CHEER

The Canadian Collaboration for Child Health:
Efficiency and Excellence in the Ethics Review of Research (CHEER)

Queen's University
HEALTH SCIENCES

# CHEER Research Program:
# **Study Design**

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**Please note:** This course was designed to be interacted and engaged with using the online modules. This **Module Companion Guide** is a resource created to complement the online slides. If there is a discrepancy between this guide and the online module, please refer to the module.

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## TABLE OF CONTENTS

INTRODUCTION ..... 3
SECTION 01: Introduction to Study Design for Child Health Research ..... 4
SECTION 02: Study Population Design Considerations ..... 13
SECTION 03: Study Procedures and Interventions ..... 20
SECTION 04: Selecting and Measuring Study Outcomes ..... 27
CONCLUSION ..... 34

## INTRODUCTION

*Please see the online learning module for the full experience of interactions within this document.*

To be ethical, research involving children must be scientifically sound. Well-designed studies provide the evidence needed to address children's unique health needs. It is essential to include children in research, rather than exclude them, so they have fair access to advancements in research and clinical care. Designing child health studies requires careful consideration of numerous scientific, practical, and ethical factors.

**Module Learning Outcomes**

Following completion of this module, learners will be able to:

1. Define key concepts and terms used in child health research study design.
2. Describe essential design considerations in child health research, incorporating relevant practical, ethical, and scientific perspectives.
3. Identify and use relevant resources for the design of high-quality and impactful child health research studies.

**Continue to Section 01**

## SECTION 01: INTRODUCTION TO STUDY DESIGN FOR CHILD HEALTH RESEARCH

A well-designed child health research study generates reliable, trustworthy results while minimizing risks to participants, contributing to improved health outcomes for children and their families. Sound design choices enable research teams to effectively and efficiently address important health questions while respecting the unique developmental and ethical needs of children. In this section, you will learn about different types of study designs that are commonly used in child health research.

**Note:** The term "children" includes infants, toddlers, preschoolers, and adolescents. The term "youth" is often used in government to categorize 16-25 year olds (i.e., younger adults). Throughout the module, the terms "child" or "children" will be predominantly used.

A "decision maker" can include parent(s), guardian(s), caregiver(s), a representative from a child protective service, social worker, legally acceptable substitute/alternative decision maker, sibling(s), or any other relative(s). The decision maker refers to an authorized third party who holds the legal right to make decisions on behalf of a child. Researchers should be aware of applicable legal and regulatory requirements with respect to legal decision makers, as these may vary among jurisdictions.

**Types of Study Designs in Child Health Research**

There are two major types of clinical study designs commonly used in child health research: **observational** and **interventional**.

*Learn about each type of study design.*

**Observational Studies**

Observational studies involve monitoring participants in their natural settings without the research team changing anything. For example, researchers might observe how a child's diet affects their growth over time without altering the child's normal eating habits.

**Interventional Studies**

Interventional studies are used to evaluate the effect or assess the outcomes of an intervention introduced to improve a child's health (e.g, medications, lifestyle changes, or preventive measures like vaccines). These studies typically involve assigning participants to different groups and actively testing the intervention to compare outcomes.

**Observational Studies**

The main types of observational studies are **cohort**, **case-control**, and **cross-sectional** studies. These studies can help identify patterns, risks, and potential areas for future studies in child health research.

*Explore three types of observational studies.*

**Cohort Studies**

In cohort studies, researchers follow a group of children over time to observe how certain events, conditions, or behaviours affect their outcomes. For example, a cohort study may be used to examine the impact of air pollution on the risk of asthma development in children.

**Case-Control Studies**

In case-control studies, researchers compare "cases," which are children with a specific condition (e.g., children with obesity), to "controls," which are those without (e.g., children without obesity), to identify potential risk factors (e.g., dietary habits, lack of physical activity).

**Cross-Sectional Studies**

In cross-sectional studies, researchers collect data at a single point in time, usually from a large group of people, to investigate relationships. For example, a cross-sectional study could be used to investigate if there is a relationship between screen time and obesity in children.

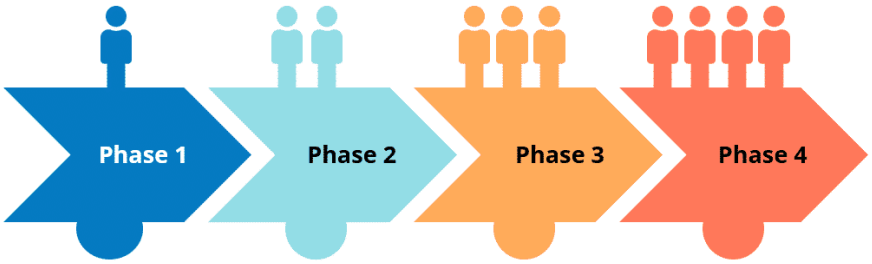
Another relevant, but less common, type of observational study is a **case study**. A case study, or case report, is a detailed report of a single person on a specific health issue or treatment. It is most often used when the situation is rare or unusual. When the individual details of children with the same condition or treatment are described and reported together, it is called a **case series**.

**Interventional Studies**

The most common form of interventional study is a **clinical trial**. A clinical trial is a type of research design that tests the safety and efficacy of an intervention in children. In clinical trials, especially those that are designed to test efficacy rather than safety, children are typically assigned to different groups so that comparisons can be made between them. There are many different types of clinical trial designs that can be used to answer research questions in children, depending on what the research question is and what is already known about the intervention.

Clinical trials are often conducted in phases, which may be referenced in documents such as consent forms. Each phase has a specific goal: the initial phases are mainly assessing safety, while later phases may compare an intervention against what is currently available on a larger scale. For example, a new cream for eczema may first be tested with a small number of participants to gauge safety, and later tested on many more participants.

*Explore how to define the phases of clinical trials.*




*Clinical trial phases.*[1]

**Phase 1**

A small group of people takes the intervention to check for safety and side effects.[2]

**Phase 2**

The intervention is given to see if it works and to monitor for more side effects.[2]

**Phase 3**

A larger group of participants takes the intervention, and it may be compared to current treatments to confirm effectiveness and safety.[2]

**Phase 4**

After approval, the intervention is monitored in the general population to catch any long-term or rare side effects.[2]

A **controlled trial** is a specific type of clinical trial where the results of an intervention group (i.e., those receiving the treatment) are compared against a control group (i.e., not receiving the treatment or receiving a standard treatment). This comparison helps researchers determine the true effects of the intervention.

When participants are randomly assigned to the intervention or control group—for example, through random numbers generated by a computer—the study is referred to as a **randomized controlled trial (RCT)**.

