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.
Spotting the study design

All Studies

Descriptive

Survey (cross-sectional)

Qualitative

Analytic

Experimental

Randomized (parallel group)

Randomized (Cross-over)

Observational analytic

Cohort study

Cross-sectional (Analytic)

Case-control study

What was the aim of the study?

When were the outcomes determined?

Exposure assigned

Some time after the exposure or intervention

At the same time as the exposure or intervention

Before the exposure was determined

Exposure not assigned
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:

  - Systematic Reviews & Meta-Analyses
  - RCTs
  - Cohort Studies
  - Cross Sectional studies
  - Case Control Studies
  - Case Studies
  - Ideas, Editorials, Opinions
  - Anecdotal
Randomized controlled trials

Past

Present

Future

Appropriate patient spectrum

Patient population

Randomize

Exposure

Experimental

Outcome

No outcome

No exposure

Control

Outcome

No outcome

Evaluate for outcome

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

Past  Present  Future

Patient population

Appropriate patient spectrum

Exposed

Outcome

No outcome

Not exposed

Outcome

No outcome

Evaluate for outcome

Measurement:
Multiple times possible

Slide courtesy: Dr. Kumar A.
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.
Cross-sectional study

Pastpresentfuture

Appropriate patient spectrum

Patient population

Exposure 1

Exposure 2

Outcome

No outcome

Outcome

No outcome

Evaluation 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**

**Past**
- Evaluate for exposure
  - Exposure
  - No exposure

**Present**
- Outcome
  - Case
  - Control

**Future**
- Appropriate patient spectrum
  - Patient population

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

Past

Patient population

Present

Appropriate patient spectrum

Randomize

Future

Evaluate for outcome

Exposure

Chili pepper

No chili pepper

No exposure

No PU

PU

No PU

Past

Present

Future
Cohort study

Past

Present

Future

Evaluate for outcome

Appropriate patient spectrum

Patient population

Chili eaters

Chili free

PU

No PU

PU

No PU
Chili pepper consumption and PU prevalence assessed at the same time
Case-control study

**Past**
- Evaluate for exposure
  - High chili diet
  - Low chili diet

**Present**
- Outcome
  - PU Patients

**Future**
- Appropriate patient spectrum
- Patient population

- Patients w/o PU
- High chili diet
- Low chili diet

**Patient population**

- Evaluate for exposure:
  - High chili diet
  - Low chili diet

- Outcome:
  - PU Patients

- Future:
- Appropriate patient spectrum
- Patient population

- Patients w/o PU
- High chili diet
- Low chili diet
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

Slide courtesy: Dr. Kumar A.
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 a 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

Slide courtesy: Dr. Kumar A.
Following up on our cirrhotic patient the capsule endoscopy revealed 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
3. Cross-sectional
4. Randomized controlled trial

Slide courtesy: Dr. Kumar A.
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>
<thead>
<tr>
<th>Varices Identified by Esophageal Capsule</th>
<th>Varices Not Identified by EGD</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varices identified by PillCam ESO</td>
<td>152</td>
<td>165</td>
</tr>
<tr>
<td>Varices not identified by PillCam ESO</td>
<td>28</td>
<td>123</td>
</tr>
<tr>
<td>Total</td>
<td>180</td>
<td>288</td>
</tr>
</tbody>
</table>

$kappa = 0.73$; 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 $0.14$, $0.23$).

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.

Discussion

Thank you

Questions ?