Designing Trial Outcomes That Matter

The Rare Disease Clinical Trial Outcome Assessment and Design Template for Patient and Family Partners (ROAD-PF) and Template for Trialists (ROAD-TT)

A toolkit to support researchers and patient and family partners in deciding together what a paediatric rare disease trial should measure, how, and by whom

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About this Toolkit

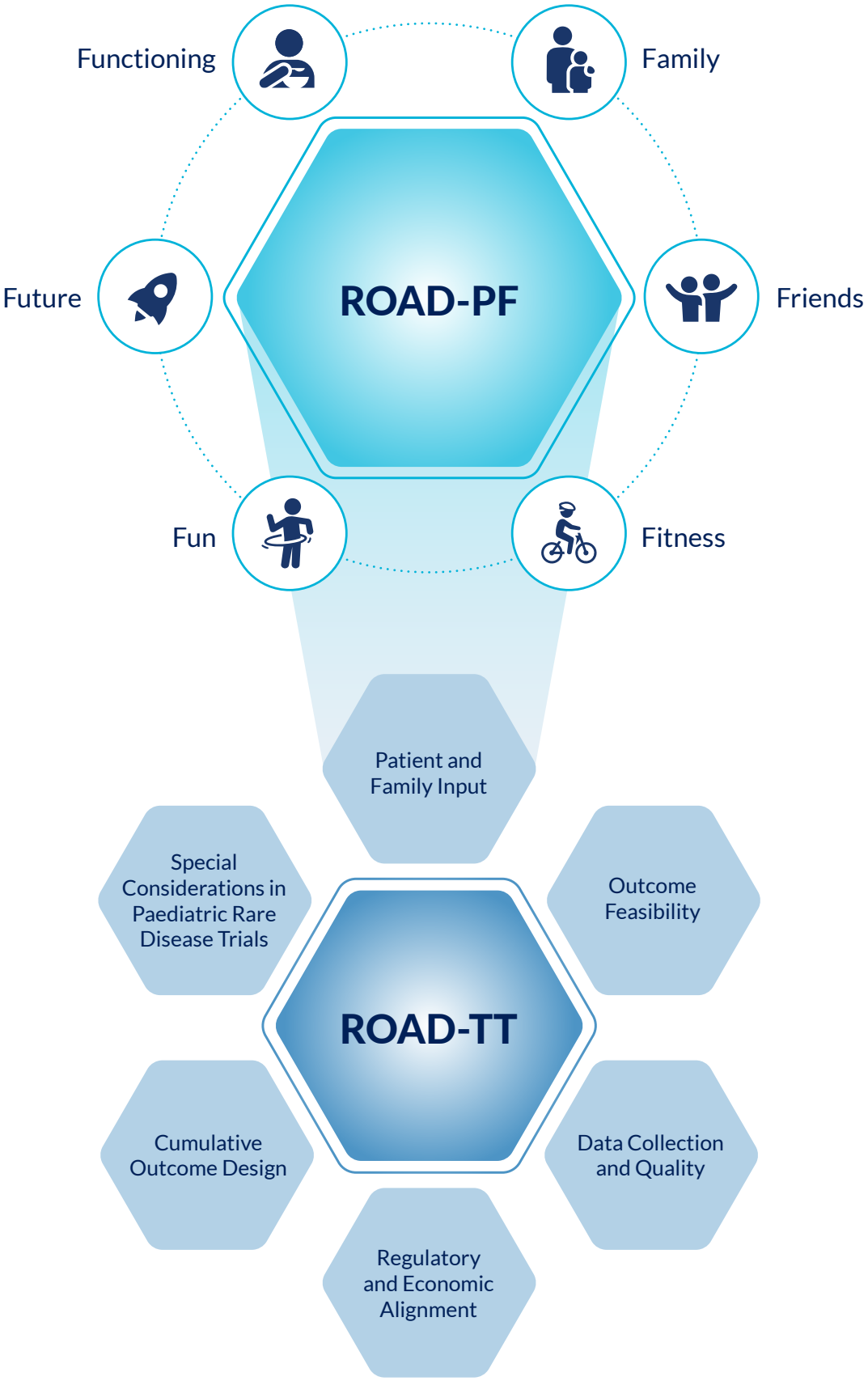
Choosing what outcome(s) a clinical trial will measure is one of the most important decisions in trial design. In paediatric rare diseases, outcomes are often selected based on previous studies or instrument availability rather than what matters most to children and families in their everyday life. This toolkit provides two companion templates that make trial outcome design (i.e., selection, definition, measurement, and reporting) a structured, documented, and collaborative process. This toolkit serves two audiences working together for meeting preparation: patients and their families, and trialists who design and conduct clinical trials. Both templates are designed to be used together in a shared meeting.

