# Assignments

- **Significance**. Use PubMed/Web of Science to do a computerized literature search, and word-process a first draft of your "Significance" section for your research question with an adequate set of references (preferably inserted with EndNote or equivalent software).

- Prepare a **brief outline** of your research protocol using the excel sheet provided earlier on

- Present your results to the class (5 min).

# Mapping the methods

## Introduction and study population

# Key elements of the methods

- Overview of the study design
- Study population
- Measurements
- Statistics
  - Statistical analyses
  - Sample size and power
- Quality control and data management
- Timetable
- Ethics
- Strengths and limitations
- References
- Appendices (draft of the questionnaire, …)

# **Your study design?**

- **Cross-sectional studies**

- **Case-control studies**

- **Cohort studies**

- **Intervention studies**

# **Study population**

- Who are your subjects and how will they be selected?
  - Selection criteria?
  - Design for sampling?
  - Plans for recruitment, increasing response

# ->The study should reflect „real life"

# Target population - study population

**Target population**

All those the researcher is interested in

# Example: ISAAC study in Germany

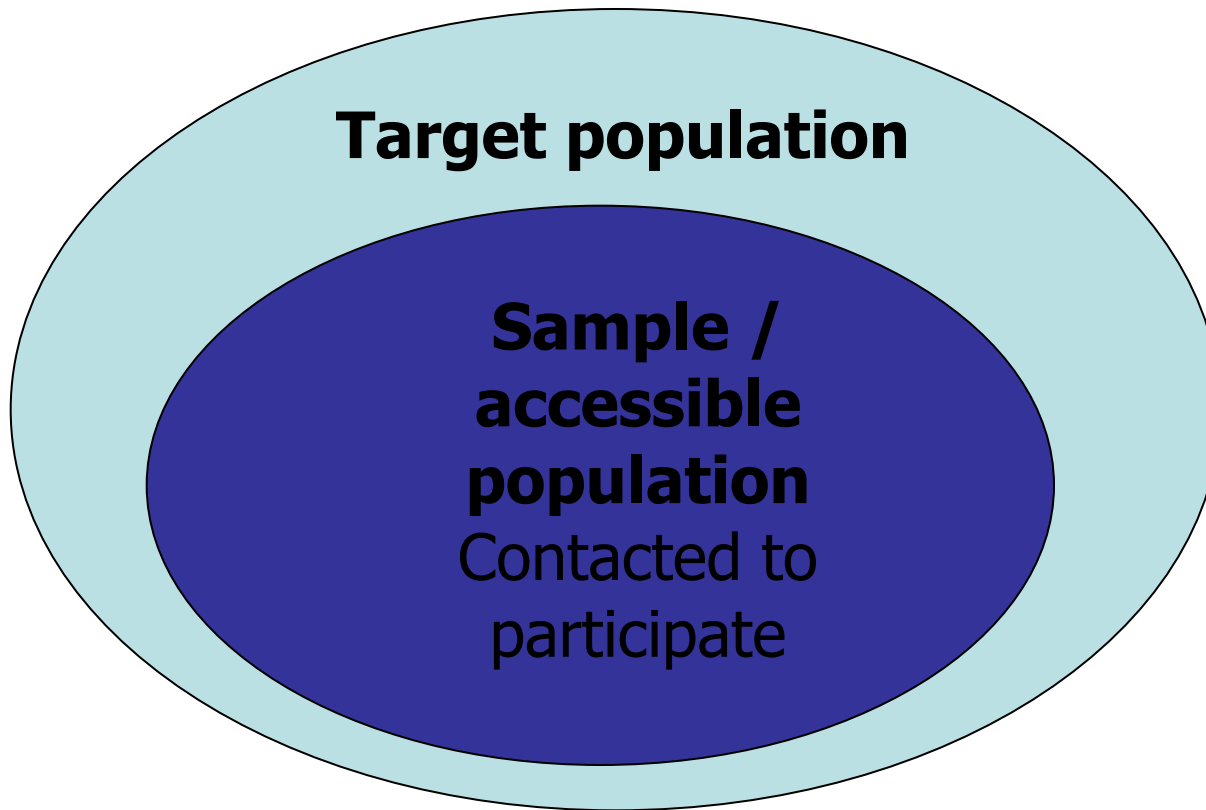**Target population**

Children aged 9-11 years in Munich and Dresden

Weiland et al. ERJ 1999
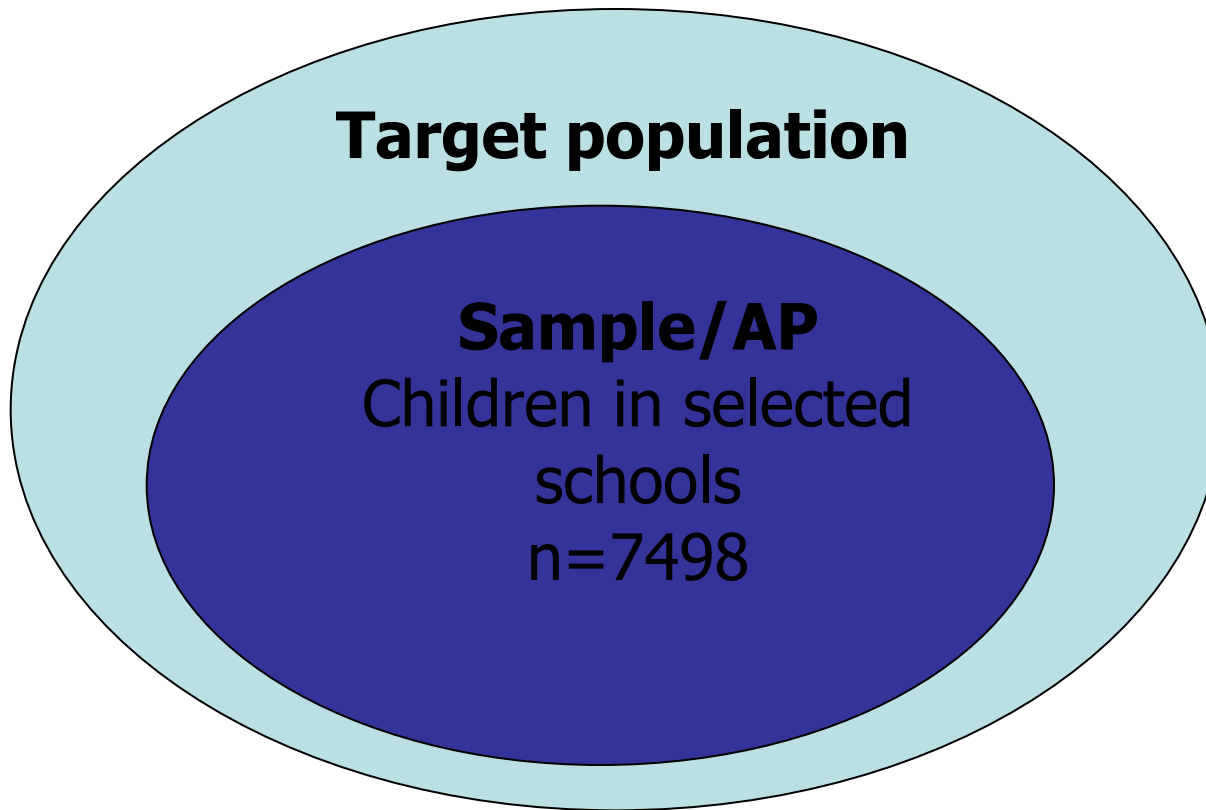
# What about your study?

√ How do you select your target population?

