Coming to grips with Quantitative Research

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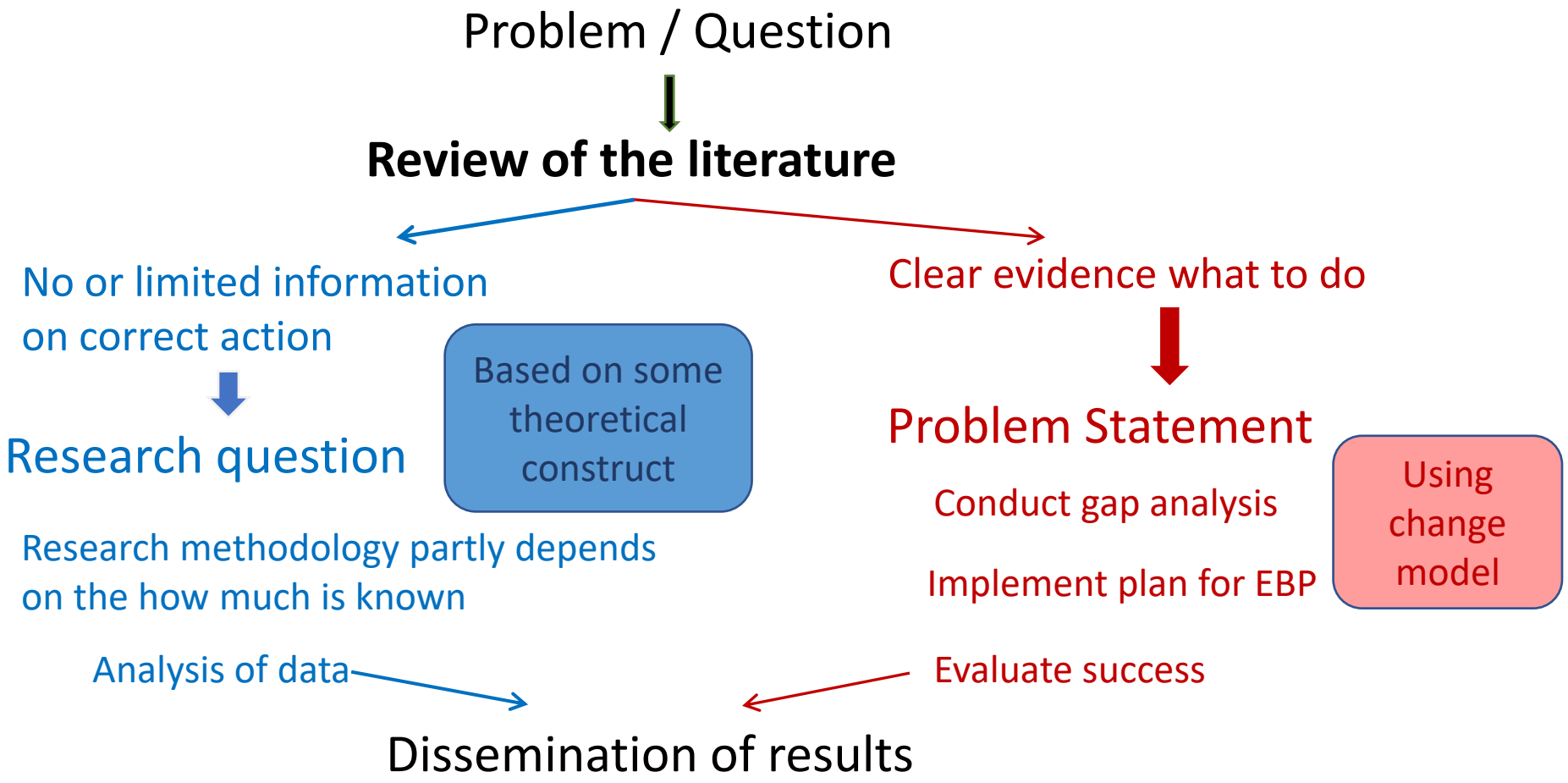
Today's objectives

- Contrast knowledge-generating research with quality improvement projects.
- Explain the basic principles of all quantitative research design to achieve valid and unbiased results.
- Describe how design of observational studies can approximate the design principles of a randomized control trial.
- Match appropriate study designs with different study aims.
- Describe essential elements in the methodology section of a quantitative research proposal.
- Discuss solutions to common biases in questionnaire development and administration.

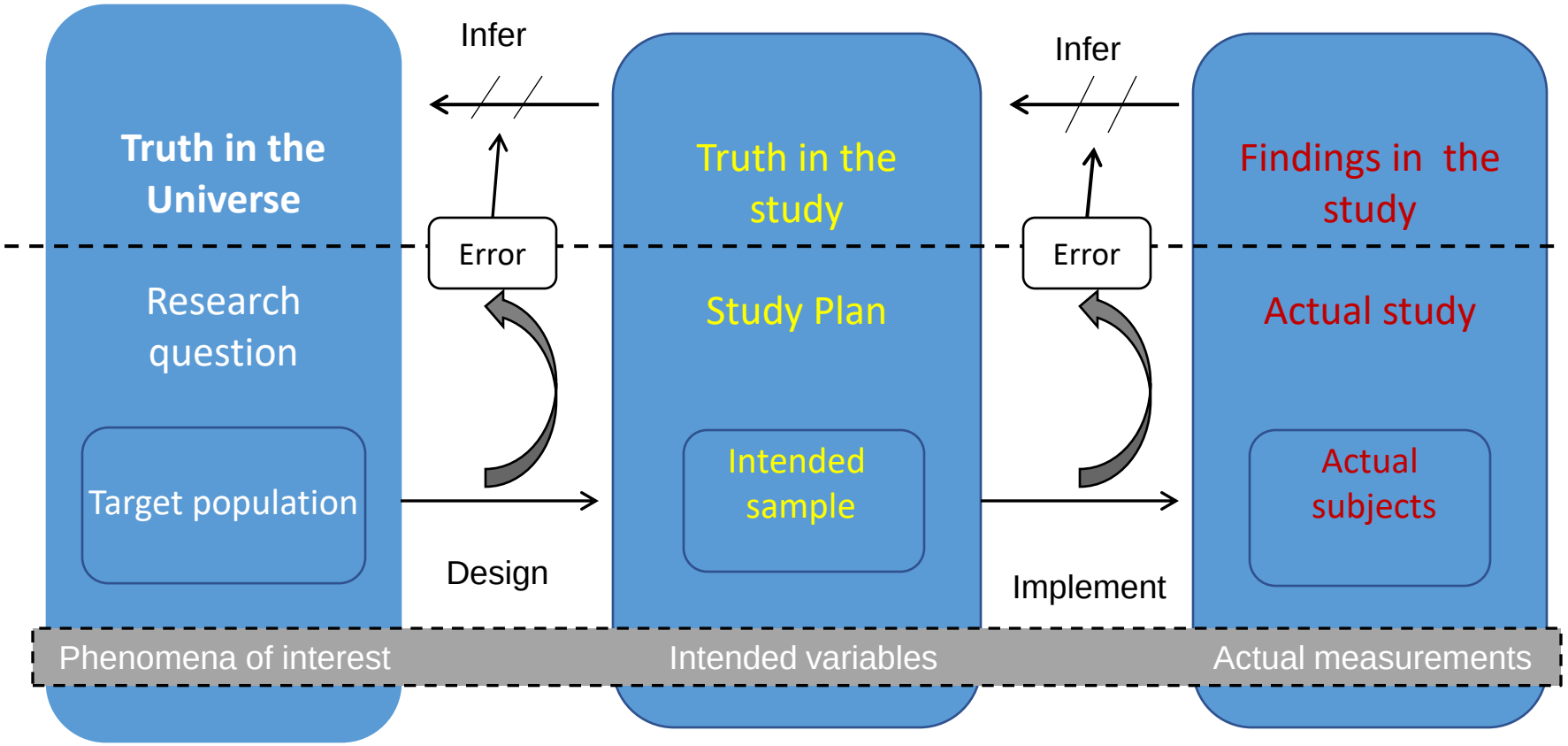
Knowledge generating research
versus
Evidenced-based /Quality Improvement projects



