

DOSE-EFFECT RELATIONSHIP: The dose-response curves

The intensity and duration of the effect of drugs are a function of the drug dose and of the drug concentration at the effect site

Dose-Effect Endpoints

Two types of Dose-response curves:

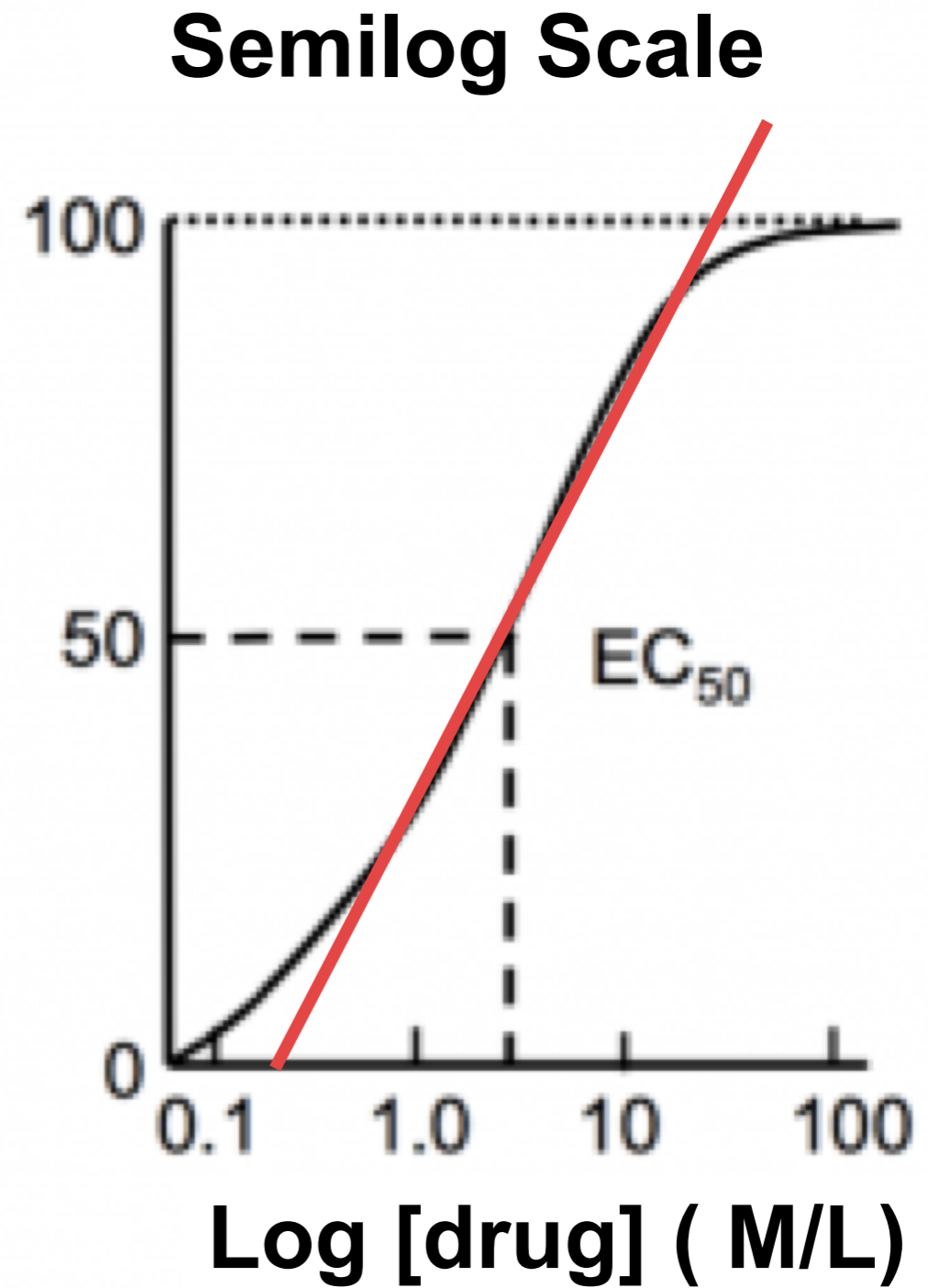
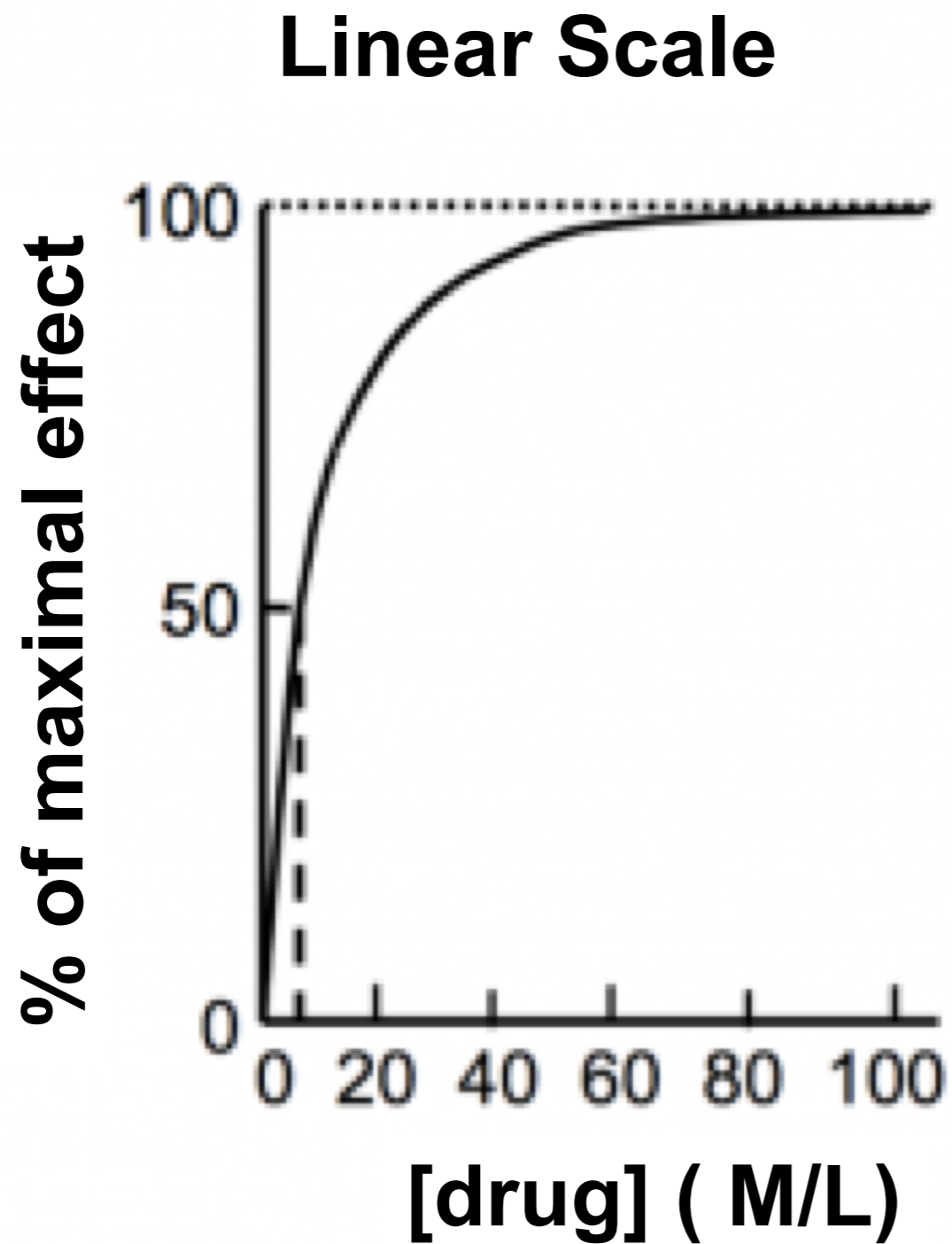
Graded