- If you're a patient or family partner, start **with Template 1, The Rare Disease Clinical Trial Outcome Assessment and Design Template for Patient and Family Partners (ROAD-PF), page 4:** This template comprises 12 co-design Outcome Design Considerations (ODCs) items across five thematic steps. It is intended to be used with the research team in a trial co-design meeting (refer to the top hexagon in the next page).

- If you're a researcher, **Template 2, The Rare Disease Clinical Trial Outcome Assessment and Design Template for Trialists (ROAD-TT), page 8** is for you: This template contains 23 ODCs across six sections, to be used by the research team during protocol development (refer to the bottom hexagon in the next page).

This toolkit was developed within the Rare Disease Clinical Trial Outcome Assessment and Design (ROAD) project, an initiative of RareKids-CAN: the Paediatric Rare Disease Clinical Trials and Treatment Network (rarekidscan.com). Established in 2024 and funded by the Canadian Institutes of Health Research, RareKids-CAN works to strengthen how children, families, and researchers connect and share information to improve access to clinical trials and treatments for children with rare diseases in Canada. This toolkit contributes to RareKids-CAN's Strategic Priority #1: *strengthening the capacity to develop and conduct high-quality paediatric rare disease clinical trials, including trials of advanced therapy medicinal products such as gene and cell therapies.*

Some terms in the templates are established concepts in clinical trial design. Rather than replace them with simpler wording, we kept these terms and defined them in the Glossary, so that patients, families, and trialists share a common vocabulary. To access the Glossary and learn more about how this toolkit was developed, visit the ROAD webpage: rarekidscan.com/resources/road


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Template 1.

The ROAD Template for Patient and Family Partners (ROAD-PF)

For patient and family partners co-designing trial outcomes with the research team

The ROAD-PF is for patient and family partners to use together with the research team. It guides a structured conversation about trial outcome co-design: what a trial should measure, how, and by whom. It contains 12 co-design items known as outcome design considerations (ODCs), organized across five thematic steps (A–E: What, Who, Meaningful Difference, Qualitative Evidence, Feasibility), grounded in CanChild's F-words for Child Development.

When discussing outcomes, the time between starting a treatment and seeing meaningful changes can vary by condition and intervention. For some conditions, the research team may need to use "proxy" measures. These are indirect signs of change, such as biomarkers, that can be measured before clinical changes are visible. In other conditions, no change in a patient-centred outcome may still be an improvement if the disease usually gets worse over time.

Instructions

1. Complete Steps 1-2 on the next page from the trial protocol. In Step 3, patient and family partners have the opportunity to detail what matters most to them or their child. What are your priorities, hopes, or concerns about what this trial should measure?

2. Review the CanChild F-words preparatory tool from canchild.ca/research-in-practice/f-words-in-childhood-disability (Step 4).

3. Work through the 12 ODCs across the five thematic steps (A–E), adding notes in the last column before, during, or after the discussion (Step 5).

   If you need more space for Notes, create a separate document.

4. After the meeting, record agreed outcomes, outstanding questions, and follow-up actions (Step 6). Keep the completed template with the completed ROAD-TT (page 8) as part of the trial's audit trail of outcome design decisions.

Follow the **6 steps** and make notes below

Trial name: _____ Meeting date: _____

Research team members present: _____

STEP 1 **Write out** trial participant inclusion criteria:
(take from the trial protocol)

STEP 2 **Write out** trial experimental and comparator intervention: (from trial protocol)

STEP 3 **List** trial outcome(s): (already stated in trial protocol)

Patient and family partners: What are your priorities, hopes, or concerns about what this trial should measure?

STEP 4 Review **CanChild's F-words for Child Development: Preparing for Co-designing Outcomes in Paediatric Rare Disease Clinical Trials** to reflect on how the F-words might apply.

STEP 5 Prepare the outcome design considerations (ODCs) before meeting with the research team, using steps A–E on the next pages. Add notes in the last column before, during, or after the discussion.

