Research Course

October 23, 2024

Study Design

Obervational & more

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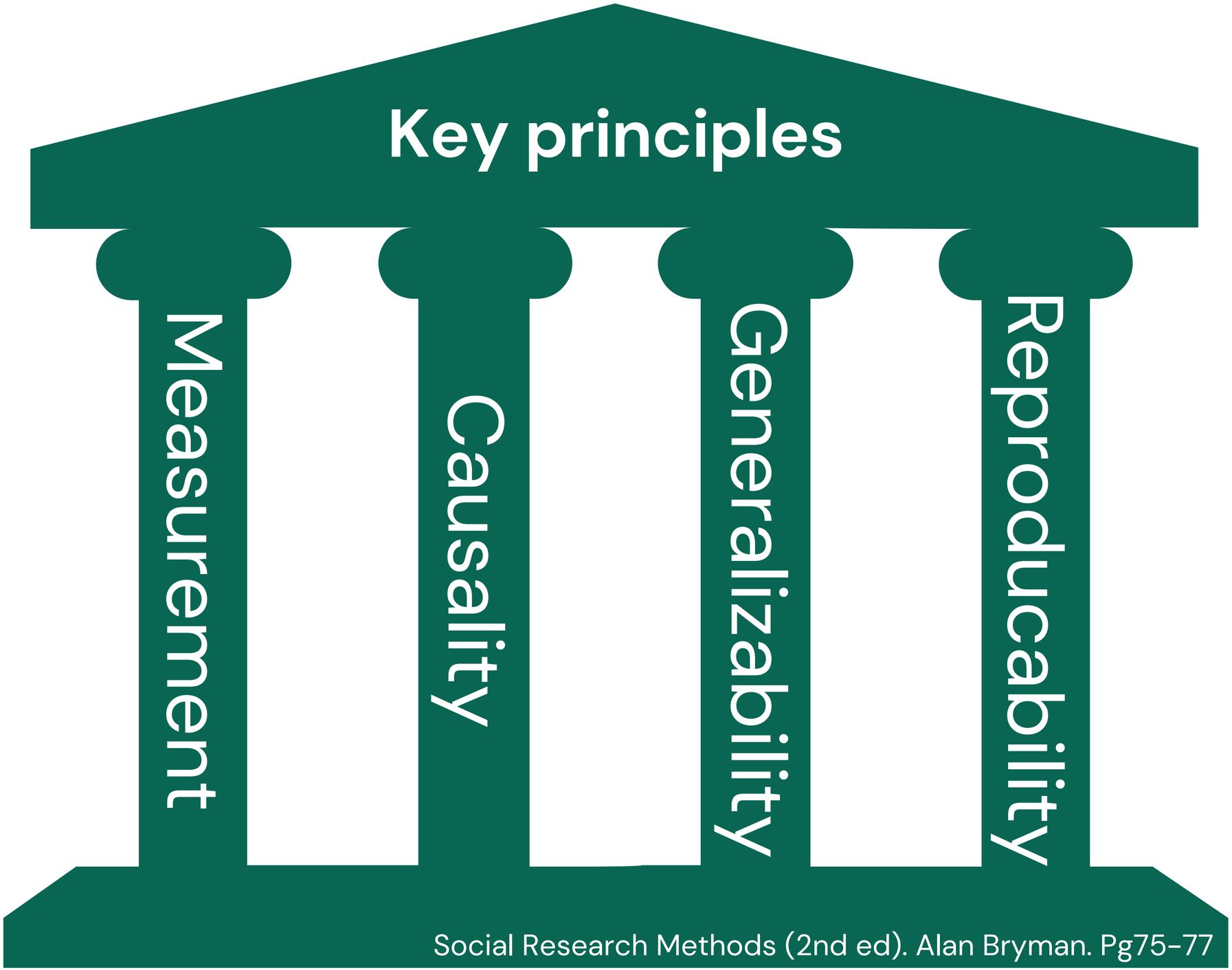
Learning Objectives

1. Be able to differentiate different types of observational study designs
2. Know when to use different study design based on research question
3. Critically appraise studies based on study design



Social Research Methods (2nd ed). Alan Bryman. Pg75-77

Before we talk about study design, let's review types of Bias...

1. Selection
2. Measurement/ Information
3. Confounding

VALIDITY

RELIABILITY

Types of Internal Validity

1

FACE

Does the indicator make intuitive sense?

How to measure:
Survey or consensus among experts. No statistical test.

2

CONTENT

Degree to which instrument measures depth & breadth of construct or concept.

How to measure:
Survey or consensus among experts. No statistical test.

3

CRITERION

Degree to which measure relates to a criterion. Predictive.

How to measure:
Statistical agreement (e.g. kappa, correlation)

4

CONSTRUCT

Degree to which measure relates to other variables within a system/theory

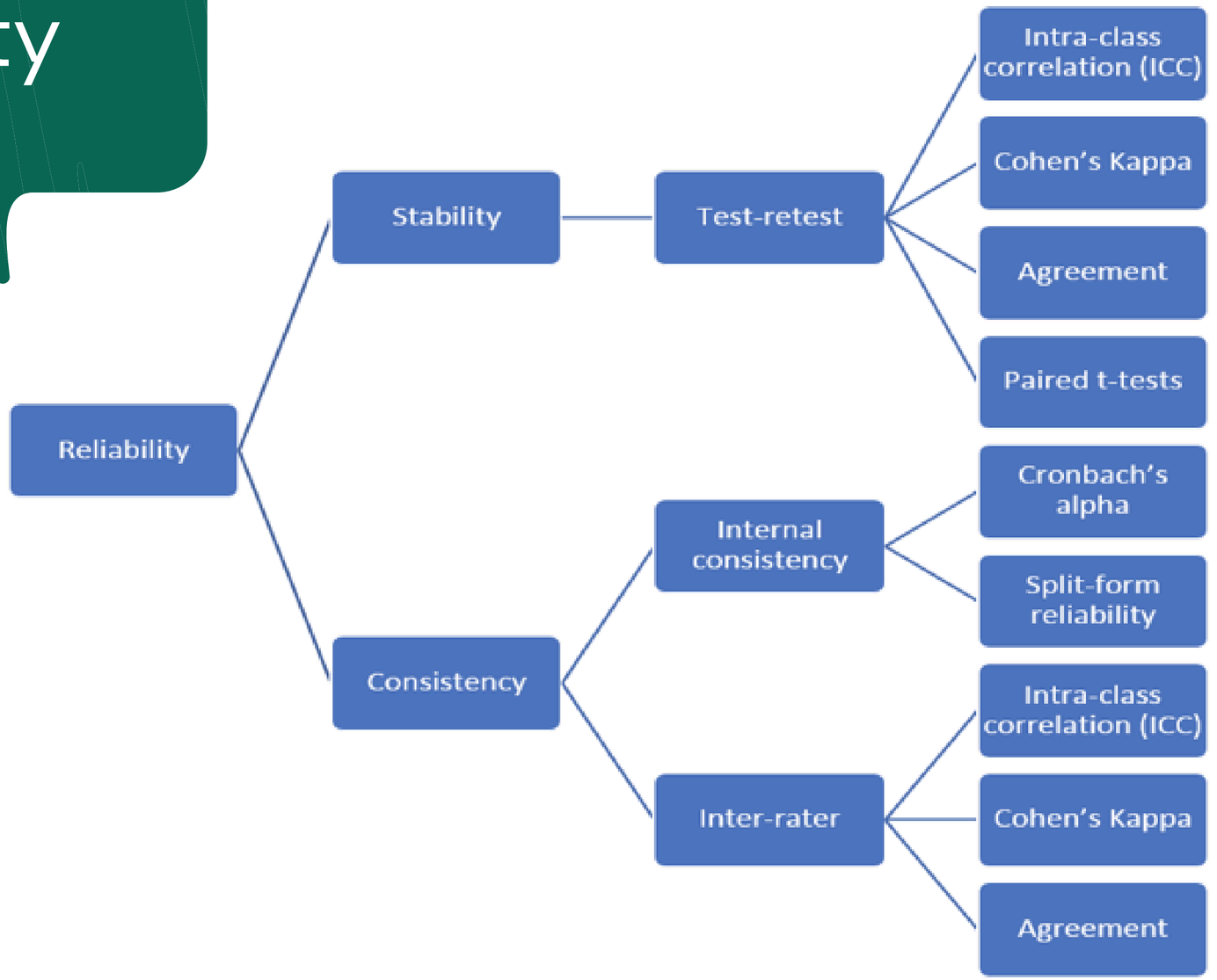
How to measure:
Statistical measures of association