- Continuous scale (\uparrow dose , \uparrow effect)
- Measured in a single biologic unit
- Relates dose to intensity of effect

Quantal

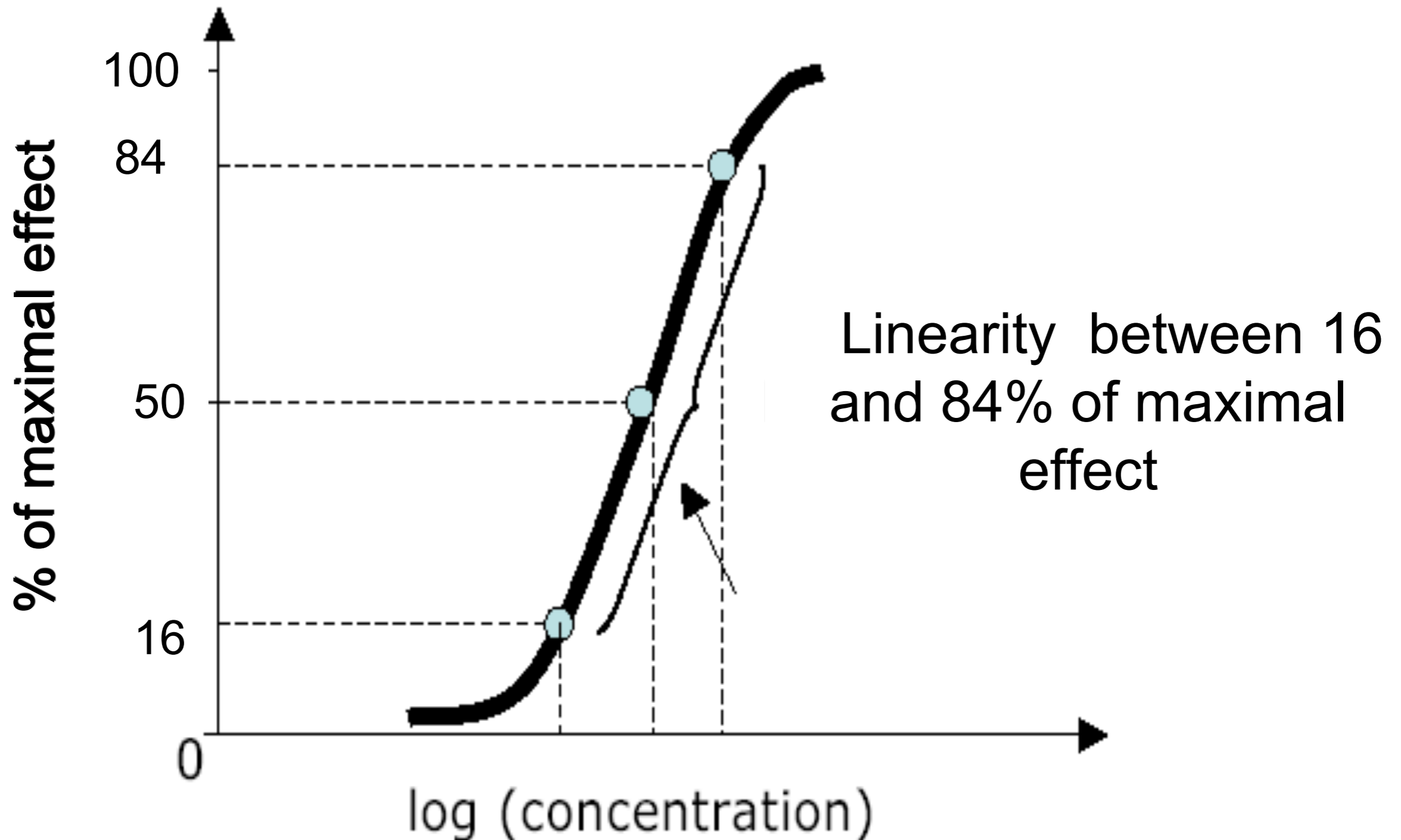
- All-or-none pharmacologic effect
- Population studies
- Relates dose to frequency of effect

