biostat/epi:
for the USMLE Step 1 +
a light primer for topics in EBM

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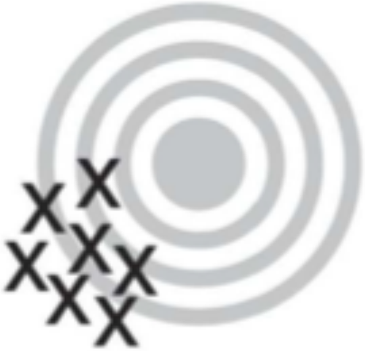
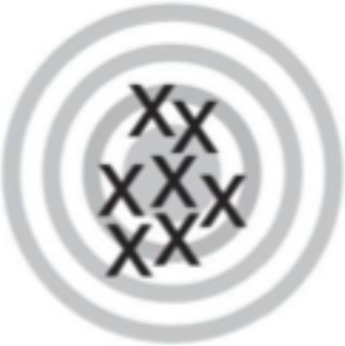
how well do we measure something

precision

consistent, reproducible, reliable

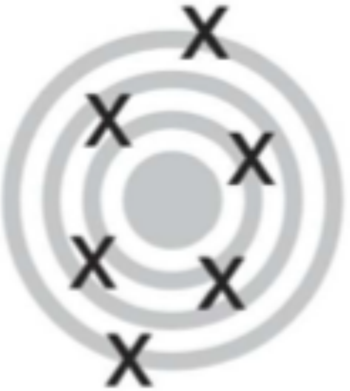


precise and accurate

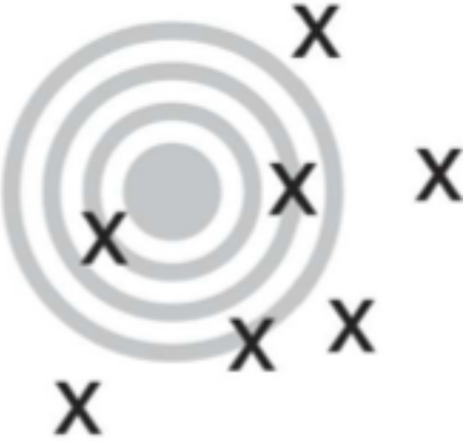


accuracy

validity



not precise and not accurate



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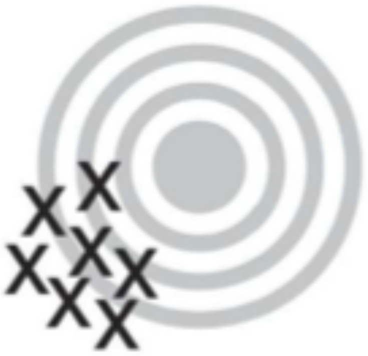
images from First Aid for the USMLE Step1, 2011

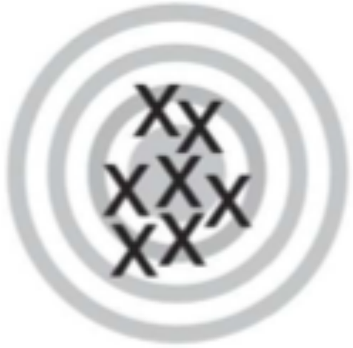
how well do we measure something

precision

random errors = low precision

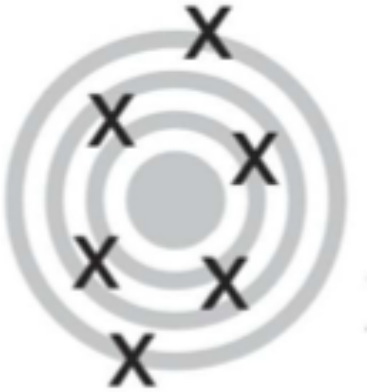


precise and accurate

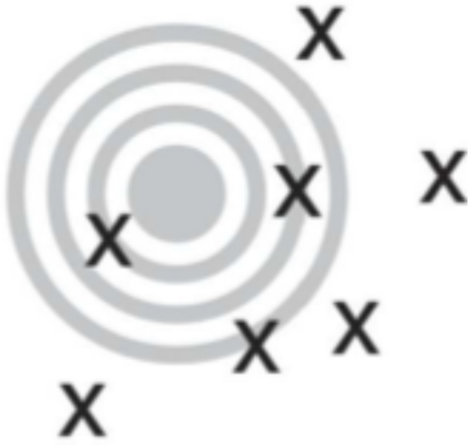


accuracy

systematic errors = low accuracy



not precise and not accurate



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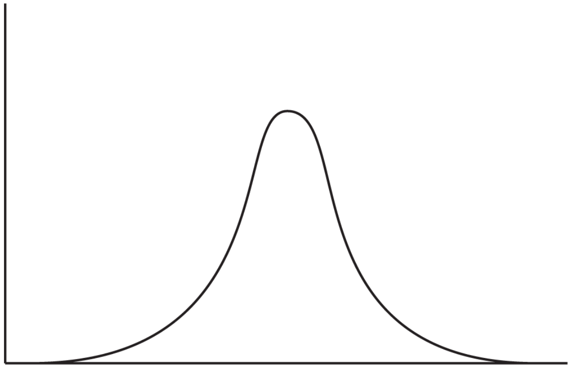
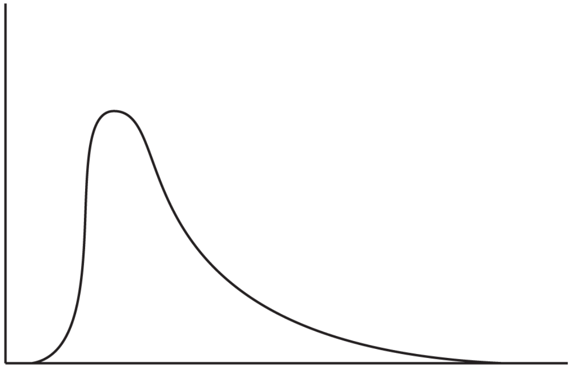
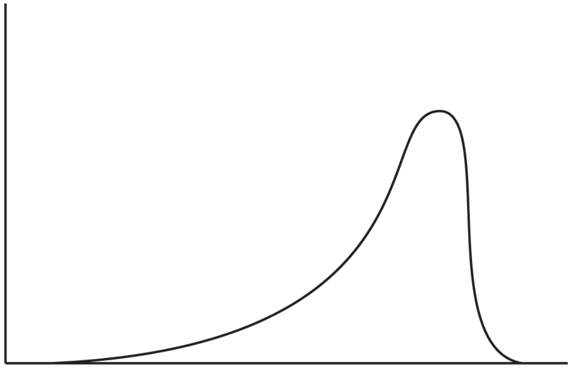
images from First Aid for the USMLE Step1, 2011

distribution

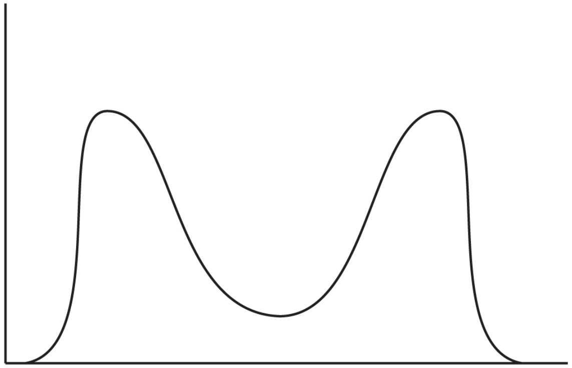




right skew



left skew



bimodal

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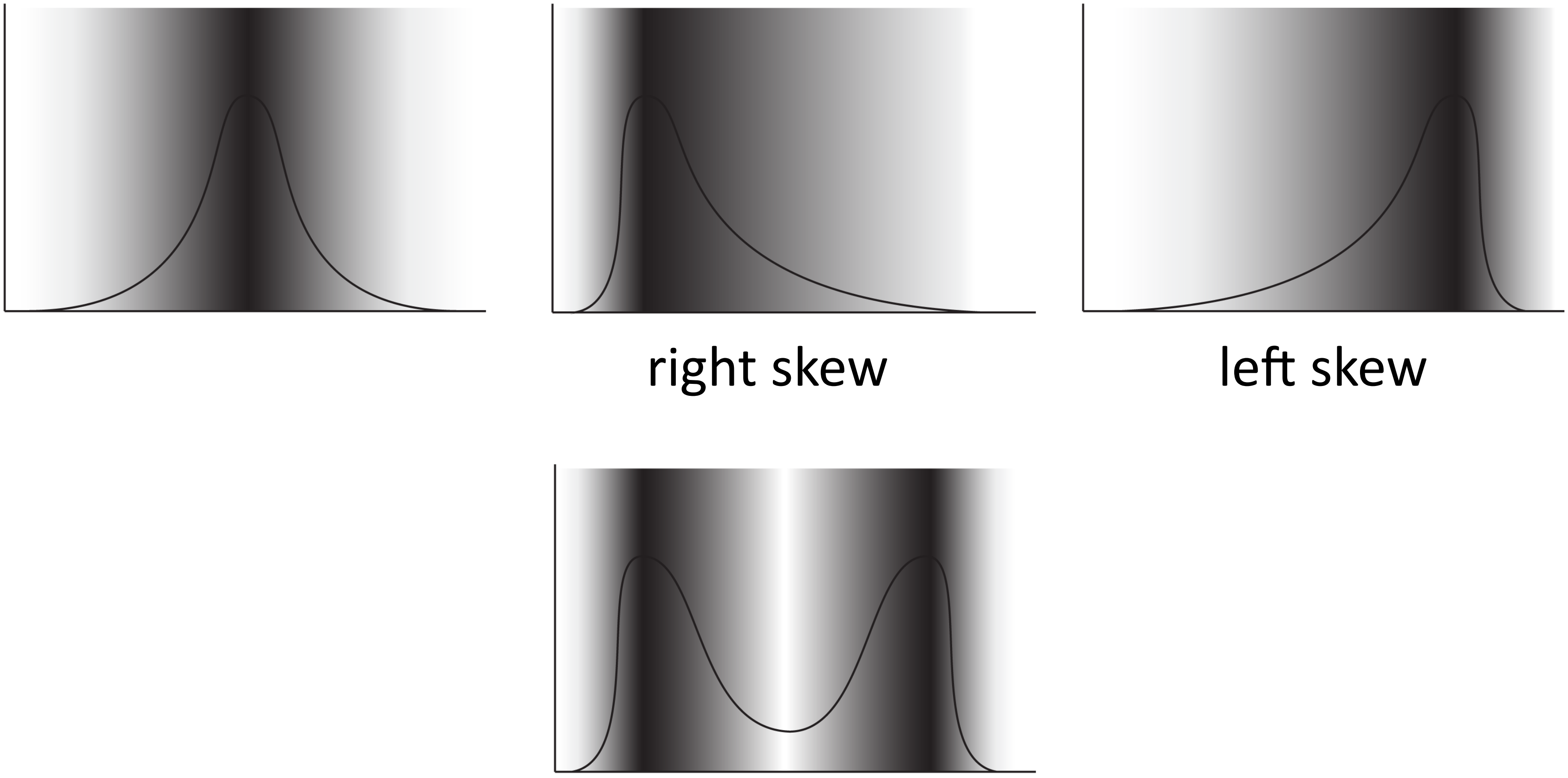
distribution



right skew

left skew

bimodal

sample density

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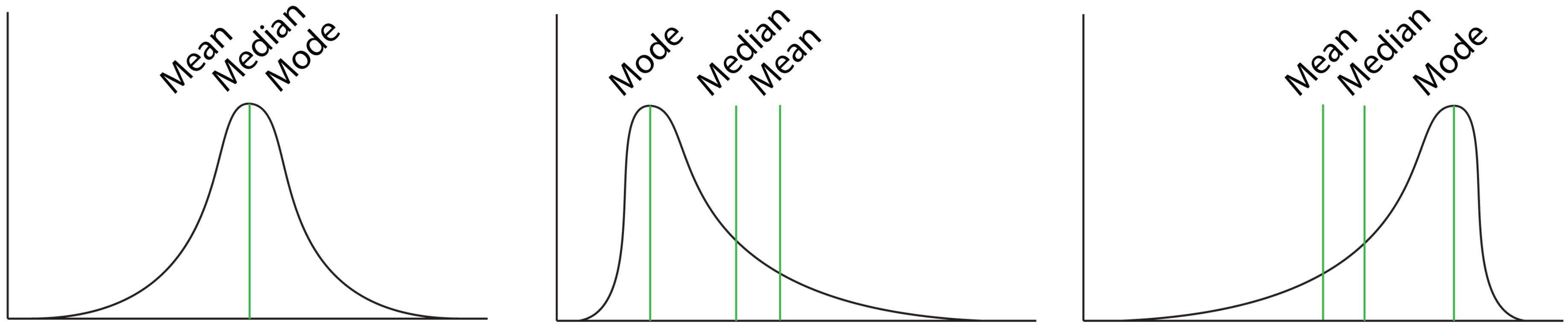
distribution



right skew

left skew

central tendency

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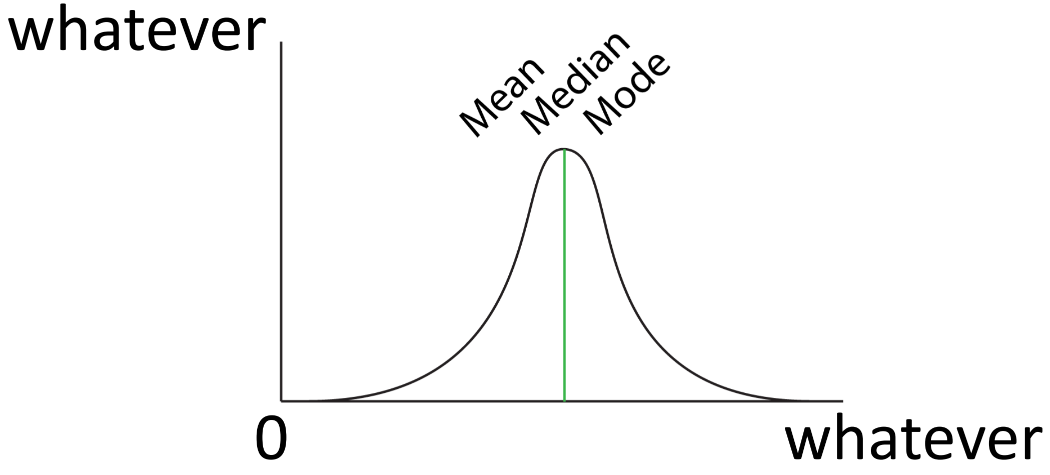
distribution



Gaussian aka Normal

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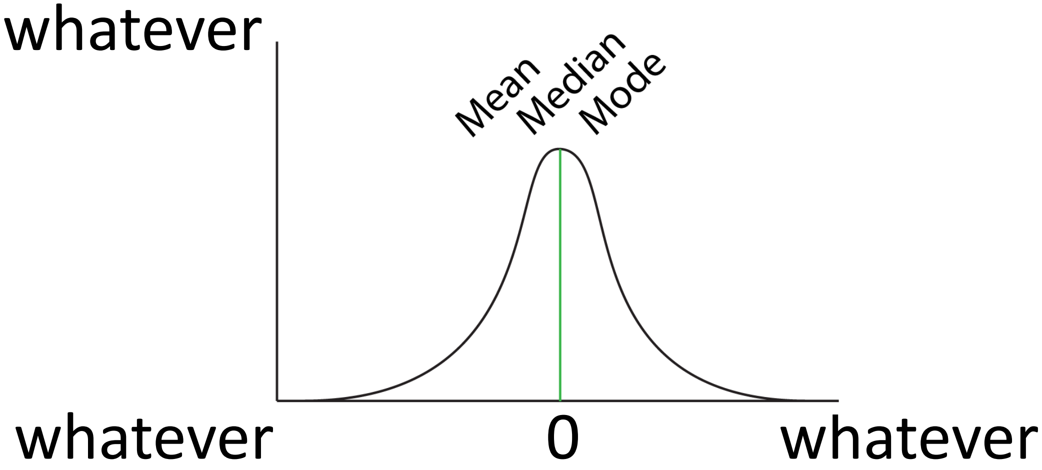
distribution



Standard Normal

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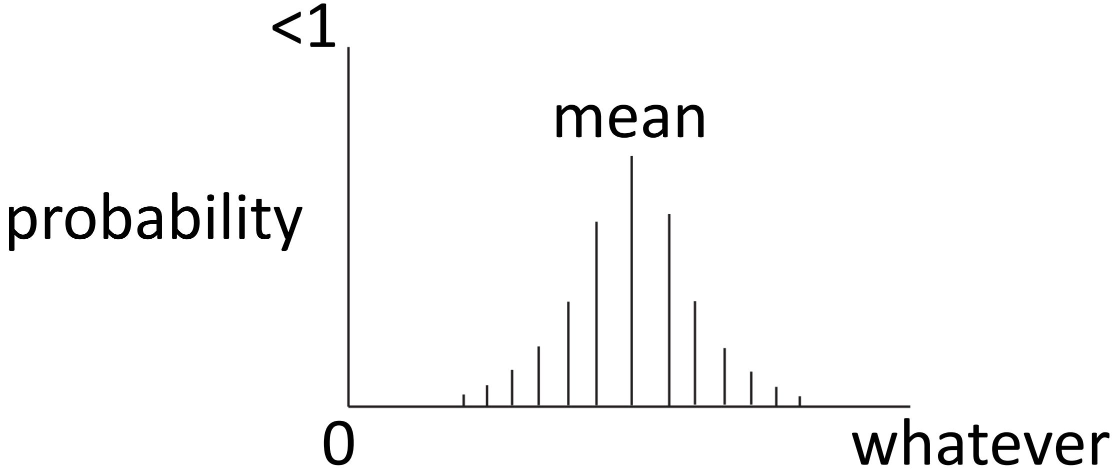
distribution