Differentiating Research and Quality Improvement (QI)

	Research	Quality Improvement
Generalizability	Designed to be generalizable	Limited scope generalizability; methods, lessons learned
Role of Theory	Goal to prove/disprove an underlying theory	**Program is being tested** – not theory How to make the program better?
Methodology	Often uses experimental controls	Pre-, post-evaluation; matching or control charts
Assumption of benefit	Use of **equipoise** e.g. treatment not expected to be beneficial	QI intervention to all patients and assumed to be safe and effective
Informed consent	Required – ethically and there is no promise of benefits	Patient consent to treatment sufficient; QI ethically required since leads to better care
Other	Serves investigator goals	Serves organizational goals

Designing a Study to get to "Truth"



Hulley SB, et al. *Designing Clinical Research, 3rd ed*.

Components of an Experiment

	Lind Survy Clinical Trial
Population e.g., persons, mice, organisms	Sailors with scurvy (n=12) Paired together with similar symptoms
Setting – place where study takes place	HMS Salisbury ship
Treatment (intervention): **independent variable**	- Apple cider -Vinegar - Mustard & garlic purges - 2 oranges & 1 lemon - Elixir of vitriol -Sea water
Timeframe: period of research; data points	?7-14 days
Observations (measurements): what/how variables collected, measured, analyzed, interpreted • Outcome (dependent) variables • Variable to check/control for confounding	Not well written up but the 2 who received oranges and lemons recovered Typically: simple relative risk

Meaning of ‘Control’ in Randomized Clinical Trial

Ruling out ‘all’ threats to valid inference

- Eliminate as many sources of **systematic bias** as possible
  - Control the situation or environment of the experiment
  - Make groups as equal as possible on baseline characteristics
    - Requires a balance between inclusion and exclusion criteria
  - Determine which groups receive a particular treatment at a particular time i.e. strict control of independent variable
  - Use blinding to reduce treatment or outcome assessment bias
- Eliminate threats to valid inference by design
  - Control factors that can affect outcome e.g change behavior (Hawthorne) by using placebo
  - Statistical control of imbalances

Three key characteristics of **all** studies

- **Comparability of populations**
  - In RCT, random assignment and CONSORT figure for drop-outs and Table 1
- **Comparability of information**
  - In RCT, double/triple blinding
- **Comparability of effects**
  - Use of ‘placebo’/ control condition esp attention-control
    - Minimizes: expectation bias, performance bias (Hawthorn effect), detection bias
  - Request subjects not use other treatments during the study

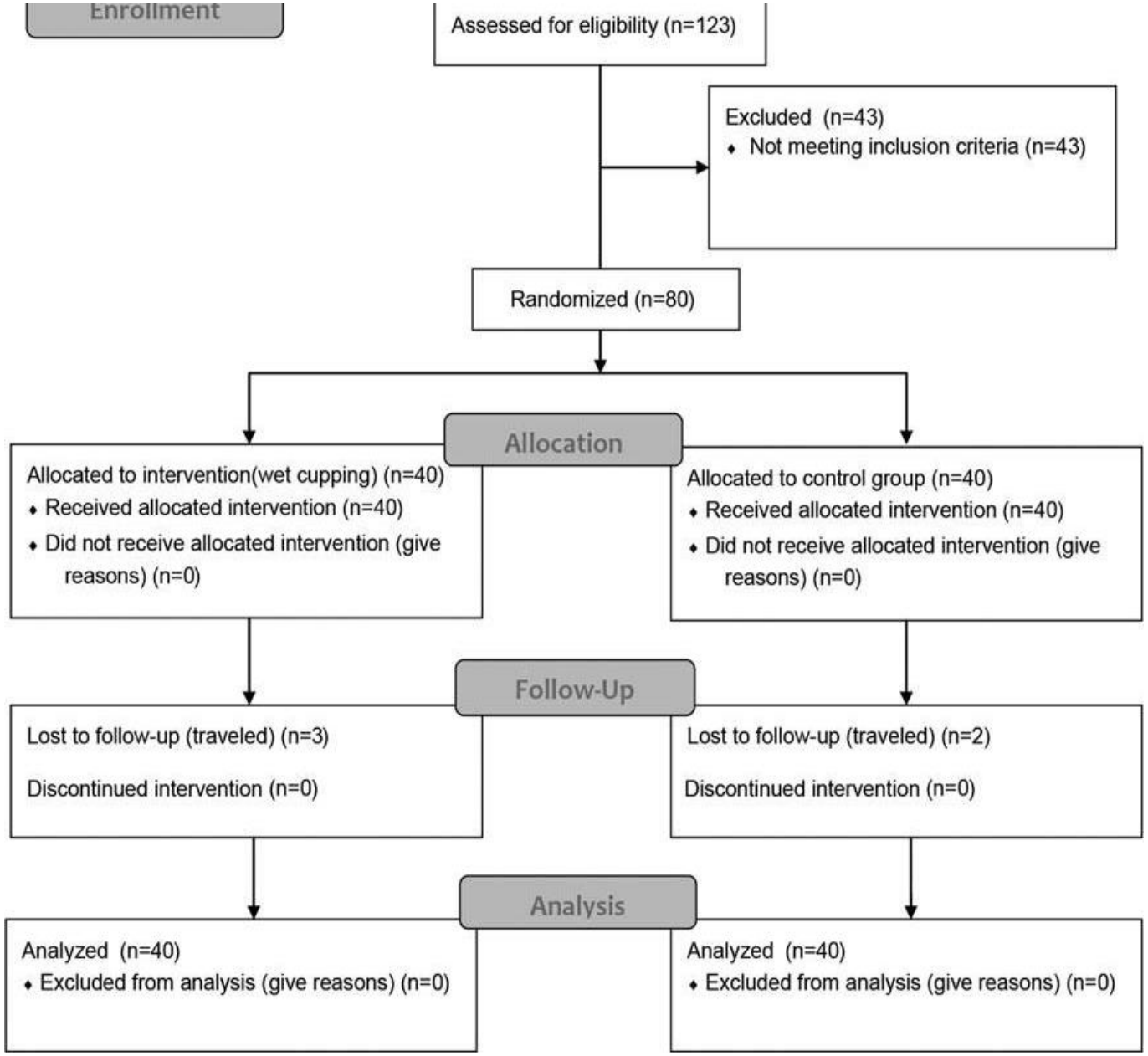


Table 1. Baseline Characteristics in Intervention (Wet Cupping) and Control Groups

Characteristic	Wet cupping (n = 40)	Control (n = 40)
Age (y)	36.48 (9.3)	36.43 (9.4)
Men/women (n/n)	22/18	17/23
Prognosis expectation on Likert scale	4.88 (0.9)	4.87 (1.1)
Age at onset (y)	31.88 (9.2)	32.48 (9.4)
Duration of illness (y)	4.45 (4.8)	3.85 (3.9)
NRS score	60.50 (19.7)	56.25 (17.5)
ODQ score	38.33 (19.2)	32.05 (15.9)
PPI score	2.35 (1.2)	2.13 (0.9)

Unless noted, values are the mean (standard deviation).
NRS, Numeric Rating Scale; ODQ, Oswestry Disability Questionnaire; PPI, Present Pain Intensity.

