

<https://t.me/UWorldNotesStep2>

BIOSTATISTICS & EPIDEMIOLOGY

UWorld Step 2 Tables and Images (Subject)

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Epidemiology and population health

X-linked recessive inheritance

Affected father

		Mother		
		X	X	
Father	X _d	XX _d	XX _d	All daughters are carriers
	Y	XY	XY	All sons are unaffected

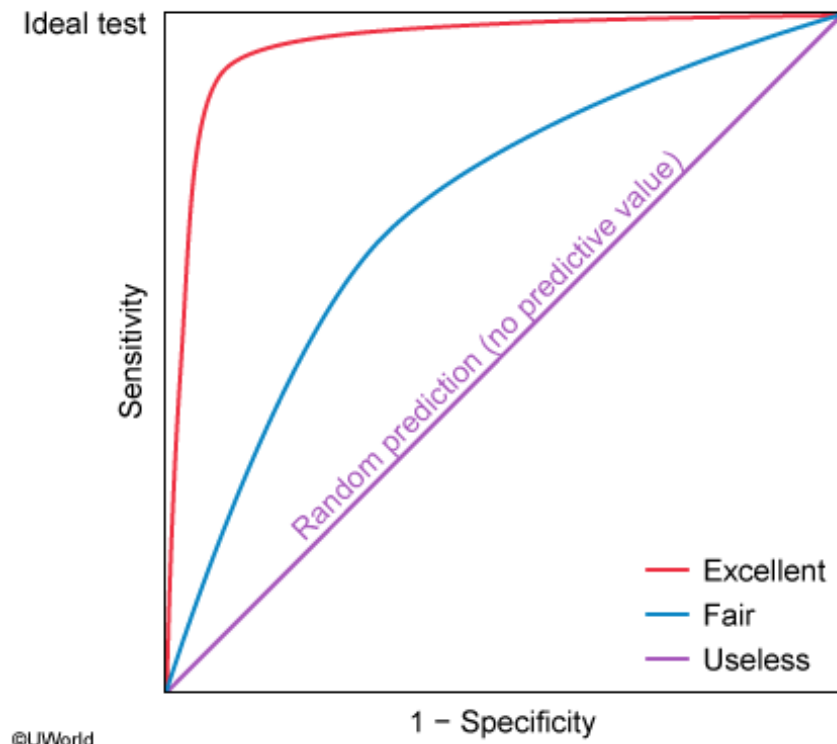
Carrier mother

		Mother		
		X	X _d	
Father	X	XX	XX _d	Daughters have 50% chance of becoming carriers
	Y	XY	X _d Y	Sons have 50% chance of being affected

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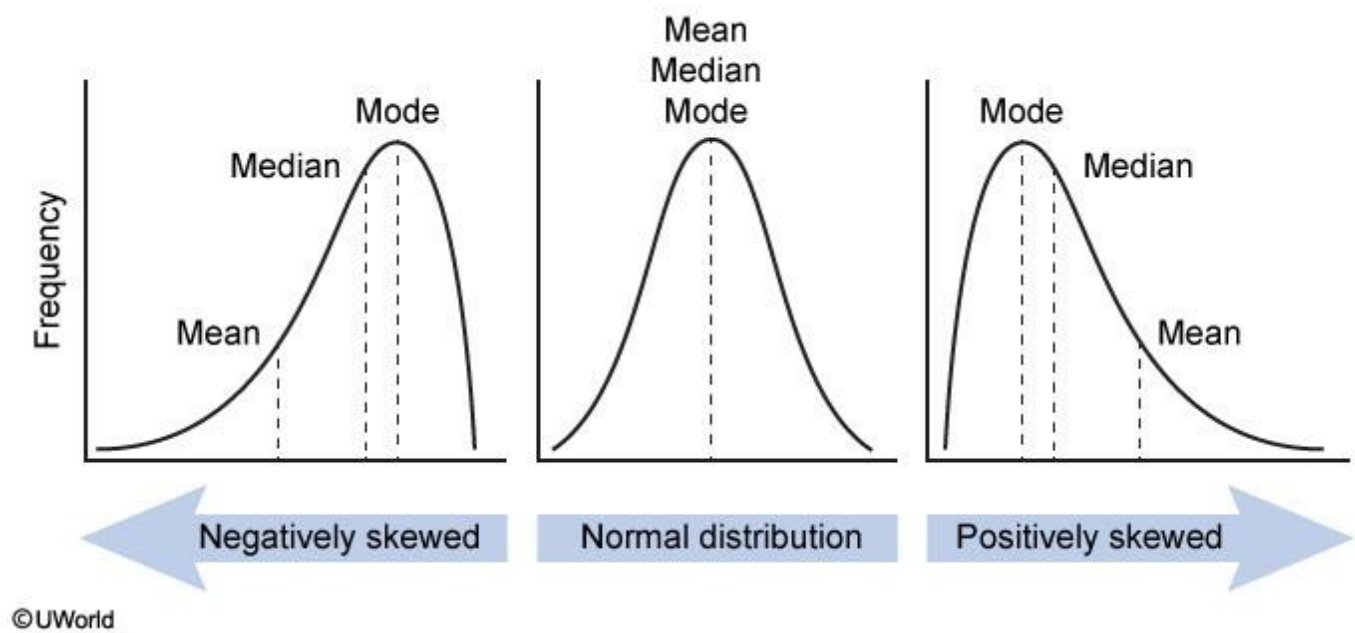
X-linked recessive inheritance