Poisson:
average rate over time or distance

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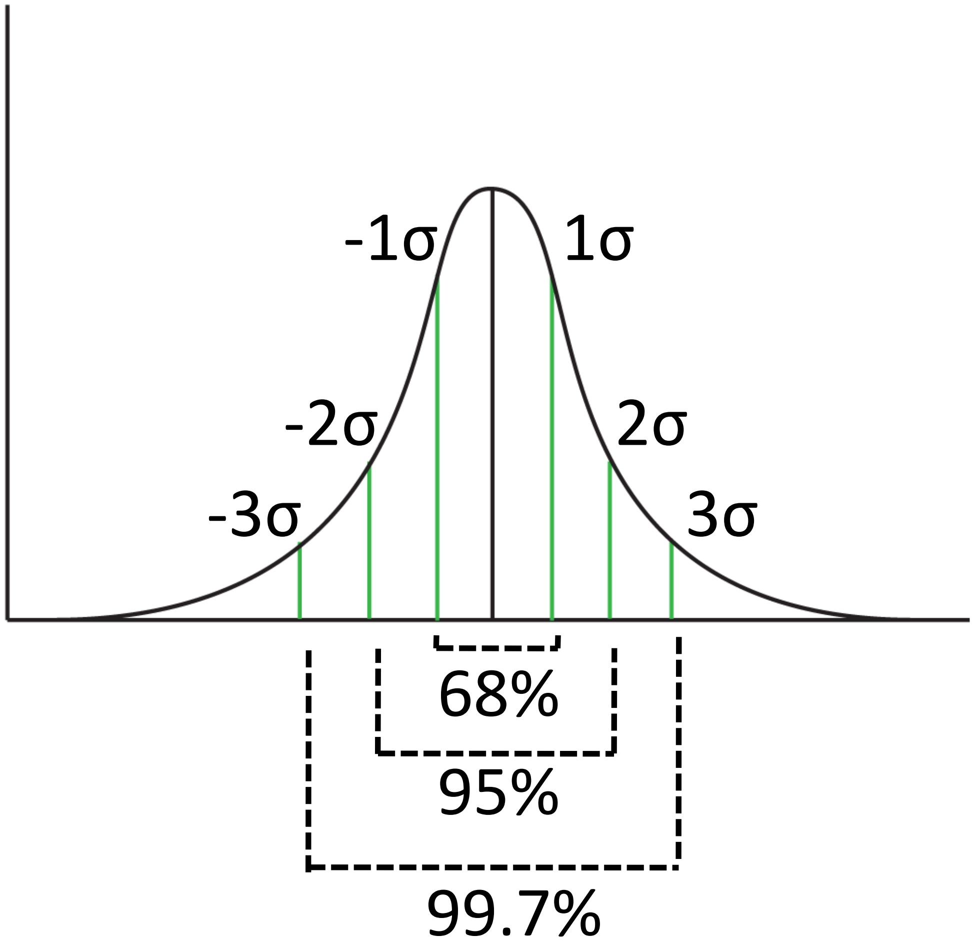
distribution characterization

σ = standard deviation

σ/√n = standard error of the mean



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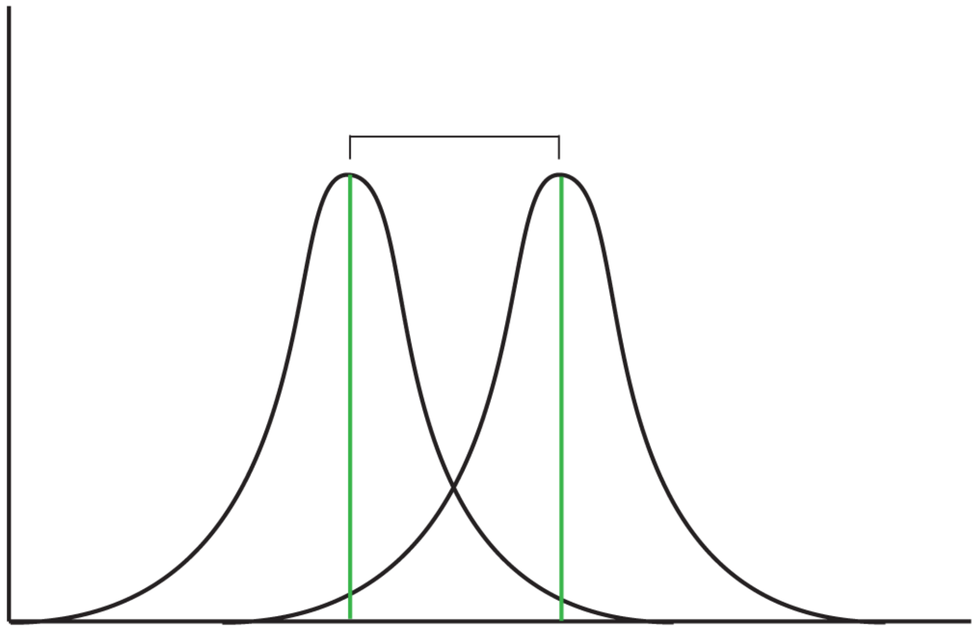
are they different?

2 means



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hypothesis testing

Study Results

		Ho	H1
Reality	Ho		false hit
	H1	false miss	power

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hypothesis testing

		Study Results	
		Ho	H1
Reality	Ho		type 1 error
	H1	type 2 error	power

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hypothesis testing

Study Results

Reality		Ho	H1
	Ho		α
	H1	β	(1-β)

→ p-value

0.05 (5%)

↓

power

depends on:

- **sample size “n” (more = better)**
- size of effect
- subject compliance

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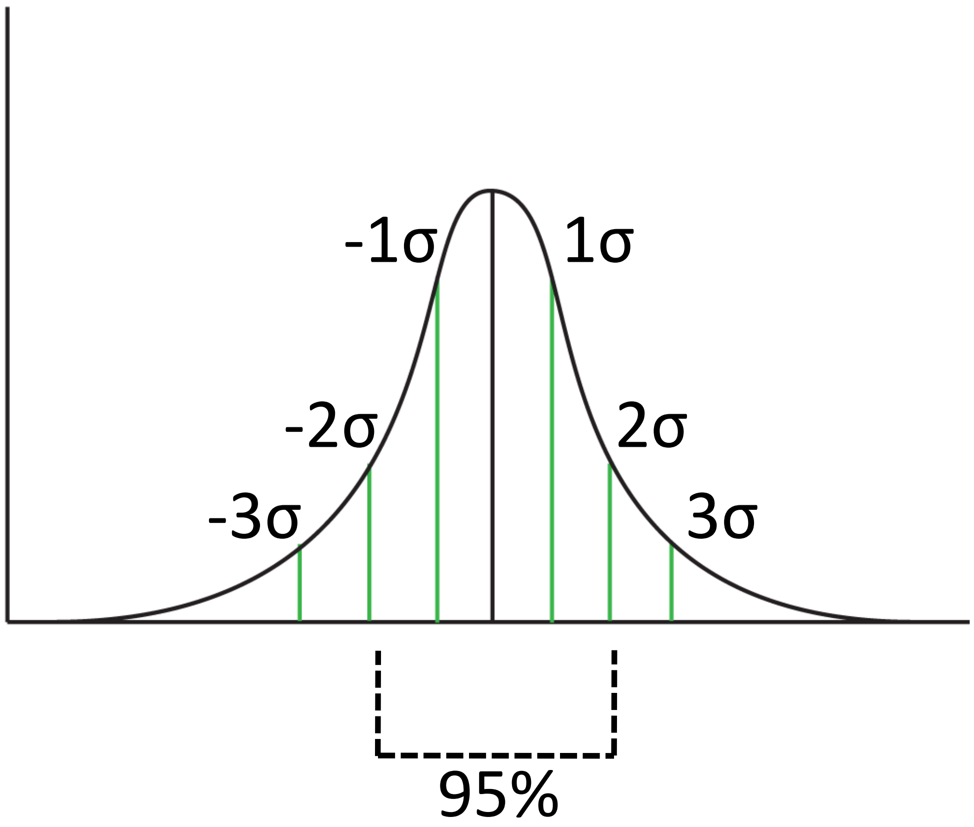
are they different?

confidence interval = range for repeated/multiple samples

mean +/- #



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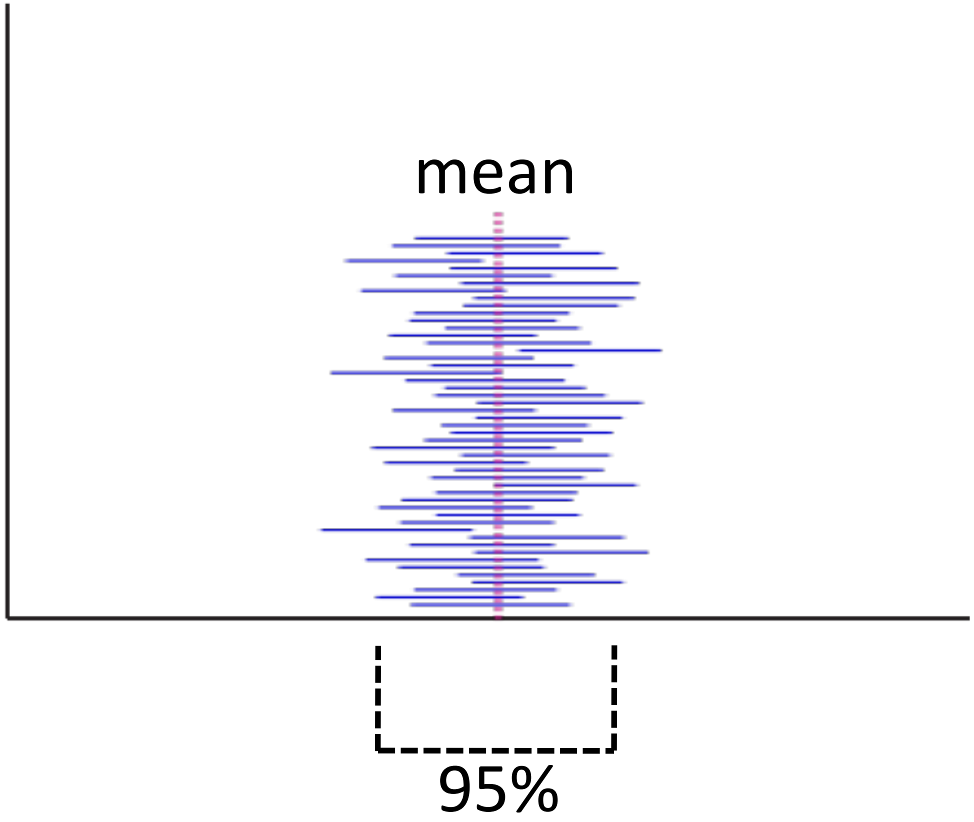
are they different?

confidence interval = range for repeated/multiple samples

mean +/- #



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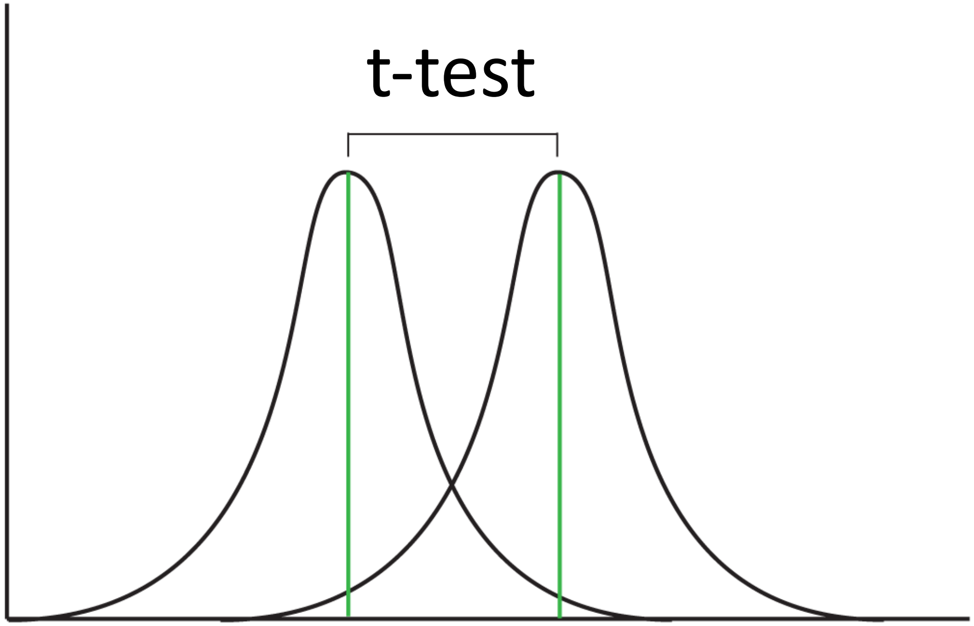
are they different?

2 means



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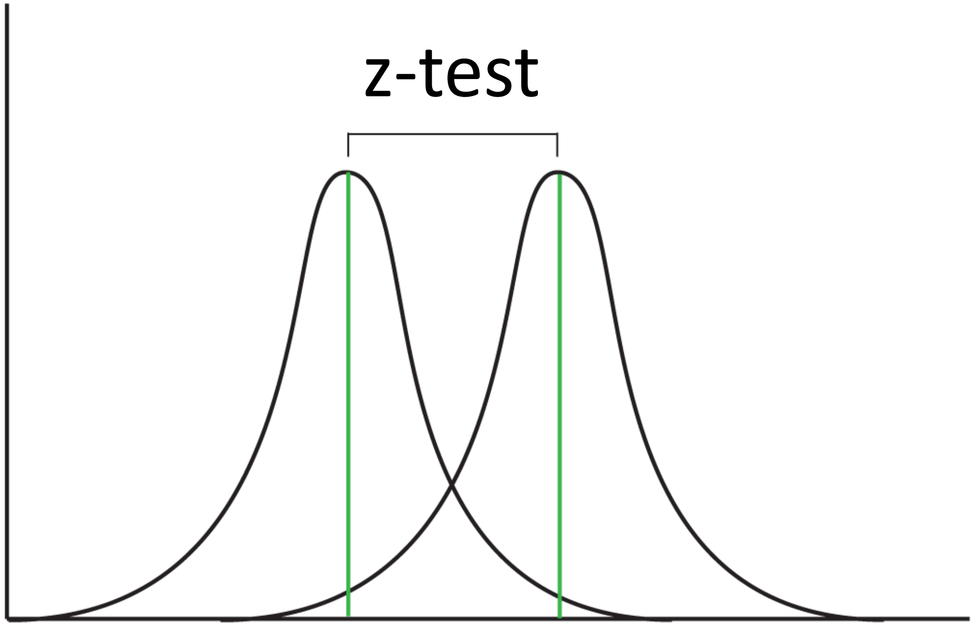
are they different?

2 means



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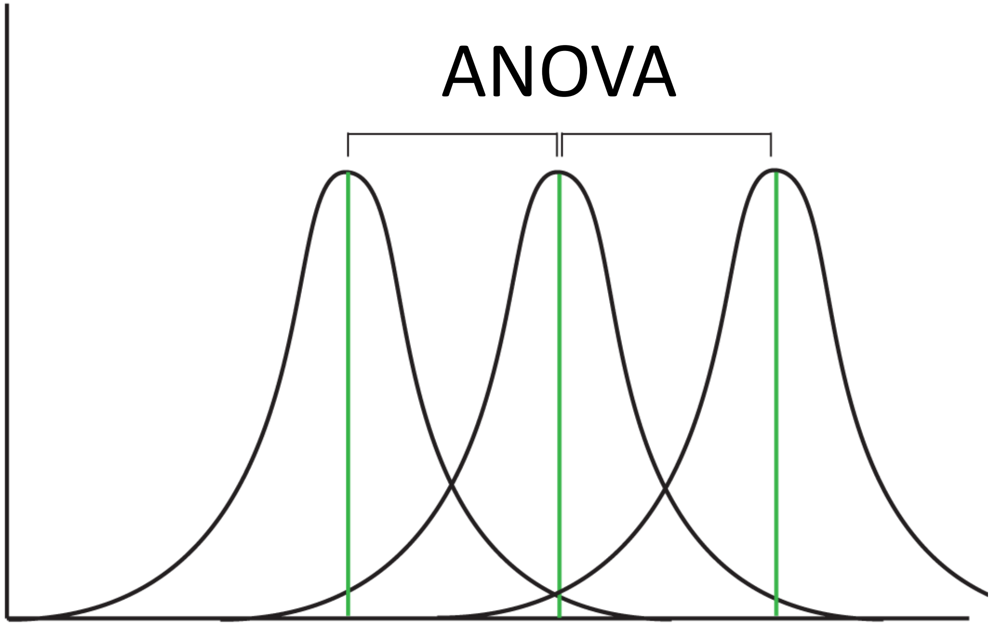
are they different?