Albedah A, et al. The use of wet cupping for non-specific low back pain: randomized controlled clinical trial. J Alt Comp Med 2015; 21(8):504

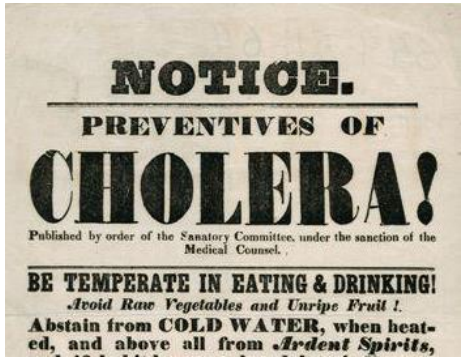
John Snow intervenes in a cholera epidemic

Situation

1865 cholera breaks out in London
Cholera: severe diarrhea, vomiting, rapid dehydration with death within hours; 50% fatality rate
Killed millions in 1800's in India, N. AM, Europe

What was unknown

Understanding of bacteria
Role of sanitary conditions


NOTICE.
PREVENTIVES OF
CHOLERA!
Published by order of the Sanatory Committee, under the sanction of the Medical Counsel.
BE TEMPERATE IN EATING & DRINKING!
Avoid Raw Vegetables and Unripe Fruit!
Abstain from COLD WATER, when heated, and above all from *Ardent Spirits,*

Questions

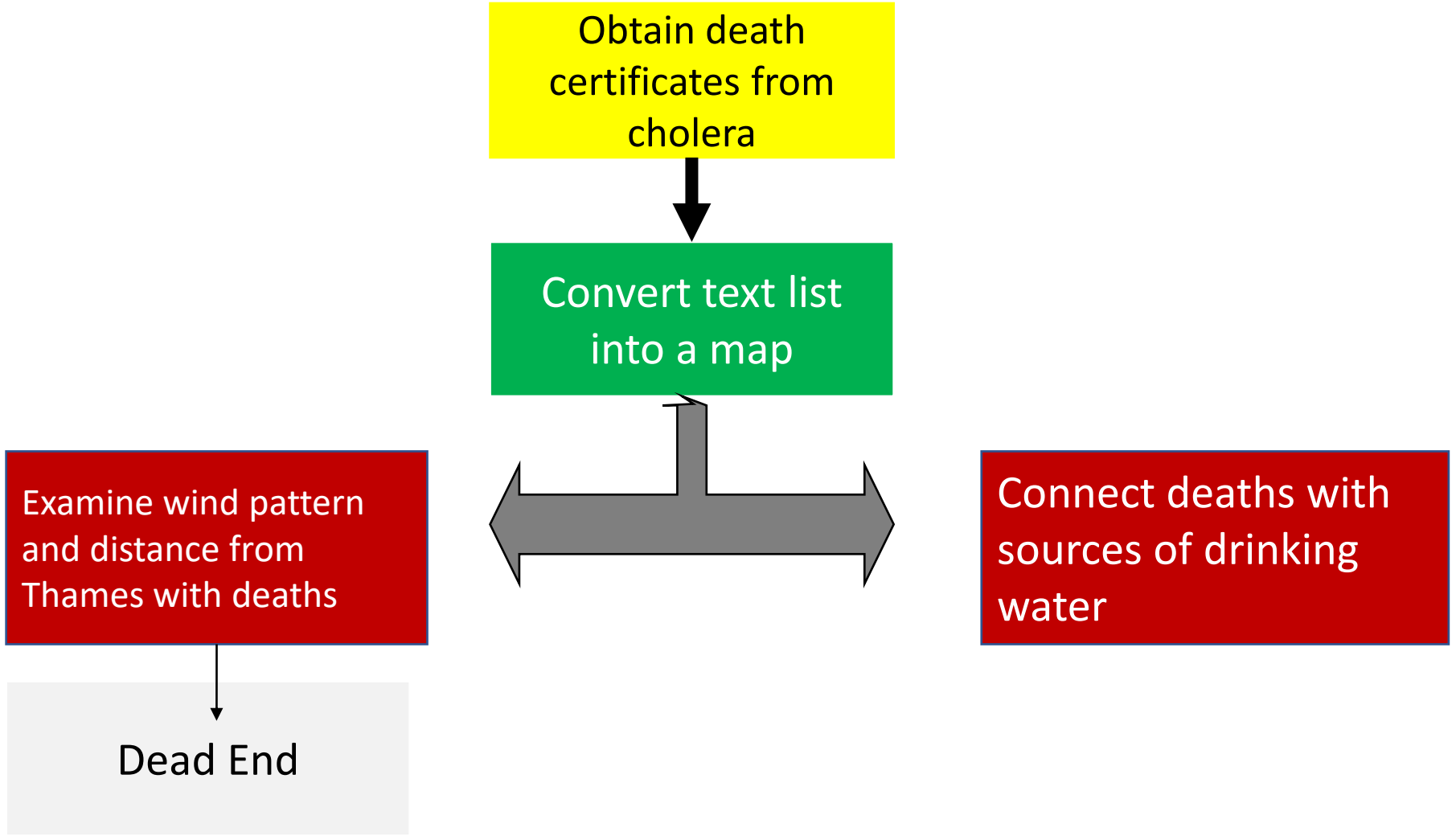
How is cholera transmitted?
How can we stop this cholera epidemic in central London?