VALIDITY

External

Internal

Reliability



Slide used with permission from: Dr. Gavin McCormack. MDCH681 2020

Mitigating Risk of Bias

1

Study Design

Randomization
Restricting
Matching

2

Measurement

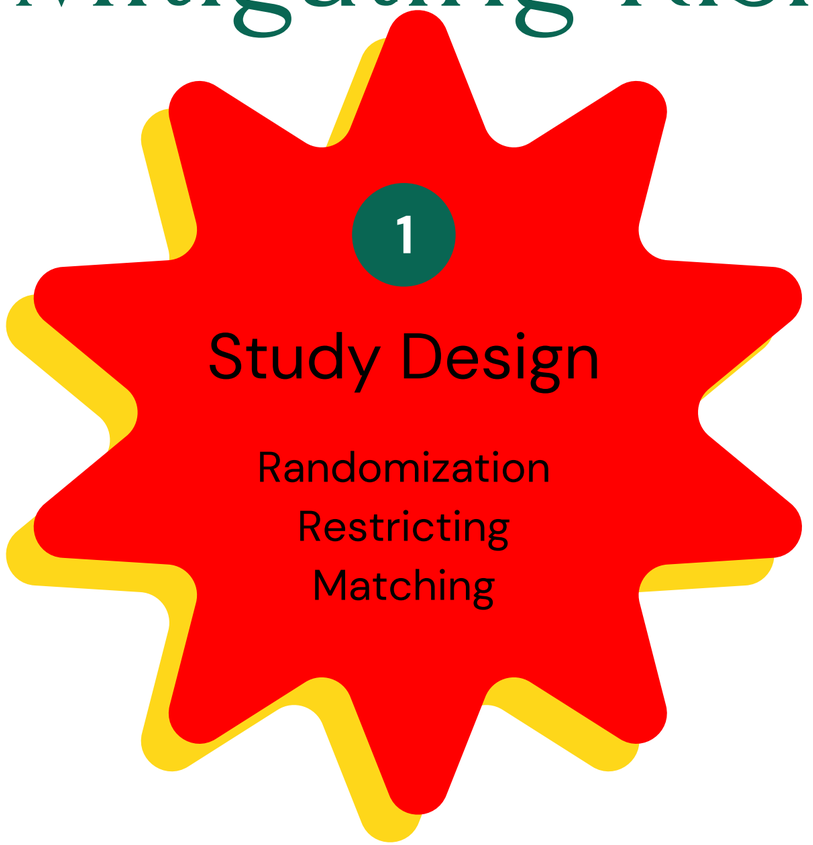
Blinding
Standardizing
Valid
Reliable

3

Statistical

Stratification
Modeling
Matching

Mitigating Risk of Bias



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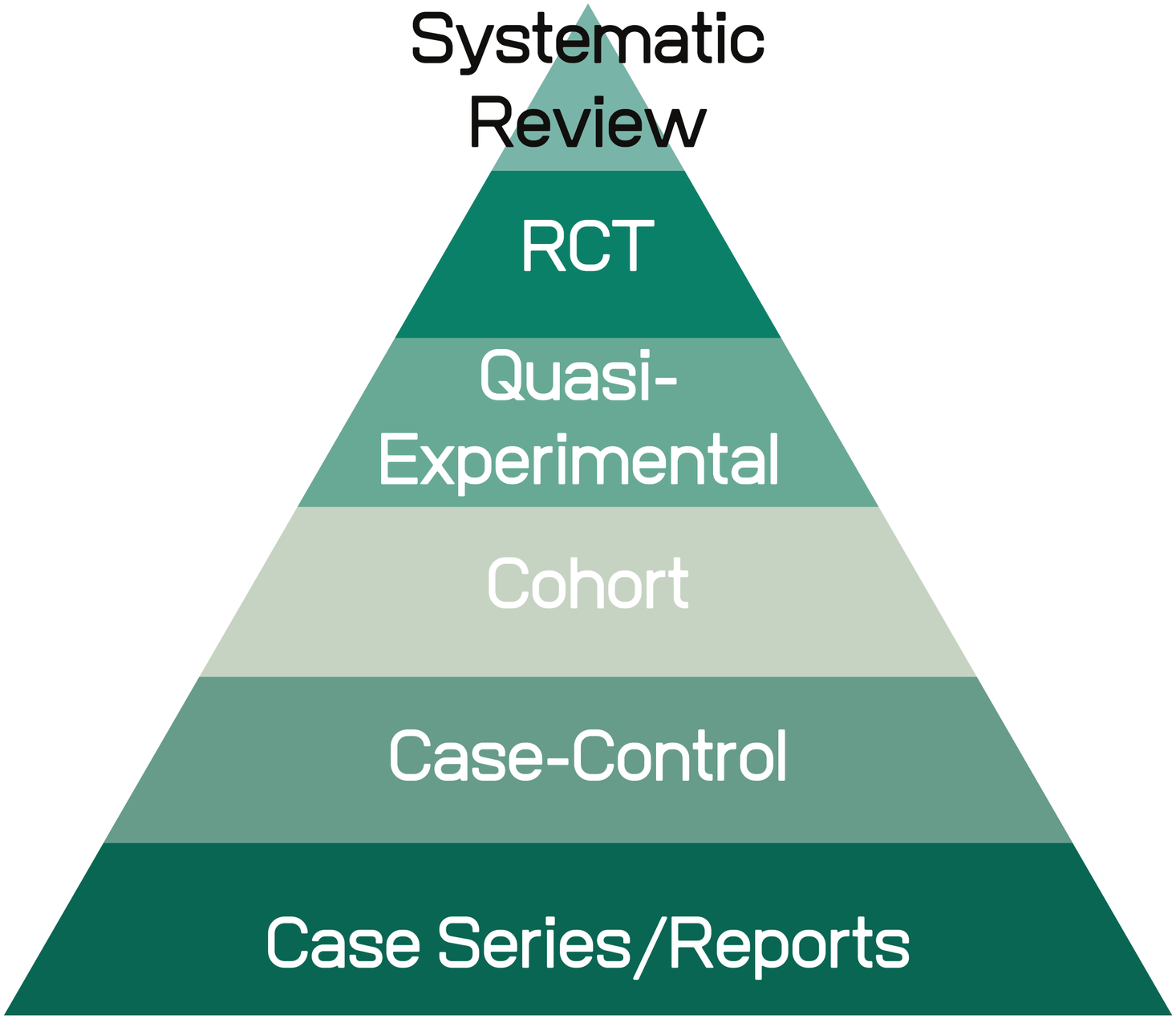