# Target population - study population

# Target population - study population



Target population

Sample/AP
Children in selected schools
n=7498
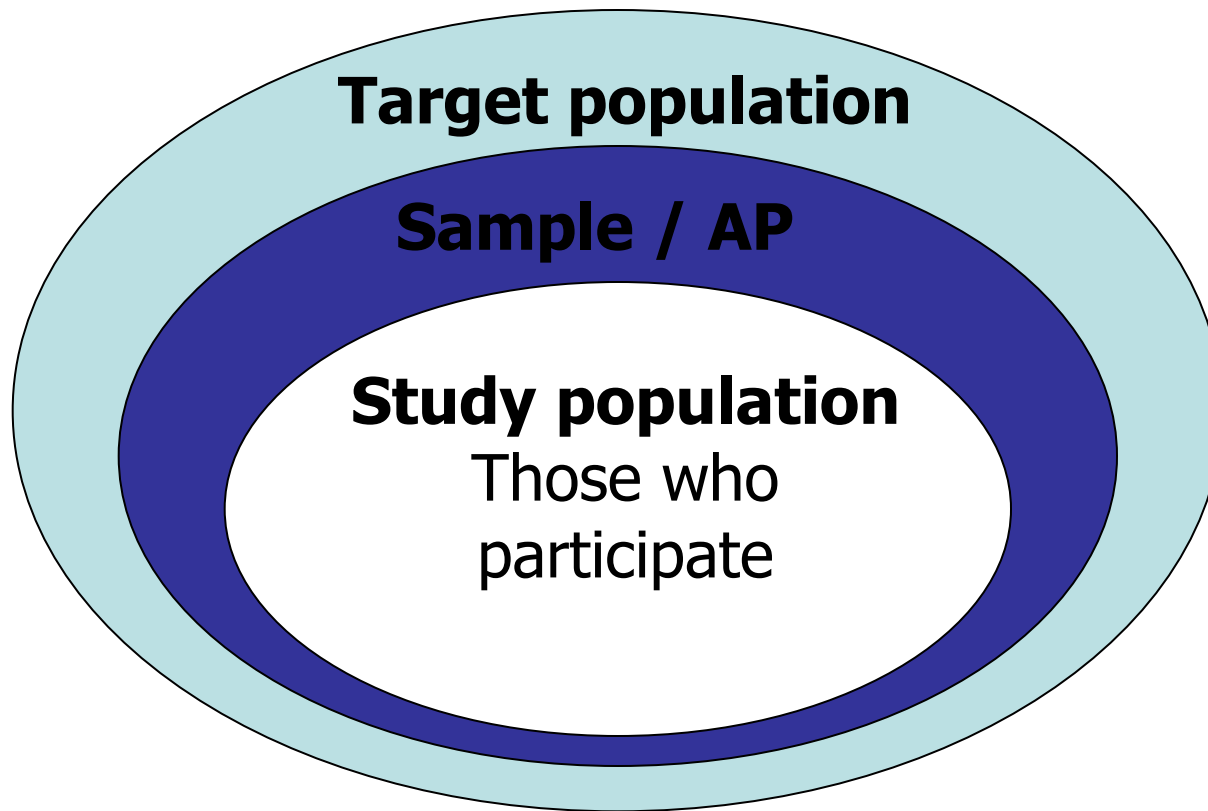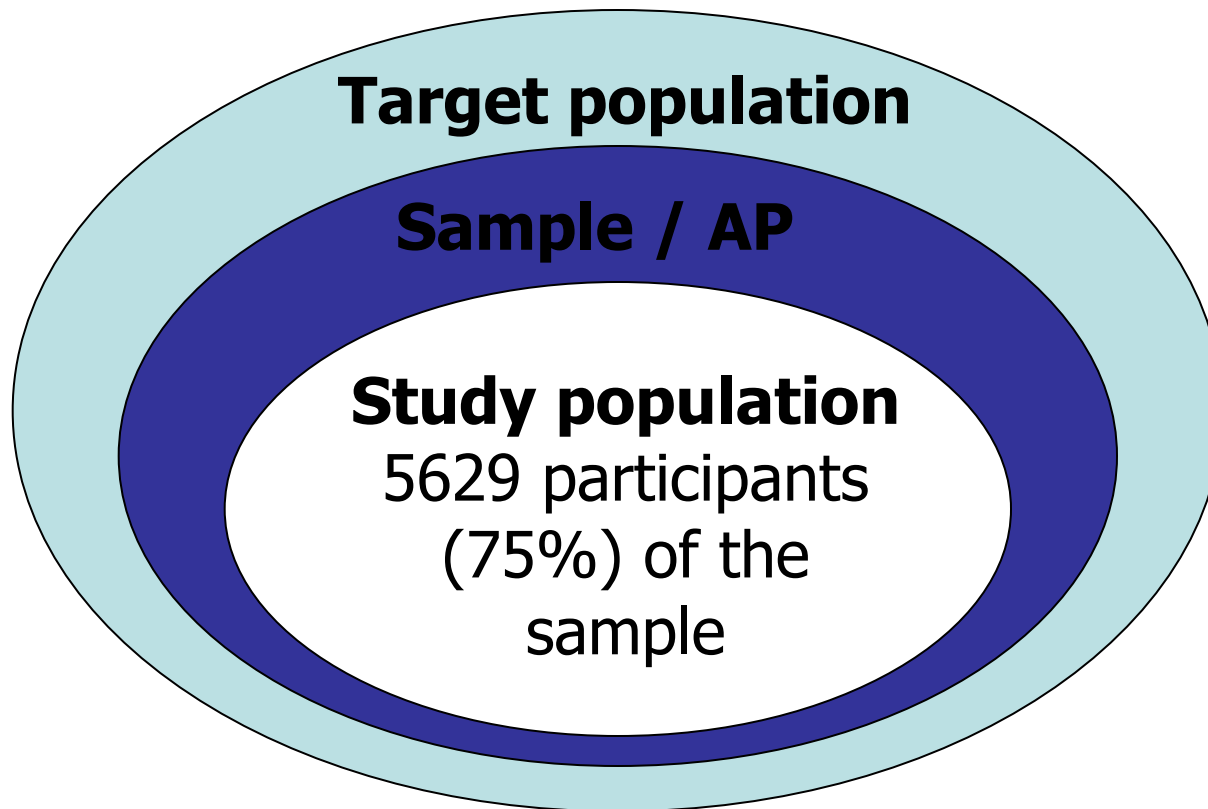
# What about your study?

