

Using Graphs to Discover and Explore

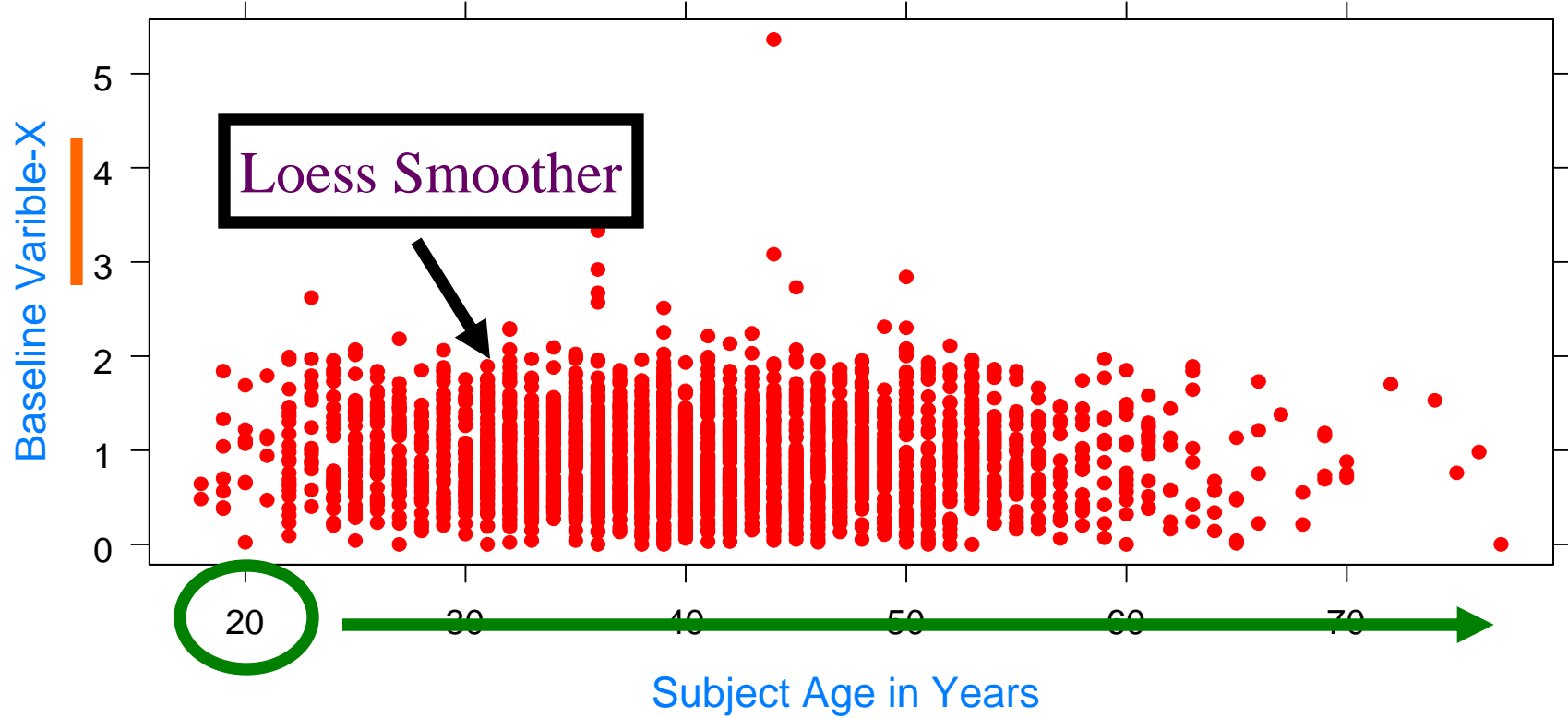
Julia Wang, Ph.D

Aug. 1, 2007

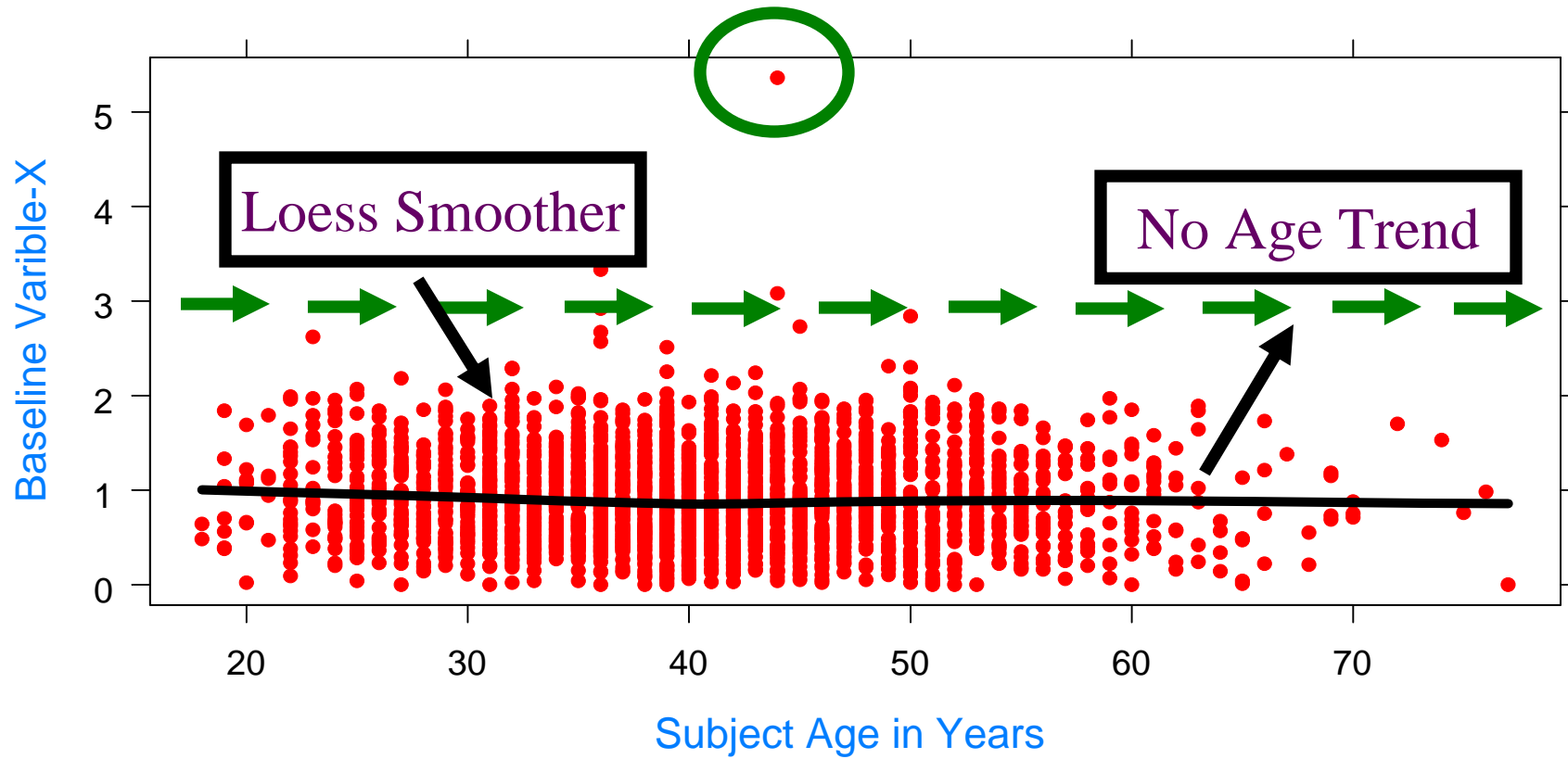
Major Theme

- Whenever possible, all data analysis should start with the **graphing of subject-level data.**

