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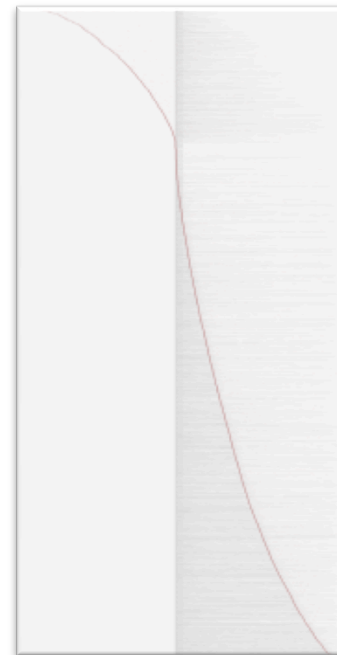
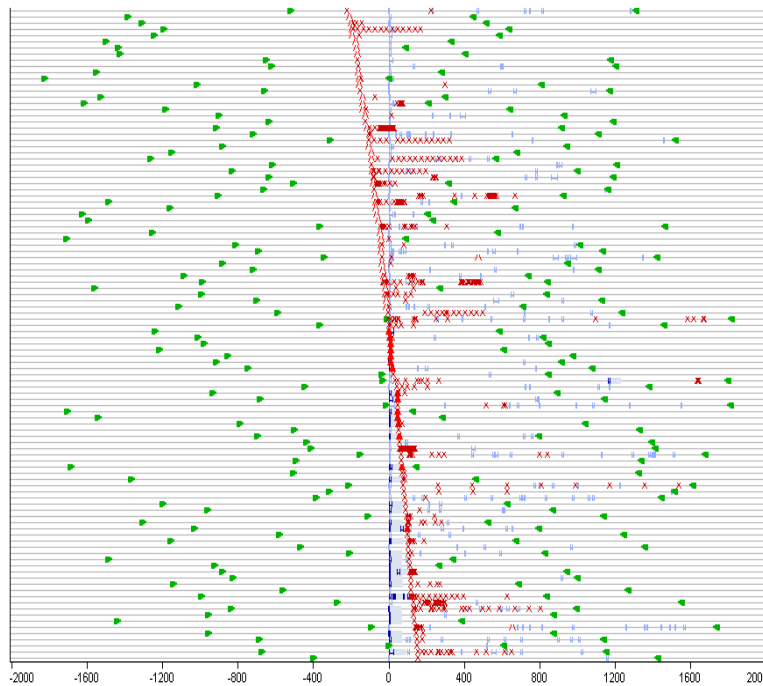
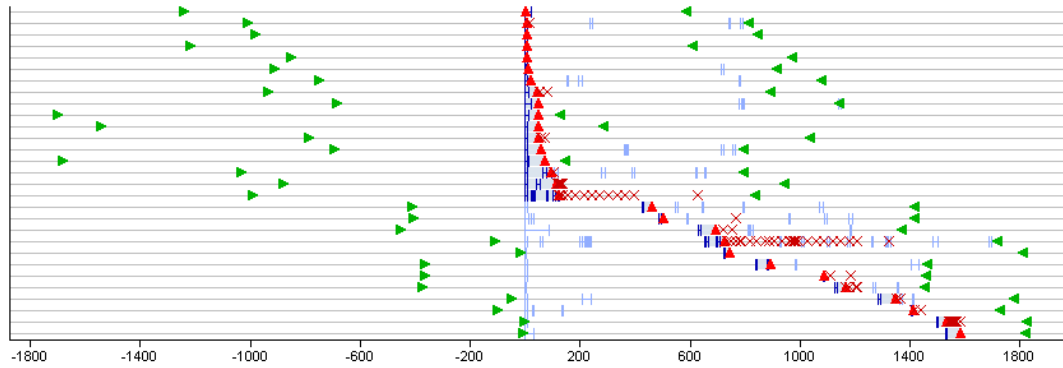
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Visual Representation of Exposure Patterns in Drug Safety Research