It is important to note that clinical trials are subject to specific regulations and oversight in Canada, including the Tri-Council Policy Statement (TCPS2), the International Council for Harmonisation of Technical Requirements of Pharmaceuticals for Human Use (ICH) guidelines, relevant privacy legislation, local Research Ethics Boards (REBs), and Health Canada.

*Learn about some of these regulations.*

**TCPS2 (2022) - Chapter 11: Clinical Trials**

**ICH Guidelines**

**Health Canada**

While most clinical trials involve groups of participants, there are also specialized designs that focus on individual cases. One such approach is the "N-of-1 trial," which involves just a single participant. In this design, a child switches between a treatment and a comparison treatment (or no treatment), sometimes in a randomized order. This type of trial design can help study treatments for rare/chronic diseases and conditions, or when different children respond differently to the same treatment.

Single-patient clinical trials can also be used to test gene therapies. For example, a single-patient gene therapy trial was conducted at The Hospital for Sick Children for four-year-old Michael Pirovolakis, with the aim of treating Michael's ultra-rare genetic condition, spastic paraplegia type 50 (SPG50).

*Read more about this trial.*

**Single-Patient Gene Therapy Clinical Trial at SickKids Carves a Path for Precision Child Health**

**Pre-Clinical Research Designs**

Pre-clinical research studies for children focus on understanding biological mechanisms, safety, and efficacy before conducting clinical research studies involving children and their families.

Pre-clinical studies can help minimize risks before involving children in clinical research and identify important biological discoveries that help us understand the causes and potential treatments of paediatric diseases and conditions.

*Explore some examples of pre-clinical studies.*

**In Vitro Studies**

*In vitro* studies are conducted in a controlled laboratory environment using biological samples such as cell cultures or tissues.

**Computational Methods**

Computational methods can utilize computer simulations to predict treatment responses or disease progression in children.

**In Vivo Studies**

Animal models (also known as *in vivo* studies) involve the study of juvenile or pregnant animals.

**Quality Improvement (QI) Studies**

Quality improvement (QI) or quality assurance (QA) studies are typically designed and conducted to implement knowledge or assess a process or program in terms of health care service delivery. These types of studies would not be considered research. Unlike traditional research, which focuses on generating new knowledge, QI/QA studies prioritize practical, real-world applications.

QA/QI studies, by design, do not increase risk to children or cause excessive burden to patients or staff.

Sometimes, the line between research and QA/QI studies may not be clear. To address this, A pRoject Ethics Community Consensus Initiative (ARECCI) has developed a tool that can help determine if a study is likely to be considered QA/QI (ethics approval not necessarily required) or research (ethics approval required).

*Access the ARECCI Ethics Screening Tool.*

**ARECCI Ethics Screening Tool**

**Note:** Although the ARECCI tool can help predict the need for an ethics review, the final determination of the requirement for ethical review always lies with the local REB.

*Answer the questions using your knowledge of QA/QI studies.*

**Question 1 of 2:** Hospital administrators at a major paediatric hospital wish to collect and measure health care provider performance data (e.g., time spent with patients) following a training session with hospital staff. Their aim is to improve wait times in their emergency department. Based on this description, would this initiative most likely be considered a QA/QI study or a research study?

a) QA/QI

b) Research Study

**Feedback:**

**The correct answer is a)**

Because the purpose of this study is to assess and improve a local process, it would typically be considered a QA/QI study.

**Question 2 of 2:** After looking at the data, the administrators realize their training session was highly effective and wish to share the findings with others. They discuss publishing the results. Would this change your opinion about whether this was research or QA/QI?

a) Yes
b) No

**Feedback:**

**The correct answer is b)**

Results of QA/QI initiatives can be published and often are. QA/QI findings that are published must relate specifically to that initiative or program. Care must be taken that broad generalizations are not

made, as this would indicate a goal of contributing to generalizable knowledge, shifting the study from QA/QI to research.

**Choosing a Study Design**

Choosing a study design for a child health research project is a critical decision that involves balancing several factors. It is critical to have a multidisciplinary team involved in the study design process that brings the appropriate expertise to help make the best design decisions possible. Team members can include scientists, clinicians, biostatisticians, as well as decision maker(s), children, community members, and others with interests in the study. Lived experience can provide critical insights into study design that can set a study up for success.

**Note:** To learn more about how to engage with patients and the public in research, refer to the *Patient and Public Engagement* module.

The research team is typically led by a Principal Investigator (PI), who is ultimately responsible for ensuring that the study design aligns with the goal of the research and that all relevant ethical approvals are obtained. Working collaboratively with a diverse team on study design can help ensure the planned study is robust, ethical, and feasible.

When selecting a study design for child health research, the team's first consideration is whether the study design aligns with the study's primary objectives. For example, if the objective is to explore cause and effect (e.g., new drug X improves symptom Z), an experimental design would be most appropriate. If the objective is to describe trends (e.g., risk factor Y is associated with condition Z), an observational design would be the best choice.

*Learn more about several other considerations that are relevant when choosing a study design for a child health research project.*

**Consideration 1**

**Ethical Concerns**

Children, as a vulnerable population, require designs that minimize risks and invasiveness as much as possible. The study team must balance the study's goals with its potential burden and risk to participants, regardless of the design type.

**Consideration 2**

**Feasibility**

Study budget, resources, sample size, and the level and type of expertise needed to successfully conduct the study can play a role in design decisions. For example, clinical trials, while offering the highest level of scientific evidence, require significant time, money, and often specialized training. Observational studies, on the other hand, may be a more cost-effective and faster way to help answer a research question, but they provide less definitive causal evidence that is unlikely to be acceptable to regulators and policy-makers. The study design should align with available resources and achievable timelines without compromising its primary objectives.

**Consideration 3**

**Acceptability**

The design must be acceptable to the participants and communities involved and respectful of relevant cultural values and practices. This can be achieved through meaningful consultations and co-designing the study together from an early phase.

**Consideration 4**

**Generalizability**

The study team must decide whether the study aims for broad applicability (which may be better addressed through multi-site studies from different geographical regions) or specific, localized insights (e.g, studies conducted at a single site, like a paediatric hospital).

In all cases, the chosen study design must be able to answer the research question at hand while upholding ethical research principles, maintaining privacy, and minimizing the risk of harm as much as possible to children and their families. If it's not designed properly, the results might not answer the research question. Conducting research that can't give clear answers is generally considered unethical.

*For your interest, access some additional resources relating to study design.*

**Maternal Infant Child and Youth Research Network (MICYRN)**

A pan-Canadian, not-for-profit organization that facilitates multijurisdictional paediatric studies. They provide expertise and support high-quality child health research in Canada.

