Interactive Cohort Analysis and Hypothesis Discovery by Exploring Temporal Patterns in Population-Level Health Records

Tianyi Zhang*
Purdue University

Thomas H. McCoy Jr.† Roy H. Perlis‡
Massachusetts General Hospital
Harvard Medical School

Finale Doshi-Velez§ Elena Glassman¶
Harvard University

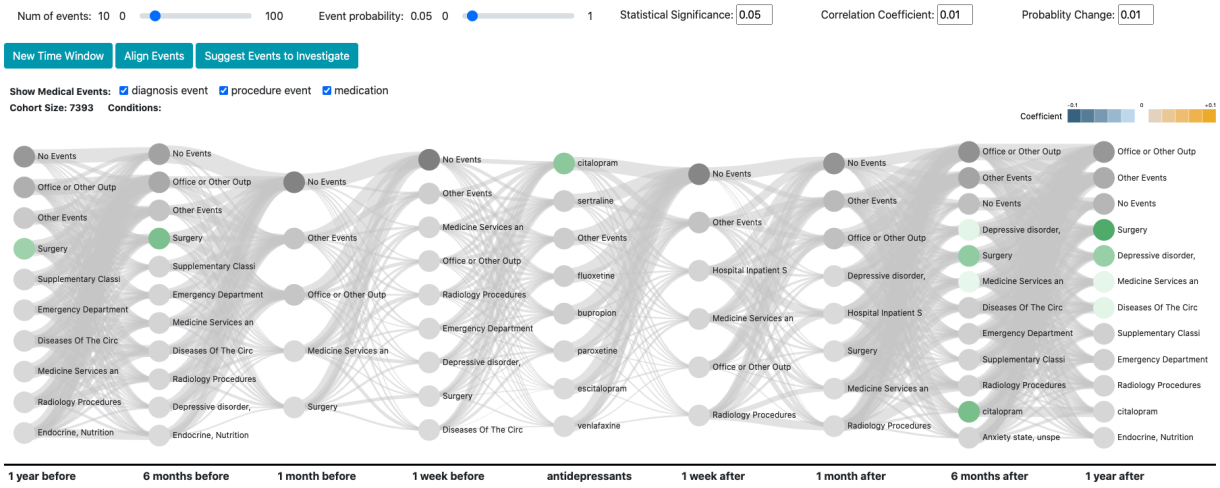

Figure 1: A holistic view of medical events with information scents (green) in different time windows

Abstract

It is challenging to visualize temporal patterns in electronic health records (EHRs) due to the high volume and high dimensionality of EHRs. In this paper, we conduct a formative study with three clinical researchers to understand their needs of exploring temporal patterns in EHRs. Based on those insights, we develop a new visualization interface that renders medical event trajectories in a holistic timeline view and guides users towards interesting patterns using an information scent based method. We demonstrate how a clinical researcher can use our tool to discover interesting sub-cohorts with unique disease progression and treatment trajectories in a case study.

Index Terms: Human-centered computing—Visualization—Visualization techniques; Human-centered computing—Visualization—Visualization design and evaluation methods

1 Introduction

The availability of electronic health records (EHRs) enables clinical researchers to discover data-driven insights about diseases and treatments. However, EHRs often include data spanning several years from hundreds of thousands of patients (i.e., large volume), which are encoded using hundreds of thousands of unique medical event types (i.e., high dimensionality). As a result, clinical researchers cannot easily gain insights from EHRs with bare eyes or primitive data analysis tools [10]. For example, it is hard to answer questions like "What are the patients with similar disease progression patterns?", "What are the commonality among them and how are they different from other patients?", "What comorbidities have they developed?", "Does the ordering of drugs tried matter?", etc.