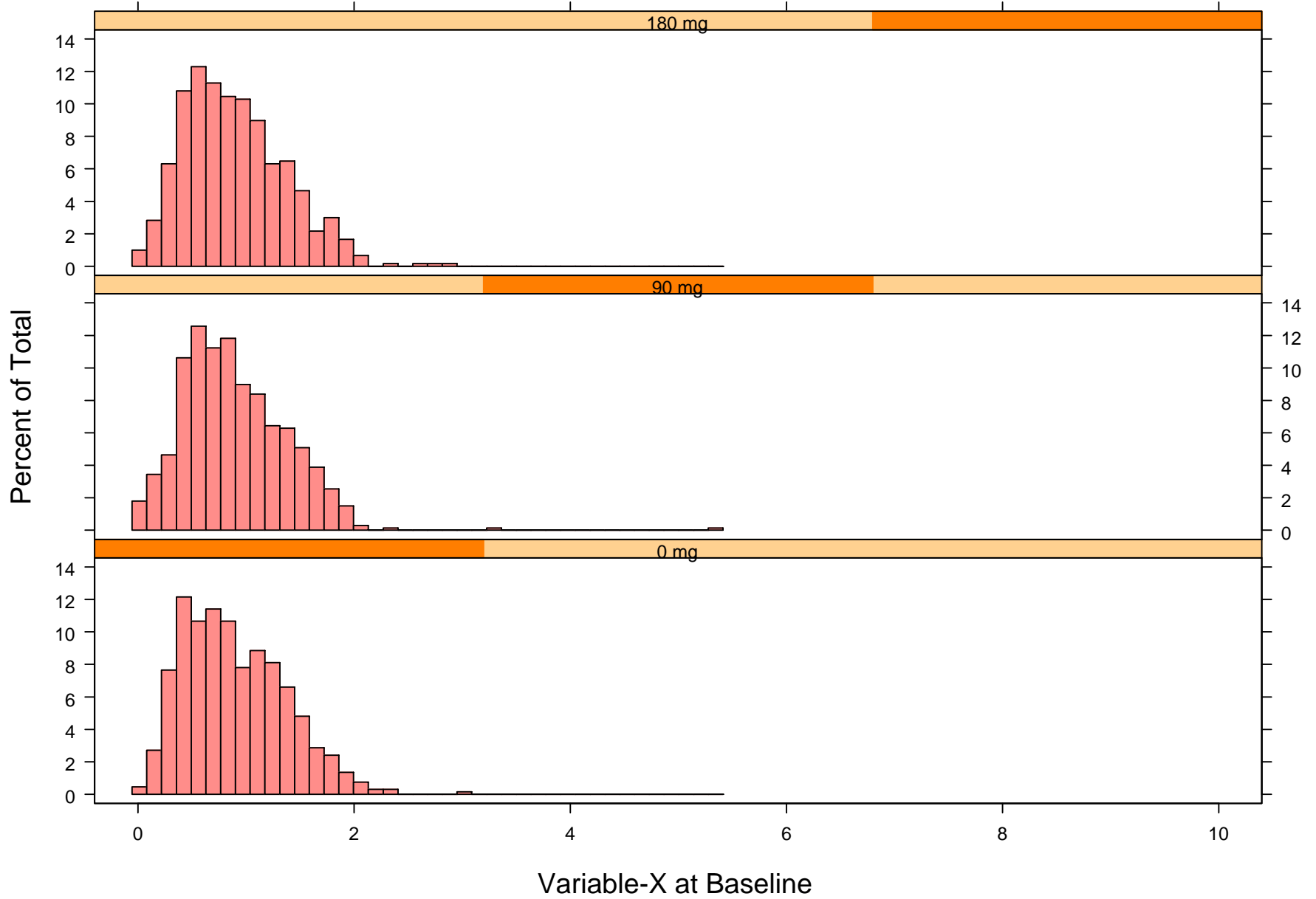
Variable-X at Baseline vs. Age



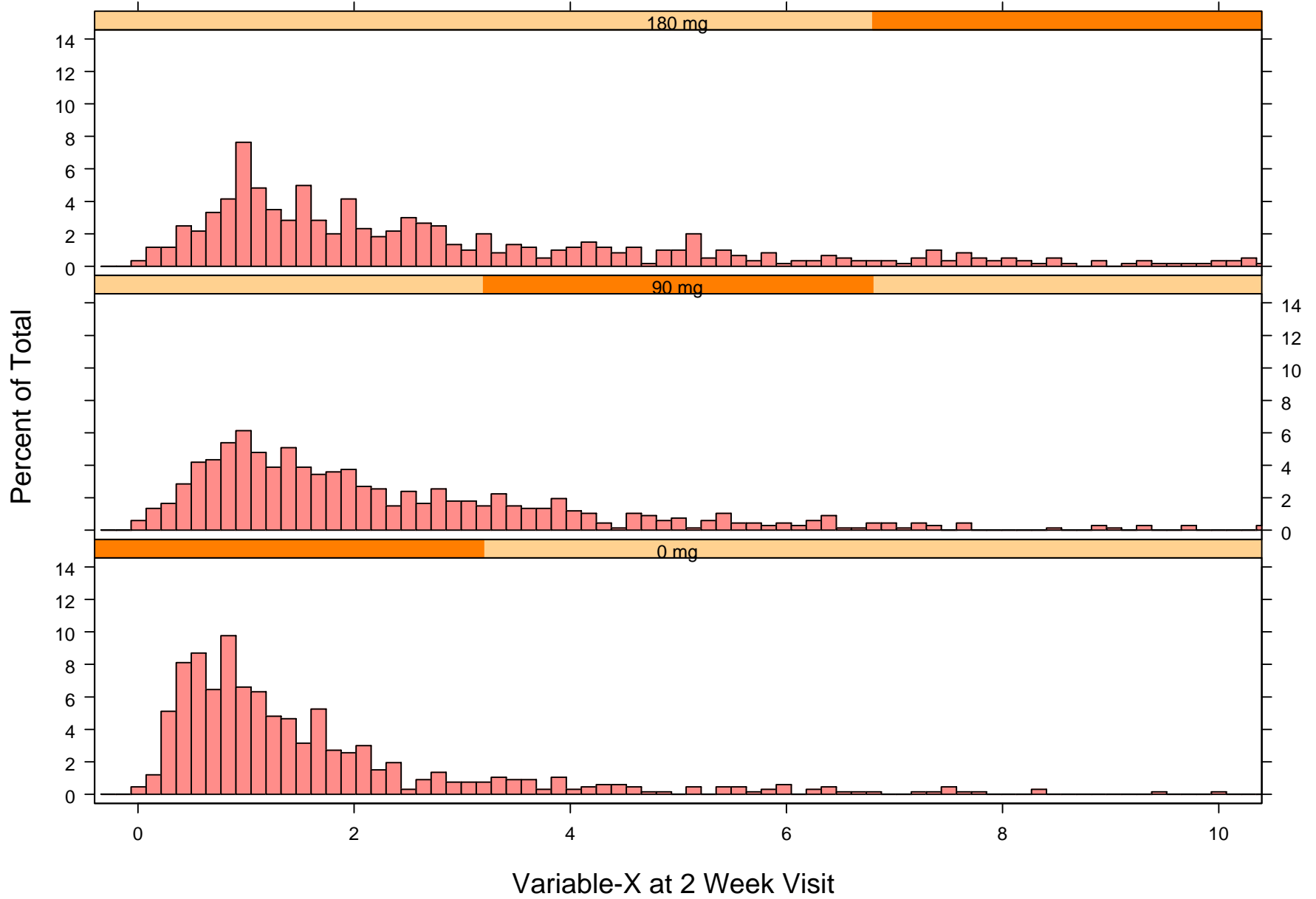
Variable-X at Baseline vs. Age



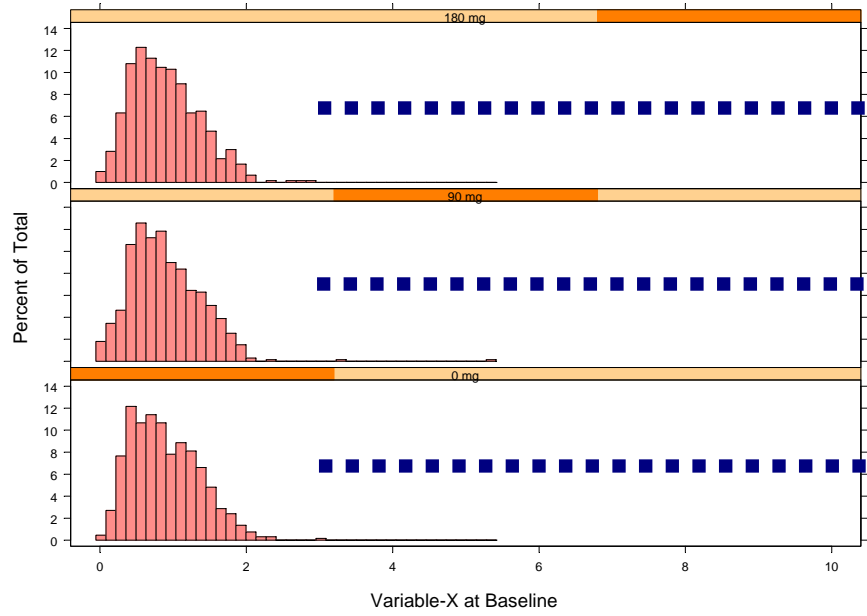
Histogram of Variable-X at Baseline



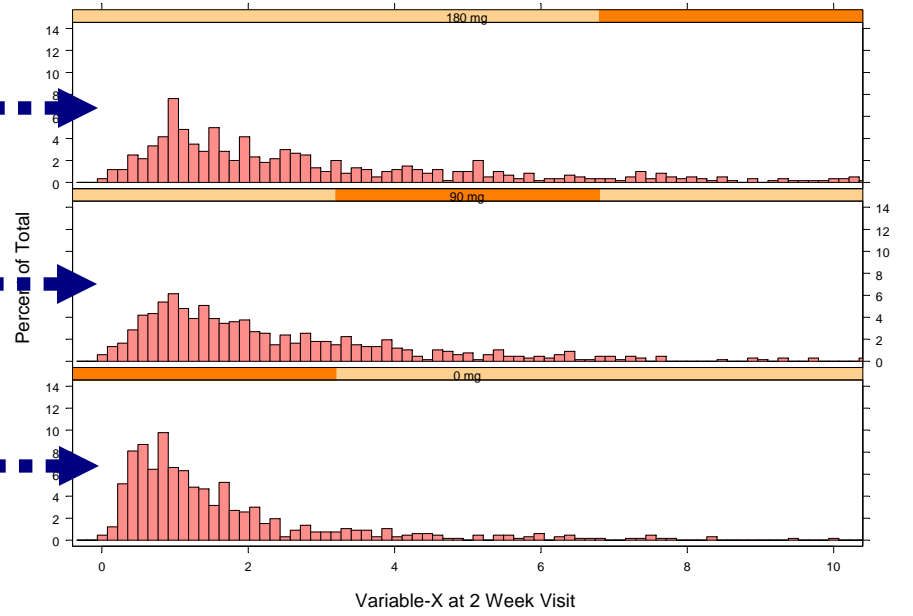
Histogram of Variable-X at 2 Week Visit



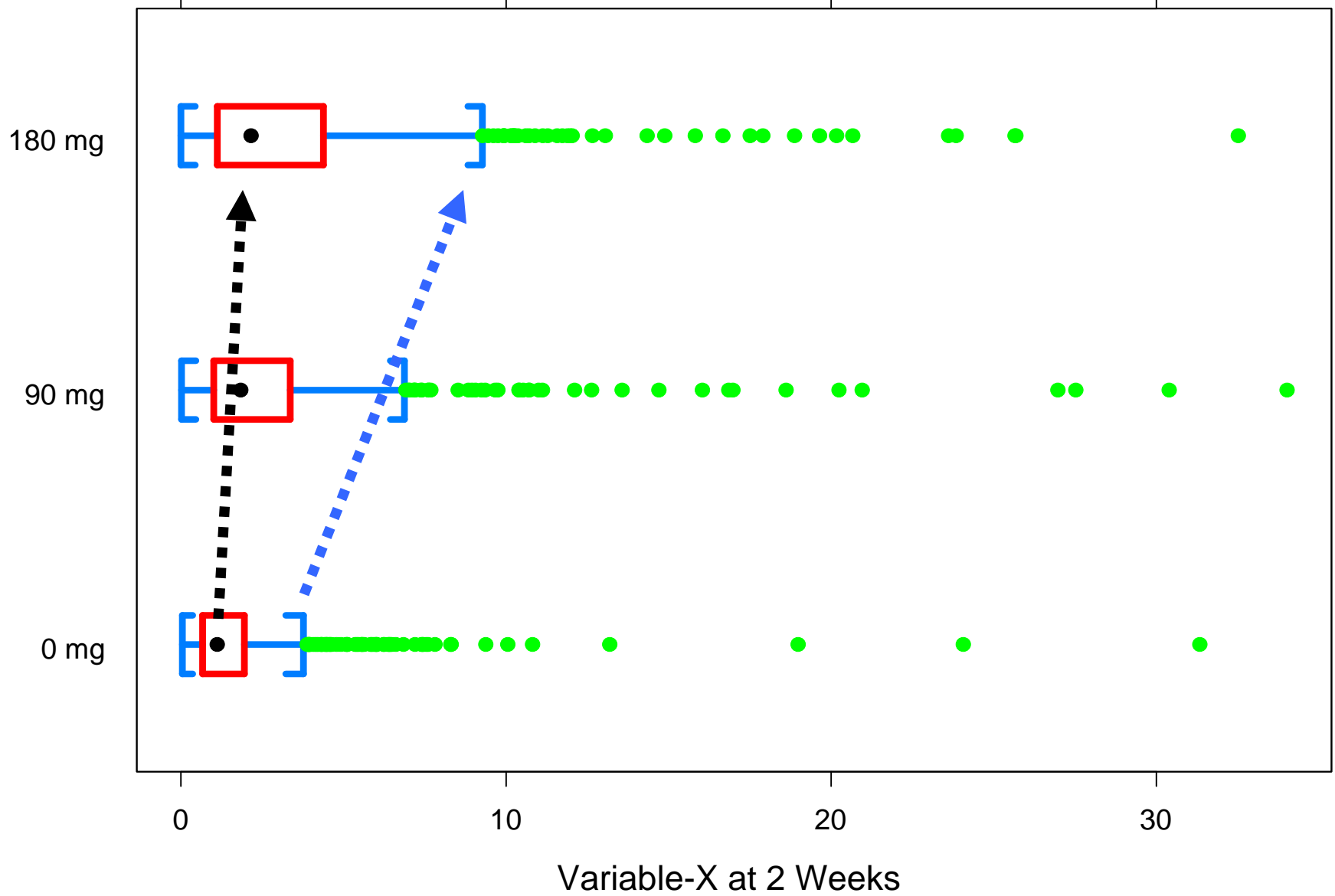
Histogram of Variable-X at Baseline



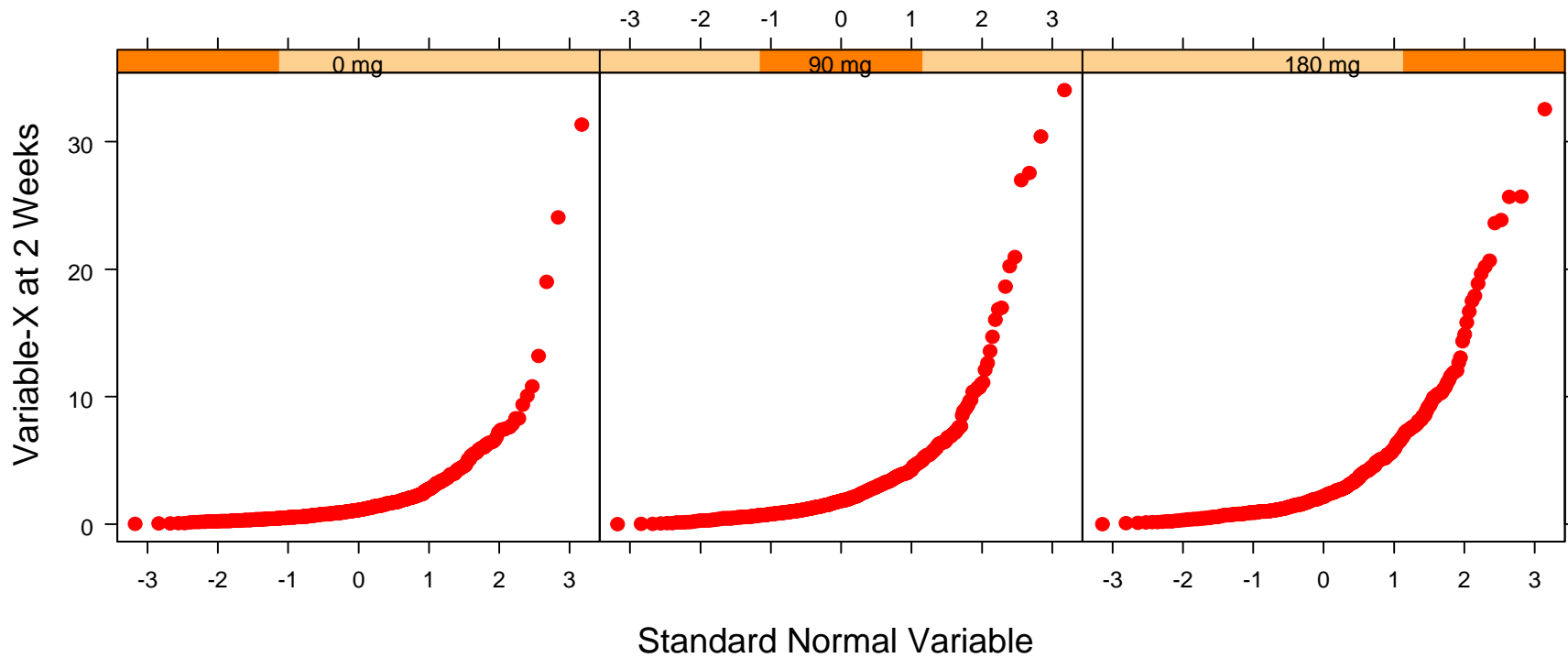
Histogram of Variable-X at 2 Week Visit



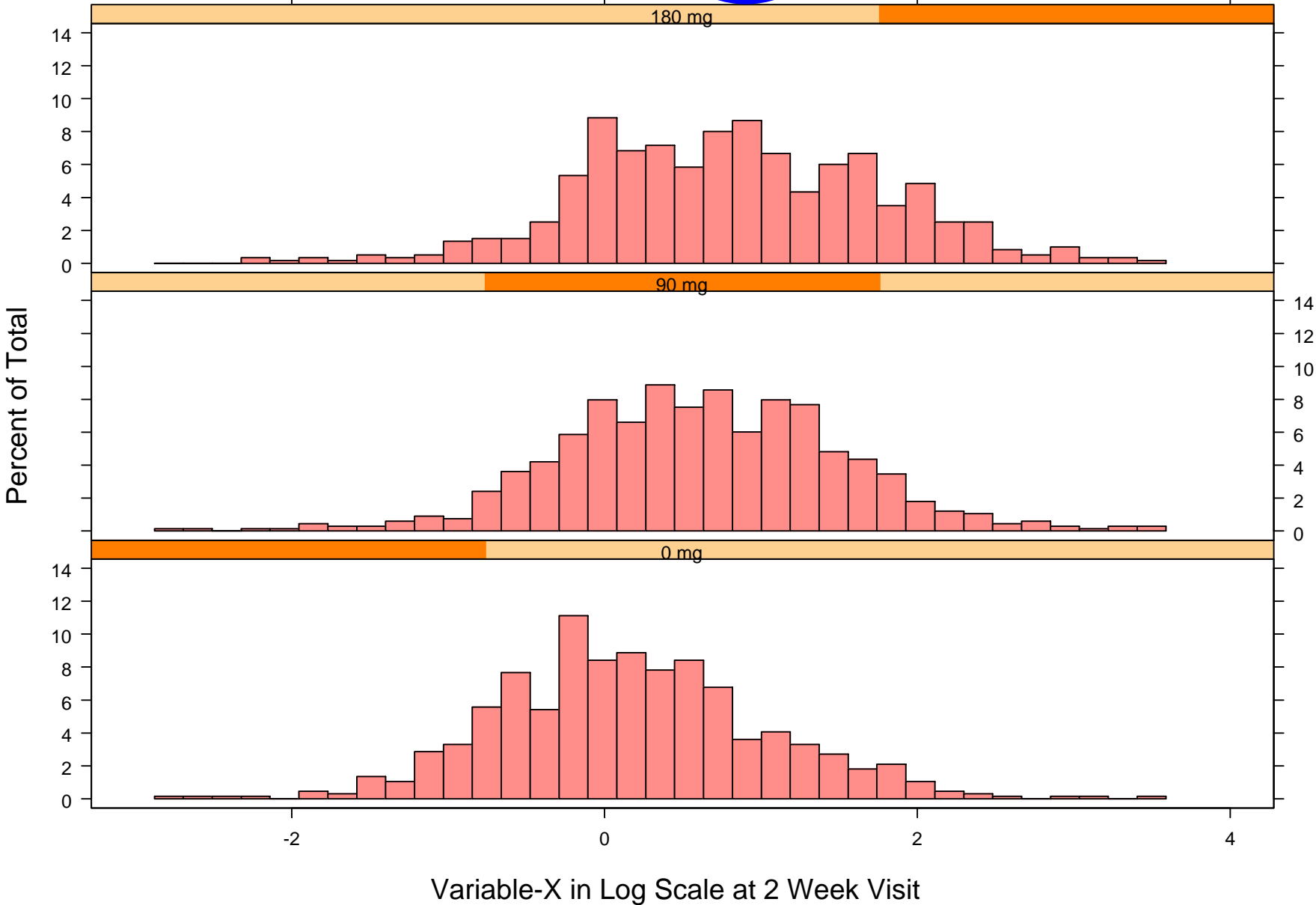
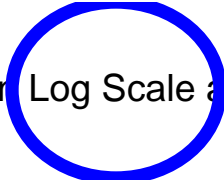
Box-Whisker Plot for Distribution Comparison



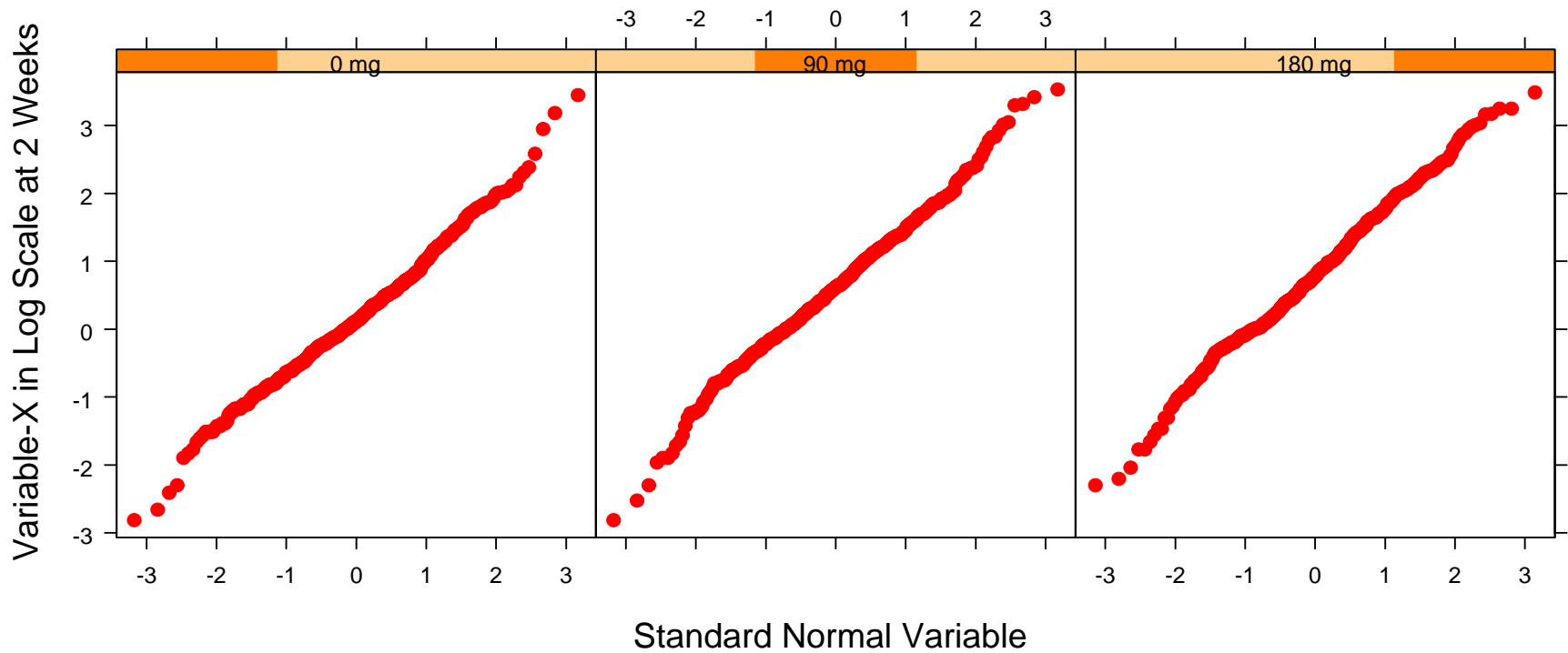
QQnorm to Check Normality



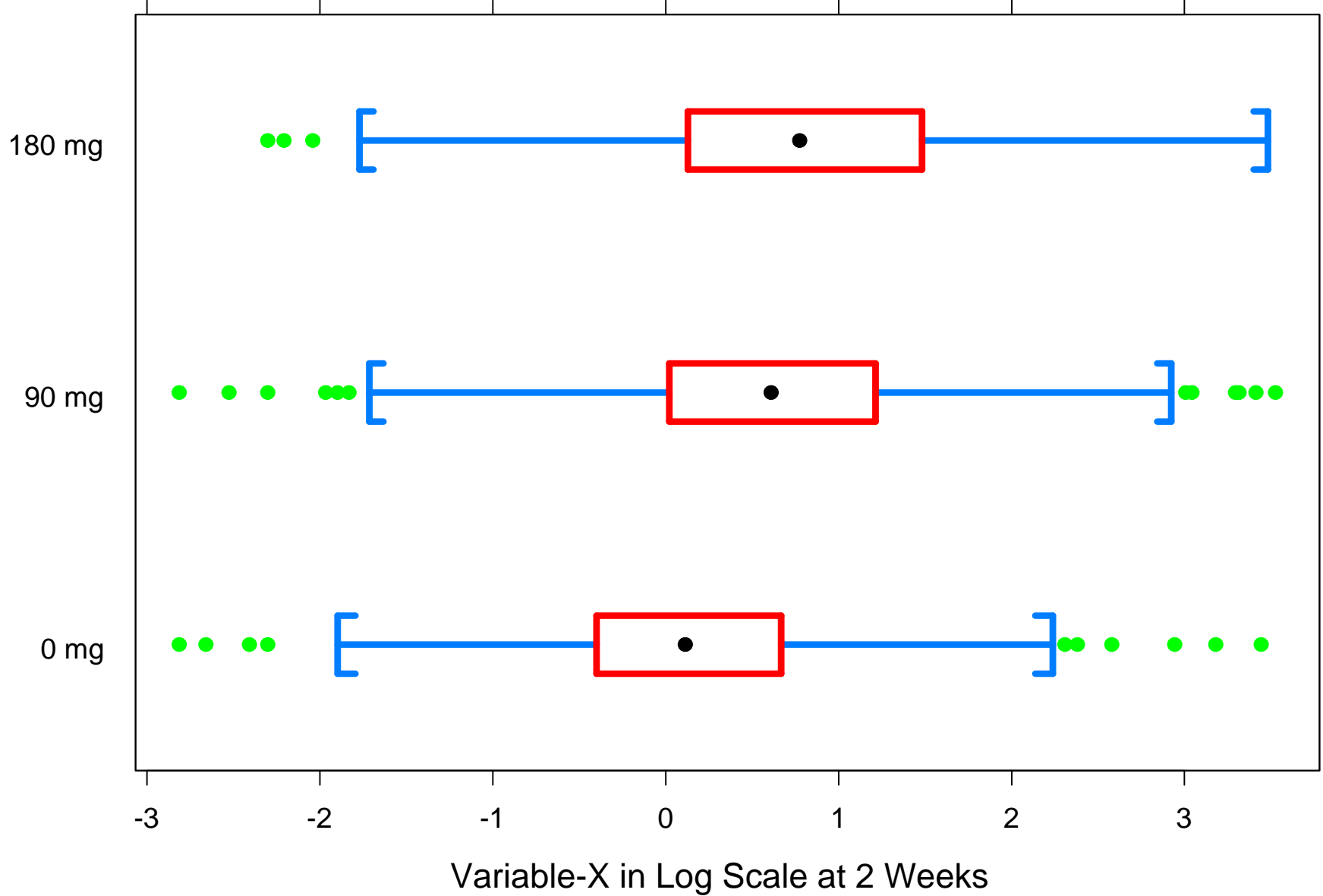
Histogram of Variable-X in Log Scale at 2 Week Visit



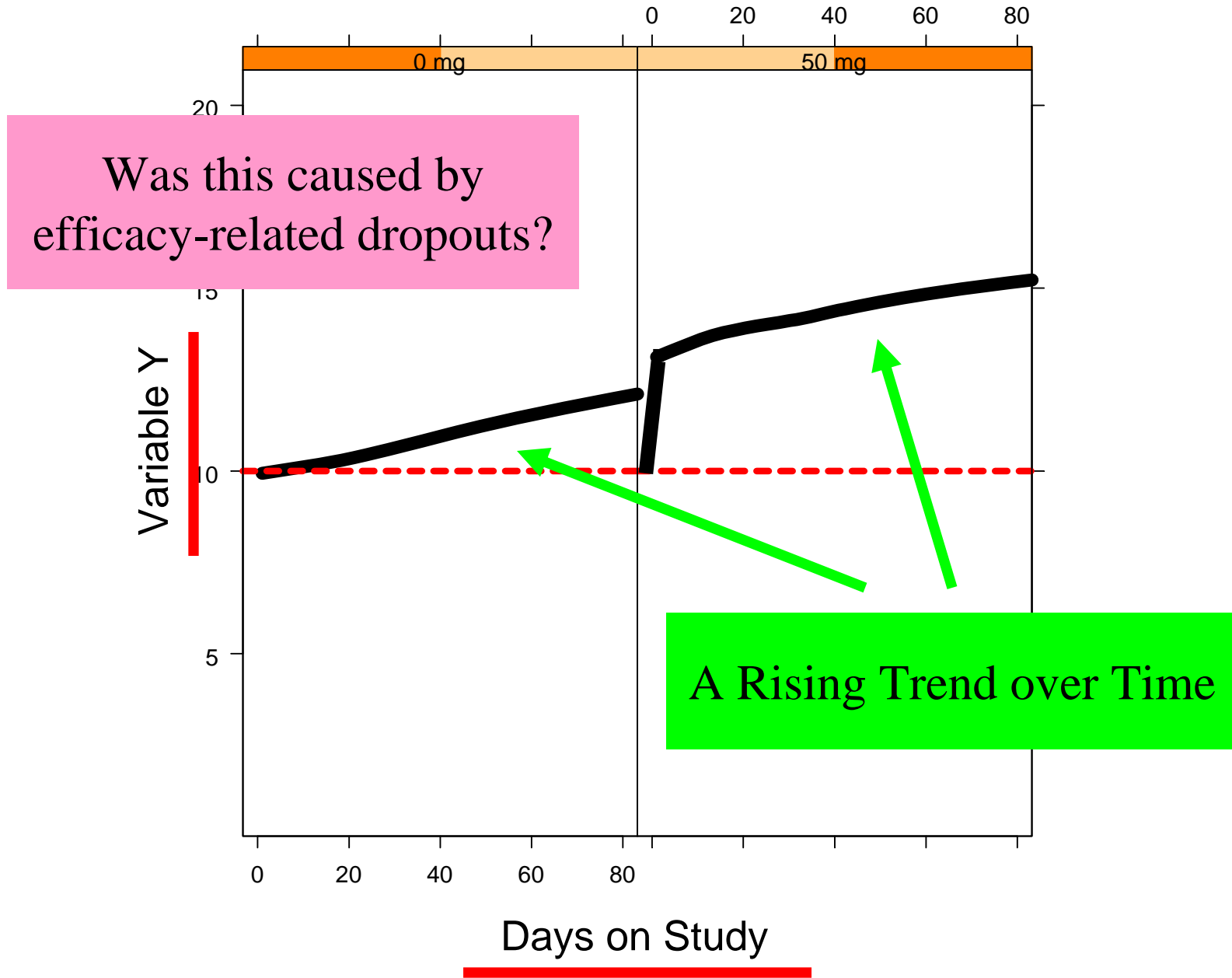
QQnorm to Check Normality



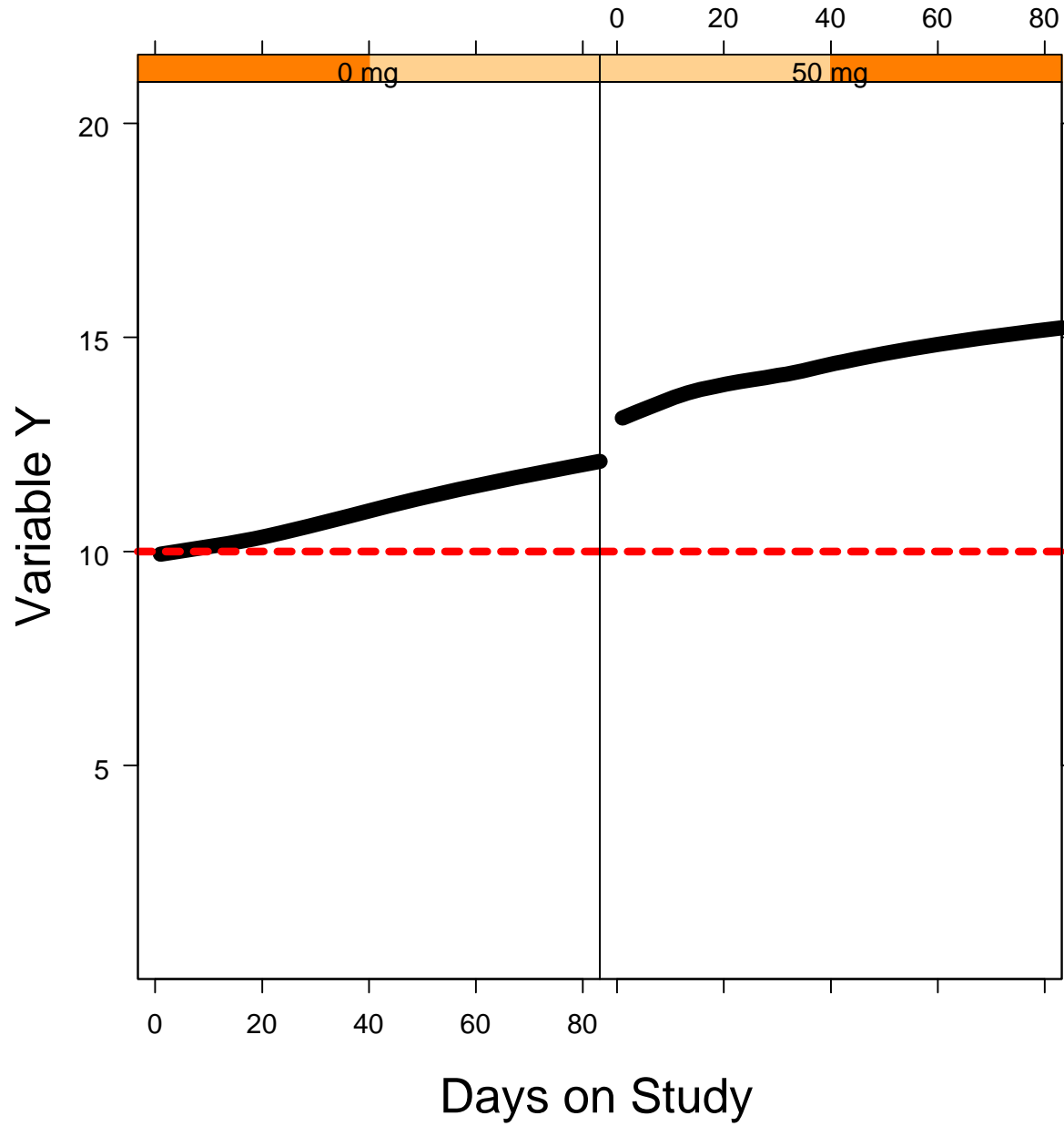
Box-Whisker Plot for Distribution Comparison



