Study Design and Statistical Planning

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Agenda

1. S.M.A.R.T. Study Planning
2. Sampling Bias considerations
3. Study Designs common at NCHS
4. What data to collect: S.M.A.R.T. variables
5. Clinical Significance vs. Statistical Significance

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S.M.A.R.T. Study Planning

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Building on S.M.A.R.T.

- Specific
- Measurable
- Achievable/Attainable
  - Does the study design you select allow for the right data to be analyzed?
- Relevant/Reasonable/Realistic/Resourced
  - Do you have the resources to complete a study base on the design you select?
- Time bound
  - Every study ends eventually. Do you have time to complete the study design and analyses you want to select?

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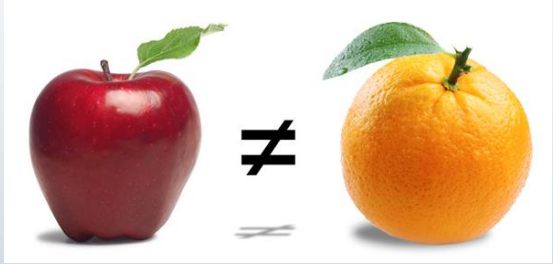
S.M.A.R.T. - Specific

"We will test health outcomes"

- **Research Question** – what has not been yet addressed by others?
- **Aims or goals of the study** – specific deliverables to answer the research question
- **Specific outcomes of the study** - what you want to measure to address the goals?
- **Hypothesis** – assumption that you are trying to prove



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S.M.A.R.T. - Measurable

- You need *operational definitions of each variable you will collect.*

- You need to be specific about how the variable with be collected and measured in terms of units, timing, frequency of the observations (scores, lab results, etc.)

- Examples:
  - ML, IU/mL, log IU/mL, (which log scale, base 10?) CAN BE VERY DIFFERENT!!!

  - Quality of life will be determined by a sum score on *validated measure* (cite measure).

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S.M.A.R.T. - Achievable

"Research doesn't grow on trees"

- Research takes *more* time, effort, and money than does a standard-of-care process or QI project alone.

Data

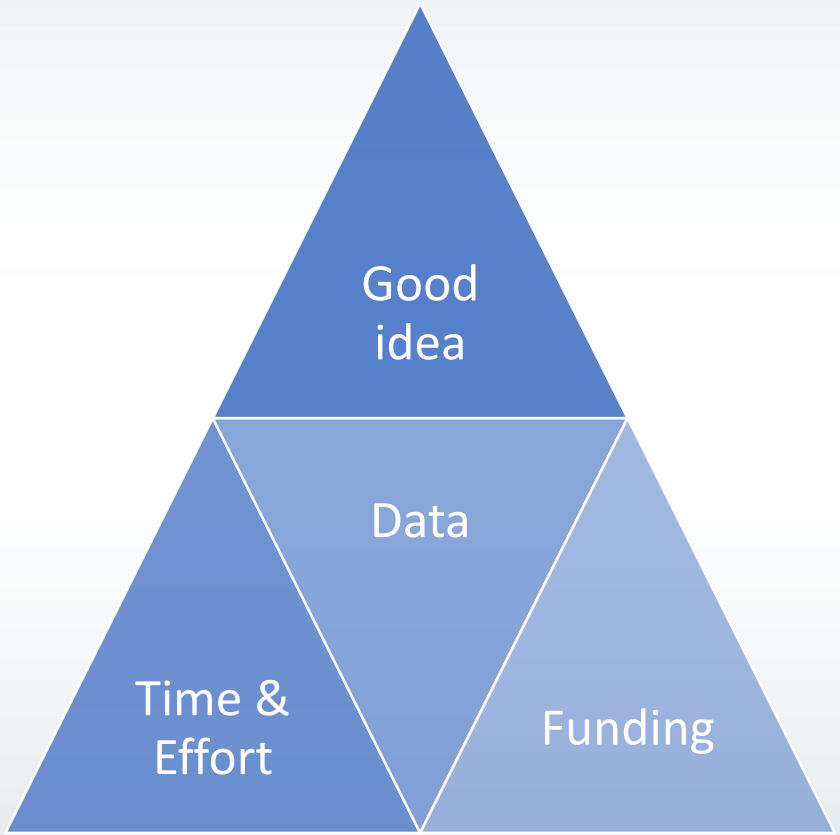
- Do you have access to this data?

