

Study types

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Where to start?

- A good clinical study starts with an appropriate question , which, in turn, is based on comprehensive review of the available pre-clinical and clinical data.
- Type of study type depends on the question to be answered.

Clinical study types

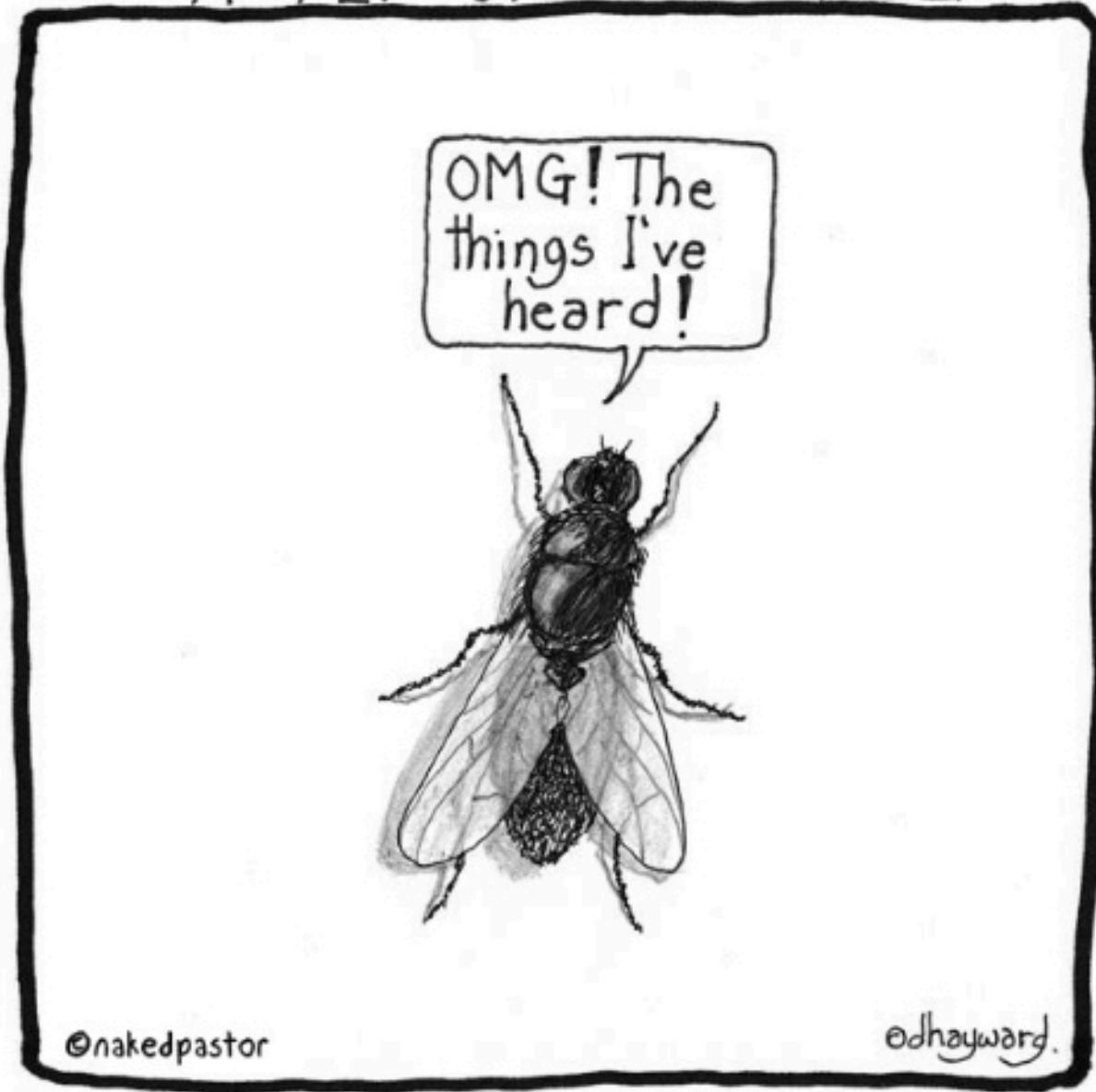
- **Observational studies**

- Cross-sectional
- Cohort
- Case-control
- Case report
- Case series

- **Experimental studies**

- Uncontrolled trials
- Controlled trials

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@nakedpastor

edhayward.