Systematic Review
RCT
Quasi-Experimental
Cohort
Case-Control
Case Series/Reports

TYPES OF STUDY DESIGNS

Observational

- Ecological
- Cross Section
- Cohort
- Case-control

Experimental

- Randomized Control Trials

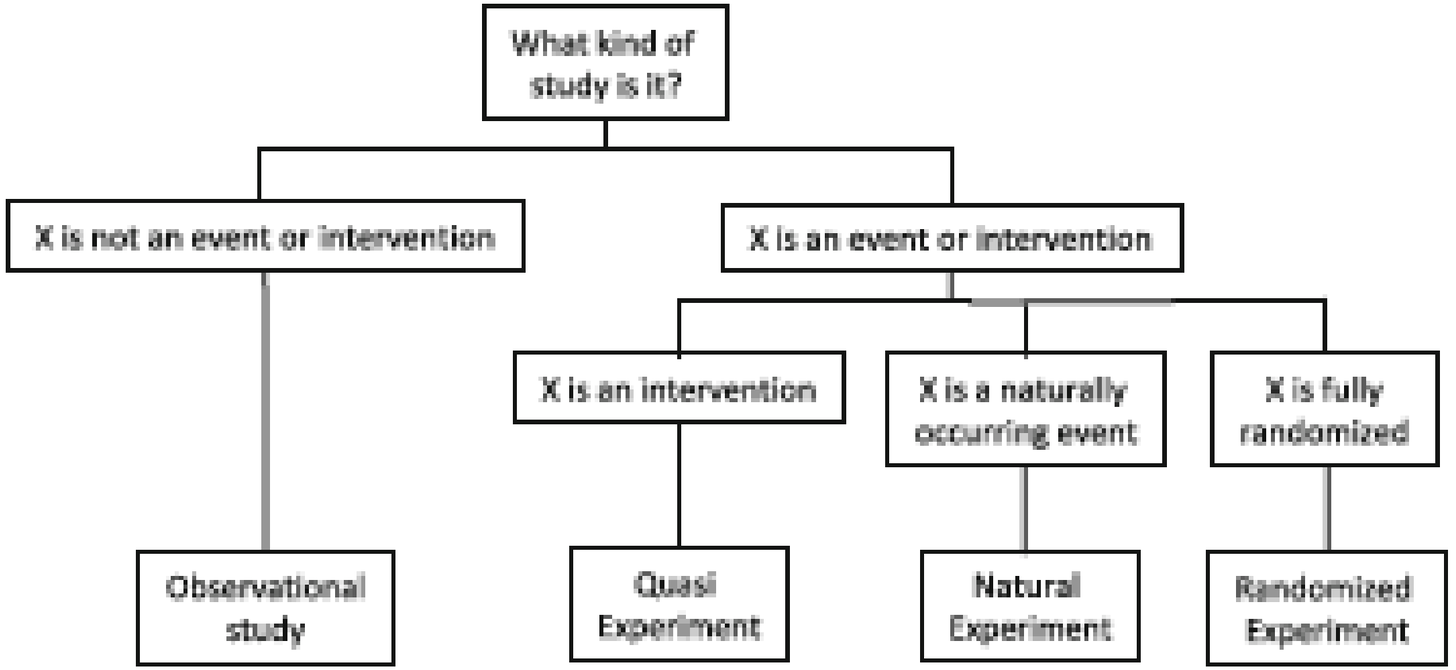
Observational

Natural Experiments / Quasi Experimental

Before-After

Step-wedge

Experimental



1a. Graphical overview of Shadish, Cook and Campbell [1]

Shadish WR, Cook TD, Campbell DT. Experimental and Quasi-Experimental Designs. 2nd ed. Wadsworth, Cengage Learning: Belmont; 2002.
In: de Vocht et al. BMC Medical Research Methodology (2021) 21:32
https://doi.org/10.1186/s12874-021-01224-x

OBSERVATIONAL

Ecological Studies

Studies of associations between risk factors and outcomes both measured at the population-level, not the individual-level (unit of analysis is communities, countries).

Ecological Studies

Research

Open Access

Air pollution and case fatality of SARS in the People's Republic of China: an ecologic study

Yan Cui[1], Zuo-Feng Zhang*[1], John Froines[2], Jinkou Zhao[3], Hua Wang[3], Shun-Zhang Yu[4] and Roger Detels[1]

Environmental Health: A Global Access Science Source 2003, 2:1

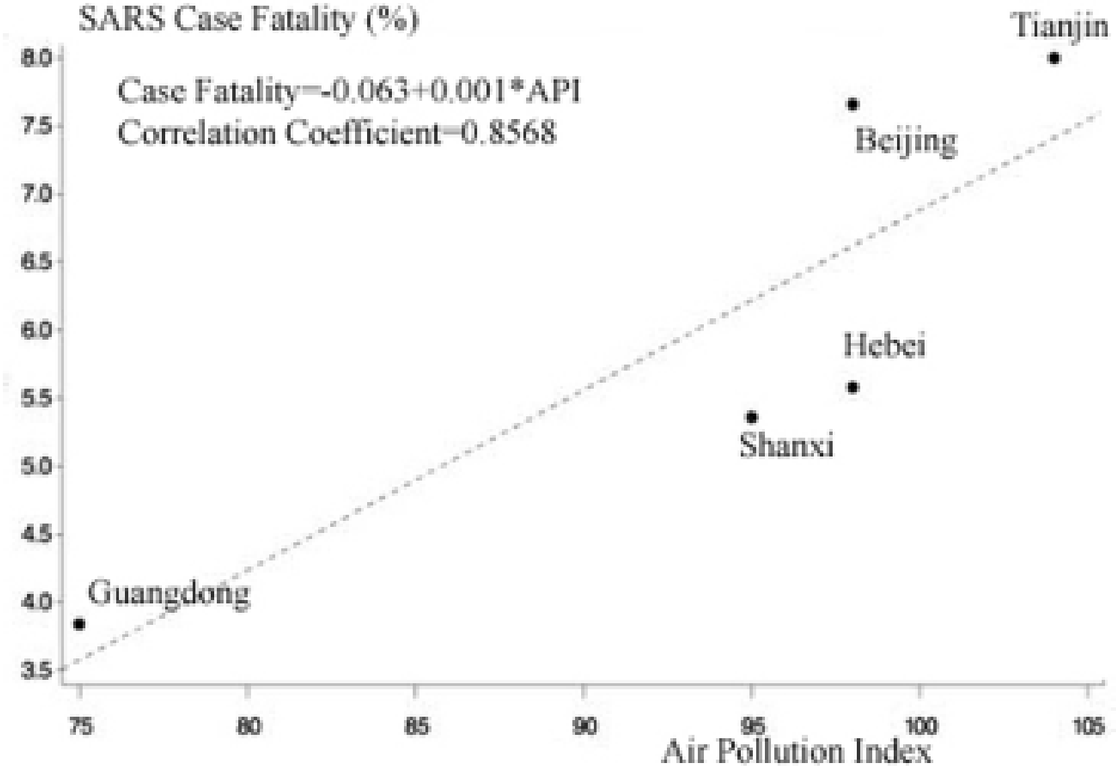


Figure 1
The Correlation and Association between Short-term Exposure to Ambient Air Pollution and Case Fatality of SARS in People's Republic of China.

