

Visualizing Clinical Trial Design and Results in 20 Graphical Displays – Achieving 20-20 in 2020

Munish Mehra, PhD (Biostats), M.S (C.S), M.Sc. (Math), Tigermed, USA
munish.mehra@Tigermed.net
+240-477-3700

**PhUSE CONNECT 2020
Orlando, FL**

**Monday 8 March, 2020
3:00-3:30 PM**

OVERVIEW



- Significant advances in software, programming and creativity to graphically display complex data
- Most applications are within a well defined domain (e.g. visualizing adverse events data, safety signals, genomics data, clinical operations data, metrics, etc.)
- This presentation takes a different approach to see how the best displays can be used to **summarizing a clinical trial design and results in 20 graphical displays**
- Look forward to lots of input
- Intend is to get input and consensus on 20 best displays so most clinical trials can be summarized using these 20 standard displays

Figure 1 - Trial Design Schema

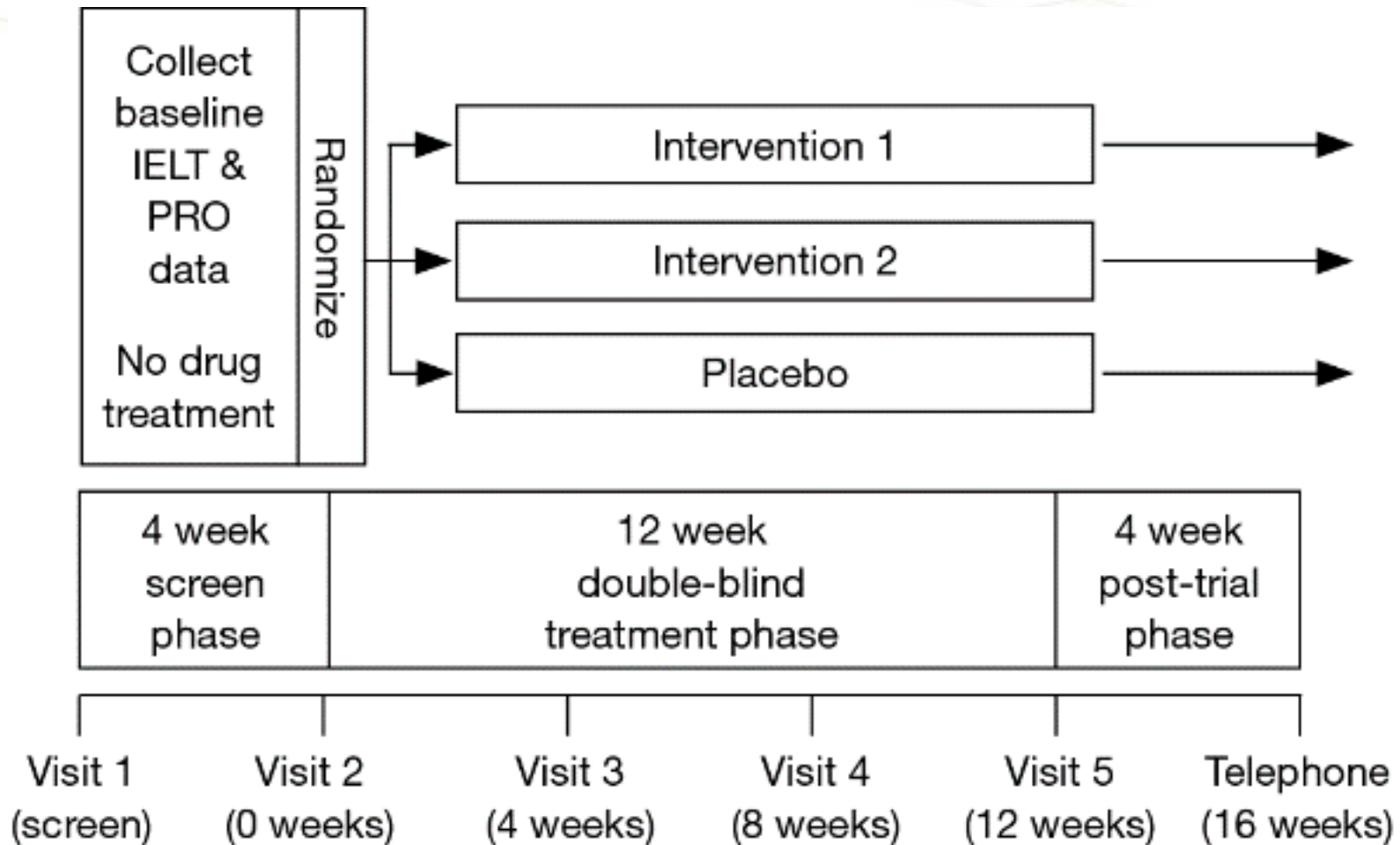


Figure 2 – Schedule of Assessments

	V1 (Screening)	V2 V1 + 1 Wk (± 3 days)	V3 V2+1 Wk (± 3 days)	V4 (Day 1)	V5 (Wk 8 ± 1 Wk)	V6 (Wk 12 ± 1 Wk)	V7 (Wk 16 ± 1 Wk)
	Run-in period			Treat ment Start	Post-Treatment Visits		
IC	X						
MH	X						
DM	X						
AE	X	X	X	X	X	X	X
VS	X			X	X	X	X
PRO	X			X	X	X	X
etc.							

Figure 3 – CONSORT Diagram for Disposition

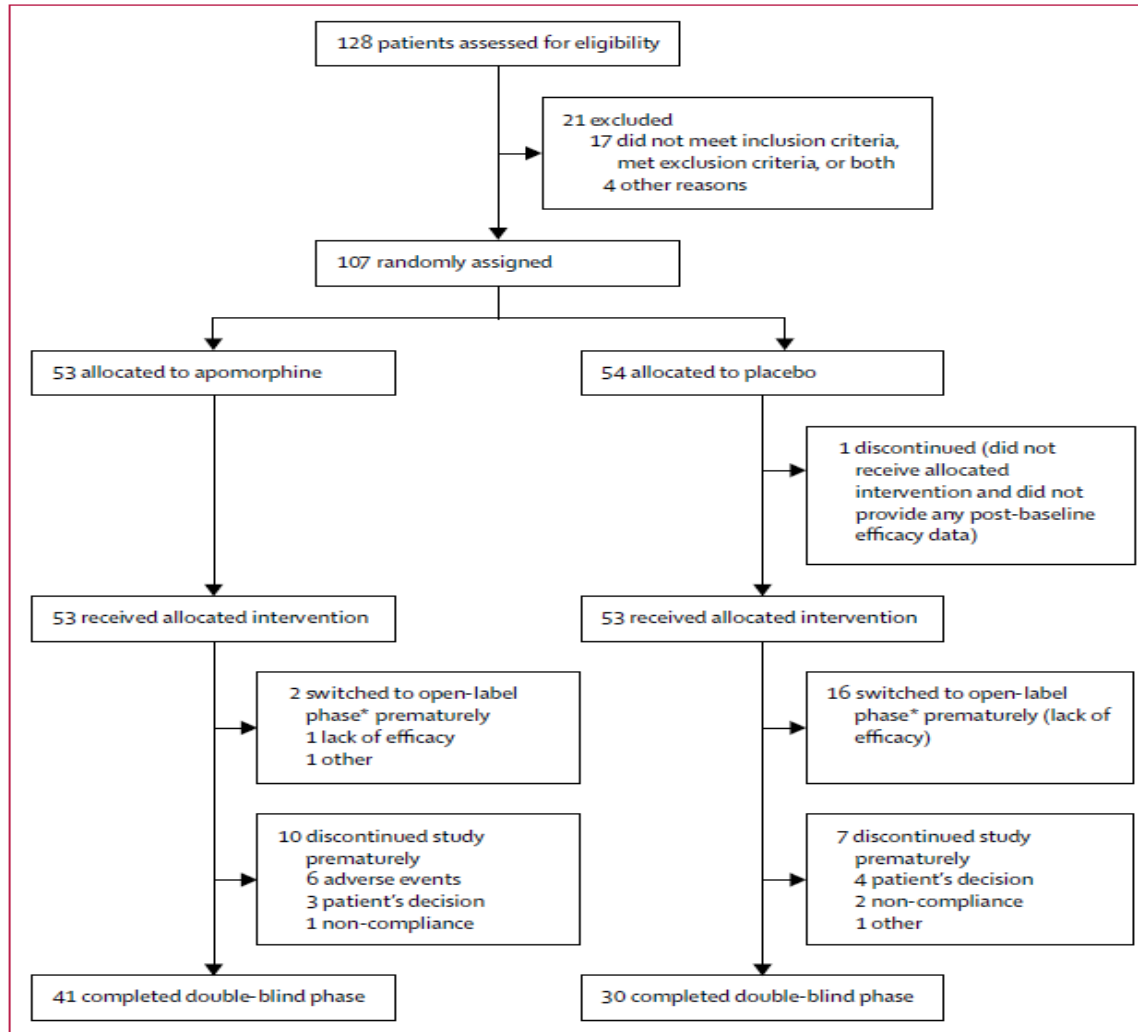


Figure 2: Trial profile

*In the open-label phase, all patients received apomorphine infusion.

