Protocol development

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What are required in a research proposal?

- ✓Study title
- ✓Proposing individual's name & contributors' name and their main roles
- ✓Introduction & statement of the problem
- ✓Purpose of the study
- ✓Methodology
- ✓Expected results
- ✓Budget
- ✓Ethical issues
- ✓References

Introduction

"The introduction is the part of the paper that provides readers with the background information for the research reported in the paper.

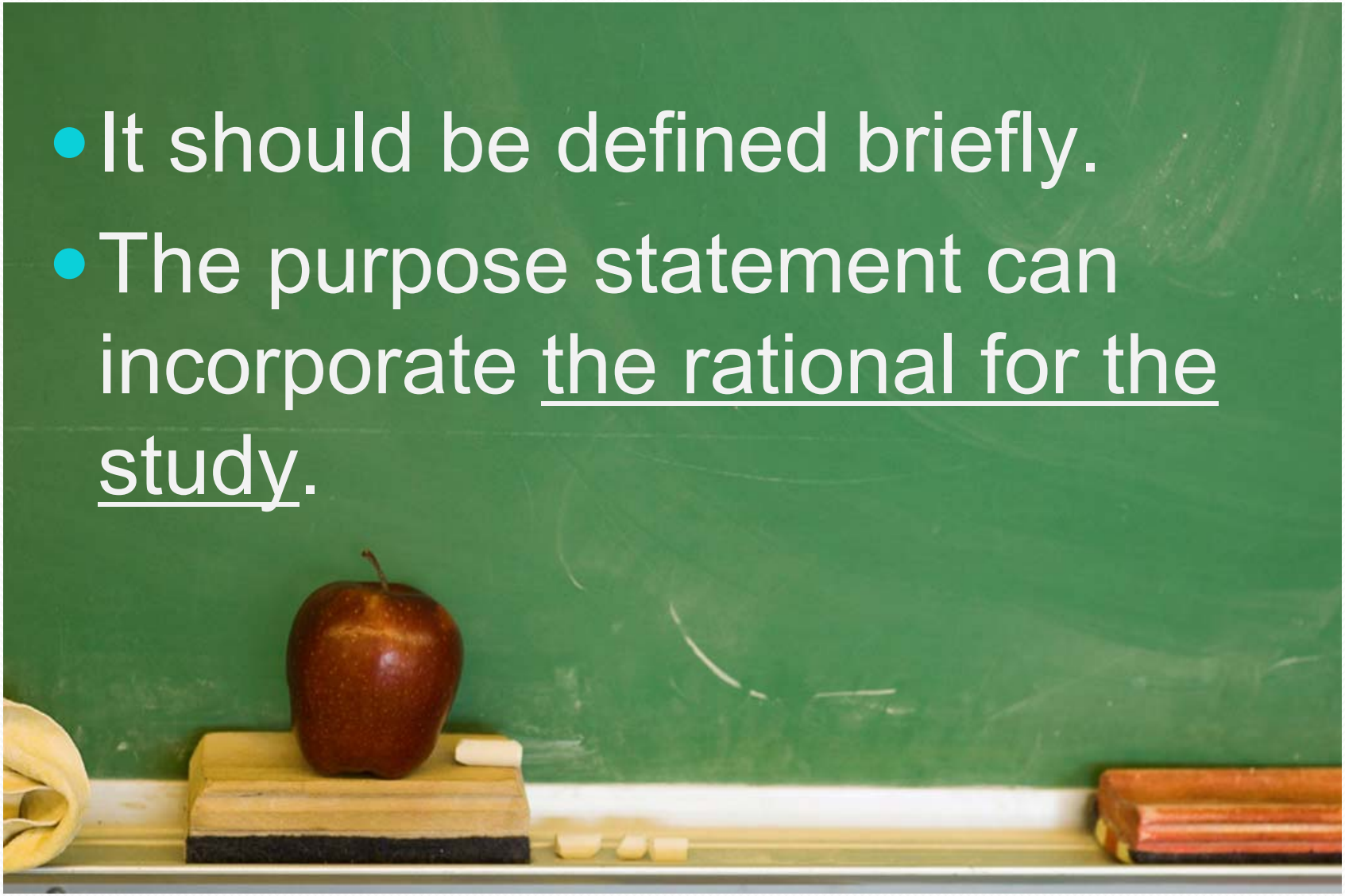
Its purpose is to establish a framework for the research , so that readers can understand how it is related to other research" (Wilkinson, 1991)

Statement of the problem

- It is important in a proposal that the problem stand out
  - The reader can easily recognize it.
- A problem statement should be written within a context briefly, and intelligibly.
- Effective problem statements answer the question "**Why does this research need to be conducted**."