3 means



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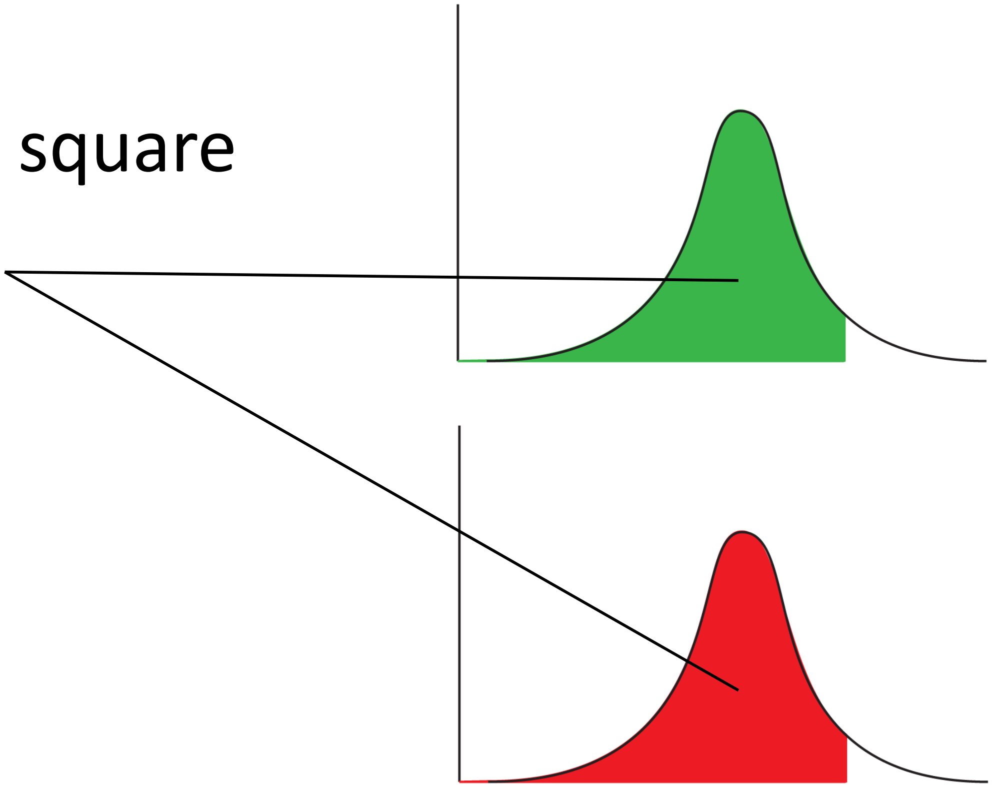
are they different?

percentage or proportions, compare to a known standard
(think Punnett square)

Chi square

χ2



is the observed frequency consistent with the expected frequency?

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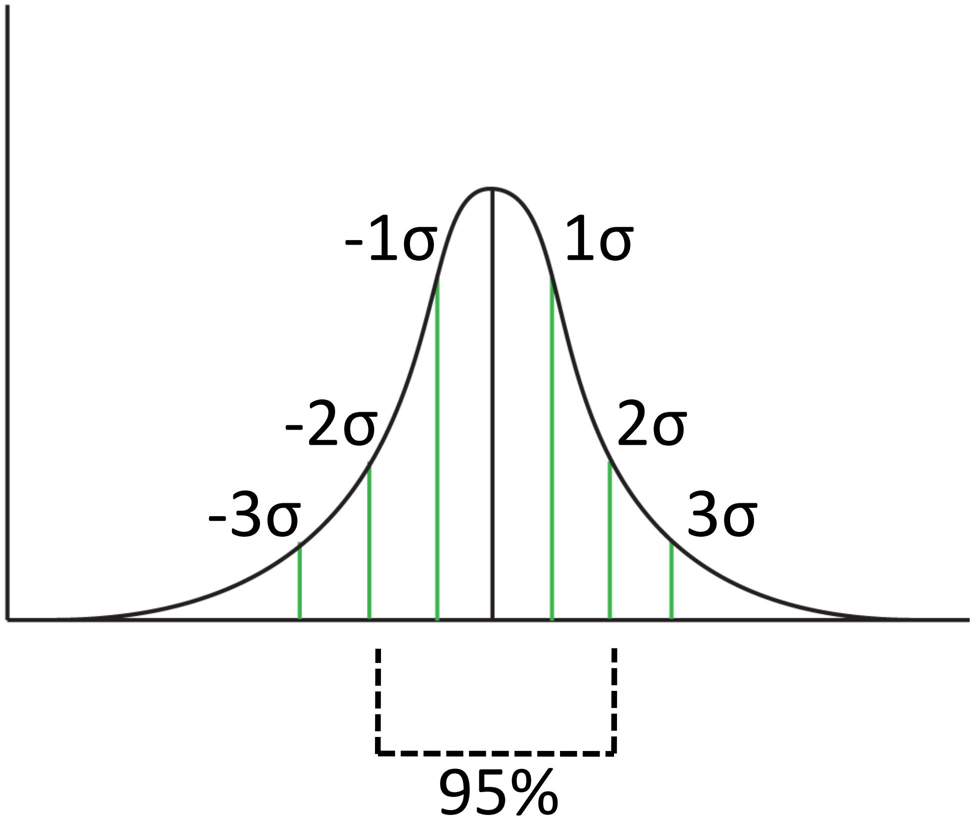
are they different?

confidence interval = range for repeated/multiple samples

mean +/- 1.96(SEM)

z-score for
95% CI



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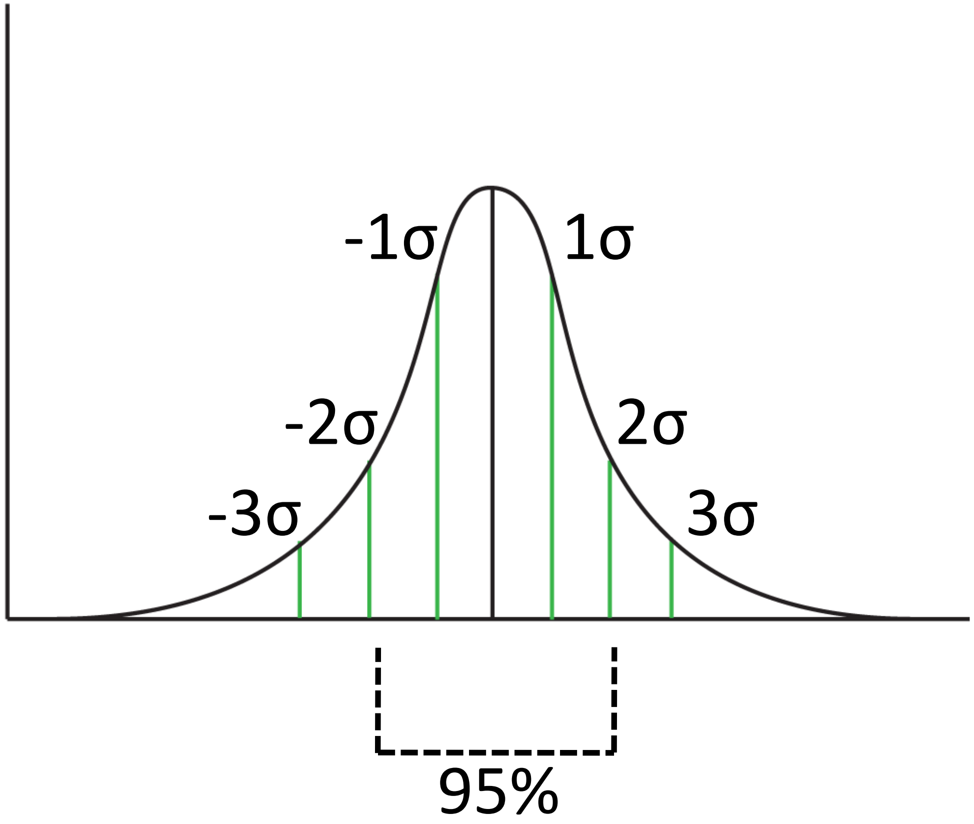
are they different?

confidence interval = range for repeated/multiple samples

mean +/- 1.96(SEM)



beware: CI overlapping = not significantly different

beware: CI including 0 when difference between means

beware: CI including 1 when “relative” or “ratio” statistic

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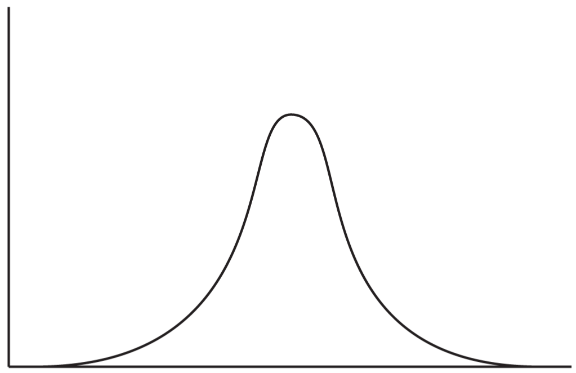
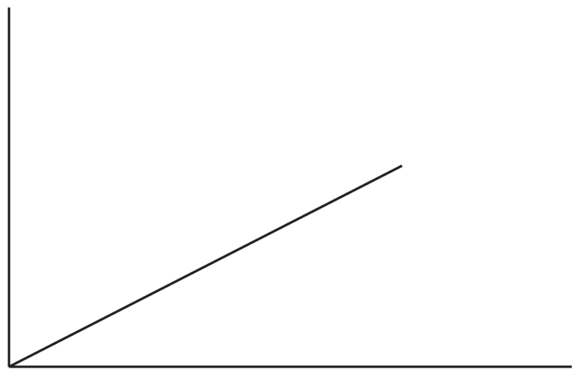
linear vs. non-linear comparisons

non-linear



linear



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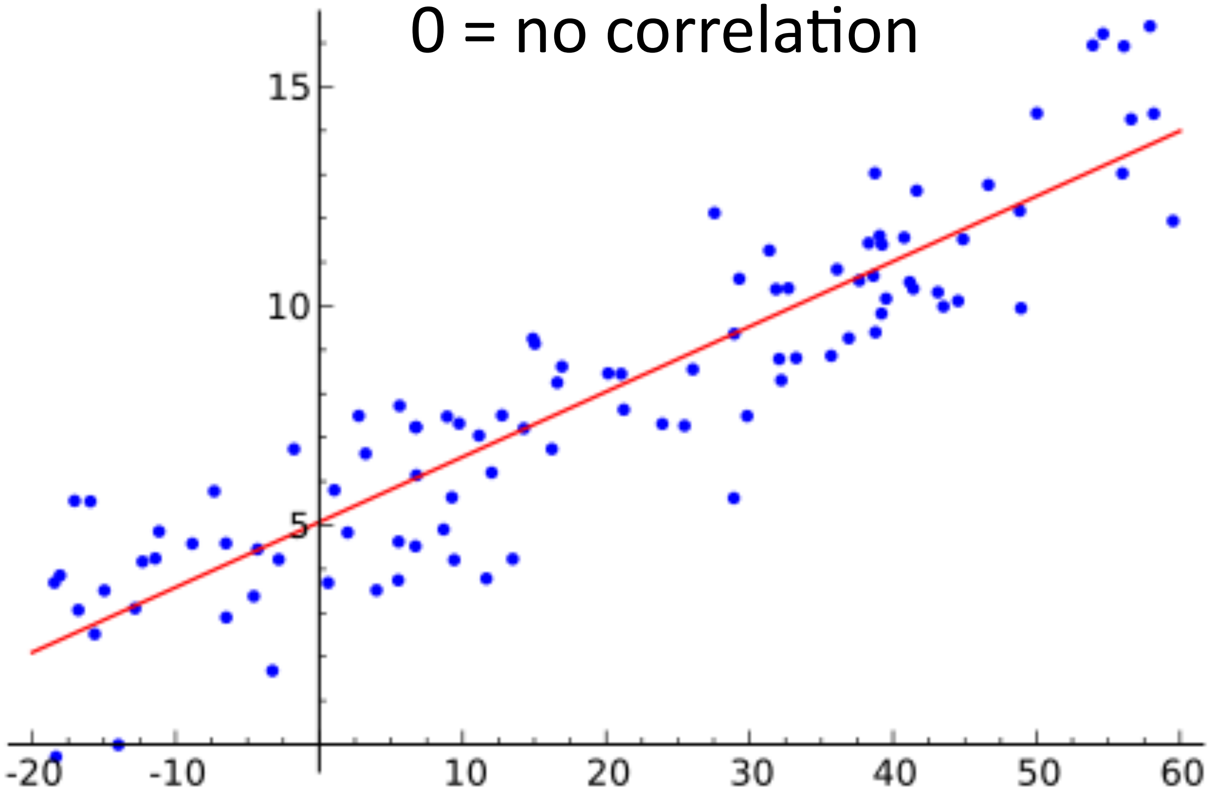
linear comparisons

regression ➔ r-value (correlation coefficient)

-1 to 1

closer to -1 or 1 = high correlation

0 = no correlation



http://en.wikipedia.org/wiki/File:Linear_regression.svg

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linear comparisons

regression ➔ r-value (correlation coefficient)

-1 to 1

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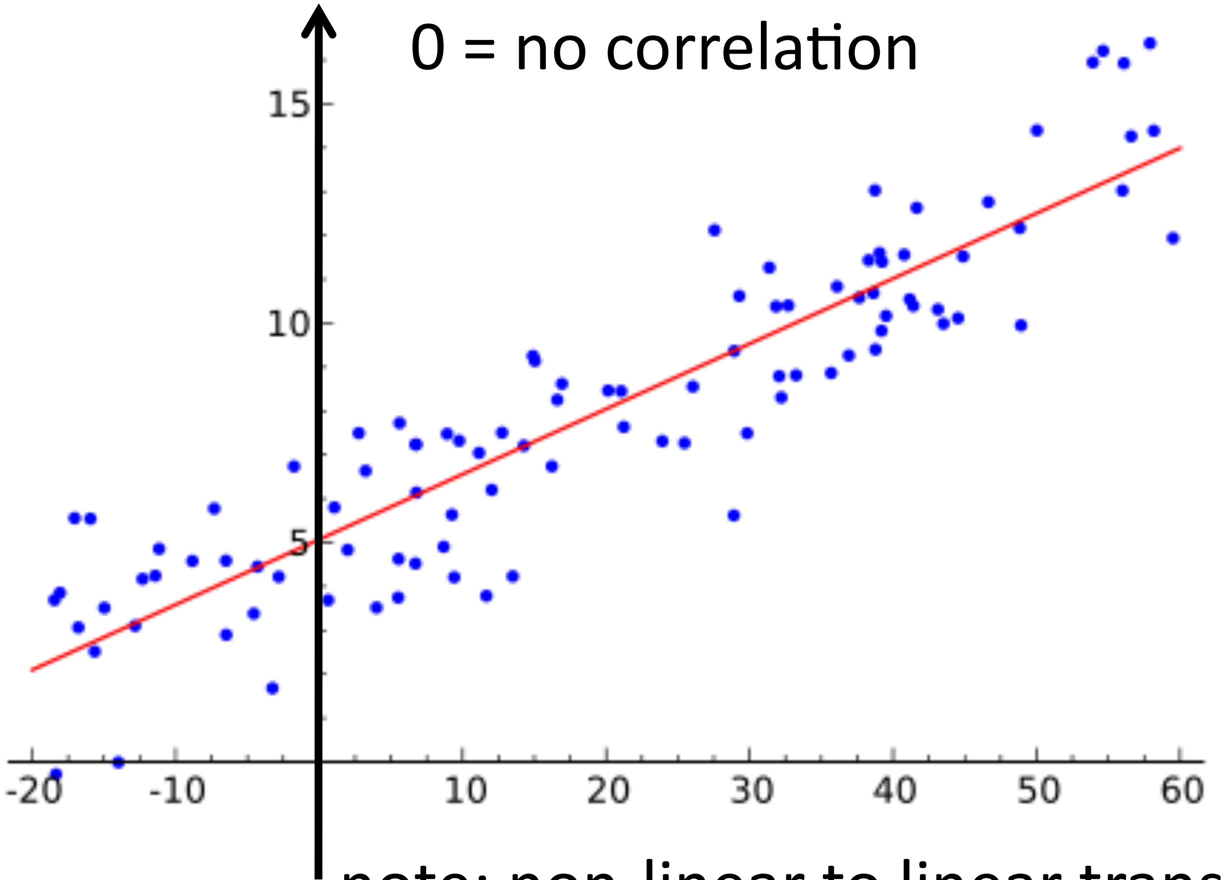

note: non-linear to linear transformations (think logs)

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http://en.wikipedia.org/wiki/File:Linear_regression.svg

contingency tables

	+	-
+		
-		

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contingency tables

diagnostic tests

		disease	
		+	-
test	+	TP	FP
	-	FN	TN

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contingency tables

diagnostic tests

		disease	
		+	-
test	+	TP	FP
	-	FN	TN

↓

sensitivity

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contingency tables

diagnostic tests

		disease	
		+	-
test	+	TP	FP
	-	FN	TN

↓

TP/(TP+FN)