Time & effort

- Do you have that time?
- Do a few "mock reviews" to time yourself

Money

- Research is not free—requires funds from Service Line or a Grant



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S.M.A.R.T. -- Relevant

Relevance

Ask yourself: Who cares?

Is it innovative? Impactful? Addresses gaps in existing knowledge?

Tips:

- ✓Do a *thorough* literature review (not just clinical input) before formulating Aims and outcomes
- ✓Check the "future directions" of discussion sections from recently published articles in the area you are interested in (e.g., in 2019 or 2020)
- ✓"Exploratory" research still needs to be at least somewhat theoretically sound in methods and approach.

Reasonable/Realistic/Resourced

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S.M.A.R.T. -- Time Bound

Will you be able to observe your outcomes in the time you have to complete your research?

You should plan to have your data collected at least 6 months to a year before you finish your Fellowship in order to get it published.

Helpful tool: Develop a **Gantt chart**

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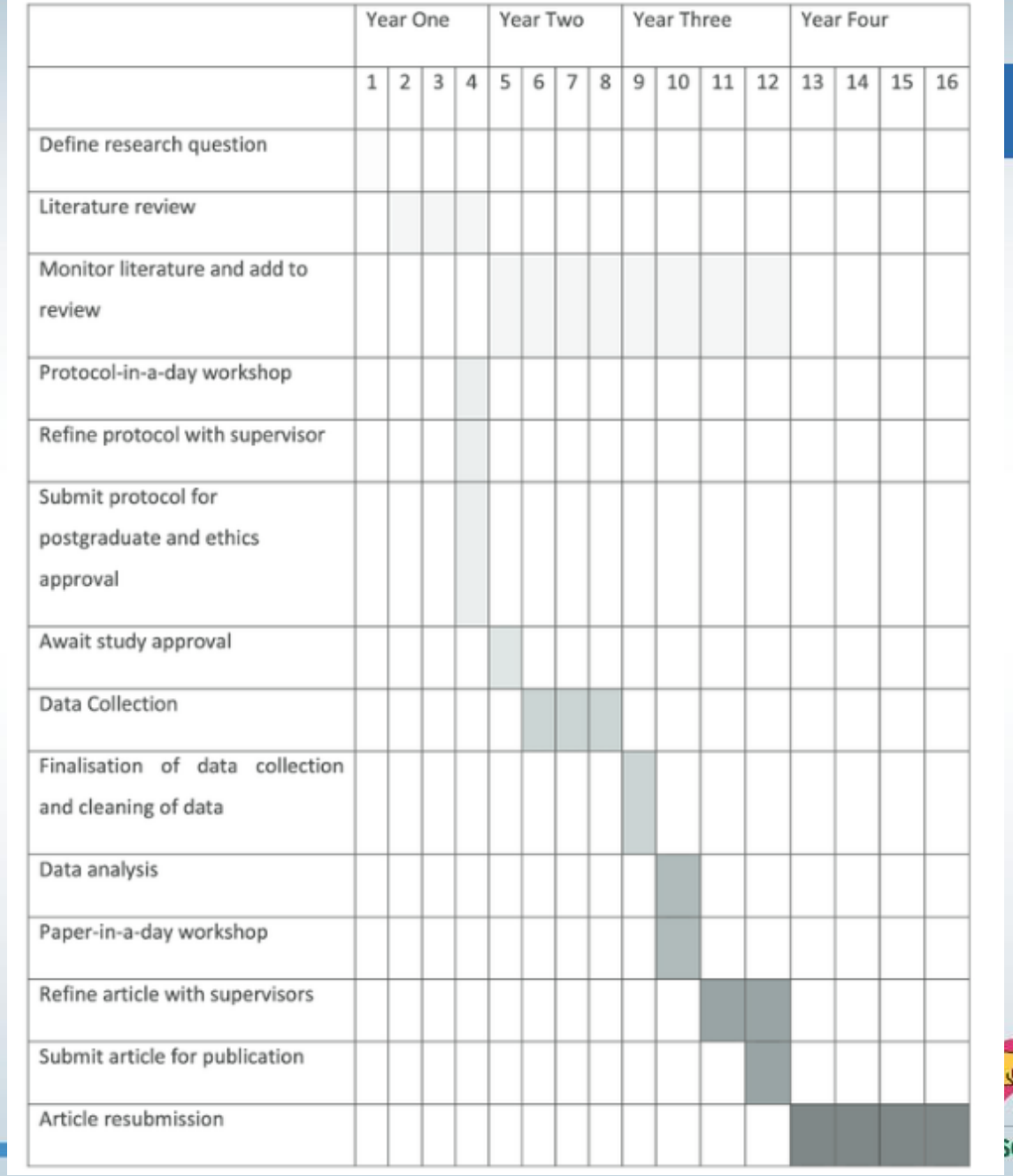
Gantt Chart Example: Medical Research Project Timeline

