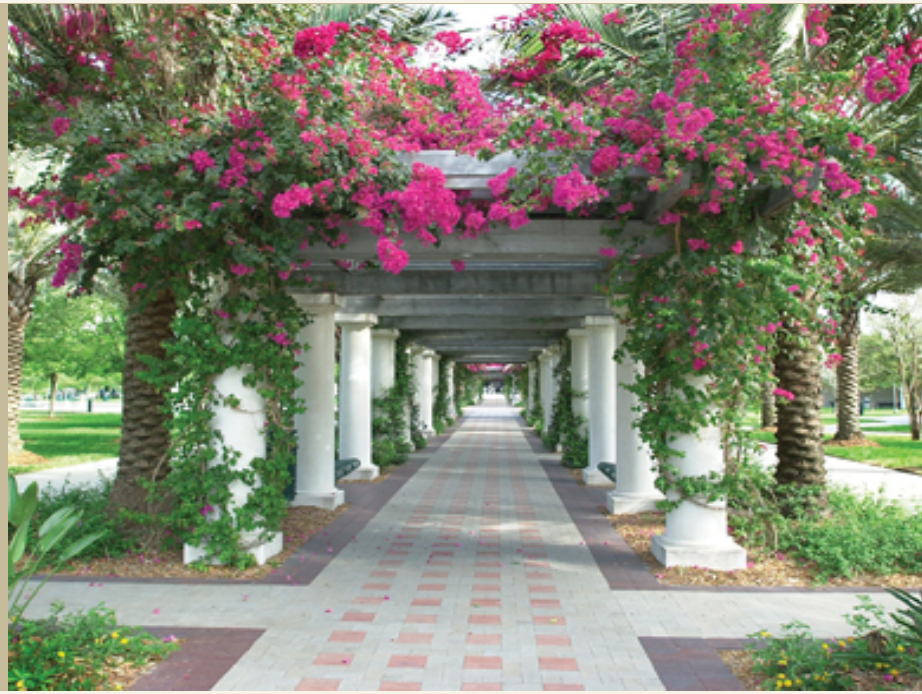
# Matching study design to research question-Interactive learning session

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# Outline

- Learning format
  - Interactive (i.e. informal)
- Questioning/interruption
  - Expected and encouraged

- What is a research question
- Introduction to study design
- Matching the study design to the research question

# What is a research question?

The researcher asks a very specific question and tests a specific hypothesis.

Broad questions are usually broken into smaller, testable hypotheses or questions.

Often called an objective or aim, though calling it a question tends to help with focusing the hypothesis and thinking about how to find an answer

- PICOTS format

# What makes a poor research question? Discussion

- a question that matters to nobody, even you
- hoping one emerges from routine clinical records
  - the records will be biased and confounded
  - they'll lack information you need to answer your question reliably, because they were collected for another reason
- fishing expedition/data dredging – gathering new data and hoping a question will emerge

# What makes a good question?

## Specificity / focus ! : PICOTS format

**P** - who are the patients or what's the problem?

**I** - what is the intervention or exposure?

**C** – what is the comparison group?

**O** - what is the outcome or endpoint?

**T**- What is the type of the question?

**S**- what is an optimal study design to answer this question?

# How to focus your question?

Some ideas:

- brief literature search for previous evidence
- discuss with colleagues
- narrow down the question – time, place, group
- what answer do you expect to find?

# From a research question to a proposal

- who am I collecting information from?
- what kinds of information do I need?
- how much information will I need? *
- how will I use the information?
- how will I minimise chance/bias/confounding?
- how will I collect the information ethically?

* sample size – ask a statistician for help

# What are the main study designs a clinician should be familiar with?

**Slide courtesy: Dr. Kumar A.**

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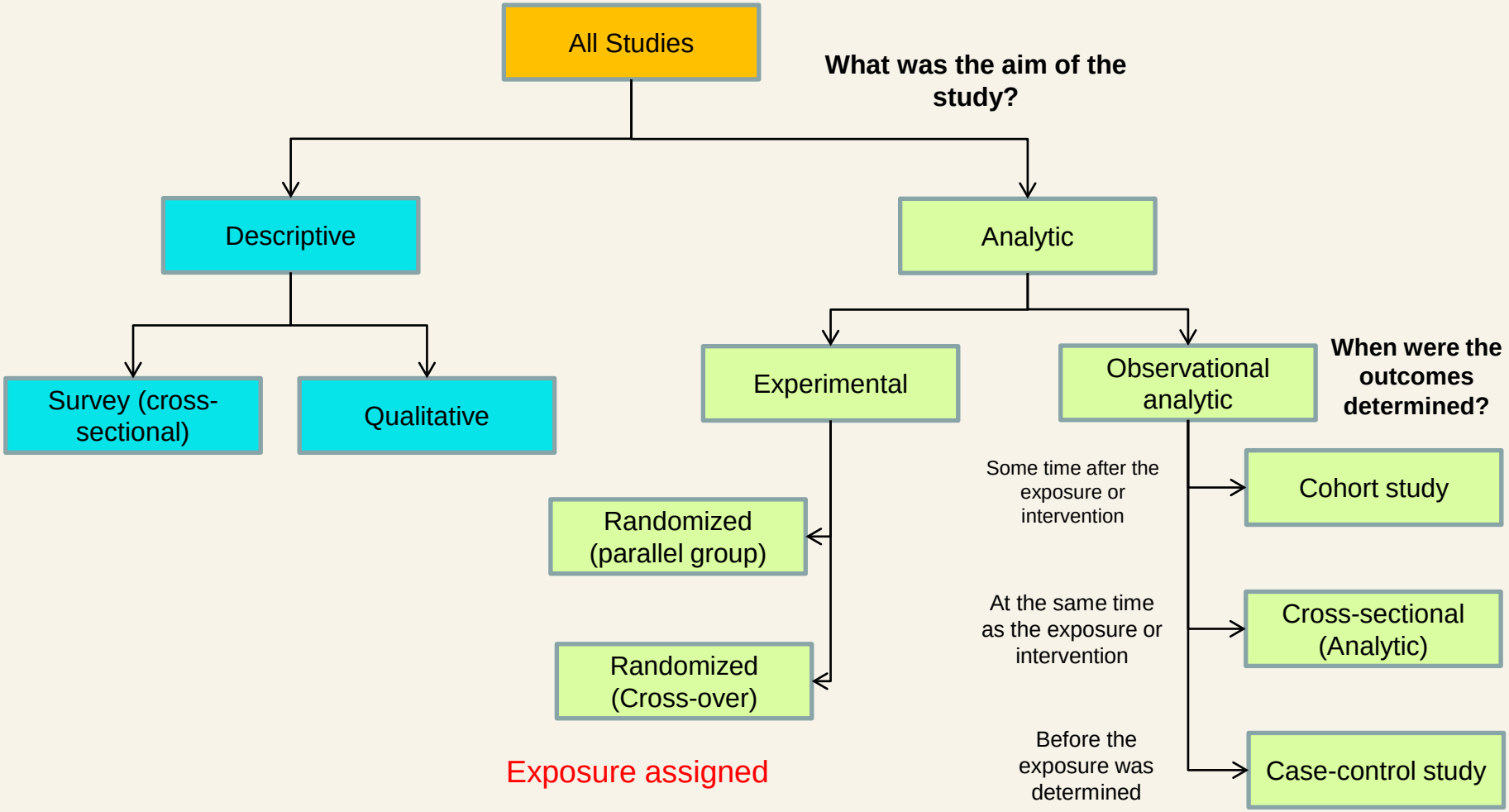
# Spotting the study design

