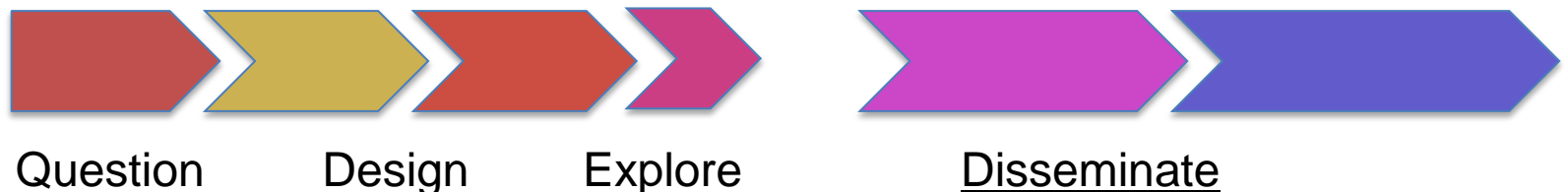


Principles of Clinical Research

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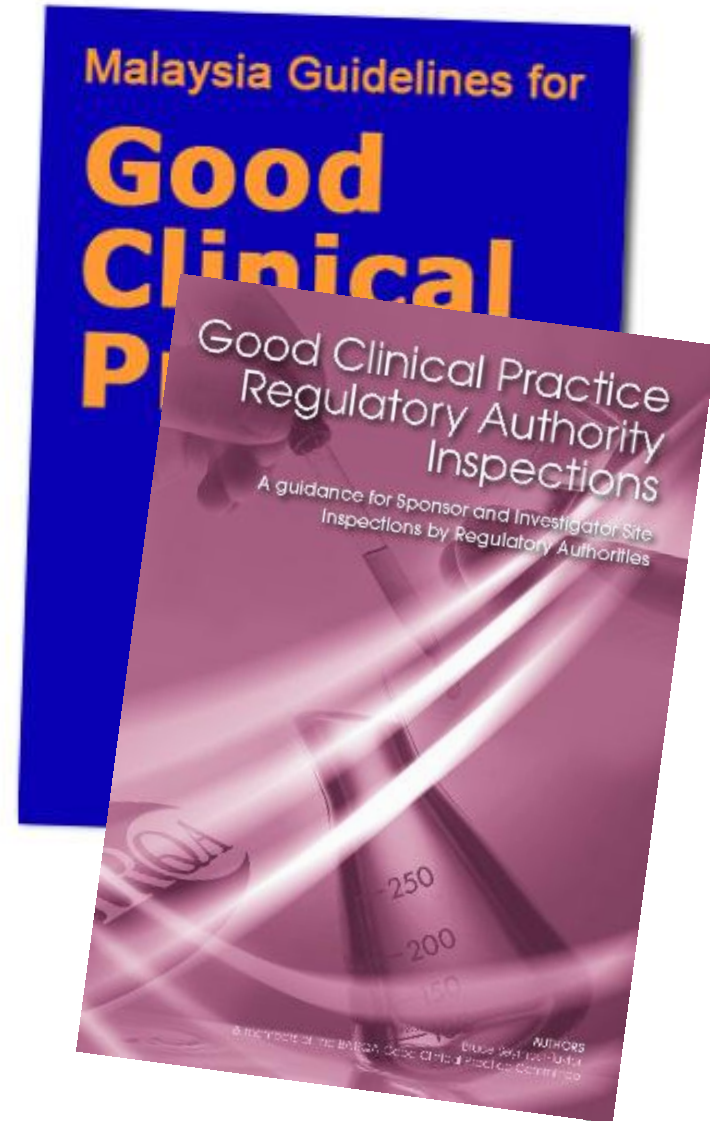
Objectives

Be aware of the importance of:

- Good Clinical Practice
- Strategies on how to answer your scientific question?
 - Research Design
 - Quantitative methods
 - Qualitative methods

What is Good Clinical Practice in research?