Interpretation of areas under the ROC curve



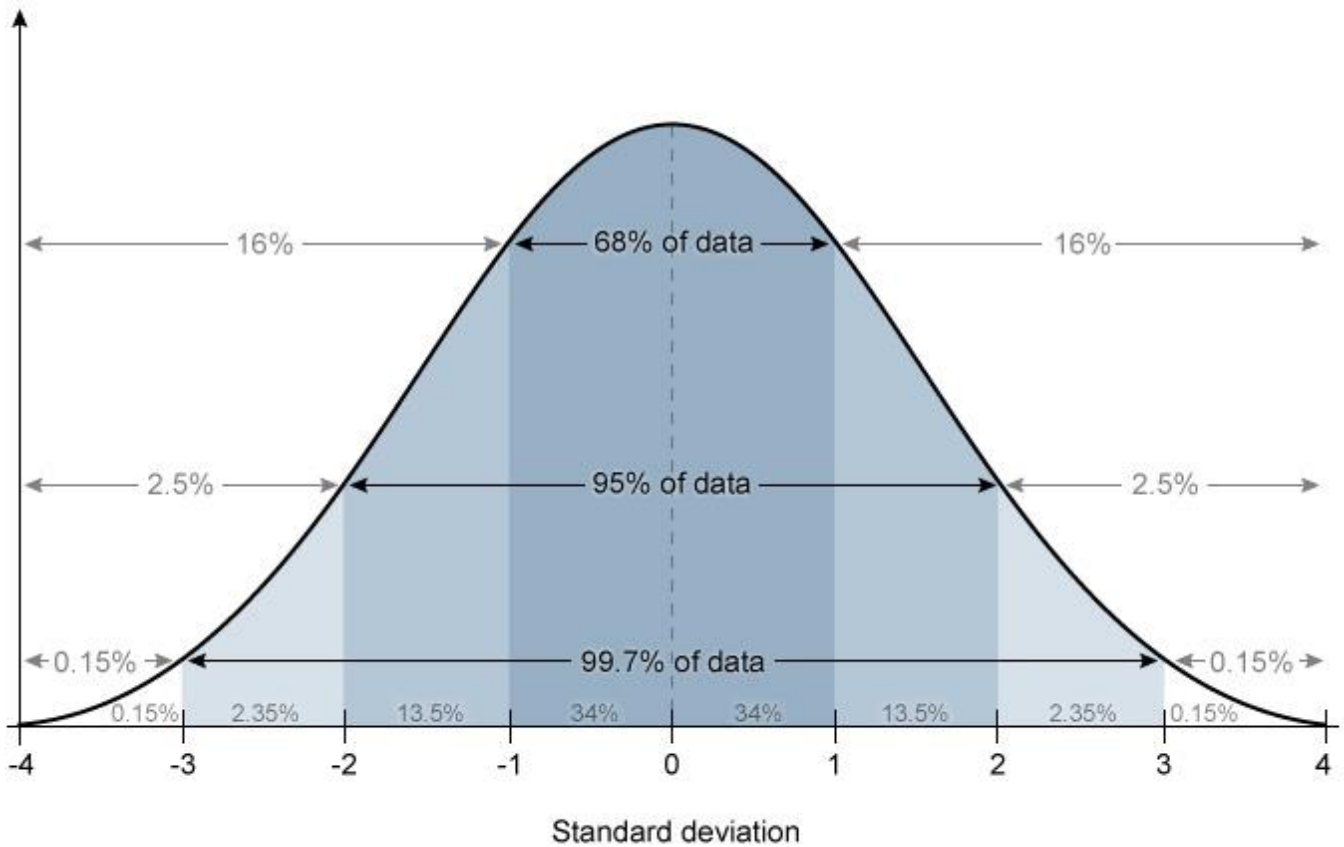
Interpretation of areas under the ROC curve

Measures and distribution of data



Mean

68-95-99.7 rule



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68-95-99.7 rule

Factors affecting power

Factor		Power	Note
Sample size	↓	↓	More difficult to detect effects
	↑	↑	Easier to detect effects
Variability of outcome	↑	↓	More difficult to detect effects
	↓	↑	Easier to detect effects
Effect size	↓	↓	More difficult to identify small effect
	↑	↑	Easier to identify large effect
Significance level (alpha, α)	↓	↓	Stringent threshold for statistical significance
	↑	↑	Lenient threshold for statistical significance

Effect size = difference between compared groups.

