Key learnings from Rare Disease Project ECHO®

Series 4, Session 5
Unlocking Tomorrow's Treatments Today: Navigating Clinical Trials and New Therapies for Your Rare Disease Patients
9 December 2025

Presentation 1: Unlocking Tomorrow's Treatments Today

Speaker: Dr Michelle Lorentzos (Paediatric Neurologist and Advanced Therapeutics Medical Lead, Sydney Children's Hospitals Network)

Dr Lorentzos draws on her experience of leading neuromuscular clinical services and clinical trials to explore the practical and ethical complexities clinicians and families face when considering participation in clinical trials.

Why clinical trials are complex for rare disease patients

- New therapies typically take 17 years to move from concept to clinical availability. This timeline feels untenable for families facing progressive conditions.
- Rare diseases magnify this challenge as patient cohorts are small and traditional trial models often don't align with the urgency of treatment for conditions.
- Clinical trials are **designed to answer questions about safety and efficacy**, not to guarantee benefit for an individual child.
- Families often equate trial participation with treatment, but in reality, it offers access to **a question, not a cure**.

Uncertainty and emotional burden

"We tell people all the time, don't make decisions when you're stressed. And then we diagnose children with catastrophic conditions and ask them to decide about a trial in a tiny window."

- Trials involve lots of unknowns: dosing regimens, eligibility criteria, and even trial continuity can change abruptly.
- Decision-making occurs during periods of grief, stress, and urgency, often within narrow time windows. Families must weigh potential benefits against risks while coping with diagnosis shock.
- Participation can disrupt daily life, strain family dynamics, and create isolation (e.g., restrictions on sharing trial involvement publicly).
- Dr Lorentzos advocated for psychosocial support alongside trial enrolment, including social work, psychology, and screening for family stress.

Choosing or declining trials

Motivations for participation	Reasons for declining
Access to investigational therapies unavailable elsewhere.	Risks and side effects.
Desire for close monitoring and contribution to knowledge that may help future patients	Burdensome schedules (e.g., weekly hospital infusions).
	Randomization or placebo requirements.
	Ethical discomfort with enrolling a child in an experimental process.

Emerging therapies and shifting attitudes
Advanced therapies such as **gene replacement therapy** and **CRISPR gene editing** are groundbreaking but highly complex interventions. These treatments aim to address the root cause of genetic conditions rather than just symptoms, which is exciting for rare disease patients. However, there are several critical considerations:

- **Irreversible nature:** Once a gene therapy is delivered, it permanently alters the patient's genetic footprint. This means:
    - If the therapy doesn't work, there's no second chance.
    - Patients may become ineligible for future trials using similar technology.
- **One-time opportunity:** Because the body develops antibodies to the viral vector used for delivery, most current gene therapies can only be administered once.
- **High-risk process:** These therapies often require **high-dose immunosuppression**, introducing additional risks and side effects.
- **Impact on future options:** Participation in such a therapy may exclude patients from other clinical trials later.

Practical Advice for Clinicians
- Encourage families to check eligibility criteria early, as age, comorbidities, and concomitant medications often exclude participation.
- Direct families to clinicaltrials.gov and patient advocacy networks for up-to-date trial information.
- Emphasise gold-standard care while waiting, as optimising health improves trial eligibility.
- Consider Natural History studies where feasible; they strengthen future trial design but must include psychological support for families receiving sensitive findings.

"Please allow my child the dignity of risk" – a powerful reminder that families want to be partners in decision-making, not passive recipients of paternalistic caution.

Discussion
The interactive discussion explored real-world dilemmas clinicians face when supporting families through trial decisions.

Case scenario: A child with a progressive neuromuscular condition whose parents were weighing participation in a high-burden trial requiring weekly infusions and potential placebo allocation.

Group reflections:

- **Primary care perspective**: GPs highlighted the challenge of counselling families when trial details are opaque and rapidly changing.
- **Navigation gaps**: Participants stressed the need for a centralised navigator role to streamline access to accurate trial information and reduce reliance on ad hoc clinician knowledge.
- **Ethical tension**: Clinicians debated balancing protection from harm with respecting family autonomy and risk appetite.
- **Practical strategies**: Suggestions included connecting families to advocacy groups, leveraging registries, and ensuring psychosocial supports are embedded in trial design.
- The discussion reinforced that shared decision-making, transparency, and timely communication are critical to reducing distress and empowering families.

Further resources

Links to supportive organisations and resources:

- ClinicalTrials.gov
- Rare Voices Australia – RARE Portal

Educational resources to support timely diagnosis from the RArEST project including:

- National Recommendations for Rare Disease Health Care: recommendation 2 which includes Red Flags for Rare Disease and AI assisted diagnostic platforms
- Rare Disease 101 Australia, an RACGP accredited e learning module
- RACGP check on Rare Diseases [Unit 607]

Read previous summaries of presentations from the Rare Disease Project ECHO series here.

Send us questions, discuss presenting a case, or let us know your go-to resources by emailing us at RareDiseasesNSW@unsw.edu.au.