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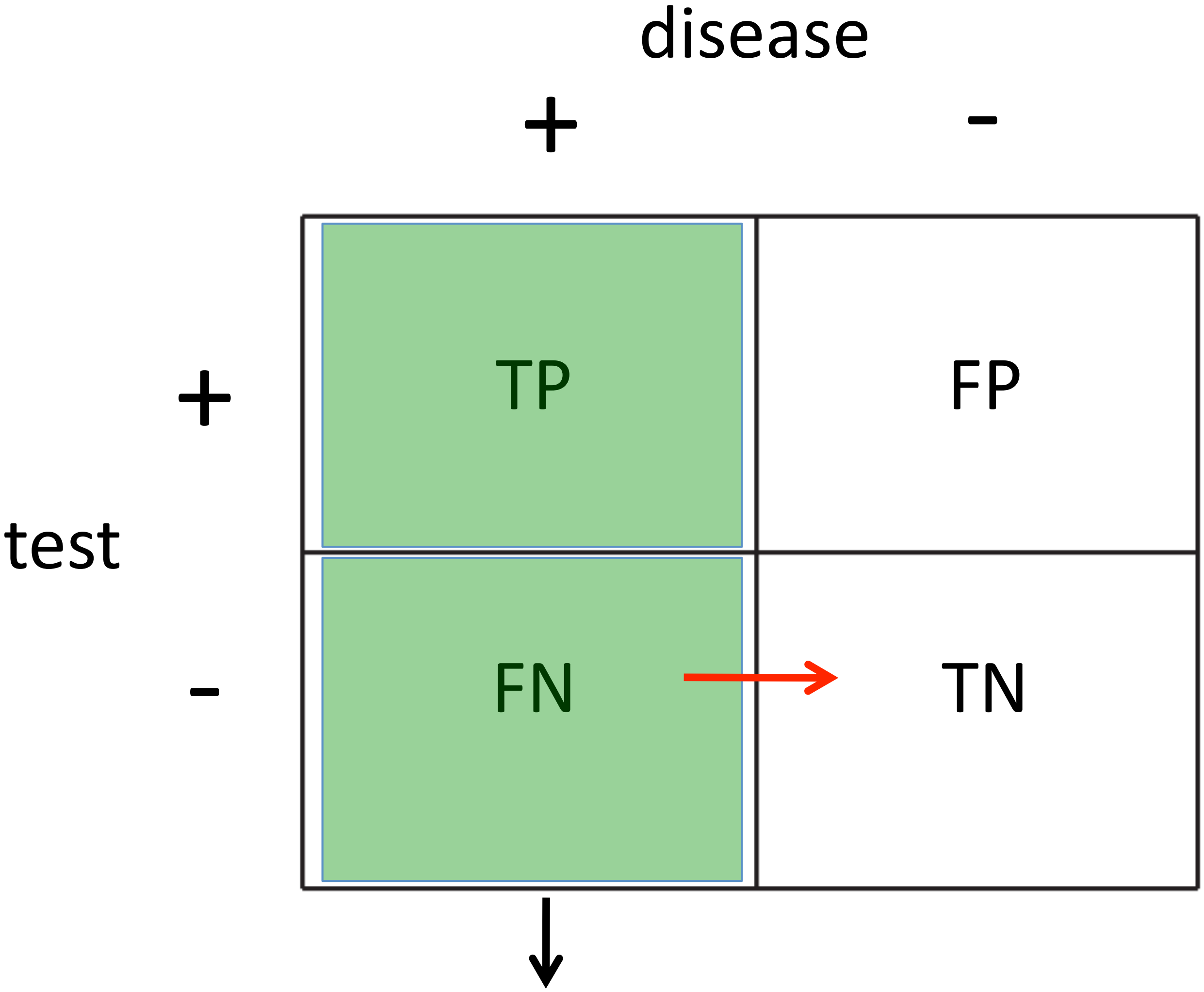
contingency tables

diagnostic tests



		disease	
		+	-
test	+	TP	FP
	-	FN	TN

rules disease out

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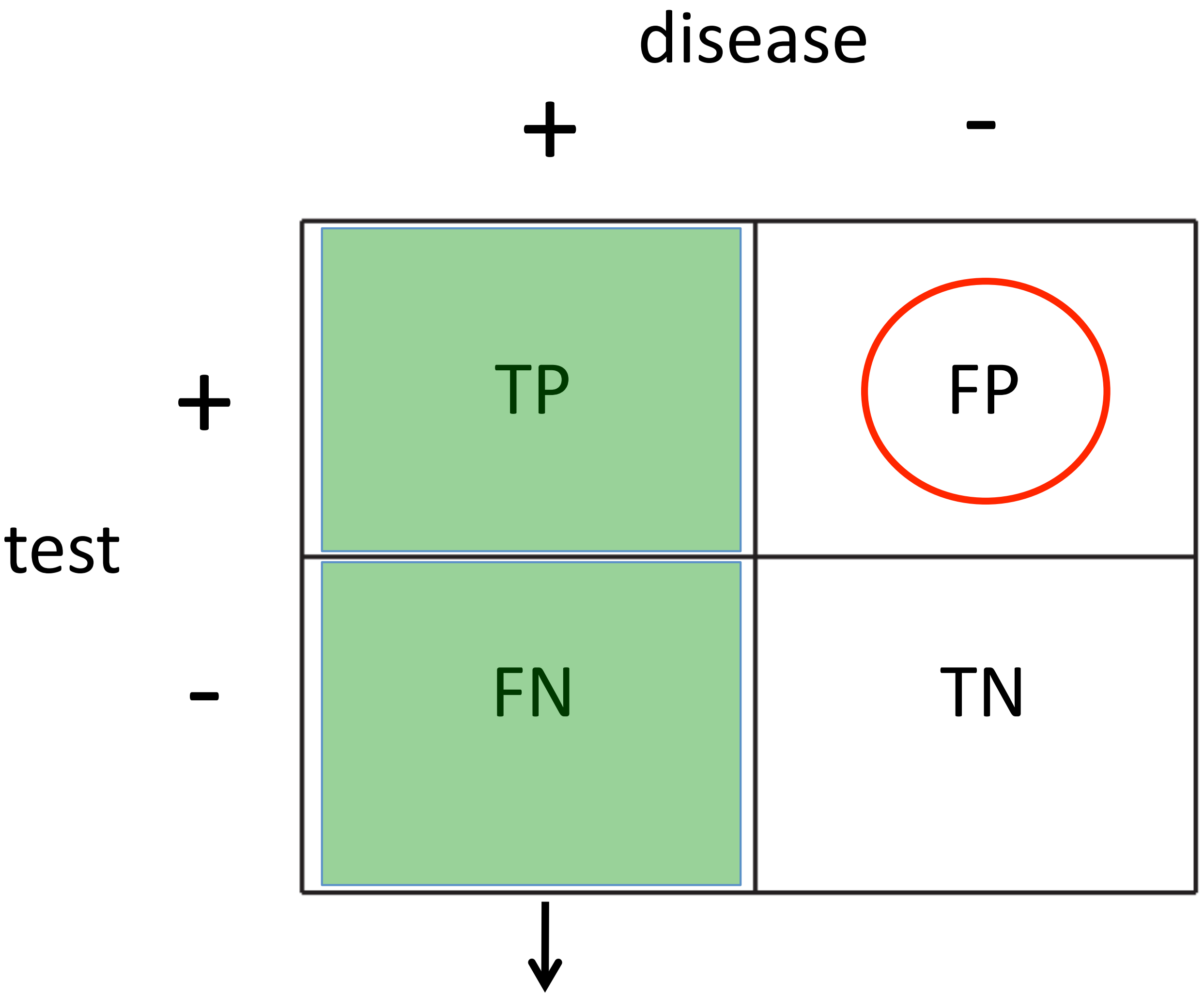
contingency tables

diagnostic tests



		disease	
		+	-
test	+	TP	FP
	-	FN	TN

rules disease out

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contingency tables

diagnostic tests

		disease	
		+	-
test	+	TP	FP
	-	FN	TN

example: ELISA

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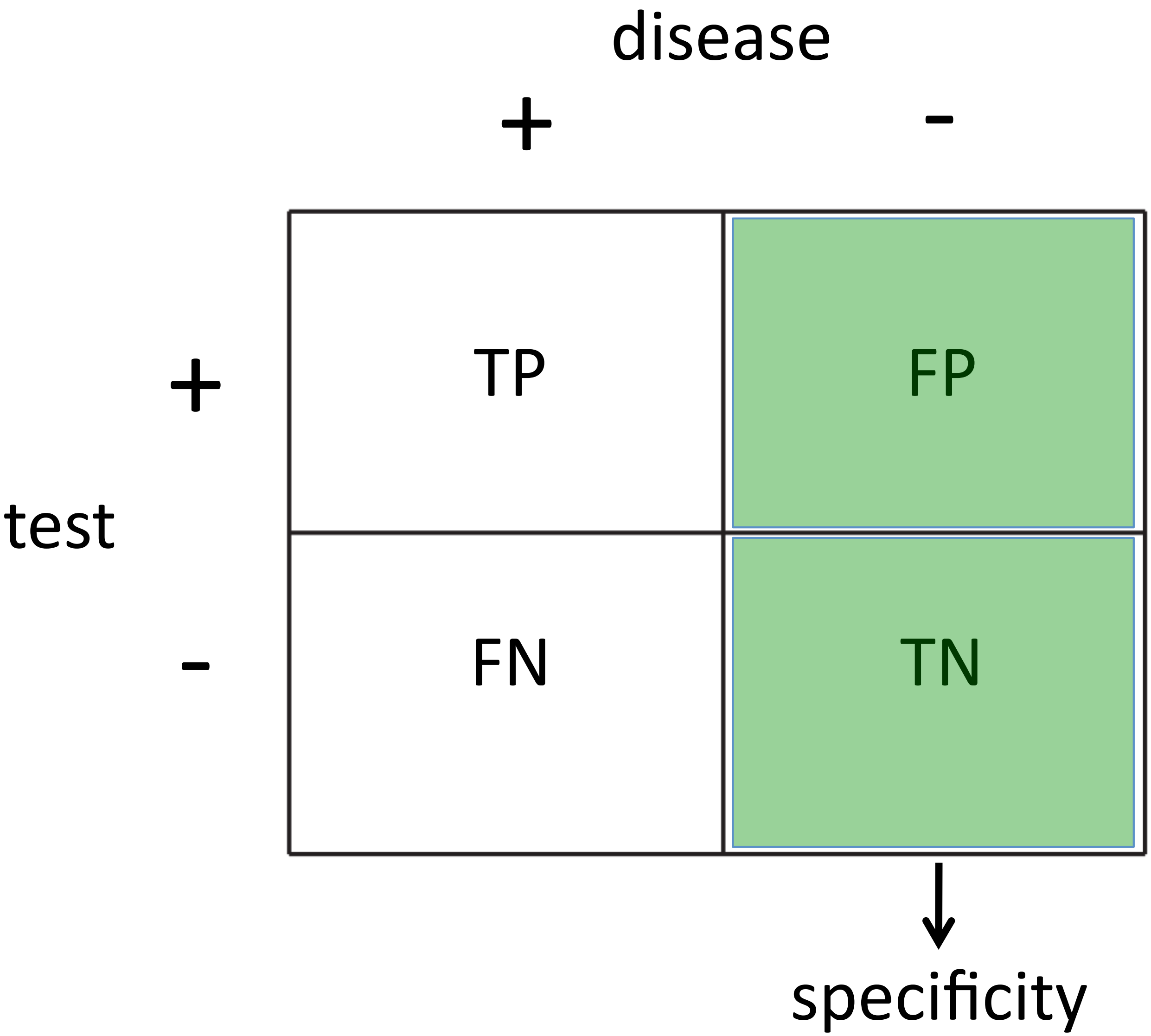
contingency tables

diagnostic tests



		disease	
		+	-
test	+	TP	FP
	-	FN	TN

specificity

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contingency tables

diagnostic tests

		disease	
		+	-
test	+	TP	FP
	-	FN	TN

↓

TN/(TN+FP)

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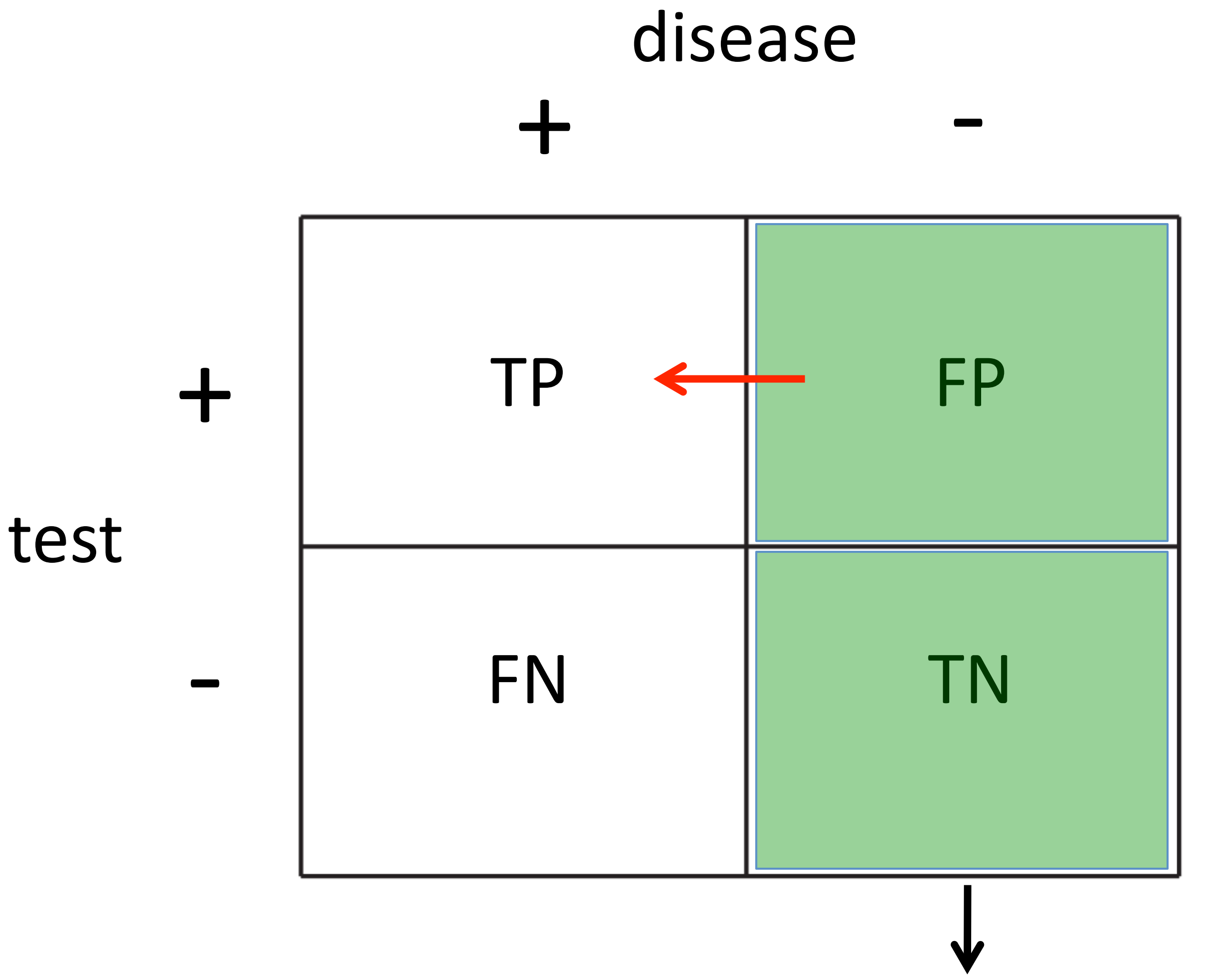
contingency tables

diagnostic tests



		disease	
		+	-
test	+	TP	🟩 FP
	-	FN	🟩 TN

rules disease in

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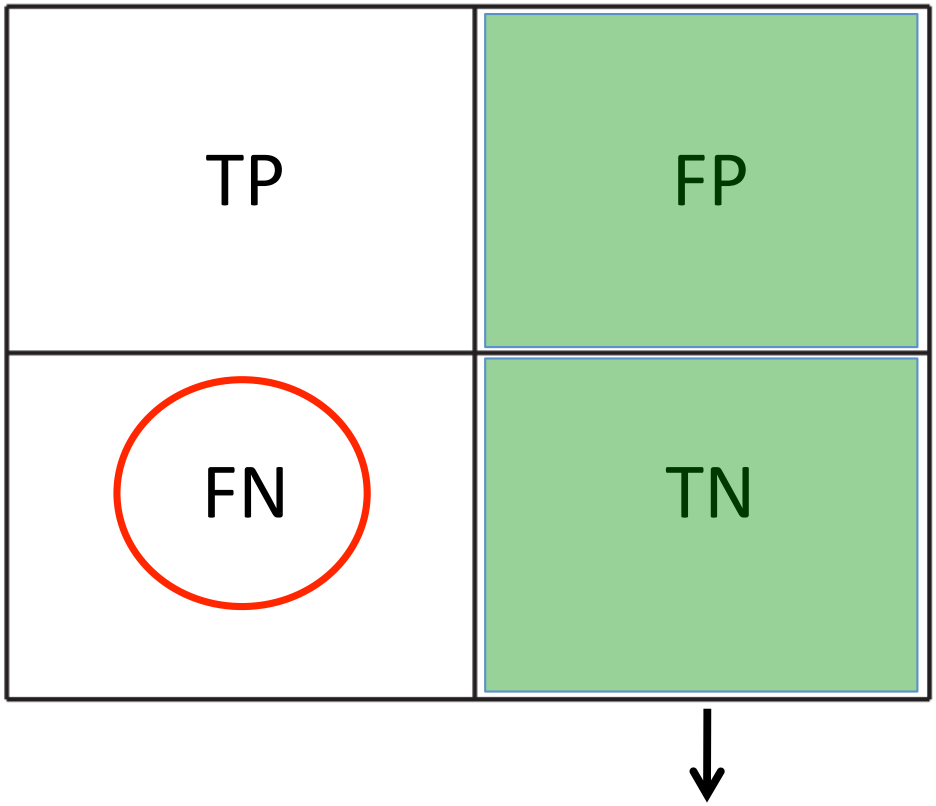
contingency tables

