Clinical Epidemiology

Dovepress
Taylor & Francis Group

Open Access Full Text Article

METHODOLOGY

Logistical Challenges in Platform Randomized Trials - Operational Realities That Curb the Promise of Efficiency

Kristian Thorlund[1,2], Jay JH Park[1,3], Matt P Wise[4], Brett Doleman[5], Johanne Juul Petersen[2], Theis Lange[6], Ole Mathiesen[7,8], Markus B Skrifvars[9], Manoj Saxena[10], Niklas Nielsen[11], Edward J Mills[1], Johannes Grand[12], Janus C Jakobsen[2,13]

[1]Department Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, ON, Canada; [2]Copenhagen Trial Unit, Centre for Clinical Intervention Research, Copenhagen University Hospital Rigshospitalet, Copenhagen Ø, Denmark; [3]Core Clinical Sciences Inc., Vancouver, BC, Canada; [4]Adult Critical Care, University Hospital of Wales, Cardiff, UK; [5]School of Medicine, University of Nottingham, Nottingham, UK; [6]Department of Public Health, Copenhagen University, Copenhagen, Denmark; [7]Centre for Anaesthesiological Research, Department Anaesthesiology, Zealand University Hospital, Koege, Denmark; [8]Department of Clinical Medicine, Copenhagen University, Copenhagen, Denmark; [9]Department of Anaesthesiology and Intensive Care Medicine, University of Helsinki and Helsinki University Hospital, Helsinki, Finland; [10]Faculty of Medicine, UNSW, Sydney, Australia; [11]Department of Clinical Sciences Lund, Lund University, Lund, Sweden; [12]Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark; [13]Department of Regional Health Research, The Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark

Correspondence: Kristian Thorlund, Email thorluk@mcmaster.ca

Abstract: Platform randomized trials offer a flexible framework for evaluating multiple therapies within a shared long-term infrastructure, yet their implementation poses substantial logistical and operational challenges. This paper examines three interrelated features that frequently determine the feasibility and efficiency of platform trials: 1) infrastructure and setup costs; 2) training, site management, and partial center participation; and 3) adapting to changing clinical practice and diagnostic criteria. While platform designs are often promoted for their efficiency, the establishment and maintenance of long-term infrastructure require greater upfront investment, more complex governance structures, and ongoing retraining compared to conventional randomized trials. Site heterogeneity and partial participation can create inconsistencies in implementation, data quality, and recruitment momentum. Over the long term, evolving standards of care and diagnostic definitions further complicate cross-arm comparability and risk introducing time-confounding. Rather than assuming platform trials are inherently more efficient, we argue that their success depends on sustained resourcing, harmonization efforts, sustained dedication from trial sites, and a robust training infrastructure. To address these challenges, we describe a trial-to-platform approach: a phased strategy in which a conventional multicenter trial is launched with modular, expandable systems that can later evolve to a platform trial. This approach allows for early learning, milestone-based funding, harmonization before full expansion, thereby reducing cost inefficiency and operational drift. Practical recommendations are provided for funders and trialists on how to structure, resource, and govern platforms to ensure scalability, reproducibility, and long-term sustainability.

Keywords: platform trials, clinical trial logistics: trial-to-platform approach, protocol adaptations

Introduction

Platform trials have gained prominence as a novel approach for evaluating multiple therapies under a unified core (master) protocol, typically allowing interventions to be added or dropped over time within a shared infrastructure. Their flexibility and efficiency, particularly the ability to add or drop treatment arms without launching a new trial, are often described as transformative features in both the methodological literature and educational resources.[1–3] Proponents highlight their potential for cost savings, improved recruitment efficiency, and accelerated evidence generation compared to traditional two-arm randomized controlled trials.[4,5] However, while their conceptual and methodological benefits are well described, the logistical demands of implementing and sustaining platform trials are often underappreciated. Their dynamic nature introduces continual demands on personnel, investigator and staff motivation, infrastructure, governance,

https://doi.org/10.2147/CLEP.S580997
Received: 12 November 2025
Accepted: 21 April 2026
Published: 11 May 2026

and coordination across trial sites.[6] Anticipated resource efficiencies may not materialize without sustained investment in operational support, data systems, and training.

In practice, many platform trial teams face recurrent obstacles in onboarding and retraining sites, maintaining version control across centers, and adapting to evolving treatment arms, eligibility criteria, or outcome definitions. Frequent updates to standard operating procedures (SOPs) and data systems create additional costs, complexity, and oversight requirements that are rarely captured in early planning, including substantial documentation and statistical complexity, as reported in platform trials.

This paper examines three overarching themes that pose recurrent logistical challenges in platform trial operations: (1) infrastructure and setup costs; (2) training, site management, and partial center participation; and (3) adapting to changing clinical practice and diagnostic criteria. By focusing on operational feasibility rather than theoretical efficiency, we aim to help investigators, funders, and regulators make informed decisions about when and how to pursue platform trial designs.

