HOW TO MAKE ADVERSE EVENTS LOOK PRETTY

Robert Snijder

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DISPLAY OF ADVERSE EVENTS

TRADITIONAL

ADVERSE EVENTS OVERVIEW (A FIRST IMPRESSION)

Post Randomization Adverse Event (MedDRA V 13.1)	Treatment A (N=156)	Treatment B (N=157)	Placebo (N=155)
Subjects Experiencing Adverse Events	105 (67.3%)	109 (69.4%)	75 (48.4%)
Subjects Experiencing Serious Adverse Events	20 (12.8%)	13 (8.3%)	15 (9.7%)
Subjects Experiencing Adverse Events Leading to Permanent Discontinuation of Study/ Study Drug	7 (4.5%)	8 (5.1%)	3 (1.9%)
Death	1 (0.6%)	1 (0.6%)	2 (1.3%)

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AND WITH A BIT MORE DETAIL

Post Randomization Adverse Event (MedDRA V 13.1)	Treatment A (N=156)	Treatment B (N=157)	Placebo (N=155)
General disorders and administration site conditions			
Application site erythema	12 (7.7%)	14 (8.9%)	0
Application site pain	44 (28.2%)	46 (29.3%)	0
Infections and infestations			
Bronchitis	0	8 (5.1%)	1 (0.6%)
Nasopharyngitis	4 (2.6%)	9 (5.7%)	8 (5.2%)
Investigations			
Blood triglycerides increased	8 (5.1%)	3 (1.9%)	4 (2.6%)
Glycosylated haemoglobin increased	9 (5.8%)	5 (3.2%)	7 (4.5%)
Musculoskeletal and connective tissue disorders			
Arthralgia	8 (5.1%)	5 (3.2%)	3 (1.9%)
Pain in extremity	8 (5.1%)	14 (8.9%)	3 (1.9%)
Nervous system disorders			
Burning sensation	15 (9.6%)	15 (9.6%)	0
Vascular disorders			
Hypertension	3 (1.9%)	10 (6.4%)	6 (3.9%)

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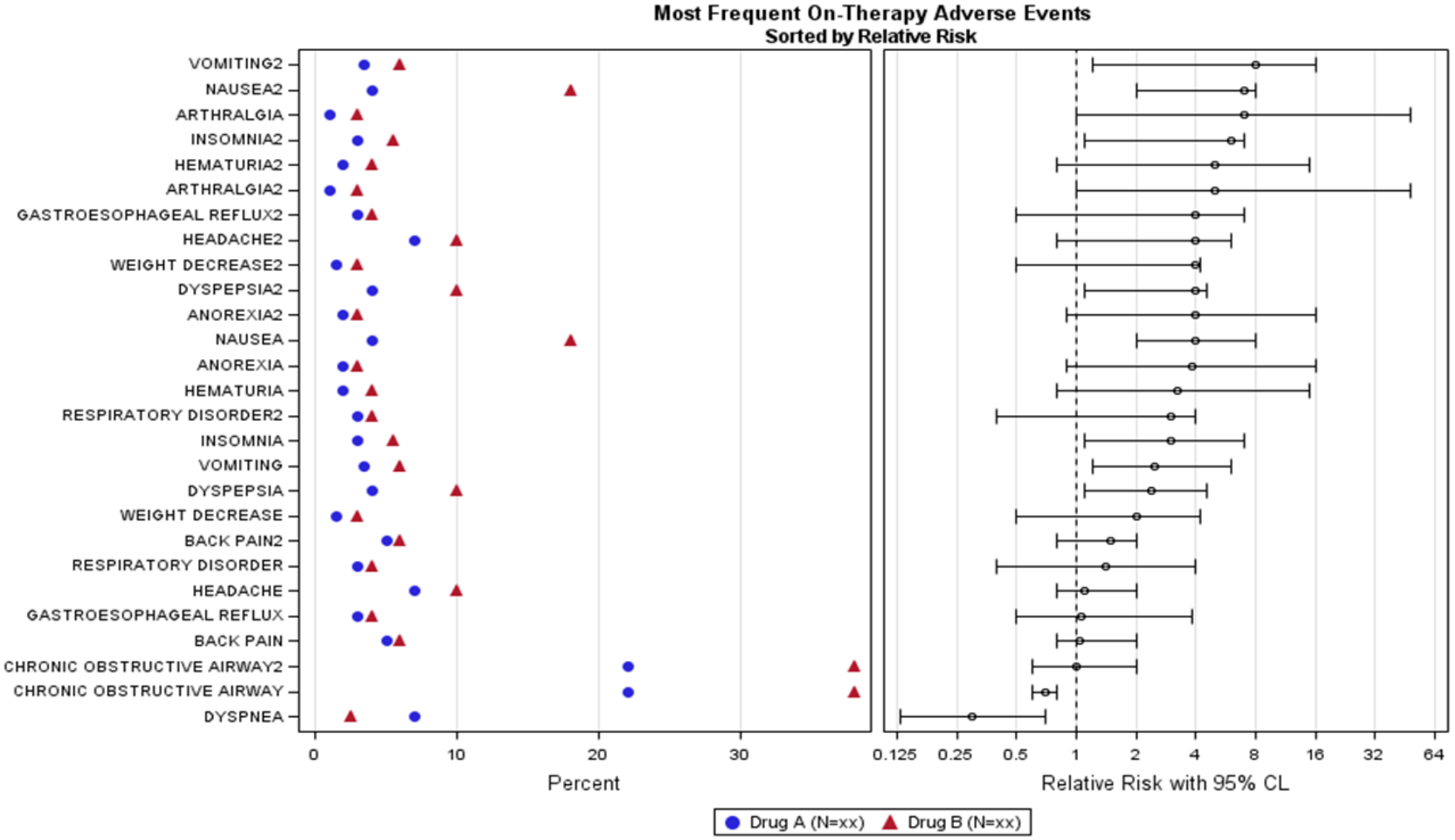
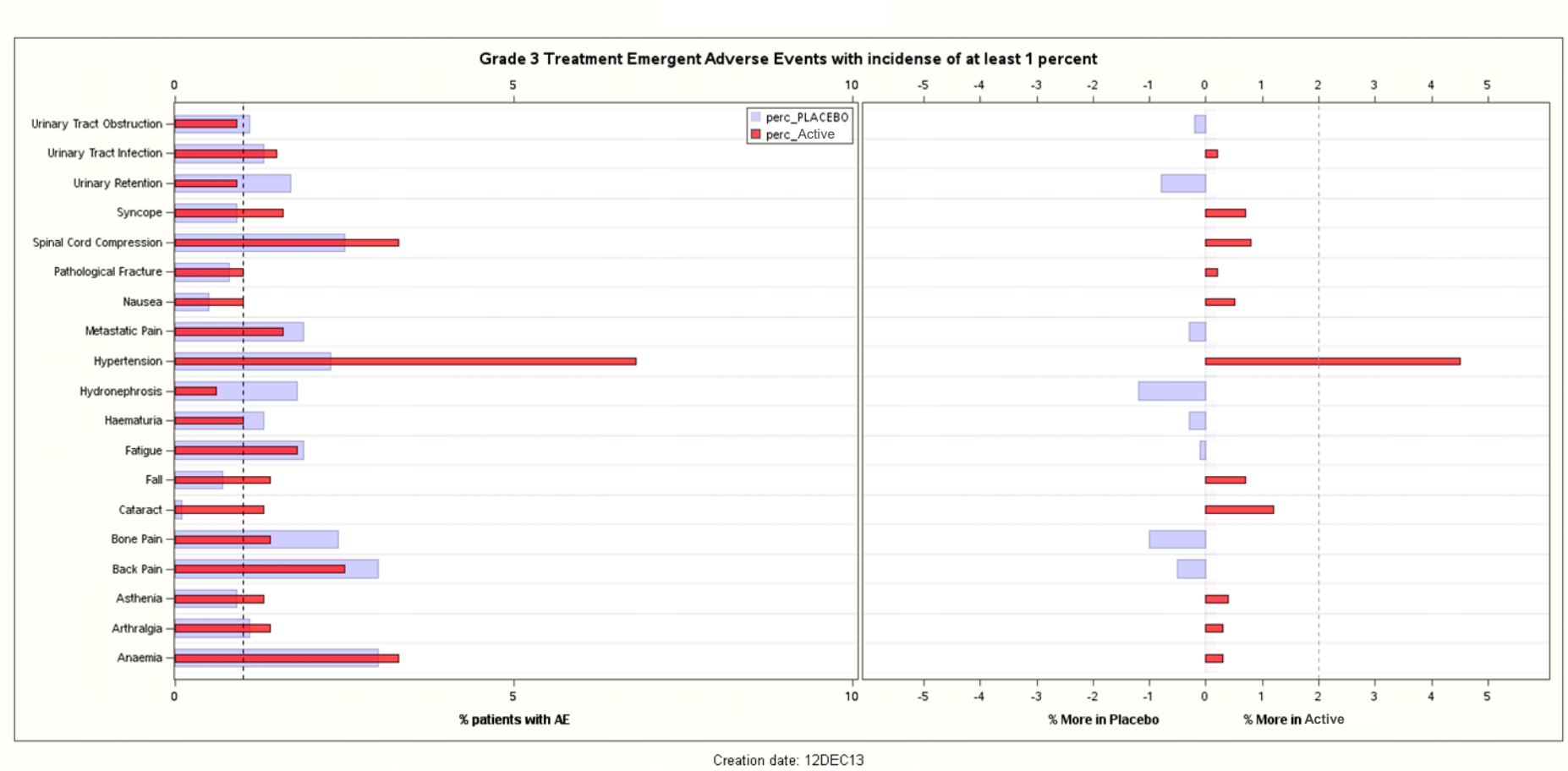
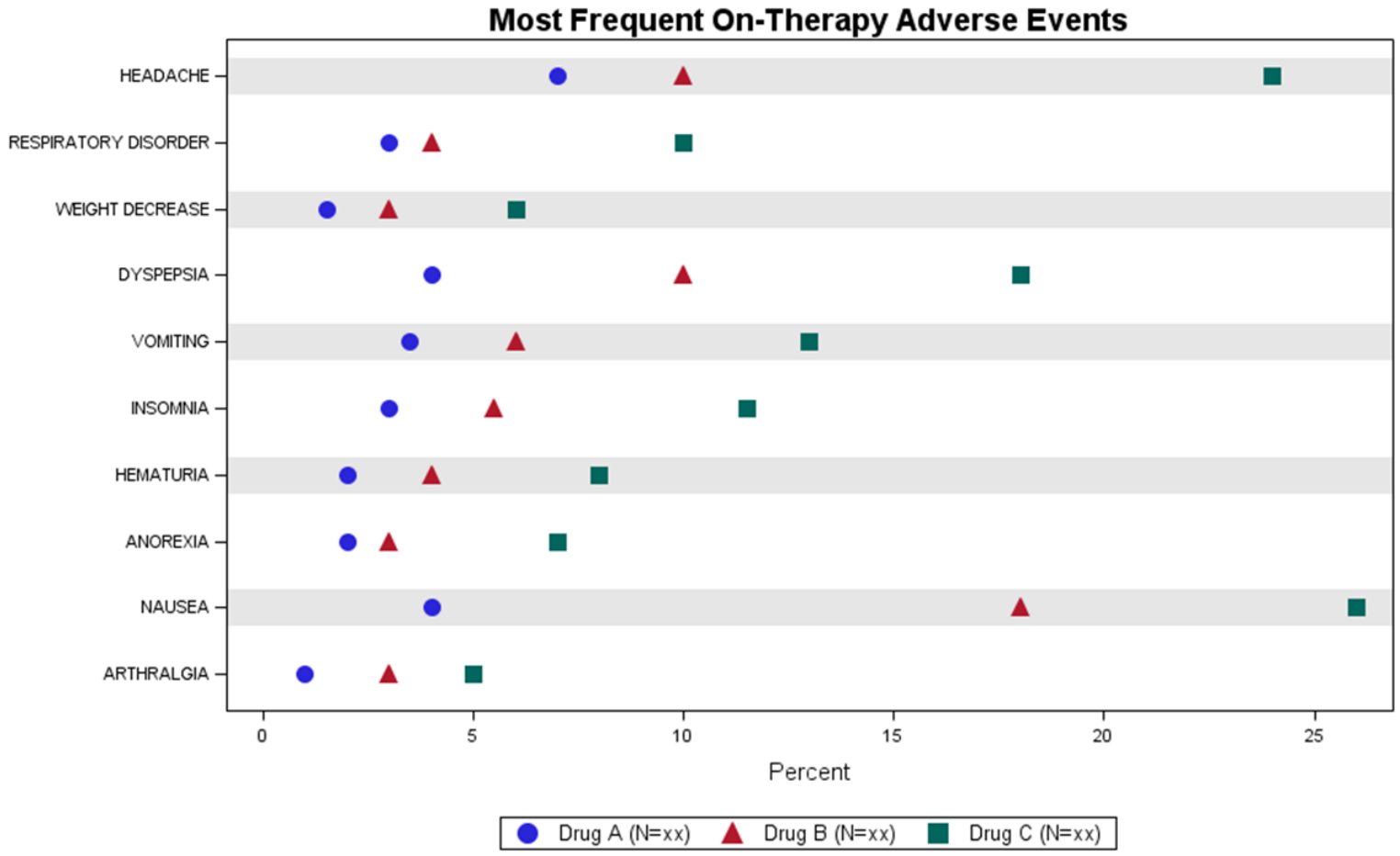
HEAD TO HEAD COMPARISON – PART 1