**Clinical Research Study Designs: The Essentials**

A 2019 journal article written by Chidambaram and Josephson outlining the basics of clinical research study designs.

**"Jargon Buster" for Research Terms**

A "Jargon Buster" document that describes key definitions and concepts for health research and design. Canadian Institutes of Health Research.

**Introduction to Clinical Trials and Regulations Course**

A course developed by N2 and the Increasing Capacity for Maternal and Paediatric Clinical Trials (IMPaCT) training network. The course is free, but you'll need to create an account to access it.

**Guidance Document**

Part C, Division 5 of the Food and Drug Regulations "Drugs for Clinical Trials Involving Human Subjects."

Now that you have explored the basics of choosing an appropriate study design for child health research, it's time to apply your knowledge. In this activity, you will consider a study focused on the relationship between **natural sleep patterns and memory**.

The objective of this study is to examine the relationship between natural sleep patterns and memory performance in typically developing children aged 9 - 12 years who have no history of diagnosed sleep disorders or recent concussions.

*Answer the question using what you have learned throughout this section.*

**Question 1 of 1:** Based on this study objective, is the study design observational or interventional?

a) Observational Design
b) Interventional Design

**Feedback:**

**The correct answer is a)**

This study is observational because it explores a naturally occurring relationship between sleep patterns and memory performance without introducing any intervention or experimental manipulation. Researchers are simply observing existing behaviours within a specific population, aiming to identify associations rather than determine cause and effect.

In Section 02, you will continue working with this case study, shifting focus to the study population.

In this section, you learned the basics of choosing a study design for child health research. You first defined and compared the two major types of clinical study designs: observational and interventional. Then, you learned about the importance of pre-clinical research designs for minimizing risks to children. You were also introduced to QI/QA studies as a way to improve the research experience itself. Lastly, you learned about the process for choosing a study design and what factors a research team should consider during that process to uphold ethical research principles.

**Page Links:**

https://ethics.gc.ca/eng/tcps2-eptc2_2022_chapter11-chapitre11.html

https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/international-council-harmonisation/guidelines.html

https://www.canada.ca/en/health-canada/services/clinical-trials.html

https://www.sickkids.ca/en/news/archive/2022/single-patient-gene-therapy-clinical-trial-carves-path-precision-child-health/

https://arecci.albertainnovates.ca/?_gl=1%2A1ekl2x8%2A_ga%2AMTMyNTU5NzMyOC4xNzM2NjA1ODY4%2A_ga_G52HF03V5D%2AMTczNjYwNTg2OC4xLjEuMTczNjYwNTg5MS4wLjAuMA

https://www.micyrn.ca/

https://pmc.ncbi.nlm.nih.gov/articles/PMC7331444/

https://cihr-irsc.gc.ca/e/documents/cihr_jargon_buster-en.pdf

https://www.impactrials.ca/online-learning

https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-clinical-practices/guidance-documents/guidance-drugs-clinical-trials-human-subjects-gui-0100.html

**Continue to Section 02**

## SECTION 02: STUDY POPULATION DESIGN CONSIDERATIONS

In this section, you will learn about the design decisions that impact who can participate in a child health research study, including study inclusion and exclusion criteria, age cut-offs and terminology, and relevant equity considerations.

Defining the Study Population

A critical design decision is setting criteria outlining who is eligible to participate in the study and who is not. These are commonly referred to as the study **inclusion** and **exclusion criteria** that are set before the study begins.

*Compare inclusion and exclusion criteria.*

**Inclusion Criteria**

The study's inclusion criteria define the characteristics participants must have to be eligible for a study, ensuring the study population aligns with the objectives of the research. These criteria may include:

- Specific age range (e.g, 6-12 years).
- Required medical condition or diagnosis (e.g, asthma).
- Defined stage or severity of the disease (e.g, mild to moderate).

Additional factors might encompass demographic characteristics, such as:

- Race and ethnicity.
- Gender-specific eligibility.
- Geographic residency.
- Language proficiency.
- The presence of specific biological markers or genetic traits, when relevant.

However, demographic characteristics should only be included when there is a clear reason for doing so; otherwise, the research may not be inclusive.

**Exclusion Criteria**

The exclusion criteria define the characteristics participants cannot have and that would disqualify them from participating in the study. Exclusion criteria should be carefully chosen to ensure safety, data reliability, and study integrity, while also not unnecessarily excluding participants who could benefit from the research or its results. These may include characteristics such as:

- The presence of other medical conditions that could interfere with the study's focus.
- Current use of medications or therapies that could impact the study's outcomes.
- Inability to complete the study tasks.

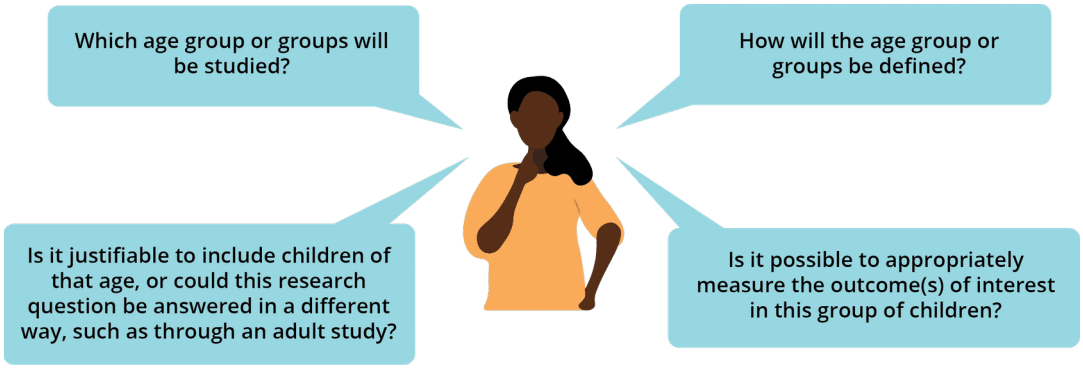
Reasons for exclusion should be clear and justifiable.

Some study designs can have highly restrictive criteria. For example, clinical trials often include a long list of inclusion and exclusion criteria for safety and regulatory reasons. In contrast, observational studies are generally more flexible, allowing for the inclusion of a broader range of children.

In all cases, the inclusion and exclusion criteria should be tailored to ensure the inclusion of participants who are able to answer the study's research question and not be unnecessarily restrictive or exclusionary.

**Defining Ages in Child Health Research**

A unique aspect of defining the population in child health research is the design decisions needed around which age group or groups will be eligible for the study and why. Children span a large range of ages and developmental stages. Several questions should be considered during study design:




**Note:** For drug studies, the selected age grouping and inclusion criteria must also consider developmental biology and pharmacology during study design.

