

# **Big Data and Health Analytics (to appear)**

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## **Chapter 12: Interactive Visualization**

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### **Abstract:**

This chapter focuses on the central role of information visualization in health analytics. From the early x-rays to 3D volume visualizations rapid progress has been made, but the most exciting growth is now in the area of information visualization which offer interactive environments and analytic processes that help support exploration of EHR data, monitoring, or insight discovery. For example, a health organization might want to investigate patterns of drug prescriptions in patients with asthma, and compare prescribing practices with current guidelines. Temporal patterns are critical to this analysis, and interactive visualizations are beginning to support powerful temporal queries, present rich result summaries, and offer fluid interactions to identify the clinically relevant patterns hidden in the data. Visualization should soon help clinicians identify cohorts of patients who match selection criteria for clinical trials, or need to be brought back to the office. Visualization can also reveal data quality problems, which are common when repurposing clinical data for secondary analysis. After a quick summary of the state-of-the-art of information visualization systems for exploring and querying EHR data, we describe in detail one recent system (EventFlow) developed by the Human-Computer Interaction Lab at the University of Maryland, and illustrate its use with an asthma prescription study example.

## 1.1 Introduction

Visual analytics is the science of analytical reasoning facilitated by interactive visual interfaces (Kielman et al., 2009; Ward et al., 2010). Visual analytics tools often combine multiple components such as analytical reasoning, data representations, human-computer interactions, tools for collaboration and for communicating the results of the analysis. Information Visualization can be defined as the use of computer-supported interactive visual representation of abstract data to amplify cognition (Card et al., 1999). It aims to visualize and manipulate large numbers of items (10<sup>2</sup>-10<sup>6</sup>), possibly extracted or aggregated from far larger datasets, or brought to the attention of users by analytics algorithms. It uses the enormous visual bandwidth and the remarkable human visual system to enable clinical researchers, epidemiologists, policy makers and even clinicians and patients to make discoveries, make decisions, or propose explanations. While visualization tools are becoming available the field is still in its infancy. In particular, the US Institute for Medicine's 2011 Report (IOM 2011) noted that "Information visualization is not as advanced in parts of clinical medicine as compared with other scientific disciplines."

After a quick overview of the range of opportunities for the use of information visualization in health informatics, we describe in detail one example of a state of the art visualization system: EventFlow, and illustrate its use with a case study of patterns of asthma drug prescriptions. EventFlow is a project of the Human-Computer Interaction Lab at the University of Maryland, College Park. The lab has a long history of transforming the experience people have with new technologies. From understanding user needs, to developing and evaluating those technologies, the lab's faculty, staff, and students have been leaders in developing innovative technology, in particular in the area of information visualization.

## 1.2 Many opportunities

While medical imagery based on x-rays, CT scans and MRIs have early on transformed medical care by providing 3D volume visualizations, commercial visualization tools such as Spotfire ([www.spotfire.com](http://www.spotfire.com)) are now routinely used for pharmaceutical drug discovery, genomic expression analyses and other applications (see example of Figure 1). Researchers are actively developing novel techniques and strategies using information visualization to harness the benefits of health informatics databases and networks (e.g. Rind et al., 2013; Faisal et al., 2013). Many technologies need substantial advances to produce reliable, effective, safe, and validated systems, but the potential societal benefits are enormous. Shneiderman et al. (2013) describes the state of the art of interactive visualization within three domains of health informatics (clinical, personal and public health) then gives seven challenges to researchers. Examples of promising applications of visualization abound.

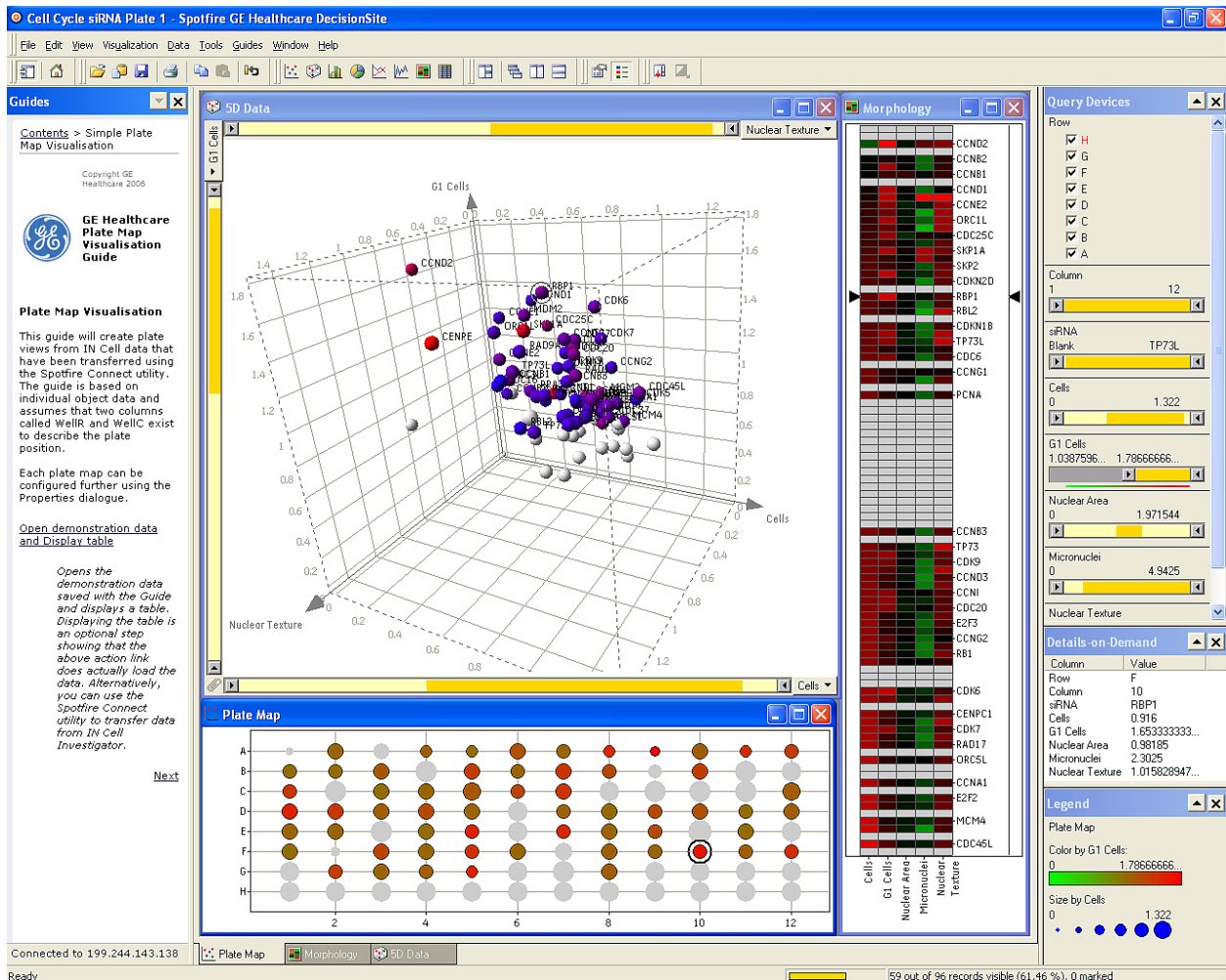


Figure 1: Using Spotfire, analysts revealed the previously unknown involvement of the retinol binding protein RBP1 in cell cycle control. (Stubbs S, & Thomas N. 2006 Methods in Enzymology; 414:1-21.)