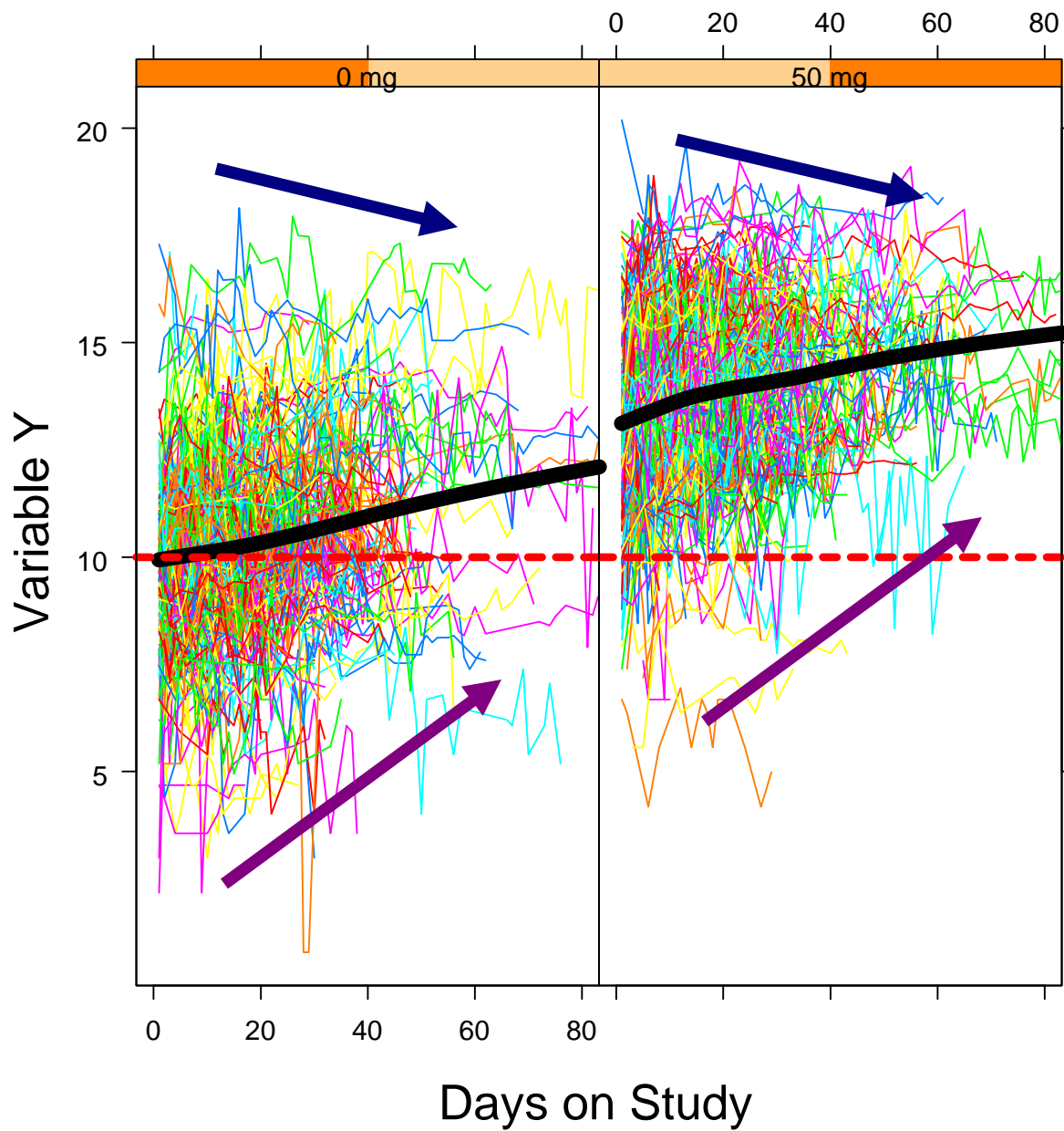
Variable Y Over Time



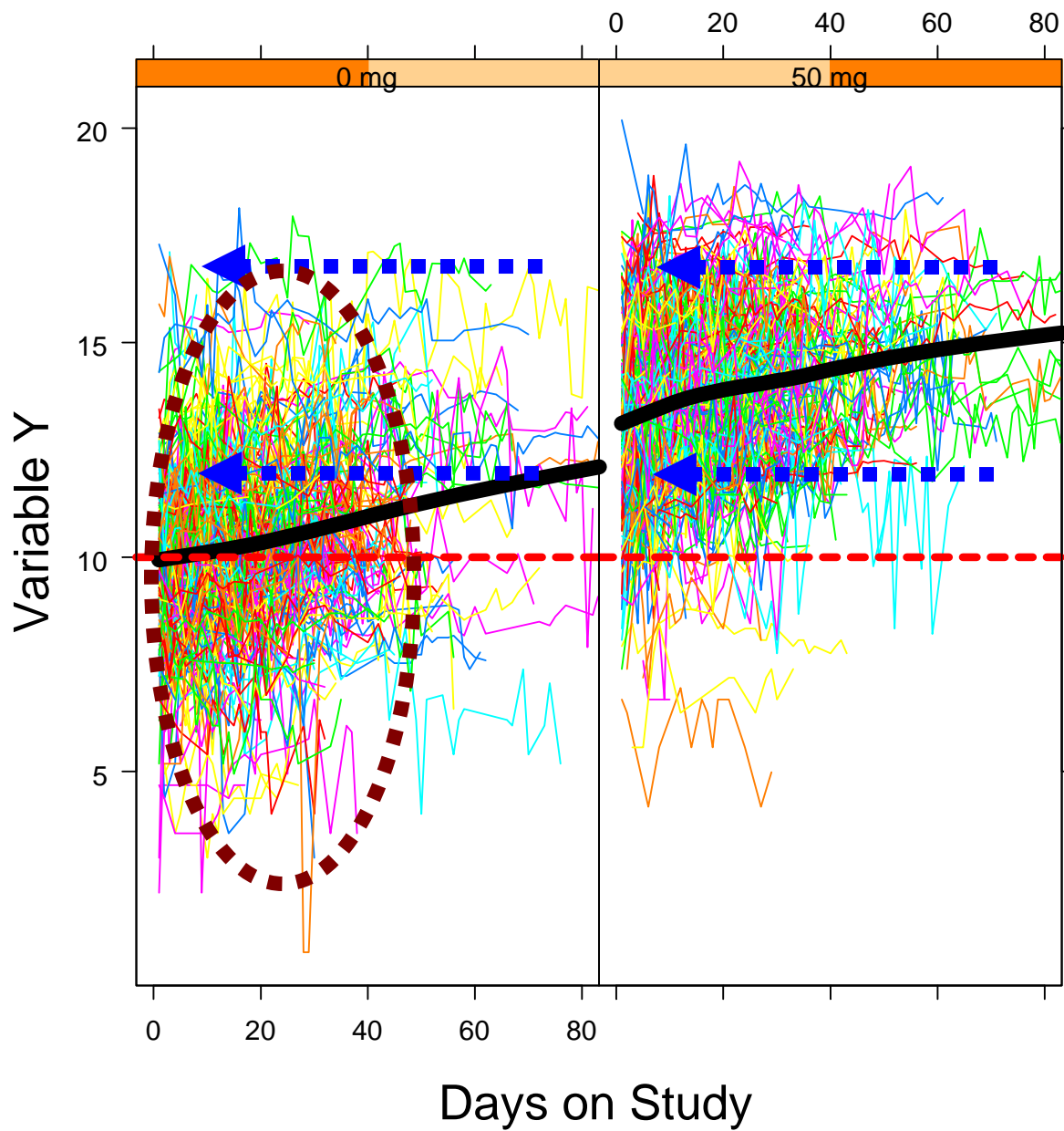
Variable Y Over Time



Variable Y Over Time



Variable Y Over Time



A Pediatric Morphine Sparing Study

- Study treatments plus **free** access to morphine.
- **Same level of pain relief across groups.**
- Efficacy variable is the **amount of morphine used.**

Table 1: Tablet Dosage by Body Weight
(Protocol XXX)

Weight (kg)	25 mg ^a <u>1/2 tablet</u>	50 mg ^a <u>1 tablet</u>	75 mg ^a <u>1.5 tablets</u>	100 mg ^a <u>2 tablets</u>
20-29.9	A	B		
30-34.9	A		B	
35-44.9		A	B	
≥45		A		B

^a This study used 50 mg scored tablets of drug X

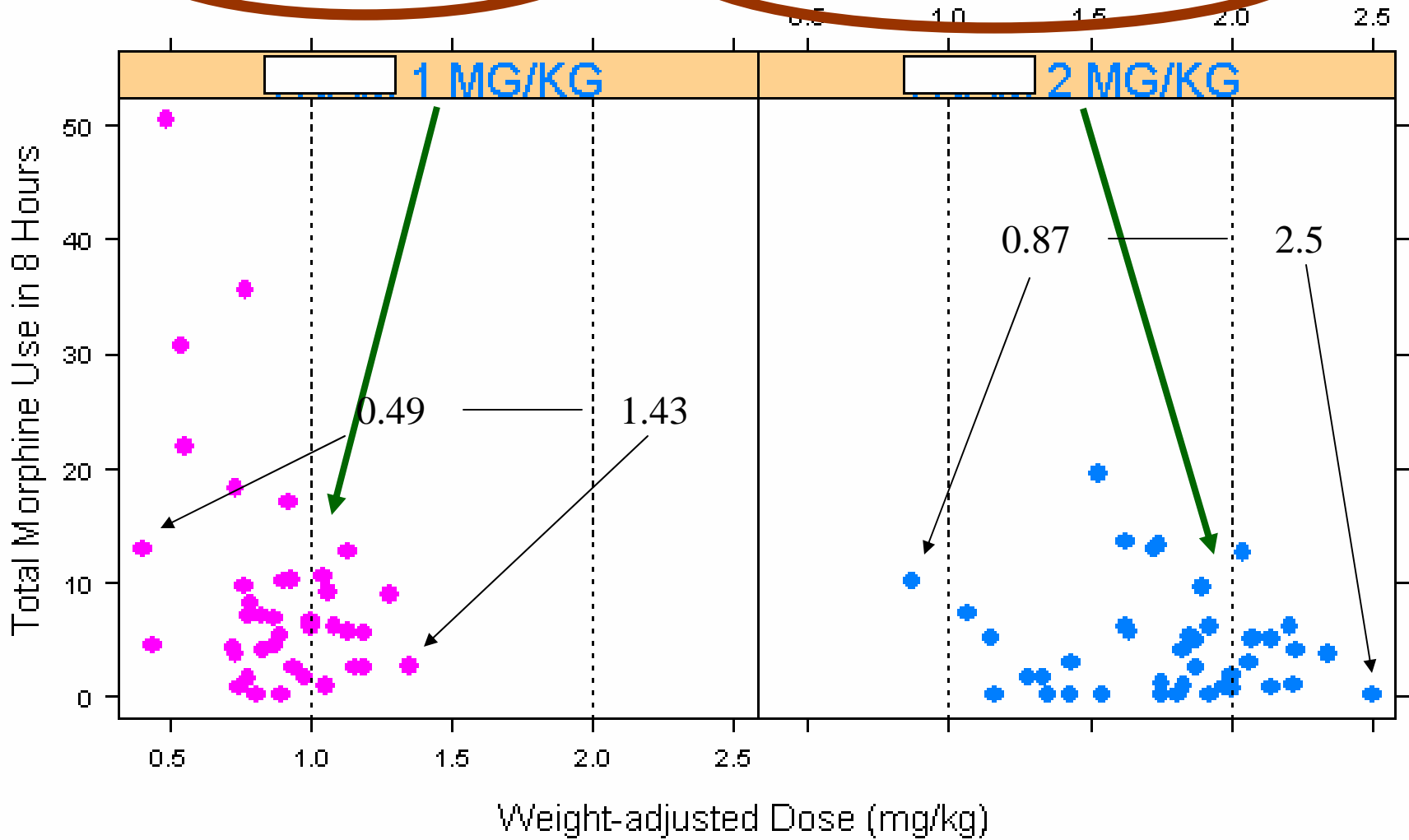
A = approximately 1 mg/kg

B = approximately 2 mg/kg

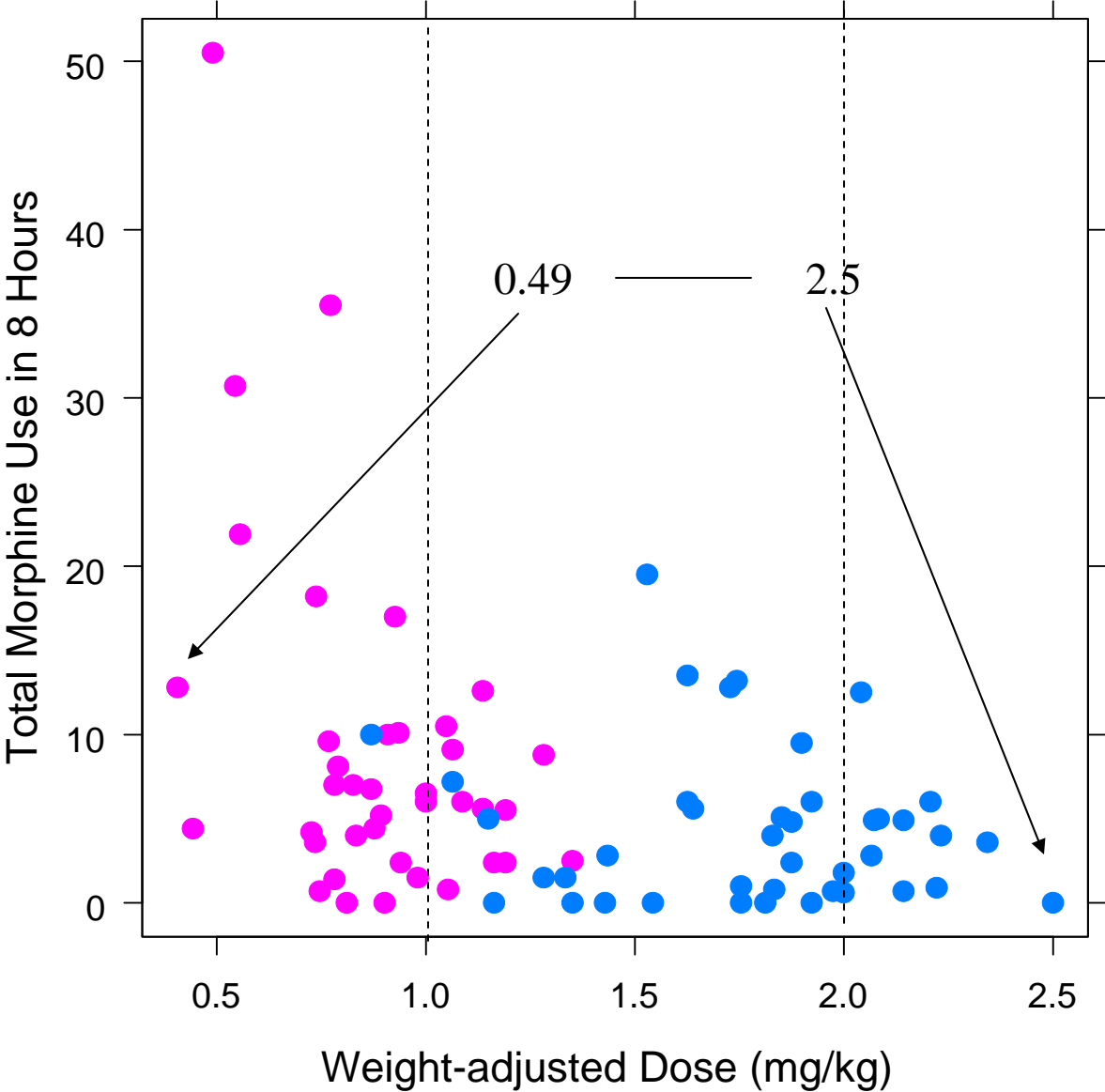
Efficacy Finding

- The 2 mg/kg group needed an average of 65% less morphine than the 1 mg/kg group.