It is important to note that age ranges and what constitutes "infants," "children," and "adolescents" can vary across institutions, organizations, geographical regions, and cultures. Researchers must clearly communicate and justify how they are using and applying relevant age categorizations for their research study.

*Review the tables to learn how the International Council of Harmonisation (ICH) E11 Guidance defines age groups compared to the National Institute of Child Health and Human Development (*NICHD*) Paediatric Terminology.*

| **ICH E11 Guidance** | |
|---|---|
| Preterm newborn infants | Newborn infants born preterm; not a homogeneous group |
| Term newborn infants | 0 to 27 days |
| Infants and toddlers | 28 days to 23 months |

| | |
|---|---|
| Children | 2-11 Years |
| Adolescents | 12 to 16-18 years (depending on the region) |

| **NICHD Paediatric Terminology** | |
|---|---|
| Preterm neonatal | The period at birth when a newborn is born before the full gestational period |
| Term neonatal | Birth to 27 days |
| Infancy | 28 days to 12 months |
| Toddler | 13 months to 2 years |
| Early childhood | 2 - 5 years |
| Middle childhood | 6 - 11 years |
| Early adolescence | 12 to 18 years |
| Late adolescence | 19 to 21 years |

The chronological age of a child, based on their birth date, is not always the only relevant factor in child health research during study design. For studies involving children with neurodevelopmental conditions, considering the child's **mental age** can be equally important.

*Explore how to define mental age.*

**Mental Age**

Mental age refers to the level of cognitive, emotional, or intellectual development a child has achieved compared to the typical abilities expected at a given chronological age. For example, a twelve-year-old with cognitive abilities like a typical six-year-old would have a mental age of six.

For research studying growth and development in children who were born preterm, it may be relevant to consider the use of a child's **corrected age** (rather than their gestational age). For instance, if a preterm baby was born at 30 weeks' gestation and is six months old by their actual birth date, their corrected age would be four months, because they missed two months of growth and development in the womb. Corrected age helps to ensure that research and clinical assessments are fair and that preterm babies are not inaccurately labelled as delayed simply because they were born early.

**Designing Inclusive and Accessible Studies**

In child health research, inclusion and exclusion criteria must be fair and equitable, avoiding the exclusion of participants who are relevant to the research. Working with members of the study population and/or their communities at an early stage of the research design can help ensure appropriate and inclusive design decisions are made.

Beyond the formal inclusion and exclusion criteria, there are other aspects of the study design that can greatly impact who is able to participate in studies that require active participation by children and their decision maker(s).

*Explore some aspects of a study design that can impact participation.*

**Aspect 1**

**Scheduling Difficulties**

The timing, frequency, and duration of study visits might not align with a family's schedule, including school, extracurricular activities, and their decision maker(s)' work and other caregiving obligations.

**Aspect 2**

**Accessibility Concerns**

Specific transportation and parking logistics, the child's mobility and cognitive abilities, and the accessibility of the study site may impact study participation.

**Aspect 3**

**Communication Barriers**

Language barriers, immigration status, and other responsibilities of their decision maker(s) might create barriers to participation if the study design does not consider and make plans to mitigate these factors.

When studies are designed for children, steps can be taken to help ensure it is inclusive and feasible for families.

*Complete the sorting activity by matching potential solutions to participation barriers.*

**Solutions:** Accessible study sites, Adding the study to medical appointments, Bilingual staff, Remote or virtual visits, Well-trained staff, Mobility aids, and Child-friendly spaces

| Participation Barriers | Solutions |
|---|---|
| Scheduling Difficulties | |
| Accessibility Concerns | |
| Communication Barriers | |

**Feedback:**

| Participation Barriers | Solutions |
|---|---|

| | |
|---|---|
| Scheduling Difficulties | Adding the study to medical appointments, Remote or virtual visits |
| Accessibility Concerns | Accessible study sites, Mobility aids, Child-friendly spaces |
| Communication Barriers | Bilingual staff, Well-trained staff |

**Sample Sizes in Child Health Research Studies**

Sample size refers to the number of children included in a research study. In child health research, selecting an appropriate sample size is crucial to ensure the study answers its questions accurately while minimizing unnecessary effort or harm to participants.

If the chosen number is too small, the results might not be able to reveal real differences or effects because there is not enough data.

If the sample size is too large, limited research resources may be wasted, and more children than necessary may be involved, raising ethical concerns.

Compared to research involving adults, the pool of eligible participants in child health research is much smaller. Children comprise only 20 - 25% of the population globally, and this percentage shrinks further with the application of study inclusion and exclusion criteria. For example, if a study aims to test a treatment for cancer, the rarity of childhood cancers further limits the pool of eligible participants.

To prevent overloading patients with research requests or procedures, for some paediatric conditions, families and clinicians must carefully consider which studies are best suited for a child if multiple options exist. Additionally, REBs may evaluate whether to permit multiple studies involving the same paediatric population to run simultaneously at one institution, as it can overburden patients.

Determining an appropriate sample size, or the right number of participants, usually involves the help of a biostatistician and is calculated using statistical techniques and software. Study design can also influence sample size requirements; for instance, repeated-measure studies can reduce the number of participants needed.

*Learn more about repeated-measure studies.*

**Repeated-Measure Study**

A repeated-measure study is a type of research where the same group of participants is measured multiple times under different conditions or at different points in time. This approach helps track changes in each child over time (instead of comparing different groups). A repeated-measure design can be either observational or experimental, depending on how the study is conducted. For example, tracking blood pressure in patients at baseline, after 4 weeks, and after 8 weeks of treatment.

Other ways to maximize participant numbers include the design of multi-site studies, such as recruiting from several clinical offices instead of just one, avoiding overly restrictive inclusion and exclusion criteria, and designing the study to be as accessible to as many patients as possible.

In long-term child health research studies, it is important to account for paediatric patients transitioning between age categories for sample size planning. The study design and statistical plans should consider changes in the number of participants within each age group over time. Since not all children will complete long studies, researchers often over-enroll by 10-15 percent at the start to compensate for potential dropouts.

Recall the sleep and memory study introduced in Section 01. In this activity, you will revisit the study with a focus on how the study population is defined.