In the area of personal health information, personal sensors are becoming popular. Products such as Fitbit (fitbit.com) collect movement data and the associated website shows retrospective temporal patterns of activity, sleep or diet with timelines, which help users reflect on their behaviors. The PatientsLikeMe web site has an Openness Philosophy and encourages members to report in great detail on their status, treatments and side effects, for more than a thousand conditions. It then presents visual summaries of the aggregated data to the public (Figure 2).

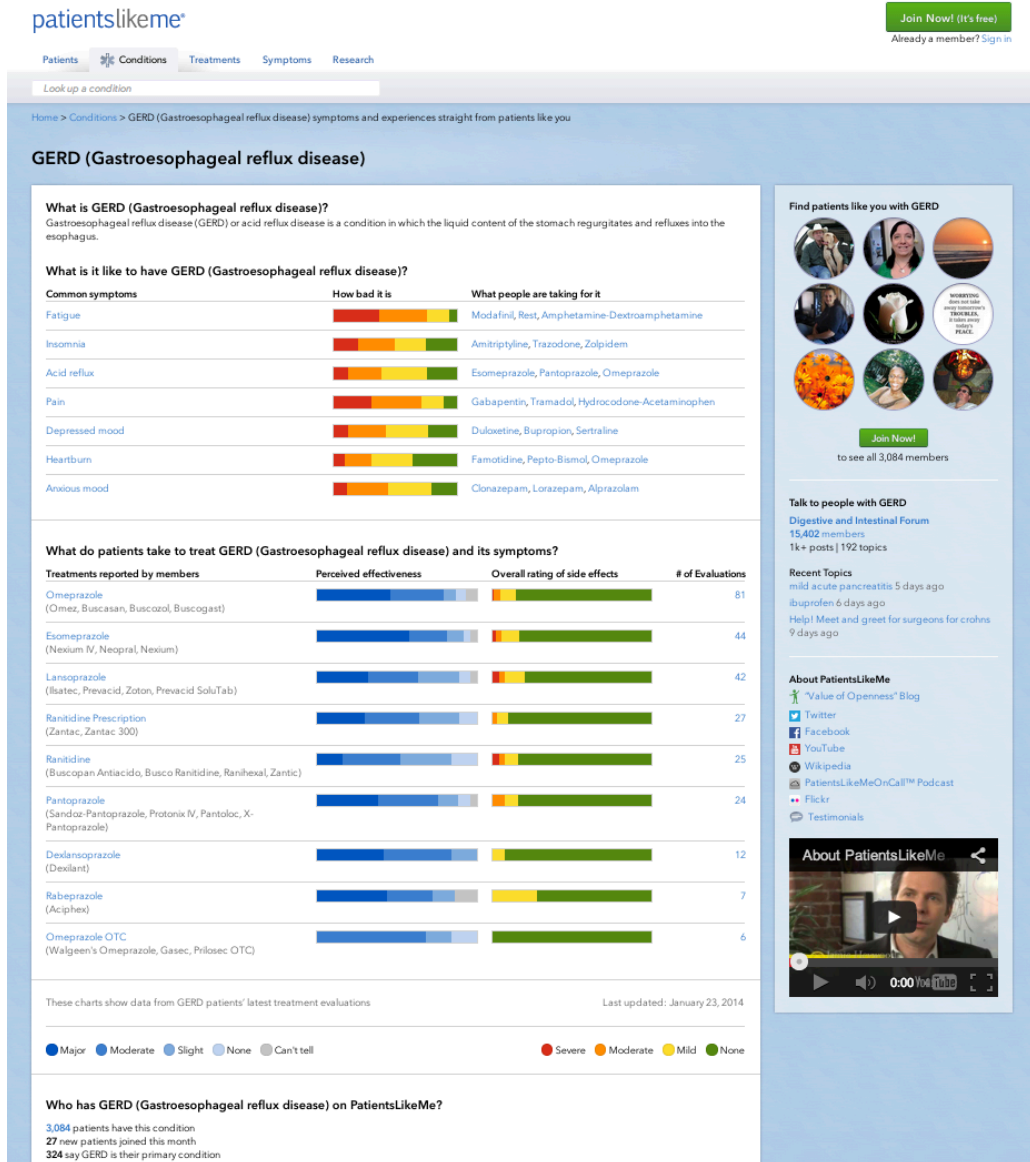


Figure 2: A PatientsLikeMe summary on GERD (Gastroesophageal reflux disease) based on reports from more than 3000 participants. [http://www.patientslikeme.com/conditions/78]

Courtesy of PatientsLikeMe ®

In the area of public health information, visualization provides novel opportunities to present the huge volume of information collected by government organizations in compelling ways. Interactive tools can help analysts spot patterns and issues, while visual presentation of the results can guide policy makers. For example the University of Washington's Institute for Health Metrics and Evaluation has developed a revealing visualization tool, GBD Compare, based on the Global Burden of Disease. GBD Compare makes good use of treemaps to enable users to explore causes of death and their impact worldwide (Figure 3, and IHME, 2014). Controlling the spread of new infectious diseases or responding to biological attacks is also an opportunity for visual analytics solutions.