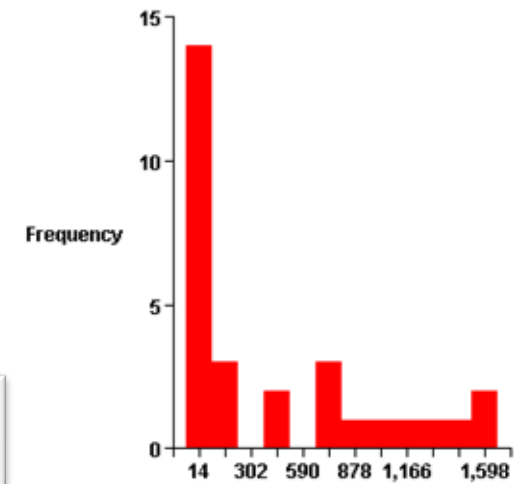
Sigfried Gold
Medical Informaticist

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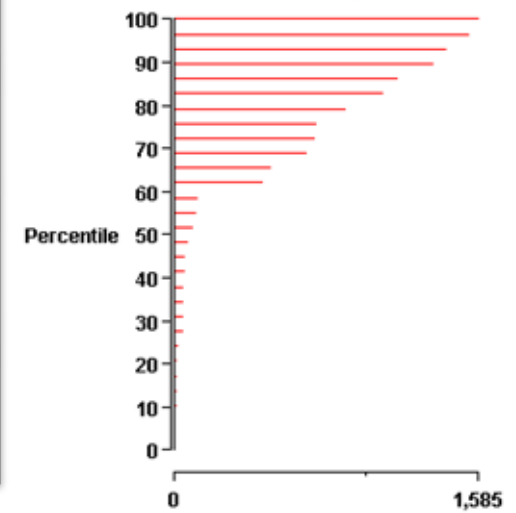
Multi-patient timeline; time to onset



Time to Onset Histogram (29 patients)



Time to Onset Plot (29 patients)



Histogram of focus events after aligning by index event. (Norén, et al.)

Temporal Pattern Discovery for Trends and Transient Effects: Its Application to Patient Records

G. Niklas Norén
WHO Collaborating Centre for
International Drug Monitoring
Uppsala, Sweden

niklas.noren
@who-umc.org

Andrew Bate
WHO Collaborating Centre for
International Drug Monitoring
Uppsala, Sweden

andrew.bate
@who-umc.org

Johan Hopstadius
WHO Collaborating Centre for
International Drug Monitoring
Uppsala, Sweden

johan.hopstadius
@who-umc.org

Kristina Star
WHO Collaborating Centre for
International Drug Monitoring
Uppsala, Sweden

kristina.star
@who-umc.org

I. Ralph Edwards
WHO Collaborating Centre for
International Drug Monitoring
Uppsala, Sweden

ralph.edwards
@who-umc.org

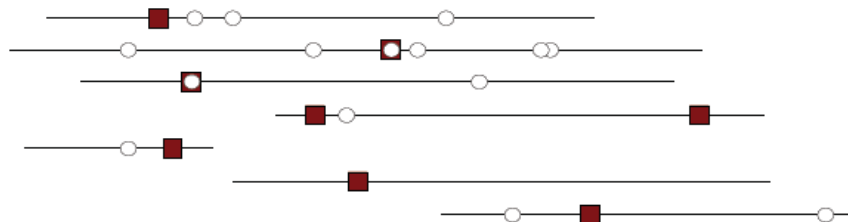


Figure 1: Abstract representation of an event history data set. Each line represents an event history, where the index event of interest is marked with squares and the focus event of interest is marked with circles.