*Explore the table and evaluate the appropriateness and equity of the inclusion and exclusion criteria.*

As you review the criteria, consider whether they might inadvertently limit participation for certain populations or raise potential ethical concerns regarding fairness and accessibility. Specifically, reflect on the exclusion of:

- Children with neurodevelopmental disorders.
- Children taking medications or supplements that affect sleep.
- Children or their decision maker(s) who are not fluent in English.

| **Inclusion Criteria** | **Exclusion Criteria** |
|---|---|
| Between 9 and 12 years old | Children with a diagnosis of neurodevelopmental disorders (e.g., attention-deficit/hyperactivity disorder [ADHD]) |
| No history of diagnosed sleep disorders (e.g., sleep apnea) | Currently taking medications or supplements that can impact sleep |
| Fluent in English (decision maker(s) and child) | History of head injury or concussion in the past year |

*Answer the question using your knowledge of inclusion and exclusion criteria.*

**Question 1 of 1:** How might these criteria affect the diversity of the participant pool, and therefore, the generalizability of the study results? Would enough participants be able to meet these criteria so that the study can realistically be completed? Are there any measures that could be taken to ensure the study design is inclusive without compromising its scientific goals?

**Feedback:** Excluding children and their decision maker(s) based on their English language proficiency would affect the diversity of the participant pool since it would exclude a large section of Canadian society, such as those who speak French, Inuktut, or any other language as their first language.

Recall that "the objective of this study is to examine the relationship between natural sleep patterns and memory performance in typically developing children aged 9 - 12 years who have no history of diagnosed sleep disorders or recent concussions." The research is looking at neurotypical children, and in order to answer the research question, children with a diagnosis of ADHD or another neurodevelopmental disorder should be excluded from this research. Including children with neurodevelopmental conditions or recent concussions may not benefit them. In a large cohort of

children, data from the children with neurodevelopmental conditions or recent concussions would likely be overshadowed by the rest of the data and it would be very challenging to make any conclusions for these specific populations.

However, research in this population of children is just as important as in other populations of children and future research could conduct the same study in children with neurodevelopmental conditions or children with concussions to compare to the children without these criteria.

In Section 03, you'll continue working with this study as you explore key concepts related to study procedures in child health research, including how interventions are introduced and tested, along with important practical and ethical considerations.

In this section, you learned about the importance of setting inclusion and exclusion criteria when designing child health research studies. You compared how different organizations categorize ages in research, and also considered the impact of mental age on results. To create inclusive and accessible studies, you learned how to work with decision maker(s) during the early stages of the research design to ensure maximum participation. Lastly, you learned how to select an appropriate sample size to accurately answer your research question while minimizing harm to participants.

**Continue to Section 03**

## SECTION 03: STUDY PROCEDURES AND INTERVENTIONS

In this section, you will be introduced to key concepts and considerations with respect to study procedures in child health research. You will also learn more about the ways interventions or treatments can be studied in clinical trials, and the relevant practical and ethical implications.

**Study Procedures Across Study Designs**

Designing studies for paediatric populations requires thoughtful consideration of both the child and their decision maker(s). Study designs and the required procedures must be acceptable and practical to encourage participation while respecting patient preferences and adhering to local REB guidelines. For example, limitations on the volume and frequency of blood draws, particularly when conducted solely for research purposes, may be specified by the ethics board.

Flexibility in study design in terms of the required procedures can be key to preventing unnecessary exclusion of children. For example, if a child declines a blood draw for an optional component of a study, their decision should be respected, and the study protocol should allow them to continue participating in other aspects of the study.

Some study designs require little to no active participation or additional procedures, beyond providing informed consent.

*Learn about some common study designs.*

**Case Studies**

Case studies are typically based on patients' medical records and need no additional input.

**Retrospective Observational Studies**

Retrospective observational studies analyze existing data or records, minimizing participant involvement.

**Prospective Observational Studies**

Prospective observational studies involve identifying participants and actively collecting data over time. These studies often investigate the development of conditions, the effects of exposures (e.g., lifestyle or environmental factors), disease progression, or long-term outcomes. For instance, researchers might recruit children exposed to second-hand smoke and follow them for 10 years to study respiratory conditions. Prospective studies frequently use standardized methods like surveys or interviews, along with practical steps and procedures such as updating participant contact information and sending reminders to complete study procedures.

**Clinical Trials**

As you learned earlier in Section 01, clinical trials demand active participation and significant commitment from children and their families. They can be intensive due to the numerous procedures, outcome measurements, and study visits involved. Before a trial begins, the study protocol must

outline the design, procedures, schedule, responsible personnel, and number of visits in detail. These specifics should be clearly communicated to children and their families during the informed consent process to ensure understanding and informed decision-making.

*For your interest, explore a checklist of items to include in clinical trial protocols.*

**Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) Reporting Guidelines**

**Interventions and Comparators in Paediatric Clinical Trials**

Clinical trials are the foundation of evidence-based medicine. Designing paediatric clinical trials requires special attention to the trial's **intervention** (e.g, what is being tested) and **comparator** (e.g, what it is being tested against).

In child health studies, **trial interventions** often involve medical devices or drugs. Paediatric device trials test medical devices for children, such as glucose monitors or mobility aids. Drug trials may evaluate new treatments for safety and efficacy, or assess existing drugs with modifications, such as different doses, routes of administration (e.g, oral or intravenous), or new age groups (e.g, testing a drug in children ages two to five years old that is already approved for children six and older).

To support the successful administration of interventions, trial protocols should incorporate strategies tailored to children's needs, such as distraction techniques or audiovisual tools. Paediatric drug and device trials must also address the unique anatomical, physiological, and developmental needs of children, which differ significantly from those of adults.

*Explore some examples of how paediatric trials adapt devices and drug interventions to meet these unique needs.*

**Devices**

When evaluating the use of medical devices in paediatric trials, several factors must be considered:

- Ability to withstand growth and developmental changes (e.g., a device for a two-year-old may not fit or function the same as for a five-year-old).
- Need to be smaller and less invasive than adult devices.
- Ability to withstand wear.
- Ability of children and/or their decision maker(s) to easily and safely operate.
- Need for enhanced safety features to mitigate risks to young users.

**Paediatric Drugs**

When evaluating the use of drugs in paediatric trials, several factors must be considered:

- Dose amounts must be carefully selected using the best available information, as children, especially neonates, metabolize drugs differently due to immature organ systems (e.g., liver, kidneys).

- Need for age-appropriate, accessible formulations (e.g., liquids or chewable tablets), since many children under the age of seven years old cannot swallow pills.
- Requirement that the taste be acceptable and palatable for children if ingested orally.
- Flexibility within the trial protocol to accommodate different doses and routes of administration, when appropriate and relevant (e.g., permitting crushing pills into applesauce for children with swallowing difficulties).
- Preference for minimal frequency of administration and minimal impact on lifestyle (e.g, once a day would likely be preferable to four times a day, which could necessitate taking medicine at school or daycare).

*Access a template checklist and guide that can help you plan and report study interventions.*

**The Template for Intervention Description and Replication (TIDieR)**

**Comparator Choice and the Use of Placebos in Clinical Trials**

In clinical trials, a key design decision is the choice of the **comparator**, or the "control" group, meaning what the intervention is going to be tested against. Most trials have one control group, though there may be more than one or none.