Graded Dose-Response Curves



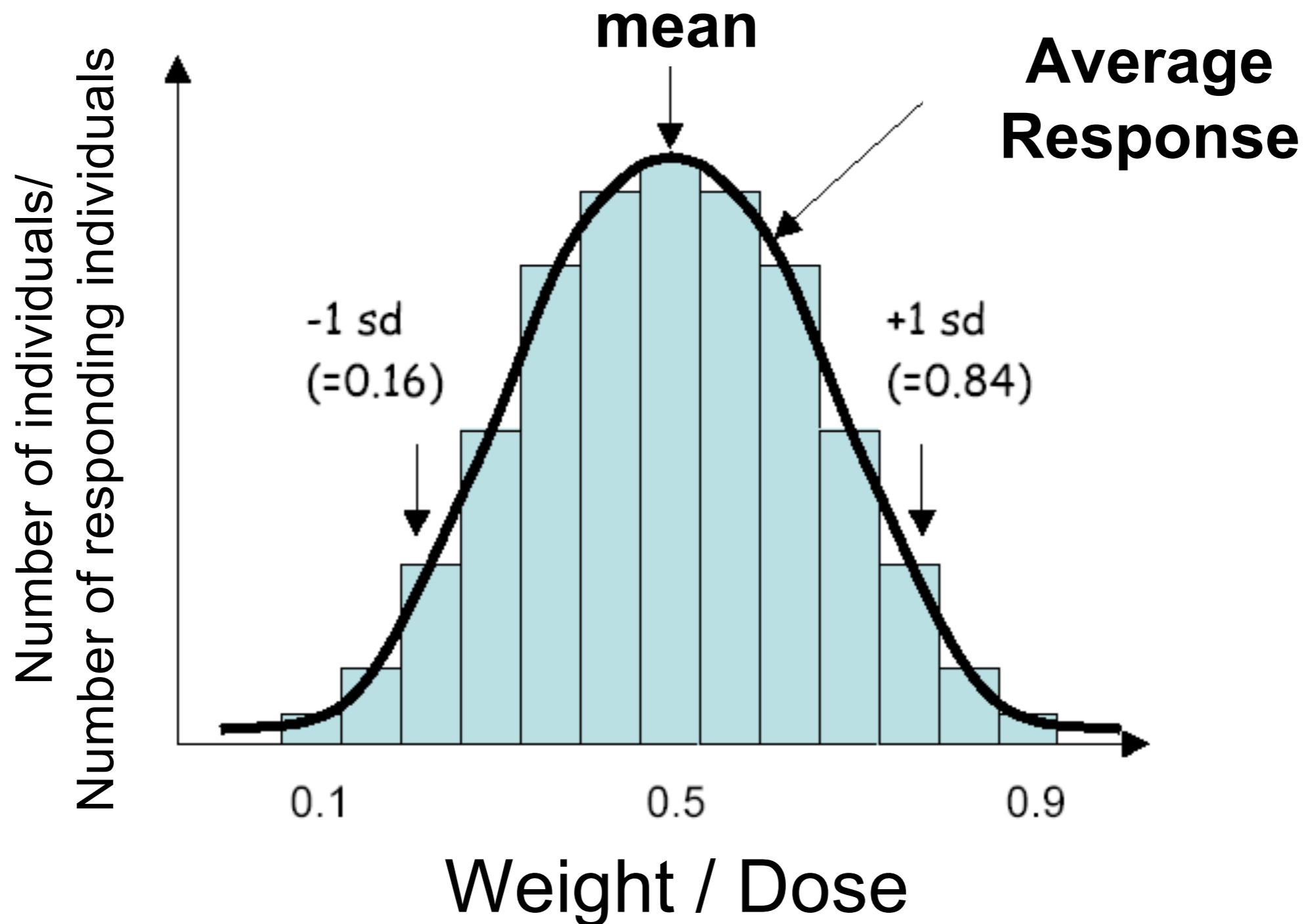
EC₅₀: concentration that gives the half maximal effect

Litchfield-Wilcoxon method for determining EC_{50}



Quantal Dose-Response Curves

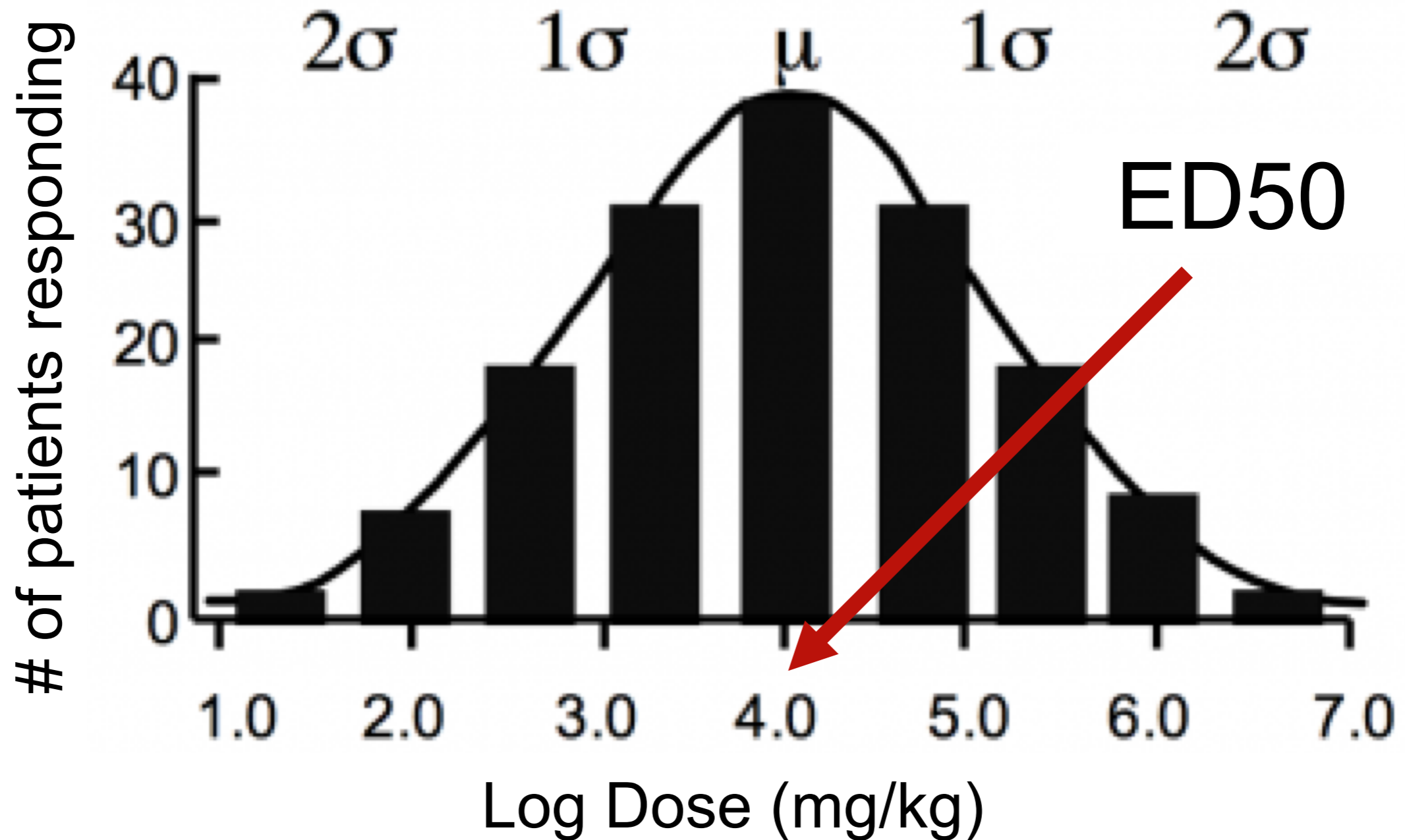
Quantal Dose-response models are based on normal distribution of biological variables



