Increasing awareness and understanding of adaptive platform trials

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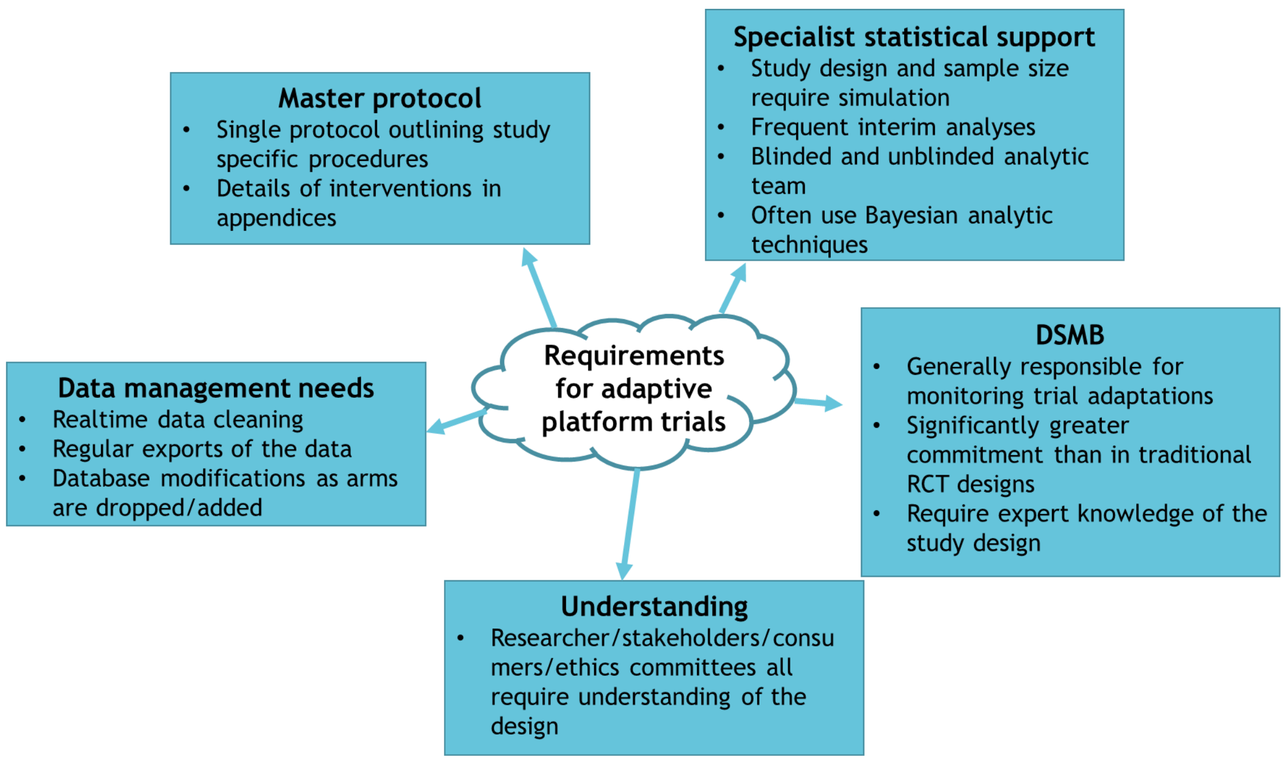
Introduction

- Adaptive platform trials are growing in popularity in Australia and globally, particularly since the emergence of COVID-19, for which decisions regarding vaccine approval and treatment strategy have been required urgently.
- These innovative designs are revolutionising how trials are conducted by enabling multiple interventions within different treatment modalities to be compared simultaneously in one or more populations.
- Such trials rapidly generate knowledge about how best to treat a disease, enabling expediated translation into practice, but are poorly understood

The Pros & Cons of adaptive platform trials

Pros	Cons
Generally has reduced participant numbers, cost and time compared with conventional two-arm, parallel group designs	Much more complex/time-consuming to develop, design and set-up than conventional designs
Enables multiple research questions to be addressed simultaneously	Need specialist statistical support
May allow fewer patients to be exposed to potentially inferior treatments	Logistical challenges with frequent interim analyses
Enables improved understanding of intervention effects, e.g. can determine efficacy in subgroups of participants	Overall design is more difficult to understand.
Greater acceptability to stakeholders (due to added flexibility)	Requires a more complex governance structure to oversee the trial

Figure 1. Additional requirements for an adaptive platform trial



What are adaptive trials?

Adaptive trials are those in which the study design changes based on the accumulating data in a pre-defined manner which is outlined in the study protocol. Examples of adaptations are:

- Response adaptive randomisation
- Early stopping for futility/efficacy
- Sample size re-estimation
- Participant population (adaptive enrichment)

What are adaptive platform trials?

