227)	0.272691	0.262008
Relative Change (%) at 19 Months after Intervention 1	4.08	(-1.26, 9.42)	0.272691	0.262008
Absolute Change at 20 Months after Intervention 1	0.011060	(-0.003144, 0.025263)	0.272440	0.261380
Relative Change (%) at 20 Months after Intervention 1	4.23	(-1.38, 9.85)	0.272440	0.261380
Absolute Change at 21 Months after Intervention 1	0.011436	(-0.003430, 0.026303)	0.272188	0.260751
Relative Change (%) at 21 Months after Intervention 1	4.39	(-1.51, 10.28)	0.272188	0.260751
Absolute Change at 22 Months after Intervention 1	0.011813	(-0.003720, 0.027346)	0.271936	0.260123
Relative Change (%) at 22 Months after Intervention 1	4.54	(-1.63, 10.72)	0.271936	0.260123
Absolute Change at 23 Months after Intervention 1	0.012190	(-0.004012, 0.028392)	0.271684	0.259494
Relative Change (%) at 23 Months after Intervention 1	4.70	(-1.76, 11.16)	0.271684	0.259494
Absolute Change at 24 Months after Intervention 1	0.012566	(-0.004308, 0.029440)	0.271432	0.258866
Relative Change (%) at 24 Months after Intervention 1	4.85	(-1.89, 11.60)	0.271432	0.258866
Absolute Change at 25 Months after Intervention 1	0.012943	(-0.004605, 0.030491)	0.271180	0.258237
Relative Change (%) at 25 Months after Intervention 1	5.01	(-2.02, 12.05)	0.271180	0.258237
Absolute Change at 26 Months after Intervention 1	0.013320	(-0.004905, 0.031544)	0.270928	0.257609
Relative Change (%) at 26 Months after Intervention 1	5.17	(-2.15, 12.50)	0.270928	0.257609
Absolute Change at 27 Months after Intervention 1	0.013696	(-0.005206, 0.032598)	0.270676	0.256980
Absolute Change at 27 Months after Intervention 1	0.013696	(-0.005206, 0.032598)	0.270676	0.256980
Relative Change (%) at 27 Months after Intervention 1	5.33	(-2.29, 12.95)	0.270676	0.256980
Relative Change (%) at 27 Months after Intervention 1	5.33	(-2.29, 12.95)	0.270676	0.256980

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 23. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of ARB Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.294168	(0.289913, 0.298422)	<.001
Baseline trend	-0.000066	(-0.000222, 0.000090)	0.403
Level Change (After Intervention 1)	-0.001463	(-0.006109, 0.003182)	0.532
Trend Change (After Intervention 1)	0.000551	(0.000186, 0.000917)	0.004
Most Parsimonious Final Model Parameters (df = 71)[2,3]			
Intercept	0.292329	(0.289808, 0.294850)	<.001
Trend Change (After Intervention 1)	0.000364	(0.000136, 0.000593)	0.002

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 24. Absolute and Relative Changes in Proportion of ARB Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000364	(0.000136, 0.000593)	0.292693	0.292329
Relative Change (%) at 1 Months after Intervention 1	0.12	(0.05, 0.20)	0.292693	0.292329
Absolute Change at 2 Months after Intervention 1	0.000729	(0.000272, 0.001185)	0.293058	0.292329
Relative Change (%) at 2 Months after Intervention 1	0.25	(0.09, 0.41)	0.293058	0.292329
Absolute Change at 3 Months after Intervention 1	0.001093	(0.000409, 0.001778)	0.293422	0.292329
Relative Change (%) at 3 Months after Intervention 1	0.37	(0.14, 0.61)	0.293422	0.292329
Absolute Change at 4 Months after Intervention 1	0.001458	(0.000545, 0.002370)	0.293787	0.292329
Relative Change (%) at 4 Months after Intervention 1	0.50	(0.18, 0.81)	0.293787	0.292329
Absolute Change at 5 Months after Intervention 1	0.001822	(0.000681, 0.002963)	0.294151	0.292329
Relative Change (%) at 5 Months after Intervention 1	0.62	(0.23, 1.02)	0.294151	0.292329
Absolute Change at 6 Months after Intervention 1	0.002186	(0.000817, 0.003556)	0.294515	0.292329
Relative Change (%) at 6 Months after Intervention 1	0.75	(0.28, 1.22)	0.294515	0.292329
Absolute Change at 7 Months after Intervention 1	0.002551	(0.000953, 0.004148)	0.294880	0.292329
Relative Change (%) at 7 Months after Intervention 1	0.87	(0.32, 1.42)	0.294880	0.292329
Absolute Change at 8 Months after Intervention 1	0.002915	(0.001090, 0.004741)	0.295244	0.292329
Relative Change (%) at 8 Months after Intervention 1	1.00	(0.37, 1.63)	0.295244	0.292329
Absolute Change at 9 Months after Intervention 1	0.003280	(0.001226, 0.005334)	0.295609	0.292329
Relative Change (%) at 9 Months after Intervention 1	1.12	(0.41, 1.83)	0.295609	0.292329
Absolute Change at 10 Months after Intervention 1	0.003644	(0.001362, 0.005926)	0.295973	0.292329
Relative Change (%) at 10 Months after Intervention 1	1.25	(0.46, 2.03)	0.295973	0.292329
Absolute Change at 11 Months after Intervention 1	0.004008	(0.001498, 0.006519)	0.296337	0.292329
Relative Change (%) at 11 Months after Intervention 1	1.37	(0.51, 2.24)	0.296337	0.292329
Absolute Change at 12 Months after Intervention 1	0.004373	(0.001634, 0.007111)	0.296702	0.292329
Relative Change (%) at 12 Months after Intervention 1	1.50	(0.55, 2.44)	0.296702	0.292329
Absolute Change at 13 Months after Intervention 1	0.004737	(0.001771, 0.007704)	0.297066	0.292329
Relative Change (%) at 13 Months after Intervention 1	1.62	(0.60, 2.64)	0.297066	0.292329
Absolute Change at 14 Months after Intervention 1	0.005102	(0.001907, 0.008297)	0.297431	0.292329
Relative Change (%) at 14 Months after Intervention 1	1.75	(0.64, 2.85)	0.297431	0.292329
Absolute Change at 15 Months after Intervention 1	0.005466	(0.002043, 0.008889)	0.297795	0.292329
Relative Change (%) at 15 Months after Intervention 1	1.87	(0.69, 3.05)	0.297795	0.292329
Absolute Change at 16 Months after Intervention 1	0.005831	(0.002179, 0.009482)	0.298160	0.292329
Relative Change (%) at 16 Months after Intervention 1	1.99	(0.74, 3.25)	0.298160	0.292329

Table 24. Absolute and Relative Changes in Proportion of ARB Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 17 Months after Intervention 1	0.006195	(0.002315, 0.010075)	0.298524	0.292329
Relative Change (%) at 17 Months after Intervention 1	2.12	(0.78, 3.46)	0.298524	0.292329
Absolute Change at 18 Months after Intervention 1	0.006559	(0.002452, 0.010667)	0.298888	0.292329
Relative Change (%) at 18 Months after Intervention 1	2.24	(0.83, 3.66)	0.298888	0.292329
Absolute Change at 19 Months after Intervention 1	0.006924	(0.002588, 0.011260)	0.299253	0.292329
Relative Change (%) at 19 Months after Intervention 1	2.37	(0.87, 3.86)	0.299253	0.292329
Absolute Change at 20 Months after Intervention 1	0.007288	(0.002724, 0.011852)	0.299617	0.292329
Relative Change (%) at 20 Months after Intervention 1	2.49	(0.92, 4.07)	0.299617	0.292329
Absolute Change at 21 Months after Intervention 1	0.007653	(0.002860, 0.012445)	0.299982	0.292329
Relative Change (%) at 21 Months after Intervention 1	2.62	(0.97, 4.27)	0.299982	0.292329
Absolute Change at 22 Months after Intervention 1	0.008017	(0.002996, 0.013038)	0.300346	0.292329
Relative Change (%) at 22 Months after Intervention 1	2.74	(1.01, 4.47)	0.300346	0.292329
Absolute Change at 23 Months after Intervention 1	0.008381	(0.003133, 0.013630)	0.300710	0.292329
Relative Change (%) at 23 Months after Intervention 1	2.87	(1.06, 4.68)	0.300710	0.292329
Absolute Change at 24 Months after Intervention 1	0.008746	(0.003269, 0.014223)	0.301075	0.292329
Relative Change (%) at 24 Months after Intervention 1	2.99	(1.10, 4.88)	0.301075	0.292329
Absolute Change at 25 Months after Intervention 1	0.009110	(0.003405, 0.014815)	0.301439	0.292329
Relative Change (%) at 25 Months after Intervention 1	3.12	(1.15, 5.08)	0.301439	0.292329
Absolute Change at 26 Months after Intervention 1	0.009475	(0.003541, 0.015408)	0.301804	0.292329
Relative Change (%) at 26 Months after Intervention 1	3.24	(1.20, 5.29)	0.301804	0.292329
Absolute Change at 27 Months after Intervention 1	0.009839	(0.003677, 0.016001)	0.302168	0.292329
Absolute Change at 27 Months after Intervention 1	0.009839	(0.003677, 0.016001)	0.302168	0.292329
Relative Change (%) at 27 Months after Intervention 1	3.37	(1.24, 5.49)	0.302168	0.292329
Relative Change (%) at 27 Months after Intervention 1	3.37	(1.24, 5.49)	0.302168	0.292329

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 25. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Beta Blocker Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.429055	(0.412916, 0.445195)	<.001
Baseline trend	-0.000934	(-0.001509, -0.000359)	0.002
Level Change (After Intervention 1)	0.006633	(-0.003457, 0.016723)	0.194
Trend Change (After Intervention 1)	0.000249	(-0.001118, 0.001616)	0.718
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.427687	(0.413507, 0.441868)	<.001
Baseline trend	-0.000853	(-0.001226, -0.000480)	<.001
Level Change (After Intervention 1)	0.006729	(-0.003117, 0.016575)	0.178

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 26. Absolute and Relative Changes in Proportion of Beta Blocker Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.396028	0.389300
Relative Change (%) at 1 Months after Intervention 1	1.73	(-0.98, 4.43)	0.396028	0.389300
Absolute Change at 2 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.395175	0.388447
Relative Change (%) at 2 Months after Intervention 1	1.73	(-0.98, 4.45)	0.395175	0.388447
Absolute Change at 3 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.394322	0.387594
Relative Change (%) at 3 Months after Intervention 1	1.74	(-0.98, 4.46)	0.394322	0.387594
Absolute Change at 4 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.393469	0.386741
Relative Change (%) at 4 Months after Intervention 1	1.74	(-0.99, 4.47)	0.393469	0.386741
Absolute Change at 5 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.392616	0.385887
Relative Change (%) at 5 Months after Intervention 1	1.74	(-0.99, 4.48)	0.392616	0.385887
Absolute Change at 6 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.391763	0.385034
Relative Change (%) at 6 Months after Intervention 1	1.75	(-0.99, 4.49)	0.391763	0.385034
Absolute Change at 7 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.390910	0.384181
Relative Change (%) at 7 Months after Intervention 1	1.75	(-1.00, 4.50)	0.390910	0.384181
Absolute Change at 8 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.390057	0.383328
Relative Change (%) at 8 Months after Intervention 1	1.76	(-1.00, 4.51)	0.390057	0.383328
Absolute Change at 9 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.389204	0.382475
Relative Change (%) at 9 Months after Intervention 1	1.76	(-1.00, 4.52)	0.389204	0.382475
Absolute Change at 10 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.388351	0.381622
Relative Change (%) at 10 Months after Intervention 1	1.76	(-1.01, 4.53)	0.388351	0.381622
Absolute Change at 11 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.387498	0.380769
Relative Change (%) at 11 Months after Intervention 1	1.77	(-1.01, 4.54)	0.387498	0.380769
Absolute Change at 12 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.386645	0.379916
Relative Change (%) at 12 Months after Intervention 1	1.77	(-1.01, 4.56)	0.386645	0.379916
Absolute Change at 13 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.385792	0.379063
Relative Change (%) at 13 Months after Intervention 1	1.78	(-1.02, 4.57)	0.385792	0.379063
Absolute Change at 14 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.384939	0.378210
Relative Change (%) at 14 Months after Intervention 1	1.78	(-1.02, 4.58)	0.384939	0.378210
Absolute Change at 15 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.384086	0.377357
Relative Change (%) at 15 Months after Intervention 1	1.78	(-1.02, 4.59)	0.384086	0.377357
Absolute Change at 16 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.383233	0.376504
Relative Change (%) at 16 Months after Intervention 1	1.79	(-1.03, 4.60)	0.383233	0.376504
Absolute Change at 17 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.382380	0.375651

Table 26. Absolute and Relative Changes in Proportion of Beta Blocker Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Relative Change (%) at 17 Months after Intervention 1	1.79	(-1.03, 4.61)	0.382380	0.375651
Absolute Change at 18 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.381527	0.374798
Relative Change (%) at 18 Months after Intervention 1	1.80	(-1.03, 4.62)	0.381527	0.374798
Absolute Change at 19 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.380674	0.373945
Relative Change (%) at 19 Months after Intervention 1	1.80	(-1.04, 4.64)	0.380674	0.373945
Absolute Change at 20 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.379820	0.373092
Relative Change (%) at 20 Months after Intervention 1	1.80	(-1.04, 4.65)	0.379820	0.373092
Absolute Change at 21 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.378967	0.372239
Relative Change (%) at 21 Months after Intervention 1	1.81	(-1.04, 4.66)	0.378967	0.372239
Absolute Change at 22 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.378114	0.371386
Relative Change (%) at 22 Months after Intervention 1	1.81	(-1.05, 4.67)	0.378114	0.371386
Absolute Change at 23 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.377261	0.370533
Relative Change (%) at 23 Months after Intervention 1	1.82	(-1.05, 4.68)	0.377261	0.370533
Absolute Change at 24 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.376408	0.369679
Relative Change (%) at 24 Months after Intervention 1	1.82	(-1.05, 4.69)	0.376408	0.369679
Absolute Change at 25 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.375555	0.368826
Relative Change (%) at 25 Months after Intervention 1	1.82	(-1.06, 4.71)	0.375555	0.368826
Absolute Change at 26 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.374702	0.367973
Relative Change (%) at 26 Months after Intervention 1	1.83	(-1.06, 4.72)	0.374702	0.367973
Absolute Change at 27 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.373849	0.367120
Absolute Change at 27 Months after Intervention 1	0.006729	(-0.003704, 0.017162)	0.373849	0.367120
Relative Change (%) at 27 Months after Intervention 1	1.83	(-1.06, 4.73)	0.373849	0.367120
Relative Change (%) at 27 Months after Intervention 1	1.83	(-1.06, 4.73)	0.373849	0.367120

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 27. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of CCB Combination Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.251828	(0.238910, 0.264746)	<.001
Baseline trend	-0.000094	(-0.000548, 0.000359)	0.680
Level Change (After Intervention 1)	0.003939	(-0.002295, 0.010173)	0.212
Trend Change (After Intervention 1)	0.000022	(-0.001035, 0.001080)	0.966
Most Parsimonious Final Model Parameters (df = 72)[2,3]			
Intercept	0.250651	(0.242637, 0.258666)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 28. Absolute and Relative Changes in Proportion of CCB Combination Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 1 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 2 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 2 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 3 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 3 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 4 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 4 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 5 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 5 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 7 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 7 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 8 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 8 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 9 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 9 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 10 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 10 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 11 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 11 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 13 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 13 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 14 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 14 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 15 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 15 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 16 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 16 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651

Table 28. Absolute and Relative Changes in Proportion of CCB Combination Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 17 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 17 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 18 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 18 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 19 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 19 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 20 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 20 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 21 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 21 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 22 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 22 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 23 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 23 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 24 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 24 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 25 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 25 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 26 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 26 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Absolute Change at 27 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Absolute Change at 27 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.250651	0.250651
Relative Change (%) at 27 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651
Relative Change (%) at 27 Months after Intervention 1	0.00	(0.00, 0.00)	0.250651	0.250651

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 29. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Loop Diuretics Combination Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.103381	(0.090760, 0.116001)	<.001
Baseline trend	-0.000331	(-0.000777, 0.000115)	0.143
Level Change (After Intervention 1)	-0.000135	(-0.005144, 0.004874)	0.957
Trend Change (After Intervention 1)	0.000174	(-0.000876, 0.001225)	0.742
Most Parsimonious Final Model Parameters (df = 71)[2,3]			
Intercept	0.105424	(0.091537, 0.119310)	<.001
Baseline trend	-0.000328	(-0.000623, -0.000033)	0.030

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 30. Absolute and Relative Changes in Proportion of Loop Diuretics Combination Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.090664	0.090664
Relative Change (%) at 1 Months after Intervention 1	0.00	(0.00, 0.00)	0.090664	0.090664
Absolute Change at 2 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.090336	0.090336
Relative Change (%) at 2 Months after Intervention 1	0.00	(0.00, 0.00)	0.090336	0.090336
Absolute Change at 3 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.090008	0.090008
Relative Change (%) at 3 Months after Intervention 1	0.00	(0.00, 0.00)	0.090008	0.090008
Absolute Change at 4 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.089680	0.089680
Relative Change (%) at 4 Months after Intervention 1	0.00	(0.00, 0.00)	0.089680	0.089680
Absolute Change at 5 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.089352	0.089352
Relative Change (%) at 5 Months after Intervention 1	0.00	(0.00, 0.00)	0.089352	0.089352
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.089024	0.089024
Relative Change (%) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.089024	0.089024
Absolute Change at 7 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.088696	0.088696
Relative Change (%) at 7 Months after Intervention 1	0.00	(0.00, 0.00)	0.088696	0.088696
Absolute Change at 8 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.088368	0.088368
Relative Change (%) at 8 Months after Intervention 1	0.00	(0.00, 0.00)	0.088368	0.088368
Absolute Change at 9 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.088040	0.088040
Relative Change (%) at 9 Months after Intervention 1	0.00	(0.00, 0.00)	0.088040	0.088040
Absolute Change at 10 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.087712	0.087712
Relative Change (%) at 10 Months after Intervention 1	0.00	(0.00, 0.00)	0.087712	0.087712
Absolute Change at 11 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.087384	0.087384
Relative Change (%) at 11 Months after Intervention 1	0.00	(0.00, 0.00)	0.087384	0.087384
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.087056	0.087056
Relative Change (%) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.087056	0.087056
Absolute Change at 13 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.086728	0.086728
Relative Change (%) at 13 Months after Intervention 1	0.00	(0.00, 0.00)	0.086728	0.086728
Absolute Change at 14 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.086400	0.086400
Relative Change (%) at 14 Months after Intervention 1	0.00	(0.00, 0.00)	0.086400	0.086400
Absolute Change at 15 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.086072	0.086072
Relative Change (%) at 15 Months after Intervention 1	0.00	(0.00, 0.00)	0.086072	0.086072
Absolute Change at 16 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.085744	0.085744
Relative Change (%) at 16 Months after Intervention 1	0.00	(0.00, 0.00)	0.085744	0.085744
Absolute Change at 17 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.085416	0.085416

Table 30. Absolute and Relative Changes in Proportion of Loop Diuretics Combination Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Relative Change (%) at 17 Months after Intervention 1	0.00	(0.00, 0.00)	0.085416	0.085416
Absolute Change at 18 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.085088	0.085088
Relative Change (%) at 18 Months after Intervention 1	0.00	(0.00, 0.00)	0.085088	0.085088
Absolute Change at 19 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.084760	0.084760
Relative Change (%) at 19 Months after Intervention 1	0.00	(0.00, 0.00)	0.084760	0.084760
Absolute Change at 20 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.084432	0.084432
Relative Change (%) at 20 Months after Intervention 1	0.00	(0.00, 0.00)	0.084432	0.084432
Absolute Change at 21 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.084104	0.084104
Relative Change (%) at 21 Months after Intervention 1	0.00	(0.00, 0.00)	0.084104	0.084104
Absolute Change at 22 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.083776	0.083776
Relative Change (%) at 22 Months after Intervention 1	0.00	(0.00, 0.00)	0.083776	0.083776
Absolute Change at 23 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.083448	0.083448
Relative Change (%) at 23 Months after Intervention 1	0.00	(0.00, 0.00)	0.083448	0.083448
Absolute Change at 24 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.083120	0.083120
Relative Change (%) at 24 Months after Intervention 1	0.00	(0.00, 0.00)	0.083120	0.083120
Absolute Change at 25 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.082792	0.082792
Relative Change (%) at 25 Months after Intervention 1	0.00	(0.00, 0.00)	0.082792	0.082792
Absolute Change at 26 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.082464	0.082464
Relative Change (%) at 26 Months after Intervention 1	0.00	(0.00, 0.00)	0.082464	0.082464
Absolute Change at 27 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.082136	0.082136
Absolute Change at 27 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.082136	0.082136
Relative Change (%) at 27 Months after Intervention 1	0.00	(0.00, 0.00)	0.082136	0.082136
Relative Change (%) at 27 Months after Intervention 1	0.00	(0.00, 0.00)	0.082136	0.082136

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 31. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Potassium Sparing Combination Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.032094	(0.030404, 0.033784)	<.001
Baseline trend	0.000078	(0.000021, 0.000136)	0.008
Level Change (After Intervention 1)	0.000084	(-0.000742, 0.000910)	0.840
Trend Change (After Intervention 1)	0.000127	(-0.000002, 0.000257)	0.053
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.032090	(0.030400, 0.033781)	<.001
Baseline trend	0.000079	(0.000022, 0.000136)	0.008
Trend Change (After Intervention 1)	0.000129	(0.000002, 0.000256)	0.047

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 32. Absolute and Relative Changes in Proportion of Potassium Sparing Combination Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000129	(-0.000008, 0.000266)	0.035775	0.035646
Relative Change (%) at 1 Months after Intervention 1	0.36	(-0.04, 0.76)	0.035775	0.035646
Absolute Change at 2 Months after Intervention 1	0.000258	(-0.000015, 0.000532)	0.035983	0.035725
Relative Change (%) at 2 Months after Intervention 1	0.72	(-0.07, 1.52)	0.035983	0.035725
Absolute Change at 3 Months after Intervention 1	0.000387	(-0.000023, 0.000797)	0.036191	0.035804
Relative Change (%) at 3 Months after Intervention 1	1.08	(-0.11, 2.27)	0.036191	0.035804
Absolute Change at 4 Months after Intervention 1	0.000516	(-0.000030, 0.001063)	0.036399	0.035883
Relative Change (%) at 4 Months after Intervention 1	1.44	(-0.15, 3.03)	0.036399	0.035883
Absolute Change at 5 Months after Intervention 1	0.000646	(-0.000038, 0.001329)	0.036607	0.035962
Relative Change (%) at 5 Months after Intervention 1	1.80	(-0.19, 3.78)	0.036607	0.035962
Absolute Change at 6 Months after Intervention 1	0.000775	(-0.000045, 0.001595)	0.036815	0.036041
Relative Change (%) at 6 Months after Intervention 1	2.15	(-0.23, 4.53)	0.036815	0.036041
Absolute Change at 7 Months after Intervention 1	0.000904	(-0.000053, 0.001861)	0.037024	0.036120
Relative Change (%) at 7 Months after Intervention 1	2.50	(-0.27, 5.27)	0.037024	0.036120
Absolute Change at 8 Months after Intervention 1	0.001033	(-0.000061, 0.002126)	0.037232	0.036199
Relative Change (%) at 8 Months after Intervention 1	2.85	(-0.31, 6.01)	0.037232	0.036199
Absolute Change at 9 Months after Intervention 1	0.001162	(-0.000068, 0.002392)	0.037440	0.036278
Relative Change (%) at 9 Months after Intervention 1	3.20	(-0.35, 6.76)	0.037440	0.036278
Absolute Change at 10 Months after Intervention 1	0.001291	(-0.000076, 0.002658)	0.037648	0.036357
Relative Change (%) at 10 Months after Intervention 1	3.55	(-0.39, 7.49)	0.037648	0.036357
Absolute Change at 11 Months after Intervention 1	0.001420	(-0.000083, 0.002924)	0.037856	0.036436
Relative Change (%) at 11 Months after Intervention 1	3.90	(-0.44, 8.23)	0.037856	0.036436
Absolute Change at 12 Months after Intervention 1	0.001549	(-0.000091, 0.003190)	0.038064	0.036515
Relative Change (%) at 12 Months after Intervention 1	4.24	(-0.48, 8.97)	0.038064	0.036515
Absolute Change at 13 Months after Intervention 1	0.001678	(-0.000099, 0.003455)	0.038272	0.036594
Relative Change (%) at 13 Months after Intervention 1	4.59	(-0.52, 9.70)	0.038272	0.036594
Absolute Change at 14 Months after Intervention 1	0.001808	(-0.000106, 0.003721)	0.038480	0.036673
Relative Change (%) at 14 Months after Intervention 1	4.93	(-0.57, 10.43)	0.038480	0.036673
Absolute Change at 15 Months after Intervention 1	0.001937	(-0.000114, 0.003987)	0.038689	0.036752
Relative Change (%) at 15 Months after Intervention 1	5.27	(-0.61, 11.15)	0.038689	0.036752
Absolute Change at 16 Months after Intervention 1	0.002066	(-0.000121, 0.004253)	0.038897	0.036831
Relative Change (%) at 16 Months after Intervention 1	5.61	(-0.66, 11.88)	0.038897	0.036831

Table 32. Absolute and Relative Changes in Proportion of Potassium Sparing Combination Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 17 Months after Intervention 1	0.002195	(-0.000129, 0.004519)	0.039105	0.036910
Relative Change (%) at 17 Months after Intervention 1	5.95	(-0.71, 12.60)	0.039105	0.036910
Absolute Change at 18 Months after Intervention 1	0.002324	(-0.000136, 0.004785)	0.039313	0.036989
Relative Change (%) at 18 Months after Intervention 1	6.28	(-0.76, 13.32)	0.039313	0.036989
Absolute Change at 19 Months after Intervention 1	0.002453	(-0.000144, 0.005050)	0.039521	0.037068
Relative Change (%) at 19 Months after Intervention 1	6.62	(-0.80, 14.04)	0.039521	0.037068
Absolute Change at 20 Months after Intervention 1	0.002582	(-0.000152, 0.005316)	0.039729	0.037147
Relative Change (%) at 20 Months after Intervention 1	6.95	(-0.85, 14.76)	0.039729	0.037147
Absolute Change at 21 Months after Intervention 1	0.002711	(-0.000159, 0.005582)	0.039937	0.037226
Relative Change (%) at 21 Months after Intervention 1	7.28	(-0.90, 15.47)	0.039937	0.037226
Absolute Change at 22 Months after Intervention 1	0.002841	(-0.000167, 0.005848)	0.040145	0.037305
Relative Change (%) at 22 Months after Intervention 1	7.61	(-0.95, 16.18)	0.040145	0.037305
Absolute Change at 23 Months after Intervention 1	0.002970	(-0.000174, 0.006114)	0.040354	0.037384
Relative Change (%) at 23 Months after Intervention 1	7.94	(-1.00, 16.89)	0.040354	0.037384
Absolute Change at 24 Months after Intervention 1	0.003099	(-0.000182, 0.006379)	0.040562	0.037463
Relative Change (%) at 24 Months after Intervention 1	8.27	(-1.06, 17.60)	0.040562	0.037463
Absolute Change at 25 Months after Intervention 1	0.003228	(-0.000189, 0.006645)	0.040770	0.037542
Relative Change (%) at 25 Months after Intervention 1	8.60	(-1.11, 18.30)	0.040770	0.037542
Absolute Change at 26 Months after Intervention 1	0.003357	(-0.000197, 0.006911)	0.040978	0.037621
Relative Change (%) at 26 Months after Intervention 1	8.92	(-1.16, 19.01)	0.040978	0.037621
Absolute Change at 27 Months after Intervention 1	0.003486	(-0.000205, 0.007177)	0.041186	0.037700
Absolute Change at 27 Months after Intervention 1	0.003486	(-0.000205, 0.007177)	0.041186	0.037700
Relative Change (%) at 27 Months after Intervention 1	9.25	(-1.21, 19.71)	0.041186	0.037700
Relative Change (%) at 27 Months after Intervention 1	9.25	(-1.21, 19.71)	0.041186	0.037700

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 33. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Thiazide-like Diuretics Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.016194	(0.016008, 0.016380)	<.001
Baseline trend	0.000027	(0.000020, 0.000034)	<.001
Level Change (After Intervention 1)	0.000827	(0.000516, 0.001139)	<.001
Trend Change (After Intervention 1)	-0.000043	(-0.000060, -0.000026)	<.001
Most Parsimonious Final Model Parameters (df = 69)[2,3]			
Intercept	0.016194	(0.016008, 0.016380)	<.001
Baseline trend	0.000027	(0.000020, 0.000034)	<.001
Level Change (After Intervention 1)	0.000827	(0.000516, 0.001139)	<.001
Trend Change (After Intervention 1)	-0.000043	(-0.000060, -0.000026)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 34. Absolute and Relative Changes in Proportion of Thiazide-like Diuretics Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000784	(0.000458, 0.001111)	0.018185	0.017401
Relative Change (%) at 1 Months after Intervention 1	4.51	(2.60, 6.42)	0.018185	0.017401
Absolute Change at 2 Months after Intervention 1	0.000742	(0.000422, 0.001062)	0.018169	0.017427
Relative Change (%) at 2 Months after Intervention 1	4.26	(2.39, 6.13)	0.018169	0.017427
Absolute Change at 3 Months after Intervention 1	0.000699	(0.000385, 0.001013)	0.018153	0.017454
Relative Change (%) at 3 Months after Intervention 1	4.00	(2.17, 5.84)	0.018153	0.017454
Absolute Change at 4 Months after Intervention 1	0.000656	(0.000347, 0.000964)	0.018137	0.017481
Relative Change (%) at 4 Months after Intervention 1	3.75	(1.95, 5.55)	0.018137	0.017481
Absolute Change at 5 Months after Intervention 1	0.000613	(0.000309, 0.000917)	0.018121	0.017508
Relative Change (%) at 5 Months after Intervention 1	3.50	(1.73, 5.27)	0.018121	0.017508
Absolute Change at 6 Months after Intervention 1	0.000570	(0.000270, 0.000871)	0.018105	0.017535
Relative Change (%) at 6 Months after Intervention 1	3.25	(1.50, 5.00)	0.018105	0.017535
Absolute Change at 7 Months after Intervention 1	0.000527	(0.000230, 0.000825)	0.018089	0.017561
Relative Change (%) at 7 Months after Intervention 1	3.00	(1.27, 4.73)	0.018089	0.017561
Absolute Change at 8 Months after Intervention 1	0.000485	(0.000188, 0.000781)	0.018073	0.017588
Relative Change (%) at 8 Months after Intervention 1	2.75	(1.04, 4.47)	0.018073	0.017588
Absolute Change at 9 Months after Intervention 1	0.000442	(0.000146, 0.000737)	0.018057	0.017615
Relative Change (%) at 9 Months after Intervention 1	2.51	(0.80, 4.22)	0.018057	0.017615
Absolute Change at 10 Months after Intervention 1	0.000399	(0.000103, 0.000695)	0.018041	0.017642
Relative Change (%) at 10 Months after Intervention 1	2.26	(0.56, 3.97)	0.018041	0.017642
Absolute Change at 11 Months after Intervention 1	0.000356	(0.000059, 0.000653)	0.018025	0.017669
Relative Change (%) at 11 Months after Intervention 1	2.01	(0.31, 3.72)	0.018025	0.017669
Absolute Change at 12 Months after Intervention 1	0.000313	(0.000014, 0.000613)	0.018009	0.017695
Relative Change (%) at 12 Months after Intervention 1	1.77	(0.05, 3.49)	0.018009	0.017695
Absolute Change at 13 Months after Intervention 1	0.000270	(-0.000033, 0.000573)	0.017993	0.017722
Relative Change (%) at 13 Months after Intervention 1	1.52	(-0.20, 3.25)	0.017993	0.017722
Absolute Change at 14 Months after Intervention 1	0.000227	(-0.000080, 0.000534)	0.017977	0.017749
Relative Change (%) at 14 Months after Intervention 1	1.28	(-0.47, 3.03)	0.017977	0.017749
Absolute Change at 15 Months after Intervention 1	0.000185	(-0.000127, 0.000497)	0.017960	0.017776
Relative Change (%) at 15 Months after Intervention 1	1.04	(-0.73, 2.81)	0.017960	0.017776
Absolute Change at 16 Months after Intervention 1	0.000142	(-0.000176, 0.000460)	0.017944	0.017803
Relative Change (%) at 16 Months after Intervention 1	0.80	(-1.00, 2.59)	0.017944	0.017803
Absolute Change at 17 Months after Intervention 1	0.000099	(-0.000226, 0.000424)	0.017928	0.017830

Table 34. Absolute and Relative Changes in Proportion of Thiazide-like Diuretics Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Relative Change (%) at 17 Months after Intervention 1	0.55	(-1.28, 2.38)	0.017928	0.017830
Absolute Change at 18 Months after Intervention 1	0.000056	(-0.000276, 0.000388)	0.017912	0.017856
Relative Change (%) at 18 Months after Intervention 1	0.31	(-1.55, 2.18)	0.017912	0.017856
Absolute Change at 19 Months after Intervention 1	0.000013	(-0.000327, 0.000353)	0.017896	0.017883
Relative Change (%) at 19 Months after Intervention 1	0.07	(-1.83, 1.98)	0.017896	0.017883
Absolute Change at 20 Months after Intervention 1	-0.000030	(-0.000379, 0.000319)	0.017880	0.017910
Relative Change (%) at 20 Months after Intervention 1	-0.17	(-2.11, 1.78)	0.017880	0.017910
Absolute Change at 21 Months after Intervention 1	-0.000073	(-0.000431, 0.000286)	0.017864	0.017937
Relative Change (%) at 21 Months after Intervention 1	-0.40	(-2.40, 1.59)	0.017864	0.017937
Absolute Change at 22 Months after Intervention 1	-0.000115	(-0.000484, 0.000253)	0.017848	0.017964
Relative Change (%) at 22 Months after Intervention 1	-0.64	(-2.68, 1.40)	0.017848	0.017964
Absolute Change at 23 Months after Intervention 1	-0.000158	(-0.000537, 0.000221)	0.017832	0.017990
Relative Change (%) at 23 Months after Intervention 1	-0.88	(-2.97, 1.21)	0.017832	0.017990
Absolute Change at 24 Months after Intervention 1	-0.000201	(-0.000591, 0.000189)	0.017816	0.018017
Relative Change (%) at 24 Months after Intervention 1	-1.12	(-3.26, 1.03)	0.017816	0.018017
Absolute Change at 25 Months after Intervention 1	-0.000244	(-0.000646, 0.000158)	0.017800	0.018044
Relative Change (%) at 25 Months after Intervention 1	-1.35	(-3.56, 0.85)	0.017800	0.018044
Absolute Change at 26 Months after Intervention 1	-0.000287	(-0.000700, 0.000127)	0.017784	0.018071
Relative Change (%) at 26 Months after Intervention 1	-1.59	(-3.85, 0.67)	0.017784	0.018071
Absolute Change at 27 Months after Intervention 1	-0.000330	(-0.000755, 0.000096)	0.017768	0.018098
Absolute Change at 27 Months after Intervention 1	-0.000330	(-0.000755, 0.000096)	0.017768	0.018098
Relative Change (%) at 27 Months after Intervention 1	-1.82	(-4.14, 0.50)	0.017768	0.018098
Relative Change (%) at 27 Months after Intervention 1	-1.82	(-4.14, 0.50)	0.017768	0.018098

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 35. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ/ACEI Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.231035	(0.228435, 0.233635)	<.001
Baseline trend	-0.000336	(-0.000430, -0.000242)	<.001
Level Change (After Intervention 1)	-0.001541	(-0.003648, 0.000567)	0.150
Trend Change (After Intervention 1)	-0.000470	(-0.000700, -0.000240)	<.001
Most Parsimonious Final Model Parameters (df = 69)[2,3]			
Intercept	0.231035	(0.228435, 0.233635)	<.001
Baseline trend	-0.000336	(-0.000430, -0.000242)	<.001
Level Change (After Intervention 1)	-0.001541	(-0.003648, 0.000567)	0.150
Trend Change (After Intervention 1)	-0.000470	(-0.000700, -0.000240)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 36. Absolute and Relative Changes in Proportion of HCTZ/ACEI Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	-0.002010	(-0.004226, 0.000206)	0.213900	0.215910
Relative Change (%) at 1 Months after Intervention 1	-0.93	(-1.95, 0.09)	0.213900	0.215910
Absolute Change at 2 Months after Intervention 1	-0.002480	(-0.004683, -0.000277)	0.213095	0.215574
Relative Change (%) at 2 Months after Intervention 1	-1.15	(-2.17, -0.14)	0.213095	0.215574
Absolute Change at 3 Months after Intervention 1	-0.002949	(-0.005163, -0.000736)	0.212289	0.215238
Relative Change (%) at 3 Months after Intervention 1	-1.37	(-2.39, -0.35)	0.212289	0.215238
Absolute Change at 4 Months after Intervention 1	-0.003419	(-0.005667, -0.001171)	0.211483	0.214902
Relative Change (%) at 4 Months after Intervention 1	-1.59	(-2.62, -0.56)	0.211483	0.214902
Absolute Change at 5 Months after Intervention 1	-0.003888	(-0.006193, -0.001584)	0.210677	0.214566
Relative Change (%) at 5 Months after Intervention 1	-1.81	(-2.87, -0.75)	0.210677	0.214566
Absolute Change at 6 Months after Intervention 1	-0.004358	(-0.006740, -0.001976)	0.209872	0.214230
Relative Change (%) at 6 Months after Intervention 1	-2.03	(-3.13, -0.94)	0.209872	0.214230
Absolute Change at 7 Months after Intervention 1	-0.004828	(-0.007306, -0.002350)	0.209066	0.213894
Relative Change (%) at 7 Months after Intervention 1	-2.26	(-3.39, -1.12)	0.209066	0.213894
Absolute Change at 8 Months after Intervention 1	-0.005297	(-0.007888, -0.002706)	0.208260	0.213558
Relative Change (%) at 8 Months after Intervention 1	-2.48	(-3.67, -1.30)	0.208260	0.213558
Absolute Change at 9 Months after Intervention 1	-0.005767	(-0.008485, -0.003048)	0.207455	0.213221
Relative Change (%) at 9 Months after Intervention 1	-2.70	(-3.95, -1.46)	0.207455	0.213221
Absolute Change at 10 Months after Intervention 1	-0.006236	(-0.009095, -0.003377)	0.206649	0.212885
Relative Change (%) at 10 Months after Intervention 1	-2.93	(-4.23, -1.62)	0.206649	0.212885
Absolute Change at 11 Months after Intervention 1	-0.006706	(-0.009716, -0.003696)	0.205843	0.212549
Relative Change (%) at 11 Months after Intervention 1	-3.16	(-4.53, -1.78)	0.205843	0.212549
Absolute Change at 12 Months after Intervention 1	-0.007176	(-0.010346, -0.004005)	0.205038	0.212213
Relative Change (%) at 12 Months after Intervention 1	-3.38	(-4.83, -1.93)	0.205038	0.212213
Absolute Change at 13 Months after Intervention 1	-0.007645	(-0.010984, -0.004306)	0.204232	0.211877
Relative Change (%) at 13 Months after Intervention 1	-3.61	(-5.13, -2.08)	0.204232	0.211877
Absolute Change at 14 Months after Intervention 1	-0.008115	(-0.011629, -0.004600)	0.203426	0.211541
Relative Change (%) at 14 Months after Intervention 1	-3.84	(-5.44, -2.23)	0.203426	0.211541
Absolute Change at 15 Months after Intervention 1	-0.008584	(-0.012280, -0.004888)	0.202621	0.211205
Relative Change (%) at 15 Months after Intervention 1	-4.06	(-5.75, -2.38)	0.202621	0.211205
Absolute Change at 16 Months after Intervention 1	-0.009054	(-0.012936, -0.005171)	0.201815	0.210869
Relative Change (%) at 16 Months after Intervention 1	-4.29	(-6.07, -2.52)	0.201815	0.210869
Absolute Change at 17 Months after Intervention 1	-0.009523	(-0.013597, -0.005450)	0.201009	0.210533

Table 36. Absolute and Relative Changes in Proportion of HCTZ/ACEI Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Relative Change (%) at 17 Months after Intervention 1	-4.52	(-6.39, -2.66)	0.201009	0.210533
Absolute Change at 18 Months after Intervention 1	-0.009993	(-0.014261, -0.005725)	0.200204	0.210197
Relative Change (%) at 18 Months after Intervention 1	-4.75	(-6.71, -2.80)	0.200204	0.210197
Absolute Change at 19 Months after Intervention 1	-0.010463	(-0.014928, -0.005997)	0.199398	0.209860
Relative Change (%) at 19 Months after Intervention 1	-4.99	(-7.03, -2.94)	0.199398	0.209860
Absolute Change at 20 Months after Intervention 1	-0.010932	(-0.015598, -0.006266)	0.198592	0.209524
Relative Change (%) at 20 Months after Intervention 1	-5.22	(-7.35, -3.08)	0.198592	0.209524
Absolute Change at 21 Months after Intervention 1	-0.011402	(-0.016271, -0.006533)	0.197786	0.209188
Relative Change (%) at 21 Months after Intervention 1	-5.45	(-7.68, -3.22)	0.197786	0.209188
Absolute Change at 22 Months after Intervention 1	-0.011871	(-0.016946, -0.006797)	0.196981	0.208852
Relative Change (%) at 22 Months after Intervention 1	-5.68	(-8.01, -3.36)	0.196981	0.208852
Absolute Change at 23 Months after Intervention 1	-0.012341	(-0.017623, -0.007059)	0.196175	0.208516
Relative Change (%) at 23 Months after Intervention 1	-5.92	(-8.34, -3.49)	0.196175	0.208516
Absolute Change at 24 Months after Intervention 1	-0.012811	(-0.018302, -0.007320)	0.195369	0.208180
Relative Change (%) at 24 Months after Intervention 1	-6.15	(-8.68, -3.63)	0.195369	0.208180
Absolute Change at 25 Months after Intervention 1	-0.013280	(-0.018982, -0.007579)	0.194564	0.207844
Relative Change (%) at 25 Months after Intervention 1	-6.39	(-9.01, -3.77)	0.194564	0.207844
Absolute Change at 26 Months after Intervention 1	-0.013750	(-0.019663, -0.007836)	0.193758	0.207508
Relative Change (%) at 26 Months after Intervention 1	-6.63	(-9.35, -3.90)	0.193758	0.207508
Absolute Change at 27 Months after Intervention 1	-0.014219	(-0.020346, -0.008093)	0.192952	0.207172
Absolute Change at 27 Months after Intervention 1	-0.014219	(-0.020346, -0.008093)	0.192952	0.207172
Relative Change (%) at 27 Months after Intervention 1	-6.86	(-9.69, -4.04)	0.192952	0.207172
Relative Change (%) at 27 Months after Intervention 1	-6.86	(-9.69, -4.04)	0.192952	0.207172