- GCP is the international standard for:
 - designing,
 - conducting,
 - recording, and
 - reporting clinical trials
- Protects research subjects
- Ensuring that process and data are accurate
- Minimizes possible fraud



GCP Responsibilities

Researchers must:

- strictly conduct a clinical trial according to the protocol,
 - document and maintain records and procedures,
 - comply with regulatory requirements.
- and*
- ensure that all ethical requirements are met



What are SOPs?

Standard operating procedures

(SOPs) are defined by the International conference on Harmonization (ICH) GCP as:

"detailed, written instructions to achieve uniformity of the performance of a specific function."



Written instructions, needed for a consistent approach to a research process.

How to make corrections to study documentation?

GCP defines procedures for changes to records. Person responsible must justify each correction.

- Draw a line through the entry,
- Show corrected entry and date beside it.
- Write initials of person making the correction.

Example:

Patient fell at home ~~office~~: (25/6/2010 R.B.)

* Never erase or conceal the original entry.

Types of Health Research

Basic Science:



Clinical Studies:



Health Services:

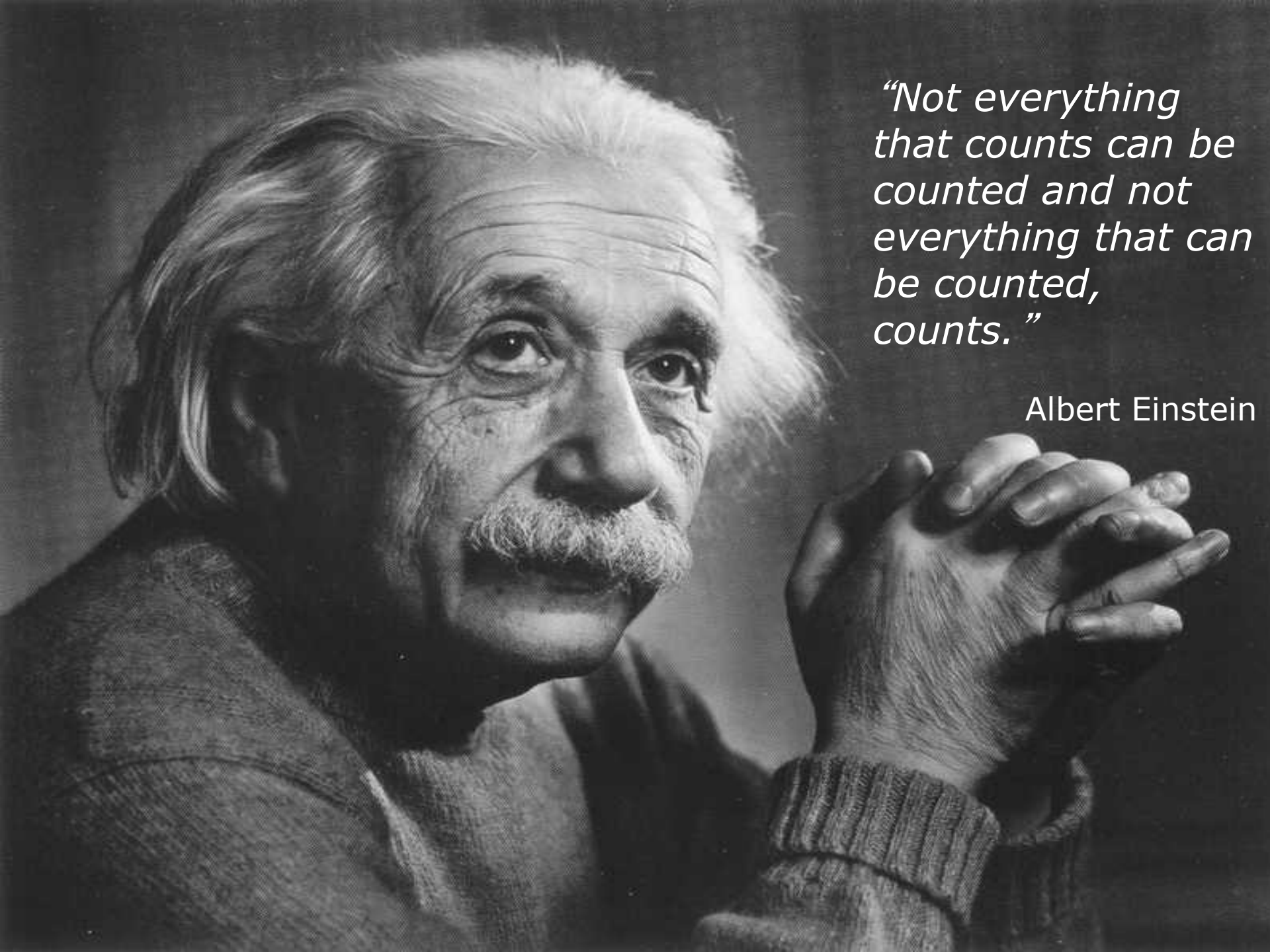


Population Health:

Types of Methods

- Qualitative
- Quantitative





“Not everything that counts can be counted and not everything that can be counted, counts.”

Albert Einstein

Qualitative Research

- Focuses on the meanings people attach to their experiences of the social world
- Interprets social phenomena (interactions & behaviours)
- Asks question about “Why?” and “How?” (not just; what, when, where?)

(Creswell, 1998)

Qualitative Research

When can we use it?

- Classify phenomena
 - Answer the 'what is X?'
 - Complement quantitative research- provide a different perspective on the same social phenomenon
 - Stand alone to explore a social phenomenon
- Results may be used to build a quantitative study*

Qualitative Question Examples



Clinical: Improve patient adherence to clinical recommendations

Educational: Determine what influences career choices of graduate trainees

Administrative: Assess local needs and operations when implementing new programs