√ How do you select your target population?
√ How do you select your sample?

# Target population - study population



Target population

Sample / AP

**Study population**
Those who participate

# Target population - study population

Target population

Sample / AP

**Study population**
5629 participants (75%) of the sample

# What about your study?

√ How do you select your target population?

√ How do you select your sample?

√ What do you expect about your study population?

# Validity and selection of the study population

- **Internal Validity**
  - Results are correct for the target population
  - Sources of error:
    Selection bias, Information bias, Confounding

- **External Validity**
  - The results can be generalized to the general population (common problem clinical trials)
    - -> take care when choosing your target population

# **Inclusion criteria**

Specifying characteristics that define populations that are relevant to the research question and efficient for study, including:

- Demographics
- Clinical Characteristics
- Geographic Characteristics
- Temporal Characteristics

# Inclusion criteria: whom to include?

- ## Only one level of training?
  (Residents)

- ## Only one speciality?
  (Cardiology)

- ## All residents from hospitals with different shift schedules?

- ## Only one type of hospitals?
  (Rehabilitation clinics, university hospitals, …)

- ## Study region?
  (Germany or Munich)

# Example

| | Case group 1: Asthma | Case group 2: IBD | Surgical controls: Appendectomy, Strabismus, … |
|---|---|---|---|
| **Centres** | Hospital Base Valdivia, Universidad Austral, Valdivia, Chile Clinica Alemana, Valdivia, Chile | | |
| **Invited** | n=190 | n=125 | N=430 for asthma n=290 for IBD |
| **Participants (questionnaire, clinical measurements)** | n=150 | n=100 | n=300 for asthma n=200 for IBD |
| **Participants (home sampling)** | n=120 | n=80 | n=240 for asthma n=160 for IBD |
| **Contact** | Asthma outpatients and inpatients | IBD inpatients and outpatients | Inpatient files and outpatients |
| **Inclusion** | 6-15 years old | 6-40 years old | 6-15 years old (asthma) 6-40 years old (IBD) |
| **criteria** | Born in Chile | Born in Chile | Born in Chile |
| **Matching** | | | Frequency matching: Age, hospital, place of living (urban, rural) |

*Table 2.6: Selection of cases and controls in Valdivia*

# Example: Inclusion criteria

Inclusion criteria are:

- Age range between 6 and 18 years.
  The upper age limit is chosen as the Centre treats patients until the age of 18 years only. The lower age range is chosen as a surgery for strabismus usually is done around age 6 years.

