Research design & study execution workshop series

Session 4

SEPTEMBER 2, 2015

- **Quick review**
- **Variables and their measurement**

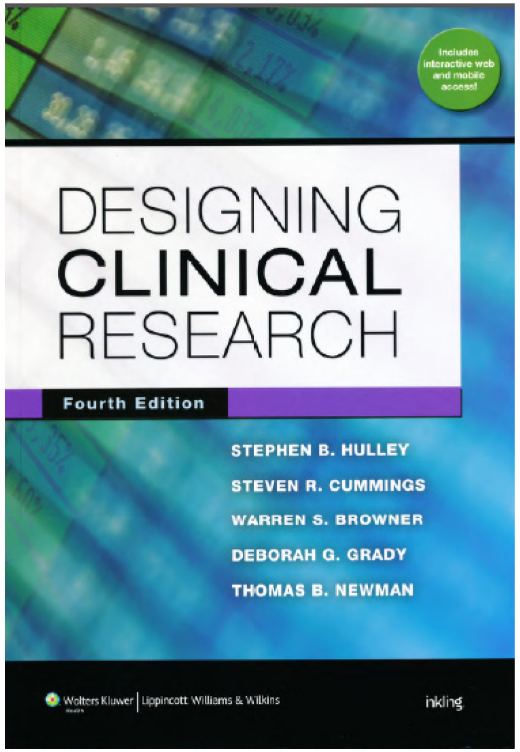
Goals & learning objectives

- Name 5 key types of variables
- Describe how your choice of study design + variables affects your ability to do the study you want

Background reading for today

Designing clinical research

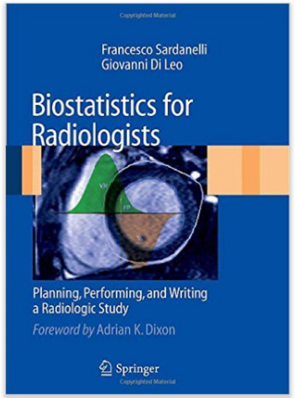
Chapter 4. Planning the Measurements: Precision, Accuracy, and Validity (p 32-41)



Extra material for today

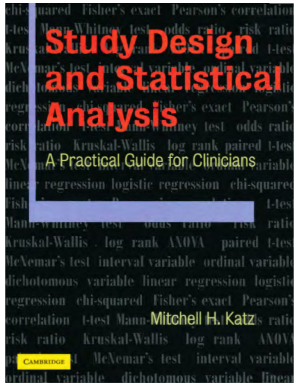
Biostatistics for radiologists

Chapter 2. Variables and measurement scales, normal distribution, and confidence intervals (p 41-65)



Study Design and Statistical Analysis

All Tables about choosing statistical tests, etc.



Quick review

Sessions 1, 2 & 3

Research questions

- FINER, ‘predictor & outcome’ format

Overview of study designs

- Case report, case series, cross-sectional study, cohort study, case-control study

Choosing appropriate study subjects

- Populations vs. samples; inclusion/exclusion criteria; developing a sampling plan

Montage teams sports challenge

- Sports injuries; published literature about football

Background readings

What makes a good research question?

Chapter 1. Getting started: The Anatomy and Physiology of Clinical Research

Chapter 2. Conceiving the research question and developing the study plan

Choosing appropriate study subjects

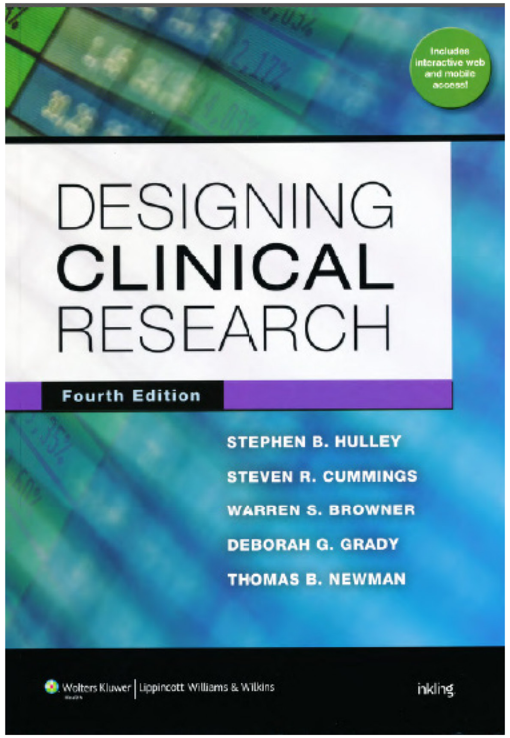
Chapter 3. Choosing the study subjects: Specification, sampling and recruitment