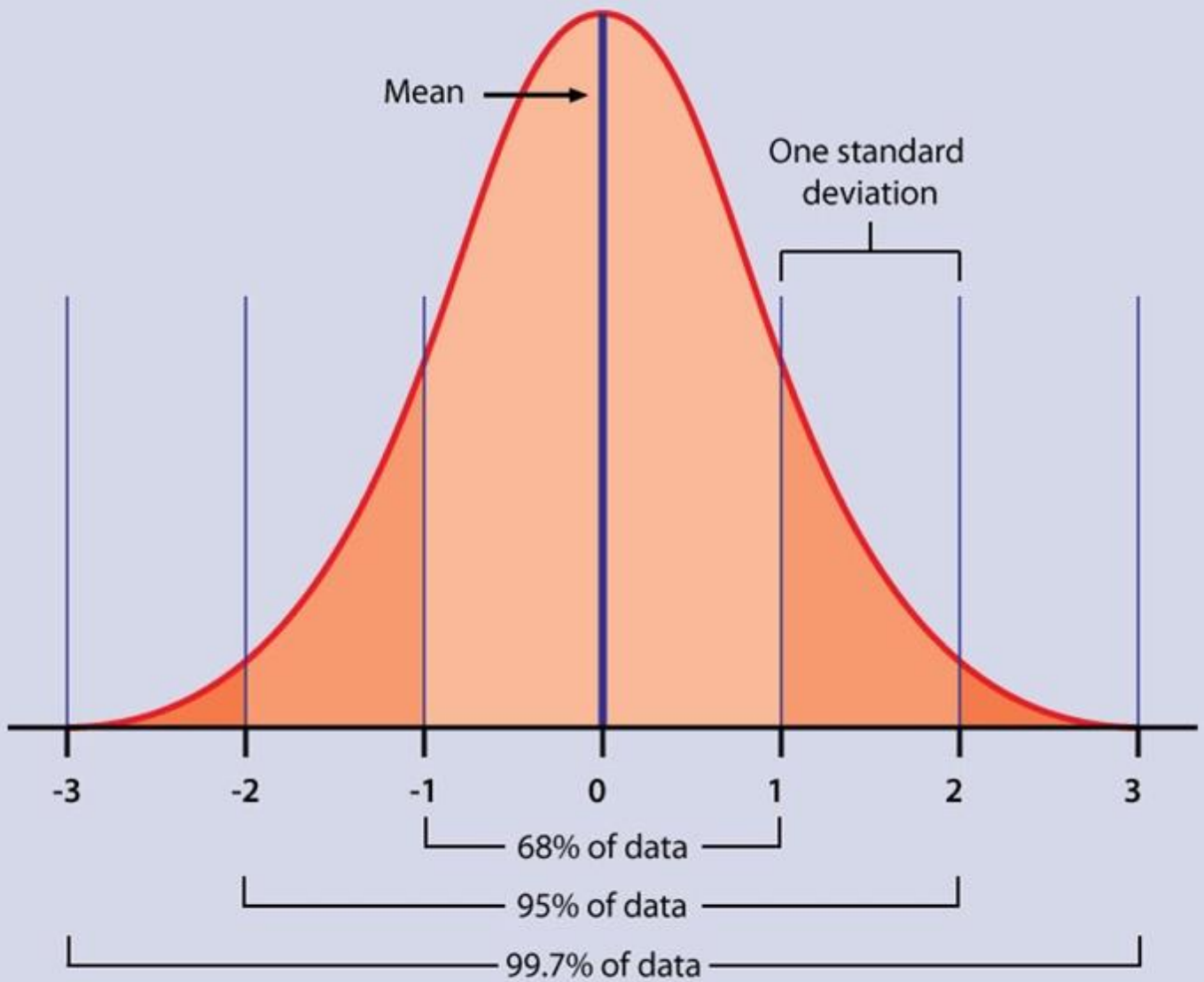
Factors affecting power

SENSITIVITY AND SPECIFICITY

	Positive condition	Negative condition	
Positive test result	TP	FP	PPV = TP / (TP + FP)
Negative test result	FN	TN	NPV = TN / (TN + FN)
	Sensitivity = TP / (TP + FN)	Specificity = TN / (TN + FP)	

FN = false negative; **FP** = false positive; **NPV** = negative predictive value; **PPV** = positive predictive value; **TN** = true negative; **TP** = true positive.

Standard deviation of a normal distribution



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Standard deviation of a normal distribution

Precision & accuracy



Low precision
Low accuracy



Low precision
High accuracy



High precision
Low accuracy



High precision
High accuracy

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Precision & accuracy

		Truth about the null hypothesis H_0	
		H_0 true	H_0 false
Decision based on test results	Reject H_0	Type I error (α)	Correct conclusion ($1 - \beta$) = power
	Fail to reject H_0	Correct conclusion ($1 - \alpha$)	Type II error (β)

Hypothesis testing

MEASURES OF ASSOCIATION

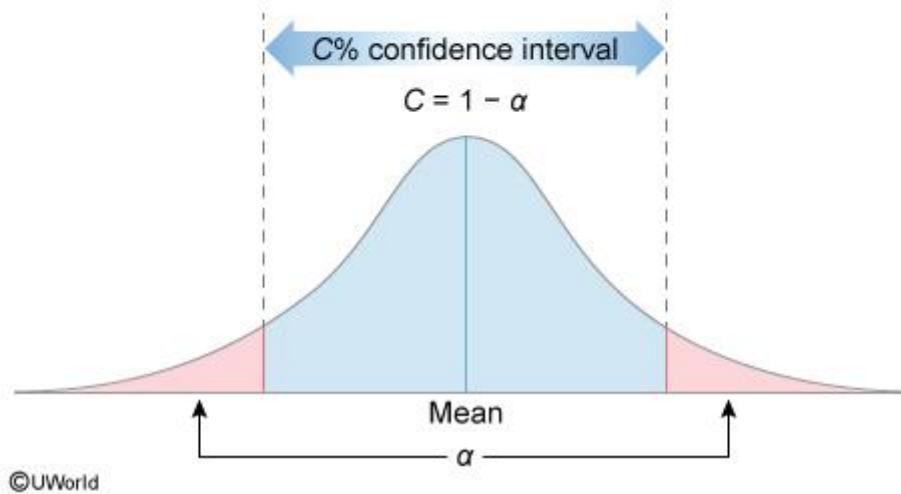
	MS +	MS -
CCSVI +	25 (a)	10 (b)
CCSVI -	125 (c)	200 (d)
Total	150	210

NUMBER NEEDED TO TREAT

Common measures of therapeutic efficacy

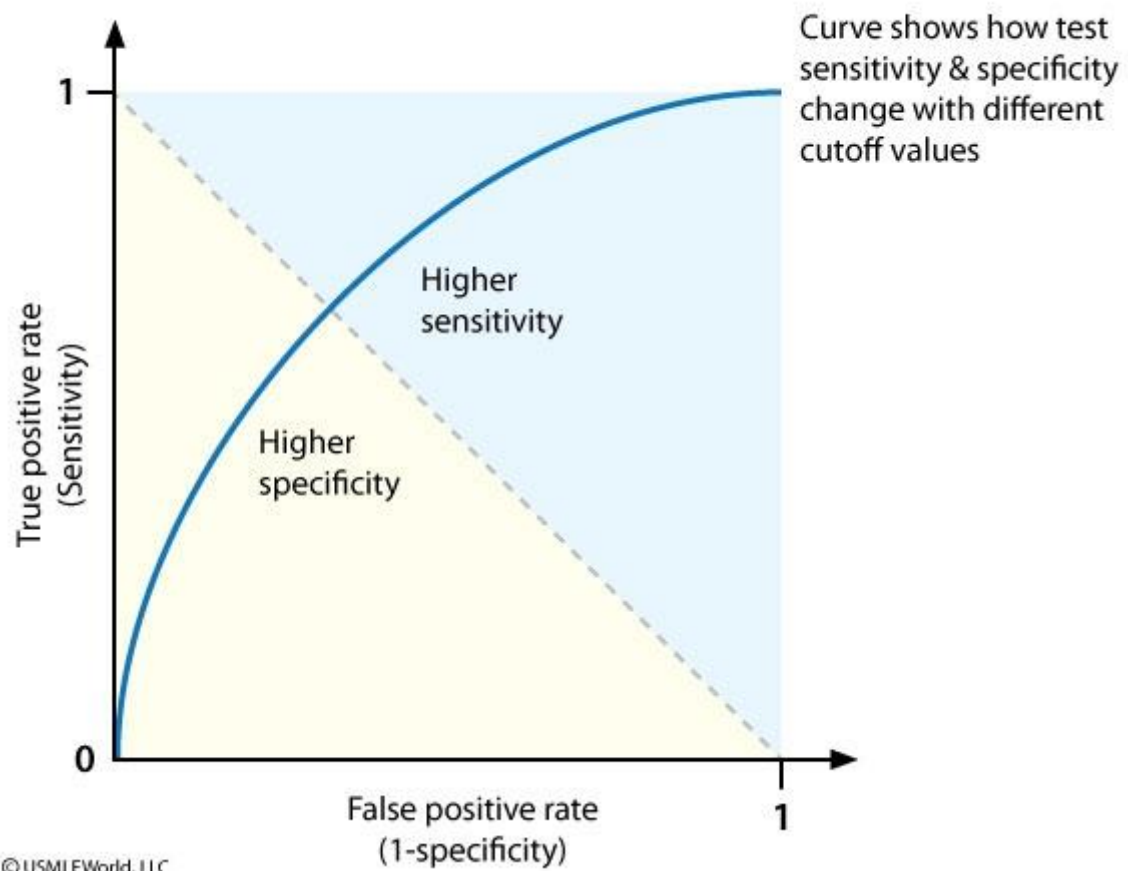
Term	Definition	Calculation
Absolute risk reduction (ARR)	Percentage indicating the actual difference in event rate between control & treatment groups	ARR = control rate – treatment rate
Relative risk reduction (RRR)	Percentage indicating relative reduction in the treatment event rate compared to the control group	RRR = ARR / control rate
Relative risk (RR)	Ratio of the probability of an event occurring in the treatment group compared to the control group	RR = treatment rate / control rate
Number needed to treat (NNT)	Number of individuals who need to be treated to prevent a negative outcome in 1 patient	NNT = 1 / ARR