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# Are you going to observe or experiment?

**observational** – cross sectional, case series, case-control studies, cohort studies

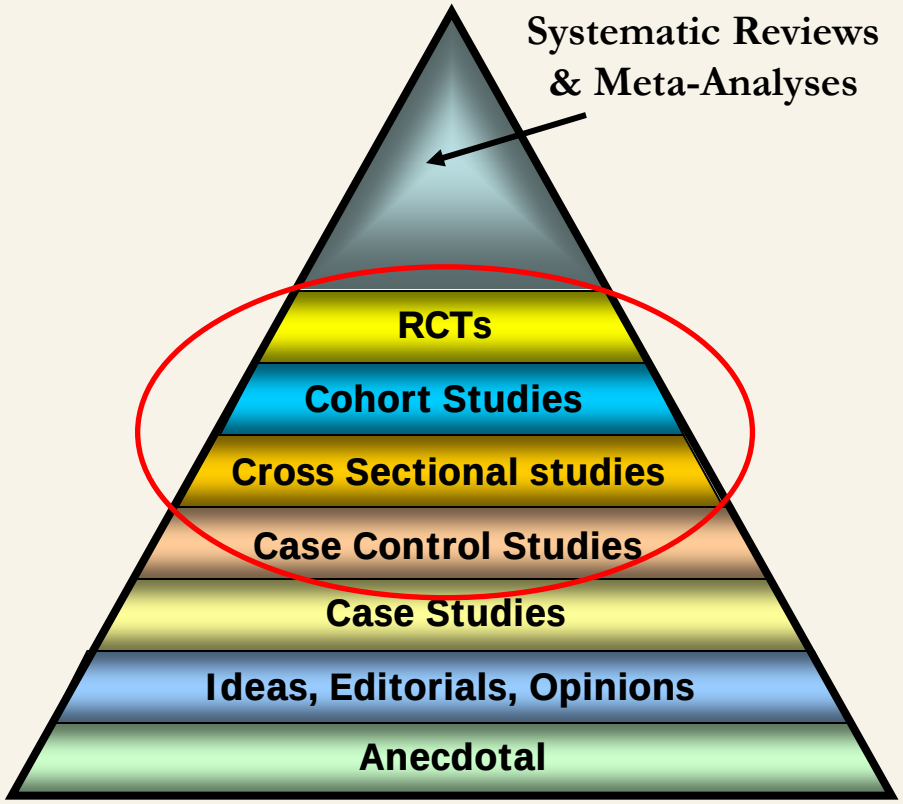
- identify participants
- observe and record characteristics
- look for associations

**experimental** – before and after studies, comparative trials (controlled or head to head), randomised trials (ditto)

- identify participants
- place in common context
- intervene
- observe/evaluate effects of intervention

# What constitutes BEST Evidence?

- For treatment questions:

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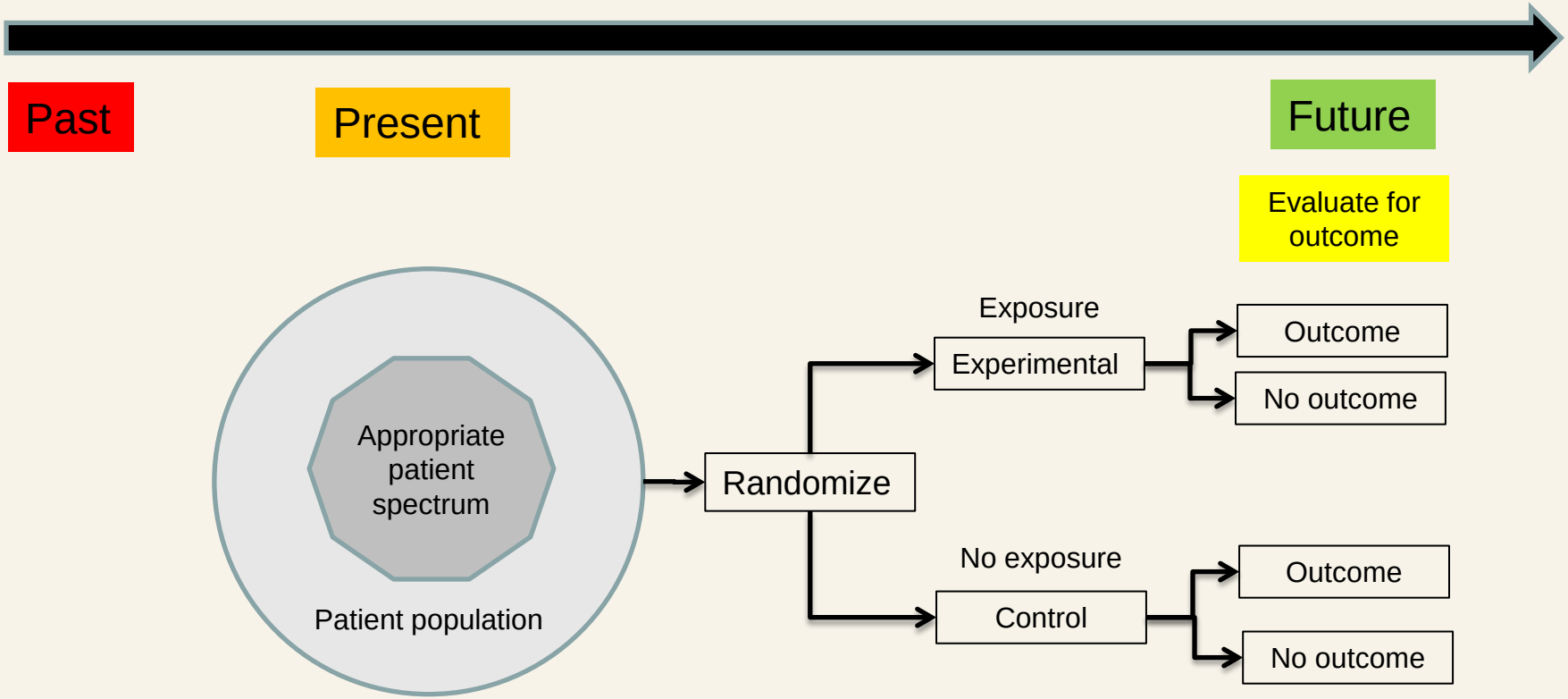
# Randomized controlled trials