Control groups must be carefully chosen to ensure they are scientifically valid while meeting the highest ethical standards. In clinical trials, researchers must justify their choice. The design of clinical trials is centred around the concept of clinical equipoise.

*Explore the definition of clinical equipoise.*

**Clinical Equipoise**

Clinical equipoise means that "a genuine uncertainty exists on the part of the relevant expert community about what interventions are most effective for a given condition," so a trial is both necessary and ethically justifiable.[5]

What to select as the comparator should include consideration of current evidence, current standard of care (e.g., usual treatment), and, if a placebo is to be used as the comparator, any risks of delaying active treatment.

*Explore the definition of placebo.*

A placebo is an inactive therapy (such as a drug or device) resembling the active treatment being tested but with no therapeutic effect. Typically, it is a tablet or capsule with no active ingredients (e.g., a sugar pill) or a "sham treatment" designed to mimic a medical procedure (e.g., an injection that contains no active medication).

**Placebo**

Placebos can be used when no standard treatment exists or when withholding treatment would be ethical, such as for mild or self-limiting conditions. Placebos can be necessary to demonstrate the true

efficacy of an intervention, particularly in conditions with spontaneous improvement (i.e., where symptoms resolve over time without treatment).

Some people understandably may not wish to participate in a study if there is a placebo arm where they may not have a chance of receiving an active treatment; however, it is important to note that participants should not be denied care in order to be in research.

*Explore some examples of using placebos ethically in trial interventions.*

If a standard of care treatment exists, clinical trials can compare two groups: one receiving the standard treatment combined with the trial intervention, and the other receiving the standard treatment alone. This approach ensures that all participants are receiving treatment as part of the trial. For example, children in a cancer trial might receive standard chemotherapy alongside a novel treatment under investigation so that all are receiving at least the typical standard of care.

An alternative approach is to compare a trial intervention against a placebo. This can be harder to justify ethically, but with an appropriate trial design, this can be accommodated; for example, some participants could be delayed in receiving the intervention, but eventually all participants will receive it.

When a study involves the use of placebos, participants must always be informed. This is especially important for children, as treatment delays could have an impact on growth and development as well as on their long-term health outcomes.

According to the **Declaration of Helsinki**, the benefits, risks, burdens, and effectiveness of a new intervention must be tested against those of the best proven intervention(s); however, exceptions for this rule exist.[6]

*Learn about exceptions to the Declaration of Helsinki.*

**Exceptions to the Declaration of Helsinki**

Circumstances where the Declaration of Helsinki is exempt include:

- If no proven intervention exists, the use of a placebo or no intervention is acceptable.
- If, for compelling and scientifically sound methodological reasons, the use of any intervention other than the best proven one(s), the use of a placebo, or no intervention is necessary to determine the efficacy or safety of an intervention.
- The participants who receive any intervention other than the best proven one(s), placebo, or no intervention, will not be subject to additional risks of serious or irreversible harm as a result of not receiving the best proven intervention.

Extreme care must be taken to avoid abuse of these options.

*Answer the questions using your knowledge of the ethics of placebos.*

**Question 1 of 2:** Is it appropriate to study a novel drug therapy for treatment-resistant epilepsy against a placebo in children ages 2 - 12 years?

a) Yes

b) No

**Feedback:**

**The correct answer is a)**

Yes. As this is treatment-resistant epilepsy, there is currently no effective treatment for the condition being studied, so a placebo **may be** justified. This would be specific to the study and the participants.

**Question 2 of 2:** Is delaying the testing of a treatment for hay fever against a placebo suitable in children?

a) Yes
b) No

**Feedback:**

**The correct answer is a)**

Yes. Delaying treatment for hay fever may cause discomfort but poses minimal harm to children. After the blinded study period, all children would receive active treatment.

The use of placebos in neonates, infants, and young children requires careful consideration, particularly when the intervention involves injections. Injections cause pain, and researchers must account for this when designing studies with placebo injections (i.e, injecting an inactive substance) in the control group. Subjecting infants to unnecessary pain is ethically **unacceptable**.[7] When placebo injections are necessary, pain mitigation strategies such as topical analgesics (e.g., skin-numbing creams) should be implemented.

*Discover three alternatives that can help minimize or avoid the use of painful placebos in neonatal research, while still preserving study integrity.*

**Alternative 1**

**"Sham" Injections**

**"Sham" injections** can serve as an alternative placebo approach. For instance, a trial nurse might briefly take the infant out of sight, apply a bandage where an injection would have been, and return the child to maintain the appearance of an injection. This method can help minimize measurement bias for the trial team and decision maker(s) while avoiding unnecessary pain for the infant.

**Alternative 2**

**Design Choice**

Risks associated with placebo use can be minimized through design choices. For instance, in cases where delaying treatment is not harmful, a trial might use a "waitlist" control group. In this design, all participants eventually receive the active intervention, but one group starts with a placebo for a set period before transitioning to the active treatment.

**Alternative 3**

**Adaptive Trial Design**

Adaptive trial designs can help reduce placebo use. These designs allow for adjustments during the trial, such as randomizing more participants into treatment arms, showing promising results based on early data. This approach helps limit exposure to a placebo while still gathering robust evidence.

*For your interest, review the list of resources available for furthering your research on the ethics of placebo trials.*

**Clinical Trial Design Course**

**The Ethics of Placebo-Controlled Trials: Methodological Justifications**

**Time to Stop Placebo Injections in Neonatal Research Projects**

**Non-Static Framework for Understanding Adaptive Designs: An Ethical Justification in Paediatric Trials**

Recall the sleep and memory study you've applied throughout Sections 01 and 02. You previously identified this study as observational, but as you've just learned, there are different types of observational designs, each with its own procedures depending on the study's objective.

*Answer the questions using what you have learned in this section.*

**Question 1 of 1:** For the sleep and memory study you've been working on, what type of observational study design best describes the planned data collection approach?

a) Case study design
b) Retrospective design
c) Prospective design

**Feedback:**

**The correct answer is c)**

This is a prospective study because it involves collecting new data. Unlike retrospective studies, which analyze existing data from the past, this design observes participants in real time. It is also not a case study, as it focuses on a broader group rather than an individual case.

In Section 04, you will return to the sleep and memory study one final time, this time with a focus on defining and measuring study outcomes.

By the end of the next section, you will bring everything together to complete your study design, applying all that you've learned throughout the module to create a well-rounded child health research study.