Study designs

Chapter 7. Designing cross-sectional and cohort studies

Chapter 8. Designing case-control studies

Journal article "Difference between case series and cohort studies"



Need help clarifying your research question? Ask yourself…

- What unresolved issue (lack of information) do I want to address?
- Do any published studies exist?
- Am I trying to replicate or refute those findings?
- In the same (or a different) study population?
- Under the same (or different) clinical circumstances?
- Using the same (or different) measurement techniques?
- What were the key limitations of the previous studies?

Why do a literature search?

- To help you clarify your research question
- To ensure that your study hasn’t been done (published) before
- To identify key limitations of the previous studies
- To help you design a stronger study (better design, subject selection, etc.)
- To identify standard ways of measuring key variables
- To identify accepted statistical analysis techniques
- To identify compelling methods of data presentation

Variables and their measurement

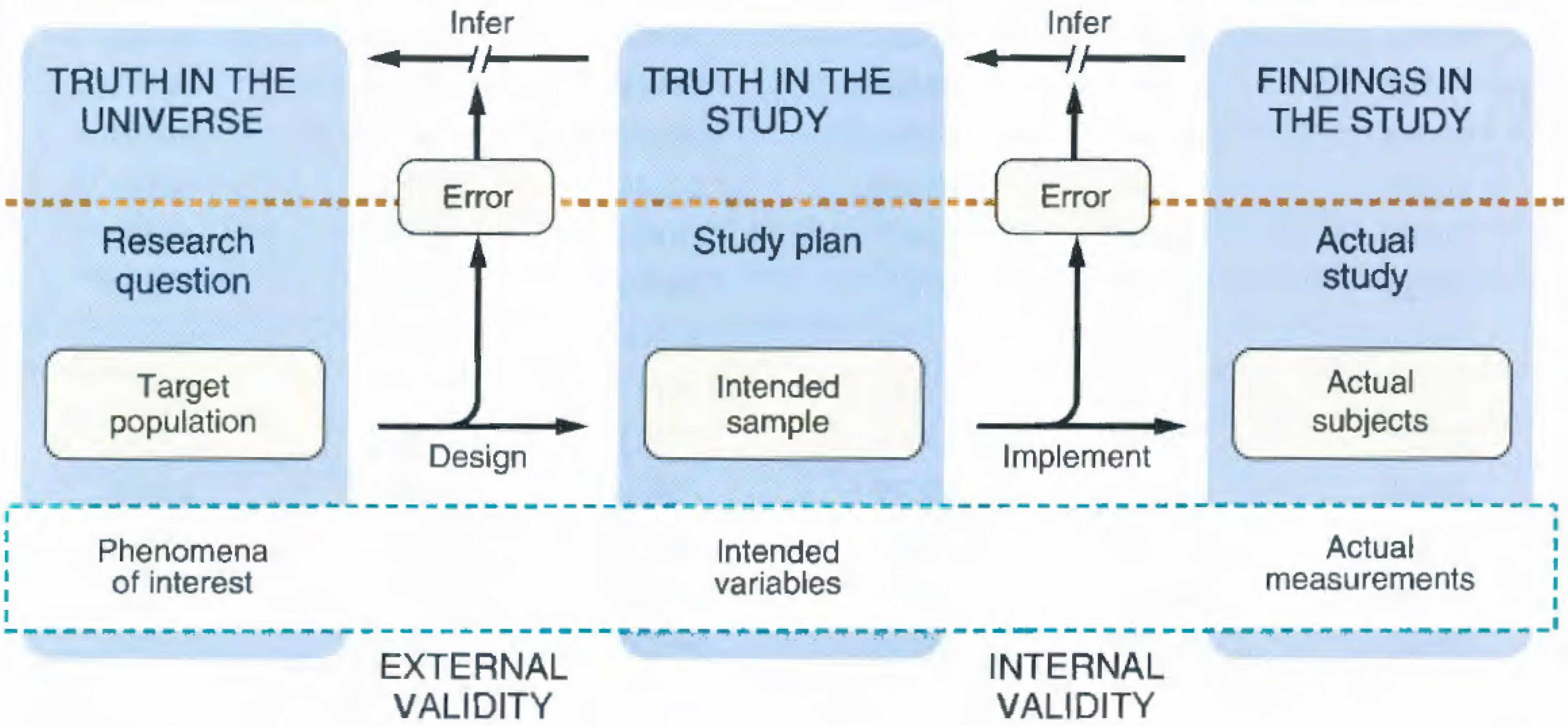


FIGURE 4.1 Designing measurements that represent the phenomena of interest.

TABLE 4.1 MEASUREMENT SCALES

TYPE OF MEASUREMENT	CHARACTERISTICS OF VARIABLE	EXAMPLE	DESCRIPTIVE STATISTICS	STATISTICAL POWER
Categorical				
Dichotomous	Two categories	Vital status (alive or dead)	Counts, proportions	Low
Nominal	Unordered categories	Race; blood type	Same as above	Low
Ordinal	Ordered categories with intervals that are not quantifiable	Degree of pain; social class	In addition to the above: medians	Intermediate
Numeric				
Continuous or discrete†	Ranked spectrum with quantifiable intervals	Weight; number of cigarettes/day	In addition to the above: means, standard deviations	High