Measurement:
Multiple times possible

**Slide courtesy: Dr. Kumar A.**

# RCT with parallel design

- ***Advantages:***
  - unbiased distribution of confounders;
  - blinding more likely;
  - randomization facilitates fair statistical analysis.
- ***Disadvantages:***
  - expensive: time and money;
  - volunteer bias;
  - ethically problematic at times.

**Slide courtesy: Dr. Kumar A.**

# Cross-over RCT

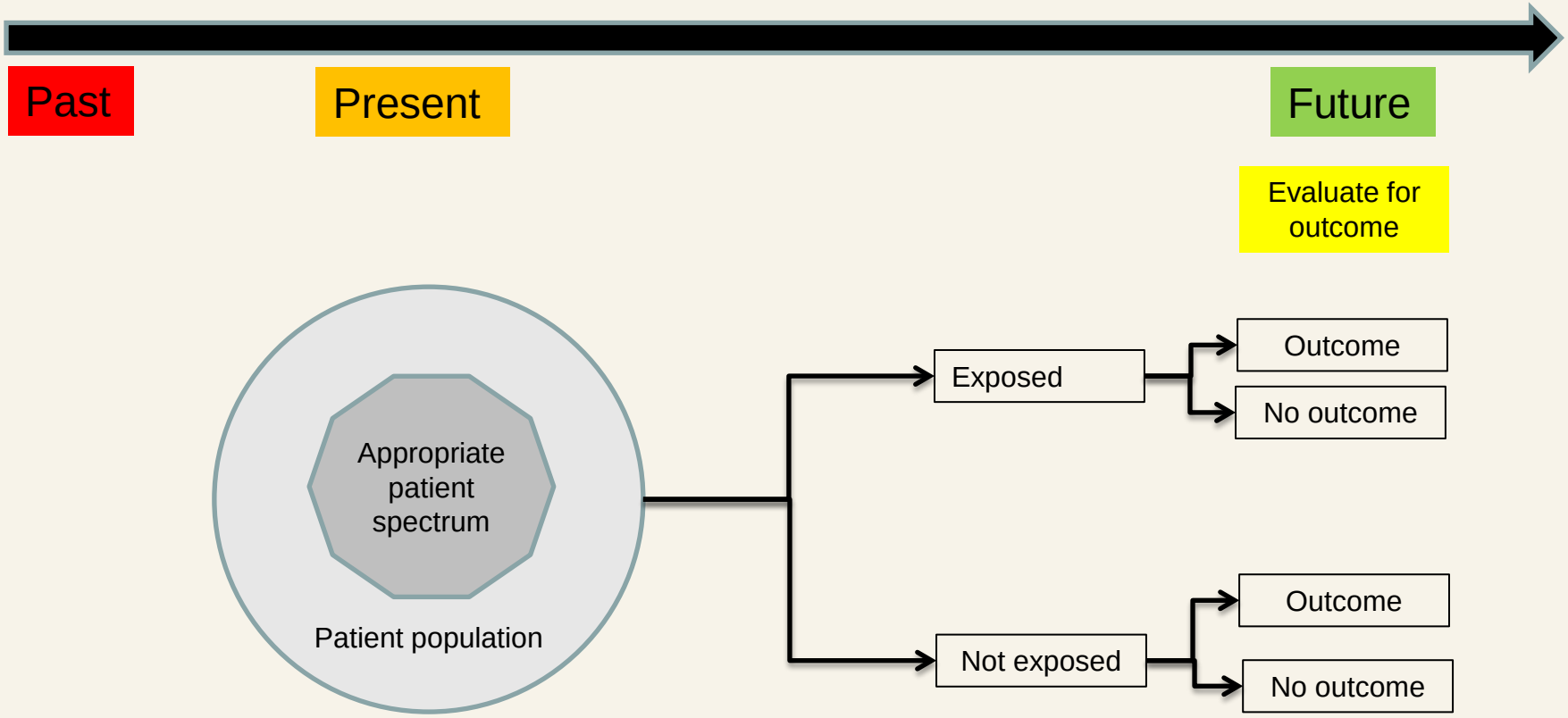
***Advantages:***

- all participants serve as own controls and error variance is reduced, thus reducing sample size needed
- all participants receive treatment (at least some of the time)
- statistical tests assuming randomisation can be used
- blinding can be maintained

***Disadvantages:***

- all participants receive placebo or alternative treatment at some point
- washout period lengthy or unknown
- cannot be used for treatments with permanent effects

# Cohort study




Measurement:
Multiple times possible

**Slide courtesy: Dr. Kumar A.**

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# Cohort study

- *Advantages:*
  - ethically safe;
  - subjects can be matched;
  - can establish timing and directionality of events;
  - eligibility criteria and outcome assessments can be standardized;
  - administratively easier and cheaper than RCT.
- *Disadvantages:*
  - controls may be difficult to identify;
  - exposure may be linked to a hidden confounder;
  - blinding is difficult;
  - randomization not present;
  - for rare disease, large sample sizes or long follow-up necessary.

