Visualization of Titrated Dose and recurrent Events Using R/ggplot2

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Medical Monitoring of On-going Clinical Studies

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- Visualization of overall trend and individual data is a powerful tool in Medical Monitoring
- Efficient open-source solution for internal monitoring is welcomed

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- Ideal tool for quick visualization
- Grammar of graphics helps to nail down the exact specification of plot in communication with clinical colleagues

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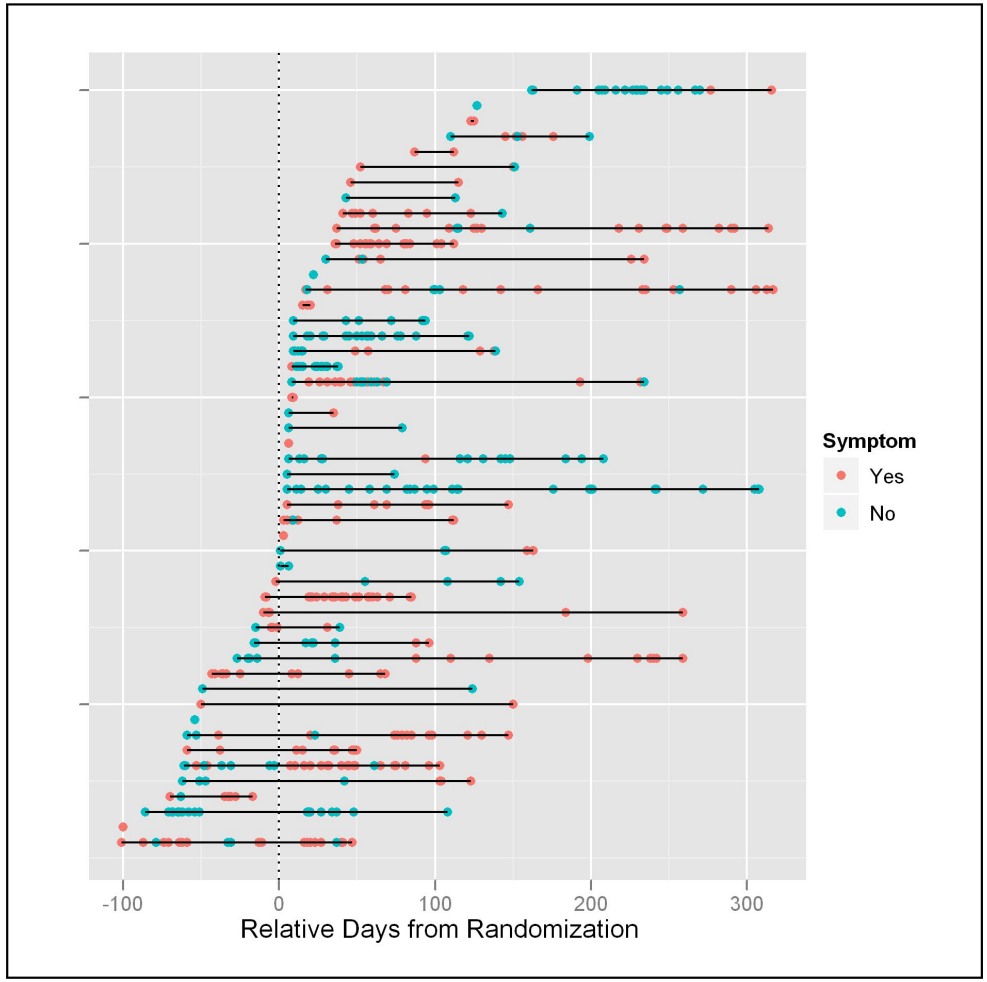
- The same metric over time need to be seen simultaneously to understand the progression of the event accumulation
- Individual contribution to the accumulating events is equally important to understand

Individual Events over Time

- Straightforward visualization of recurring events, one patient a row



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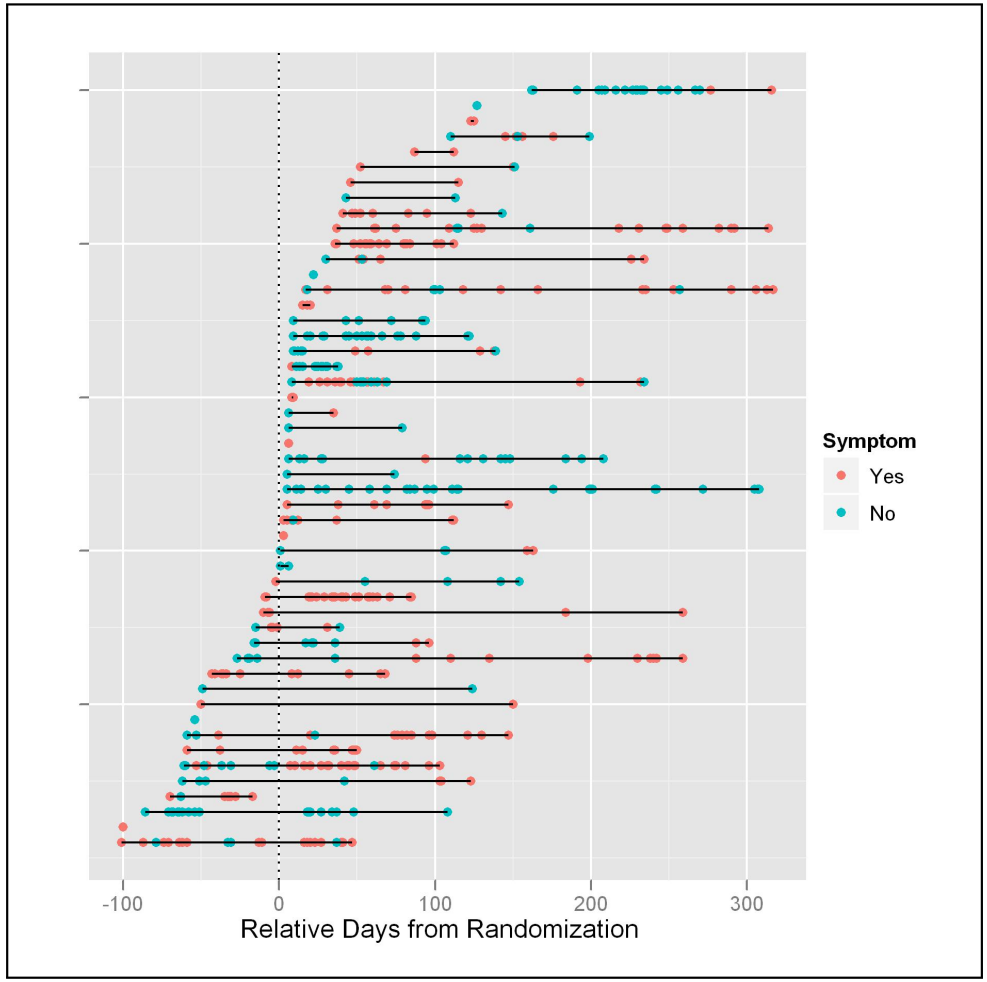

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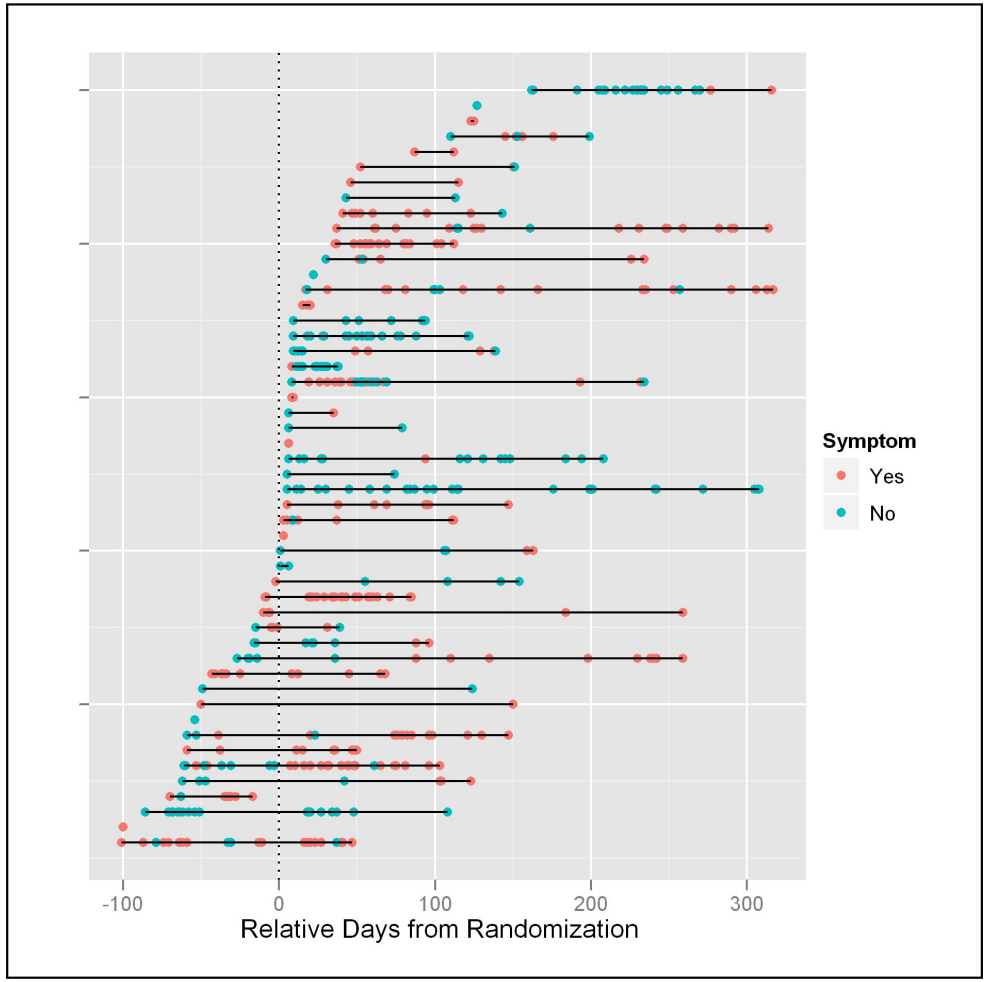
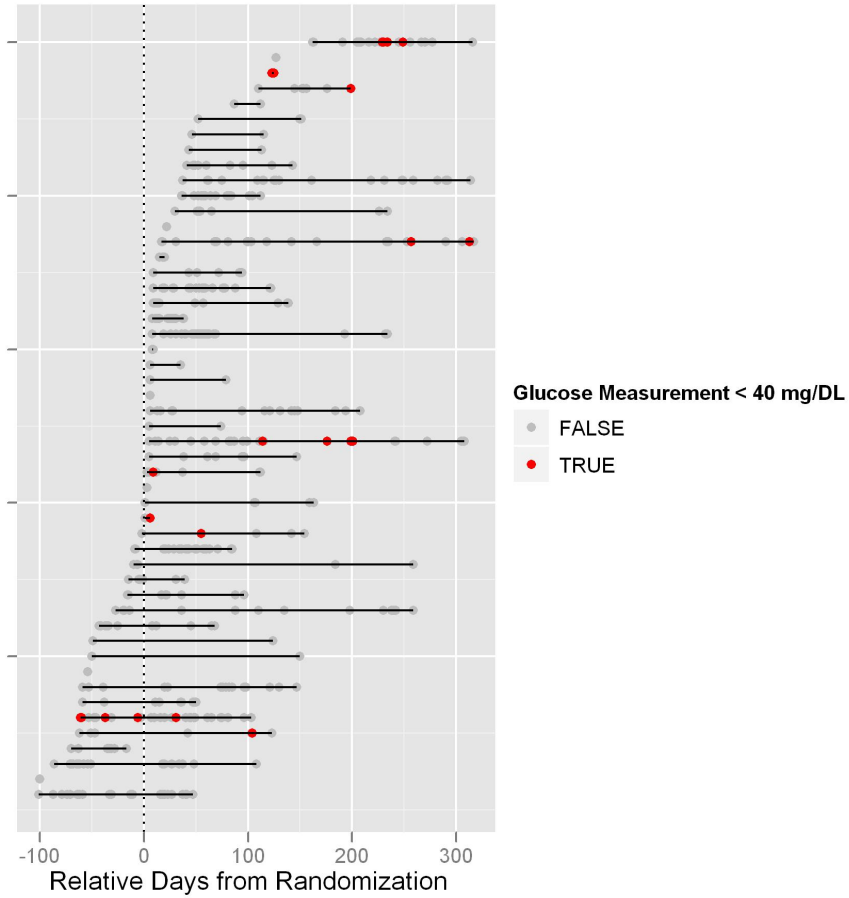
- Order on y-axis can depend on various information to explore relation with covariates