Over the years, the information visualization community has made great efforts to visualize EHRs. Of particular interest to us are the visualization techniques that identify and render temporal patterns in EHRs [4, 6, 7, 9, 13, 14, 17, 18, 20, 25, 29–32]. To understand how clinical researchers use such visualization tools in exploratory cohort analysis, we conducted a formative study with three clinical researchers at Massachusetts General Hospital and asked them to try out a state-of-the-art visualization tool called Cadence [13]. Participants gave three major pieces of feedback. First, they wished the visualization could make interesting patterns more recognizable or at least provide some hints about which medical events to consider investigating first, instead of users composing their own hypotheses or queries with little assistance or information scent from the system. Second, instead of only showing relative temporal ordering, they suggested time be better represented in the visualization, as an event occurring a week vs. a month after another event has significantly different clinical implications. Third, they found it difficult to translate their clinical questions into queries supported by Cadence. For example, they found it hard to define a *meta-event* like "seizure" using several diagnosis codes, and they were also not able to define a query to answer an exploratory question such as "What symptoms did patients develop while taking a drug over a time period?"

Based on the formative study, we designed an interactive visualization interface for exploring temporal patterns in electronic health records. Figure 1 shows an overview of our tool. Our tool provides a holistic view of disease and treatment trajectories in a timeline view, where users are given the flexibility to bin medical events into different time windows. Frequent medical events are rendered in each time window. The flow between two events in adjacent time windows indicates the conditional probability of having one event given another event, which is computed based on the frequency of each event in the cohort. We also developed a novel algorithm to

*e-mail: tianyi@purdue.edu
†e-mail: tmccoy@mgh.harvard.edu
‡e-mail: rperlis@mgh.harvard.edu
§e-mail: finale@seas.harvard.edu
¶e-mail: glassman@seas.harvard.edu

identify medical events that may lead to a sub-cohort with unique temporal patterns. These medical events are highlighted to guide the data exploration process, inspired by the idea of information scents in the information foraging theory [8]. Furthermore, our tool supports a rich set of user interactions to allow clinical researchers to create a query that answers their clinical questions. For example, users can group multiple events to form a meta-event. Users can also define the inclusion or exclusion of an event to filter the cohort of patients. Clinical researchers can further run statistical tests to assess the correlation between two medical events.

This paper is organized as follows. Section 2 discusses related work and elaborates on how our tool is different from existing visualization, clustering, and data mining techniques for EHRs. Section 3 describes the formative study and our findings. Section 4 describes the tool design. Section 5 demonstrates how a clinical researcher can use our tool to arrive at a sub-cohort of patients with interesting and unique temporal patterns. Section 6 concludes this work and discusses future work.

2 Related Work

2.1 Visualization for temporal patterns in EHRs

Many visualization techniques have been proposed to discover temporal patterns in EHRs [1, 4, 6, 7, 9, 13, 17, 18, 20, 25, 29–32]. To reduce the volume and dimensionality of medical records, many of these techniques require a priori event selection, e.g., only including a small set of events for analysis and ignoring the rest. While several tools such as EventFlow [20] provide a faithful overview of event sequences in medical records, the resulting sequence view can be quite complex and cluttered given the high dimensional structure of medical events and the rich variations in individual patients' medical histories. Therefore, users have to manually filter and aggregate medical events before they can arrive at a simple and clean sequence view with recognizable patterns. This manual process is tedious and time-consuming. OutFlow [30] and Cadence [13] use automated hierarchical event aggregation algorithms to simplify event sequences, where users can control the aggregation level through a slider. However, clinical researchers in our formative study found such automated aggregation obscure. They wished to have more transparency and control over the automated aggregation process.

Query-based visualization tools [11, 13, 16, 17, 21] allow users to define a query to filter a dataset and then visualize the query result for further investigation. However, our formative study shows that, for exploratory analysis, clinical researchers found it difficult to decide where to start and which event to further investigate on. They wished the tool could provide some hints to guide them towards interesting patterns, rather than coming up with their own hypothesis or queries. To support this need, we propose a novel algorithm to compute the information scent of a medical event based on how likely patients having this event have unique patterns compared with patients without this event. By following the information scent of medical events, users can interactively filter the dataset and identify a sub-cohort of patients with unique temporal patterns.