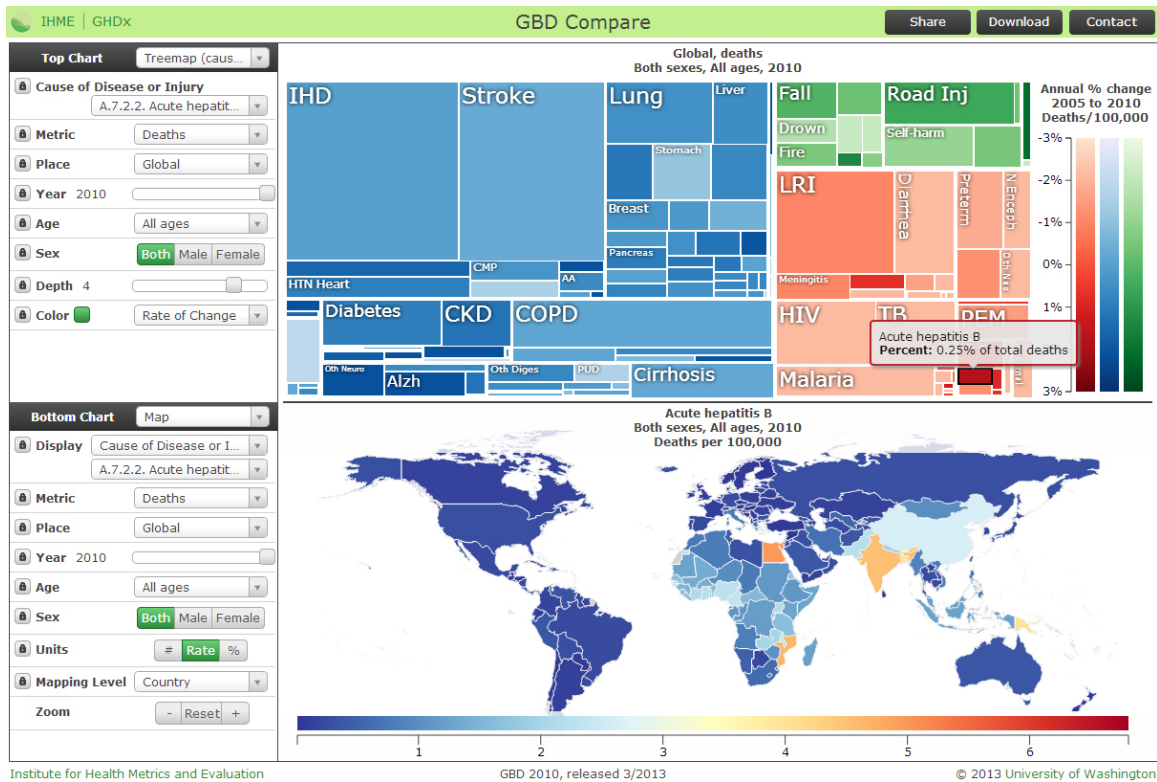


Figure 3: GBD Compare, based on the Global Burden of Disease. At the top a treemap shows all the causes of deaths. The size of the box is proportional to the number of deaths, and the color indicates the change over time (light for improving, dark for worsening). Acute Hepatitis is selected, and the map below shows where the problem is most prevalent.

Coupled with models of disease spread, visualizations are starting to help decision makers predict the future course of the outbreak, and evaluate strategies that can be applied to control an epidemic (Afzal et al., 2011). Improved syndromic surveillance includes the analysis of over the counter drug sales. Data from social media is especially interesting for public health analysts (Christakis et al., 2011). Clustering algorithms can sort out the active communities of discussions and network analysis metrics help to detect key influencers (Hansen et al, 2010; Hesse et al, 2010) (Figure 4).



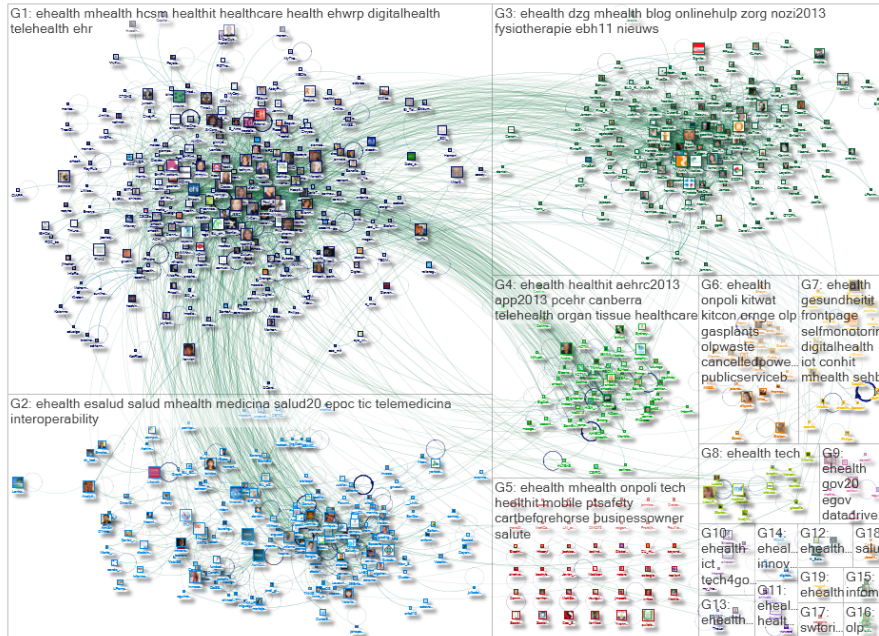


Figure 4: NodeXL ([www.codeplex.com/nodexl](http://www.codeplex.com/nodexl)) graph of 695 Twitter users whose recent tweets contained "#ehealth". Each of the 6177 edges corresponds to a "follows", "replies-to" or "mention" relationship between those users. Users can scan representative keywords for each cluster, the most active tweeters, the URLs mentioned the most often, etc. The largest cluster is placed at the top left. It is in English – with mostly American Twitter users. Its focus is on on digital health and EHR. The second largest in lower left corner is mainly for Spanish tweets. The top right is a large network of mostly Dutch tweets. Those 2 clusters are well connected to the US group but less so to each other. Courtesy of Marc Smith.

Finally, in the area of clinical health information Rind et al. make a survey of interactive visualization to explore and query electronic health records (Rind et al., 2013). Visual temporal summaries of single patient visual histories have been inspired by the early Lifelines prototype (Plaisant et al. 98) (Figure 5), as are body maps showing the location of previous and current conditions, surgeries, or injuries, but no strategy has emerged to be widely accepted. While clinical trials remain the work horse of clinical research+ there is now a shift toward the use of existing clinical data for discovery research, leading researchers to analyze large warehouses of patient histories (e.g., [btris.nih.gov](http://btris.nih.gov)). Visualization can reveal data quality problems, which are common when reusing data created for other purposes. Temporal patterns are critical to this research, so novel visualizations now support powerful graphical temporal queries and summarization of clinically relevant temporal patterns hidden in the data (Monroe et al., 2013). Visualizations can also help clinicians identify cohorts of patients who match selection criteria for clinical trials (e.g. using [i2b2.org](http://i2b2.org)).