- Born in Germany.
  This is done because early childhood environments which might differ considerably from country to country.

- No malformation.
  All malformations which might be associated with strabismus and contact with animals in infancy are excluded.

- Persistent and extended oligoarticular JIA (OA JIA).
  Because different risk factors might underlie different subtypes of JIA, cases are restricted to those with persistent or extended OA JIA.

# **Exclusion criteria**

Specifying subsets of the population that will not be studied because of:

- Likelihood of being lost to follow-up
- An inability to provide good data
- Being at high risk for side effects
- Characteristics that make it unethical to withhold treatment

# Exclusion criteria example

- Not able to speak German

- Other ethnicity

- Outside age range

- Controls:
  - living in other areas than cases

# How can you ensure that the results are valid for your target population?

Minimize bias and confounding!!!

# Selection Bias

- **Sampling bias**
  - Bias in the way your study population is selected

- **Participation bias**
  - Response of your sample depends on exposure and disease

# Sampling: Case-control study

**Exposed cases have a different chance of admission than controls**

|  | Cases of lung cancer | Controls from surgical wards |
|---|:---:|:---:|
| **Contact with asbestos** | a | b |
| **No contact with asbestos** | c | d |

- Professor "Super-X", Head of respiratory department, world capacity on asbestos exposure, 145 publications on subject

- Lung cancer cases exposed to asbestos not representative of lung cancer cases

# Sampling – example

- The majority of physicians working 24-hour shifts in Munich live in walking distance to the hospitals

- The majority of physicians working 8-hour shifts in Munich have to take their car to get home

➢ The results of your study indicate that 24-hour shifts protect from traffic accidents

# Sampling

- Convenience Samples

- Probability Samples
  - Simple Random Sample
  - Stratified Random Sample
  - Cluster Sample
  - Systematic Sample

# **Convenience sampling**

- People who

  – meet entry requirements that are

  – easily accessible to investigators.

- Might be consecutive samples:

  – All patients who show up in the ER over a four week interval and meet the inclusion criteria. Whether they are representative of the target population has to be judged by the investigator.

# Simple random sample

- Provide numerical values to units of the population and select a subset at random.
- Can use random number lists or generators to pick the sample
- Examples:
  - Sample from the population registry
  - Sample of the patients with strabismus surgery

# Systematic sample

- Take e.g. every second patient on a list
- Might be biased
- No real advantage over simple random sample