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 37. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ/ARB/CCB Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.012379	(0.011698, 0.013059)	<.001
Baseline trend	-0.000032	(-0.000056, -0.000008)	0.011
Level Change (After Intervention 1)	-0.000072	(-0.000380, 0.000236)	0.642
Trend Change (After Intervention 1)	-0.000130	(-0.000192, -0.000069)	<.001
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.012399	(0.011565, 0.013232)	<.001
Baseline trend	-0.000034	(-0.000063, -0.000004)	0.027
Trend Change (After Intervention 1)	-0.000128	(-0.000200, -0.000056)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 38. Absolute and Relative Changes in Proportion of HCTZ/ARB/CCB Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	-0.000128	(-0.000216, -0.000040)	0.010762	0.010890
Relative Change (%) at 1 Months after Intervention 1	-1.17	(-1.91, -0.44)	0.010762	0.010890
Absolute Change at 2 Months after Intervention 1	-0.000256	(-0.000432, -0.000079)	0.010600	0.010856
Relative Change (%) at 2 Months after Intervention 1	-2.36	(-3.82, -0.89)	0.010600	0.010856
Absolute Change at 3 Months after Intervention 1	-0.000384	(-0.000648, -0.000119)	0.010439	0.010823
Relative Change (%) at 3 Months after Intervention 1	-3.54	(-5.74, -1.35)	0.010439	0.010823
Absolute Change at 4 Months after Intervention 1	-0.000511	(-0.000864, -0.000159)	0.010278	0.010789
Relative Change (%) at 4 Months after Intervention 1	-4.74	(-7.67, -1.81)	0.010278	0.010789
Absolute Change at 5 Months after Intervention 1	-0.000639	(-0.001081, -0.000198)	0.010116	0.010756
Relative Change (%) at 5 Months after Intervention 1	-5.94	(-9.60, -2.29)	0.010116	0.010756
Absolute Change at 6 Months after Intervention 1	-0.000767	(-0.001297, -0.000238)	0.009955	0.010722
Relative Change (%) at 6 Months after Intervention 1	-7.16	(-11.54, -2.77)	0.009955	0.010722
Absolute Change at 7 Months after Intervention 1	-0.000895	(-0.001513, -0.000277)	0.009793	0.010688
Relative Change (%) at 7 Months after Intervention 1	-8.37	(-13.48, -3.27)	0.009793	0.010688
Absolute Change at 8 Months after Intervention 1	-0.001023	(-0.001729, -0.000317)	0.009632	0.010655
Relative Change (%) at 8 Months after Intervention 1	-9.60	(-15.43, -3.77)	0.009632	0.010655
Absolute Change at 9 Months after Intervention 1	-0.001151	(-0.001945, -0.000357)	0.009471	0.010621
Relative Change (%) at 9 Months after Intervention 1	-10.83	(-17.38, -4.29)	0.009471	0.010621
Absolute Change at 10 Months after Intervention 1	-0.001279	(-0.002161, -0.000396)	0.009309	0.010588
Relative Change (%) at 10 Months after Intervention 1	-12.08	(-19.34, -4.81)	0.009309	0.010588
Absolute Change at 11 Months after Intervention 1	-0.001407	(-0.002377, -0.000436)	0.009148	0.010554
Relative Change (%) at 11 Months after Intervention 1	-13.33	(-21.31, -5.35)	0.009148	0.010554
Absolute Change at 12 Months after Intervention 1	-0.001534	(-0.002593, -0.000476)	0.008986	0.010521
Relative Change (%) at 12 Months after Intervention 1	-14.58	(-23.28, -5.89)	0.008986	0.010521
Absolute Change at 13 Months after Intervention 1	-0.001662	(-0.002809, -0.000515)	0.008825	0.010487
Relative Change (%) at 13 Months after Intervention 1	-15.85	(-25.26, -6.44)	0.008825	0.010487
Absolute Change at 14 Months after Intervention 1	-0.001790	(-0.003025, -0.000555)	0.008664	0.010454
Relative Change (%) at 14 Months after Intervention 1	-17.12	(-27.24, -7.01)	0.008664	0.010454
Absolute Change at 15 Months after Intervention 1	-0.001918	(-0.003242, -0.000595)	0.008502	0.010420
Relative Change (%) at 15 Months after Intervention 1	-18.41	(-29.23, -7.59)	0.008502	0.010420
Absolute Change at 16 Months after Intervention 1	-0.002046	(-0.003458, -0.000634)	0.008341	0.010387
Relative Change (%) at 16 Months after Intervention 1	-19.70	(-31.22, -8.17)	0.008341	0.010387
Absolute Change at 17 Months after Intervention 1	-0.002174	(-0.003674, -0.000674)	0.008179	0.010353

Table 38. Absolute and Relative Changes in Proportion of HCTZ/ARB/CCB Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Relative Change (%) at 17 Months after Intervention 1	-21.00	(-33.22, -8.77)	0.008179	0.010353
Absolute Change at 18 Months after Intervention 1	-0.002302	(-0.003890, -0.000713)	0.008018	0.010320
Relative Change (%) at 18 Months after Intervention 1	-22.30	(-35.23, -9.38)	0.008018	0.010320
Absolute Change at 19 Months after Intervention 1	-0.002429	(-0.004106, -0.000753)	0.007857	0.010286
Relative Change (%) at 19 Months after Intervention 1	-23.62	(-37.24, -10.00)	0.007857	0.010286
Absolute Change at 20 Months after Intervention 1	-0.002557	(-0.004322, -0.000793)	0.007695	0.010253
Relative Change (%) at 20 Months after Intervention 1	-24.94	(-39.26, -10.63)	0.007695	0.010253
Absolute Change at 21 Months after Intervention 1	-0.002685	(-0.004538, -0.000832)	0.007534	0.010219
Relative Change (%) at 21 Months after Intervention 1	-26.28	(-41.28, -11.27)	0.007534	0.010219
Absolute Change at 22 Months after Intervention 1	-0.002813	(-0.004754, -0.000872)	0.007372	0.010185
Relative Change (%) at 22 Months after Intervention 1	-27.62	(-43.31, -11.93)	0.007372	0.010185
Absolute Change at 23 Months after Intervention 1	-0.002941	(-0.004970, -0.000912)	0.007211	0.010152
Relative Change (%) at 23 Months after Intervention 1	-28.97	(-45.34, -12.59)	0.007211	0.010152
Absolute Change at 24 Months after Intervention 1	-0.003069	(-0.005186, -0.000951)	0.007050	0.010118
Relative Change (%) at 24 Months after Intervention 1	-30.33	(-47.39, -13.27)	0.007050	0.010118
Absolute Change at 25 Months after Intervention 1	-0.003197	(-0.005403, -0.000991)	0.006888	0.010085
Relative Change (%) at 25 Months after Intervention 1	-31.70	(-49.43, -13.96)	0.006888	0.010085
Absolute Change at 26 Months after Intervention 1	-0.003325	(-0.005619, -0.001030)	0.006727	0.010051
Relative Change (%) at 26 Months after Intervention 1	-33.08	(-51.49, -14.67)	0.006727	0.010051
Absolute Change at 27 Months after Intervention 1	-0.003452	(-0.005835, -0.001070)	0.006565	0.010018
Absolute Change at 27 Months after Intervention 1	-0.003452	(-0.005835, -0.001070)	0.006565	0.010018
Relative Change (%) at 27 Months after Intervention 1	-34.46	(-53.54, -15.38)	0.006565	0.010018
Relative Change (%) at 27 Months after Intervention 1	-34.46	(-53.54, -15.38)	0.006565	0.010018

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 39. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ/ARB Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.293571	(0.275333, 0.311809)	<.001
Baseline trend	-0.001610	(-0.002259, -0.000960)	<.001
Level Change (After Intervention 1)	-0.001089	(-0.004843, 0.002666)	0.565
Trend Change (After Intervention 1)	0.002074	(0.000478, 0.003670)	0.012
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.292898	(0.274492, 0.311304)	<.001
Baseline trend	-0.001581	(-0.002235, -0.000927)	<.001
Trend Change (After Intervention 1)	0.001943	(0.000381, 0.003504)	0.016

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 40. Absolute and Relative Changes in Proportion of HCTZ/ARB Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.001943	(0.000369, 0.003516)	0.223696	0.221753
Relative Change (%) at 1 Months after Intervention 1	0.88	(0.11, 1.64)	0.223696	0.221753
Absolute Change at 2 Months after Intervention 1	0.003885	(0.000738, 0.007032)	0.224057	0.220172
Relative Change (%) at 2 Months after Intervention 1	1.76	(0.21, 3.31)	0.224057	0.220172
Absolute Change at 3 Months after Intervention 1	0.005828	(0.001107, 0.010549)	0.224419	0.218591
Relative Change (%) at 3 Months after Intervention 1	2.67	(0.32, 5.02)	0.224419	0.218591
Absolute Change at 4 Months after Intervention 1	0.007770	(0.001476, 0.014065)	0.224781	0.217010
Relative Change (%) at 4 Months after Intervention 1	3.58	(0.41, 6.75)	0.224781	0.217010
Absolute Change at 5 Months after Intervention 1	0.009713	(0.001845, 0.017581)	0.225142	0.215429
Relative Change (%) at 5 Months after Intervention 1	4.51	(0.51, 8.51)	0.225142	0.215429
Absolute Change at 6 Months after Intervention 1	0.011656	(0.002214, 0.021097)	0.225504	0.213848
Relative Change (%) at 6 Months after Intervention 1	5.45	(0.60, 10.31)	0.225504	0.213848
Absolute Change at 7 Months after Intervention 1	0.013598	(0.002583, 0.024613)	0.225866	0.212267
Relative Change (%) at 7 Months after Intervention 1	6.41	(0.68, 12.13)	0.225866	0.212267
Absolute Change at 8 Months after Intervention 1	0.015541	(0.002953, 0.028129)	0.226227	0.210686
Relative Change (%) at 8 Months after Intervention 1	7.38	(0.76, 13.99)	0.226227	0.210686
Absolute Change at 9 Months after Intervention 1	0.017484	(0.003322, 0.031646)	0.226589	0.209105
Relative Change (%) at 9 Months after Intervention 1	8.36	(0.83, 15.89)	0.226589	0.209105
Absolute Change at 10 Months after Intervention 1	0.019426	(0.003691, 0.035162)	0.226950	0.207524
Relative Change (%) at 10 Months after Intervention 1	9.36	(0.90, 17.82)	0.226950	0.207524
Absolute Change at 11 Months after Intervention 1	0.021369	(0.004060, 0.038678)	0.227312	0.205943
Relative Change (%) at 11 Months after Intervention 1	10.38	(0.96, 19.79)	0.227312	0.205943
Absolute Change at 12 Months after Intervention 1	0.023311	(0.004429, 0.042194)	0.227674	0.204362
Relative Change (%) at 12 Months after Intervention 1	11.41	(1.02, 21.80)	0.227674	0.204362
Absolute Change at 13 Months after Intervention 1	0.025254	(0.004798, 0.045710)	0.228035	0.202781
Relative Change (%) at 13 Months after Intervention 1	12.45	(1.07, 23.84)	0.228035	0.202781
Absolute Change at 14 Months after Intervention 1	0.027197	(0.005167, 0.049227)	0.228397	0.201200
Relative Change (%) at 14 Months after Intervention 1	13.52	(1.11, 25.92)	0.228397	0.201200
Absolute Change at 15 Months after Intervention 1	0.029139	(0.005536, 0.052743)	0.228759	0.199619
Relative Change (%) at 15 Months after Intervention 1	14.60	(1.15, 28.05)	0.228759	0.199619
Absolute Change at 16 Months after Intervention 1	0.031082	(0.005905, 0.056259)	0.229120	0.198038
Relative Change (%) at 16 Months after Intervention 1	15.69	(1.17, 30.22)	0.229120	0.198038
Absolute Change at 17 Months after Intervention 1	0.033025	(0.006274, 0.059775)	0.229482	0.196457

Table 40. Absolute and Relative Changes in Proportion of HCTZ/ARB Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Relative Change (%) at 17 Months after Intervention 1	16.81	(1.19, 32.43)	0.229482	0.196457
Absolute Change at 18 Months after Intervention 1	0.034967	(0.006643, 0.063291)	0.229843	0.194876
Relative Change (%) at 18 Months after Intervention 1	17.94	(1.20, 34.68)	0.229843	0.194876
Absolute Change at 19 Months after Intervention 1	0.036910	(0.007012, 0.066807)	0.230205	0.193295
Relative Change (%) at 19 Months after Intervention 1	19.10	(1.21, 36.98)	0.230205	0.193295
Absolute Change at 20 Months after Intervention 1	0.038852	(0.007381, 0.070324)	0.230567	0.191714
Relative Change (%) at 20 Months after Intervention 1	20.27	(1.20, 39.33)	0.230567	0.191714
Absolute Change at 21 Months after Intervention 1	0.040795	(0.007750, 0.073840)	0.230928	0.190133
Relative Change (%) at 21 Months after Intervention 1	21.46	(1.18, 41.73)	0.230928	0.190133
Absolute Change at 22 Months after Intervention 1	0.042738	(0.008119, 0.077356)	0.231290	0.188552
Relative Change (%) at 22 Months after Intervention 1	22.67	(1.16, 44.18)	0.231290	0.188552
Absolute Change at 23 Months after Intervention 1	0.044680	(0.008488, 0.080872)	0.231652	0.186971
Relative Change (%) at 23 Months after Intervention 1	23.90	(1.12, 46.68)	0.231652	0.186971
Absolute Change at 24 Months after Intervention 1	0.046623	(0.008858, 0.084388)	0.232013	0.185390
Relative Change (%) at 24 Months after Intervention 1	25.15	(1.07, 49.23)	0.232013	0.185390
Absolute Change at 25 Months after Intervention 1	0.048566	(0.009227, 0.087905)	0.232375	0.183809
Relative Change (%) at 25 Months after Intervention 1	26.42	(1.01, 51.84)	0.232375	0.183809
Absolute Change at 26 Months after Intervention 1	0.050508	(0.009596, 0.091421)	0.232736	0.182228
Relative Change (%) at 26 Months after Intervention 1	27.72	(0.93, 54.50)	0.232736	0.182228
Absolute Change at 27 Months after Intervention 1	0.052451	(0.009965, 0.094937)	0.233098	0.180647
Absolute Change at 27 Months after Intervention 1	0.052451	(0.009965, 0.094937)	0.233098	0.180647
Relative Change (%) at 27 Months after Intervention 1	29.03	(0.85, 57.22)	0.233098	0.180647
Relative Change (%) at 27 Months after Intervention 1	29.03	(0.85, 57.22)	0.233098	0.180647

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 41. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ/BB Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.025969	(0.025459, 0.026480)	<.001
Baseline trend	-0.000121	(-0.000138, -0.000103)	<.001
Level Change (After Intervention 1)	-0.000013	(-0.000271, 0.000246)	0.923
Trend Change (After Intervention 1)	0.000041	(0.000002, 0.000080)	0.042
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.025970	(0.025459, 0.026482)	<.001
Baseline trend	-0.000121	(-0.000138, -0.000103)	<.001
Trend Change (After Intervention 1)	0.000040	(0.000002, 0.000079)	0.042

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 42. Absolute and Relative Changes in Proportion of HCTZ/BB Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000040	(0.000000, 0.000081)	0.020576	0.020535
Relative Change (%) at 1 Months after Intervention 1	0.20	(0.00, 0.40)	0.020576	0.020535
Absolute Change at 2 Months after Intervention 1	0.000081	(0.000000, 0.000162)	0.020495	0.020414
Relative Change (%) at 2 Months after Intervention 1	0.40	(-0.01, 0.80)	0.020495	0.020414
Absolute Change at 3 Months after Intervention 1	0.000121	(0.000000, 0.000242)	0.020415	0.020294
Relative Change (%) at 3 Months after Intervention 1	0.60	(-0.01, 1.21)	0.020415	0.020294
Absolute Change at 4 Months after Intervention 1	0.000162	(0.000000, 0.000323)	0.020335	0.020173
Relative Change (%) at 4 Months after Intervention 1	0.80	(-0.02, 1.62)	0.020335	0.020173
Absolute Change at 5 Months after Intervention 1	0.000202	(0.000000, 0.000404)	0.020254	0.020052
Relative Change (%) at 5 Months after Intervention 1	1.01	(-0.02, 2.04)	0.020254	0.020052
Absolute Change at 6 Months after Intervention 1	0.000243	(0.000000, 0.000485)	0.020174	0.019931
Relative Change (%) at 6 Months after Intervention 1	1.22	(-0.03, 2.46)	0.020174	0.019931
Absolute Change at 7 Months after Intervention 1	0.000283	(0.000000, 0.000566)	0.020093	0.019810
Relative Change (%) at 7 Months after Intervention 1	1.43	(-0.03, 2.89)	0.020093	0.019810
Absolute Change at 8 Months after Intervention 1	0.000324	(0.000001, 0.000647)	0.020013	0.019690
Relative Change (%) at 8 Months after Intervention 1	1.64	(-0.04, 3.33)	0.020013	0.019690
Absolute Change at 9 Months after Intervention 1	0.000364	(0.000001, 0.000727)	0.019933	0.019569
Relative Change (%) at 9 Months after Intervention 1	1.86	(-0.05, 3.77)	0.019933	0.019569
Absolute Change at 10 Months after Intervention 1	0.000404	(0.000001, 0.000808)	0.019852	0.019448
Relative Change (%) at 10 Months after Intervention 1	2.08	(-0.06, 4.21)	0.019852	0.019448
Absolute Change at 11 Months after Intervention 1	0.000445	(0.000001, 0.000889)	0.019772	0.019327
Relative Change (%) at 11 Months after Intervention 1	2.30	(-0.06, 4.67)	0.019772	0.019327
Absolute Change at 12 Months after Intervention 1	0.000485	(0.000001, 0.000970)	0.019692	0.019206
Relative Change (%) at 12 Months after Intervention 1	2.53	(-0.07, 5.13)	0.019692	0.019206
Absolute Change at 13 Months after Intervention 1	0.000526	(0.000001, 0.001051)	0.019611	0.019086
Relative Change (%) at 13 Months after Intervention 1	2.76	(-0.08, 5.59)	0.019611	0.019086
Absolute Change at 14 Months after Intervention 1	0.000566	(0.000001, 0.001132)	0.019531	0.018965
Relative Change (%) at 14 Months after Intervention 1	2.99	(-0.09, 6.06)	0.019531	0.018965
Absolute Change at 15 Months after Intervention 1	0.000607	(0.000001, 0.001212)	0.019451	0.018844
Relative Change (%) at 15 Months after Intervention 1	3.22	(-0.10, 6.54)	0.019451	0.018844
Absolute Change at 16 Months after Intervention 1	0.000647	(0.000001, 0.001293)	0.019370	0.018723
Relative Change (%) at 16 Months after Intervention 1	3.46	(-0.11, 7.02)	0.019370	0.018723

Table 42. Absolute and Relative Changes in Proportion of HCTZ/BB Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 17 Months after Intervention 1	0.000688	(0.000001, 0.001374)	0.019290	0.018603
Relative Change (%) at 17 Months after Intervention 1	3.70	(-0.12, 7.52)	0.019290	0.018603
Absolute Change at 18 Months after Intervention 1	0.000728	(0.000001, 0.001455)	0.019210	0.018482
Relative Change (%) at 18 Months after Intervention 1	3.94	(-0.14, 8.01)	0.019210	0.018482
Absolute Change at 19 Months after Intervention 1	0.000769	(0.000001, 0.001536)	0.019129	0.018361
Relative Change (%) at 19 Months after Intervention 1	4.19	(-0.15, 8.52)	0.019129	0.018361
Absolute Change at 20 Months after Intervention 1	0.000809	(0.000001, 0.001617)	0.019049	0.018240
Relative Change (%) at 20 Months after Intervention 1	4.43	(-0.16, 9.03)	0.019049	0.018240
Absolute Change at 21 Months after Intervention 1	0.000849	(0.000001, 0.001697)	0.018969	0.018119
Relative Change (%) at 21 Months after Intervention 1	4.69	(-0.18, 9.55)	0.018969	0.018119
Absolute Change at 22 Months after Intervention 1	0.000890	(0.000001, 0.001778)	0.018888	0.017999
Relative Change (%) at 22 Months after Intervention 1	4.94	(-0.19, 10.08)	0.018888	0.017999
Absolute Change at 23 Months after Intervention 1	0.000930	(0.000002, 0.001859)	0.018808	0.017878
Relative Change (%) at 23 Months after Intervention 1	5.20	(-0.21, 10.61)	0.018808	0.017878
Absolute Change at 24 Months after Intervention 1	0.000971	(0.000002, 0.001940)	0.018728	0.017757
Relative Change (%) at 24 Months after Intervention 1	5.47	(-0.22, 11.16)	0.018728	0.017757
Absolute Change at 25 Months after Intervention 1	0.001011	(0.000002, 0.002021)	0.018647	0.017636
Relative Change (%) at 25 Months after Intervention 1	5.73	(-0.24, 11.71)	0.018647	0.017636
Absolute Change at 26 Months after Intervention 1	0.001052	(0.000002, 0.002102)	0.018567	0.017515
Relative Change (%) at 26 Months after Intervention 1	6.00	(-0.26, 12.27)	0.018567	0.017515
Absolute Change at 27 Months after Intervention 1	0.001092	(0.000002, 0.002182)	0.018487	0.017395
Absolute Change at 27 Months after Intervention 1	0.001092	(0.000002, 0.002182)	0.018487	0.017395
Relative Change (%) at 27 Months after Intervention 1	6.28	(-0.28, 12.83)	0.018487	0.017395
Relative Change (%) at 27 Months after Intervention 1	6.28	(-0.28, 12.83)	0.018487	0.017395

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 43. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ/Central Alpha-2 Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.000022	(0.000017, 0.000027)	<.001
Baseline trend	-0.000000	(-0.000001, -0.000000)	<.001
Level Change (After Intervention 1)	-0.000005	(-0.000008, -0.000001)	0.008
Trend Change (After Intervention 1)	0.000000	(-0.000000, 0.000001)	0.428
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.000021	(0.000016, 0.000025)	<.001
Baseline trend	-0.000000	(-0.000000, -0.000000)	<.001
Level Change (After Intervention 1)	-0.000004	(-0.000008, -0.000001)	0.011

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 44. Absolute and Relative Changes in Proportion of HCTZ/Central Alpha-2 Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	-0.000004	(-0.000008, -0.000001)	0.000005	0.000009
Relative Change (%) at 1 Months after Intervention 1	-47.94	(-78.76, -17.13)	0.000005	0.000009
Absolute Change at 2 Months after Intervention 1	-0.000004	(-0.000008, -0.000001)	0.000004	0.000009
Relative Change (%) at 2 Months after Intervention 1	-49.35	(-80.79, -17.91)	0.000004	0.000009
Absolute Change at 3 Months after Intervention 1	-0.000004	(-0.000008, -0.000001)	0.000004	0.000009
Relative Change (%) at 3 Months after Intervention 1	-50.84	(-82.96, -18.73)	0.000004	0.000009
Absolute Change at 4 Months after Intervention 1	-0.000004	(-0.000008, -0.000001)	0.000004	0.000008
Relative Change (%) at 4 Months after Intervention 1	-52.42	(-85.28, -19.57)	0.000004	0.000008
Absolute Change at 5 Months after Intervention 1	-0.000004	(-0.000008, -0.000001)	0.000004	0.000008
Relative Change (%) at 5 Months after Intervention 1	-54.11	(-87.78, -20.44)	0.000004	0.000008
Absolute Change at 6 Months after Intervention 1	-0.000004	(-0.000008, -0.000001)	0.000003	0.000008
Relative Change (%) at 6 Months after Intervention 1	-55.91	(-90.50, -21.32)	0.000003	0.000008
Absolute Change at 7 Months after Intervention 1	-0.000004	(-0.000008, -0.000001)	0.000003	0.000007
Relative Change (%) at 7 Months after Intervention 1	-57.83	(-93.45, -22.21)	0.000003	0.000007
Absolute Change at 8 Months after Intervention 1	-0.000004	(-0.000008, -0.000001)	0.000003	0.000007
Relative Change (%) at 8 Months after Intervention 1	-59.89	(-96.68, -23.10)	0.000003	0.000007
Absolute Change at 9 Months after Intervention 1	-0.000004	(-0.000008, -0.000001)	0.000003	0.000007
Relative Change (%) at 9 Months after Intervention 1	-62.10	(-100.24, -23.95)	0.000003	0.000007
Absolute Change at 10 Months after Intervention 1	-0.000004	(-0.000008, -0.000001)	0.000002	0.000007
Relative Change (%) at 10 Months after Intervention 1	-64.48	(-104.19, -24.76)	0.000002	0.000007
Absolute Change at 11 Months after Intervention 1	-0.000004	(-0.000008, -0.000001)	0.000002	0.000006
Relative Change (%) at 11 Months after Intervention 1	-67.04	(-108.61, -25.48)	0.000002	0.000006
Absolute Change at 12 Months after Intervention 1	-0.000004	(-0.000008, -0.000001)	0.000002	0.000006
Relative Change (%) at 12 Months after Intervention 1	-69.83	(-113.59, -26.06)	0.000002	0.000006
Absolute Change at 13 Months after Intervention 1	-0.000004	(-0.000008, -0.000001)	0.000002	0.000006
Relative Change (%) at 13 Months after Intervention 1	-72.85	(-119.25, -26.45)	0.000002	0.000006
Absolute Change at 14 Months after Intervention 1	-0.000004	(-0.000008, -0.000001)	0.000001	0.000006
Relative Change (%) at 14 Months after Intervention 1	-76.14	(-125.73, -26.56)	0.000001	0.000006
Absolute Change at 15 Months after Intervention 1	-0.000004	(-0.000008, -0.000001)	0.000001	0.000005
Relative Change (%) at 15 Months after Intervention 1	-79.75	(-133.21, -26.30)	0.000001	0.000005
Absolute Change at 16 Months after Intervention 1	-0.000004	(-0.000008, -0.000001)	0.000001	0.000005
Relative Change (%) at 16 Months after Intervention 1	-83.72	(-141.92, -25.53)	0.000001	0.000005

Table 44. Absolute and Relative Changes in Proportion of HCTZ/Central Alpha-2 Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 17 Months after Intervention 1	-0.000004	(-0.000008, -0.000001)	0.000001	0.000005
Relative Change (%) at 17 Months after Intervention 1	-88.10	(-152.14, -24.07)	0.000001	0.000005
Absolute Change at 18 Months after Intervention 1	-0.000004	(-0.000008, -0.000001)	0.000000	0.000005
Relative Change (%) at 18 Months after Intervention 1	-92.97	(-164.25, -21.70)	0.000000	0.000005
Absolute Change at 19 Months after Intervention 1	-0.000004	(-0.000008, -0.000001)	0.000000	0.000004
Relative Change (%) at 19 Months after Intervention 1	-98.41	(-178.70, -18.11)	0.000000	0.000004
Absolute Change at 20 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 20 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 21 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 21 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 22 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 22 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 23 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 23 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 24 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 24 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 25 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 25 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 26 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 26 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 27 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 27 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 27 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 27 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 August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 45. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ-Containing Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.337660	(0.334947, 0.340373)	<.001
Baseline trend	-0.000865	(-0.000964, -0.000767)	<.001
Level Change (After Intervention 1)	-0.000542	(-0.003299, 0.002214)	0.696
Trend Change (After Intervention 1)	-0.000043	(-0.000280, 0.000193)	0.715
Most Parsimonious Final Model Parameters (df = 71)[2,3]			
Intercept	0.338112	(0.335901, 0.340322)	<.001
Baseline trend	-0.000891	(-0.000944, -0.000838)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 46. Absolute and Relative Changes in Proportion of HCTZ-Containing Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.298033	0.298033
Relative Change (%) at 1 Months after Intervention 1	0.00	(0.00, 0.00)	0.298033	0.298033
Absolute Change at 2 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.297143	0.297143
Relative Change (%) at 2 Months after Intervention 1	0.00	(0.00, 0.00)	0.297143	0.297143
Absolute Change at 3 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.296252	0.296252
Relative Change (%) at 3 Months after Intervention 1	0.00	(0.00, 0.00)	0.296252	0.296252
Absolute Change at 4 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.295361	0.295361
Relative Change (%) at 4 Months after Intervention 1	0.00	(0.00, 0.00)	0.295361	0.295361
Absolute Change at 5 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.294471	0.294471
Relative Change (%) at 5 Months after Intervention 1	0.00	(0.00, 0.00)	0.294471	0.294471
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.293580	0.293580
Relative Change (%) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.293580	0.293580
Absolute Change at 7 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.292690	0.292690
Relative Change (%) at 7 Months after Intervention 1	0.00	(0.00, 0.00)	0.292690	0.292690
Absolute Change at 8 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.291799	0.291799
Relative Change (%) at 8 Months after Intervention 1	0.00	(0.00, 0.00)	0.291799	0.291799
Absolute Change at 9 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.290908	0.290908
Relative Change (%) at 9 Months after Intervention 1	0.00	(0.00, 0.00)	0.290908	0.290908
Absolute Change at 10 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.290018	0.290018
Relative Change (%) at 10 Months after Intervention 1	0.00	(0.00, 0.00)	0.290018	0.290018
Absolute Change at 11 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.289127	0.289127
Relative Change (%) at 11 Months after Intervention 1	0.00	(0.00, 0.00)	0.289127	0.289127
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.288236	0.288236
Relative Change (%) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.288236	0.288236
Absolute Change at 13 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.287346	0.287346
Relative Change (%) at 13 Months after Intervention 1	0.00	(0.00, 0.00)	0.287346	0.287346
Absolute Change at 14 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.286455	0.286455
Relative Change (%) at 14 Months after Intervention 1	0.00	(0.00, 0.00)	0.286455	0.286455
Absolute Change at 15 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.285565	0.285565
Relative Change (%) at 15 Months after Intervention 1	0.00	(0.00, 0.00)	0.285565	0.285565
Absolute Change at 16 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.284674	0.284674
Relative Change (%) at 16 Months after Intervention 1	0.00	(0.00, 0.00)	0.284674	0.284674

Table 46. Absolute and Relative Changes in Proportion of HCTZ-Containing Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 17 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.283783	0.283783
Relative Change (%) at 17 Months after Intervention 1	0.00	(0.00, 0.00)	0.283783	0.283783
Absolute Change at 18 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.282893	0.282893
Relative Change (%) at 18 Months after Intervention 1	0.00	(0.00, 0.00)	0.282893	0.282893
Absolute Change at 19 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.282002	0.282002
Relative Change (%) at 19 Months after Intervention 1	0.00	(0.00, 0.00)	0.282002	0.282002
Absolute Change at 20 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.281111	0.281111
Relative Change (%) at 20 Months after Intervention 1	0.00	(0.00, 0.00)	0.281111	0.281111
Absolute Change at 21 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.280221	0.280221
Relative Change (%) at 21 Months after Intervention 1	0.00	(0.00, 0.00)	0.280221	0.280221
Absolute Change at 22 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.279330	0.279330
Relative Change (%) at 22 Months after Intervention 1	0.00	(0.00, 0.00)	0.279330	0.279330
Absolute Change at 23 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.278440	0.278440
Relative Change (%) at 23 Months after Intervention 1	0.00	(0.00, 0.00)	0.278440	0.278440
Absolute Change at 24 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.277549	0.277549
Relative Change (%) at 24 Months after Intervention 1	0.00	(0.00, 0.00)	0.277549	0.277549
Absolute Change at 25 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.276658	0.276658
Relative Change (%) at 25 Months after Intervention 1	0.00	(0.00, 0.00)	0.276658	0.276658
Absolute Change at 26 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.275768	0.275768
Relative Change (%) at 26 Months after Intervention 1	0.00	(0.00, 0.00)	0.275768	0.275768
Absolute Change at 27 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.274877	0.274877
Absolute Change at 27 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.274877	0.274877
Relative Change (%) at 27 Months after Intervention 1	0.00	(0.00, 0.00)	0.274877	0.274877
Relative Change (%) at 27 Months after Intervention 1	0.00	(0.00, 0.00)	0.274877	0.274877

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 47. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ-Containing Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.957547	(0.956265, 0.958830)	<.001
Baseline trend	-0.000458	(-0.000504, -0.000412)	<.001
Level Change (After Intervention 1)	-0.000099	(-0.000711, 0.000513)	0.748
Trend Change (After Intervention 1)	0.000090	(-0.000020, 0.000200)	0.106
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.957520	(0.956210, 0.958831)	<.001
Baseline trend	-0.000458	(-0.000504, -0.000411)	<.001
Trend Change (After Intervention 1)	0.000086	(-0.000024, 0.000195)	0.124

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 48. Absolute and Relative Changes in Proportion of HCTZ-Containing Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000086	(-0.000027, 0.000199)	0.937009	0.936923
Relative Change (%) at 1 Months after Intervention 1	0.01	(0.00, 0.02)	0.937009	0.936923
Absolute Change at 2 Months after Intervention 1	0.000171	(-0.000055, 0.000397)	0.936637	0.936466
Relative Change (%) at 2 Months after Intervention 1	0.02	(-0.01, 0.04)	0.936637	0.936466
Absolute Change at 3 Months after Intervention 1	0.000257	(-0.000082, 0.000596)	0.936265	0.936008
Relative Change (%) at 3 Months after Intervention 1	0.03	(-0.01, 0.06)	0.936265	0.936008
Absolute Change at 4 Months after Intervention 1	0.000343	(-0.000109, 0.000794)	0.935893	0.935550
Relative Change (%) at 4 Months after Intervention 1	0.04	(-0.01, 0.08)	0.935893	0.935550
Absolute Change at 5 Months after Intervention 1	0.000428	(-0.000136, 0.000993)	0.935521	0.935093
Relative Change (%) at 5 Months after Intervention 1	0.05	(-0.01, 0.11)	0.935521	0.935093
Absolute Change at 6 Months after Intervention 1	0.000514	(-0.000164, 0.001191)	0.935149	0.934635
Relative Change (%) at 6 Months after Intervention 1	0.05	(-0.02, 0.13)	0.935149	0.934635
Absolute Change at 7 Months after Intervention 1	0.000599	(-0.000191, 0.001390)	0.934777	0.934177
Relative Change (%) at 7 Months after Intervention 1	0.06	(-0.02, 0.15)	0.934777	0.934177
Absolute Change at 8 Months after Intervention 1	0.000685	(-0.000218, 0.001588)	0.934405	0.933719
Relative Change (%) at 8 Months after Intervention 1	0.07	(-0.02, 0.17)	0.934405	0.933719
Absolute Change at 9 Months after Intervention 1	0.000771	(-0.000245, 0.001787)	0.934032	0.933262
Relative Change (%) at 9 Months after Intervention 1	0.08	(-0.03, 0.19)	0.934032	0.933262
Absolute Change at 10 Months after Intervention 1	0.000856	(-0.000273, 0.001985)	0.933660	0.932804
Relative Change (%) at 10 Months after Intervention 1	0.09	(-0.03, 0.21)	0.933660	0.932804
Absolute Change at 11 Months after Intervention 1	0.000942	(-0.000300, 0.002184)	0.933288	0.932346
Relative Change (%) at 11 Months after Intervention 1	0.10	(-0.03, 0.23)	0.933288	0.932346
Absolute Change at 12 Months after Intervention 1	0.001028	(-0.000327, 0.002383)	0.932916	0.931889
Relative Change (%) at 12 Months after Intervention 1	0.11	(-0.04, 0.26)	0.932916	0.931889
Absolute Change at 13 Months after Intervention 1	0.001113	(-0.000355, 0.002581)	0.932544	0.931431
Relative Change (%) at 13 Months after Intervention 1	0.12	(-0.04, 0.28)	0.932544	0.931431
Absolute Change at 14 Months after Intervention 1	0.001199	(-0.000382, 0.002780)	0.932172	0.930973
Relative Change (%) at 14 Months after Intervention 1	0.13	(-0.04, 0.30)	0.932172	0.930973
Absolute Change at 15 Months after Intervention 1	0.001284	(-0.000409, 0.002978)	0.931800	0.930515
Relative Change (%) at 15 Months after Intervention 1	0.14	(-0.04, 0.32)	0.931800	0.930515
Absolute Change at 16 Months after Intervention 1	0.001370	(-0.000436, 0.003177)	0.931428	0.930058
Relative Change (%) at 16 Months after Intervention 1	0.15	(-0.05, 0.34)	0.931428	0.930058

Table 48. Absolute and Relative Changes in Proportion of HCTZ-Containing Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 17 Months after Intervention 1	0.001456	(-0.000464, 0.003375)	0.931056	0.929600
Relative Change (%) at 17 Months after Intervention 1	0.16	(-0.05, 0.36)	0.931056	0.929600
Absolute Change at 18 Months after Intervention 1	0.001541	(-0.000491, 0.003574)	0.930684	0.929142
Relative Change (%) at 18 Months after Intervention 1	0.17	(-0.05, 0.38)	0.930684	0.929142
Absolute Change at 19 Months after Intervention 1	0.001627	(-0.000518, 0.003772)	0.930312	0.928685
Relative Change (%) at 19 Months after Intervention 1	0.18	(-0.06, 0.41)	0.930312	0.928685
Absolute Change at 20 Months after Intervention 1	0.001713	(-0.000546, 0.003971)	0.929940	0.928227
Relative Change (%) at 20 Months after Intervention 1	0.18	(-0.06, 0.43)	0.929940	0.928227
Absolute Change at 21 Months after Intervention 1	0.001798	(-0.000573, 0.004169)	0.929568	0.927769
Relative Change (%) at 21 Months after Intervention 1	0.19	(-0.06, 0.45)	0.929568	0.927769
Absolute Change at 22 Months after Intervention 1	0.001884	(-0.000600, 0.004368)	0.929195	0.927312
Relative Change (%) at 22 Months after Intervention 1	0.20	(-0.07, 0.47)	0.929195	0.927312
Absolute Change at 23 Months after Intervention 1	0.001970	(-0.000627, 0.004566)	0.928823	0.926854
Relative Change (%) at 23 Months after Intervention 1	0.21	(-0.07, 0.49)	0.928823	0.926854
Absolute Change at 24 Months after Intervention 1	0.002055	(-0.000655, 0.004765)	0.928451	0.926396
Relative Change (%) at 24 Months after Intervention 1	0.22	(-0.07, 0.51)	0.928451	0.926396
Absolute Change at 25 Months after Intervention 1	0.002141	(-0.000682, 0.004964)	0.928079	0.925938
Relative Change (%) at 25 Months after Intervention 1	0.23	(-0.07, 0.54)	0.928079	0.925938
Absolute Change at 26 Months after Intervention 1	0.002226	(-0.000709, 0.005162)	0.927707	0.925481
Relative Change (%) at 26 Months after Intervention 1	0.24	(-0.08, 0.56)	0.927707	0.925481
Absolute Change at 27 Months after Intervention 1	0.002312	(-0.000736, 0.005361)	0.927335	0.925023
Absolute Change at 27 Months after Intervention 1	0.002312	(-0.000736, 0.005361)	0.927335	0.925023
Relative Change (%) at 27 Months after Intervention 1	0.25	(-0.08, 0.58)	0.927335	0.925023
Relative Change (%) at 27 Months after Intervention 1	0.25	(-0.08, 0.58)	0.927335	0.925023