Other: Discover what influences the behaviours of patients and health workers for quality improvement



Qualitative Methods

- Interview (e.g. key informants)
- Focus Group Discussions
- Observations
- Review new documents (e.g. journals)
- Review existing documents
- Open-ended survey question

Focus Groups

- Structured discussion with small number of subjects
- An interview guide is prepared beforehand and the researcher usually 'chairs- facilitates' the group
- Discussion is tape-recorded, then transcribed and analyzed
- Discussion continues until no new information comes out



Other Methods

Interviews

- Key informants,
- Stakeholders

Role-play and simulation

- Participants play a role, or observe role-play, then asked to rate behaviour, report feelings, and predict further events.

Data Analysis: Organize into codes, categories & themes

MR Helpers for Qualitative Analysis

Memory Stick Modules:

Helper for Qualitative Design

By O'Hearn, Turyakira and Graham

- Understand common study designs.
- Identify pros and cons to various methods.
- Practical design for two types of studies

Introduction to Qualitative Research

By Kielmann, Cataldo, Seeley

- Interviews
- Focus Groups
- Observation
- Fieldwork
- Ethics and Logistics
- Data Analysis

Quantitative Analysis

“Statistics deals with collection, analysis, interpretation, and presentation of numerical data.

Statistical tests makes sense of data collected on a small sample of the population to allows us to extrapolate to more general conclusions.”

- Explore relationships among factors
- Explain outcomes in terms of exposures
 - Higher levels of arsenic and mercury lead to higher rates of birth defects
- Investigate causality vs. correlation
- Hawthorne Effect

Features of a good Quantitative Research Design

- ◆ Has a clear & answerable research question
- ◆ Has valid and reliable measures
- ◆ Enables us to compare variables
 - between groups, or
 - before and after an intervention
- ◆ Allow us to
 - quantify differences
 - establish temporal sequence
 - minimizes bias
 - control for confounding variables

Types of Clinical Studies

Observational Studies:

- Case Series
- Cross sectional
- Case Control
- Cohort study

Experimental Studies:

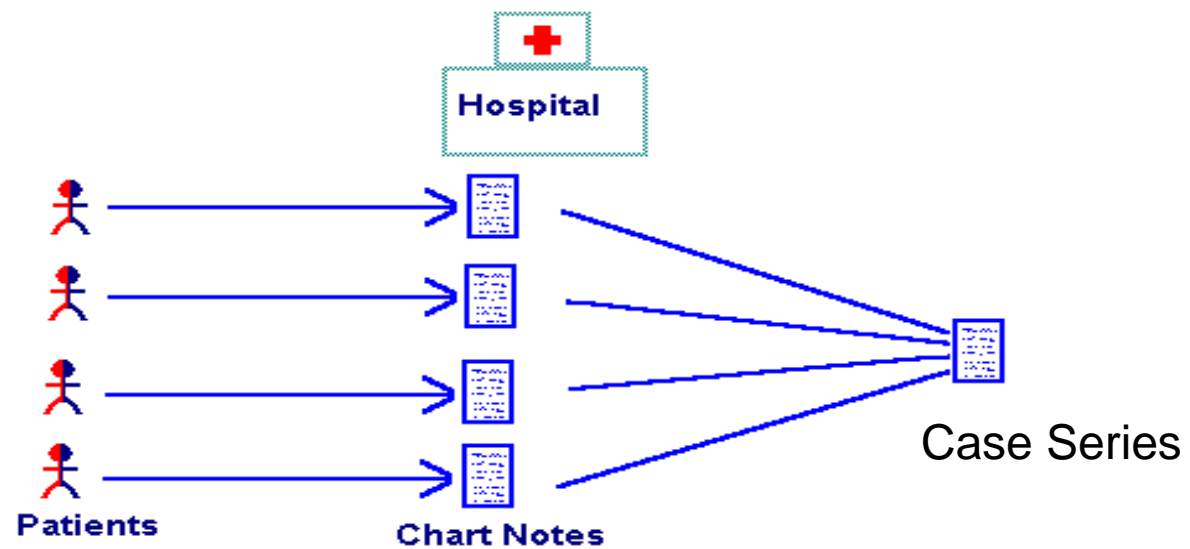
- Randomized controlled trials
- Nonrandomized controlled trials

Case Reports and Case Series

Case report: detailed report on a single case

Case series: collection of similar cases

Both can teach a lesson and **help develop a hypothesis** based on insight gained from the report.



Case Reports and Case Series

Advantages:

- Easy to do
- recognition of new diseases
- **formulation of hypotheses**



Disadvantages:

- based on the experience of one person, or just a few people
- presence of any risk factor may be coincidental
- lack of an appropriate comparison group

Cross-sectional Study

Study population at a single point in time-
useful to determine: prevalence of factors
frequency of a disease.
current health status
Helpful to plan health services.

Advantages:

- quick and easy
- **hypothesis generating**

Disadvantages:

- May be hard to say if 'exposure' really preceded 'outcome'.
- Poor for testing hypotheses.

Case-control study



Selection of a control group is an critically important issue in any case-control study.



Ideal control group should be representative of the population from which the cases are derived (the *source population*).