HEAD TO HEAD COMPARISON – PART 2



HEAD TO HEAD COMPARISON - MORE THEN TWO TREATMENTS



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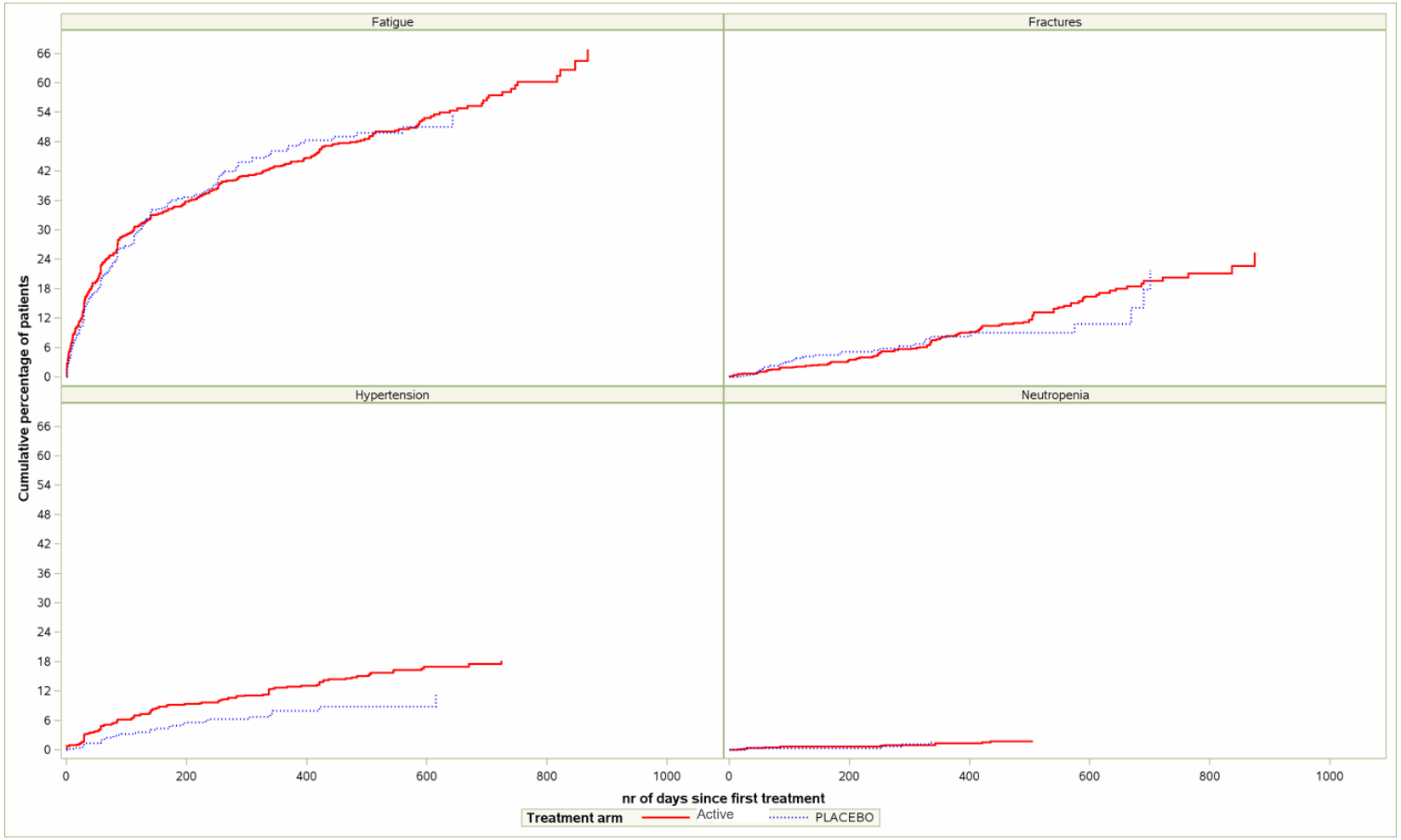
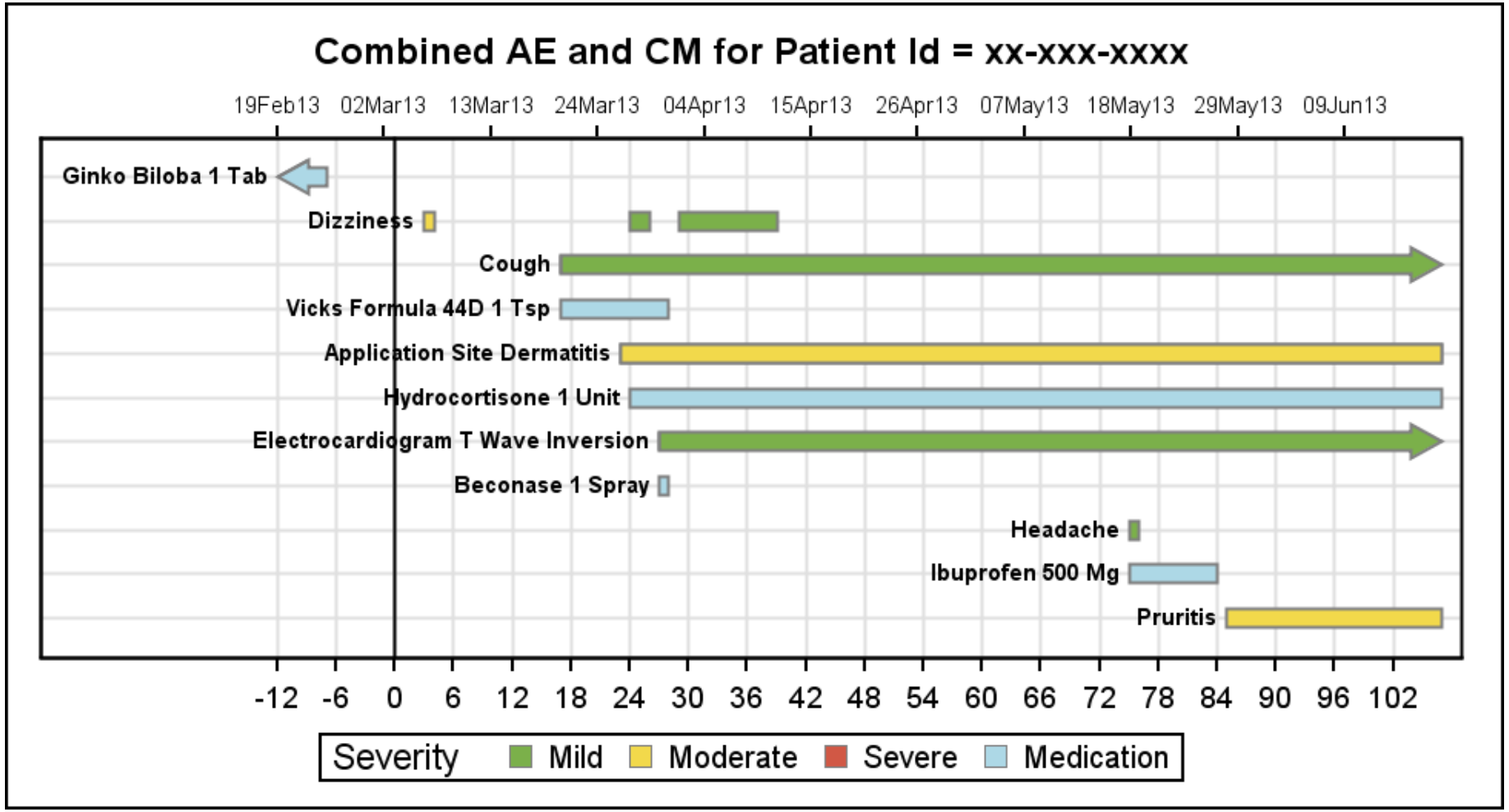
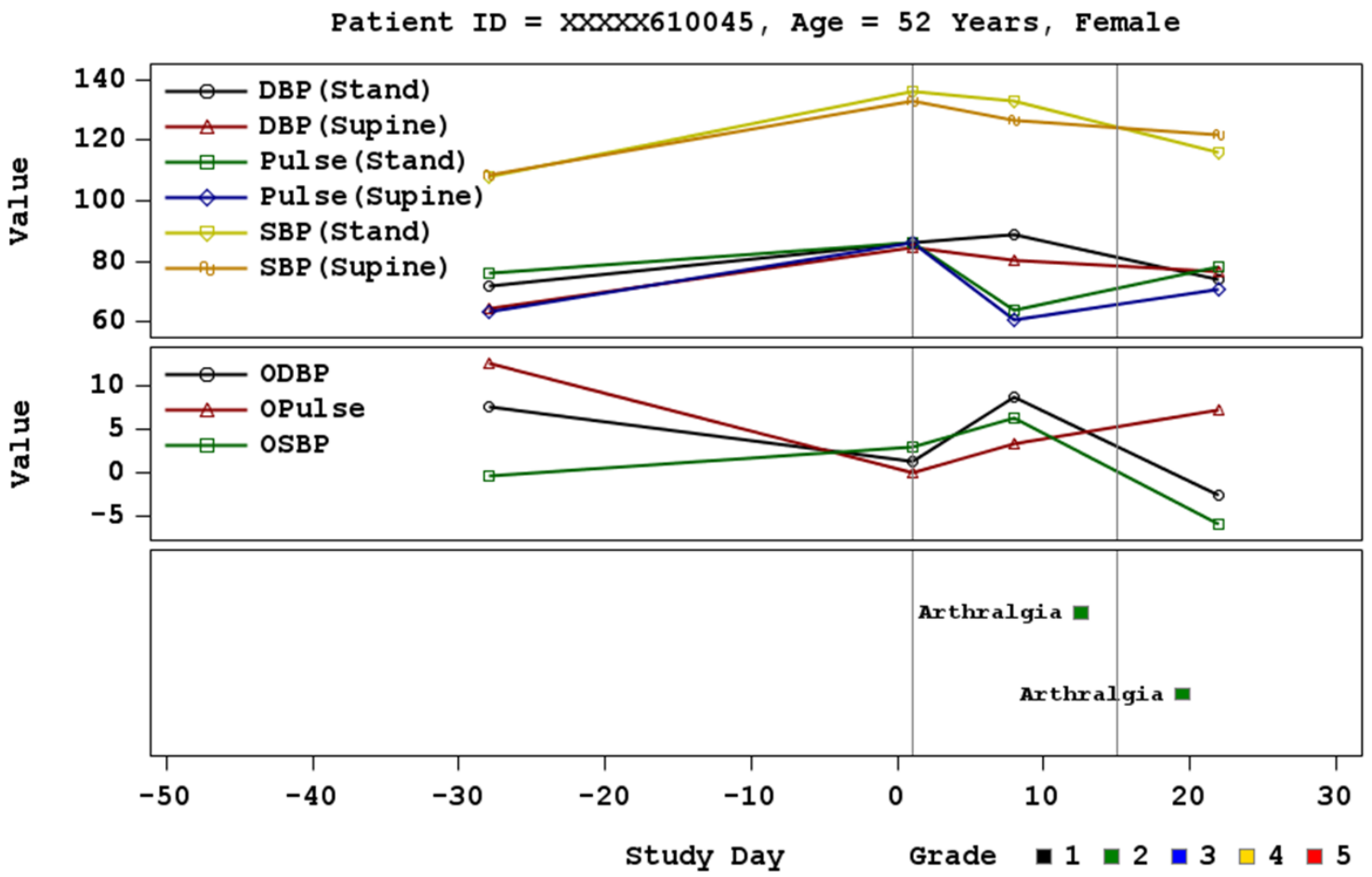
TIME TO EVENT