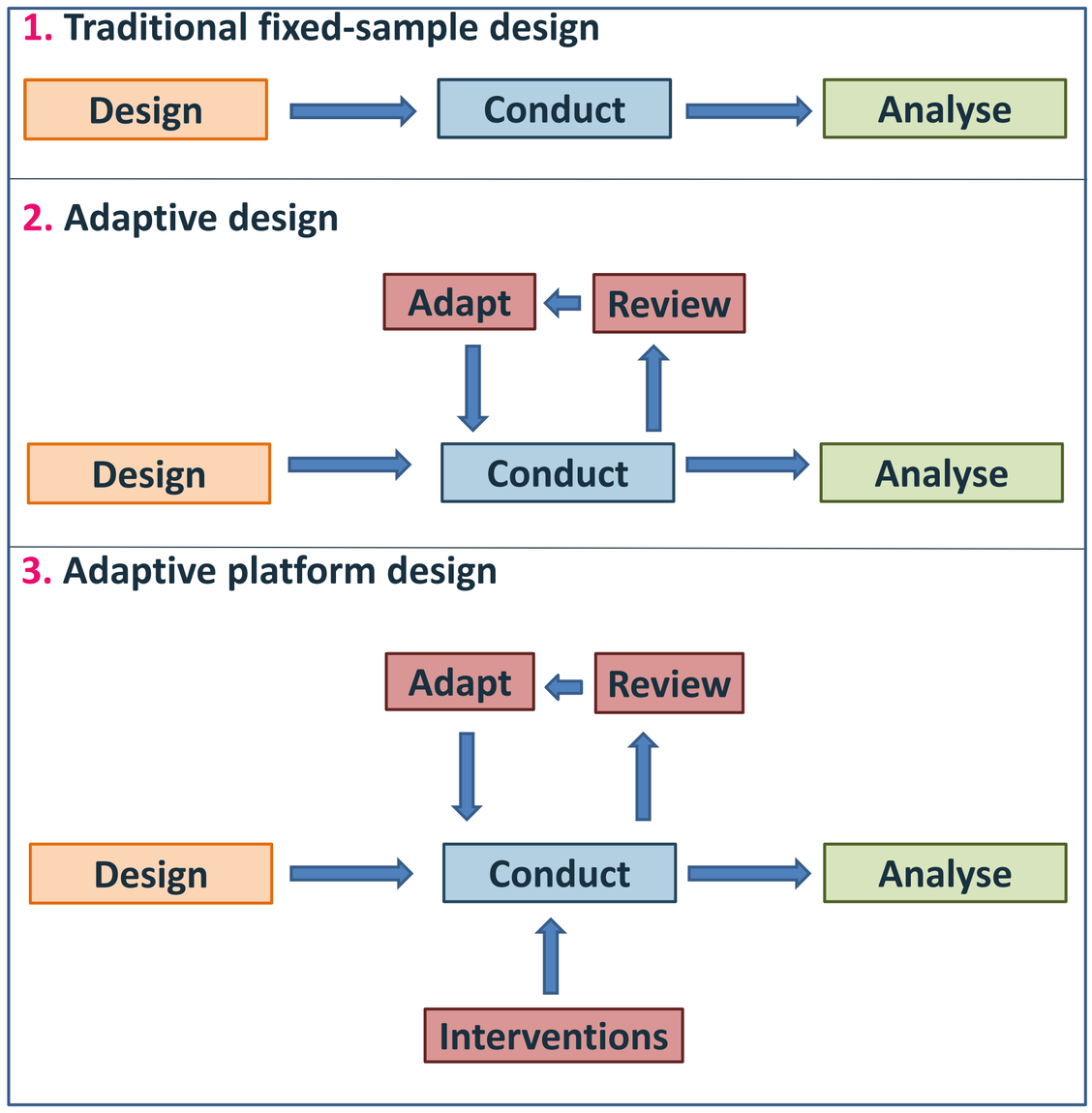
Adaptive platform trials offer further efficiency by comparing multiple interventions to a single control within different subgroups of participants under a single "master" protocol, with the ability to add interventions and to share information across subgroups of participants.

Key Features of Adaptive Platform Trials:

- Any number of subgroups
- Involves regular interim analyses
- No maximum sample size
- Has predefined decision rules for adaptation
- Treatments can be added or removed
- Treatment assignment controlled by accruing data
- Governed by a single master protocol

Figure 2: Schematic of different trial designs

Figure adapted *from Pallmann et al, 2018, Adaptive designs in clinical trials: why use them, and how to run and report them, BMC Medicine 2018 16:29*



Initiatives of ACTA-STInG & the Innovative Trial Designs Working Group

Initiative	Description
Innovative trials nomenclature document	Development of a glossary which would be available as as a web-resource defining all of the complex nomenclature relating to innovative trials
Discussion paper on the funding strategies for innovative designs*	This discussion paper will provide an outline of potential funding strategies for adaptive platform trials
Discussion paper on ethical issues in innovative designs*	This paper will provide an overview of the ethical considerations for researchers when considering using an innovative trial design
Discussion paper for consumer representatives on different types of innovative designs*	This paper will be aimed at consumer representatives outlining the key features of a range of innovative trial designs
Training in innovative designs	Workshops and webinars on innovative trial designs, for example the workshop at the ACTA ASM, and webinar series on N-of-1 studies for early 2023.
Web-reference document	Development of a document outlining when conventional designs are appropriate, and when innovative designs should be considered. May include a library of resources and case studies

* Initially these documents will be focused on adaptive platform trials, but the longer-term plan is to expand these to cover a range of innovative trial designs, for example cluster randomized, cluster-crossover and stepped wedge designs.

www.clinicaltrialsalliance.org.au

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