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 49. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ/Direct Renin Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.000627	(0.000588, 0.000667)	<.001
Baseline trend	-0.000009	(-0.000011, -0.000008)	<.001
Level Change (After Intervention 1)	0.000000	(-0.000020, 0.000020)	0.995
Trend Change (After Intervention 1)	0.000005	(0.000002, 0.000008)	<.001
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.000628	(0.000589, 0.000666)	<.001
Baseline trend	-0.000009	(-0.000011, -0.000008)	<.001
Trend Change (After Intervention 1)	0.000005	(0.000002, 0.000008)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 50. Absolute and Relative Changes in Proportion of HCTZ/Direct Renin Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000005	(0.000002, 0.000008)	0.000212	0.000206
Relative Change (%) at 1 Months after Intervention 1	2.55	(0.61, 4.48)	0.000212	0.000206
Absolute Change at 2 Months after Intervention 1	0.000011	(0.000004, 0.000017)	0.000208	0.000197
Relative Change (%) at 2 Months after Intervention 1	5.34	(1.20, 9.47)	0.000208	0.000197
Absolute Change at 3 Months after Intervention 1	0.000016	(0.000006, 0.000025)	0.000203	0.000188
Relative Change (%) at 3 Months after Intervention 1	8.40	(1.77, 15.04)	0.000203	0.000188
Absolute Change at 4 Months after Intervention 1	0.000021	(0.000008, 0.000034)	0.000199	0.000178
Relative Change (%) at 4 Months after Intervention 1	11.79	(2.28, 21.30)	0.000199	0.000178
Absolute Change at 5 Months after Intervention 1	0.000026	(0.000011, 0.000042)	0.000195	0.000169
Relative Change (%) at 5 Months after Intervention 1	15.56	(2.72, 28.39)	0.000195	0.000169
Absolute Change at 6 Months after Intervention 1	0.000032	(0.000013, 0.000050)	0.000191	0.000160
Relative Change (%) at 6 Months after Intervention 1	19.76	(3.04, 36.48)	0.000191	0.000160
Absolute Change at 7 Months after Intervention 1	0.000037	(0.000015, 0.000059)	0.000187	0.000150
Relative Change (%) at 7 Months after Intervention 1	24.49	(3.19, 45.80)	0.000187	0.000150
Absolute Change at 8 Months after Intervention 1	0.000042	(0.000017, 0.000067)	0.000183	0.000141
Relative Change (%) at 8 Months after Intervention 1	29.85	(3.09, 56.62)	0.000183	0.000141
Absolute Change at 9 Months after Intervention 1	0.000047	(0.000019, 0.000076)	0.000179	0.000131
Relative Change (%) at 9 Months after Intervention 1	35.98	(2.61, 69.35)	0.000179	0.000131
Absolute Change at 10 Months after Intervention 1	0.000053	(0.000021, 0.000084)	0.000175	0.000122
Relative Change (%) at 10 Months after Intervention 1	43.04	(1.58, 84.50)	0.000175	0.000122
Absolute Change at 11 Months after Intervention 1	0.000058	(0.000023, 0.000092)	0.000171	0.000113
Relative Change (%) at 11 Months after Intervention 1	51.27	(-0.27, 102.81)	0.000171	0.000113
Absolute Change at 12 Months after Intervention 1	0.000063	(0.000025, 0.000101)	0.000166	0.000103
Relative Change (%) at 12 Months after Intervention 1	60.99	(-3.35, 125.34)	0.000166	0.000103
Absolute Change at 13 Months after Intervention 1	0.000068	(0.000027, 0.000109)	0.000162	0.000094
Relative Change (%) at 13 Months after Intervention 1	72.65	(-8.34, 153.64)	0.000162	0.000094
Absolute Change at 14 Months after Intervention 1	0.000074	(0.000030, 0.000118)	0.000158	0.000085
Relative Change (%) at 14 Months after Intervention 1	86.88	(-16.35, 190.12)	0.000158	0.000085
Absolute Change at 15 Months after Intervention 1	0.000079	(0.000032, 0.000126)	0.000154	0.000075
Relative Change (%) at 15 Months after Intervention 1	104.65	(-29.32, 238.63)	0.000154	0.000075
Absolute Change at 16 Months after Intervention 1	0.000084	(0.000034, 0.000134)	0.000150	0.000066
Relative Change (%) at 16 Months after Intervention 1	127.47	(-50.84, 305.78)	0.000150	0.000066

Table 50. Absolute and Relative Changes in Proportion of HCTZ/Direct Renin Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 17 Months after Intervention 1	0.000089	(0.000036, 0.000143)	0.000146	0.000057
Relative Change (%) at 17 Months after Intervention 1	157.82	(-87.98, 403.63)	0.000146	0.000057
Absolute Change at 18 Months after Intervention 1	0.000095	(0.000038, 0.000151)	0.000142	0.000047
Relative Change (%) at 18 Months after Intervention 1	200.20	(-156.12, 556.53)	0.000142	0.000047
Absolute Change at 19 Months after Intervention 1	0.000100	(0.000040, 0.000160)	0.000138	0.000038
Relative Change (%) at 19 Months after Intervention 1	263.52	(-293.40, 820.44)	0.000138	0.000038
Absolute Change at 20 Months after Intervention 1	0.000105	(0.000042, 0.000168)	0.000134	0.000029
Relative Change (%) at 20 Months after Intervention 1	368.36	(-614.40, 1351.12)	0.000134	0.000029
Absolute Change at 21 Months after Intervention 1	0.000110	(0.000044, 0.000176)	0.000130	0.000019
Relative Change (%) at 21 Months after Intervention 1	575.53	(-1592.70, 2743.75)	0.000130	0.000019
Absolute Change at 22 Months after Intervention 1	0.000116	(0.000046, 0.000185)	0.000125	0.000010
Relative Change (%) at 22 Months after Intervention 1	1177.62	(-7031.68, 9386.92)	0.000125	0.000010
Absolute Change at 23 Months after Intervention 1	0.000121	(0.000048, 0.000193)	0.000121	0.000000
Relative Change (%) at 23 Months after Intervention 1	26281.78	(-3673156, 3725719)	0.000121	0.000000
Absolute Change at 24 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 24 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 25 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 25 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 26 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 26 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 27 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Absolute Change at 27 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 27 Months after Intervention 1	N/A	(N/A, N/A)	N/A	N/A
Relative Change (%) at 27 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 August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 51. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ Single Ingredient Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.306528	(0.287830, 0.325226)	<.001
Baseline trend	0.002273	(0.001611, 0.002936)	<.001
Level Change (After Intervention 1)	0.000217	(-0.002736, 0.003170)	0.884
Trend Change (After Intervention 1)	-0.002330	(-0.003954, -0.000706)	0.006
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.306749	(0.288307, 0.325192)	<.001
Baseline trend	0.002263	(0.001615, 0.002912)	<.001
Trend Change (After Intervention 1)	-0.002291	(-0.003829, -0.000753)	0.004

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 52. Absolute and Relative Changes in Proportion of HCTZ Single Ingredient Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	-0.002291	(-0.003815, -0.000767)	0.406310	0.408601
Relative Change (%) at 1 Months after Intervention 1	-0.56	(-0.91, -0.21)	0.406310	0.408601
Absolute Change at 2 Months after Intervention 1	-0.004582	(-0.007630, -0.001535)	0.406282	0.410865
Relative Change (%) at 2 Months after Intervention 1	-1.12	(-1.82, -0.41)	0.406282	0.410865
Absolute Change at 3 Months after Intervention 1	-0.006873	(-0.011445, -0.002302)	0.406255	0.413128
Relative Change (%) at 3 Months after Intervention 1	-1.66	(-2.71, -0.62)	0.406255	0.413128
Absolute Change at 4 Months after Intervention 1	-0.009165	(-0.015259, -0.003070)	0.406227	0.415391
Relative Change (%) at 4 Months after Intervention 1	-2.21	(-3.59, -0.82)	0.406227	0.415391
Absolute Change at 5 Months after Intervention 1	-0.011456	(-0.019074, -0.003837)	0.406199	0.417655
Relative Change (%) at 5 Months after Intervention 1	-2.74	(-4.46, -1.02)	0.406199	0.417655
Absolute Change at 6 Months after Intervention 1	-0.013747	(-0.022889, -0.004605)	0.406171	0.419918
Relative Change (%) at 6 Months after Intervention 1	-3.27	(-5.32, -1.22)	0.406171	0.419918
Absolute Change at 7 Months after Intervention 1	-0.016038	(-0.026704, -0.005372)	0.406144	0.422182
Relative Change (%) at 7 Months after Intervention 1	-3.80	(-6.17, -1.42)	0.406144	0.422182
Absolute Change at 8 Months after Intervention 1	-0.018329	(-0.030519, -0.006139)	0.406116	0.424445
Relative Change (%) at 8 Months after Intervention 1	-4.32	(-7.01, -1.62)	0.406116	0.424445
Absolute Change at 9 Months after Intervention 1	-0.020620	(-0.034334, -0.006907)	0.406088	0.426708
Relative Change (%) at 9 Months after Intervention 1	-4.83	(-7.84, -1.82)	0.406088	0.426708
Absolute Change at 10 Months after Intervention 1	-0.022911	(-0.038149, -0.007674)	0.406060	0.428972
Relative Change (%) at 10 Months after Intervention 1	-5.34	(-8.66, -2.02)	0.406060	0.428972
Absolute Change at 11 Months after Intervention 1	-0.025203	(-0.041963, -0.008442)	0.406032	0.431235
Relative Change (%) at 11 Months after Intervention 1	-5.84	(-9.47, -2.21)	0.406032	0.431235
Absolute Change at 12 Months after Intervention 1	-0.027494	(-0.045778, -0.009209)	0.406005	0.433498
Relative Change (%) at 12 Months after Intervention 1	-6.34	(-10.28, -2.41)	0.406005	0.433498
Absolute Change at 13 Months after Intervention 1	-0.029785	(-0.049593, -0.009977)	0.405977	0.435762
Relative Change (%) at 13 Months after Intervention 1	-6.84	(-11.07, -2.60)	0.405977	0.435762
Absolute Change at 14 Months after Intervention 1	-0.032076	(-0.053408, -0.010744)	0.405949	0.438025
Relative Change (%) at 14 Months after Intervention 1	-7.32	(-11.85, -2.80)	0.405949	0.438025
Absolute Change at 15 Months after Intervention 1	-0.034367	(-0.057223, -0.011511)	0.405921	0.440289
Relative Change (%) at 15 Months after Intervention 1	-7.81	(-12.62, -2.99)	0.405921	0.440289
Absolute Change at 16 Months after Intervention 1	-0.036658	(-0.061038, -0.012279)	0.405894	0.442552
Relative Change (%) at 16 Months after Intervention 1	-8.28	(-13.39, -3.18)	0.405894	0.442552
Absolute Change at 17 Months after Intervention 1	-0.038949	(-0.064853, -0.013046)	0.405866	0.444815

Table 52. Absolute and Relative Changes in Proportion of HCTZ Single Ingredient Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Relative Change (%) at 17 Months after Intervention 1	-8.76	(-14.15, -3.37)	0.405866	0.444815
Absolute Change at 18 Months after Intervention 1	-0.041241	(-0.068667, -0.013814)	0.405838	0.447079
Relative Change (%) at 18 Months after Intervention 1	-9.22	(-14.89, -3.56)	0.405838	0.447079
Absolute Change at 19 Months after Intervention 1	-0.043532	(-0.072482, -0.014581)	0.405810	0.449342
Relative Change (%) at 19 Months after Intervention 1	-9.69	(-15.63, -3.74)	0.405810	0.449342
Absolute Change at 20 Months after Intervention 1	-0.045823	(-0.076297, -0.015348)	0.405783	0.451605
Relative Change (%) at 20 Months after Intervention 1	-10.15	(-16.36, -3.93)	0.405783	0.451605
Absolute Change at 21 Months after Intervention 1	-0.048114	(-0.080112, -0.016116)	0.405755	0.453869
Relative Change (%) at 21 Months after Intervention 1	-10.60	(-17.09, -4.11)	0.405755	0.453869
Absolute Change at 22 Months after Intervention 1	-0.050405	(-0.083927, -0.016883)	0.405727	0.456132
Relative Change (%) at 22 Months after Intervention 1	-11.05	(-17.80, -4.30)	0.405727	0.456132
Absolute Change at 23 Months after Intervention 1	-0.052696	(-0.087742, -0.017651)	0.405699	0.458396
Relative Change (%) at 23 Months after Intervention 1	-11.50	(-18.51, -4.48)	0.405699	0.458396
Absolute Change at 24 Months after Intervention 1	-0.054987	(-0.091557, -0.018418)	0.405672	0.460659
Relative Change (%) at 24 Months after Intervention 1	-11.94	(-19.21, -4.66)	0.405672	0.460659
Absolute Change at 25 Months after Intervention 1	-0.057279	(-0.095371, -0.019186)	0.405644	0.462922
Relative Change (%) at 25 Months after Intervention 1	-12.37	(-19.90, -4.84)	0.405644	0.462922
Absolute Change at 26 Months after Intervention 1	-0.059570	(-0.099186, -0.019953)	0.405616	0.465186
Relative Change (%) at 26 Months after Intervention 1	-12.81	(-20.59, -5.02)	0.405616	0.465186
Absolute Change at 27 Months after Intervention 1	-0.061861	(-0.103001, -0.020720)	0.405588	0.467449
Absolute Change at 27 Months after Intervention 1	-0.061861	(-0.103001, -0.020720)	0.405588	0.467449
Relative Change (%) at 27 Months after Intervention 1	-13.23	(-21.27, -5.20)	0.405588	0.467449
Relative Change (%) at 27 Months after Intervention 1	-13.23	(-21.27, -5.20)	0.405588	0.467449

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 53. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of HCTZ/Potassium-Sparing Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.097390	(0.094644, 0.100136)	<.001
Baseline trend	-0.000413	(-0.000510, -0.000316)	<.001
Level Change (After Intervention 1)	0.000037	(-0.001072, 0.001147)	0.947
Trend Change (After Intervention 1)	0.000236	(0.000006, 0.000467)	0.045
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.097495	(0.094647, 0.100342)	<.001
Baseline trend	-0.000414	(-0.000514, -0.000315)	<.001
Trend Change (After Intervention 1)	0.000236	(0.000005, 0.000466)	0.045

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 54. Absolute and Relative Changes in Proportion of HCTZ/Potassium-Sparing Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000236	(-0.000020, 0.000491)	0.079089	0.078853
Relative Change (%) at 1 Months after Intervention 1	0.30	(-0.03, 0.63)	0.079089	0.078853
Absolute Change at 2 Months after Intervention 1	0.000471	(-0.000040, 0.000983)	0.078910	0.078439
Relative Change (%) at 2 Months after Intervention 1	0.60	(-0.07, 1.27)	0.078910	0.078439
Absolute Change at 3 Months after Intervention 1	0.000707	(-0.000060, 0.001474)	0.078732	0.078025
Relative Change (%) at 3 Months after Intervention 1	0.91	(-0.11, 1.92)	0.078732	0.078025
Absolute Change at 4 Months after Intervention 1	0.000943	(-0.000080, 0.001966)	0.078553	0.077610
Relative Change (%) at 4 Months after Intervention 1	1.22	(-0.15, 2.58)	0.078553	0.077610
Absolute Change at 5 Months after Intervention 1	0.001179	(-0.000100, 0.002457)	0.078375	0.077196
Relative Change (%) at 5 Months after Intervention 1	1.53	(-0.19, 3.24)	0.078375	0.077196
Absolute Change at 6 Months after Intervention 1	0.001414	(-0.000120, 0.002949)	0.078196	0.076782
Relative Change (%) at 6 Months after Intervention 1	1.84	(-0.23, 3.91)	0.078196	0.076782
Absolute Change at 7 Months after Intervention 1	0.001650	(-0.000140, 0.003440)	0.078018	0.076368
Relative Change (%) at 7 Months after Intervention 1	2.16	(-0.27, 4.59)	0.078018	0.076368
Absolute Change at 8 Months after Intervention 1	0.001886	(-0.000160, 0.003932)	0.077839	0.075953
Relative Change (%) at 8 Months after Intervention 1	2.48	(-0.31, 5.28)	0.077839	0.075953
Absolute Change at 9 Months after Intervention 1	0.002122	(-0.000180, 0.004423)	0.077661	0.075539
Relative Change (%) at 9 Months after Intervention 1	2.81	(-0.36, 5.97)	0.077661	0.075539
Absolute Change at 10 Months after Intervention 1	0.002357	(-0.000200, 0.004915)	0.077482	0.075125
Relative Change (%) at 10 Months after Intervention 1	3.14	(-0.40, 6.68)	0.077482	0.075125
Absolute Change at 11 Months after Intervention 1	0.002593	(-0.000220, 0.005406)	0.077304	0.074711
Relative Change (%) at 11 Months after Intervention 1	3.47	(-0.45, 7.39)	0.077304	0.074711
Absolute Change at 12 Months after Intervention 1	0.002829	(-0.000240, 0.005898)	0.077125	0.074296
Relative Change (%) at 12 Months after Intervention 1	3.81	(-0.50, 8.12)	0.077125	0.074296
Absolute Change at 13 Months after Intervention 1	0.003065	(-0.000260, 0.006389)	0.076947	0.073882
Relative Change (%) at 13 Months after Intervention 1	4.15	(-0.55, 8.85)	0.076947	0.073882
Absolute Change at 14 Months after Intervention 1	0.003300	(-0.000280, 0.006881)	0.076768	0.073468
Relative Change (%) at 14 Months after Intervention 1	4.49	(-0.60, 9.59)	0.076768	0.073468
Absolute Change at 15 Months after Intervention 1	0.003536	(-0.000300, 0.007372)	0.076590	0.073054
Relative Change (%) at 15 Months after Intervention 1	4.84	(-0.66, 10.34)	0.076590	0.073054
Absolute Change at 16 Months after Intervention 1	0.003772	(-0.000320, 0.007864)	0.076411	0.072639

Table 54. Absolute and Relative Changes in Proportion of HCTZ/Potassium-Sparing Combination Product Users among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Relative Change (%) at 16 Months after Intervention 1	5.19	(-0.71, 11.10)	0.076411	0.072639
Absolute Change at 17 Months after Intervention 1	0.004008	(-0.000340, 0.008355)	0.076233	0.072225
Relative Change (%) at 17 Months after Intervention 1	5.55	(-0.77, 11.87)	0.076233	0.072225
Absolute Change at 18 Months after Intervention 1	0.004243	(-0.000360, 0.008846)	0.076054	0.071811
Relative Change (%) at 18 Months after Intervention 1	5.91	(-0.83, 12.65)	0.076054	0.071811
Absolute Change at 19 Months after Intervention 1	0.004479	(-0.000380, 0.009338)	0.075876	0.071397
Relative Change (%) at 19 Months after Intervention 1	6.27	(-0.89, 13.44)	0.075876	0.071397
Absolute Change at 20 Months after Intervention 1	0.004715	(-0.000400, 0.009829)	0.075697	0.070982
Relative Change (%) at 20 Months after Intervention 1	6.64	(-0.96, 14.24)	0.075697	0.070982
Absolute Change at 21 Months after Intervention 1	0.004951	(-0.000420, 0.010321)	0.075519	0.070568
Relative Change (%) at 21 Months after Intervention 1	7.02	(-1.02, 15.05)	0.075519	0.070568
Absolute Change at 22 Months after Intervention 1	0.005186	(-0.000440, 0.010812)	0.075340	0.070154
Relative Change (%) at 22 Months after Intervention 1	7.39	(-1.09, 15.87)	0.075340	0.070154
Absolute Change at 23 Months after Intervention 1	0.005422	(-0.000460, 0.011304)	0.075162	0.069740
Relative Change (%) at 23 Months after Intervention 1	7.77	(-1.16, 16.71)	0.075162	0.069740
Absolute Change at 24 Months after Intervention 1	0.005658	(-0.000480, 0.011795)	0.074983	0.069325
Relative Change (%) at 24 Months after Intervention 1	8.16	(-1.23, 17.55)	0.074983	0.069325
Absolute Change at 25 Months after Intervention 1	0.005894	(-0.000500, 0.012287)	0.074805	0.068911
Relative Change (%) at 25 Months after Intervention 1	8.55	(-1.30, 18.41)	0.074805	0.068911
Absolute Change at 26 Months after Intervention 1	0.006129	(-0.000520, 0.012778)	0.074626	0.068497
Relative Change (%) at 26 Months after Intervention 1	8.95	(-1.38, 19.28)	0.074626	0.068497
Absolute Change at 27 Months after Intervention 1	0.006365	(-0.000540, 0.013270)	0.074448	0.068083
Absolute Change at 27 Months after Intervention 1	0.006365	(-0.000540, 0.013270)	0.074448	0.068083
Relative Change (%) at 27 Months after Intervention 1	9.35	(-1.46, 20.16)	0.074448	0.068083
Relative Change (%) at 27 Months after Intervention 1	9.35	(-1.46, 20.16)	0.074448	0.068083

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 55. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of ACEI Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.304169	(0.302177, 0.306160)	<.001
Baseline trend	-0.000506	(-0.000561, -0.000452)	<.001
Level Change (After Intervention 1)	0.001916	(0.000584, 0.003248)	0.006
Trend Change (After Intervention 1)	-0.000373	(-0.000479, -0.000268)	<.001
Most Parsimonious Final Model Parameters (df = 69)[2,3]			
Intercept	0.304169	(0.302177, 0.306160)	<.001
Baseline trend	-0.000506	(-0.000561, -0.000452)	<.001
Level Change (After Intervention 1)	0.001916	(0.000584, 0.003248)	0.006
Trend Change (After Intervention 1)	-0.000373	(-0.000479, -0.000268)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 56. Absolute and Relative Changes in Proportion of ACEI Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.001543	(0.000205, 0.002881)	0.282934	0.281391
Relative Change (%) at 1 Months after Intervention 1	0.55	(0.07, 1.03)	0.282934	0.281391
Absolute Change at 2 Months after Intervention 1	0.001170	(-0.000175, 0.002514)	0.282055	0.280885
Relative Change (%) at 2 Months after Intervention 1	0.42	(-0.06, 0.90)	0.282055	0.280885
Absolute Change at 3 Months after Intervention 1	0.000797	(-0.000565, 0.002158)	0.281175	0.280379
Relative Change (%) at 3 Months after Intervention 1	0.28	(-0.20, 0.77)	0.281175	0.280379
Absolute Change at 4 Months after Intervention 1	0.000423	(-0.000966, 0.001813)	0.280296	0.279873
Relative Change (%) at 4 Months after Intervention 1	0.15	(-0.35, 0.65)	0.280296	0.279873
Absolute Change at 5 Months after Intervention 1	0.000050	(-0.001376, 0.001477)	0.279417	0.279367
Relative Change (%) at 5 Months after Intervention 1	0.02	(-0.49, 0.53)	0.279417	0.279367
Absolute Change at 6 Months after Intervention 1	-0.000323	(-0.001796, 0.001150)	0.278538	0.278860
Relative Change (%) at 6 Months after Intervention 1	-0.12	(-0.64, 0.41)	0.278538	0.278860
Absolute Change at 7 Months after Intervention 1	-0.000696	(-0.002223, 0.000832)	0.277658	0.278354
Relative Change (%) at 7 Months after Intervention 1	-0.25	(-0.80, 0.30)	0.277658	0.278354
Absolute Change at 8 Months after Intervention 1	-0.001069	(-0.002659, 0.000521)	0.276779	0.277848
Relative Change (%) at 8 Months after Intervention 1	-0.38	(-0.95, 0.18)	0.276779	0.277848
Absolute Change at 9 Months after Intervention 1	-0.001442	(-0.003100, 0.000216)	0.275900	0.277342
Relative Change (%) at 9 Months after Intervention 1	-0.52	(-1.11, 0.07)	0.275900	0.277342
Absolute Change at 10 Months after Intervention 1	-0.001815	(-0.003548, -0.000083)	0.275021	0.276836
Relative Change (%) at 10 Months after Intervention 1	-0.66	(-1.28, -0.03)	0.275021	0.276836
Absolute Change at 11 Months after Intervention 1	-0.002188	(-0.004000, -0.000376)	0.274141	0.276330
Relative Change (%) at 11 Months after Intervention 1	-0.79	(-1.44, -0.14)	0.274141	0.276330
Absolute Change at 12 Months after Intervention 1	-0.002561	(-0.004457, -0.000666)	0.273262	0.275823
Relative Change (%) at 12 Months after Intervention 1	-0.93	(-1.61, -0.25)	0.273262	0.275823
Absolute Change at 13 Months after Intervention 1	-0.002935	(-0.004918, -0.000951)	0.272383	0.275317
Relative Change (%) at 13 Months after Intervention 1	-1.07	(-1.78, -0.35)	0.272383	0.275317
Absolute Change at 14 Months after Intervention 1	-0.003308	(-0.005382, -0.001233)	0.271503	0.274811
Relative Change (%) at 14 Months after Intervention 1	-1.20	(-1.95, -0.46)	0.271503	0.274811
Absolute Change at 15 Months after Intervention 1	-0.003681	(-0.005850, -0.001512)	0.270624	0.274305
Relative Change (%) at 15 Months after Intervention 1	-1.34	(-2.12, -0.56)	0.270624	0.274305
Absolute Change at 16 Months after Intervention 1	-0.004054	(-0.006319, -0.001788)	0.269745	0.273799
Relative Change (%) at 16 Months after Intervention 1	-1.48	(-2.30, -0.67)	0.269745	0.273799
Absolute Change at 17 Months after Intervention 1	-0.004427	(-0.006791, -0.002062)	0.268866	0.273293

Table 56. Absolute and Relative Changes in Proportion of ACEI Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Relative Change (%) at 17 Months after Intervention 1	-1.62	(-2.47, -0.77)	0.268866	0.273293
Absolute Change at 18 Months after Intervention 1	-0.004800	(-0.007265, -0.002335)	0.267986	0.272786
Relative Change (%) at 18 Months after Intervention 1	-1.76	(-2.65, -0.87)	0.267986	0.272786
Absolute Change at 19 Months after Intervention 1	-0.005173	(-0.007741, -0.002605)	0.267107	0.272280
Relative Change (%) at 19 Months after Intervention 1	-1.90	(-2.83, -0.97)	0.267107	0.272280
Absolute Change at 20 Months after Intervention 1	-0.005546	(-0.008219, -0.002874)	0.266228	0.271774
Relative Change (%) at 20 Months after Intervention 1	-2.04	(-3.00, -1.08)	0.266228	0.271774
Absolute Change at 21 Months after Intervention 1	-0.005919	(-0.008697, -0.003141)	0.265349	0.271268
Relative Change (%) at 21 Months after Intervention 1	-2.18	(-3.19, -1.18)	0.265349	0.271268
Absolute Change at 22 Months after Intervention 1	-0.006292	(-0.009177, -0.003408)	0.264469	0.270762
Relative Change (%) at 22 Months after Intervention 1	-2.32	(-3.37, -1.28)	0.264469	0.270762
Absolute Change at 23 Months after Intervention 1	-0.006666	(-0.009658, -0.003673)	0.263590	0.270256
Relative Change (%) at 23 Months after Intervention 1	-2.47	(-3.55, -1.38)	0.263590	0.270256
Absolute Change at 24 Months after Intervention 1	-0.007039	(-0.010141, -0.003937)	0.262711	0.269749
Relative Change (%) at 24 Months after Intervention 1	-2.61	(-3.73, -1.49)	0.262711	0.269749
Absolute Change at 25 Months after Intervention 1	-0.007412	(-0.010623, -0.004200)	0.261831	0.269243
Relative Change (%) at 25 Months after Intervention 1	-2.75	(-3.92, -1.59)	0.261831	0.269243
Absolute Change at 26 Months after Intervention 1	-0.007785	(-0.011107, -0.004463)	0.260952	0.268737
Relative Change (%) at 26 Months after Intervention 1	-2.90	(-4.10, -1.69)	0.260952	0.268737
Absolute Change at 27 Months after Intervention 1	-0.008158	(-0.011592, -0.004724)	0.260073	0.268231
Absolute Change at 27 Months after Intervention 1	-0.008158	(-0.011592, -0.004724)	0.260073	0.268231
Relative Change (%) at 27 Months after Intervention 1	-3.04	(-4.29, -1.79)	0.260073	0.268231
Relative Change (%) at 27 Months after Intervention 1	-3.04	(-4.29, -1.79)	0.260073	0.268231

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 57. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of ARB Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.279421	(0.274151, 0.284691)	<.001
Baseline trend	0.000200	(0.000015, 0.000386)	0.035
Level Change (After Intervention 1)	-0.000440	(-0.003925, 0.003046)	0.802
Trend Change (After Intervention 1)	0.000753	(0.000325, 0.001181)	<.001
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.279444	(0.274142, 0.284746)	<.001
Baseline trend	0.000197	(0.000013, 0.000380)	0.036
Trend Change (After Intervention 1)	0.000743	(0.000320, 0.001167)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 58. Absolute and Relative Changes in Proportion of ARB Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000743	(0.000316, 0.001170)	0.289034	0.288290
Relative Change (%) at 1 Months after Intervention 1	0.26	(0.11, 0.41)	0.289034	0.288290
Absolute Change at 2 Months after Intervention 1	0.001486	(0.000632, 0.002341)	0.289973	0.288487
Relative Change (%) at 2 Months after Intervention 1	0.52	(0.21, 0.82)	0.289973	0.288487
Absolute Change at 3 Months after Intervention 1	0.002229	(0.000948, 0.003511)	0.290913	0.288684
Relative Change (%) at 3 Months after Intervention 1	0.77	(0.32, 1.23)	0.290913	0.288684
Absolute Change at 4 Months after Intervention 1	0.002973	(0.001264, 0.004681)	0.291853	0.288880
Relative Change (%) at 4 Months after Intervention 1	1.03	(0.42, 1.64)	0.291853	0.288880
Absolute Change at 5 Months after Intervention 1	0.003716	(0.001580, 0.005851)	0.292793	0.289077
Relative Change (%) at 5 Months after Intervention 1	1.29	(0.53, 2.05)	0.292793	0.289077
Absolute Change at 6 Months after Intervention 1	0.004459	(0.001896, 0.007022)	0.293732	0.289273
Relative Change (%) at 6 Months after Intervention 1	1.54	(0.63, 2.45)	0.293732	0.289273
Absolute Change at 7 Months after Intervention 1	0.005202	(0.002212, 0.008192)	0.294672	0.289470
Relative Change (%) at 7 Months after Intervention 1	1.80	(0.73, 2.86)	0.294672	0.289470
Absolute Change at 8 Months after Intervention 1	0.005945	(0.002528, 0.009362)	0.295612	0.289667
Relative Change (%) at 8 Months after Intervention 1	2.05	(0.84, 3.27)	0.295612	0.289667
Absolute Change at 9 Months after Intervention 1	0.006688	(0.002844, 0.010533)	0.296551	0.289863
Relative Change (%) at 9 Months after Intervention 1	2.31	(0.94, 3.68)	0.296551	0.289863
Absolute Change at 10 Months after Intervention 1	0.007431	(0.003160, 0.011703)	0.297491	0.290060
Relative Change (%) at 10 Months after Intervention 1	2.56	(1.04, 4.08)	0.297491	0.290060
Absolute Change at 11 Months after Intervention 1	0.008175	(0.003476, 0.012873)	0.298431	0.290256
Relative Change (%) at 11 Months after Intervention 1	2.82	(1.14, 4.49)	0.298431	0.290256
Absolute Change at 12 Months after Intervention 1	0.008918	(0.003792, 0.014044)	0.299371	0.290453
Relative Change (%) at 12 Months after Intervention 1	3.07	(1.24, 4.90)	0.299371	0.290453
Absolute Change at 13 Months after Intervention 1	0.009661	(0.004108, 0.015214)	0.300310	0.290650
Relative Change (%) at 13 Months after Intervention 1	3.32	(1.35, 5.30)	0.300310	0.290650
Absolute Change at 14 Months after Intervention 1	0.010404	(0.004424, 0.016384)	0.301250	0.290846
Relative Change (%) at 14 Months after Intervention 1	3.58	(1.45, 5.71)	0.301250	0.290846
Absolute Change at 15 Months after Intervention 1	0.011147	(0.004740, 0.017554)	0.302190	0.291043
Relative Change (%) at 15 Months after Intervention 1	3.83	(1.55, 6.11)	0.302190	0.291043
Absolute Change at 16 Months after Intervention 1	0.011890	(0.005056, 0.018725)	0.303130	0.291239
Relative Change (%) at 16 Months after Intervention 1	4.08	(1.65, 6.52)	0.303130	0.291239

Table 58. Absolute and Relative Changes in Proportion of ARB Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 17 Months after Intervention 1	0.012633	(0.005372, 0.019895)	0.304069	0.291436
Relative Change (%) at 17 Months after Intervention 1	4.33	(1.75, 6.92)	0.304069	0.291436
Absolute Change at 18 Months after Intervention 1	0.013377	(0.005688, 0.021065)	0.305009	0.291632
Relative Change (%) at 18 Months after Intervention 1	4.59	(1.85, 7.33)	0.305009	0.291632
Absolute Change at 19 Months after Intervention 1	0.014120	(0.006004, 0.022236)	0.305949	0.291829
Relative Change (%) at 19 Months after Intervention 1	4.84	(1.94, 7.73)	0.305949	0.291829
Absolute Change at 20 Months after Intervention 1	0.014863	(0.006320, 0.023406)	0.306888	0.292026
Relative Change (%) at 20 Months after Intervention 1	5.09	(2.04, 8.14)	0.306888	0.292026
Absolute Change at 21 Months after Intervention 1	0.015606	(0.006636, 0.024576)	0.307828	0.292222
Relative Change (%) at 21 Months after Intervention 1	5.34	(2.14, 8.54)	0.307828	0.292222
Absolute Change at 22 Months after Intervention 1	0.016349	(0.006952, 0.025746)	0.308768	0.292419
Relative Change (%) at 22 Months after Intervention 1	5.59	(2.24, 8.94)	0.308768	0.292419
Absolute Change at 23 Months after Intervention 1	0.017092	(0.007268, 0.026917)	0.309708	0.292615
Relative Change (%) at 23 Months after Intervention 1	5.84	(2.34, 9.35)	0.309708	0.292615
Absolute Change at 24 Months after Intervention 1	0.017835	(0.007584, 0.028087)	0.310647	0.292812
Relative Change (%) at 24 Months after Intervention 1	6.09	(2.43, 9.75)	0.310647	0.292812
Absolute Change at 25 Months after Intervention 1	0.018578	(0.007900, 0.029257)	0.311587	0.293009
Relative Change (%) at 25 Months after Intervention 1	6.34	(2.53, 10.15)	0.311587	0.293009
Absolute Change at 26 Months after Intervention 1	0.019322	(0.008216, 0.030428)	0.312527	0.293205
Relative Change (%) at 26 Months after Intervention 1	6.59	(2.63, 10.55)	0.312527	0.293205
Absolute Change at 27 Months after Intervention 1	0.020065	(0.008532, 0.031598)	0.313467	0.293402
Absolute Change at 27 Months after Intervention 1	0.020065	(0.008532, 0.031598)	0.313467	0.293402
Relative Change (%) at 27 Months after Intervention 1	6.84	(2.72, 10.96)	0.313467	0.293402
Relative Change (%) at 27 Months after Intervention 1	6.84	(2.72, 10.96)	0.313467	0.293402

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 59. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Beta Blocker Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.345395	(0.334451, 0.356338)	<.001
Baseline trend	-0.000394	(-0.000768, -0.000020)	0.039
Level Change (After Intervention 1)	0.000498	(-0.004955, 0.005951)	0.856
Trend Change (After Intervention 1)	0.000638	(-0.000202, 0.001478)	0.135
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.345347	(0.334368, 0.356327)	<.001
Baseline trend	-0.000388	(-0.000760, -0.000017)	0.041
Trend Change (After Intervention 1)	0.000645	(-0.000184, 0.001475)	0.126

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 60. Absolute and Relative Changes in Proportion of Beta Blocker Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000645	(-0.000265, 0.001556)	0.328513	0.327868
Relative Change (%) at 1 Months after Intervention 1	0.20	(-0.09, 0.48)	0.328513	0.327868
Absolute Change at 2 Months after Intervention 1	0.001291	(-0.000530, 0.003112)	0.328770	0.327479
Relative Change (%) at 2 Months after Intervention 1	0.39	(-0.17, 0.96)	0.328770	0.327479
Absolute Change at 3 Months after Intervention 1	0.001936	(-0.000795, 0.004668)	0.329027	0.327091
Relative Change (%) at 3 Months after Intervention 1	0.59	(-0.26, 1.45)	0.329027	0.327091
Absolute Change at 4 Months after Intervention 1	0.002582	(-0.001060, 0.006223)	0.329284	0.326702
Relative Change (%) at 4 Months after Intervention 1	0.79	(-0.35, 1.93)	0.329284	0.326702
Absolute Change at 5 Months after Intervention 1	0.003227	(-0.001325, 0.007779)	0.329541	0.326314
Relative Change (%) at 5 Months after Intervention 1	0.99	(-0.44, 2.42)	0.329541	0.326314
Absolute Change at 6 Months after Intervention 1	0.003873	(-0.001590, 0.009335)	0.329798	0.325925
Relative Change (%) at 6 Months after Intervention 1	1.19	(-0.53, 2.90)	0.329798	0.325925
Absolute Change at 7 Months after Intervention 1	0.004518	(-0.001855, 0.010891)	0.330055	0.325537
Relative Change (%) at 7 Months after Intervention 1	1.39	(-0.62, 3.39)	0.330055	0.325537
Absolute Change at 8 Months after Intervention 1	0.005164	(-0.002120, 0.012447)	0.330312	0.325148
Relative Change (%) at 8 Months after Intervention 1	1.59	(-0.71, 3.89)	0.330312	0.325148
Absolute Change at 9 Months after Intervention 1	0.005809	(-0.002385, 0.014003)	0.330569	0.324760
Relative Change (%) at 9 Months after Intervention 1	1.79	(-0.80, 4.38)	0.330569	0.324760
Absolute Change at 10 Months after Intervention 1	0.006455	(-0.002650, 0.015559)	0.330826	0.324372
Relative Change (%) at 10 Months after Intervention 1	1.99	(-0.89, 4.87)	0.330826	0.324372
Absolute Change at 11 Months after Intervention 1	0.007100	(-0.002914, 0.017115)	0.331083	0.323983
Relative Change (%) at 11 Months after Intervention 1	2.19	(-0.99, 5.37)	0.331083	0.323983
Absolute Change at 12 Months after Intervention 1	0.007745	(-0.003179, 0.018670)	0.331340	0.323595
Relative Change (%) at 12 Months after Intervention 1	2.39	(-1.08, 5.87)	0.331340	0.323595
Absolute Change at 13 Months after Intervention 1	0.008391	(-0.003444, 0.020226)	0.331597	0.323206
Relative Change (%) at 13 Months after Intervention 1	2.60	(-1.17, 6.37)	0.331597	0.323206
Absolute Change at 14 Months after Intervention 1	0.009036	(-0.003709, 0.021782)	0.331854	0.322818
Relative Change (%) at 14 Months after Intervention 1	2.80	(-1.27, 6.87)	0.331854	0.322818
Absolute Change at 15 Months after Intervention 1	0.009682	(-0.003974, 0.023338)	0.332111	0.322429
Relative Change (%) at 15 Months after Intervention 1	3.00	(-1.36, 7.37)	0.332111	0.322429
Absolute Change at 16 Months after Intervention 1	0.010327	(-0.004239, 0.024894)	0.332368	0.322041
Relative Change (%) at 16 Months after Intervention 1	3.21	(-1.46, 7.87)	0.332368	0.322041

Table 60. Absolute and Relative Changes in Proportion of Beta Blocker Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 17 Months after Intervention 1	0.010973	(-0.004504, 0.026450)	0.332625	0.321653
Relative Change (%) at 17 Months after Intervention 1	3.41	(-1.56, 8.38)	0.332625	0.321653
Absolute Change at 18 Months after Intervention 1	0.011618	(-0.004769, 0.028006)	0.332882	0.321264
Relative Change (%) at 18 Months after Intervention 1	3.62	(-1.65, 8.89)	0.332882	0.321264
Absolute Change at 19 Months after Intervention 1	0.012264	(-0.005034, 0.029561)	0.333139	0.320876
Relative Change (%) at 19 Months after Intervention 1	3.82	(-1.75, 9.40)	0.333139	0.320876
Absolute Change at 20 Months after Intervention 1	0.012909	(-0.005299, 0.031117)	0.333396	0.320487
Relative Change (%) at 20 Months after Intervention 1	4.03	(-1.85, 9.91)	0.333396	0.320487
Absolute Change at 21 Months after Intervention 1	0.013555	(-0.005564, 0.032673)	0.333653	0.320099
Relative Change (%) at 21 Months after Intervention 1	4.23	(-1.95, 10.42)	0.333653	0.320099
Absolute Change at 22 Months after Intervention 1	0.014200	(-0.005829, 0.034229)	0.333910	0.319710
Relative Change (%) at 22 Months after Intervention 1	4.44	(-2.05, 10.93)	0.333910	0.319710
Absolute Change at 23 Months after Intervention 1	0.014845	(-0.006094, 0.035785)	0.334167	0.319322
Relative Change (%) at 23 Months after Intervention 1	4.65	(-2.15, 11.45)	0.334167	0.319322
Absolute Change at 24 Months after Intervention 1	0.015491	(-0.006359, 0.037341)	0.334424	0.318933
Relative Change (%) at 24 Months after Intervention 1	4.86	(-2.25, 11.97)	0.334424	0.318933
Absolute Change at 25 Months after Intervention 1	0.016136	(-0.006624, 0.038897)	0.334681	0.318545
Relative Change (%) at 25 Months after Intervention 1	5.07	(-2.36, 12.49)	0.334681	0.318545
Absolute Change at 26 Months after Intervention 1	0.016782	(-0.006889, 0.040453)	0.334938	0.318157
Relative Change (%) at 26 Months after Intervention 1	5.27	(-2.46, 13.01)	0.334938	0.318157
Absolute Change at 27 Months after Intervention 1	0.017427	(-0.007154, 0.042008)	0.335195	0.317768
Absolute Change at 27 Months after Intervention 1	0.017427	(-0.007154, 0.042008)	0.335195	0.317768
Relative Change (%) at 27 Months after Intervention 1	5.48	(-2.56, 13.53)	0.335195	0.317768
Relative Change (%) at 27 Months after Intervention 1	5.48	(-2.56, 13.53)	0.335195	0.317768

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 61. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of CCB Combination Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.225270	(0.216907, 0.233633)	<.001
Baseline trend	0.000553	(0.000272, 0.000834)	<.001
Level Change (After Intervention 1)	0.000151	(-0.003577, 0.003879)	0.936
Trend Change (After Intervention 1)	0.000141	(-0.000481, 0.000764)	0.652
Most Parsimonious Final Model Parameters (df = 71)[2,3]			
Intercept	0.224589	(0.216604, 0.232574)	<.001
Baseline trend	0.000603	(0.000427, 0.000780)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 62. Absolute and Relative Changes in Proportion of CCB Combination Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.251739	0.251739
Relative Change (%) at 1 Months after Intervention 1	0.00	(0.00, 0.00)	0.251739	0.251739
Absolute Change at 2 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.252342	0.252342
Relative Change (%) at 2 Months after Intervention 1	0.00	(0.00, 0.00)	0.252342	0.252342
Absolute Change at 3 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.252945	0.252945
Relative Change (%) at 3 Months after Intervention 1	0.00	(0.00, 0.00)	0.252945	0.252945
Absolute Change at 4 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.253549	0.253549
Relative Change (%) at 4 Months after Intervention 1	0.00	(0.00, 0.00)	0.253549	0.253549
Absolute Change at 5 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.254152	0.254152
Relative Change (%) at 5 Months after Intervention 1	0.00	(0.00, 0.00)	0.254152	0.254152
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.254755	0.254755
Relative Change (%) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.254755	0.254755
Absolute Change at 7 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.255358	0.255358
Relative Change (%) at 7 Months after Intervention 1	0.00	(0.00, 0.00)	0.255358	0.255358
Absolute Change at 8 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.255962	0.255962
Relative Change (%) at 8 Months after Intervention 1	0.00	(0.00, 0.00)	0.255962	0.255962
Absolute Change at 9 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.256565	0.256565
Relative Change (%) at 9 Months after Intervention 1	0.00	(0.00, 0.00)	0.256565	0.256565
Absolute Change at 10 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.257168	0.257168
Relative Change (%) at 10 Months after Intervention 1	0.00	(0.00, 0.00)	0.257168	0.257168
Absolute Change at 11 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.257772	0.257772
Relative Change (%) at 11 Months after Intervention 1	0.00	(0.00, 0.00)	0.257772	0.257772
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.258375	0.258375
Relative Change (%) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.258375	0.258375
Absolute Change at 13 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.258978	0.258978
Relative Change (%) at 13 Months after Intervention 1	0.00	(0.00, 0.00)	0.258978	0.258978
Absolute Change at 14 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.259582	0.259582
Relative Change (%) at 14 Months after Intervention 1	0.00	(0.00, 0.00)	0.259582	0.259582
Absolute Change at 15 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.260185	0.260185
Relative Change (%) at 15 Months after Intervention 1	0.00	(0.00, 0.00)	0.260185	0.260185
Absolute Change at 16 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.260788	0.260788
Relative Change (%) at 16 Months after Intervention 1	0.00	(0.00, 0.00)	0.260788	0.260788
Absolute Change at 17 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.261392	0.261392