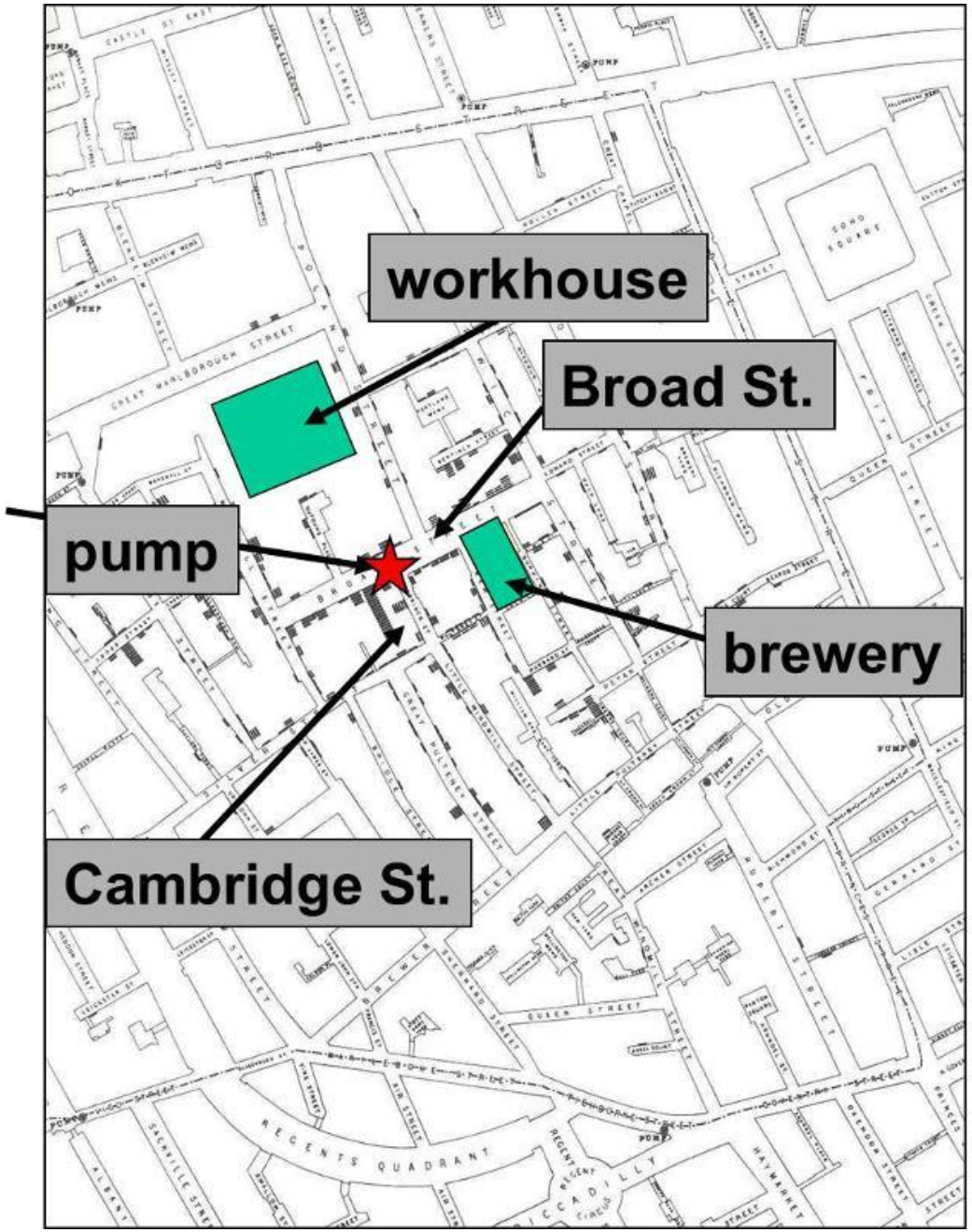
Hypothesis

Cholera is spread by:
1) Breathing vapors of decaying matter
2) Drinking contaminated water

John Snow's Designs and Methods:

Searches for correlations between water and cholera





Snow correlates death locations with a water source

Broad street pump

Residence of cholera victim

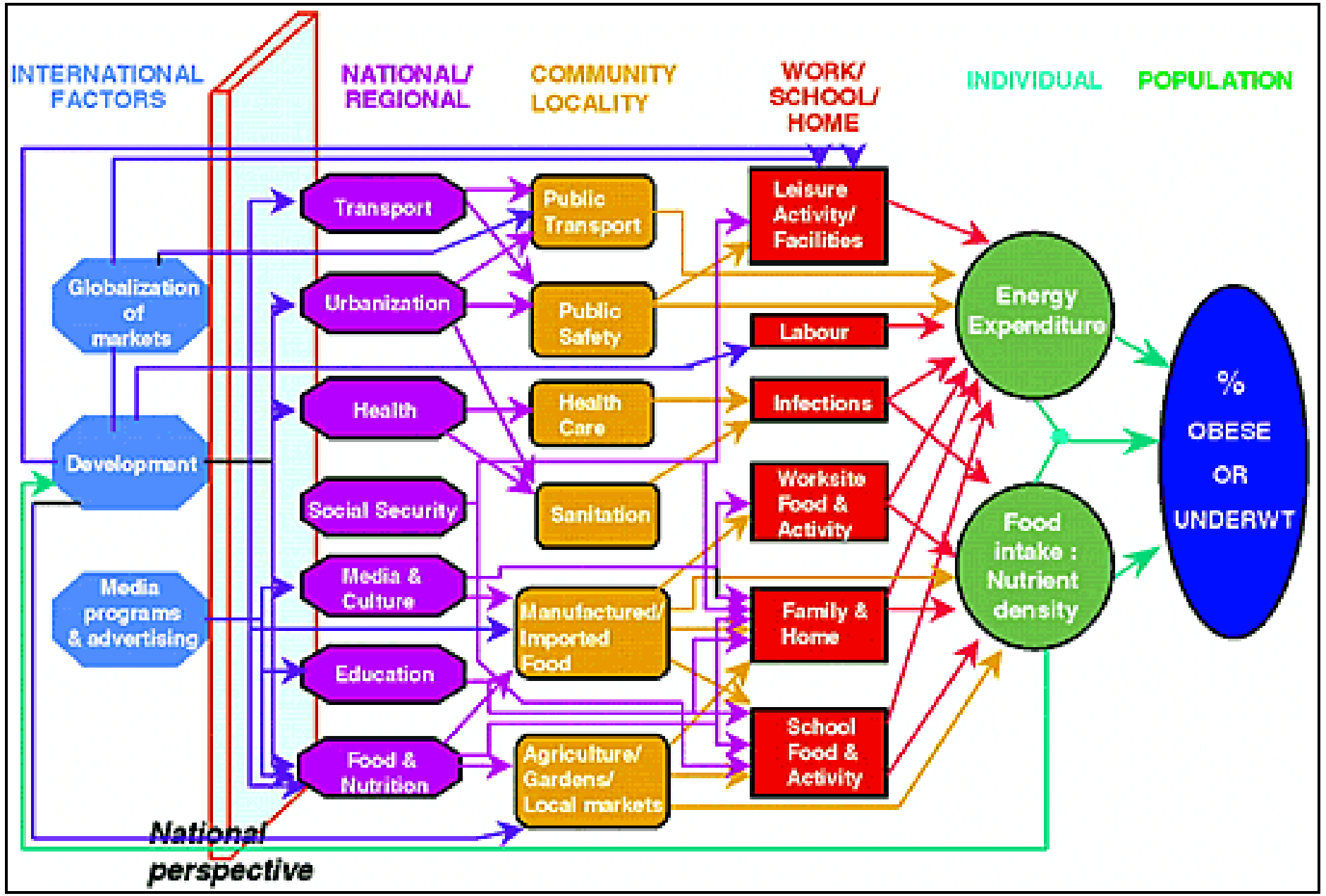
Different water source not Broad St. pump

Strong correlation of cholera victims drinking water from Broad St. pump!

Why do we need observational studies?