†Continuous variables have an infinite number of values (e.g., weight), whereas discrete numeric variables are more limited (e.g., number of cigarettes/day). Discrete variables that have a large number of possible values resemble continuous variables for practical purposes of power and analysis.

Type of measurement	Characteristics of variable
Categorical	
Dichotomous	Two categories
Nominal	Unordered categories
Ordinal	Ordered categories with intervals that are not quantifiable
Numeric	
Continuous	Infinite number of quantifiable intervals
Discrete	Limited number of quantifiable intervals

Type of measurement	Characteristics of variable
Categorical	
Dichotomous	Two categories
Examples	
Gender	Male or female
Disease status	Has disease or does not have disease
Age	Young or old

Type of measurement	Characteristics of variable
Categorical	
Nominal	Unordered categories
Examples	
Race	African-American, Caucasian, Hispanic
Eye color	Blue, Brown, Green, Hazel
Blood type	A, B, AB, O

Type of measurement	Characteristics of variable
Categorical	
Ordinal	Ordered categories with intervals that are not quantifiable
Examples	
Stage of disease	I, II, III, IV
Degree of pain	Low, medium, medium-high, high
Age group	Infant, toddler, preschooler, school-age child

Type of measurement	Characteristics of variable
Numeric	
Continuous	Infinite number of quantifiable intervals
Examples	
Birth weight	Measured in grams (pounds, ounces)
Height	Measured in cm (inches)
Age	Measured in days, weeks, months, years

Type of measurement	Characteristics of variable
Numeric	
Discrete	Limited number of quantifiable intervals
Examples	
Number of pregnancies	1, 2, 3, 4, etc.
Age	In days, months, years (when sampling strategy restricts the number of categories)

J Neurotrauma. 2015 Jul 17. [Epub ahead of print]

Cavum Septum Pellucidum in Retired American Pro-Football Players.

Gardner RC[1,2], Hess CP[3], Brus-Ramer M[3], Possin KL[1], Cohn-Sheehy BI[1], Kramer JH[1], Berger MS[4], Yaffe K[2,5,6], Miller B[1], Rabinovici GD[1].

