

# Visualizing Patterns of Drug Prescriptions with EventFlow: A Pilot Study of Asthma Medications in the Military Health System

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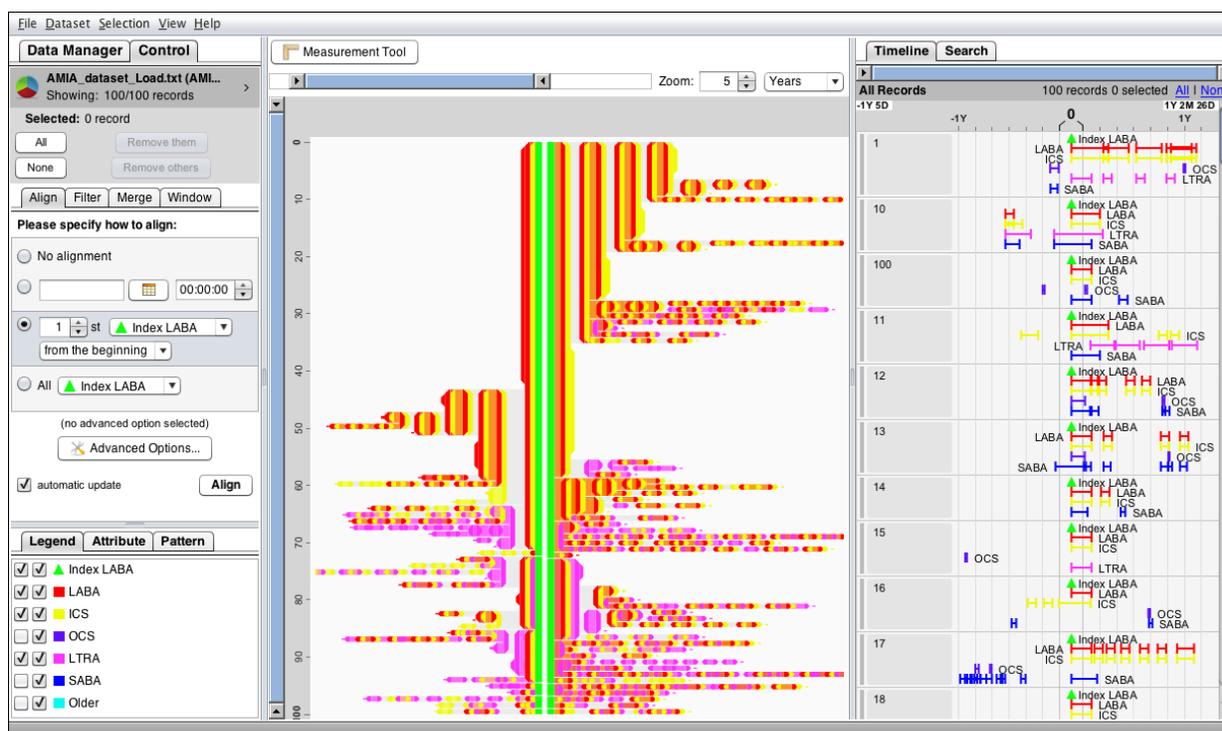
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## Abstract

The Food and Drug Administration and Department of Defense were interested in detecting sub-optimal use of long-acting beta-agonists (LABAs) in asthmatics within the Military Health System (MHS). Visualizing the patterns of asthma medication use surrounding a LABA prescription is a quick way to detect possible sub-optimal use for further evaluation. Analysis of 100 asthma patients was conducted in EventFlow to display and summarize time-point and interval data. Epidemiologists reported that EventFlow was a powerful tool for rapidly visualizing possible patterns of sub-optimal LABA use that can be targeted for intervention.