**Slide courtesy: Dr. Kumar A.**

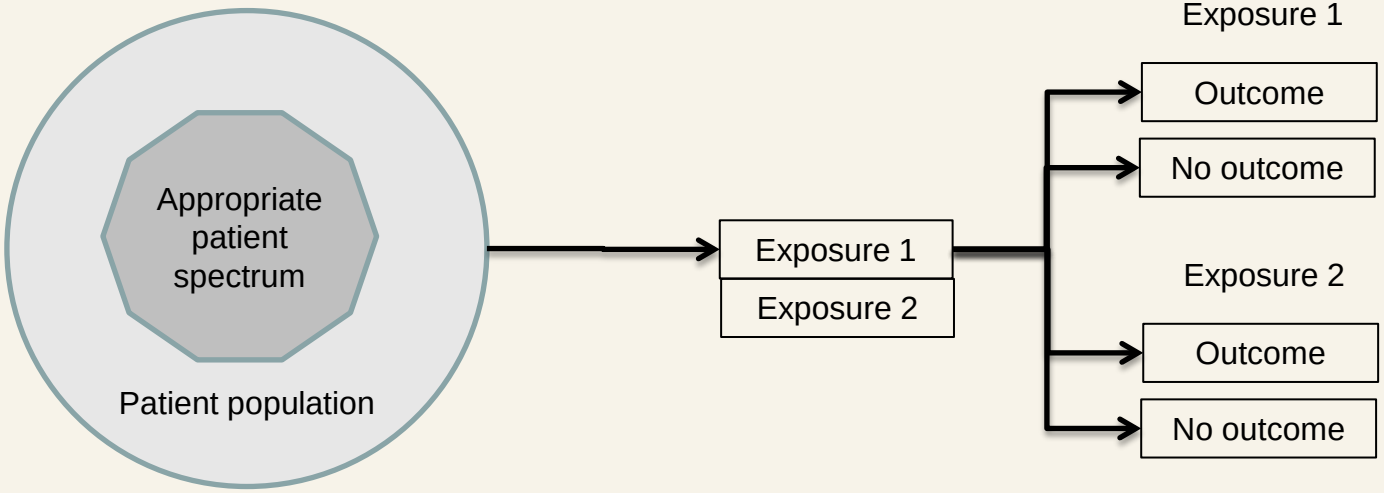
# Cross-sectional study

Past

Present

Future

Evaluate for outcome





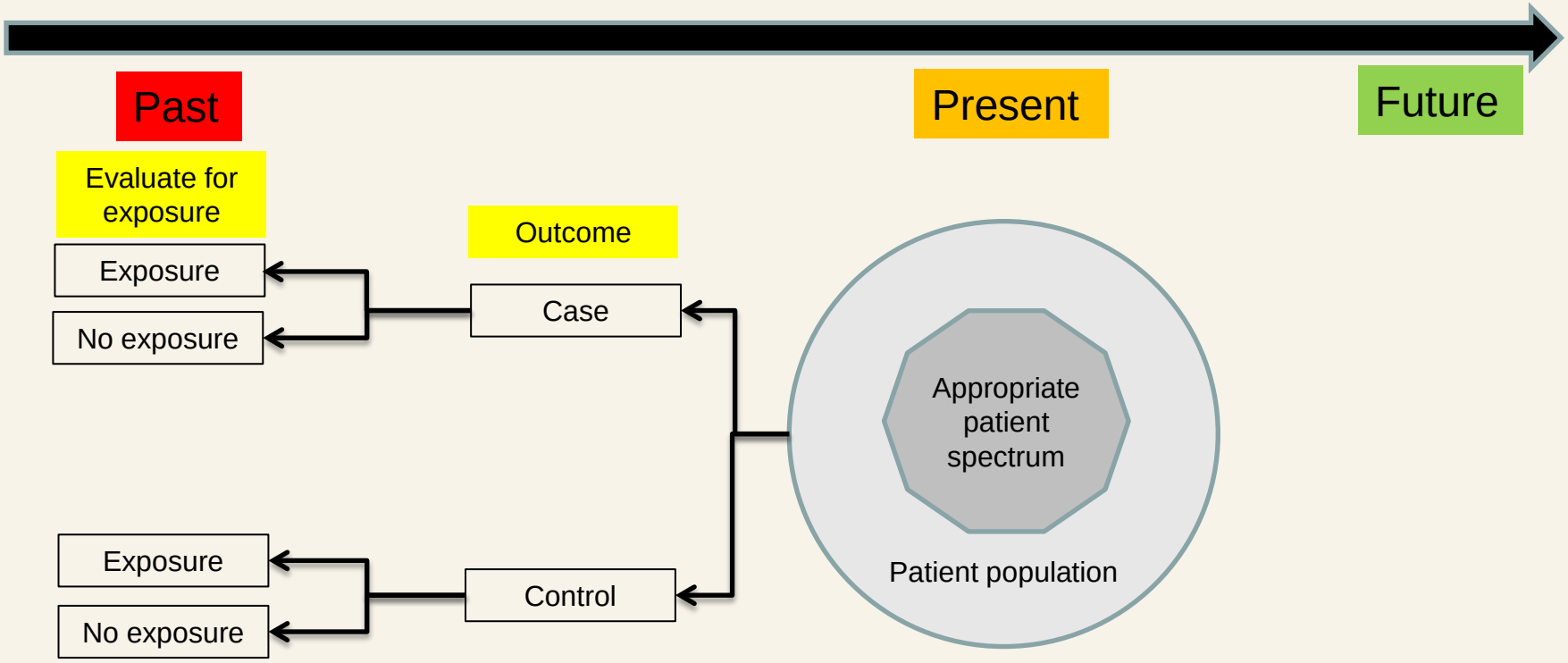
Measurement:
One point in time

**Slide courtesy: Dr. Kumar A.**

# Cross-sectional study

- *Advantages:*
  - cheap and simple;
  - ethically safe.
- *Disadvantages:*
  - establishes association at most, not causality;
  - recall bias susceptibility (e.g. surveys);
  - confounders may be unequally distributed;
  - group sizes may be unequal.

