

MASTER PROTOCOL REFERENCES & RESOURCES

The articles listed below provide a range of references and resources for learning about the basic overview on the concept of master protocol, adaptive platform trials, basket trials, emerging best practices, and regulatory guidance related to master protocols.

OVERVIEW ON MASTER PROTOCOLS

- ◆ Woodcock J, LaVange LM. Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both. *New England Journal of Medicine*. 2017;377(1):62-70. doi: 10.1056/NEJMra1510062.
 - This seminal paper sparked broad interest in master protocol studies. It provides an overview of basic design and operational characteristics of master protocol studies.
 - Available at: <https://www.nejm.org/doi/10.1056/NEJMra1510062>
- ◆ Renfro LA, Sargent DJ. Statistical controversies in clinical research: basket trials, umbrella trials, and other master protocols: a review and examples. *Ann Oncol*. 2017 Jan 1;28(1):34-43. doi: 10.1093/annonc/mdw413.
 - Provides a detailed overview of advantages and limitations of basket and umbrella designs, as well as examples of adaptive platform studies and master protocols that use a hybrid design approach.
 - Available at: <https://pubmed.ncbi.nlm.nih.gov/28177494/>
- ◆ Siden EG, Park JJ, Zoratti MJ, Dron L, Harari O, Thorlund K, Mills EJ. Reporting of master protocols towards a standardized approach: A systematic review. *Contemp Clin Trials Commun*. 2019 Jul 4;15: 100406. doi: 10.1016/j.conctc.2019.100406.
 - Highlights persistent inconsistencies in the description of basket, umbrella, and platform trials. The appendices offer very helpful tools that can be used to support early adopters' efforts to conduct their own review of master protocol studies.
 - Available at: <https://www.sciencedirect.com/science/article/pii/S2451865419301103>
- ◆ Park JJH, Siden E, Zoratti MJ, Dron L, Harari O, Singer J, Lester RT, Thorlund K, Mills EJ. Systematic review of basket trials, umbrella trials, and platform trials: a landscape analysis of master protocols. *Trials*. 2019 Sep 18;20(1):572. doi: 10.1186/s13063-019-3664-1.
 - Provides a through overview of key master protocol trial characteristics, disease characteristics, and global geographic representation. It also highlights the need to strengthen the landscape of existing master trials through ongoing nomenclature development and the development of master protocol studies in diverse global regions and therapeutic areas.
 - Available at: <https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-019-3664-1>

- ◆ Lesser, N, Naaz B. “Master Protocols: Shifting the drug development paradigm” Deloitte Insights. 2018. Available at: <https://www2.deloitte.com/us/en/insights/industry/life-sciences/master-protocol-clinical-trial-drug-development-process.html>
 - Describes the benefits and tradeoffs of master protocol studies for biopharmaceutical companies, including factors that contribute to overall time and cost savings associated with the master protocol approach
- ◆ Degenarro L, LaVange L, Manax V, Baker A. So you want to start a master protocol trial [Webinar]. 2018. Available from: <https://www.fastercures.org/events/webinars/show/so-you-want-to-start-a-master-protocol-trial>
 - Provides an overview of the benefits and challenges of utilizing the master protocol approach. Additionally, the Leukemia & Lymphoma Society and the Pancreatic Cancer Action Network describe study characteristics and lessons learned from recently developed master protocol studies.

ADDITIONAL ADAPTIVE PLATFORM TRIAL RESOURCES

- ◆ Saville BR, Berry SM. Efficiencies of platform clinical trials: A vision of the future. *Clinical Trials*. 2016;13(3):358-66. doi: 10.1177/1740774515626362.
 - Compares and contrasts design and operational efficiencies in platform trials and traditional randomized control trials.
 - Available at: <https://journals.sagepub.com/doi/abs/10.1177/1740774515626362>
- ◆ Stern, AD, Metha, S. “Adaptive Platform Trials: The Clinical Trial of the Future?” Harvard Business School Case 618-025, September 2017. [Revised January 2018.]
 - Provides a detailed description of the development of the GBM-AGILE trial and reviews important nomenclature, statistical characteristics, stakeholder engagement considerations, and creative funding strategies relevant to the design and implementation of adaptive platform trials.
 - Available at: <https://www.hbs.edu/faculty/Pages/item.aspx?num=53315>