Significance level α	Confidence level $C = 1 - \alpha$	Confidence interval $C\%$
0.10	0.90	90%
0.05	0.95	95%
0.01	0.99	99%



P-value and confidence interval

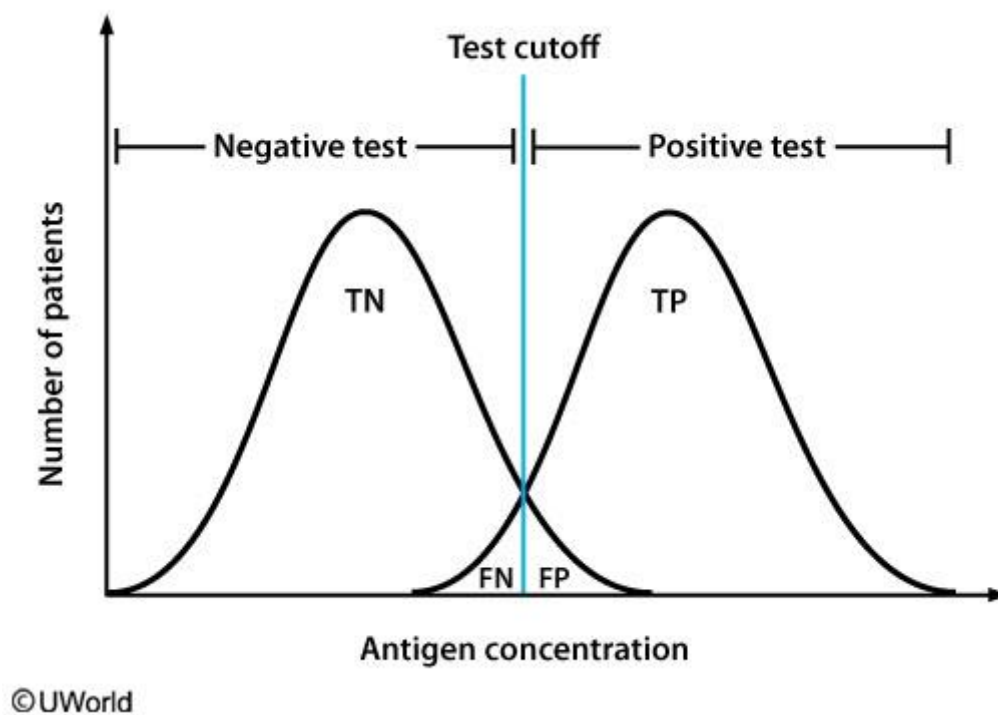
ROC curve



Receiver Operating Characteristic (ROC curve)

SENSITIVITY AND SPECIFICITY

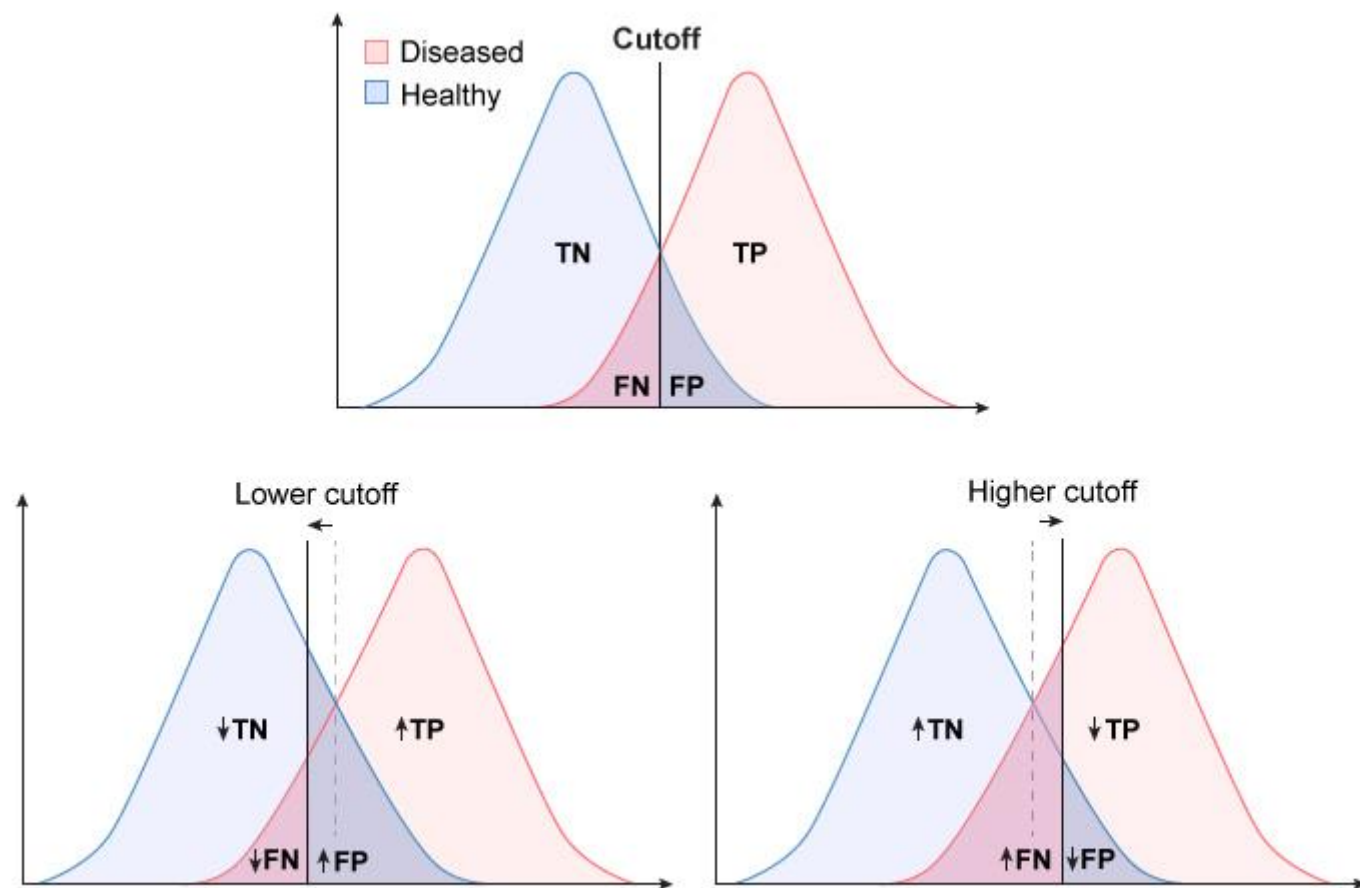
Test Results	Disease Present	Disease Absent	Total
Positive	A True positive (TP)	B False positive (FP)	A + B
Negative	C False negative (FN)	D True negative (TN)	C + D
Total	A + C	B + D	A + B + C + D