Ecological Studies

Strength

- Cheap & easy (usually use existing data)
- Can use aggregate data
- Generate hypotheses

Limitation

- Inferring to individuals (ecological fallacy)
- Unclear confounding
- Unclear temporality

OBSERVATIONAL

Cross-sectional Studies

Descriptive studies where data is collected at one point in time (both exposure and outcomes).

Cross-sectional Studies

Head & Neck. 2020;42:1591–1596.

Smell and taste disorders during COVID-19 outbreak: Cross-sectional study on 355 patients

Valeria Dell'Era MD[1] | Filippo Farri MD[1] | Giacomo Garzaro MD[2] | Miriam Gatto MD[3] | Paolo Aluffi Valletti MD[1] | Massimiliano Garzaro MD[1]

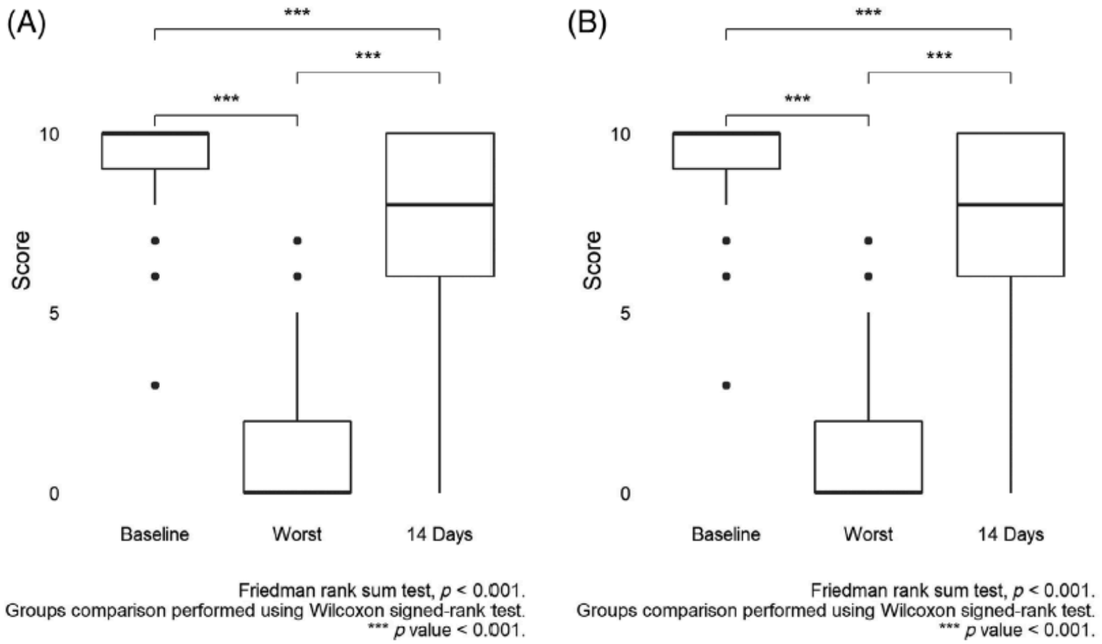


FIGURE 1 Smell, A, and taste, B, perception (score) before developing symptoms (baseline), at the highest intensity of symptoms (worst) and after 2 weeks from their onset (14 days)

Cross-sectional Studies

Strength

- Cheap & easy (usually) because no follow-up
- Good for describing burden
- Generate hypotheses

Limitation

- Temporality is unknown
- Prevalence-incidence bias
- Unclear if disease/exposure changes over time

OBSERVATIONAL

Case-control studies

Descriptive studies where cases and controls are chosen and risk factors are examined retrospectively.

Case-control Studies

Aryee *et al. BMC Geriatrics* (2017) 17:260
DOI 10.1186/s12877-017-0627-9

BMC Geriatrics

RESEARCH ARTICLE Open Access

Identifying protective and risk factors for injurious falls in patients hospitalized for acute care: a retrospective case-control study

Emmanuel Aryee[1], Spencer L. James[2], Guenola M. Hunt[3] and Hilary F. Ryder[1,4,5*]

Table 4 Univariate analysis of predictors of injurious fall

	Variable	Patients with injurious falls (n = 117) [number (%)]	Controls (n = 320) [number (%)]	OR	CI	P Value
Demographics	Age > 70	48 (41)	111 (34.7)	1.31	(0.85–2.02)	0.223
	Male sex	80 (68.4)	166 (54.9)	2	(1.28–3.13)	0.002
Medical history						
	Cognitive Impairment	20 (17.1)	33 (10.3)	1.79	(0.98–3.27)	0.057
	History of fragility fracture	12 (10.3)	30 (6.3)	1.71	(0.81–3.63)	0.159
	History of joint replacement	9 (7.7)	7 (2.2)	3.73	(1.36–10.25)	0.011
	Recent surgery	32 (27.4)	146 (45.8)	0.45	(0.28–0.71)	0.001
	Current smoker	20 (17.9)	45 (14.9)	1.25	(0.70–2.22)	0.455
	Mean Charlston Comorbidity Index (SD)	6 (SD 3.6)	5.0 (SD 2.7)			0.001
Active treatments						
	CNS agents	79 (67.5)	144 (45.0)	2.54	(1.63–3.97)	<0.0001
	Vasoactive agents	71 (60.7)	150 (46.9)	1.75	(1.14–2.69)	0.011
	Therapeutic dose anticoagulants	19 (16.2)	47 (14.7)	1.13	(0.63–2.01)	0.688
Characteristics						
	Assessed "at risk to fall"	57 (48.7)	123 (38.6)	1.51	(0.99–2.32)	0.057
	History of fall	27 (23.1)	32 (10.0)	2.69	(1.53–4.73)	0.001

Case-control Studies

Strength

- Can study rare diseases
- Relatively cheap & quick
- Examine multiple risk factors
- Latency from onset long

Limitation

- Rare exposure
- Measurement & selection bias
- Can't assess incidence, risk or rates

OBSERVATIONAL

Cohort studies

Descriptive studies where a group of participants are followed over time.

