Session 3: A brighter future for clinical trials in the EU: continuing the journey

Panel discussion

ACT EU multi-stakeholder platform annual meeting

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European Network of Excellence for Paediatric Research

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Innovative Approaches in Clinical Trials: *High Potentiality, Limited Application*

Fostering innovation in clinical research practice is a key objective in creating a more welcoming environment for both stakeholders and patients

Innovative methodological approaches, including **Master Protocols** (such as Umbrella, Platform, and Basket trials), **Adaptive Study Designs**, **Seamless** and **Decentralized Clinical Trials**, are critical for enhancing the **efficiency** of clinical trials and the evaluation of medicines, particularly in **small populations** like paediatric and rare disease patients.

ADVANTAGES:

- ***Increase Efficiency*** *in testing novel therapies*
- ***Decrease the patient populations***
- *Easier patient* ***access****, higher* ***retention***
- *Ensure* ***feasibility*** *and* ***validity*** *of data*
- *Offer* ***flexibility*** *in trial design as data emerges allowing for adaptation of therapies, reduction of trial duration and patient burden*
  - ***Improvement*** *of Ethical Standards*
  - ***Patient-Centric*** *Approaches*
  - ***Safety*** *Monitoring*
- ***Optimization*** *of resource use*

LIMITATIONS:

- ***Conservatism and Resistance to Change*** *as new approaches can appear risky or insufficiently validated compared to traditional methods*
- ***Complexity in planning*** *and* ***management***
- ***Regulatory Concerns*** *regarding the interpretation and generalization of results*
- ***Specialized expertise*** *in advanced methodologies and statistical analysis contributes to* ***increased costs***
- ***Limited familiarity*** *and* ***lack of specialized training*** *among researchers and clinicians*

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Despite their advantages and endorsement in scientific and regulatory guidelines, the implementation of these innovative approaches in clinical research practice remains very limited.

Strategies & Actions for Innovation

1) Promoting Engagement of Medical and Research Professionals

- Regular organization of **Workshops and Seminars** to share insights about innovative study design.
- Incorporation of them in modules in **Continuing Medical Education (CME**) programs.
- Distributing **Publications and Case Studies** to highlight their successful implementation and effects.

2) Fostering Engagement and Empowerment of Patients

- Promotion of **Patient Advisory Boards** involving patients in trial design and planning to better align with patient needs (YPAG for children).
- Use of **Patient-friendly Information Materials**, understandable to laypersons and specific patient populations, to make clearer the communication and increase patient trust and participation.

3) Promote Regulatory Flexibility

- Use **Regulatory Sandboxes** for testing innovative designs to encourage creativity and reduce fear of non-compliance.
- **Streamlined approvals** to accelerate pathways for innovative approaches.
- **Harmonize global regulations** to simplify multi-country trials and expands access to diverse populations.

4) Promote International and Collaborative Partnerships

- Foster global and cross-sector collaborations to speed up innovation by exchanging ideas, **pooling resources and expertise**.
- Embrace **open science** by creating an open **data-sharing environment** to leverage existing datasets, reduce duplication, and drive more efficient clinical trials.
- Enhance **recruitment for small populations** by increased pool of potential participants.