diagnostic tests



		disease	
		+	-
test	+	TP	FP
	-	FN	TN

rules disease in

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diagnostic tests

		disease	
		+	-
test	+	TP	FP
	-	FN	TN

↓

example: Western

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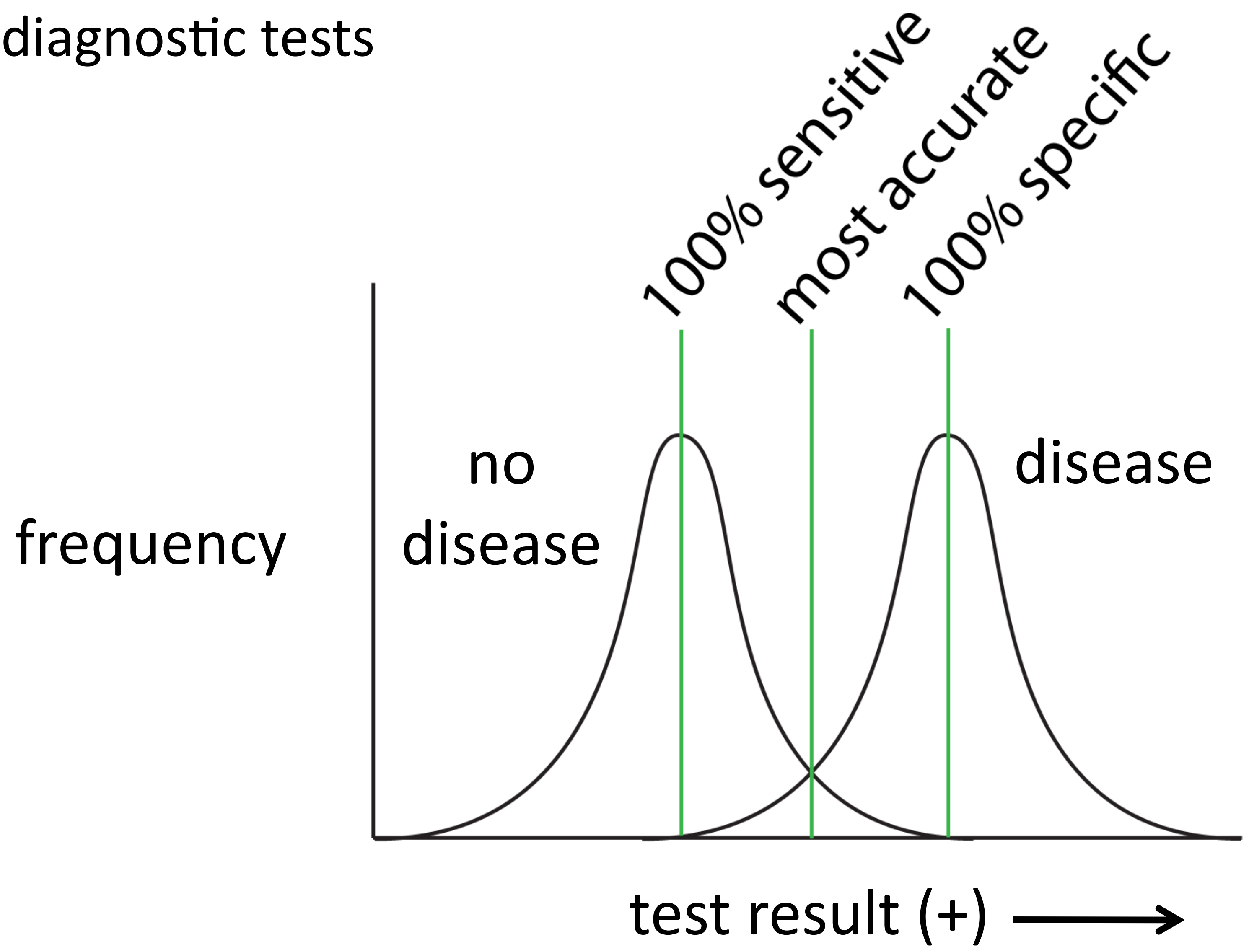
contingency tables

diagnostic tests



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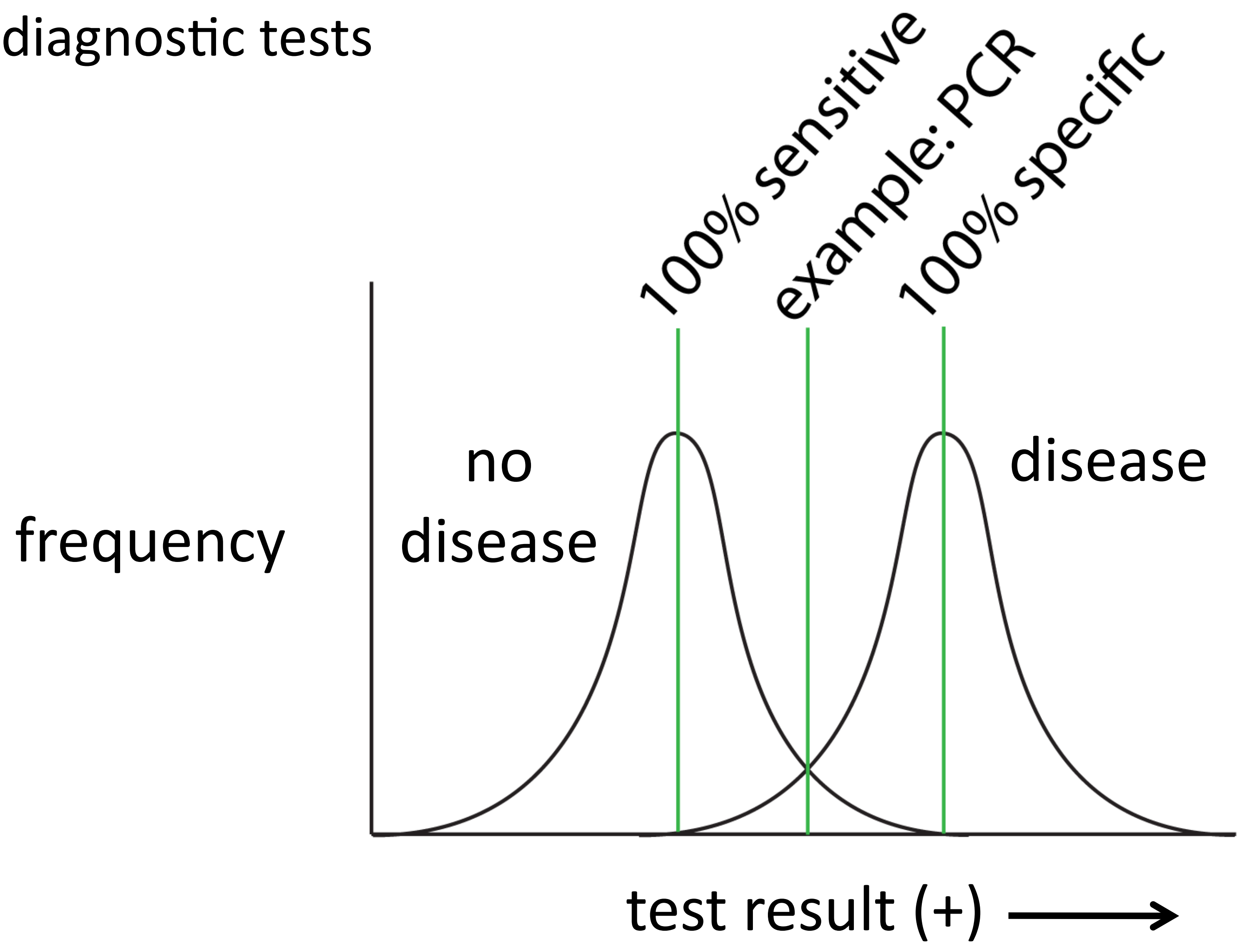
diagnostic tests



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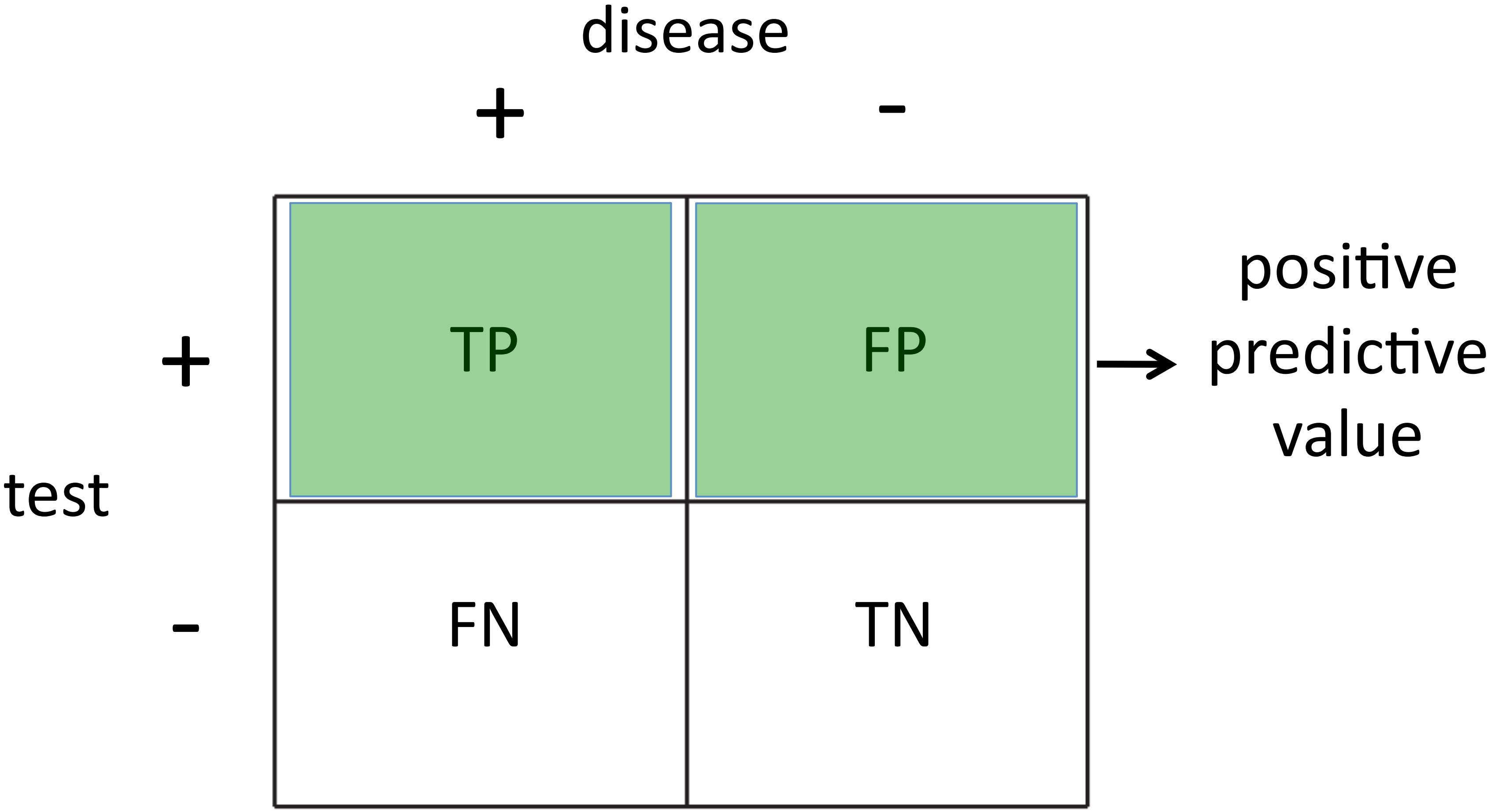
diagnostic tests



		disease	
		+	-
test	+	🟩 TP	🟩 FP
	-	FN	TN

→ positive predictive value

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diagnostic tests

		disease		
		+	-	
test	+	TP	FP	→ TP/(TP+FP)
	-	FN	TN	

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diagnostic tests

		disease		
		+	-	
test	+	TP	FP	
	-	FN	TN	→ negative predictive value

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contingency tables

diagnostic tests

		disease		
		+	-	
test	+	TP	FP	
	-	FN	TN	→TN/(TN+FN)

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contingency tables

risk factors

		disease	
		+	-
risk factor	+	a	b
	-	c	d

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risk factors: odds

		disease			odds ratio
		+	-		
risk factor	+	a	b	→	a/b
					÷
	-	c	d	→	c/d

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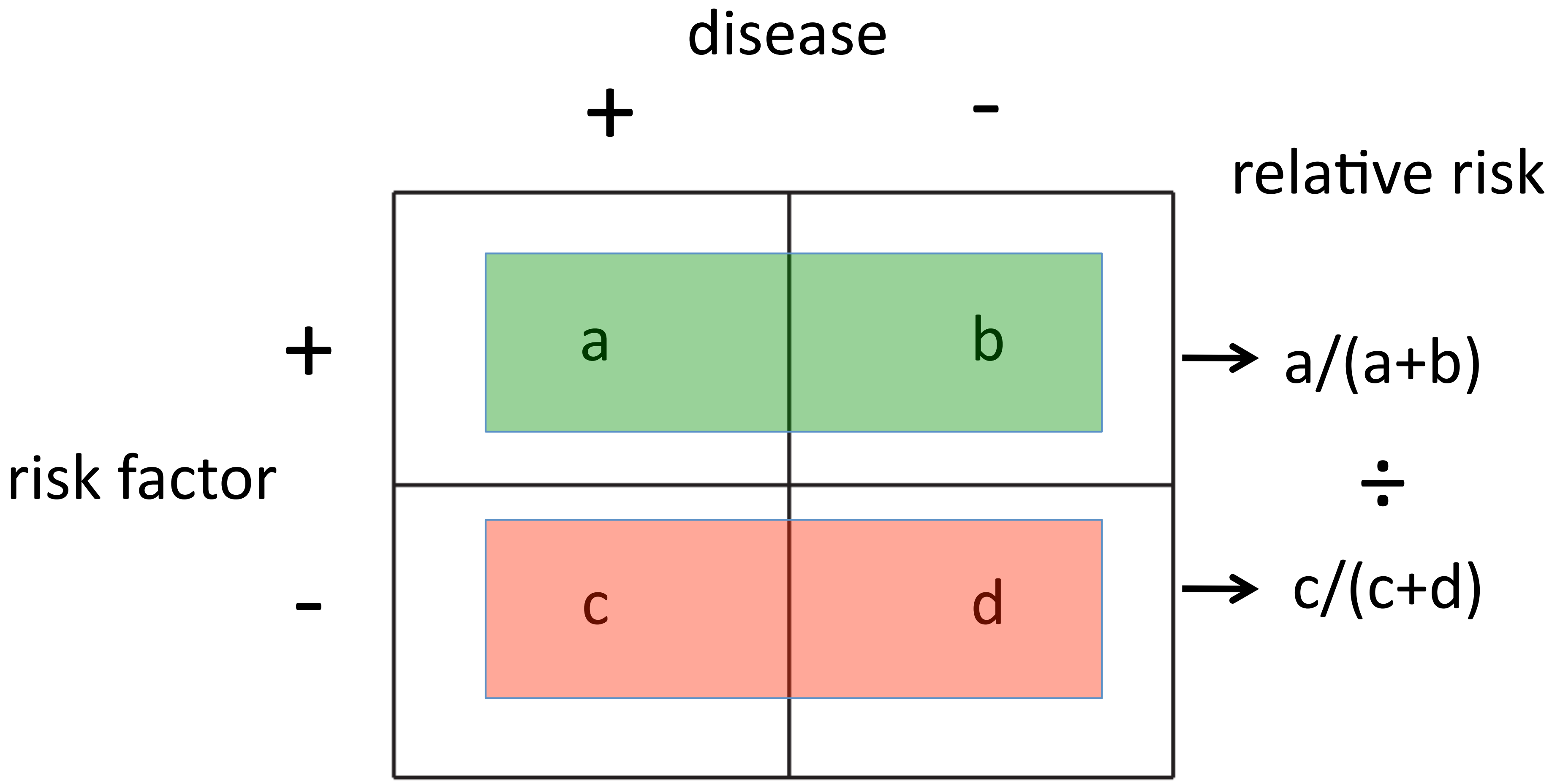
risk factors: risk



		disease	
		+	-
risk factor	+	a	b
	-	c	d

relative risk

→ $a/(a+b)$

÷

→ $c/(c+d)$

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risk factors: risk

		disease +	disease -	attributable risk
risk factor	+	a	b	→ a/(a+b)
				-
	-	c	d	→ c/(c+d)

