Framing the Question

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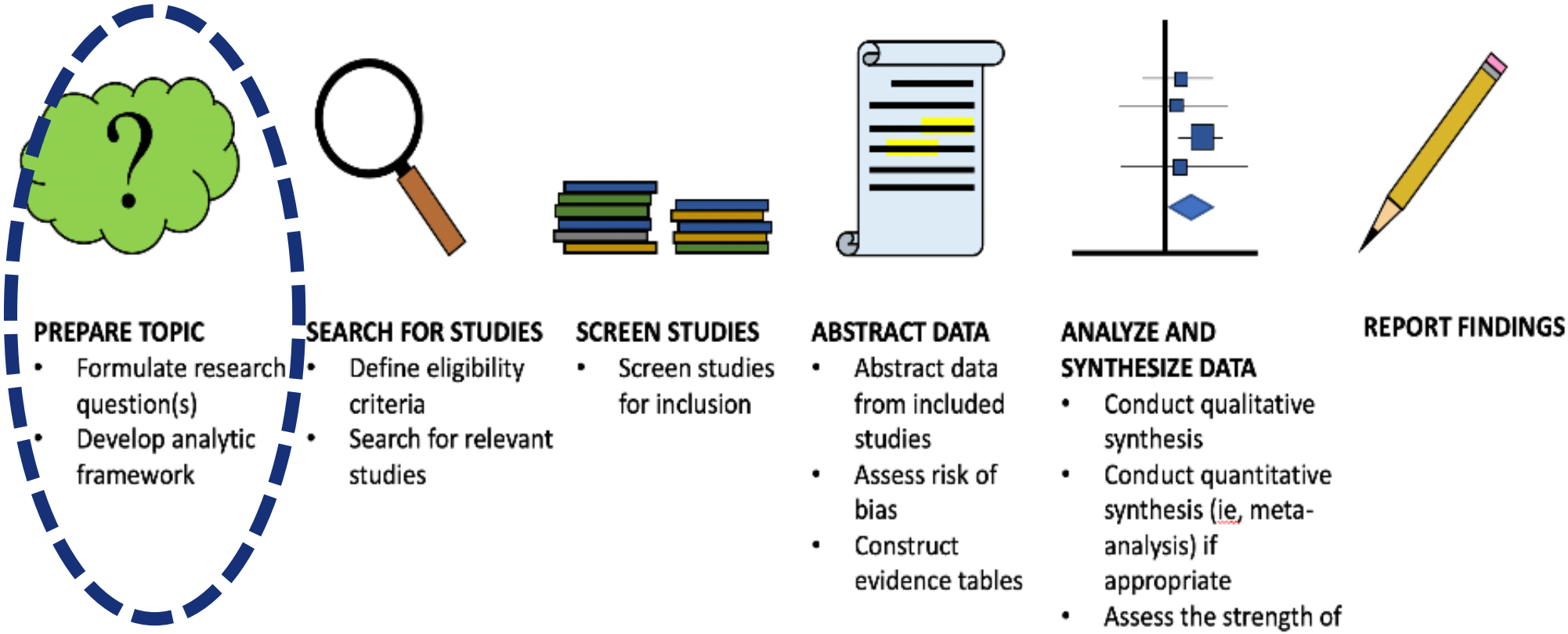
Steps in Completing a Systematic Review



PREPARE TOPIC
- Formulate research question(s)
- Develop analytic framework

SEARCH FOR STUDIES
- Define eligibility criteria
- Search for relevant studies

SCREEN STUDIES
- Screen studies for inclusion

ABSTRACT DATA
- Abstract data from included studies
- Assess risk of bias
- Construct evidence tables

ANALYZE AND SYNTHESIZE DATA
- Conduct qualitative synthesis
- Conduct quantitative synthesis (ie, meta-analysis) if appropriate
- Assess the strength of evidence

REPORT FINDINGS

A **systematic review** attempts to identify, appraise and synthesize all the empirical evidence that meets pre-specified eligibility criteria to answer a specific research question.

