A Sorting and Classification Method for Interactive Visualization of Drug/Event Patterns across Many Patient Timelines

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Abstract

Patterns of interest to a researcher using a large administrative healthcare database for pharmacovigilance include: time to onset, positive and negative instances of dechallenge and rechallenge; withdrawal effects; and continuation of treatment through an event. To analyze patient timelines according to these patterns, we define discrete exposure states for each event in relation to that event's nearest exposure; e.g., unexposed, early exposure, late exposure, within a post-exposure risk window, and beyond post-exposure risk. These and other experimental features were added to a patient timeline visualization tool and evaluated for use in signal strengthening research.

Objectives

We have an existing visualization tool for drug safety signal strengthening that displays, sorts, aligns and filters patient timelines through a fast, interactive user interface. Our objective was to explore the usefulness of several additional capabilities (see Figure 4), particularly:

- dividing exposures into user-configurable sub-periods;
- de-emphasizing events that appear to be part of an episode of care due to their proximity to an earlier event;
- ability to distinguish between first, second and other exposure eras;
- ability to highlight or filter on exposed events according to currently configured definition of exposure, or on exposures containing events;
- ability to identify and highlight patterns of event exposure.

Methods

Phase Forward and the Army Pharmacovigilance Center have collaboratively built PVDAS, the Pharmacovigilance Defense Application System, to explore questions of drug safety using the DoD's 12 million-patient medical data repository. The software uses a range of techniques to answer questions posed by the FDA and by military medical officers.

The visualization tool limits the patient population to those who, at some time, have had both the event and the exposure. Sorting and alignment parameters are highly configurable, but the default is to align by the start of the first exposure and sort by the first occurrence of the event. This gives a straight vertical line of exposures crossed by a curved line of events running from the upper left to lower right of the graphic. The shape of this curve suggests ideas about the association of drug and event in this population.

We examined data for several positive drug / event examples, including: lisinopril and angioedema (Figures 1 and 2), and warfarin and GI bleed (Figure 3). Programmer and researchers iteratively examined and discussed these examples, and modified the tool to help researchers explore patterns of interest.

Results

The purpose of exploring timeline visualizations was to see what the tool and our data could show us about these drug / event combinations. These results are not necessarily statistically significant, they simply represent a set of observations we were able to make by looking at the data with this tool. For lisinopril and angioedema the following was observed:

- most patients are removed from the drug after the event, even though one would not expect the event to be caused by the drug if it occurs late in exposure;
- for patients rechallenged after the event most had no recurrence of the event;
- patients with a history of the event were less likely to be prescribed the drug;
- the graph bears out our expectation of the event clustering during early exposure.

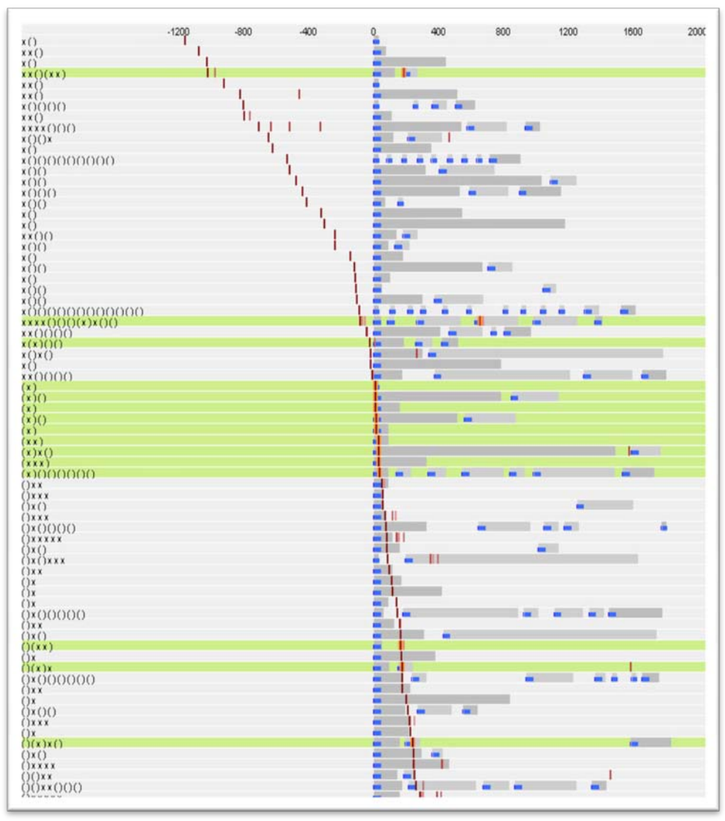

Figure 1. First 50 of 200 patients with Lisinopril and angioedema. Gray bars represent Lisinopril exposure. Blue bars represent the early part of exposure when risk is presumed highest. Red bars represent occurrence of angioedema in patients' medical records. Green highlighting flags patient with events occurring during early exposure.