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contingency tables

treatments

	disease	
	+	-
treatment	a	b
placebo	c	d

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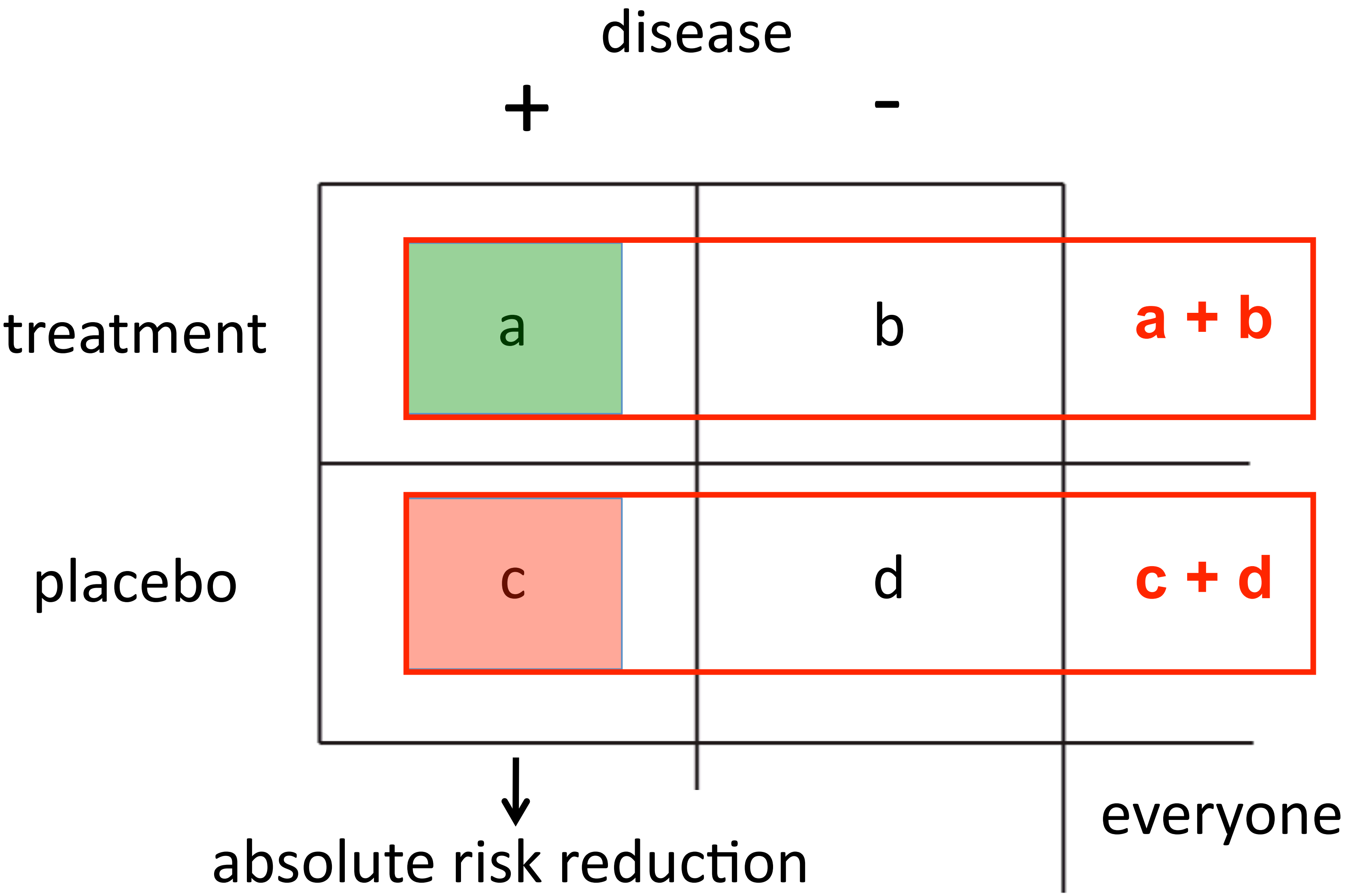
contingency tables

treatments: risk reduction



disease

	+	-	
treatment	a	b	a + b
placebo	c	d	c + d

absolute risk reduction

everyone

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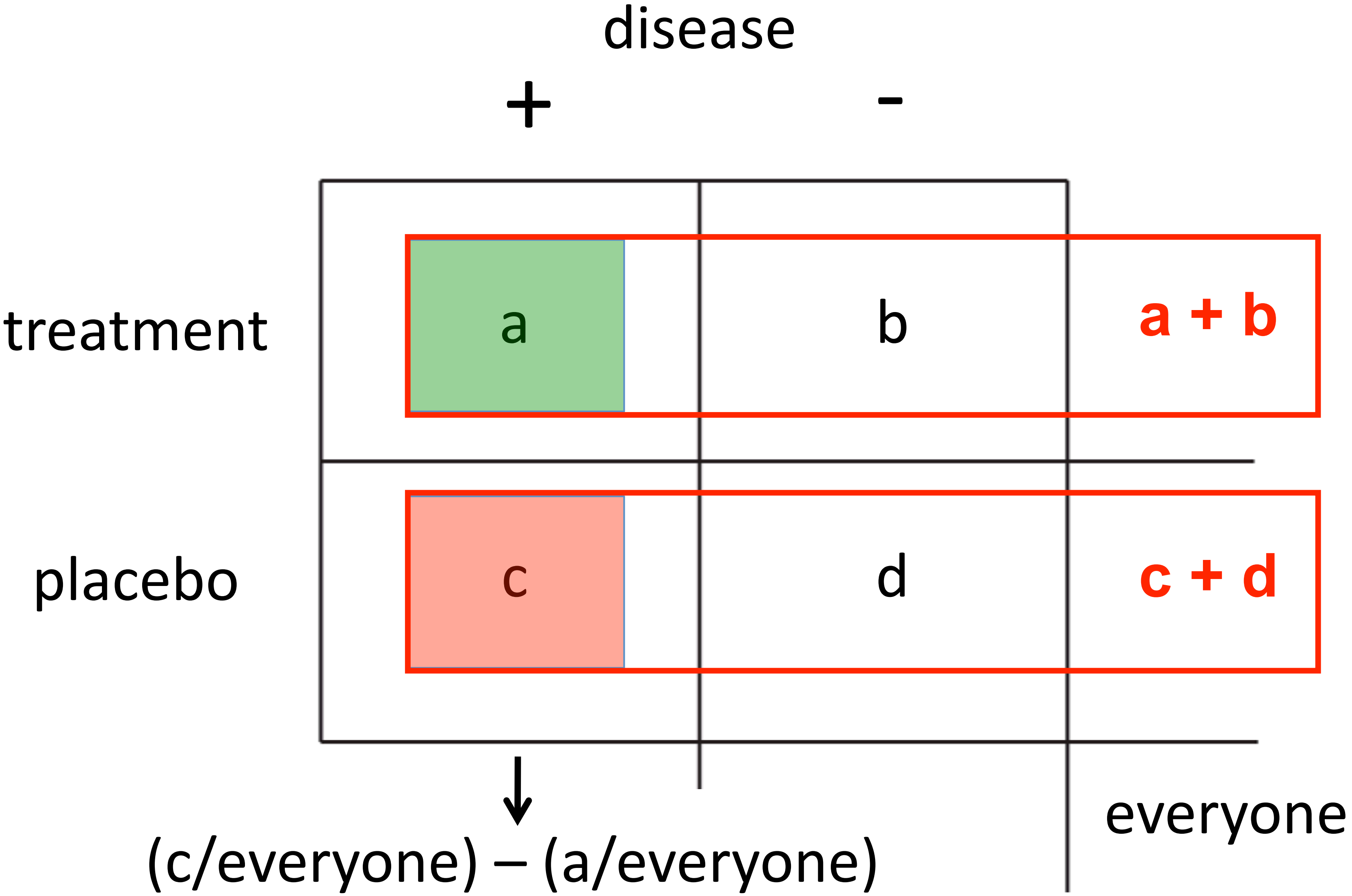
contingency tables

treatments: risk reduction



	disease		
	+	-	
treatment	a	b	a + b
placebo	c	d	c + d
			everyone

(c/everyone) – (a/everyone)

c + d a + b

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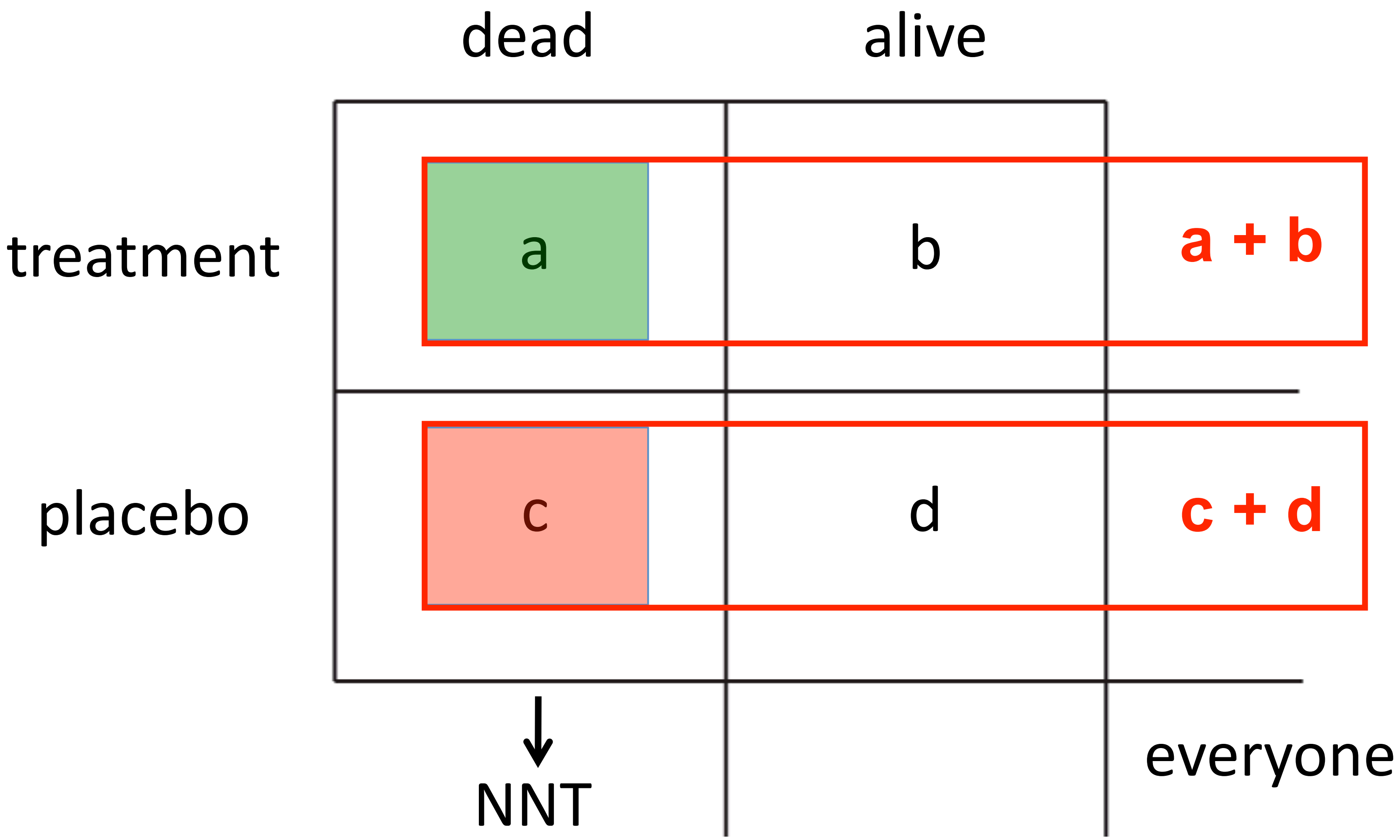
contingency tables

treatments: number needed to treat



	dead	alive	
treatment	a	b	**a + b**
placebo	c	d	**c + d**
	↓ NNT		everyone

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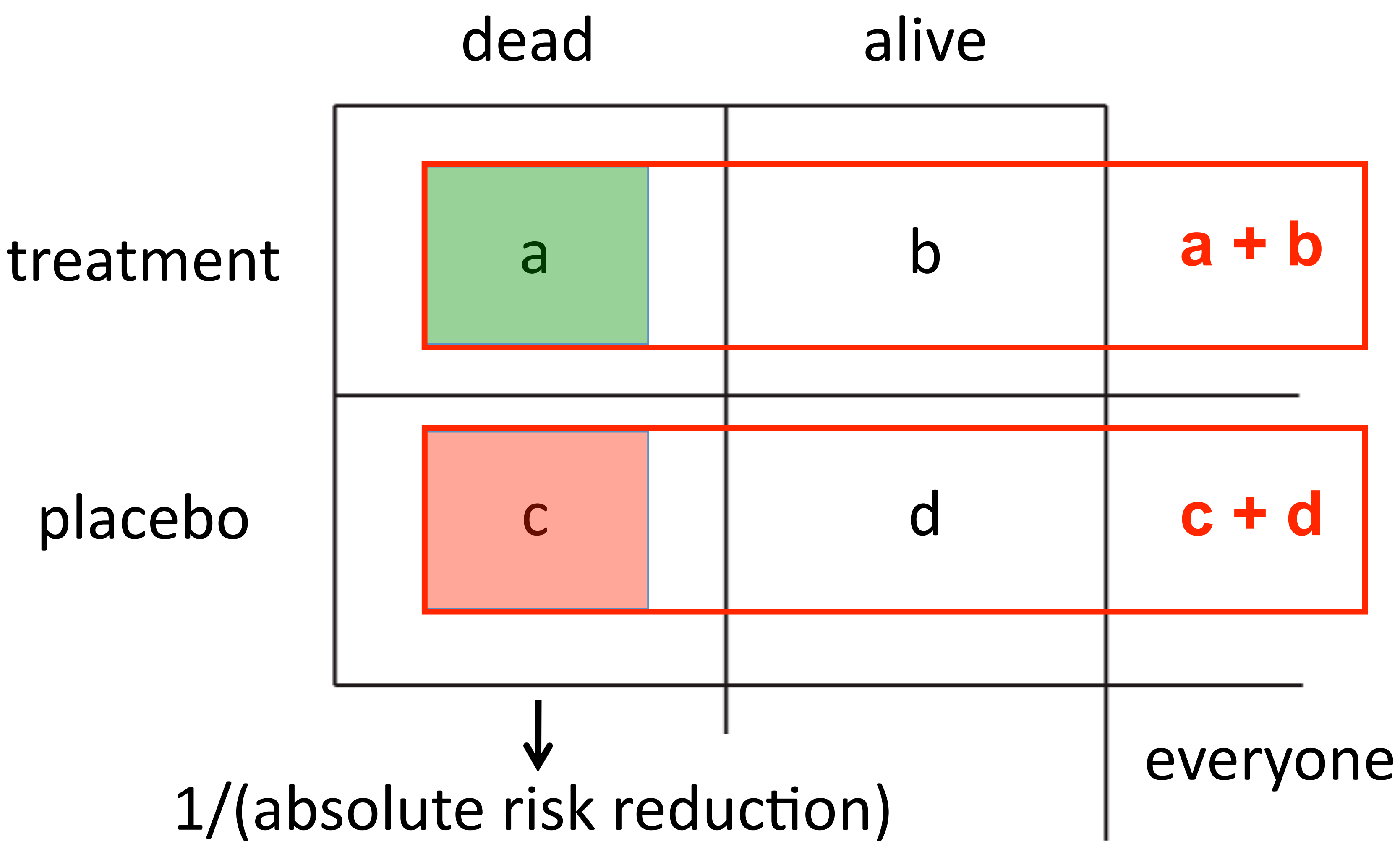
contingency tables

treatments: number needed to treat



	dead	alive	
treatment	a	b	a + b
placebo	c	d	c + d

↓

1/(absolute risk reduction)

everyone

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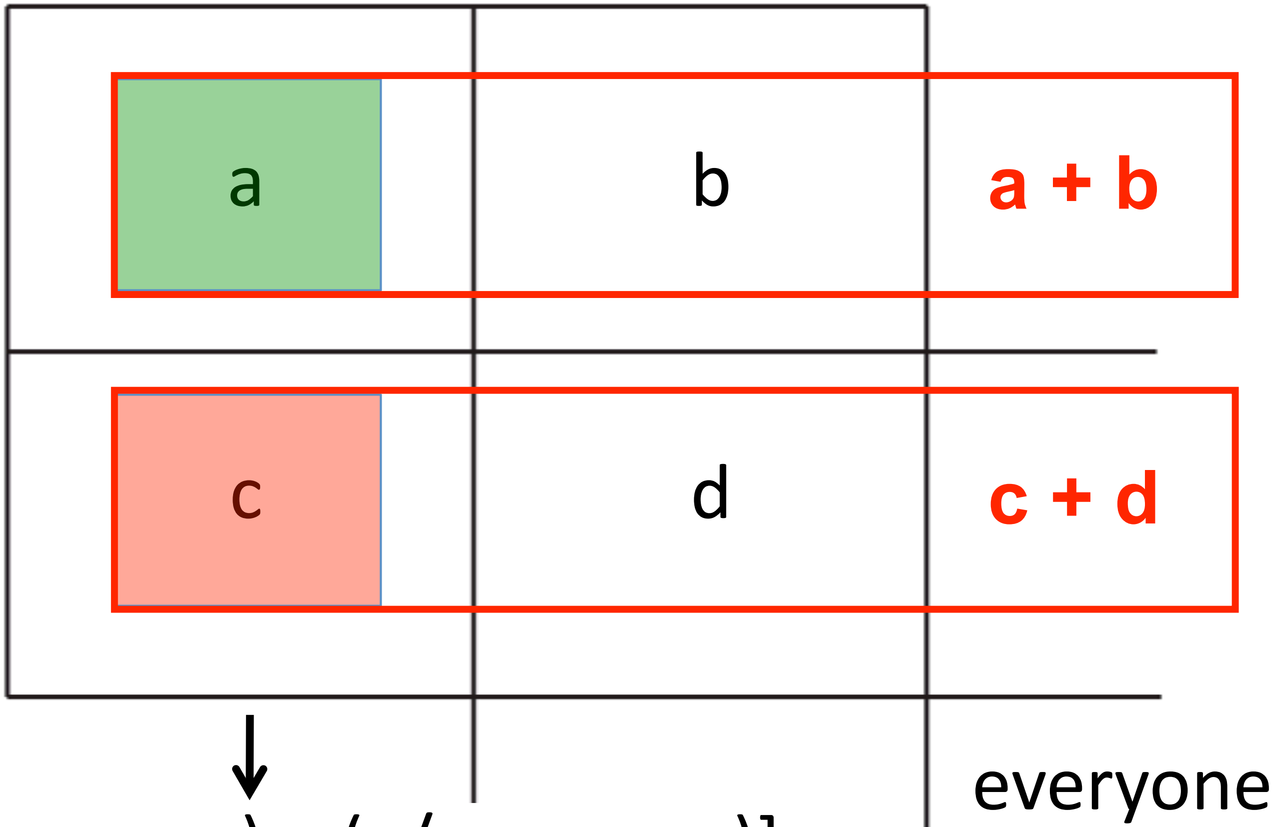
treatments: number needed to treat



	dead	alive	
treatment	a	b	**a + b**
placebo	c	d	**c + d**
			everyone

$$1/[(c/\underset{\mathbf{c + d}}{\text{everyone}}) – (a/\underset{\mathbf{a + b}}{\text{everyone}})]$$