Please answer in the chat box

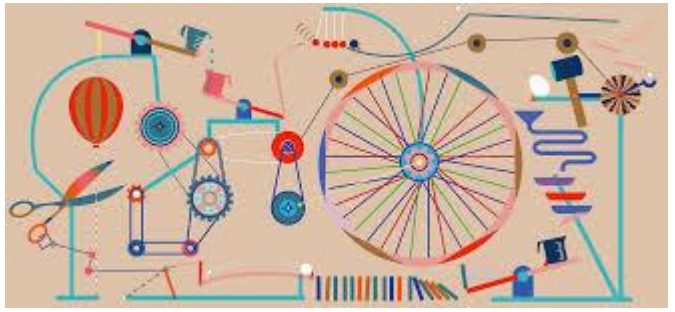
- It may be unethical or not feasible to do an experimental study
- An RCT may not answer the question you want to answer
  - RCTs are **efficacy** (what is possible under ideal conditions), not **effectiveness** trials
- Question you are studying may not suit RCT trial design
  - Very rare event
  - Complex processes


INTERNATIONAL FACTORS
NATIONAL/ REGIONAL
COMMUNITY LOCALITY
WORK/ SCHOOL/ HOME
INDIVIDUAL
POPULATION
Globalization of markets
Development
Media programs & advertising
Transport
Urbanization
Health
Social Security
Media & Culture
Education
Food & Nutrition
Public Transport
Public Safety
Health Care
Sanitation
Manufactured/ Imported Food
Agriculture/ Gardens/ Local markets
Leisure Activity/ Facilities
Labour
Infections
Worksite Food & Activity
Family & Home
School Food & Activity
Energy Expenditure
Food intake : Nutrient density
% OBESE OR UNDERWT
National perspective

Types of quantitative research

Analytic
(correlational)

Descriptive



Quasi-experimental: Causal-comparative

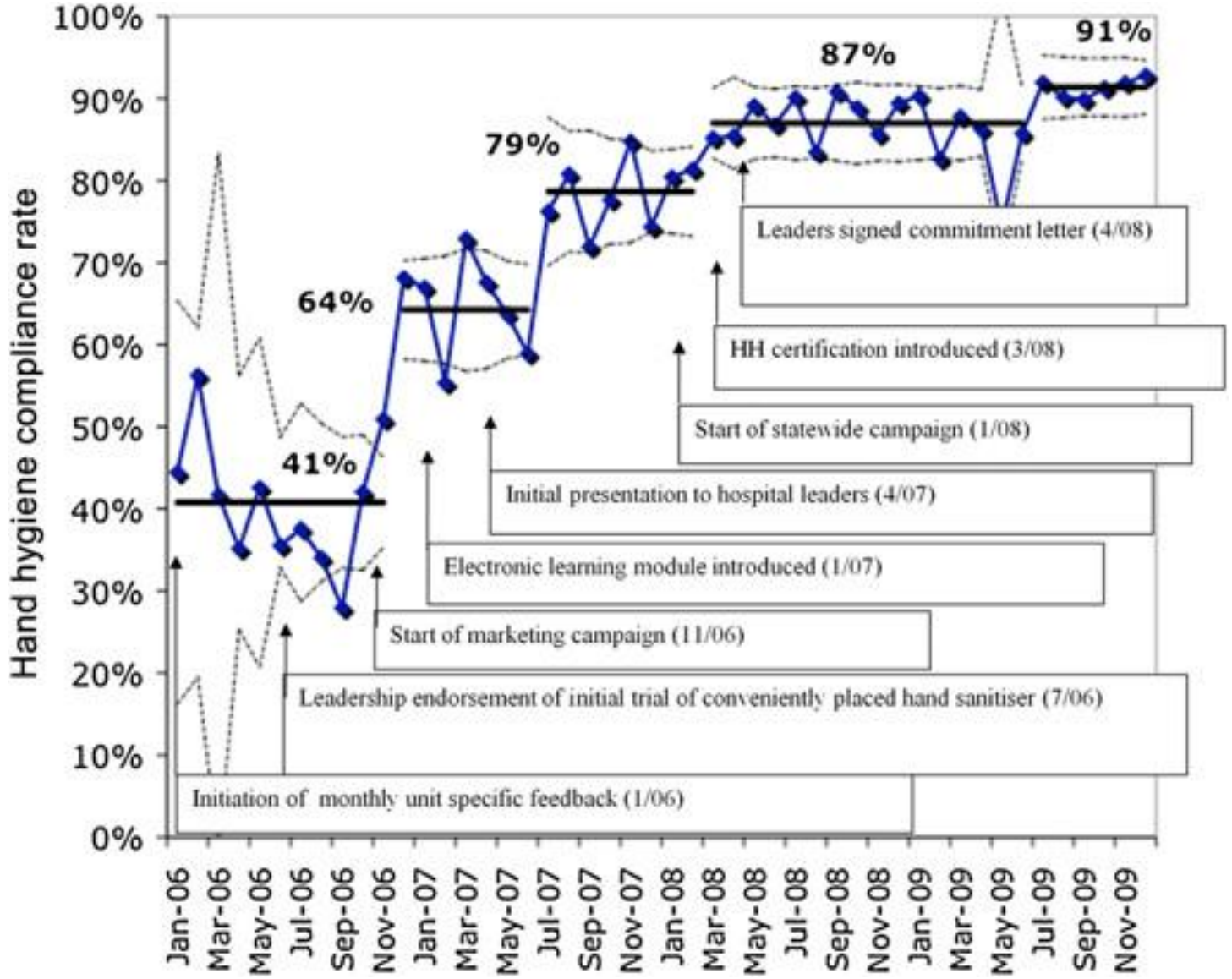
Experimental: RCT

Quasi-experimental Design

Like experiment, aims to assess cause and effect

- No random assignment of subjects but random assignment may occur e.g., by groups or setting (aka Cluster randomization)
- Control groups compensates for lack of randomization
- Intervention introduced in one group but not the other (control group)
  - Effect on subjects are measured and compared between groups
- Design variations
  - Natural experiment: event occurs naturally e.g. earthquake, disaster
  - Non-equivalent control group e.g. outcomes in a clinic before a new process is introduced and after
  - Time-series design: effects of treatment inferred from measurement taken multiple times before and after treatment

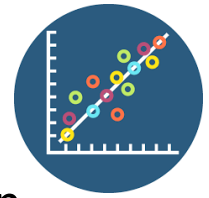
Kirkland KB, et al. Impact of hospital wide handwashing hygiene initiative on hospital-care associated infections: results of an interrupted time series. *BMJ Safe Qual*.2012; 21(12):1019.



Observational Studies

No manipulation or control or random assignment to groups
CANNOT by themselves determine cause and effect

- **Descriptive study**
  Describes characteristics/behaviors of a population or situation &/or frequency of a phenomenon.



- **Analytic/Correlational study**
  Describe size (magnitude) and direction of the relationship between 2 or more variables
  - Hypothesis generating
  - Improve or inform health-related activities
  - Inform decision-making

  Comparison between groups usually

Potential Data collection methods

- Cohort: follow group over time
- Cross-sectional: one time assessment
- Case-control: choose controls to match cases and assess exposures
- Secondary Data: can be any of the above designs depending on how data collected
- Meta-Analytic: combine study results

What are the issues related to observational studies?