Characteristics of observational studies

- No control over study units
- Study of risk factors that have serious consequences
- Study of individuals in their natural environment
- Possibility of confounding

Aim of observational studies

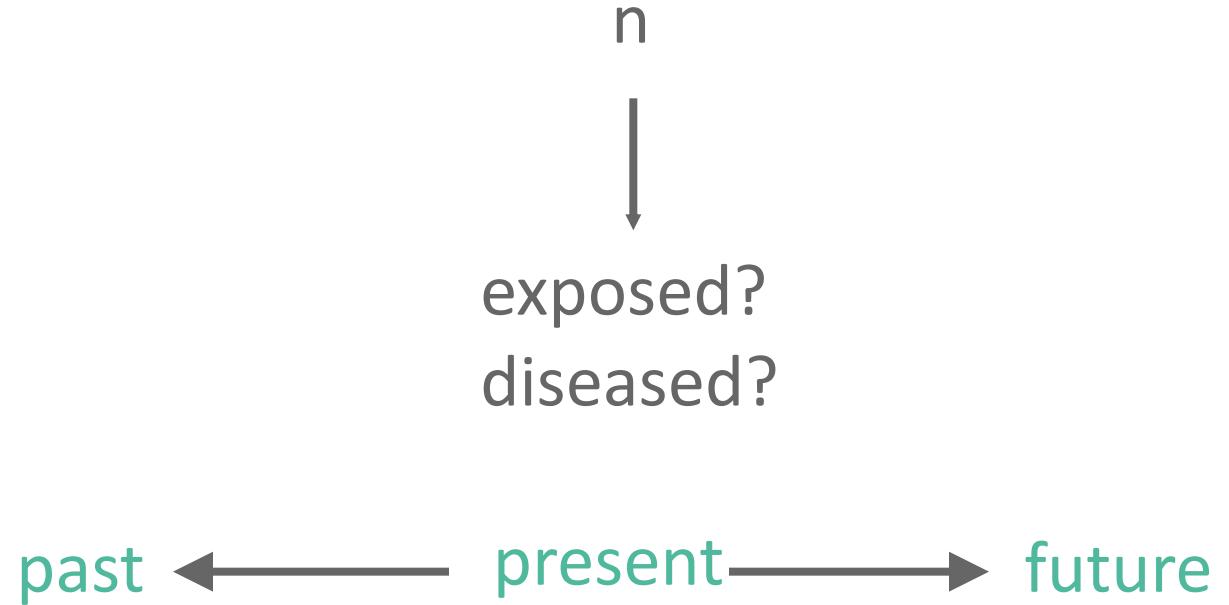
- Evaluate the effect of a suspected risk factor (exposure) on an outcome (e.g., disease)

Study types

Cross-sectional studies

Cross-sectional studies (1)

- Exposure and disease measured once, at the same point in time



Cross-sectional studies (2)

- Random sample from population
- Estimates the frequencies of both exposure and outcome in the population
- Measuring both exposure and outcome at one point in time
- Typically, a survey

Cross-sectional studies (3)

- **Advantages**

- Can study several exposure factors and outcomes simultaneously
- Determine disease prevalence
- Quick
- Low cost (e.g., mail survey)

- **Limitations**

- Do not determine causal association
- Not appropriate if either exposure or outcome is rare