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APPENDIX

Additional Information About Innovative Methodological Approaches

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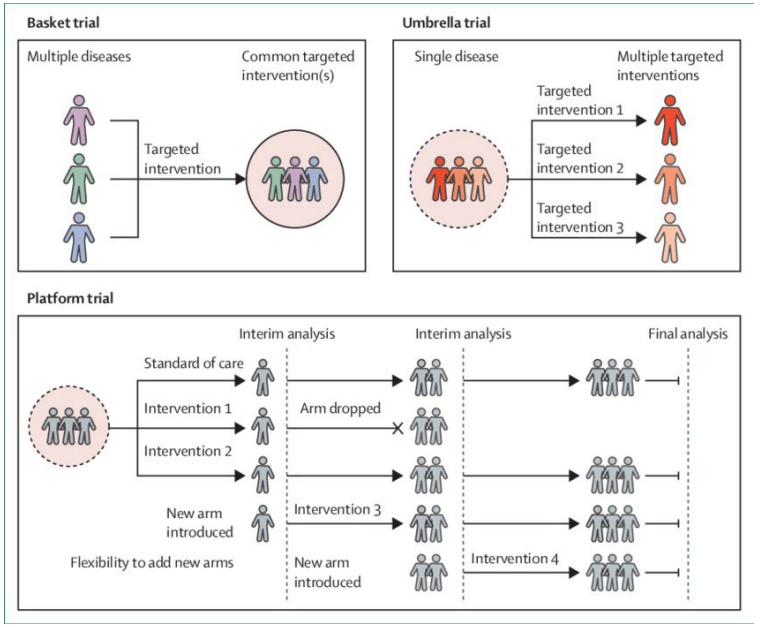
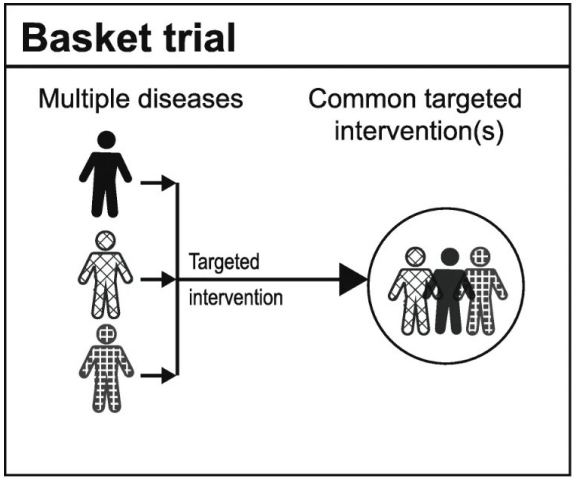
Innovative methodological approaches

A **MASTER PROTOCOL** is a unifying study construct that includes multiple subgroups and substudies, with patients having same or different diseases and that employ one or multiple drugs to treat it. The ability to use a single trial design to simultaneously evaluate multiple drugs and/or disease populations in multiple substudies, speeds up drug development and makes it more efficient.



V.,Bogin *Master protocols: New directions in drug discovery,* Contemporary Clinical Trials Communications (2020)

1) Basket trials refer to clinical trials conducted to test one treatment on multiple diseases that share common molecular alternations or other predictive risk factors. The US FDA considers a basket study to be adequate evidence for approval and recommends researchers utilize such trial designs. A basket design makes the most sense when there is clinical reason that all the indications can be improved by the same molecular drug mechanism.



Park, J.J.H., Siden, E., Zoratti, M.J. *et al.* Systematic review of basket trials, umbrella trials, and platform trials: a landscape analysis of master protocols. *Trials* **20**, 572 (2019). https://doi.org/10.1186/s13063-019-3664-1

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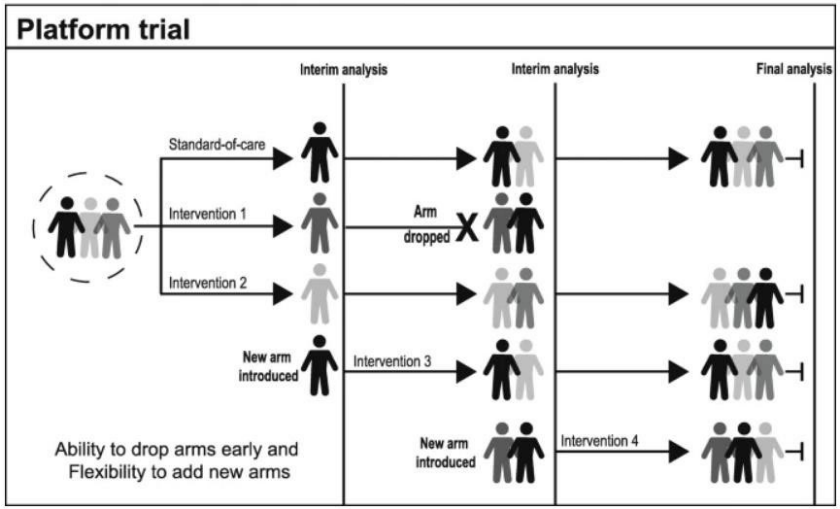
2) Platform trials referred to as Multi-Arm, Multi-Stage (MAMS) design to evaluate several interventions against a common control group. These designs help to further accept additions or exclusions of new therapies or patient populations during the clinical trial. In a platform trial, interim analyses evaluate the efficacy or futility of each targeted therapy and use their results to add new ones or exclude certain study therapies.