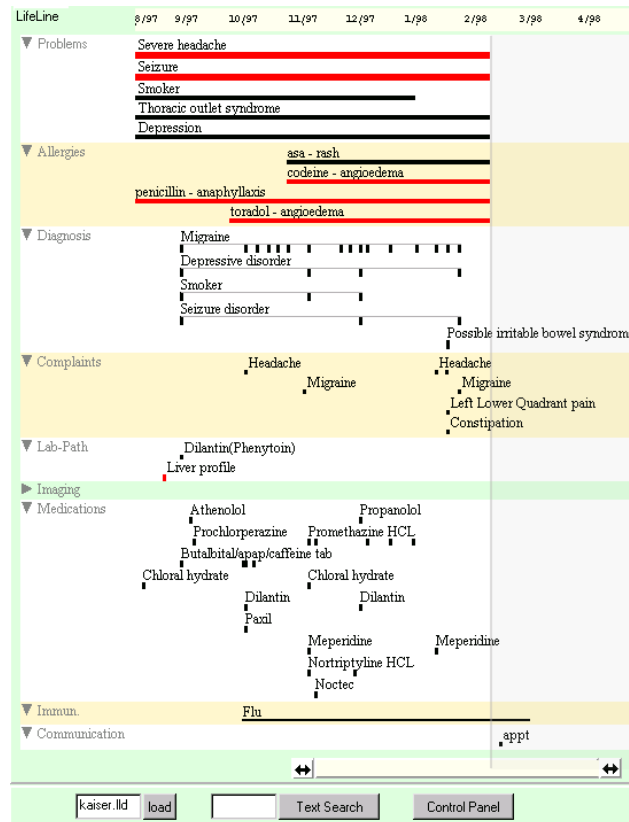


Figure 5: The Lifelines prototype shows a timeline summary of one patient. Users can zoom in and out, or click on any graphic element to reveal more details (Plaisant et al., 1998)

After this quick review of the many opportunities for information visualization in health informatics we will focus the third section on a detailed description of one example tool - called EventFlow, and the fourth section will illustrate the use of EventFlow in the study of patterns of asthma drug prescriptions.

### 1.3 EventFlow for temporal sequence analysis of EHR data

EventFlow ([www.cs.umd.edu/hcil/eventflow](http://www.cs.umd.edu/hcil/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) LifeLines2 (Wang et al., 2009) and LifeFlow (Wongsuphasawat et al., 2011). With LifeLines2 researchers used event operators (align, rank, filter and group by) to specify queries on point event data. This early effort focused on searches for patterns specified by users, for example “find all the patients who bounce back to the ICU within 24 hours of leaving the ICU”, or “find patients with high creatinine readings within 14 days of the administration of radiographic contrast materials” (in an effort to find patients who experienced reduced renal function after infusion of contrast materials). Our research showed that such temporal queries require users to refine their queries iteratively after seeing the results (*e.g.*, by seeing the results they immediately realized that they needed to remove patients with too many creatinine highs before the contrast - as they probably had chronic renal failure - or that they needed to remove patients without

normal readings before the contrast). See video demonstrations at [www.cs.umd.edu/hcil/lifelines2](http://www.cs.umd.edu/hcil/lifelines2).

The next step was to provide compact visual summaries of all sequences found in the data (Wongsuphasawat et al., 2011). This breakthrough technique allows users to explore questions such as “what happens to patients after they leave the emergency room?” or, combined with the align operator “what happens before and after patients are admitted to the ICU?”

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 include “interestingness” measures that often puzzle end-users.

## Interface description

This section introduces the main design features of EventFlow. More details are provided in section 4 in the context of a use case. The interface of EventFlow consists of three main components: interactive controls, legend, overview and timeline (Figure 6).

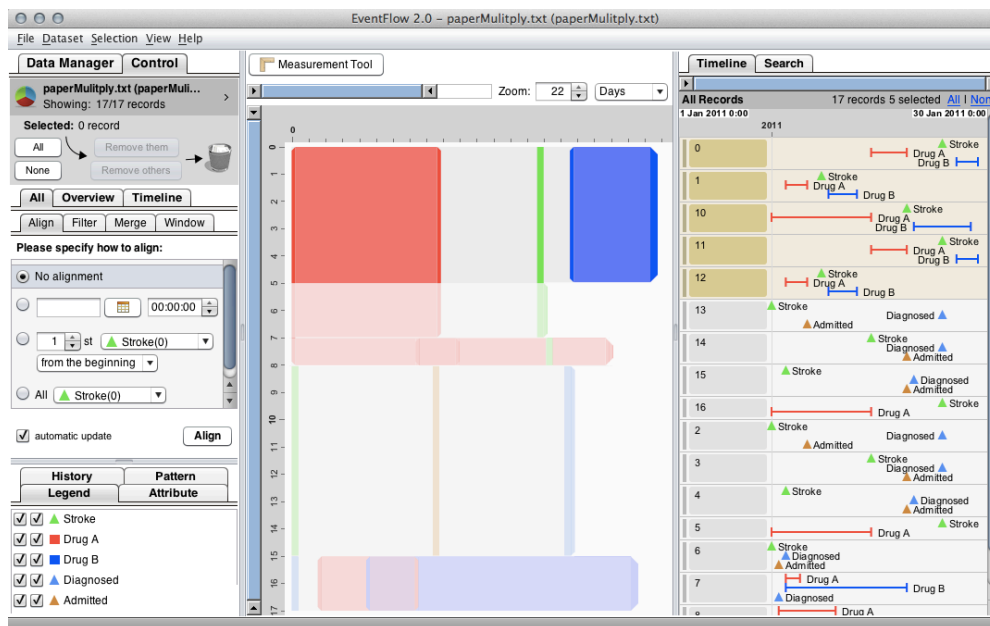




Figure 6: The EventFlow interactive analysis tool ([www.cs.umd.edu/hcil/eventflow](http://www.cs.umd.edu/hcil/eventflow)) with a small sample dataset. On the left are found controls and legend, in the middle is the overview of all sequence patterns in the dataset, and on the right a scrollable timeline browser shows all the individual records. The top sequence in the overview is selected (drug A, followed by stroke, followed by drug B). The distance between events corresponds to the average time between events. The height of the bar corresponds to the proportion of records with that sequence. The records with the selected sequence are highlighted at the top in the timeline view.