The Checklist with a timeline dimension



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2 year timeline

Months												
1		2	3	4	5	6	7	8	9	10	11	12-24
Develop objectives, testable hypothesis, outcomes, literature review, select a mentor, meet with biostatistician												
	Develop a protocol (use protocol builder)		Submit application to conduct research in eApp									
	October 12, 2020			Execute research protocol.								**Share with all coauthors 2 weeks prior to abstract submission deadline**
			January 11, 2021	Data collection (6M) & analysis (6W)								
							July 12, 2021					Complete Abstract & publish manuscript

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Sampling Bias considerations

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Common Sampling Biases in Pediatric Care Settings

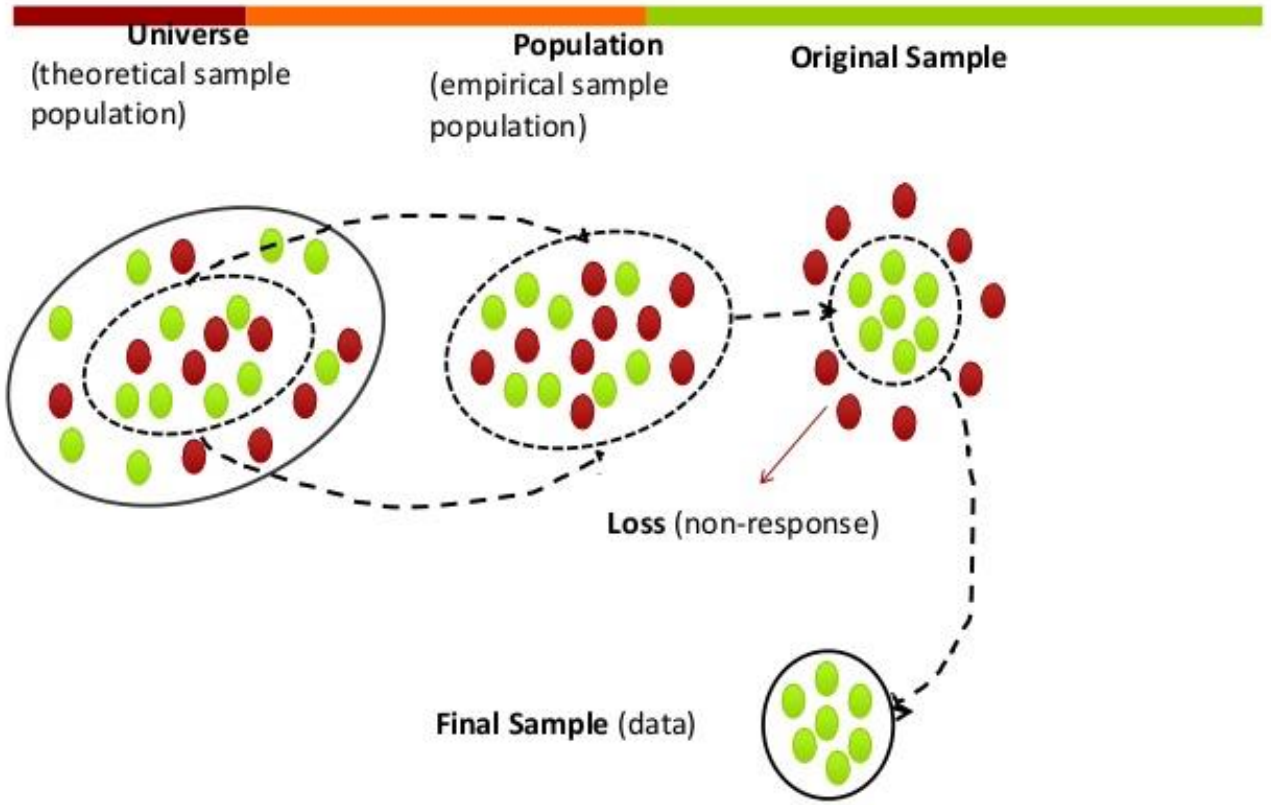
Selection

- Example--patients who are sicker may show up more in certain types of care and less in other types of care
- We don't know about the patients we don't see