Reference: Regina Katzenschlager, et. al, *Apomorphine subcutaneous infusion in patients with Parkinson's disease with persistent motor fluctuations (TOLEDO): a multicentre, double-blind, randomised, placebo-controlled trial*, Lancet Neurol 2018, [http://dx.doi.org/10.1016/S1474-4422\(18\)30239-4](http://dx.doi.org/10.1016/S1474-4422(18)30239-4)
<http://www.consort-statement.org/consort-statement/flow-diagram>

Figure 4 – Box Plots for Demographics and Baseline Data

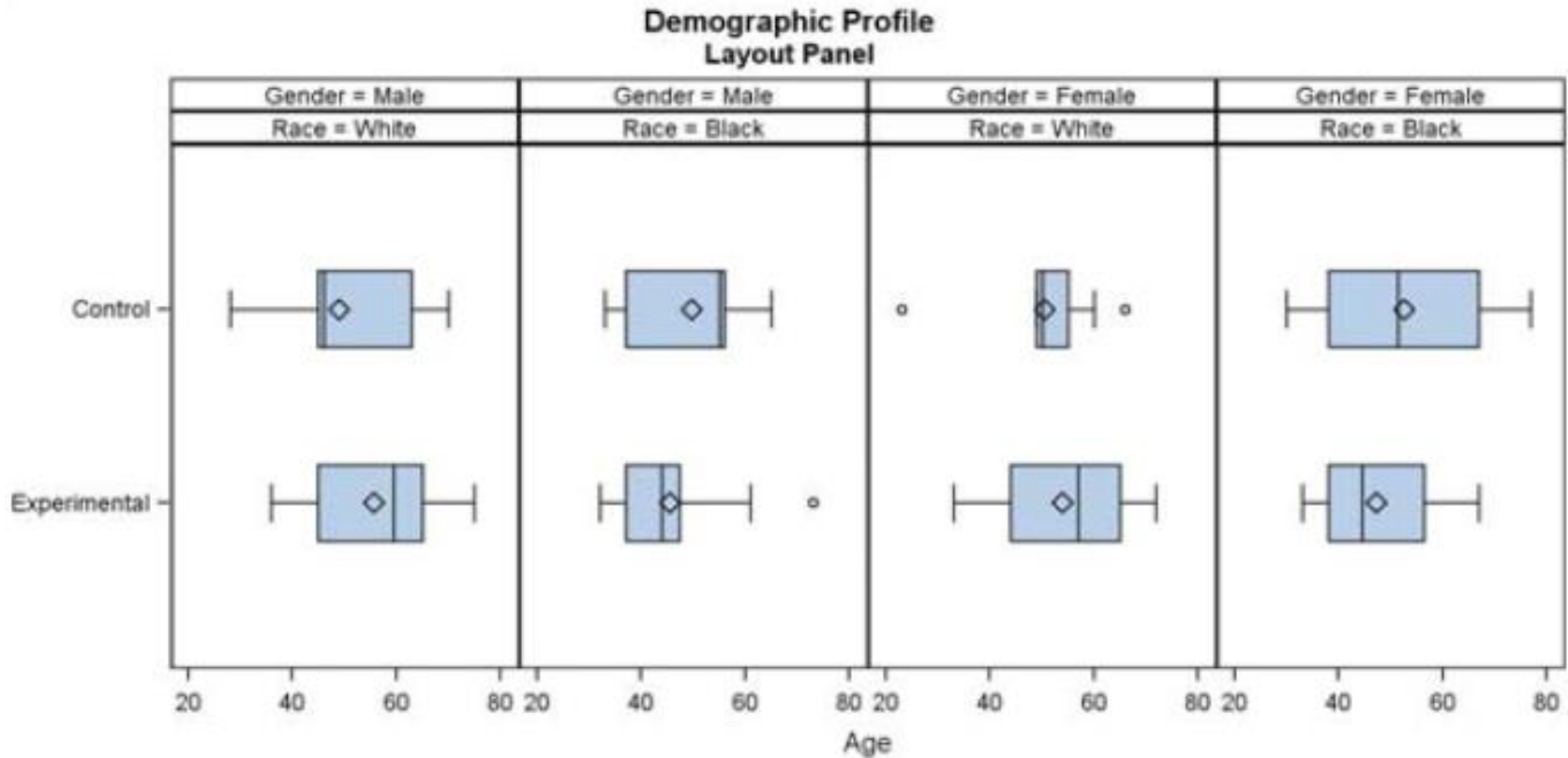


Figure 5 – Forest Plot for Baseline or Efficacy Data

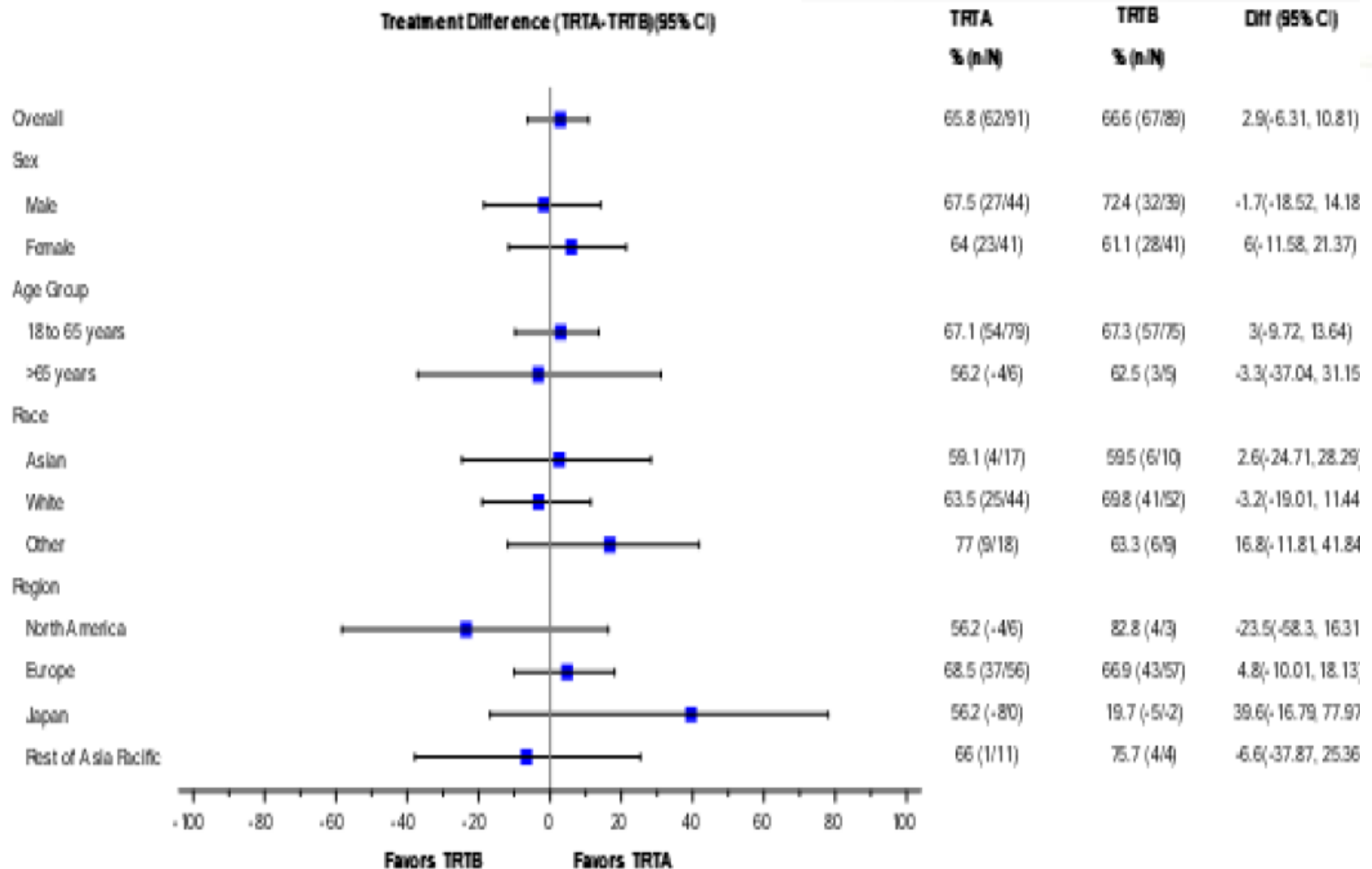
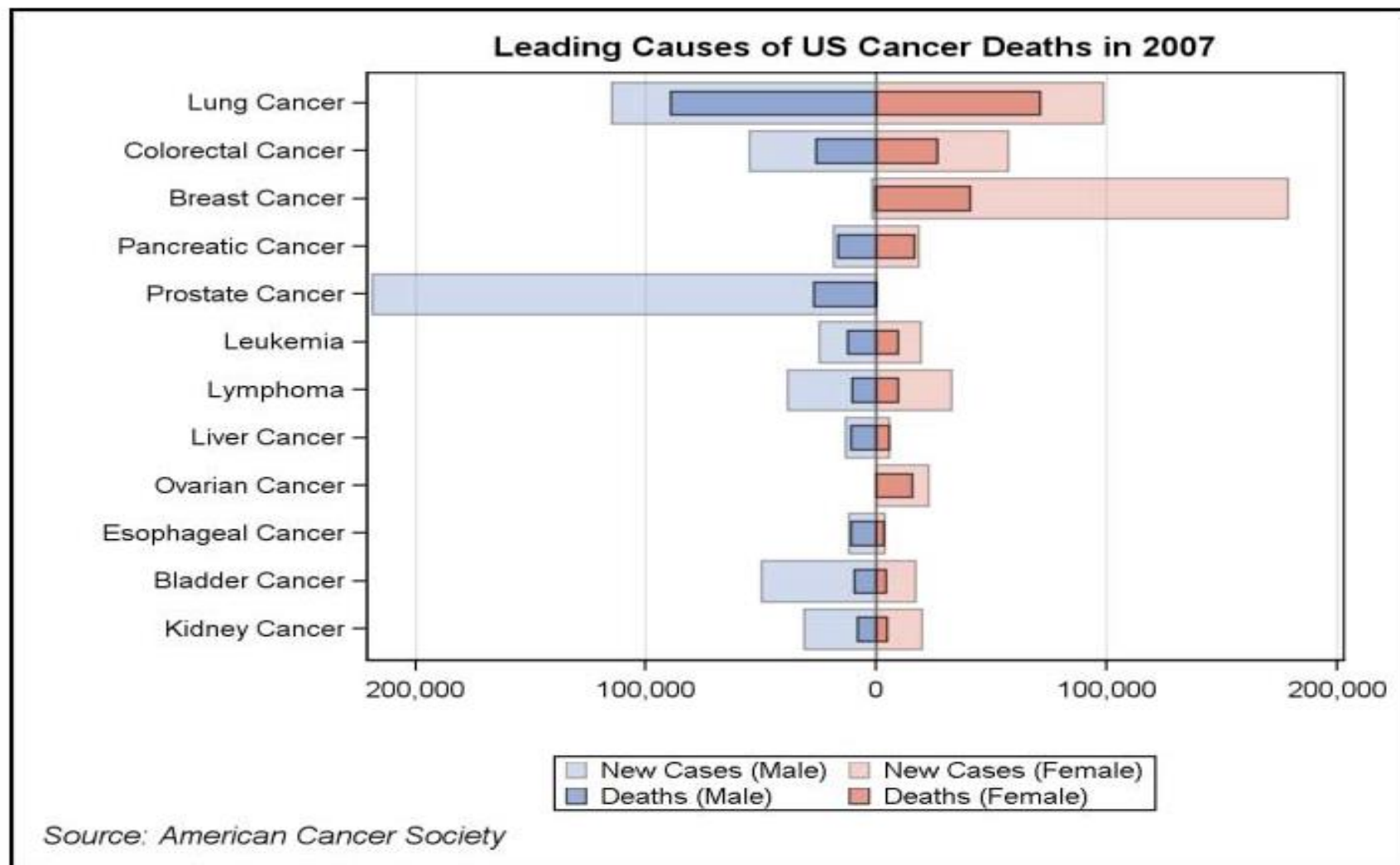
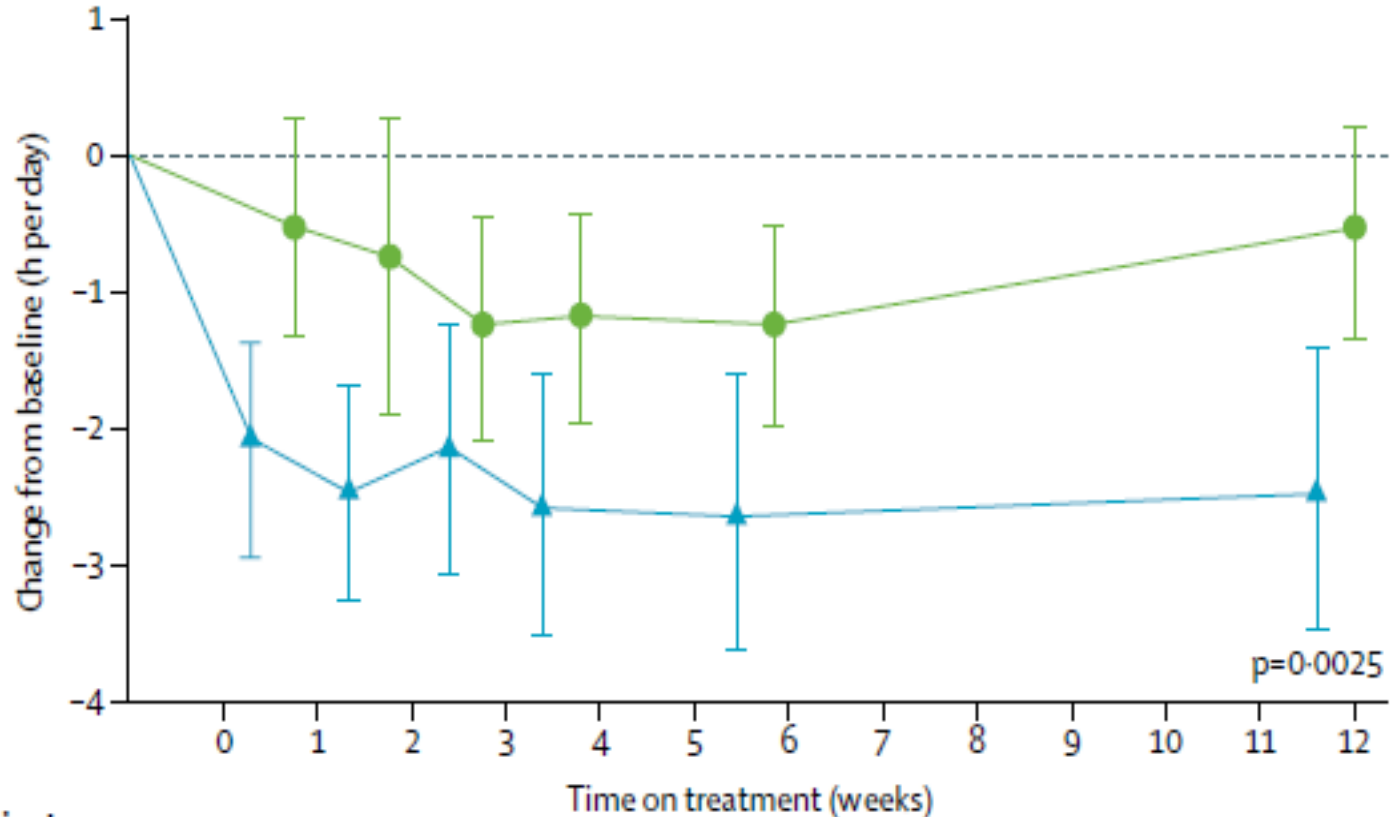