2.2 Clustering and sequence mining approaches

Clustering-based approaches have been proposed to identify patients that follow the same or similar patterns [2, 3, 5, 12, 14, 19, 22]. These approaches rely on feature selection and predefined metrics to measure the similarity between patients. This may hinder opportunities of identifying latent patterns that are not captured by selected features or similarity metrics. Furthermore, it may not be readily determinable by the user why some patients are grouped together while others are not. As a result, clinical researchers still need to dig into each cluster of patients' records to make sense of these clusters. In fact, given the complexity and temporal nature of medical records, they are often distributed in a high-dimensional space without clear boundaries as the basis for clustering.

Frequent sequence mining techniques have also been applied to identify temporal patterns from EHRs [15, 23–26]. However, these techniques often require careful data preprocessing, aggregation, or filtering to simplify the raw EHRs, e.g., removing disease and procedure events that are not related to a specific disease under investigation. Otherwise, these mining techniques often identify too many patterns. For example, we identified over 321K sequence patterns supported by at least 100 patients by running a frequent sequence mining algorithm [28] on a fully dimensional, non-filtered EHR dataset of 7K patients. A key challenge is to distill useful insights from the over-abundance of patterns. Instead of directly visualizing the large number of sequence patterns identified from an EHR dataset, we choose to use these patterns to compute the information scents of medical events and guide users to interactively narrow down to a sub-cohort of patients with unique sequence patterns.

3 Formative Study

To understand how well existing visualization techniques support temporal pattern discovery in exploratory cohort analysis, we conducted a formative study with three psychiatrists at Massachusetts General Hospital. During the study, participants did an exploratory analysis of a large EHR dataset that they were familiar with, using a state-of-the-art visualization tool called Cadence [13]. The EHR dataset contains medical records of 7393 patients diagnosed with major depressive disorders. In this dataset, diagnosis events are encoded with ICD-9 codes, procedures are encoded with CPT-4 codes, and drug prescriptions are encoded with RxNorm codes.

While the participants felt excited about the visualization support provided by Cadence, they gave three major pieces of feedback based on their experience of using Cadence.

The tool should provide more hints to guide users towards interesting patterns. Given a temporal query, Cadence visualizes the trajectories of events specified in the query. Users can interactively add more events to the timeline view and refine the query by exploring co-occurring events in a list view or a scatter plot. Due to the high dimensionality of EHRs, there are often many events in the list view and the scatter plot. As a result, participants found it difficult to navigate through these many events and figure out which event to investigate for the next step. Even though the list view shows the frequency of co-occurring events and the scatter plot also renders the statistical signifance value of correlated events, such information scents are not sufficient for users to decide whether further investigation on an event would lead them to a sub-cohort of patients with interesting patterns. P1 said, "*The distribution bars of co-occurring events do not really tell me how many patients get it one time, two times, or many times. We really care about the time density of these events, not just their frequency.*"

Time should be better represented. Though the visualization in Cadence shows the relative ordering between different events, it is hard to tell how long an event occurred before another. In clinical settings, an event occurring one week before another is quite different from the event occurring one year before another. In addition, the timeline view in Cadence does not show co-occurring events other than those specified in the query. When investigating what happened to patients who got seizure after taking bupropion, P3 wished to see co-occurring events in the timeline view so she could easily recognize other possible reasons for seizure such as a recent diagnosis of alcoholic disorder. While the scatter plot shows the correlation between events, it is hard to tell when a correlated event occurs. Participants commented that what they really cared about was the chronicity of events. They wished to see trajectories of co-occurring events in the timeline view.