"Mortality"

- Drop-out of care (and your study) is unfortunately all too common → missing data

Whom you select in your study does not always reflect the patients or families you intend to generalize to



Sampling at NCHS

History

Patient's past (and family's past) influences current observations

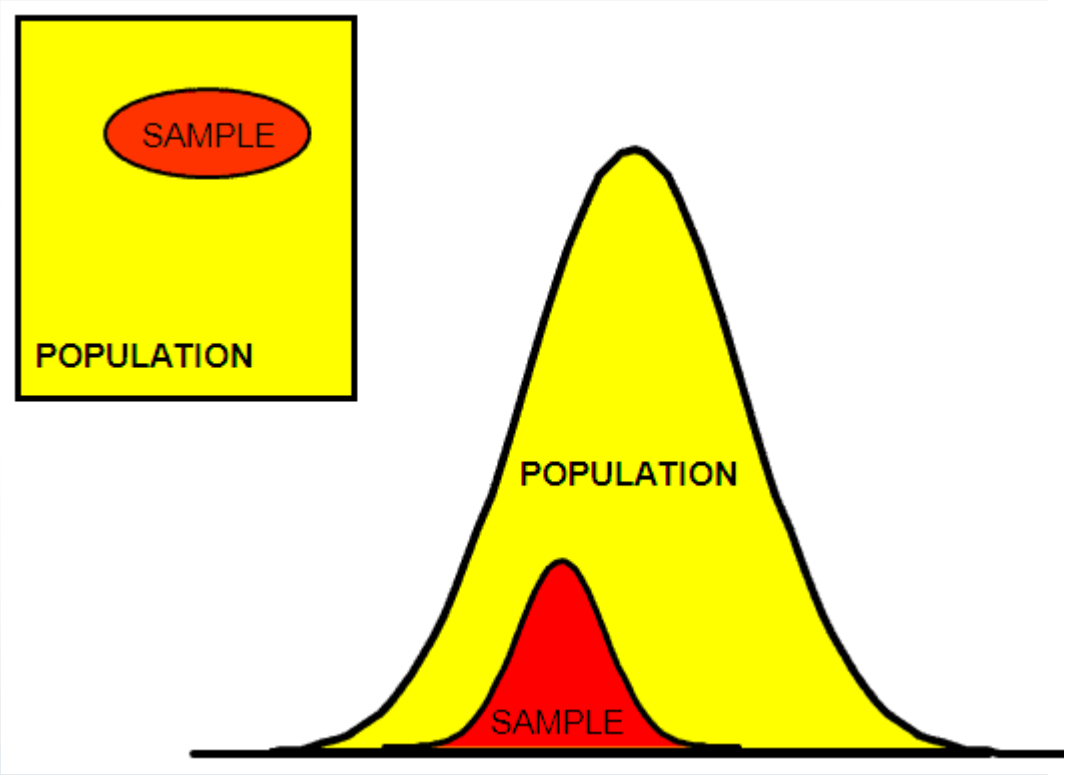
Maturation

Patients and Health Care Systems change over time ("secular trends")

Representativeness

How much you can generalize → the purpose of research.