Figure 6 – Creative Bar Graphs for Efficacy or Safety Data



Can also use Stacked Bar Graphs, 3-D Bar graphs etc.

Figure 7 – Line Graphs for Efficacy or Safety over Time

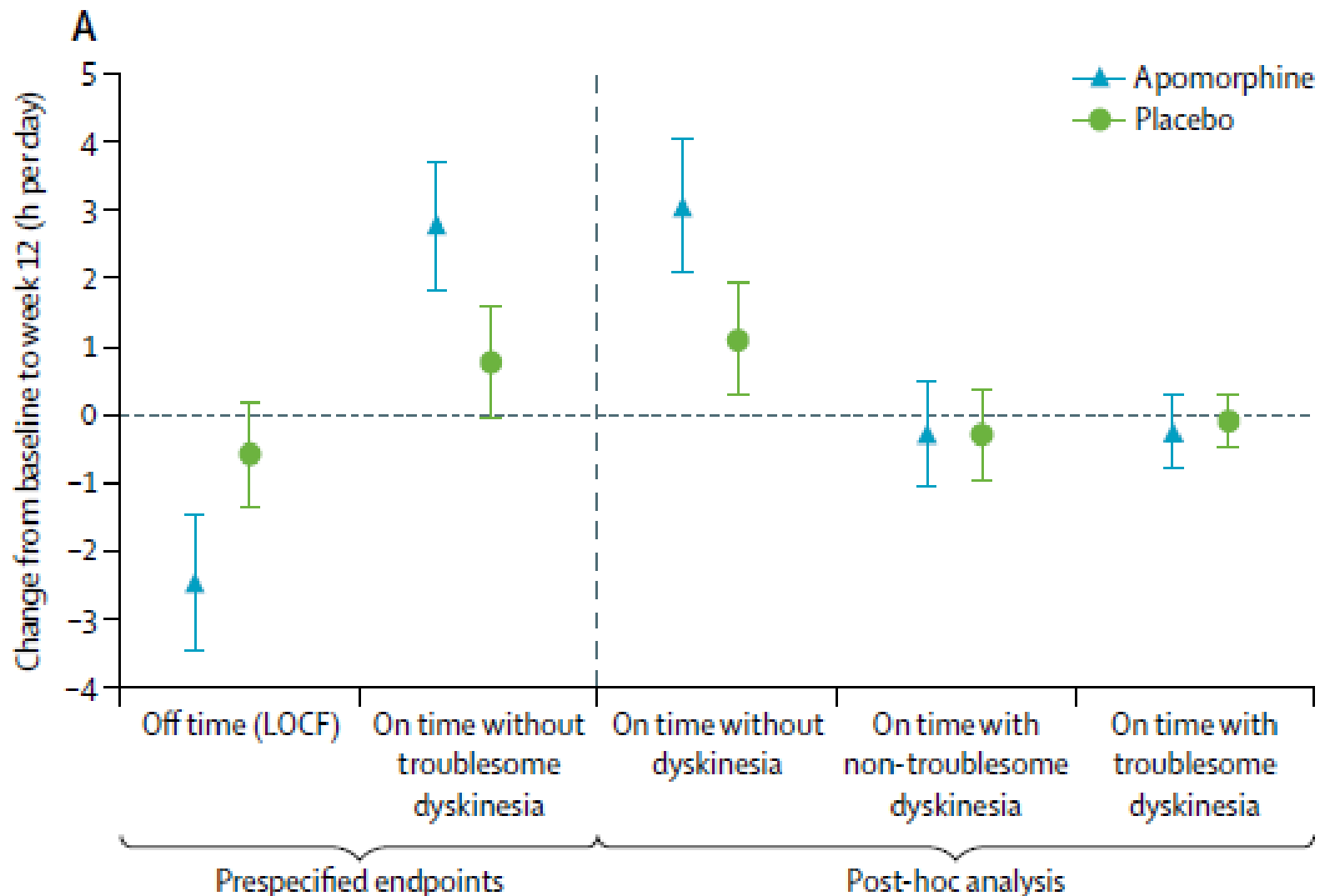


Number of patients

Apomorphine	53	52	52	52	52	..	52	..	..	..	..	..	53
Placebo	53	48	48	48	48	..	48	..	..	..	..	..	52