### *Individual records*

On the right the timeline shows details of individual records; each patient is shown on a separate timeline. In Figure 6 we see patient 0 to 16, and users need to scroll to see all patients. Triangle icons represent point events while connected rectangles represent intervals (and condense to a single rectangle when the interval duration is small). The legend shows all event categories, enabling users to change the color and order of the categories. Figure 6 only shows patients 0 to 16, forcing users to scroll to see all patients.

### *Overview of sequences*

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 (Wongsuphasawat et al., 2011) 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. Users can select other metrics such as the median, and the distribution of values is overlaid on the display when the cursor hovers over a time gap element. Multiple interval events can occur concurrently, and EventFlow handles this occurrence by rendering overlapping intervals using the combined color of the two overlapping categories. Colors selected for interval categories default to primary colors, resulting in intuitive overlap colors. 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.

The two views (overview and timeline) are coupled so that when users select an event sequence (*i.e.*, bar) all records with that sequence are selected on the timeline view (shown in dark yellow in Figure 6) and moved to the top of the timeline. Similarly, selecting a record on the right will highlight the corresponding event in the summary. The legend allows users to select or deselect which event categories they want to display on the overview or the timeline. After selecting records users can also remove either the selected or unselected records from the display. These two simple techniques allow users to easily narrow the focus of an analysis on records exhibiting particular event sequences of interest.

### *Search*

EventFlow includes two separate search interfaces. The basic menu-based search interface gives users easy access to either before and after relationships (Subsequence module) or during relationships (Overlap module). The Advanced Search allows users to specify more complex temporal features such as absolute time constraints and absence of events scenarios (Monroe et al., 2013a). The advanced search interface uses a visual query language to draw the desired

sequence of event relationships (see Figure 8 in the next section). Matching records are selected in the timeline display and moved to the top, while those that do not match remain at the bottom. This allows users to quickly see not only the records that match their query, but also records that did not match so they can check that the search behaved as expected.

A set of simplification operations allows users to focus on patterns of interest (Monroe et al., 2013b), e.g. by selecting event categories or applying search and replace operations.)

Finally the control panel gives access to many more powerful operators to zoom and filter, rank and cluster the records, adjust parameters of the views, and manage datasets.

#### **1.4 Use case: Studying patterns of prescription of asthma medications**

This section summarizes a case study conducted with the US Army, Office of the Surgeon General, Pharmacovigilance Center, where an epidemiologist worked with the EventFlow developers to understand the prescribing patterns of asthma medications. A particular question of interest was whether a type of asthma medications, i.e. long-acting beta-agonists (LABAs), was being correctly prescribed according to guidelines. Visualizing the temporal patterns of asthma medication use surrounding a LABA prescription with EventFlow is a quick way to detect possible sub-optimal use. The ultimate goal of the study was to understand LABA use in order to inform interventions to prevent morbidity and mortality from sub-optimal use.

In layman's terms, the National Asthma Education and Prevention Program clinical guidelines for the diagnosis and management of asthma (NAEPP 2007) and safety alerts published by FDA (FDA 2010a and 2010b) recommend that LABAs should only be prescribed in combination with a particular other medication (a long-term asthma controller) and only be used after the use of other drugs have failed. Similarly the guidelines recommend that LABA therapy should be de-escalated once asthma has been adequately controlled. In other words we were looking for the proportion of LABA used concomitantly with appropriate other therapies, and escalation/de-escalation patterns. For more information on the guidelines and overall study, please see (Meyer et al. 2013).

The epidemiologist selected a sample of 100 asthma patients, extracted all of their asthma medication prescriptions for the 365 days surrounding a LABA prescription, and categorized the asthma medications into groups. The file included for each prescription a de-identified patient identifier, the type of asthma medication, the start date of the prescription, and the end date of the prescription derived from the start date plus days supply of the prescription. Figure 7 shows what it looked like when first loaded in EventFlow. The color legend in the lower left corner indicates that LABAs appear as bright red intervals, inhaled corticosteroids (ICS, which are supposed to overlap with the LABA prescriptions) are blue, while the other drugs that should be prescribed before and after the LABA therapies are shown in other colors (i.e. light blue for oral corticosteroid bursts [OCS], pink for leukotriene receptor antagonists [LTRA], yellow for short-acting beta-agonists [SABA], and orange for other older drugs).