Trial Infrastructure and Setup Costs

A widely cited advantage of platform trials is their potential to reduce total resource use through shared infrastructure, common control arms, and adaptive features that allow multiple research questions to be evaluated sequentially or in parallel.[1–3] Many have adopted a platform-first model, in which a full platform trial infrastructure is established from the outset before any single comparison is launched. The intent behind this, though not always realized in practice, is to design a durable, reusable trial infrastructure from the outset before any single comparison is launched. This approach has been exemplified by several high-profile initiatives, such as the I-SPY 2 trial in breast cancer,[7] the STAMPEDE trial in prostate cancer,[8] and the HEALEY ALS Platform Trial.[9] Additional examples of platform trials and their associated logistical challenges are summarized in Table 1. Yet realizing these efficiencies requires substantial upfront investment in infrastructure, data systems, and personnel.

Table 1 Examples of Logistical Challenges and Successes in Past Platform Trials

Trial Acronym	Full Trial Name	Disease/ Therapeutic Area	Region	Logistical Focus in Manuscript
I-SPY 2[7]	*Investigation of Serial Studies to Predict Your Therapeutic Response with Imaging and Molecular Analysis 2*	Breast cancer (neoadjuvant chemotherapy)	United States (multi-center)	Early exemplar of adaptive multi-arm platform; illustrates substantial infrastructure and data system demands
STAMPEDE[8]	*Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy*	Prostate cancer	United Kingdom (multi-center, NIHR-funded)	Demonstrates high setup cost, complex CRFs, and recurring training needs
HEALEY ALS[9]	–	Amyotrophic lateral sclerosis (neurodegenerative disease)	United States (multinational expansion planned)	Example of reusable disease-specific platform infrastructure across parallel arms
FOCUS4[10]	*Molecularly Stratified Colorectal Cancer Platform Trial*	Colorectal cancer	United Kingdom (multi-center)	Highlights biomarker-based stratification, repeated training, and partial site participation
FLAIR[11]	*Front-Line Therapy in CLL (FLAIR) Platform Trial*	Chronic lymphocytic leukemia	United Kingdom (multi-center)	Operational burden of adding new arms; repeated ethics and retraining cycles
REMAP-CAP[12]	*Randomized, Embedded, Multifactorial Adaptive Platform Trial for Community-Acquired Pneumonia*	Community-acquired pneumonia / COVID-19	Europe, Australia, North America (multinational)	Contracting and regulatory complexity (140+ sites, 16 EU countries); large-scale coordination challenges

(*Continued*)

Table 1 (Continued).

Trial Acronym	Full Trial Name	Disease/ Therapeutic Area	Region	Logistical Focus in Manuscript
RECOVERY[16]	*Randomised Evaluation of COVID-19 Therapy*	COVID-19	United Kingdom (national platform)	Large pandemic-era platform; evolving endpoints and external validity concerns
TTM2[20]	*Targeted Temperature Management 2 Trial*	Post–cardiac arrest care	Scandinavia/ Europe	Served as foundation for STEPCARE; shows practical transition toward platform model
STEPCARE[21]	*Sedation, Temperature and Pressure After Cardiac Arrest and Resuscitation Platform Trial*	Post–cardiac arrest / critical care	Scandinavia/ Europe (multinational)	Illustrates successful trial-to-platform evolution; cited as model for scalable long-term infrastructure

Because most sponsors operate under traditional funding models, high setup costs can be a prohibitive barrier. Platform trials require more complex infrastructure than conventional two-arm trials, including regulatory frameworks, ethics approval pipelines, trial master files, statistical monitoring, and increasingly complex documentation and statistical frameworks, as highlighted in recent platform trial experiences such as the SNAP trial.[10] Specialized personnel such as statisticians for complex simulations, master protocol managers, modular data managers, and ongoing endpoint harmonization teams must often be in place from the outset. Experiences from the STAMPEDE (prostate cancer) and FOCUS4 (colorectal cancer) studies show that adaptability itself increases costs through continually evolving case report forms (CRFs), database updates, and retraining requirements.[8,11,12] The FLAIR trial likewise found that each arm triggered additional IT, ethics document-control work.[13] During the COVID-19 pandemic, REMAP-CAP required over 140 site contracts across 16 EU countries, illustrating the scale of coordination that may be needed.[14] Notably, some of the most successful platform trials during the COVID-19 pandemic, including REMAP-CAP and RECOVERY, benefited from pre-existing or rapidly deployable infrastructure, enabling early activation and adaptation as the pandemic emerged.[14,15] Figure 1 illustrates a hypothetical example of how platform trial costs compare to conventional clinical costs in the real world. The values shown are illustrative, based on a combination of published estimates and the authors' experience with platform trial implementation, and are intended to reflect general cost dynamics rather than precise projections.