# Stratified random sample

- Divide target population into subgroups
- Take random sample from each strata
- E.g.,
  - Population registry of Munich
  - Subgroup 1: Children aged 8-12 years
    Subgroup 2: Teenagers aged 13-17 years
  - Random sample of 1000 from each group
- Useful when a less common group of the population is of special interest to the investigator
  (e.g., children living in Munich born in Australia)
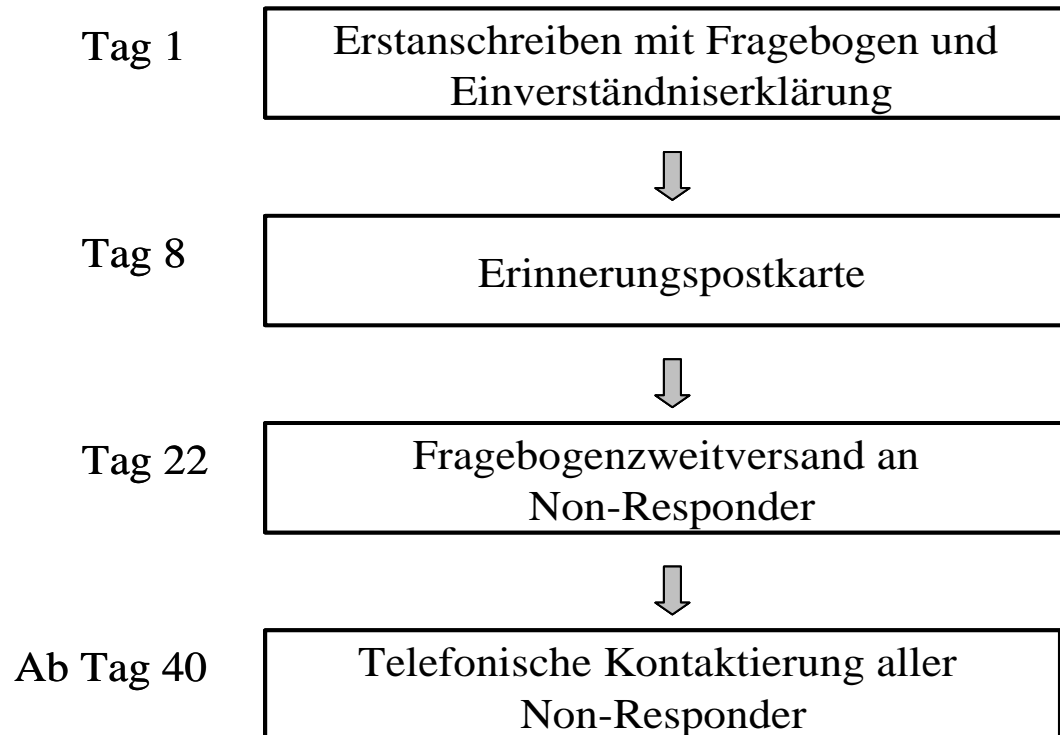
# **Cluster sample**

- Select some schools from all primary schools in Munich

- Invite all 4th grade students to take part in your study

- Useful when population is widely dispersed

- Disadvantage: loss of power (clustering has to be taken into account in the statistical analysis)
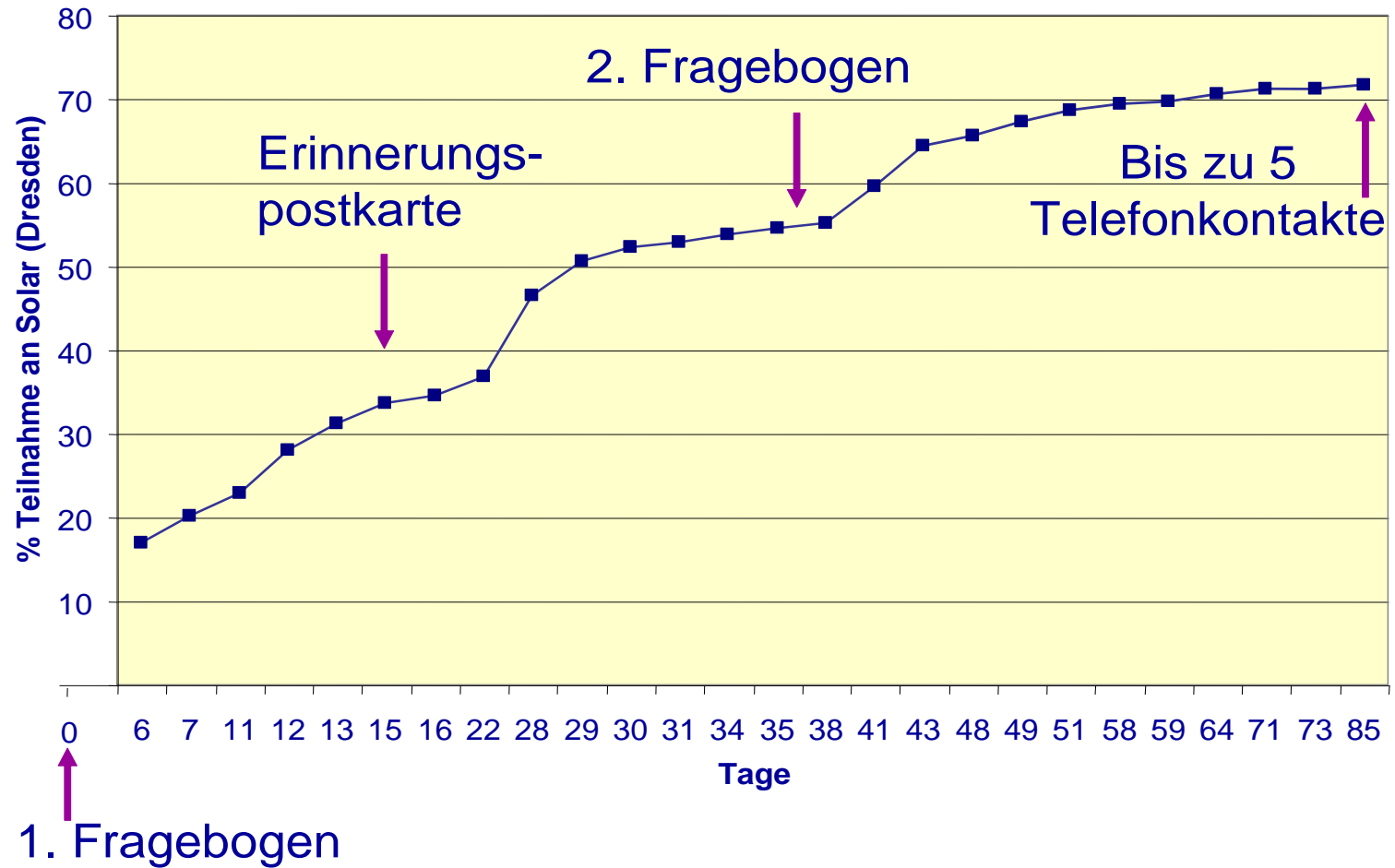
# How to minimize participation bias

