VIEWPOINT

INTEGRATING CLINICAL TRIALS AND PRACTICE

Embedding Patient and Health Care Professional Voices in Clinical Trials

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There is growing evidence that a substantial proportion of trials do not generate informative results due to suboptimal design or underrecruitment.[1] For every funded study that is uninformative due to poor design, the opportunity is lost to fund an alternative study. This leads to fiscal waste but, more importantly, it represents an ethical issue: every uninformative study has put undue burden on patients who willingly contributed for zero benefits, leading to a negative benefit-risk ratio.

Research shows that integrating patients' views on how to improve trial features (such as burden of data collection, travel for study procedures, consent materials, and relevance of outcomes) can lead to improved trial recruitment.[2] Similarly, early engagement with health care professionals (including clinicians, nurses, and health care managers who coordinate and deliver care) charged with delivering an intervention can identify potential barriers to the conduct of a trial that can then be addressed before launch.[3] Engaging key stakeholders, such as patients and health care professionals, early in the trial development process to codesign trial key features is thus likely to improve trial design and conduct, ultimately leading to more informative trial results.

> To ensure the clinical trials ecosystem of the future is optimized, we should seek to ensure that patient and health care professional perspectives are routinely integrated.

Various tools and guidance have been developed by national and international groups to support the coinvolvement of patients and health care professionals in the trial design process (coproduction of trial design). Broad guidance includes that developed by the Patient Focused Medicines Development initiative, which provides a step-by-step guide to building partnerships and integrating input as well as providing suggestions for methodological approaches. Similarly, the 10-step process for continuous engagement in comparative effectiveness research developed by Mullins and colleagues[4] covers aspects from topic solicitation to study dissemination, with each examined for the purpose of patient engagement. Other tools focus on specific elements of trial design or implementation. For example, the Perceived Research Burden Assessment tool solicits responses from patients and families regarding perceived logistical, psychological, and physical burdens to trial participation. By responding to this information during the trial design process, adaptations can be made to overcome potential challenges that may impact recruitment and retention.

In addition to these tools, formal organizations have also been established to support input from patients and the public on other aspects of trial design. The James Lind Alliance in the UK, for example, facilitates Priority Setting Partnerships that bring together patients and health care professionals to jointly identify and agree on areas of health and care that should be prioritized in future research. To date, hundreds of research priorities have been identified across a wide range of conditions and health care settings.[5] Another example is the Core Outcome Measures in Effectiveness Trials (COMET) initiative, which has established processes to create stakeholder-prioritized lists of trial outcomes that should be measured and reported in all clinical trials in a specific area of health or health care. These lists of standardized outcomes (ie, core outcome sets [COS]) are developed using formal process standards that stipulate the inclusion of patients, health care professionals, and clinical trialists as well as transparent processes for determining consensus.[6] To date, hundreds of COS have been developed, with a database maintained on the COMET initiative website. A list of these and other resources to facilitate the inclusion of patient and health care professional perspectives in the trial development process are presented in the **Table**.

Despite the extensive evidence-based tools and frameworks already available internationally to support patient and health care professional involvement in the trial design process, their uptake and use remains low—reviews of clinical trials have found levels of reported patient involvement ranging from less than 1% to 18% of identified trials. Further, even when patient perspectives are integrated, it is mainly in the logistical conduct of research, with much less engagement reported in the development of trial questions, design, or outcomes. The uptake of COS within clinical trials also varies dramatically, with little to no use in some clinical areas. Thus, there remains a major discrepancy between the evidence demonstrating the benefits of patient and health care professional engagement in the design and conduct of clinical trials and the use of tools or the products of involvement in practice. This represents a key challenge for the clinical trials enterprise that urgently needs to be addressed.

Reviews have identified that as many as 60 different frameworks already exist to support the involvement of

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Table. Resources to Support the Inclusion of Patient and Clinician Voices in Clinical Trials