Sensitivity and specificity (Test cutoff)

SENSITIVITY, SPECIFICITY, NPV, PPV

Test results	Disease		Total
	Present	Absent	
Positive	A True positive (TP)	B False positive (FP)	A+B
Negative	C False Negative (FN)	D True Negative (TN)	C+D
Total	A+C	B+D	A+B+C+D



FN = false negatives; FP = false positives; TN = true negatives; TP = true positives

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Sensitivity, specificity, NPV, PPV

Prevalence & PPV/NPV	
Prevalence ↑	<ul style="list-style-type: none"> • PPV ↑ • NPV ↓
Prevalence ↓	<ul style="list-style-type: none"> • PPV ↓ • NPV ↑

NPV = negative predictive value;
 PPV = positive predictive value.

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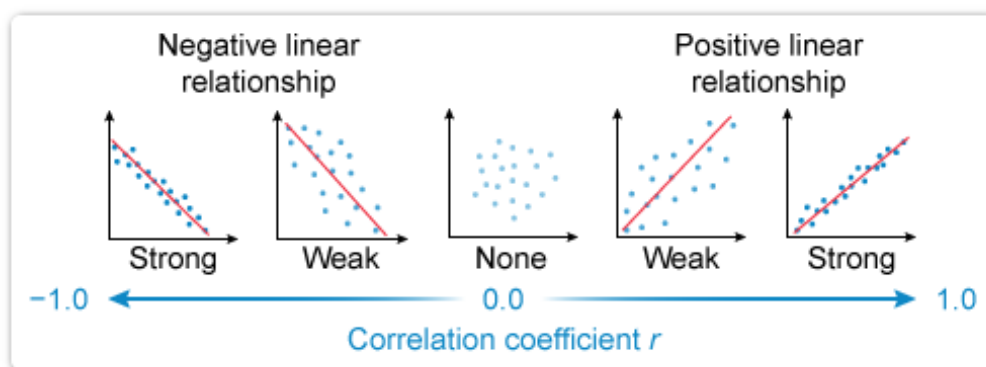
Sensitivity, specificity, NPV, PPV

		Dependent variable	
		Qualitative (categorical)	Quantitative
Independent variable	Qualitative (categorical)	Chi-square, logistic regression*	t-test, ANOVA, linear regression
	Quantitative	Logistic regression*	Correlation, linear regression

* Dependent variable must be dichotomous.

ANOVA = analysis of variance.

Direction and strength of a linear relationship



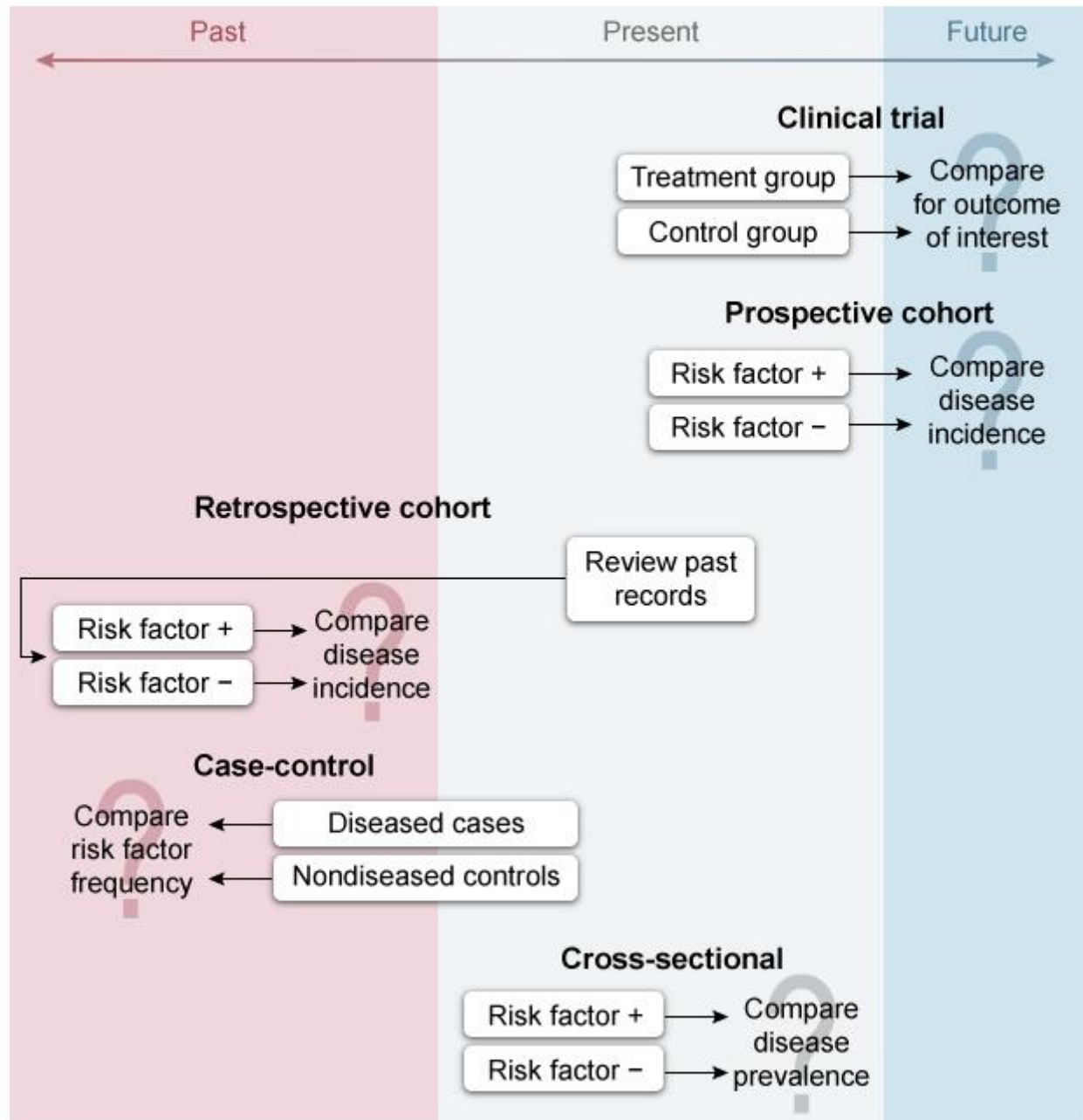
Direction and strength of a linear relationship