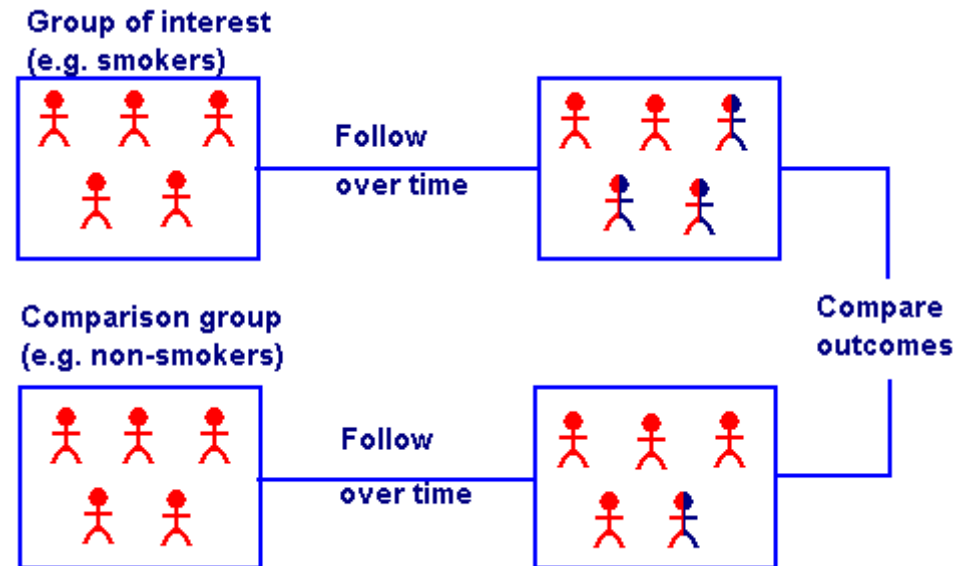


Observational: Cohort Study

Observational study: well-defined group of research participants followed over time to see if different exposures lead to different outcomes.

Characteristics:

- must follow-up study with forward direction,
- can start in the present or the past



From Google images

Cohort Study

Advantages:

- least prone to bias compared to other observational designs
- exposures and causes are observed before effects
- Can be used to study several exposures and several outcomes
- Can assess impacts of treatments

Disadvantages:

- costly and time consuming to follow cohort forward in time
- loss-to-follow-up may lead to bias
- expensive design to study rare or diseases with long latencies
- for treatment, more prone to bias than RCT

Controlled Trials

- **Randomized Control Trials (RCTs):**
 - Eliminates *bias* so statistical tests valid (e.g. t-test)
 - Improves chance of having comparable groups
 - Groups may differ in small studies ($n < 100$)
- **Blinding**
 - ideal if patient and/or investigator unaware of treatment assigned.
- **Registering Trials*****
 - All clinical trial must be registered as part of the Consolidated Standards of Reporting Trials (CONSORT)
 - **Standard required for publication**
 - To register go to the Pan African Clinical Trials Registry <http://www.pactr.org/ic>

***An RCT is the “gold standard”
to evaluate an intervention***

Controlled trials

Advantage:

- Allows investigator to control the research process.
- Randomized Control Trial (RCT) is “*Gold Standard*” of evaluation
- Outcome more likely to be accepted.

Disadvantages:

- Time and cost
- Restricted to interventions or exposures that can be randomized,
- Research participants may be so narrowly defined that it is difficult to generalize

Quantitative

Qualitative

Research Aims	Test hypotheses and establish cause and effect	Understand social phenomena in their natural settings
Study Design	Formal, objective, and systematic	Observational, holistic, and flexible
Sampling	Unbiased cross-section representative of the study population	Strategically selected to collect the most meaningful data
Methods	Measurement yielding numeric data	Interviews and observations yielding textual data
Analysis	Emphasis on statistical techniques to determine significance	Identify themes that emerge from the data

MicroResearch Program

Here are 4 proposed MR projects questions – what type of design would you use?

- What are the knowledge, practice and attitudes about blood donation in Kiruhura District in SW Uganda?
- What are the causes of death in first week of life in rural Uganda?
- What are the effects of the government decreed free maternity delivery services on the quality of maternal health care services at Pumoni hospital in Nairobi?
- Can cell phone reminders improve the antenatal care attendance of pregnant women in Semi-urban Tanzania?

Helpful Material

1. Good Clinical Practice: Consolidated Guidelines (International).
<http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/EducationalMaterials/ucm112925.htm>
2. Tutorials on clinical trials
<http://library.downstate.edu/EBM2/contents.htm>
3. Users' Guides to the Medical Literature:
http://ugi.usersguides.org/usersguides/hg/hh_start.asp
4. **On Memory Stick**
 - *Quantitative design a general overview*
 - *Helper for Quantitative Design (Draft)*
 - *Qualitative Design general overview*
 - *Helper for Qualitative design (Draft)*