Study types

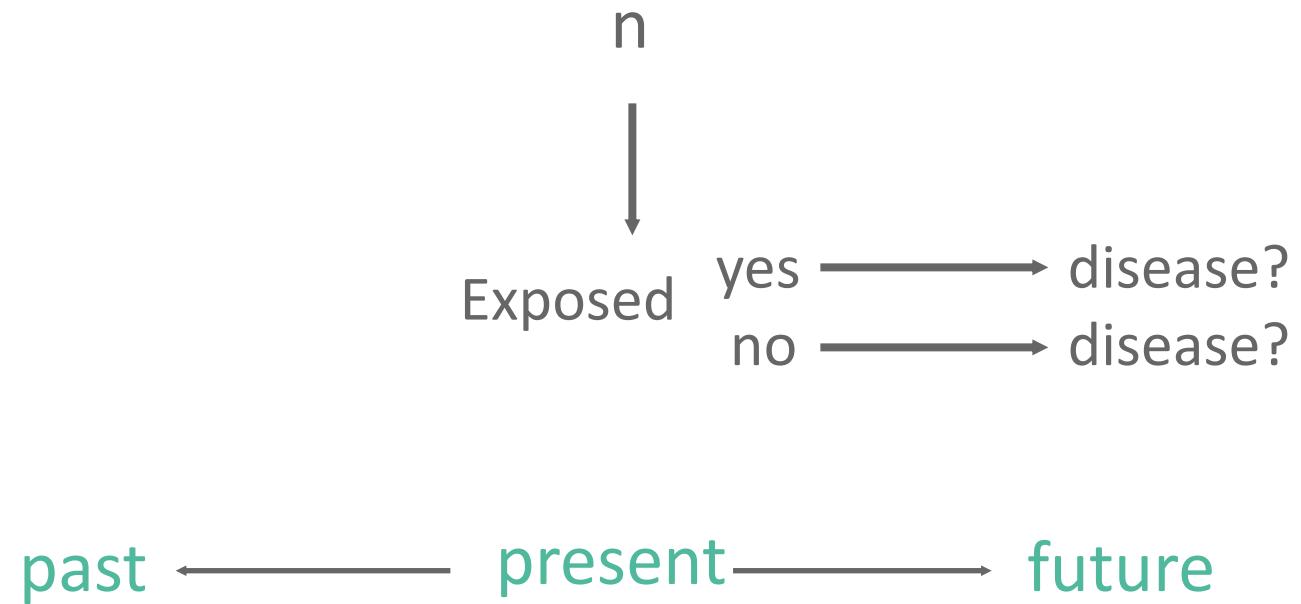
Cohort studies

Cohort studies (1)

- Follow-up studies; subjects are selected on presence or absence of exposure and absence of disease at one point in time.
- Disease is then assessed for all subjects at another point in time.