The tool should provide more support to express exploratory queries and sophisticated temporal patterns. The query interface in Cadence can be used to specify temporal patterns such as "dis-

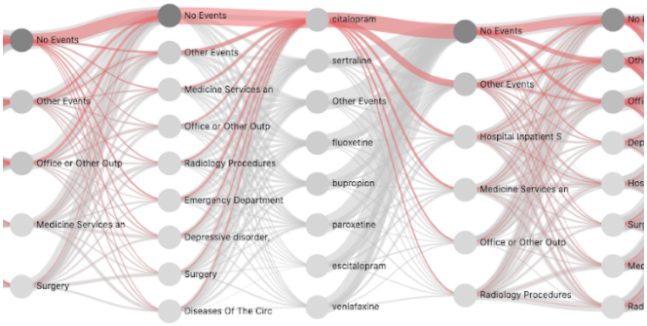

Figure 2: Hovering over an event shows the flow of patients conditioned on this event.

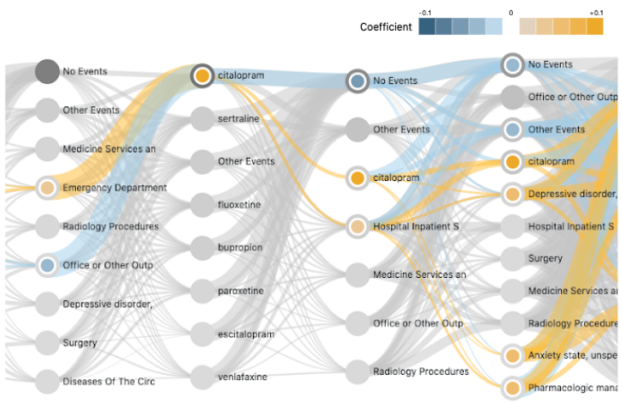

Figure 3: A user pinned an event and viewed positively or negatively correlated events in the timeline view.

charged from a hospital ten days after transferred into the ICU." However, participants found it hard to define a query to answer more open-ended questions such as "are there groups of patients that are different from other groups of patients in the way that we are not aware of?" Furthermore, since medical events in the EHR dataset were encoded with low-level codes in CPT, ICD, and RxNorm, participants often had to manually bundle multiple low-level codes based on their clinical questions. It is cumbersome since there are many codes. While Cadence allows users to aggregate events using a slider, participants found it hard to interpret which events were aggregated together when moving the slider. Furthermore, when informed that this dynamic event aggregation feature was based on ICD and CPT hierarchies, P2 said, "*ICD and CPT hierarchies should not be used to infer event aggregation strategies, since these hierarchies are primarily designed for billing. They do not reflect the appropriate bundling clinicians need to answer their questions.*" Participants wished to have better tool support for medical event bundling.

4 Tool Design

Based on the feedback from the formative study, we designed an interactive visualization interface for exploring temporal patterns in EHRs, as shown in Figure 1.

4.1 A Holistic View of Temporal Patterns

To help users recognize temporal patterns in a large EHR dataset, our interface provides a holistic view of medical events in different timeline windows. Users need to first define an anchoring point to initiate the visualization, such as the first prescription of any antidepressants. We choose to ask users to provide an anchoring point since patients' health record often span across many years and the resulting timeline view can be extremely lengthy and complex without a focus. By default, our interface shows frequent medical events in multiple time windows up to a year before and after the anchoring point. Users are allowed to add or delete a time window to adjust the timeline view. The width of the flow between two events indicates how likely patients having one event would then have another event, which is a kind of conditional probability.

$$Flow(x_{t1} \rightarrow y_{t2}) = \frac{|Patient(x_{t1}) \cap Patient(y_{t2})|}{|Patient(x_{t1})|}$$

In the formula above, the function $Patient(x_t)$ returns the set of patients who have medical event x in the time window t. An alternative way to compute the flow width is to use the relative frequency of having x_{t1} and y_{t2}, i.e., $\frac{|Patient(x_{t1}) \cap Patient(y_{t2})|}{|Cohort\ Size|}$. After consulting our clinician collaborators, we decided to use conditional probability since it was more preferred to interpret the time dependency between events in a temporal pattern. In addition, when a user hovers over an event in the timeline view, the flows in a sub-cohort with that event are highlighted and overlaid on the current timeline view, as shown in Figure 2.