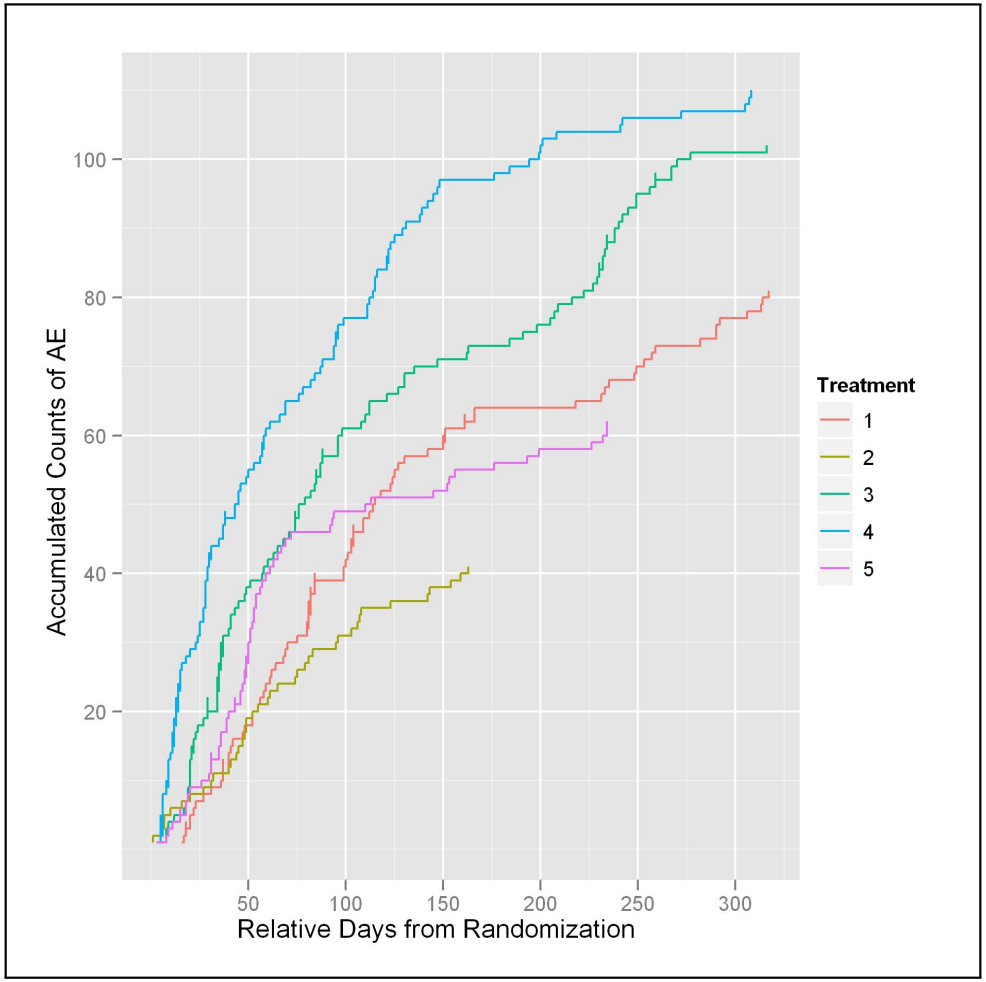
Individual Events over Time, Another Colored Coding

Individual points may be color coded to indicate severity



Accumulated Count of Occurence

- Total count of accumulated events over time plotted using `geom_step`



Accumulated Count of Occurence

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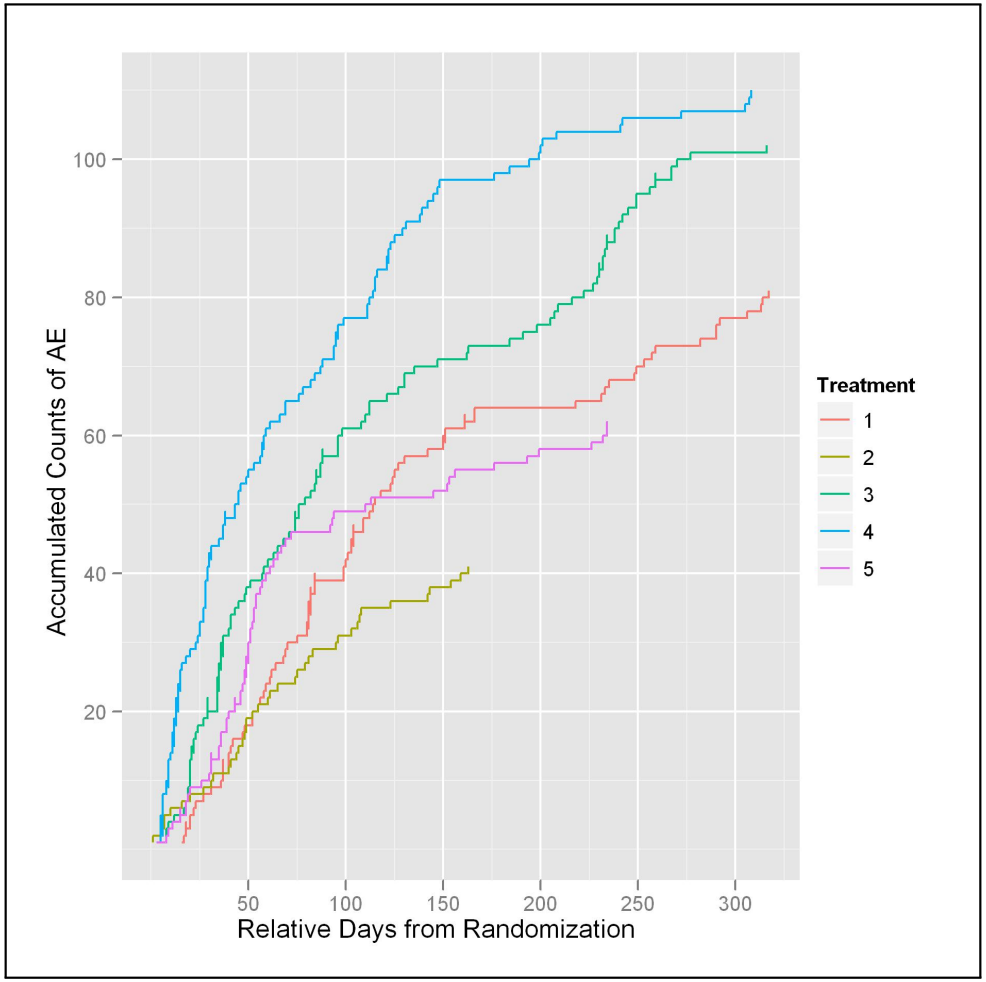
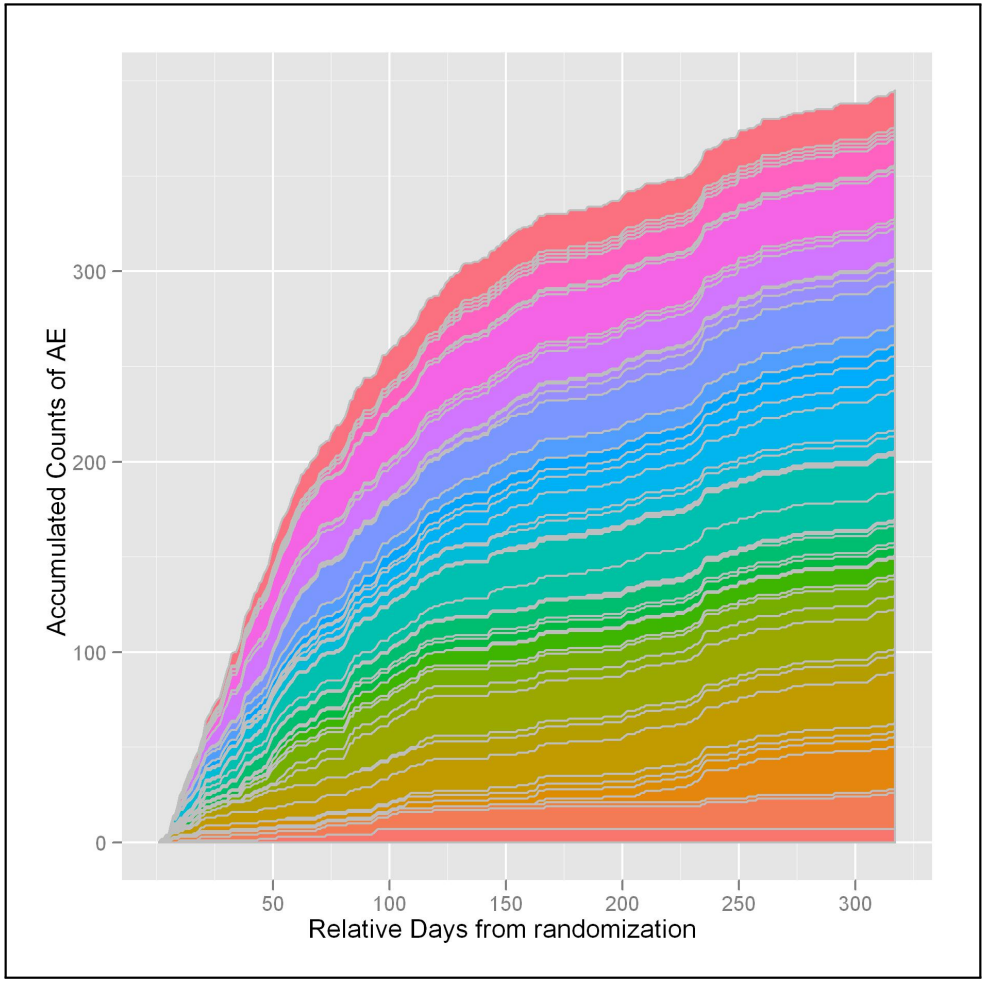
- Useful for comparing different dose level but individual contributions to the total count is not reflected in the graph