Quantal Dose-Effect Study

Dose	No. of Responding Subjects
1	0
2	1
3	3
4	5
5	7
6	2
7	1
8	1

Quantal Dose-Effect Curve: Frequency distribution

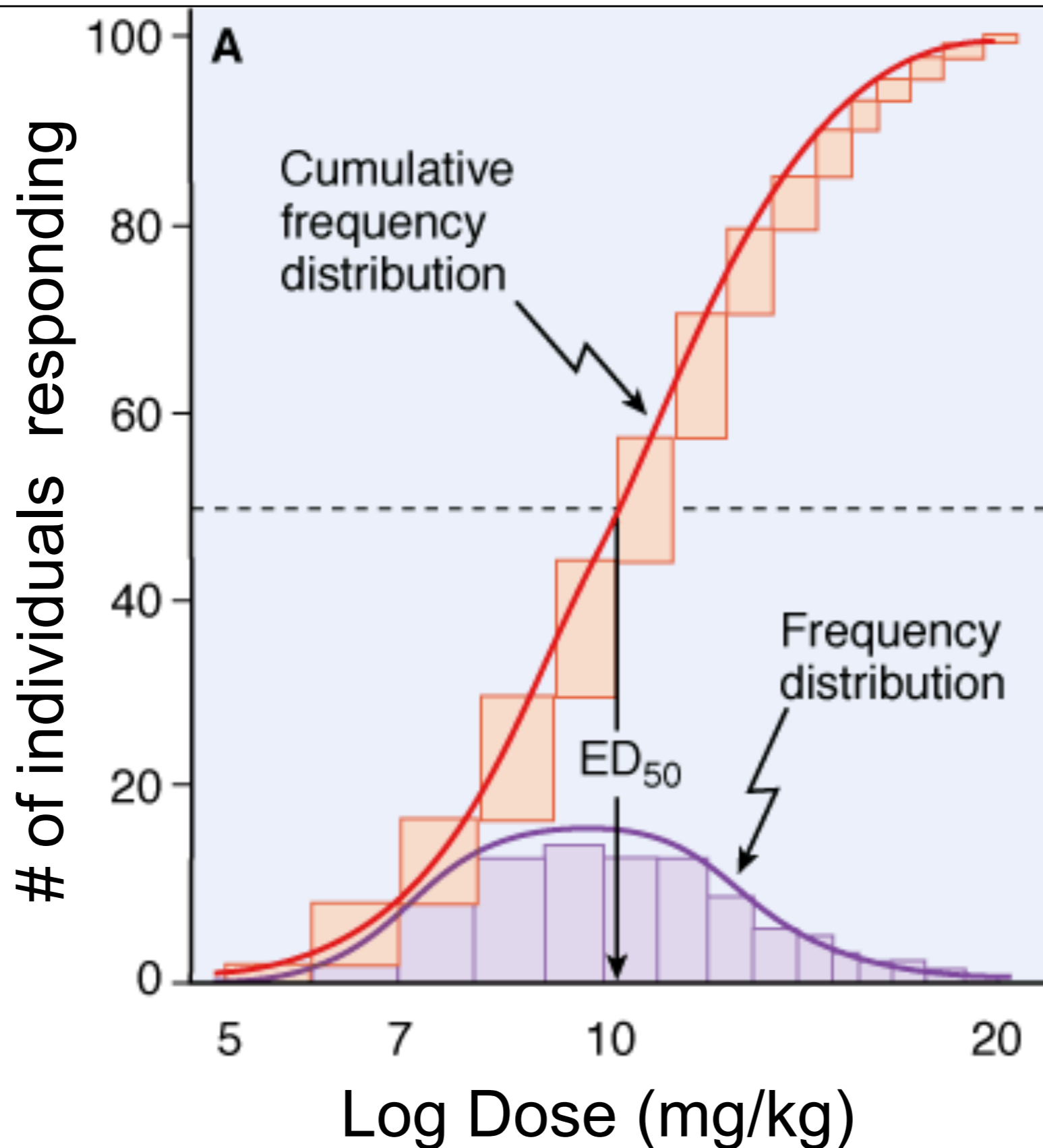


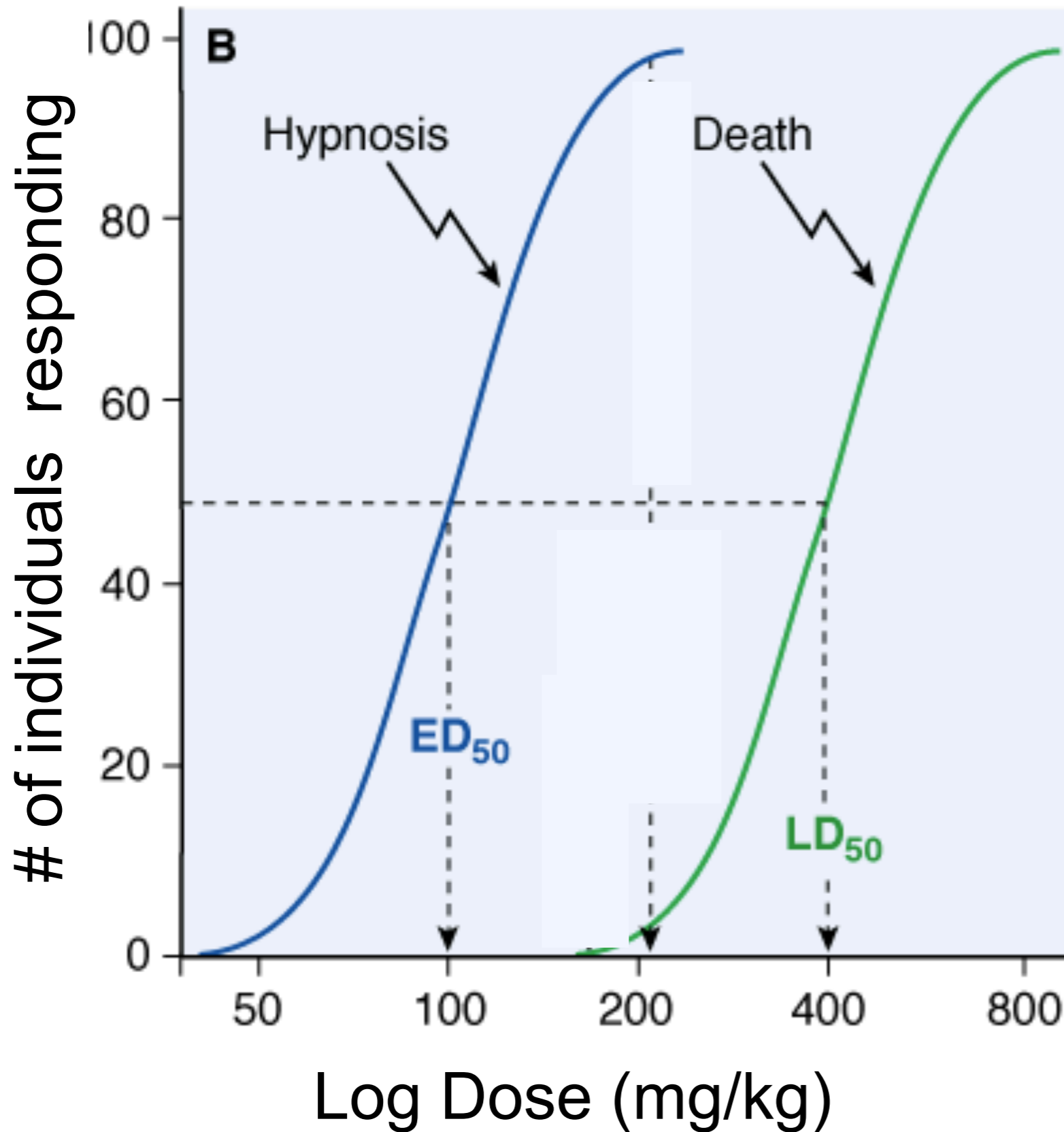
ED50: dose required to produce the therapeutic effect in 50% of the population