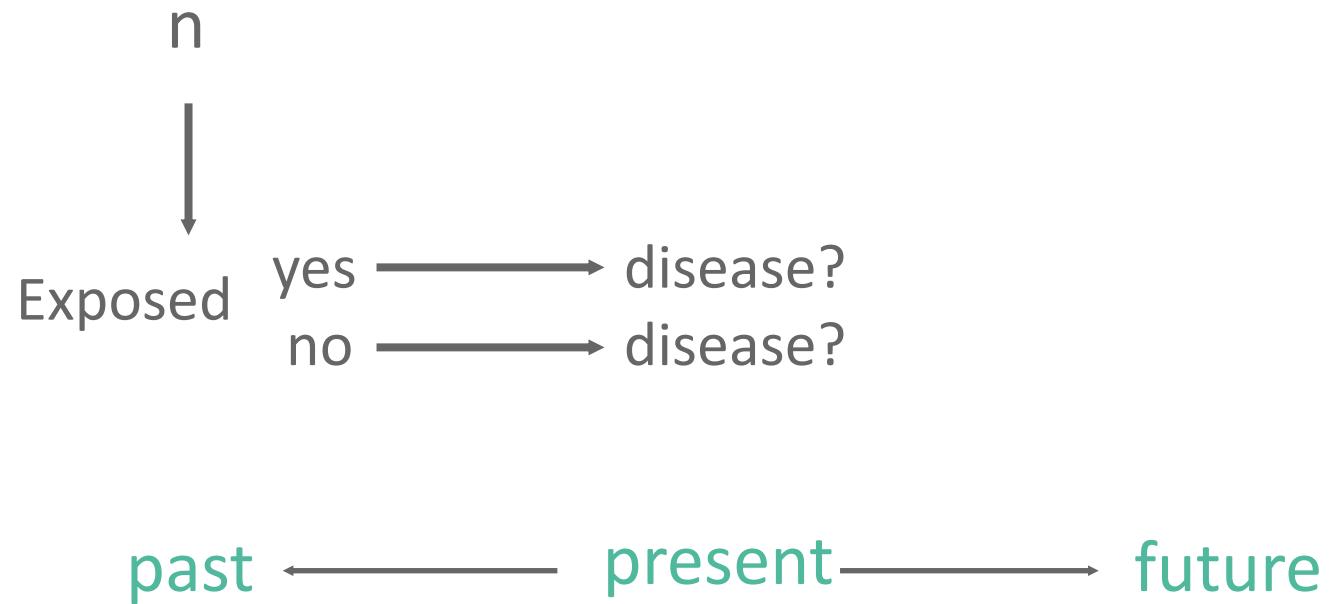
Cohort studies (2)

- Individuals selected by exposure status and future occurrence of disease measured



Cohort studies (3)

- Individuals selected by exposure status and future occurrence of disease measured



Cohort studies (4)

- **Advantages**

- Establishment of a temporal sequence between exposure and disease
- Assessment of the direct measurement of incidence
- Examination of multiple effects of a single exposure

Cohort studies (5)

- **Limitations**

- Time consuming and expensive
- Loss to follow-up and data unavailability
- Potential confounding factors
- Inefficient for rare diseases