Common types of systematic errors in statistical studies	
Selection biases	<p><i>Inappropriate selection or poor retention of study subjects</i></p> <ul style="list-style-type: none">• Ascertainment (sampling) bias: Study population differs from target population due to nonrandom selection methods• Nonresponse bias: High nonresponse rate to surveys/questionnaires can cause errors if nonresponders differ in some way from responders• Berkson bias: Disease studied using only hospital-based patients may lead to results not applicable to target population• Prevalence (Neyman) bias: Exposures that happen long before disease assessment can cause study to miss diseased patients that die early or recover• Attrition bias: Significant loss of study participants may cause bias if those lost to follow-up differ significantly from remaining subjects
Observational biases	<p><i>Inaccurate measurement or classification of disease, exposure, or other variable</i></p> <ul style="list-style-type: none">• Recall bias: Common in retrospective studies, subjects with negative outcomes are more likely to report certain exposures than control subjects• Observer bias: Observers misclassify data due to individual differences in interpretation or preconceived expectations regarding study• Reporting bias: Subjects over- or under-report exposure history due to perceived social stigmatization• Surveillance (detection) bias: Risk factor itself causes increased monitoring in exposed group relative to unexposed group, which increases probability of identifying a disease

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Common types of systematic errors in statistical studies

Temporality of different study designs

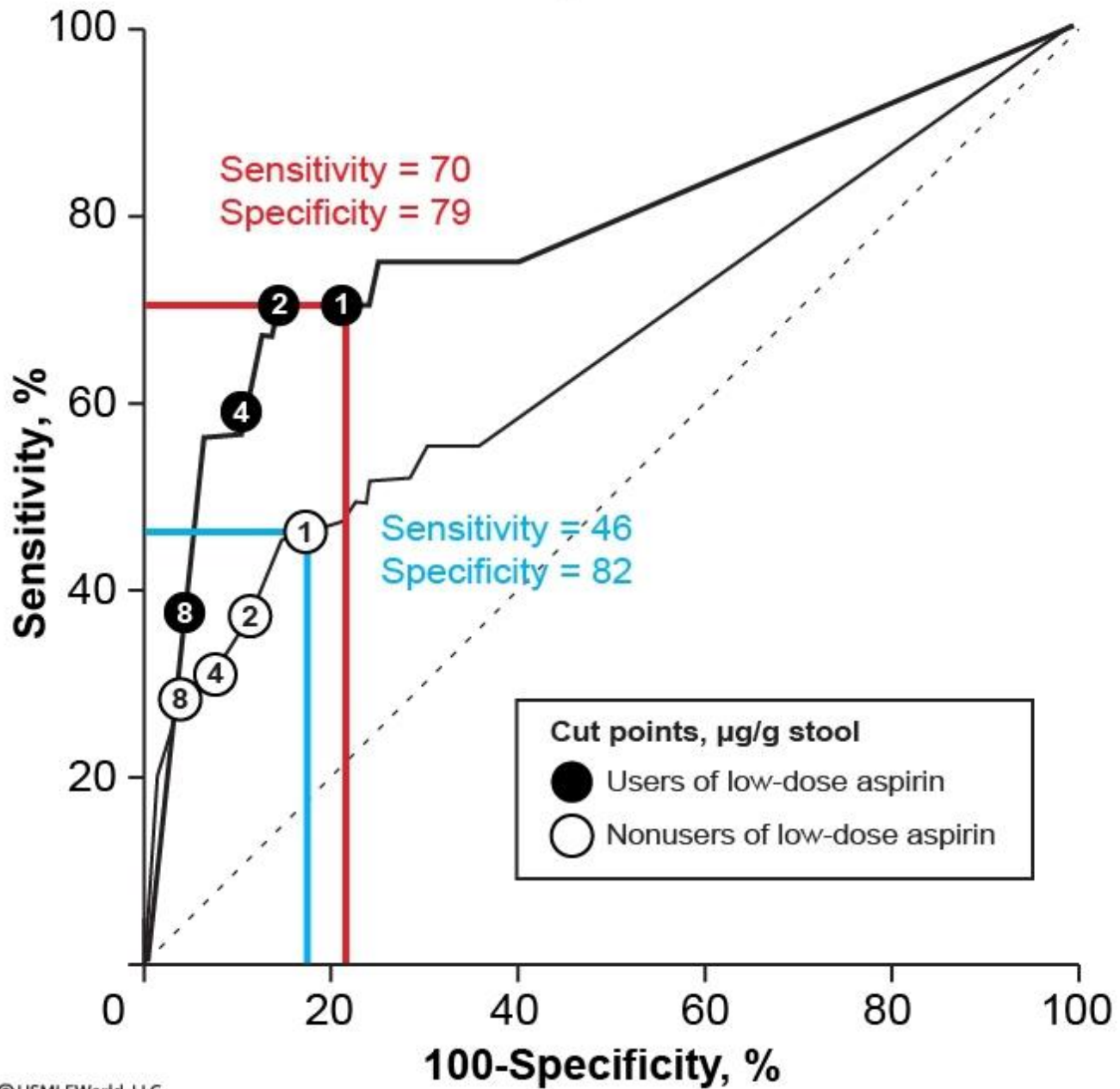


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Temporality of different study designs