Author information

Abstract

Previous studies report that cavum septum pellucidum (CSP) is frequent among athletes with a history of repeated traumatic brain injury (TBI), such as boxers. Few studies of CSP in athletes, however, have assessed detailed features of the septum pellucidum in a case-control fashion. This is important because prevalence of CSP in the general population varies widely (2% to 85%) between studies. Further, rates of CSP among American pro-football players have not been described previously. We sought to characterize MRI features of the septum pellucidum in a series of retired pro-football players with a history of repeated concussive/subconcussive head traumas compared with controls. We retrospectively assessed retired American pro-football players presenting to our memory clinic with cognitive/behavioral symptoms in whom structural MRI was available with slice thickness ≤2 mm (n=17). Each player was matched to a memory clinic control patient with no history of TBI. Scans were interpreted by raters blinded to clinical information and TBI/football history, who measured CSP grade (0-absent, 1-equivocal, 2-mild, 3-moderate, 4-severe) and length according to a standard protocol. Sixteen of 17 (94%) players had a CSP graded ≥2 compared with 3 of 17 (18%) controls. CSP was significantly higher grade (p<0.001) and longer in players than controls (mean length±standard deviation: 10.6 mm±5.4 vs. 1.1 mm±1.3, p<0.001). Among patients presenting to a memory clinic, long high-grade CSP was more frequent in retired pro-football players compared with patients without a history of TBI.

KEYWORDS: concussion; magnetic resonance imaging; septum pellucidum; traumatic brain injury

Numerical:

Discrete (Limited number of quantifiable intervals)

TABLE 1. CLINICAL CHARACTERISTICS

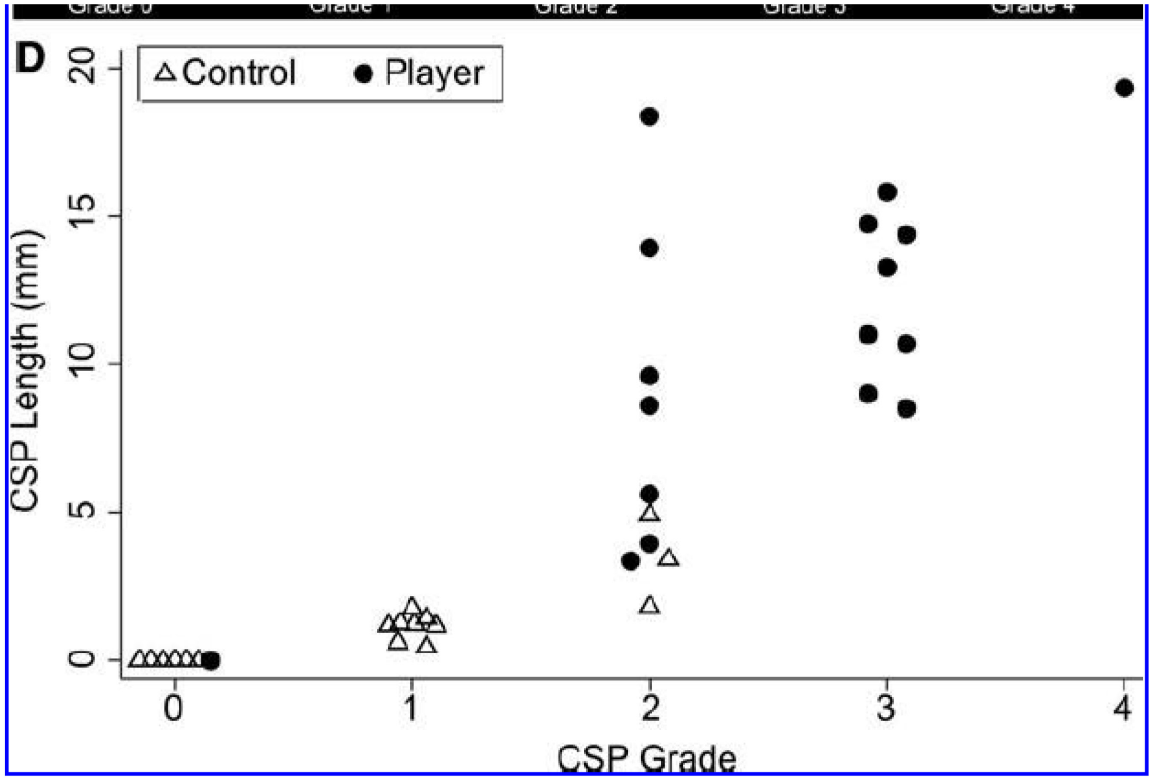
	Controls (n = 17)	*Players (n = 17)*
Age, years; mean (SD)	54.7 (15.8)	54.6 (15.8)
Male	17/17	17/17
Education, years; mean (SD)	17.3 (5.2)	17.7 (3.3)
MMSE; mean (SD)*	26.5 (4.5)	26.5 (2.5)
Total lifetime football exposure (childhood, high-school, college, pro), years; mean (SD)	N/A	17.3 (4.5)
Total pro-football exposure, years; mean (SD)	N/A	7.7 (3.8)
Patient reported repeated concussions	0/17	15/17
Patient reported at least one concussion with LOC	0/17	11/17
Pro-football position played	N/A	Defensive back (2), defensive end (1), defensive linebacker (6), defensive safety (1), long-snapper (1), offensive lineman (1), offensive tackle (4), offensive wide-receiver (1)
Years since retired from pro-football; mean (SD)	N/A	24.5 (15.5)
Clinical diagnoses (n)	MCI (9), AD (3), FTLD gene-carrier (2), bvFTD (1), HD (1), svPPA (1)	CPCS (5), MCI (6), HAND (1), cognitive disorder NOS (1), early-onset AD (1), mild dementia NOS (2), nfvPPA (1)