Cohort Studies

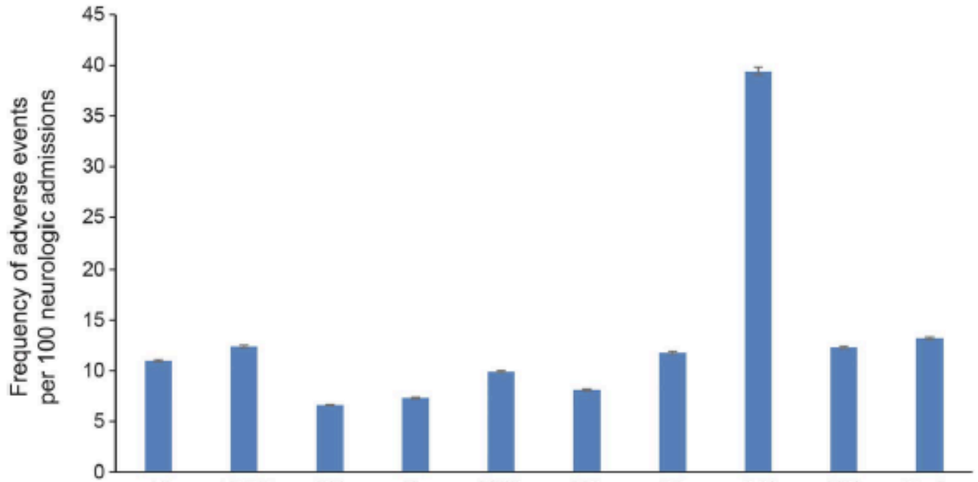
Hospital safety among neurologic patients

A population-based cohort study of adverse events

Khara M. Sauro, PhD
Hude Quan, PhD
Khokan C. Sikdar, PhD
Peter Faris, PhD
Nathalie Jette, MD, MSc

Neurology® 2017;89:284–290

Figure **Frequency of admissions (per 100 admissions) with an AE**



	All	ADRD	BT	Ep	MND	MS	PD	SCI	TBI	Stroke
Odds ratio		1.25	0.54	0.60	0.89	0.70	1.08	5.36	1.14	1.31
95% CI (Upper)		1.21	0.51	0.57	0.75	0.64	1.02	4.81	1.09	1.27
95% CI (Lower)		1.29	0.58	0.63	1.10	0.75	1.14	5.98	1.20	1.36

Overall frequency of admissions (per 100 neurologic admissions) with an AE and frequency by neurologic condition. Error bars indicate 95% CIs associated with the proportion of AEs. Odds ratios represent the odds of having an AE compared to all other neurologic conditions combined. ADRD = Alzheimer disease and related dementia; AE = adverse event; BT = brain tumor; CI = confidence interval; Ep = epilepsy; MND = motor neuron disease; MS = multiple sclerosis; PD = parkinsonism/Parkinson disease; SCI = spinal cord injury; TBI = traumatic brain injury.

Cohort Studies

Strength

- Can study temporality
- Can study rare exposures
- Examine multiple outcomes from one exposure
- Less subject to bias

Limitation

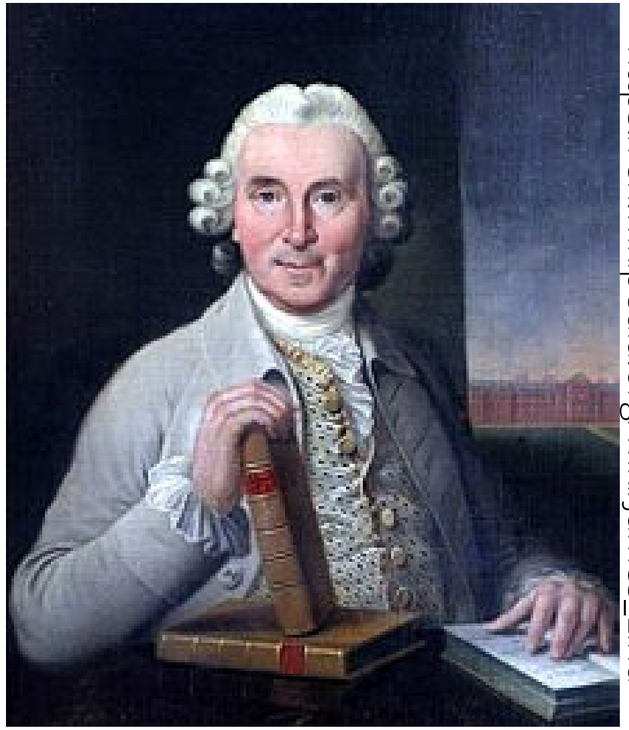
- Resource intensive
- Attrition bias

EXPERIMENTAL

Randomized Control Trials

1. Randomization
2. Intervention / Control
3. Observed over time

Randomized Control Trials



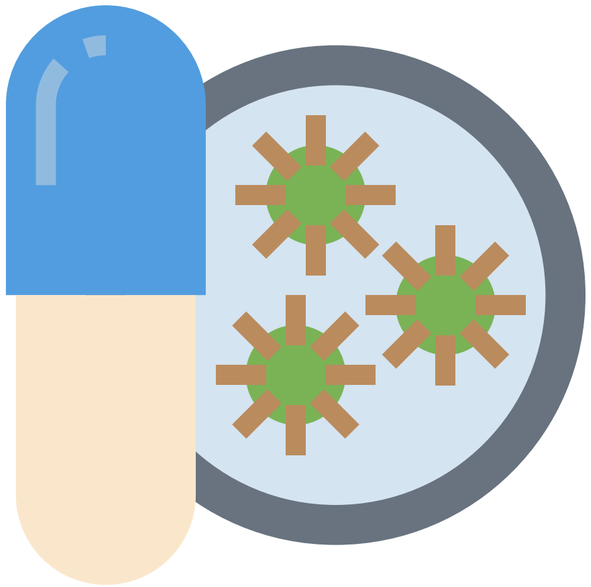
https://en.wikipedia.org/wiki/James_Lind

VINEGAR

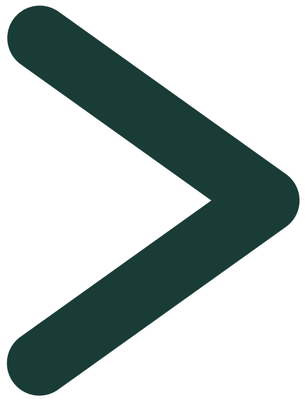
SEA AIR

CIDER

Randomized Control Trials



Streptomycin



QUASI-EXPERIMENTAL

Design Components

1. Intervention / Control
2. Observe outcome

Quasi-experimental design components

E C O X

QUASI EXPERIMENTAL

1. **Quasi Experimental**
   Exposure to the event/intervention not completely controlled by researcher

2. **Natural Experiments**
   Exposure to the event/intervention not manipulated by researcher

3. **Pragmatic Trials**
   Evidence of intervention in real-world setting

QUASI-EXPERIMENTAL DESIGNS

1. Case study
2. One-group Pretest-Posttest
3. Posttest Control Group
4. Pretest-posttest Control Group
5. Interrupted time series

QUASI-EXPERIMENTAL

"...quasi-experimental study to evaluate the outcome of training maternal and child health workers on common blinding childhood diseases."

- Data collected using questionnaires before and after (3 months) a training intervention.
- Total and percentage scores before and after for each participant.

Olowoyeye AO, et al. O BMC Health Serv Res. 2019 Jun 27;19(1):430.

QUASI-EXPERIMENTAL

"The aim of the present study was to assess the effectiveness of implementing an educational module based on...guidelines on the nurses' knowledge and self-confidence regarding central line catheters (CVCs) caring, complications, and application."

- 100 oncology nurses from oncology units in two groups, experimental group (N = 50) and control group (N = 50).
- Participants completed a knowledge test and a self-confidence scale before and after the educational program.

Abu Sharour L et al. J Vasc Nurs. 2018 Dec;36(4):203-207.

QUASI-EXPERIMENTAL

"The aim of this study was to implement and evaluate an evidence-based intervention targeting staff to promote early mobilisation in older patients admitted to general medical inpatient units."

Evaluate the impact of the staff intervention on the primary outcome, patient mobilisation, over 3 time periods—pre-intervention (10 weeks), during intervention (8 weeks) and post-intervention (20 weeks).