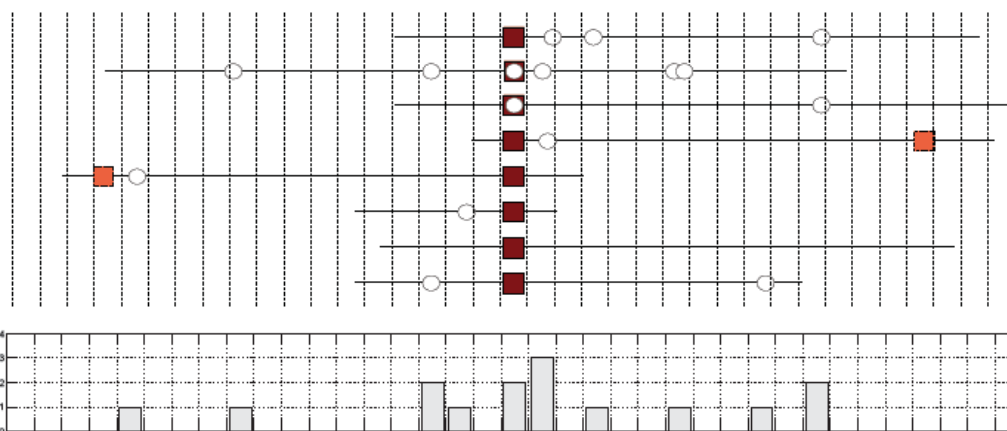


Figure 2: The same event histories as in Figure 1 aligned by their index events. Note that the event history with two index events is represented twice here. The histogram in the bottom panel is a simple summary of the number of index events with a focus event in each given time period.

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Chronograph (Norén, et al. continued)

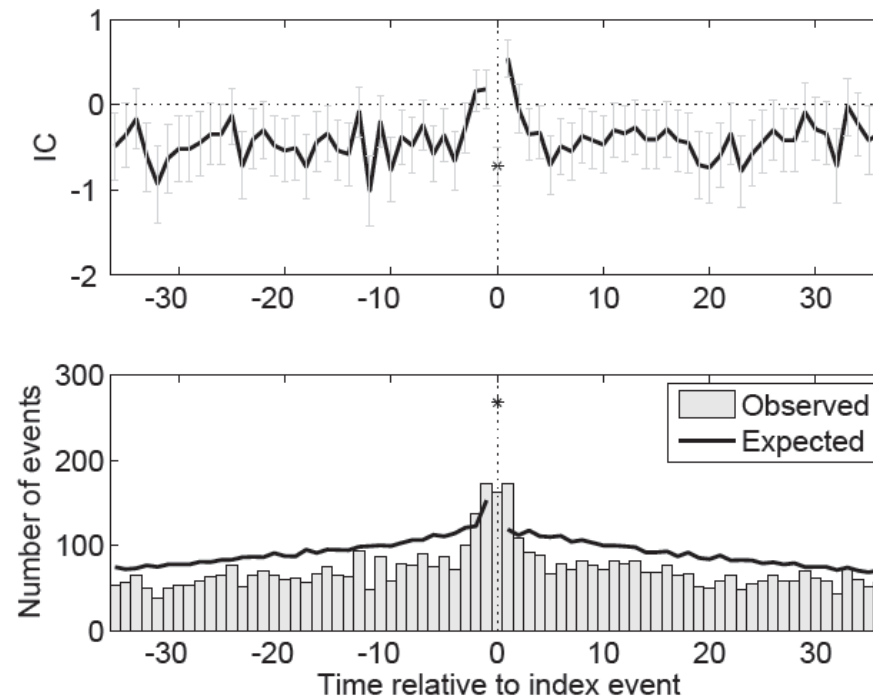


Figure 3: Example of a chronograph. The bottom panel displays the observed and expected numbers of index events with a focus event in different time periods relative to the index event. The top panel displays the corresponding variation in the IC value.

Chronograph examples (Norén, et al. continued)

Adverse drug reactions

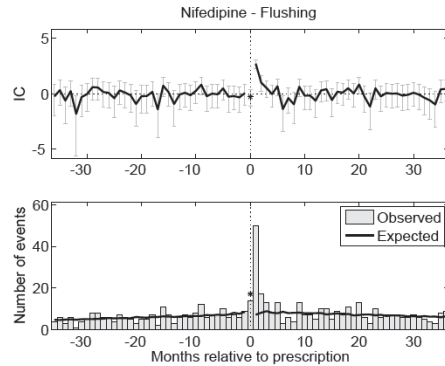


Figure 4: Chronograph for the registration of *flushing* relative to first prescriptions of *nifedipine*.

