PP32: Visual Monitoring of Intercurrent Events with Heatmap

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Abstract

Problem

Identification, analysis, and visualisation of intercurrent events (IEs) are becoming an integral part of clinical studies implementing the estimands framework[1]. Heatmaps are an effective visualisation for displaying many data points on a 2D canvas. Events such as concomitant medications, adverse events, study milestones or other events of interest are overlaid on the heatmap with different shapes, allowing for clear visual exploration. In order to enlarge the image without losing quality, it is essential to produce it in a vector format like SVG.

Summary

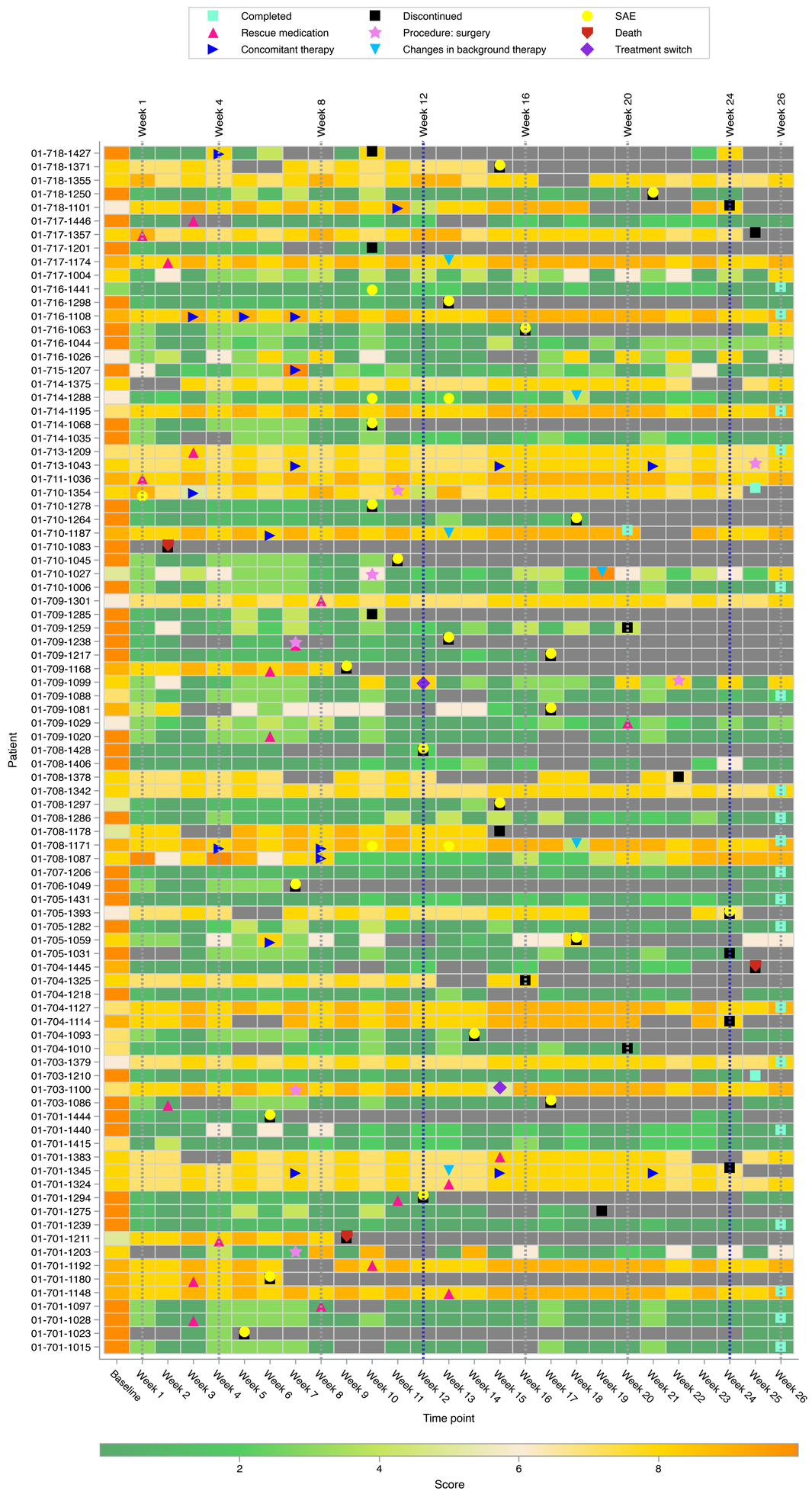
In this poster we construct a heatmap with y-axis for patient, x-axis for time point, cell color for a data point (categorical or continuous endpoint, e.g. score or scale) and intercurrent events with different shapes overlaid. Keeping the image in SVG format allows easy embedding in HTML or high quality printing on oversized paper such as posters.

Takeaway

Heatmap is an efficient way to display 2-dimensional data (patient, variable) and still has a room to overlay additional datapoints like IEs on top and other patient data as interactive pop-ups. Raw data can be plotted allowing visual reviews while collected.