## Introduction

Electronic health record (EHR) and administrative medical claims databases contain millions of patient records showing medication therapy (e.g., initiation, change of dose, switch to a different medication, augmentation with additional medication for the same condition) for various medical conditions. Clinical researchers and quality improvement analysts have a need to characterize the nature and frequency of such patterns of medication use and, ultimately, to build and test hypotheses regarding the reasons for changes, the benefits and risks of real-world prescribing patterns, and to make recommendations for improved medication management (see <sup>1</sup> for a survey of tools available). We believe that interactive information visualization tools such as EventFlow<sup>2</sup> (Figure 1) can lead to a dramatic improvement in a clinical researcher's ability to obtain deep knowledge of the types of medication usage patterns that occur within a medical practice/healthcare system.



**Figure 1:** Overview of 100 patients' prescription records. Limiting the display to LABA (long-acting beta-agonist), ICS (inhaled corticosteroid), and LTRA (leukotriene receptor antagonist) simplifies the overview. The data is aligned on the green index LABA (the alignment point is shown as a green vertical line).

This paper summarizes the early stages of a case study being conducted with the US Army, Office of the Surgeon General, Pharmacovigilance Center (PVC) where epidemiologists and clinicians worked with HCIL researchers to understand the prescribing patterns of asthma medications. The PVC is collaborating with the Food and Drug Administration (FDA) and Allergy/Immunology clinicians from the Walter Reed National Military Medical Center to determine if long-acting beta-agonists (LABAs), a type of asthma medication, are being mis-prescribed within the Military Health System (MHS).

## Related Work

EventFlow builds on the past research by the HCIL on the visualization of temporal sequences of point events (*i.e.*, events with a single timestamp) LifeLines<sup>2</sup> and LifeFlow<sup>1</sup>. While those tools have been successfully used by clinical researchers and quality assurance administrators to answer many questions, they only operated on point event data (diagnoses, orders, admissions etc.) and therefore had no notion of episodes, partial or complete overlaps, or gaps between events. EventFlow introduces the ability to interactively search and visualize interval data, which is an important step forward. Intervals, such as uninterrupted periods of medication use or episodes of disease, are a central aspect of the analysis of medication use.

In a broader context, temporal database storage, retrieval, interpretation, analysis, and visualization constitute a huge set of research topics. Still the relational database model can be too limiting for many temporal queries. Extensions such as TSQL and other temporal database query languages solve some problems, but the semantics of meaningful temporal queries is difficult or impossible to express in these temporal languages and logics, especially in the presence of interval events<sup>3</sup>. Data mining strategies that can extract common patterns in baskets of items have been cleverly extended to deal with categorical sequences<sup>4</sup>. However, when events in a sequence have different amounts of time between them, data mining approaches become difficult to apply, leading researchers to adopt more selective approaches that often include “interestingness” measures. Work on extracting common temporal patterns in interval event data is still in its infancy<sup>5</sup>.

## EventFlow interface description

The main interface of EventFlow consists of three main components: interactive controls, legend, overview and timeline (Figure 1). On the right the timeline browser shows details of individual records; each patient is shown on a separate timeline. Triangle icons represent point events while connected rectangles represent intervals (and condense to a single rectangle when the interval duration is small). In the center, the overview aggregates all records with the same sequence of events into a single bar. This method was first introduced in LifeFlow<sup>5</sup> and has now been extended to interval data in EventFlow. The height of a bar is determined by the number of records in the group and the horizontal gap between events is proportional to the mean time between the two events among the records in the group. EventFlow renders overlapping intervals using the combined color of the two overlapping categories. For example, when a red interval intersects a blue interval, the resulting overlap is purple. When two intervals of the same category intersect, the color saturation is increased. While this technique works best when limited to a small number of event categories (*i.e.*, colors) our experience suggests that being able to see overlaps of just two or three event categories is already an important improvement over existing techniques for many users. A basic, menu-based search interface is complemented by an Advanced Search to allow users to specify more complex temporal features such as absolute time constraints and absence of events scenarios<sup>6</sup>. The advanced search interface uses a visual query language to draw the desired sequence of event relationships (see Figure 2). Finally, a set of simplification operations allows users to focus on patterns of interest<sup>7</sup> (e.g. by selecting event categories or applying search and replace operations<sup>8</sup>.)