Regina Katzenschlager, et. al, *Apomorphine subcutaneous infusion in patients with Parkinson's disease with persistent motor fluctuations (TOLEDO): a multicentre, double-blind, randomised, placebo-controlled trial*, Lancet Neurol 2018, [http://dx.doi.org/10.1016/S1474-4422\(18\)30239-4](http://dx.doi.org/10.1016/S1474-4422(18)30239-4)

Figure 8 – Continuous non-longitudinal data by categories for Efficacy

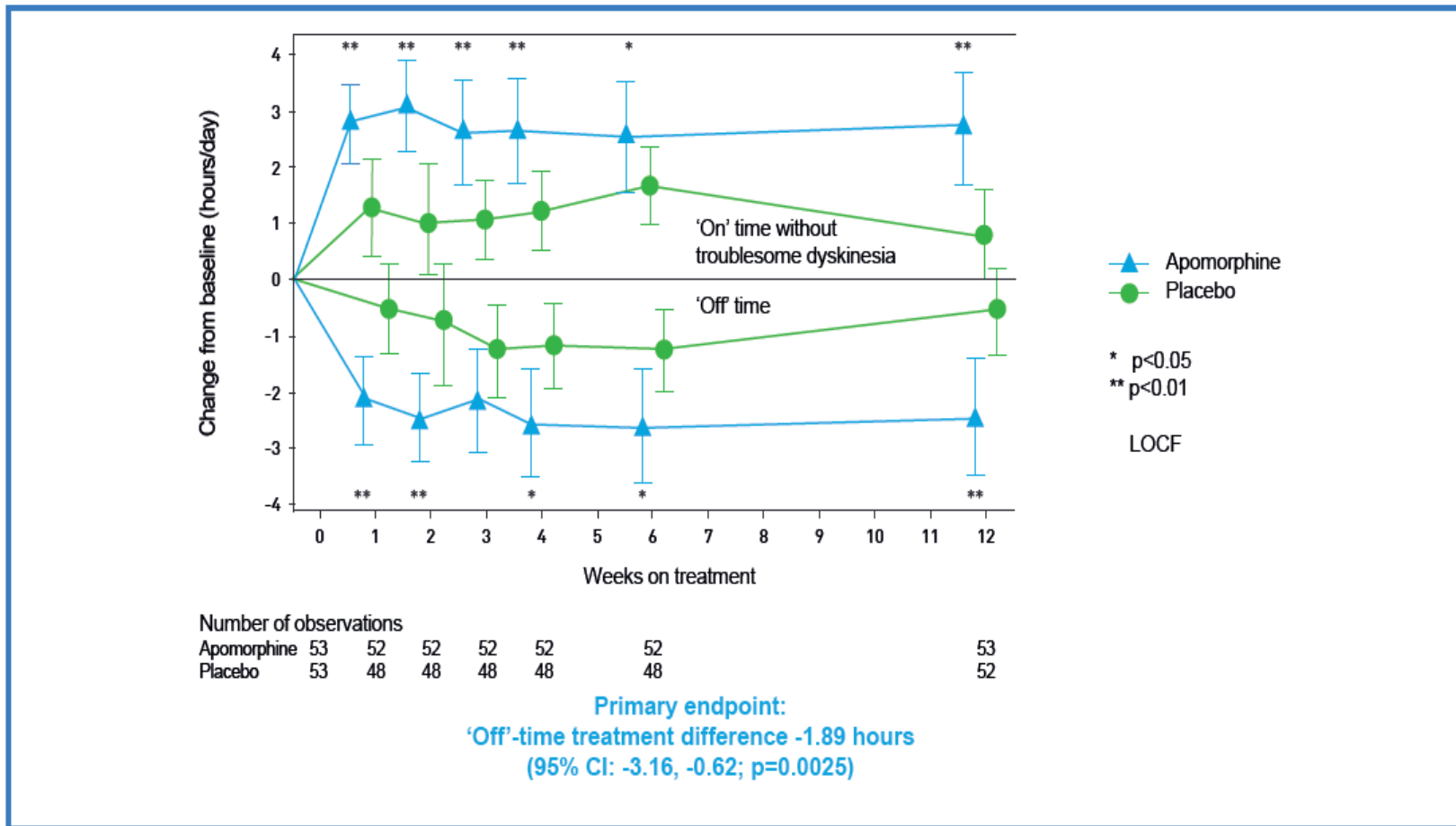


Regina Katzenschlager, et. al, *Apomorphine subcutaneous infusion in patients with Parkinson's disease with persistent motor fluctuations (TOLEDO): a multicentre, double-blind, randomised, placebo-controlled trial*, Lancet Neurol 2018, [http://dx.doi.org/10.1016/S1474-4422\(18\)30239-4](http://dx.doi.org/10.1016/S1474-4422(18)30239-4)

Figure 9 – Mirror plot for Efficacy Data Over Time

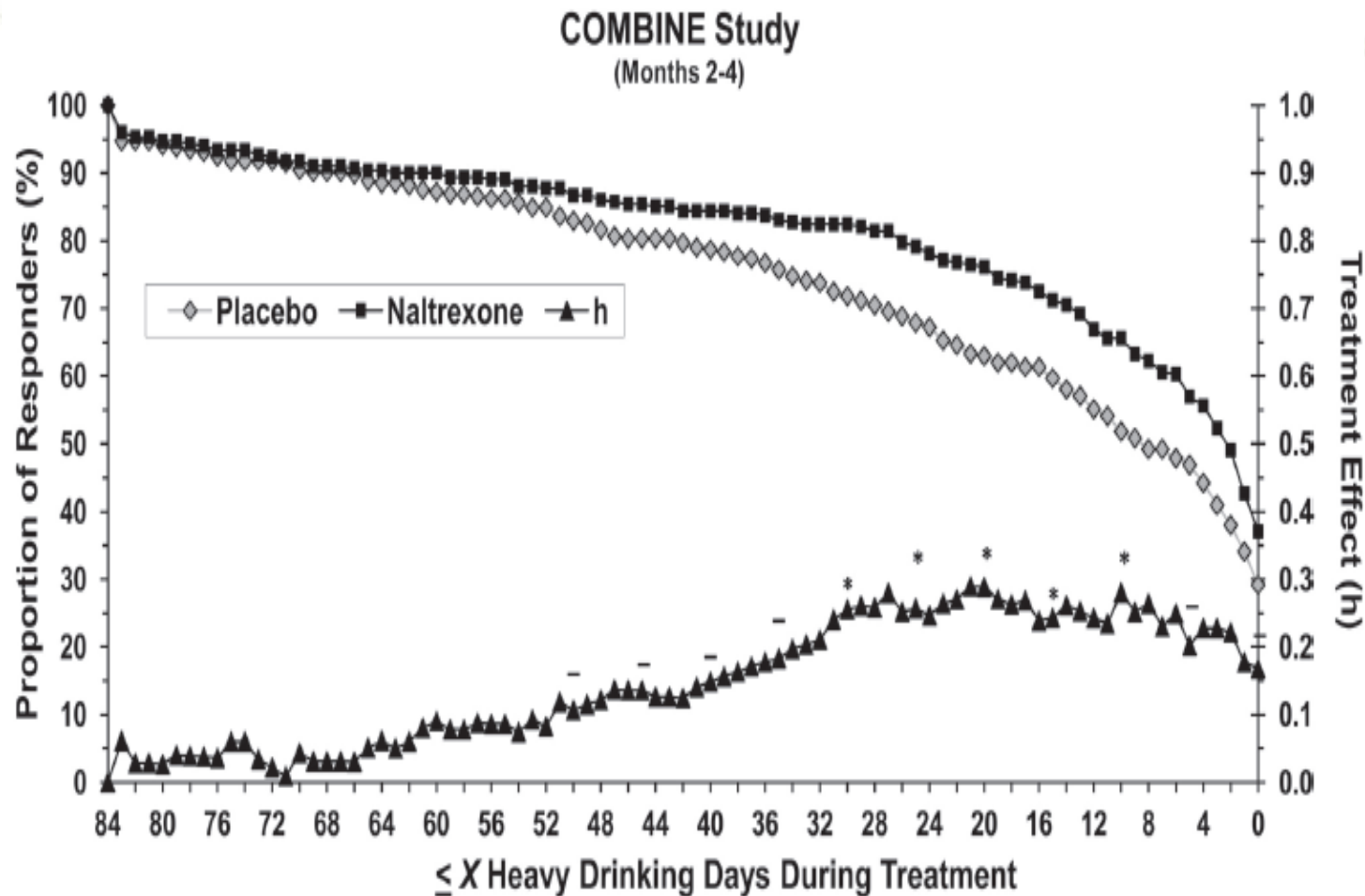


Figure 3: PD motor states at each visit based on home diary results



For each variable, data shown are the average from the motor symptom diary for the 2 consecutive days prior to the visit. Error bars are 95% confidence interval for the mean. LOCF, last observation carried forward. p-values are APO versus placebo.