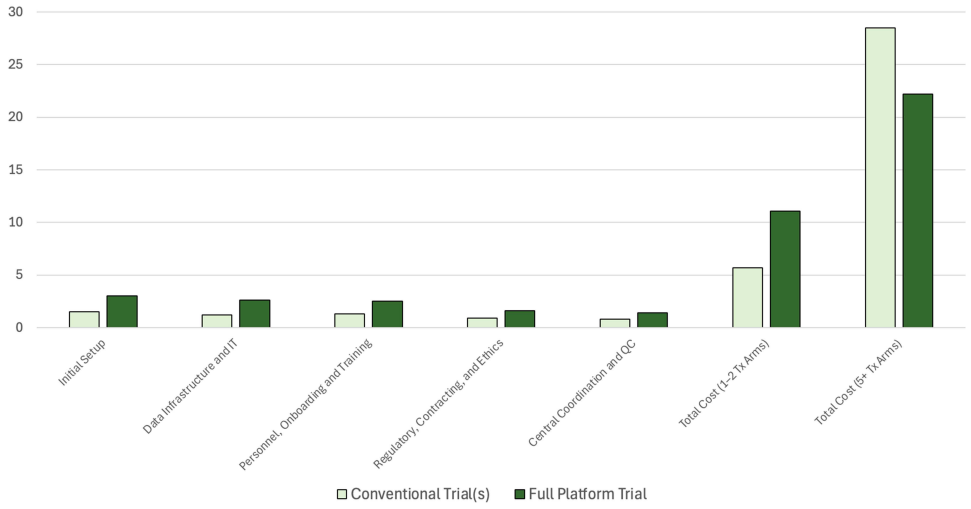

Figure 1 Illustration comparison of the cost ($M, y-axis) of multiple conventional trials versus a full platform trial, by individual operational components, totalled for 1–2 experimental treatment arms, and totalled for 5+ experimental treatment arms.
Abbreviations: QC, Quality Checks; Tx Arms, Treatment Arms.

https://doi.org/10.2147/CLEP.S580997

Park et al estimated that, despite higher setup costs, well-populated platform trials could reduce total expenditure by 17–57% compared to running multiple conventional trials.[5] However, such simulations assume fully harmonized data systems, uniform site capability, continuous accrual, and minimal downtime between arms–conditions that are rarely achieved in practice. Real-world platform trials commonly face onboarding delays, protocol complexity, and delayed site readiness, all of which can introduce hidden costs that materially erode projected savings.[16] Some of these costs can be anticipated through early feasibility assessments, pilot phases, and scenario-based planning that account for site onboarding delays, protocol amendments, and periods of low recruitment. Furthermore, fixed-cost infrastructure (eg, central trial coordination, safety monitoring boards, and IT maintenance) remains active even during less active periods when few or no arms are recruiting. The need for perpetual data-system readiness further increases ongoing staff costs. In turn, establishing a platform trial infrastructure can require not only higher upfront costs but also higher maintenance costs.

Many real-world platform trials investigate only a limited number of interventions before terminating due to various factors, including funding constraints, operational complexity, and insufficient recruitment.[16,17] Under-utilization can make a short-lived platform more expensive than independent trials. Savings depend not only on sample size or shared controls but on sustained use of the infrastructure. However, grant systems typically fund discrete research questions rather than large infrastructure projects such as long-term platform trials. Although agencies such as NIHR and CIHR have begun offering platform-specific calls,[18,19] most public and industry sponsors still fund conventional trials, increasing the risk of premature termination. During the COVID-19 pandemic, over 59 platform trials were registered, but only a handful added new interventions. Economic justification, therefore, depends less on theoretical efficiency than on actual durability and utilization.[16]

Mitigating Setup Cost and Strain with a Trial-to-Platform Approach

An alternative strategy to mitigate the high upfront costs and complexity of launching a full-scale platform trial is to adopt a trial-to-platform model. In this approach, infrastructure is initially established to support a well-designed conventional randomized multicenter trial, with foundational components such as modular data systems, adaptable governance structures, and flexible CRFs, all intentionally built to accommodate potential future platform expansion. This phased build-out allows resources to be allocated gradually, with each stage informed by operational experience and emerging clinical questions. Rather than incurring the substantial costs of a platform-ready architecture from the outset, sponsors can make incremental investments that are justified by trial performance, recruitment velocity, and emerging therapeutic opportunities. In this sense, the trial-to-platform model provides a natural "testbed" for stress-testing infrastructure elements in a lower-complexity environment that utilize milestone-based funding decisions for a high performing long-term trial infrastructure.

Figure 2 introduces the stages of a trial-to-platform approach as an alternative to the commonly used platform-first approach. Table 2 further highlights key actions and processes for each stage within the three operational domains covered in this article. Lastly, Figure 3 illustrates the time, cost, and feasibility of the trial-to-platform approach versus both multiple conventional trials and a platform-first approach. Figure 3 covers these aspects for both trial infrastructure and setup costs, as well as the operational domains in the following two sections. While the trial-to-platform approach may mitigate early logistical and funding risks, platform-first designs may offer advantages in settings with sustained funding and a stable clinical infrastructure, particularly for rapid adaptation to evolving clinical practice. However, perusal of the platform clinical trial literature strongly suggests that such settings (ie. favoring platform-first) are the exception rather than the rule.