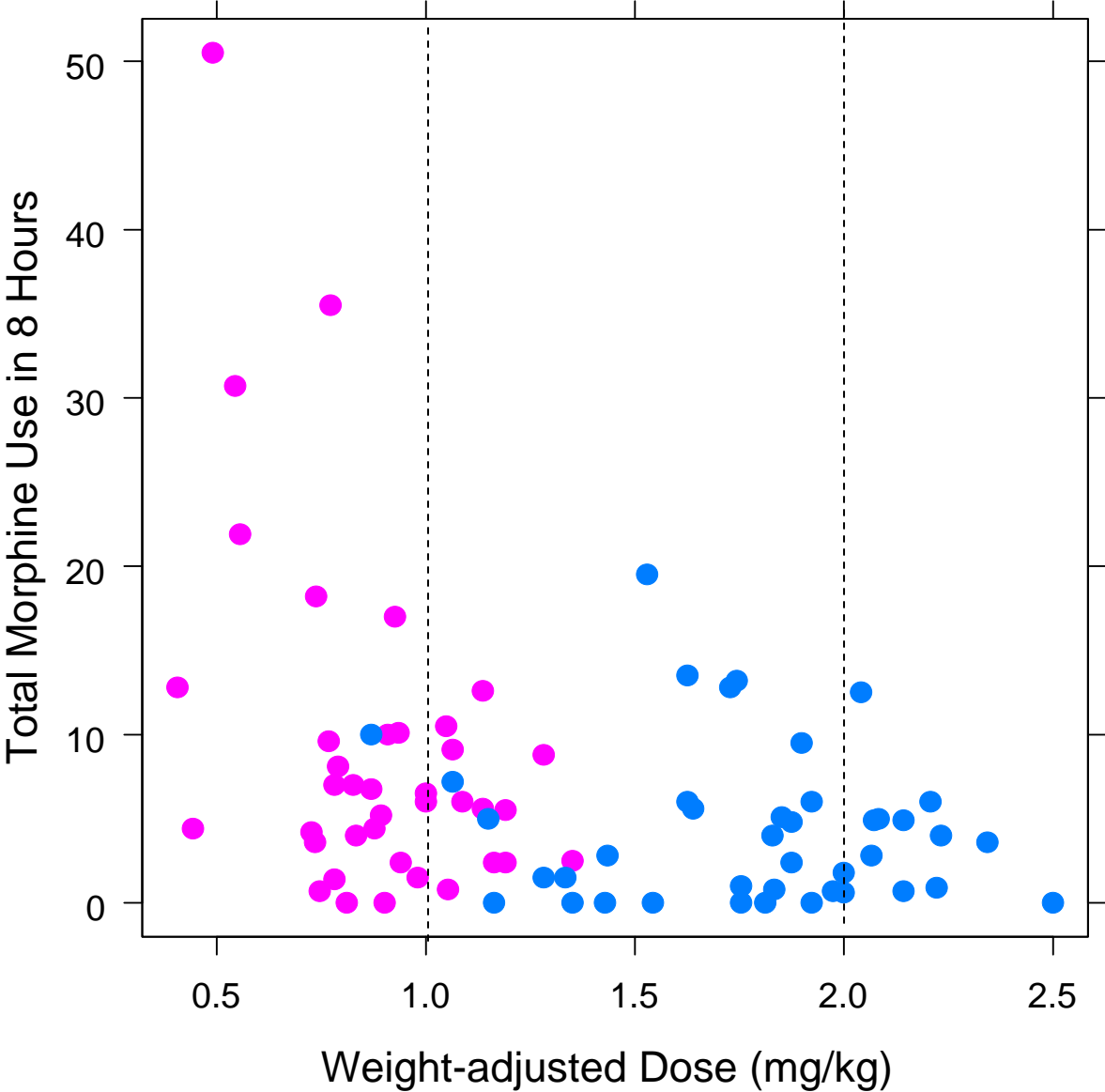
Morphine Use vs. Weight-adjusted Dose



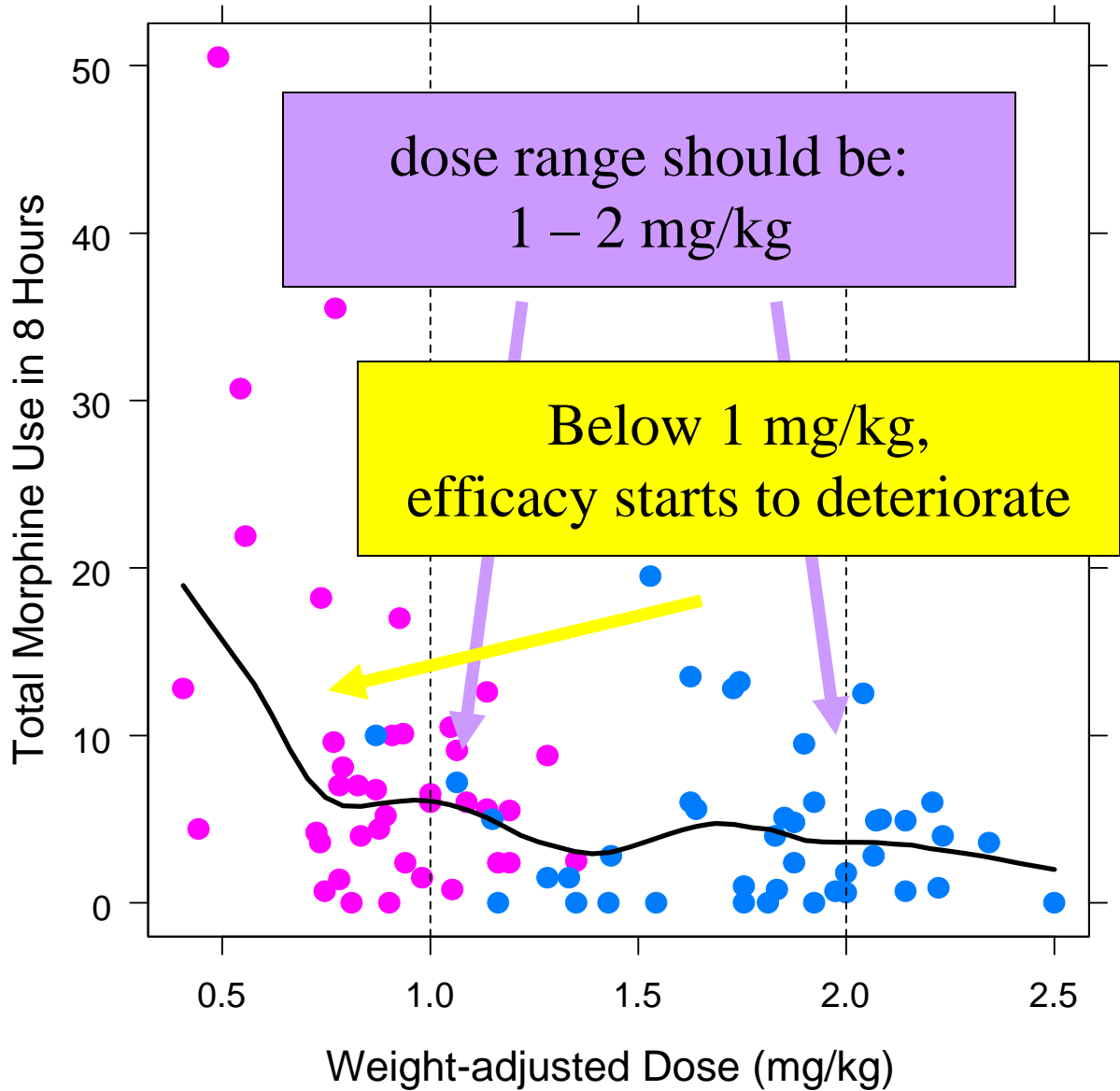
Morphine Use vs. Weight-adjusted Dose



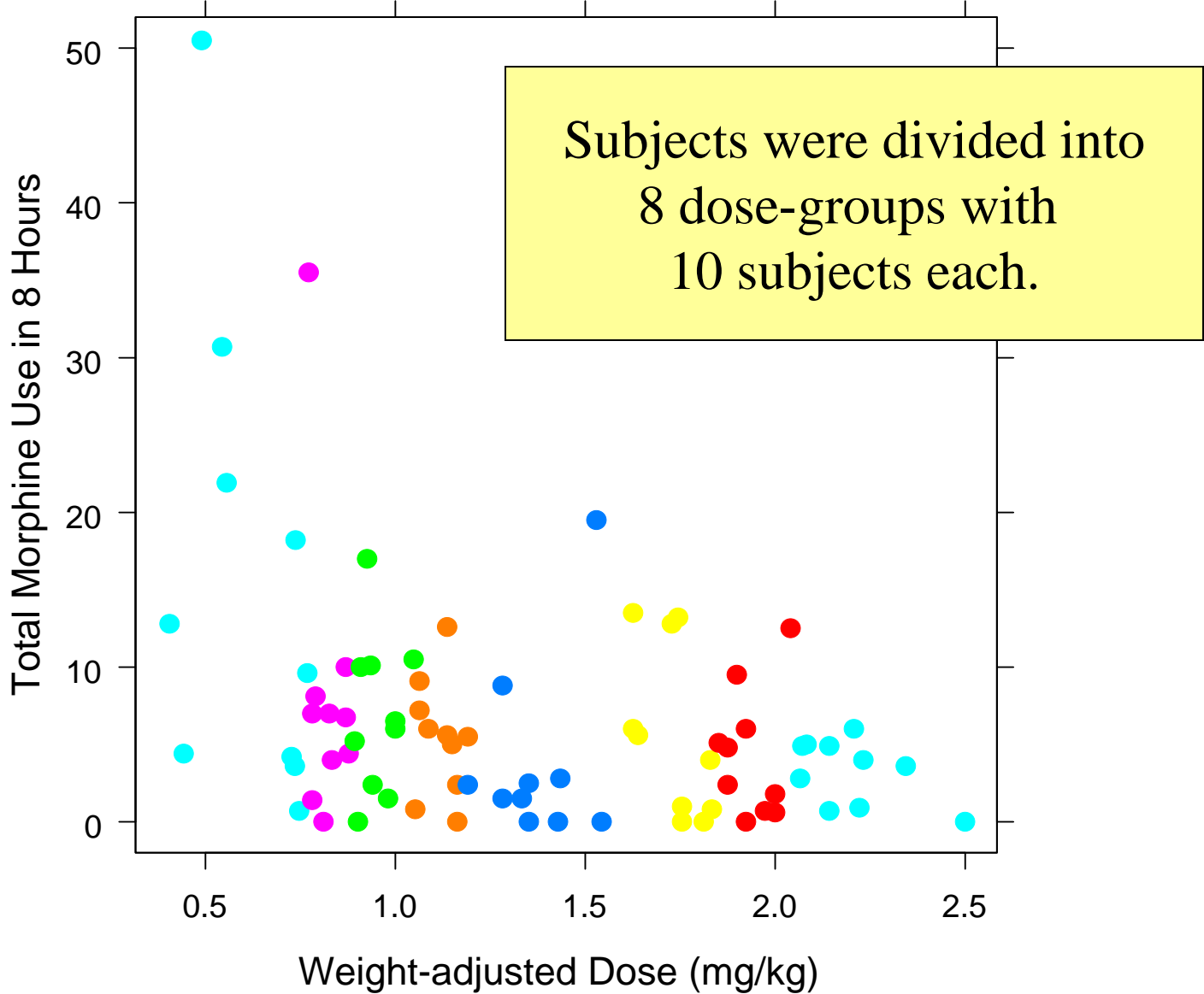
Morphine Use vs. Weight-adjusted Dose



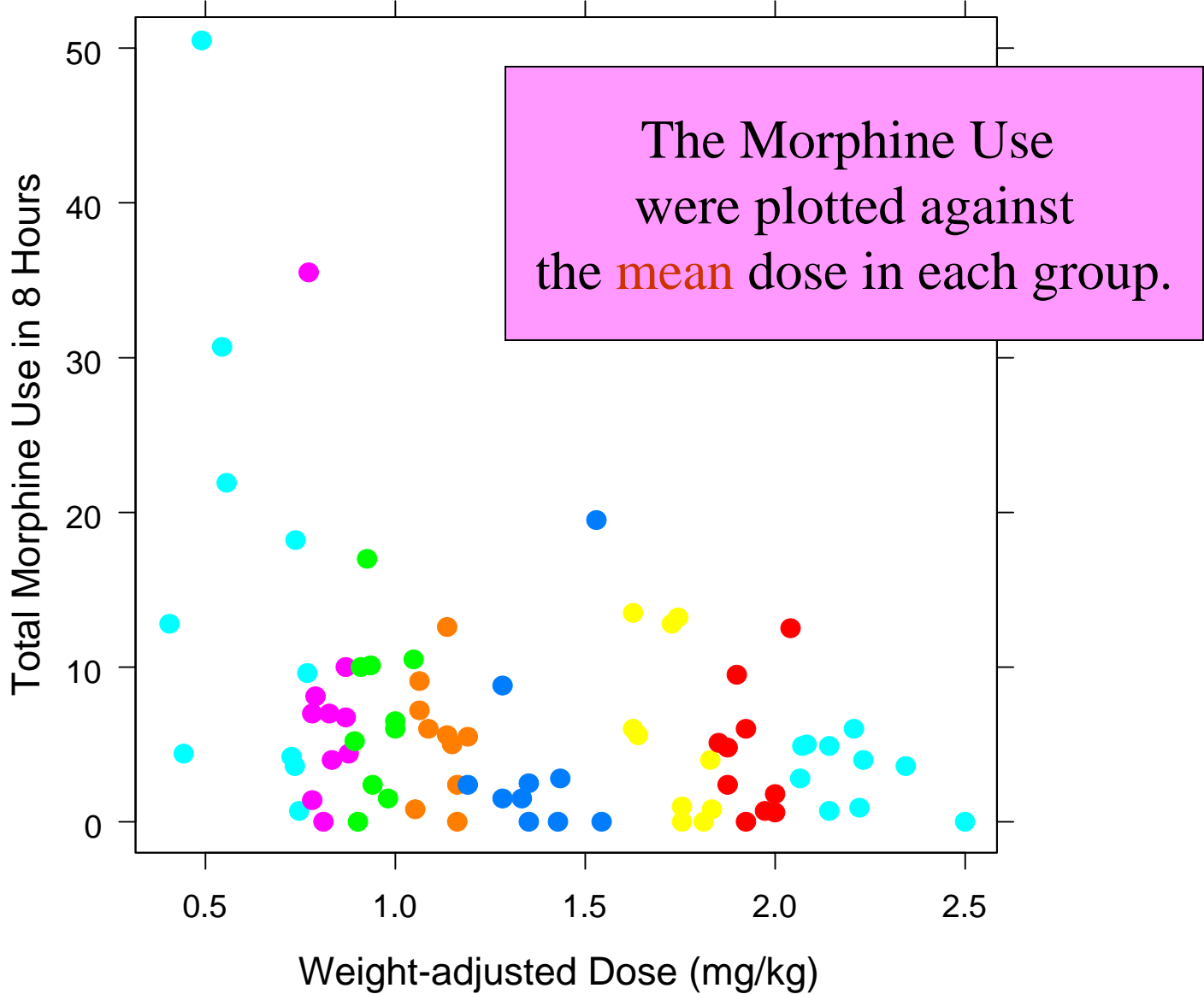
Morphine Use vs. Weight-adjusted Dose



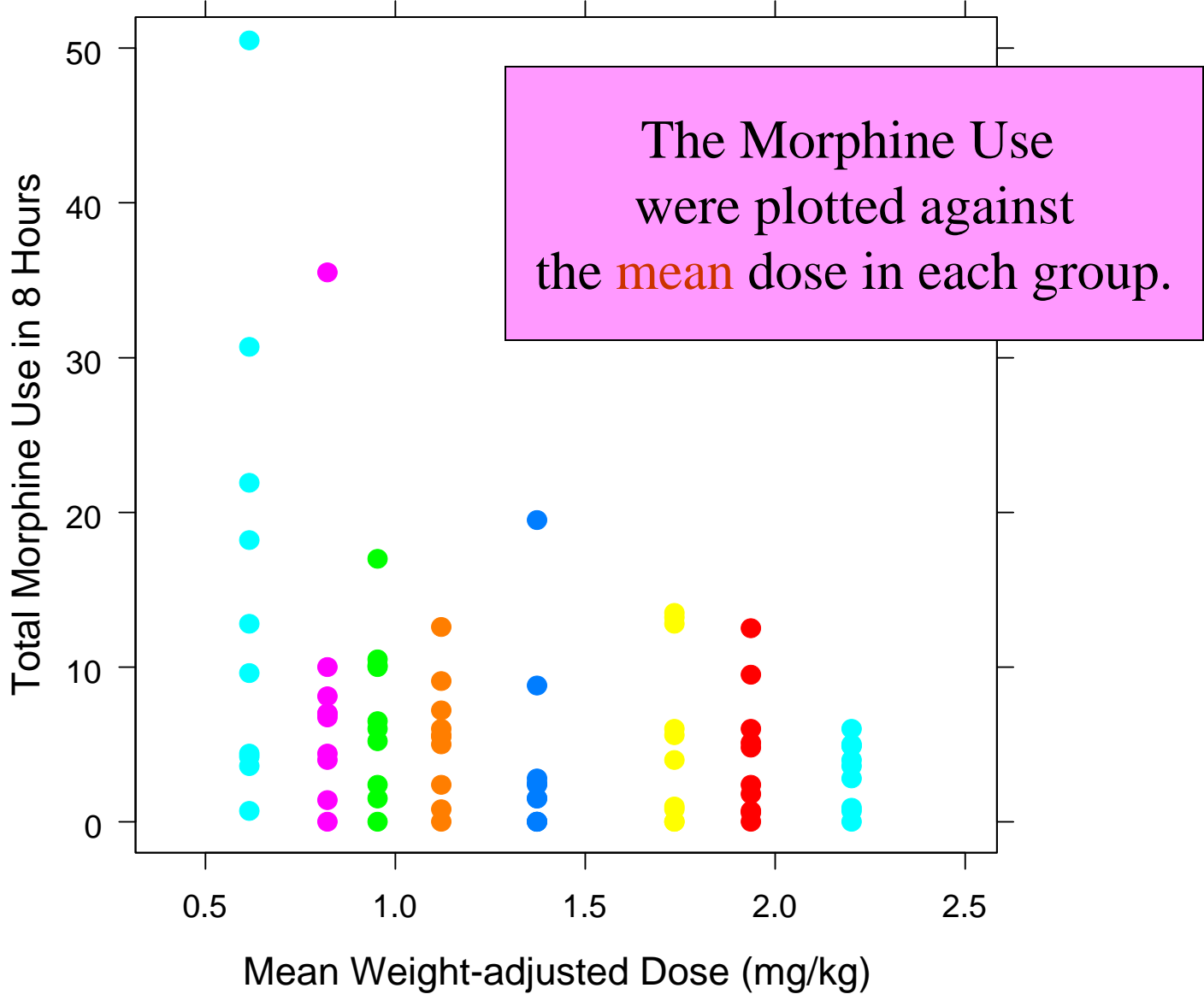
Morphine Use vs. Weight-adjusted Dose



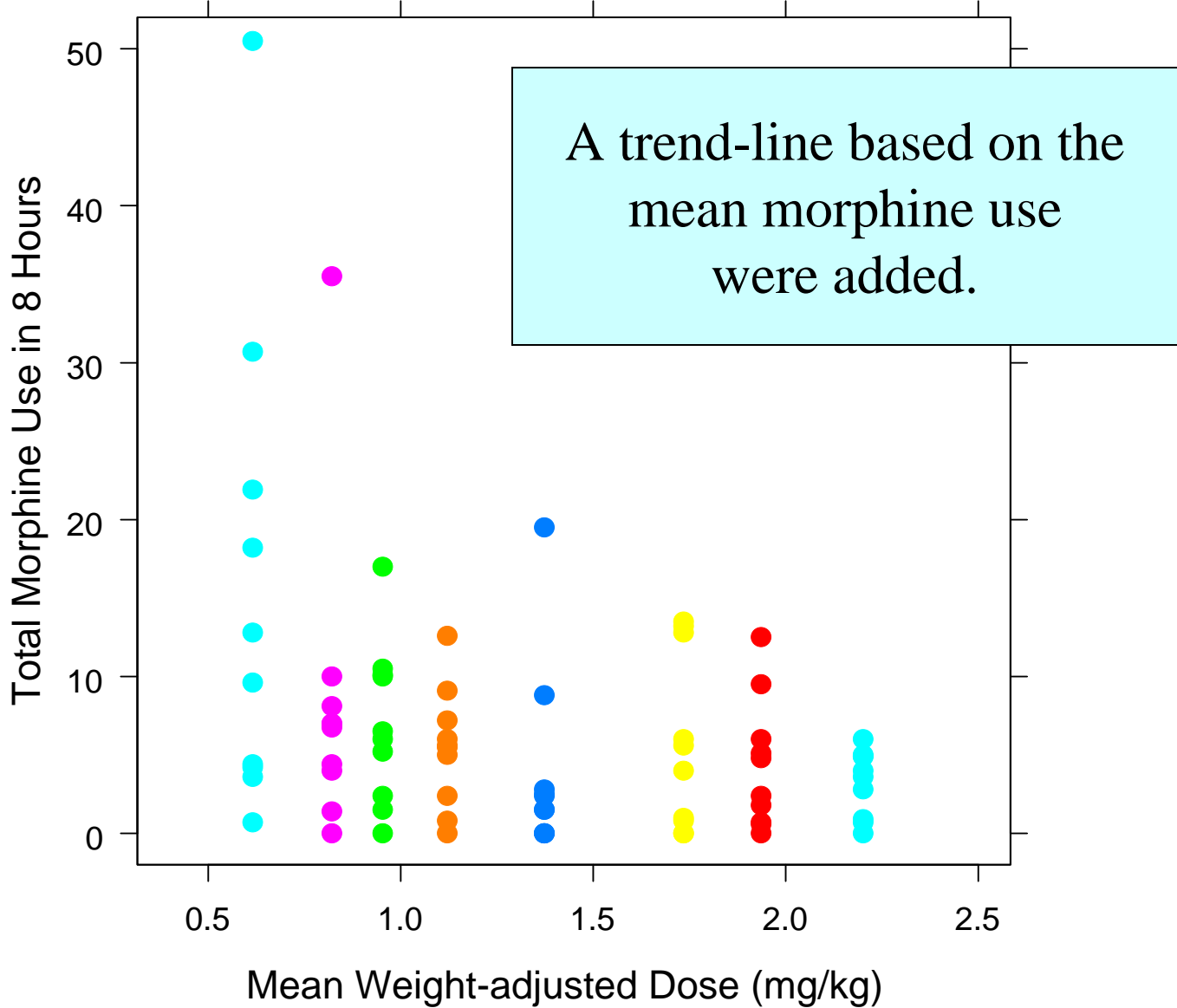
Morphine Use vs. Weight-adjusted Dose



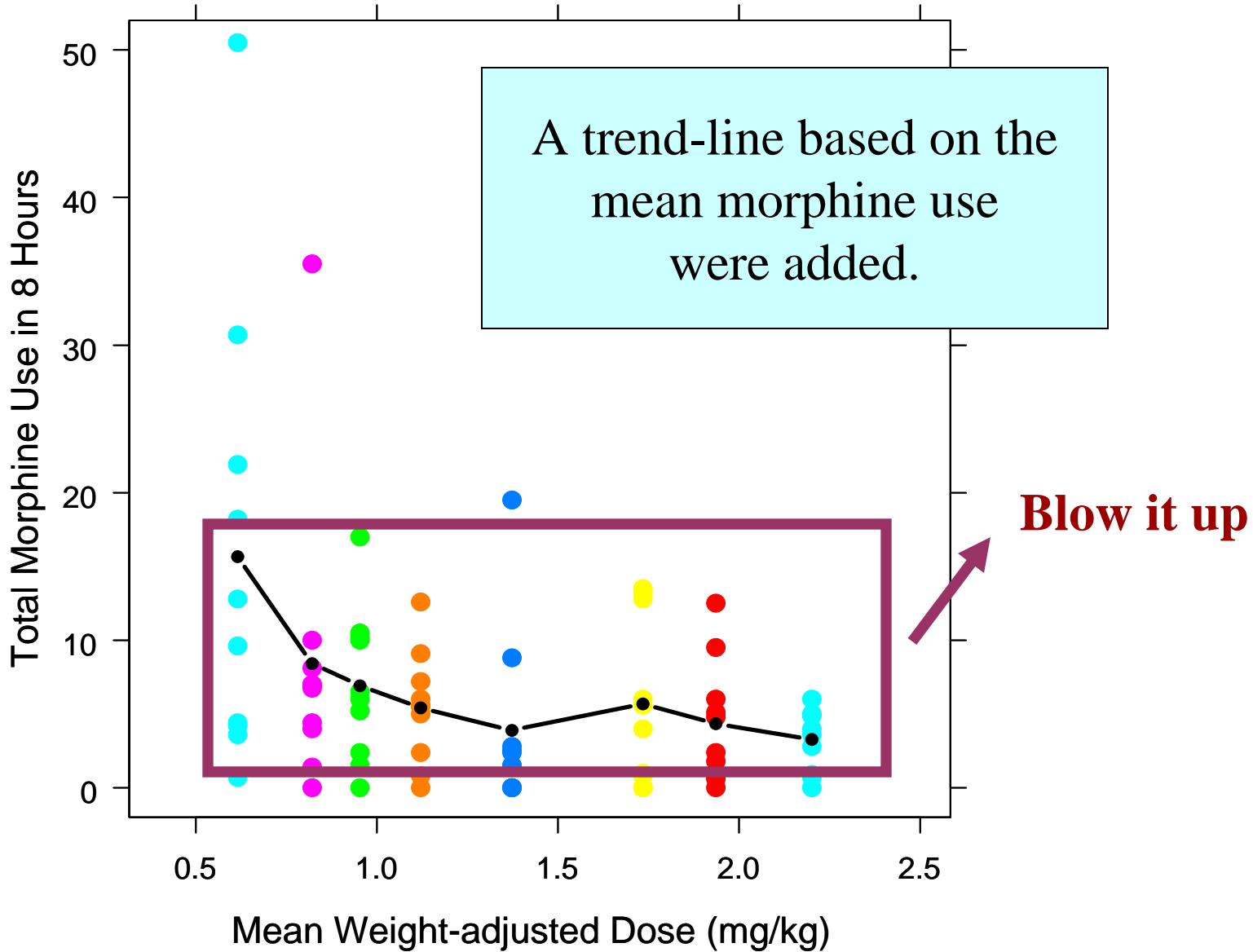
Morphine Use vs. Weight-adjusted Dose



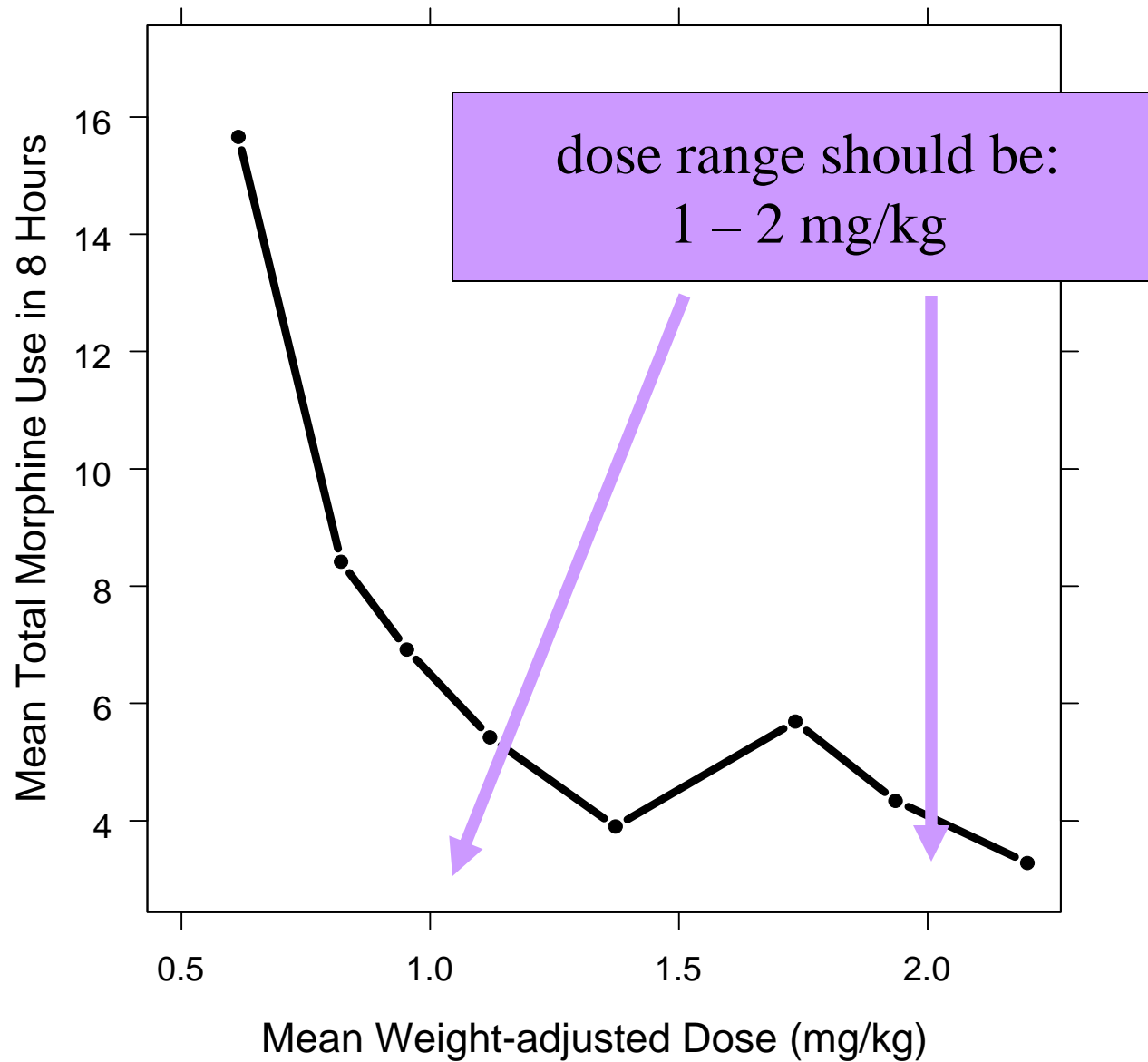
Morphine Use vs. Weight-adjusted Dose



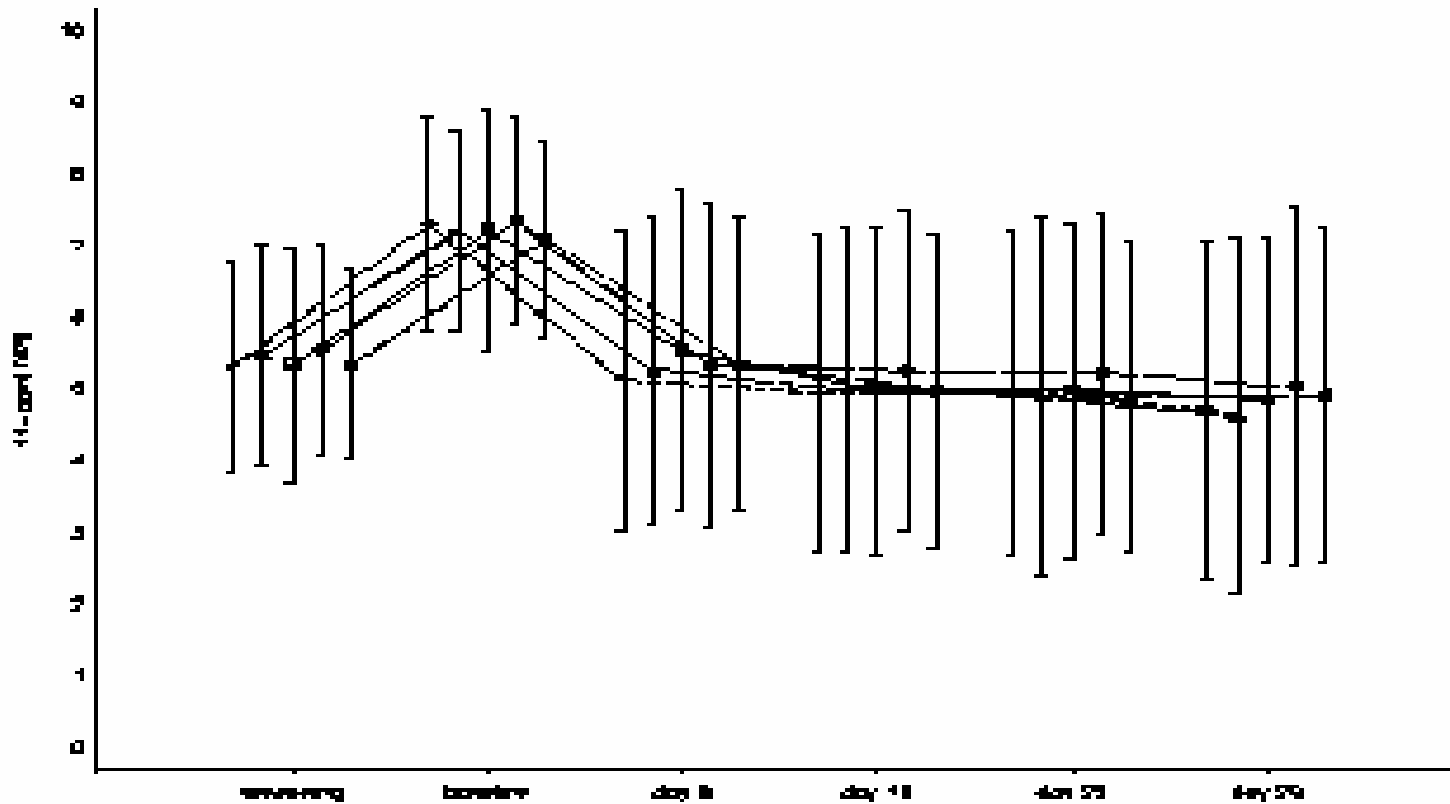
Morphine Use vs. Weight-adjusted Dose



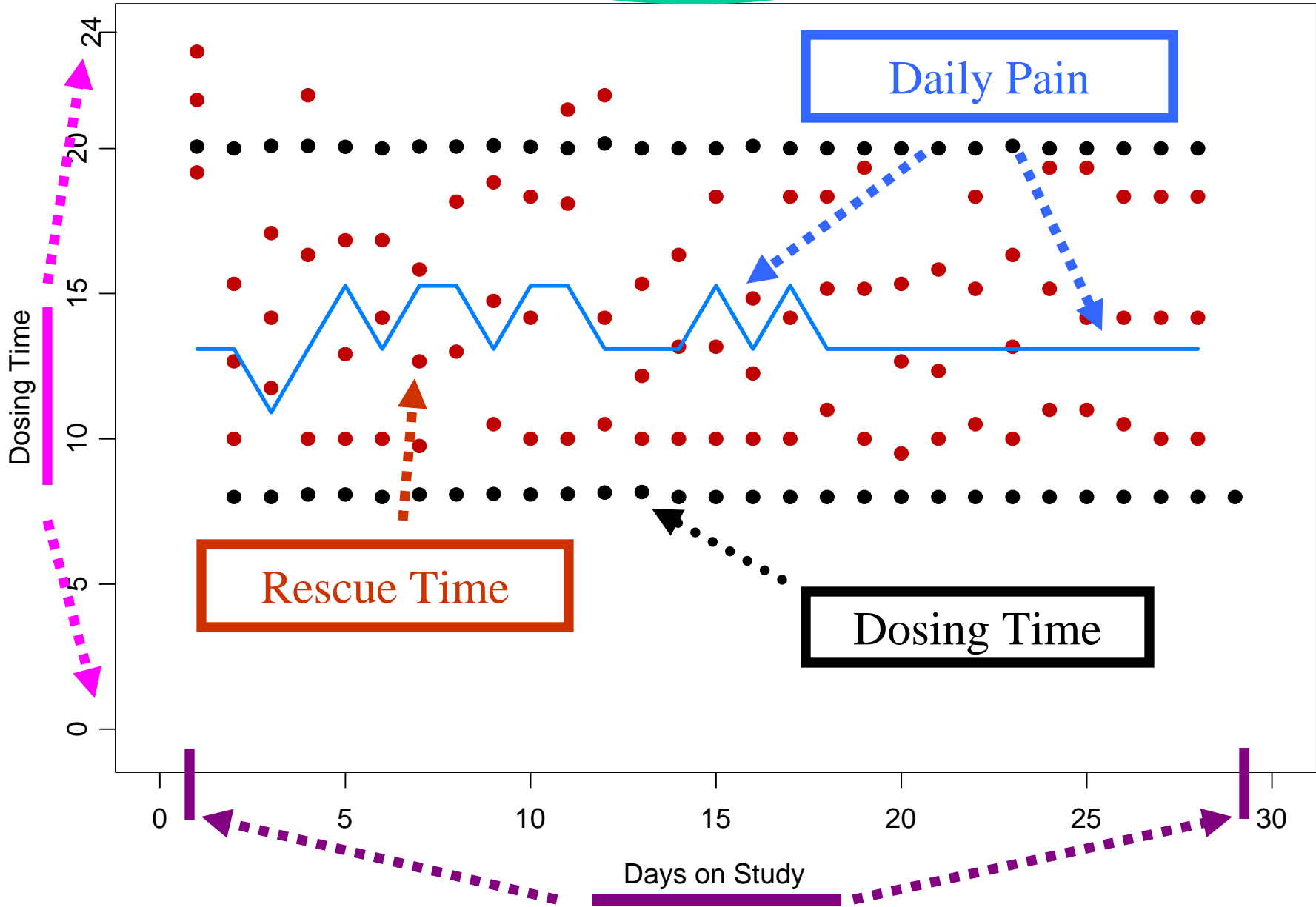
Mean Morphine Use vs. Mean Weight-adjusted Dose



