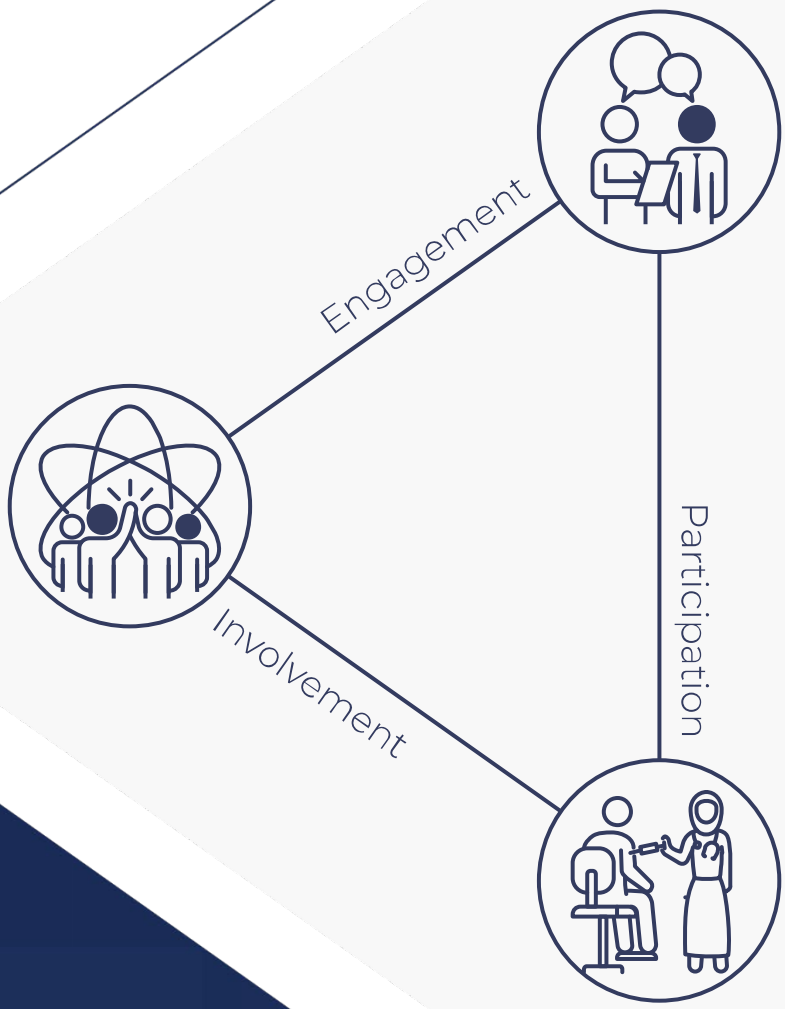
Australian Clinical Trials Alliance



Information and resources on Adaptive and Platform Trials for consumer representatives

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Healthcare and research are constantly evolving.

In recent years new clinical trial designs have been developed so that trials provide greater benefits to both researchers and those people who participate in the trial.

Adaptive Trials are one group of Innovative Trial Designs that allow for greater flexibility in the way trials are conducted.

We have prepared this information sheet to describe what Adaptive Trials are and to explain why these may be more attractive to consumers.

Traditional trial designs

Traditional clinical trials are an important part of medical research. They help researchers figure out if new treatments work and if they are safe.

One common traditional clinical trial design is called a Randomized Controlled Trial (RCT). In these trials, people are randomly put into groups: one group gets the new treatment, and the other gets a dummy treatment (known as placebo) or nothing. This is important when considering how well a new treatment works, as without treatment, the two groups should on average be the same. This means that any differences seen between the groups are because of the treatment, not other things.

In a traditional randomised controlled trial, the design of the trial is set upfront including the details of the treatment and the control, how participants will be randomised between the groups and the number of participants that will be recruited into the trial. Once the trial begins, no changes can be made, which is why this trial type is also known as a fixed trial design.

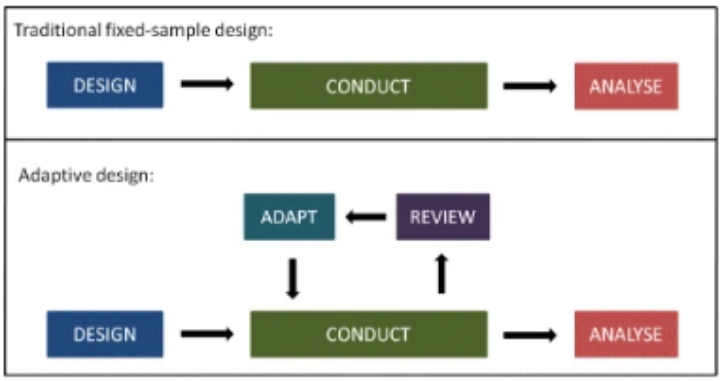
These types of trials are important, but they can be slow and not always answer all the questions we have about treatments. Fortunately, there are now new ways to design clinical trials. Adaptive Trials can be more efficient, involving more trial participants and providing results more quickly. This helps improve healthcare for everyone.