Adapted from Wallace C et al. J Compar Effect Res 2013; 2(3):273-282

Key Messages

- Well-framed research questions inform the process of conducting a systematic review.
- The type of question determines the appropriate type of evidence to address it.
- “PICO” describes the components of answerable questions for systematic reviews.

Outline

- Describe some general considerations
- Describe the steps in framing a research question:
  1. What is the question? (PICO)
  2. What is the question type?
  3. What type of evidence to look for?
- Review an example of a research question

The Question Informs the Process

Well-framed questions determine:

- Criteria used to select studies
- Development of the search strategy
- Data to be abstracted

Typical Clinical Questions

- Is completing root canal treatment in a single visit as effective and safe as completing the treatment over multiple visits?
- Is intensive glycemic control (e.g., HbA1c<7% or equivalents) more effective than conventional glycemic control for reducing mortality and cardiovascular disease in patients with T2D?
- Is fluid restriction effective for treating heart failure patients?

Broad vs. Narrow Questions

	Broad Questions
Advantages	• Comprehensive • Can explore consistency/ inconsistency
Disadvantages	• More resource intensive • Potentially complex and unwieldy • Interpretation may be challenging

Adapted from Higgins et al (Associate Editors). *Cochrane Handbook for Systematic Reviews of Interventions.* 2nd Edition. Chichester (UK): John Wiley & Sons, 2019.

Broad vs. Narrow Questions

	Broad Questions	Narrow Questions
Advantages	• Comprehensive • Can explore consistency/ inconsistency	• More manageable • Easier to read
Disadvantages	• More resource intensive • Potentially complex and unwieldy • Interpretation may be challenging	• Evidence may be sparse • Limited applicability • May result in spurious conclusions • Increased burden for accessing and summarizing multiple reviews

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Classify Your Question

2. What is the question type?

- **Example: Infant with severe eczema**
  - What is the cause of this condition? Heredity? Environmental exposures? *(etiology)*
  - Likelihood of getting worse? Getting better? (*prognosis*)
  - Potential benefits of topical corticosteroids? (*therapy*)
  - Potential harms of topical corticosteroids? (*harm*)
  - Potential differences in outcome if the patient is treated earlier rather than later? (*screening; prognosis*)

Classifying Question Types

Question	*Classification/Type*
• What proportion of the population is newly diagnosed with this problem each year?	**Incidence**
• What proportion of the population is currently living with this problem?	**Prevalence**
• What should be done to treat this problem?	**Therapy**
• Will detecting this problem early, before symptoms, make a difference in my health?	**Screening**
• How good is this test at detecting this problem?	**Diagnostic Accuracy**
• What is the likely outcome of this problem?	**Prognosis**
• Will there be any negative effects (of an intervention)?	**Harm**
• What causes this problem?	**Etiology**
• How can this problem be prevented?	**Prevention**

Classifying Question Types

Example	*Classification/Type*
• Is treatment with remdesivir more effective than placebo in reducing severity of COVID-19?	**Therapy**
• What is the incidence/prevalence of COVID-19 in Rhode Island?	**Incidence/Prevalence**
• Compared with pulmonologists, how effective are primary care doctors in detecting COVID-19?	
• What is the probability that an otherwise healthy 40-year-old with COVID-19 will need a ventilator in the next 2 weeks?	
• Is screening for symptoms outside grocery stores effective in identifying COVID-19?	
• What proportion of patients receiving remdesivir for COVID-19 develop liver damage?	
• Is hypertension a risk factor for the development of COVID-19 in adults?	
• I don't think I have COVID-19? How might I best protect myself?	

Poll Question 3.

What type of question is this?

Compared with pulmonologists, how effective are primary care doctors in detecting COVID-19?