Table 62. Absolute and Relative Changes in Proportion of CCB Combination Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Relative Change (%) at 17 Months after Intervention 1	0.00	(0.00, 0.00)	0.261392	0.261392
Absolute Change at 18 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.261995	0.261995
Relative Change (%) at 18 Months after Intervention 1	0.00	(0.00, 0.00)	0.261995	0.261995
Absolute Change at 19 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.262598	0.262598
Relative Change (%) at 19 Months after Intervention 1	0.00	(0.00, 0.00)	0.262598	0.262598
Absolute Change at 20 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.263202	0.263202
Relative Change (%) at 20 Months after Intervention 1	0.00	(0.00, 0.00)	0.263202	0.263202
Absolute Change at 21 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.263805	0.263805
Relative Change (%) at 21 Months after Intervention 1	0.00	(0.00, 0.00)	0.263805	0.263805
Absolute Change at 22 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.264408	0.264408
Relative Change (%) at 22 Months after Intervention 1	0.00	(0.00, 0.00)	0.264408	0.264408
Absolute Change at 23 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.265012	0.265012
Relative Change (%) at 23 Months after Intervention 1	0.00	(0.00, 0.00)	0.265012	0.265012
Absolute Change at 24 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.265615	0.265615
Relative Change (%) at 24 Months after Intervention 1	0.00	(0.00, 0.00)	0.265615	0.265615
Absolute Change at 25 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.266218	0.266218
Relative Change (%) at 25 Months after Intervention 1	0.00	(0.00, 0.00)	0.266218	0.266218
Absolute Change at 26 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.266822	0.266822
Relative Change (%) at 26 Months after Intervention 1	0.00	(0.00, 0.00)	0.266822	0.266822
Absolute Change at 27 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.267425	0.267425
Absolute Change at 27 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.267425	0.267425
Relative Change (%) at 27 Months after Intervention 1	0.00	(0.00, 0.00)	0.267425	0.267425
Relative Change (%) at 27 Months after Intervention 1	0.00	(0.00, 0.00)	0.267425	0.267425

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 63. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Loop Diuretics Combination Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.055790	(0.049197, 0.062384)	<.001
Baseline trend	-0.000114	(-0.000345, 0.000117)	0.330
Level Change (After Intervention 1)	-0.000060	(-0.002905, 0.002784)	0.966
Trend Change (After Intervention 1)	0.000241	(-0.000297, 0.000779)	0.374
Most Parsimonious Final Model Parameters (df = 72)[2,3]			
Intercept	0.053988	(0.048974, 0.059003)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 64. Absolute and Relative Changes in Proportion of Loop Diuretics Combination Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 1 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 2 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 2 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 3 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 3 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 4 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 4 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 5 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 5 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 7 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 7 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 8 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 8 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 9 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 9 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 10 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 10 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 11 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 11 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 13 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 13 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 14 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 14 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 15 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 15 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 16 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 16 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988

Table 64. Absolute and Relative Changes in Proportion of Loop Diuretics Combination Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 17 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 17 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 18 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 18 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 19 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 19 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 20 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 20 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 21 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 21 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 22 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 22 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 23 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 23 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 24 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 24 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 25 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 25 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 26 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 26 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Absolute Change at 27 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Absolute Change at 27 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053988	0.053988
Relative Change (%) at 27 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988
Relative Change (%) at 27 Months after Intervention 1	0.00	(0.00, 0.00)	0.053988	0.053988

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 65. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Potassium Sparing Combination Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.037649	(0.037177, 0.038121)	<.001
Baseline trend	0.000325	(0.000307, 0.000342)	<.001
Level Change (After Intervention 1)	-0.000074	(-0.000589, 0.000440)	0.774
Trend Change (After Intervention 1)	0.000010	(-0.000033, 0.000052)	0.648
Most Parsimonious Final Model Parameters (df = 71)[2,3]			
Intercept	0.037608	(0.037235, 0.037982)	<.001
Baseline trend	0.000327	(0.000318, 0.000336)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 66. Absolute and Relative Changes in Proportion of Potassium Sparing Combination Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.052305	0.052305
Relative Change (%) at 1 Months after Intervention 1	0.00	(0.00, 0.00)	0.052305	0.052305
Absolute Change at 2 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.052632	0.052632
Relative Change (%) at 2 Months after Intervention 1	0.00	(0.00, 0.00)	0.052632	0.052632
Absolute Change at 3 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.052958	0.052958
Relative Change (%) at 3 Months after Intervention 1	0.00	(0.00, 0.00)	0.052958	0.052958
Absolute Change at 4 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053285	0.053285
Relative Change (%) at 4 Months after Intervention 1	0.00	(0.00, 0.00)	0.053285	0.053285
Absolute Change at 5 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053612	0.053612
Relative Change (%) at 5 Months after Intervention 1	0.00	(0.00, 0.00)	0.053612	0.053612
Absolute Change at 6 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.053938	0.053938
Relative Change (%) at 6 Months after Intervention 1	0.00	(0.00, 0.00)	0.053938	0.053938
Absolute Change at 7 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.054265	0.054265
Relative Change (%) at 7 Months after Intervention 1	0.00	(0.00, 0.00)	0.054265	0.054265
Absolute Change at 8 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.054591	0.054591
Relative Change (%) at 8 Months after Intervention 1	0.00	(0.00, 0.00)	0.054591	0.054591
Absolute Change at 9 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.054918	0.054918
Relative Change (%) at 9 Months after Intervention 1	0.00	(0.00, 0.00)	0.054918	0.054918
Absolute Change at 10 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.055245	0.055245
Relative Change (%) at 10 Months after Intervention 1	0.00	(0.00, 0.00)	0.055245	0.055245
Absolute Change at 11 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.055571	0.055571
Relative Change (%) at 11 Months after Intervention 1	0.00	(0.00, 0.00)	0.055571	0.055571
Absolute Change at 12 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.055898	0.055898
Relative Change (%) at 12 Months after Intervention 1	0.00	(0.00, 0.00)	0.055898	0.055898
Absolute Change at 13 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.056224	0.056224
Relative Change (%) at 13 Months after Intervention 1	0.00	(0.00, 0.00)	0.056224	0.056224
Absolute Change at 14 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.056551	0.056551
Relative Change (%) at 14 Months after Intervention 1	0.00	(0.00, 0.00)	0.056551	0.056551
Absolute Change at 15 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.056878	0.056878
Relative Change (%) at 15 Months after Intervention 1	0.00	(0.00, 0.00)	0.056878	0.056878
Absolute Change at 16 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.057204	0.057204
Relative Change (%) at 16 Months after Intervention 1	0.00	(0.00, 0.00)	0.057204	0.057204
Absolute Change at 17 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.057531	0.057531

Relative Change (%) at 17 Months after Intervention 1	0.00	(0.00, 0.00)	0.057531	0.057531
Absolute Change at 18 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.057857	0.057857
Relative Change (%) at 18 Months after Intervention 1	0.00	(0.00, 0.00)	0.057857	0.057857
Absolute Change at 19 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.058184	0.058184
Relative Change (%) at 19 Months after Intervention 1	0.00	(0.00, 0.00)	0.058184	0.058184
Absolute Change at 20 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.058511	0.058511
Relative Change (%) at 20 Months after Intervention 1	0.00	(0.00, 0.00)	0.058511	0.058511
Absolute Change at 21 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.058837	0.058837
Relative Change (%) at 21 Months after Intervention 1	0.00	(0.00, 0.00)	0.058837	0.058837
Absolute Change at 22 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.059164	0.059164
Relative Change (%) at 22 Months after Intervention 1	0.00	(0.00, 0.00)	0.059164	0.059164
Absolute Change at 23 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.059490	0.059490
Relative Change (%) at 23 Months after Intervention 1	0.00	(0.00, 0.00)	0.059490	0.059490
Absolute Change at 24 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.059817	0.059817
Relative Change (%) at 24 Months after Intervention 1	0.00	(0.00, 0.00)	0.059817	0.059817
Absolute Change at 25 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.060144	0.060144
Relative Change (%) at 25 Months after Intervention 1	0.00	(0.00, 0.00)	0.060144	0.060144
Absolute Change at 26 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.060470	0.060470
Relative Change (%) at 26 Months after Intervention 1	0.00	(0.00, 0.00)	0.060470	0.060470
Absolute Change at 27 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.060797	0.060797
Absolute Change at 27 Months after Intervention 1	0.000000	(0.000000, 0.000000)	0.060797	0.060797
Relative Change (%) at 27 Months after Intervention 1	0.00	(0.00, 0.00)	0.060797	0.060797
Relative Change (%) at 27 Months after Intervention 1	0.00	(0.00, 0.00)	0.060797	0.060797

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Table 67. Parameter Estimates from the Segmented Regression Model of Monthly Proportion of Thiazide-like Diuretics Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1]

	Estimate	95% CI	Approximate Pr > |t|
Initial Model Parameters (df = 69)[2]			
Intercept	0.015673	(0.015308, 0.016038)	<.001
Baseline trend	0.000115	(0.000105, 0.000124)	<.001
Level Change (After Intervention 1)	0.000090	(-0.000116, 0.000296)	0.388
Trend Change (After Intervention 1)	-0.000072	(-0.000091, -0.000053)	<.001
Most Parsimonious Final Model Parameters (df = 70)[2,3]			
Intercept	0.015664	(0.015302, 0.016026)	<.001
Baseline trend	0.000116	(0.000106, 0.000125)	<.001
Trend Change (After Intervention 1)	-0.000070	(-0.000089, -0.000051)	<.001

[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

[2]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 0.2

Table 68. Absolute and Relative Changes in Proportion of Thiazide-like Diuretics Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

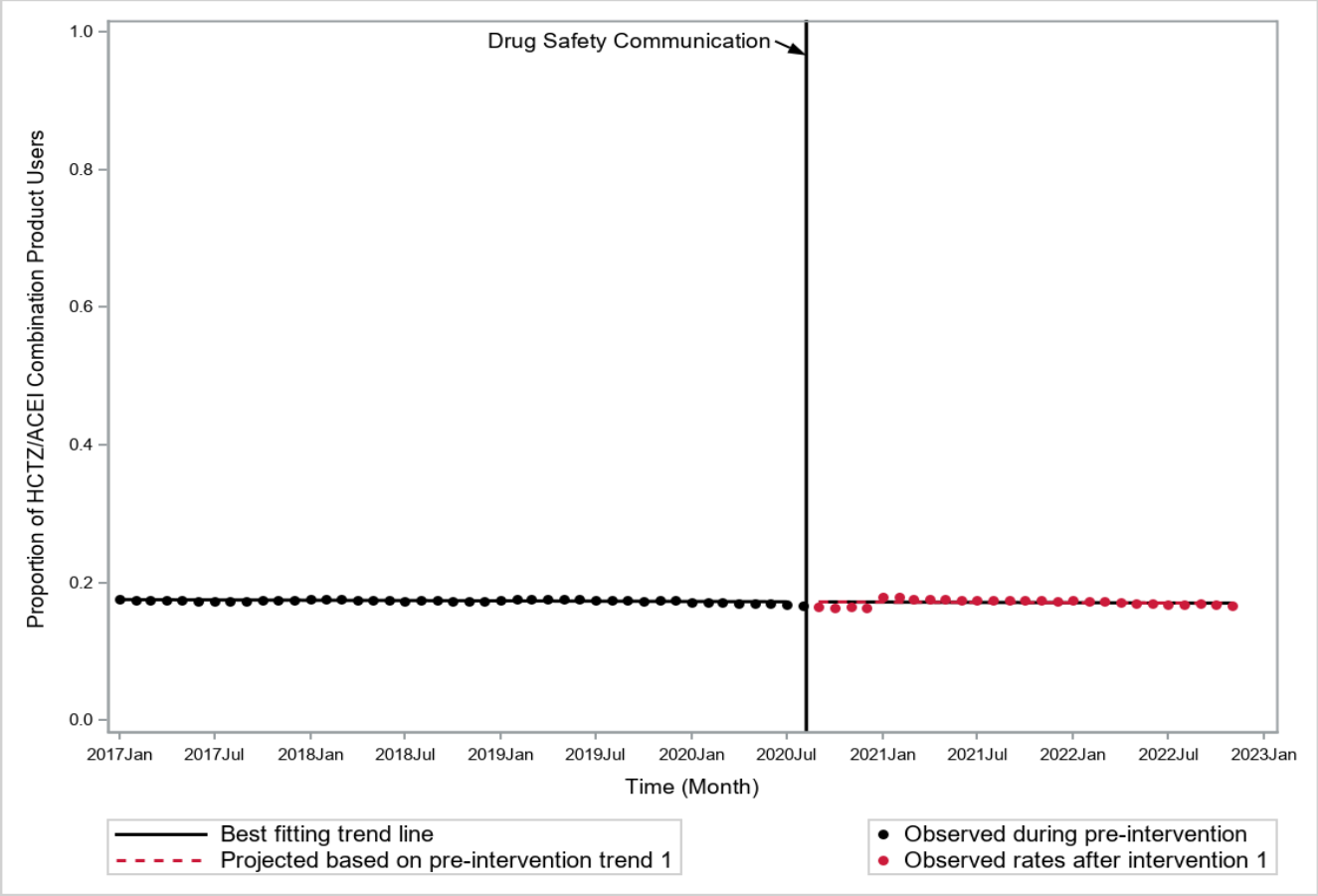
Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 1 Months after Intervention 1	-0.000070	(-0.000093, -0.000047)	0.020794	0.020865
Relative Change (%) at 1 Months after Intervention 1	-0.34	(-0.44, -0.23)	0.020794	0.020865
Absolute Change at 2 Months after Intervention 1	-0.000140	(-0.000187, -0.000094)	0.020840	0.020980
Relative Change (%) at 2 Months after Intervention 1	-0.67	(-0.88, -0.46)	0.020840	0.020980
Absolute Change at 3 Months after Intervention 1	-0.000211	(-0.000280, -0.000141)	0.020885	0.021096
Relative Change (%) at 3 Months after Intervention 1	-1.00	(-1.31, -0.68)	0.020885	0.021096
Absolute Change at 4 Months after Intervention 1	-0.000281	(-0.000373, -0.000189)	0.020930	0.021211
Relative Change (%) at 4 Months after Intervention 1	-1.32	(-1.74, -0.91)	0.020930	0.021211
Absolute Change at 5 Months after Intervention 1	-0.000351	(-0.000466, -0.000236)	0.020976	0.021327
Relative Change (%) at 5 Months after Intervention 1	-1.65	(-2.16, -1.13)	0.020976	0.021327
Absolute Change at 6 Months after Intervention 1	-0.000421	(-0.000560, -0.000283)	0.021021	0.021442
Relative Change (%) at 6 Months after Intervention 1	-1.96	(-2.58, -1.35)	0.021021	0.021442
Absolute Change at 7 Months after Intervention 1	-0.000491	(-0.000653, -0.000330)	0.021066	0.021558
Relative Change (%) at 7 Months after Intervention 1	-2.28	(-2.99, -1.57)	0.021066	0.021558
Absolute Change at 8 Months after Intervention 1	-0.000562	(-0.000746, -0.000377)	0.021112	0.021673
Relative Change (%) at 8 Months after Intervention 1	-2.59	(-3.40, -1.78)	0.021112	0.021673
Absolute Change at 9 Months after Intervention 1	-0.000632	(-0.000839, -0.000424)	0.021157	0.021789
Relative Change (%) at 9 Months after Intervention 1	-2.90	(-3.81, -1.99)	0.021157	0.021789
Absolute Change at 10 Months after Intervention 1	-0.000702	(-0.000933, -0.000472)	0.021202	0.021905
Relative Change (%) at 10 Months after Intervention 1	-3.21	(-4.20, -2.21)	0.021202	0.021905
Absolute Change at 11 Months after Intervention 1	-0.000772	(-0.001026, -0.000519)	0.021248	0.022020
Relative Change (%) at 11 Months after Intervention 1	-3.51	(-4.60, -2.42)	0.021248	0.022020
Absolute Change at 12 Months after Intervention 1	-0.000843	(-0.001119, -0.000566)	0.021293	0.022136
Relative Change (%) at 12 Months after Intervention 1	-3.81	(-4.99, -2.62)	0.021293	0.022136
Absolute Change at 13 Months after Intervention 1	-0.000913	(-0.001213, -0.000613)	0.021339	0.022251
Relative Change (%) at 13 Months after Intervention 1	-4.10	(-5.38, -2.83)	0.021339	0.022251
Absolute Change at 14 Months after Intervention 1	-0.000983	(-0.001306, -0.000660)	0.021384	0.022367
Relative Change (%) at 14 Months after Intervention 1	-4.39	(-5.76, -3.03)	0.021384	0.022367
Absolute Change at 15 Months after Intervention 1	-0.001053	(-0.001399, -0.000707)	0.021429	0.022482
Relative Change (%) at 15 Months after Intervention 1	-4.68	(-6.14, -3.23)	0.021429	0.022482
Absolute Change at 16 Months after Intervention 1	-0.001123	(-0.001492, -0.000755)	0.021475	0.022598
Relative Change (%) at 16 Months after Intervention 1	-4.97	(-6.51, -3.43)	0.021475	0.022598

Table 68. Absolute and Relative Changes in Proportion of Thiazide-like Diuretics Product Users among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer after August 8, 2020[1] Compared with Expected Rates Derived from Baseline Trend

Outcome Measure	Estimate	95% CI	Predicted Rate (With Intervention)	Extrapolated Rate (Without Intervention)
Absolute Change at 17 Months after Intervention 1	-0.001194	(-0.001586, -0.000802)	0.021520	0.022714
Relative Change (%) at 17 Months after Intervention 1	-5.26	(-6.88, -3.63)	0.021520	0.022714
Absolute Change at 18 Months after Intervention 1	-0.001264	(-0.001679, -0.000849)	0.021565	0.022829
Relative Change (%) at 18 Months after Intervention 1	-5.54	(-7.25, -3.82)	0.021565	0.022829
Absolute Change at 19 Months after Intervention 1	-0.001334	(-0.001772, -0.000896)	0.021611	0.022945
Relative Change (%) at 19 Months after Intervention 1	-5.81	(-7.61, -4.02)	0.021611	0.022945
Absolute Change at 20 Months after Intervention 1	-0.001404	(-0.001865, -0.000943)	0.021656	0.023060
Relative Change (%) at 20 Months after Intervention 1	-6.09	(-7.97, -4.21)	0.021656	0.023060
Absolute Change at 21 Months after Intervention 1	-0.001474	(-0.001959, -0.000990)	0.021701	0.023176
Relative Change (%) at 21 Months after Intervention 1	-6.36	(-8.32, -4.40)	0.021701	0.023176
Absolute Change at 22 Months after Intervention 1	-0.001545	(-0.002052, -0.001037)	0.021747	0.023291
Relative Change (%) at 22 Months after Intervention 1	-6.63	(-8.67, -4.59)	0.021747	0.023291
Absolute Change at 23 Months after Intervention 1	-0.001615	(-0.002145, -0.001085)	0.021792	0.023407
Relative Change (%) at 23 Months after Intervention 1	-6.90	(-9.02, -4.78)	0.021792	0.023407
Absolute Change at 24 Months after Intervention 1	-0.001685	(-0.002238, -0.001132)	0.021837	0.023523
Relative Change (%) at 24 Months after Intervention 1	-7.16	(-9.37, -4.96)	0.021837	0.023523
Absolute Change at 25 Months after Intervention 1	-0.001755	(-0.002332, -0.001179)	0.021883	0.023638
Relative Change (%) at 25 Months after Intervention 1	-7.43	(-9.71, -5.15)	0.021883	0.023638
Absolute Change at 26 Months after Intervention 1	-0.001826	(-0.002425, -0.001226)	0.021928	0.023754
Relative Change (%) at 26 Months after Intervention 1	-7.69	(-10.04, -5.33)	0.021928	0.023754
Absolute Change at 27 Months after Intervention 1	-0.001896	(-0.002518, -0.001273)	0.021973	0.023869
Absolute Change at 27 Months after Intervention 1	-0.001896	(-0.002518, -0.001273)	0.021973	0.023869
Relative Change (%) at 27 Months after Intervention 1	-7.94	(-10.38, -5.51)	0.021973	0.023869
Relative Change (%) at 27 Months after Intervention 1	-7.94	(-10.38, -5.51)	0.021973	0.023869

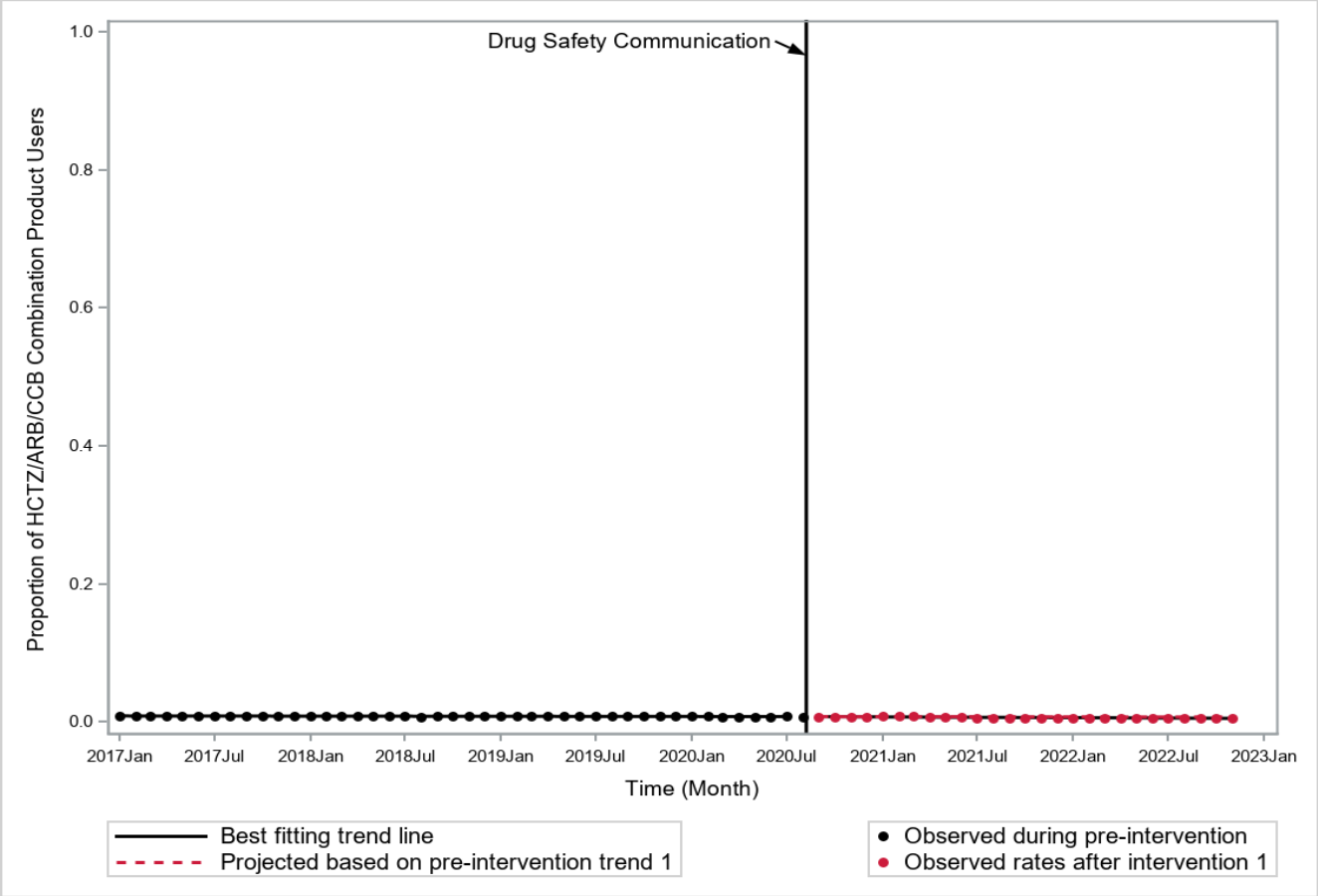
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 1. Proportion of HCTZ/ACEI Combination Product Users Among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer Before and After August 8, 2020[1]



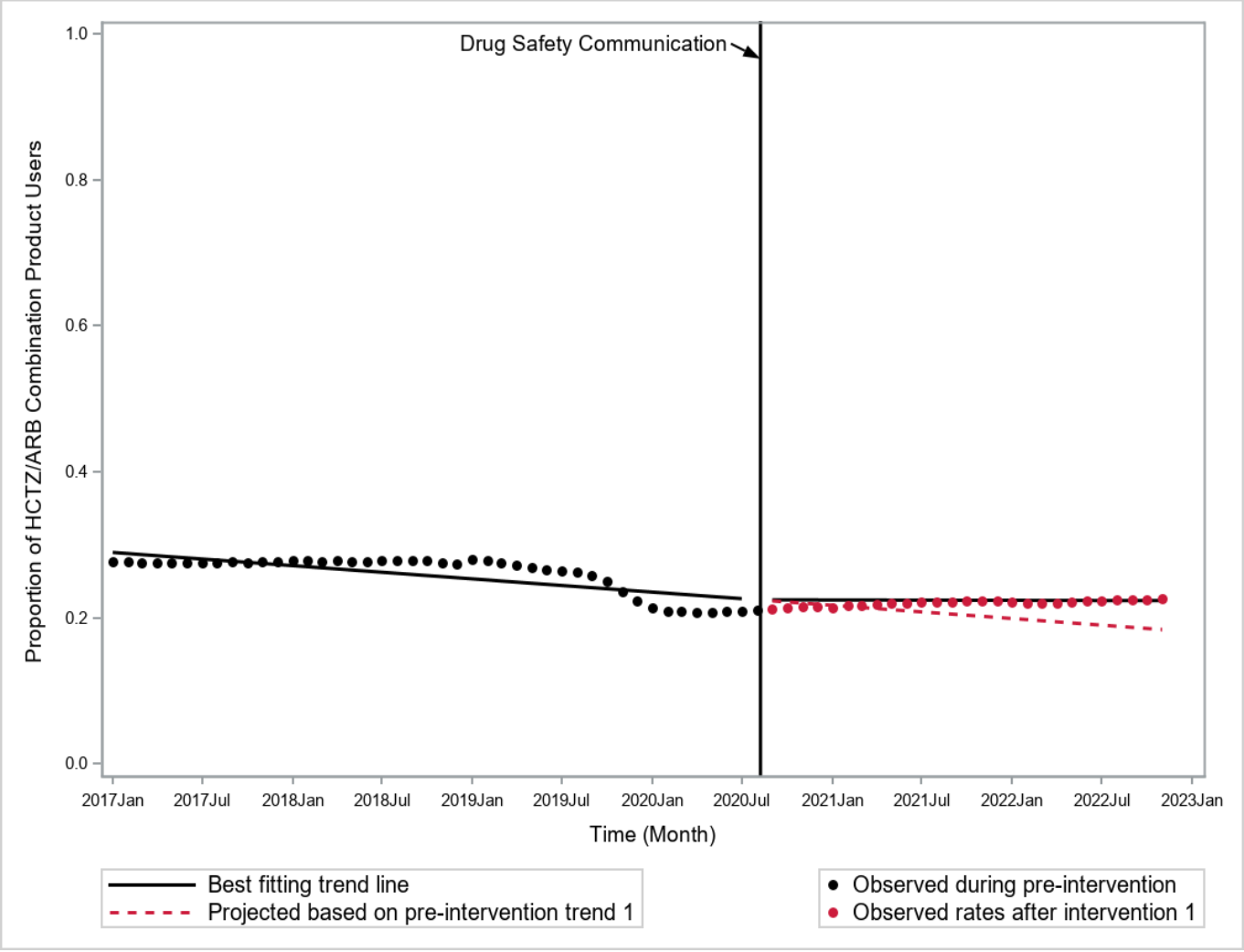
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 2. Proportion of HCTZ/ARB/CCB Combination Product Users Among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer Before and After August 8, 2020[1]



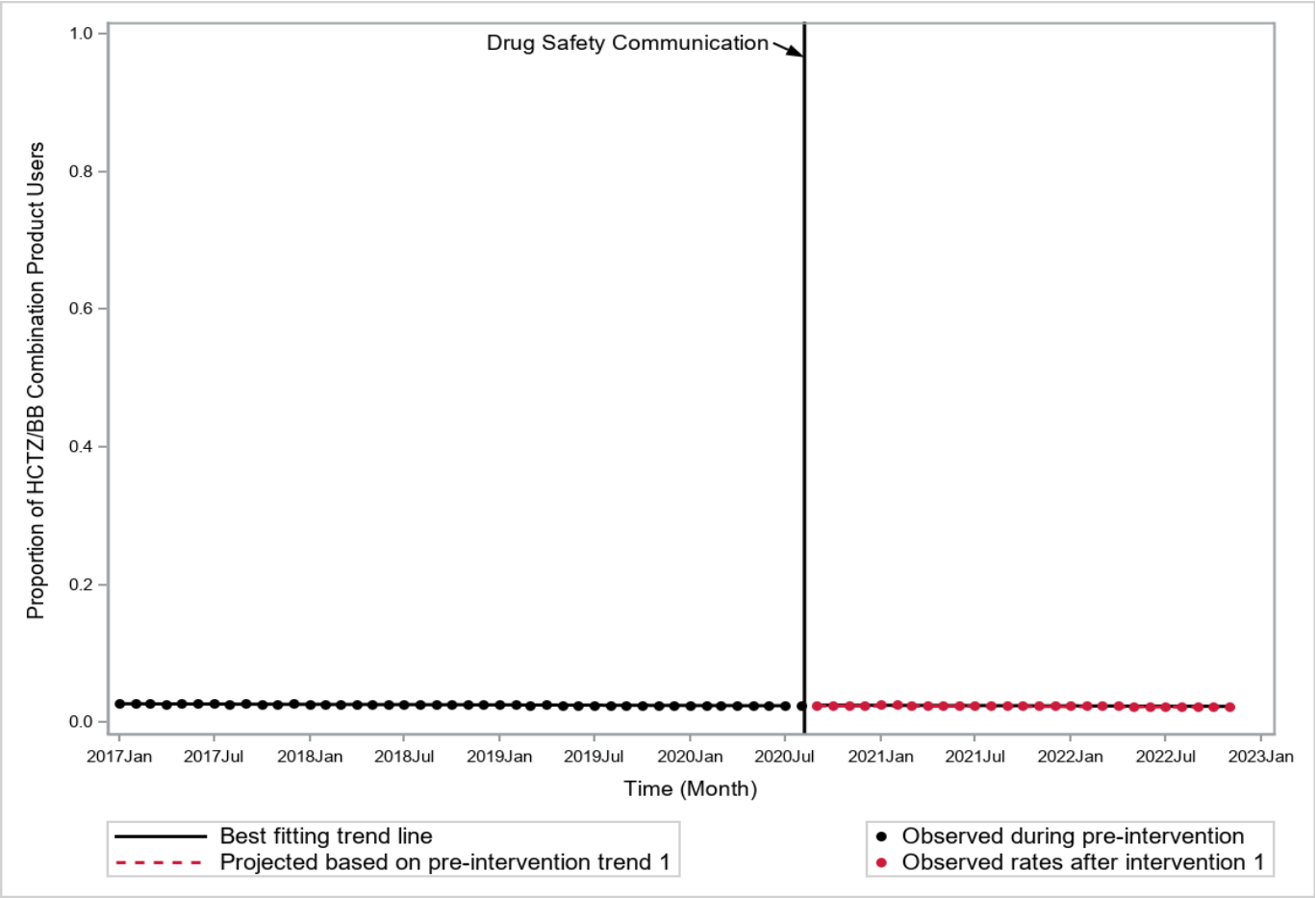
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 3. Proportion of HCTZ/ARB Combination Product Users Among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer Before and After August 8, 2020[1]



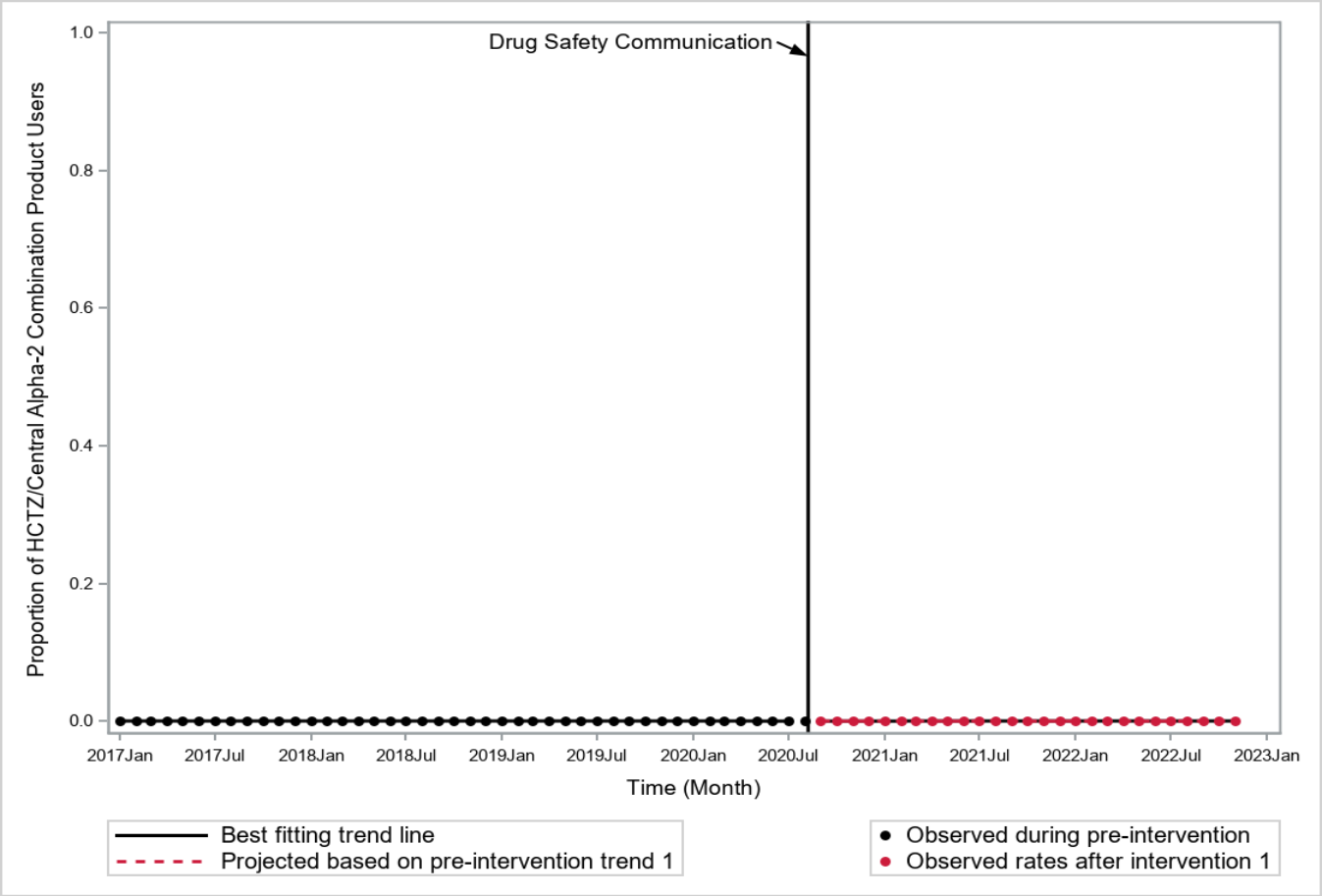
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 4. Proportion of HCTZ/BB Combination Product Users Among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer Before and After August 8, 2020[1]



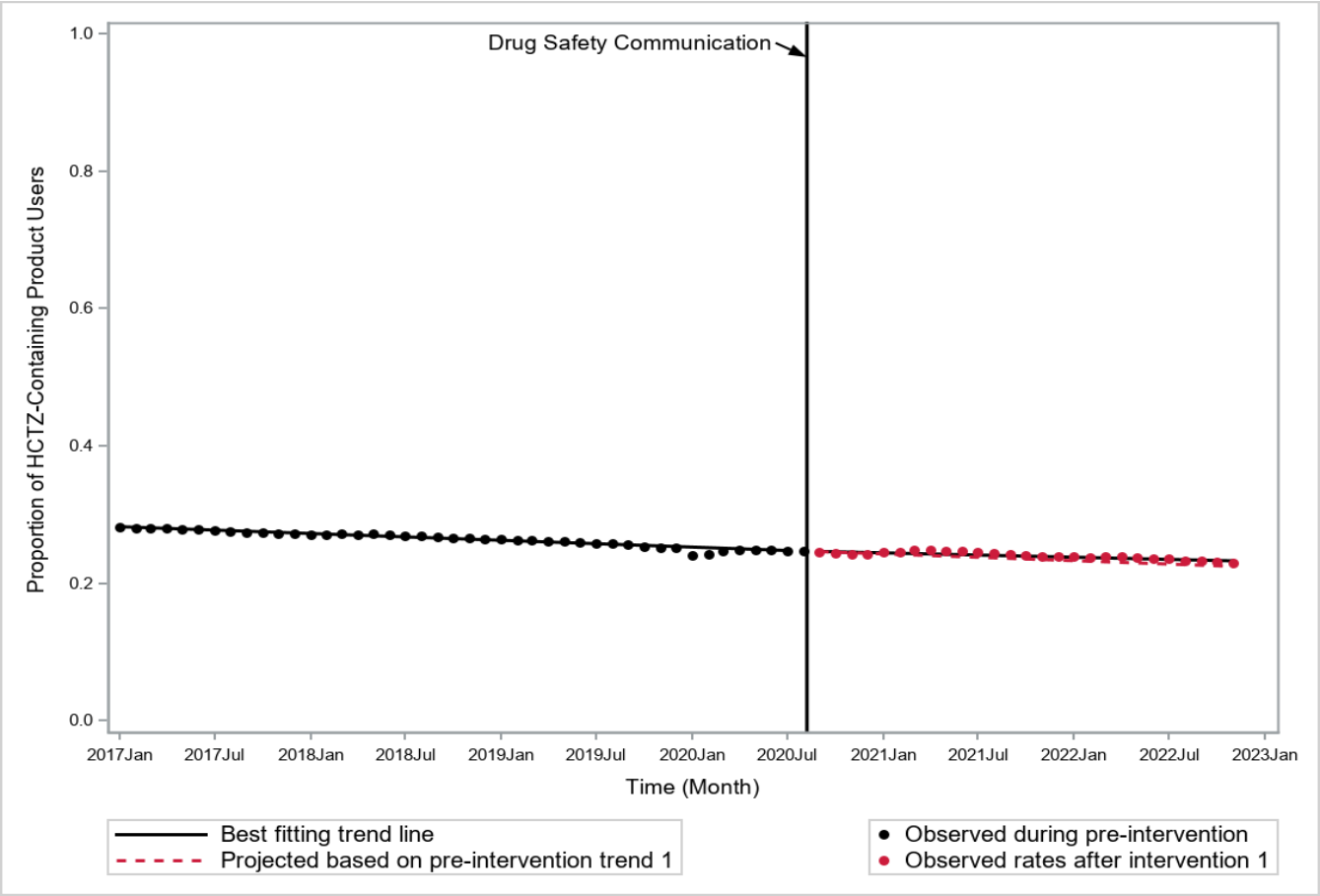
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 5. Proportion of HCTZ/Central Alpha-2 Combination Product Users Among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer Before and After August 8, 2020[1]



