Sentinel

A New Analytic Tool for Interrupted Time Series Analysis to Assess the Impact of FDA Regulatory Actions

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Disclosures

- The views expressed in this presentation represent those of the presenters and do not necessarily represent the official views of the U.S. FDA.
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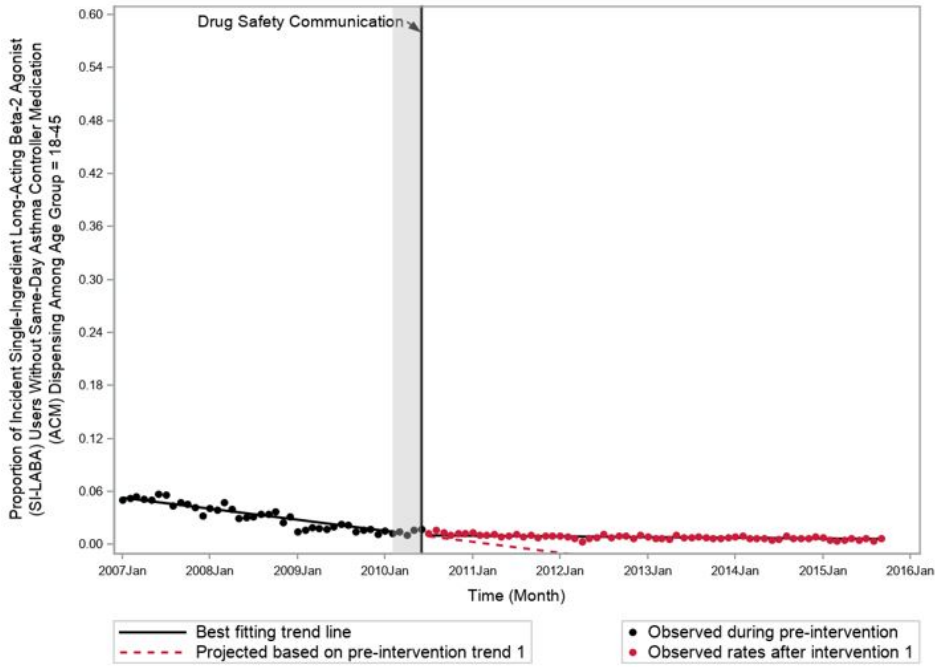
Purpose & Methods

- **Background and Objective:** Regulatory actions by the US Food and Drug Administration (FDA) often influence prescribing practice and drug use. A flexible, scalable population-based tool to assess the impact of regulatory actions would be valuable. Interrupted time series (ITS) is a quasi-experimental method that is stronger than pre-post analyses as it controls for secular trends. We developed a reusable statistical program to conduct ITS analyses in electronic healthcare data formatted to the Sentinel Common Data Model.
- **Methods:** The program was tested using an FDA drug safety communication from 2010 related to the safety of long-acting beta2-agonists (LABA) in adult asthma patients; FDA recommended against use of LABA alone without the use of long-term asthma controller medications (ACM).
- ***Data source:*** We used healthcare claims data (2007-2015) from 16 Data Partners in the FDA's Sentinel System.
- ***Participants:*** Patients aged 18-45 years with asthma and those with poorly controlled asthma, based on previously used diagnosis and medication algorithms.
- ***Outcome measures:*** monthly proportions of (1) single ingredient LABA initiators among all LABA initiators (including initiators of fixed-dose combination LABA) [initiation is defined based on 183-day washout], and (2) LABA initiators with same-day dispensing of ACM or fixed-dose combination LABA among LABA-naïve patients with asthma.
- **Analyses:** Time series of population monthly proportions were divided into three segments: (1) pre-intervention period: 01/2007 – 01/2010; (2) the anticipatory period: 02/2010 – 06/2010; and (3) post-intervention period: 07/2010 – 09/2015.
  - Our tool generated ITS graphs and used segmented regression to estimate baseline slope, level change, slope change, absolute and relative changes at up to two user-specified time point(s) after the intervention.
  - The tool was validated by comparing our results against a prior analysis of the impact of FDA communications on LABA that used similar measures and customized programming (Zhou E, et al. 2017 J Asthma Allergy).
  - These analyses were designed on Sentinel Query Request Package (QRP) v. 9.3.1, with custom programming.

Results & Conclusions

Results: Initiation of LABA alone declined among all LABA initiators before the FDA's communications in June 2010. (-0.10% per quarter; 95% CI: -0.11% to -0.09%) and the downward trend continued after (Fig 1). This finding was consistent with the FDA's previous study, which validated performance of the newly developed ITS tool.

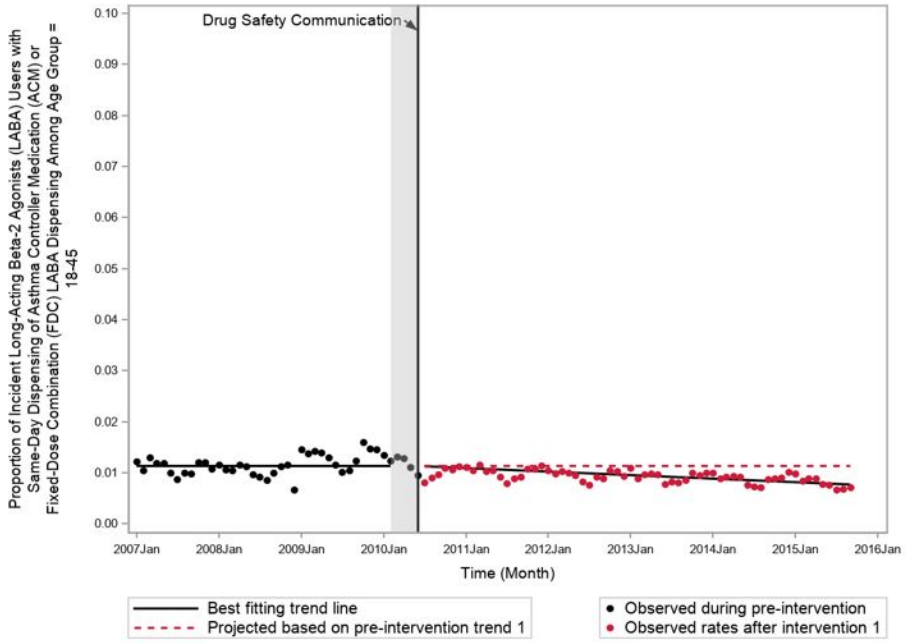
Figure 1. Proportion of Single-Ingredient LABA Initiators among all LABA Initiators Before and After June 2, 2010



https://dev.sentinelsystem.org/projects/SENTINEL/repos/sentinel-routine-querying-tool-documentation/browse/files/file470-type02-itsfunctional.md

Concomitant use of LABA and ACM was stable among adult asthma patients before the FDA communications (Fig 2). After the FDA communications, there was a small but statistically significant trend decrease of 0.006% per quarter (95% CI: -0.008% to -0.003%).

Figure 2. Proportion of LABA Initiators with Same-Day Dispensing of ACM or Fixed-Dose Combination LABA Among LABA-Naive Patients with Asthma Before and After June 2, 2010



Conclusions: We developed and validated an ITS tool using FDA communications on LABA as the test case. The reusable tool can be applied to real-world databases formatted to the Sentinel Common Data Model for assessment of the impact of FDA regulatory actions on drug use.