NCHS patients are not general population



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Study Designs common at NCHS

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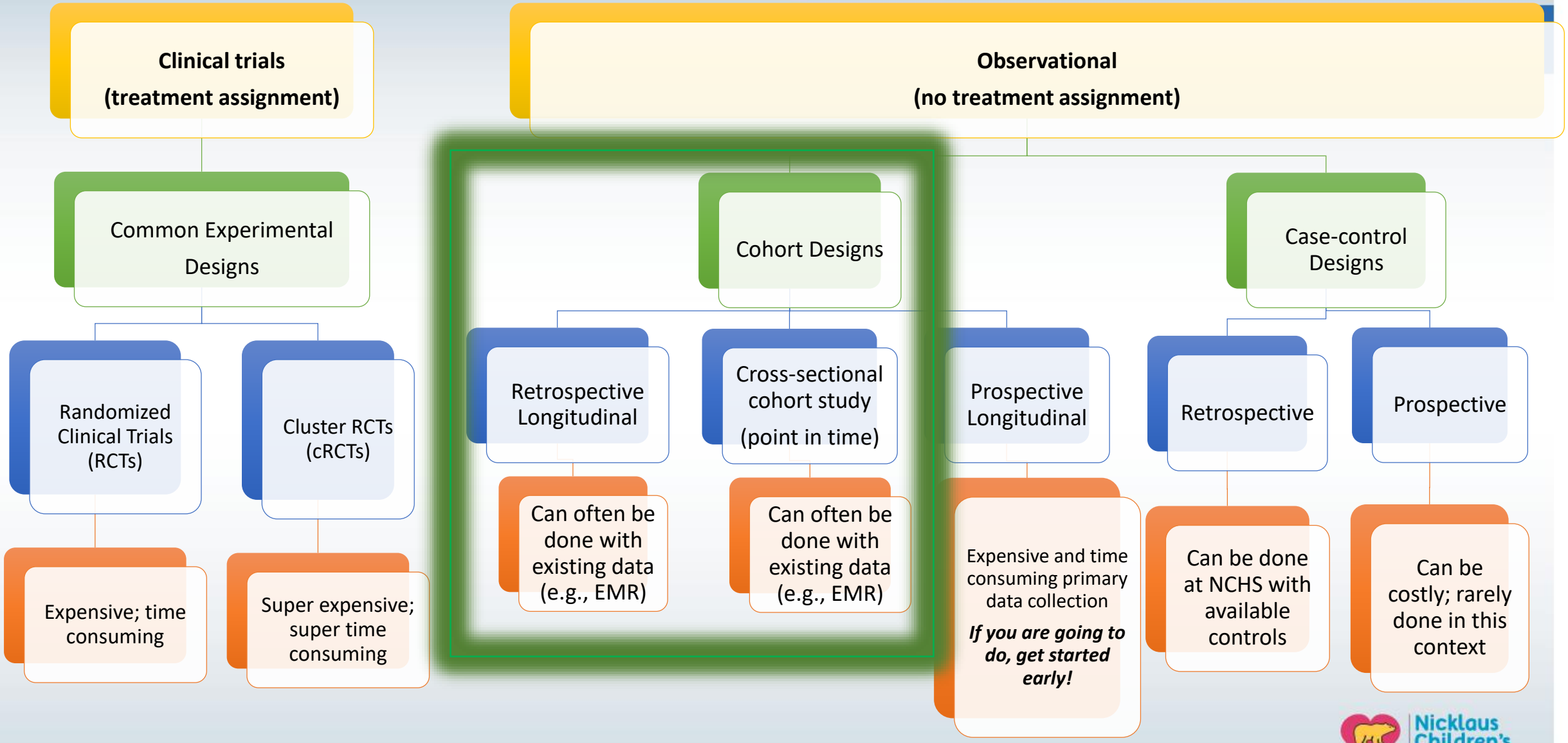