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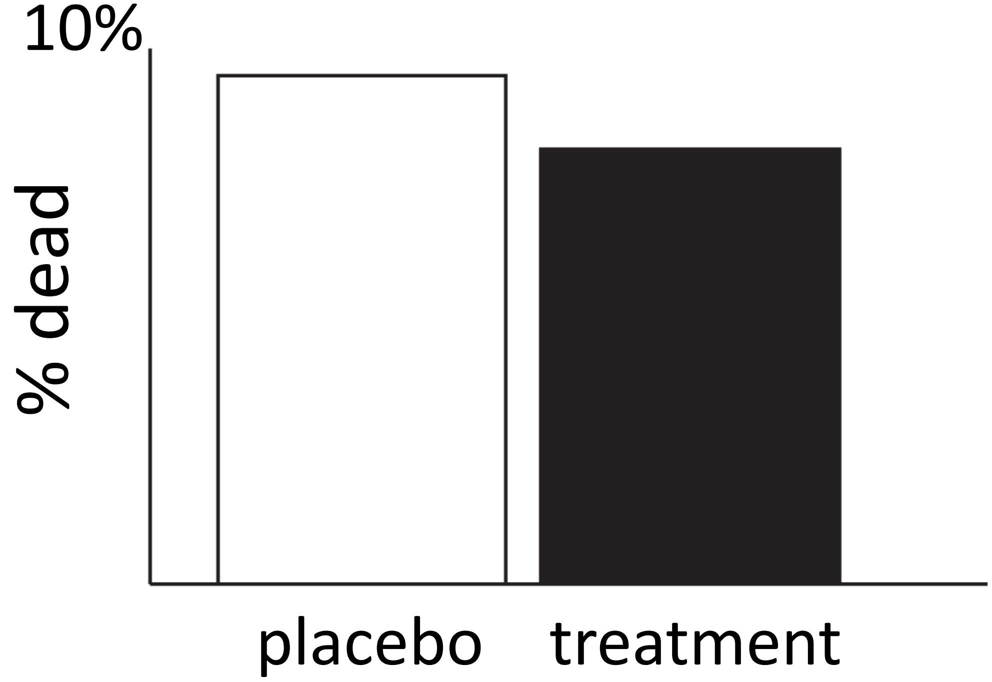
treatments: number needed to treat



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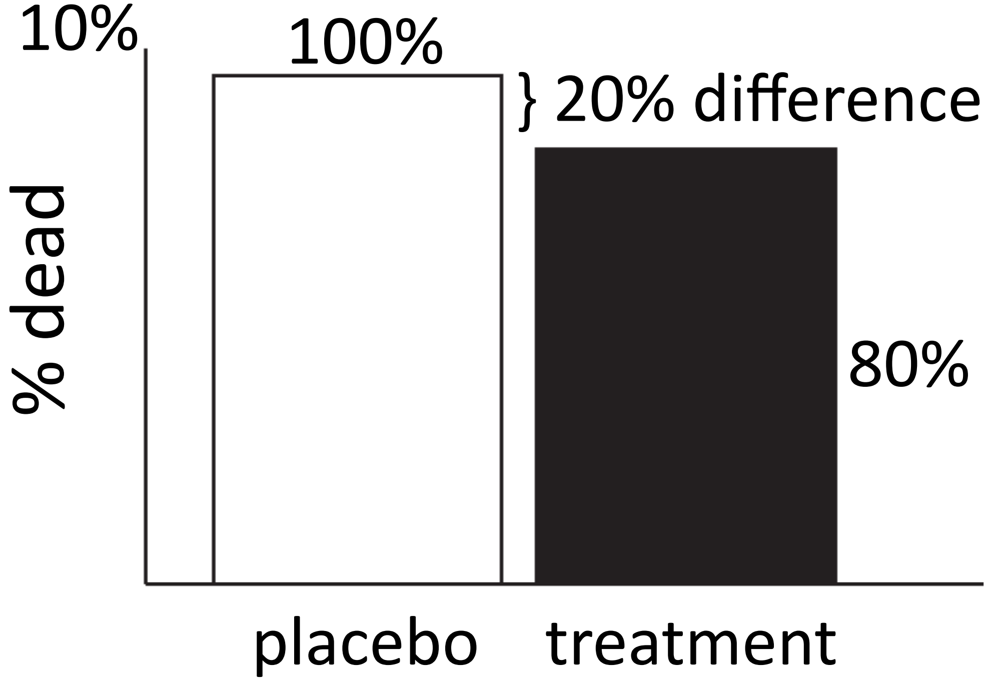
for more, see: http://www.thennt.com/

contingency tables

treatments: number needed to treat



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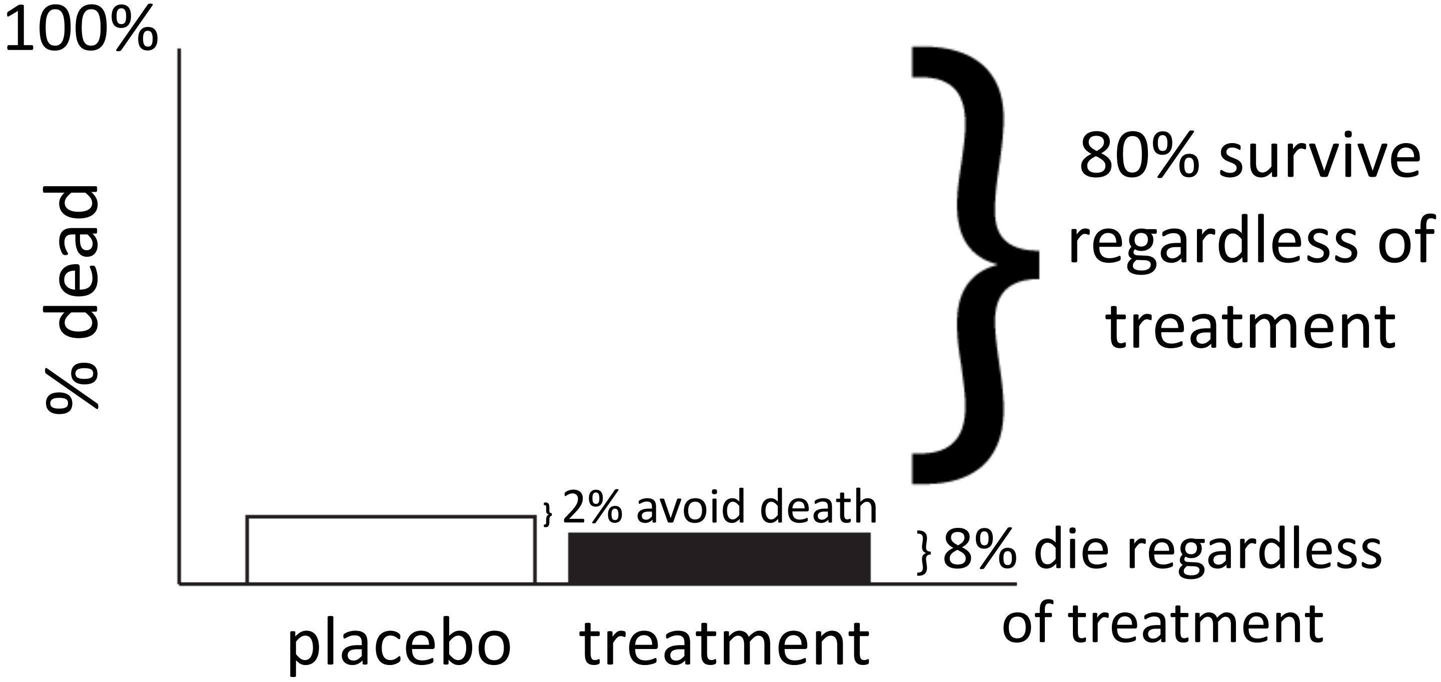
for more, see: http://www.thennt.com/

contingency tables

treatments: number needed to treat



everyone!!!

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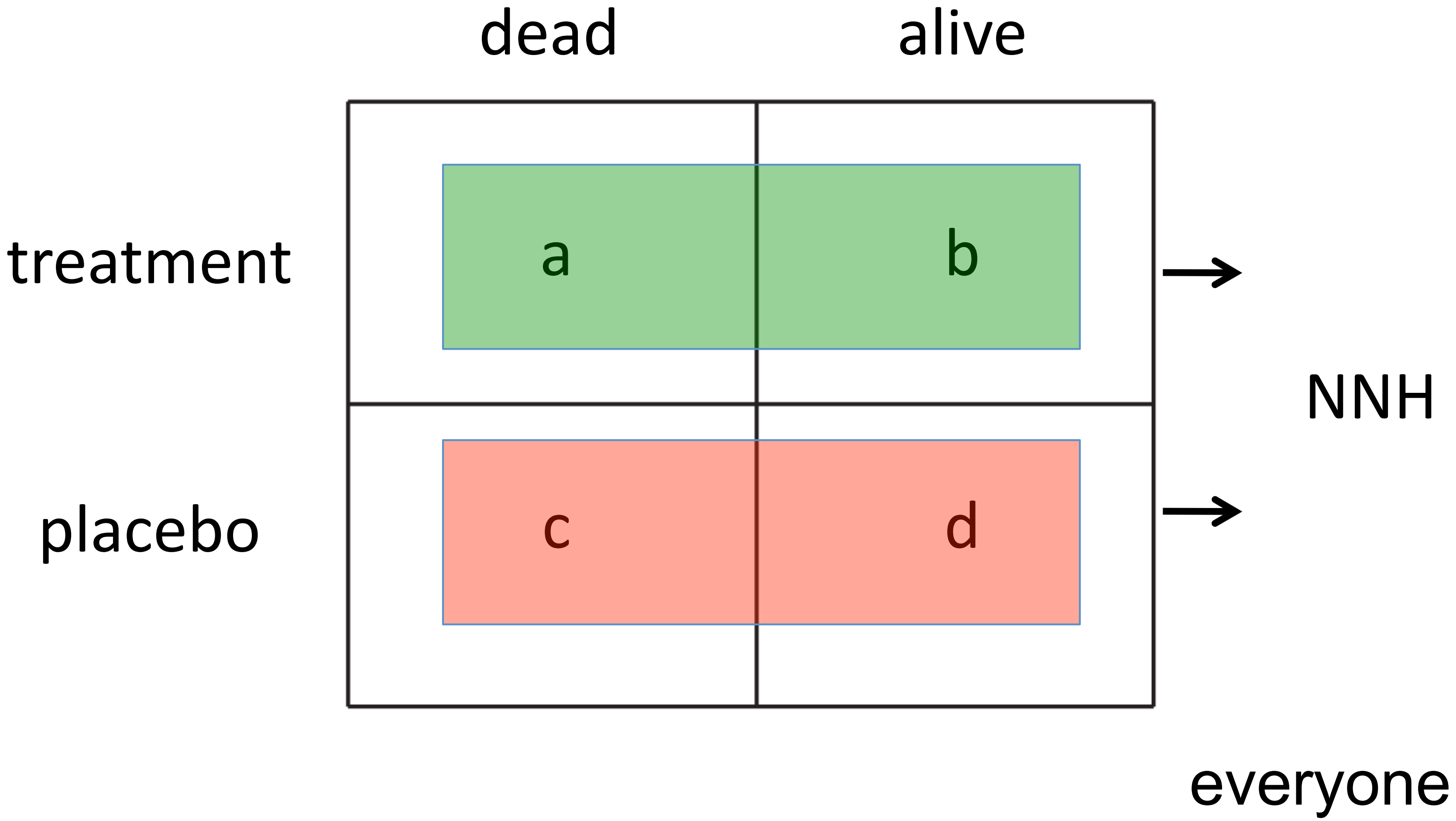
contingency tables

treatments: number needed to harm



	dead	alive
treatment	a	b
placebo	c	d

→ NNH →

everyone

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contingency tables

treatments: number needed to harm

	dead	alive	attributable risk
treatment	a	b	→ a/(a+b)
			-
placebo	c	d	→ c/(c+d)
			everyone

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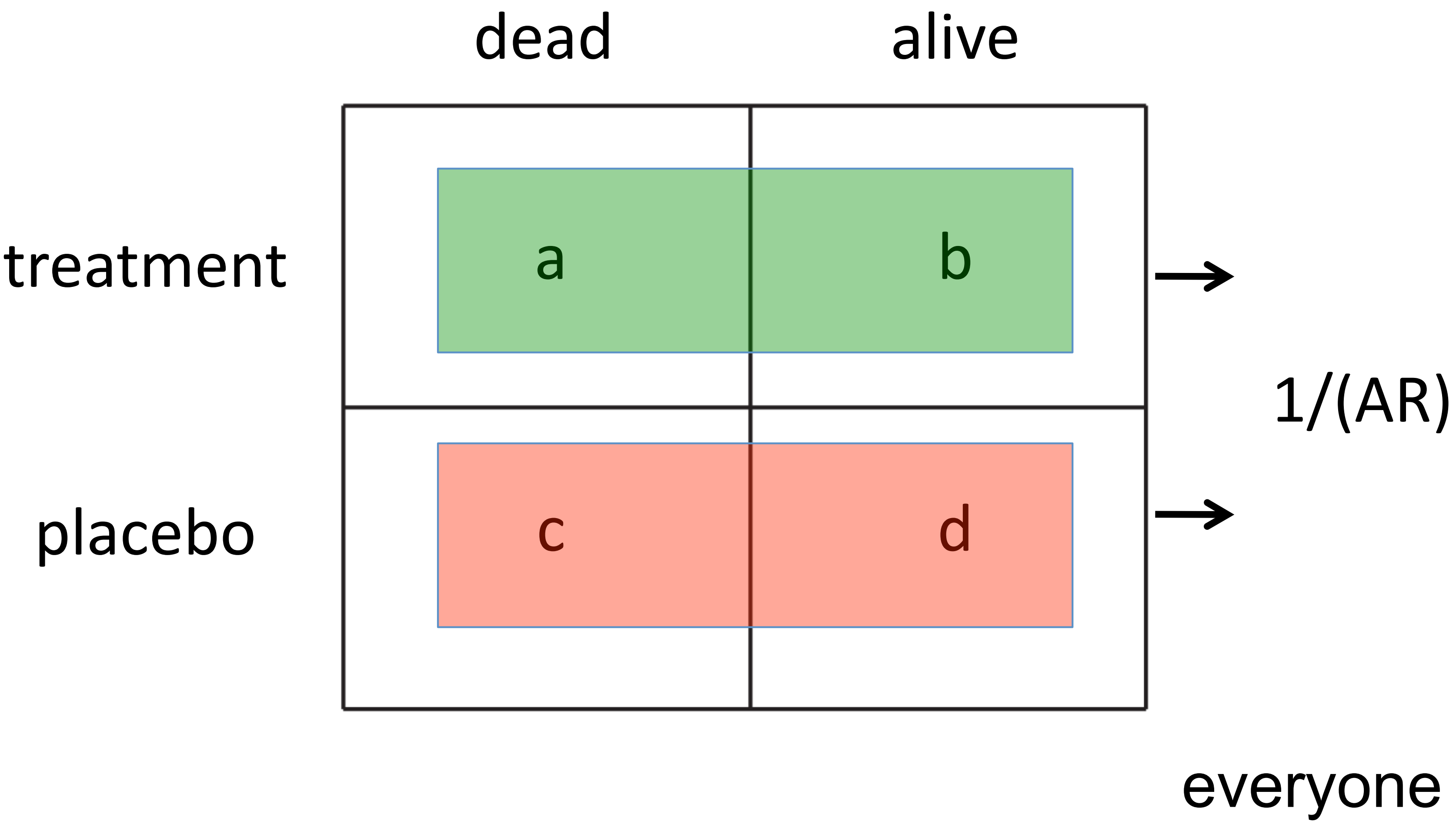
contingency tables

treatments: number needed to harm



	dead	alive
treatment	a	b
placebo	c	d

→

→

1/(AR)