Accumulated Counts, Individuals Stacked

- Different patients' accumulated counts stacked together using `geom_area(stat="identity", position="stack")`



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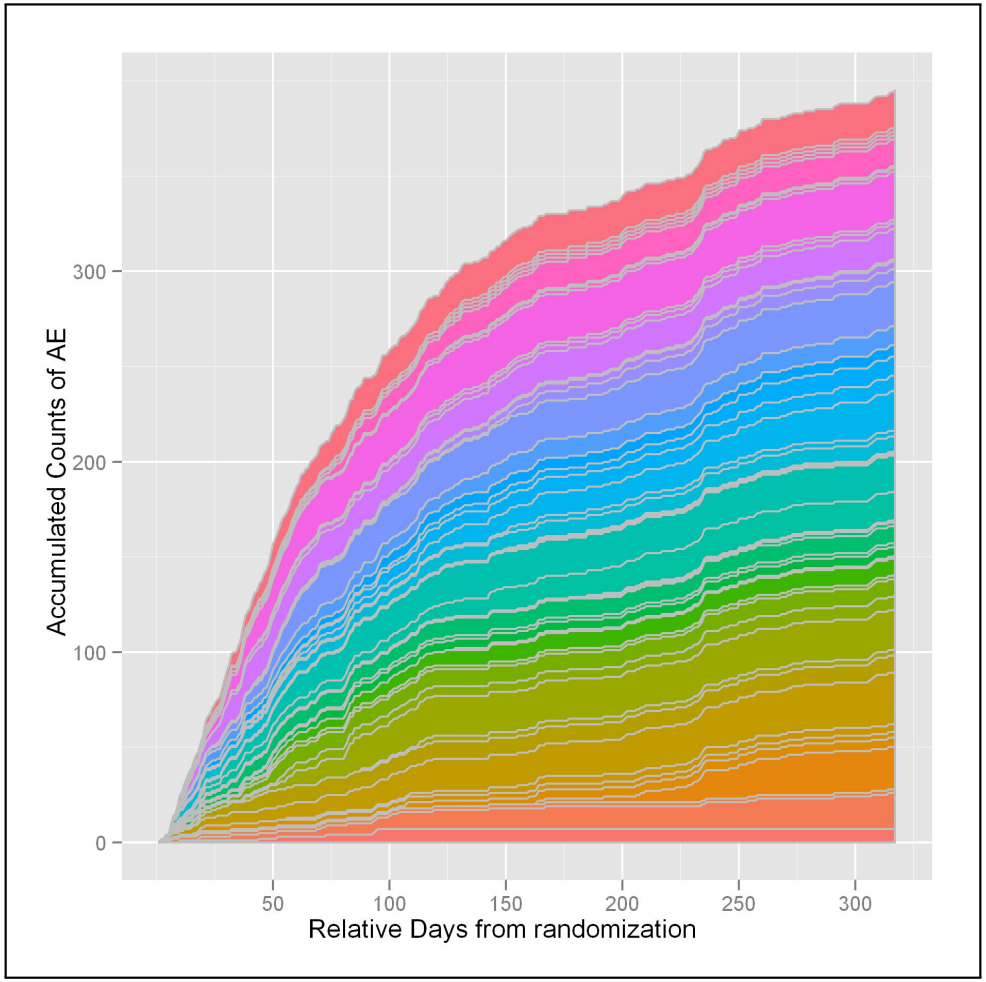
- Each patient is color coded to enable clear distinction between individual contribution



Mean Cumulative Function Over Time + Individual Counts over Time

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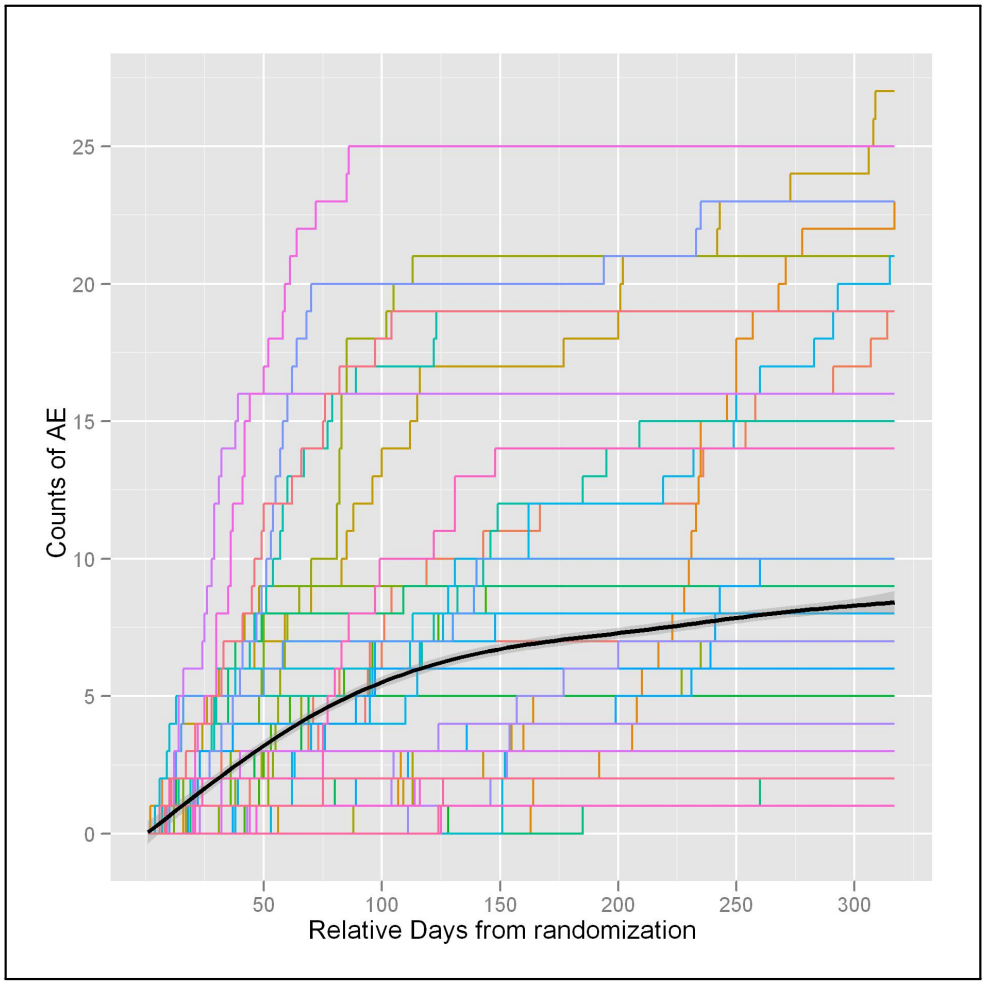

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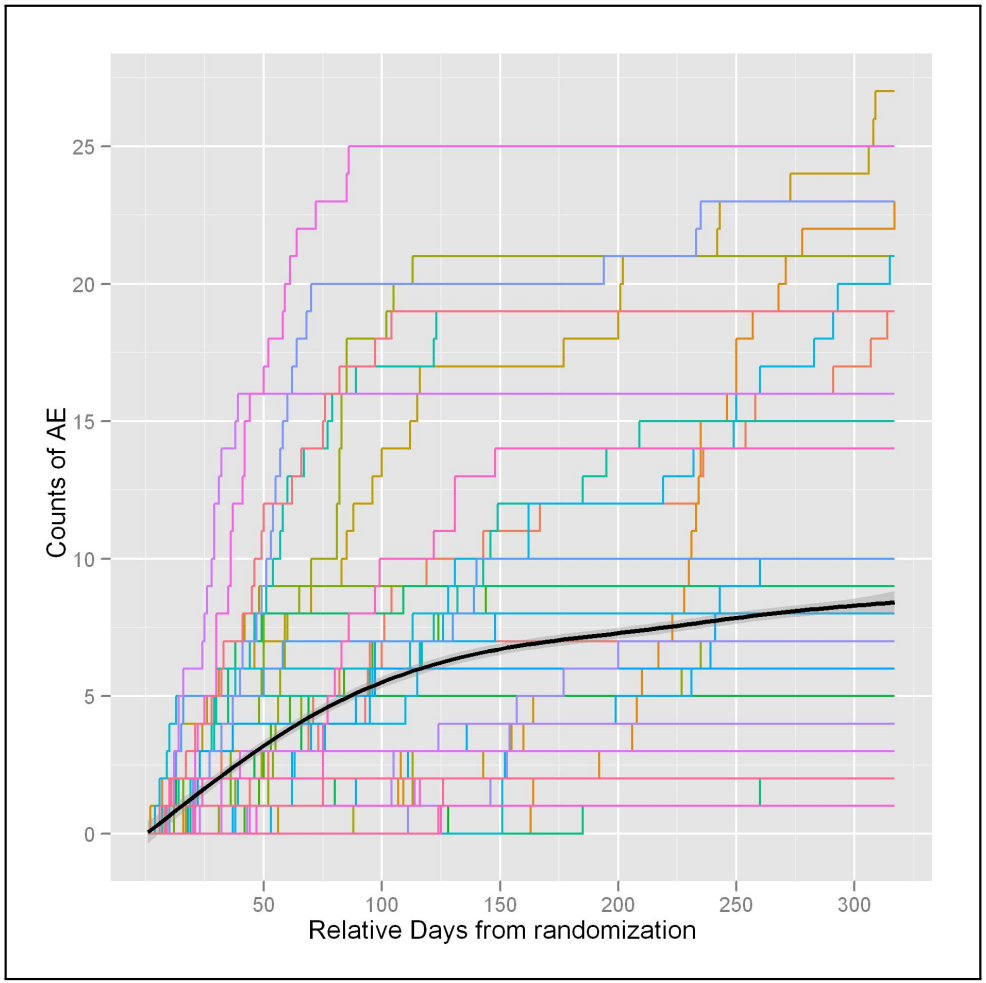

