Integrating Patient and Public Involvement and Engagement in Translational Medicine

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Translational Medicine (TM), an interdisciplinary branch of biomedical research, aims to rapidly transform scientific discoveries into interventions for testing in clinical settings and adoption into practice.[1] Its potential for global benefit came into sharp focus during the Coronavirus disease (COVID-19) pandemic. However, despite the successful development of effective COVID-19 vaccines, the complex issue of vaccine hesitancy, revealed the critical role of social determinants and public trust in TM.[2] Whilst Patient and Public Involvement and Engagement (PPIE) is increasingly adopted in clinical and applied research, it is under-utilised and under-reported in preclinical research where it is typically confined to the priority-setting stages of research and often a one-time occurrence.[3,4] The successful translation of new scientific discoveries into interventions for patient benefit must involve public contributors, including patients, throughout the TM pathway.[5,6] This has been recognised and endorsed internationally by several research funders including governmental agencies such as the UK's National Institute for Health and Care Research (NIHR),[7] the US National Institutes of Health (NIH)[8] and Australia's National Health and Medical Research Council[9] as well as charitable organisations including the pan-African Science for Africa Foundation[10] and the India Alliance.[11] There are several potential benefits of implementing PPIE for TM including helping to bridge the gap between preclinical and clinical research (Box 1).[3,4,12]

However, PPIE is associated with several barriers, some of which are particularly challenging in TM (Box 1).[3,4,12] A potential barrier to effective PPIE is the absence of established relationships between researchers and public contributors. Researchers need to develop relationships with patients and the public which value 'expertise by experience' and address inequalities.[6] Developing meaningful partnerships with patients and the public requires time and concerted effort to succeed and the ideal model of interaction is co-production which is characterised by power sharing.[13]

Another barrier could be communication issues between researchers and public contributors. Laboratory-based researchers, who typically have limited direct contact and experience of interacting with patients and the public, often feel ill-equipped to convey technical information beyond their own scientific community.[3,4] They may also be uncertain about the public having sufficient scientific and ethical literacy to engage in meaningful discussions. This can be further complicated by issues of language, culture and public distrust, controversy or politics. Opportunities should be provided for researchers, including those involved in preclinical research, to interact with patient and public partners. Such opportunities may include informal meetings where researchers present and discuss their work in lay terms to the public contributors, 'lab tour' for the public contributors and pairing

PhD researchers with public contributors, building on similar models that have worked within a TM context.[14] The experiential learning that occurs during these relationship-building activities could be mutually beneficial and effective in breaking down barriers. Public contributors may gain a better understanding of research being conducted while researchers become better at communicating their work to lay audiences. The compelling testimonies from our public contributors and researchers demonstrate that differences in knowledge are not barriers to PPIE, but opportunities to produce new learning, competencies and tangible outcomes (Box 1). However, facilitating these opportunities require substantial investments in terms of time and financial resources.

Patent laws governing new discoveries can create additional dilemmas. While these are intended to benefit society by motivating innovation (through temporary exclusive rights on new therapies and technologies), they prohibit the sharing of information with the public. TM also involves long timescales, with lags between different phases of the translational continuum. Conducting PPIE over these lengthy periods may be costly and some public contributors may be unable to participate for the duration of the programme.

It is important that TM research programmes develop strategies to address these challenges and effectively integrate PPIE in research. For instance, the NIHR-funded Blood and Transplant Research Unit in Precision Cellular Therapeutics (BTRU-PCT)[15] co-produced a PPIE Strategy and Delivery Plan with public contributors.[16] The Canadian Institutes of Health Research also developed a patient engagement framework to establish key concepts, principles and areas for patient engagement.[17] However, well-developed strategy documents for PPIE does not automatically address the challenges. The ideas need to be implemented appropriately. Relationship building also takes time, particularly the development of mutually beneficial relationships with underserved groups.

Prioritisation, planning and appropriate costing at the outset is a key enabler for PPIE, particularly when conducted across research programmes that span multiple disciplines, methods and settings. This involves working with community groups at the grant development stage to clarify who the research is relevant to, and working with these individuals to plan the research, including PPIE.[6] Early involvement could facilitate the integration of PPIE across the TM continuum and throughout the research cycle (including research prioritisation, commissioning, conduct, dissemination and implementation).

