LMU KLINIKUM DER UNIVERSITÄT MÜNCHEN

Unit for Occupational and Environemtal Epidemiology & Net Teaching
Head: Prof. Dr. Katja Radon, MSc

Institute and Outpatient Clinic for Occupational, Social a. Environmental Medicine
Director: Prof. Dr. med. Dennis Nowak

Mapping the methods:

Exposure, outcome, confounders

Non-differential misclassifcation

- Unreliable measures
  (random measurement error)
  = attenuation of true association
  = increased amount of variation,
  unexplained by independent variable
- Solutions:
  - Improve your measurement
  - Increase your sample size

Differential misclassification

- Biased measurements (systematic measurement error)
  = estimated effects are higher or lower than the true association
- Solutions:
  - Improve your measurement
  - Balance your design so systematic errors in measurement are equally represented in the comparison group (to cancel out the effect)
  - Blind the observers and subjects to exposure/ outcome/ intervention status

Sources and remedies for unreliability and bias in measurement

Source	Possible reason	Remedy
Subject	Biological variation (e.g. RR) Sampling error (e.g. electrosensitivity)	Repeated measurements on same subject Increase number of items used to measure the attribute
Obser-ver	Different interpretation / data collection methods	- train observers - standardized data collection method - get rid of observers - remove/revise items ob-servers can't agree upon

Sources and remedies for unreliability and bias in measurement

Source	Possible reason	Remedy
Proce-dure	Procedure for data collection varies (e.g., humidity, time…)	Standardize the data collection methods
Instru-ment	Different instruments used, instrument variability (e.g., lab measures)	- Standardize the instruments - Calibrate instruments regularly

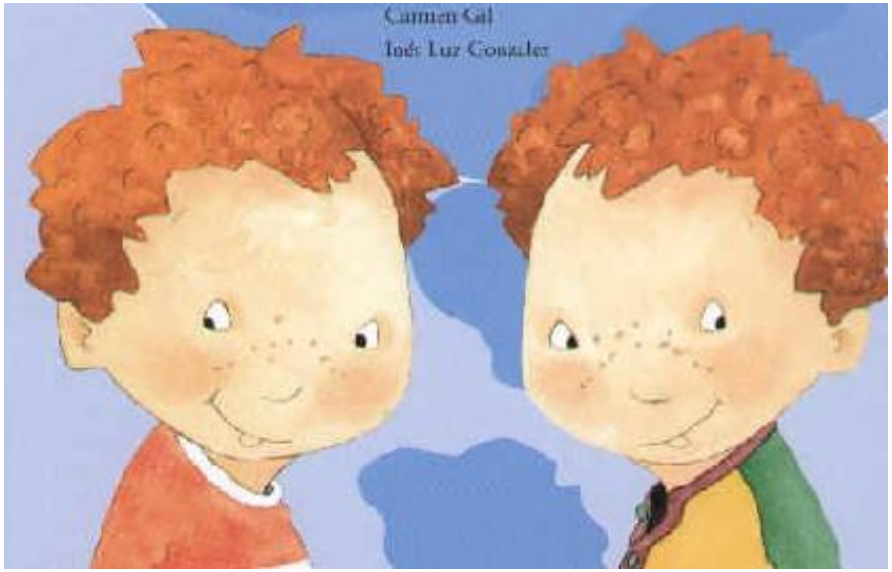
Variables / measurements

- Keep in mind the value of efficiency and parsimony
- Collect useful data at an affordable cost in time and money

Back to your protocol

1. Design
2. Population
   Inclusion / exclusion criteria (who, where)
   Sampling
3. Define variables / measurements
   How to ascertain exposure
   How to ascertain outcome
   How to measure potential confounders
4. Procedures: how to collect
5. Analysis
6. Sample Size / Power
7. Limitations

Confounding



Confounder

A confounder is an unknown or unaccounted for factor in a research study.