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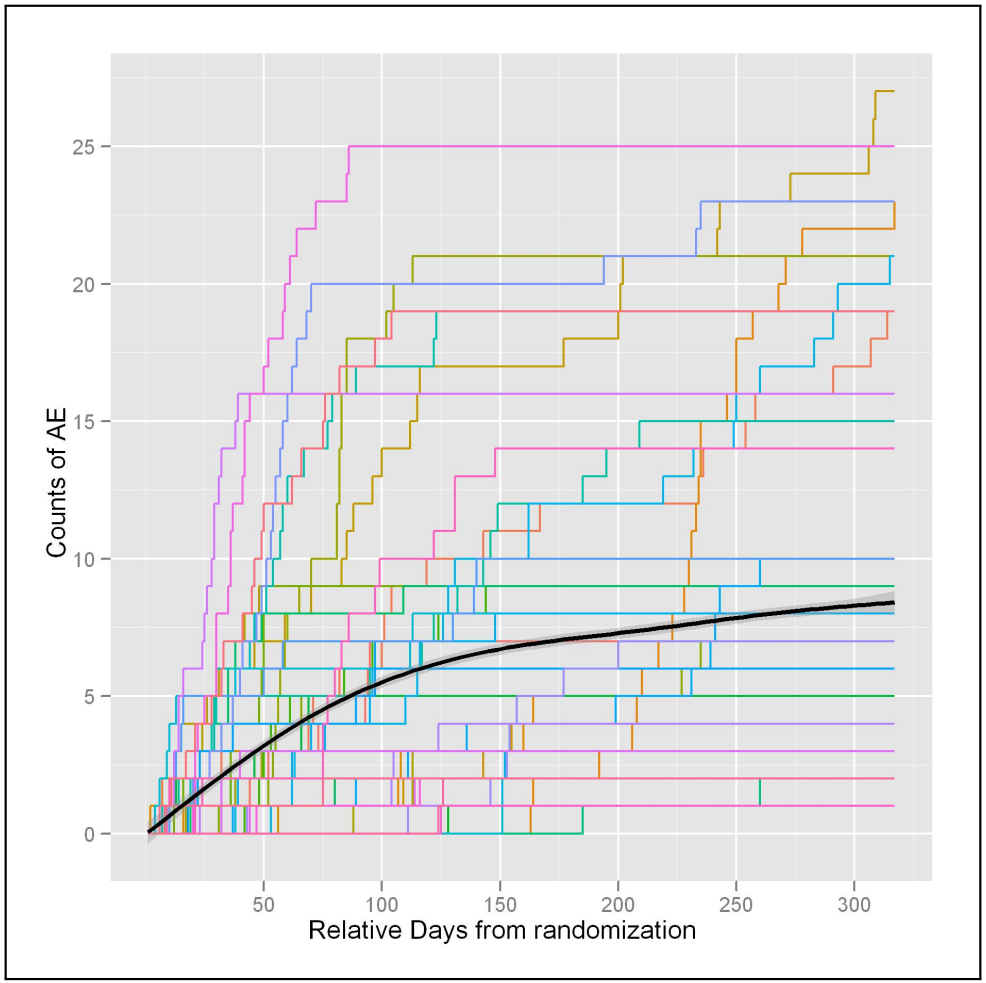
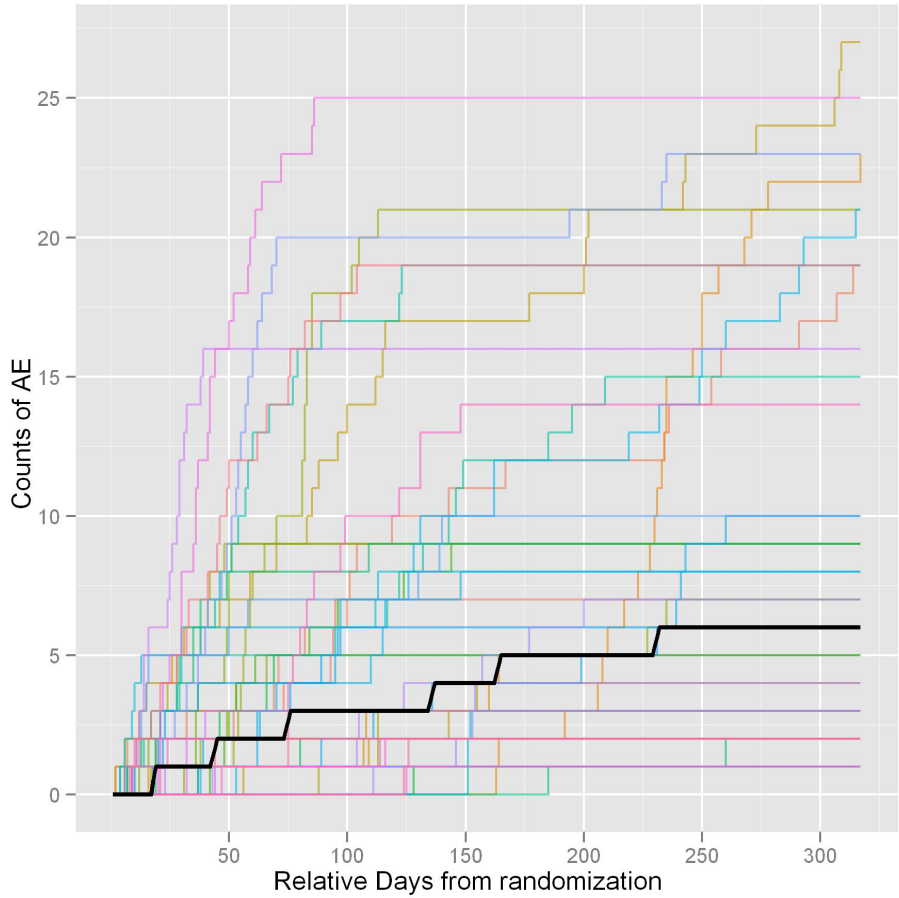
- More appropriate MCF estimate accounting for censoring is available, but requires additional coding outside of ggplot2



Median Cumulative Function

Median of cumulative counts over time gives a robust estimate of a typical time-dependent path of event accumulation



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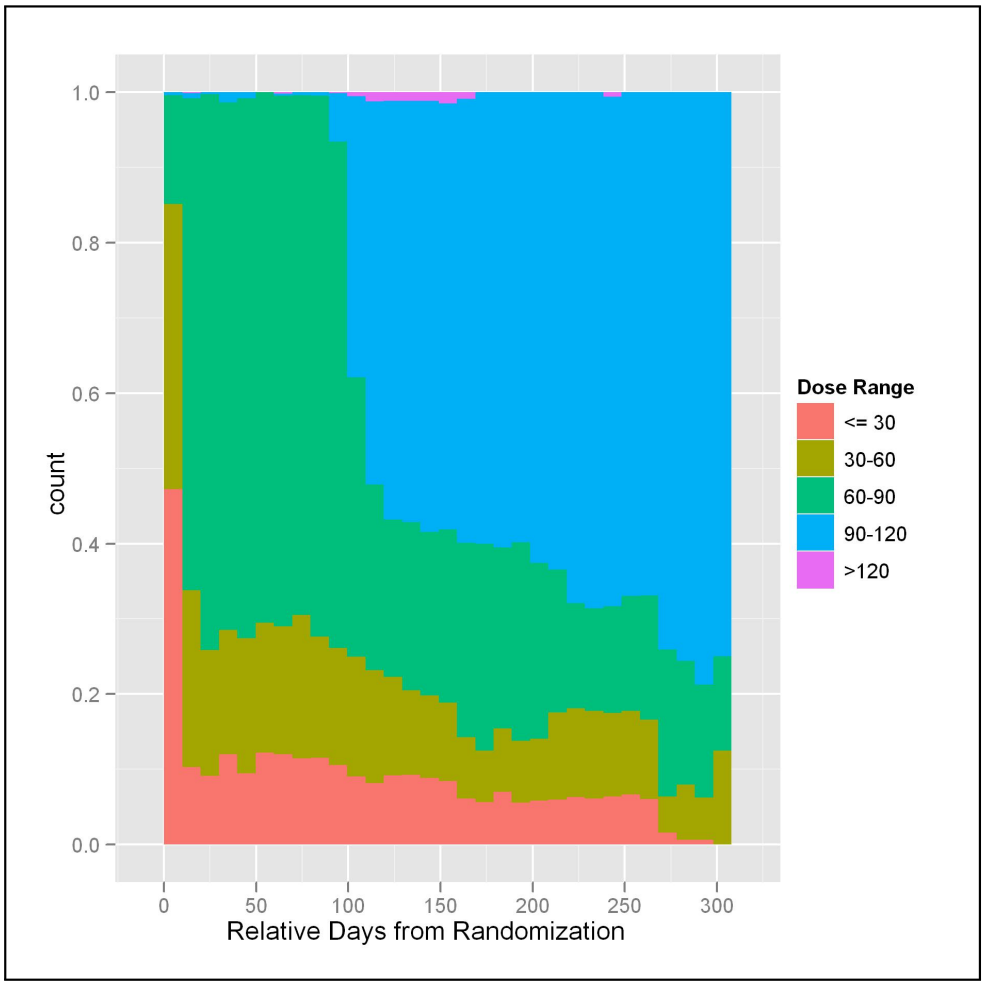
- Individual titration path relates to both efficacy and safety signals