STEP 6 After the meeting has ended, note down:
A. Agreed outcomes · B. Outstanding questions ·
C. Follow-up actions

Step		
A. What is being measured and how		**F-words / Notes**
1	Identify which trial outcomes go beyond biological or disease-specific measures and capture everyday life. For example, consider whether the outcome measures how a child or adolescent functions, participates, communicates, or feels. This may include communication ability, adaptive behavior, social participation, and caregiver wellbeing. Describe any guiding ideas or frameworks, such as the F-words framework or the ICF, that were used to support this discussion.	☐ Functioning ☐ Fitness ☐ Family ☐ Fun ☐ Friends ☐ Future
2	Clearly describe what each outcome is intended to measure and why it is understandable, age-appropriate, and relevant in paediatric rare disease contexts. If standardized tools are used, explain whether these tools have been tested for the target population. Also explain whether they capture the full range of abilities, including non-verbal communication modalities such as gestures, facial expressions and body language.	☐ Functioning ☐ Fitness ☐ Family ☐ Fun ☐ Friends ☐ Future
B. Who is doing the reporting?		**Notes**
3	Clearly state who is reporting each outcome, such as the child, adolescent, sibling, caregiver, or clinician. State how the outcome will be reported, such as through a verbal report, an observer report, or augmentative and alternative communication. Describe when and how children and adolescents will be supported to self-report.	
4	Describe how different perspectives, such as from children/adolescents, their caregivers, and clinicians, can each provide valuable information. Explain how information from different people can help to build a complete picture of the outcome.	
5	Describe how priorities of patients and families at different points in the disease course are considered. Acknowledge that what matters most can change as a child grows or as a disease progresses.	

C. Meaningful difference		Notes
6	Explain how the selected trial outcomes will help children/adolescents, their caregivers, and clinicians decide whether a treatment is worthwhile.	
7	Define what meaningful change looks like, how it affects daily life, and how this may differ by age, development, condition, and family situation. Consider the time needed between when the intervention is done and when measurable change can be seen. For some conditions, no change months after treatment may be an improvement if the disease usually gets worse over time.	
8	Report whether outcome measurement tools can detect meaningful changes for trial participants at different points in the disease course. Consider floor and ceiling effects: whether the tool can pick up improvements when someone starts with very low or very high scores. For example, communication measures may have floor effects in groups with limited verbal speech. Also explain how baseline scores affect interpretation of change, and whether meaningful score differences or meaningful score regions have been established for the tools used.	
D. Qualitative evidence (e.g., information from interviews, focus groups, observations, or open-ended responses)		**Notes**
9	Describe why qualitative evidence is essential. Discuss how it complements quantitative outcomes, and how it explains why outcomes change or do not change. Describe how this information will be included in the analysis and in knowledge translation.	
E. Feasibility (e.g., it is realistic to complete, can it be done)		**Notes**
10	Identify barriers and decide whether the outcome assessments and schedules are realistic for different family circumstances. Consider the frequency, intensity, and timing of the assessments. Other factors to consider include (a) practical barriers, such as travel, scheduling, and technology; (b) energy and recovery needs such as fatigue and limited daily energy; and (c) equity-related factors such as time, financial resources, mobility, and caregiving responsibilities.	
11	Be explicit about the trade-offs between the information gained and what is required from children/adolescents and families. Consider the total impact and potential challenges over the full length of the trial, including things such as the number of assessments, the time involved, travel, and fatigue.	
12	Make sure that feasibility is built into outcome design from the start, not treated as an afterthought.	

Template 2.

The ROAD Template for Trialists (ROAD-TT)

For researchers and trial teams designing paediatric rare disease trials

The ROAD-TT supports research teams in designing, explaining, and documenting paediatric rare disease trial outcomes during protocol development and facilitates reporting. It aggregates and organizes existing methodological and regulatory guidance for the paediatric rare disease context. It does not introduce new requirements. It is a decision-support template, not a compliance checklist.

The ROAD-TT contains 23 outcome design considerations (ODCs), organized in six sections, to be considered before the trial outcomes are finalized. Ideally, the ROAD-TT is completed alongside the ROAD-PF during a trial co-design meeting with patient and family partners, so partner input can shape decisions.

Instructions

1. Complete the template during protocol development, before outcome selection is finalized.
2. For each item, read the "Consideration" and the "What to record" prompt, then document your team's response in the notes column.
   If you need more space for Notes, create a separate document.
3. ODCs marked ‡ are conditional on the study type, design, or inferential framework. If an item does not apply to your trial, mark it "N/A" and briefly explain why.
4. ODCs marked * flag considerations where the anticipated number of participants directly limits the outcome measures and analyses available. Report the assumed number and justify the selection.
5. Where partner input informed your decisions, cross-reference the completed ROAD-PF Template.
6. Retain the completed template with the trial protocol as a documented record of outcome design decisions.