Reply in chat box

Example: If we want to examine the relationship between smoking and a health outcome since we can't randomize

- Comparability of populations
  - Baseline characteristic differences
- Comparability of effects
  - Confounding or bias
- Comparability of information

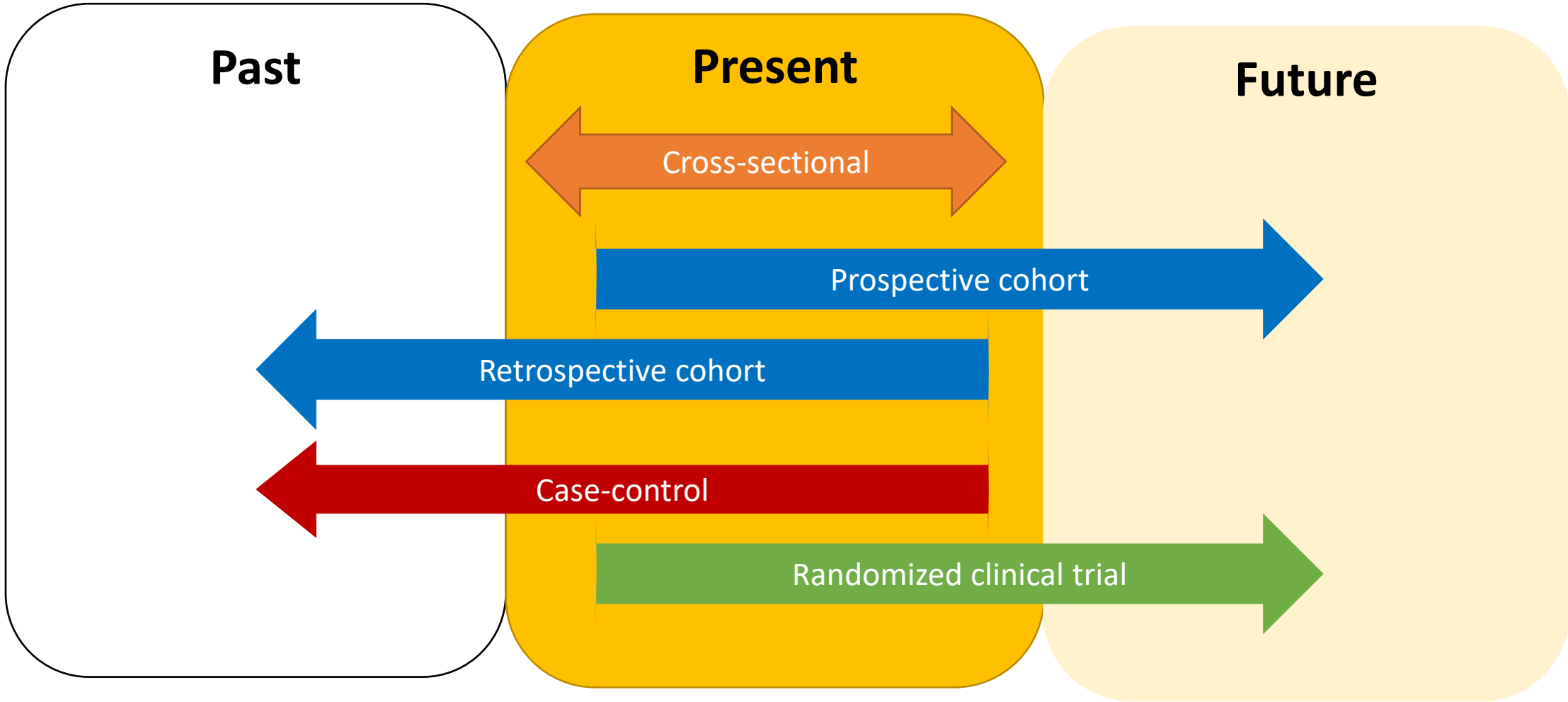
- Differences by gender and age of smokers
- In observational studies, people self- select their exposures which may be associated with many other behaviors/issues (exposures) e.g. mental health, drug use, exercise activity
- Need objective measures that can't be influenced by participant or researcher
- Researcher must use same source for information
- If proxy person used, how to assure comparable information

Cohort study example of excellent ‘comparabilites’

Risk of myocardial infarction, death, and diabetes in identified twins with different BMI (Nordstrom et al JAMA Int Med, 2016)

- Comparability of populations
  - Monozygotic twins
    - Same genetics
    - Same gender
- Comparability of effects
  - Sociodemograpahic and behavior information collected at same time with same instrument before outcomes measured
- Comparability of information
  - As above plus used same Swedish health database to measure outcomes

Study Designs and Time



Cohort compared to RCT

Similarities

- Comparison across two or more exposure groups
- Follow subjects to monitor outcomes
- Select groups to achieve comparability and efficiency
- Proportion in the compared groups does not reflect the general population
- Statistical measure: relative risk (both have complete denominators)

Differences

- RCT: random allocation of exposure

  Cohort: self-selection of exposure
- RCT: randomize for baseline comparability

  Cohort: must carefully select groups to achieve comparability or adjust statistically
- RCT: use placebo to match group experiences' and mask assignment

  Cohort: select groups carefully to do this; masking possible sometimes
- TIME: RCT – prospective

  Cohort – either direction

Cross-sectional Studies

Advantages

- Fast and inexpensive to do
- No loss to follow-up
- Many exposures and outcomes can be assessed
  - Hypothesis generating
- Can be highly generalizable if using population-based data

Disadvantages

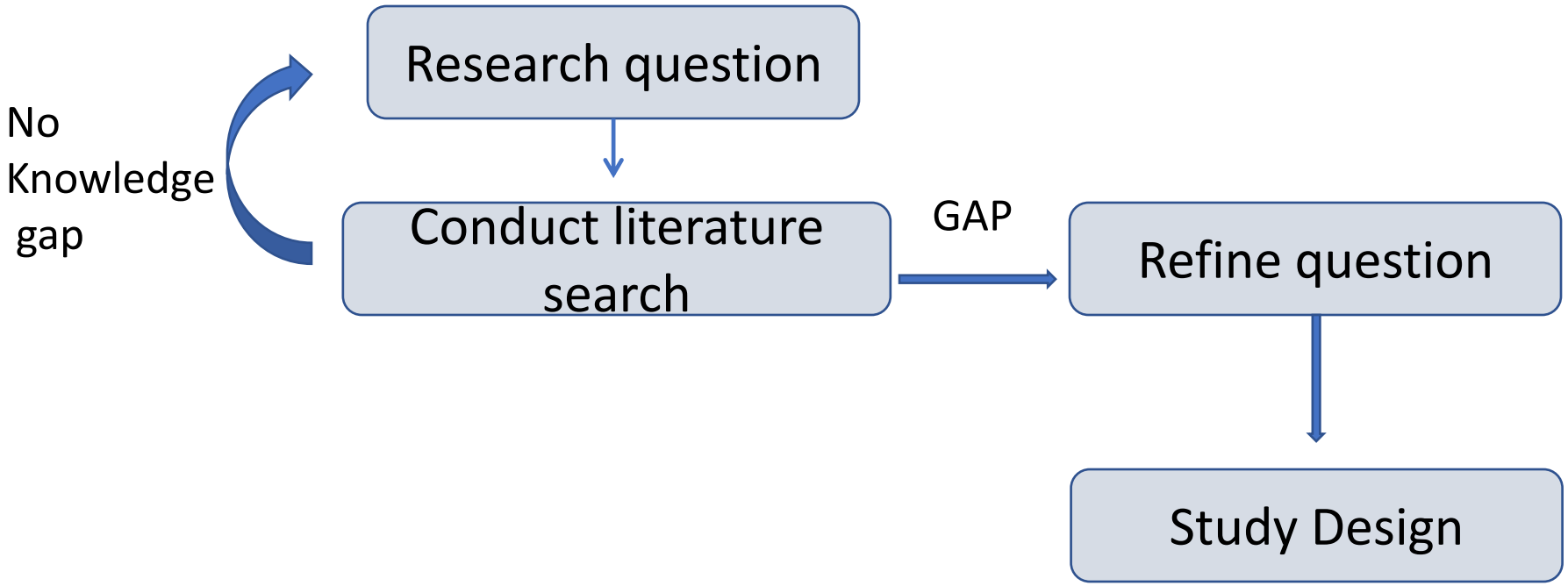
- Temporal sequence uncertainty making causal inference difficult
- Impractical if the focus is a rare disease
- Preponderance of prevalent cases of long duration leading to ‘healthy worker/survivor bias’ (bias against finding an association)

Since there is no true denominator, measure of association is the odds ratio.