What are Adaptive Trials?

Adaptive Trials refer to trial designs that can be changed (ie adapted) while the trial is happening. While the trial is being conducted, data is reviewed, and the trial adapted as appropriate (see Figure 1).

For example, depending on the data collected, researchers can stop before reaching the planned sample size, change the number of participants they aim to recruit, change how participants are randomised into the groups, or even drop or add intervention arms (see Figure 2). This flexibility helps in finding the best treatment more quickly and often requires fewer participants, making the process more efficient.

Figure 1:



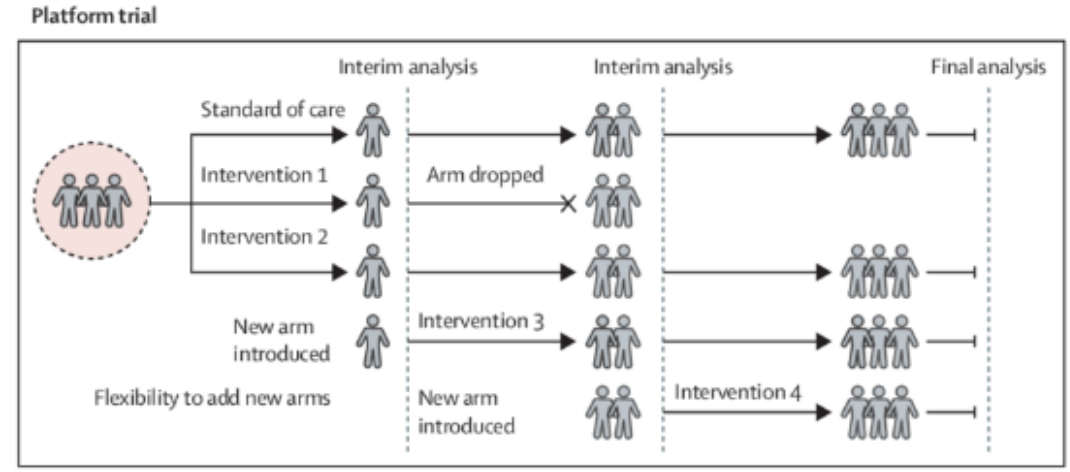
Schematic of a traditional clinical trial design with fixed sample size, and an adaptive design with pre-specified review(s) and adaptation(s)

Pallmann, P., Bedding, A.W., Choodari-Oskooei, B. *et al.* Adaptive designs in clinical trials: why use them, and how to run and report them. *BMC Med* **16**, 29 (2018). https://doi.org/10.1186/s12916-018-1017-7

What are Adaptive Platform Trials?

Adaptive Platform Trials take the concept of Adaptive Trials a step further by including multiple treatments for the same disease at the same time within a single trial. They also allow researchers to remove treatments or add new treatments as they become available without starting a new trial each time. Figure 2 outlines how data is analysed at different timepoints, and based on the result, certain treatment arms may be dropped (discontinued) or a new treatment arm may be added, all while the trial is in progress.

Figure 2:



Park JJH, Ford N, Xavier D, Ashorn P, Grais RF, Bhutta ZA, Goossens H, Thorlund K, Socias ME, Mills EJ. Randomised trials at the level of the individual. Lancet Glob Health. 2021 May;9(5):e691-e700. doi: 10.1016/S2214-109X(20)30540-4.

Key features of an Adaptive Platform Trial

- **Multiple Treatments**: an Adaptive Platform Trial can include several different treatments at the same time to see which works best. It allows researchers to answer more than one question at a time.
- **Flexible Design**: an Adaptive Platform Trial can adapt based on the data of the trial as it progresses, such as adding new treatments or stopping those that don't work well, adjusting the number of participants, and so on.
- **Continuous Learning**: the researchers in the Adaptive Platform Trial regularly review the data during the trial to make informed decisions quickly.
- **Patient-Centered**: Aims to find effective treatments faster, benefiting patients sooner.
- **Resource-Efficient**: Saves time and resources by evaluating multiple treatments together rather than in separate trials.
- **More complex**. Adaptive platform trials are not needed nor the best design for some questions. They are more complex to design and conduct than traditional clinical trials.