everyone

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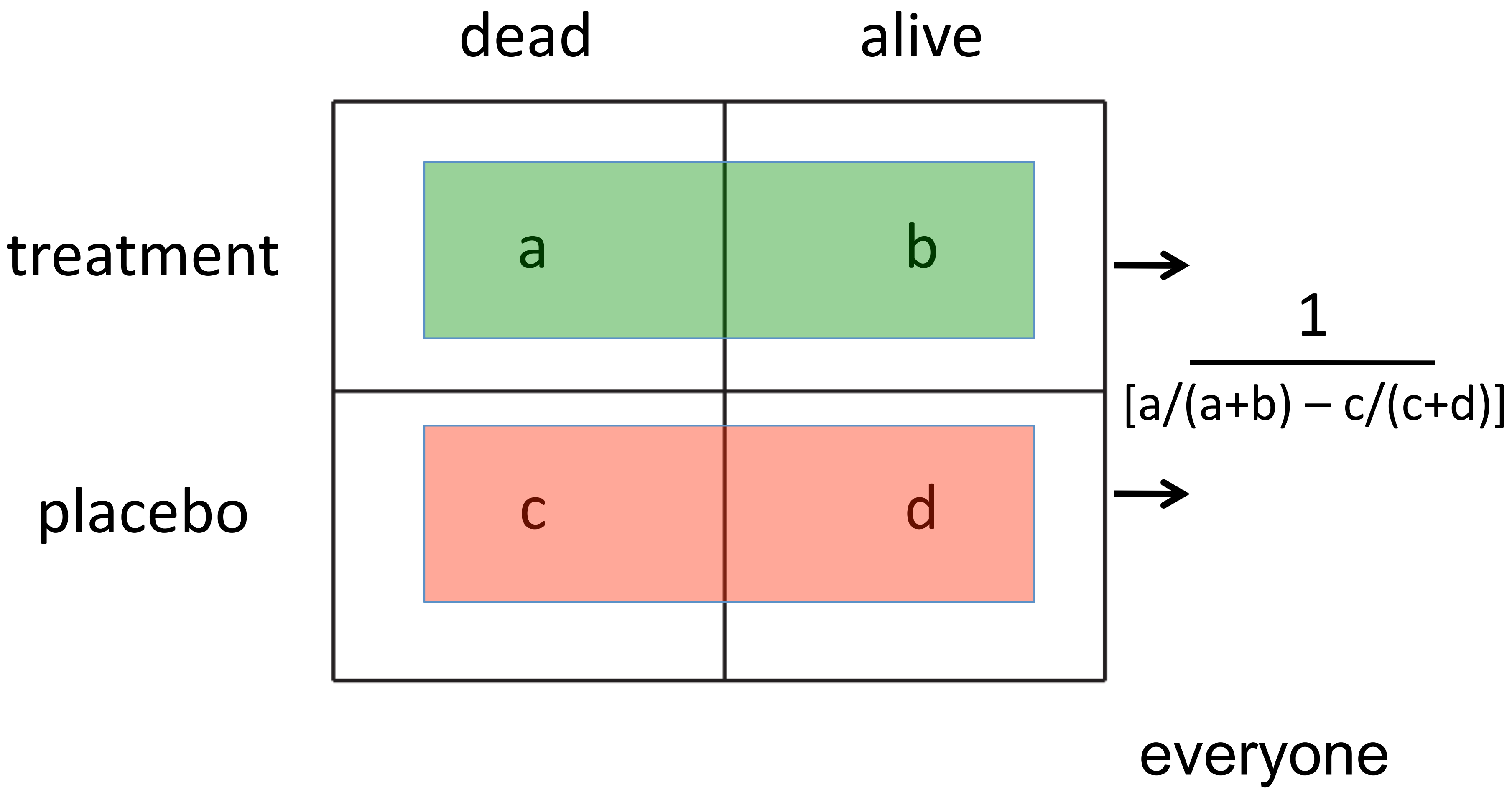
contingency tables

treatments: number needed to harm



	dead	alive
treatment	a	b
placebo	c	d

$$\frac{1}{[a/(a+b) - c/(c+d)]}$$

everyone

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contingency tables

treatments: NNT vs. NNH

What happens when NNT > NNH?

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how many sick people are there?

prevalence = how many people are sick

single time point

point prevalence = (total # sick)/(total population)

incidence = how many people are getting sick, new cases

time interval

incidence = (new cases over time)/(total population **at risk***)

at risk* = excludes currently have disease or previously positive

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how many sick people are there?

prevalence = how many people are sick

- single time point
- point prevalence = (total # sick)/(total population)

incidence = how many people are getting sick, new cases

- time interval
- incidence = (new cases over time)/(total population **at risk***)

prevalence ≅ incidence x disease duration
chronic disease: prevalence > incidence
acute disease: prevalence ≅ incidence

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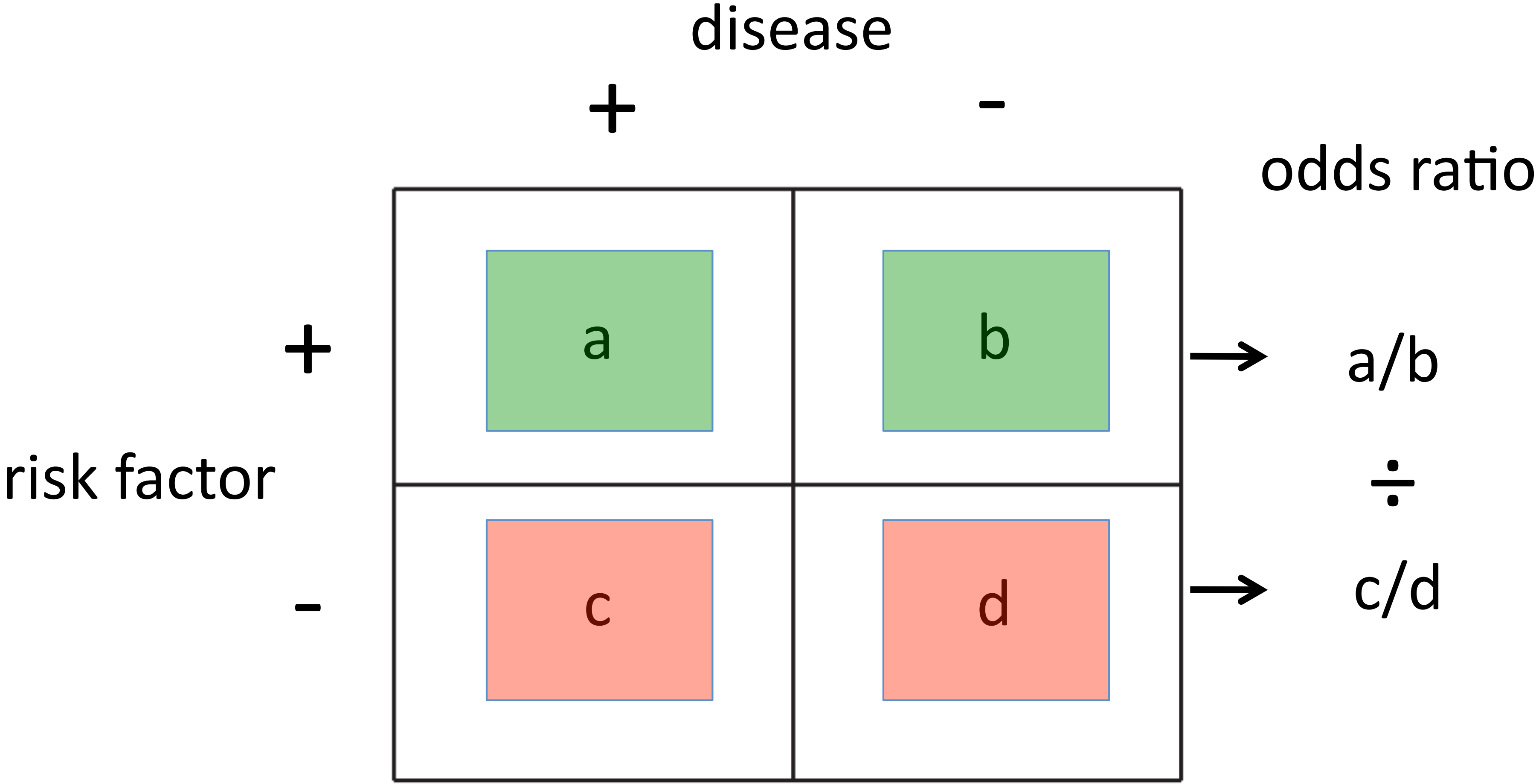
study types

- case control: retrospective, observational

  disease vs. no disease → look for risk factor

  statistic: **odds ratio**



		disease	
		+	-
risk factor	+	a	b
	-	c	d

odds ratio

a/b

÷

c/d

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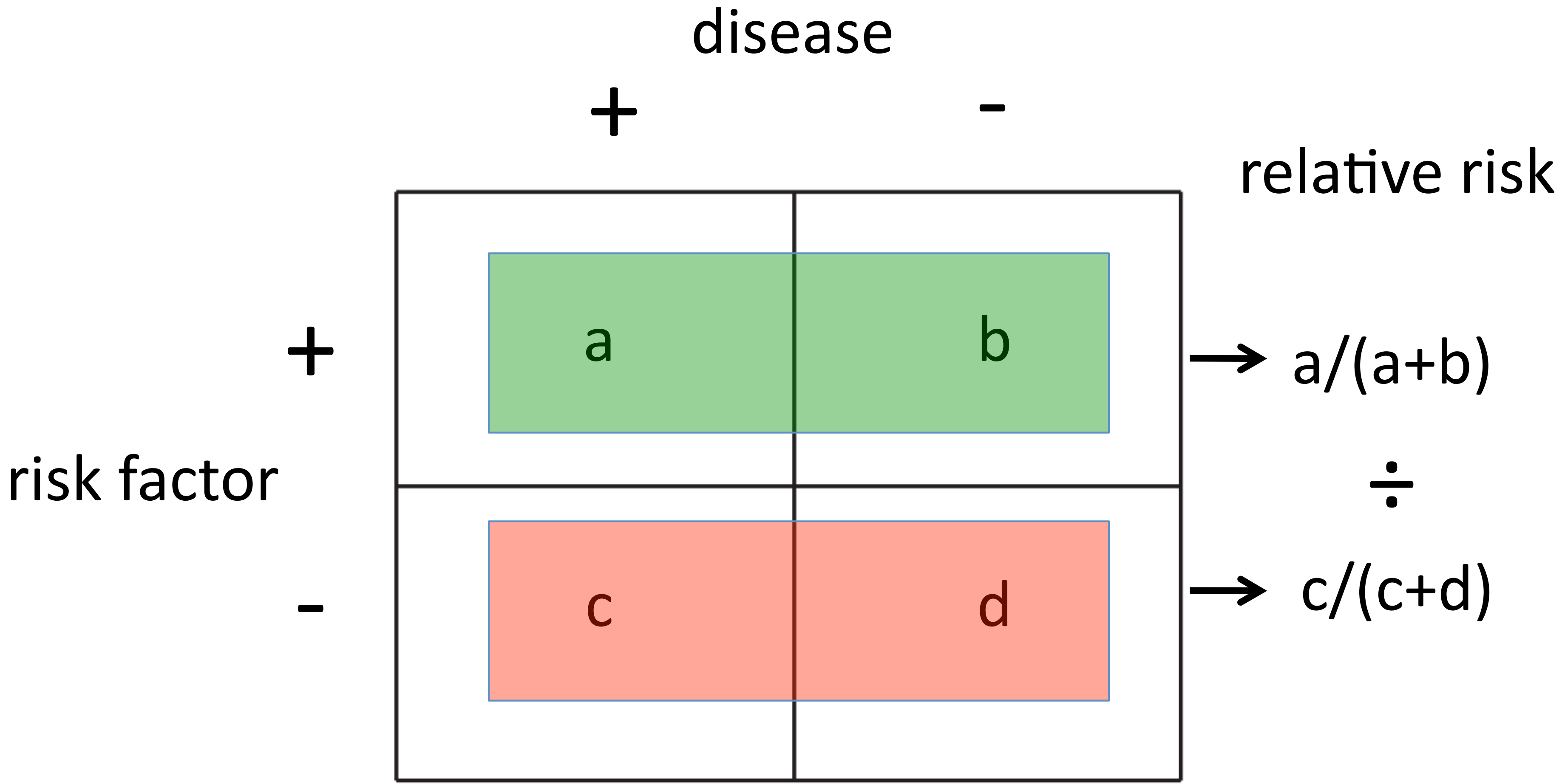
study types

- cohort: prospective, observational

risk factor present vs. absent → look for disease

statistic: **relative risk**



		disease		relative risk
		+	-	
risk factor	+	a	b	→ a/(a+b)
				÷
	-	c	d	→ c/(c+d)

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study types

- cross sectional: single time point, observational

  disease or risk factor presence

  statistic: **prevalence**

prevalence = how many people are sick

single time point

point prevalence = (total # sick)/(total population)

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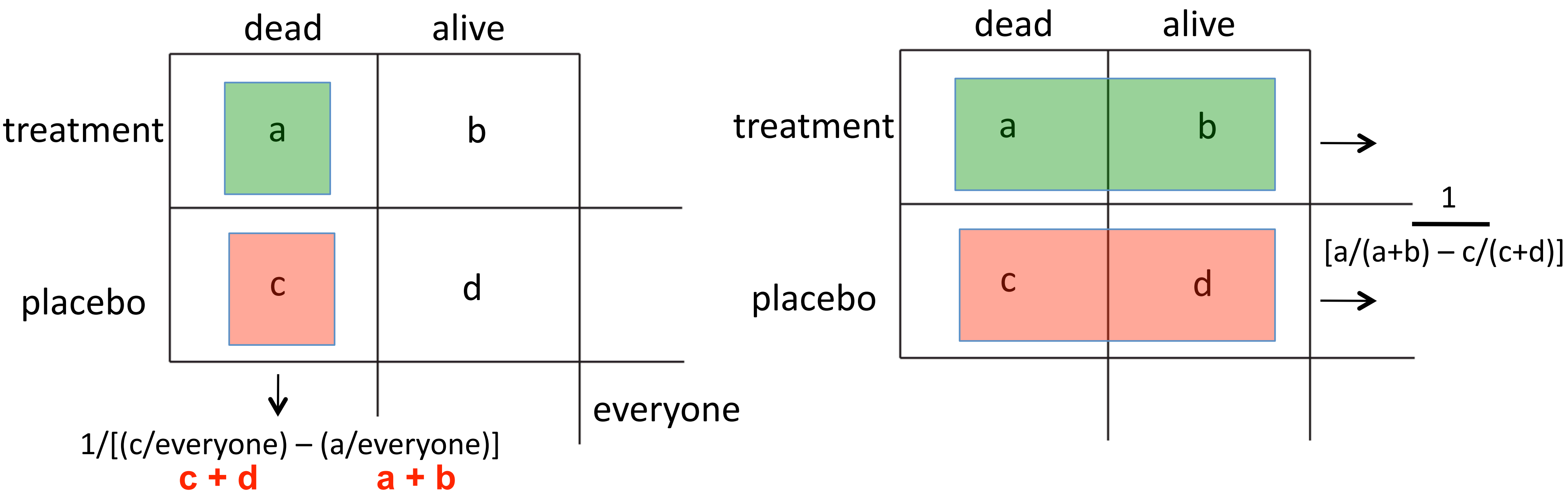
study types

- randomized controlled trial: prospective, interventional, gold

  treatment vs. placebo → outcome

  statistic: NNT/NNH, multiple comparisons

NNT | NNH



NNT

	dead	alive
treatment	🟩 a	b
placebo	🟥 c	d

everyone

1/[(c/everyone) – (a/everyone)]

c + d a + b

NNH

	dead	alive
treatment	🟩 a	🟩 b
placebo	🟥 c	🟥 d

$$\frac{1}{[a/(a+b) - c/(c+d)]}$$

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study types

- randomized controlled trial: prospective, interventional, gold
  treatment vs. placebo → outcome
  statistic: NNT/NNH, multiple comparisons

phase I:
small # pts, healthy volunteers = **safety**, toxicity, pharmacokinetics

phase II:
small # pts, have dz, placebo control = tx **efficacy**, dosing, adverse rxns

phase III:
large #pts, randomly assigned tx vs control = new vs old SOP tx or placebo

APPROVAL

phase IV:
post-marketing **surveillance** = for rare, long term effects

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study types

- meta-analysis: retrospective, chart review, platinum
  pools data from multiple studies, usually RCTs

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study types

- twin concordance study

    genes vs. environment questions
    genetic heritability: monozygotic vs. dizygotic
    think early life, autism etiology

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study types

- adoption study
  - genes vs. environment questions
  - think later life, schizophrenia etiology

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bias

bias = systematic error

- selection bias: nonrandom assignment into groups, loss to follow up
- recall bias: knowledge of presence of dz changes subject’s response
- sampling bias: subjects are not representative of population, non-generalizable
- late-look bias: information gathered at inappropriate time, eg: giving survey on fatal dz to alive pts
- procedure bias: subjects in different groups not treated the same
- confounding bias: one factor distorts/confuses the effect of another closely related one
- lead-time bias: early detection confused with ↑survival...seen with improved screening
- pygmalion effect: researchers belief changes outcome of tx...researcher's behavior
- hawthorne effect: subjects change behavior when the they know they’re being studied...subject's behavior
- observer bias: researcher's decision affected by prior knowledge of subject’s exposure status

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