A Failed Chronic Pain Study

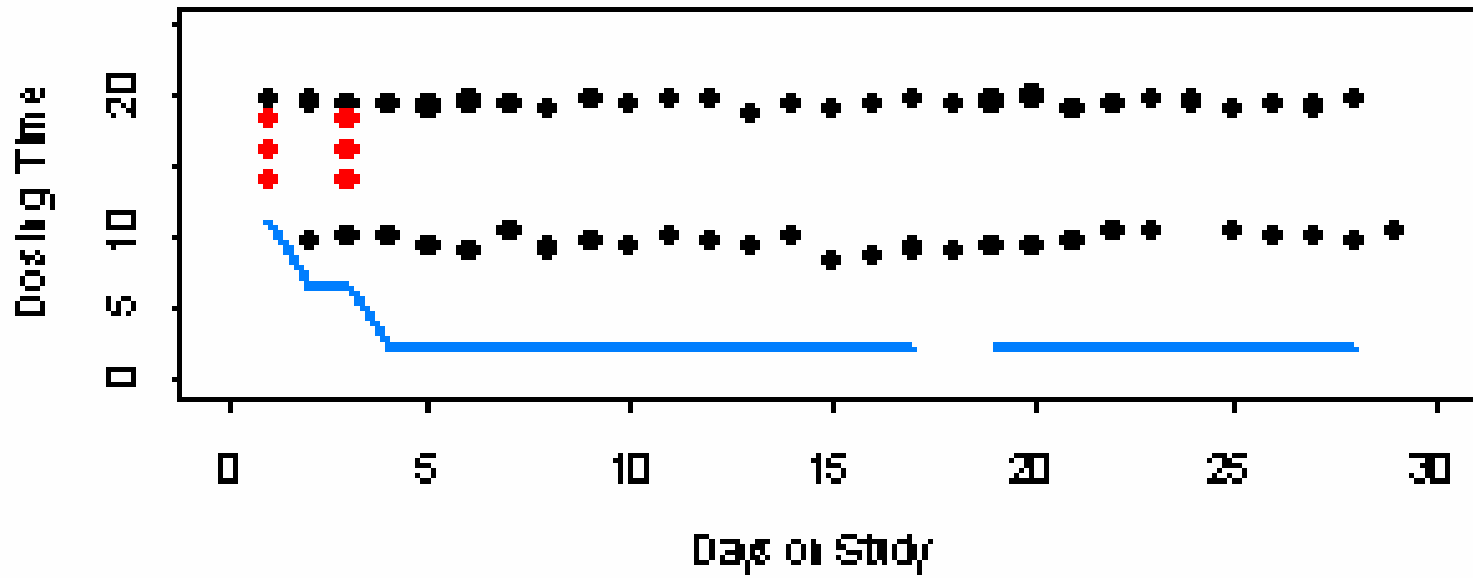


Subj 503 in Drug X

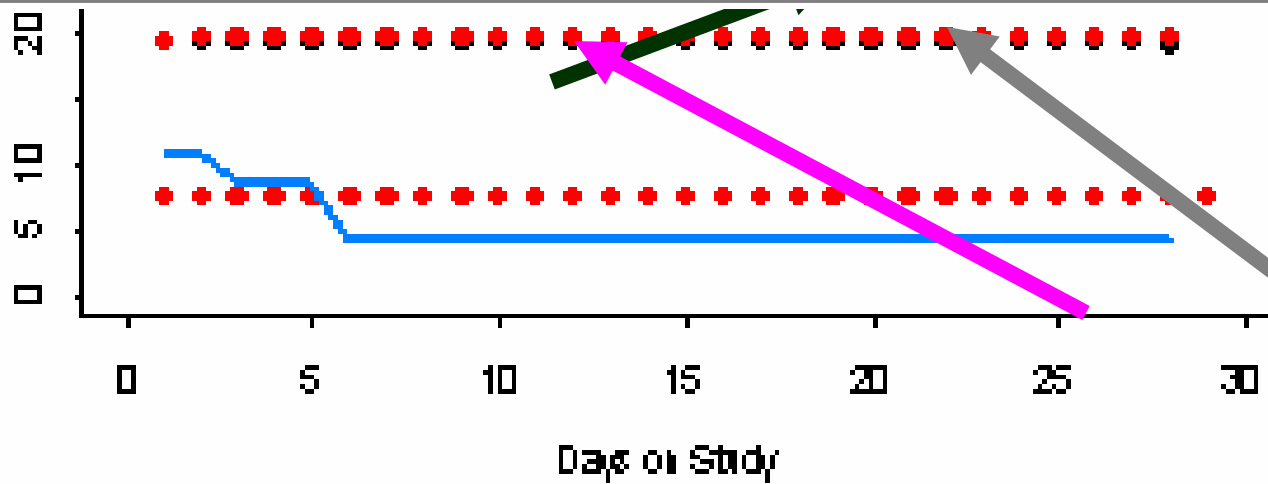


Subj 530 in Drug X

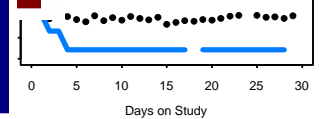
Dosing Time



Dosing Time



30

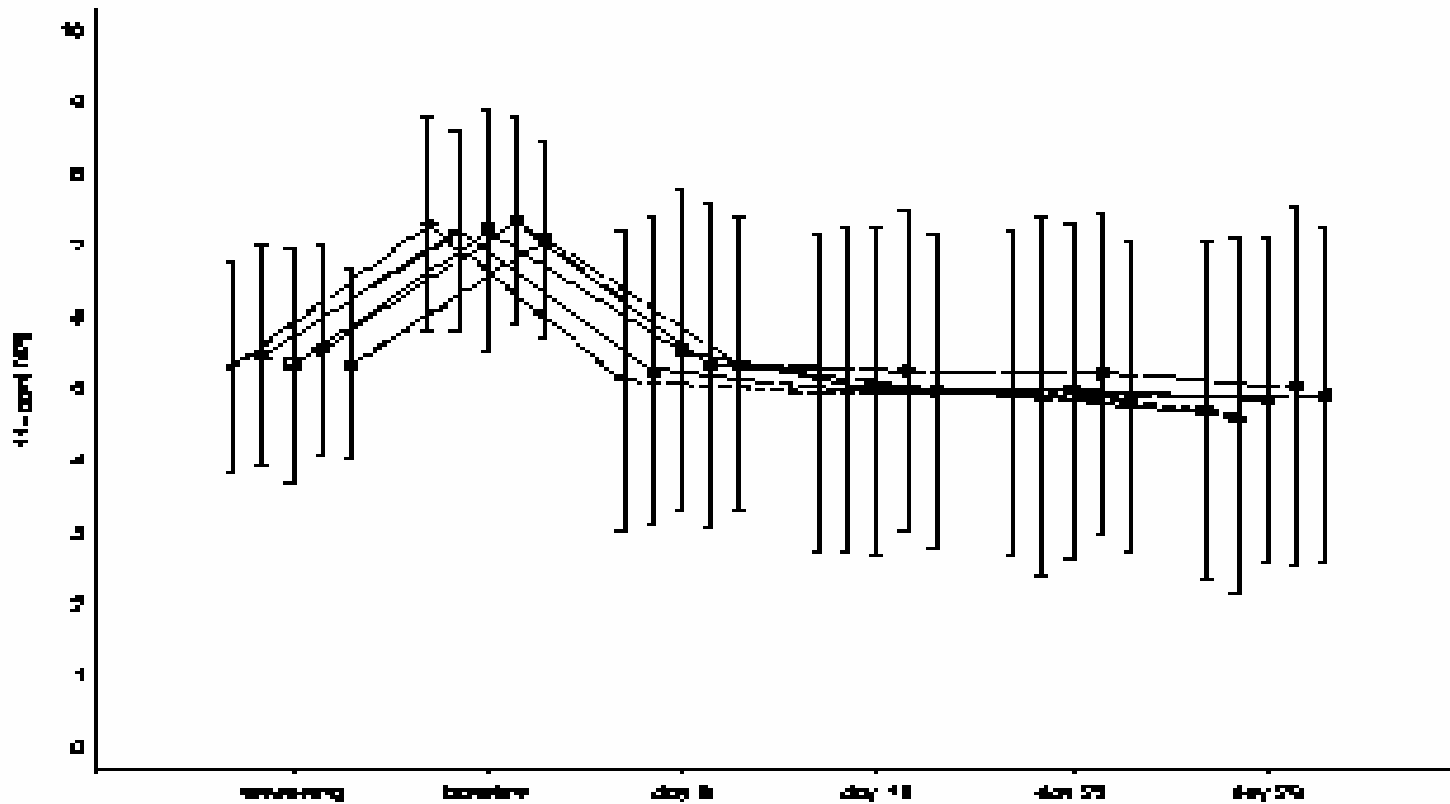


A Morphine

This study was turned into a morphine sparing-type of a study.

- Study treatments plus **free** access to morphine.
- **Same level of pain relief across groups.**
- Efficacy variable is the amount of rescues used.

A Failed Chronic Pain Study

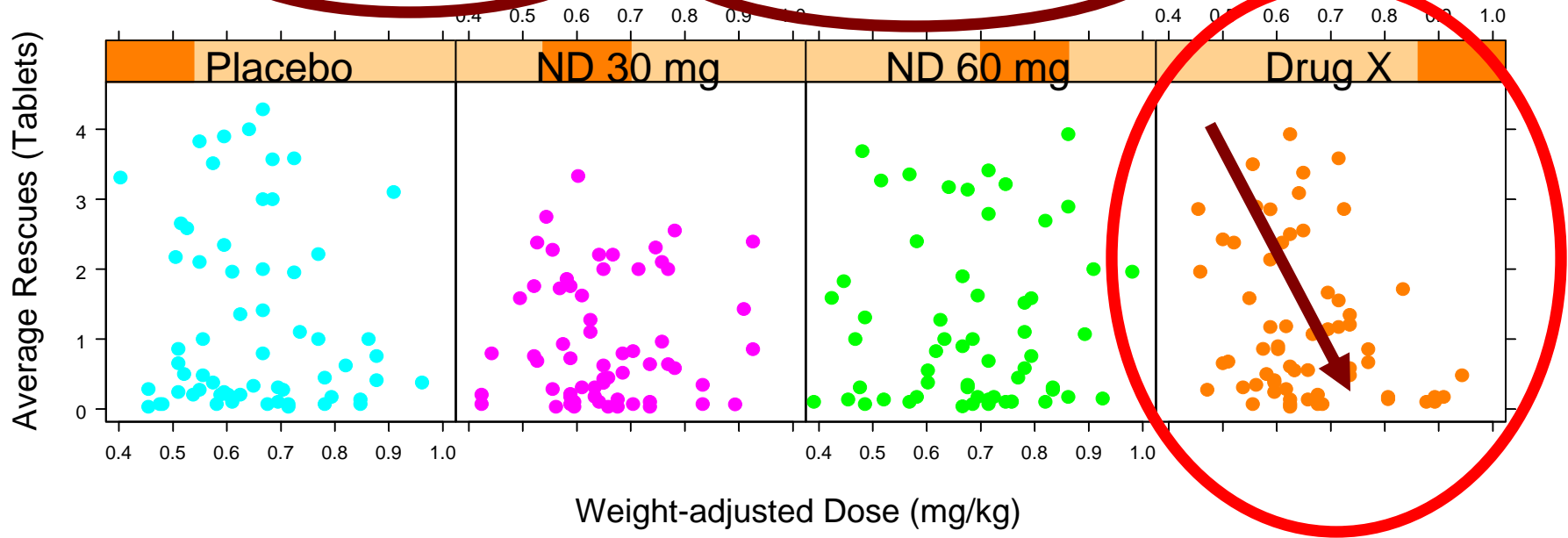


A Morphine

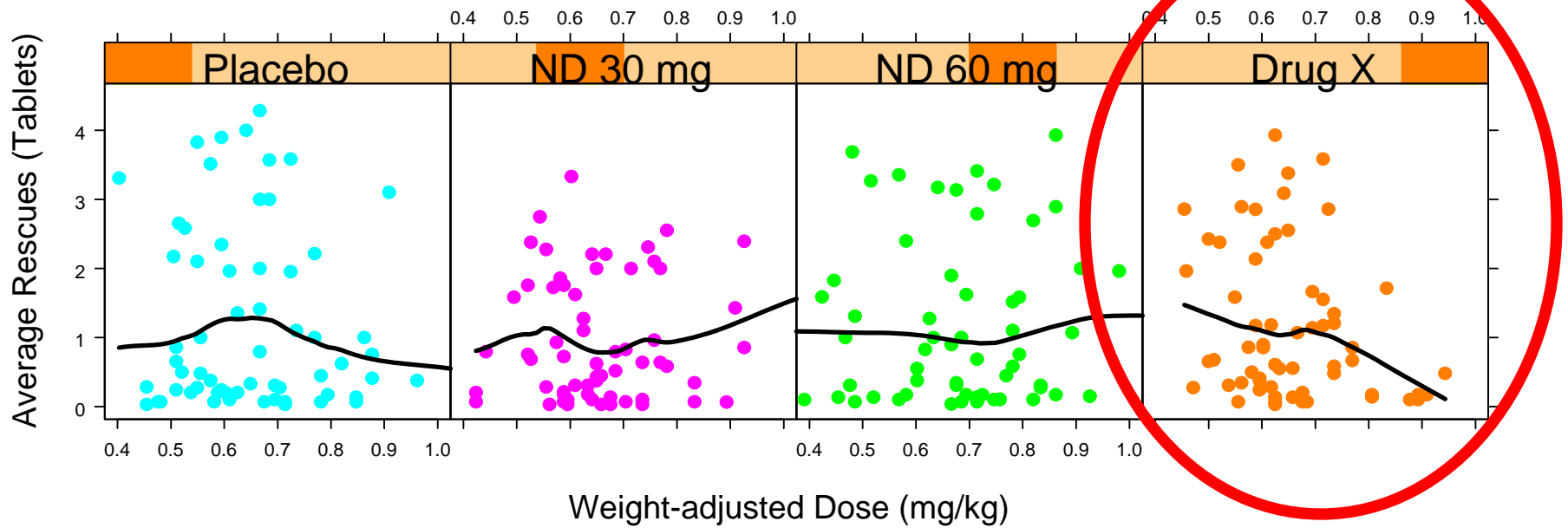
This study was turned into a morphine sparing-type of a study.

- Study treatments plus free access to morphine.
- **Same level of pain relief across groups.**
- Efficacy variable is the amount of rescues used.

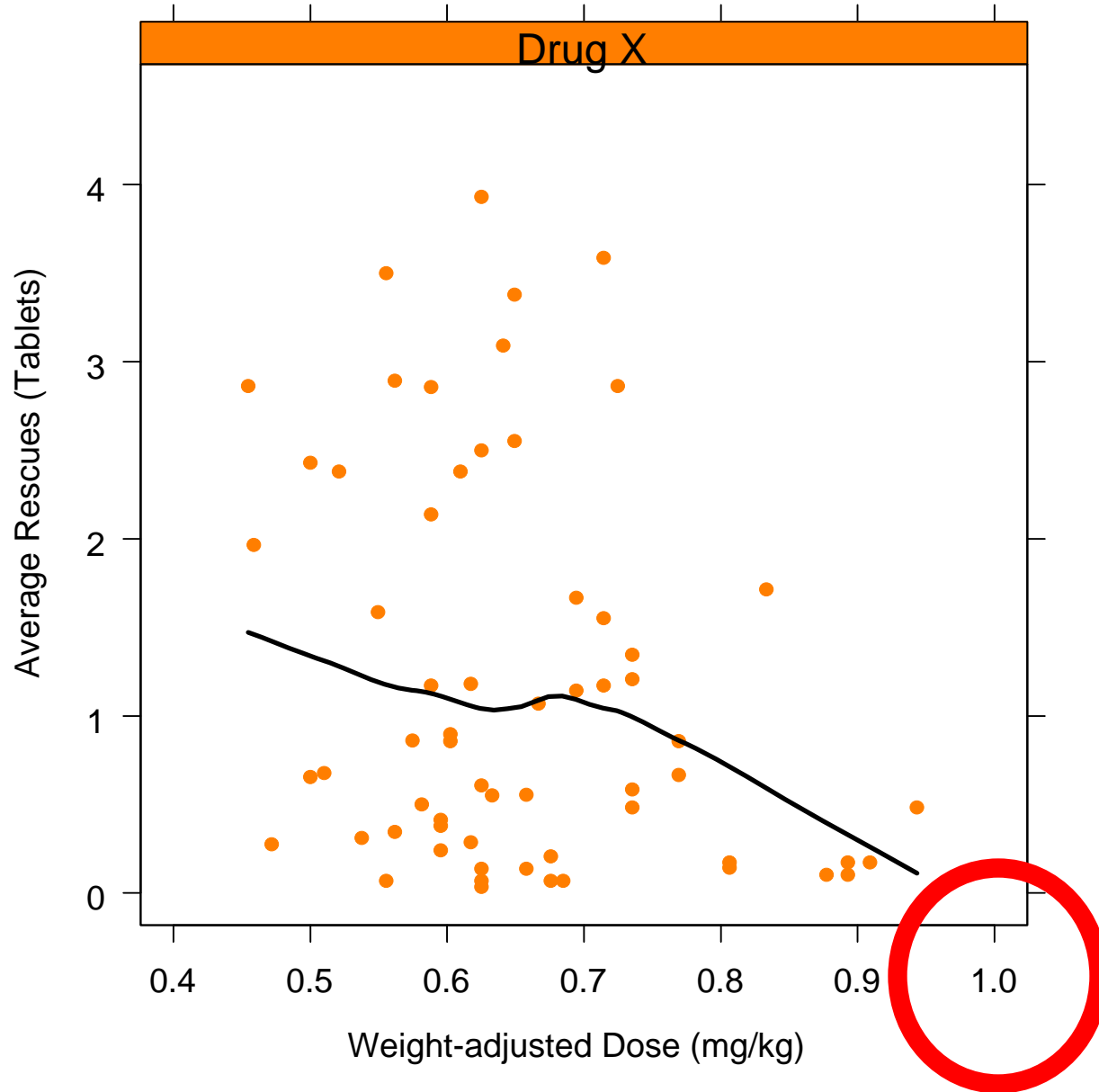
Rescue Usage vs. Weight-adjusted Dose (mg/kg)



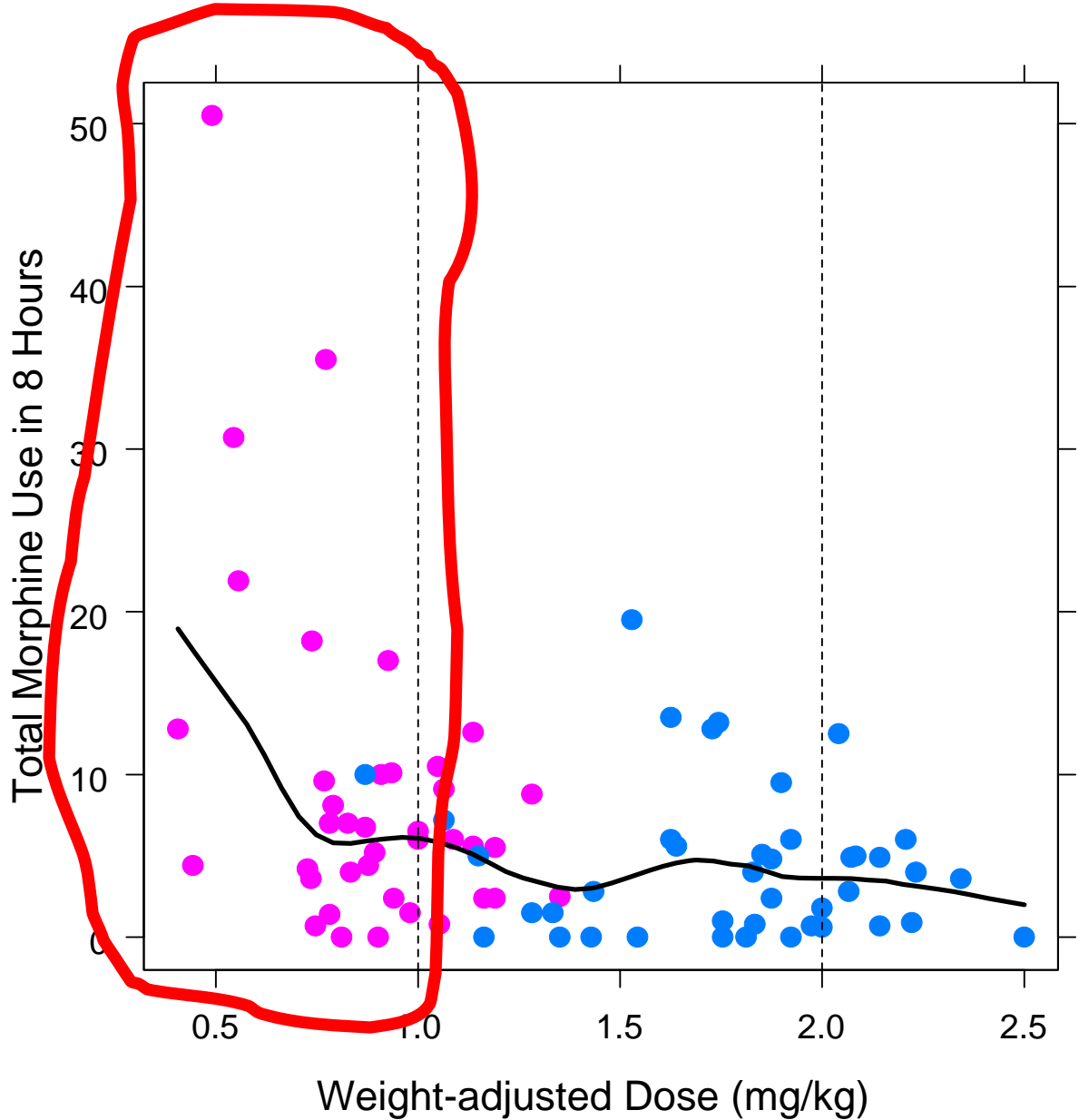
Rescue Usage vs. Weight-adjusted Dose (mg/kg)