Liu B et al. Age Ageing. 2018;47(1):112-119.

QUASI-EXPERIMENTAL

Natural study designs

- Naturally-occurring dichotomy between a treatment and comparator.
- Assess impact of population-level policies

Craig P et al. J Epi Community Health. 2012; 66:1182-1186.

Natural study designs - Example

McLaren *et al. International Journal for Equity in Health* (2016) 15:24
DOI 10.1186/s12939-016-0312-1

International Journal for Equity in Health

RESEARCH Open Access

Equity in children's dental caries before and after cessation of community water fluoridation: differential impact by dental insurance status and geographic material deprivation

Lindsay McLaren[1*], Deborah A. McNeil[2], Melissa Potestio[3,1], Steve Patterson[4], Salima Thawer[1], Peter Faris[5], Congshi Shi[1] and Luke Shwart[6]

Natural study designs - Examples

Objective: Explore removing fluoride from Calgary's water on equity (socio-economic patterns of dental caries in children).

Methods: Surveys of children in grade 2 and dental exam conducted through schools before and after removal of fluroide in Calgary water.

McLaren et al. Int'l JEquity of Health. (2016) 15:24

Natural study designs - Examples

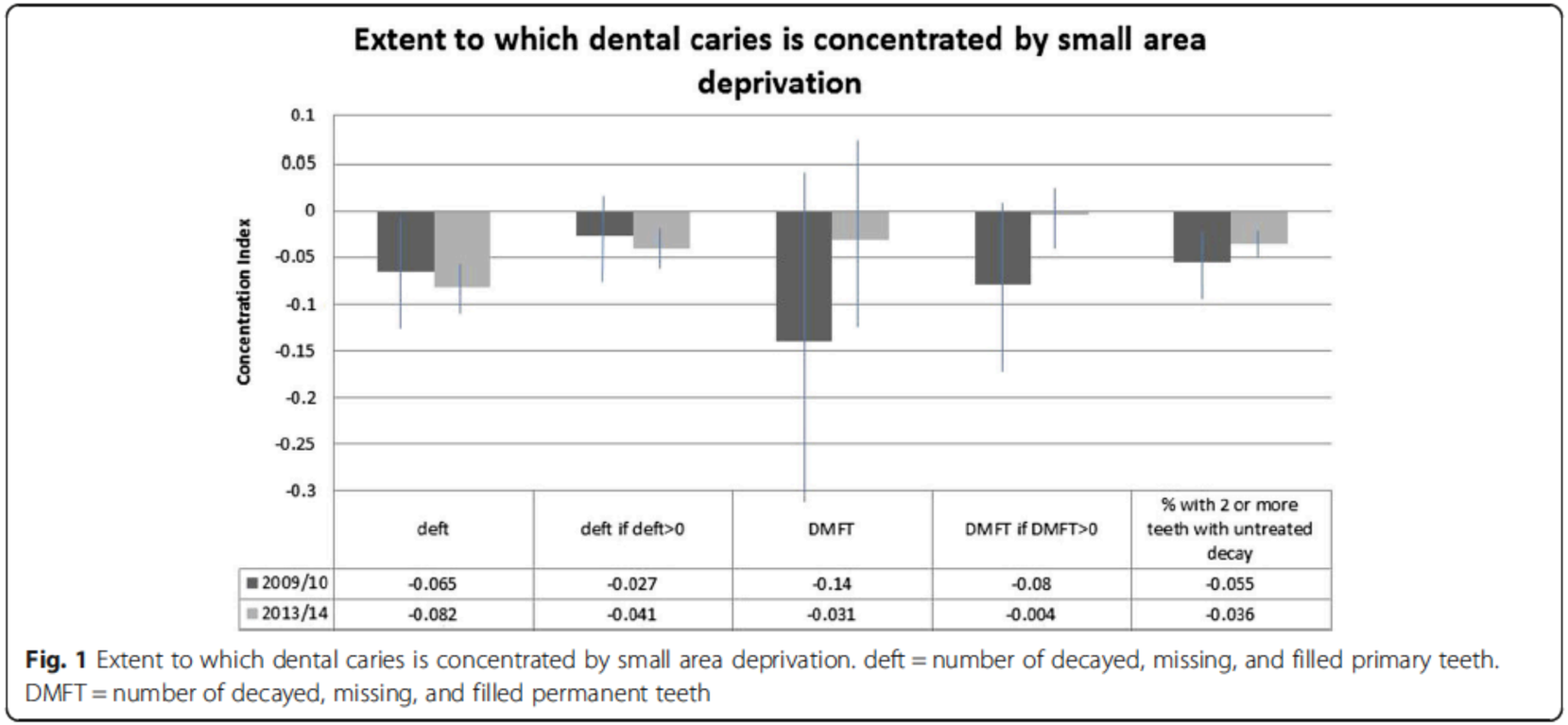


Fig. 1 Extent to which dental caries is concentrated by small area deprivation. deft = number of decayed, missing, and filled primary teeth. DMFT = number of decayed, missing, and filled permanent teeth

McLaren et al. Int'l JEquity of Health. (2016) 15:24

QUASI-EXPERIMENTAL

Pragmatic study designs

Recruitment of investigators and participants, the intervention (and delivery within trial), follow-up and analysis are as close to usual care and setting as possible.

Drazen JM et al. NEJM. 2016. 375(5): 454-463.

Table 1. Nine Dimensions for Assessing the Level of Pragmatism in a Trial, as Proposed in the Pragmatic–Explanatory Continuum Indicator Summary 2 (PRECIS-2) Tool.*