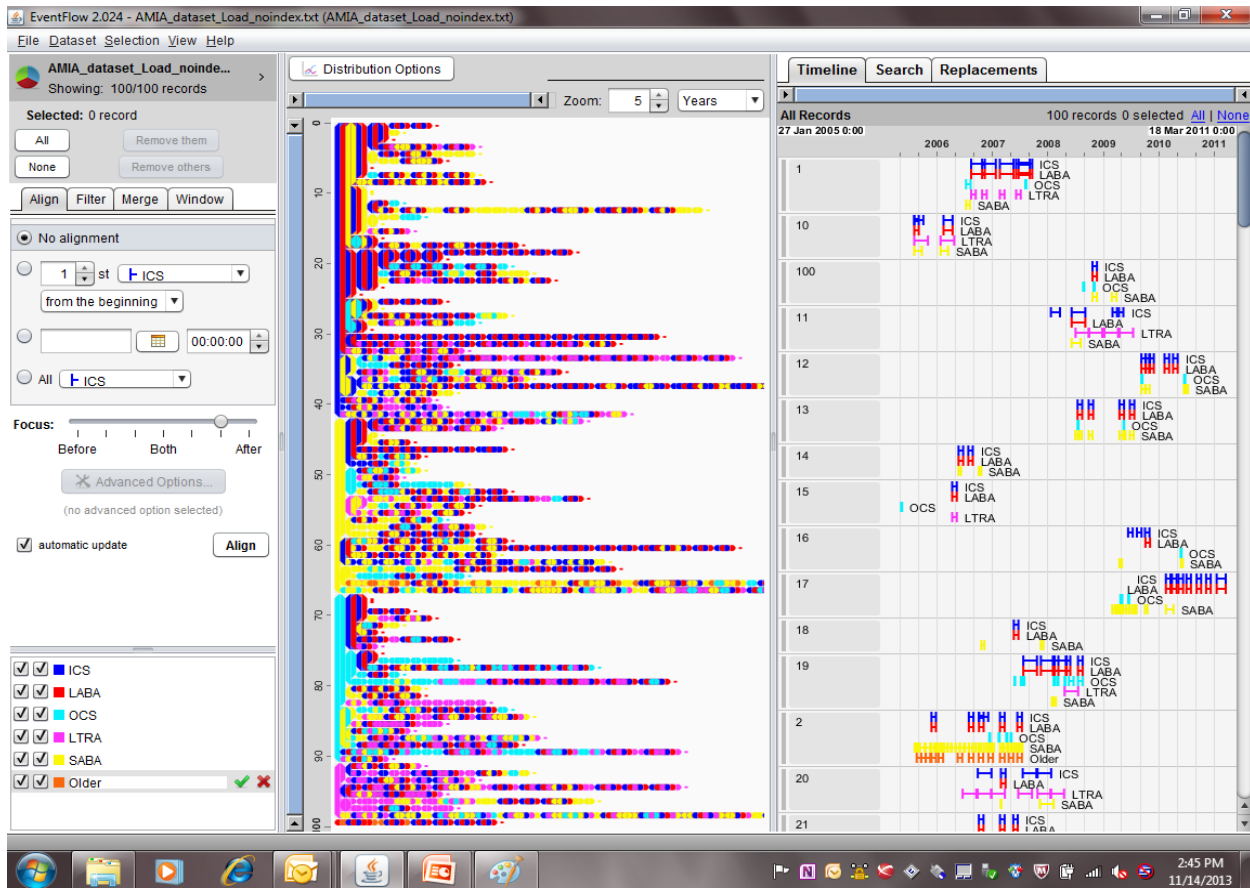


Figure 7: Initial EventFlow overview of 100 patients’ prescription records. LABAs are shown in bright red, ICS is blue (and supposed to always overlap with LABA), while the other drugs that should be prescribed before and after the LABA therapies are shown in other colors (light blue, pink or yellow).

At first the display appeared very busy and did not reveal clear patterns, but we could immediately see that most of the patients had more than one LABA prescription. To compare with the guidelines, we needed to find the “new” LABA prescriptions which are defined in simple terms as “new LABA prescriptions for patients who did not have a LABA in the previous 90 days.” EventFlow graphical Search and Replace feature was found to be very helpful for that (see Figure 8). By using menu selections we placed the set of events and constraints on the search control panel to specify the search pattern (i.e. a red LABA interval, followed by no LABA for at least 90 days, then another red LABA interval.), then specified that a new type of event be created (“Index LABA”, colored black) and that this event be inserted at the time of the start of the second interval. After the insertion was completed we realized, by looking at the visualization, that we had forgotten the cases where patients had never had a LABA before, so we repeated the search and replace with a second pattern (Figure 8 – right side).

The search results separate the records that match the search pattern from those that do not match. Because we were able to quickly and visually inspect the non-matches we could see that several patients had a LABA more than 90 days but less than a year before the index LABA suggesting that using a longer “washout” period (i.e. period without LABA) may be useful in

future analyses. Still we decided to stick with the 90-day washout period because washing out for 365 days resulted in similar patients included.

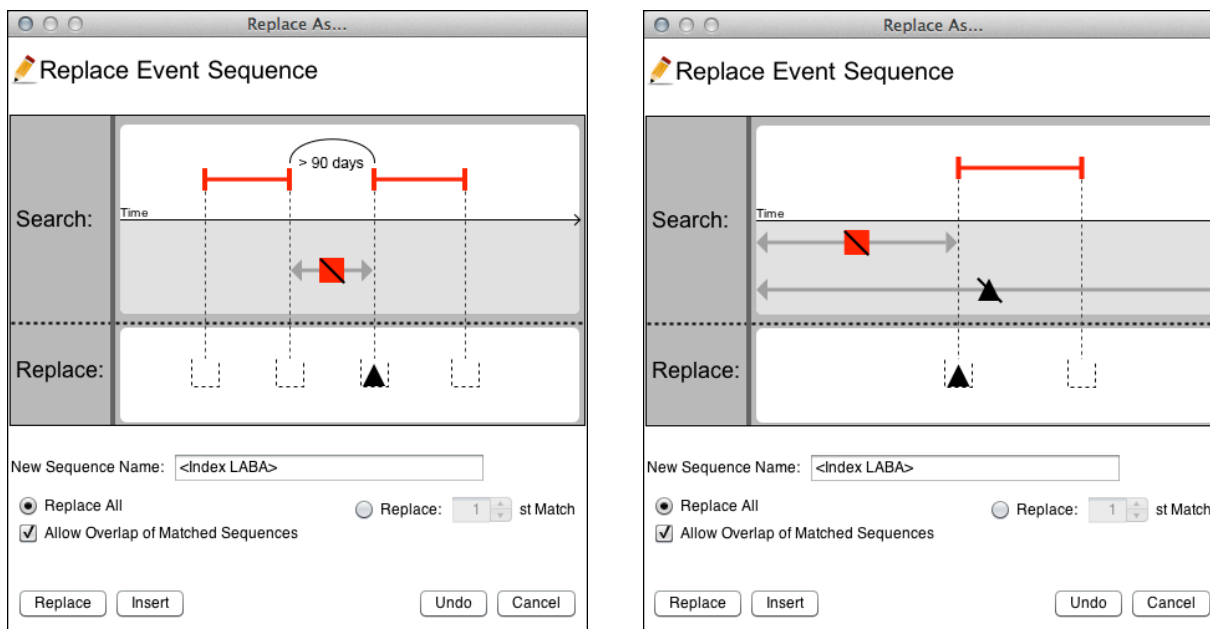


Figure 8- EventFlow advanced search interface. Using menus to select event type and control panels to set constraints users specify search patterns, e.g. on the left the search pattern is to be a red LABA interval, followed by no LABA for at least 90 days, then another red LABA interval.

If needed users specify what the pattern should be replaced by, here a black “index LABA” event.

Next, since we wanted to examine patterns surrounding the index LABA we used the powerful alignment tool in EventFlow to align all records by the time of the index LABA prescription (Figure 9).