Dose Distribution over Time



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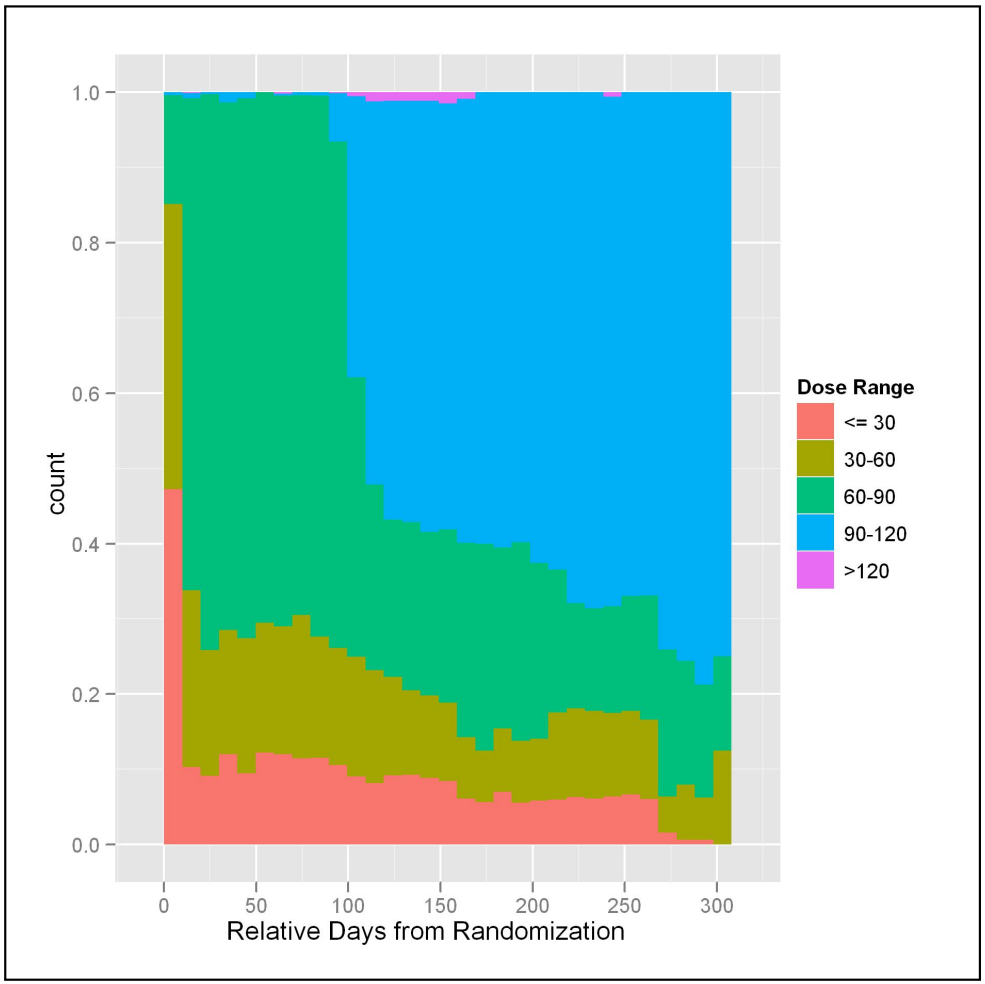

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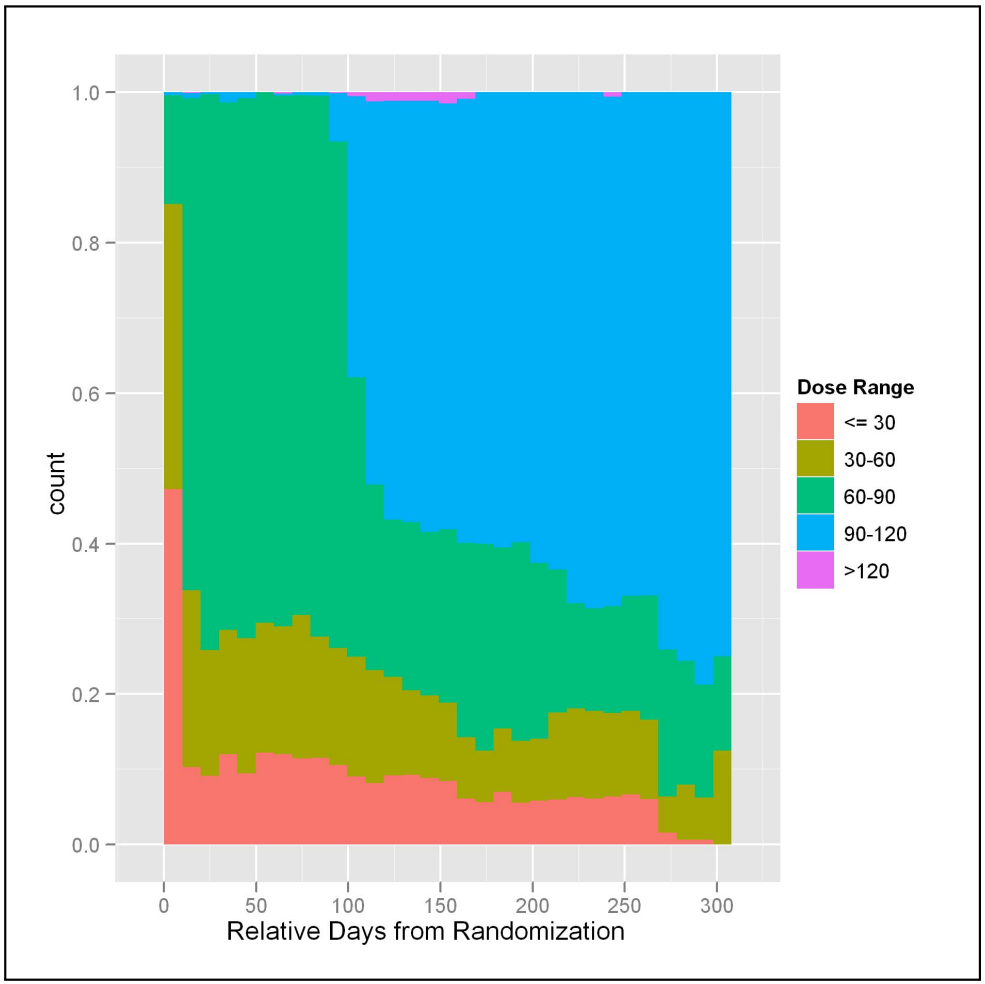

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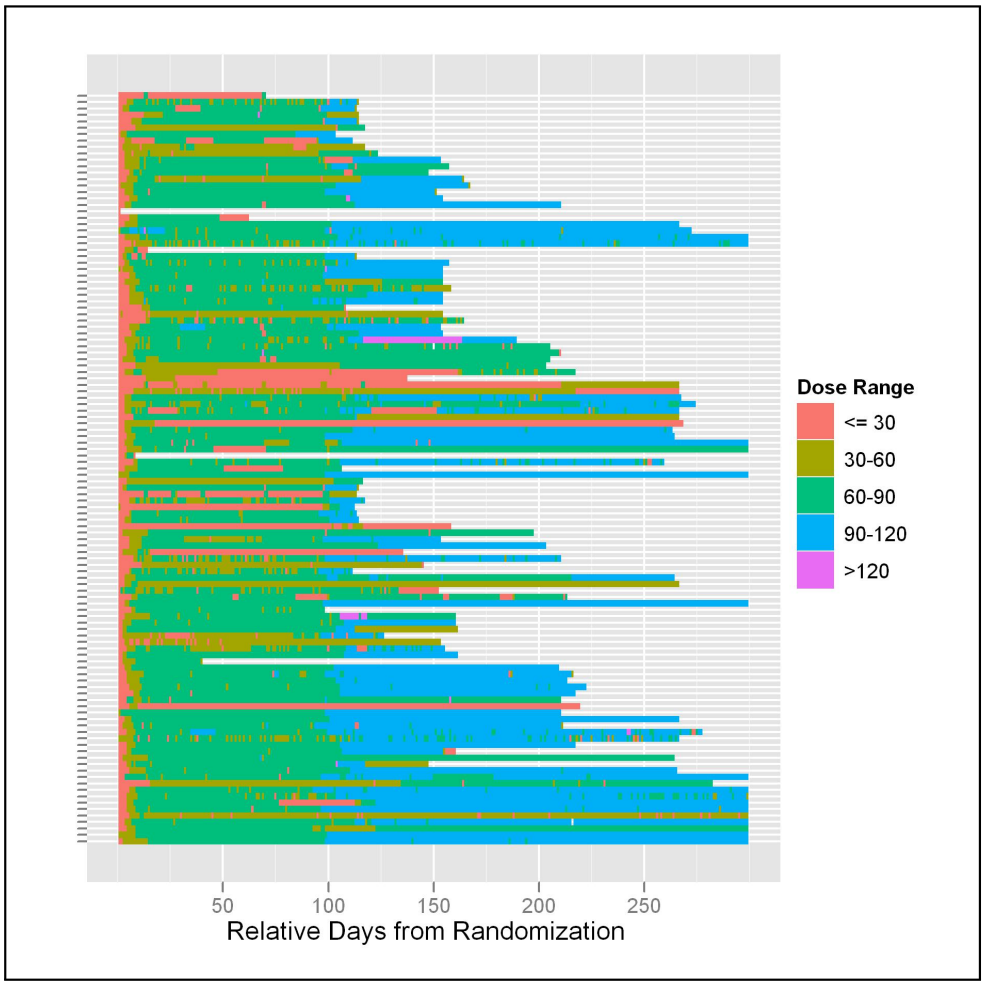
- Use `geom_bar(position="fill")` to visualize the relative proportion of doses over time
- Overdose easily identified by graph