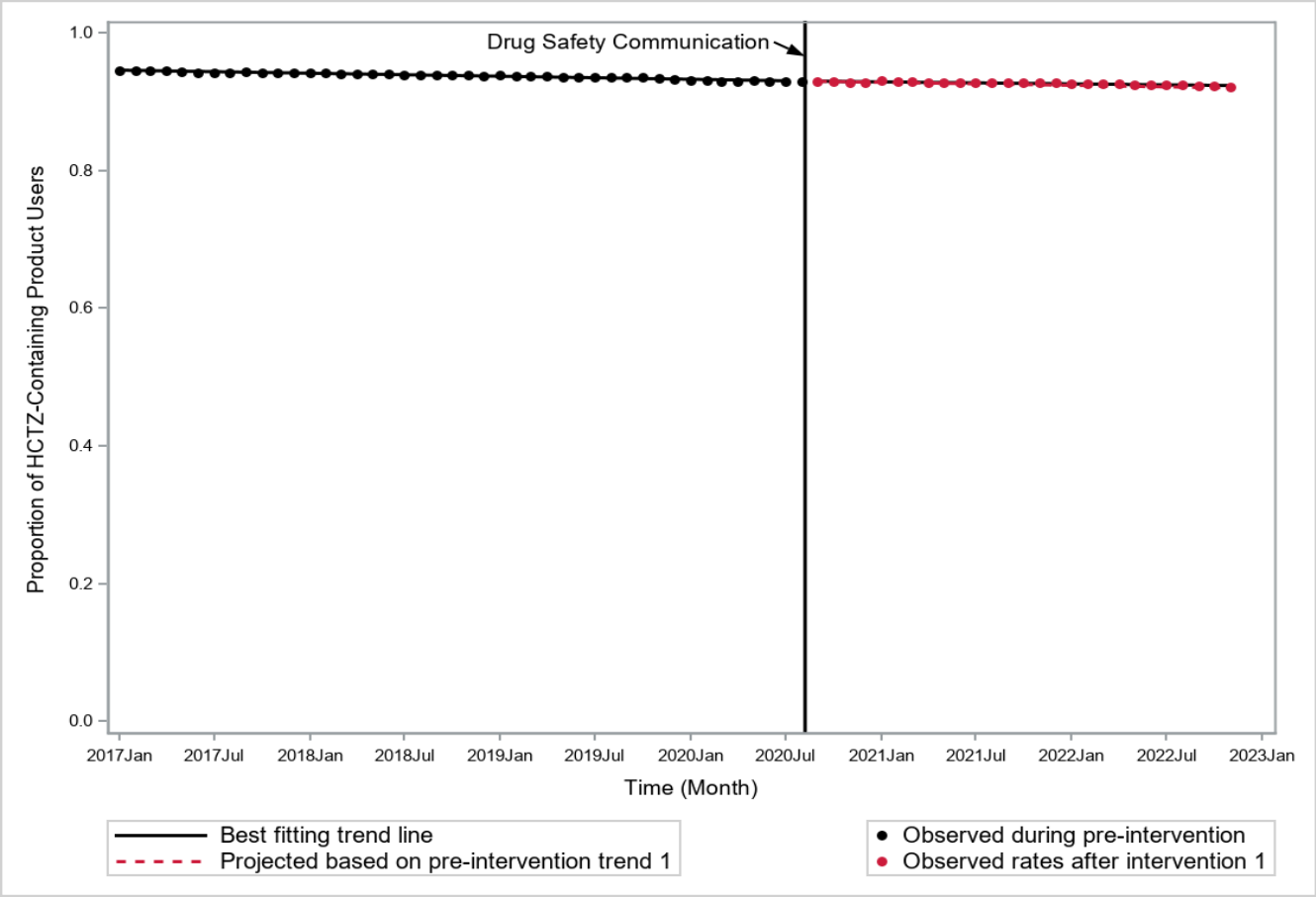
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 6. Proportion of HCTZ-Containing Product Users Among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer Before and After August 8, 2020[1]



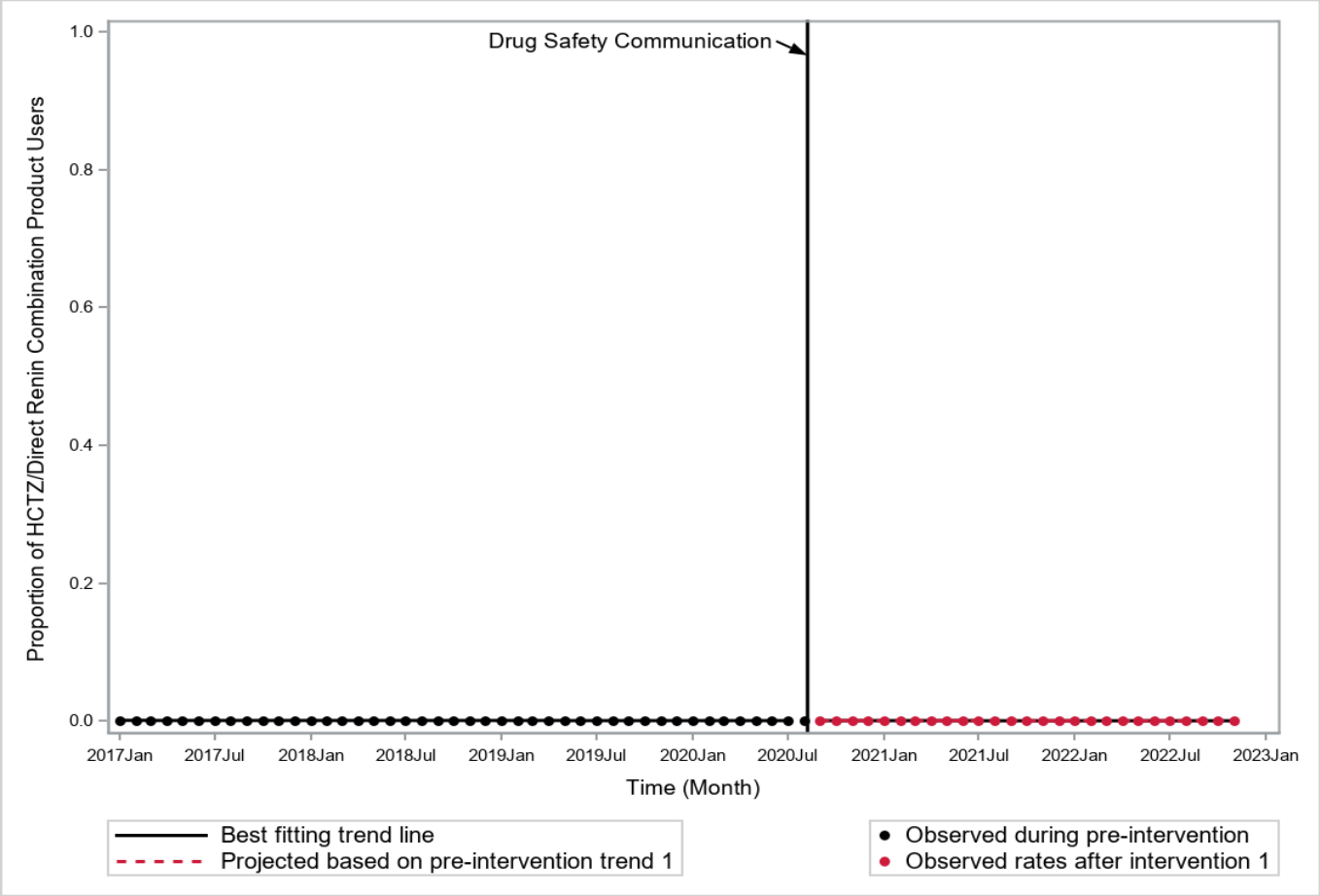
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 7. Proportion of HCTZ-Containing Product Users Among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer Before and After August 8, 2020[1]



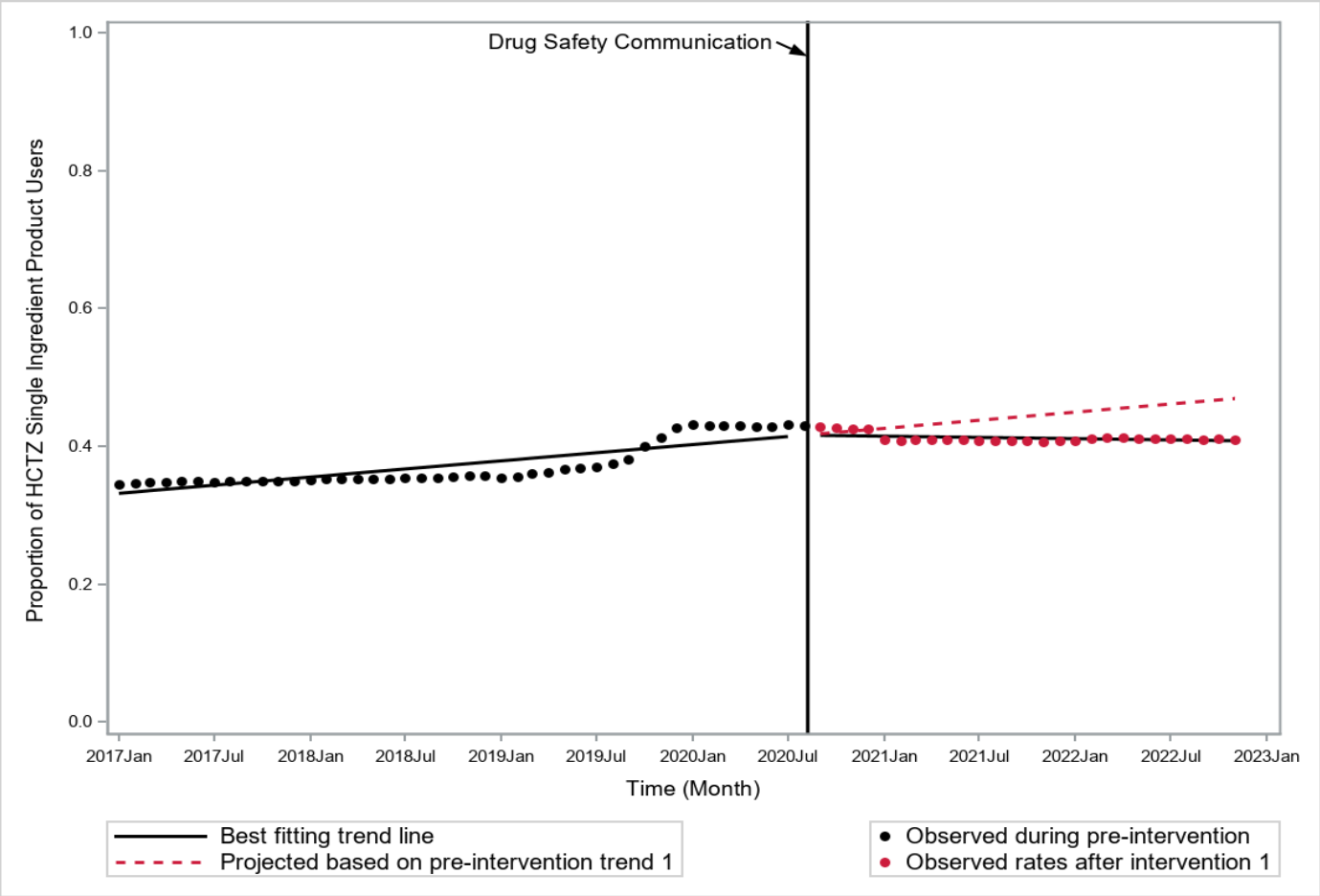
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 8. Proportion of HCTZ/Direct Renin Combination Product Users Among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer Before and After August 8, 2020[1]



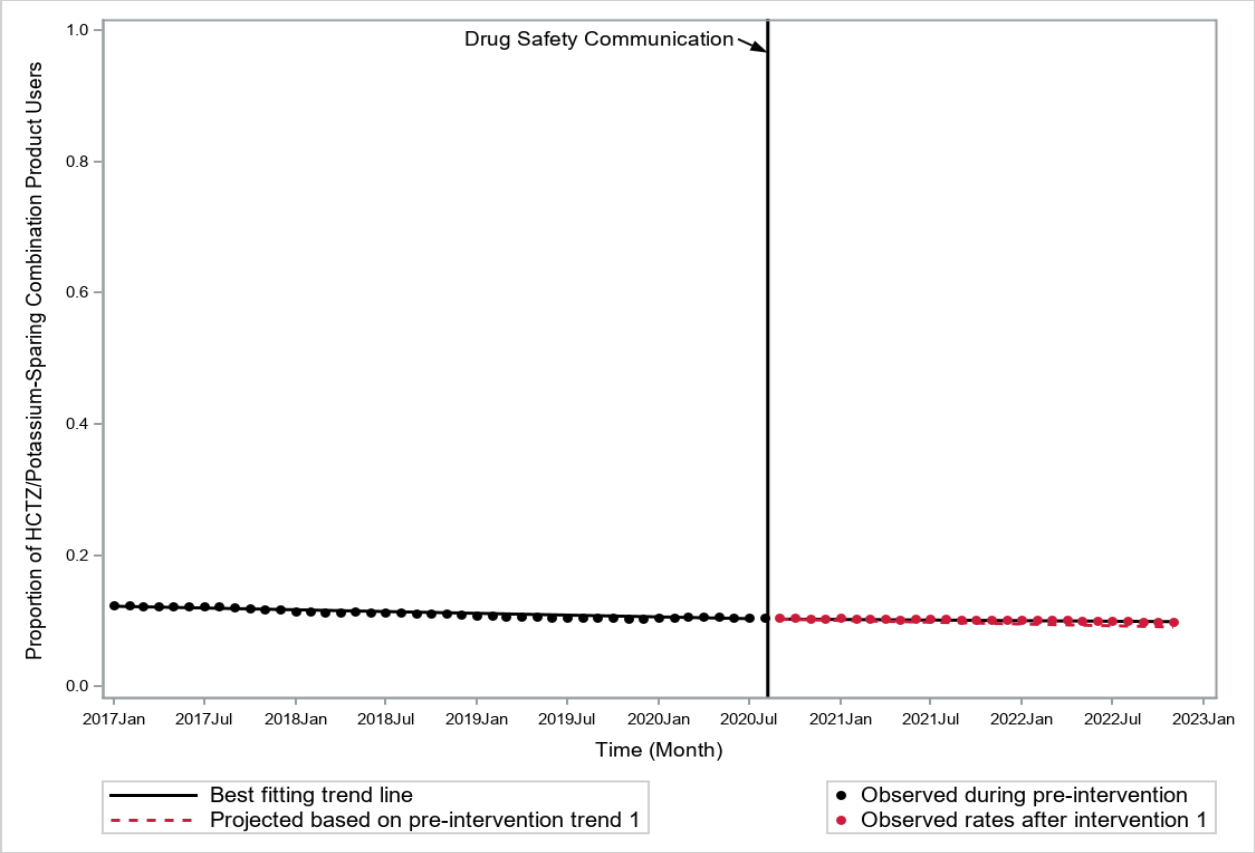
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 9. Proportion of HCTZ Single Ingredient Product Users Among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer Before and After August 8, 2020[1]



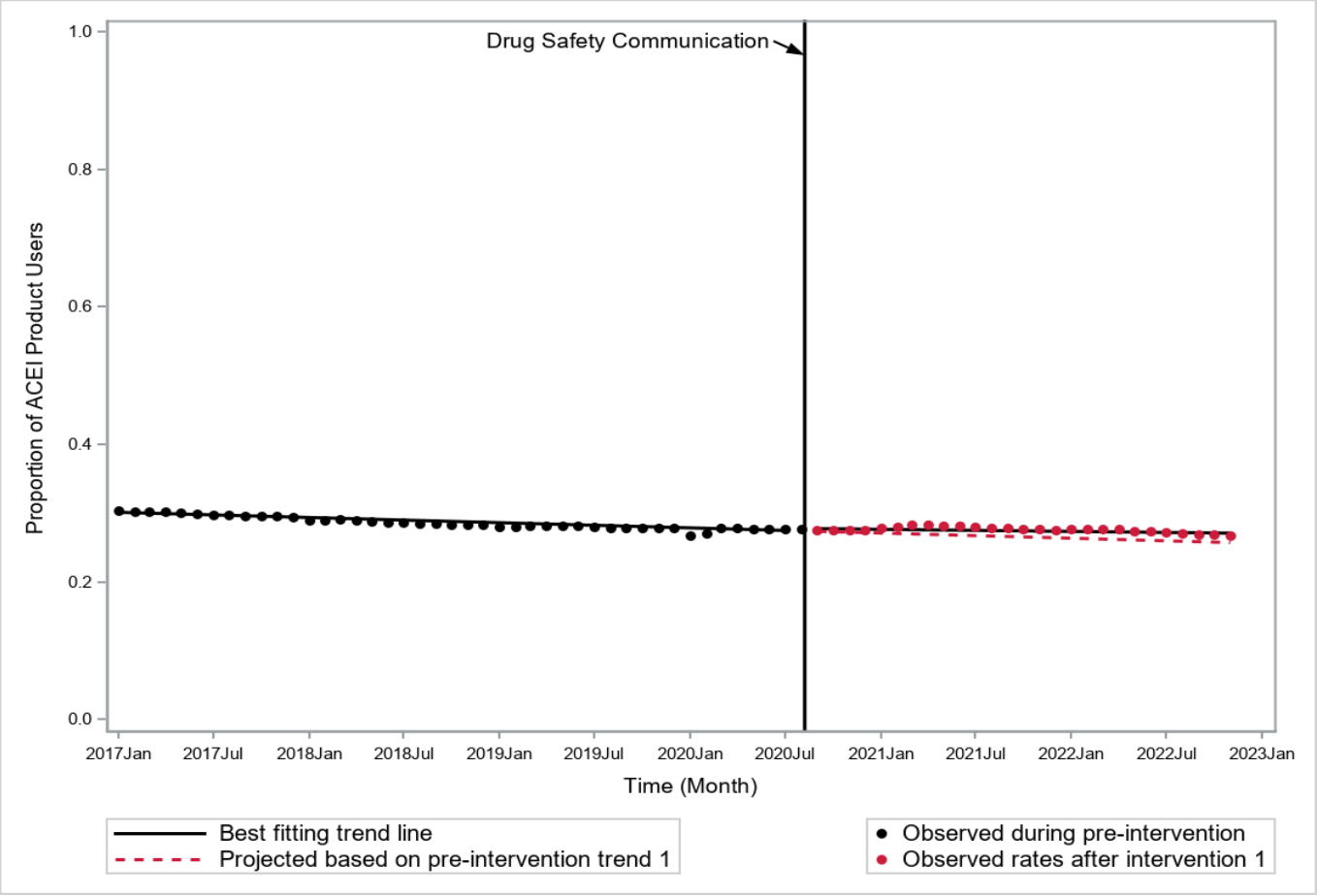
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 10. Proportion of HCTZ/Potassium-Sparing Combination Product Users Among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with history of skin cancer Before and After August 8, 2020[1]



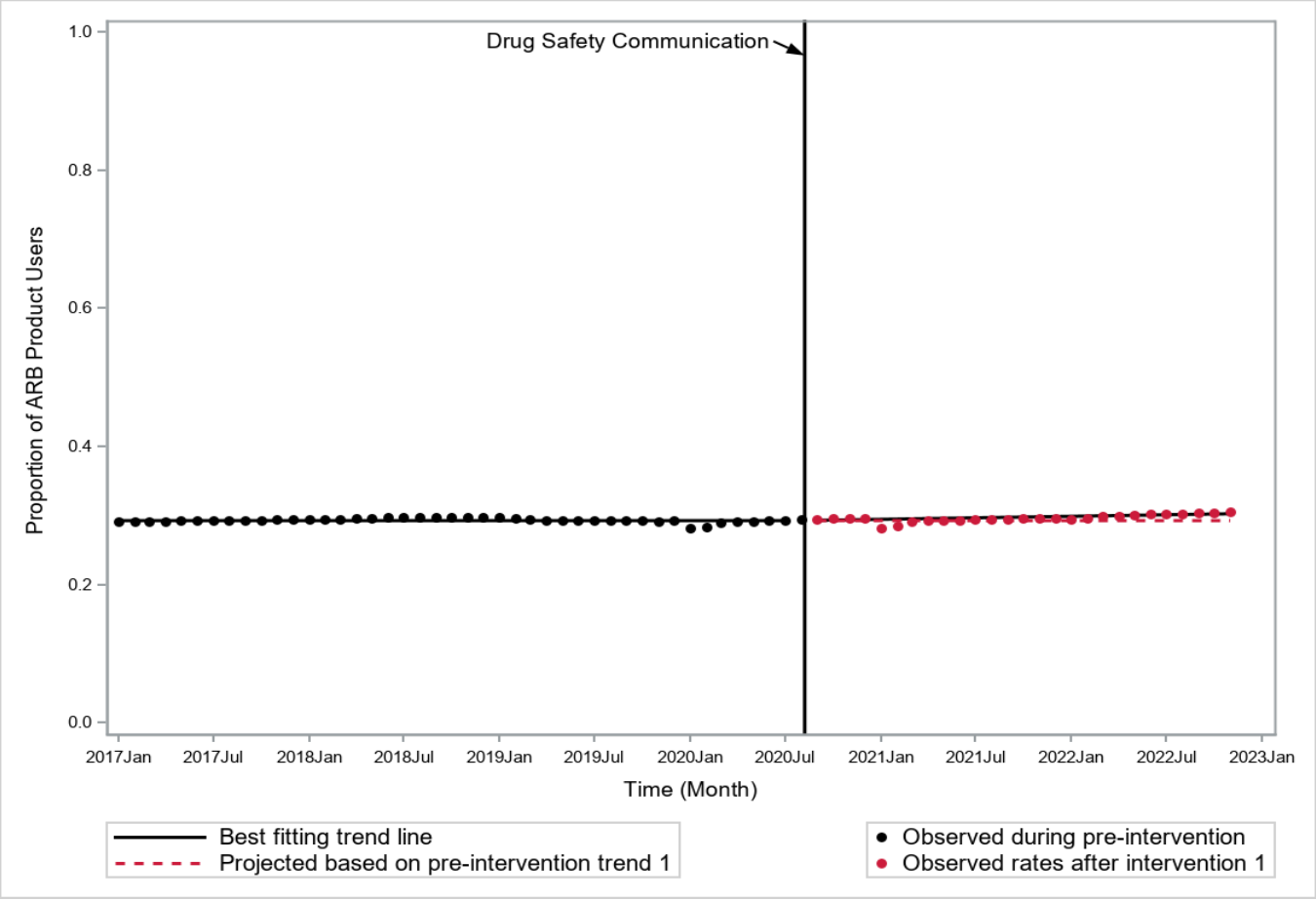
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 11. Proportion of ACEI Product Users Among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer Before and After August 8, 2020[1]



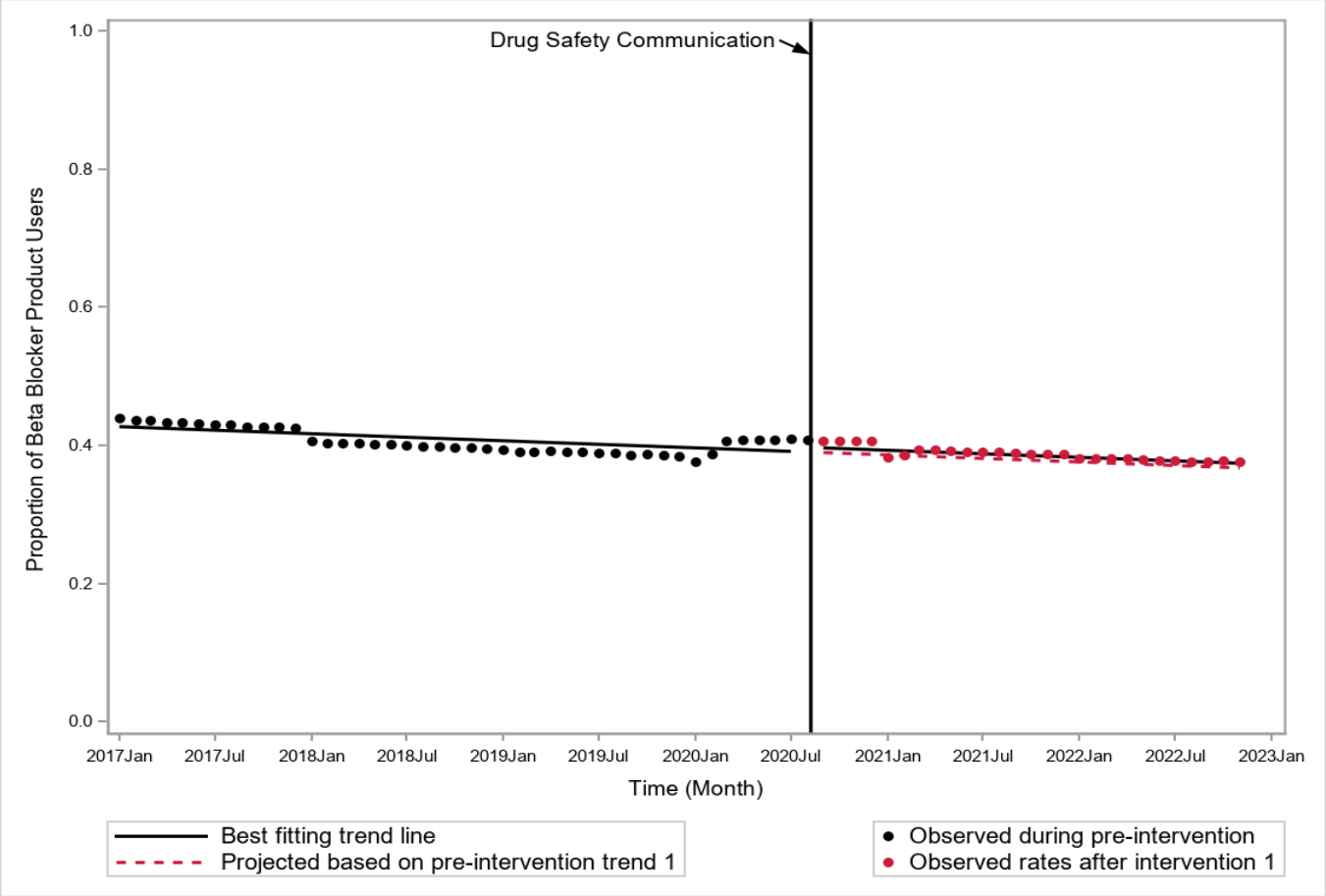
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 12. Proportion of ARB Product Users Among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer Before and After August 8, 2020[1]



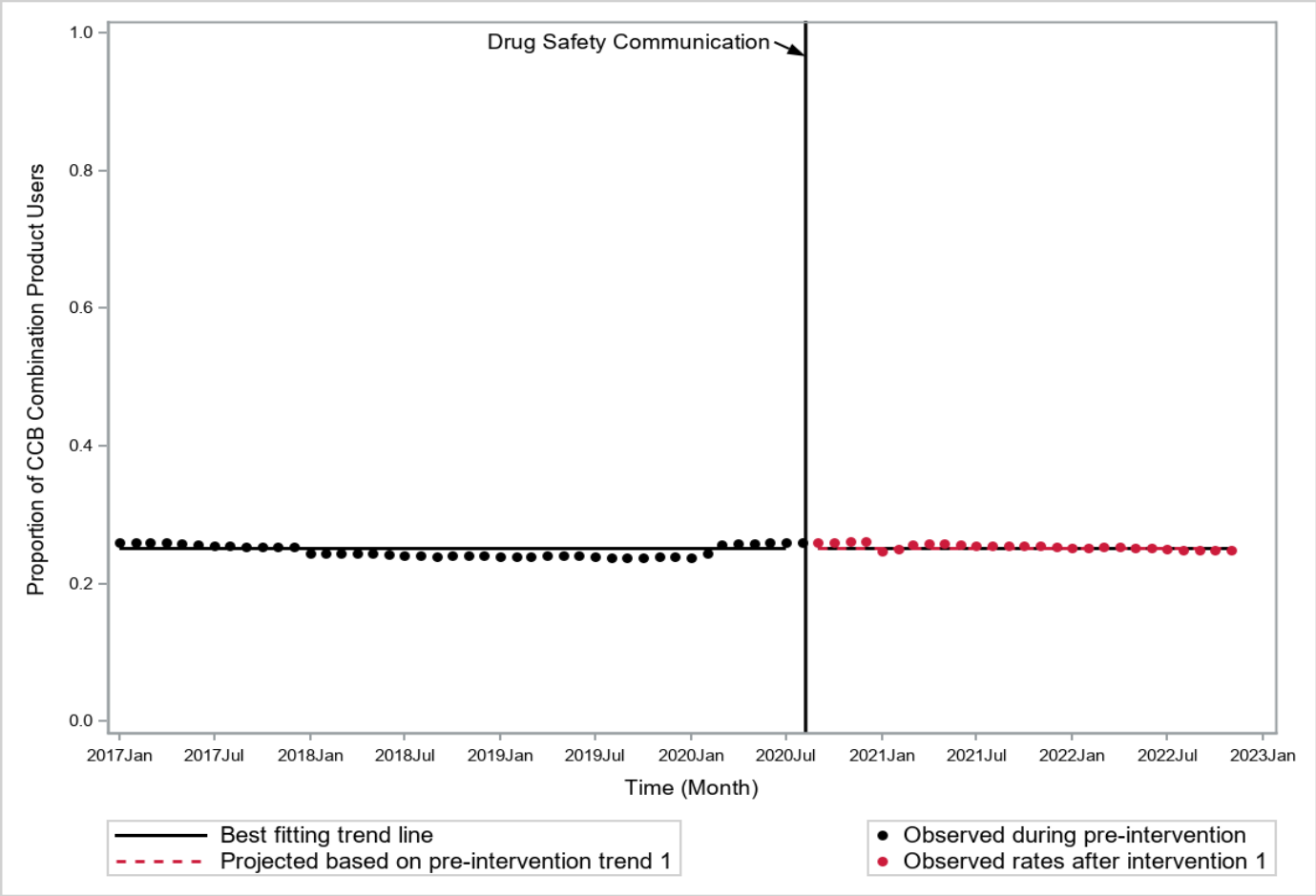
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 13. Proportion of Beta Blocker Product Users Among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer Before and After August 8, 2020[1]



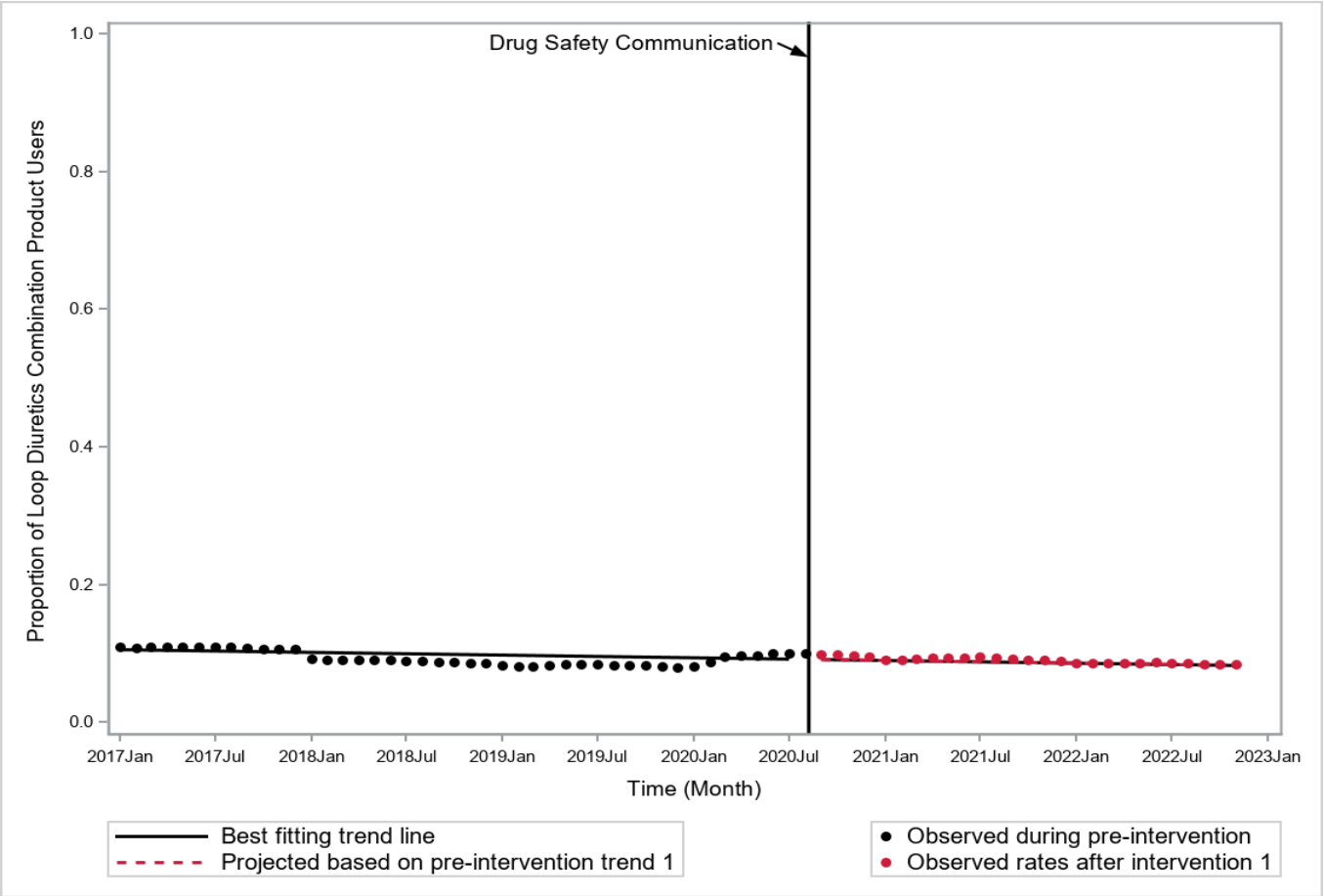
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 14. Proportion of CCB Combination Product Users Among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer Before and After August 8, 2020[1]



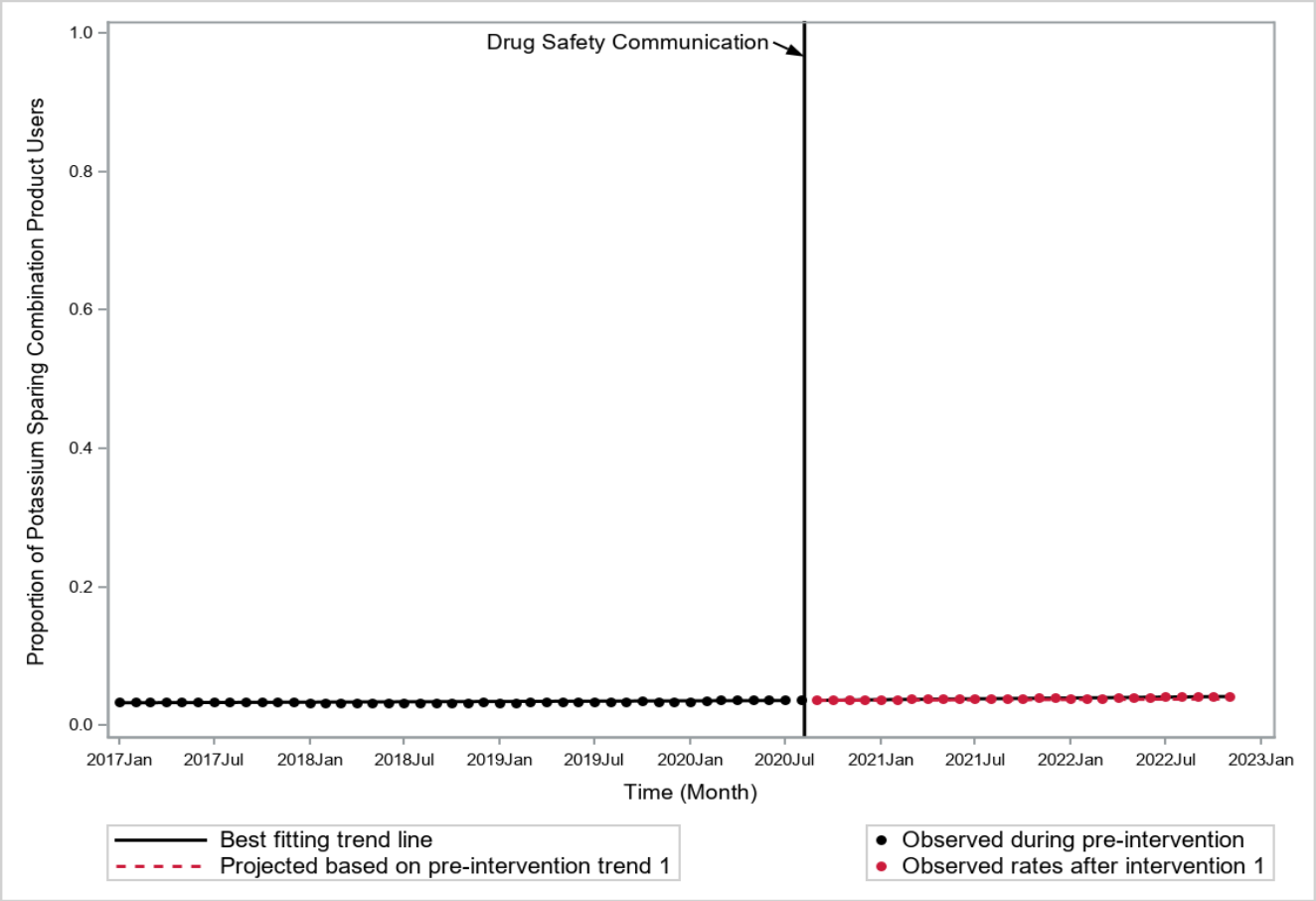
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 15. Proportion of Loop Diuretics Combination Product Users Among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer Before and After August 8, 2020[1]



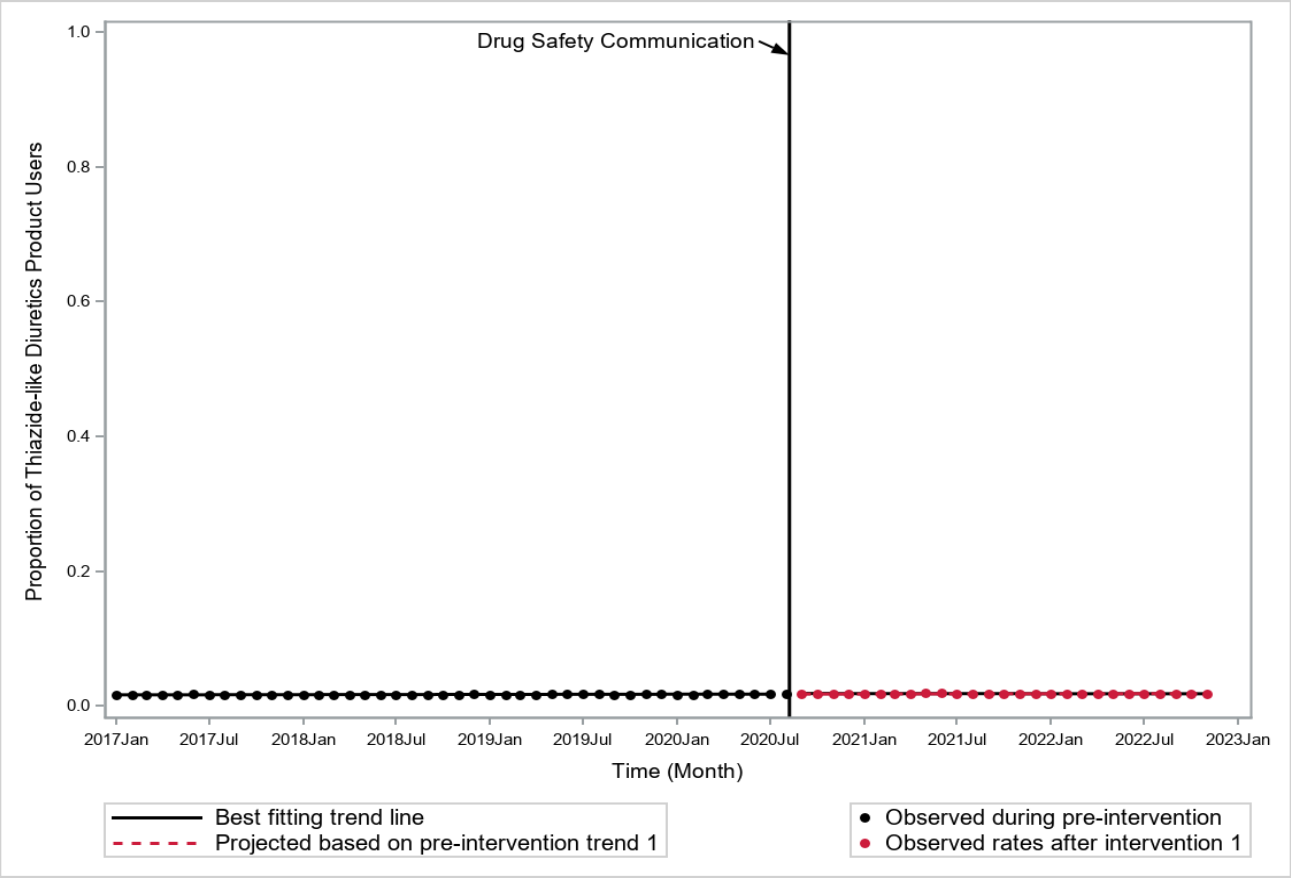
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 16. Proportion of Potassium Sparing Combination Product Users Among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer Before and After August 8, 2020[1]



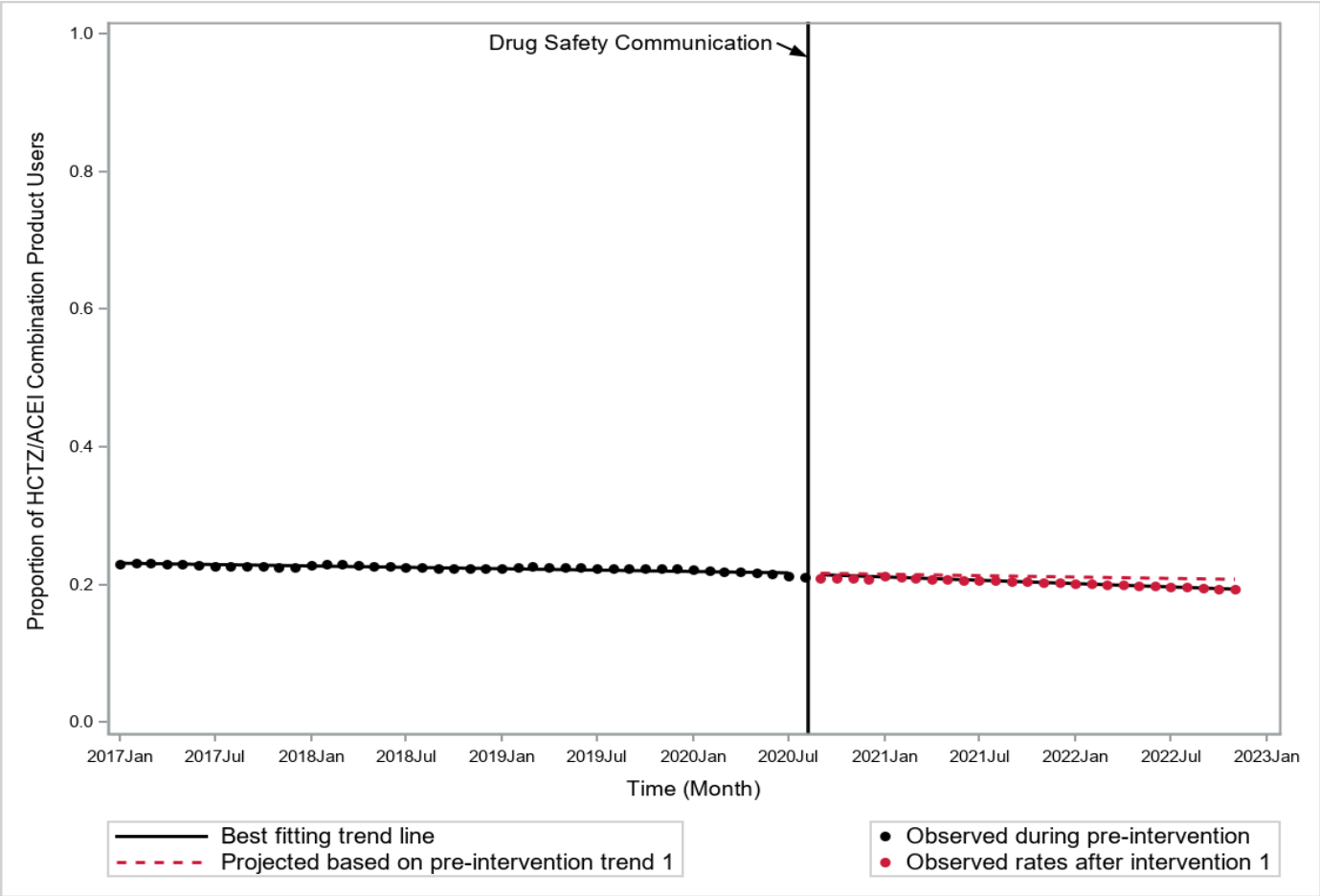
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 17. Proportion of Thiazide-like Diuretics Product Users Among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with history of skin cancer Before and After August 8, 2020[1]