If a user is interested in one particular event, she can pin the event in the timeline view. Our interface will then test the correlation between the pinned event and every other events in the timeline view. Currently, we use chi-squared test of independence to calculate the coefficients and p-values. For example, if a user pins the first prescription of citalopram, other correlated events with statistical significance, such as admitted to an emergency room a week before the citalopram prescription, are highlighted in the timeline view, as shown in Figure 3. Yellow color indicates a positive correlation, while blue indicates a negative correlation. The color hue is adjusted based on the correlation coefficient value. The default p-value and coefficient thresholds are 0.05 and 0.01 respectively. A user can adjust these thresholds along with other thresholds, such as the number of events rendered in each time window, using the control knobs on top of the interface.

4.2 Information Scents

Due to the high dimensionality of EHRs, the timeline view often renders many medical events in different time windows. Based on our formative study, users may find it hard to navigate through these many events and decide which one to investigate for the next step. To address this challenge, we have developed a novel algorithm that identifies medical events that will lead to a sub-cohort with unique temporal sequence patterns compared to other sub-cohorts without these events.

$$Scent(x_t) = |PSet(x_t) - PSet(\neg x_t)| \times |PSet(\neg x_t) - PSet(x_t)|$$

The formula above shows the method to calculate the information scent of an event x in a time window t. The function $PSet(x_t)$ returns the set of temporal patterns in a sub-cohort of patients with x_t, while $PSet(\neg x_t)$ returns the set of temporal patterns in a sub-cohort without x_t. We choose to multiply the number of unique temporal patterns in the sub-cohort with x_t and the number of unique patterns in the sub-cohort without x_t, since during the experiment, we observed that selecting an event sometimes split the cohort to two sub-cohorts, one of which contains a super set of temporal patterns of another. Currently, we use a frequent closed sequence mining algorithm called BIDE [28] to identify temporal sequence patterns in a cohort. Since it is computationally expensive to run frequent sequence mining on the fly, we precompute all frequent sequence patterns in the entire cohort using a minimum support threshold of 100. In other word, each identified pattern is followed by at least 100 patients. For each sequence pattern, we also cache the IDs of

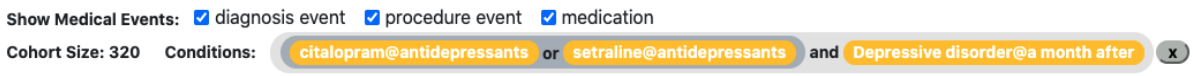

Figure 4: An example inclusion criterion that bundles multiple events

those patients who follow the pattern. In this way, we can efficiently compute $PSet(x_t)$ by checking whether there are at least 100 patients in the intersection of the patients with x_t and the patients that support a pattern p in the pre-computed pattern set.

As shown in Figure 1, the events with information scent scores above a threshold are highlighted in green. The green color hue is adjusted based on the information scent score. For example, the surgery events in multiple time windows are highlighted in Figure 1. This indicates that further investigation of these surgery events will lead to a sub-cohort of patients with unique temporal sequence patterns. A user can filter the dataset by selecting one or more of these events and make further investigation.

4.3 Event bundling

While navigating through medical events in the timeline view, users can bundle multiple events using conjunction and disjunction operators to filter events and create a sub-cohort. Users can either add an event via drag and drop or through a look up table. Our interface also supports specifying exclusion criteria such as not including an event x_t. Figure 4 shows an example inclusion criterion that bundles three events. Filtering the dataset with this criterion creates a sub-cohort of 320 patients who were given either citalopram or sertraline in their first antidepressant prescription and were then diagnosed with depressive disorder again a month after the first prescription. Every time the dataset is filtered, the set of pre-computed sequence patterns and their supporting patients are also filtered accordingly.