In this section, you explored how designing studies for the paediatric population requires careful consideration. You learned about interventions and comparators, and the importance of tailoring

study design to account for age and developmental differences across groups. Providing child-friendly supports is essential for maximum safety and effectiveness. When selecting a comparator, criteria in paediatric trials must be meaningful, ethical, and aligned with current standards and best practices, particularly when considering the use of placebo injections in neonates.

**Page Links:**

https://pubmed.ncbi.nlm.nih.gov/40294521/

https://www.bmj.com/content/348/bmj.g1687

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https://linkinghub.elsevier.com/retrieve/pii/S1551714413001547

https://neonatalresearch.org/2022/10/27/time-to-stop-placebo-injections-in-neonatal-research-projects/

https://jme.bmj.com/content/48/11/825

**Continue to Section 04**

## SECTION 04: SELECTING AND MEASURING STUDY OUTCOMES

In this section, you will first learn how study outcomes are categorized. Then, you will explore how outcomes for child research studies can be selected, including choosing a core outcome set. Next, you will learn how study outcomes are measured and what practical and ethical considerations to account for when making measurement decisions during study design. Lastly, you will be introduced to the importance of communicating study outcomes to participants and their families.

**Study Outcomes in Child Health Research**

Outcomes are what are measured in a child health research study. In clinical trials, they are sometimes called the trial's "endpoints." The measured outcomes are what is going to answer the research question by providing the necessary data. Many different types of outcomes can be measured.

Some examples of study outcomes include:

- Treatment effectiveness (e.g., symptom improvement, such as reduced pain or fever).
- Growth and development (e.g., weight gain and reaching developmental milestones).
- Functional abilities (e.g., ability to attend school).

Outcomes can be categorized as either **single** or **composite**.

*Learn more about each type of outcome.*

**Single Outcome**

A single outcome measures one specific result, such as death. This approach is clear and easy to interpret because it avoids confusion about what is being measured.

**Composite Outcome**

A composite outcome combines multiple results, such as the number of participants who die or have a nonfatal stroke. While this approach can improve statistical efficiency by increasing the number of events, it comes with challenges. The combined outcomes must move in the same direction (e.g., both improve or worsen together), and differences in clinical importance or unexpected responses can make results harder to interpret.

Different types of outcomes can be collected, and there are various methods to collect and protect participant data. It is important to decide the best way to collect the outcome data and plan for the relevant steps to protect participant data during the study design phase.

**Note:** Refer to the *Research Data* module to learn more about how to collect and protect participants' data.

Deciding what to measure in a child health research study is a key study decision. The selected outcomes should:

- Directly address the study's research question.

- Be useful and meaningful to those impacted by the study and its findings (e.g., children, their decision maker(s), health professionals, and policymakers).
- Be able to be measured safely, accurately, and practically in children.

Deciding what is going to be measured in the study can drive other important design decisions.

*Discover what must be considered when choosing a study outcome measure.*

**Frequency**

Consider **how often** the outcome can and should be measured.

**Roles**

Consider **who** is going to do the measurement and related data collection (e.g., is a nurse necessary or can a decision maker do it?).

**Location**

Consider **where** the outcome can be measured (e.g., it is possible to measure it at home, or does it require a hospital visit?).

When researching the same health condition, many child health research studies can measure and report on different outcomes. This is a problem because it makes it difficult to compare or combine findings from child health research studies conducted by different people in different places. A **core outcome set** can be a helpful way to ensure the outcomes in a child health research study are both meaningful and practical, and that the results of a study can be combined or compared with other similar studies occurring in children.

*Explore the definition of a core outcome set.*

**Core Outcome Set**

A core outcome set is a minimum set of outcomes that should be measured and reported in all clinical trials or other types of research studies undertaken in a specific health condition.

*Watch the video to learn more about core outcome sets (3:23).*

As you watch, note how core outcome sets are collaboratively developed with input from patients, researchers, and healthcare professionals.

**Start of Video Transcript**

*Hello, I'm Laura. As a patient with asthma, I'm interested in health research. I think research is the best way to help improve treatments and develop new and better ones. That's why I'm keen to help researchers design studies that make a difference to people's lives. Researchers develop and test treatments to make sure they work and are safe. To do this, they look at the effects treatments have on patients by measuring outcomes. For example, last year I took part in Dr. Smith's study that tested a new asthma treatment. Dr. Smith measured an outcome of how often I used my reliever inhaler before and after taking the new treatment.*

*But there is a problem, because the same outcomes aren't always measured for the same health condition, and different researchers throughout the world often measure different outcomes. So, for example, Dr. Lopez in Spain might be looking at the number of times patients have to go into hospital with their asthma as an outcome, while Dr. Bedi in India may decide to measure nighttime wheeze. When these asthma treatment studies are finished they can't be compared or combined, because they've used different outcomes. It's then difficult to know which treatment is best. It's a bit like trying to compare apples with bananas. This isn't just a challenge for asthma, but for many different health conditions affecting patients throughout the world.*

*So, how can we solve this problem? It's simple, really. If all studies in a particular health condition measure the same set of outcomes, they can be easily compared and combined. Once agreed, this set of outcomes is called a 'core outcome set.' But deciding on which outcomes are core requires discussions and input from the right people. The core outcomes need to be relevant to patients, like me, health professionals, and researchers, so that we can design studies that are more relevant to patients. People working on core outcome sets need to make sure that patients and health professionals both have their say. To do this, they often use 'consensus methods.' Consensus methods include surveys, meetings, and discussions where everybody's views can be heard and taken into account.*

When a core outcome set has been agreed, the hope is that researchers will use it in all studies for that health condition. We'll be able to learn more about the condition because findings can be compared and combined. In the long run, this means treatments that work will be available to patients more quickly.

**End of Video Transcript**


*COMET Initiative logo.*[8]

The Core Outcome Measures in Effectiveness Trials (COMET) Initiative's website provides a publicly available, free-to-use, searchable repository of core outcomes sets. It is kept updated through regular systematic review updates, citation alerts, and notifications from core outcome set developers. There are many paediatric core outcome sets available, and more are being developed all the time.

*For your interest, search for core outcome sets using COMET's advanced search tool.*

**COMET Initiative - Advanced Search**

**Measuring Study Outcomes**

Once the study outcomes are chosen, the related study design decision is choosing how the outcomes should be measured. Different ways of obtaining measurements may include, for example:

- Clinical rating scales.
- Questionnaires.
- Laboratory tests.
- Physical exams.
- Observations of an image or behaviour.
- Responses to a single question.

For child health research studies, it is essential that the outcomes are measured in a way that is age-appropriate, fit-for-purpose, and minimizes burden on children and their decision maker(s) as much as possible. For example, if it is a study questionnaire that children will be completing, it should be easily understandable by a child, capture information that is important and relevant to the child's age and condition, and be as brief as possible.