- Screening
- Prognosis
- Diagnostic accuracy
- Prevention

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• Is screening for symptoms outside grocery stores effective in identifying COVID-19?	**Screening**
• What proportion of patients receiving remdesivir for COVID-19 develop liver damage?	**Harm**
• Is hypertension a risk factor for the development of COVID-19 in adults?	**Etiology**
• I don't think I have COVID-19? How might I best protect myself?	**Prevention**

3. What type of evidence to look for?

Use your question classification to seek the appropriate type of evidence

Question:	Look for evidence from:
Incidence, prevalence	Cohort studies, cross-sectional studies
Therapy	Clinical trials, cohort studies
Screening	Clinical trials, cohort studies
Diagnostic accuracy	Clinical trials, cohort/cross-sectional studies
Prognosis	Clinical trials, cohort studies
Harm	Cohort studies, clinical trials, case-control studies
Etiology	Cohort & case-control studies

Components of "Answerable" Clinical Questions

1. What is the question?

P Patients or populations

I Intervention

C Comparison group(s)

O Outcomes

Populations or patients (P)

- Define condition or disease, including explicit diagnostic criteria
- Population and setting of interest (age, race, sex, community, hospital, outpatient)

Interventions (I)

- Mode of delivery (including personnel who delivery it)
- Dosage and intensity
- Duration and timing of therapy
- Co-intervention

Comparators (C)

- No treatment
- Placebo
- Standard therapy
- Active treatment (head-to-head)

Outcomes (O)

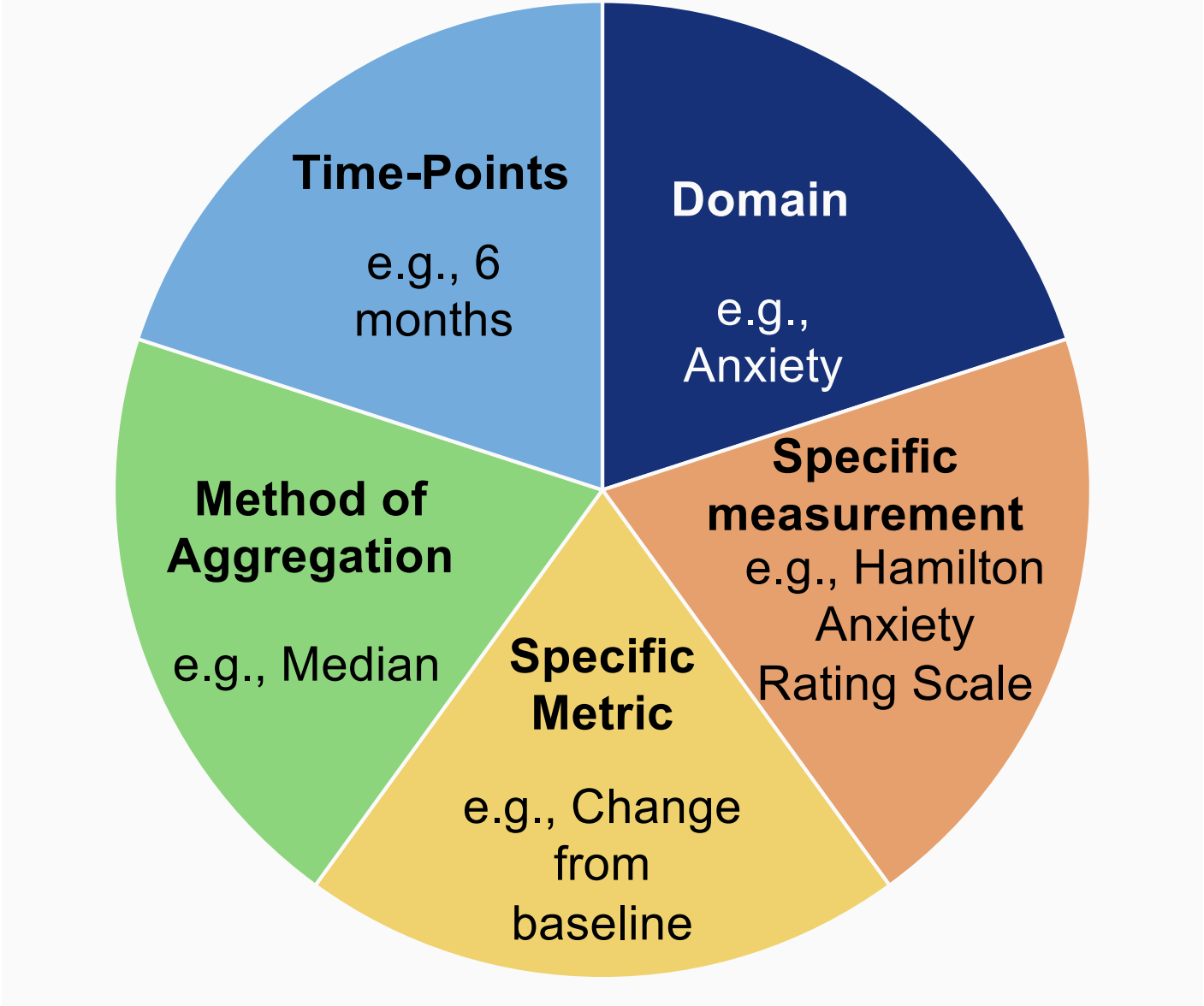
- Measures or events used to determine whether an intervention is effective and/or safe
- "Dependent" variable (in a regression)
- Yardsticks