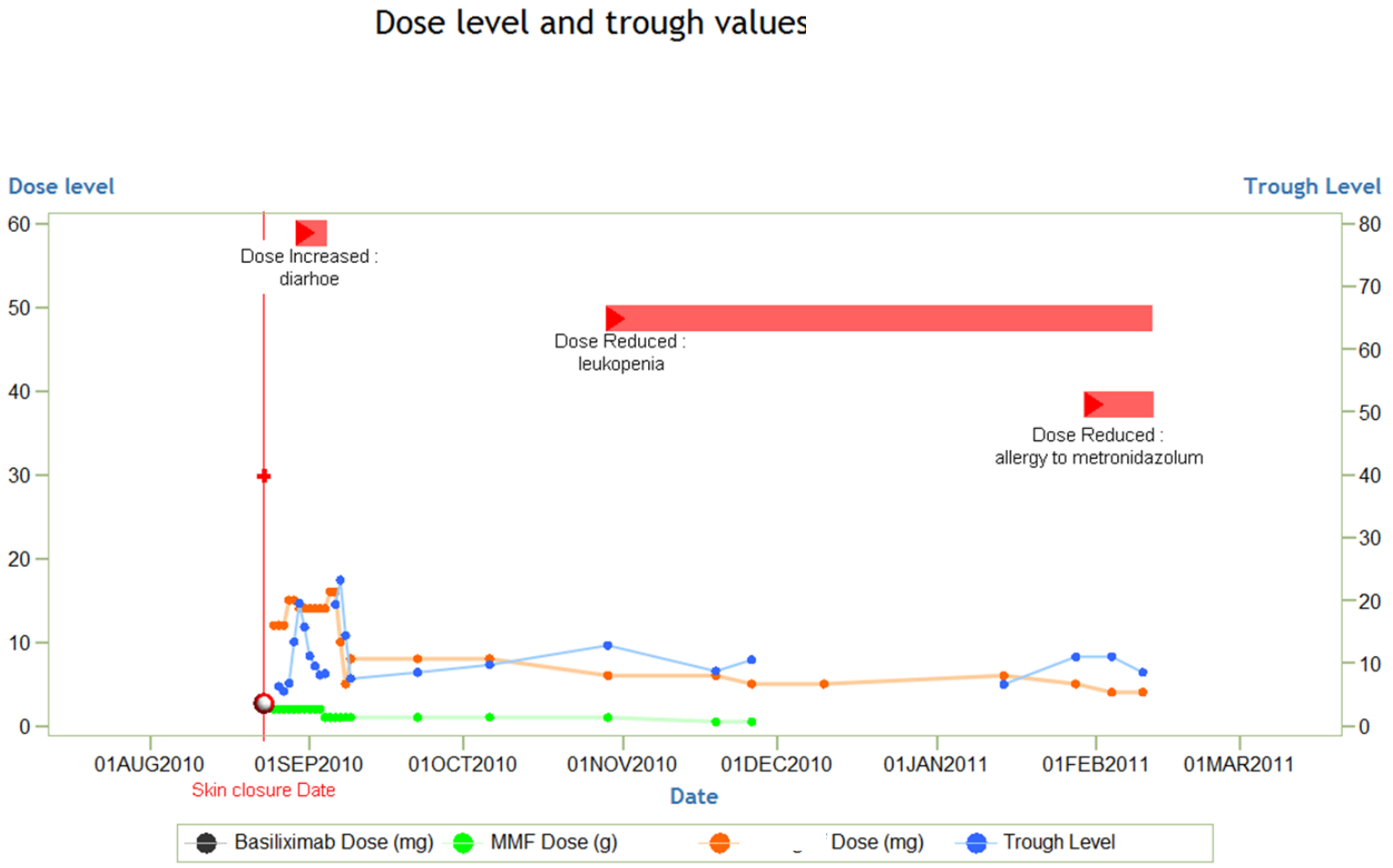
AE'S IN TIME


Combined AE and CM for Patient Id = xx-xxx-xxxx
19Feb13
02Mar13
13Mar13
24Mar13
04Apr13
15Apr13
26Apr13
07May13
18May13
29May13
09Jun13
Ginko Biloba 1 Tab
Dizziness
Cough
Vicks Formula 44D 1 Tsp
Application Site Dermatitis
Hydrocortisone 1 Unit
Electrocardiogram T Wave Inversion
Beconase 1 Spray
Headache
Ibuprofen 500 Mg
Pruritis
-12 -6 0 6 12 18 24 30 36 42 48 54 60 66 72 78 84 90 96 102
Severity
Mild
Moderate
Severe
Medication