Training, Site Management and Partial Center Participation

Platform trials impose training and management requirements that are often very different in scale and duration from those of conventional randomized controlled trials. Traditional trials frequently involve a concentrated burst of startup training followed by stable implementation, whereas platform trials require ongoing adaptation as new arms are introduced, eligibility criteria revised, or endpoints redefined. Coordinating centers must repeatedly re-engage sites through updated documentation and training. Without sufficient support, these evolving demands may result in recruitment delays from site disengagement, increased logistical overhead, or risk to the internal validity of the trial.[13,14]

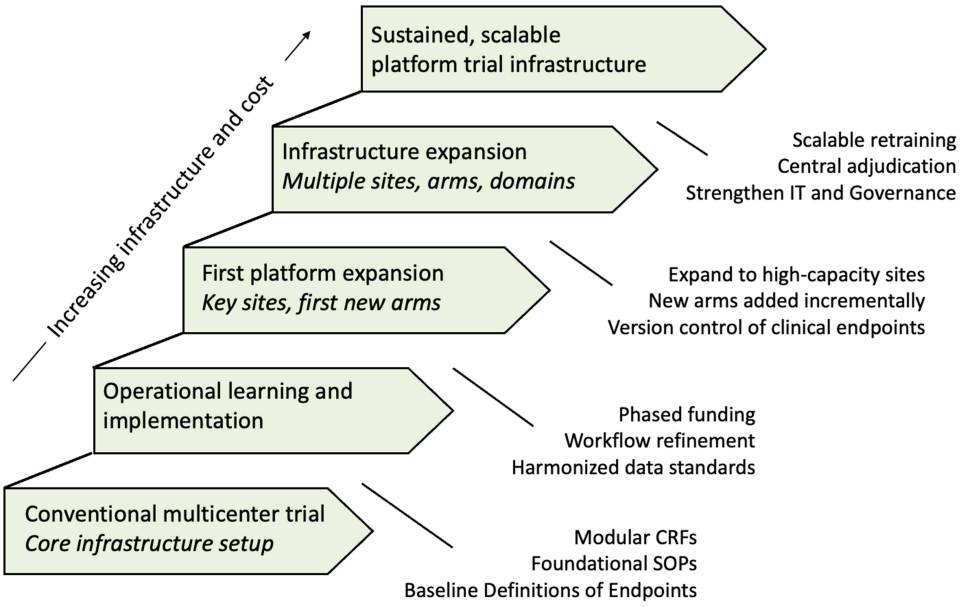

Figure 2 Stages of a *trial-to-platform* approach with increasing cost and infrastructure complexity.
Abbreviations: CRF, Case Report Form; SOC, Standard Operating Procedure.

Initial Onboarding and Ongoing Re-Training

Launching a platform trial requires a higher baseline of staff engagement and operational readiness than a conventional two-arm trial.[6,16,17] Trial coordinators, investigators, research nurses, and pharmacists must understand not only the master protocol but also the control structures, arm-specific CRFs, and dynamic randomization schemes that evolve as arms are added or removed. This is especially challenging for institutions with limited prior exposure to adaptive or modular trial designs.[2,6] Trials employing biomarker-stratified randomisation or real-time subgroup allocation also require training on sample collection, testing logistics, and subgroup-specific workflows. The FOCUS4 trial team

Table 2 Trial-to-Platform Considerations and Implementations Across Key Operational Domains

	Mitigating Setup Cost and Strain	**Streamlining Training and Site Management**	**Maintaining Temporal and Diagnostic Consistency**
Conventional Trial	Begin with modular data systems and flexible CRFs designed for later platform integration.	Use the initial conventional trial as a *training incubator* to test onboarding, SOPs, and workflows.	Pilot outcome definitions and diagnostic criteria under a fixed, conventional trial structure.
Operational Learning and Implementation	Allocate resources in phases tied to early performance, recruitment velocity, and feasibility milestones.	Evaluate training routines, communication channels, and site engagement to identify operational bottlenecks.	Monitor how clinical assessments and outcome ascertainment vary across sites and refine data-capture standards.
First Platform Expansion	Introduce new arms or modules only after demonstrating readiness and stable trial operations.	Expand to additional, high-performing sites based on demonstrated capacity and engagement.	Synchronize endpoint definitions and implement version control as new arms are added.
Infrastructure Expansion	Strengthen IT systems, governance structures, and central coordination to support multiple arms.	Scale retraining and documentation systems efficiently while maintaining consistent interpretation across sites.	Establish central adjudication processes and harmonized definitions for consistent comparisons across arms.
Sustained, Scalable Infrastructure	Maintain continuous operations through milestone-based funding and adaptive infrastructure.	Embed ongoing training, SOP updates, and communication loops for long-term sustainability.	Ensure temporal consistency through controlled updates, minimizing drift and preserving analytic comparability.