A confounder is

1. associated with the **exposure** under study **AND**
2. associated with the **disease** (outcome) under study
3. is **not** in the causal pathway between exposure and disease

Instrument	Category	Group	Parameter
Question-naire	Animal contact	E	(Farm) animal contact during pregnancy
		E	(Farm) animal contact in infancy
	Markers of hygiene	E	Consumption of raw farm milk and cheese
		E	Infectious disease (Tbc, Worms, …)
		E	Vaccination
		E	Siblings, day care attendants
		E	Day care attendants
		E	Housing / Heating
		E	Fleas / cockroaches / mice / rats
	Nutrition	E	Nutrition (traditional / modern food), vitamin D supplementation
	Phenotype	C	Family history of AD/IBD
	Confounder	C	Breast feeding
		C	Birth weight
		C	Socio-demographics
		C	ETS exposure
Clinical parameter	Skin prick test	O	House dust mites, storage mites, bla g 1, mice, Alternaria tenuis, cat, dog, local grass mix
	Blood sample	O/E	Total IgE (O), eosinophilia (E)
	Stool	E	Giardia lamblia, Ascaris
	Anthropometric measurements	E	Weight, height (BMI)
Genetics	Blood sample	E	Golden Gate Assay analyzing 1.500 candidate SNPs
Home sampling	Dust samples	E	Endotoxin Allergens: Der p1, bla 1, mice, cat, dog

E=Exposure, O=Outcome, C=Confounder

Classification of measurement types of scales

Type	Definition
• Nominal	• 2 or more mutually exclusive categories, no ordering among categories Example: ?
• Ordinal	• 2 or more mutually exclusive categories that are ordered; distance between categories might not be equal Examples: ?
• Interval	• multiple categories and the distance between categories equal Examples: ?
• Ratio	• Multiple categories, distance equal, zero=absence of the attribute (e.g.weight)

Classification of types of variables

By their measurement characteristic

Type	Scales	Summary Statistics
• Continuous	• Ratio • Interval • *Ordinal	• Mean, mode, median
• Discrete	• *Ordinal • Nominal	• Proportion • Frequency

Back to your protocol

1. How do you measure
   Exposure?
   Outcome?
   Confounders?
2. What about (non-)differential misclassification?
3. What about the feasibility of your measurements?

Generic structure of the measurement section

1. **Predictors / exposure**
   e.g., intervention,
   risk factor,
   individual characteristic
   policy change
2. **Outcomes**
   e.g., Morbidity
   Mortality
   Quality of life
   Satisfaction
   Costs
3. **Confounders**
   e.g., disease severity
   individual characteristic
   Opportunity for detection
   Co-intervention

Generic structure of the write-up per variable measured

1. Definition
2. Source of information
3. Reliability
4. Validity
5. (Feasibility)
6. Variable creation (e.g., compliance = number of pills taken/ number of pills required per months)
7. Type of variable (e.g., compliance will be treated as continuous=% required taken) and dichotomous (=compliance with therapeutic effectiveness range 80-110%) variable

Generic structure of the write-up per variable measured

Describe your main outcome variable according to the structure described

Back to your protocol

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3. Define variables / measurements
   How to ascertain exposure
   How to ascertain outcome
   How to measure potential confounders
4. Procedures: how to collect the data
5. Data analysis
6. Sample Size / Power
7. Limitations

Data analysis

1. Restate the hypothesis to be tested including predictor, outcome and pot. confounders in general terms
   This study will test the hypothesis that living in a rural area during infancy protects from allergies at age 6-16 yrs independent of sex, SES, parental atopy.

Data analysis

2. Operationalize each variable (table)

Variable	Definition	Type	Scale
Farm-contact in infancy	Questionnaire q32	Exposure	Dichotomous
Asthma	Bronchial challenge(+) symptoms (+) Symptoms score	Outcome	Dichotomous Ordinal
BMI etc…	Height+Weight measured	Confoun-der	Continous

Data analysis

3. Define type of analysis (make linkt to measurement scale)
4. Unit of analysis (group, individual, tissue)
5. Criteria for including/excluding variables
6. Complexity of your data
   (Multiple explanatory variables, Repeated measures over time, Missing data…)

Last but not least: ETHICS

http://www.ethikkommission.med.uni-muenchen.de/

http://www.blaek.de/beruf_recht/ethik/ethik_formulare.cfm

Assignment 2

Compose the following sections of your research protocol:

- Variables and their measurement
- Data collection
- Data analysis (as far as possible)
- Sample size/Power (as far as possible)
- Limitations of your study

Submit the final protocol until

05.12.2012 to

katja.radon@gmail.com

On December 6th 2012 your group will receive the protocol of another group for review!

Further information will be given via email.