Categorical:

Nominal (Unordered categories)

Categorical
Dichotomous (Two categories)

Numerical
Continuous
(infinite number
of quantifiable
intervals)



Categorical
Ordinal (Ordered categories with intervals that are not quantifiable)

Type of measurement	Characteristics of variable
Categorical	
Dichotomous	Gender (male)
Nominal	Type of pro-football position played (wide-receiver, lineman, etc.)
Ordinal	CSP category (1, 2, 3, 4, 5)
Numeric	
Continuous	Length of CSP (mm)
Discrete	Number of concussions

Title of study	Trends in football-related injuries investigated at a tertiary care children's hospital: 2000-2014
Research question	Has the total number or nature of exams associated with football-related injuries changed over the past 15 years?
Significance	Increased public awareness about the long-term impact of concussions, rules of football have changed, etc.
Study design	Time-series analysis
Subjects	Exams on 6-17 year old males (Jan 1, 1990-Dec 31, 2014) who reported playing football prior to the injury being investigated
Predictor variable(s)	Time period, age group
Outcome variable	Number and type of radiology procedures (defined by the modality and anatomical location of the injury)
Primary null hypothesis	No change in the overall number or type of exams associated with football-related injuries

Type of measurement	Example
Categorical	
Dichotomous	Patient gender (male or female)
Nominal	Organization Body part (group using exam code)
Ordinal	Time period (collapse year of exam into groups) Patient age (collapsed into multiple groups)
Numeric	
Continuous	Date exam completed

Why is it essential to think about how to measure your variables from the beginning of your study?

The study design + type of variables determine

- Information needs for sample size planning
- How the study data should be collected
- How you should code & record the data
- How you can analyze the data
- How you are able present the findings

Type of measurement	Descriptive statistics	Statistical power
Categorical		
Dichotomous	Counts, proportions	Low
Nominal	Counts, proportions	Low
Ordinal	Counts, proportions, medians, IQR	Intermediate
Numeric		
Continuous	Counts, proportions, medians, IQR, means, SD	High
Discrete	Counts, proportions, medians, IQR, means, SD	High

Table 5.1. Statistics for assessing an association between two variables, unpaired data