# Case-control study




Measurement:
not applicable

**Slide courtesy: Dr. Kumar A.**

# Case-control studies

- *Advantages:*
  - quick and cheap;
  - only feasible method for very rare disorders or those with long lag between exposure and outcome
  - fewer subjects needed than cross-sectional studies.
- *Disadvantages:*
  - reliance on recall or records to determine exposure status;
  - confounders;
  - selection of control groups is difficult;
  - potential bias: recall, selection.

**Slide courtesy: Dr. Kumar A.**

# Eat Chili pepper

- **Chili pepper** is the key to good health
- Be sure to eat **Chili pepper** with every meal
- **Chili pepper** –it kills harmful bacteria

**Chili pepper is wonderful**

# Hypothetical Research Question

- Your mission:

  Reduce the incidence of *peptic ulcer*

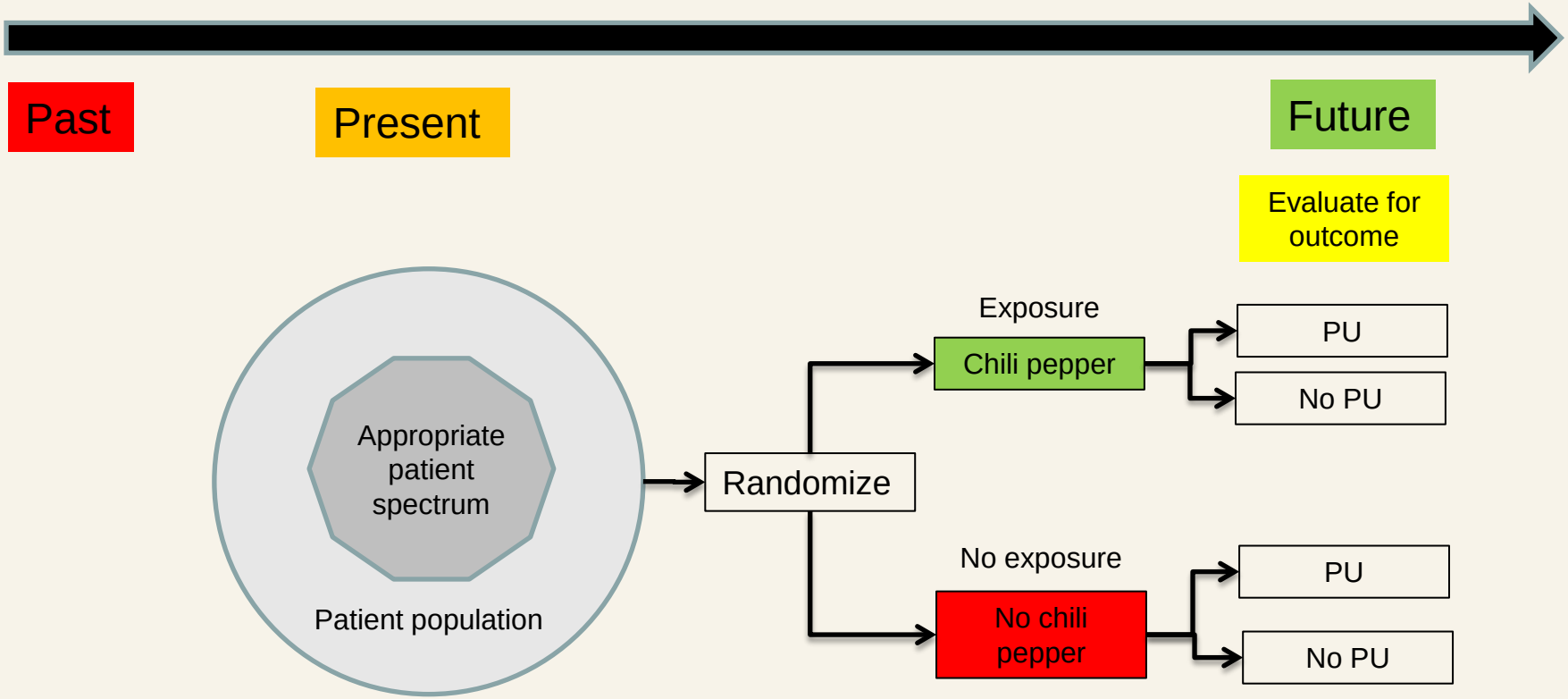
- Your belief:

  Chili pepper consumption is the key to good health

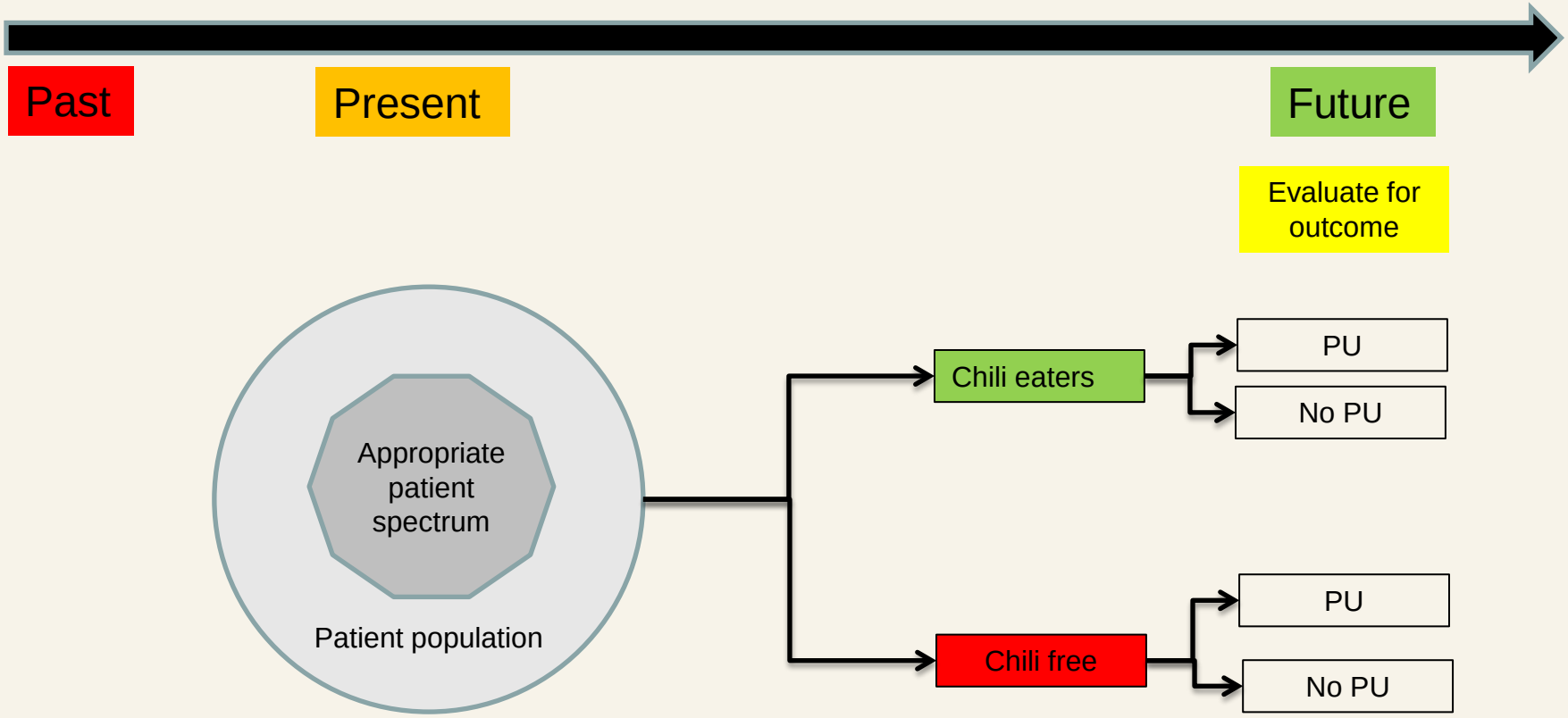
- Your hypothesis

  Chili pepper intake decreases the risk of *peptic ulcer (PU)*

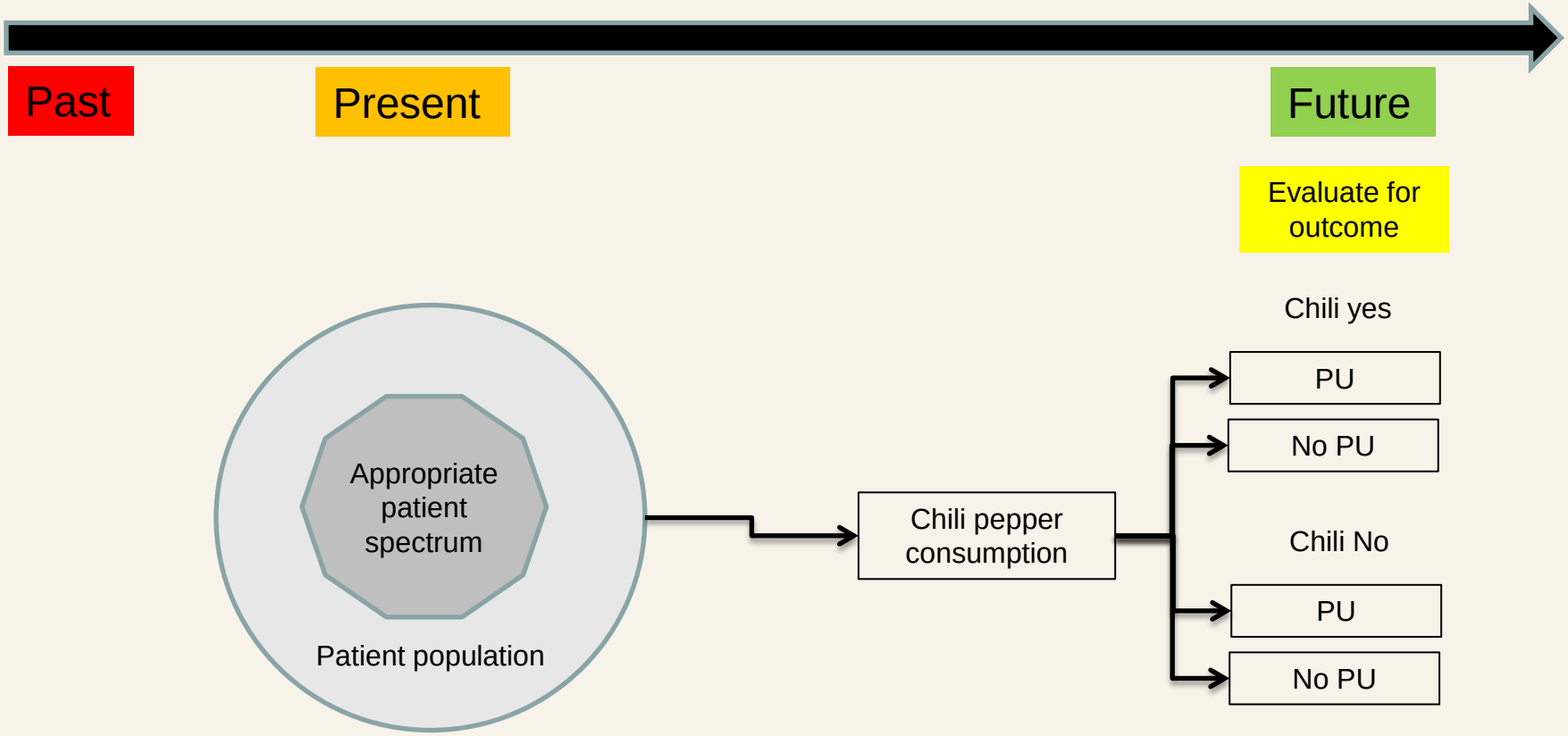
# Randomized controlled trials



# Cohort study

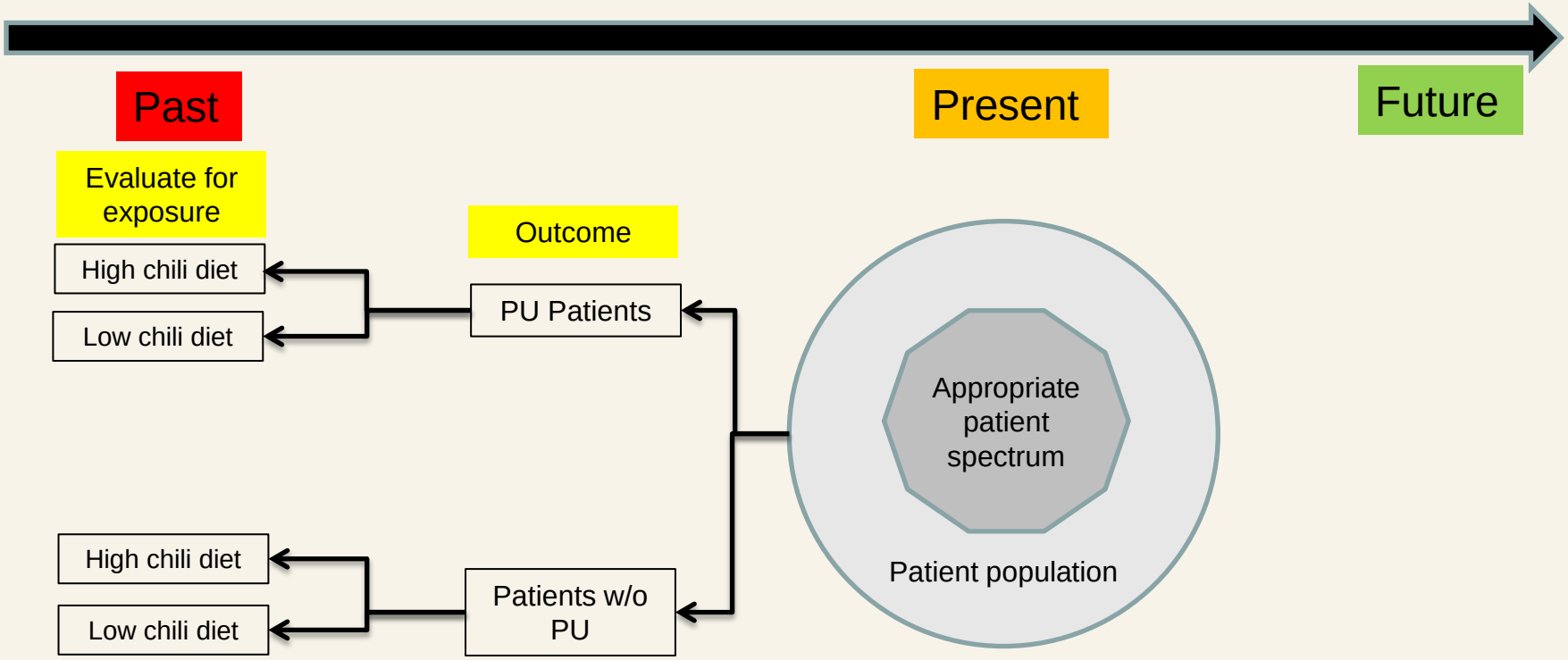


# Cross-sectional study




**Chili pepper consumption and PU prevalence assessed at the same time**

# Case-control study

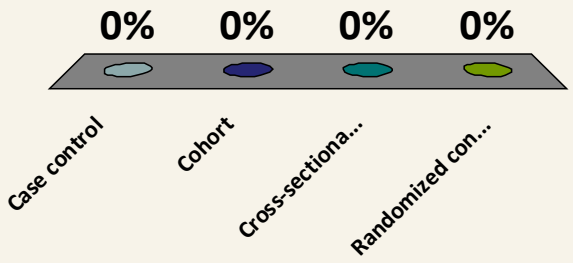


# Part II

Matching the study design to the research question

A 38-year-old man presents to the emergency department for severe alcohol abuse with nausea and vomiting. He reports no other significant medical problems. The patient is confused and slightly obtunded, and hepatomegaly is discovered on physical exam. You establish that patient is cirrhotic and most cirrhotic patients develop esophageal varices, with a lifetime incidence as high as 80-90%. You decide to send the patient for EGD which you know is not a very pleasing experience for the patient. You remember that recently a colleague mentioned that why not use capsule endoscopy. Being a logical person you wonder how effective is capsule endoscopy in accurately identifying esophageal varices in cirrhotic patients? In your search for an answer you would attempt to find a study employing which of the following study designs?

1. Case control
2. Cohort
3. Cross-sectional