- „neutral" Invitation letter

  („Study on traffic accidents among residents" not mentioning shift models)

- Follow-up procedures!!!

- Incentives (voucher, money, pen)

# How to minimize selective participation

| | |
|---|---|
| Tag 1 | Erstanschreiben mit Fragebogen und Einverständniserklärung |

⇩

| | |
|---|---|
| Tag 8 | Erinnerungspostkarte |

⇩

| | |
|---|---|
| Tag 22 | Fragebogenzweitversand an Non-Responder |

⇩

| | |
|---|---|
| Ab Tag 40 | Telefonische Kontaktierung aller Non-Responder |

# Follow-up procedures

# Describing your study population

| Country | Expected number of cases | |
|---|---|---|
| | Per year | Study period |
| Austria | 35 | 86 |
| France | 94 | 235 |
| Germany | 125 | 313 |
| Greece | 25 | 63 |
| Israel | 40 | 120 |
| Italy | 68 | 169 |
| Netherlands | 63 | 158 |
| Spain | 125 | 313 |
| Total – with EU funding | 574 | 1 455 |

Table 1.2b – Expected number of brain tumour cases (malignant and benign) per country in the age range 10-24.
**_Benign tumours represent about 20% of the numbers shown here._**

# Describing your follow-up procedures



| | |
|---|---|
| Tag 1 | **1. Anschreiben mit Fragebogen** |
| Tag 8 | **Erinnerungspostkarte an Non-Responder** |
| Tag 22 | **Fragebogen-Zweitversand an Non-Responder** |
| Woche 6-7 | **Telefonischer Kontakt aller Non-Responder** |

# Sampling –
# Your example

- Please draw a summary table / graph displaying your

1. Target population

2. Sample

3. Study population

    including the response you anticipate and inclusion / exclusion criteria.

- Describe the selection bias that might occur and how you will minimize it.

- Present your results to the class

# Assignment 1

Compose an amplification of the "Study Subjects" section of your research protocol in less than one page.

This section should include the following:

1. A description of the target and accessible population (sample). Specify and justify the selection criteria.
2. A description of how the study subjects will be sampled from the target/accessible population (sample).
3. A description of how you plan to recruit potential subjects identified by your sampling process.
4. A description of your strategies for retaining your study subjects.
5. Propose and comment on some strategies for making your sample more representative of the population you wish to generalize to.