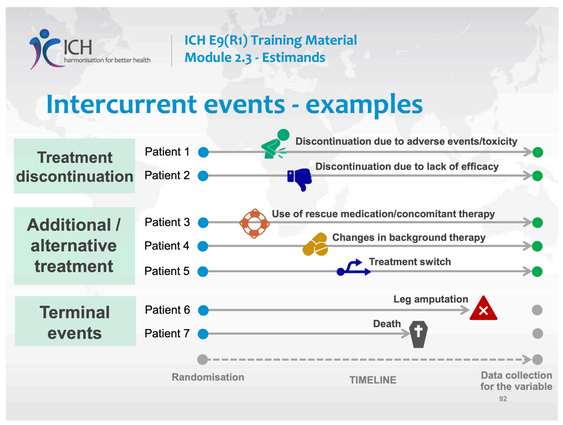
Heatmap

Figure: Score of interest with intercurrent events (Full Analysis Set)



Note: Missing values are represented in gray color.

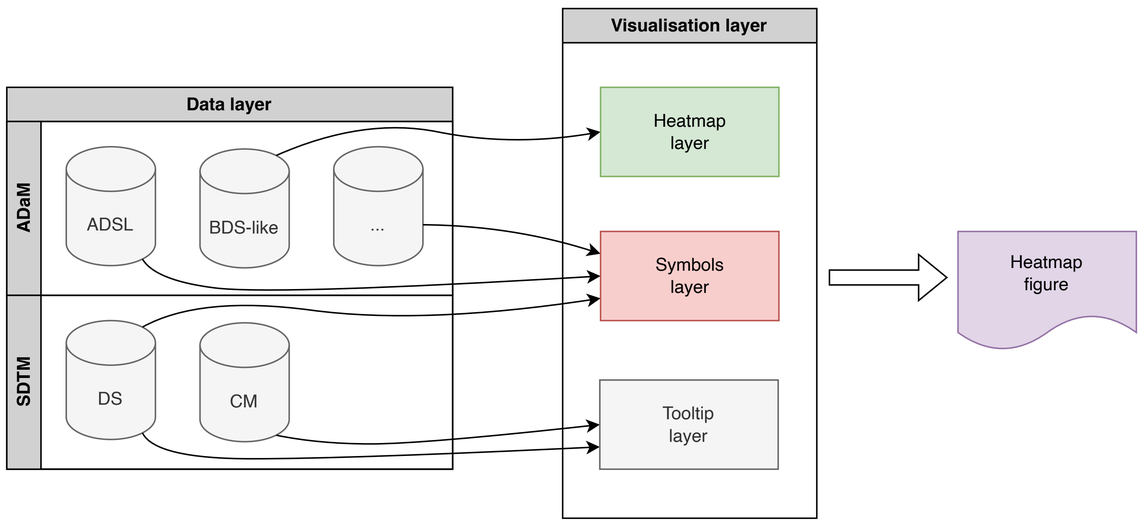
ICH guidance



ICH training material[2] provides examples of IEs based on

- concomitant medications,
- adverse events,
- study milestones,
- disposition and terminal events.

Dataflow



Components

Heatmap layer

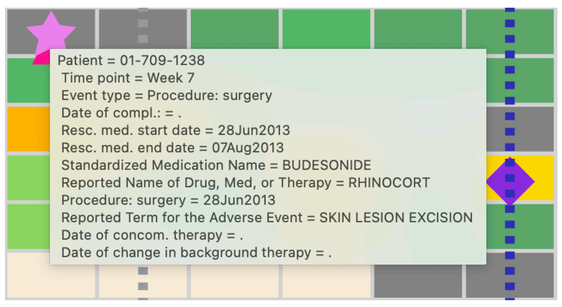
Heatmap itself visualizes any parameter of interest at analysis timepoint, for example continuous score at `Week`. Parameter is usually served from a BDS-like ADaM dataset. It's useful to display missing data separately to make a clear distinguishment when a value is missing, as such scenarios should be considered separately by the ICH guidance.

Symbols layer

Each cell of a heatmap may have several differently shaped symbols plotted on top. Symbols layer overlays different intercurrent events as distinguishable symbols.

- Treatment discontinuation
  - Discontinuation due to adverse events/toxicity
  - Discontinuation due to lack of efficacy
- Additional / alternative treatment
  - Use of rescue medication/concomitant therapy
  - Changes in background therapy
  - Treatment switch
- Terminal events
  - Leg amputation
  - Death

Tooltip layer



When heatmap and symbols layers are not sufficient for data exploration – additional information can be overlaid as a tooltip, for example:

- dates or relevant to event information,
- data-points from other parameters.

Links

Data source[3] used for the figure is a modified & augmented version of CDISC Pilot data. For more information, visit the Github[4] page.

References

(1) ICH E9(R1) Estimands and Sensitivity Analysis in Clinical Trials <https://database.ich.org/sites/default/files/E9-R1_Step4_Guideline_2019_1203.pdf>.

(2) ICH E9(R1) Estimands and Sensitivity Analysis in Clinical Trials – Training Material – December 2021 <https://database.ich.org/sites/default/files/E9%28R1%29%20Training%20Material%20-%20PDF_0.pdf>.

(3) CDISC Pilot data <https://github.com/phuse-org/phuse-scripts/tree/master/data/adam/cdisc>.

(4) Poster Github <https://github.com/alnbln/phuse2024eu-pp32>.