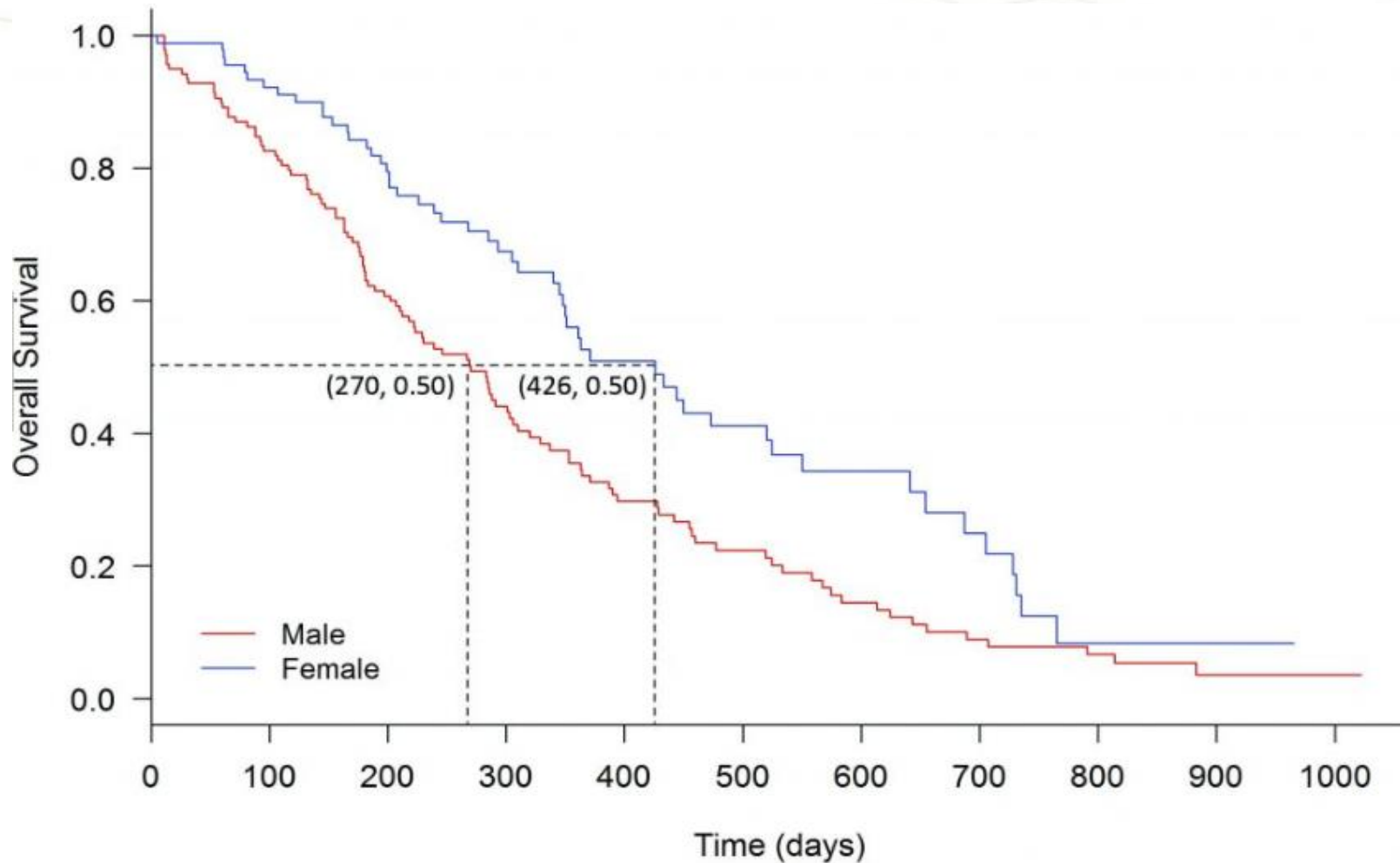
Figure 10 – Cumulative Proportion of Responders for Efficacy Data



<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3965687/pdf/jsad335.pdf>

For another Example with 95% CI see: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3125671/pdf/nihms-295566.pdf>

Figure 11 – Kaplan-Meier plot (Survival or Time to event analyses)



Reference for above plot: <https://www.quantics.co.uk/blog/introduction-survival-analysis-clinical-trials/>

Figure 12 – Spider Plot or Spaghetti Plot for Individual Subject Efficacy Responses Over Time

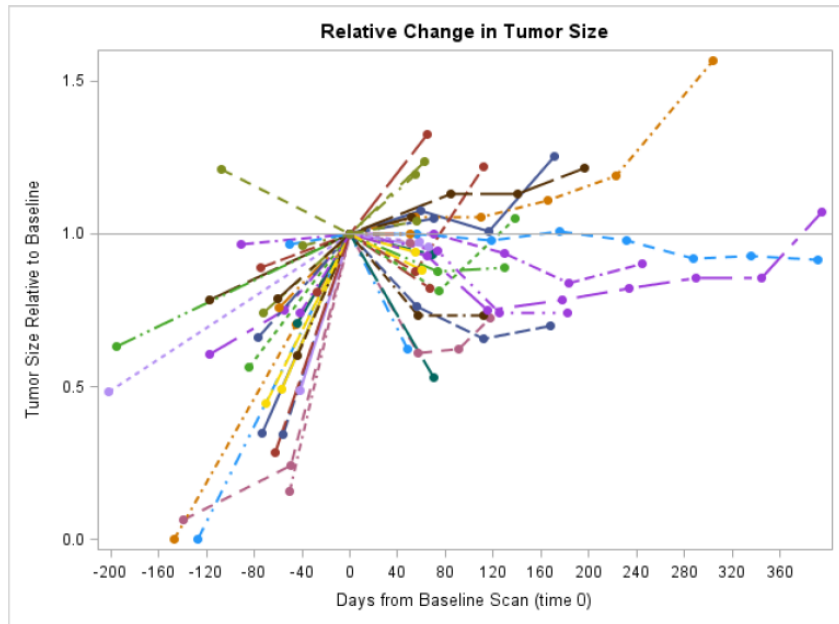


Figure 3. Spider Plot, displaying change in tumor size, starting in pre-treatment phase

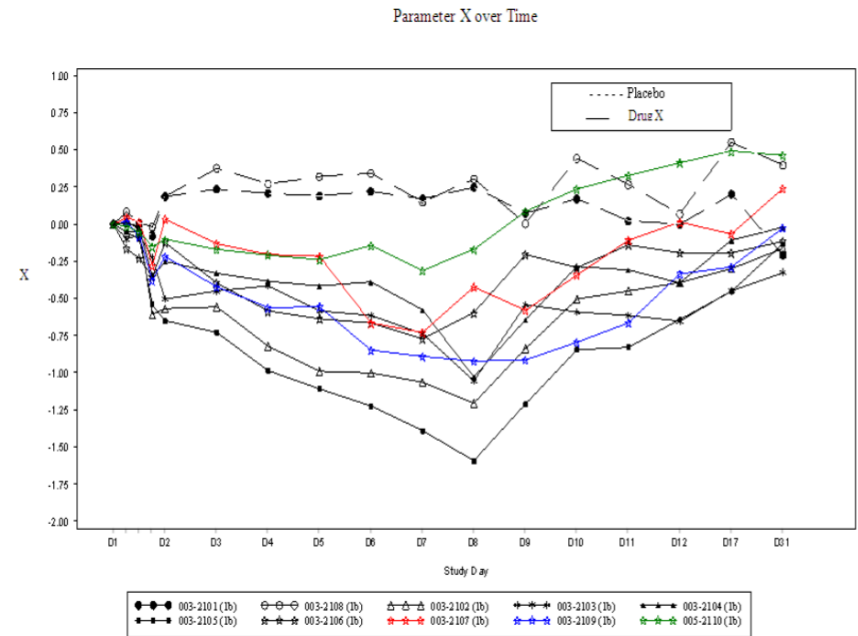


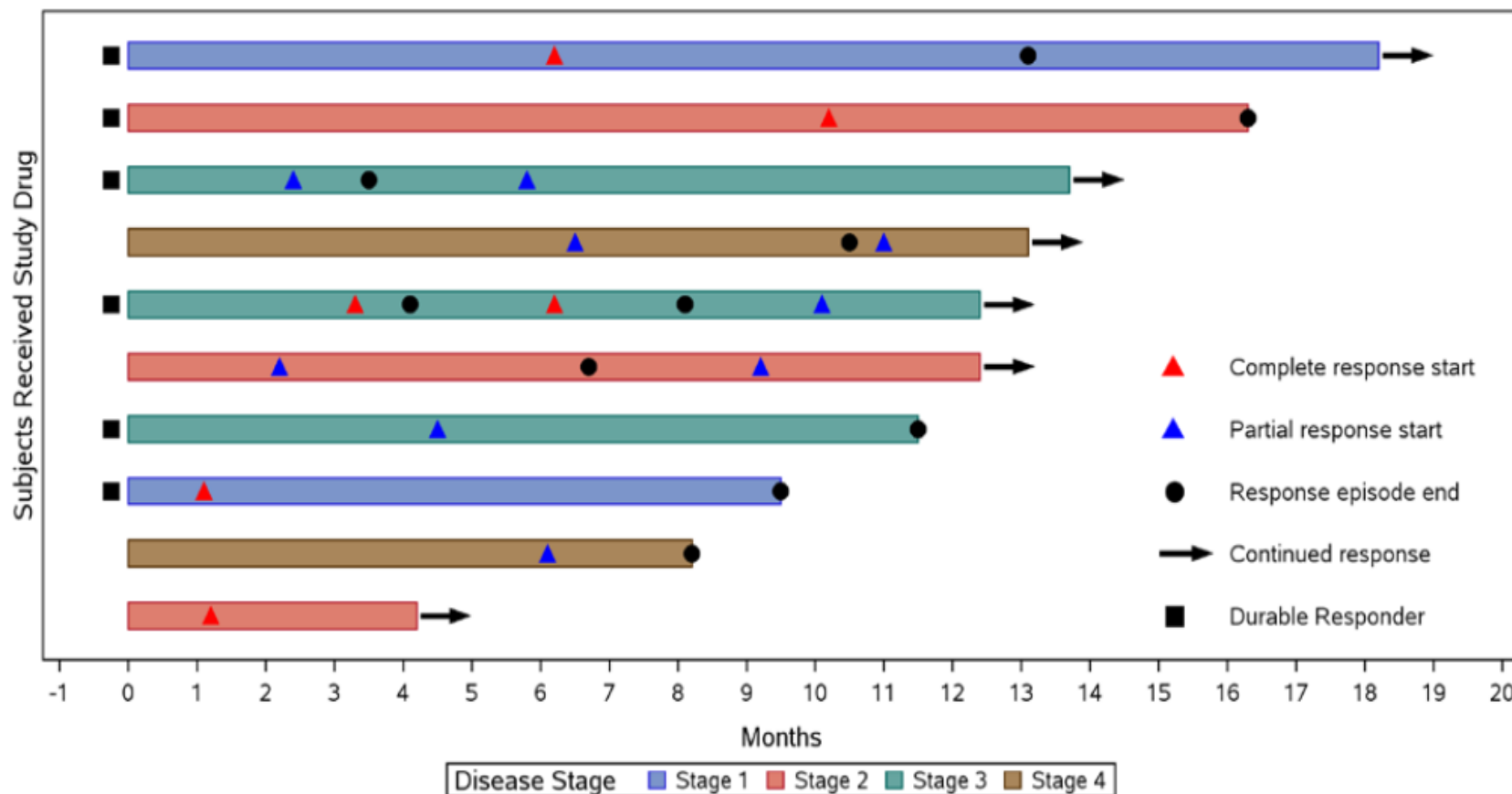
Figure 1. Illustration of graph of interest: Parameter X over time