Basic criterion to establish causality	Explanation
Analogy	Similar associations known
Biological gradient	Dose-response relationship between cause & effect
Biological plausibility	Probable given established knowledge
Coherence	Association should not conflict with known facts
Consistency	Cause widely associated with effect
Experimental evidence	Effect evidenced by experimental designs
Specificity	Cause uniquely associated with effect
Strength of association	Cause associated with a substantive effect
Temporality	Cause precedes effect

Hemoglobin test



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Hemoglobin test

Confounding vs effect modification

Confounding

Crude analysis

Alcohol use $\xrightarrow[\text{RR} = 1.81 \text{ (95\%CI: 1.06, 3.10)}]{\text{Significant association}}$ Bladder cancer

Stratified by smoking

Smokers

Alcohol use $\xrightarrow[\text{RR} = 0.95 \text{ (95\%CI: 0.51, 1.76)}]{\text{No association}}$ Bladder cancer

Non-smokers

Alcohol use $\xrightarrow[\text{RR} = 1.03 \text{ (95\%CI: 0.34, 3.13)}]{\text{No association}}$ Bladder cancer

Effect modification

Crude analysis

Use of oral contraceptive $\xrightarrow[\text{RR} = 1.40 \text{ (95\%CI: 1.01, 1.96)}]{\text{Significant association}}$ Breast cancer

Stratified by family history

Family history of breast cancer

Use of oral contraceptive $\xrightarrow[\text{RR} = 3.33 \text{ (95\%CI: 2.51, 4.41)}]{\text{Strong significant association}}$ Breast cancer

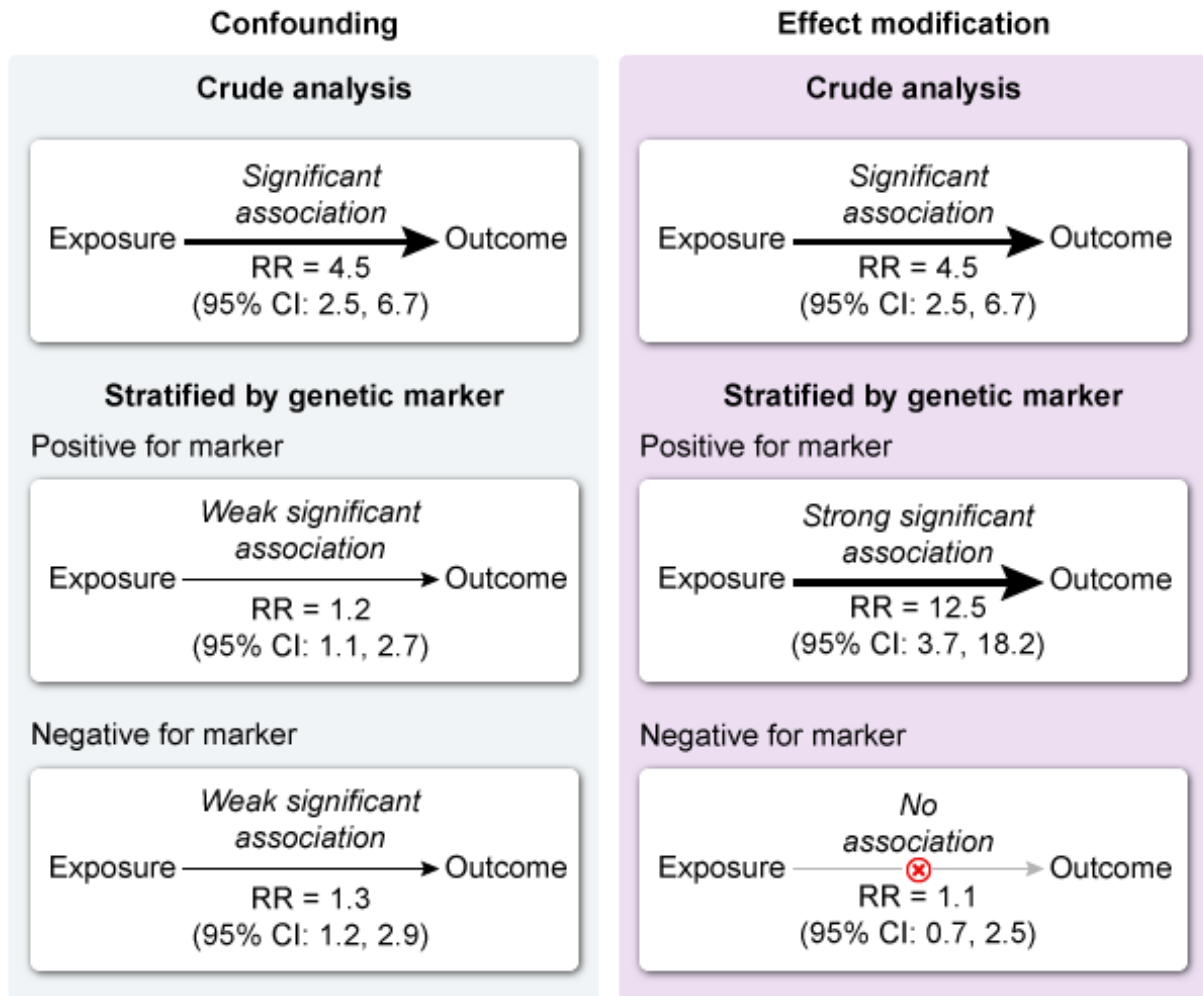
No family history of breast cancer

Use of oral contraceptive $\xrightarrow[\text{RR} = 1.27 \text{ (95\%CI: 1.01, 1.60)}]{\text{Weak significant association}}$ Breast cancer

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Confounding vs effect modification

Confounding vs effect modification



RR = relative risk; CI = confidence interval.