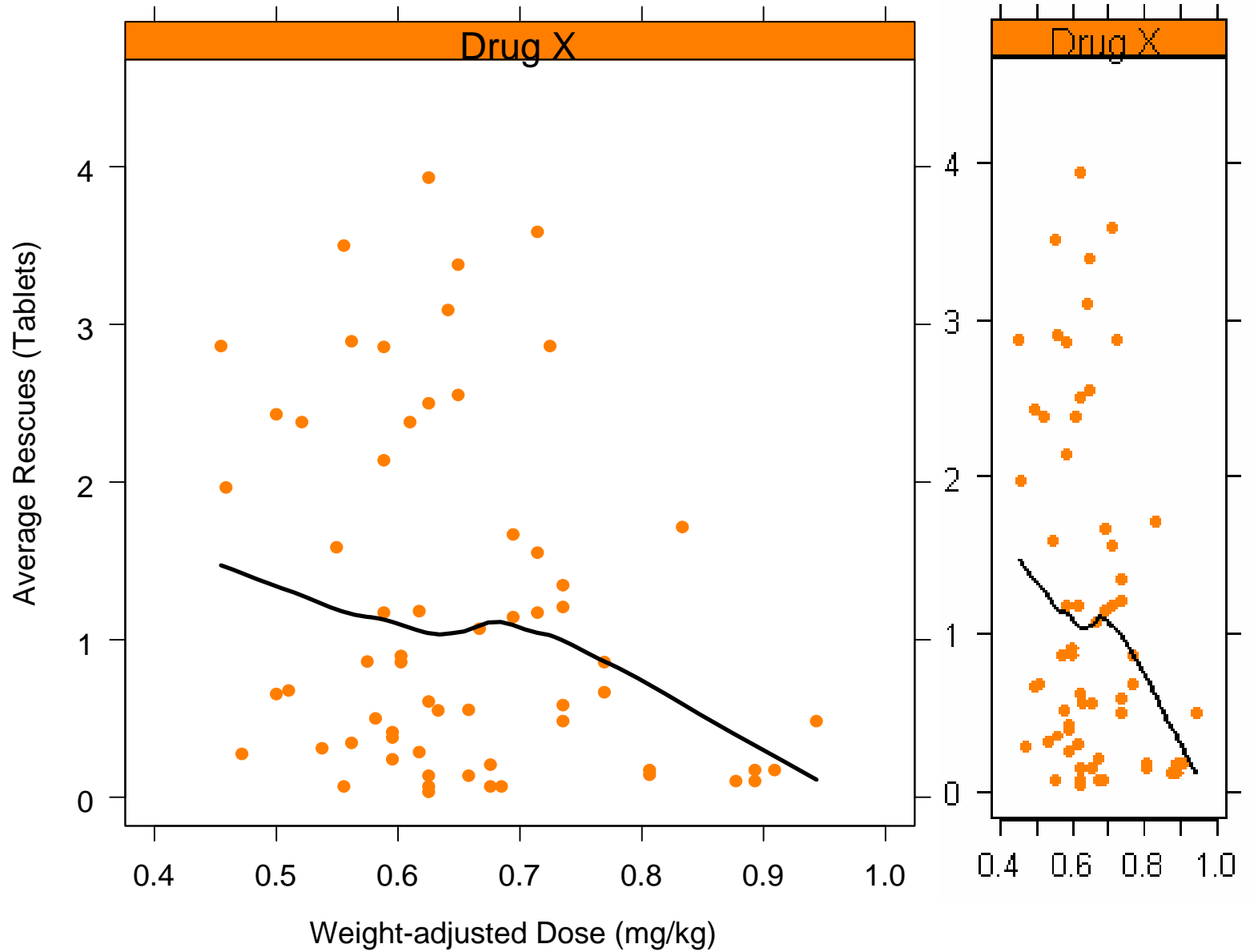
Rescue Usage vs. Weight-adjusted Dose (mg/kg)



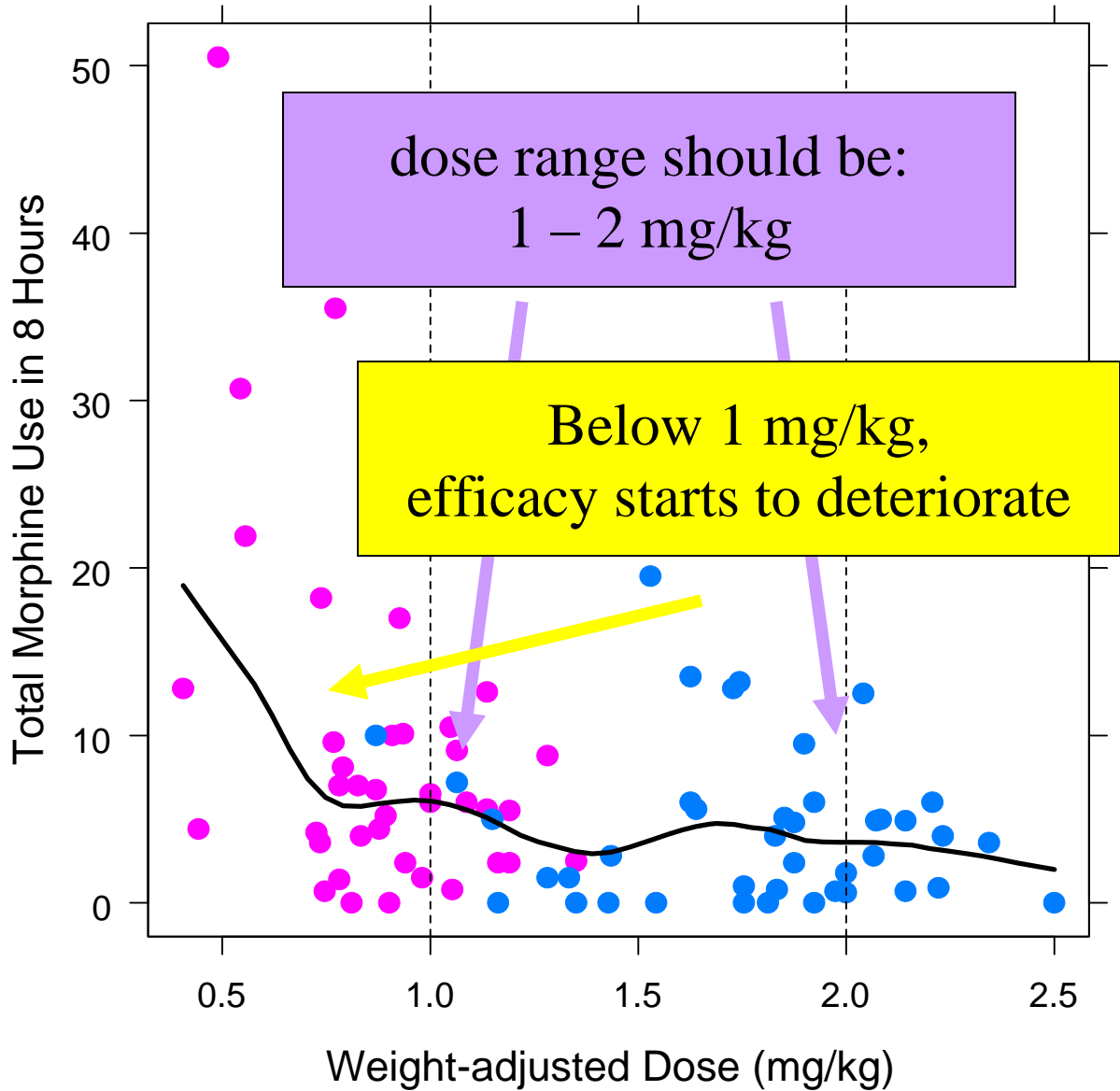
Morphine Use vs. Weight-adjusted Dose



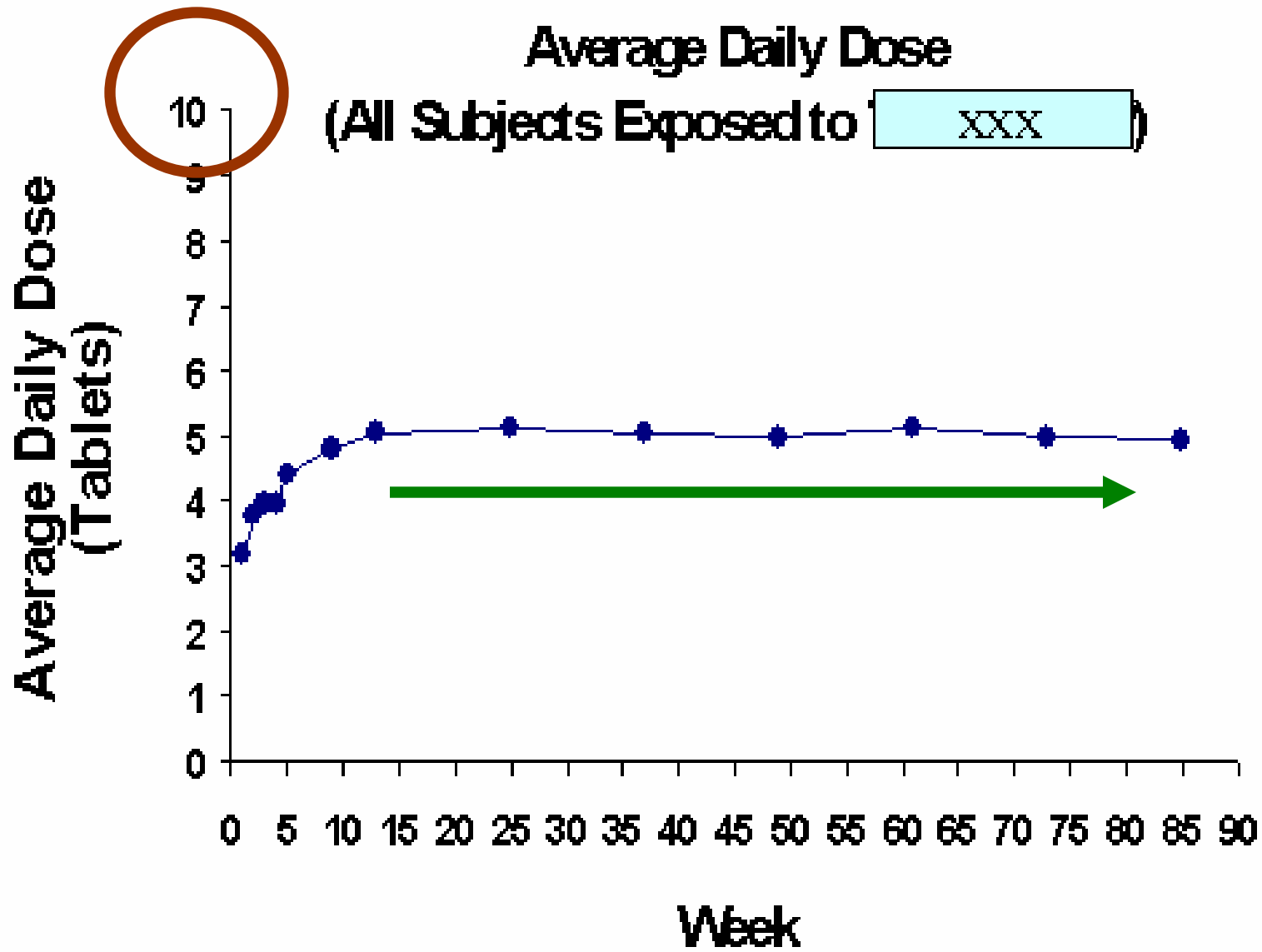
Rescue Usage vs. Weight-adjusted Dose (mg/kg)

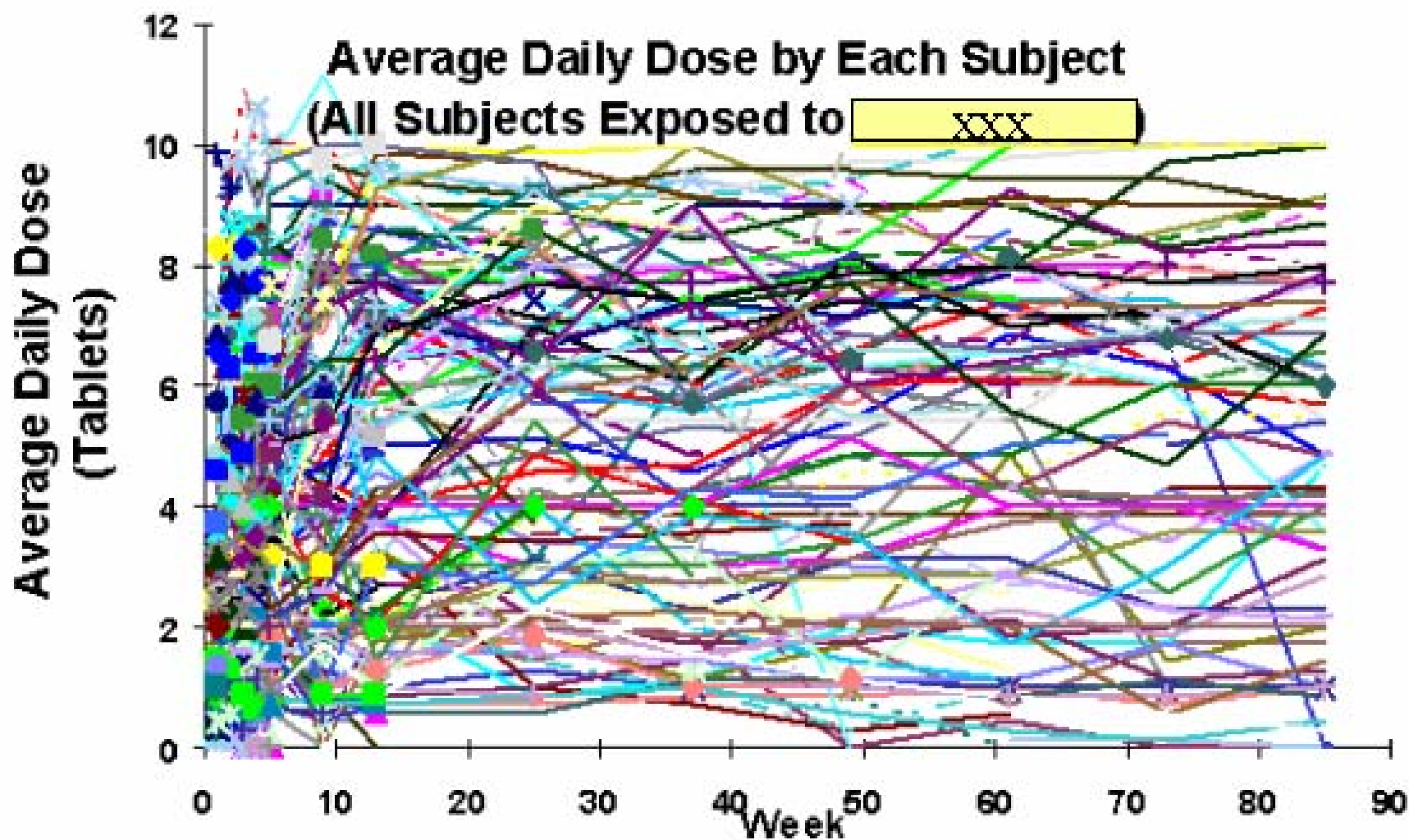


Morphine Use vs. Weight-adjusted Dose



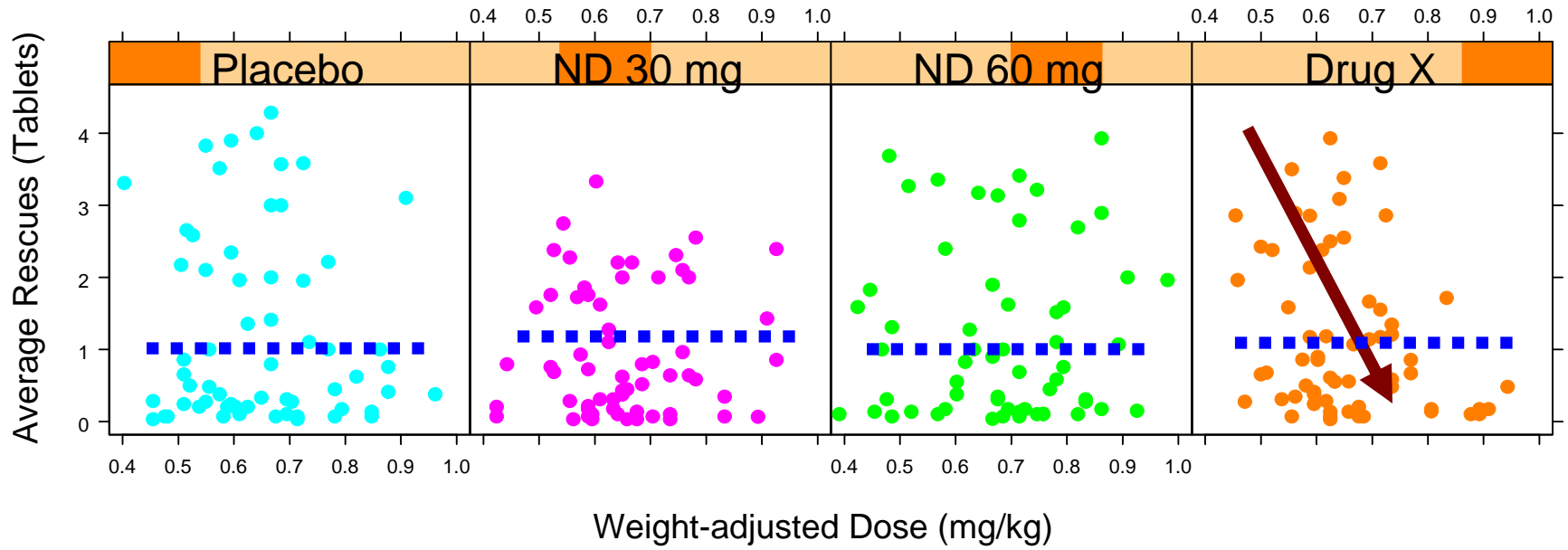
- The Drug X dose is too low.
- Study drug doses are also low.



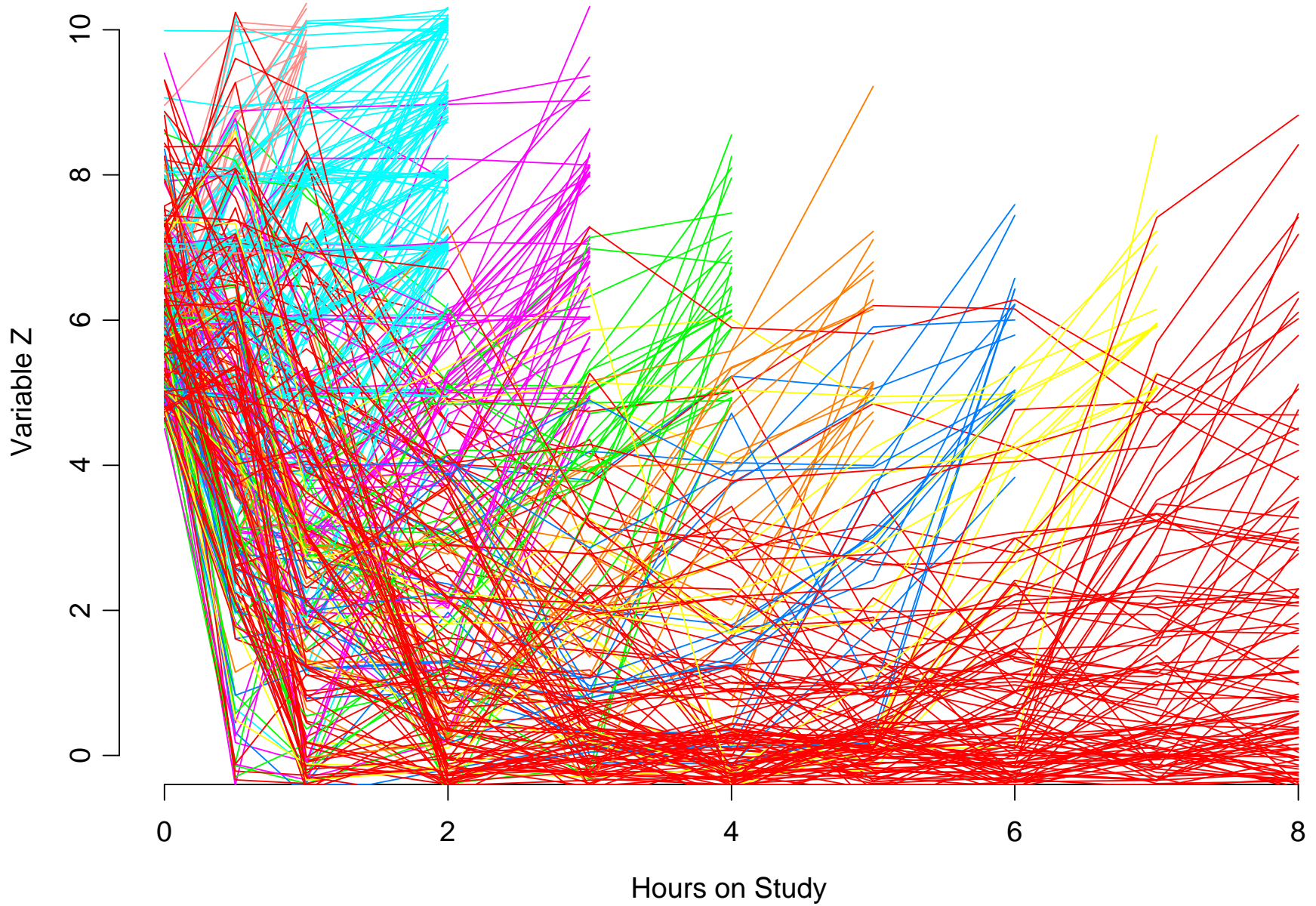


Overall **summary** statistics
can hide important
patterns in
the **subject-level** data.