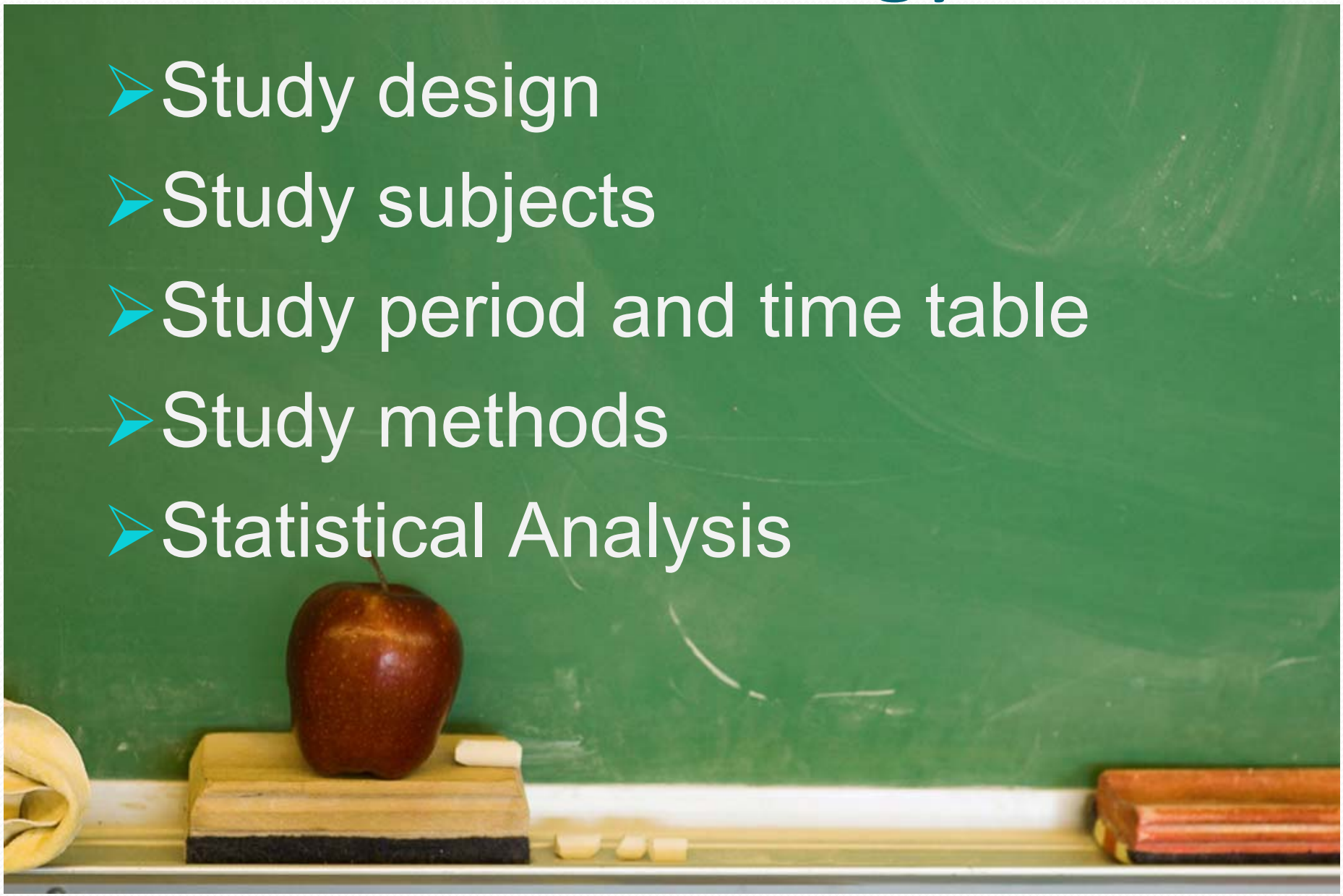
You should be able to answer this question Clearly.

Purpose of the study



- It should be defined briefly.
- The purpose statement can incorporate the rational for the study.