Section 1. Special Considerations in Paediatric Rare Disease Trials (4 items)

Item	Consideration	What to record	Notes
1.1*	Patient heterogeneity and expected trajectories in (a) natural history and (b) developmental stage to inform outcome selection and timing of measurement.	Describe how patient heterogeneity has been considered in (1) outcome selection and (2) design or analytic strategies (e.g., repeated-measures, stratification, covariate adjustment, individualized responder definitions). Specify how heterogeneity has been reflected in each attribute of the estimand(s).	☐ Addressed ☐ N/A
1.2	Age- and (neuro)developmental stage appropriateness of each outcome and measurement instrument.	Describe how the outcome and measurement instrument are age- and developmentally appropriate for the target paediatric population. Provide the rationale for selecting a paediatric-specific or an (adapted) adult measurement instrument.	☐ Addressed ☐ N/A
1.3	Floor and ceiling effects of the outcome measurement instrument in the target paediatric population.	Specify the score metric, and describe the expected impact of floor and ceiling effects, both on baseline scores and the detection of meaningful change. If applicable, provide implications for trial eligibility or planned mitigation strategies.	☐ Addressed ☐ N/A
1.4‡	"Disease stabilization" as a meaningful outcome in progressive disease, and how stabilization will be measured and interpreted.	Describe and justify how stabilization is defined and measured, including the quantitative criteria and instruments used. Detail the natural history data used for contextualization, and any patient input or regulatory precedent supporting this choice.	☐ Addressed ☐ N/A

‡ Indicates ODCs that are conditional on the study type, design, or inferential framework. If an item does not apply to your trial, mark it "N/A" and briefly explain why.

* Indicates ODCs where the anticipated number of participants directly limits the outcome measures and analyses available. Report the assumed number and justify the selection.



Section 2. Patient and Family Input (4 items)

Item	Consideration	What to record	Response/Notes
2.1	Involving patients, caregivers, and advocacy groups in designing the trial outcomes.	Describe how patients, caregivers, and/or advocacy groups are involved in outcome design (i.e., selection, definition, measurement, and reporting). Prospectively document the impact of their involvement, to be reported in accordance with an established engagement reporting guideline (e.g., GRIPP2).	☐ Addressed ☐ N/A
2.1a	Timing of initiation to ensure their input occurs early enough to influence outcome selection.	Describe when and how patient and family engagement (PFE) informed the choice of outcome domains.	☐ Addressed ☐ N/A
2.1b	The characteristics of engaged patients and families, including diversity of disease severity, age, socioeconomic status, and geographic/cultural background.	Describe how the diversity of engaged patients and families was considered (or, why it was not) and whether the diversity goals were achieved.	☐ Addressed ☐ N/A
2.2	Conceptual or theoretical framework(s) that guide child-specific patient-centred outcome selection.	Justify the selection of patient-centred outcomes and state PRO-specific objectives and hypotheses (e.g., ICF framework, CanChild's F-word approach). Describe which of the 12 items in the five ROAD-PF Template steps (A–E) that patient partners prepared were discussed. Describe and justify the reporter for each outcome. Report any adaptations to be used to enable child self-report.	☐ Addressed ☐ N/A
2.3	Acceptability of selected outcome measures and assessment schedules for patients and families.	Describe how measures and assessment schedules are acceptable for trial participants and their families. Address how respondent fear, pain, and distress will be assessed and minimized.	☐ Addressed ☐ N/A
2.4	Cultural appropriateness, accessibility, and inclusiveness of outcome measures.	Describe how outcome measures are culturally appropriate, accessible, and inclusive. Report the use of validated translations, accessibility accommodations, and any cultural adaptations made.	☐ Addressed ☐ N/A

Section 3. Outcome Feasibility (2 items)

Item	Consideration	What to record	Response/Notes
3.1	Number of selected outcome measures and timing of assessment schedules.	Justify the number of outcomes and the timing and clustering of assessments given the constraints of the rare disease trial. Describe how measures and assessment schedules are (made) feasible and acceptable for trial participants and their families.	☐ Addressed ☐ N/A
3.2	Outcome-related retention and follow-up plan, and missing data handling.	Describe plans for outcome-related retention and follow-up. Document which outcomes will be collected after treatment discontinuation – for any reason – during the trial. Describe how missing outcome data will be handled analytically.	☐ Addressed ☐ N/A

Section 4. Data Collection and Quality (3 items)

Item	Consideration	What to record	Response/Notes
4.1	Suitability of the setting in which the outcome is assessed.	Justify the suitability of the setting(s) in which each outcome has been assessed. Describe which assessments, if any, have been conducted remotely or through decentralized trial methods, and how.	☐ Addressed ☐ N/A
4.2‡	Integration, reconciliation, or analysis of data from multiple reporters, and necessary training and certification for outcome assessors/reporters.	Describe the reporter(s) for each outcome and the training provided to outcome assessors/reporters. Give the rationale and the approaches used to prevent, reconcile, and analyse discrepancies between reporters.	☐ Addressed ☐ N/A
4.3‡	Standardization procedures for outcome assessment across study sites.	Describe the standardization procedures implemented across sites, including assessor training, certification, and monitoring for inter-site variability.	☐ Addressed ☐ N/A

‡ Indicates ODCs that are conditional on the study type, design, or inferential framework. If an item does not apply to your trial, mark it "N/A" and briefly explain why.