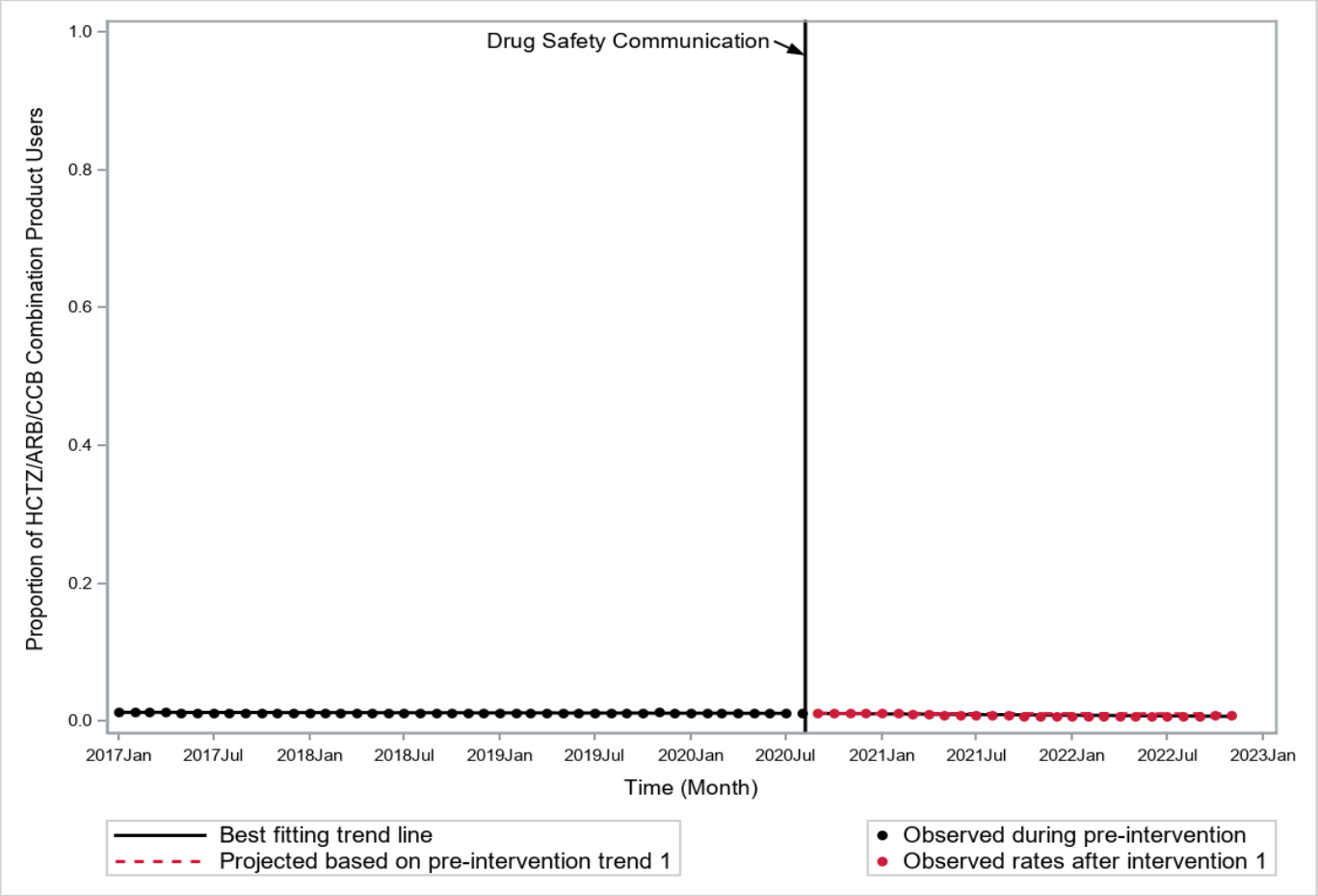
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 18. Proportion of HCTZ/ACEI Combination Product Users Among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer Before and After August 8, 2020[1]



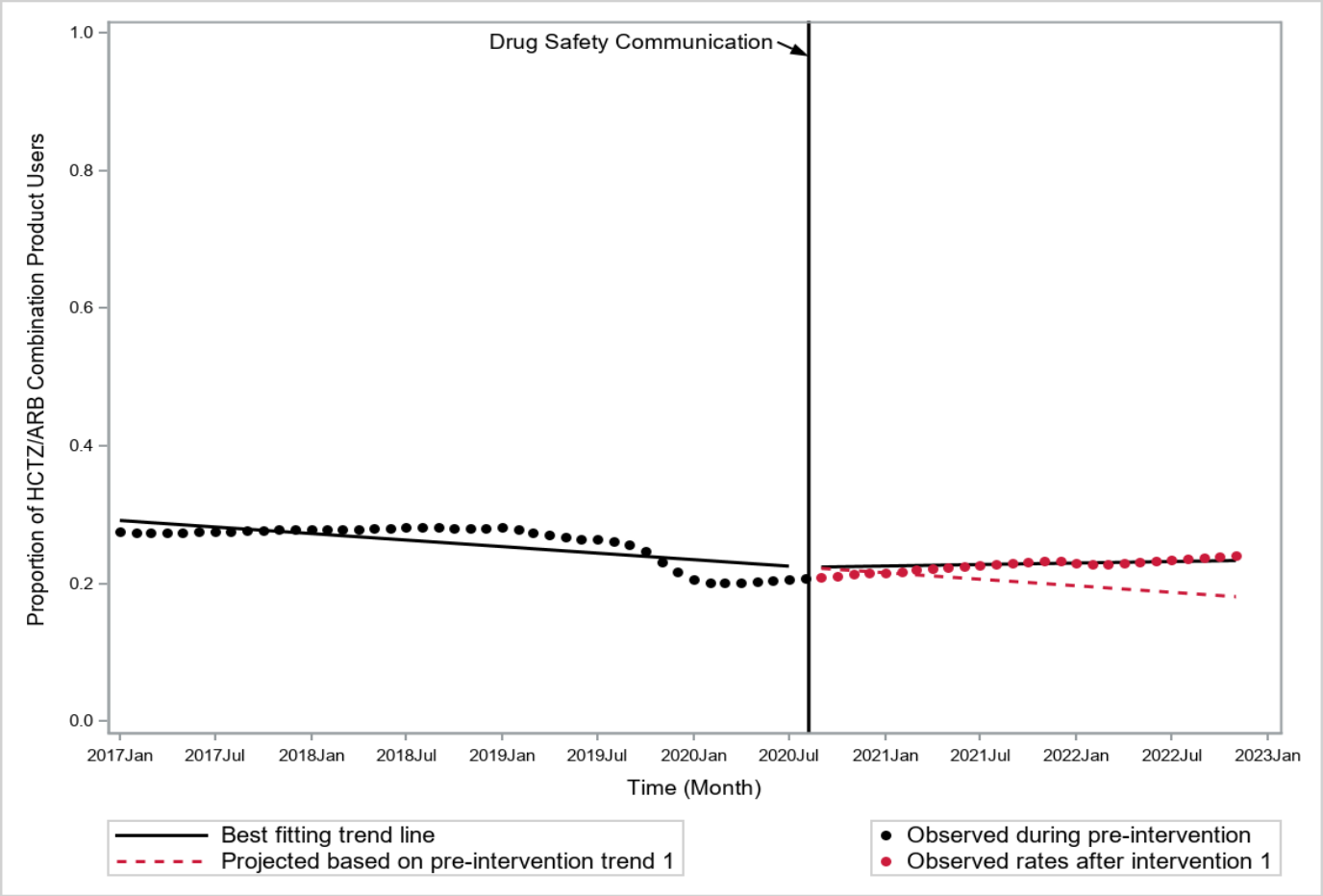
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 19. Proportion of HCTZ/ARB/CCB Combination Product Users Among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer Before and After August 8, 2020[1]



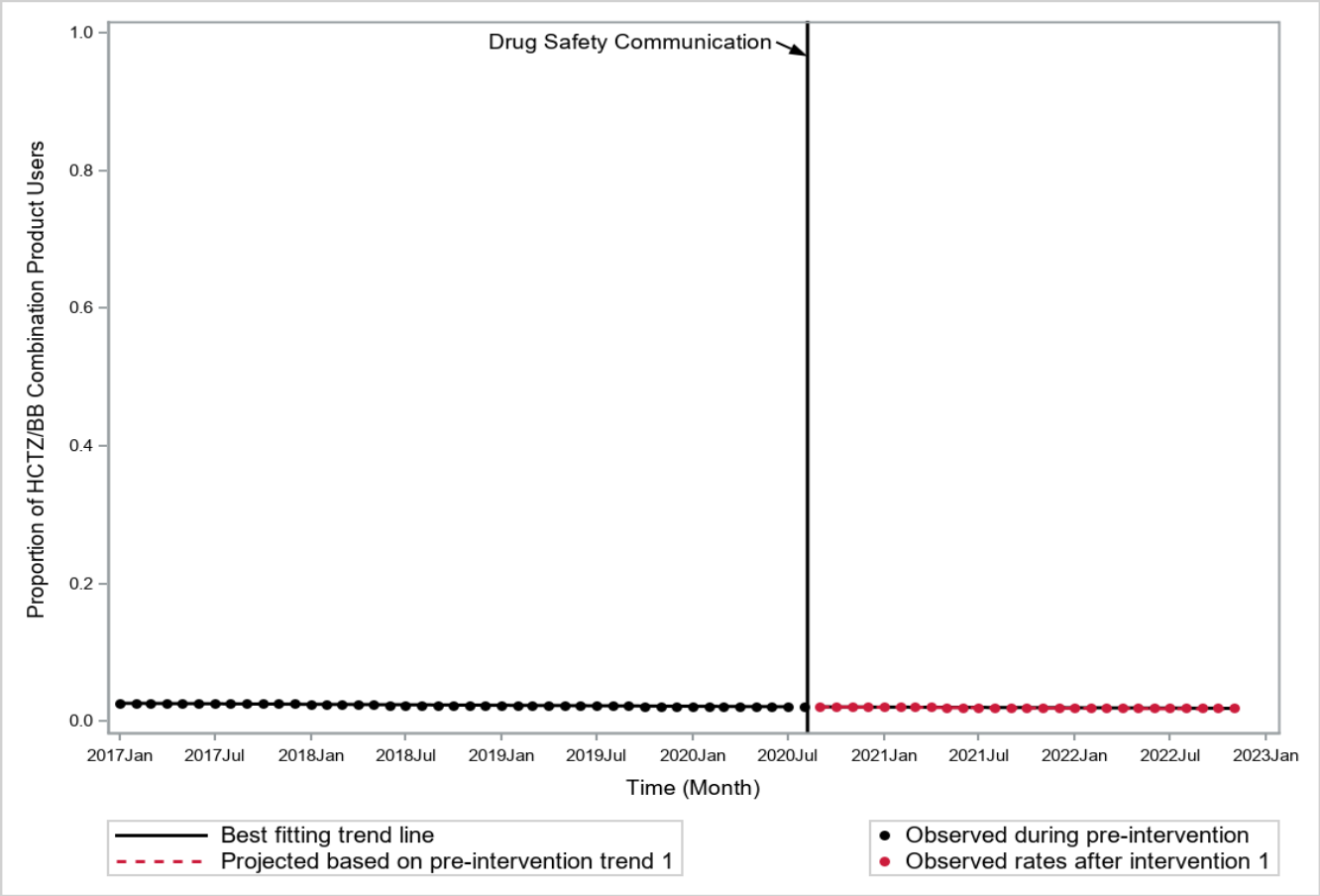
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 20. Proportion of HCTZ/ARB Combination Product Users Among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer Before and After August 8, 2020[1]



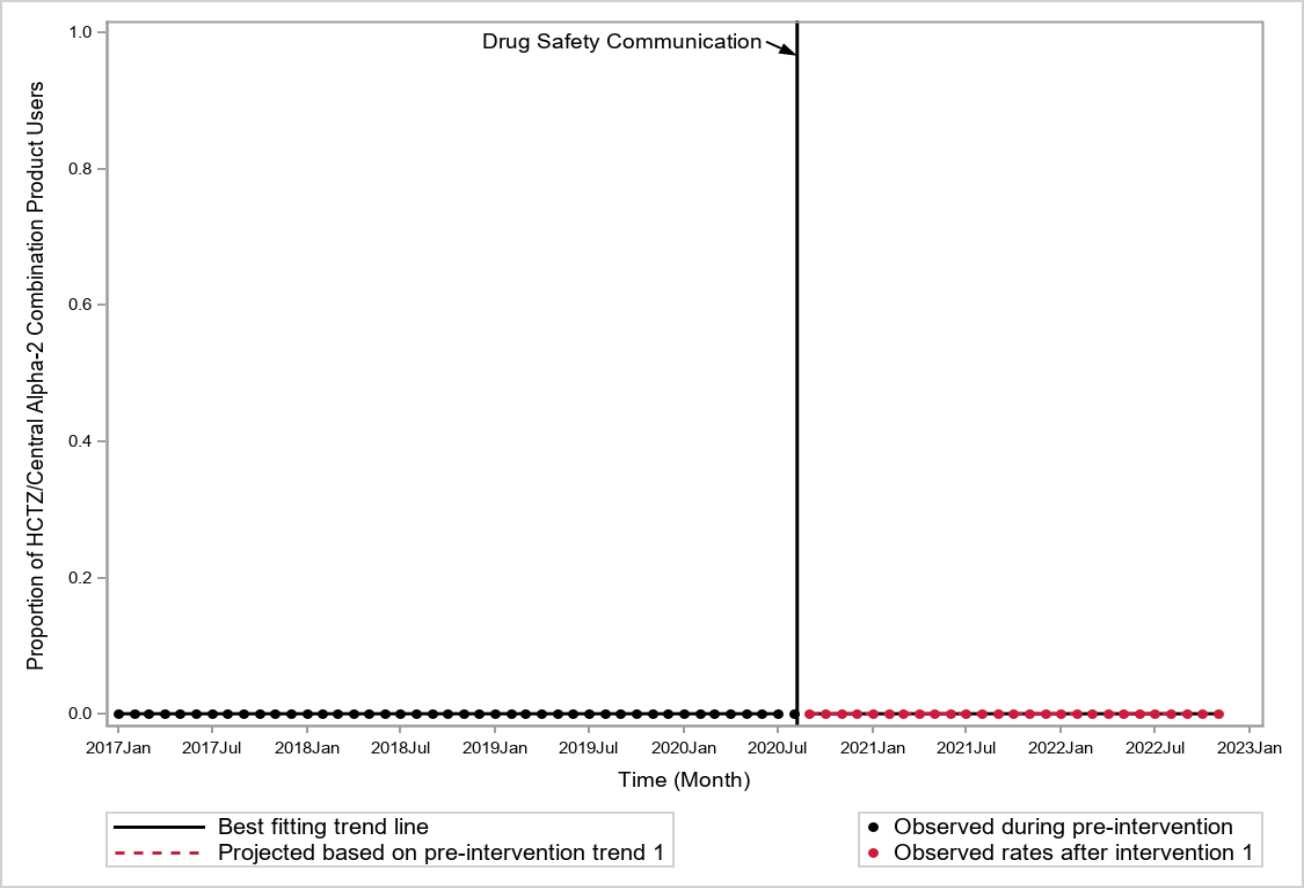
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 21. Proportion of HCTZ/BB Combination Product Users Among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer Before and After August 8, 2020[1]



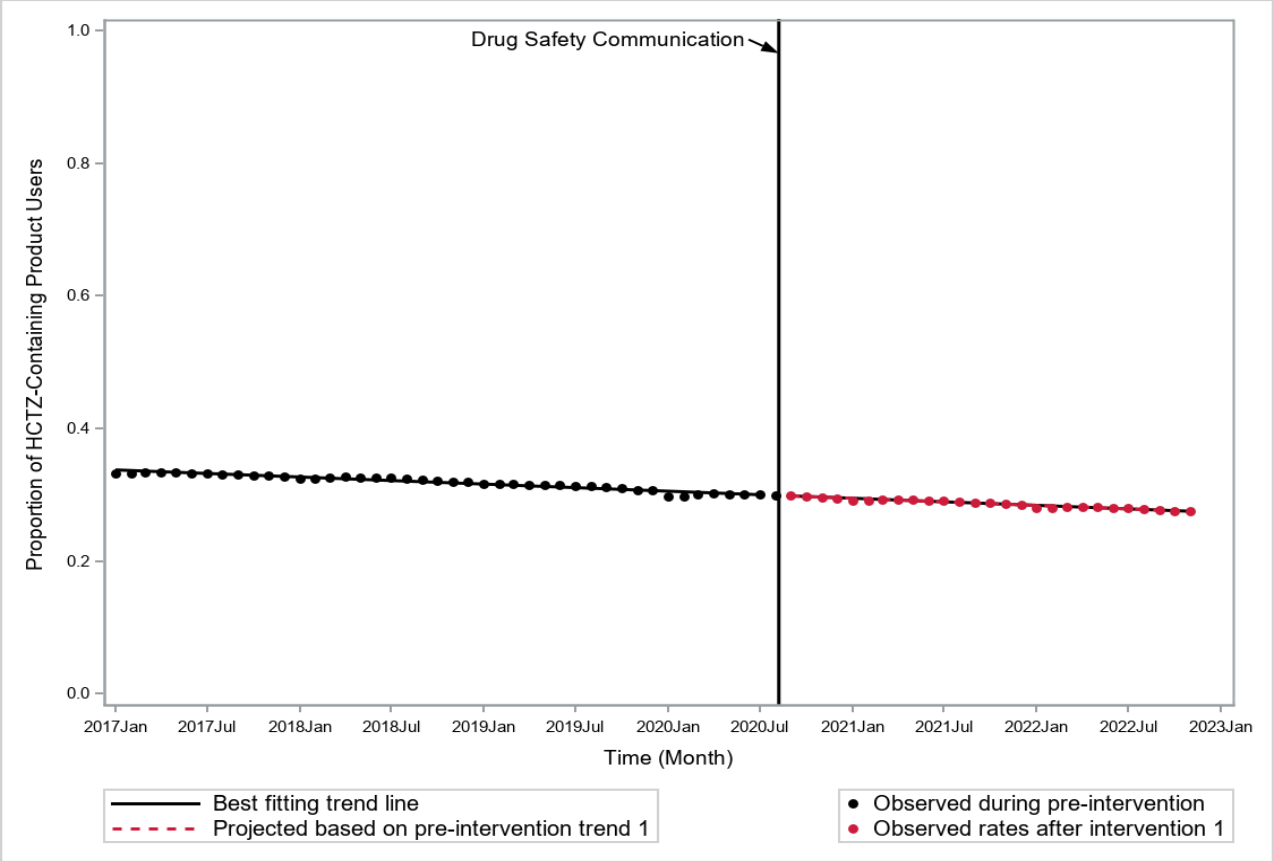
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 22. Proportion of HCTZ/Central Alpha-2 Combination Product Users Among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer Before and After August 8, 2020[1]



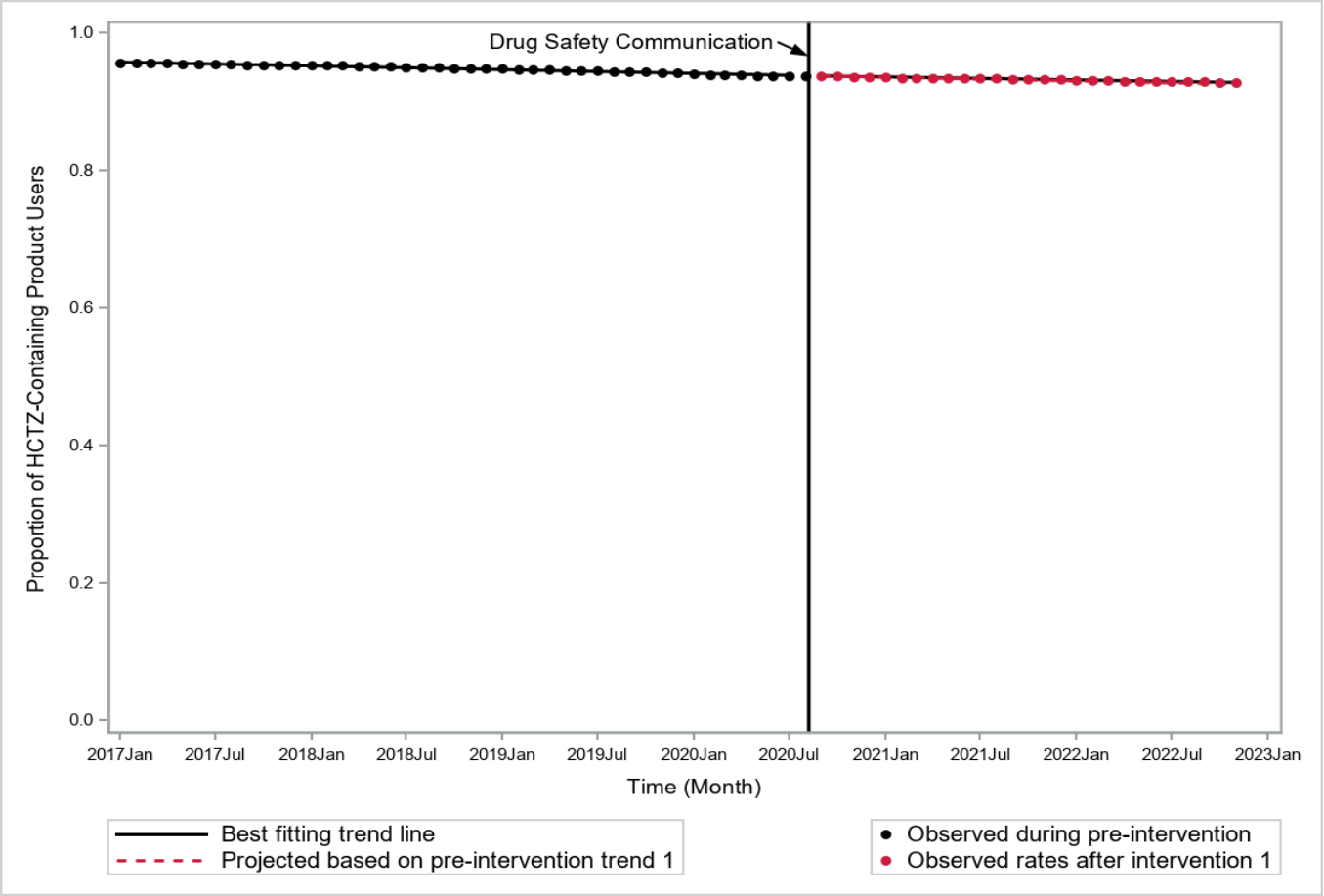
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 23. Proportion of HCTZ-Containing Product Users Among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer Before and After August 8, 2020[1]



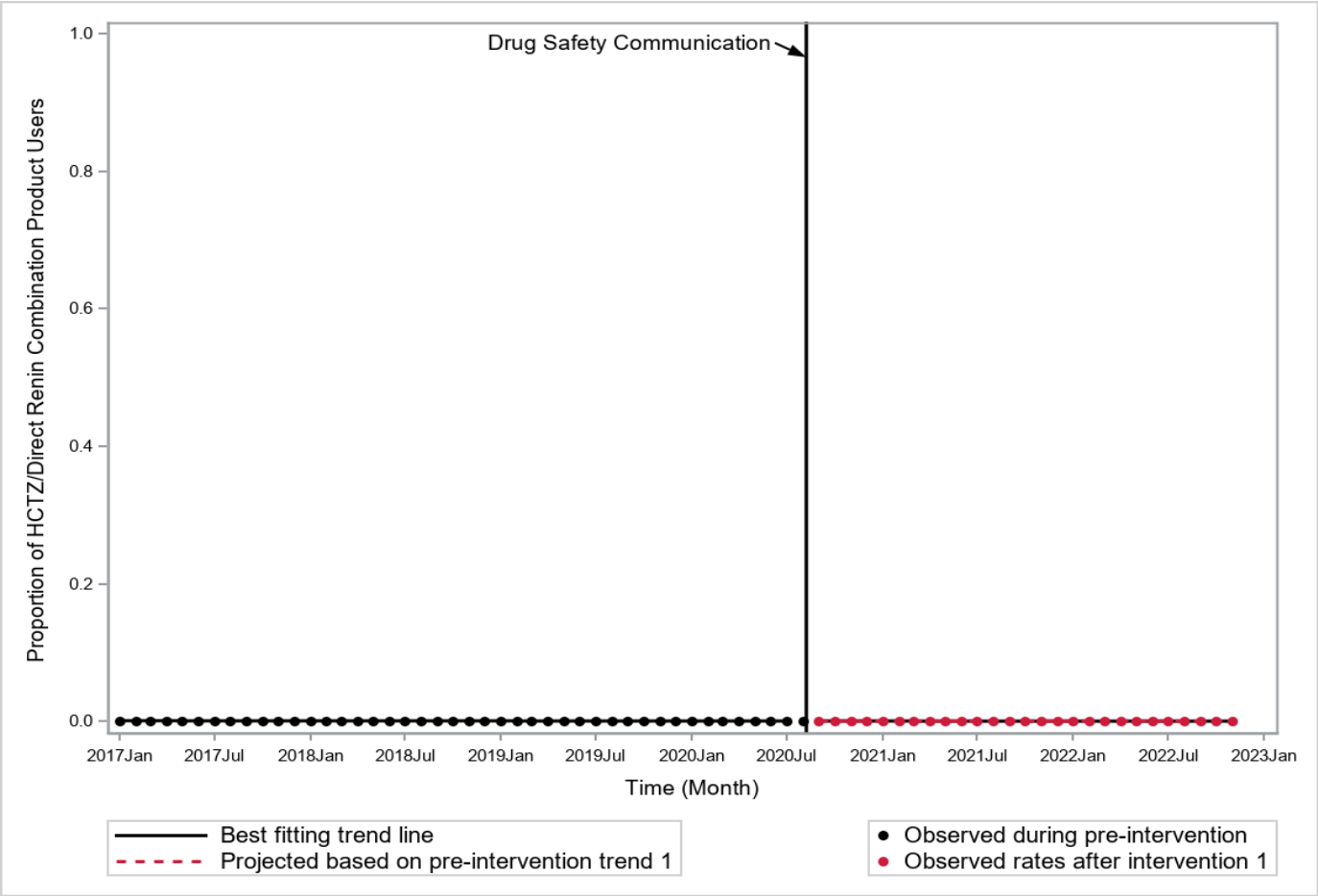
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 24. Proportion of HCTZ-Containing Product Users Among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer Before and After August 8, 2020[1]



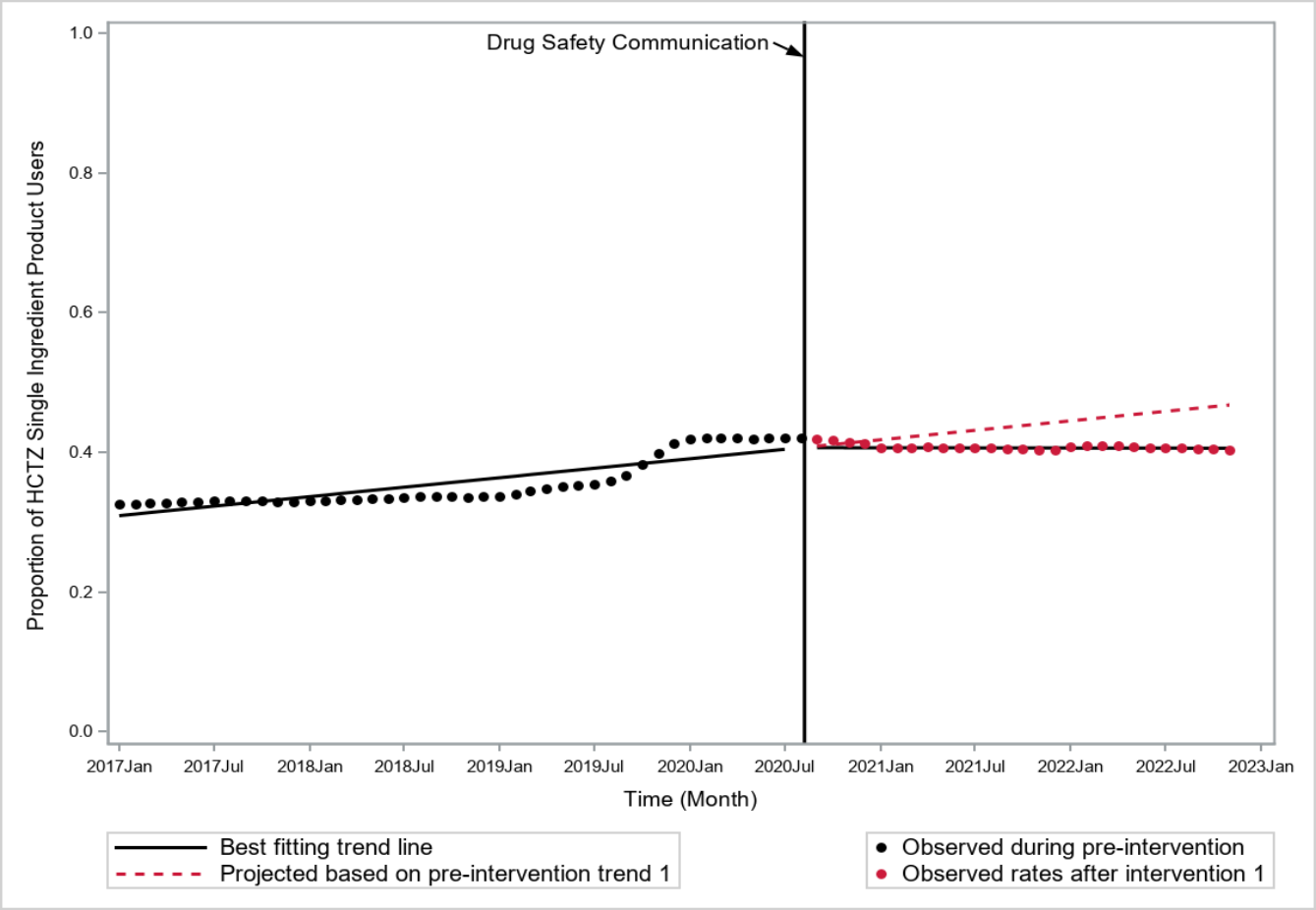
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 25. Proportion of HCTZ/Direct Renin Combination Product Users Among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer Before and After August 8, 2020[1]



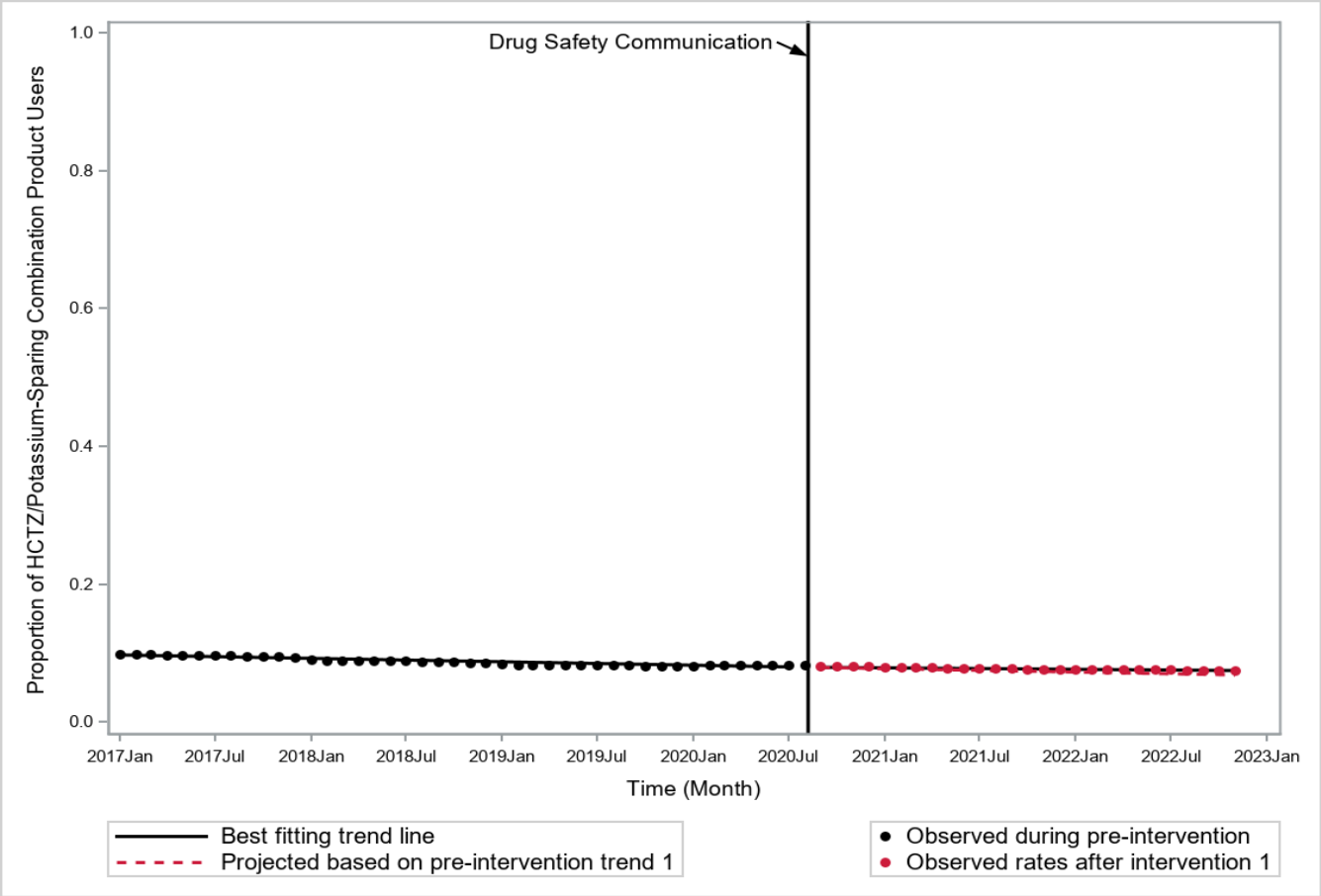
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 26. Proportion of HCTZ Single Ingredient Product Users Among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer Before and After August 8, 2020[1]



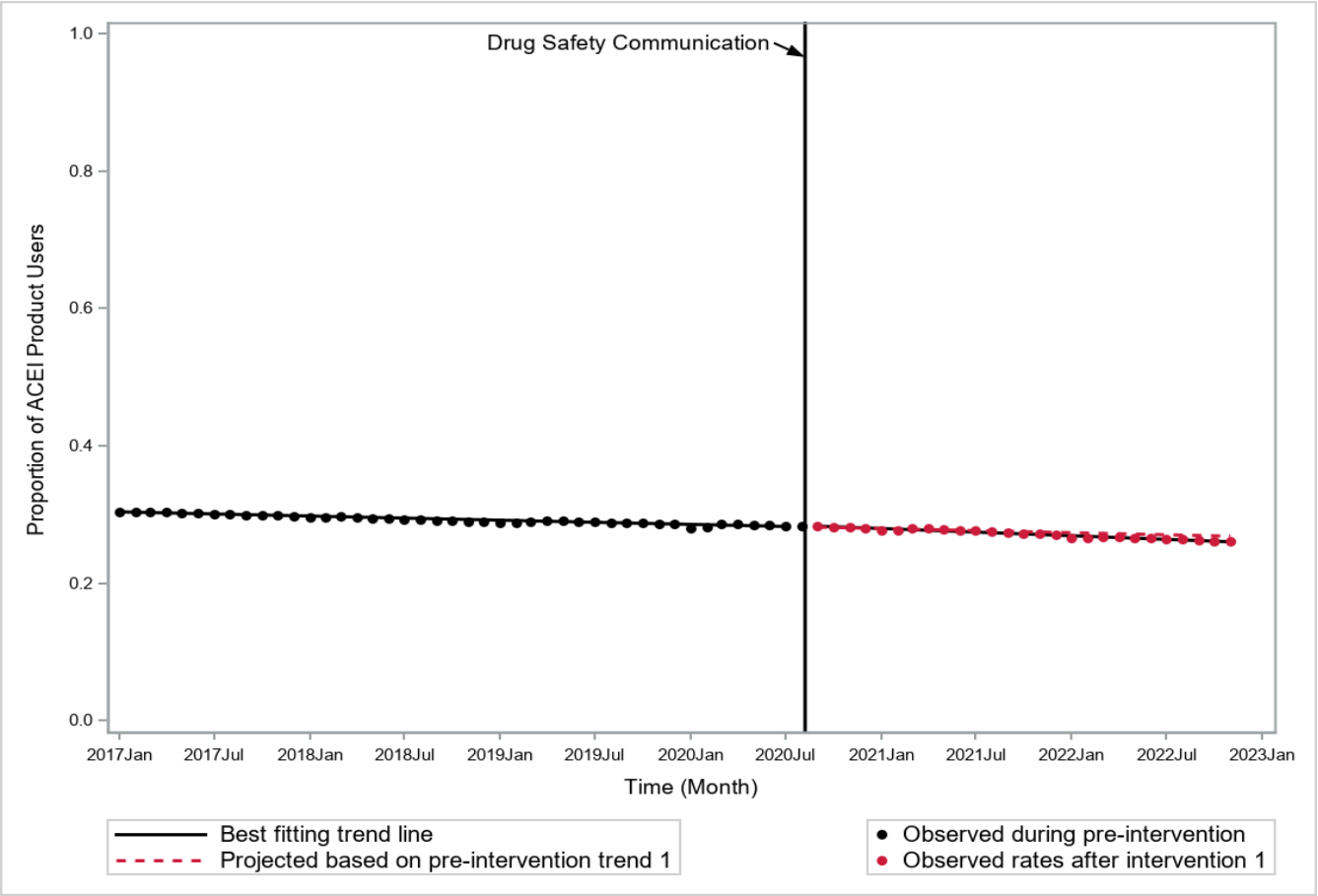
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 27. Proportion of HCTZ/Potassium-Sparing Combination Product Users Among Number of patients with use of HCTZ-containing products or thiazide-like diuretics with no history of skin cancer Before and After August 8, 2020[1]



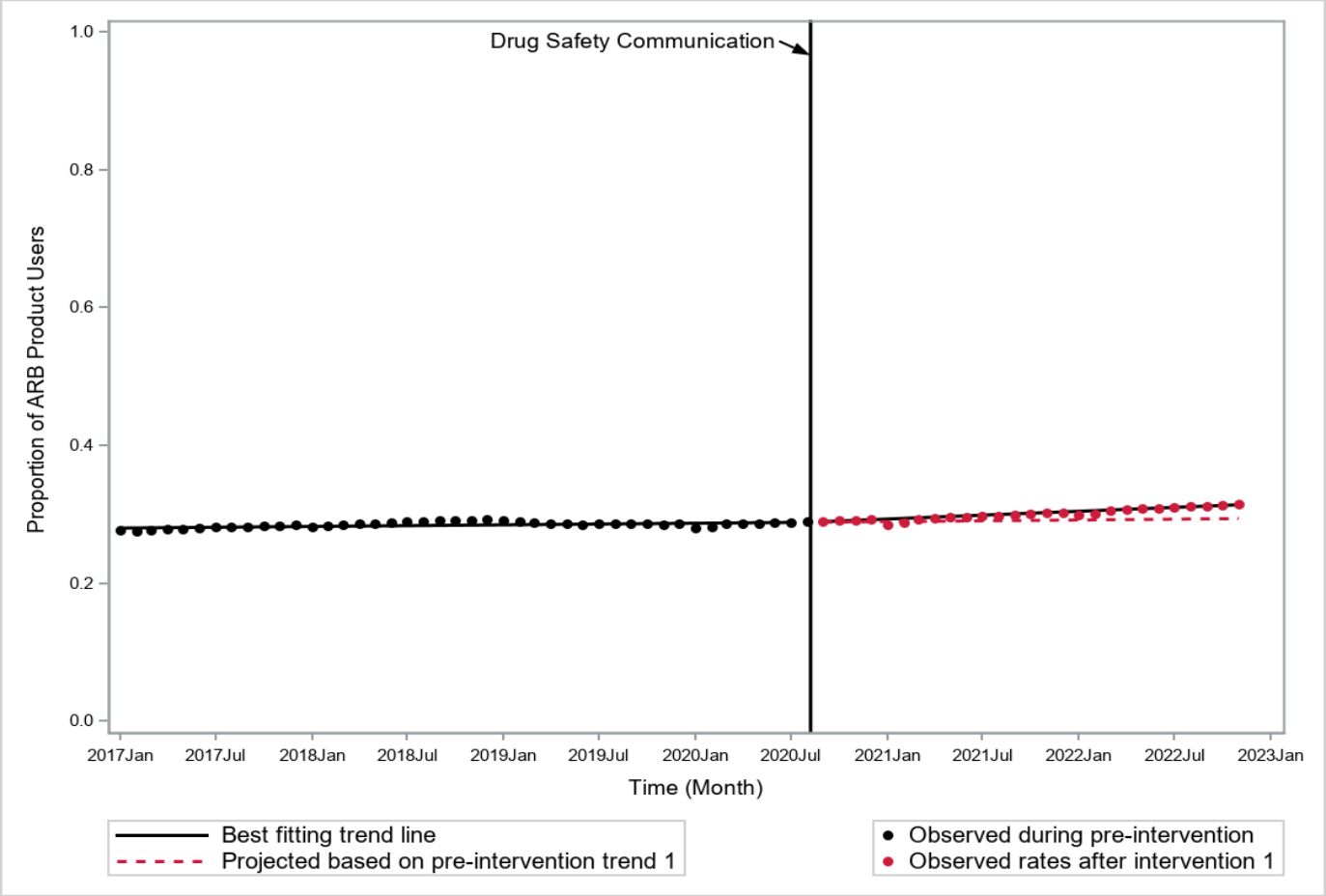
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 28. Proportion of ACEI Product Users Among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer Before and After August 8, 2020[1]