COMBINING ADVERSE EVENTS WITH LAB DATA

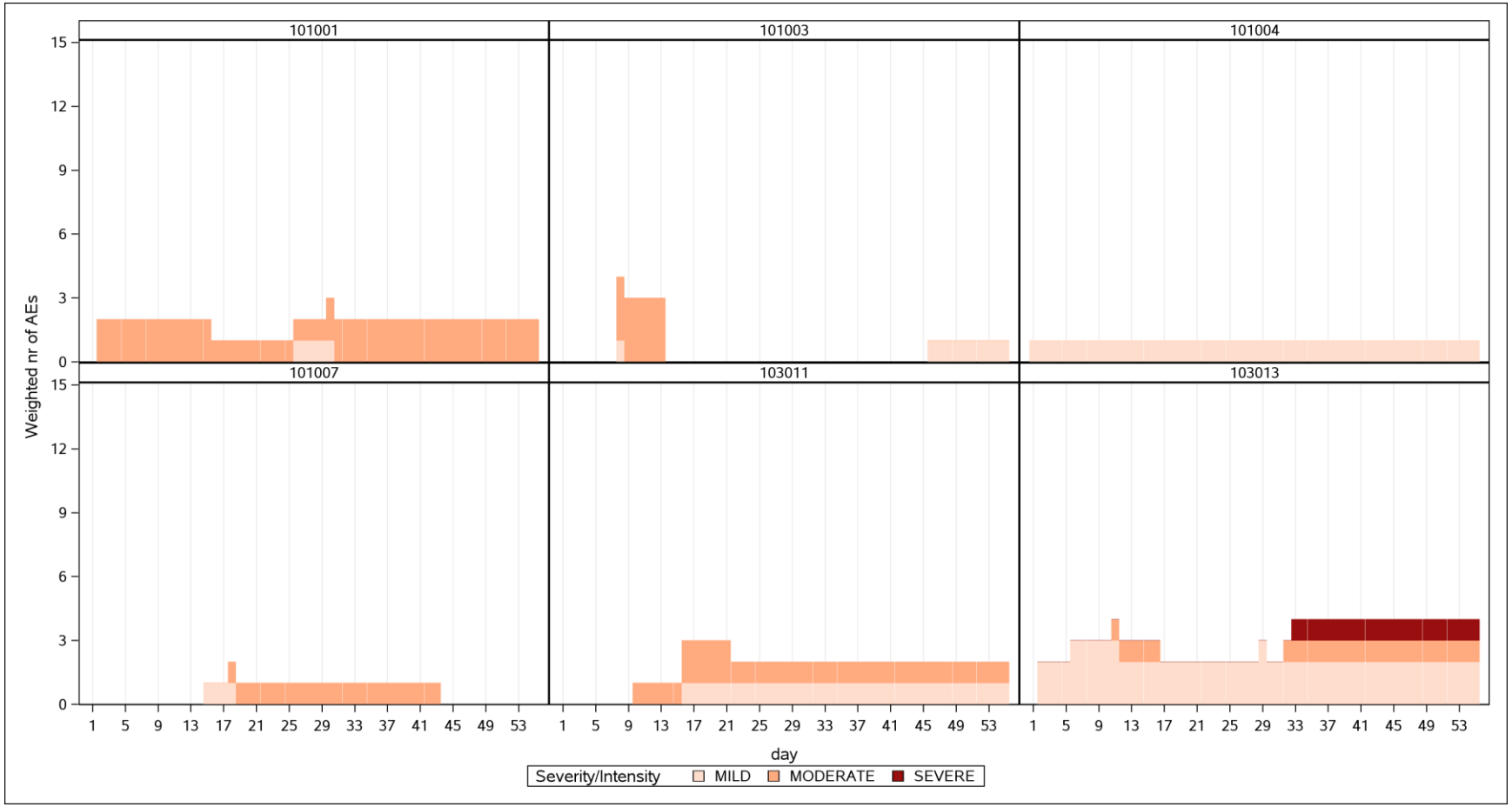


COMBINING AE'S WITH DOSE LEVELS



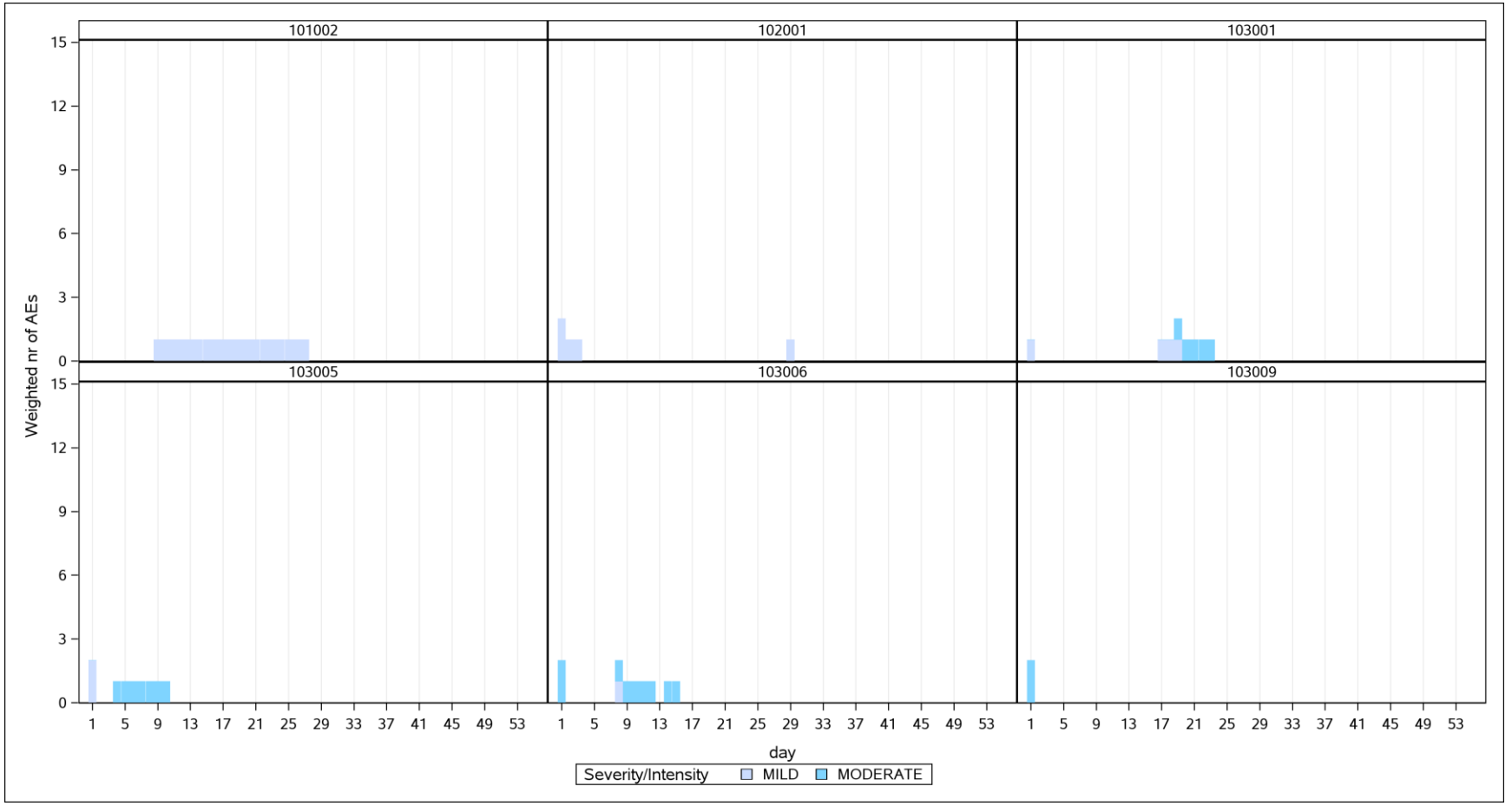
BURDEN OF THERAPY

EXAMPLE PATIENTS – TREATMENT A



On each day (day 1 to day 55) the number of AE's present in a single patient are counted, colored by severity

EXAMPLE PATIENTS – TREATMENT B



GENERAL IDEA

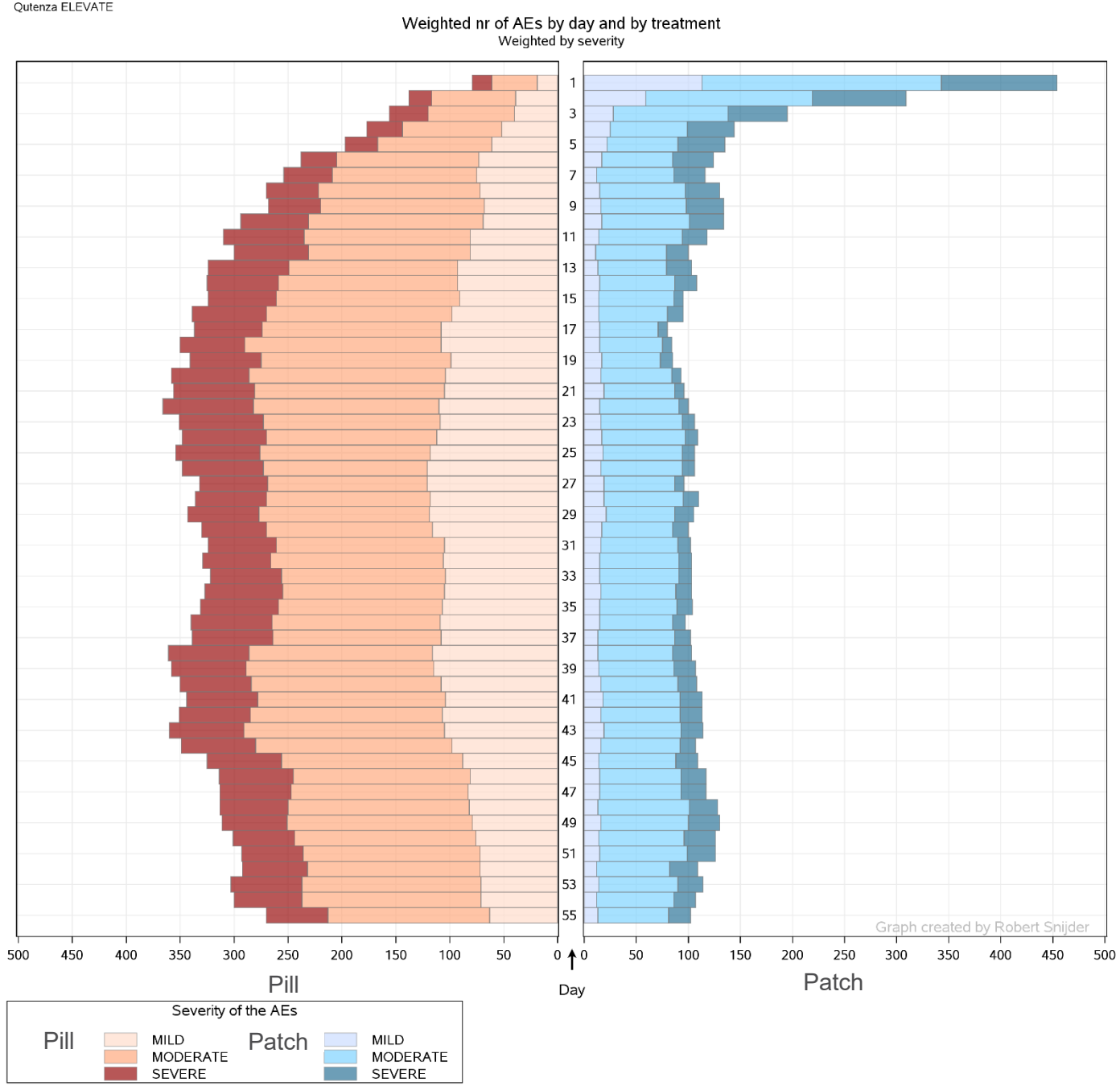
The presence of TEAEs was plotted against study day, such that if a patient reported a TEAE from Days 3 to 5, this TEAE was considered present on Days 3, 4 and 5. If that patient reported TEAEs of differing severity on a single day, the worst severity was taken into account in the analysis.