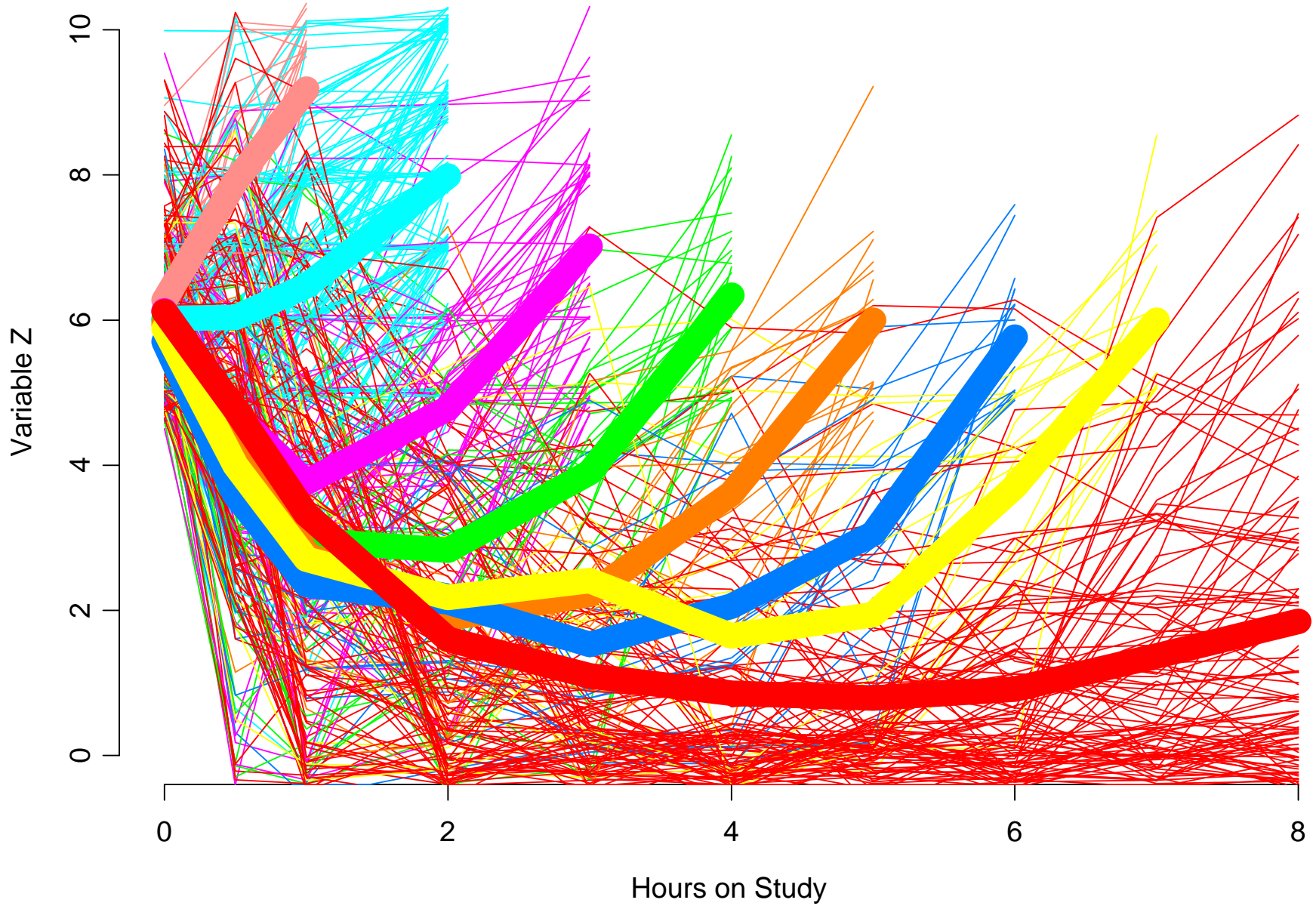
Rescue Usage vs. Weight-adjusted Dose (mg/kg)



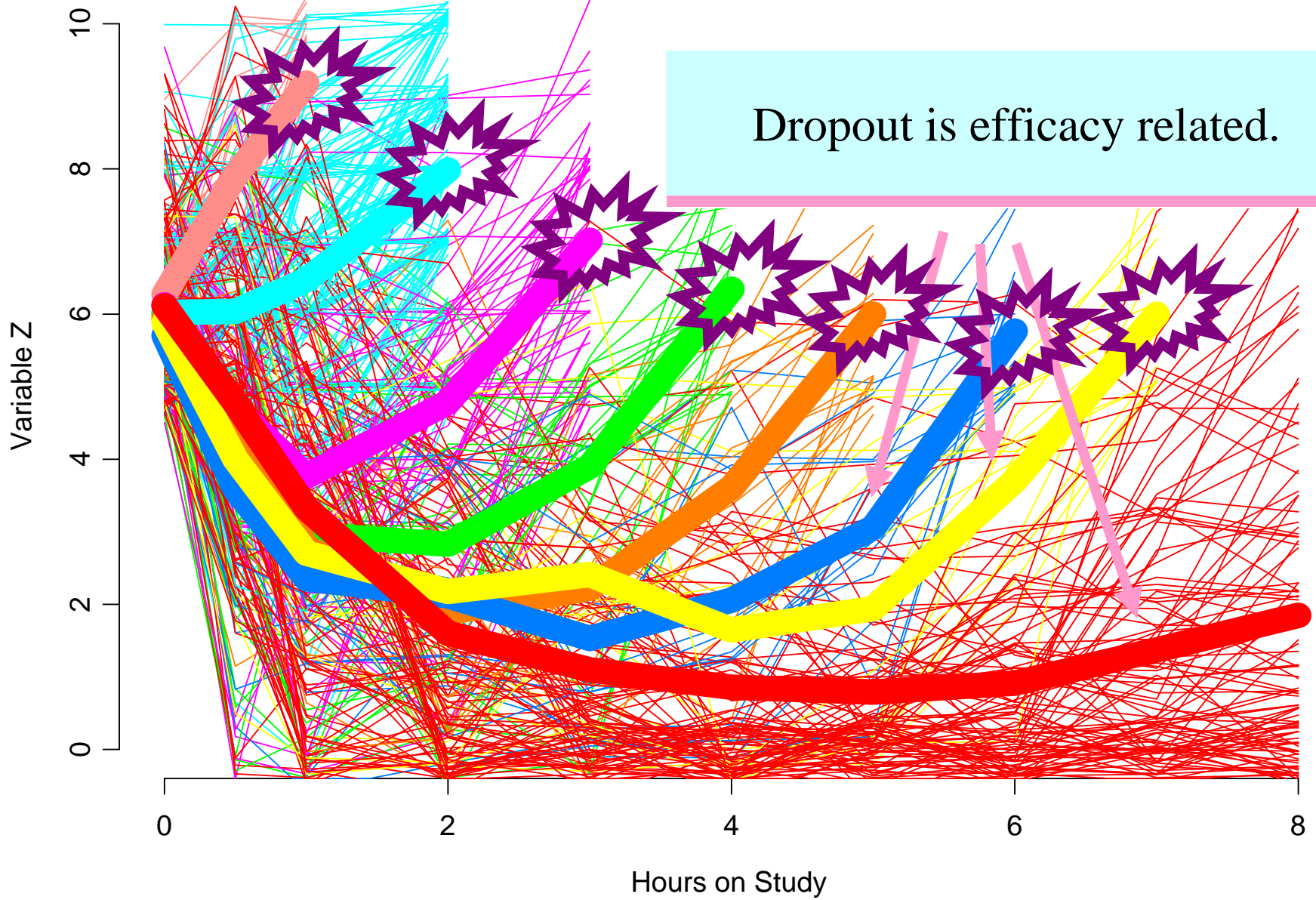
Individual Profile Over Time



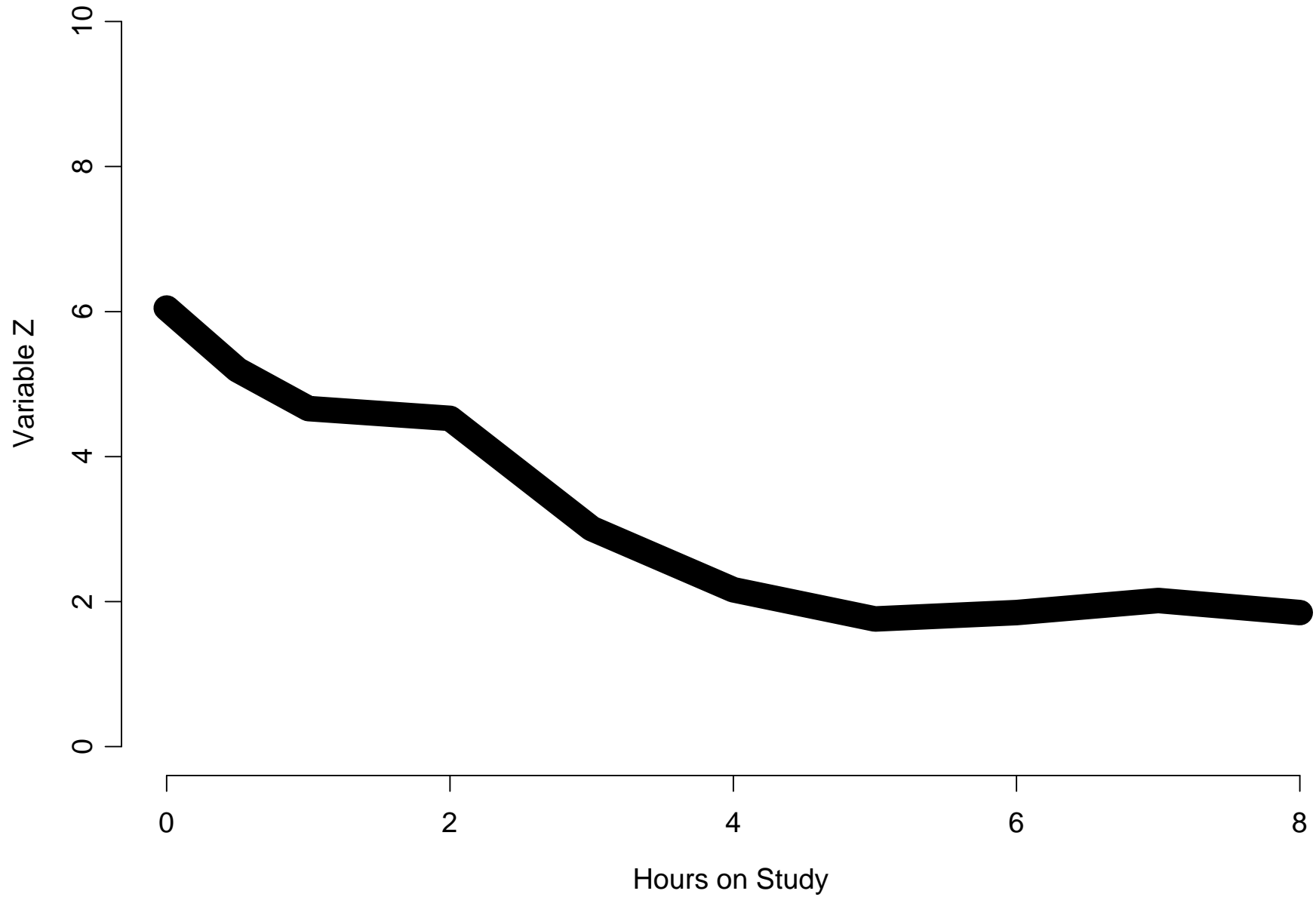
Individual Profile Over Time



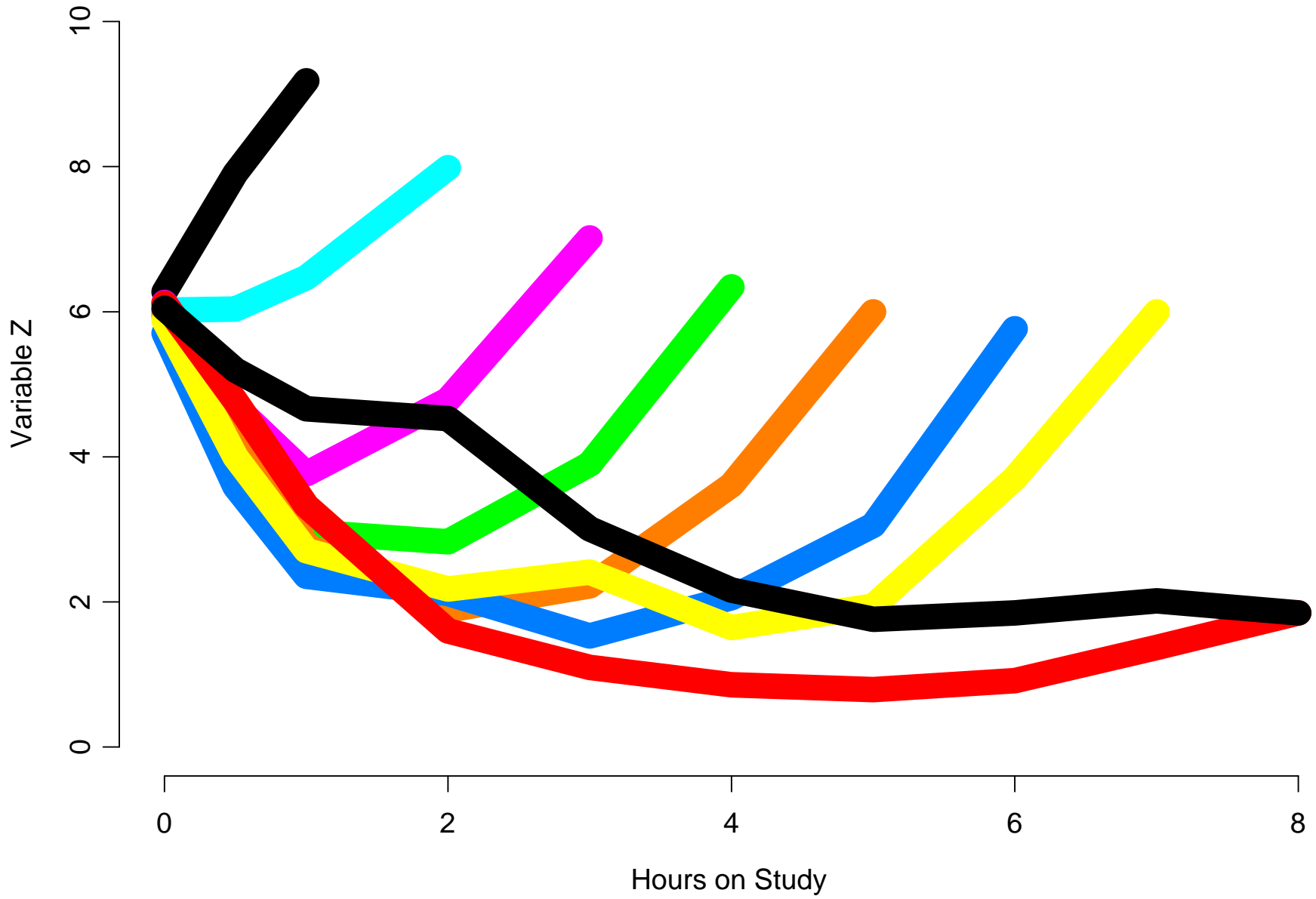
Individual Profile Over Time



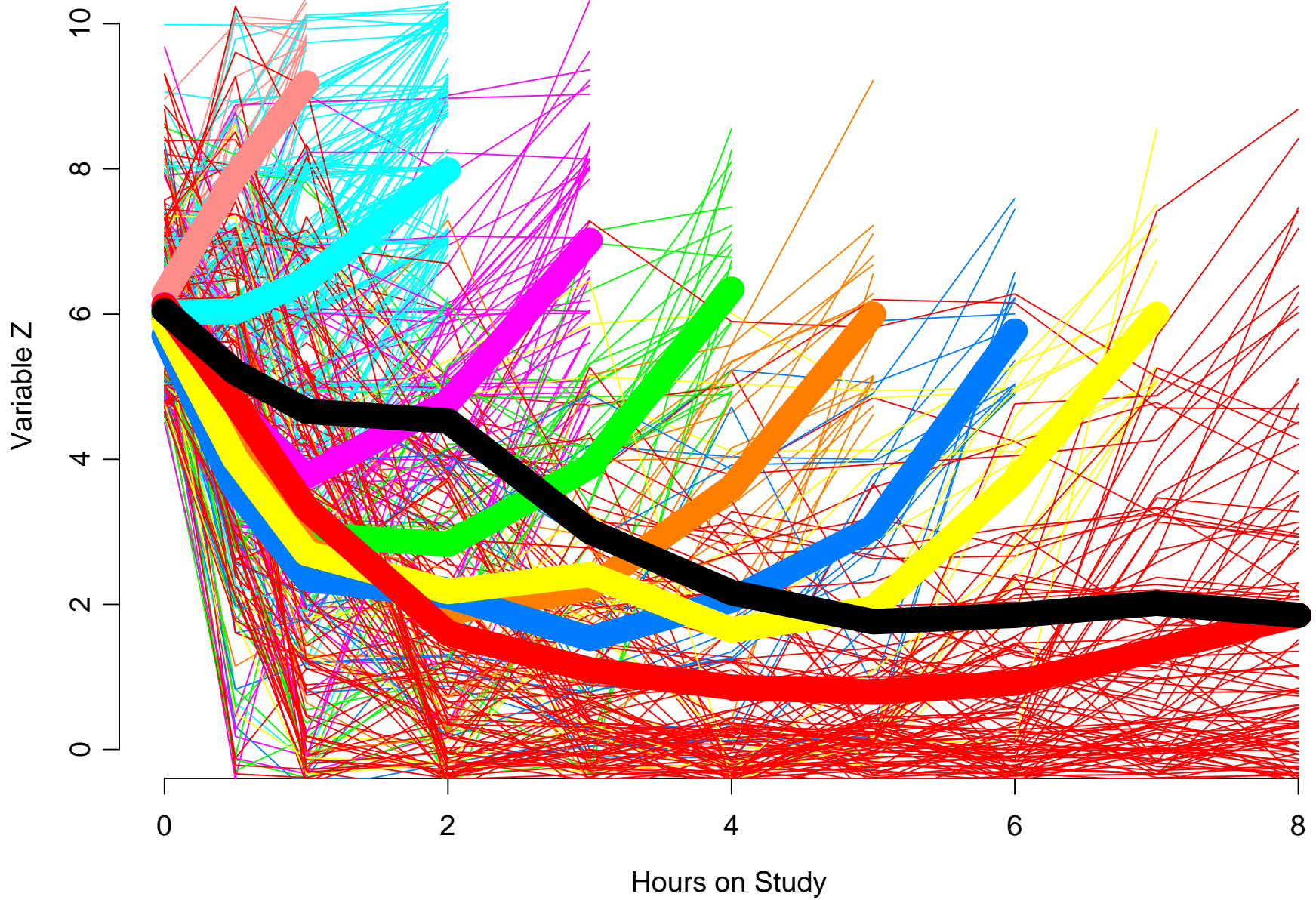
Mean Profile Over Time



Mean Profile Over Time

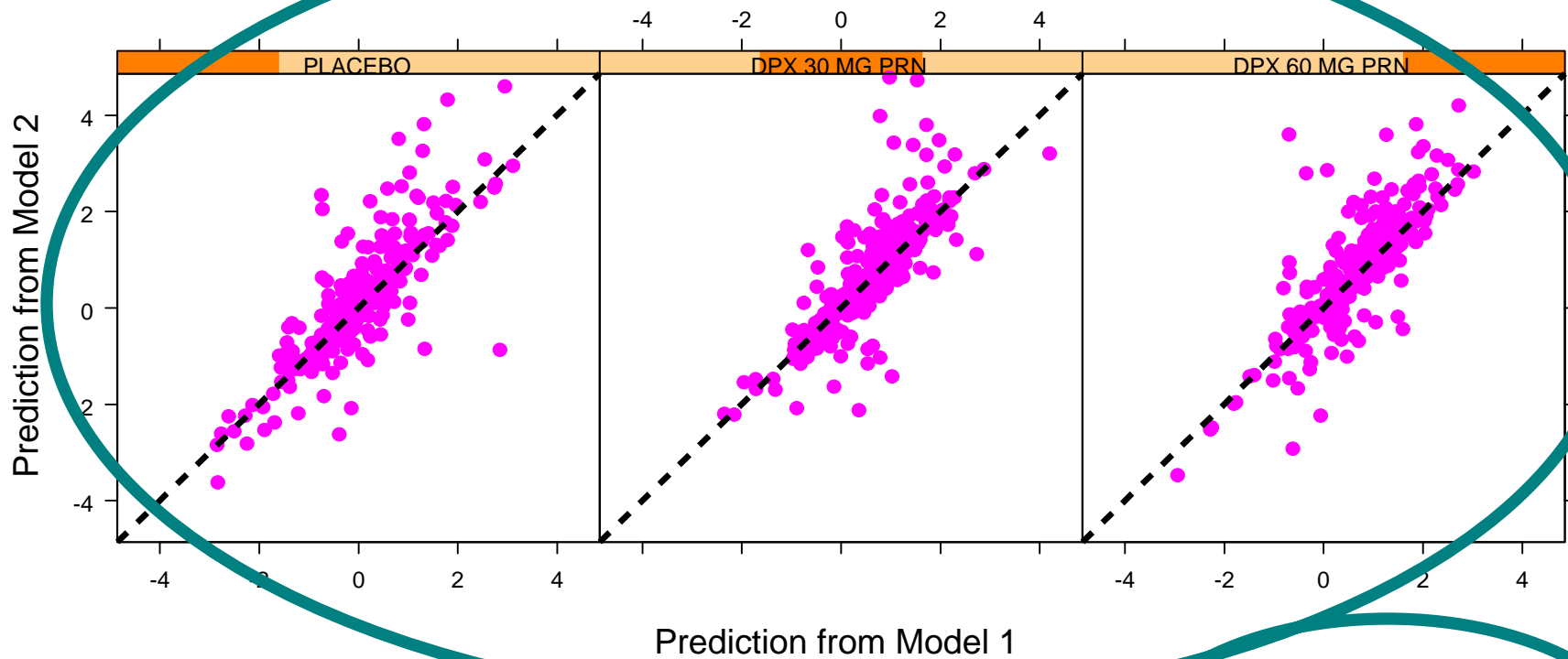


Mean Profile Over Time



Whenever possible,
we should start with the
subject-level data.