Resource	Area of focus	Source
Consumer Involvement and Engagement Toolkit	Framework for engagement	Australian Clinical Trials Alliance (ACT) Consumer Involvement and Engagement Toolkit: https://involvementtoolkit.clinicaltrialsalliance.org.au/toolkit
CTTI Prioritization Tool for Sponsors and Patient Groups	Identification of engagement opportunities	Clinical Trials Transformation Initiative: https://prioritizationtool.ctti-clinicaltrials.org/
James Lind Alliance: Priority Setting Partnerships	Topic identification	James Lind Alliance Priority Setting Partnerships: https://www.jla.nihr.ac.uk/about-the-james-lind-alliance/templates-and-useful-documents.htm
How-to Guide on Patient Engagement in Clinical Trial Protocol Design	Trial protocol design	Patient Focused Medicines Development (PFMD): https://pemsuite.org/How-to-Guides/Patient-engagement-in-clinical-trial-protocol-design.pdf
Patient Protocol Engagement Toolkit (P-PET)	Trial protocol design	TransCelerate Biopharma, Inc: https://www.transceleratebiopharmainc.com/ppet/planning-for-patient-engagement/
Action, actor, context, target, time (AACTT) framework	Description of behaviors for implementing trial interventions	Presseau J, McCleary N, Lorencatto F, Patey AM, Grimshaw JM, Francis J. Action, actor, context, target, time (AACTT): a framework for specifying behavior. *Implement Sci*. 2019;14(1):102. doi:10.1186/s13012-019-0951-x
Perceived Research Burden Assessment (PeRBA) instrument	Assessment of patient burden and benefits of trial participation	Lingler JH, Schmidt K, Gentry A, Hu L, Terhorst L. Perceived research burden assessment (PeRBA): instrument development and psychometric evaluation. *J Empir Res Hum Res Ethics*. 2014;9(4):46-49. doi:10.1177/1556264614545037
Patient Friction Coefficient (PFC)	Assessment of patient burden and benefits of trial participation	Cameron D, Willoughby C, Messer D, Lux M, Aitken M, Getz K. Assessing participation burden in clinical trials: introducing the patient friction coefficient. *Clin Ther*. 2020;42(8):e150-e159. doi:10.1016/j.clinthera.2020.06.015
Stages of Patient Reported Outcome (PRO) development	Outcome selection and measurement	Addario B, Geissler J, Horn MK, et al. Including the patient voice in the development and implementation of patient-reported outcomes in cancer clinical trials. *Health Expect*. 2020;23(1):41-51. doi:10.1111/hex.12997
The Core Outcome Measures in Effectiveness Trials (COMET) Handbook: version 1.0	Outcome selection and measurement	Williamson PR, Altman DG, Bagley H, et al. The COMET Handbook: version 1.0. *Trials*. 2017;18(suppl 3):280. doi:10.1186/s13063-017-1978-4
Core Outcome Set-Standards for Development (COS-STAD)	Outcome selection and measurement	Kirkham JJ, Davis K, Altman DG, et al. Core outcome set-standards for development: the COS-STAD recommendations. *PLoS Med*. 2017;14(11):e1002447. doi:10.1371/journal.pmed.1002447

patients and health care professionals in research. As such, the need is not for more methods or frameworks, which will likely lead to duplication and confusion, but rather for how to ensure the current evidence base is adopted into practice.

Adopting insights from implementation science can help. The field of implementation science is the study of approaches used to promote the systematic uptake of evidence-based practice and research.[7] By applying an implementation science lens, we can begin to address key implementation questions such as "what are the incentives and drivers that can promote the adoption of these tools?" and "what are the barriers to the use of identified research priorities, frameworks, or COS?" From there it will be possible to develop solutions using proven implementation techniques to address the identified barriers and improve use. For example, early work in COS has found that a lack of awareness among key stakeholders—trialists, trial networks, and funders—is a barrier to use. Addressing this issue points to the need for improved dissemination strategies that actively engage with those in a position to promote and support the uptake of a COS.

The integration of patient and health care professional perspectives in trials has been shown to yield improvements in clinical trial design and delivery. Despite recognition of these benefits, and the existence of frameworks and tools to support adoption, uptake remains variable. To ensure the clinical trials ecosystem of the future is optimized, we should seek to ensure that patient and health care professional perspectives are routinely integrated. Applying an implementation science lens to identify and address challenges in the use of identified research priorities, frameworks, and COS that seek to embed the perspectives of patients and health care professionals is needed. This will allow the development of more informative clinical trials through improved designs and ultimately, through their findings, provide better evidence to inform better health care.

ARTICLE INFORMATION

Published Online: July 1, 2024. doi:10.1001/jama.2024.6314

Conflict of Interest Disclosures: Dr Campbell reported receiving grants from NIHR, MRC, and NHS outside the submitted work. No other disclosures were reported.

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