5 Demonstration

This section describes a usage scenario to demonstrate how clinical researchers can use our tool to discover interesting temporal patterns in a cohort. We use the same psychiatry dataset as in Section 3 in this usage scenario. Suppose Alex is a psychiatry researcher who is conducting an exploratory analysis on the psychiatry dataset. He wants to find some interesting patterns that he is not aware of before and use them to form new hypotheses in his research. Alex defines the first prescription of any antidepressants as an anchoring point. Then a timeline view is rendered in the interface. While it is interesting to see the trajectories of patients in such a timeline view, Alex finds it tedious to look into so many events one by one. Alex clicks on the "Suggest Events to Investigate" button to solicit some recommendations from the tool. Several medical events are highlighted in green to indicate what to investigate next (Figure 1). Alex notices that patients whose first antidepressant prescription is citalopram are likely to have unique temporal patterns. He decides to make some further investigation and pins this event in the timeline view. Then, several events that are correlated with the first prescription of citalopram are highlighted in the timeline view (Figure 3). Alex finds that there is a strong positive correlation between the first prescription of citalopram and the subsequent prescriptions of citalopram, which is not surprising. On the other hand, Alex is surprised to see a positive correlation between the prescription of citalopram and being admitted to an emergency. This makes Alex wonder whether this is because citalopram is a common antidepressant choice for those ER doctors. Alex also wonders whether other kinds of antidepressants also have such a positive correlation with ER. He pins the first prescription of another antidepressant, sertraline, in the timeline view. This time, the timeline view highlights a different set of correlated events for sertraline, as shown in Figure 5. Alex notices the first prescription of sertraline has a positive correlation with radiology procedures

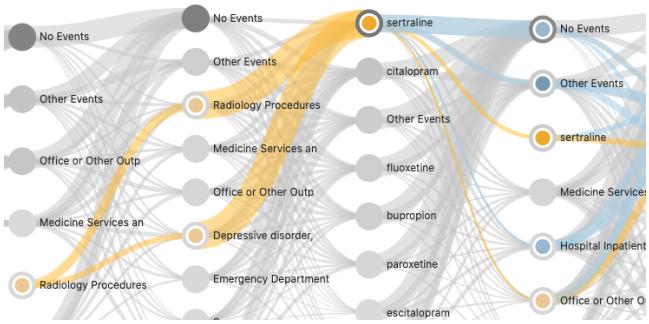

Figure 5: Medical events correlated with the first sertraline prescription

a week and a month before the first sertraline prescription. This implies a contrastingly different trajectory compared with patients who were given citalopram as the first antidepressant. Alex finds this observation quite interesting. He decides to conduct more rigorous experiments to validate this hypothesis and check if any scientific conclusions can be reached.

6 Conclusion

This paper presents an interactive visualization interface for exploring temporal sequence patterns in population-level electronic health records (EHRs). The design of this interface is informed by a formative study with clinical researchers on their needs and experiences of using a state-of-the-art visualization tool for EHRs. Three key features in this tool include: (1) a holistic view of medical events in different time windows, (2) information scents that guide users towards sub-cohorts of patients with unique sequence patterns, (3) a rich set of interactions that allow users to identify statistically correlated events, bundle multiple events, and define sophisticated inclusion and exclusion criteria to filter the dataset. Using this tool, we identified several interesting temporal patterns that were not known before in a psychiatry dataset.

In future work, we will continue to implement several tool features suggested by our clinician collaborators to further support exploratory cohort analysis. For example, our clinician collaborators found it hard to compare patterns in two sub-cohorts, e.g., a sub-cohort of patients who prescribed citalopram and another sub-cohort who prescribed sertraline. They wished they could compare the timeline views of multiple sub-cohorts side by side. Some existing work such as LifeLines2 [29] allows users to compare temporal summaries of two cohorts. It is worth investigating how well such cohort comparison design can support clinicians' need. Another promising tool feature is to recommend what events to bundle together using concept learning or ontology learning. In addition, we will conduct case studies with clinical researchers to comprehensively evaluate the usability and effectiveness of our tool, following the evaluation guidelines from prior work [27].

Acknowledgments

We would like to thank anonymous participants for the formative study and anonymous reviewers for their valuable feedback. This work was supported in part by NIH R01 MH123804-01A1.