Study types

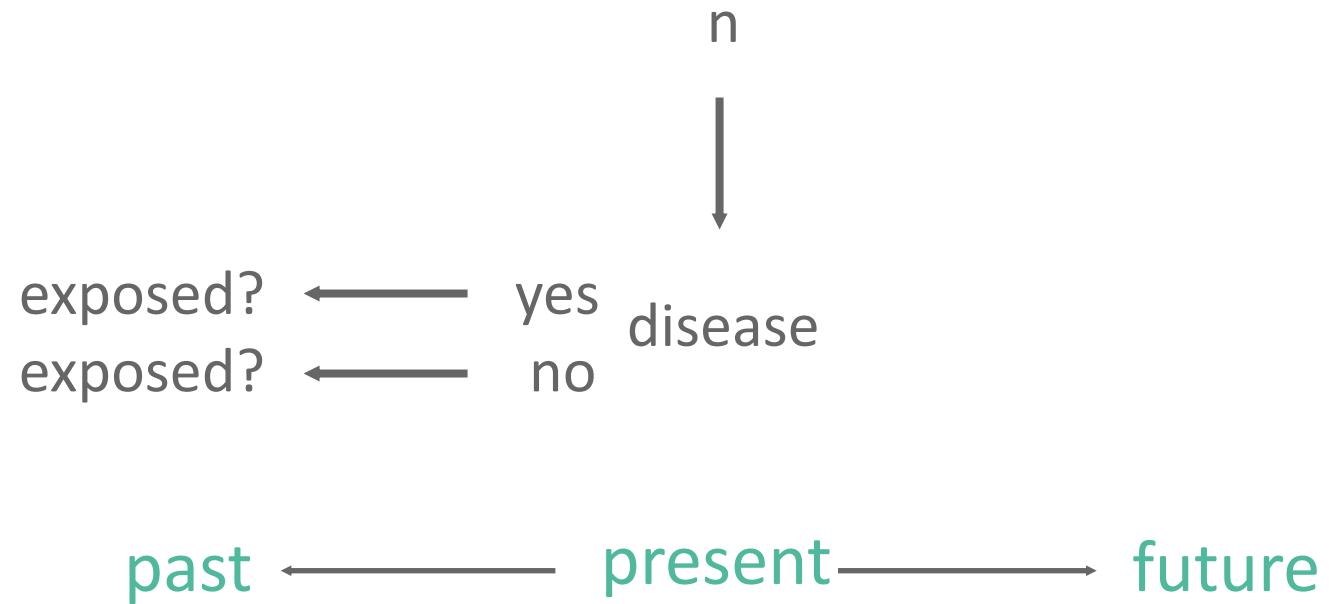
Case-control studies

Case-control studies (1)

- Retrospective
- First, identify cases
- Then, identify suitable controls
 - Hardest part: who is suitable?
- Then, inquire or retrieve previous exposure
 - By interview
 - By databases

Case-control studies (2)

- Diseased and non-diseased individuals are selected
- Past exposure status is retrieved



Case-control studies (3)

- **Advantages**

- Suitable for rare disease
- Can study several risk factors at the same time
- Usually, low-cost
- Confounding likely

Case-control studies (5)

- **Limitations**

- Susceptible to bias (particularly selection and recall)
- Difficulties in selection of controls
- Ascertainment of disease and exposure status
- Inefficient for rare exposures