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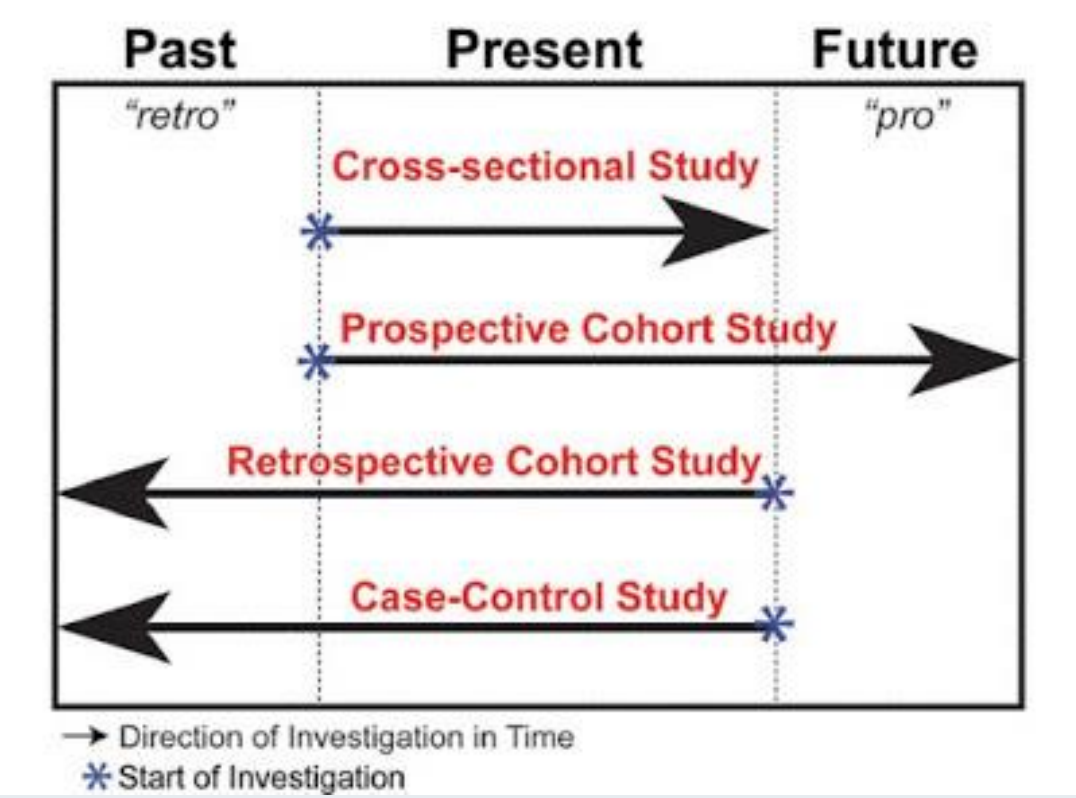
When time starts for cohort and case-control studies



- Cross Sectional Study Example
  - One time survey of parents
- Prospective Cohort Study Example
  - Longitudinal follow-up of patient condition after different types of surgery
- Retrospective Cohort Study Example
  - Chart review of patient care that happened in the past
- Case Control Study Example
  - Environmental exposure (e.g., food poisoning) study (match similar controls with patients who show up sick in ED)

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What data to collect: S.M.A.R.T. variables

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S.M.A.R.T. Variables

Essential Variables

- Outcomes (may be more than 1)
- Variables that ***may relate*** to outcomes
  - Treatment
  - Exposure variables
- Confounders that relate to treatment (or exposure) and outcomes

Always include important background descriptive qualities of the sample

- Gender
- Age
- Race
- Ethnicity

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Collecting Confounders

(broad statistical vs. Epidemiologically strict definition)

Independent (Treatment or Exposure)

Dependent (outcome, endpoint)

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Clinical Significance vs. Statistical Significance

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Significance and p values

p value "the probability of obtaining an effect at least as extreme as the one observed with the current sample, assuming the truth of the null hypothesis of no effect or association."

[poll]

Types of errors	Null hypothesis is True	Null hypothesis is False
You reject the null hypothesis	Type I error α (ALPHA)	Correct Decision
You fail to reject the null hypothesis	Correct Decision	Type II error β (BETA)

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Significance and p values

p value "the probability of obtaining an effect at least as extreme as the one observed with the current sample, assuming the truth of the null hypothesis of no effect or association."

Do not just rely on p values

- Report Effect Sizes (e.g., percent differences, OR, RR, etc.)
- Report measures of *uncertainty* = Confidence Intervals

Clinical Significance is not the same as statistical significance

Types of errors	Null hypothesis is True	Null hypothesis is False
You reject the null hypothesis	Type I error α (ALPHA)	Correct Decision
You fail to reject the null hypothesis	Correct Decision	Type II error β (BETA)

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Sample Size Considerations

More often though, you have this issue: you have a very small sample

- You start to get false negatives due to low statistical power
- Try to get as large a sample size as possible (with available resources)
- Power analysis (ask biostatistician)

Optimism bias

- “Things always take longer than you think they will.”
- EMR database cleaning, manipulation, restructuring, and analysis takes time
- If doing chart review, pilot test your chart reviews and time yourself