https://doi.org/10.2147/CLEP.S580997

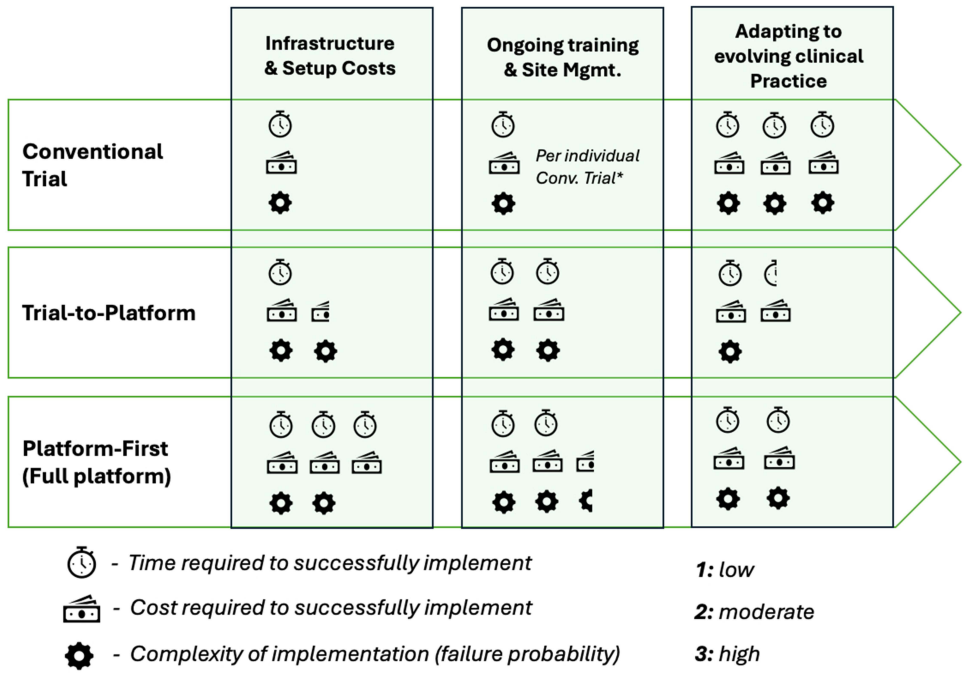

Figure 3 Comparison of the time, cost, and feasibility of the *trial-to-platform* approach versus both multiple conventional trials and a *platform-first* approach across three key operational categories.
Notes: *Cheaper per individual conventional trial; but more expensive for multiple conventional trials to match the number of treatment comparisons from a corresponding platform trial.

reported that aligning biomarker turnaround times with recruitment was one of the most operationally complex aspects of trial startup, particularly when introducing new arms.[11,12]

Because platform trials are designed to evolve, sites must be prepared for recurrent updates to training materials, consent forms, CRFs, SOPs, and recruitment procedures. Each new treatment arm may entail revised eligibility criteria or follow-up schedules, requiring re-training across participating centers. In the FLAIR platform trial, for example, each additional arm triggered documentation revisions, new pharmacy protocols, and ethics board submissions, with downstream training requirements at all participating sites.[13] Staff turnover over long trial durations further exacerbates these burdens, necessitating redundancy and ongoing training cycles.

Managing Communication, Oversight, and Protocol Drift

The dependency between the central coordinating team and sites requires a robust communication infrastructure to ensure consistent comprehension of updates. Traditional investigator meetings or static manuals are rarely sufficient. Many platform trials now rely on centralized dashboards, version-controlled documentation repositories, automated alerts, and digital training platforms that track completion and comprehension.[16] In large international platforms, regional liaisons and dedicated training coordinators are often essential to ensuring consistent interpretation of evolving protocols.[6]

As the number and frequency of amendments grow, training fatigue can emerge, where staff become desensitized to frequent updates or fail to implement changes accurately. Over time, this can lead to protocol drift–local deviations from intended conduct that undermine data quality.[14] To mitigate these risks, several trial teams have introduced milestone-linked retraining checkpoints or automated alerts highlighting updates relevant to specific site-level roles (eg, pharmacy, radiology, informed consent).

Partial Center Participation and Heterogeneity

Beyond training, platform trials face practical challenges arising from partial site participation. In practice, many centers only engage in a subset of treatment comparisons due to variations in infrastructure, staffing, regulatory approvals, and patient populations. This selective participation complicated management and interpretation. Each sub-protocol may

require tailored training sessions, ethics submissions, consent forms, or data collection pathways, creating a patchwork of eligibility criteria and protocol versions.[11,13] As seen in the FOCUS4 trial, centers joined and left the platform at different times and for different modules, requiring constant reconfiguration of site materials and workflows.[11] Similarly, in the FLAIR trial, adding new arms triggered updates to documentation and regulatory files, which did not always roll out uniformly across participating institutions.[13]

Operationally, such heterogeneity can affect recruitment rates and trial momentum. Sites not active in certain arms may experience periods of inactivity, discouraging local investigators and reducing overall accrual efficiency. Partial participation can also introduce analytic and selection biases if certain patient subgroups are disproportionately represented in specific arms.[19]