If an end date was not present in the database, or a TEAE was ongoing, the last study day of the patient was taken as the end day of the TEAE.

WEIGHTING

In order to visually represent the safety burden experienced by a patient, varied weighting was applied to TEAE severity in each arm in a consistent manner. The presented graph therefore displays the weighted TEAEs per day. For the purposes of example graphs presented in this Presentation, TEAEs that were recorded as mild, moderate, and severe were weighted to represent 1x, 2x, and 3x TEAEs per event per day, respectively.

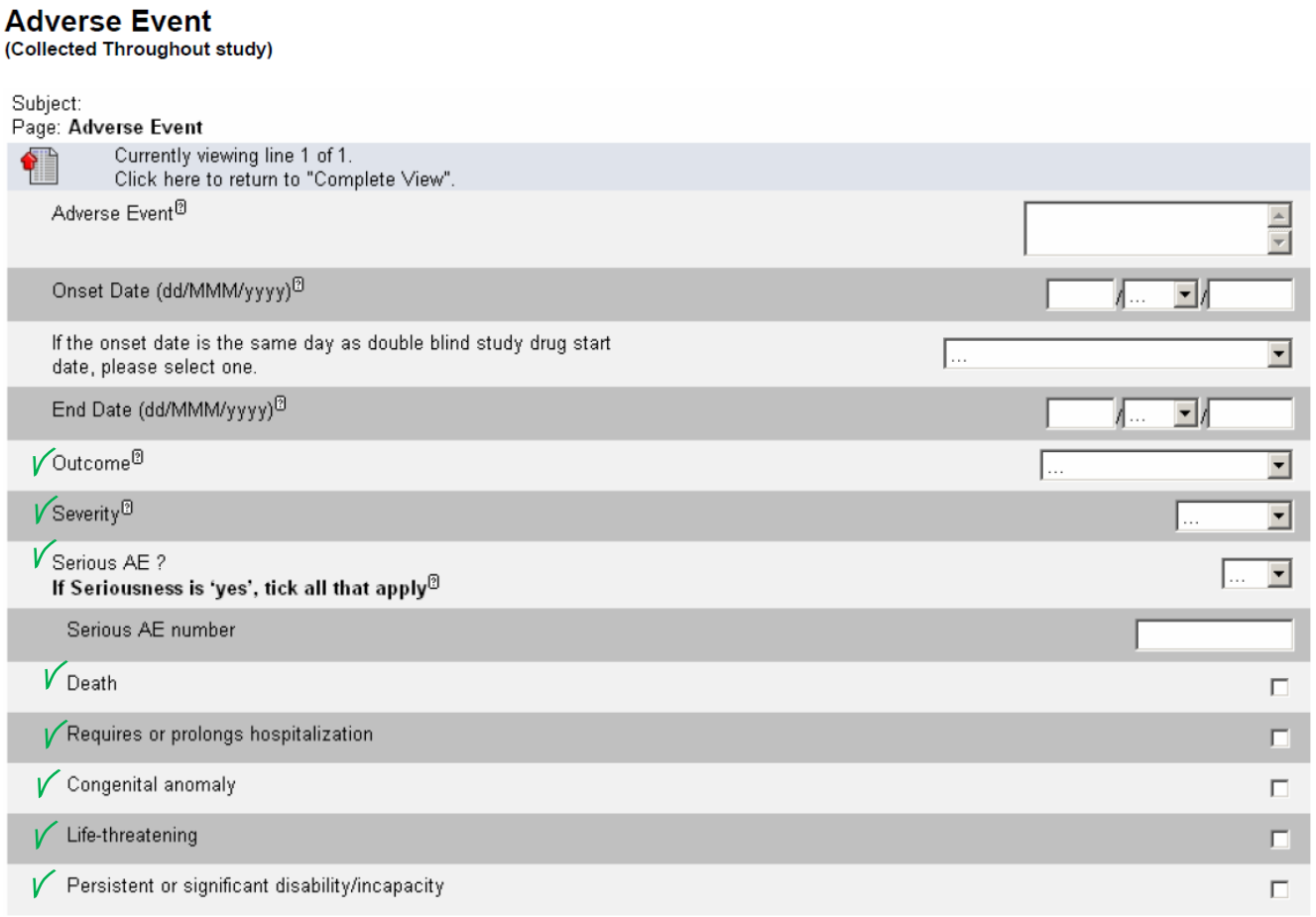
Qutenza ELEVATE



Weight: Mild=1 Moderate=2 Severe=3

Date 11 March 2014

THINGS FROM THE CRF YOU CAN USE FOR WEIGHTING



Adverse Event
(Collected Throughout study)

Subject:
Page: **Adverse Event**

Currently viewing line 1 of 1.
Click here to return to "Complete View".

Adverse Event

Onset Date (dd/MMM/yyyy)

If the onset date is the same day as double blind study drug start date, please select one.

End Date (dd/MMM/yyyy)