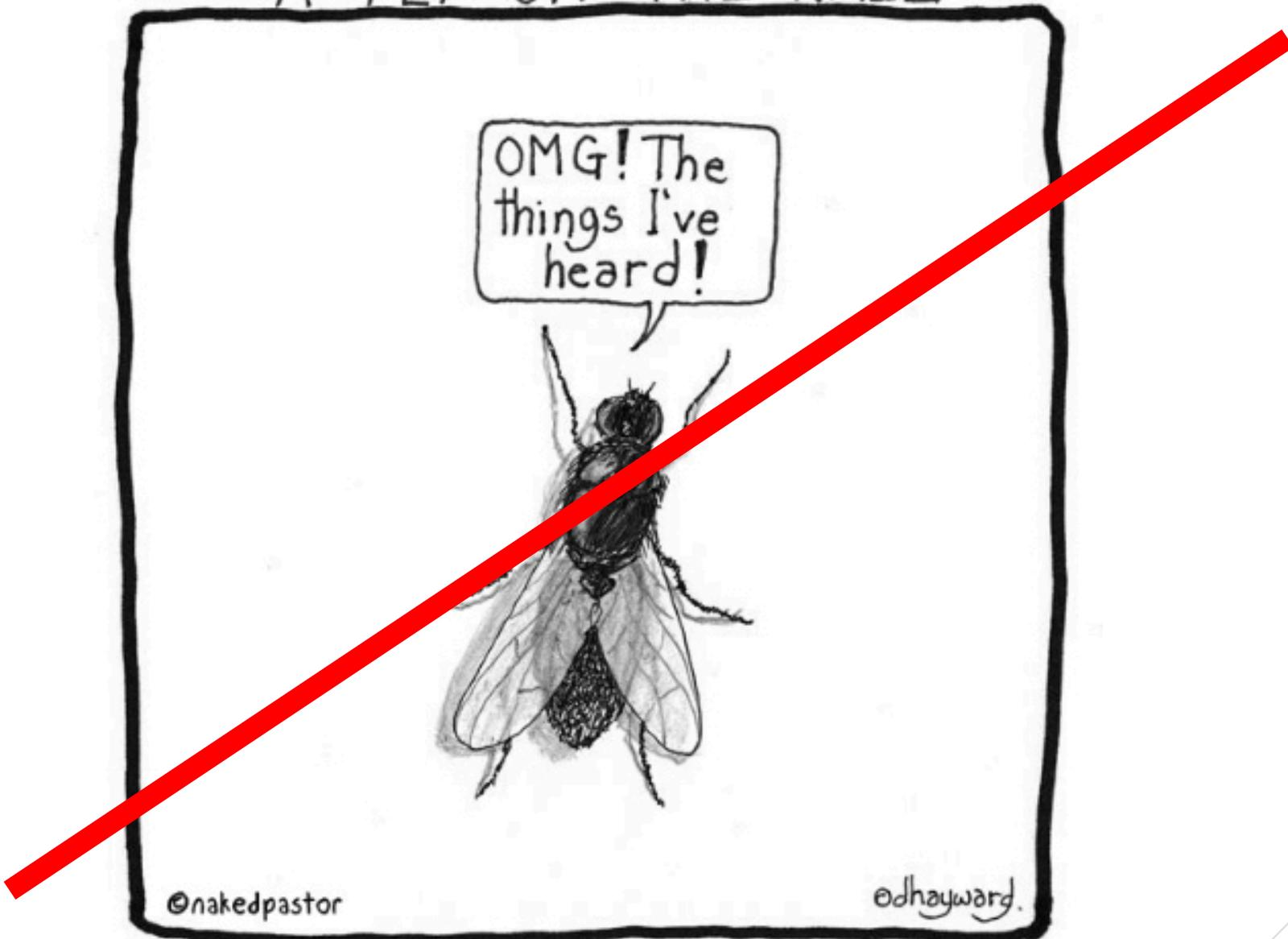
Summary of observational studies

Characteristic	Cross-sectional	Case-control	Cohort
Sampling	Random sample: population	Purposive sample: diseased / non-diseased	Purposive sample: exposed / non-exposed
Time	One point	Retrospective	Prospective
Causality	Statistical association	Screening for many risk factors	Testing one (or few) risk factors
Frequency measure	Prevalence	None	Incidence

Study types

Clinical trials

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Clinical trials: Study design

- **Uncontrolled**
- **Controlled**
 - Before/after (cross-over)
 - Historical
 - Concurrent, not randomized
 - Randomized

Advantages of clinical trials

- Randomization tends to produce comparable groups
- Assure causal association
- Randomization produces valid statistical tests

Disadvantages of clinical trials

- **Generalization**
 - Participants studied may not represent general study population
- **Recruitment**
 - Hard
- **Acceptability of randomization process**
 - Some physicians will refuse
 - Some participants will refuse
- **Administrative complexity**

Comparing treatments

- **Fundamental principle**
 - Groups must be alike in all important aspects and only differ in the intervention each group receives
- **Randomization**
 - Each participant has the same chance of receiving any of the interventions under study
 - Allocation is carried out using a chance mechanism so that neither the participant nor the investigator will know in advance which will be assigned
- **Blinding**
 - Avoidance of conscious or subconscious influence
 - Fair evaluation of outcomes

Clinical trials vs. cross-sectional studies

Clinical trials

- Individuals selected by entry condition
- Control over exposure
- Exposure groups fully comparable
- Outcome measured after allocating individuals to exposure
- Causal association likely

Cross-sectional studies

- Individuals selected randomly
- Exposure observed as occurring in nature (groups not ‘identical’)
- Exposure AND outcome measured at one point in time
- No causal interpretation

Types of studies



Types of studies

Type of Question	Ideal Type of Study
Therapy	RCT
Prevention	RCT > Cohort Study > Case Control
Diagnosis	Prospective, blind controlled trial comparison to gold standard
Prognosis	Cohort Study > Case Control > Case Series/Case Report
Etiology/Harm	RCT > Cohort Study > Case Control
Cost analysis	economic analysis

Note: Meta-analyses and systematic reviews, when available, often provide the best answers to clinical questions.

<http://www.dartmouth.edu>

Take-home messages

- Selection of design should be made based on the hypothesis to be tested with consideration of the current state of knowledge
- Consider available resources when deciding on a study design
- Observational studies are especially valuable in epidemiology
- Clinical trials carry the highest level of evidence and should be pursued whenever feasible
- A clear and organized study design leads to successful results

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