From a data-management perspective, variable participation demands highly flexible but harmonized electronic data-capture systems. CRFs and data-entry workflows must accommodate varying arm availability across centers, increasing the risk of missing data and version-control errors.[11] During the COVID-19 pandemic, for example, high-income-country sites implemented new arms more rapidly, while low- to middle-income country (LMIC) sites often lagged or opted out due to resource constraints. This asymmetry led to the underrepresentation of global populations, reducing external validity, an issue raised in reviews of REMAP-CAP and RECOVERY's multinational expansion.[14,15]

Streamlining Training and Site Management Challenges with the Trial-to-Platform Approach

A trial-to-platform model provides a practical way to address training and site management challenges. By first launching a conventional trial with embedded platform-ready features, teams can establish core onboarding routines, communication systems, and SOPs in a stable environment. Sites gradually build familiarity with shared control structures and adaptive processes before full platform rollout. This staged process is illustrated in Figure 2 and Table 2, showing how training, site readiness, and infrastructure capacity can be scaled iteratively to support sustained platform growth. As the platform expands, these early experiences streamline retraining and document control, reducing the disruption of repeated large-scale updates. This phased approach also identifies high-performing centers for future participation, ensuring that training resources are targeted and scalable. Such progressive onboarding is particularly valuable in regions or therapeutic areas with limited prior experience with platform trials.

Adapting to Changing Clinical Practice and Diagnostic Criteria

Platform trials are often intended to run for years and to adapt flexibly to evolving medical knowledge. However, the focus of this flexibility has predominantly been on treatments, largely ignoring the dynamic nature of clinical practice, outcome definitions, and evolving interpretations of clinical outcomes. As medical standards evolve and clinical practice shifts, the consistency and applicability of prespecified trial outcomes may therefore be compromised. These dynamics introduce potential confounding effects that threaten both the internal validity and external generalizability of findings.

Changing Standards of Care and Diagnostic Criteria

Over the course of a multi-year platform trial, real-world diagnostic criteria and clinical thresholds may undergo substantial changes after trial initiation. These changes can occur due to the introduction of new diagnostic technologies, shifts in biomarker thresholds, or consensus redefinitions of clinical syndromes. For example, historically, the diagnosis of myocardial infarction has evolved from autopsy-based criteria to dynamic troponin-based biomarkers, with increasing sensitivity and declining specificity over time.[22] Successive updates to the Universal Definition of myocardial infarction have altered both the incidence and clinical significance of diagnosed infarctions, thereby reshaping the populations eligible for trial enrollment and endpoint adjudication. Similarly, hypoglycemia outcomes in diabetes trials are subject to wide heterogeneity, with inconsistent thresholds, symptom reporting criteria, and inclusion of biochemical confirmation.[20,21] During the COVID-19 pandemic, evolving knowledge about disease progression and variant behavior led to shifting endpoints, ranging from early definitions based on hospitalization to later ones emphasizing viral load,

symptom duration, or need for oxygen therapy.[23–25] Lastly, a shift in diagnosis of Alzheimers disease from a predominantly clinical syndrome to criteria incorporating biomarkers and neuroimaging, including amyloid PET, CSF tau/amyloid, MRI atrophy patterns, represents a more recent example.[26,27] These transitions often occurred mid-trial, complicating the ability to generate consistent longitudinal comparisons, especially when treatment arms are continually added or dropped.

Time-Confounded Comparisons

As new arms are added over time to a platform trial, there is an inherent risk of time confounding. Later arms are often compared against a control population accrued earlier, under different clinical conditions, background therapies, or diagnostic standards. This is not merely a statistical artifact but a real-world operational hazard. For example, background corticosteroid use changed substantially in COVID-19 trials after mid-2020, altering the context in which antiviral or immunomodulatory therapies were tested.[28] Even with statistical adjustment, residual confounding from evolving care standards remains likely.

Maintaining Temporal and Diagnostic Consistency Through a Trial-to-Platform Approach

A trial-to-platform model offers a structured way to manage changes in clinical practice and diagnostic criteria over time. Beginning with a conventional multicenter trial allows investigators to identify variation in assessments and outcome definitions across sites before scaling to a broader platform. This early phase helps reveal where diagnostic drift or inconsistencies may arise as technologies or care standards evolve. As the platform matures, these experiences inform clear procedures for version control, endpoint updates, and central adjudication. Definitions can then be revised prospectively and consistently across all trial arms, thereby preserving comparability and reducing time confounding. In this way, the trial-to-platform approach aligns operational flexibility with methodological stability, ensuring that evolving science does not compromise interpretability. The staged mechanisms illustrated in Figure 2 and Table 2 demonstrate how diagnostic alignment and endpoint consistency can be sustained as platforms evolve. Figure 3 further illustrates the comparative feasibility, cost and complexity of the trial-to-platform approach compared to both (multiple) conventional trials and a platform-first approach.