Outcome

Severity

Serious AE ?
If Seriousness is 'yes', tick all that apply

Serious AE number

Death

Requires or prolongs hospitalization

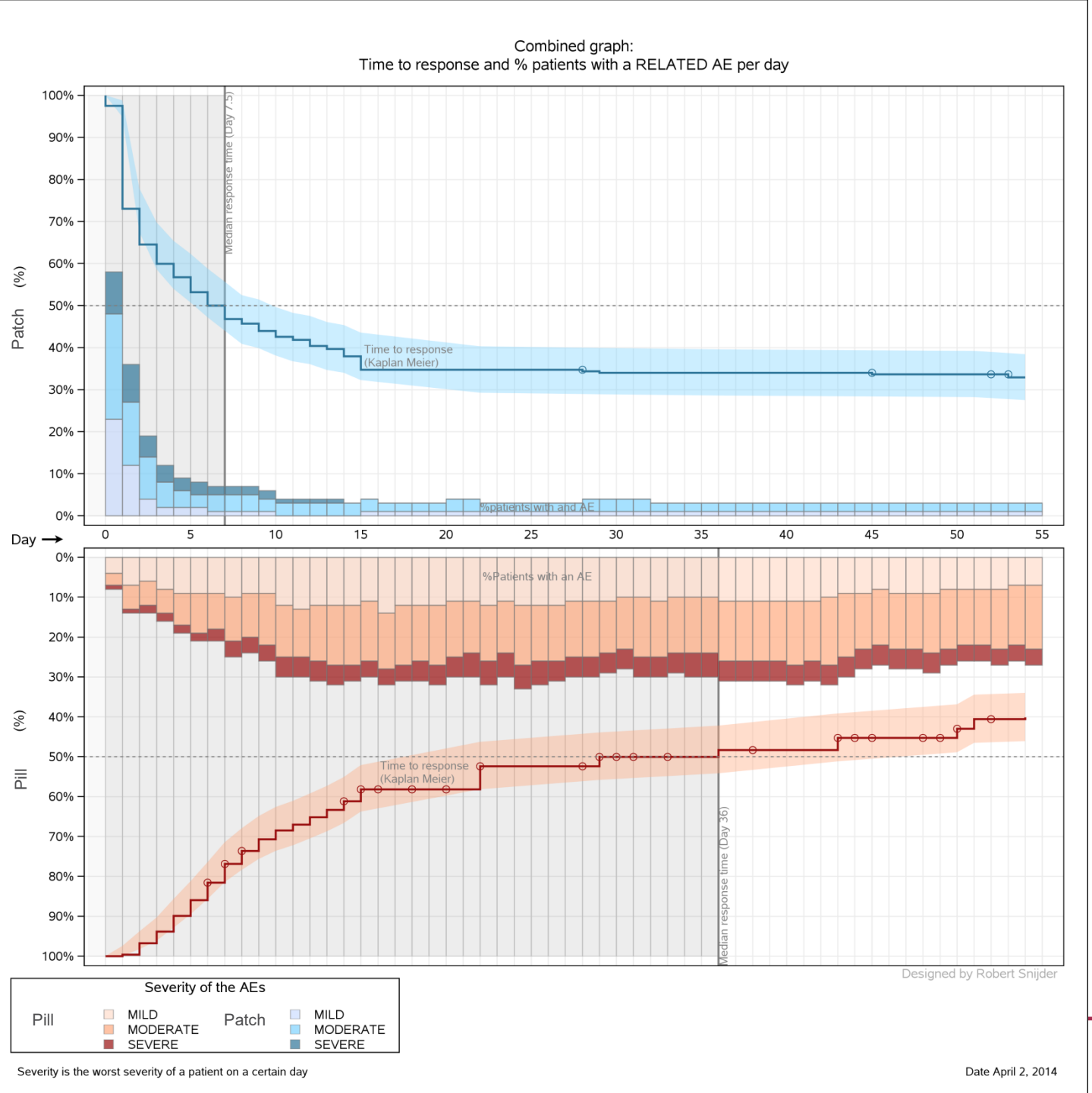
Congenital anomaly

Life-threatening

Persistent or significant disability/incapacity

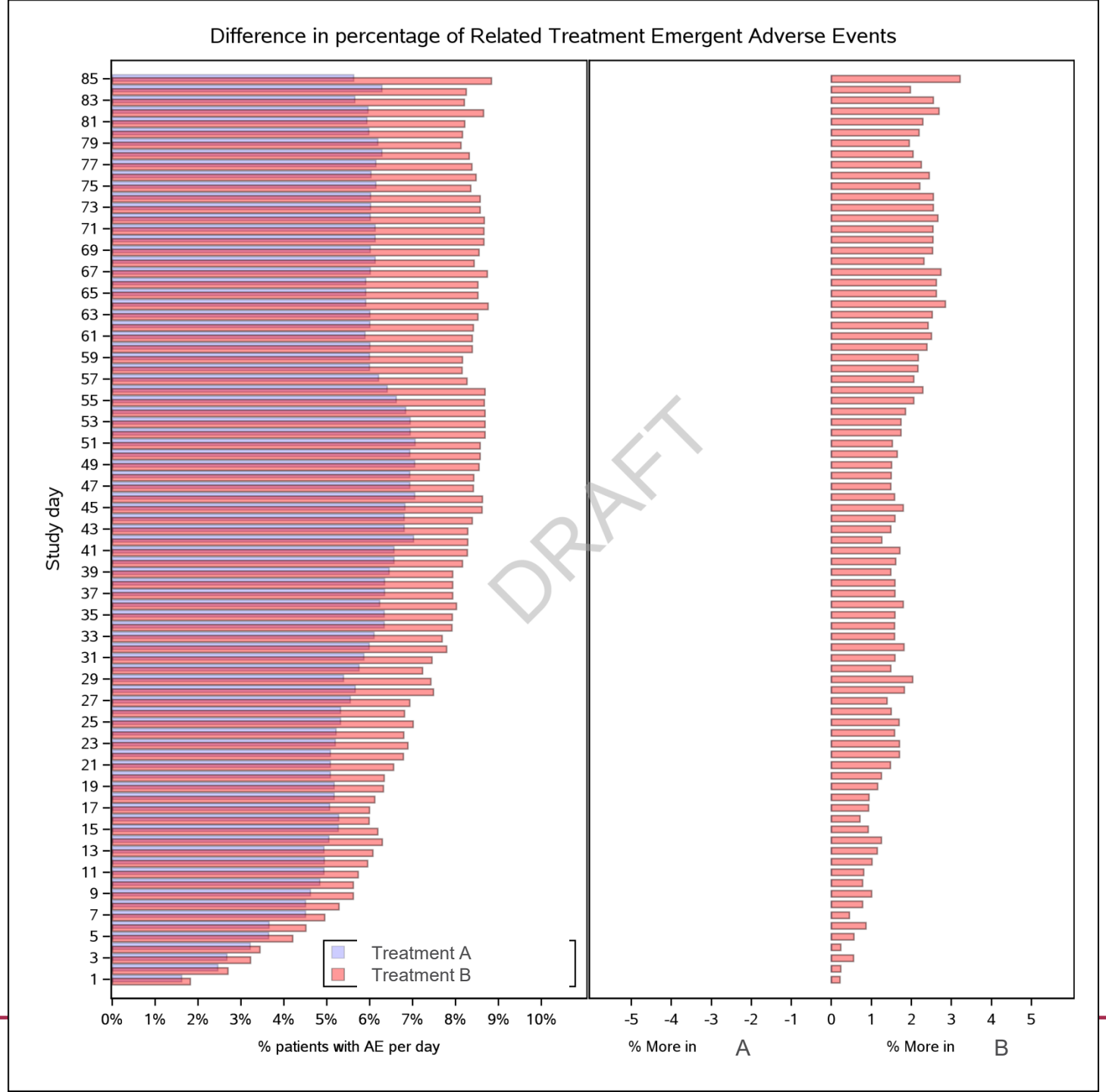
Other weighting tools might include Utility functions estimated with discrete choice experiments

COMBINED WITH EFFICACY



Severity is the worst severity of a patient on a certain day

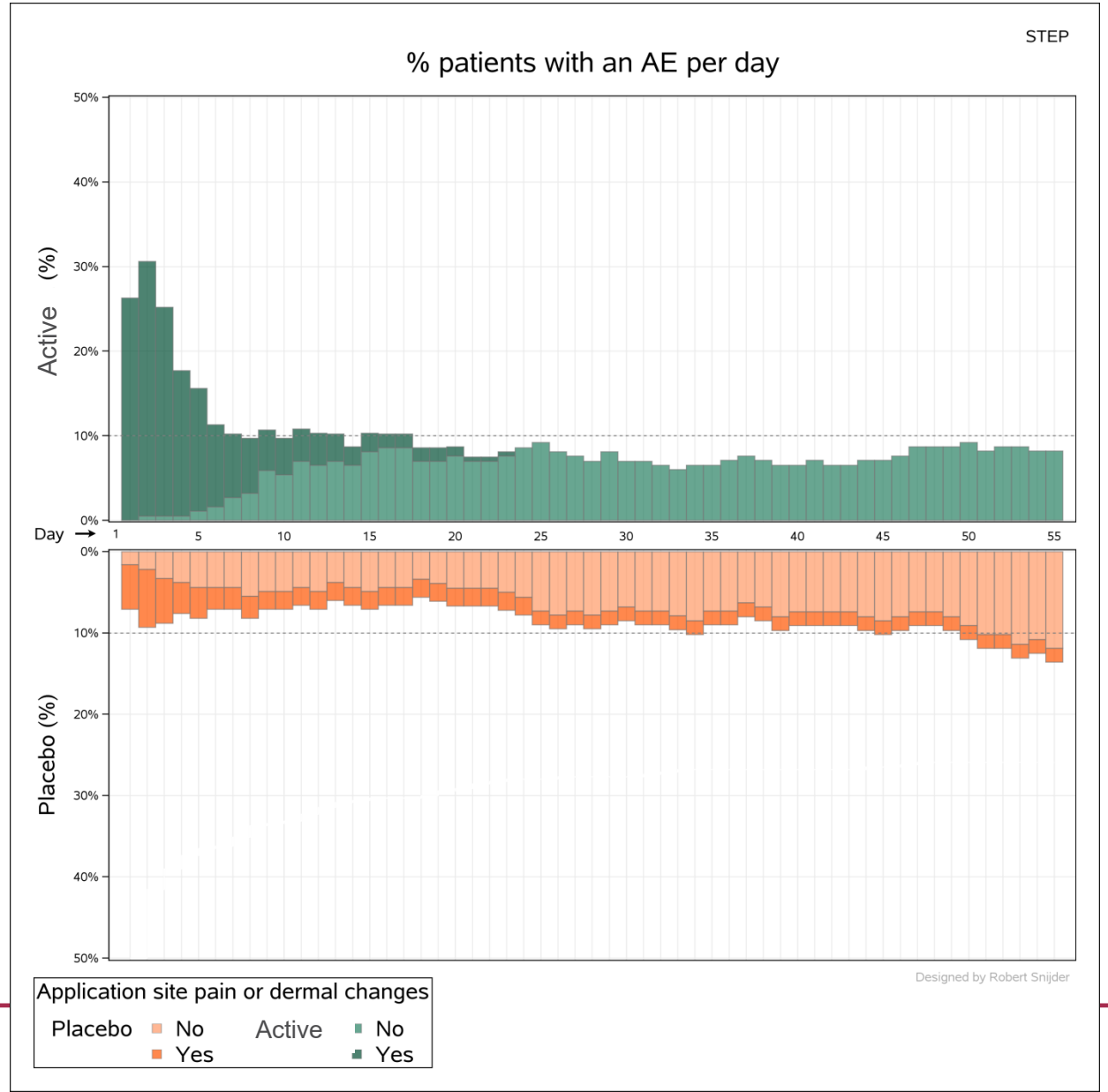
Date April 2, 2014


Difference in percentage of Related Treatment Emergent Adverse Events
Study day
85
83
81
79
77
75
73
71
69
67
65
63
61
59
57
55
53
51
49
47
45
43
41
39
37
35
33
31
29
27
25
23
21
19
17
15
13
11
9
7
5
3
1
Treatment A
Treatment B
0% 1% 2% 3% 4% 5% 6% 7% 8% 9% 10%
% patients with AE per day
-5 -4 -3 -2 -1 0 1 2 3 4 5
% More in A
% More in B
DRAFT