Methodology



- Study design
- Study subjects
- Study period and time table
- Study methods
- Statistical Analysis

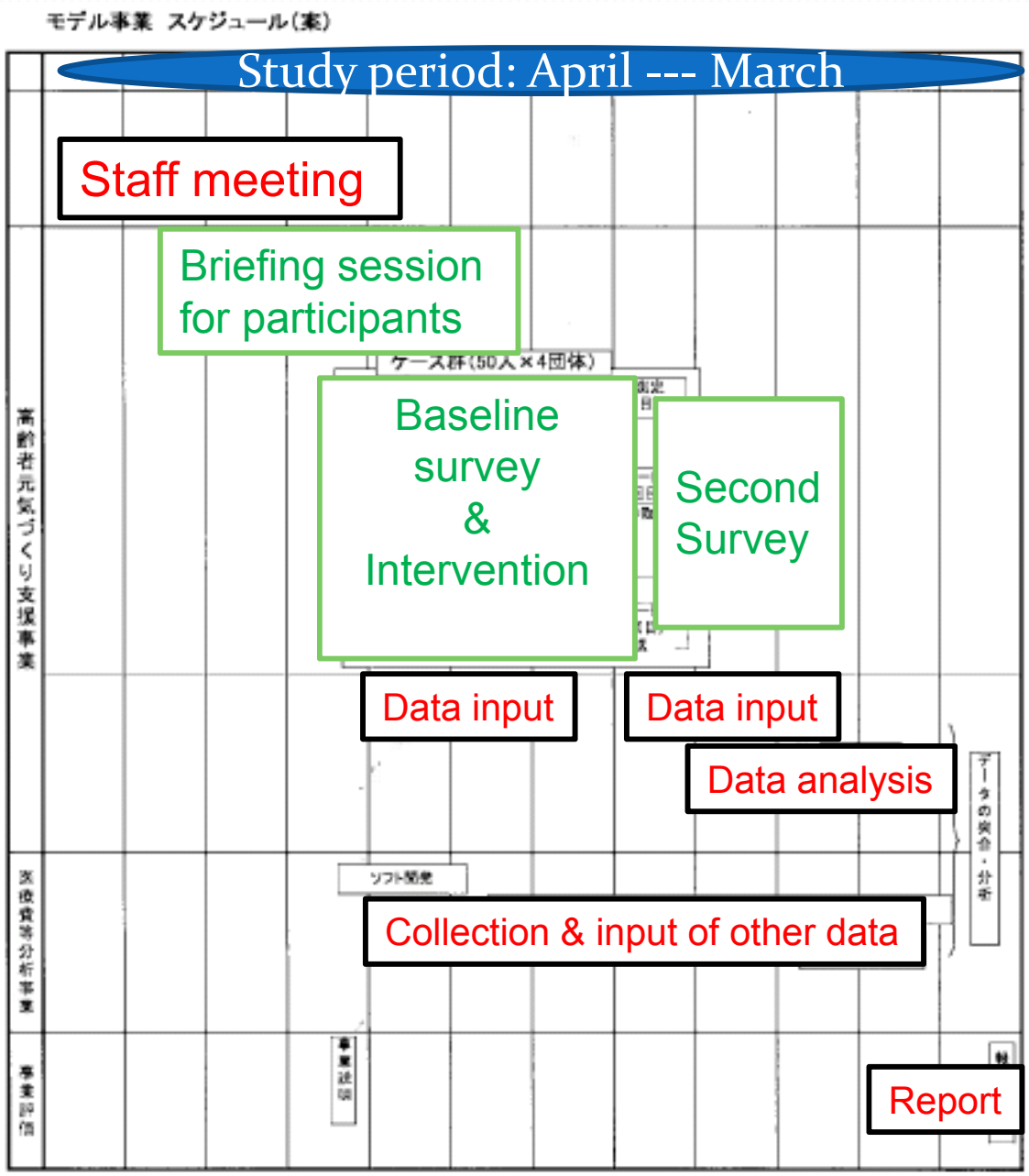
Study design

- **Observational study**
  - Descriptive study
  - Cross-sectional study
  - Case-control study
  - Cohort study
- **Intervention**
  - Hospital-based (clinical)
  - Community-based

Study subjects

- When?
  - Study period
- Where?
  - Which hospital, area?
- Who?
  - Inclusion & exclusion criteria
  - Matched control?
- How many?
  - Sample size

Study period and time table



An example of intervention Study in a community

- Operation of the intervention & data collection
- Data input & analysis
- Data collection from other Resources (medical service fee)
- Evaluations

Study methods

- **Data collection**
  - outcome variable
  - main exposure variable
  - confounding factors
- **Instrumentation**
- **Statistical Analysis**

Statistical methods can be chosen, once you decide the study design and outcome / exposure variable(s).