Practical Recommendations and Conclusion

Despite the substantial challenges detailed in this paper, platform trials remain one of the most promising designs for accelerating therapeutic evaluation. The aim of this paper is not to discourage their use but to align expectations with practical realities. Effective implementation depends on the thoughtful sequencing of trial design, infrastructure development, and governance. Each should be scaled to demonstrate feasibility rather than theoretical efficiency.

A trial-to-platform approach can serve as a pragmatic entry point. Beginning with a conventional multicenter trial enables teams to establish site readiness, operational stability, and reliable data systems before expanding to a full platform. Once feasibility is proven, the infrastructure can evolve through modular trial extensions, shared governance, and harmonized protocols. This staged model reduces early cost and training burdens and ensures resources are not wasted if expansion proves infeasible. The TTM2 trial, which randomized 1900 adults following cardiac arrest,[29] exemplifies this strategy and laid the foundation for The CARE Platform Trial, which has already enrolled over 3000 patients and continues to add new interventions.[30]

Regardless of the initial model, success depends on establishing an organizational structure that efficiently manages both comparison-specific and platform-level issues. At the comparison level, considerations include intervention availability, site readiness, recruitment challenges, data requirements, statistical analysis plans, and interim analyses. In practice, these structures are often complemented by pragmatic workflow adaptations, such as centralized screening processes or dedicated support personnel, to reduce burden on frontline clinicians and maintain recruitment efficiency. At the platform level, responsibilities extend to strategic oversight, long-term funding, governance of shared controls,

overarching methodological principles governing the platform, and integration of new collaborators. Maintaining clear communication between these layers is essential to avoid duplication of effort and decision fatigue.

While an ideal structure might include separate steering groups for each comparison and for the overarching platform, this can become unmanageable. In practice, addressing platform-specific topics during steering group meetings, or vice versa, can reduce the number of required meetings while preserving oversight. Streamlining governance in this way helps teams remain responsive to operational needs without overwhelming trial staff.

Ultimately, platform trials are not plug-and-play. Their complexity requires planning, realistic funding horizons, and sustained commitment from sites and sponsors. Choosing the right developmental pathway–trial-to-platform or platform-first–should depend on the maturity of the research network and the anticipated longevity of the platform. With careful planning, continuous training, and disciplined governance, platform trials can fulfill their promise as efficient adaptive engines of clinical discovery.

Disclosure

Dr. Jay Park reports an ownership stake in Core Clinical Sciences Inc. Dr Matt Wise reports personal fees for serving in the advisory board from Diagnostics for the Real World and personal fees as a clinical expert for NICE advice service, outside the submitted work. Dr Theis served in Data and Safety Monitoring Board (DSMB) for Novo Nordisk study and Leo Pharma study, outside the submitted work. The authors report no other conflicts of interest in this work.

References

1. Woodcock J, LaVange LM. Master protocols to study multiple therapies, multiple diseases, or both. *N Engl J Med*. 2017;377(1):62–70. doi:10.1056/NEJMra1510062
2. Park JJH, Harari O, Dron L, et al. An overview of platform trials with a checklist for clinical readers. *J Clin Epidemiol*. 2020;125:1–8. doi:10.1016/j.jclinepi.2020.04.025
3. Saville BR, Berry SM. Efficiencies of platform clinical trials: a vision of the future. *Clin Trials*. 2016;13(3):358–366. doi:10.1177/1740774515626362
4. Berry DA. The platform trial: a new paradigm for evaluating multiple treatments. *Nat Rev Clin Oncol*. 2021;18(2):87–88.
5. Park JJH, Sharif B, Harari O, et al. Economic evaluation of cost and time required for a platform trial vs conventional trials. *JAMA Netw Open*. 2022;5(7):e2221140. doi:10.1001/jamanetworkopen.2022.21140
6. van Hout D, Mouncey P, Harrison D, et al. Hurdles for the delivery of multinational randomized clinical trials. *JAMA Network Open*. 2025;8(7):e2518503. doi:10.1001/jamanetworkopen.2025.18503
7. Barker AD, Sigman CC, Kelloff GJ, et al. I-SPY 2: an adaptive breast cancer trial design in the setting of neoadjuvant chemotherapy. *Clin Pharmacol Ther*. 2009;86(1):97–100. doi:10.1038/clpt.2009.68
8. James ND, Sydes MR, Clarke NW, et al. STAMPEDE: a multi-arm, multi-stage randomized controlled trial platform in prostate cancer. *Br J Cancer*. 2012;106(5):882–888.
9. Paganoni S, Macklin EA, Hendrix S, et al. The HEALEY ALS platform trial: design, rationale, and novel approach to disease management. *Neurology*. 2020;95(9):e1497–e1507.
10. Mahar RK, McGlothlin A, Dymock M, et al; on behalf of the SNAP Global Trial Steering Committee. Statistical documentation for multi-disease, multi-domain platform trials: our experience with the Staphylococcus aureus network adaptive platform trial. *Trials*. 2025;26(1):49. doi:10.1186/s13063-024-08684-8
11. Hague D, Townsend S, Masters L, et al. Changing platforms without stopping the train: experiences of data management and data management systems when adapting platform protocols by adding and closing comparisons. *Trials*. 2019;20(1):294. doi:10.1186/s13063-019-3322-7
12. Kaplan R. The FOCUS4 design for biomarker stratified trials. *Chin Clin Oncol*. 2015;4(3):35. doi:10.3978/j.issn.2304-3865.2015.02.03
13. Howard DR, Hockaday A, Brown JM, et al. A platform trial in practice: adding a newexperimental research arm to the ongoing confirmatory FLAIR trial in chronic lymphocytic leukaemia. *Trials*. 2021;22(1):38. doi:10.1186/s13063-020-04971-2
14. Goossens H, Derde L, Horby P, Bonten M. The European clinical research response to optimise treatment of patients with COVID-19: lessons learned, future perspective, and recommendations. *Lancet Infect Dis*. 2022;22(5):e153–58. doi:10.1016/S1473-3099(21)00705-2
15. Vanderbeek AM, Bliss JM, Yin Z, Yap C. Implementation of platform trials in the COVID-19 pandemic: a rapid review. *Contemp Clin Trials*. 2022;119:106892. doi:10.1016/j.cct.2022.106892
16. Schiavone F, Bathia R, Letchemanan K, et al. This is a platform alteration: a trial management perspective on the operational aspects of adaptive and platform and umbrella protocols. *Trials*. 2019;20(1):264. doi:10.1186/s13063-019-3216-8
17. Koenig F, Spiertz C, Millar D, et al. Current state-of-the-art and gaps in platform trials: 10 things you should know—insights from EU-PEARL. *eClinicalMedicine*. 2024;67:102384. doi:10.1016/j.eclinm.2023.102384
18. National Institute for Health and Care Research (NIHR). Australia–UK platform studies in areas of unmet clinical need (Reference ID: 97018). NIHR; 2024. Available from: https://www.nihr.ac.uk/funding/australia-uk-platform-studies-areas-unmet-clinical-need/97018. Accessed April 22, 2026.
19. Government of Canada. Canadian Institutes of Health Research (CIHR): funding opportunities related to platform trials. *Canada Gazette*. 2025. Available from: https://gazette.gc.ca/rp-pr/p1/2025/2025-12-20/html/reg2-eng.html. Accessed April 22, 2026.