## Ongoing PVC study of long-acting beta-agonist (LABA) therapy

FDA guidelines recommend that patients with asthma who are using LABA therapy also receive a long-term asthma controller medication (LTACM) such as an inhaled corticosteroid (ICS)<sup>22-23</sup>. Single-ingredient LABA prescribing has been linked with increased risk of asthma-related hospitalizations, intubations, and death. The FDA has issued drug safety communications and required label changes to all LABA products detailing that, in asthmatics, LABAs should only be prescribed in combination with a LTACM and only after attempts to optimize other LTACM therapies have failed. According to FDA guidelines, LABA therapy should be de-escalated once asthma has been adequately controlled. LABA prescribing patterns in the MHS were unknown, so the PVC and FDA undertook a study to characterize LABA use among asthmatics in the MHS over time. Metrics of interest were the proportion with concomitant LTACM therapies, length of therapy, and escalation/de-escalation practices. The ultimate goal of the study was to understand LABA use in the MHS in order to inform interventions to prevent morbidity and mortality from sub-optimal LABA use.

The PVC performed a retrospective cohort study using administrative health claims from the MHS from January 1, 2006 to March 1, 2010. The study was approved by the US Army Medical Research and Materiel Command, Office of Research Protections, Institutional Review Board. Eligible patients were identified from the prescription files by

searching for records containing LABA product names. Patients were further limited to asthma patients while excluding COPD patients and limited to patients that did not have LABA in the previous 90 days.

### Case study of the use of EventFlow

We randomly selected 100 patients, extracted all of their asthma medication prescriptions for the 365 days surrounding the index LABA prescription date, categorized the asthma medications into useful groups (LABA, ICS, leukotriene receptor antagonists [LTRA], oral corticosteroid bursts [OCS], and short-acting beta-agonists [SABA]) and imported the data into EventFlow. The input file included a de-identified patient identifier, the asthma medication group, the start date of the prescription, and the end date of the prescription derived from the start date plus days supply of the prescription. An indicator to mark the index LABA date was added to each patient's records. We looked for patterns of asthma medication dispensing surrounding the index LABA prescription that suggested good compliance with FDA guidelines<sup>22-23</sup>. These patterns included 1) a LABA only in conjunction with an ICS, 2) use of other LTACM such as LTRA or ICS prior to the LABA, and 3) exchange of LABA for other LTACM after the asthma is under control.

We examined patterns surrounding the index LABA using the alignment tool in EventFlow and aligned on the point of interest, the index LABA prescription (Figure 1). To focus on patterns of step-up therapy from a non-LABA LTACM to a LABA and step-down therapy from a LABA to other LTACM, we limited the display to LABA and the other common LTACM: ICS and LTRA. In the absence of significant asthma exacerbations or clinical presentations, we expected to see step up from an ICS or LTRA to a LABA and then step down to an LTRA or ICS alone once the asthma was under control. Using the display, we noted that:

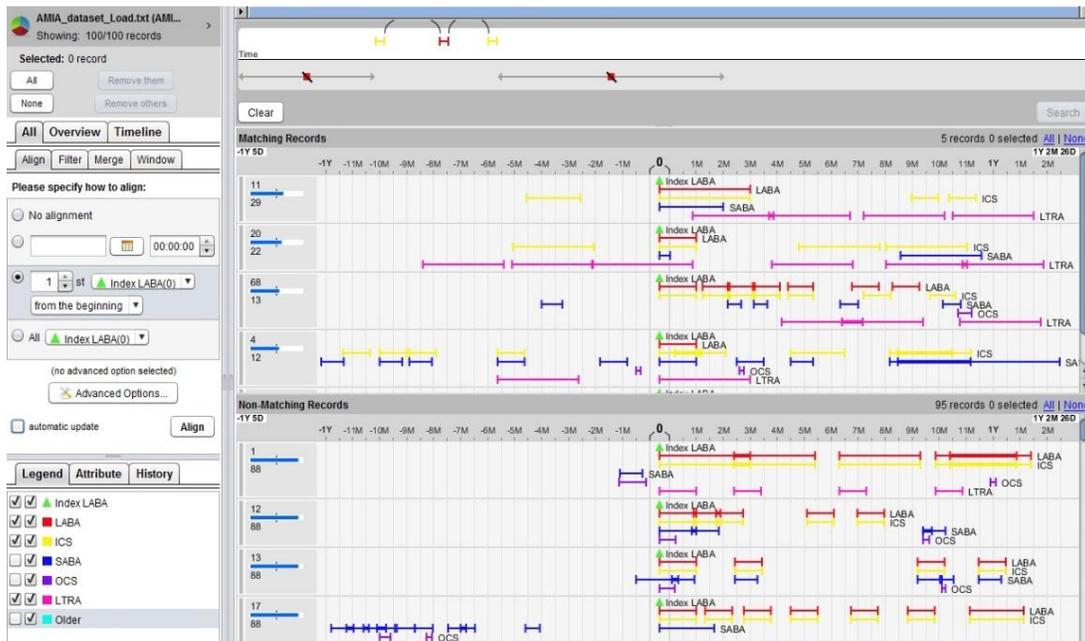
1. About 65% of patients did not have another LTACM before the LABA (*i.e.* started with red LABA or green index LABA) and about half had no evidence of step down to an LTRA or ICS alone. . We were looking for other LTACM like yellow ICS or pink LTRA surrounding the LABA. However, starting on a LABA may be appropriate in the case of a significant asthma exacerbation or symptomatic presentation.
2. We noted that very few LABAs were prescribed without an inhaled corticosteroid (*i.e.* red LABA usually overlaps with the yellow ICS) which is consistent with FDA guidelines.
3. Several patients had a non-index LABA greater than 90 days but less than a year before the index LABA suggesting that a longer washout period may be useful in identifying new (index) LABA prescriptions.

However, we saw that, again, these patterns are not necessarily inconsistent with FDA guidelines<sup>22-23</sup> if asthma symptoms warranted immediate or continued use of LABA. Nevertheless, these patterns do highlight areas for further investigation and possible clinical intervention especially for patients with no evidence of a step-down trial. We are currently working with allergy/immunology specialists at Walter Reed National Military Medical Center, Bethesda, Maryland to evaluate patients who continued on LABA therapy but lacked clinical outpatient follow-up visits after the index LABA.

Finally, we constructed multiple queries to view the patterns that were consistent with FDA guidelines<sup>22-23</sup> by finding patients who were prescribed an ICS, the most common LTACM, within 3 months of both the start and end date of a LABA prescription. We added the additional query to exclude patient therapies that started or ended with a LABA (Figure 2). The query identified five patients that met the FDA guidelines based on prescription patterns of step-up therapy from an ICS to a LABA, use of LABA concomitantly with an ICS, and step-down to an ICS alone. Because the exploration was done on a sample of 100 patients, to confirm these exploratory findings, the entire patient population was evaluated using traditional SQL and SAS queries. These analyses supported the exploratory results. The epidemiologists and clinicians commented that the interface was much easier to learn and use than the command-based, statistical software that they normally employ. Furthermore, these command-based languages offered no simple option of visualizing the patterns in a meaningful way - a feature that is central to the standard search model as well as both of our query interfaces.

### Conclusion

EventFlow was effective in uncovering important patterns of LABA use in the data used in this pilot study. Our results provide evidence that secondary use of electronic health records databases could be dramatically expanded if easy-to-use interfaces allowed clinical researchers to specify queries, review results, and find temporal patterns without needing to default to the time-consuming traditional SQL or SAS queries. We believe that the future of user interfaces is moving toward larger, information- abundant interactive visual displays similar to EventFlow, and this will help researchers compare populations, discover relationships, and spot anomalies that are medically-actionable.



**Figure 2:** Using the advanced query panel, we searched for patients who received an ICS (yellow) within 3 months of both the start and end date of the LABA (red). We also wanted to ensure that this sequence was neither preceded nor followed by a LABA. Matching records move to the top, but we can also check that the search behaved as expected by looking at the records that did not match.

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\*Krist Wongsuphasawat is now at Twitter, but contributed to this work while a PhD student at U. of Maryland.

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