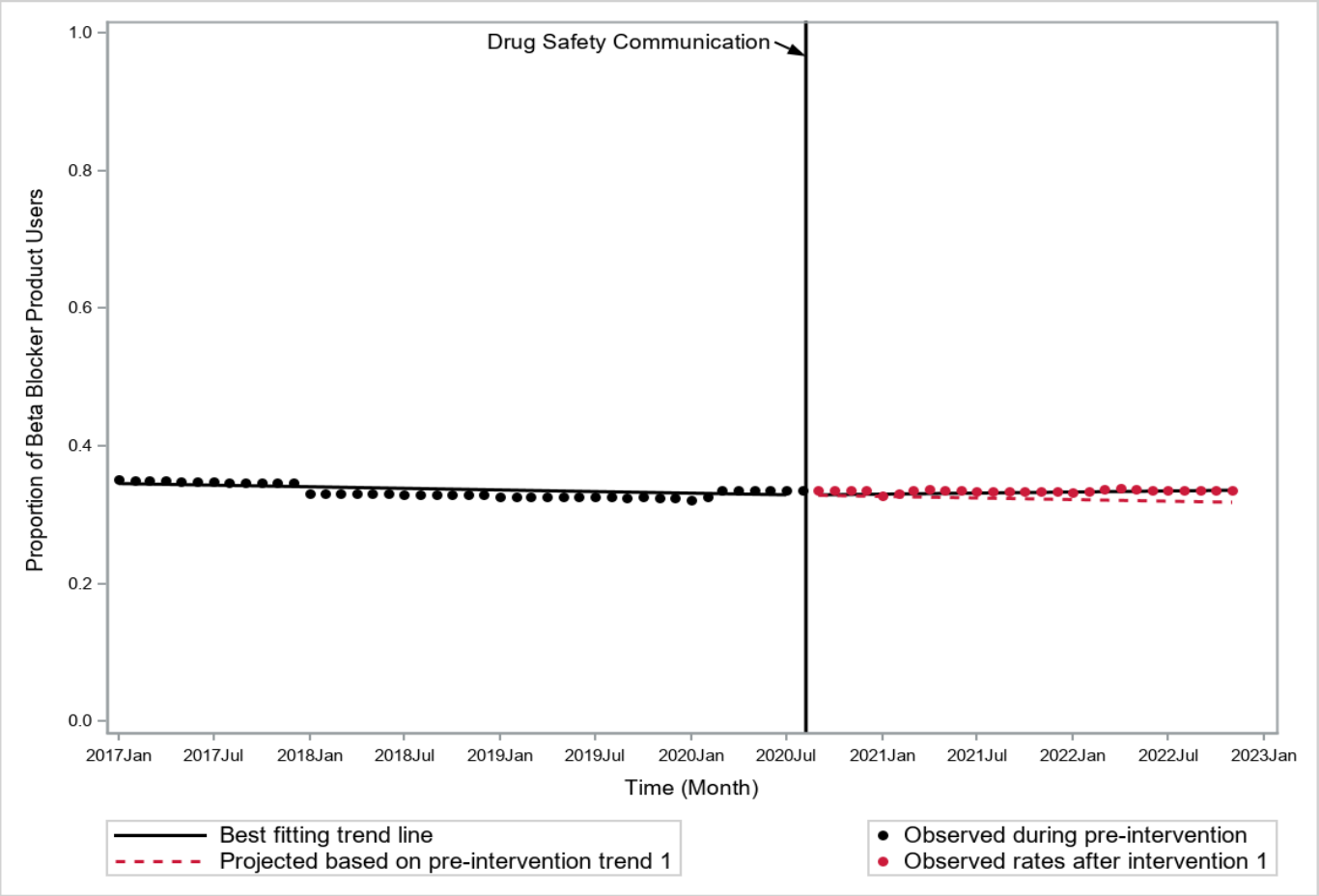
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 29. Proportion of ARB Product Users Among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer Before and After August 8, 2020[1]



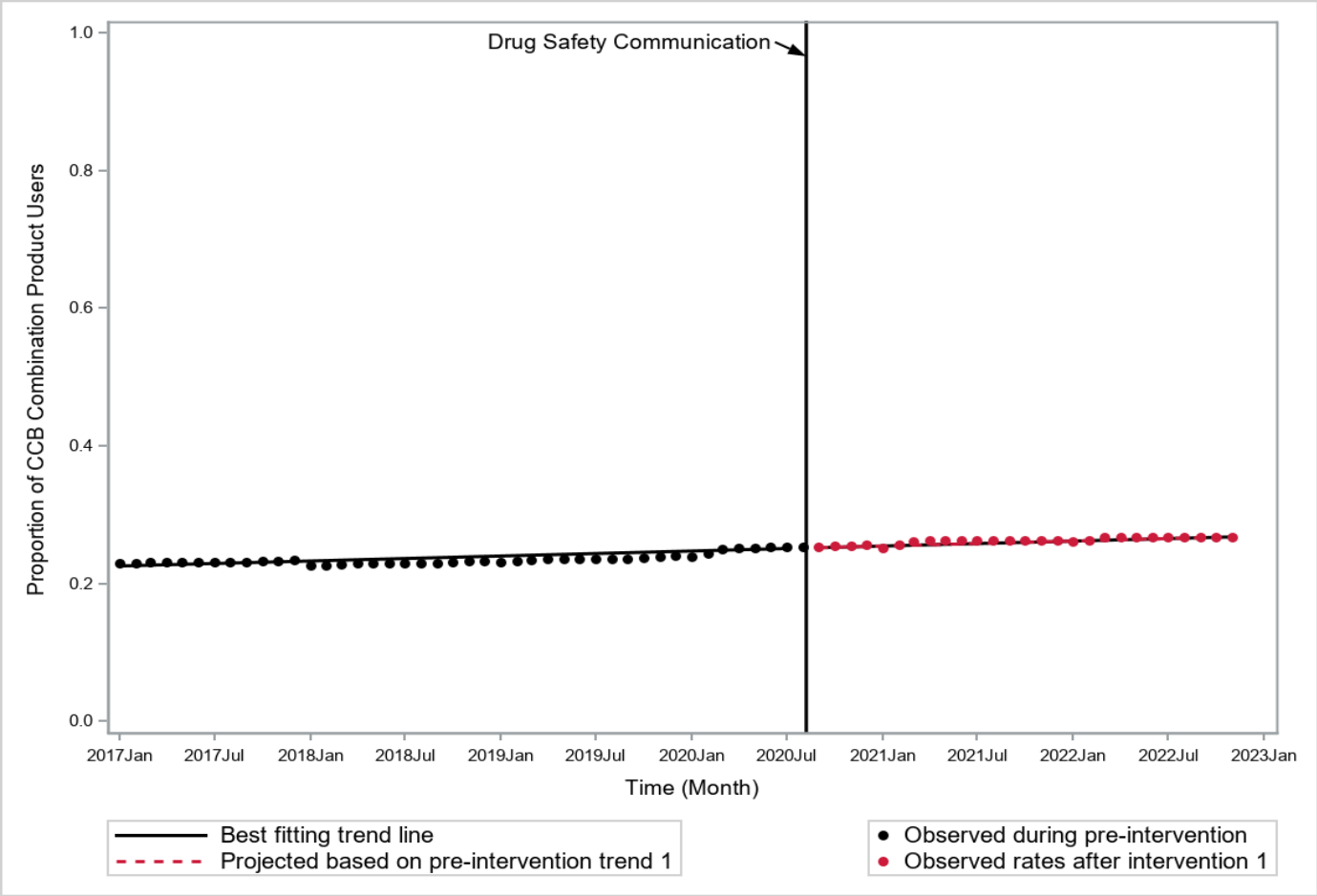
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 30. Proportion of Beta Blocker Product Users Among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer Before and After August 8, 2020[1]



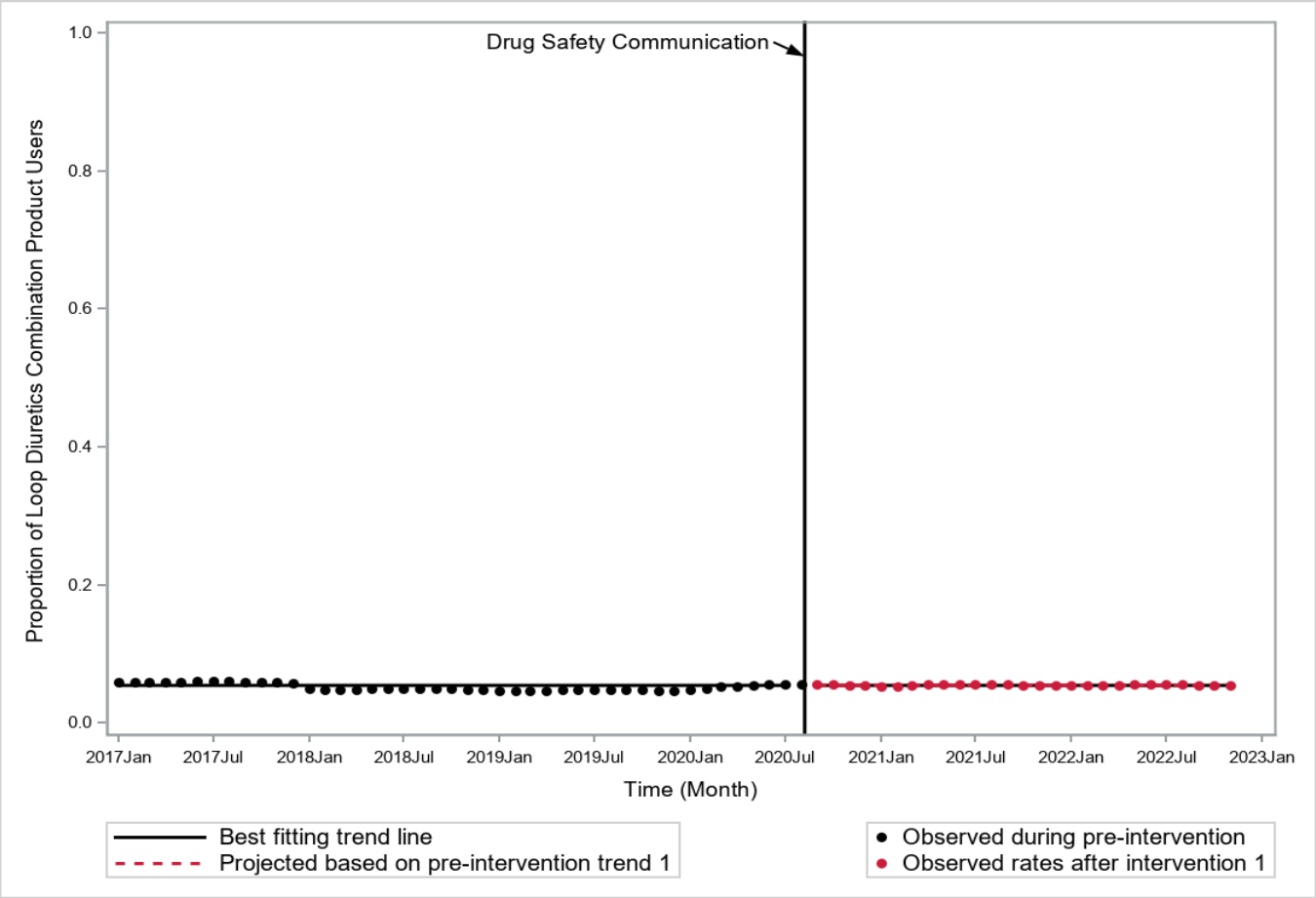
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 31. Proportion of CCB Combination Product Users Among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer Before and After August 8, 2020[1]



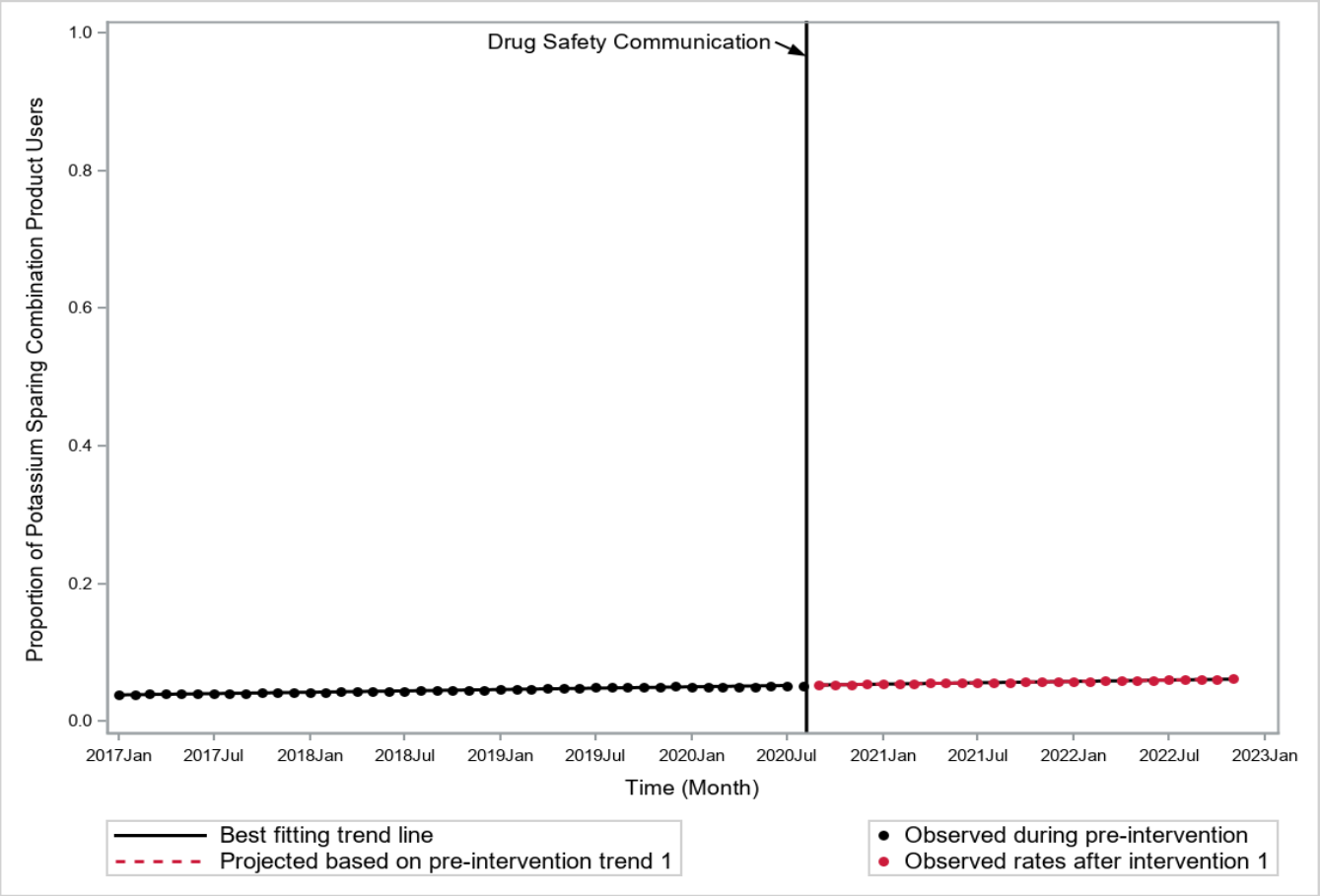
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 32. Proportion of Loop Diuretics Combination Product Users Among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer Before and After August 8, 2020[1]



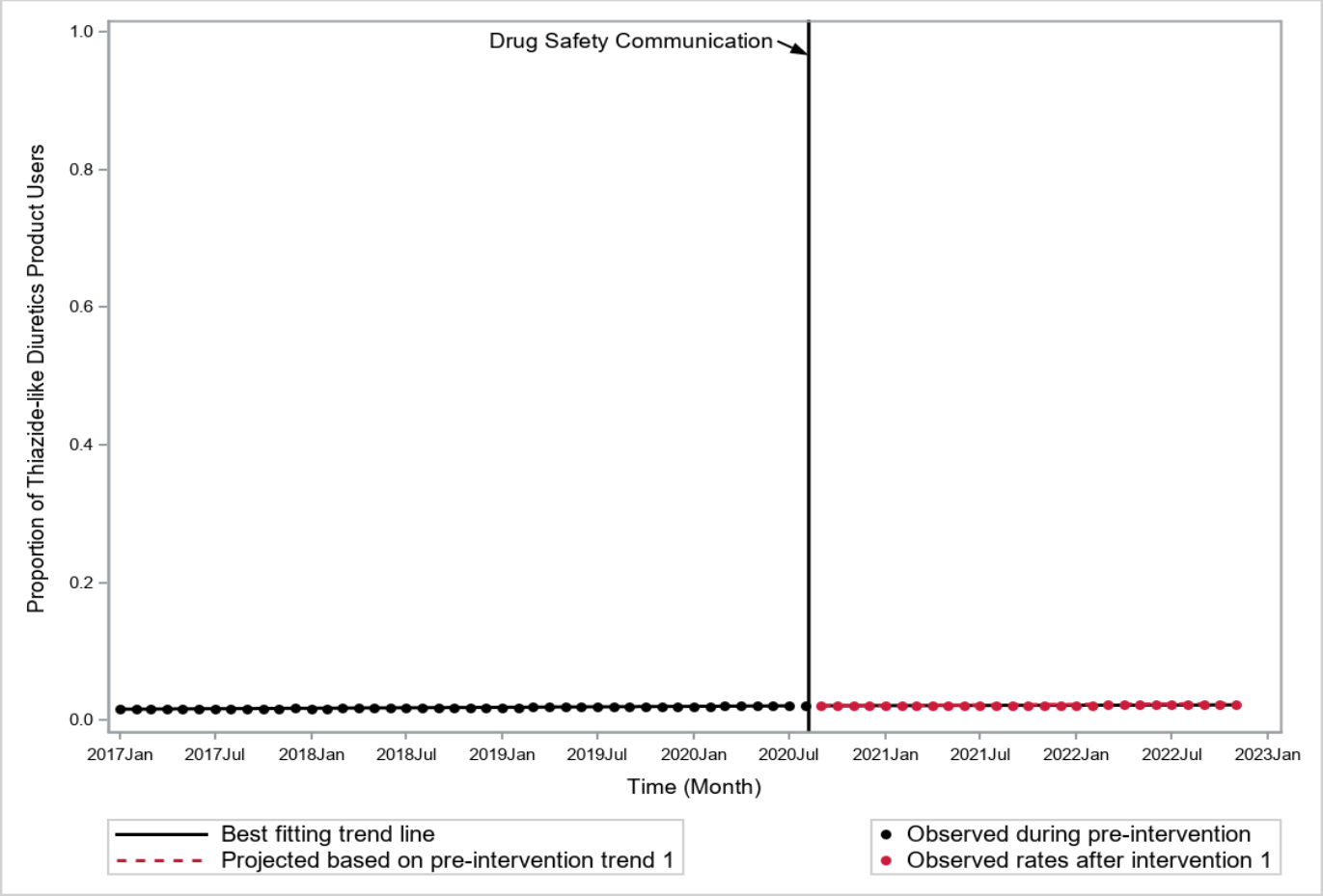
[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 33. Proportion of Potassium Sparing Combination Product Users Among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer Before and After August 8, 2020[1]



[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Figure 34. Proportion of Thiazide-like Diuretics Product Users Among Number of patients with use of HCTZ-containing products or any diuretics or any antihypertensives with no history of skin cancer Before and After August 8, 2020[1]



[1]The ITS model is performed with rounding to the nearest subsequent month for August 8, 2020 as the start of Drug Safety Communication. Data from January 1, 2017 to November 30, 2022 is used to create the model.

Appendix A. Dates of Available Data for Each Data Partner (DP) as of Request Distribution Date (August 30, 2023)

Masked DP ID	DP Start Date	DP End Date[1]
DP01	01/01/2010	12/31/2022

[1]End Date represents the earliest of: (1) query end date, or (2) last day of the most recent month for which all of a Data Partner's data tables (enrollment, dispensing, etc.) have at least 80% of the record count relative to the prior month.

Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name	Brand Name
HCTZ single ingredient/monotherapy	
hydrochlorothiazide	hydrochlorothiazide
hydrochlorothiazide	Microzide
HCTZ combination products	
benazepril HCl/hydrochlorothiazide	benazepril-hydrochlorothiazide
benazepril HCl/hydrochlorothiazide	Lotensin HCT
captopril/hydrochlorothiazide	captopril-hydrochlorothiazide
enalapril maleate/hydrochlorothiazide	enalapril-hydrochlorothiazide
enalapril maleate/hydrochlorothiazide	Vaseretic
fosinopril sodium/hydrochlorothiazide	fosinopril-hydrochlorothiazide
lisinopril/hydrochlorothiazide	lisinopril-hydrochlorothiazide
lisinopril/hydrochlorothiazide	Zestoretic
moexipril HCl/hydrochlorothiazide	moexipril-hydrochlorothiazide
quinapril HCl/hydrochlorothiazide	Accuretic
quinapril HCl/hydrochlorothiazide	quinapril-hydrochlorothiazide
amlodipine besylate/valsartan/hydrochlorothiazide	amlodipine-valsartan-hcthiazid
amlodipine besylate/valsartan/hydrochlorothiazide	Exforge HCT
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide	olmesartan-amlodipin-hcthiazid
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide	Tribenzor
candesartan cilexetil/hydrochlorothiazide	Atacand HCT
candesartan cilexetil/hydrochlorothiazide	candesartan-hydrochlorothiazid
irbesartan/hydrochlorothiazide	Avalide
irbesartan/hydrochlorothiazide	irbesartan-hydrochlorothiazide
losartan potassium/hydrochlorothiazide	Hyzaar
losartan potassium/hydrochlorothiazide	losartan-hydrochlorothiazide
olmesartan medoxomil/hydrochlorothiazide	Benicar HCT
olmesartan medoxomil/hydrochlorothiazide	olmesartan-hydrochlorothiazide
telmisartan/hydrochlorothiazide	Micardis HCT
telmisartan/hydrochlorothiazide	telmisartan-hydrochlorothiazid
valsartan/hydrochlorothiazide	Diovan HCT
valsartan/hydrochlorothiazide	valsartan-hydrochlorothiazide
bisoprolol fumarate/hydrochlorothiazide	bisoprolol-hydrochlorothiazide
bisoprolol fumarate/hydrochlorothiazide	Ziac
metoprolol succinate/hydrochlorothiazide	Dutoprol
metoprolol succinate/hydrochlorothiazide	metoprolol su-hydrochlorothiaz
metoprolol tartrate/hydrochlorothiazide	metoprolol ta-hydrochlorothiaz
propranolol HCl/hydrochlorothiazide	propranolol-hydrochlorothiazid
methyldopa/hydrochlorothiazide	methyldopa-hydrochlorothiazide
aliskiren hemifumarate/hydrochlorothiazide	Tekturna HCT
amiloride HCl/hydrochlorothiazide	amiloride-hydrochlorothiazide

Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name	Brand Name
spironolactone/hydrochlorothiazide	Aldactazide
spironolactone/hydrochlorothiazide	spironolacton-hydrochlorothiaz
triamterene/hydrochlorothiazide	Dyazide
triamterene/hydrochlorothiazide	Maxzide
triamterene/hydrochlorothiazide	Maxzide-25mg
triamterene/hydrochlorothiazide	triamterene-hydrochlorothiazid
HCTZ ACE inhibitor combination	
benazepril HCl/hydrochlorothiazide	benazepril-hydrochlorothiazide
benazepril HCl/hydrochlorothiazide	Lotensin HCT
captopril/hydrochlorothiazide	captopril-hydrochlorothiazide
enalapril maleate/hydrochlorothiazide	enalapril-hydrochlorothiazide
enalapril maleate/hydrochlorothiazide	Vaseretic
fosinopril sodium/hydrochlorothiazide	fosinopril-hydrochlorothiazide
lisinopril/hydrochlorothiazide	lisinopril-hydrochlorothiazide
lisinopril/hydrochlorothiazide	Zestoretic
moexipril HCl/hydrochlorothiazide	moexipril-hydrochlorothiazide
quinapril HCl/hydrochlorothiazide	Accuretic
quinapril HCl/hydrochlorothiazide	quinapril-hydrochlorothiazide
HCTZ ARB combination	
amlodipine besylate/valsartan/hydrochlorothiazide	amlodipine-valsartan-hcthiazid
candesartan cilexetil/hydrochlorothiazide	Atacand HCT
candesartan cilexetil/hydrochlorothiazide	candesartan-hydrochlorothiazid
irbesartan/hydrochlorothiazide	Avalide
irbesartan/hydrochlorothiazide	irbesartan-hydrochlorothiazide
losartan potassium/hydrochlorothiazide	Hyzaar
losartan potassium/hydrochlorothiazide	losartan-hydrochlorothiazide
olmesartan medoxomil/hydrochlorothiazide	Benicar HCT
olmesartan medoxomil/hydrochlorothiazide	olmesartan-hydrochlorothiazide
telmisartan/hydrochlorothiazide	Micardis HCT
telmisartan/hydrochlorothiazide	telmisartan-hydrochlorothiazid
valsartan/hydrochlorothiazide	Diovan HCT
valsartan/hydrochlorothiazide	valsartan-hydrochlorothiazide
HCTZ potassium sparing diuretics combination	
amiloride HCl/hydrochlorothiazide	amiloride-hydrochlorothiazide
spironolactone/hydrochlorothiazide	Aldactazide
spironolactone/hydrochlorothiazide	spironolacton-hydrochlorothiaz
triamterene/hydrochlorothiazide	Dyazide
triamterene/hydrochlorothiazide	Maxzide
triamterene/hydrochlorothiazide	Maxzide-25mg
triamterene/hydrochlorothiazide	triamterene-hydrochlorothiazid
HCTZ beta blocker combination	
bisoprolol fumarate/hydrochlorothiazide	bisoprolol-hydrochlorothiazide

Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name	Brand Name
bisoprolol fumarate/hydrochlorothiazide	Ziac
metoprolol succinate/hydrochlorothiazide	Dutoprol
metoprolol succinate/hydrochlorothiazide	metoprolol su-hydrochlorothiaz
metoprolol tartrate/hydrochlorothiazide	metoprolol ta-hydrochlorothiaz
propranolol HCl/hydrochlorothiazide	propranolol-hydrochlorothiazid
HCTZ ARB calcium channel blocker combination	
amlodipine besylate/valsartan/hydrochlorothiazide	amlodipine-valsartan-hcthiazid
amlodipine besylate/valsartan/hydrochlorothiazide	Exforge HCT
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide	olmesartan-amlodipin-hcthiazid
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide	Tribenzor
Chlorothiazide, Bendroflumethiazide, or Thiazide-like diuretics	
chlorthalidone	chlorthalidone
chlorthalidone	Thalitone
indapamide	indapamide
metolazone	metolazone
chlorothiazide	chlorothiazide
chlorothiazide	Diuril
nadolol/bendroflumethiazide	Corzide
nadolol/bendroflumethiazide	nadolol-bendroflumethiazide
Chlorothiazide	
chlorothiazide	chlorothiazide
chlorothiazide	Diuril
Bendroflumethiazide	
nadolol/bendroflumethiazide	Corzide
nadolol/bendroflumethiazide	nadolol-bendroflumethiazide
Thiazide-like diuretics	
chlorthalidone	chlorthalidone
chlorthalidone	Thalitone
indapamide	indapamide
metolazone	metolazone
ACE inhibitors	
amlodipine besylate/benazepril HCl	amlodipine-benazepril
amlodipine besylate/benazepril HCl	Lotrel
benazepril HCl	benazepril
benazepril HCl	Lotensin
captopril	captopril
enalapril maleate	enalapril maleate
enalapril maleate	Epaned
enalapril maleate	Vasotec
fosinopril sodium	fosinopril

Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name	Brand Name
lisinopril	lisinopril
lisinopril	Prinivil
lisinopril	Qbrelis
lisinopril	Zestril
moexipril HCl	moexipril
perindopril arginine/amlodipine besylate	Prestalia
perindopril erbumine	Aceon
perindopril erbumine	perindopril erbumine
quinapril HCl	Accupril
quinapril HCl	quinapril
ramipril	Altace
ramipril	ramipril
trandolapril	Mavik
trandolapril	trandolapril
trandolapril/verapamil HCl	Tarka
trandolapril/verapamil HCl	trandolapril-verapamil
Calcium channel blockers	
amlodipine benzoate	Katerzia
amlodipine besylate	amlodipine
amlodipine besylate	Norliqva
amlodipine besylate	Norvasc
amlodipine besylate/celecoxib	Consensi
diltiazem HCl	Cardizem
diltiazem HCl	Cardizem CD
diltiazem HCl	Cardizem LA
diltiazem HCl	Cartia XT
diltiazem HCl	diltiazem HCl
diltiazem HCl	DILT-XR
diltiazem HCl	Matzim LA
diltiazem HCl	Taztia XT
diltiazem HCl	Tiadylt ER
diltiazem HCl	Tiazac
felodipine	felodipine
isradipine	isradipine
levamlodipine maleate	Conjupri
levamlodipine maleate	levamlodipine
nicardipine HCl	nicardipine
nifedipine	Adalat CC
nifedipine	Afeditab CR
nifedipine	Nifedical XL
nifedipine	nifedipine
nifedipine	Procardia

Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name	Brand Name
nifedipine	Procardia XL
nimodipine	nimodipine
nimodipine	Nymalize
nisoldipine	nisoldipine
nisoldipine	Sular
verapamil HCl	Calan
verapamil HCl	Calan SR
verapamil HCl	verapamil
verapamil HCl	Verelan
verapamil HCl	Verelan PM
Potassium-sparing diuretics	
amiloride HCl	amiloride
eplerenone	eplerenone
eplerenone	Inspra
spironolactone	Aldactone
spironolactone	CaroSpir
spironolactone	spironolactone
triamterene	Dyrenium
triamterene	triamterene
Loop diuretics	
bumetanide	bumetanide
ethacrynic acid	Edecrin
ethacrynic acid	ethacrynic acid
furosemide	furosemide
furosemide	Lasix
torsemide	Demadex
torsemide	Soaanz
torsemide	torsemide
Limited denominator (any HCTZ-containing product, chlorothiazide, bendroflumethiazide or thiazide-like diuretics)	
aliskiren hemifumarate/hydrochlorothiazide	Tekturna HCT
amiloride HCl/hydrochlorothiazide	amiloride-hydrochlorothiazide
amlodipine besylate/valsartan/hydrochlorothiazide	amlodipine-valsartan-hcthiazid
amlodipine besylate/valsartan/hydrochlorothiazide	Exforge HCT
benazepril HCl/hydrochlorothiazide	benazepril-hydrochlorothiazide
benazepril HCl/hydrochlorothiazide	Lotensin HCT
bisoprolol fumarate/hydrochlorothiazide	bisoprolol-hydrochlorothiazide
bisoprolol fumarate/hydrochlorothiazide	Ziac
candesartan cilexetil/hydrochlorothiazide	Atacand HCT
candesartan cilexetil/hydrochlorothiazide	candesartan-hydrochlorothiazid
captopril/hydrochlorothiazide	captopril-hydrochlorothiazide

Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name	Brand Name
enalapril maleate/hydrochlorothiazide	enalapril-hydrochlorothiazide
enalapril maleate/hydrochlorothiazide	Vaseretic
fosinopril sodium/hydrochlorothiazide	fosinopril-hydrochlorothiazide
hydrochlorothiazide	hydrochlorothiazide
hydrochlorothiazide	Microzide
irbesartan/hydrochlorothiazide	Avalide
irbesartan/hydrochlorothiazide	irbesartan-hydrochlorothiazide
lisinopril/hydrochlorothiazide	lisinopril-hydrochlorothiazide
lisinopril/hydrochlorothiazide	Zestoretic
losartan potassium/hydrochlorothiazide	Hyzaar
losartan potassium/hydrochlorothiazide	losartan-hydrochlorothiazide
methyldopa/hydrochlorothiazide	methyldopa-hydrochlorothiazide
metoprolol succinate/hydrochlorothiazide	Dutoprol
metoprolol succinate/hydrochlorothiazide	metoprolol su-hydrochlorothiaz
metoprolol tartrate/hydrochlorothiazide	metoprolol ta-hydrochlorothiaz
moexipril HCl/hydrochlorothiazide	moexipril-hydrochlorothiazide
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide	olmesartan-amlodipin-hcthiazid
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide	Tribenzor
olmesartan medoxomil/hydrochlorothiazide	Benicar HCT
olmesartan medoxomil/hydrochlorothiazide	olmesartan-hydrochlorothiazide
propranolol HCl/hydrochlorothiazide	propranolol-hydrochlorothiazid
quinapril HCl/hydrochlorothiazide	Accuretic
quinapril HCl/hydrochlorothiazide	quinapril-hydrochlorothiazide
spironolactone/hydrochlorothiazide	Aldactazide
spironolactone/hydrochlorothiazide	spironolacton-hydrochlorothiaz
telmisartan/hydrochlorothiazide	Micardis HCT
telmisartan/hydrochlorothiazide	telmisartan-hydrochlorothiazid
triamterene/hydrochlorothiazide	Dyazide
triamterene/hydrochlorothiazide	Maxzide
triamterene/hydrochlorothiazide	Maxzide-25mg
triamterene/hydrochlorothiazide	triamterene-hydrochlorothiazid
valsartan/hydrochlorothiazide	Diovan HCT
valsartan/hydrochlorothiazide	valsartan-hydrochlorothiazide
chlorothiazide	chlorothiazide
chlorothiazide	Diuril
nadolol/bendroflumethiazide	Corzide
nadolol/bendroflumethiazide	nadolol-bendroflumethiazide
chlorthalidone	chlorthalidone
chlorthalidone	Thalitone
indapamide	indapamide

Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name	Brand Name
metolazone	metolazone
Full denominator (any HCTZ-containing products, any thiazide diuretics, any diuretics or any antihypertensives)	
aliskiren hemifumarate/hydrochlorothiazide	Tekturna HCT
amiloride HCl/hydrochlorothiazide	amiloride-hydrochlorothiazide
amlodipine besylate/valsartan/hydrochlorothiazide	amlodipine-valsartan-hcthiazid
amlodipine besylate/valsartan/hydrochlorothiazide	Exforge HCT
benazepril HCl/hydrochlorothiazide	benazepril-hydrochlorothiazide
benazepril HCl/hydrochlorothiazide	Lotensin HCT
bisoprolol fumarate/hydrochlorothiazide	bisoprolol-hydrochlorothiazide
bisoprolol fumarate/hydrochlorothiazide	Ziac
candesartan cilexetil/hydrochlorothiazide	Atacand HCT
candesartan cilexetil/hydrochlorothiazide	candesartan-hydrochlorothiazid
captopril/hydrochlorothiazide	captopril-hydrochlorothiazide
enalapril maleate/hydrochlorothiazide	enalapril-hydrochlorothiazide
enalapril maleate/hydrochlorothiazide	Vaseretic
fosinopril sodium/hydrochlorothiazide	fosinopril-hydrochlorothiazide
hydrochlorothiazide	hydrochlorothiazide
hydrochlorothiazide	Microzide
irbesartan/hydrochlorothiazide	Avalide
irbesartan/hydrochlorothiazide	irbesartan-hydrochlorothiazide
lisinopril/hydrochlorothiazide	lisinopril-hydrochlorothiazide
lisinopril/hydrochlorothiazide	Zestoretic
losartan potassium/hydrochlorothiazide	Hyzaar
losartan potassium/hydrochlorothiazide	losartan-hydrochlorothiazide
methyldopa/hydrochlorothiazide	methyldopa-hydrochlorothiazide
metoprolol succinate/hydrochlorothiazide	Dutoprol
metoprolol succinate/hydrochlorothiazide	metoprolol su-hydrochlorothiaz
metoprolol tartrate/hydrochlorothiazide	metoprolol ta-hydrochlorothiaz
moexipril HCl/hydrochlorothiazide	moexipril-hydrochlorothiazide
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide	olmesartan-amlodipin-hcthiazid
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide	Tribenzor
olmesartan medoxomil/hydrochlorothiazide	Benicar HCT
olmesartan medoxomil/hydrochlorothiazide	olmesartan-hydrochlorothiazide
propranolol HCl/hydrochlorothiazide	propranolol-hydrochlorothiazid
quinapril HCl/hydrochlorothiazide	Accuretic
quinapril HCl/hydrochlorothiazide	quinapril-hydrochlorothiazide
spironolactone/hydrochlorothiazide	Aldactazide
spironolactone/hydrochlorothiazide	spironolacton-hydrochlorothiaz

Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name	Brand Name
telmisartan/hydrochlorothiazide	Micardis HCT
telmisartan/hydrochlorothiazide	telmisartan-hydrochlorothiazid
triamterene/hydrochlorothiazide	Dyazide
triamterene/hydrochlorothiazide	Maxzide
triamterene/hydrochlorothiazide	Maxzide-25mg
triamterene/hydrochlorothiazide	triamterene-hydrochlorothiazid
valsartan/hydrochlorothiazide	Diovan HCT
valsartan/hydrochlorothiazide	valsartan-hydrochlorothiazide
chlorothiazide	chlorothiazide
chlorothiazide	Diuril
nadolol/bendroflumethiazide	Corzide
nadolol/bendroflumethiazide	nadolol-bendroflumethiazide
chlorthalidone	chlorthalidone
chlorthalidone	Thalitone
indapamide	indapamide
metolazone	metolazone
amlodipine besylate/benazepril HCl	amlodipine-benazepril
amlodipine besylate/benazepril HCl	Lotrel
benazepril HCl	benazepril
benazepril HCl	Lotensin
captopril	captopril
enalapril maleate	enalapril maleate
enalapril maleate	Epaned
enalapril maleate	Vasotec
fosinopril sodium	fosinopril
lisinopril	lisinopril
lisinopril	Prinivil
lisinopril	Qbrelis
lisinopril	Zestril
moexipril HCl	moexipril
perindopril arginine/amlodipine besylate	Prestalia
perindopril erbumine	Aceon
perindopril erbumine	perindopril erbumine
quinapril HCl	Accupril
quinapril HCl	quinapril
ramipril	Altace
ramipril	ramipril
trandolapril	Mavik
trandolapril	trandolapril
trandolapril/verapamil HCl	Tarka
trandolapril/verapamil HCl	trandolapril-verapamil
amlodipine benzoate	Katerzia

Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name	Brand Name
amlodipine besylate	amlodipine
amlodipine besylate	Norliqva
amlodipine besylate	Norvasc
amlodipine besylate/celecoxib	Consensi
diltiazem HCl	Cardizem
diltiazem HCl	Cardizem CD
diltiazem HCl	Cardizem LA
diltiazem HCl	Cartia XT
diltiazem HCl	diltiazem HCl
diltiazem HCl	DILT-XR
diltiazem HCl	Matzim LA
diltiazem HCl	Taztia XT
diltiazem HCl	Tiadylt ER
diltiazem HCl	Tiazac
felodipine	felodipine
isradipine	isradipine
levamlodipine maleate	Conjupri
levamlodipine maleate	levamlodipine
nicardipine HCl	nicardipine
nifedipine	Adalat CC
nifedipine	Afeditab CR
nifedipine	Nifedical XL
nifedipine	nifedipine
nifedipine	Procardia
nifedipine	Procardia XL
nimodipine	nimodipine
nimodipine	Nymalize
nisoldipine	nisoldipine
nisoldipine	Sular
verapamil HCl	Calan
verapamil HCl	Calan SR
verapamil HCl	verapamil
verapamil HCl	Verelan
verapamil HCl	Verelan PM
amiloride HCl	amiloride
eplerenone	eplerenone
eplerenone	Inspra
spironolactone	Aldactone
spironolactone	CaroSpir
spironolactone	spironolactone
triamterene	Dyrenium
triamterene	triamterene

Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name	Brand Name
bumetanide	bumetanide
ethacrynic acid	Edecrin
ethacrynic acid	ethacrynic acid
furosemide	furosemide
furosemide	Lasix
torsemide	Demadex
torsemide	Soaanz
torsemide	torsemide
ARB Generics	
amlodipine besylate/olmesartan medoxomil	amlodipine-olmesartan
amlodipine besylate/olmesartan medoxomil	amlodipine-olmesartan
amlodipine besylate/olmesartan medoxomil	amlodipine-olmesartan
amlodipine besylate/olmesartan medoxomil	amlodipine-olmesartan
amlodipine besylate/olmesartan medoxomil	Azor
amlodipine besylate/olmesartan medoxomil	Azor
amlodipine besylate/olmesartan medoxomil	Azor
amlodipine besylate/olmesartan medoxomil	Azor
amlodipine besylate/valsartan	amlodipine-valsartan
amlodipine besylate/valsartan	amlodipine-valsartan
amlodipine besylate/valsartan	amlodipine-valsartan
amlodipine besylate/valsartan	amlodipine-valsartan
amlodipine besylate/valsartan	Exforge
amlodipine besylate/valsartan	Exforge
amlodipine besylate/valsartan	Exforge
amlodipine besylate/valsartan	Exforge
amlodipine besylate/valsartan/hydrochlorothiazide	amlodipine-valsartan-hcthiazid
amlodipine besylate/valsartan/hydrochlorothiazide	amlodipine-valsartan-hcthiazid
amlodipine besylate/valsartan/hydrochlorothiazide	amlodipine-valsartan-hcthiazid
amlodipine besylate/valsartan/hydrochlorothiazide	amlodipine-valsartan-hcthiazid
amlodipine besylate/valsartan/hydrochlorothiazide	amlodipine-valsartan-hcthiazid
amlodipine besylate/valsartan/hydrochlorothiazide	Exforge HCT
amlodipine besylate/valsartan/hydrochlorothiazide	Exforge HCT
amlodipine besylate/valsartan/hydrochlorothiazide	Exforge HCT
amlodipine besylate/valsartan/hydrochlorothiazide	Exforge HCT
amlodipine besylate/valsartan/hydrochlorothiazide	Exforge HCT
azilsartan medoxomil	Edarbi
azilsartan medoxomil	Edarbi
azilsartan medoxomil/chlorthalidone	Edarbyclor
azilsartan medoxomil/chlorthalidone	Edarbyclor
candesartan cilexetil	Atacand
candesartan cilexetil	Atacand
candesartan cilexetil	Atacand

Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name	Brand Name
candesartan cilexetil	Atacand
candesartan cilexetil	candesartan
candesartan cilexetil	candesartan
candesartan cilexetil	candesartan
candesartan cilexetil	candesartan
candesartan cilexetil/hydrochlorothiazide	Atacand HCT
candesartan cilexetil/hydrochlorothiazide	Atacand HCT
candesartan cilexetil/hydrochlorothiazide	Atacand HCT
candesartan cilexetil/hydrochlorothiazide	candesartan-hydrochlorothiazid
candesartan cilexetil/hydrochlorothiazide	candesartan-hydrochlorothiazid
candesartan cilexetil/hydrochlorothiazide	candesartan-hydrochlorothiazid
eprosartan mesylate	eprosartan
irbesartan	Avapro
irbesartan	Avapro
irbesartan	Avapro
irbesartan	irbesartan
irbesartan	irbesartan
irbesartan	irbesartan
irbesartan/hydrochlorothiazide	Avalide
irbesartan/hydrochlorothiazide	Avalide
irbesartan/hydrochlorothiazide	irbesartan-hydrochlorothiazide
irbesartan/hydrochlorothiazide	irbesartan-hydrochlorothiazide
losartan potassium	Cozaar
losartan potassium	Cozaar
losartan potassium	Cozaar
losartan potassium	losartan
losartan potassium	losartan
losartan potassium	losartan
losartan potassium/hydrochlorothiazide	Hyzaar
losartan potassium/hydrochlorothiazide	Hyzaar
losartan potassium/hydrochlorothiazide	Hyzaar
losartan potassium/hydrochlorothiazide	losartan-hydrochlorothiazide
losartan potassium/hydrochlorothiazide	losartan-hydrochlorothiazide
losartan potassium/hydrochlorothiazide	losartan-hydrochlorothiazide
nebivolol HCl/valsartan	Byvalson
olmesartan medoxomil	Benicar
olmesartan medoxomil	Benicar
olmesartan medoxomil	Benicar
olmesartan medoxomil	olmesartan
olmesartan medoxomil	olmesartan
olmesartan medoxomil	olmesartan

Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name	Brand Name
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide	olmesartan-amlodipin-hcthiazid
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide	olmesartan-amlodipin-hcthiazid
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide	olmesartan-amlodipin-hcthiazid
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide	olmesartan-amlodipin-hcthiazid
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide	olmesartan-amlodipin-hcthiazid
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide	Tribenzor
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide	Tribenzor
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide	Tribenzor
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide	Tribenzor
olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide	Tribenzor
olmesartan medoxomil/hydrochlorothiazide	Benicar HCT
olmesartan medoxomil/hydrochlorothiazide	Benicar HCT
olmesartan medoxomil/hydrochlorothiazide	Benicar HCT
olmesartan medoxomil/hydrochlorothiazide	olmesartan-hydrochlorothiazide
olmesartan medoxomil/hydrochlorothiazide	olmesartan-hydrochlorothiazide
olmesartan medoxomil/hydrochlorothiazide	olmesartan-hydrochlorothiazide
sacubitril/valsartan	Entresto
sacubitril/valsartan	Entresto
sacubitril/valsartan	Entresto
telmisartan	Micardis
telmisartan	Micardis
telmisartan	Micardis
telmisartan	telmisartan
telmisartan	telmisartan
telmisartan	telmisartan
telmisartan/amlodipine besylate	telmisartan-amlodipine
telmisartan/amlodipine besylate	telmisartan-amlodipine
telmisartan/amlodipine besylate	telmisartan-amlodipine
telmisartan/amlodipine besylate	telmisartan-amlodipine
telmisartan/amlodipine besylate	Twynsta
telmisartan/amlodipine besylate	Twynsta
telmisartan/amlodipine besylate	Twynsta

Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name	Brand Name
telmisartan/amlodipine besylate	Twynsta
telmisartan/hydrochlorothiazide	Micardis HCT
telmisartan/hydrochlorothiazide	Micardis HCT
telmisartan/hydrochlorothiazide	Micardis HCT
telmisartan/hydrochlorothiazide	telmisartan-hydrochlorothiazid
telmisartan/hydrochlorothiazide	telmisartan-hydrochlorothiazid
telmisartan/hydrochlorothiazide	telmisartan-hydrochlorothiazid
valsartan	Diovan
valsartan	Diovan
valsartan	Diovan
valsartan	Diovan
valsartan	valsartan
valsartan	valsartan
valsartan	valsartan
valsartan	valsartan
valsartan	valsartan
valsartan/hydrochlorothiazide	Diovan HCT
valsartan/hydrochlorothiazide	Diovan HCT
valsartan/hydrochlorothiazide	Diovan HCT
valsartan/hydrochlorothiazide	Diovan HCT
valsartan/hydrochlorothiazide	Diovan HCT
valsartan/hydrochlorothiazide	valsartan-hydrochlorothiazide
valsartan/hydrochlorothiazide	valsartan-hydrochlorothiazide
valsartan/hydrochlorothiazide	valsartan-hydrochlorothiazide
valsartan/hydrochlorothiazide	valsartan-hydrochlorothiazide
valsartan/hydrochlorothiazide	valsartan-hydrochlorothiazide
Beta Blockers Generic	
acebutolol HCl	acebutolol
acebutolol HCl	acebutolol
acebutolol HCl	Sectral
acebutolol HCl	Sectral
atenolol	atenolol
atenolol	atenolol
atenolol	atenolol
atenolol	Tenormin
atenolol	Tenormin
atenolol	Tenormin
atenolol/chlorthalidone	atenolol-chlorthalidone
atenolol/chlorthalidone	atenolol-chlorthalidone
atenolol/chlorthalidone	Tenoretic 100
atenolol/chlorthalidone	Tenoretic 50
betaxolol HCl	betaxolol

Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name	Brand Name
betaxolol HCl	betaxolol
bisoprolol fumarate	bisoprolol fumarate
bisoprolol fumarate	bisoprolol fumarate
bisoprolol fumarate	Zebeta
bisoprolol fumarate	Zebeta
bisoprolol fumarate/hydrochlorothiazide	bisoprolol-hydrochlorothiazide
bisoprolol fumarate/hydrochlorothiazide	bisoprolol-hydrochlorothiazide
bisoprolol fumarate/hydrochlorothiazide	bisoprolol-hydrochlorothiazide
bisoprolol fumarate/hydrochlorothiazide	Ziac
bisoprolol fumarate/hydrochlorothiazide	Ziac
bisoprolol fumarate/hydrochlorothiazide	Ziac
carvedilol	carvedilol
carvedilol	carvedilol
carvedilol	carvedilol
carvedilol	carvedilol
carvedilol	Coreg
carvedilol	Coreg
carvedilol	Coreg
carvedilol	Coreg
carvedilol phosphate	carvedilol phosphate
carvedilol phosphate	carvedilol phosphate
carvedilol phosphate	carvedilol phosphate
carvedilol phosphate	carvedilol phosphate
carvedilol phosphate	Coreg CR
carvedilol phosphate	Coreg CR
carvedilol phosphate	Coreg CR
carvedilol phosphate	Coreg CR
esmolol HCl	Brevibloc
esmolol HCl	esmolol
esmolol HCl	esmolol
esmolol HCl in sodium chloride, iso-osmotic	Brevibloc in NaCl (iso-osm)
esmolol HCl in sodium chloride, iso-osmotic	Brevibloc in NaCl (iso-osm)
esmolol HCl in sodium chloride, iso-osmotic	esmolol in NaCl (iso-osm)
esmolol HCl in sodium chloride, iso-osmotic	esmolol in NaCl (iso-osm)
esmolol HCl in sterile water	esmolol in sterile water
esmolol HCl in sterile water	esmolol in sterile water
labetalol HCl	labetalol
labetalol HCl	labetalol
labetalol HCl	labetalol
labetalol HCl	labetalol
labetalol HCl	labetalol
labetalol HCl	labetalol

Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name	Brand Name
labetalol HCl	labetalol
labetalol HCl	labetalol
labetalol HCl in dextrose, iso-osmotic	labetalol in dextrose,iso-osm
labetalol HCl in sodium chloride, iso-osmotic	labetalol in NaCl (iso-osmot)
labetalol in dextrose 5 % in water	labetalol in dextrose 5 %
metoprolol succinate	Kapspargo Sprinkle
metoprolol succinate	Kapspargo Sprinkle
metoprolol succinate	Kapspargo Sprinkle
metoprolol succinate	Kapspargo Sprinkle
metoprolol succinate	metoprolol succinate
metoprolol succinate	metoprolol succinate
metoprolol succinate	metoprolol succinate
metoprolol succinate	metoprolol succinate
metoprolol succinate	Toprol XL
metoprolol succinate	Toprol XL
metoprolol succinate	Toprol XL
metoprolol succinate	Toprol XL
metoprolol succinate/hydrochlorothiazide	Dutoprol
metoprolol succinate/hydrochlorothiazide	Dutoprol
metoprolol succinate/hydrochlorothiazide	Dutoprol
metoprolol succinate/hydrochlorothiazide	metoprolol su-hydrochlorothiaz
metoprolol succinate/hydrochlorothiazide	metoprolol su-hydrochlorothiaz
metoprolol succinate/hydrochlorothiazide	metoprolol su-hydrochlorothiaz
metoprolol tartrate	Lopressor
metoprolol tartrate	Lopressor
metoprolol tartrate	Lopressor
metoprolol tartrate	metoprolol tartrate
metoprolol tartrate	metoprolol tartrate
metoprolol tartrate	metoprolol tartrate
metoprolol tartrate	metoprolol tartrate
metoprolol tartrate	metoprolol tartrate
metoprolol tartrate	metoprolol tartrate
metoprolol tartrate	metoprolol tartrate
metoprolol tartrate/hydrochlorothiazide	metoprolol ta-hydrochlorothiaz
metoprolol tartrate/hydrochlorothiazide	metoprolol ta-hydrochlorothiaz
metoprolol tartrate/hydrochlorothiazide	metoprolol ta-hydrochlorothiaz
nadolol	Corgard
nadolol	Corgard
nadolol	Corgard
nadolol	nadolol
nadolol	nadolol
nadolol	nadolol

Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name	Brand Name
nadolol/bendroflumethiazide	Corzide
nadolol/bendroflumethiazide	Corzide
nadolol/bendroflumethiazide	nadolol-bendroflumethiazide
nadolol/bendroflumethiazide	nadolol-bendroflumethiazide
nebivolol HCl	Bystolic
nebivolol HCl	Bystolic
nebivolol HCl	Bystolic
nebivolol HCl	Bystolic
nebivolol HCl	nebivolol
nebivolol HCl	nebivolol
nebivolol HCl	nebivolol
nebivolol HCl	nebivolol
pindolol	pindolol
pindolol	pindolol
propranolol HCl	Hemangeol
propranolol HCl	Inderal LA
propranolol HCl	Inderal LA
propranolol HCl	Inderal LA
propranolol HCl	Inderal LA
propranolol HCl	Inderal XL
propranolol HCl	Inderal XL
propranolol HCl	InnoPran XL
propranolol HCl	InnoPran XL
propranolol HCl	propranolol
propranolol HCl	propranolol
propranolol HCl	propranolol
propranolol HCl	propranolol
propranolol HCl	propranolol
propranolol HCl	propranolol
propranolol HCl	propranolol
propranolol HCl	propranolol
propranolol HCl	propranolol
propranolol HCl	propranolol
propranolol HCl	propranolol
propranolol HCl	propranolol
propranolol HCl/hydrochlorothiazide	propranolol-hydrochlorothiazid
propranolol HCl/hydrochlorothiazide	propranolol-hydrochlorothiazid
sotalol HCl	Betapace
sotalol HCl	Betapace
sotalol HCl	Betapace
sotalol HCl	Betapace
sotalol HCl	Betapace AF

Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request

Generic Name	Brand Name
sotalol HCl	Betapace AF
sotalol HCl	Betapace AF
sotalol HCl	Sorine
sotalol HCl	Sorine
sotalol HCl	Sorine
sotalol HCl	Sorine
sotalol HCl	sotalol
sotalol HCl	sotalol
sotalol HCl	sotalol
sotalol HCl	sotalol
sotalol HCl	sotalol
sotalol HCl	Sotalol AF
sotalol HCl	Sotalol AF
sotalol HCl	Sotalol AF
sotalol HCl	Sotylize
timolol maleate	timolol maleate
timolol maleate	timolol maleate
timolol maleate	timolol maleate

Appendix C.1. Specifications for Type 2, Interrupted Time Series Request, Skin Cancer History Analysis, Full Denominator

		Multiple Events Group 1	Multiple Events Group 2	Multiple Events Group 3
		Numerator: HCTZ-containing products	**Numerator: HCTZ single ingredient/monotherapy**	**Numerator: ACEI + HCTZ**
Multiple Events	**Multiple Events Composition (Primary)**	denom_limited_no	denom_limited_no	denom_limited_no
	Multiple Events Composition (Secondary)	hctz_containing_all_no	hctz_mono_all_no	hctz_acei_combo_no
	ITS Denominator	Number of patients with use of HCTZ-containing products, chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ-containing products, chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ-containing products, chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer in enrollment history
	ITS Numerator	Number of patients with use of any HCTZ-containing product; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ single ingredient; NO evidence of skin cancer in enrollment history	Number of patients with use of ACEI + HCTZ combo product; NO evidence of skin cancer in enrollment history
	Observation window around primary episode	Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode
	Secondary episode to use for time metrics	First occurrence of secondary index	First occurrence of secondary index	First occurrence of secondary index
	Minimum cutoff to be considered adherent	1 adherent episode	1 adherent episode	1 adherent episode
	Categories for length of primary episode	N/A	N/A	N/A

Appendix C.1. Specifications for Type 2, Interrupted Time Series Request, Skin Cancer History Analysis, Full Denominator

		ITS Analysis 1A	ITS Analysis 2A	ITS Analysis 3A
		Intervention date 8/8/2020	**Intervention date 8/8/2020**	**Intervention date 8/8/2020**
ITS Analysis	**Data range start, end**	1/1/2017 - most recent available data	1/1/2017 - most recent available data	1/1/2017 - most recent available data
	Anticipatory date period	N/A	N/A	N/A
	Intervention date	20/08/08	20/08/08	20/08/08
	Truncation of exposure episode at intervention date?	Yes	Yes	Yes
	Interval length	Monthly	Monthly	Monthly
	p-value	0.05	0.05	0.05
	Autoregression lag	12 (12 months)	12 (12 months)	12 (12 months)
	Autoregression model parameter cutoff	0.2	0.2	0.2
	Time points at which to report difference metrics	All available months between intervention date and data range end	All available months between intervention date and data range end	All available months between intervention date and data range end
	Continuous enrollment required?	No	No	No

Appendix C.1. Specifications for Type 2, Interrupted Time Series Request, Skin Cancer History Analysis, Full Denominator

ITS Analysis

	ITS Analysis 1B	ITS Analysis 2B	ITS Analysis 3B
	Anticipatory/lag period from 6/1/2020 - 10/1/2020	Anticipatory/lag period from 6/1/2020 - 10/1/2020	Anticipatory/lag period from 6/1/2020 - 10/1/2020
Data range start, end	1/1/2017 - most recent available data	1/1/2017 - most recent available data	1/1/2017 - most recent available data
Anticipatory/lag period	6/1/2020 - 10/1/2020	6/1/2020 - 10/1/2020	6/1/2020 - 10/1/2020
Intervention date	20/08/08	20/08/08	20/08/08
Truncation of exposure episode at intervention date?	Yes	Yes	Yes
Interval length	Monthly	Monthly	Monthly
p-value	0.05	0.05	0.05
Autoregression lag	12 (12 months)	12 (12 months)	12 (12 months)
Autoregression model parameter cutoff	0.2	0.2	0.2
Time points at which to report difference metrics	All available months between intervention date and data range end	All available months between intervention date and data range end	All available months between intervention date and data range end
Continuous enrollment required?	No	No	No

Appendix C.1. Specifications for Type 2, Interrupted Time Series Request, Skin Cancer History Analysis, Full Denominator

Multiple Events Group 4	Multiple Events Group 5	Multiple Events Group 6	Multiple Events Group 7
Numerator: ARB + HCTZ	**Numerator: Potassium-sparing diuretic + HCTZ**	**Numerator: Beta blocker + HCTZ**	**Numerator: ARB + CCB + HCTZ**
denom_limited_no	denom_limited_no	denom_limited_no	denom_limited_no
hctz_arb_combo_no	hctz_potass_combo_no	hctz_beta_combo_no	hctz_arb_ccb_combo_no
Number of patients with use of HCTZ-containing products, chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ-containing products, chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ-containing products, chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ-containing products, chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer in enrollment history
Number of patients with use of ARB + HCTZ combo product; NO evidence of skin cancer in enrollment history	Number of patients with use of potassium-sparing diuretic + HCTZ combo product; NO evidence of skin cancer in enrollment history	Number of patients with use of beta blocker + HCTZ combo product; NO evidence of skin cancer in enrollment history	Number of patients with use of ARB + CCB + HCTZ combo product; NO evidence of skin cancer in enrollment history
Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode
First occurrence of secondary index	First occurrence of secondary index	First occurrence of secondary index	First occurrence of secondary index
1 adherent episode	1 adherent episode	1 adherent episode	1 adherent episode
N/A	N/A	N/A	N/A

Appendix C.1. Specifications for Type 2, Interrupted Time Series Request, Skin Cancer History Analysis, Full Denominator

ITS Analysis 4A	ITS Analysis 5A	ITS Analysis 6A	ITS Analysis 7A
Intervention date 8/8/2020	**Intervention date 8/8/2020**	**Intervention date 8/8/2020**	**Intervention date 8/8/2020**
1/1/2017 - most recent available data	1/1/2017 - most recent available data	1/1/2017 - most recent available data	1/1/2017 - most recent available data
N/A	N/A	N/A	N/A
20/08/08	20/08/08	20/08/08	20/08/08
Yes	Yes	Yes	Yes
Monthly	Monthly	Monthly	Monthly
0.05	0.05	0.05	0.05
12 (12 months)	12 (12 months)	12 (12 months)	12 (12 months)
0.2	0.2	0.2	0.2
All available months between intervention date and data range end	All available months between intervention date and data range end	All available months between intervention date and data range end	All available months between intervention date and data range end
No	No	No	No

Appendix C.1. Specifications for Type 2, Interrupted Time Series Request, Skin Cancer History Analysis, Full Denominator

ITS Analysis 4B	ITS Analysis 5B	ITS Analysis 6B	ITS Analysis 7B
Anticipatory/lag period from 6/1/2020 - 10/1/2020	Anticipatory/lag period from 6/1/2020 - 10/1/2020	Anticipatory/lag period from 6/1/2020 - 10/1/2020	Anticipatory/lag period from 6/1/2020 - 10/1/2020
1/1/2017 - most recent available data	1/1/2017 - most recent available data	1/1/2017 - most recent available data	1/1/2017 - most recent available data
6/1/2020 - 10/1/2020	6/1/2020 - 10/1/2020	6/1/2020 - 10/1/2020	6/1/2020 - 10/1/2020
20/08/08	20/08/08	20/08/08	20/08/08
Yes	Yes	Yes	Yes
Monthly	Monthly	Monthly	Monthly
0.05	0.05	0.05	0.05
12 (12 months)	12 (12 months)	12 (12 months)	12 (12 months)
0.2	0.2	0.2	0.2
All available months between intervention date and data range end	All available months between intervention date and data range end	All available months between intervention date and data range end	All available months between intervention date and data range end
No	No	No	No

Appendix C.1. Specifications for Type 2, Interrupted Time Series Request, Skin Cancer History Analysis, Full Denominator

Multiple Events Group 8	Multiple Events Group 9	Multiple Events Group 10	Multiple Events Group 11
Numerator: Direct renin inhibitor + HCTZ	**Numerator: Central alpha 2 agonist + HCTZ**	**Numerator: HCTZ-containing products**	**Numerator: Chlorothiazide, bendroflumethiazide, or thiazide-like diuretics**
denom_limited_no	denom_limited_no	denom_all	denom_all
hctz_direct_no	hctz_central_no	hctz_containing_all	other_thiazide_plus
Number of patients with use of HCTZ-containing products, chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ-containing products, chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ-containing products, any thiazide diuretics, any diuretics, or any antihypertensives	Number of patients with use of HCTZ-containing products, any thiazide diuretics, any diuretics, or any antihypertensives
Number of patients with use of direct renin inhibitor + HCTZ combo product; NO evidence of skin cancer in enrollment history	Number of patients with use of central alpha 2 agonist + HCTZ combo product; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ-containing products	Number of patients with use of chlorothiazide, bendroflumethiazide, or thiazide-like diuretics
Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode
First occurrence of secondary index	First occurrence of secondary index	First occurrence of secondary index	First occurrence of secondary index
1 adherent episode	1 adherent episode	1 adherent episode	1 adherent episode
N/A	N/A	N/A	N/A

Appendix C.1. Specifications for Type 2, Interrupted Time Series Request, Skin Cancer History Analysis, Full Denominator

ITS Analysis 8A	ITS Analysis 9A	ITS Analysis 10A	ITS Analysis 11A
Intervention date 8/8/2020	**Intervention date 8/8/2020**	**Intervention date 8/8/2020**	**Intervention date 8/8/2020**
1/1/2017 - most recent available data	1/1/2017 - most recent available data	1/1/2017 - most recent available data	1/1/2017 - most recent available data
N/A	N/A	N/A	N/A
20/08/08	20/08/08	20/08/08	20/08/08
Yes	Yes	Yes	Yes
Monthly	Monthly	Monthly	Monthly
0.05	0.05	0.05	0.05
12 (12 months)	12 (12 months)	12 (12 months)	12 (12 months)
0.2	0.2	0.2	0.2
All available months between intervention date and data range end	All available months between intervention date and data range end	All available months between intervention date and data range end	All available months between intervention date and data range end
No	No	No	No

Appendix C.1. Specifications for Type 2, Interrupted Time Series Request, Skin Cancer History Analysis, Full Denominator

ITS Analysis 8B	ITS Analysis 9B	ITS Analysis 10B	ITS Analysis 11B
Anticipatory/lag period from 6/1/2020 - 10/1/2020	Anticipatory/lag period from 6/1/2020 - 10/1/2020	Anticipatory/lag period from 6/1/2020 - 10/1/2020	Anticipatory/lag period from 6/1/2020 - 10/1/2020
1/1/2017 - most recent available data	1/1/2017 - most recent available data	1/1/2017 - most recent available data	1/1/2017 - most recent available data
6/1/2020 - 10/1/2020	6/1/2020 - 10/1/2020	6/1/2020 - 10/1/2020	6/1/2020 - 10/1/2020
20/08/08	20/08/08	20/08/08	20/08/08
Yes	Yes	Yes	Yes
Monthly	Monthly	Monthly	Monthly
0.05	0.05	0.05	0.05
12 (12 months)	12 (12 months)	12 (12 months)	12 (12 months)
0.2	0.2	0.2	0.2
All available months between intervention date and data range end	All available months between intervention date and data range end	All available months between intervention date and data range end	All available months between intervention date and data range end
No	No	No	No

Appendix C.1. Specifications for Type 2, Interrupted Time Series Request, Skin Cancer History Analysis, Full Denominator

Multiple Events Group 12	Multiple Events Group 13	Multiple Events Group 14	Multiple Events Group 15	Multiple Events Group 16	Multiple Events Group 17
Numerator: ACEIs (non-HCTZ combination)	**Numerator: CCBs (non-HCTZ combination)**	**Numerator: Potassium-sparing diuretics (non-HCTZ combination)**	**Numerator: Loop diuretics**	**Numerator: ARBs (non-HCTZ combination)**	**Numerator: Beta blockers (non-HCTZ combination)**
denom_all	denom_all	denom_all	denom_all	denom_all	denom_all
other_acei	other_ccb	other_potass	other_loop	other_arbs	other_bb
Number of patients with use of HCTZ-containing products, any thiazide diuretics, any diuretics, or any antihypertensives	Number of patients with use of HCTZ-containing products, any thiazide diuretics, any diuretics, or any antihypertensives	Number of patients with use of HCTZ-containing products, any thiazide diuretics, any diuretics, or any antihypertensives	Number of patients with use of HCTZ-containing products, any thiazide diuretics, any diuretics, or any antihypertensives	Number of patients with use of HCTZ-containing products, any thiazide diuretics, any diuretics, or any antihypertensives	Number of patients with use of HCTZ-containing products, any thiazide diuretics, any diuretics, or any antihypertensives
Number of patients with use of ACEIs (non-HCTZ combination)	Number of patients with use of CCBs (non-HCTZ combination)	Number of patients with use of potassium-sparing diuretics (non-HCTZ combination)	Number of patients with use of loop diuretics	Number of patients with use of ARBs (non-HCTZ combination)	Number of patients with use of beta blockers (non-HCTZ combination)
Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode
First occurrence of secondary index	First occurrence of secondary index	First occurrence of secondary index	First occurrence of secondary index	First occurrence of secondary index	First occurrence of secondary index
1 adherent episode	1 adherent episode	1 adherent episode	1 adherent episode	1 adherent episode	1 adherent episode
N/A	N/A	N/A	N/A	N/A	N/A

Appendix C.1. Specifications for Type 2, Interrupted Time Series Request, Skin Cancer History Analysis, Full Denominator

ITS Analysis 12A	ITS Analysis 13A	ITS Analysis 14A	ITS Analysis 15A	ITS Analysis 14A	ITS Analysis 15A
Intervention date 8/8/2020	**Intervention date 8/8/2020**	**Intervention date 8/8/2020**	**Intervention date 8/8/2020**	**Intervention date 8/8/2020**	**Intervention date 8/8/2020**
1/1/2017 - most recent available data	1/1/2017 - most recent available data	1/1/2017 - most recent available data	1/1/2017 - most recent available data	1/1/2017 - most recent available data	1/1/2017 - most recent available data
N/A	N/A	N/A	N/A	N/A	N/A
20/08/08	20/08/08	20/08/08	20/08/08	20/08/08	20/08/08
Yes	Yes	Yes	Yes	Yes	Yes
Monthly	Monthly	Monthly	Monthly	Monthly	Monthly
0.05	0.05	0.05	0.05	0.05	0.05
12 (12 months)	12 (12 months)	12 (12 months)	12 (12 months)	12 (12 months)	12 (12 months)
0.2	0.2	0.2	0.2	0.2	0.2
All available months between intervention date and data range end	All available months between intervention date and data range end	All available months between intervention date and data range end	All available months between intervention date and data range end	All available months between intervention date and data range end	All available months between intervention date and data range end
No	No	No	No	No	No

Appendix C.1. Specifications for Type 2, Interrupted Time Series Request, Skin Cancer History Analysis, Full Denominator

ITS Analysis 12B	ITS Analysis 13B	ITS Analysis 14B	ITS Analysis 15B	ITS Analysis 14B	ITS Analysis 15B
Anticipatory/lag period from 6/1/2020 - 10/1/2020	Anticipatory/lag period from 6/1/2020 - 10/1/2020	Anticipatory/lag period from 6/1/2020 - 10/1/2020	Anticipatory/lag period from 6/1/2020 - 10/1/2020	Anticipatory/lag period from 6/1/2020 - 10/1/2020	Anticipatory/lag period from 6/1/2020 - 10/1/2020
1/1/2017 - most recent available data	1/1/2017 - most recent available data	1/1/2017 - most recent available data	1/1/2017 - most recent available data	1/1/2017 - most recent available data	1/1/2017 - most recent available data
6/1/2020 - 10/1/2020	6/1/2020 - 10/1/2020	6/1/2020 - 10/1/2020	6/1/2020 - 10/1/2020	6/1/2020 - 10/1/2020	6/1/2020 - 10/1/2020
20/08/08	20/08/08	20/08/08	20/08/08	20/08/08	20/08/08
Yes	Yes	Yes	Yes	Yes	Yes
Monthly	Monthly	Monthly	Monthly	Monthly	Monthly
0.05	0.05	0.05	0.05	0.05	0.05
12 (12 months)	12 (12 months)	12 (12 months)	12 (12 months)	12 (12 months)	12 (12 months)
0.2	0.2	0.2	0.2	0.2	0.2
All available months between intervention date and data range end	All available months between intervention date and data range end	All available months between intervention date and data range end	All available months between intervention date and data range end	All available months between intervention date and data range end	All available months between intervention date and data range end
No	No	No	No	No	No

Appendix C.2. Specifications for Type 2, Interrupted Time Series Request, No Skin Cancer History Analysis, Limited Denominator

		Multiple Events Group 18	Multiple Events Group 19
		Numerator: HCTZ-containing products; NO evidence of skin cancer prior to dispensing	**Numerator: HCTZ single ingredient/monotherapy; NO evidence of skin cancer prior to dispensing**
Multiple Events	**Multiple Events Composition (Primary)**	denom_limited_no	denom_limited_no
	Multiple Events Composition (Secondary)	hctz_containing_all_no	hctz_mono_all_no
	ITS Denominator	Number of patients with use of HCTZ-containing products, chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ-containing products, chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer in enrollment history
	ITS Numerator	Number of patients with use of any HCTZ-containing product; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ single ingredient; NO evidence of skin cancer in enrollment history
	Observation window around primary episode	Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode
	Secondary episode to use for time metrics	First occurrence of secondary index	First occurrence of secondary index
	Minimum cutoff to be considered adherent	1 adherent episode	1 adherent episode
	Categories for length of primary episode	N/A	N/A

Appendix C.2. Specifications for Type 2, Interrupted Time Series Request, No Skin Cancer History Analysis, Limited Denominator

ITS Analysis

	ITS Analysis 1A	ITS Analysis 2A
	Intervention date 8/8/2020	**Intervention date 8/8/2020**
Data range start, end	1/1/2017 - most recent available data	1/1/2017 - most recent available data
Anticipatory date period	N/A	N/A
Intervention date	20/08/08	20/08/08
Truncation of exposure episode at intervention date?	Yes	Yes
Interval length	Monthly	Monthly
p-value	0.05	0.05
Autoregression lag	12 (12 months)	12 (12 months)
Autoregression model parameter cutoff	0.2	0.2
Time points at which to report difference metrics	All available months between intervention date and data range end	All available months between intervention date and data range end
Continuous enrollment required?	No	No

ITS Analysis

	ITS Analysis 1B	ITS Analysis 2B
	Anticipatory/lag period from 6/1/2020 - 10/1/2020	**Anticipatory/lag period from 6/1/2020 - 10/1/2020**
Data range start, end	1/1/2017 - most recent available data	1/1/2017 - most recent available data
Anticipatory/lag period	6/1/2020 - 10/1/2020	6/1/2020 - 10/1/2020
Intervention date	20/08/08	20/08/08
Truncation of exposure episode at intervention date?	Yes	Yes
Interval length	Monthly	Monthly
p-value	0.05	0.05
Autoregression lag	12 (12 months)	12 (12 months)
Autoregression model parameter cutoff	0.2	0.2
Time points at which to report difference metrics	All available months between intervention date and data range end	All available months between intervention date and data range end
Continuous enrollment required?	No	No

Appendix C.2. Specifications for Type 2, Interrupted Time Series Request, No Skin Cancer History Analysis, Limited Denominator

Multiple Events Group 20	Multiple Events Group 21	Multiple Events Group 22
Numerator: ACEI + HCTZ; NO evidence of skin cancer prior to dispensing	**Numerator: ARB + HCTZ; NO evidence of skin cancer prior to dispensing**	**Numerator: Potassium-sparing diuretic + HCTZ; NO evidence of skin cancer prior to dispensing**
denom_limited_no	denom_limited_no	denom_limited_no
hctz_acei_combo_no	hctz_arb_combo_no	hctz_potass_combo_no
Number of patients with use of HCTZ-containing products, chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ-containing products, chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ-containing products, chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer in enrollment history
Number of patients with use of ACEI + HCTZ combo product; NO evidence of skin cancer in enrollment history	Number of patients with use of ARB + HCTZ combo product; NO evidence of skin cancer in enrollment history	Number of patients with use of potassium-sparing diuretic + HCTZ combo product; NO evidence of skin cancer in enrollment history
Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode
First occurrence of secondary index	First occurrence of secondary index	First occurrence of secondary index
1 adherent episode	1 adherent episode	1 adherent episode
N/A	N/A	N/A

Appendix C.2. Specifications for Type 2, Interrupted Time Series Request, No Skin Cancer History Analysis, Limited Denominator

ITS Analysis 3A
Intervention date 8/8/2020
1/1/2017 - most recent available data
N/A
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 4A
Intervention date 8/8/2020
1/1/2017 - most recent available data
N/A
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 5A
Intervention date 8/8/2020
1/1/2017 - most recent available data
N/A
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 3B
Anticipatory/lag period from 6/1/2020 - 10/1/2020
1/1/2017 - most recent available data
6/1/2020 - 10/1/2020
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 4B
Anticipatory/lag period from 6/1/2020 - 10/1/2020
1/1/2017 - most recent available data
6/1/2020 - 10/1/2020
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 5B
Anticipatory/lag period from 6/1/2020 - 10/1/2020
1/1/2017 - most recent available data
6/1/2020 - 10/1/2020
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

Appendix C.2. Specifications for Type 2, Interrupted Time Series Request, No Skin Cancer History Analysis, Limited Denominator

Multiple Events Group 23	Multiple Events Group 24	Multiple Events Group 25
Numerator: Beta blocker + HCTZ; NO evidence of skin cancer prior to dispensing	**Numerator: ARB + CCB + HCTZ; NO evidence of skin cancer prior to dispensing**	**Numerator: Direct renin inhibitor + HCTZ; NO evidence of skin cancer prior to dispensing**
denom_limited_no	denom_limited_no	denom_limited_no
hctz_beta_combo_no	hctz_arb_ccb_combo_no	hctz_direct_no
Number of patients with use of HCTZ-containing products, chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ-containing products, chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ-containing products, chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer in enrollment history
Number of patients with use of beta blocker + HCTZ combo product; NO evidence of skin cancer in enrollment history	Number of patients with use of ARB + CCB + HCTZ combo product; NO evidence of skin cancer in enrollment history	Number of patients with use of direct renin inhibitor + HCTZ combo product; NO evidence of skin cancer in enrollment history
Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode
First occurrence of secondary index	First occurrence of secondary index	First occurrence of secondary index
1 adherent episode	1 adherent episode	1 adherent episode
N/A	N/A	N/A

Appendix C.2. Specifications for Type 2, Interrupted Time Series Request, No Skin Cancer History Analysis, Limited Denominator

ITS Analysis 6A
Intervention date 8/8/2020
1/1/2017 - most recent available data
N/A
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 7A
Intervention date 8/8/2020
1/1/2017 - most recent available data
N/A
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 8A
Intervention date 8/8/2020
1/1/2017 - most recent available data
N/A
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 6B
Anticipatory/lag period from 6/1/2020 - 10/1/2020
1/1/2017 - most recent available data
6/1/2020 - 10/1/2020
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 7B
Anticipatory/lag period from 6/1/2020 - 10/1/2020
1/1/2017 - most recent available data
6/1/2020 - 10/1/2020
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 8B
Anticipatory/lag period from 6/1/2020 - 10/1/2020
1/1/2017 - most recent available data
6/1/2020 - 10/1/2020
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

Appendix C.2. Specifications for Type 2, Interrupted Time Series Request, No Skin Cancer History Analysis, Limited Denominator

Multiple Events Group 26	Multiple Events Group 27	Multiple Events Group 28
Numerator: Central alpha 2 agonist + HCTZ; NO evidence of skin cancer prior to dispensing	**Numerator: HCTZ-containing products; NO evidence of skin cancer prior to dispensing**	**Numerator: Chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer prior to dispensing**
denom_limited_no	denom_all_no	denom_all_no
hctz_central_no	hctz_containing_all_no	other_thiazide_plus_no
Number of patients with use of HCTZ-containing products, chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ-containing products, any thiazide diuretics, any diuretics, or any antihypertensives; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ-containing products, any thiazide diuretics, any diuretics, or any antihypertensives; NO evidence of skin cancer in enrollment history
Number of patients with use of central alpha 2 agonist + HCTZ combo product; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ-containing products; NO evidence of skin cancer in enrollment history	Number of patients with use of chlorothiazide, bendroflumethiazide, or thiazide-like diuretics; NO evidence of skin cancer in enrollment history
Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode
First occurrence of secondary index	First occurrence of secondary index	First occurrence of secondary index
1 adherent episode	1 adherent episode	1 adherent episode
N/A	N/A	N/A

Appendix C.2. Specifications for Type 2, Interrupted Time Series Request, No Skin Cancer History Analysis, Limited Denominator

ITS Analysis 9A
Intervention date 8/8/2020
1/1/2017 - most recent available data
N/A
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 10A
Intervention date 8/8/2020
1/1/2017 - most recent available data
N/A
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 11A
Intervention date 8/8/2020
1/1/2017 - most recent available data
N/A
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 9B
Anticipatory/lag period from 6/1/2020 - 10/1/2020
1/1/2017 - most recent available data
6/1/2020 - 10/1/2020
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 10B
Anticipatory/lag period from 6/1/2020 - 10/1/2020
1/1/2017 - most recent available data
6/1/2020 - 10/1/2020
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 11B
Anticipatory/lag period from 6/1/2020 - 10/1/2020
1/1/2017 - most recent available data
6/1/2020 - 10/1/2020
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

Appendix C.2. Specifications for Type 2, Interrupted Time Series Request, No Skin Cancer History Analysis, Limited Denominator

Multiple Events Group 29	Multiple Events Group 30	Multiple Events Group 31	Multiple Events Group 32
Numerator: ACEIs (non-HCTZ combination); NO evidence of skin cancer prior to dispensing	**Numerator: CCBs (non-HCTZ combination); NO evidence of skin cancer prior to dispensing**	**Numerator: ARBs (non-HCTZ combination); NO evidence of skin cancer prior to dispensing**	**Numerator: Beta blockers (non-HCTZ combination); NO evidence of skin cancer prior to dispensing**
denom_all_no	denom_all_no	denom_all_no	denom_all_no
other_acei_no	other_ccb_no	other_arbs_no	other_bb_no
Number of patients with use of HCTZ-containing products, any thiazide diuretics, any diuretics, or any antihypertensives; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ-containing products, any thiazide diuretics, any diuretics, or any antihypertensives; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ-containing products, any thiazide diuretics, any diuretics, or any antihypertensives; NO evidence of skin cancer in enrollment history	Number of patients with use of HCTZ-containing products, any thiazide diuretics, any diuretics, or any antihypertensives; NO evidence of skin cancer in enrollment history
Number of patients with use of ACEIs (non-HCTZ combination); NO evidence of skin cancer in enrollment history	Number of patients with use of CCBs (non-HCTZ combination); NO evidence of skin cancer in enrollment history	Number of patients with use of ARBs (non-HCTZ combination); NO evidence of skin cancer in enrollment history	Number of patients with use of beta blockers; NO evidence of skin cancer in enrollment history
Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode	Start of primary episode (index date) to end of primary episode
First occurrence of secondary index	First occurrence of secondary index	First occurrence of secondary index	First occurrence of secondary index
1 adherent episode	1 adherent episode	1 adherent episode	1 adherent episode
N/A	N/A	N/A	N/A

Appendix C.2. Specifications for Type 2, Interrupted Time Series Request, No Skin Cancer History Analysis, Limited Denominator

ITS Analysis 12A
Intervention date 8/8/2020
1/1/2017 - most recent available data
N/A
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 13A
Intervention date 8/8/2020
1/1/2017 - most recent available data
N/A
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 14A
Intervention date 8/8/2020
1/1/2017 - most recent available data
N/A
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 15A
Intervention date 8/8/2020
1/1/2017 - most recent available data
N/A
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 12B
Anticipatory/lag period from 6/1/2020 - 10/1/2020
1/1/2017 - most recent available data
6/1/2020 - 10/1/2020
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 13B
Anticipatory/lag period from 6/1/2020 - 10/1/2020
1/1/2017 - most recent available data
6/1/2020 - 10/1/2020
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
All available months between intervention date and data range end
No

ITS Analysis 14B
Anticipatory/lag period from 6/1/2020 - 10/1/2020
1/1/2017 - most recent available data
6/1/2020 - 10/1/2020
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
intervention date and data range end
No

ITS Analysis 15B
Anticipatory/lag period from 6/1/2020 - 10/1/2020
1/1/2017 - most recent available data
6/1/2020 - 10/1/2020
20/08/08
Yes
Monthly
0.05
12 (12 months)
0.2
intervention date and data range end
No