Details of statistical methods will be given later

How to collect the data

- **From written records**
  - Clinical information: Medical records, pathological reports, blood examination sheet, etc.
- **From official records**
  - Death certificate, Disease registry (such as cancer)
  - Need to get a permission to access these data
- **By questionnaire**
  - Self-report----better to check omission of recording
  - By interview----trained interviewers are required
- **Biomarkers measurements in lab**
  - Biological specimens with informed consent are required
- **Measurements of environmental levels of pollutants**
  - At household level or area level

Volume & container for biological specimens

- Volume of blood sample
  - DNA? ----- Theoretically, one drop of blood is enough if you apply PCR method.
  - Serum?----- Depend on what you are going to measure.
- Container
  - Should be sterilized? ----- Definitely, to detect microbe or virus / to obtain viable lymphocytes

How to store biological specimens

- In **liquid nitrogen**
  - Viable lymphocytes (for mRNA, culture)
- **Freezer** (at -20 or -80 degree)
  - Lymphocytes for DNA
  - Serum
- **Refrigerator**
  - urine
- **Room temperature** (cooler is better)
  - Hair, nail, paraffin-embedded tissues, blood on FTA cards

Depend on what you are going to measure
Check it before sample collection

Expected results

- Limitations and delimitations
- Significance of the study
  - How important your results are clinically / socially (for public health).
  - What suggestions for subsequent research arise from the findings?
  - What can we do the next as a result of the proposed research?