Risk factor (independent variable, exposure, group assignment)	Outcome (dependent variable)					
	Dichotomous	Nominal	Interval, normal distribution	Interval non-normal	Ordinal	Time to event, censored data
Dichotomous	Chi-squared, Fisher's exact test, risk ratio, odds ratio	Chi-squared	*t*-test	Mann-Whitney test	Chi-squared for trend, Mann-Whitney test	Log-rank, Wilcoxon, rate ratio
Nominal	Chi-squared, exact test	Chi-squared	ANOVA	Kruskal–Wallis test	Kruskal–Wallis test	Log-rank, Wilcoxon
Interval, normal distribution	*t*-test	ANOVA	Linear regression, Pearson's correlation coefficient	Spearman's rank correlation coefficient	Spearman's rank correlation coefficient	–
Interval, non-normal	Mann-Whitney test	Kruskal–Wallis test	Spearman's rank correlation coefficient	Spearman's rank correlation coefficient	Spearman's rank correlation coefficient	–
Ordinal	Chi-squared for trend, Mann-Whitney test	Kruskal–Wallis test	Spearman's rank correlation coefficient	Spearman's rank correlation coefficient	Spearman's rank correlation coefficient	–

Table 5.22. Comparison of bivariate tests for independent observations and repeated observations of the same subjects.

	Independent observations (2 groups)	Paired observations (2 observations)	Independent observations (≥3 groups)	Repeated observations (≥3 observations)
Dichotomous variable	Chi-squared Fisher's exact	McNemar's test	Chi-squared	Cochran's *Q*
Normally distributed interval variable	*t*-test	Paired *t*-test	ANOVA	Repeated-measures ANOVA
Non-normally distributed interval variable	Mann-Whitney test	Wilcoxon signed rank test	Kruskal–Wallis test	Friedman statistic
Ordinal variable	Mann-Whitney test	Wilcoxon signed rank test	Kruskal–Wallis test	Friedman statistic

Table 5.28. Comparison of bivariate tests for unmatched and matched data

	Unmatched data	Matched data
Dichotomous variable	Chi-squared Odds ratio	McNemar's test Matched odds ratio
Normally distributed interval variable	*t*-test	Paired *t*-test
Non-normally distributed variable	Mann-Whitney test	Wilcoxon signed rank test
Ordinal variable	Mann-Whitney test	Wilcoxon signed rank test
Survival time	Log-rank	No readily available test

Table 6.1. Type of outcome variable determines choice of multivariable analysis

Type of outcome	Example of outcome variable	Type of multivariable analysis
Interval	Blood pressure, weight, temperature	Multiple linear regression
Dichotomous	Death, cancer, intensive care unit admission	Multiple logistic regression
Time to outcome (dichotomous event)	Time to death, time to cancer	Proportional hazards analysis

Table 7.1. Required information for a sample size determination for univariate analyses

Dichotomous variable	Interval variable
Expected proportion	Expected standard deviation
Desired width of the confidence interval	Desired width of the confidence interval
Confidence level of interval	Confidence level of interval

Table 7.2. Required elements for sample size determination for bivariate analyses

Comparison of two proportions (association of two dichotomous variables) (chi-squared)	Comparison of two means (association of a dichotomous variable and a normally distributed interval variable) (*t*-test)	Association of two normally distributed interval variables (Pearson's correlation coefficient)	Comparison of two survival times (log-rank statistic)
Expected percentage in group 1	Effect size	Effect size	Effect size
Expected percentage in group 2	Standard deviation of interval variable		Accrual interval
Ratio of number of subjects in group 1 to number of subjects in group 2			Duration of trial
			Attrition rate
Alpha	Alpha	Alpha	Alpha
Power	Power	Power	Power

Quiz: What type of variable is age?

A. Dichotomous
B. Nominal
C. Ordinal
D. Discrete
E. Continuous
F. All of the above
G. Other

What type of variable is age?

Answer = G. Other

A. Dichotomous
C. Ordinal
D. Discrete
E. Continuous

Tasks accomplished:

Formulate your research question
Draft a study outline
Use Montage to explore the feasibility of your idea
Clarify your definitions of the ‘predictor/exposure’ and ‘outcome’ variables
Clarify your subject selection criteria

Next steps:

Create a concrete list of the type of variables in your proposed study