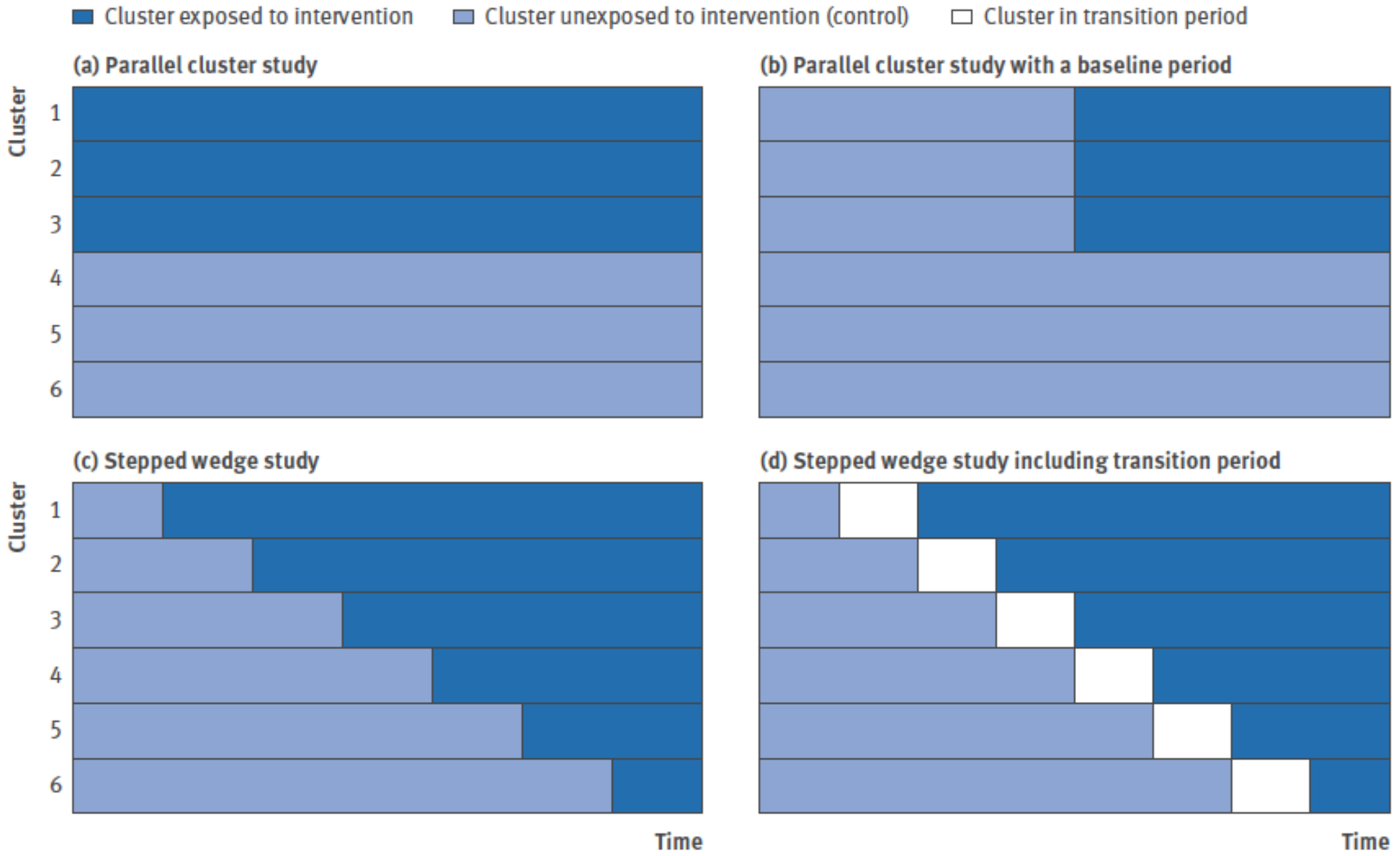
Dimension	Assessment of Pragmatism
Recruitment of investigators and participants	
Eligibility	To what extent are the participants in the trial similar to patients who would receive this intervention if it was part of usual care?
Recruitment	How much extra effort is made to recruit participants over and above what would be used in the usual care setting to engage with patients?
Setting	How different are the settings of the trial from the usual care setting?
The intervention and its delivery within the trial	
Organization	How different are the resources, provider expertise, and organization of care delivery in the intervention group of the trial from those available in usual care?
Flexibility in delivery	How different is the flexibility in how the intervention is delivered from the flexibility anticipated in usual care?
Flexibility in adherence	How different is the flexibility in how participants are monitored and encouraged to adhere to the intervention from the flexibility anticipated in usual care?
The nature of follow-up	
Follow-up	How different is the intensity of measurement and the follow-up of participants in the trial from the typical follow-up in usual care?
The nature, determination, and analysis of outcomes	
Primary outcome	To what extent is the primary outcome of the trial directly relevant to participants?
Primary analysis	To what extent are all data included in the analysis of the primary outcome?

* Information in the table is adapted from Loudon et al.[22]

Ford & Norrie. N Engl J Med 2016; 375:454–463
DOI: 10.1056/NEJMra1510059

QUASI-EXPERIMENTAL

Pragmatic study designs



Hemming K et al. BMJ 2015. 350: h391

Pragmatic study design - Example

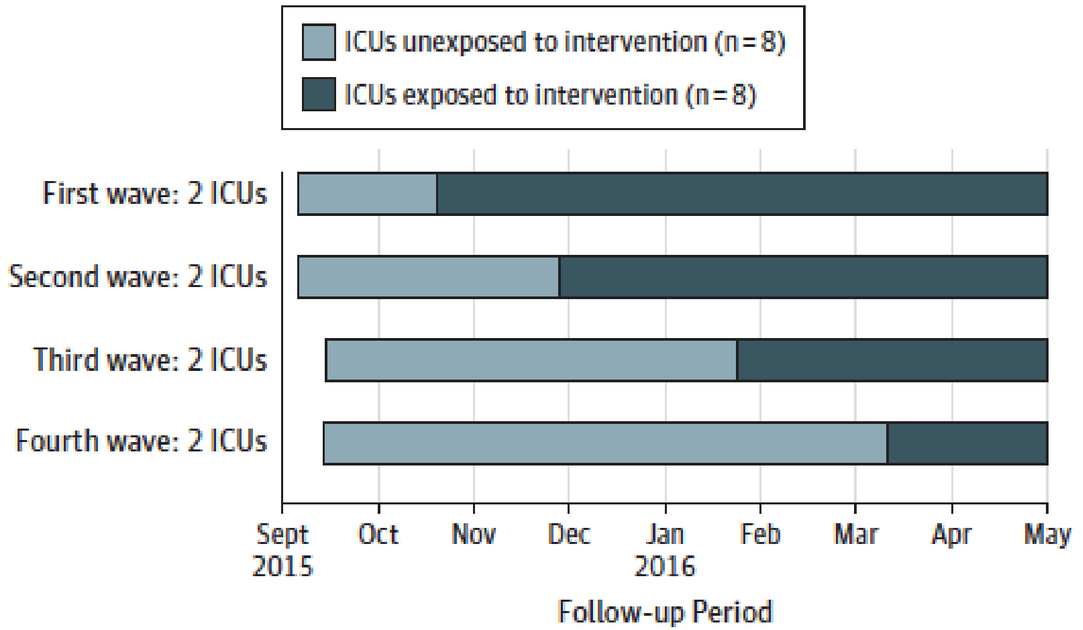
Effect of Standardized Handoff Curriculum on Improved Clinician Preparedness in the Intensive Care Unit. A Stepped-Wedge Cluster Randomized Clinical Trial

Parent B et al. JAMA Surgery. 2018; 153(5): 464-470

Objective: To determine the effect of a standardized handoff curriculum on interclinician communication and patient outcomes.

Pragmatic study design - Example

Figure 2. Stepped-Wedge Cluster Randomized Implementation of the UW-IPASS Standardized Handoff Curriculum



Conducted in 8 intensive care units (ICUs) over a period of 8 months at 2 tertiary-referral teaching hospitals.