When can an association be judged as causal?
(adapted Bradford Hill Criteria)

- Temporal relationship e.g. exposure occurs before the outcome
- Strength of association e.g. large relative risk
- Dose-response relationship (biologic gradient)
- Biologic plausibility
- Consistency with other knowledge
- Alternative relationships explored
- Cessation of exposure
- [Specificity of association]

Designing a research study

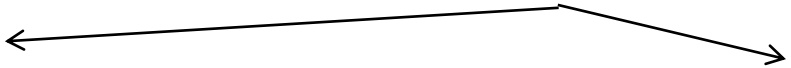


What study design?

- If focus on individual values and experiences, qualitative study
- If little is known about the topic, and doing an exploratory study: qualitative study or descriptive study
- Confirmatory study: experimental, quasi-experimental, observational analytic (correlational)

Deciding Among Study Designs

Goal: Obtaining valid and precise information on the association between exposure and disease using a minimum of resources



Observational

- Objective prevention, treatment, or causal factor
- Moderate to large effect expected
- RCT not ethical or feasible
- RCT too expensive

Experimental

-Objective: prevention or treatment
-Small effect expected
-Ethical and feasible
-Money is available

Adapted from Ashengrau and Seage, Essentials of Epidemiology in Public Health 2nd ed, pg 157

If Observational, more decisions

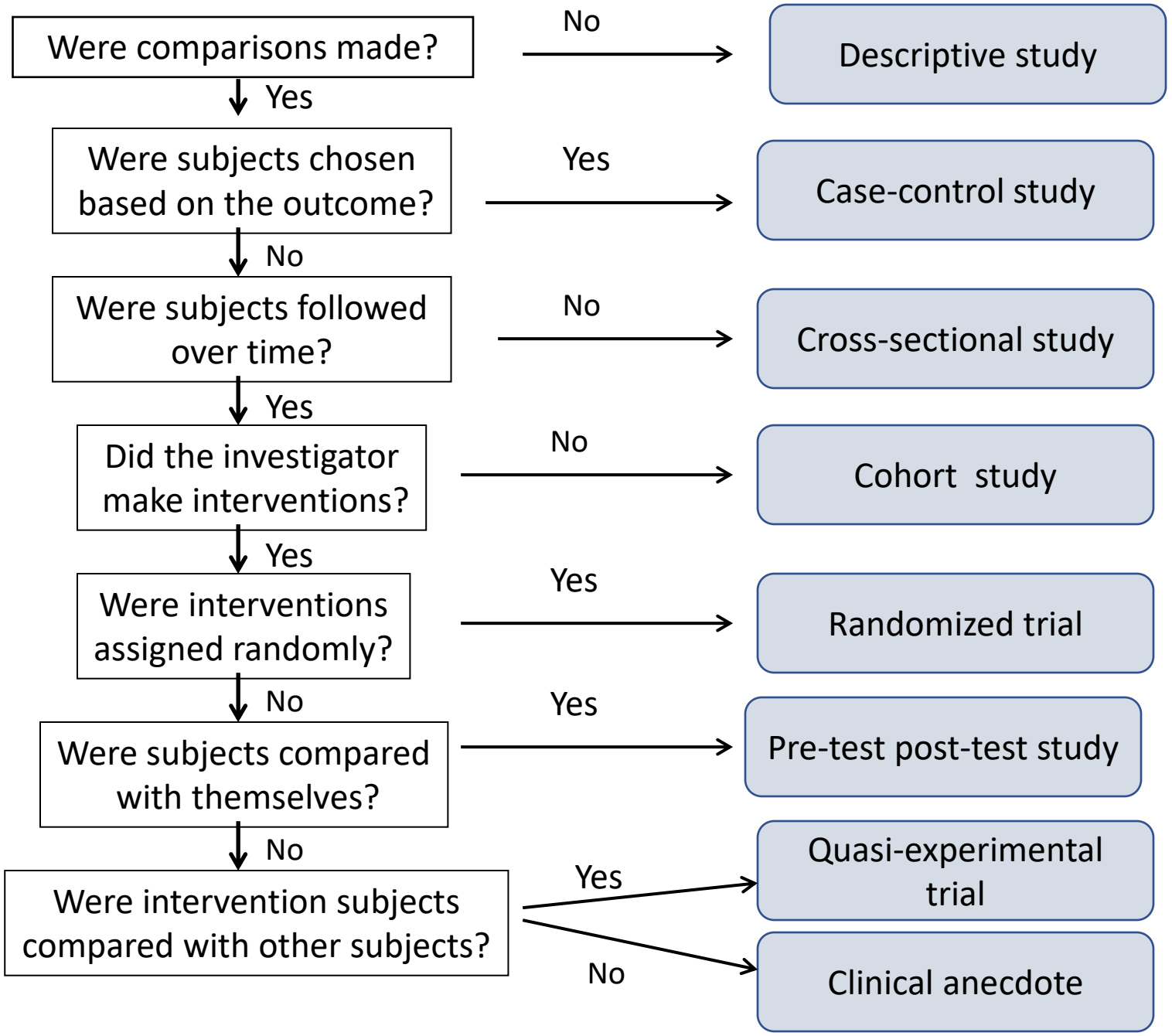
Cohort
-Little known about the exposure
-Evaluate many effects of
the exposure
-Exposure is rare
-Underlying population is fixed

Case-Control
- Little known about the disease
- Evaluate many exposures
- Disease is rare (<10-20% incidence)
- Dz has long induction and latent period
- Exposure data are expensive
- Underlying population is dynamic

Retrospective
- Dz has long induction and latent period
- Historical exposure
- Want to save time and money

Prospective
-Dz has short induction and latent period
-Current exposure
-Want high-quality data

Adapted from Ashengrau and Seage, Essentials of Epidemiology in Public Health 2nd ed, pg 157


Were comparisons made?
No
Descriptive study
Yes
Were subjects chosen based on the outcome?
Yes
Case-control study
No
Were subjects followed over time?
No
Cross-sectional study
Yes
Did the investigator make interventions?
No
Cohort study
Yes
Were interventions assigned randomly?
Yes
Randomized trial
No
Were subjects compared with themselves?
Yes
Pre-test post-test study
No
Were intervention subjects compared with other subjects?
Yes
Quasi-experimental trial
No
Clinical anecdote

Methodology Section of Research Proposal

- Study Design
- Study Population
- Study Setting
- Recruitment
- Study measures – variable table may be useful
- Study Conduct
- Analytic strategy
- Potential Barriers and Limitations
- Research ethics
- Study Timeline

Study population, setting, recruitment

- Be specific as possible about the setting and population
- Inclusion and exclusion criteria
  - Be thoughtful and only if exclude if essential
  - More criteria, less generalizability
- Sample size needed – this needs to be done early in the process
  - Depends on the effect size you anticipate in finding (as well as alpha and beta)
  - If a prospective study, need to account for drop-outs to obtain needed sample
- How will you recruit?
- What about privacy issues in recruiting and completing questionnaires?
- What about asking a group to complete the questionnaires?
  - Okay for them to talk among themselves? If not, important to provide this instruction.