Outcomes (O)

- Measures or events used to determine whether an intervention is effective and/or safe
- "Dependent" variable (in a regression)
- Yardsticks

Five Elements of an Outcome – Anxiety Example

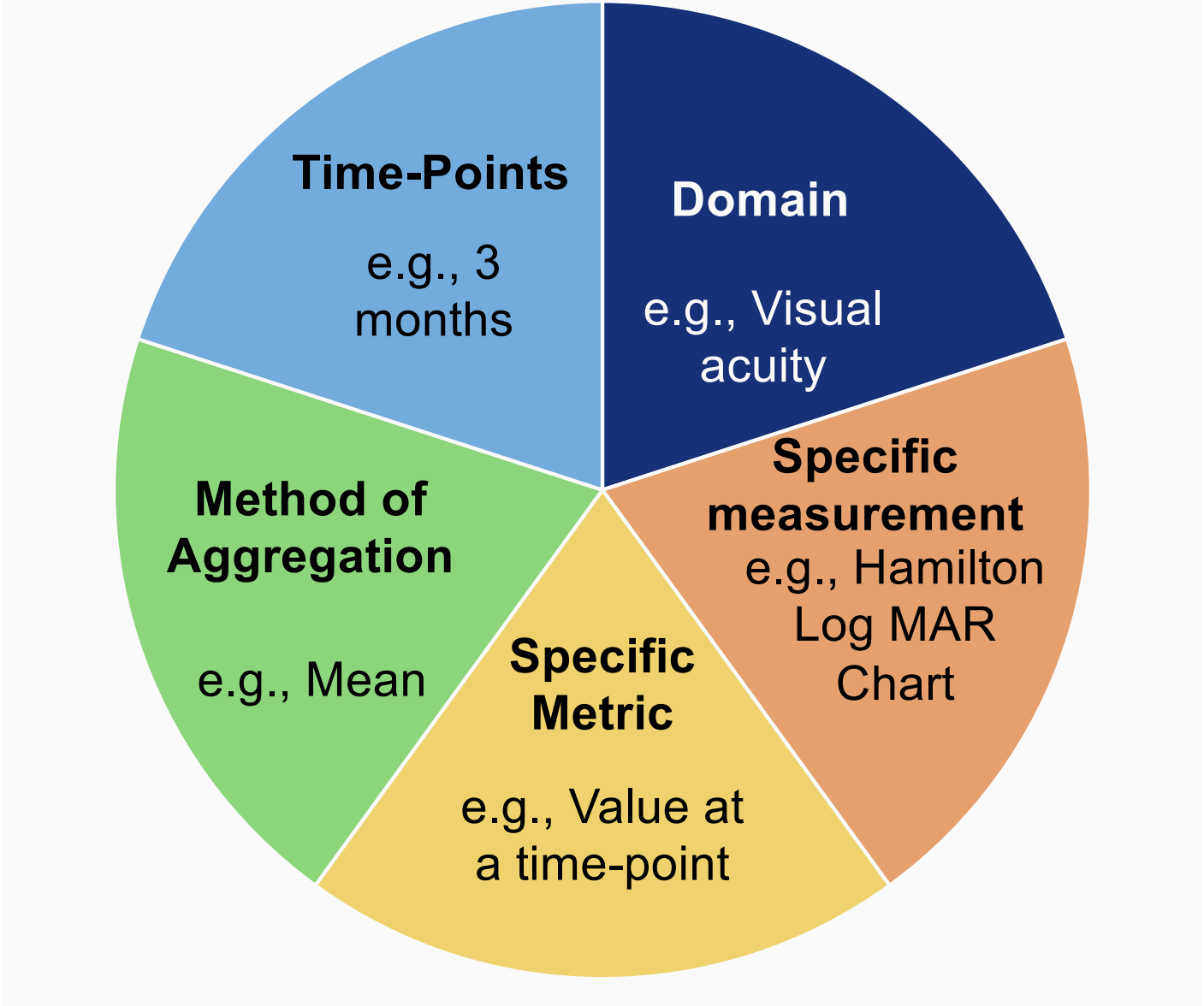
Five elements of a completely pre-specified outcome*