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Confounding vs effect modification

Methods to control confounding	
Design stage	<ul style="list-style-type: none"> • Matching • Restriction • Randomization
Analysis stage	<ul style="list-style-type: none"> • Stratified analysis • Statistical modeling

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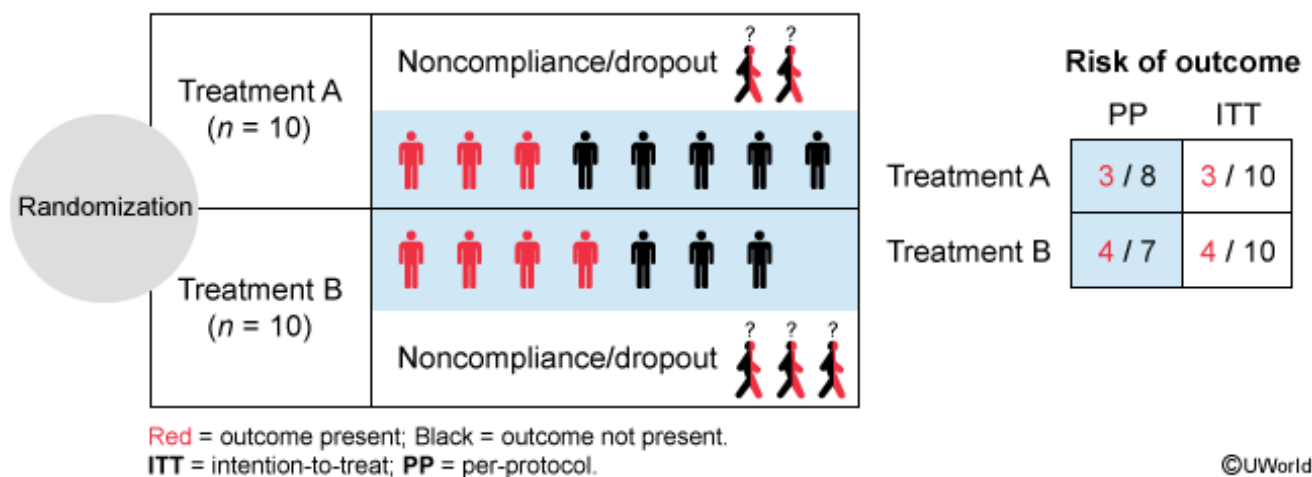
Methods to control confounding

Statistical significance:

Relationship between confidence intervals and p -values

"A ___ confidence interval that does not include the null value..."	95%	99%
"...corresponds to $p < ___$."	0.05	0.01

Per-protocol versus intention-to-treat analysis



Per-protocol versus intention-to-treat analysis

Type I (α) and type II (β) errors

		True status	
		There is a true difference (ie, H_0 is false)	There is NO true difference (ie, H_0 is true)
Study result	Difference calculated as statistically significant (ie, reject H_0)	Correctly conclude there is a difference	Type I (α) error (Falsely conclude there is a difference)
	Difference calculated as NOT statistically significant (ie, fail to reject H_0)	Type II (β) error (Falsely conclude there is NO difference)	Correctly conclude there is NO difference

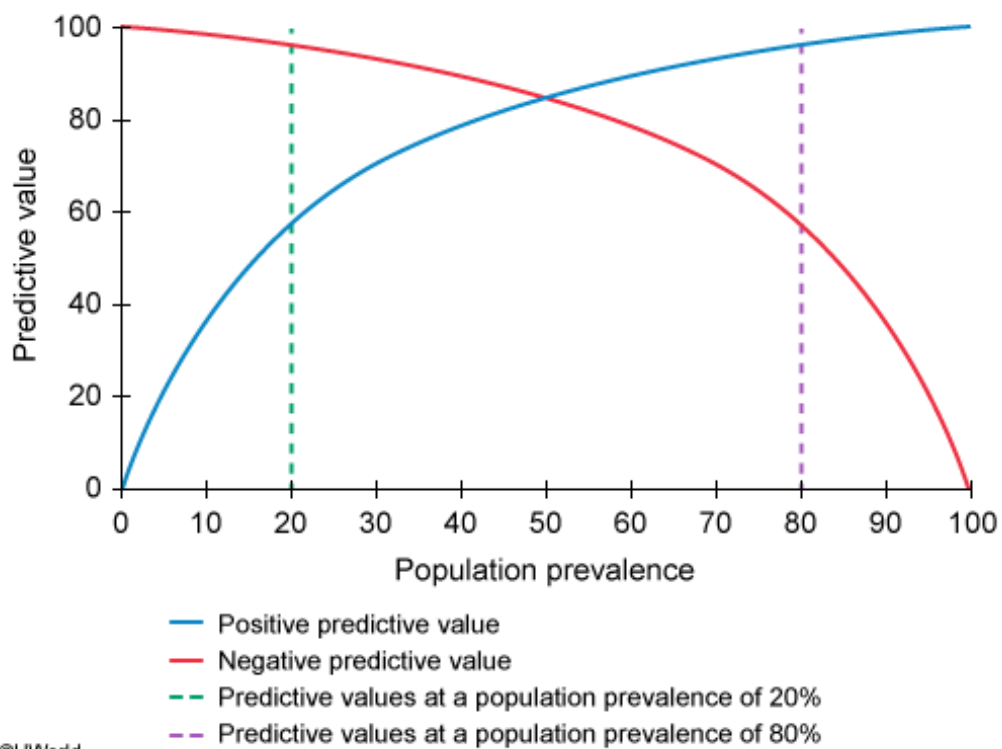
 H_0 = null hypothesis of no difference.

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	95% confidence interval	99% confidence interval
Null value outside confidence intervals	$p < 0.05$	$p < 0.01$
Null value inside confidence interval	$p \geq 0.05$	$p \geq 0.01$

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Risk



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Sensitivity, specificity, NPV, PPV

Types of studies in the health sciences

Experimental	
Randomized controlled trial	<ul style="list-style-type: none"> • Random allocation into treatment & placebo groups • Can determine efficacy of the intervention
Nonrandomized design	<ul style="list-style-type: none"> • Nonrandom allocation into treatment & placebo groups • Can determine efficacy of the intervention
Observational	
Cohort	<ul style="list-style-type: none"> • Data gathered from the same individuals over time (longitudinal) • Can assess risk factors or outcomes
Cross-sectional	<ul style="list-style-type: none"> • Data gathered at one point in time • Can determine prevalence of an outcome in a population
Case-control	<ul style="list-style-type: none"> • Data gathered from individuals with the condition of interest (cases) & compared to individuals without the condition (controls)
Case	<ul style="list-style-type: none"> • Detailed information gathered about one individual (or a small group of individuals)
Review	
Meta-analysis	<ul style="list-style-type: none"> • Data from multiple studies are statistically combined & analyzed

	Internal validity	External validity
Characteristics	Describes causality (ie, if change in independent variable causes change in dependent variable)	Describes generalizability (ie, if observed relationship applies to situations or people outside study)
	↑ As study becomes more tightly controlled	↓ As study becomes more tightly controlled
	↓ As study becomes more like the real world	↑ As study becomes more like the real world
Threats to validity	Bias due to: <ul style="list-style-type: none"> • Confounding • History • Maturation • Measurement • Regression toward the mean • Repeated testing • Selection 	Bias due to: <ul style="list-style-type: none"> • Artificial research environment • Measurement effects • Nonrepresentative sample