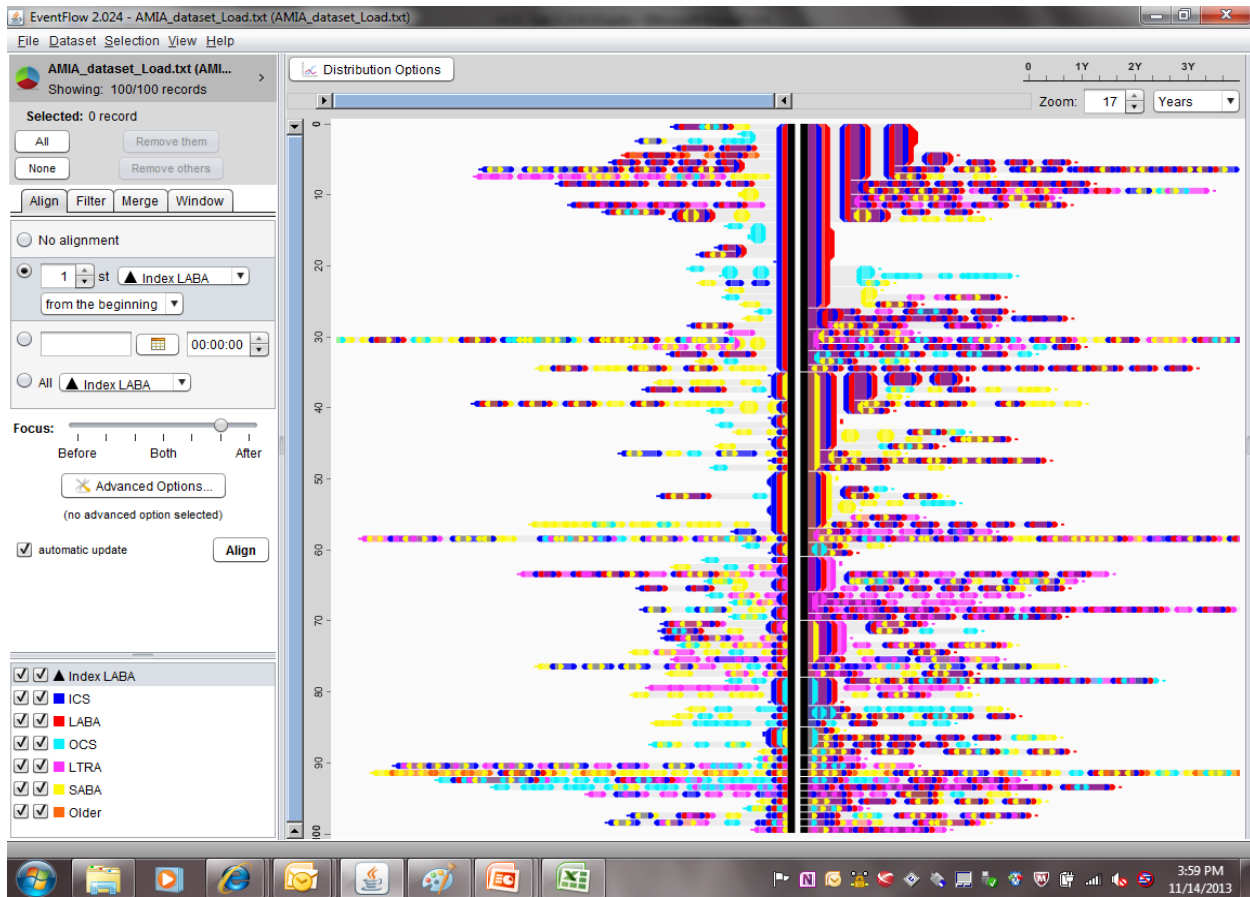


Figure 9- All records are now aligned by the black event “New LABA”

We showed this display to specialists in asthma treatment and they were immediately able to pick out troubling patterns of asthma treatment. For example, patients with a lot of yellow and light blue should most likely have been targeted for earlier step –up to a LABA. Patients with a lot of light blue or yellow after the LABA may need to be brought in for evaluation for continued LABA or other medications.

Next we wanted to check that the red LABAs were not prescribed without a blue ICS, so we started by searching for prescriptions of LABA that occurred at the same time as a prescription for an ICS then decided to replace ALL the overlapping red and blue intervals with one brown LABA + ICS interval, to more easily be able to find the remaining LABA prescriptions that did not fit the search criteria. This simplified the display so we could see that there were very few red LABAs left. Looking at the detail timeline view of individual records we could review those exceptions. E.g. one example of a remaining red LABA was a patient that had a LABA prescription happen during a longer ICS prescription so that was still according to treatment guidelines.

Another way we could simplify the display and focus on the prescriptions immediately preceding and following the LABA was to set a time window of three months on either side of the alignment point (Figure 10). This really highlighted the LABAs that were prescribed without the appropriate step-up and step-down therapy. For example we could see patients that were given

only one LABA with no other asthma therapy before or after. A possible follow up investigation would be to see if the LABAs were being prescribed for something other than asthma like an episode of bronchitis, flu, or cold.

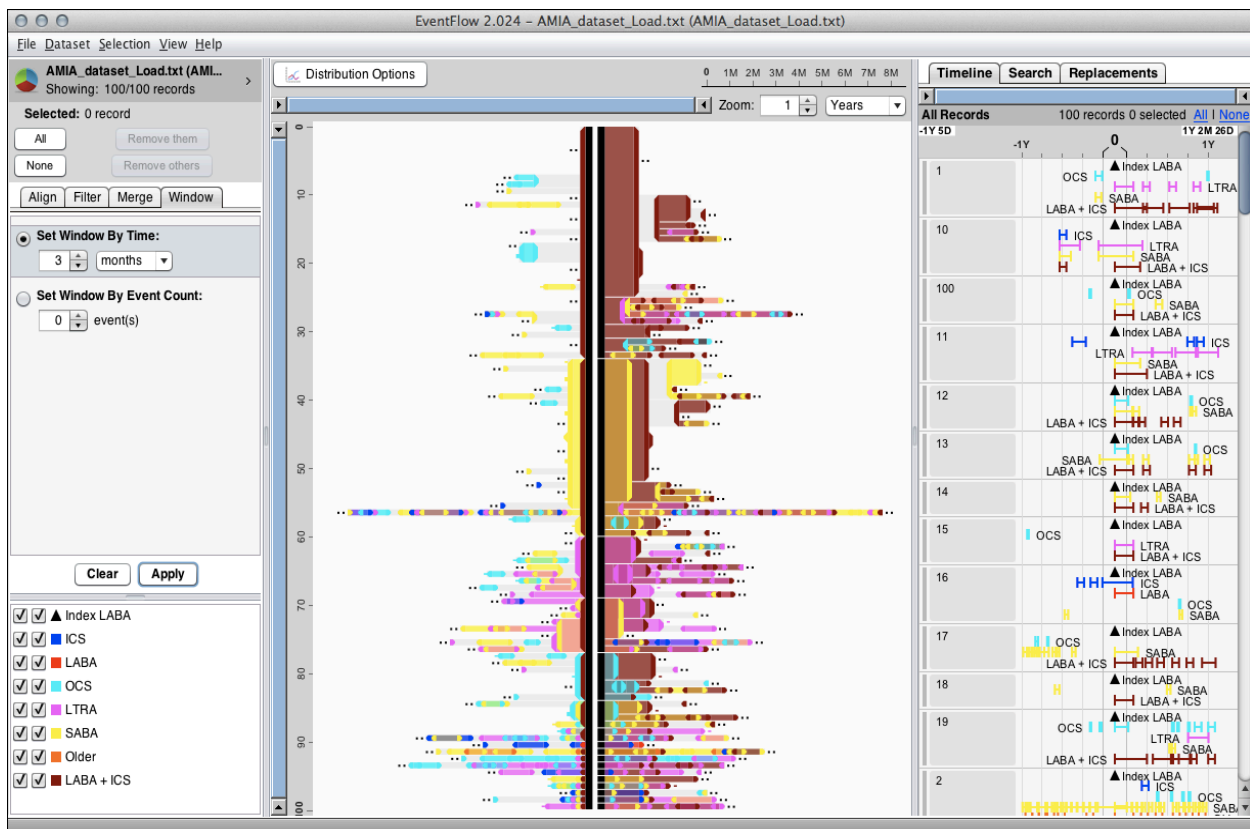


Figure 10 - Setting a windowing limit of 3 months on each side of the Index LABA reduces the number of patterns and leads to a simplified display. On the right we can also see the detailed view, which allows users to review abnormal patterns.