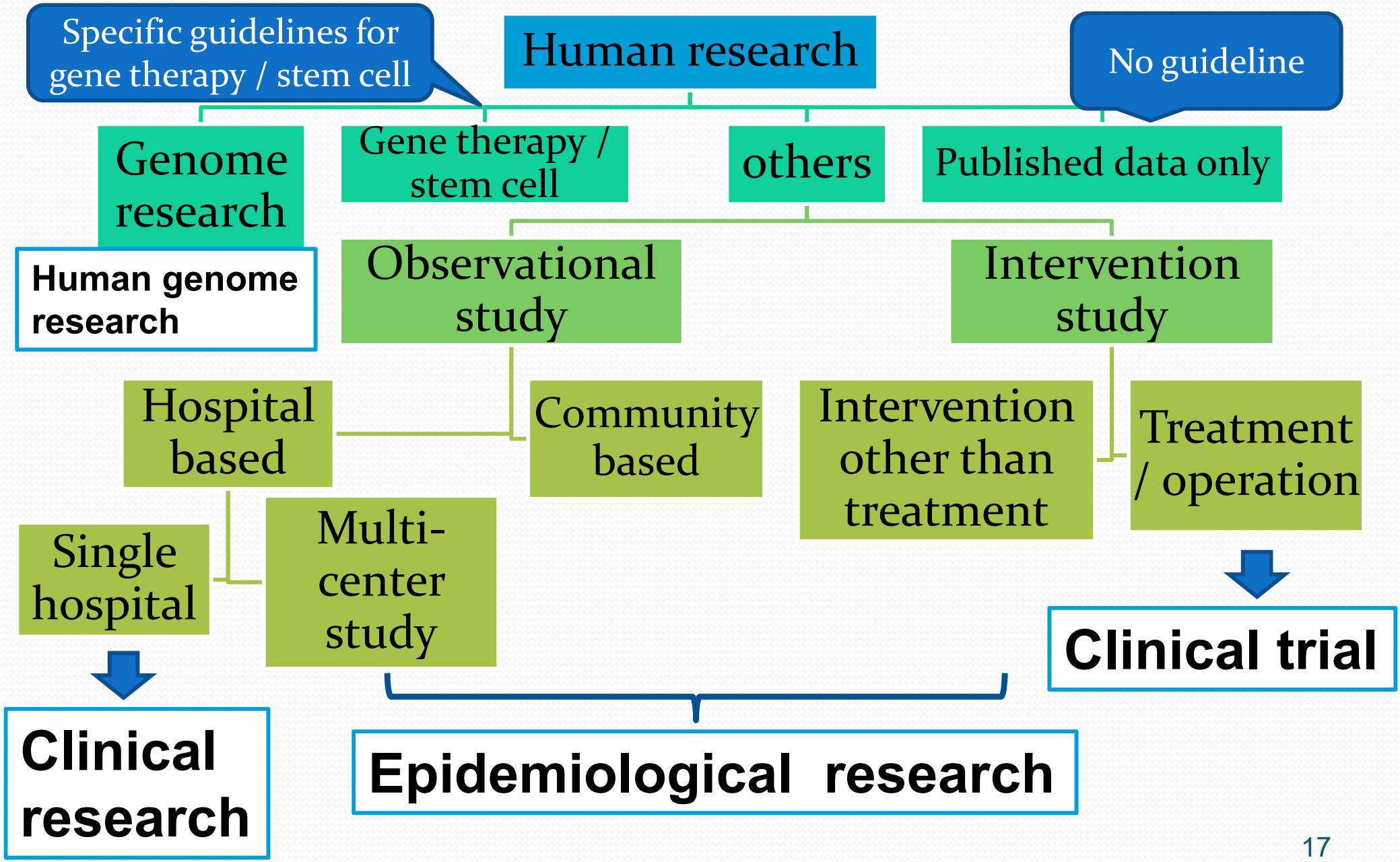
Research budget

- To operate the study
  - **Compensation** for interviewers, assistants for data collection & management, lab. technicians, etc.
  - **Printing & mailing costs** of the questionnaire
  - **License fee** if you use the standardized questionnaire
  - **Supplies expenses** including reagents and materials in lab. (if any)
  - **Travel expenses** for field surveys
- To manage the study
  - **Travel expenses** for meeting, attending conferences, etc.
  - **Communication cost** such as telephone, mail, etc.
- To publish the results
  - Publication / submission fees for papers
  - English editing

Guidelines relating to human research in Japan

- The guideline of human genome research
  - All studies examining human genome
  - Exceptions: genome analysis which are routinely used in clinical practices such as EGFR mutation
- The guideline of clinical research
- The guideline of epidemiological research
- Others
  - Clinical trials : to evaluate new treatment / operation
  - The guideline for gene therapy
  - The guideline for clinical research using stem cells

An example of flow chart for research guidelines



Guidelines set down responsibilities

- Researchers
- Head of the institute
  - Setting of IRB
  - Approval / disapproval of the research proposal based on the IRB's comments
- IRB (institutional review board)
  - Review the research proposal
  - Confidentiality of the information

Responsibility of Institutional Review Board

an example in Japanese guideline

- IRB: A committee to **approve**, **monitor**, and **review** human research with aim **to protect the rights and welfare of the study subjects**
  - Also known as an independent ethics committee (IEC) or ethical review board (ERB)

- Members: including outside members, both genders
  - Experts in basic and clinical medicine
  - Legal profession /Experts in social science
  - A representative of general public