Study Measures: Variable table example

Table 1 – Subjective and Objective Study Measures		
Measure	Instrument/Measure	Validity/reliability statistics
Demographic characteristics	Information on age, race/ethnicity, marital status, education, length of time without permanent shelter prior to present shelter, and lifetime income	
Insomnia Severity Index (ISI) (Aim 1)	7 item scale for insomnia severity. Scores range from 0-28	Internal consistency: Cronbach's 0.90; In community population: sensitivity 86.1%; specificity 87.7% with cut-off>10.[62] 8.4 pts decreased associated with moderate improvement of symptoms in clinical population[62]
PROMIS Sleep-Related Impairment Scale (Aim 1)	8 items to measure effects of sleep ion daytime activity	Correlation with full PROMIS item bank = 0.98.[63] The discrimination slope parameters range from 1.67 – 3.76.[64]
Hair cortisol (Aim 2)	Physiological distress as measured by cortisol in 3mm dimeter vertex hair sample.	Test-retest correlations 0.68-0.79[65]. Coefficient of variation <5%.
PROMIS SFv1.0 Anxiety 8a (Aim 2)	Distress scale using an 8 item anxiety scale of symptoms over last 7 days	Internal consistency reliability of .90 over a range of T-scores 42-80.[66]
PTSD Checklist v. 5 (PCL-5)(Aim 2)	New 20 item 5-point Likert scale of PTSD symptoms was revised to correspond with the DMS-5.	For mixed population of community, college students, & military:[67,68] Cronbach's alpha .89-.94; test-retest .82-.87; convergent reliability (rs=.74-.78)

Common errors in methodology section

- Definitions for independent and dependent variables do not match the study aims or questions
- Wrong study design to meet study aims
  - Measuring a complex concept that may change at only one point in time
- Lack of specificity about recruitment and study procedures
- Analytic approach does not match the variables in the study

Surveys and Their Administration

Goal of Surveys or Research Questionnaires

Obtain the minimum amount of data to provide quality data about the problem.

How do you develop a survey/questionnaire?

- Delphi study: obtain opinions from experts
- Focus groups of study target population
- Choose appropriate validated instruments
  - COSMIN (www.cosmin.nl)

    (**CO**nsensus-based **S**tandards for the selection of health **M**easure **IN**struments)
    - Find different instruments
    - Appraisal tools and checklists to assess appropriateness of the instrument

Resource: O'Connor, S. (2022) Designing and using surveys in nursing research: A contemporary discussion. *Clinical Nursing Research*. 31(4), 567-70.

Questionnaire Reliability & Validity

Validity

- Face/content validity
- Construct validity
  - Requires several studies to evaluate
- Criterion validity
  - Compared to ‘gold standard’

Reliability

- Test-retest
  - Consistency of results at 2 different times
  - ≥.70 acceptable (Pearson or Intraclass correlation)
  - Obtain for your study through pilot testing
- Inter-rater reliability
  - Consistency across raters or observers
  - Cohen’s kappa or intraclass correlation
  - Ideal ≥.75; >.50 acceptable
- Internal consistency (validated instruments)
  - Degree to which items measure a single concept
  - Cronbach’s alpha around .80 ideal (.70 OK)

Sources of Bias in Questionnaires

- Question Design
- Questionnaire Design
- Survey Administration
- Analysis

Plain Language principles

- Logical organization with reader in mind
- Use ‘you’ and other pronouns
- Use the active voice
- Use short sentences (less than 15 words)
- Incorporate easy-to-read design features
  - Use upper and lowercase text
  - Use at least 12 point font
  - Use headings and sub-headings

Sources of Bias in Question Design

Wording

- Ambiguous questions
- Overly complex questions
- Double barreled questions
- Leading questions
- Technical Jargon or uncommon words
- Vague Words

Faulty Scale

- **Forced choice**
  - Too few choices?
  - Use “Don’t Know?
- **Missing interval**
  - **C**over every choice
- **Overlapping interval**
  - Use mutually exclusive categories

Vague words encourage vague answers

Contrast:

How often do you exercise?

[ ] Regularly

[ ] Occasionally

How often do you exercise?

[ ] twice a week or more often

[ ] once a week

[ ] less than once a week

Decide on type of questions

Frequency

	During the **Past Month**, how much of the time did you:	None of the time	A little of the time	Some of the time	A good bit of the time	Most of the time	All of the time
1	have difficulty reasoning and solving problems? *(for example: making plans, decisions, learning new things)*	1	2	3	4	5	6
2	have difficulty doing activities involving concentration and thinking?	1	2	3	4	5	6

Likert Scale

My doctors spent enough time with me during my labor and birth

Strongly disagree	Disagree	Undecided	Agree	Strongly Agree
1	2	3	4	5

How SATISFIED/dissatisfied are you with your Mantram? (Circle one)

Very NOT Satisfied				Very Satisfied
1	2	3	4	5

Other question decisions

- Include open-ended question/s ?
  - May be very informative especially encouraged during pilot testing
  - Will need to decide how these will be analyzed if incorporated into study results – Content/Thematic Analysis

Questionnaire design as source of bias

- Formatting problem
  - Poor formatting leads to inaccurate responses
  - **Solution**: easy to read and visually appealing: adequate ‘white space’

Which is easier to read and enter data?

7. During the past month, how often have you taken medicine to help you sleep (prescribed or "over the counter")?

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

8. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

During the past **month**, how often have you:	Not during the past month	Less than 1 time a week	1 or 2 times a week	3 or more times a week
7. taken medicine to help you sleep (prescribed or "over the counter")?	0	1	2	3
8. had trouble staying awake while driving, eating meals, at social events?	0	1	2	3

Questionnaire design as source of bias

- **Formatting problem**
  - Poor formatting leads to inaccurate responses
  - **Solution**: easy to read and visually appealing: adequate ‘white space’
- **Questionnaire too long**
  - Result: response fatigue and answering randomly or all ‘yes’ or ‘no’
  - **Solution**: limit to the data you need to answer study aims
- **Placement and asking sensitive questions**
  - Universalize question e.g. “Many women experience domestic violence …”
  - Place at end; general agreement to put sociodemographic questions at the end

Good questionnaire design principles

- Pretest, pretest, pretest……
- Ordering of questions:
  - Pretest may help
  - Is there a logical order?
  - Start with easier ones first with more sensitive questions later
  - Group topics together
  - Don’t put more important questions last
  - If combination of open- and closed ended, start with close-ended questions

Questionnaire Administration – source of bias

Respondents

Subconscious reactions

- Central tendency bias or ‘end aversion’
- Positive satisfaction

Conscious reaction

- Faking good or bad
- Unacceptability: exposure, disease, etc

Inaccurate recall

- Primacy or recency i.e. item listed first or last more likely chosen
- Recall: using lists may help
- Proxy respondent

Researcher

- Interviewer bias
- Non-blinding