We then used several search and replace steps to find patients that had appropriate step-up and step-down therapy. First, we looked for patients who had a blue ICS before and after their index LABA. That resulted in six selected patients. Then we found patients that were taking a pink LTRA before and after the LABA. The LABA could have been started during an existing pink LTRA event (Figure 11) or with prescriptions for LTRA before and after the index LABA. At the end we found the 27 out of 100 patients that appear to have been treated according to treatment guidelines based on prescription patterns of step-up and step-down therapy.

We could remove those patients from the display and inspect the remaining 73 patients that may not have been treated according to treatment guidelines. We could see that this group still had some patterns that appear to be according to guidelines. The ones with multiple yellow SABA before the LABA or the light blue OCS before the LABA may indicate a severe asthma exacerbation that was appropriately treated with a LABA. There were also blue ICS before the LABA that switched to pink LTRA after the LABA. We were able to go back and add that pattern to our search of appropriate treatment patterns. Of course other patients could also have been appropriately treated but such analysis would require a full review of the clinical notes.



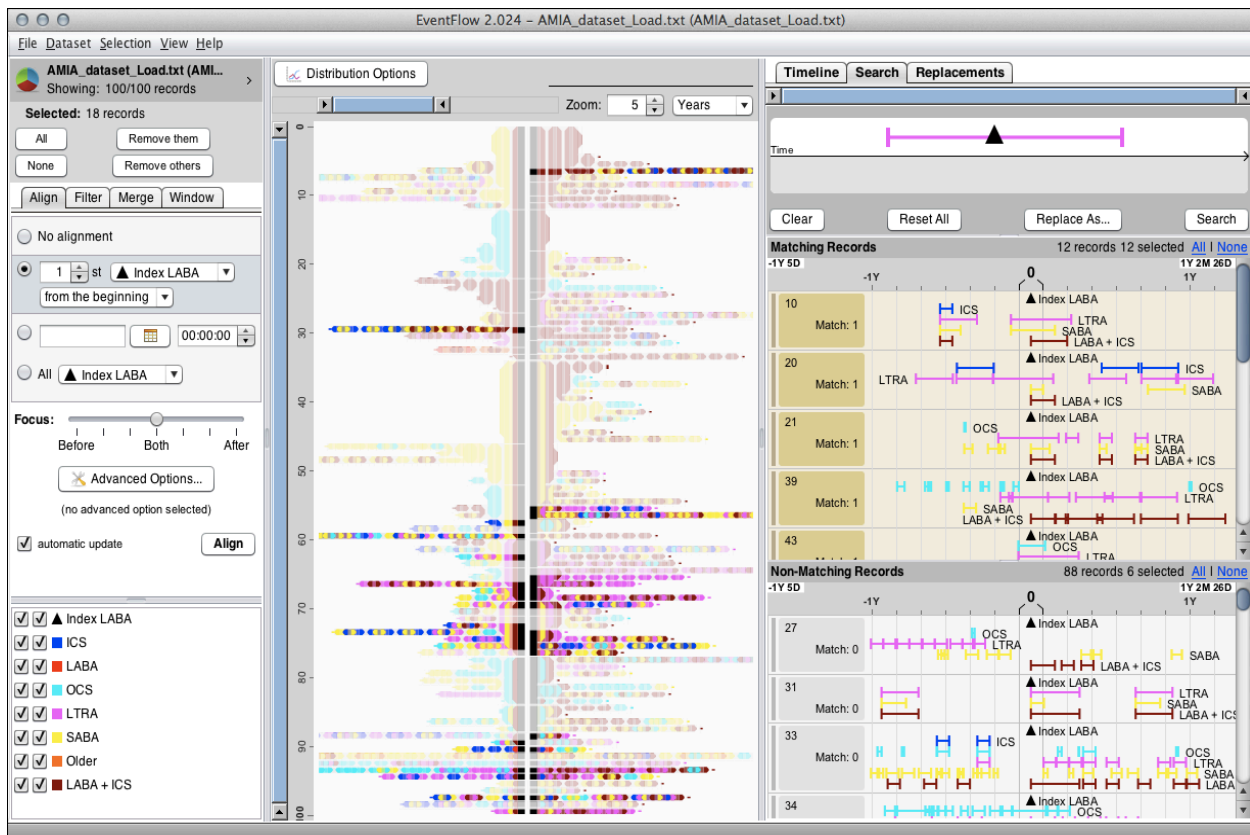


Figure 11 - Find Patients with pink LTRA before and after Index LABA. On the right we see the search panel. On the top right is the pattern being searched, below it are the records that match the pattern (also highlighted on the overview in the center of the screen), and further below the records that do not match the pattern.

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 based on the queries that had been found useful during the rapid interactive exploration. 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 way of reviewing the results in a meaningful way – while the visualization allowed rapid hypothesis generation, refinement of the queries and review of the results.

## 1.5 Conclusions

While there are many opportunities, challenges for Information Visualization remains. Some are general visualization problems, e.g. scaling to larger datasets or maintaining of provenance (i.e. records of the source of the data and of the analysis process used); others are specific to health informatics, e.g. characterizing and understanding similarity of patients, or visualizing comparative-effectiveness and cause and effect relationships. Traditional evaluation metrics for

interactive systems - such as task time completion, number of errors, or recall and precision are insufficient to quantify the utility of visual analytics tools that may be used for days or months, and new research is needed to improve our visual analytics evaluation methodology.

Still, the growing number of successful applications and case studies provides evidence that the use of electronic health records databases for research and quality assurance could be dramatically expanded when easy-to-use interfaces allow clinical researchers to specify queries, review results, and find patterns. 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.

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