Parent B et al. JAMA Surgery. 2018; 153(5): 464-470

EFFICACY = EFFECTIVENESS

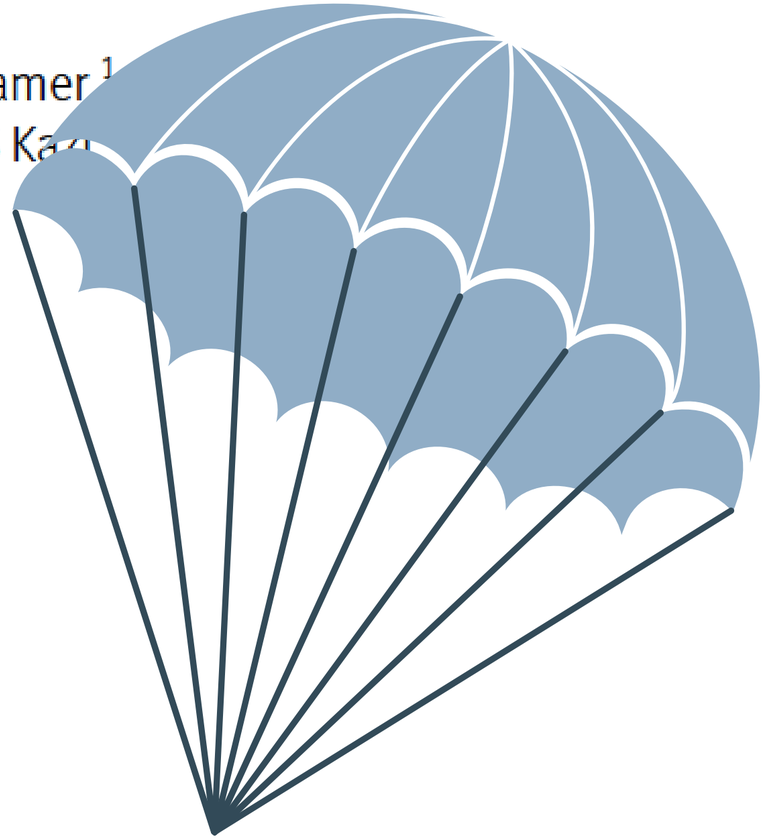
Choosing a design - considerations

1. Ethical consideration
2. Time & resource constraint
3. Sample size
4. Unit of analysis
5. Minimizing bias

BMJ, 2018. 363: k5094

Parachute use to prevent death and major trauma when jumping from aircraft: randomized controlled trial

Robert W Yeh,[1] Linda R Valsdottir,[1] Michael W Yeh,[2] Changyu Shen,[1] Daniel B Kramer,[1]
Jordan B Strom,[1] Eric A Secemsky,[1] Joanne L Healy,[1] Robert M Domeier,[3] Dhruv S Kazi,[1]
Brahmajee K Nallamothu[4] On behalf of the PARACHUTE Investigators



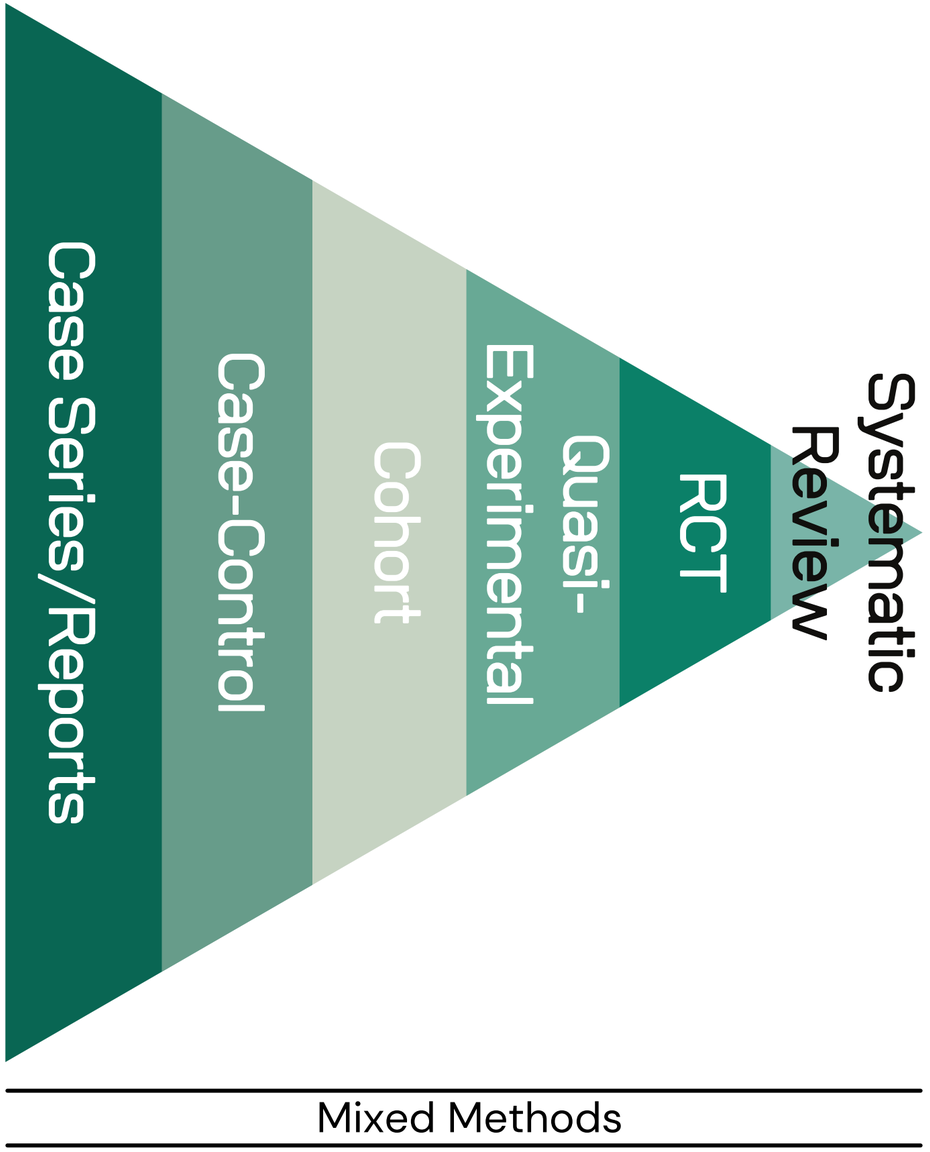
Less structure

Advantages

- Inquiry validity
- Exploratory & formative
- Inductive power
- Capture unknown/unanticipated elements

Disadvantages

- Generalizability
- Reliability
- Comparative analysis
- Association & causation



More structure

Advantages

- Precision
- Comparative capacity
- Reliability
- Association & causation
- Confirmatory

Disadvantages

- Inquiry validity
- Resource intensive
- Miss complexity
- Real-world applicability (efficacy vs. effectiveness

Adapted from: Public Health Research Methods. Eds: Guest & Namey. Page 49

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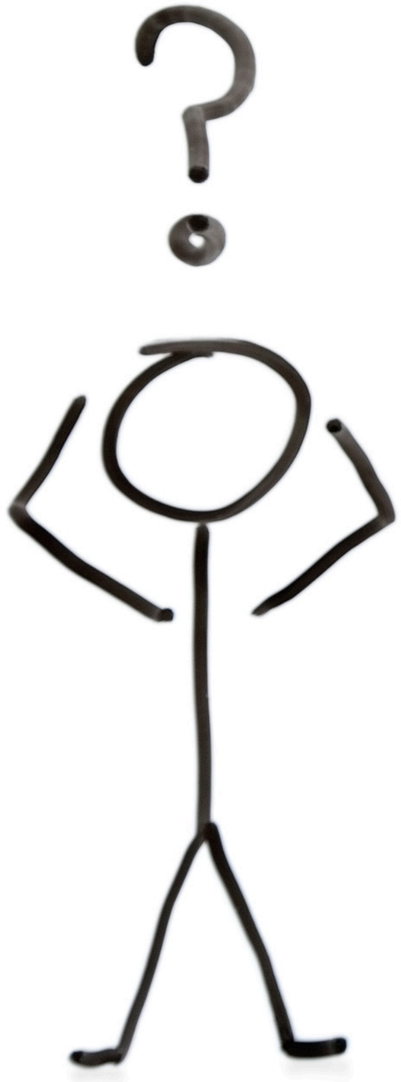

QUESTIONS