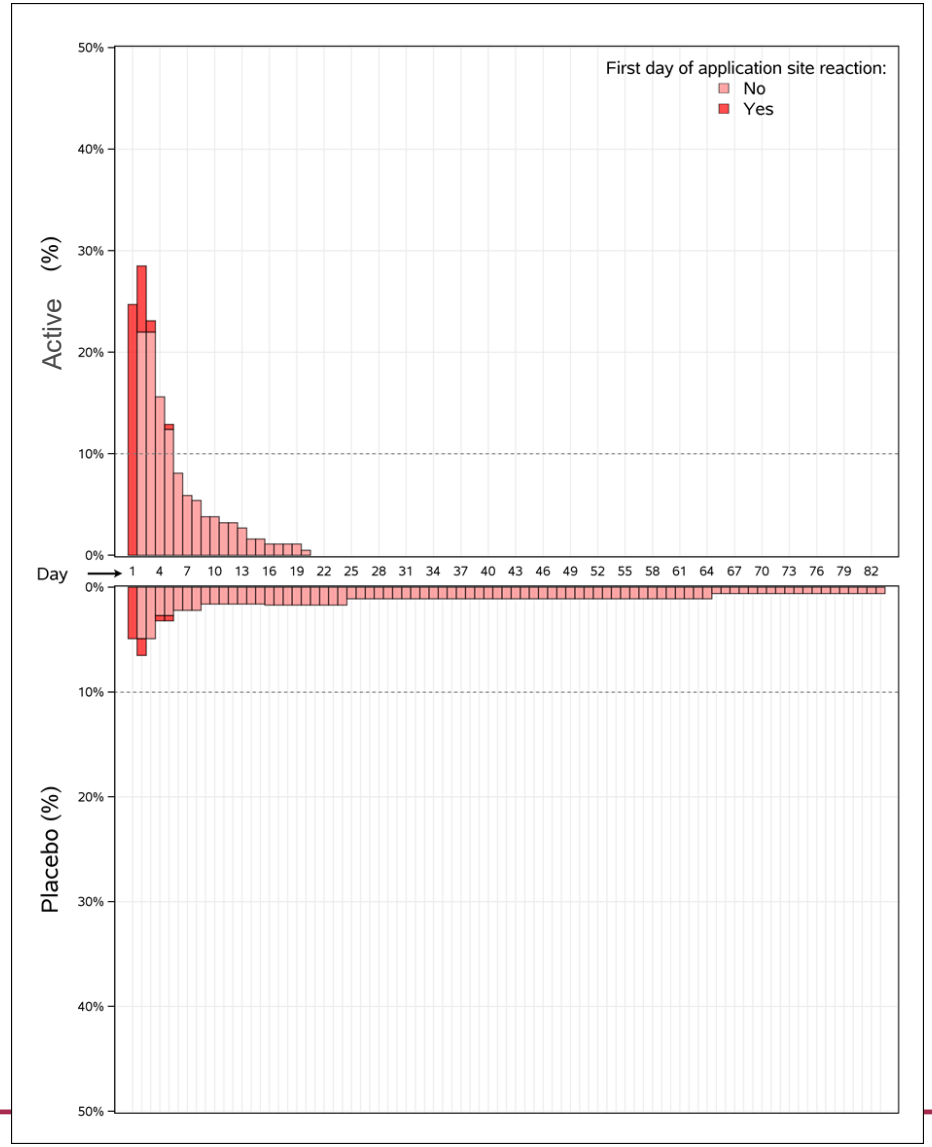
AUC

By summing up the burden of each day for each patient, with or without the weighting of events, one can derive an Area Under Curve (AUC) per patient. This will give a burden estimate for each patient (Supplementary Appendix).

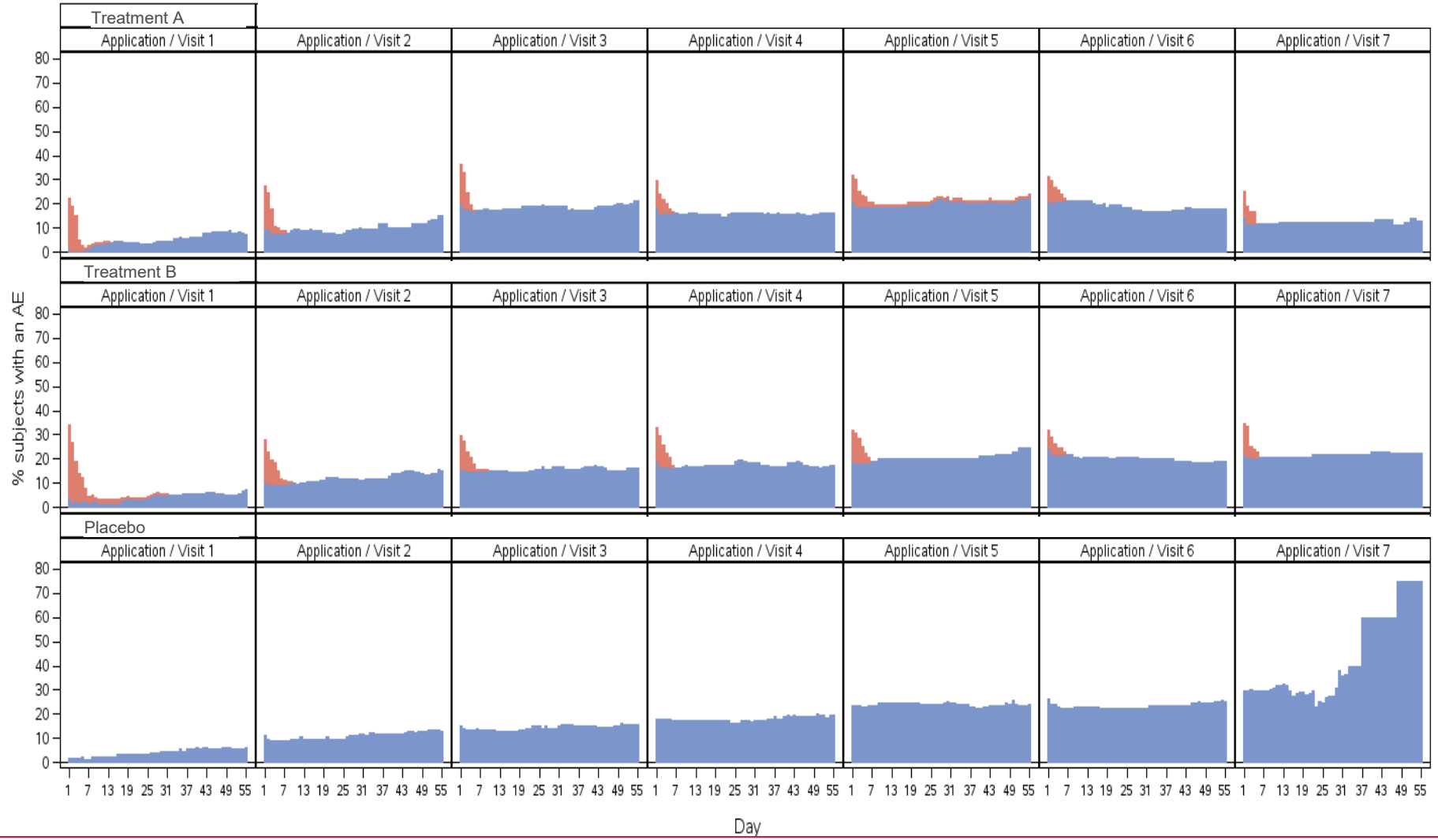
ADVERSE EVENTS



DIFFERENT COLORING



Percentage of Patients with an Adverse Event per Day, multiple periods



Application site reaction Yes No

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BURDON OF THERAPY PUBLICATION

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A novel standard to evaluate the impact of therapeutic agents on patient safety – The BURDEN OF THERAPY™©*

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