Color Coded Individual Dose



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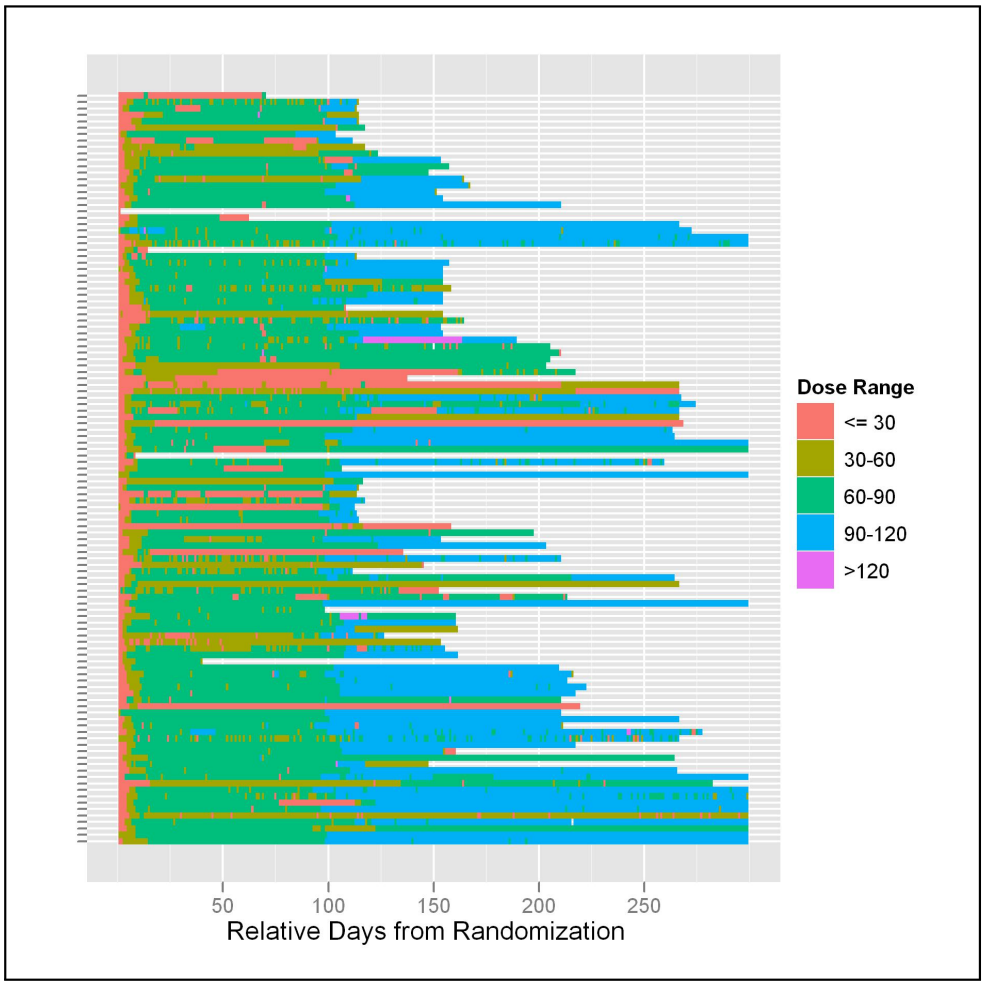

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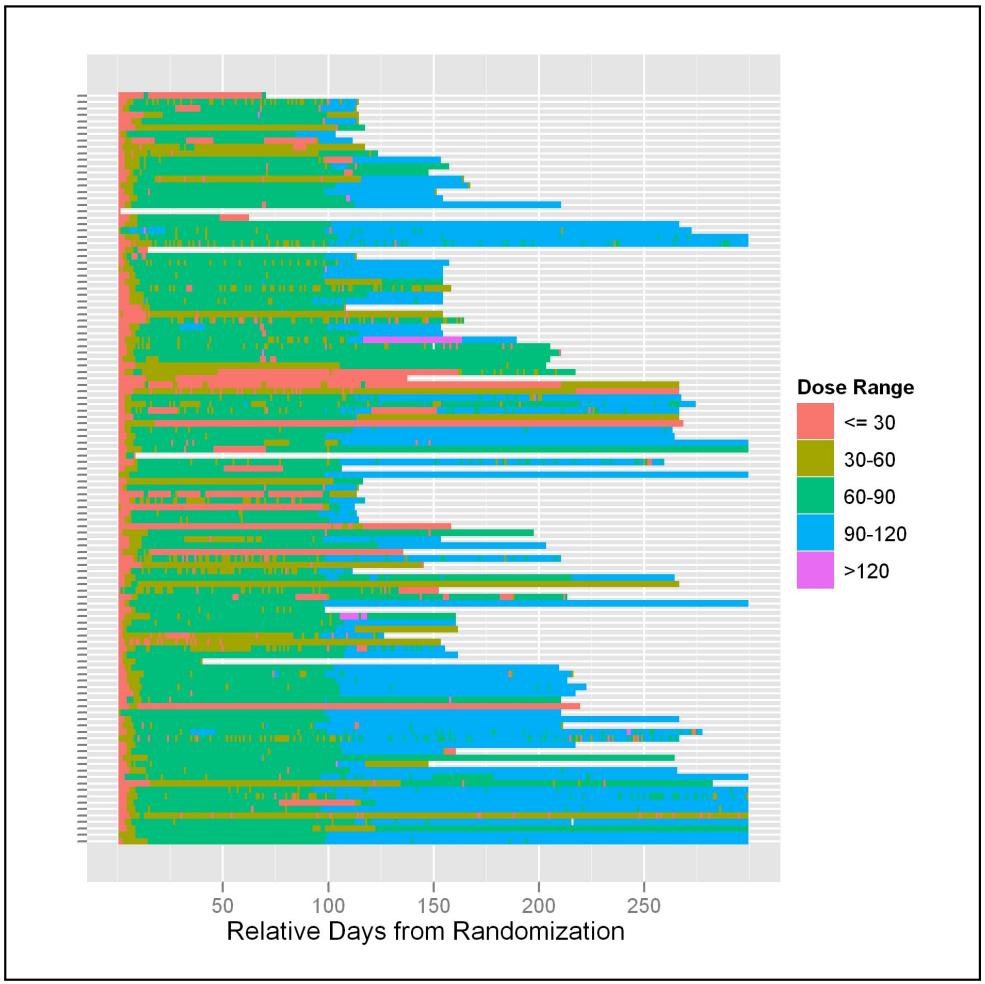

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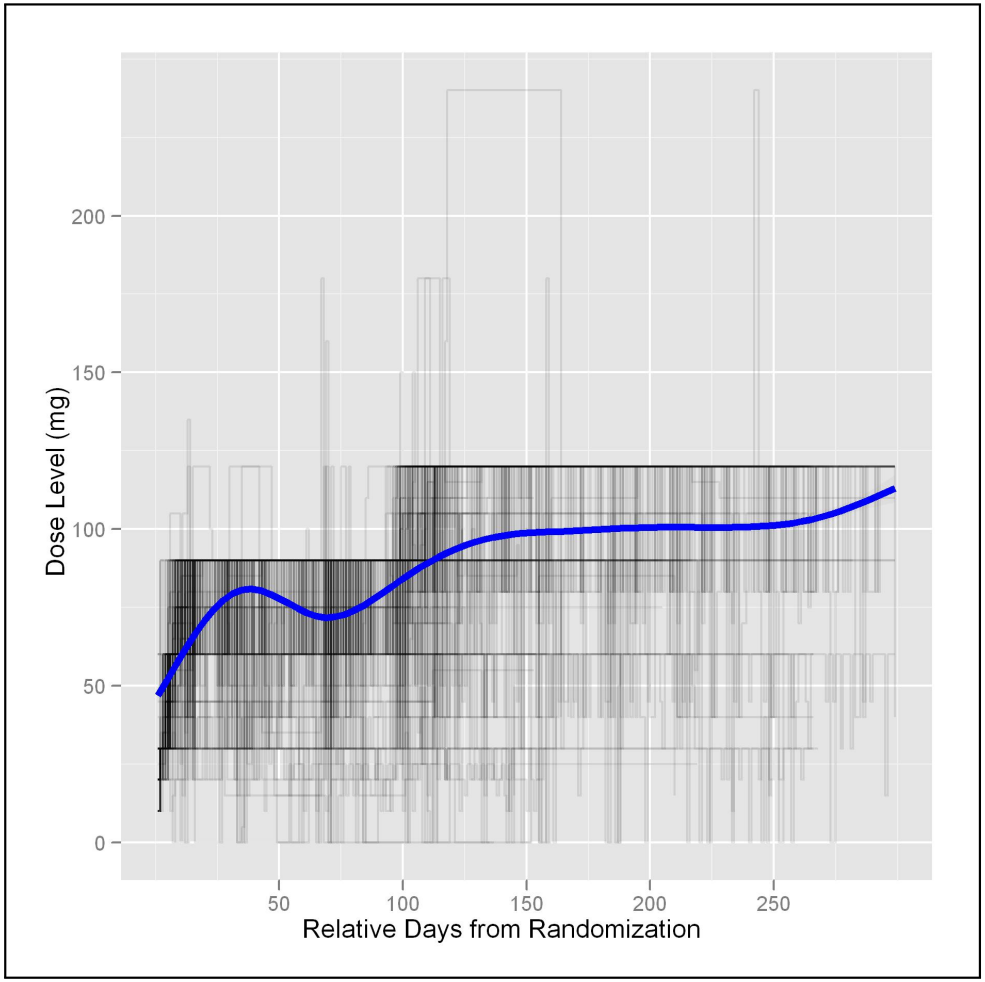
- Up-titration by design is visible in graph - study requires all patients to up-titrate to highest dose per day around 100 days
- Alternating colors indicate up or down-titration activities.

Titration Path + Average Dose over Time



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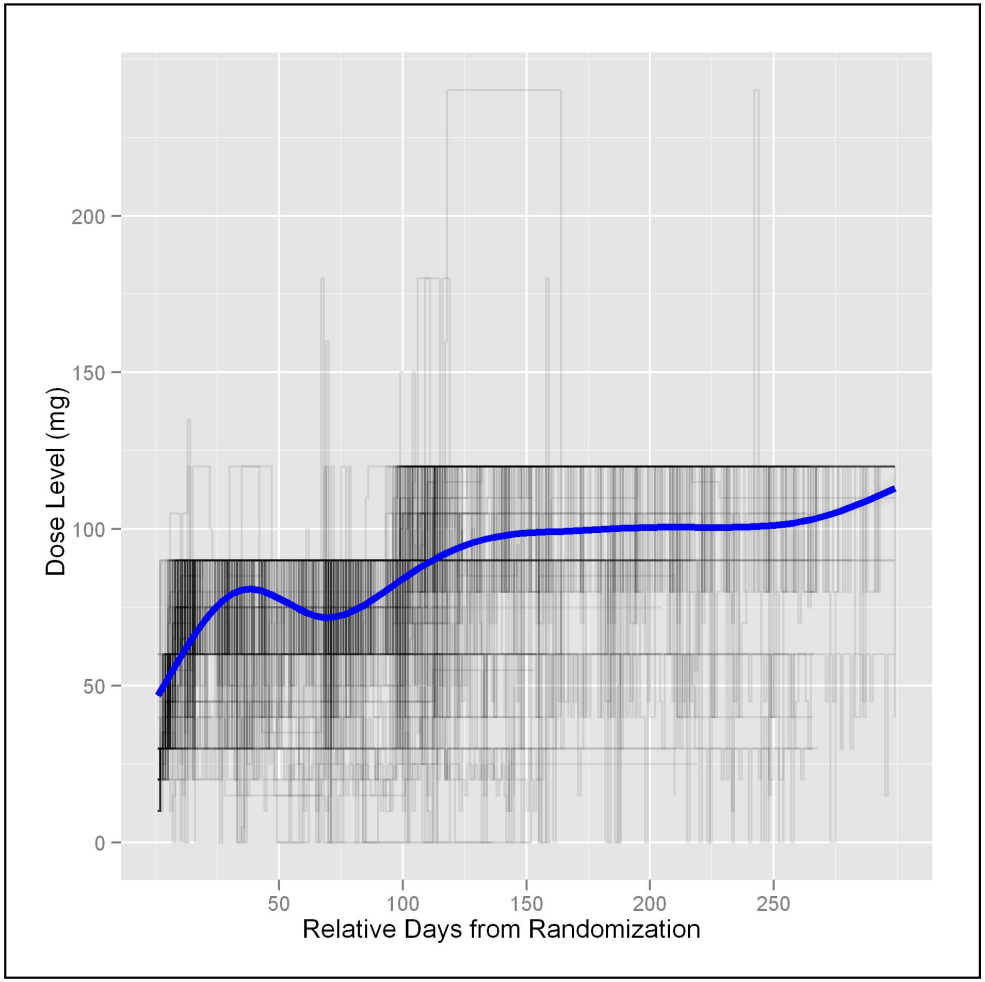