REFERENCES

[1] R. Bade, S. Schlechtweg, and S. Miksch. Connecting time-oriented data and information to a coherent interactive visualization. In *Proceedings of the SIGCHI conference on Human factors in computing systems*, pp. 105–112, 2004.

[2] I. Batal, G. F. Cooper, D. Fradkin, J. Harrison, F. Moerchen, and M. Hauskrecht. An efficient pattern mining approach for event detection in multivariate temporal data. *Knowledge and information systems*, 46(1):115–150, 2016.

[3] G. Bruno, T. Cerquitelli, S. Chiusano, and X. Xiao. A clustering-based approach to analyse examinations for diabetic patients. In *2014 IEEE International Conference on Healthcare Informatics*, pp. 45–50. IEEE, 2014.

[4] H. S. G. Caballero, A. Corvò, P. M. Dixit, and M. A. Westenberg. Visual analytics for evaluating clinical pathways. In *2017 IEEE Workshop on Visual Analytics in Healthcare (VAHC)*, pp. 39–46. IEEE, 2017.

[5] N. Cao, D. Gotz, J. Sun, and H. Qu. Dicon: Interactive visual analysis of multidimensional clusters. *IEEE transactions on visualization and computer graphics*, 17(12):2581–2590, 2011.

[6] A. T. Chen, J. H. Chang, S. Hallinan, and D. C. Mohr. Mapping user trajectories to examine behavior and outcomes in digital health intervention data. In *2019 IEEE Workshop on Visual Analytics in Healthcare (VAHC)*, pp. 1–8. IEEE, 2019.

[7] R. Chen, P. Ryan, K. Natarajan, T. Falconer, K. D. Crew, C. G. Reich, R. Vashisht, G. Randhawa, N. H. Shah, and G. Hripcsak. Treatment patterns for chronic comorbid conditions in patients with cancer using a large-scale observational data network. *JCO clinical cancer informatics*, 4:171–183, 2020.

[8] E. H. Chi, P. Pirolli, K. Chen, and J. Pitkow. Using information scent to model user information needs and actions and the web. In *Proceedings of the SIGCHI conference on Human factors in computing systems*, pp. 490–497, 2001.

[9] F. Dabek, E. Jimenez, and J. J. Caban. A timeline-based framework for aggregating and summarizing electronic health records. In *2017 IEEE Workshop on Visual Analytics in Healthcare (VAHC)*, pp. 55–61. IEEE, 2017.

[10] F. Du, B. Shneiderman, C. Plaisant, S. Malik, and A. Perer. Coping with volume and variety in temporal event sequences: Strategies for sharpening analytic focus. *IEEE transactions on visualization and computer graphics*, 23(6):1636–1649, 2016.

[11] D. Gotz and H. Stavropoulos. Decisionflow: Visual analytics for high-dimensional temporal event sequence data. *IEEE transactions on visualization and computer graphics*, 20(12):1783–1792, 2014.

[12] D. Gotz, J. Sun, N. Cao, and S. Ebadollahi. Visual cluster analysis in support of clinical decision intelligence. In *AMIA Annual Symposium Proceedings*, vol. 2011, p. 481. American Medical Informatics Association, 2011.

[13] D. Gotz, J. Zhang, W. Wang, J. Shrestha, and D. Borland. Visual analysis of high-dimensional event sequence data via dynamic hierarchical aggregation. *IEEE transactions on visualization and computer graphics*, 26(1):440–450, 2019.

[14] M. Grace Shin, M. Samuel McLean, and M. June Hu. Visualizing temporal patterns by clustering patients. pp. 41–46, 2014.

[15] Z. Huang, X. Lu, and H. Duan. On mining clinical pathway patterns from medical behaviors. *Artificial intelligence in medicine*, 56(1):35–50, 2012.

[16] J. Jin and P. Szekely. Interactive querying of temporal data using a comic strip metaphor. In *2010 IEEE Symposium on Visual Analytics Science and Technology*, pp. 163–170. IEEE, 2010.

[17] J. Krause, A. Perer, and H. Stavropoulos. Supporting iterative cohort construction with visual temporal queries. *IEEE transactions on visualization and computer graphics*, 22(1):91–100, 2015.