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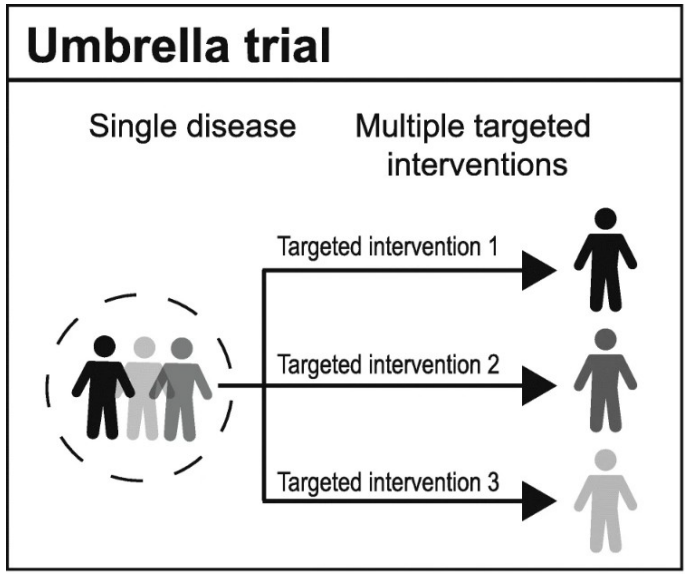
3) Umbrella trials allow for the evaluation of multiple targeted therapies in a single disease setting. Conceptually, it is simply a set of (sub)trials run in parallel. It offers a selection of appealing advantages, including that several treatment-related questions can be answered in a single trial and a potential reduction in the number of patients required (for instance, by including a common control arm).



Front Med (Lausanne). 2022; 9: 1037439.
Published online 2022 Oct 12. doi: 10.3389/fmed.2022.1037439

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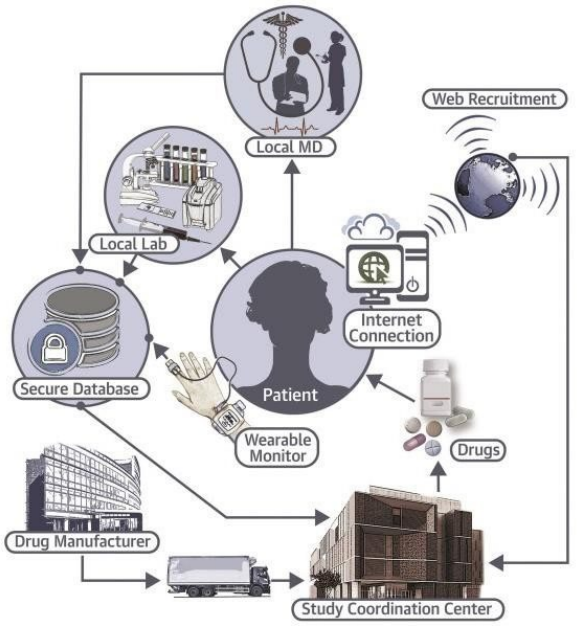
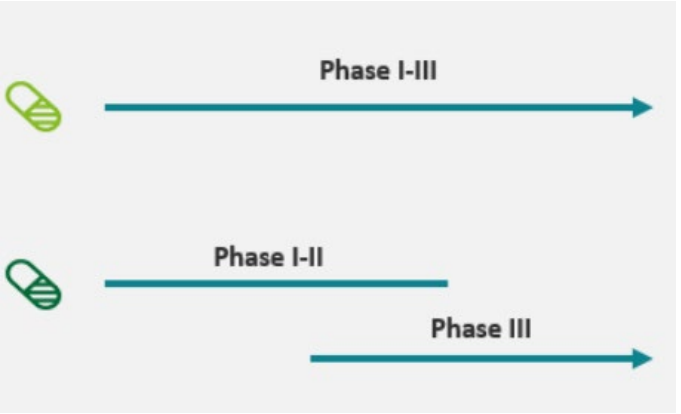
A **decentralized clinical trial** (DCT) is a type of clinical trial that reduces or eliminates the need for participants to visit clinical trial sites. Instead, much of the trial is conducted remotely, utilizing technology such as telemedicine, mobile health applications, wearable devices, and local healthcare providers. This model aims to make participation easier and more accessible, especially for patients who live far from traditional research centres or have mobility issues.