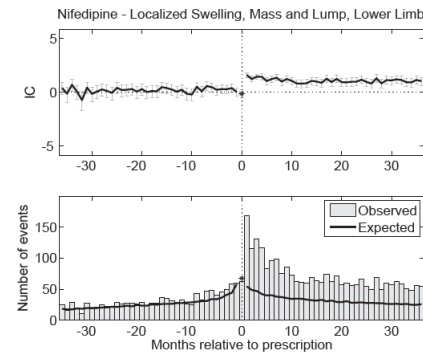


Figure 5: Chronograph for the registration of *localized swelling, mass and lump, lower limb* relative to first prescriptions of *nifedipine*.

Beneficial effects

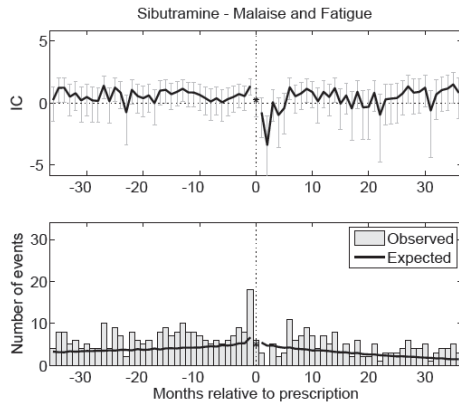


Figure 6: Chronograph for the registration of *malaise and fatigue* relative to first prescriptions of *sibutramine*.

Underlying disease

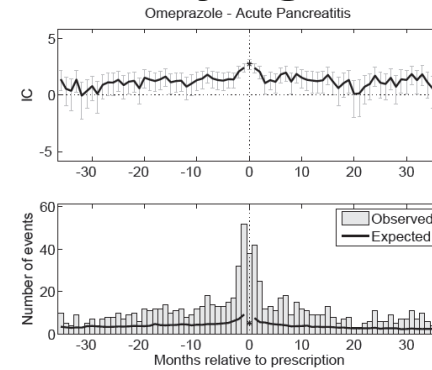


Figure 7: Chronograph for the registration of *acute pancreatitis* relative to first prescriptions of *omeprazole*.

Intervals

- We expect some AEs to occur early in exposure, others late
- But we want to see what actually happens before building our assumptions into a study model
- Interface allows user specification of early and late periods of exposure and post-exposure, and highlighting of events occurring during defined risk periods
- Pattern notation with rank and filter allows exploration of dechallenge and rechallenge scenarios
- Adherence
 - Allowable gap between prescriptions
 - Carry-over of stockpiled medication



Exposure periods

- Unexposed: Before first exposure
- Start of exposure: Day 0
- Early exposure: Day 1 to Day 40
- Fuzzy exposure: Day 1 to Day all
- Late exposure: Day 100 to end of exp
- Post-exposure risk: Post exp to day 15
- Fuzzy post-exposure: Days 16 to 50 after exp
- Long past exposure: 50 days after exp to next exp

Which exposure

- All
- First
- Second
- Last

Event Types

- None
- First event
- Continues previous event
- Fuzzy post-event
- Subsequent event

Clinical patterns

- NoExposureEvents
- atLeastOneEventExposed
- atLeastHalfEventsExposed
- allEventsExposed
- atLeastOneExposureHasEvents
- atLeastHalfExposureHasEvents
- allExposuresHaveEvents
- Multiple patterns

199 patients

Currently highlighted: Exposure periods: Start of exposure, Early exposure
 Event types: First event, Subsequent event
 Clinical patterns: atLeastOneEventExposed, atLeastOneExposureHasEvents

Sorted by: Exposure periods: Start of exposure, Early exposure
 Event types: First event, Subsequent event
 Sorted by: Exposure periods: Start of exposure, Early exposure
 Event types: First event, Subsequent event