Reference:

https://www.researchgate.net/publication/281748374_Graphical_Results_in_Clinical_Studies_A_focus_on_graphics_used_in_oncology

<https://www.pharmasug.org/proceedings/2013/CC/PharmaSUG-2013-CC27.pdf>

Figure 13 – Swimmer Plots for Individual Subject Efficacy Data Over Time



Each bar represents one subject in the study.

A Durable Responder is a subject who has confirmed response for at least 183 days (6 months).

<https://www.pharmasug.org/proceedings/2014/DG/PharmaSUG-2014-DG07.pdf>

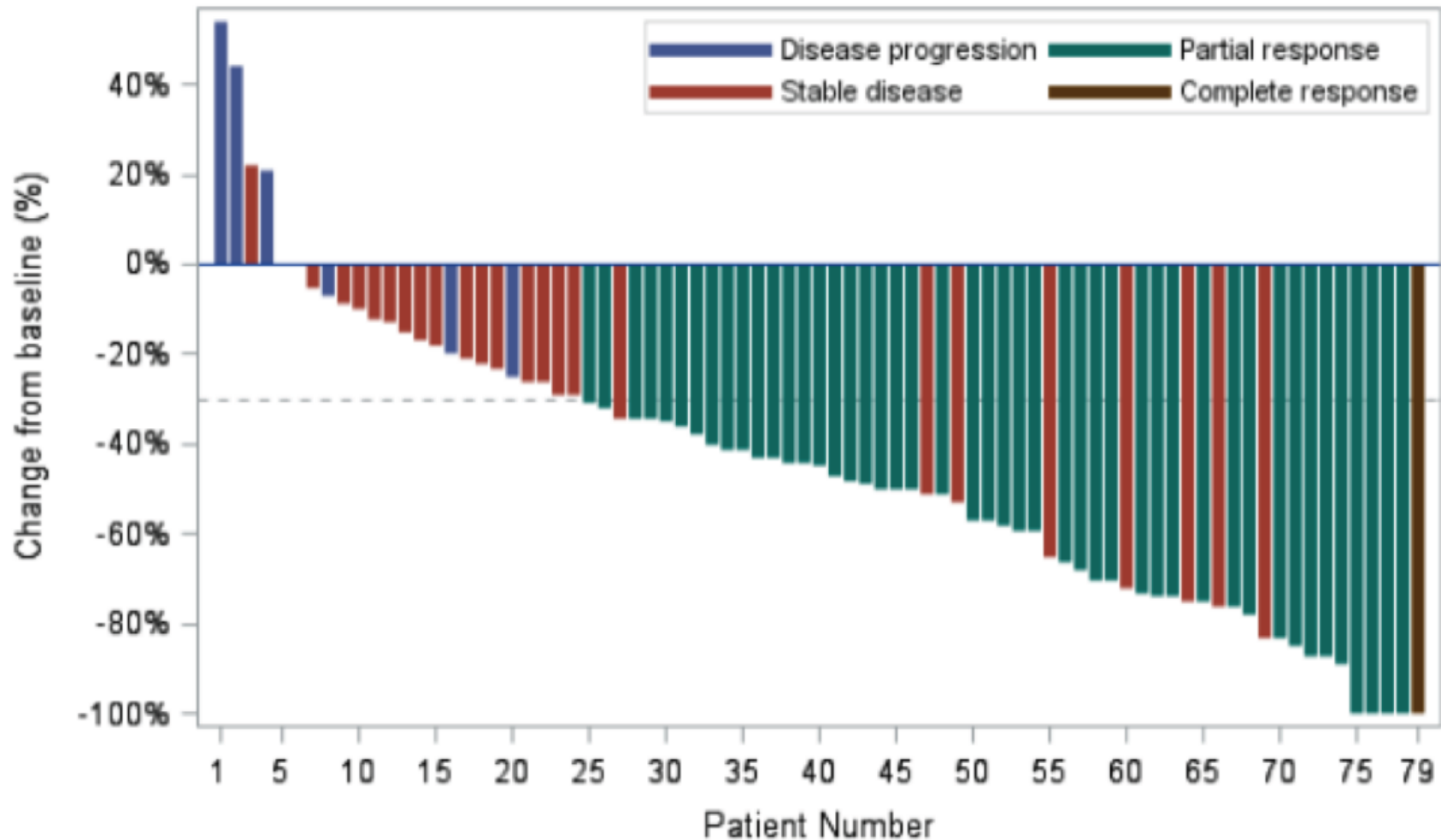
SAS code for Swimmer Plots by Matange, S. (2014, June 22) can also be found at:

<https://blogs.sas.com/content/graphicallyspeaking/2014/06/22/swimmer-plot/>

Figure 14 – Waterfall Plots for Efficacy Data by Subject

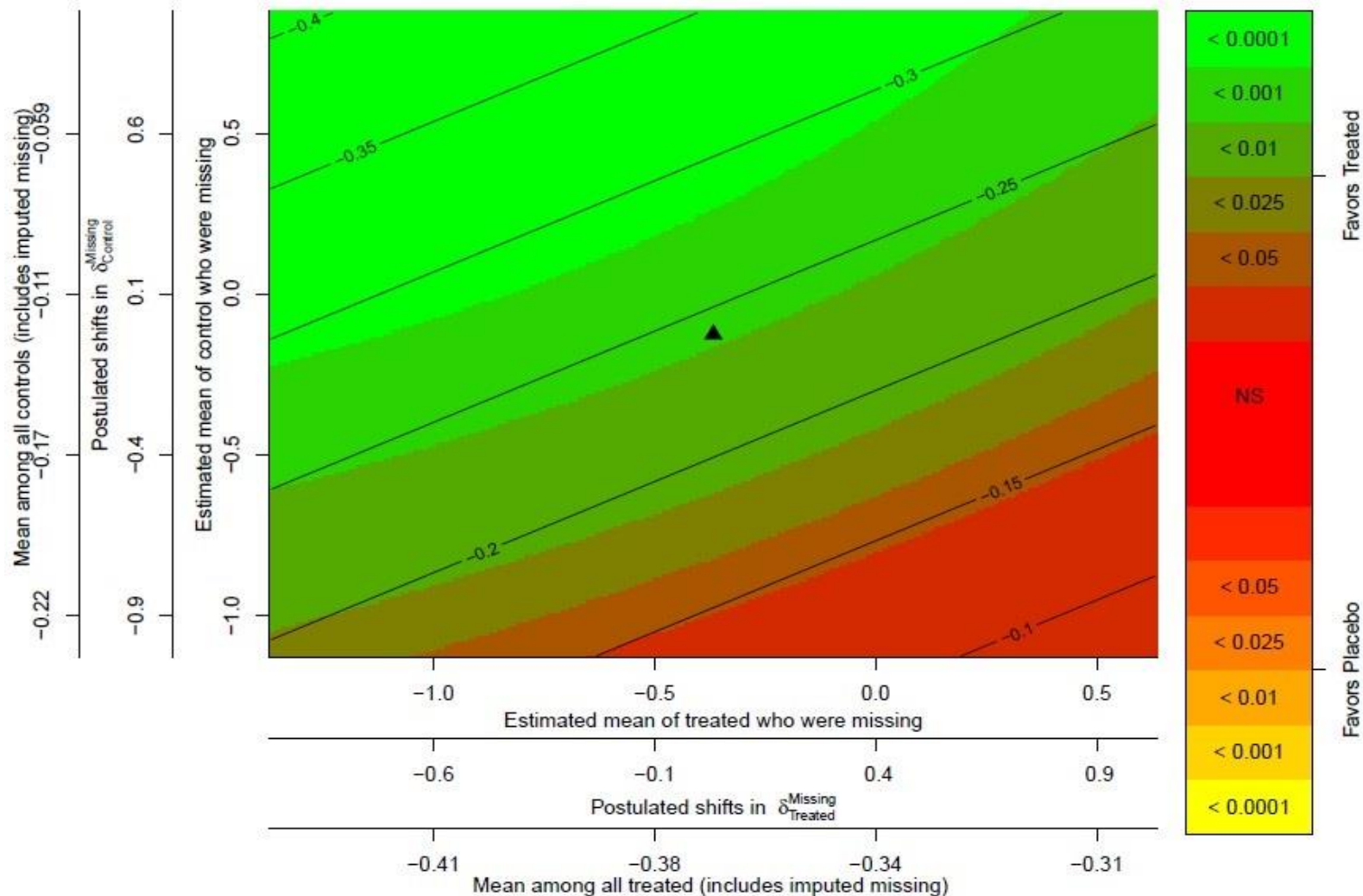


Percent Change in Tumor Burden (N=79)