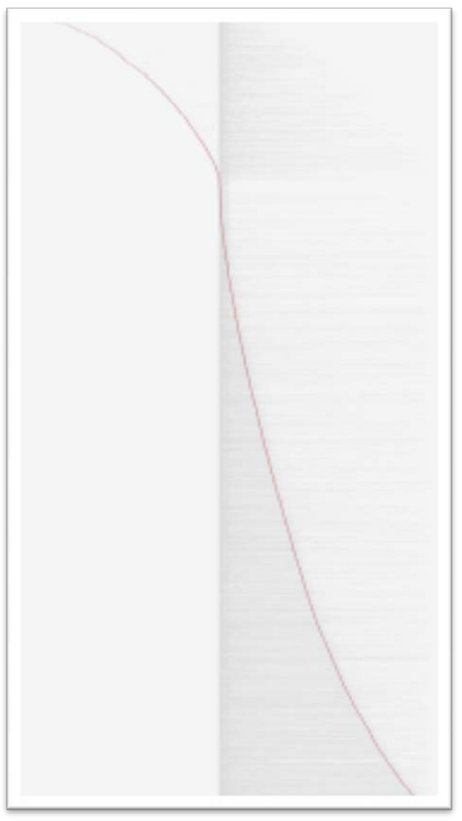

Figure 2. 9,000 patients with Lisinopril and angioedema.

Figure 3. 10,000 patients with Warfarin and GI bleed.

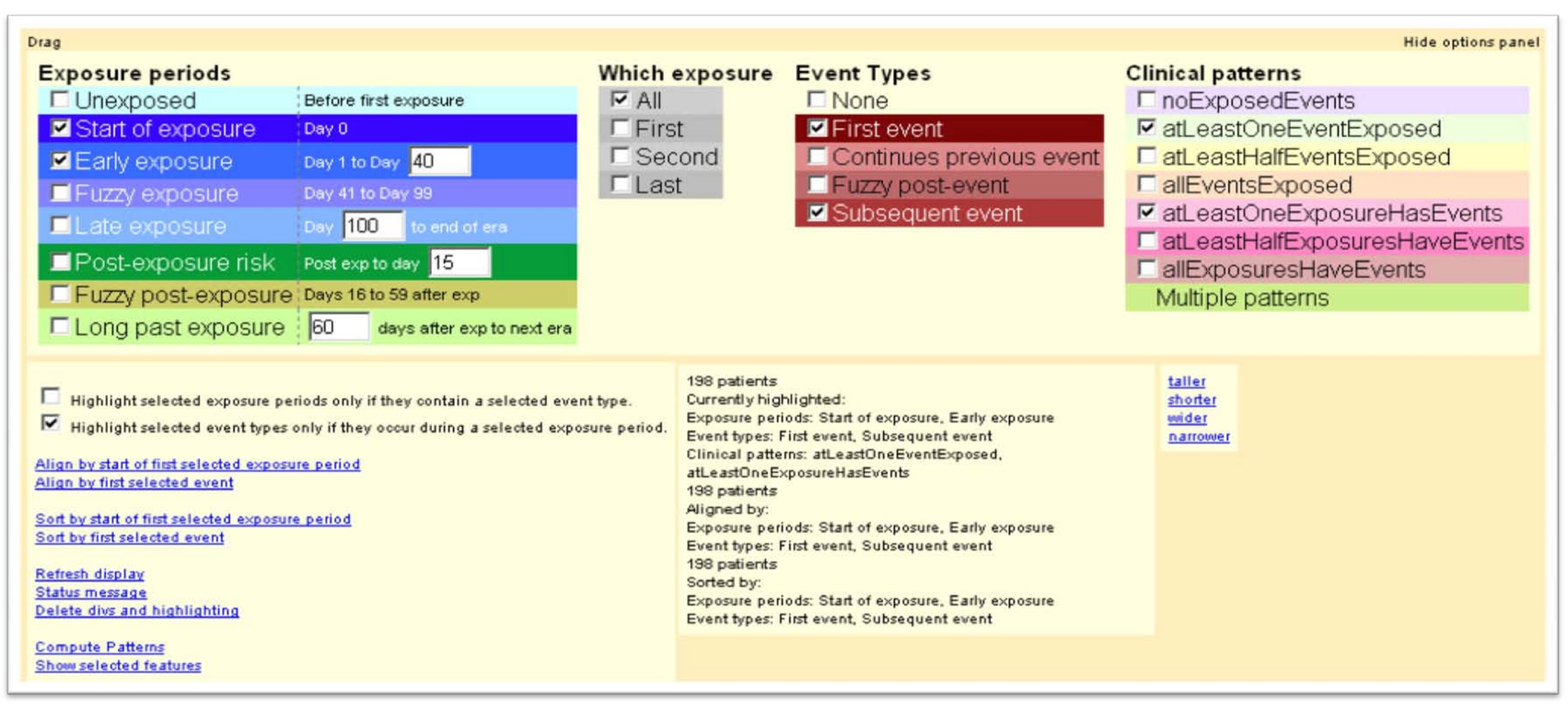

Figure 4. Patient timeline visualization prototype control panel

Conclusions

In early development of visualization tools we need to use positive cases to bring out observable patterns. The usefulness of particular features, however, will become clearer when we use the tool to explore signals that have not been verified elsewhere.

Further study is needed to determine the usefulness of dividing exposure and post-exposure eras into early and late periods and other complex features of the tool. It seems that most of our observations arose from the basic timeline layout with alignment by first exposure and sorting by first event.

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