Quantal Dose-Effect Study

Dose	No. of Responding Subjects	Cumulative Response
1	0	0
2	1	1
3	3	4 (3+1)
4	5	9 (5+4)
5	7	16 (9+7)
6	2	18 (16+2)
7	1	19 (18+1)
8	1	20 (19+1)

Quantal Dose-Effect Curve: Cumulative Frequency distribution

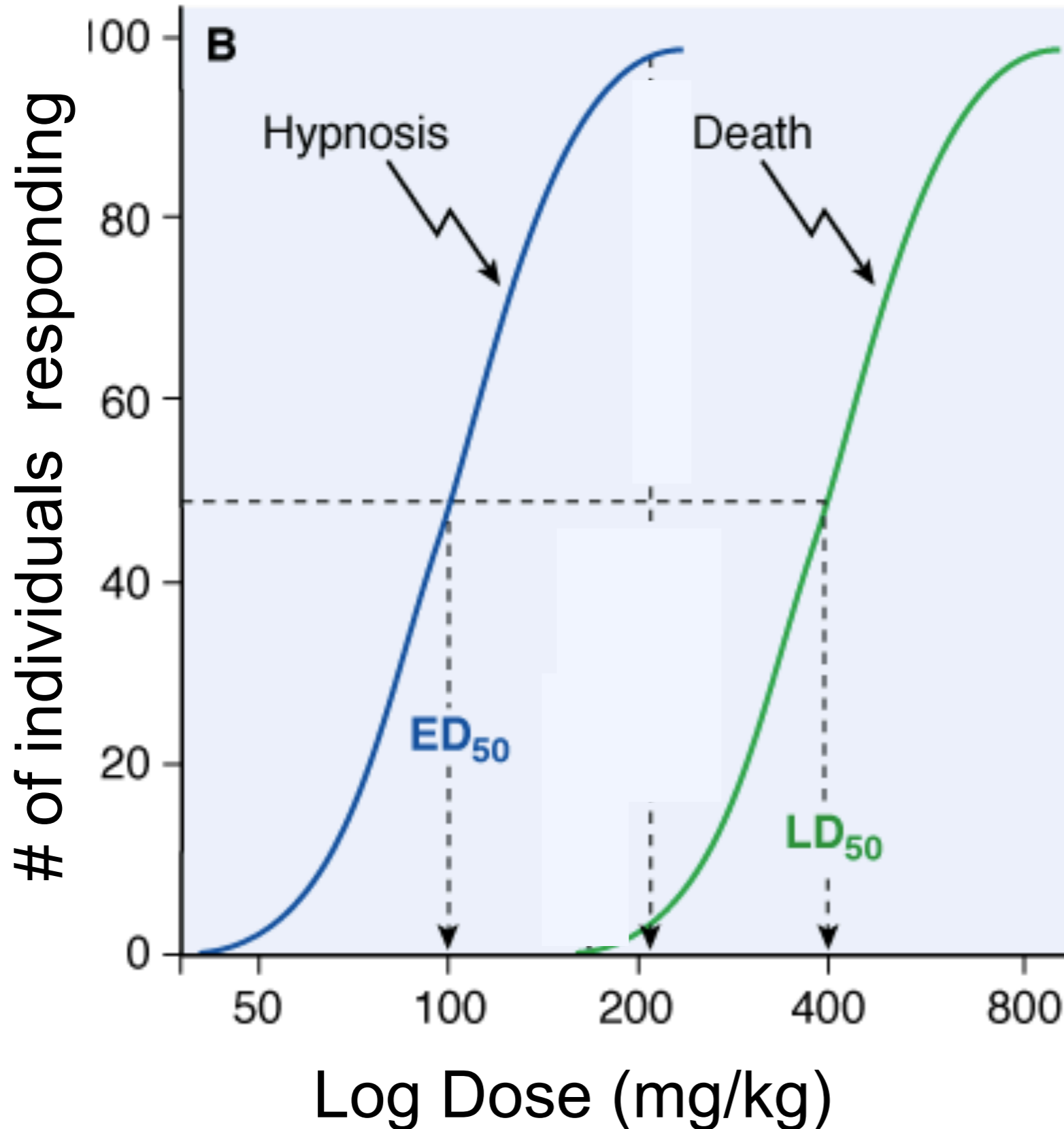




ED₅₀: dose required to produce a therapeutic effect in 50% of the population

LD₅₀: lethal dose in 50% of the population

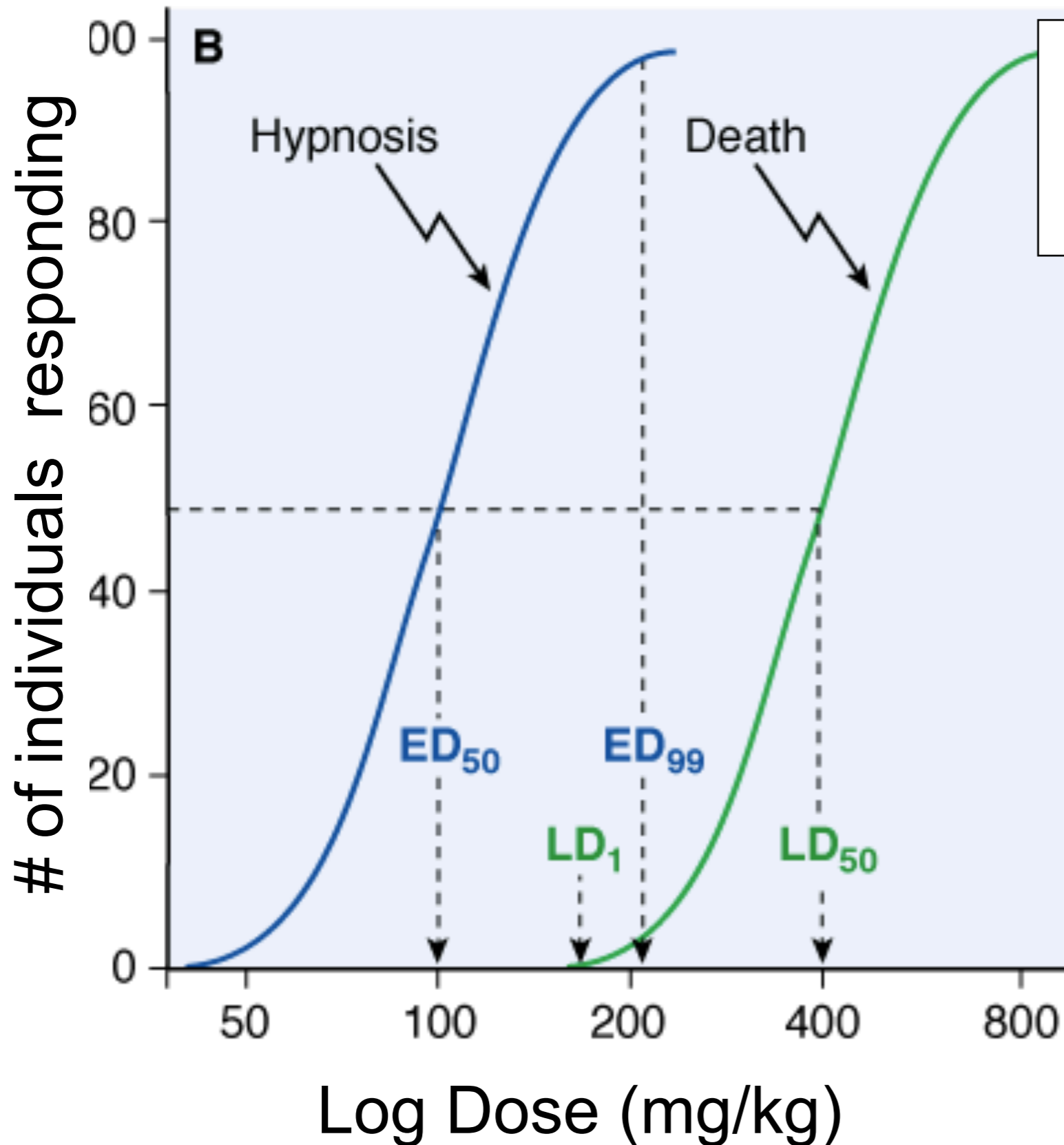
Therapeutic Index: $\frac{LD_{50}}{ED_{50}} = \frac{400}{100} = 4$



ED50: dose required to produce a therapeutic effect in 50% of the population

LD50: lethal dose in 50% of the population

$$\text{Therapeutic Index: } \frac{LD_{50}}{ED_{50}} = \frac{400}{100} = 4$$



$$\text{Margin of Safety: } \frac{LD_1}{ED_{99}} = \frac{160}{230} = 0,70$$

ED₉₉: dose required to produce a therapeutic effect in 99% of the population

LD₁: letal dose in 1% of the population

The Therapeutic Ratio does not take into account the slope of the dose-response curves

Drugs A and B have the same Therapeutic Ratio (same ED₅₀) but A is more safe than B

The Safety Factor, ratio of ED₉₉ to TD₁, better describes the safety degree of a drug