[18] S. Malik, F. Du, M. Monroe, E. Onukwugha, C. Plaisant, and B. Shneiderman. Cohort comparison of event sequences with balanced integration of visual analytics and statistics. In *Proceedings of the 20th International Conference on Intelligent User Interfaces*, pp. 38–49, 2015.

[19] B. M. Marlin, D. C. Kale, R. G. Khemani, and R. C. Wetzel. Unsupervised pattern discovery in electronic health care data using probabilistic clustering models. In *Proceedings of the 2nd ACM SIGHIT international health informatics symposium*, pp. 389–398, 2012.

[20] M. Monroe, R. Lan, H. Lee, C. Plaisant, and B. Shneiderman. Temporal event sequence simplification. *IEEE transactions on visualization and computer graphics*, 19(12):2227–2236, 2013.

[21] M. Monroe, R. Lan, J. Morales del Olmo, B. Shneiderman, C. Plaisant, and J. Millstein. The challenges of specifying intervals and absences in temporal queries: A graphical language approach. In *Proceedings of the SIGCHI Conference on Human Factors in Computing Systems*, pp. 2349–2358, 2013.

[22] A. Mustaqeem, S. M. Anwar, and M. Majid. A modular cluster based collaborative recommender system for cardiac patients. *Artificial intelligence in medicine*, 102:101761, 2020.

[23] G. N. Norén, J. Hopstadius, A. Bate, K. Star, and I. R. Edwards. Temporal pattern discovery in longitudinal electronic patient records. *Data Mining and Knowledge Discovery*, 20(3):361–387, 2010.

[24] A. Perer and F. Wang. Frequence: Interactive mining and visualization of temporal frequent event sequences. In *Proceedings of the 19th international conference on Intelligent User Interfaces*, pp. 153–162, 2014.

[25] A. Perer, F. Wang, and J. Hu. Mining and exploring care pathways from electronic medical records with visual analytics. *Journal of biomedical informatics*, 56:369–378, 2015.

[26] H. Scheuerlein, F. Rauchfuss, Y. Dittmar, R. Molle, T. Lehmann, N. Pienkos, and U. Settmacher. New methods for clinical pathways—business process modeling notation (bpmn) and tangible business process modeling (t. bpm). *Langenbeck's archives of surgery*, 397(5):755–761, 2012.

[27] B. Shneiderman and C. Plaisant. Strategies for evaluating information visualization tools: multi-dimensional in-depth long-term case studies. In *Proceedings of the 2006 AVI workshop on BEyond time and errors: novel evaluation methods for information visualization*, pp. 1–7, 2006.

[28] J. Wang, J. Han, and C. Li. Frequent closed sequence mining without candidate maintenance. *IEEE Transactions on Knowledge and Data Engineering*, 19(8):1042–1056, 2007.

[29] T. D. Wang, C. Plaisant, B. Shneiderman, N. Spring, D. Roseman, G. Marchand, V. Mukherjee, and M. Smith. Temporal summaries: Supporting temporal categorical searching, aggregation and comparison. *IEEE transactions on visualization and computer graphics*, 15(6):1049–1056, 2009.

[30] K. Wongsuphasawat and D. Gotz. Exploring flow, factors, and outcomes of temporal event sequences with the outflow visualization. *IEEE Transactions on Visualization and Computer Graphics*, 18(12):2659–2668, 2012.

[31] K. Wongsuphasawat, J. A. Guerra Gómez, C. Plaisant, T. D. Wang, M. Taieb-Maimon, and B. Shneiderman. Lifeflow: visualizing an overview of event sequences. In *Proceedings of the SIGCHI conference on human factors in computing systems*, pp. 1747–1756, 2011.

[32] Y. Zhang, K. Chanana, and C. Dunne. Idmvis: Temporal event sequence visualization for type 1 diabetes treatment decision support. *IEEE transactions on visualization and computer graphics*, 25(1):512–522, 2018.