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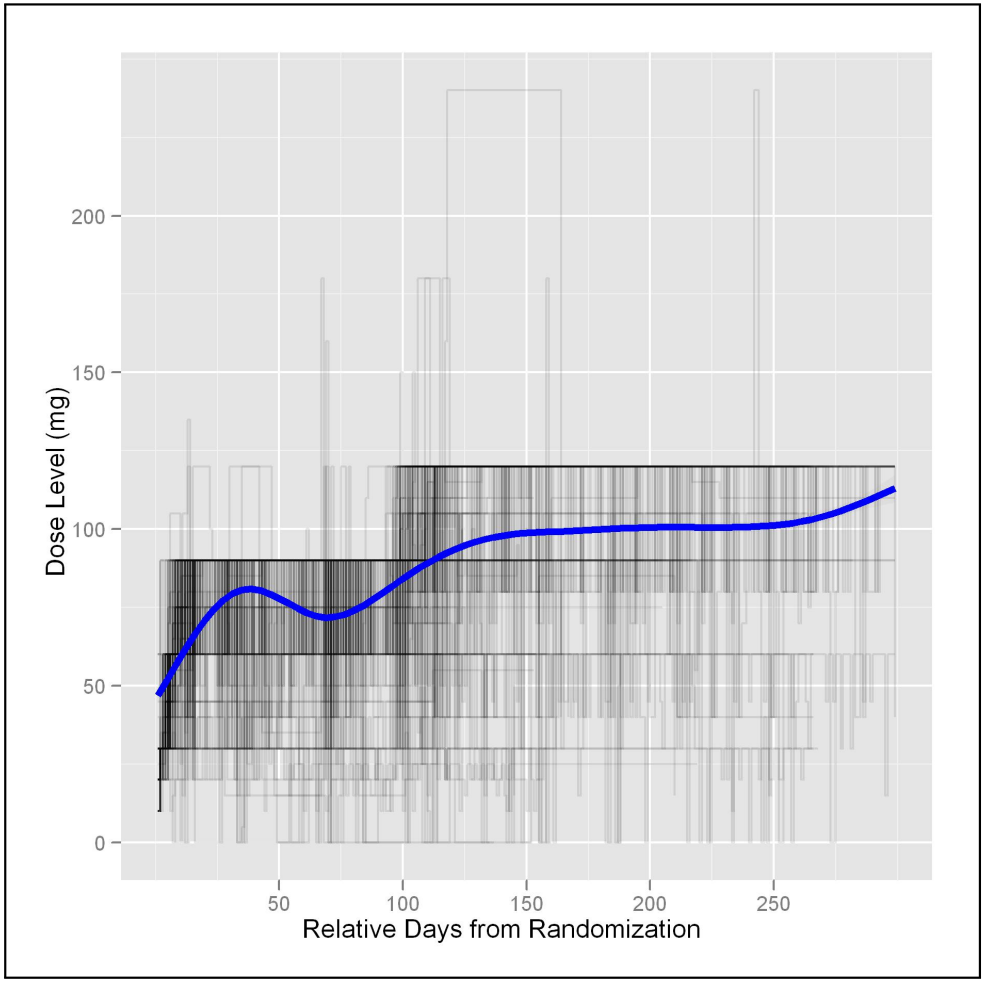

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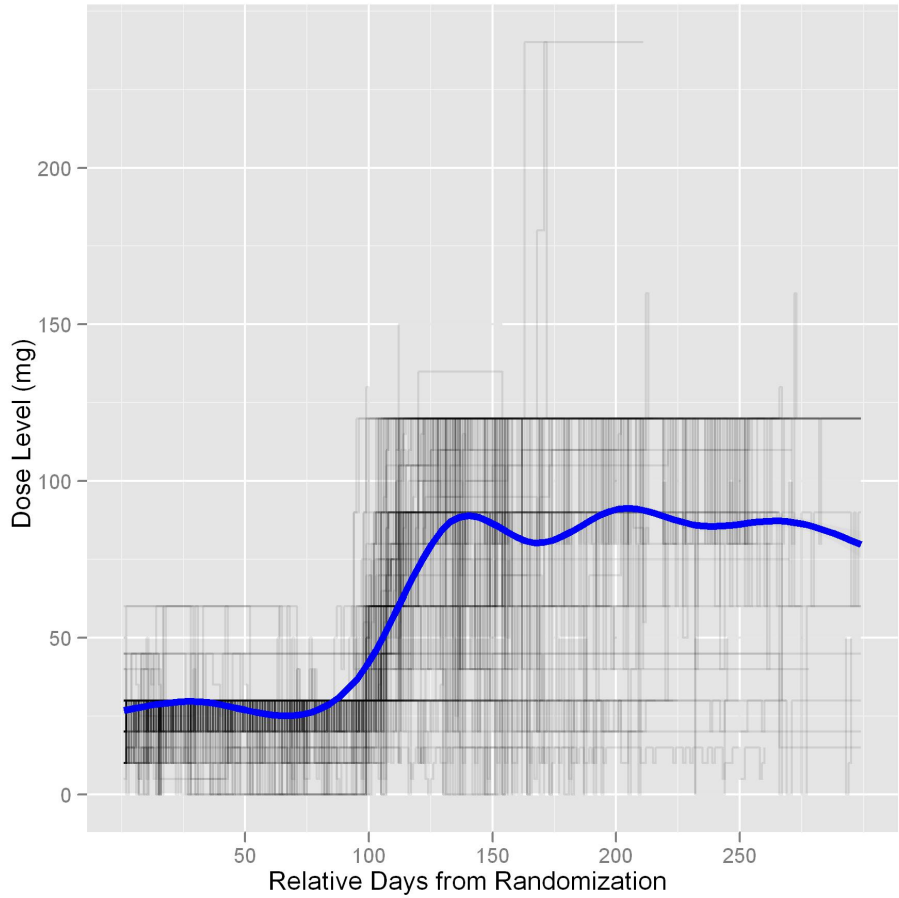
- Use alpha=0.1 to reduce overplotting
- Mean dose over time indicates the overall titration trend

Titration Path + Average Dose over Time, cont.

Titration at another dose level - note the different stable doses the majority of patients settled on



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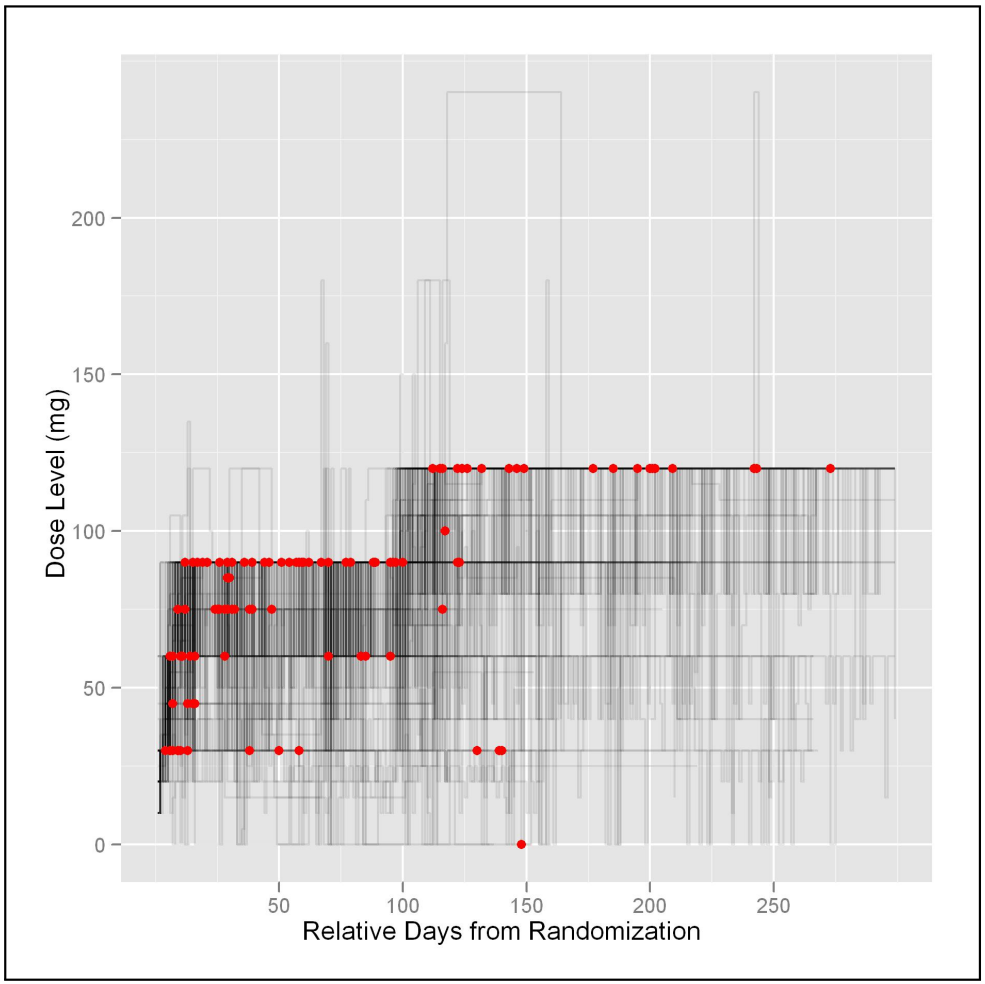
- Use `geom_step` to trace the individual titration path; use `geom_point` to connect the episodes over time with corresponding dose