Reference: Wicklin, R. (2015, April 20). Create a waterfall plot in SAS,
<https://blogs.sas.com/content/iml/2015/04/20/waterfall-plot.html>

Figure 15 – Heat Map for Tipping Point Analysis for Sensitivity Analysis



Reference: Torres, Cesar, *A Tipping Point Method to Evaluate Sensitivity to Potential Violations in Missing Data Assumptions*, ASA Biopharmaceutical Section Regulatory-Industry Statistics Workshop, September 24, 2019

Figure 16 – Dot Plot for AEs



Most Frequent On-Therapy Adverse Events Sorted by Relative Risk

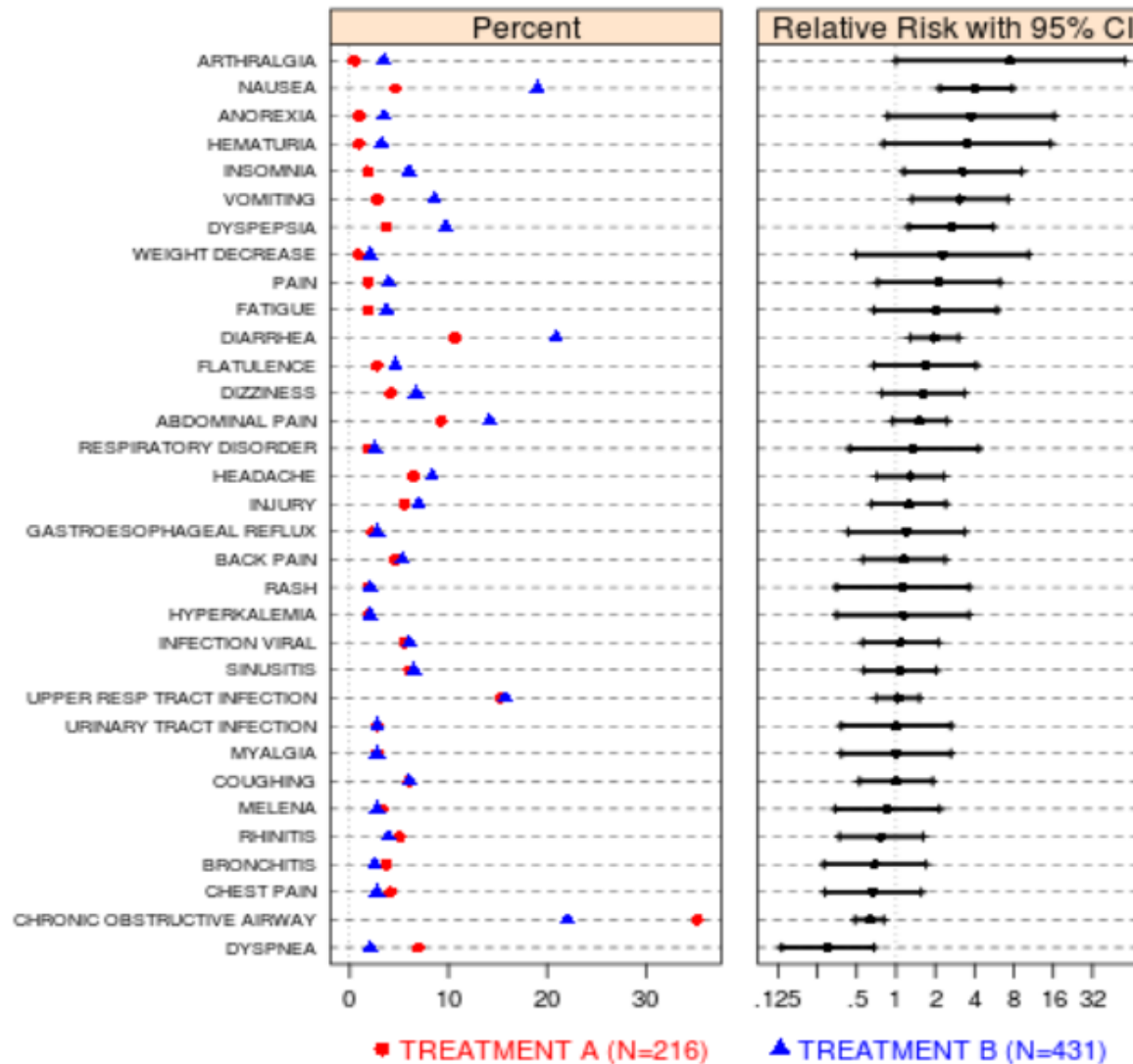


Figure 17 – Volcano Plots for AEs

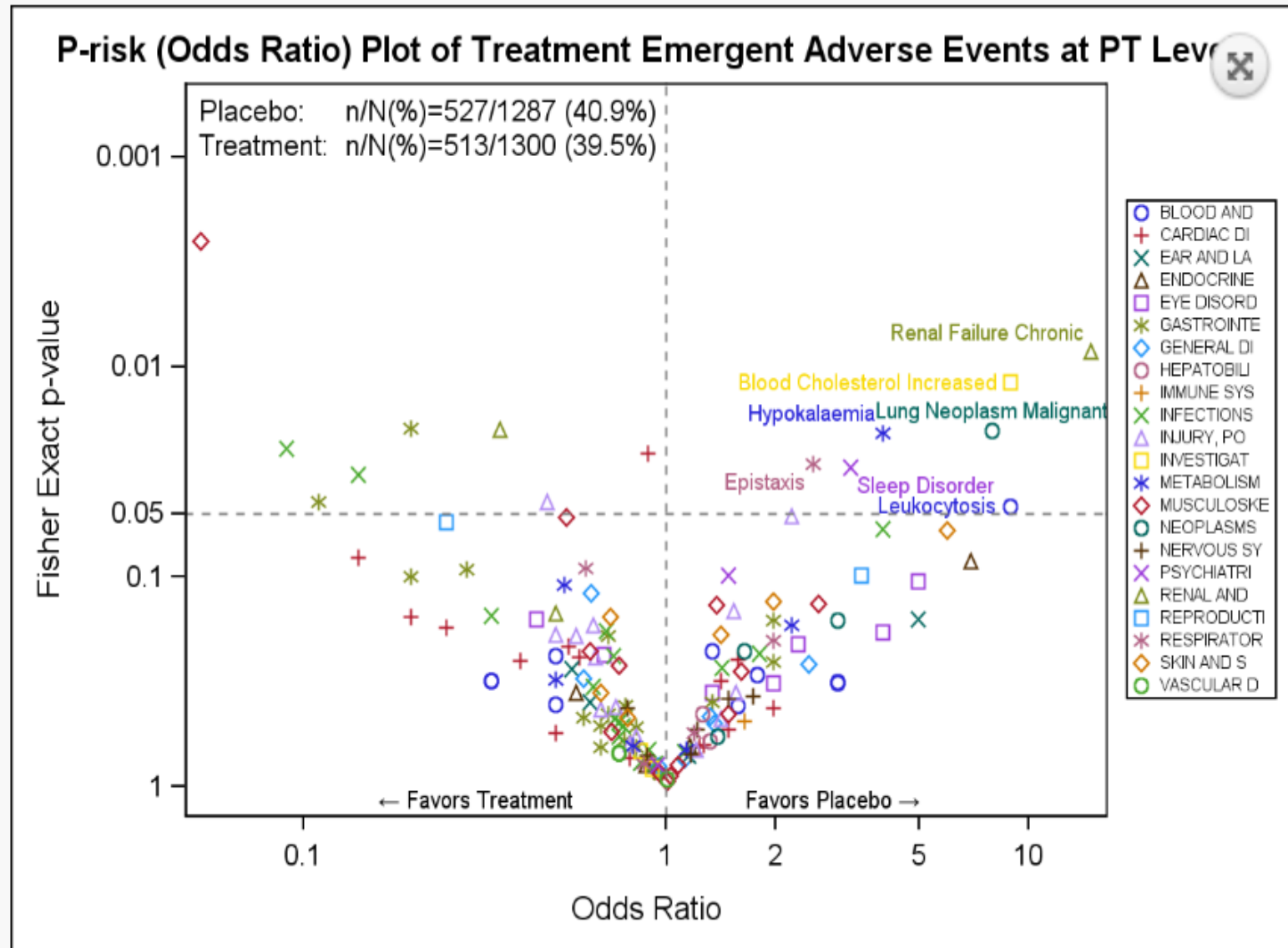


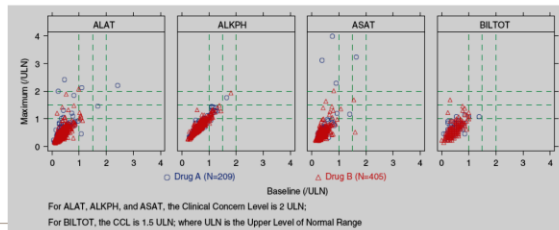
Figure 18 – Specialized Scatter Plots and Box Plots for Lab, VS, ECG Shifts etc.