Van Norman, G.A. J Am Coll Cardiol Basic Trans Science. 2021;6:384-387.



A **seamless clinical trial** is a type of clinical trial that combines different phases of the trial into a single, continuous study. Instead of conducting separate, distinct trials for each phase (e.g., Phase I, Phase II, and Phase III), a seamless trial allows the transition from one phase to another without having to start a new trial for each step. This approach can help reduce delays between phases, minimize costs, and improve efficiency.



https://pharma.be/sites/default/files/2022-05/Pharma.be_Deloitte_Whitepaper%20Innovative%20Clinical%20Trials_vfinal.pdf

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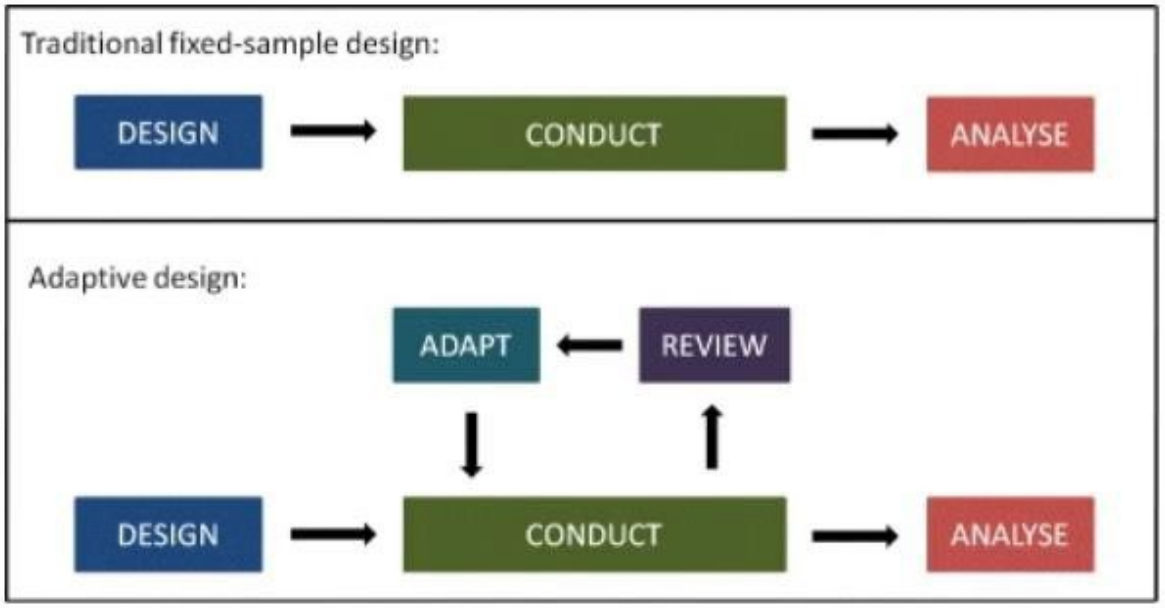
Adaptive designs can make clinical trials more flexible by utilising results accumulating in the trial to modify the trial's course in accordance with pre-specified rules. Trials with an adaptive design are often more efficient, informative and ethical than trials with a traditional fixed design since they often make better use of resources such as time and might require fewer participants.



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

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