Consumer involvement in Adaptive Trials

As with any trial, it is critical to engage consumers throughout the entire process of an Adaptive Trial. Consumers can provide valuable input into concept development and trial protocol design to ensure the trial addresses issues and outcomes that matter most to patients, and that the procedures are acceptable to consumers. This will increase participant willingness and compliance, and it builds trust through transparency and inclusivity from the start. Due to the complexity of Adaptive Trials, consumer involvement may have additional challenges, however is particularly important.

Benefits of consumer involvement in Adaptive Trial Designs

- **Patient-centred approach:** Consumer involvement ensures that adaptive trial designs are shaped by the real needs and preferences of patients, carers, communities, and the people using healthcare services. This leads to trials that are more relevant and meaningful.
- **Relevance**: Creates solutions that truly meet the needs and preferences of consumers.
- **Effectiveness**: Improves the usefulness and impact of health programs and technologies.
- **User-Friendliness**: Ensures that health interventions are easy to use and understand.
- **Engagement**: Involves patients and caregivers, making them feel valued and heard.
- **Innovation**: Brings together diverse perspectives, leading to creative and practical solutions.
- **Trust**: Builds trust between patients, caregivers, and healthcare providers.
- **Satisfaction**: Increases satisfaction with health services and products.
- **Better Outcomes**: Leads to improved health outcomes by addressing real-world needs and priorities.

For more information, such as models of consumer involvement and levels of participation, please visit the ACTA | CT:IQ Consumer Involvement and Engagement Toolkit

Common terms in Adaptive Trials

Adaptive Trial	A type of clinical trial that can change as it progresses based on the data collected within the trial.
Adaptive Platform Trial	A type of Adaptive Trial that tests multiple treatments at once and can add new treatments as they become available.
Consumer	Patients and potential patients, carers, and people who use health care services.
Control Group	A group of people in a clinical trial who receive the control treatment, this might be standard of care, a placebo or no treatment. This group is used as a comparison to see how well the new treatments work.
Efficacy	How well a treatment works if taken
Endpoint	The main outcome that the trial is measuring to see if the treatment works.
Interim Analysis	An analysis of the trial data during the conduct of the trial. The results from these analyses are used to inform the adaptations (changes) in the trial design
Randomisation	The process of assigning people by chance to different groups in a trial. This helps ensure the differences between the groups are due to only the treatment they are randomised to.
Study protocol	A document that outlines the plan for the trial, including the research question, the rational for the question, the treatments being considered and details about how the trial will be conducted. For adaptive trials, this should also include details about the adaptations/changes that may be made to the trial as the trial continues
Treatment arm	A group of participants in the trial that were randomly allocated to receive a specific treatment.
Placebo	A harmless, inactive treatment sometimes used in a trial, so that participants cannot tell if they have been allocated to the treatment or the control group.

Additional resources for consumer involvement in research

ACTA | CT:IQ
Consumer Involvement & Engagement Toolkit

AccessCR
Consumer Involvement Resources – AccessCR

Adaptive Health Intelligence Website
What is an Adaptive Clinical trial/ Tom Snelling
What are the Benefits of Adaptive Clinical Trials? Steve Webb & Tom Snelling

Australian Health Research Alliance
Consumer and Community Initative (CCI)

1. Development of a handbook with practical steps to guide stakeholders and organisations in embedding CCI in health and medical research-"*Involving Consumers in Health and Medical Research*-A practical handbook for organisations, researchers, consumers and funders".
   (Lead: Western Australian Health Translation Network)
2. Establishing a knowledge hub that brings ideas, knowledge, tools, research and activities together in a central online space. The aim of the National Knowledge Hub for Consumer and Community Involvement project was to explore the needs of consumers, clinicians, researchers and health service managers regarding CCI training and resources and access to these, and to use this information to develop a model for a national platform to meet these needs.
   (Lead: Monash Partners, SPHERE)
3. Evaluating Impact-Identifying and testing approaches that show if involving consumers in health research makes a difference, and the kinds of effects it has in different research settings.

Video resources on Adaptive Platform design for consumers

Adaptive Health Intelligence Website and ACTA Website

What is an Adaptive Clinical trial/ Tom Snelling

What are the Benefits of Adaptive Clinical Trials? Steve Webb & Tom Snelling

References

The Adaptive Platform Trials Coalition. (2019, August 28). Adaptive platform trials: definition, design, conduct and reporting considerations. *Nature Reviews Drug Discovery, 18*, 797-807

Increasing awareness and understanding of adaptive platform trials- K Lee et al. Poster Presentation, ACTA Annual Scientific Meeting, November 2022

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www.clinicaltrialsalliance.org.au

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