BASKET TRIAL RESOURCES

- ◆ Cunanan KM, Gonen M, Shen R, Hyman DM, Riely GJ, Begg CB, Lasonos A. Basket Trials in Oncology: A Trade-Off Between Complexity and Efficiency. *J Clin Oncol*. 2017 Jan 20;35(3):271-273. doi: 10.1200/JCO.2016.69.9751. Epub 2016 Nov 28.
 - Gives an overview of the overarching goals of basket trials and makes recommendations for how to address key design challenges related to basket trials.
 - Available at: <https://ascopubs.org/doi/10.1200/JCO.2016.69.9751>
- ◆ Tao JJ, Schram AM, Hyman DM. Basket Studies: Redefining Clinical Trials in the Era of Genome-Driven Oncology. 2018;69(1):319-31. doi: 10.1146/annurev-med-062016-050343.
 - Summarizes the overarching purpose basket trials and provides an overview of key biostatistical considerations to advance the use of genome-driven oncology.
 - Available at: <https://www.annualreviews.org/doi/abs/10.1146/annurev-med-062016-050343>

EMERGING BEST PRACTICES

- ◆ Burd A, Schilsky RL, Byrd JC, Levine RL, Papadimitrakopoulou VA, Herbst RS, Redman MW, Druker BJ, Gandara DR. Challenges and approaches to implementing master/basket trials in oncology. *Blood Adv*. 2019 Jul 23;3(14):2237-2243. doi: 10.1182/bloodadvances.2019031229. PMID: 31337605; PMCID: PMC6650731.
 - Builds on experiences from NCI Match, Tapur, LUNG-MAP, and Beat AML trials to provide a roadmap of emerging best practices for the design and implementation of master protocol studies in oncology.
 - Available at: <https://ashpublications.org/bloodadvances/article/3/14/2237/260091/Challenges-and-approaches-to-implementing-master>
- ◆ Blagden SP, Billingham L, Brown LC, Buckland SW, Cooper AM, Ellis S, Fisher W, Hughes H, Keatley DA, Maignen FM, Morozov A, Navaie W, Pearson S, Shaaban A, Wydenbach K, Kearns PR; Experimental Cancer Medicine Centres (ECMC) CID trials working group. Effective delivery of Complex Innovative Design (CID) cancer trials-A consensus statement. *Br J Cancer*. 2020 Feb;122(4):473-482. doi: 10.1038/s41416-019-0653-9. Epub 2020 Jan 6. PMID: 31907370; PMCID: PMC7028941.
 - Summarizes a set of 10 multi-stakeholder, consensus-based recommendations on the design and conduct of complex innovative trials, including master protocol studies. In addition to critical study-level considerations, the authors highlight key capacity building efforts within the broader clinical trial ecosystem that are needed to further the development of master protocol studies.
 - Available at: <https://www.nature.com/articles/s41416-019-0653-9>
- ◆ Angus DC, Alexander BM, Berry S, Buxton M, Lewis R, Paoloni M, et al. Adaptive platform trials: definition, design, conduct and reporting considerations. *Nature Reviews Drug Discovery*. 2019; 18(10):797-807. doi: 10.1038/s41573-019-0034-3.
 - The Adaptive Platform Trial Coalition provides a detailed overview of common features and best practices related to the design, conduct, oversight, and reporting of adaptive platform trials.
 - Available at: <https://www.nature.com/articles/s41573-019-0034-3>

REGULATORY GUIDANCE

- ◆ Food and Drug Administration. [**Master Protocols: Efficient Clinical Trial Design Strategies To Expedite Development of Oncology Drugs and Biologics**](#). Draft Guidance. October 2018.
- ◆ Clinical Trials Facilitation and Coordination Group. [**Recommendation Paper on the Initiation and Conduct of Complex Clinical Trials**](#). February 2019.