Section 5. Regulatory and Economic Alignment (5 items) ‡

Item	Consideration	What to record	Response/Notes
5.1‡	Regulatory frameworks that inform: 5.1a. Outcome selection (i.e., clinical outcome assessments (COAs)); 5.1b. Meaningful Aspect of Health (MAH); 5.1c. Concept of Interest (COI) of COA(s); 5.1d. Context of Use (COU) of COA(s).	Describe which applicable regulatory and research ethics frameworks have been identified and how they informed outcome selection, the MAH, COI, and the CoU of each COA (from FDA *Patient-Focused Drug Development (PFDD) Guidance 3*).	☐ Addressed ☐ N/A
5.2‡	Trial outcomes meet regulatory expectations.	Describe how key outcomes have been designed to meet regulatory expectations (e.g., FDA *Patient-Focused Drug Development (PFDD) Guidance 3* (Section IV, Table 2): (1) justification of the COA type, (2) content coverage, (3) administration, (4) comprehension, (5) scoring method, (6) interfering influences, (7) reliability, and (8) correspondence to the meaningful aspect of health).	☐ Addressed ☐ N/A
5.3‡	Cross-jurisdictional regulatory inconsistencies in outcome requirements.	Describe all relevant cross-jurisdictional (e.g., FDA vs. EMA vs. Health Canada) inconsistencies in outcome requirements, and how these have been dealt with. Report whether any regulatory engagement or scientific advice has been obtained, and the strategies used to align outcome design across regulatory bodies.	☐ Addressed ☐ N/A
5.4‡	Strategies to gain regulatory acceptance for novel, unvalidated, or disease-specific outcome measures.	Describe efforts made and results to gain regulatory acceptance of any novel, unvalidated, or disease-specific outcome measures. Detail whether and how any validation evidence will be generated.	☐ Addressed ☐ N/A
5.5‡	Economic outcomes.	Describe any economic and health-related utility (e.g., quality of life) outcomes that are collected. Explain which outcome measurement instruments are validated for the study population. Describe what healthcare resource-use data will be collected, and how.	☐ Addressed ☐ N/Aw

‡ Indicates ODCs that are conditional on the study type, design, or inferential framework. If an item does not apply to your trial, mark it "N/A" and briefly explain why.

Section 6. Cumulative Outcome Design (5 items)

Item	Consideration	What to record	Response/Notes
6.1	Choice of Clinical Outcome Assessment (COA) type(s) considering how the outcome(s) address the research objective(s).	Justify the selection of each trial outcome, its COA type and scores, and reporter for the domain of interest. Describe how outcome results will be interpreted in the context of the research objectives.	☐ Addressed ☐ N/A
6.2	Core elements of each defined outcome.	Describe each outcome's core elements: 6.2a. outcome domain; 6.2b. specific instrument; 6.2c. specific metric; 6.2d. cutoff (if applicable); 6.2e. variable type; 6.2f. time point(s) of assessment.	☐ Addressed ☐ N/A
6.3*	Validity, reliability, and responsiveness of selected outcome measurement instruments for the target paediatric rare disease population.	Justify the selection and appropriateness of each outcome measurement instrument in context of its measurement properties (validity, reliability, responsiveness). Describe any adaptations made, with rationale. Detail gaps in psychometric evidence.	☐ Addressed ☐ N/A
6.4	Meaningful-change threshold for each outcome.	Justify the meaningful-change threshold for each outcome. If pre-specification is not possible, detail post-hoc approaches that will inform interpretation.	☐ Addressed ☐ N/A
6.5	Core Outcome Sets.	Describe whether a Core Outcome Set (COS) exists and has been used. Where none exists, whether pre-established disease-specific measures have been adopted. Where co-primary outcomes are designated, describe the multiplicity strategy or state explicitly that no adjustment has been planned.	☐ Addressed ☐ N/A

* Indicates ODCs where the anticipated number of participants directly limits the outcome measures and analyses available. Report the assumed number and justify the selection.

Considerations

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