4. Randomized controlled trial

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You recall a conversation from your medical school days with one of your favorite anatomy professors. The professor observed that most students from his class who were good in anatomy tend to become radiologists. As believer in science you decided to explore if there is any truth to this observation. Which study design is most suited to address the hypothesis that good anatomy students are most likely to become radiologists?

1. Case control
2. Cohort
3. Cross-sectional
4. Randomized controlled trial


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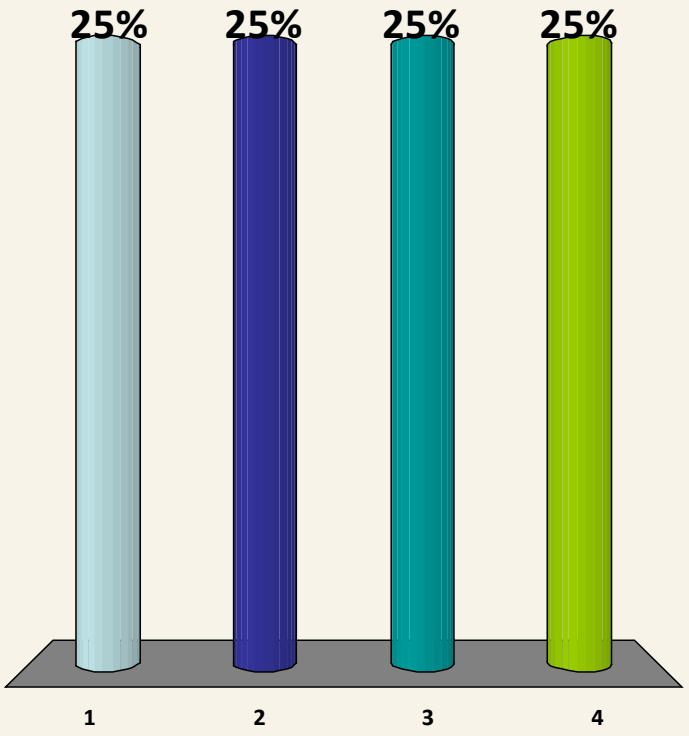
Following up on our cirrhotic patient the capsule endoscopy reveled acute variceal bleeding. You know that cirrhosis in Child–Pugh class C or those in class B who have persistent bleeding at endoscopy are at high risk for treatment failure and a poor prognosis. You decide to recommend treatment right away with a transjugular intrahepatic portosystemic shunt (TIPS). However a colleague of yours suggests to continue treatment with vasoactive-drug therapy, followed after 3 to 5 days by treatment with propranolol and long-term endoscopic band ligation (EBL), with insertion of a TIPS if needed as rescue therapy only. Which study design is best suited to provide most unbiased answer to the question of immediate versus rescue treatment with TIPS?