Measuring and comparing study outcomes in child health research can have unique challenges compared with adult studies. There is developmental variability among children, which can affect the applicability and accuracy of assessment tools. Generally, children as young as six years old can reliably complete some outcome measures. However, in some cases, obtaining accurate data can be complicated by children's limited ability to articulate symptoms or experiences. Thus, different measurement tools might be needed to accurately measure the same outcome in different ages.

*Learn about some additional practical and ethical considerations when making measurement decisions during the design of child health research studies.*

**Consideration 1**

**Risks and Burdens**

When considering how outcomes should be measured, you should evaluate the potential risk and burden of measuring the outcome. For example, if the outcome is a lab value, how often does blood work need to be drawn, and how much distress and inconvenience will this cause the study participants and their decision maker(s)?

**Consideration 2**

**Scheduling**

You should ask yourself, "How often does the outcome need to be measured?" and "How flexible is the timing of measurement?" For example, families have busy schedules and requirements for rigid daily measurements may be difficult for them to accommodate.

**Consideration 3**

**Costs**

Some outcome measurement tools can be costly (e.g., licensed questionnaires versus those that are freely and publicly available), so budgets should be considered when making a measurement decision.

**Consideration 4**

**Translations**

To support effective communication, consider whether translations are needed and available for the study population(s) the research is designed to serve.

**Consideration 5**

**Sharing Results**

Assess what, if any, information from the results will be sharable and reportable to participants. Some families may be eager to know the results of the research study test results, for example, neurocognitive testing like intelligence quotient (IQ) results or genetic test results. It is important to be transparent about what information can and cannot be shared as part of the research study back to the participant and their families. Best practices should be followed when available and approved by the local REB.

When available, core outcome sets can offer valuable guidance on selecting appropriate measurement methods and should be consulted during the study design process.

For some outcomes, a critical design decision is selecting the most appropriate measurement tool when multiple options are available. For instance, a review of outcome measures in adolescent depression trials identified 19 different tools used to assess depression symptom severity.[9]

In other cases, the key decision might involve determining who will provide the data for measurement or whether multiple sources should be used. For example, some rating scales for ADHD have decision maker(s)-report, teacher-report, and youth-report versions, which can yield different results depending on the respondent.

In addition to consulting with patient partners, clinicians, and experts in measurement science, there are various tips and resources that can help guide measurement selection.

*For your interest, explore these resources.*

**COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN)**

COSMIN provides freely accessible tools and resources to guide the selection of outcome measurement instruments.

**Patient-Reported Outcomes Measurement Information System (PROMIS)**

PROMIS has developed freely available paediatric measures for functioning, symptoms, behaviours, and feelings that can be completed by children or decision maker(s), depending on their age.

**Food and Drug Administration (FDA) Clinical Outcome Assessment Compendium**

The FDA has a database of what they consider "qualified" outcomes for use in drug trials.

**SPIRIT-Outcomes**

SPIRIT-Outcomes has outcome-specific considerations that may be helpful when developing a study protocol.

**Consolidated Standards of Reporting Trials (CONSORT) Outcomes**

CONSORT-Outcomes includes guidelines for Reporting Outcomes when publishing trial results.

**Communicating Study Outcomes**

Communicating study outcomes to the participants involved is a key part of showing appreciation for their contribution. Participants and their families have often given their time and data, so it is important they are informed about what was learned.

*Learn how to communicate study findings.*

**How to Communicate Study Findings**

Communicating the study outcomes should be done in clear, plain language, avoiding technical terms, and should explain the study's results, what they mean, and how they might be used in the future. It is also important to be honest about any limitations or unexpected findings.

Sharing results can help build trust in the research process and encourage participation in future studies. For families with children with chronic or long-term health conditions, sharing the results of the study may be an important step for them in their health care journey.

You've now explored how outcomes are selected, categorized, measured, and communicated in child health research. Return to the sleep and memory study one final time to consider what outcome(s) should be measured and how they might be assessed.

Recall the study objective: To examine the relationship between natural sleep patterns and memory performance in typically developing children aged 9 - 12 years who have no history of diagnosed sleep or neurodevelopmental disorders.

*Answer the question using what you've learned throughout this section.*

**Question 1 of 1:** Which of the following would be appropriate study outcome measures for this study? *Select all that apply.*

a) Hours of sleep recorded over a two-week period using a wearable sleep tracker
b) Decision-maker-reported questionnaire about changes in the child's mood and behaviour since starting the study
c) Scores on a standardized, age-appropriate memory test
d) Number of medical appointments attended in the past year

**Feedback:**

**The correct answers are a) and c)**

Hours of sleep recorded using a wearable tracker and scores on a standardized memory test are appropriate outcome measures because they directly align with the study's objective and can be reliably collected in school-aged children.

A guardian-reported questionnaire about mood and behaviour may provide a helpful background, but does not directly assess memory performance.

The number of medical appointments attended in the past year is unrelated to the research question and would not contribute meaningful data to answer it.

You have now completed the module and applied all key concepts to design a full, ethically sound child health research study. Well done!

In this section, you learned how to select and measure study outcomes for child health research. You compared the definitions of single and composite outcomes and learned what to consider when selecting an outcome to measure. You were also introduced to core outcome sets as a way to ensure measurable and practical results. Next, you learned how to choose a measurement for the study outcome. You considered some factors that may impact this decision, including: developmental variability, risks, scheduling, cost, translations, and how the data will be shared. Lastly, you learned how to communicate the research outcomes to the participants and their families.

**Page Links:**

https://www.youtube.com/watch?v=g1MZi2mzK1U

https://www.comet-initiative.org/Studies

https://www.cosmin.nl/

https://www.healthmeasures.net/explore-measurement-systems/promis/intro-to-promis

https://www.fda.gov/drugs/development-resources/clinical-outcome-assessment-compendium

https://jamanetwork.com/journals/jama/fullarticle/2799547

https://jamanetwork.com/journals/jama/fullarticle/2799401

**Continue to Conclusion**

## CONCLUSION

This module introduced the key concepts and terms fundamental to child health research design, including various study designs and the critical considerations involved in planning a research study for children. You explored essential design decisions, such as defining inclusion and exclusion criteria, creating inclusive and accessible studies for children and their decision maker(s), and developing study plans and procedures. The module also covered selecting and measuring study outcomes, as well as considerations around interventions and comparators for clinical trials when applicable.

By emphasizing the importance of ethical and scientifically sound research, this module has equipped you with the knowledge and tools needed to design child health studies that address children's unique health needs. Through balancing practical, scientific, and ethical considerations, you are now empowered to contribute to research that advances paediatric care and ensures equitable benefits for all children.

*Access the references for this module.*

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