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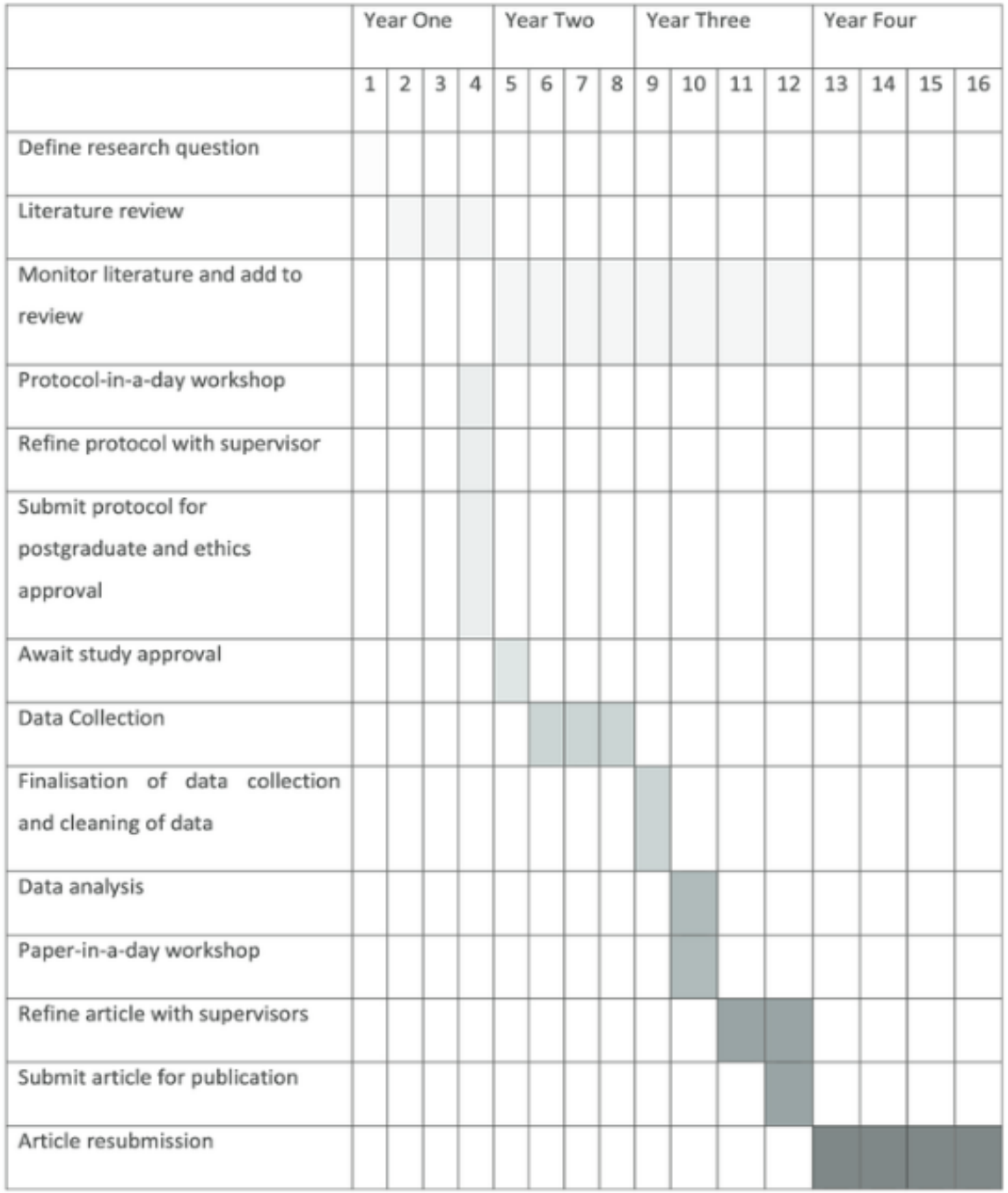
Review

- Choose a study design and analysis strategy that supports S.M.A.R.T.

- Use tools and information available to you
  - ***Both*** prior literature ***and*** clinical expertise
  - Time yourself if doing chart review (on non-study data)
  - Formal and updated Gantt charts to keep you on track



Thank you!

Questions, concerns, quejas?

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