1. Case control
2. Cohort
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# Reporting statements

- CONSORT for randomised controlled trials
- STARD for diagnostic accuracy studies
- STROBE for observational studies
- PRISMA for systematic reviews of trials
- MOOSE for meta-analyses of observational studies

EQUATOR network

equator-network.org/resource-centre/library-of-health-research reporting/

# Take home message

Types of clinical questions

- Treatment
- Diagnosis
- Prognosis
- Etiology
- Values/preferences

# Take home message

- Research design is a function of question
  - Not choice
- Matching the design to question = <unbiased results

# Diagnostic accuracy of EGD versus capsule endoscopy

**Table 2. Varices Identified by Esophageal Capsule Versus EGD**

| | Varices Identified by EGD | Varices Not Identified by EGD | Total |
|---|---|---|---|
| Varices identified by PillCam ESO | 152 | 13 | 165 |
| Varices not identified by PillCam ESO | 28 | 95 | 123 |
| Total | 180 | 108 | 288 |

kappa = 0.73; sensitivity = 84% (CI 81%, 87%); specificity = 88% (CI 82%, 92%); positive predictive value = 92% (CI 88%, 95%); negative predictive value = 77% (CI 72%, 81%); positive likelihood ratio = 7.0 (CI 4.6, 11.2); negative likelihood ratio = 0.18 (CI 0.14, 0.23).

Study: de Franchis R et. al. Esophageal capsule endoscopy for screening and surveillance of esophageal varices in patients with portal hypertension. Hepatology. 2008 May;47(5):1595-603.

# Immediate versus rescue TIPS

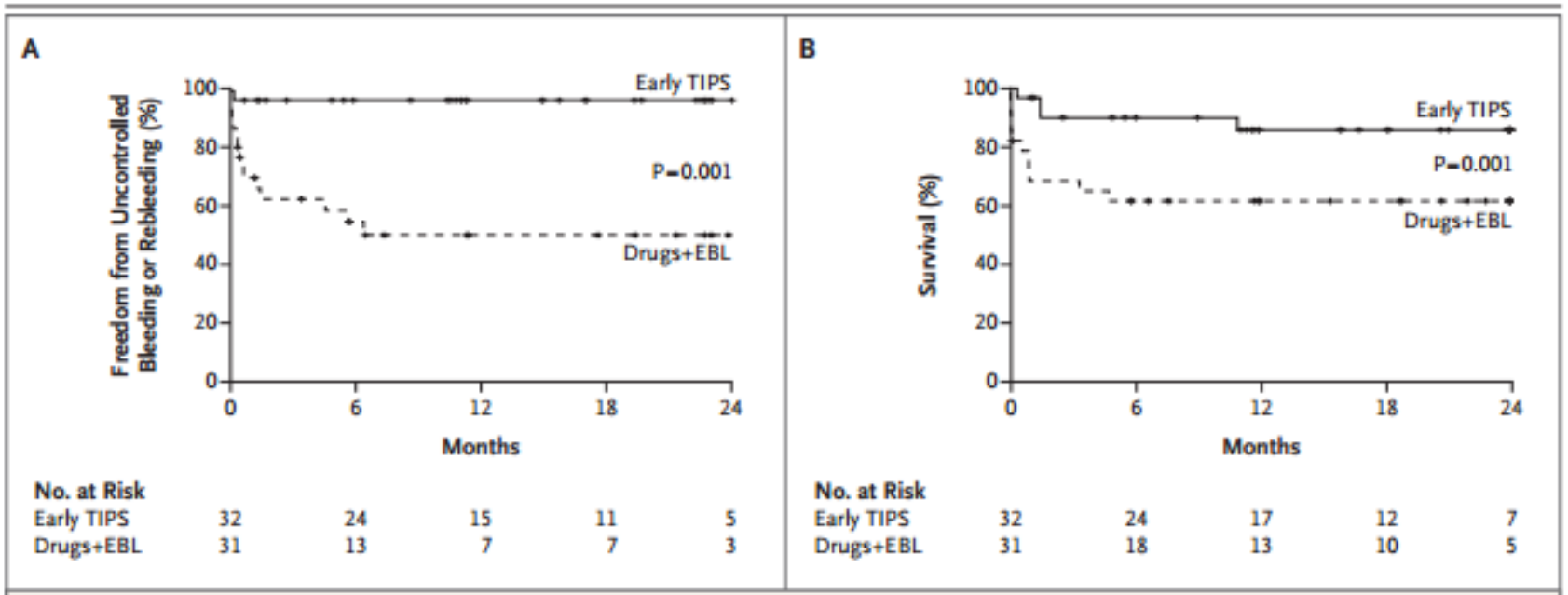


**Figure 2. Actuarial Probability of the Primary Composite End Point and of Survival, According to Treatment Group.**

The probability of remaining free from uncontrolled variceal bleeding or variceal rebleeding is shown in Panel A, and the probability of survival is shown in Panel B. EBL denotes endoscopic band ligation, and TIPS transjugular intrahepatic portosystemic shunt.

N Engl J Med 2010;362:2370-9

# Discussion

# Thank you

Questions ?