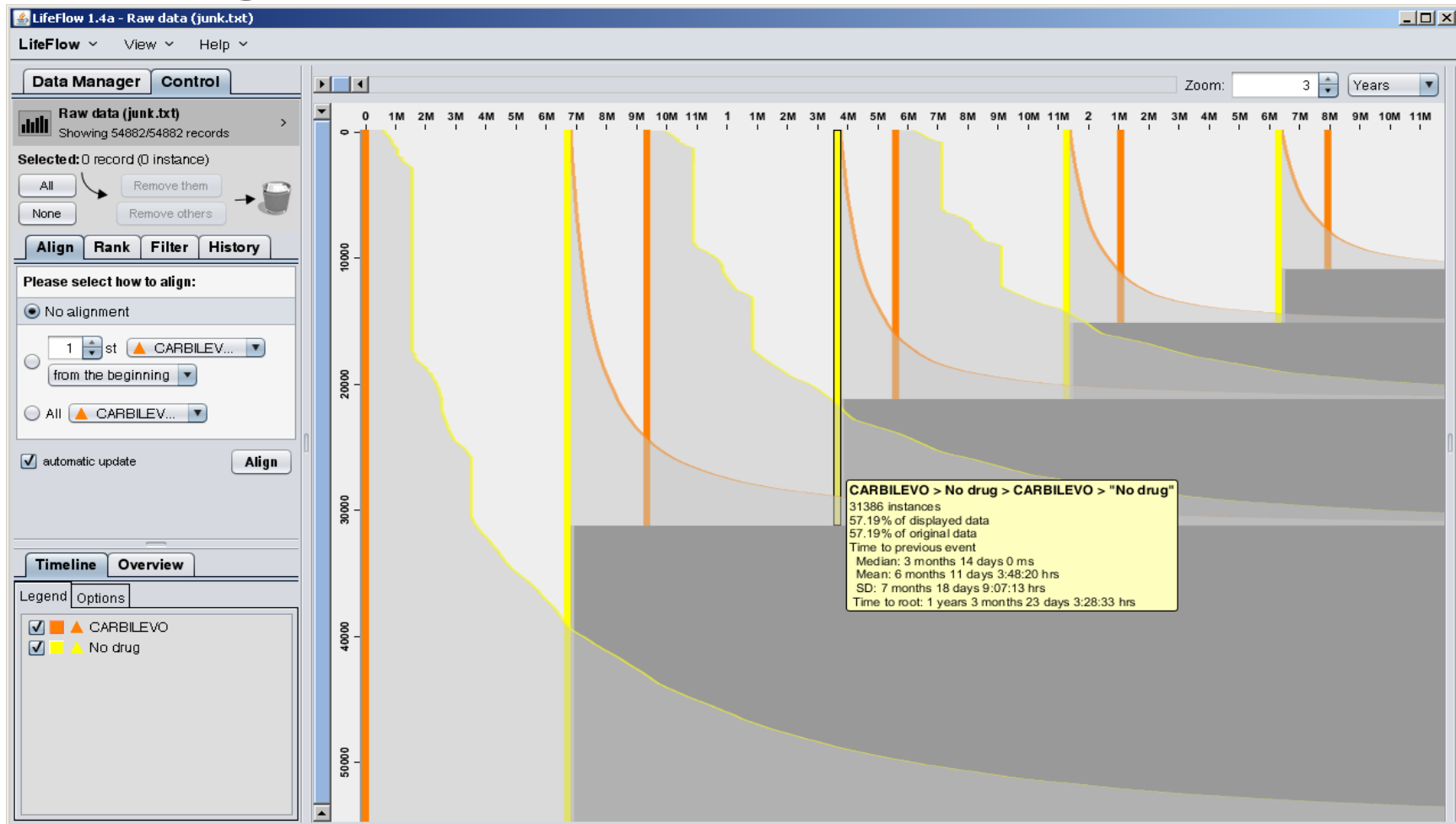
More than one exposure or event type

- Concomitance and medication history
 - Patterns of occurrence of other drugs prescribed around the same time as the drug of interest
- Co-morbidity
 - Patterns of illness, signs and symptoms surrounding index date
- Drug switching
 - Switch as evidence of adverse reaction
 - Switch as index date for study comparing two second-line drugs, index date is the switch from a common first-line drug

Actively working on ways of exploring these patterns.

Your ideas?

UMD HCIL LifeFlow, Anti-Parkinsons Drug Eras



HCIL's LifeFlow – Opioid Drug Eras