Lab Shift Scatterplots

Notes on how to use:

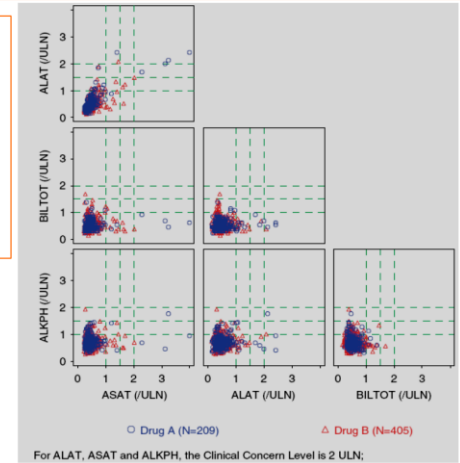
- Graphical equivalent of a "shift table"
- Reference lines at clinically important levels
- Focus on upper left quadrant of each panel
- Plot control group last to more readily identify Tx effect (not done in example below)
- Consider displaying on log scale to account for skewness in distribution
- May be useful with any lab data to pick up possible associations
- General shift of all points up and to the left
 - Distribution of max over several visits (y-axis) has a larger mean than that of a single (baseline) visit (x-axis)



Trellis of Scatterplots for Lab Tests

Notes on how to use:

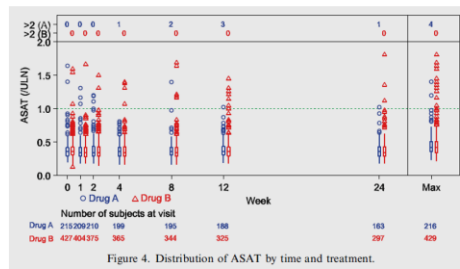
- Allows identification of simultaneous elevations
- May be useful with any lab data to pick up possible associations
- Similar graphical features to Trellis plot
- Will normalize lab results by either Upper Limit of Normal Range or Upper Limit of PCI Range and graph each lab test against the others in a matrix.



Lab Boxplots over Time

Notes on how to use:

- Standard boxplots (Tukey's schematic diagrams)
- Colour and symbol to differentiate treatments
- Time axis on continuous scale (not nominal)
- Numbers of patients for each time point displayed under x-axis
- Graphical margin shows distribution of maximum change for each patient
- Number of extreme values (>2 ULN) noted above the plot



Side-by-side Boxplots

Notes on how to use:

- Alternative display to scatterplots
- The main interest is in the outliers, so the central mass of the observations can be relegated to a simple box
- In comparison to scatterplots, includes additional information about median and distribution across all subjects
- Similar graph could be used to examine muscle injury by profiling creatinine phosphokinase (CPK), ASAT, lactate dehydrogenase (LDH)

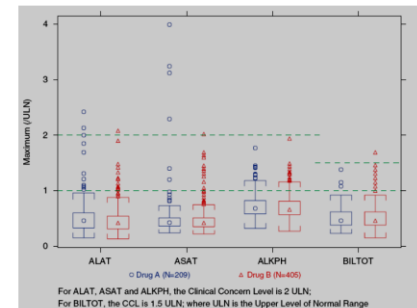


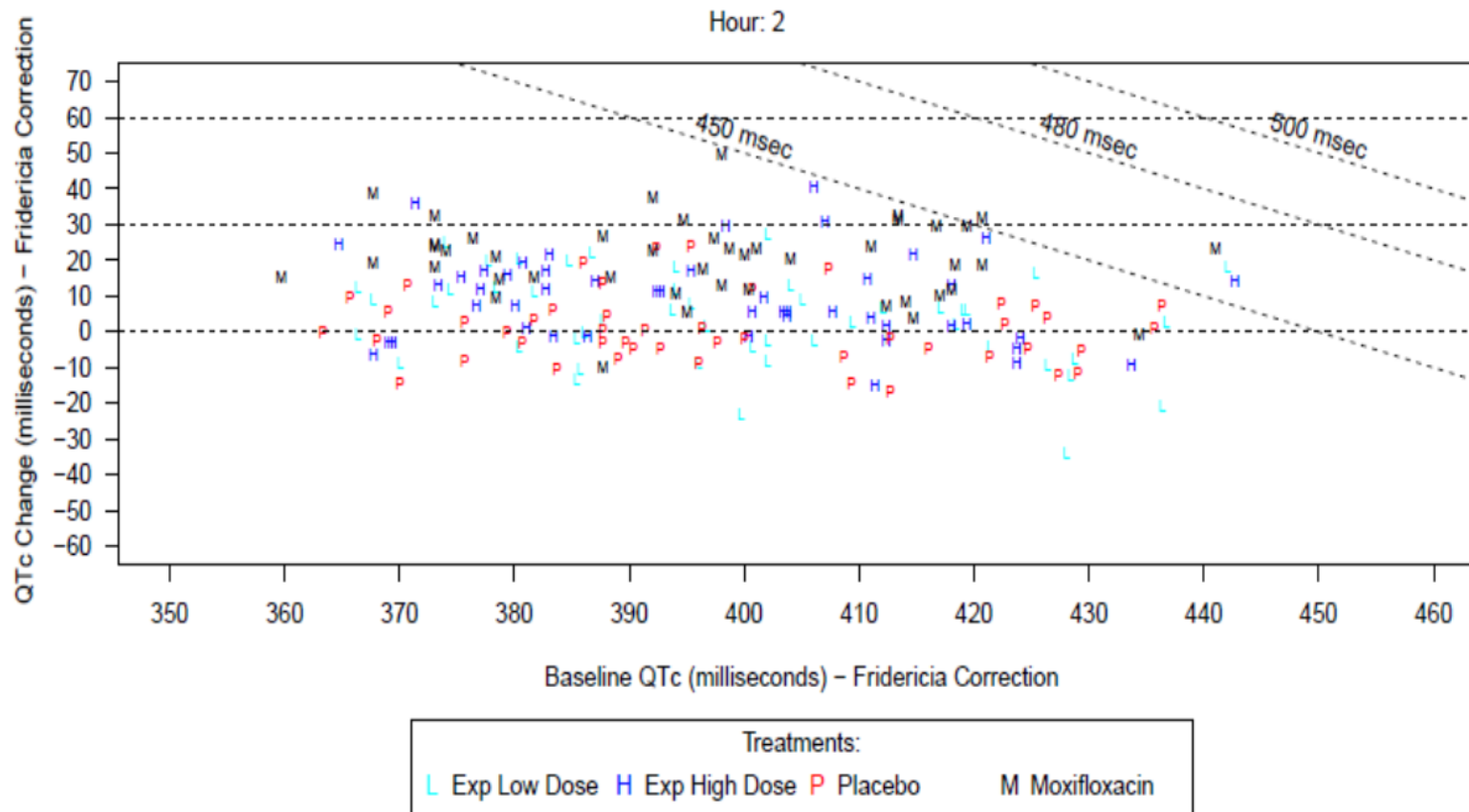
Figure 19 – ECG ICH-E14 Plot



Protocol: text
Population: Text

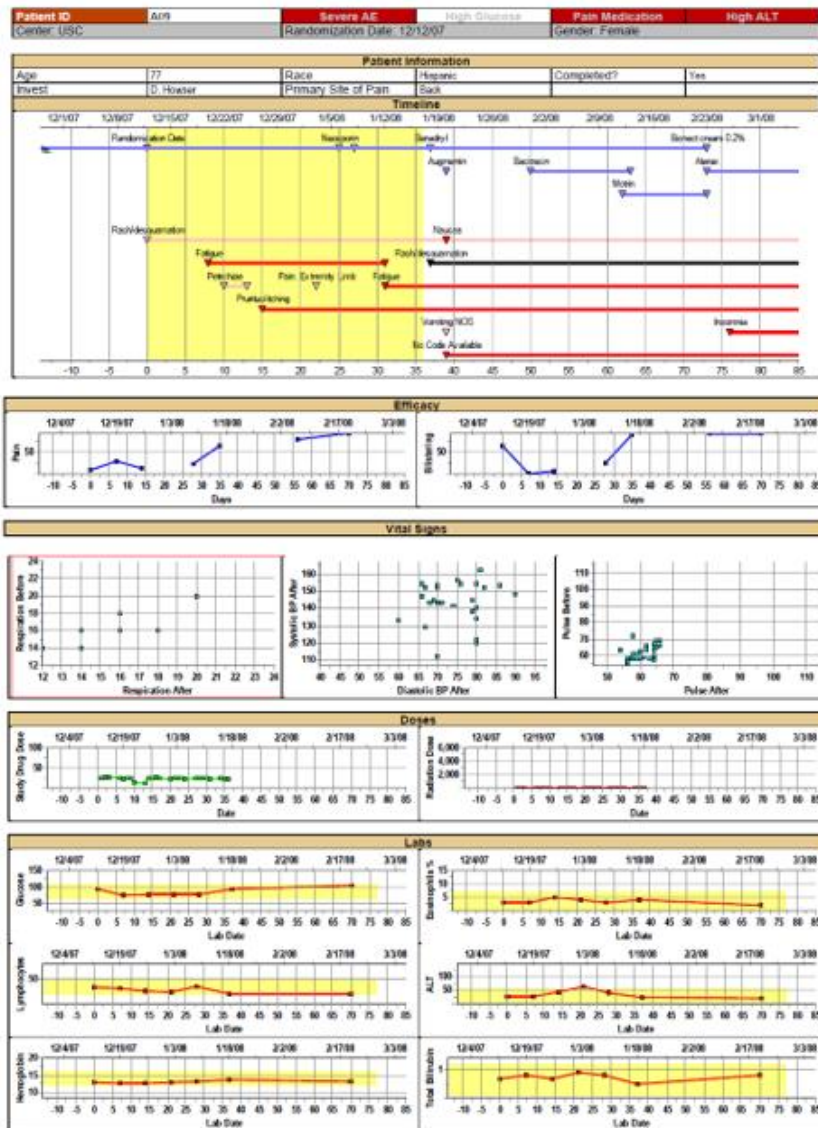
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ECG/VITALS G2
Figure Number
Title2 (Base R)



Reference: The above image and code are available at: <https://www.ctspedia.org/do/view/CTSpedia/ClinECGGraph000>

Figure 20 – Patient Profiles



Reference: www.patientprofiles.com downloaded 4 March, 2009, Can be accessed on WayBackMachine at: <https://web.archive.org/web/20091104034528/http://www.patientprofiles.com/examples.html>

**Please do reach out to me with
suggestions on better ways to display
clinical trial data**

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