Correlation between Two Predictions



correlation with 95% CI:

Placebo (N = 288)

0.775 (0.724 , 0.817)

ND 50 mg (N = 312)

0.766 (0.716 , 0.808)

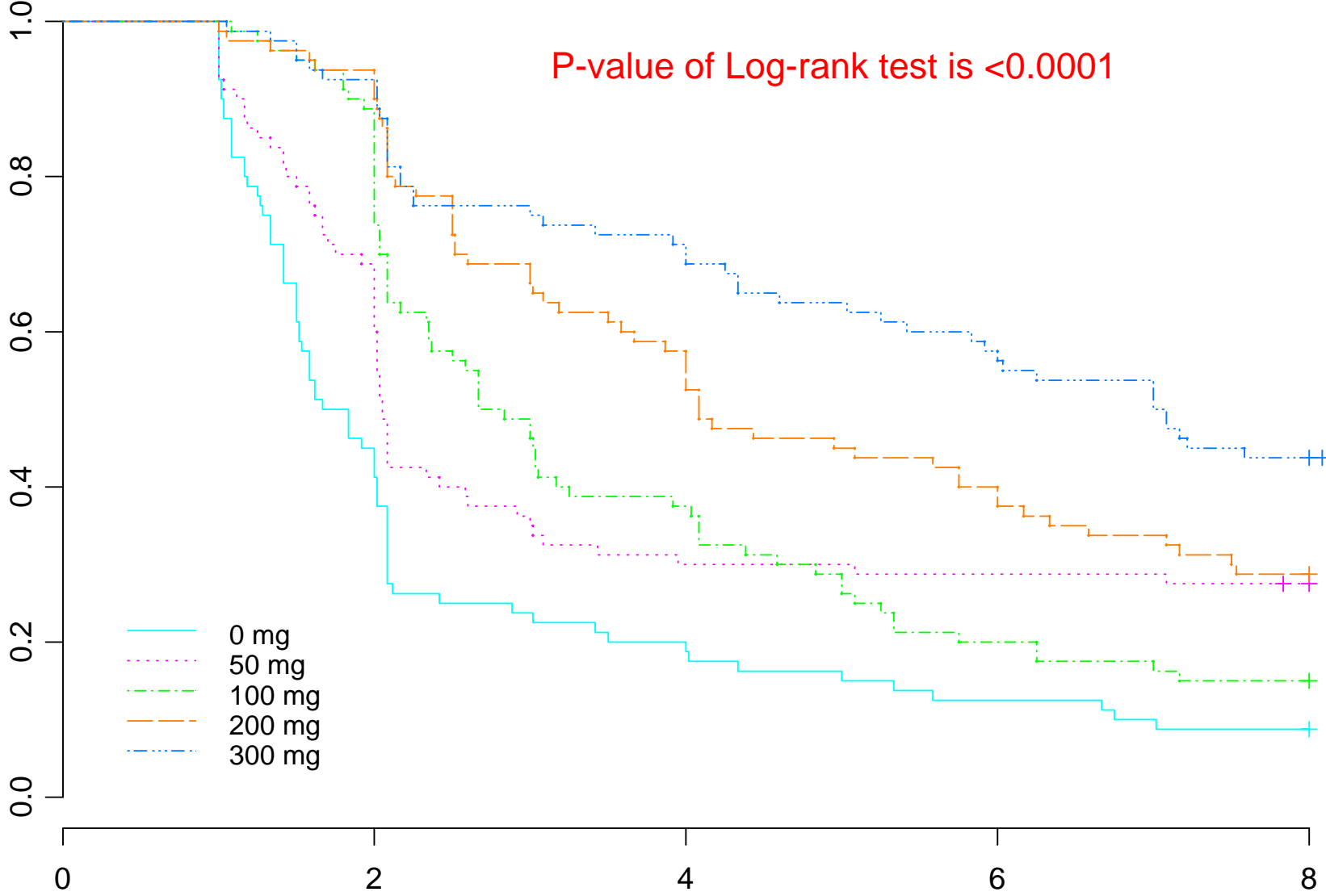
ND 100 mg (N = 292)

0.787 (0.739 , 0.827)

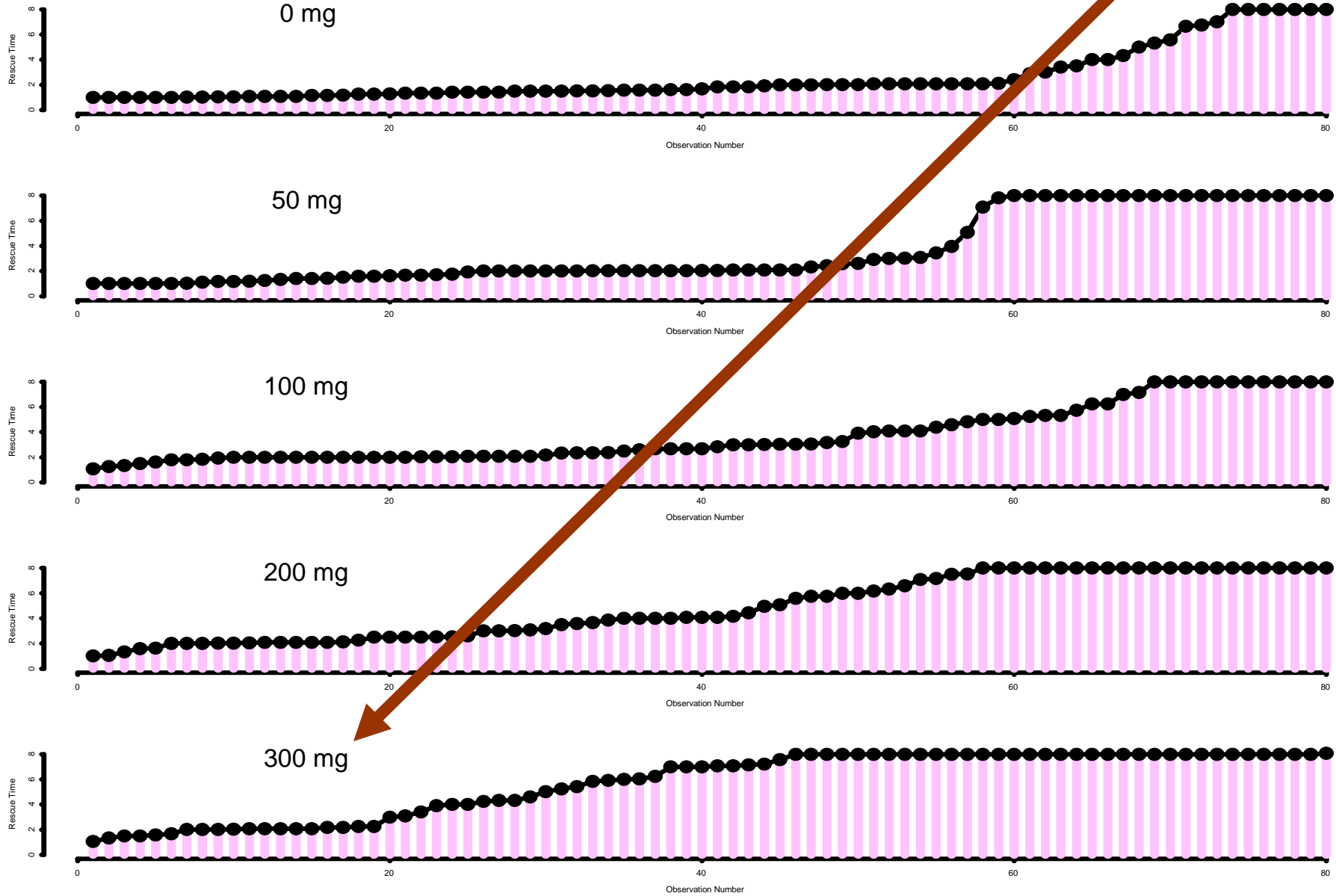
Placebo	(N=314) <u>0.391</u> <u>(0.293, 0.480)</u>	(N=288) <u>0.775</u> <u>(0.724, 0.817)</u>	(N=270) <u>0.933</u> <u>(0.915, 0.947)</u>
50 mg	(N=333) <u>0.330</u> <u>(0.231, 0.423)</u>	(N=312) <u>0.766</u> <u>(0.716, 0.808)</u>	(N=283) <u>0.919</u> <u>(0.899, 0.936)</u>
100 mg	(N=324) <u>0.332</u> <u>(0.232, 0.426)</u>	(N=292) <u>0.787</u> <u>(0.739, 0.827)</u>	(N=265) <u>0.943</u> <u>(0.928, 0.955)</u>

Kaplan-Meier Survival Curves for Time to Rescue

A Single-dose Acute Pain Study



Distribution of Time to Rescue



4 hrs

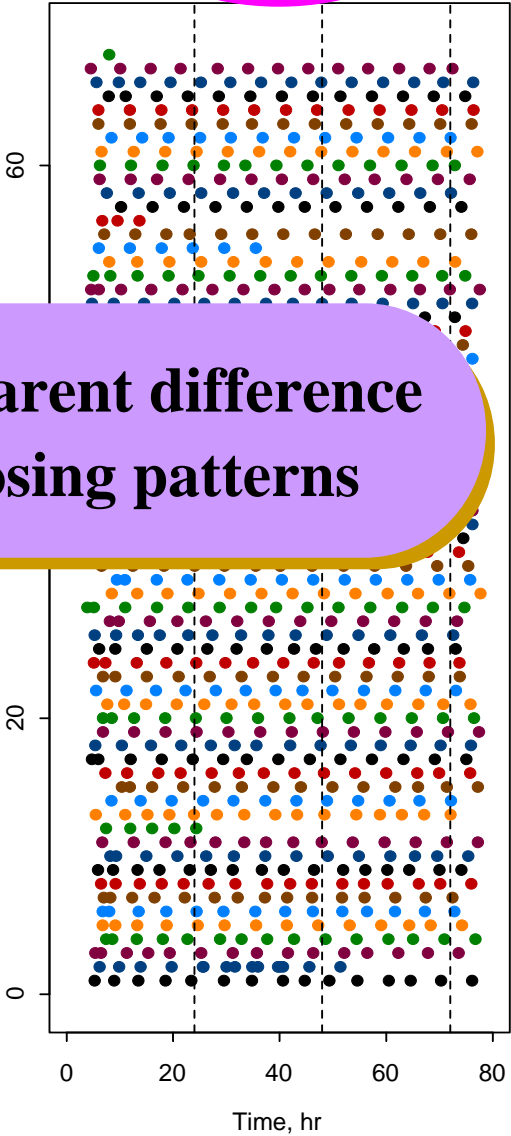
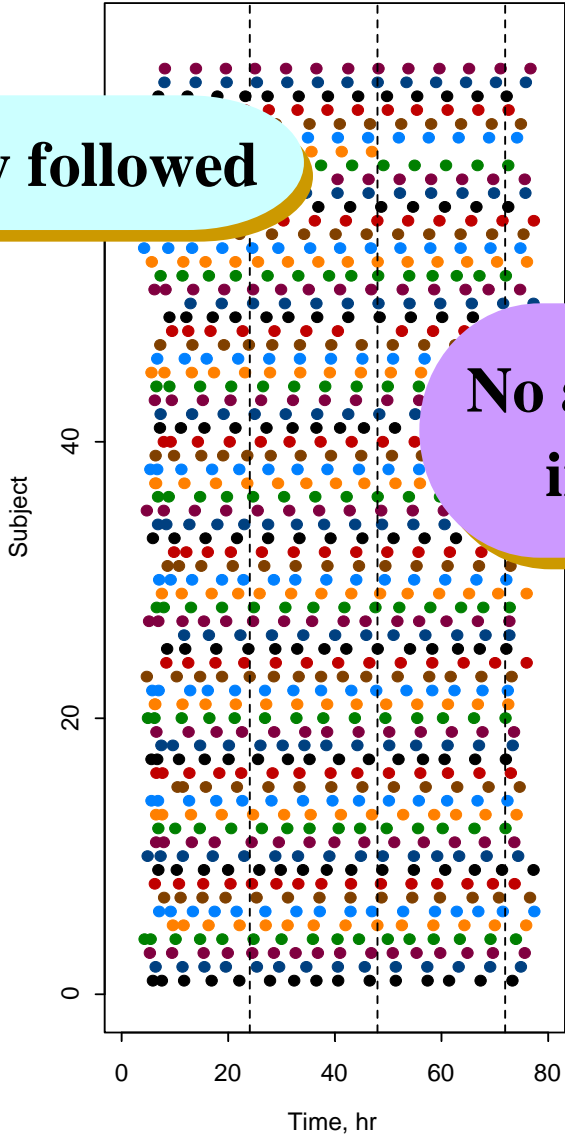
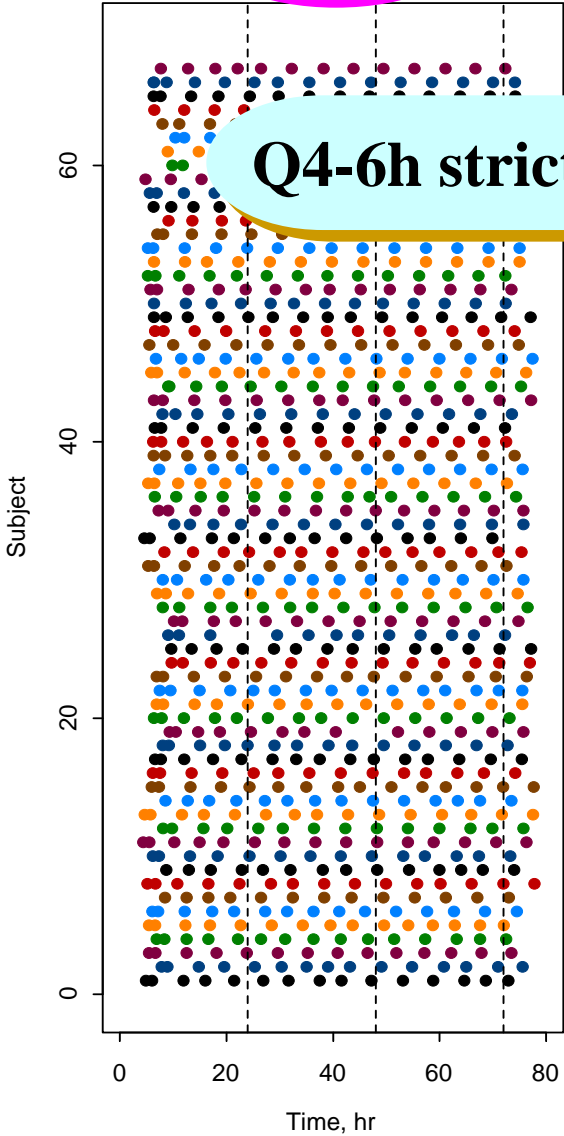
Placebo

Drug Intake

70 mg

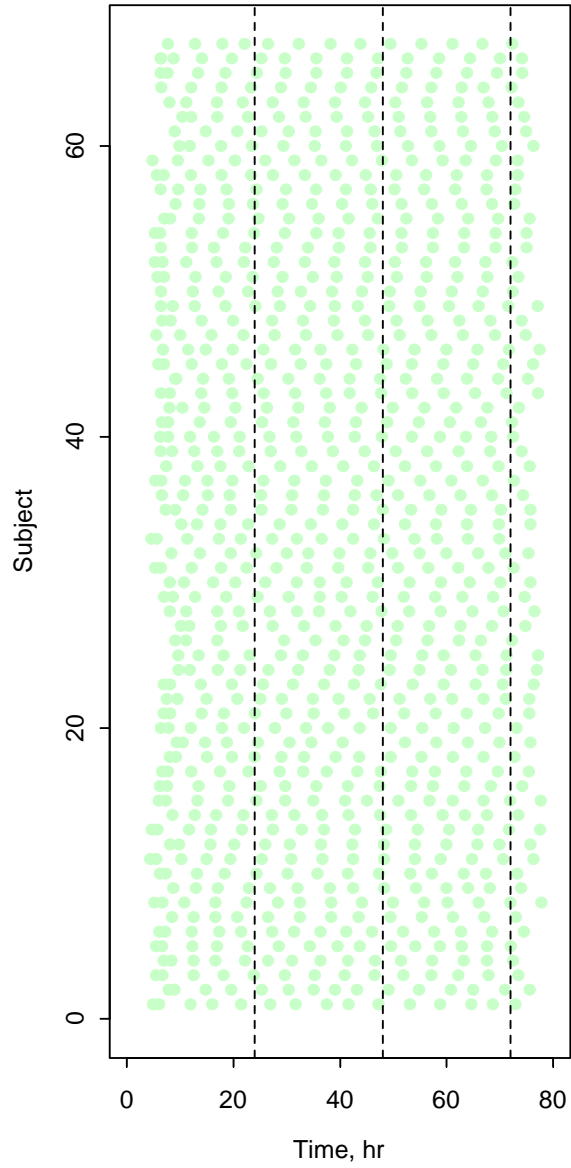
6 hrs

140 mg

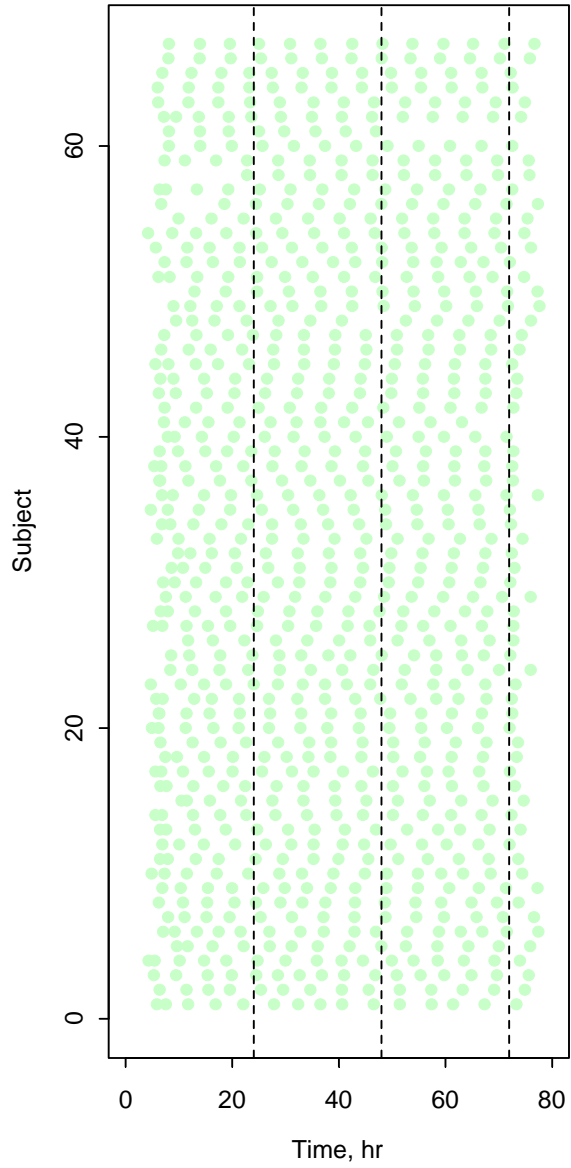


Rescue Intake

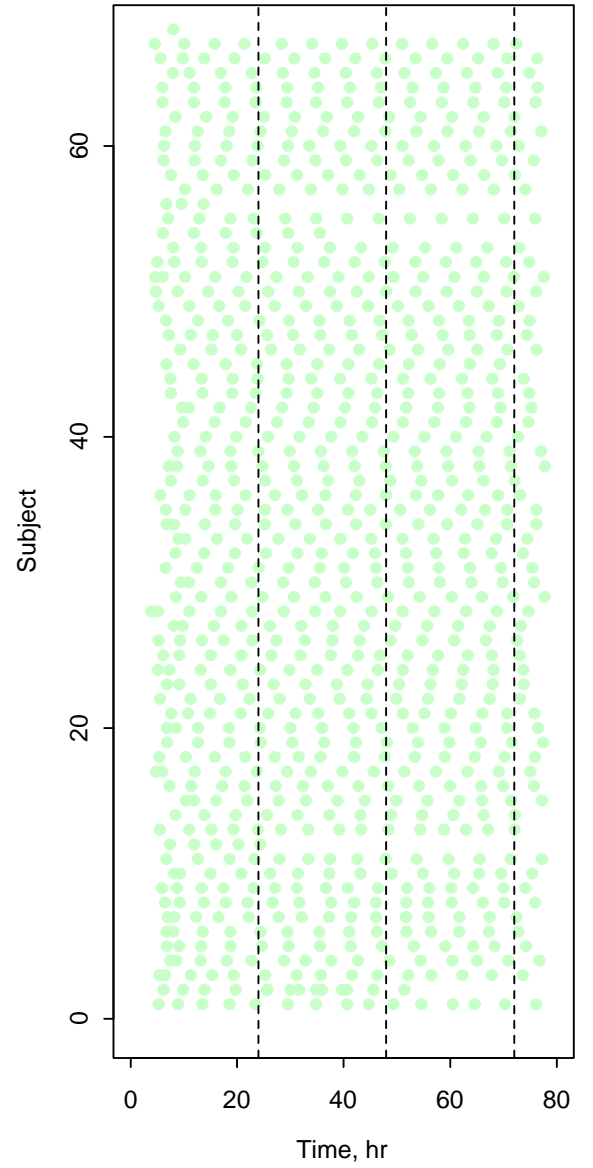
Placebo



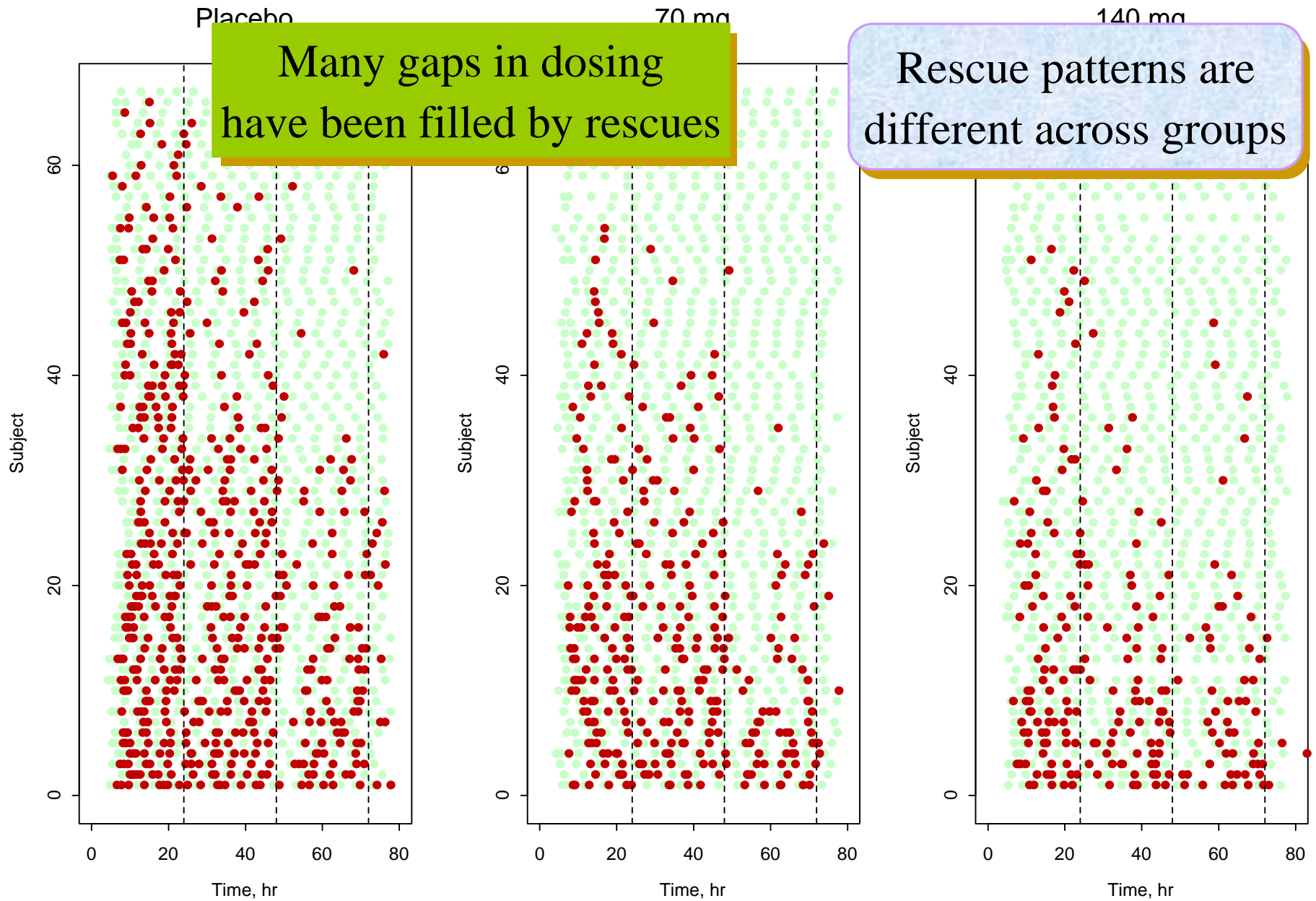
70 mg



140 mg



Rescue Intake



Conclusion

Spend more time doing graphs!