Responsibility of researchers

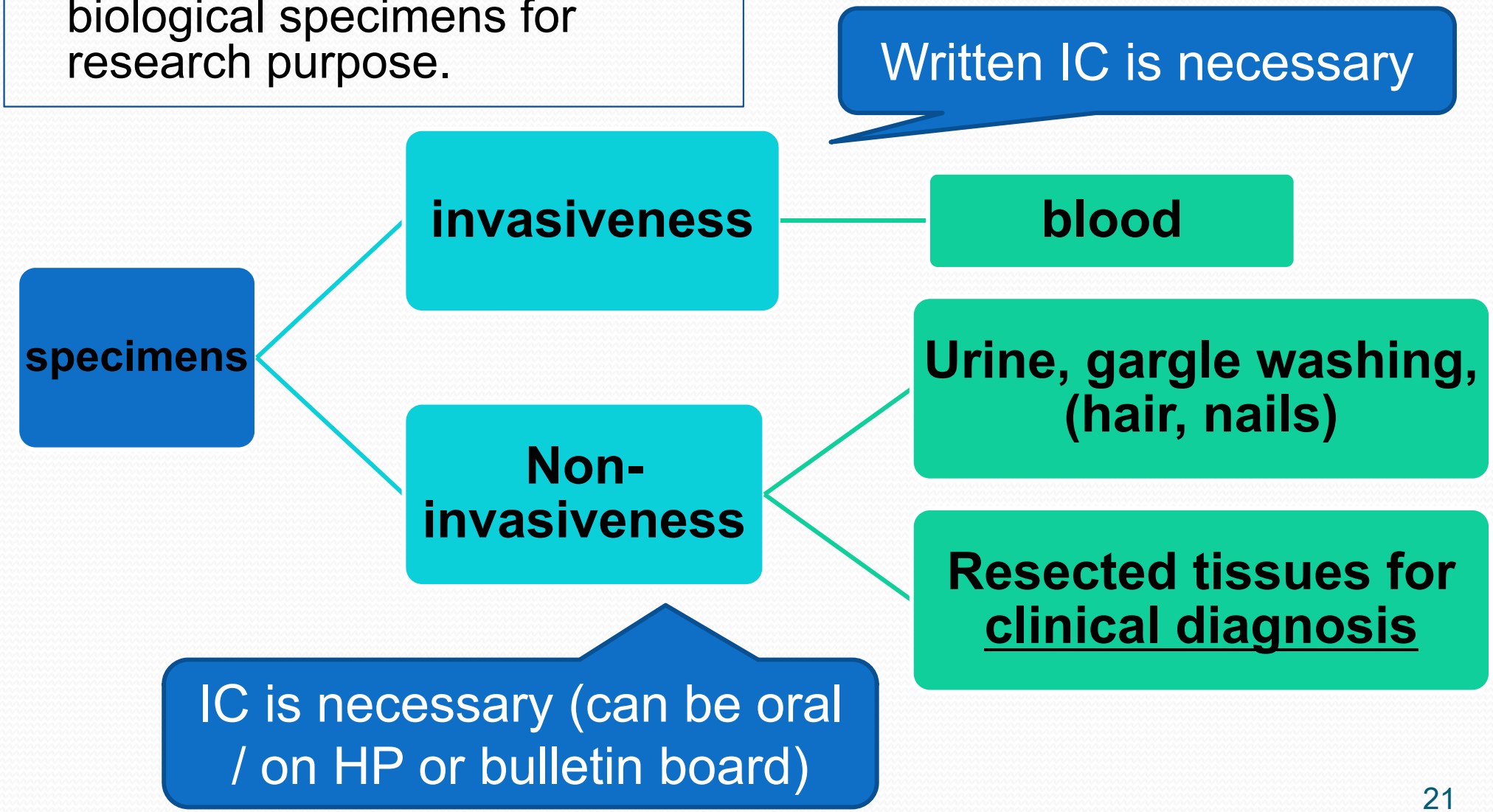
an example in Japanese guideline

- Respect for the dignity and human rights of the individual (study subject)
- Scientifically rational and ethical studies should be conducted.
- Human research protocols should be submitted to the ethics committee / IRB before study is conducted.
- Obtain the **informed consent**
- Protect the personal information
- Publication / public announcement of your results

IC for biological specimens

an example in Japanese guideline

- Informed consent is necessary when you use any kinds of biological specimens for research purpose.



IC for other data

an example in Japanese guideline

- **Questionnaire**
  - Basically, IC is not necessary
  - Study subjects have right to say “NO”.

- Use of medical records / pathological reports, etc.
  - IC is not necessary.
  - Researchers should disclose information of your research.

Protection of personal information

1. Assign an independent number (research ID) for each subject
2. Keep anonymous status during the analysis procedure including laboratory examinations
3. Written IC forms and personal information (interlinked research ID) should be kept in a locked place.
4. For human genome research, you should have a personal information handler.

Further readings for ethical issues

- Declaration of Helsinki
  - World Medical Association declaration
  - Ethical Principles for Medical Research Involving Human Subjects

http://www.wma.net/en/30publications/10policies/b3/index.html

- CONSORT (Consolidated Standards of Reporting Trials)
  - Updated guidelines for reporting parallel group randomised trials

Kenneth et al. Journal of Clinical Epidemiology 63 (2010) 834-840

Responsibility of researchers to the community (study subjects)

- Scientific reports
  - In scientific publication
  - At a scientific meeting
- Public announcement through
  - Website
  - Bulletin board in your hospital
  - Pamphlet for general readers
  - Mass media
  - Public symposium

This is also important to win the support of public for future studies