- Zarin DA et al. *N Engl J Med* 2011
- Saldanha IJ, et al. PLoS One 2014

Five Elements of an Outcome – Visual Acuity Example

Five elements of a completely pre-specified outcome*



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Context for Example

- In 2000, the American Academy of Pediatrics (AAP) recommended that children at high risk for food allergies should avoid peanut consumption until age 3.
- However, the incidence of peanut allergy more than doubled between 2000 and 2008, increasing to nearly 2%.
- In 2008, recommendations for the avoidance of allergens were withdrawn.

Rationale for the Trial

- The gut is the largest immune organ in the body.
- Experts now hypothesize that early introduction of highly allergenic foods might be the key to producing tolerance.

P – Populations

Who are the relevant patients?

- Define condition or disease, including explicit diagnostic criteria
- Population and setting of interest (age, race, sex, community, hospital, outpatient)

P: Infants less than 12 months of age with severe eczema, egg allergy, or both

Question (part 1): "For Infants less than 12 months of age with severe eczema, egg allergy, or both…"

I – Intervention

What is the intervention/risk factor/exposure of interest?

- Timing of exposure(s)
- Route of administration
- Dose intensity
- Duration of exposure or therapy

I: Consumption of peanuts

Question (part 2): "…does consumption of peanuts…"

C - Comparison

What is the comparison intervention?

- Placebo
- No treatment
- Standard of care
- Active intervention

C: Avoidance of peanuts

Question (part 3): "…when compared with avoidance of peanuts…"

O – Outcomes

What are the outcomes/conditions of interest?

- Criteria for defining outcome
- Clinically relevant with consideration of importance to patients

O: Peanut allergy

- presence of peanut allergy at 5 years of age, as measured by oral food challenge test
- presence of peanut allergy at 5 years of age, as measured by immune markers

Question (part 4): "…prevent peanut allergy at 5 years of age, as measured by oral fluid challenge test and immune markers?"

An example of a research question

For infants less than 12 months of age with severe eczema, egg allergy, or both, does consumption of peanuts, when compared with avoidance of peanuts, prevent peanut allergy at 5 years of age, as measured by oral fluid challenge test and immune markers?

An example of a research question

P

For infants less than 12 months of age with severe eczema,

I

egg allergy, or both, does consumption of peanuts, when

C

compared with avoidance of peanuts, prevent peanut allergy

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at 5 years of age, as measured by oral fluid challenge test

and immune markers?

Question type?

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