Distribution of recurrent Events and Corresponding Dose



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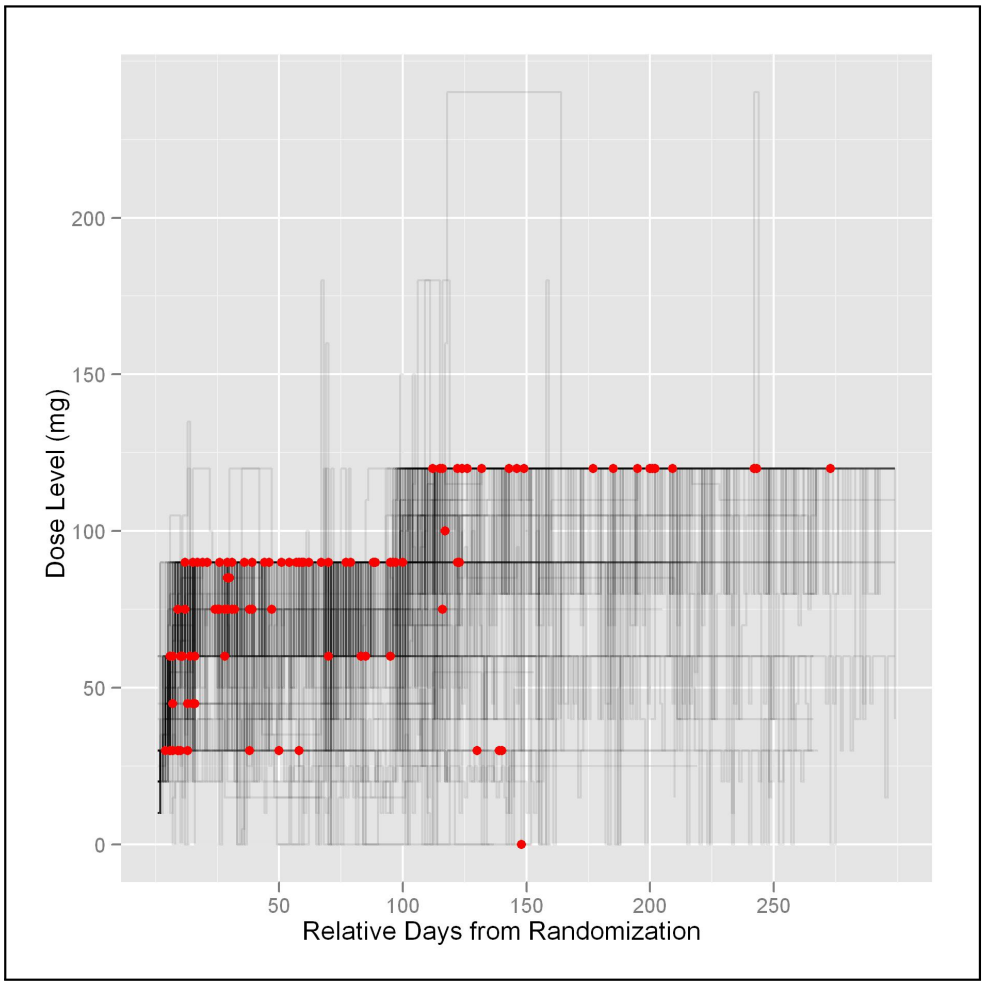

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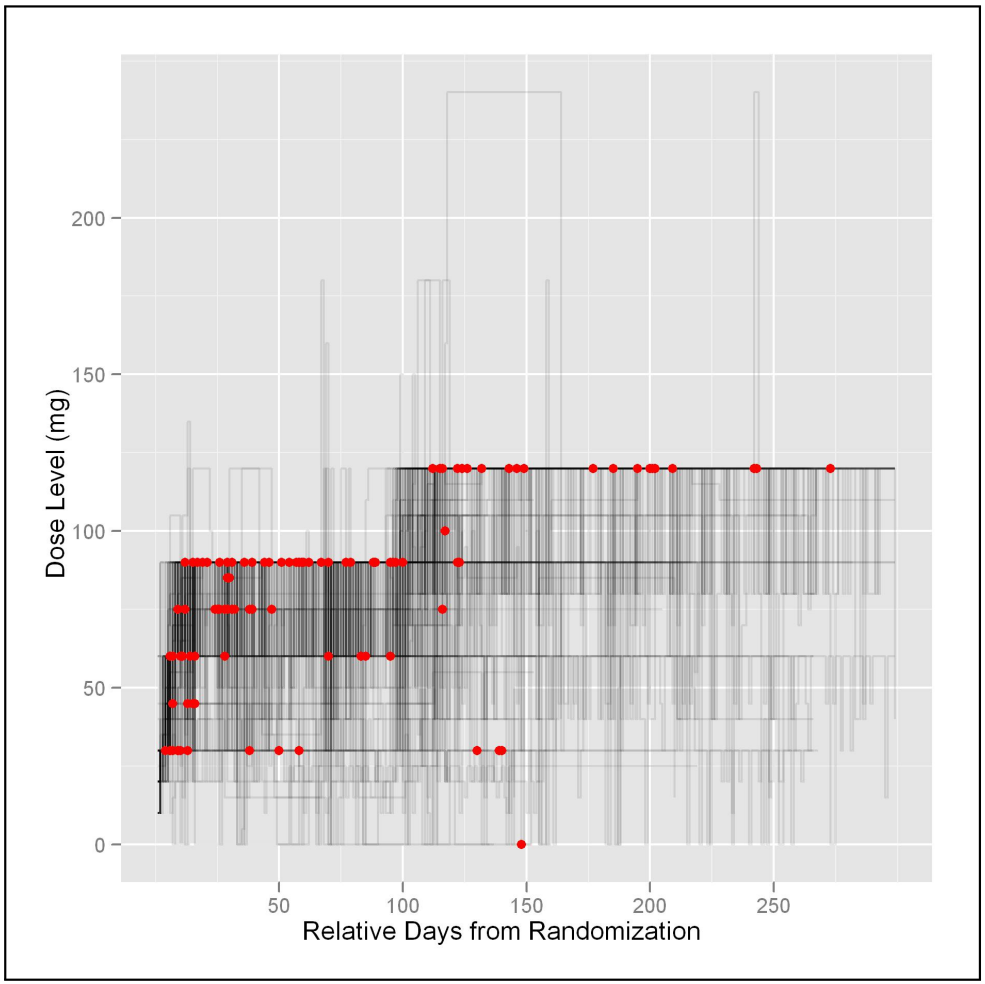
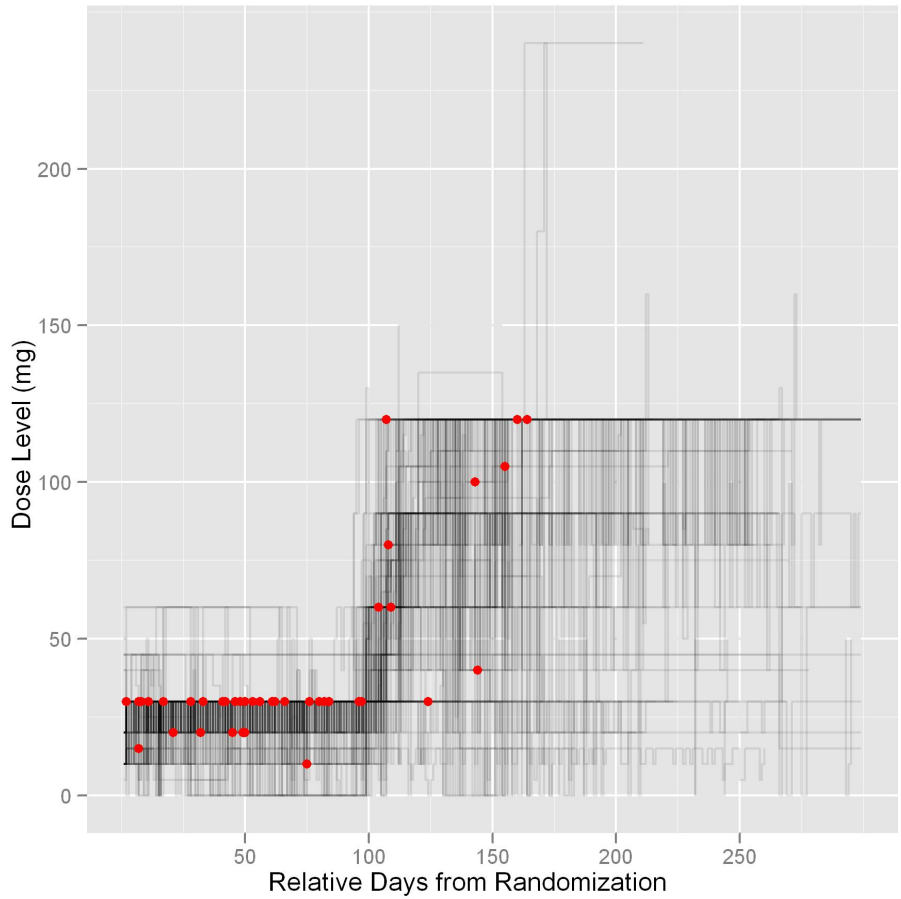


A few observations

- Distribution of events at different dose level
- How the more frequent titration activities correlate with event occurrence
- Some overdose as shown by unexpected spikes

Distribution of recurrent Events and Corresponding Dose cont.

The recurrent events and dose titration visualized at a different dose level - note the distinctive decrease in recurrence of the event after day 100.



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- The concept of mapping aesthetics to data fits in naturally when we try to communicate with clinicians regarding a proposed visualization
- Rich statistical packages in R complement the graphical capability of ggplot2

Discussion

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- How to differentiate up and down-titration in dose-titration graphs?
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- Any more ideas for clinical data visualization?

Reference


Hadley Wickham.
ggplot2: elegant graphics for data analysis, Springer New York, 2009.


Edward R. Tufte.
The Visual Display of Quantitative Information, Graphics Press, 2001.

Acknowledgement

- Bret Musser
- Gary Meininger