20. Balijepalli C, Druyts E, Siliman G, Joffres M, Thorlund K, Mills EJ. Hypoglycemia: a review of definitions used in clinical trials evaluating antihyperglycemic drugs for diabetes. *Clin Epidemiol*. 2017;9:291–296. doi:10.2147/CLEP.S129268
21. Rodríguez-Gutiérrez R, Salcido-Montenegro A, González-González JG, McCoy RG. Variation in hypoglycemia ascertainment and report in type 2 diabetes observational studies: a meta-epidemiological study. *BMJ Open Diabetes Res Care*. 2021;9(1):e001906. doi:10.1136/bmjdrc-2020-001906
22. Davis P. The evolution of the definition of myocardial infarction. *RGA Knowledge Center*. 2018. Available from: https://www.rgare.com/knowledge-center/article/the-evolution-of-the-definition-of-myocardial-infarction. Accessed April 22, 2026.
23. Thorlund K, Smith D, Linsell C, et al. The importance of appropriate selection of clinical endpoints in outpatient COVID-19 clinical trials. *Commun Med*. 2023;3(1):53. doi:10.1038/s43856-023-00281-1
24. Horby P, Lim WS, Emberson JR, et al. Dexamethasone in hospitalized patients with Covid-19. *N Engl J Med*. 2021;384(8):693–704.
25. Gordon AC, Mouncey PR, Al-Beidh F, et al; REMAP-CAP Investigators. Interleukin-6 receptor antagonists in critically ill patients with Covid-19. *N Engl J Med*. 2021;384(16):1491–1502.
26. Jack CR, Bennett DA, Blennow K, et al. NIA-AA research framework: toward a biological definition of Alzheimer's disease. *Alzheimers Dement*. 2018;14(4):535–562. doi:10.1016/j.jalz.2018.02.018
27. Jack CR, Andrews SJ, Beach TG, et al. Revised criteria for diagnosis and staging of Alzheimer's disease. *Alzheimers Dement*. 2024;20(8):5143–5169. doi:10.1002/alz.13859
28. Bugin K, Woodcock J. Trends in COVID-19 therapeutic clinical trials. *Nat Rev Drug Discov*. 2021;20(4):254–255. PMID: 33633370. doi:10.1038/d41573-021-00037-5
29. Dankiewicz J, Cronberg T, Lilja GOT, et al. Hypothermia versus normothermia after out-of-hospital cardiac arrest. *N Engl J Med*. 2021;384(24):2283–2294. doi:10.1056/NEJMoa2100591
30. Kamp CB, Dankiewicz J, Olsen MH, et al. Sedation, temperature and pressure after cardiac arrest and resuscitation-The STEPCARE trial: a statistical analysis plan. *Acta Anaesthesiol Scand*. 2025;69(5):e70033. doi:10.1111/aas.70033