PPIE expertise should be considered a fundamental part of research delivery in TM. Developing, implementing and sustaining high quality PPIE is a skilled and time-consuming endeavour that is frequently overlooked. Thus, while PPIE is ‘everyone’s business’, it is

important to recognise that many researchers are likely to have limited experience of implementing PPIE, particularly in TM. In our experience, a key enabler has been the employment of a dedicated PPIE Manager to facilitate and co-ordinate activities, liaising with the different research themes within the project. Another enabler was creating a shared understanding of PPIE, to ensure researchers and public contributors understand how they can contribute to delivery plans. Excellent resources exist for PPIE such as the NIHR Learning for Involvement Website, the European Science Engagement Platform and the US Food and Drug Administration (FDA)'s Patient-Focused Drug Development Guidance Series. However, finding and utilising these resources when there is limited experience can be daunting. Dedicated handbooks may be created to provide practical information and signposts to resources.[18,19]

Looking ahead, there is an increasing commitment to PPIE in TM. For example, World Health Organisation (WHO) Advisors for genome editing recommended that 'education, engagement and empowerment' should be embedded as 'a core feature' in emerging public health technologies, and called on the WHO to develop best practice documents.[20] There are also global efforts focused on scaling up TM in low- and middle-income countries,[21] with associated frameworks to support community engagement and involvement in global healthcare research.[22] Priority actions include more joined-up work by national leads for PPIE to support these initiatives, and robust training for TM researchers across disciplines, to ensure knowledge about PPIE is carried into their different domains of practice. There is also a need for more sustainable models for PPIE where research funders and organisations build ongoing relationships with communities, rather than just investing in project-specific approaches. This not only includes having permanent PPIE teams and public advisory boards within organisations that undertake TM, but also developing new funding models that enable community-led research expressly aimed at reducing health inequalities. Robust assessment and reporting of PPIE impact in TM is crucial for strengthening the evidence base and facilitating greater adoption.[23,24] Stakeholders such as funders, ethical review committees, and regulatory bodies can also play a critical role in encouraging the adoption of PPIE in TM and accountability among researchers by requesting high quality PPIE plans at the outset of research and evidence of its impact at the end of projects. The effective incorporation of patient and public perspectives in the TM pathway could facilitate the translation of scientific breakthroughs into interventions that would benefit patients and the society.

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Author contributions

The manuscript was conceived by KLS, MC, OLA; KLS wrote the first draft; all authors critically reviewed the manuscript, contributed content and approved the final version.

Competing interests

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Box 1: Potential benefits and challenges of Patient and Public Involvement and Engagement in Translational Medicine

Benefits of PPIE
Relevance and acceptability. Helps identify what issues matter to patients and society, in ways that rapidly lead to acceptable and beneficial treatments that have a guaranteed market.[3,4,12]
Feasibility. Can identify real world factors that shape translation e.g. information about how and why interventions reach the bedside. Supports uptake at the clinical and community level.[3,4,12]
Good financial investment. Early involvement may support quicker routes to market, by avoiding costly changes in direction, wasted resources and unintended consequences.[3,4,12]
Credibility and trustworthiness. Can help understand the range of attitudes held towards the research. Supports transparent and effective, communication. Important given fake news and misinformation.[3,4,12]
Benefits for researchers. Can support skill development (e.g. science communication with lay audiences) and enhance reputation and profile (e.g. showcasing work). Wider partnerships and networks can support research and future opportunities. Can motivate and inspire; reminding researchers about the value of their work.[3,4,12]
Benefits for patients and the public. Can provide opportunities to make a difference, shape future care, 'give something back', meet others, develop new knowledge, share existing skills or develop new ones.[3,4,12]

References

1. Cohrs RJ, Martin T, Ghahramani P, Bidaut L, Higgins PJ, Shahzad A. Translational Medicine definition by the European Society for Translational Medicine. *New Horizons in Translational Medicine* 2015; **2**(3): 86-8.
2. Lazarus JV, Wyka K, White TM, et al. A survey of COVID-19 vaccine acceptance across 23 countries in 2022. *Nature Medicine* 2023; **29**(2): 366-75.
3. Fox G, Fergusson DA, Daham Z, et al. Patient engagement in preclinical laboratory research: A scoping review. *eBioMedicine* 2021; **70**.
4. Carroll P, Dervan A, Maher A, et al. Applying Patient and Public Involvement in preclinical research: A co-created scoping review. *Health Expect* 2022; **25**(6): 2680-99.
5. Aiyegbusi OL, Macpherson K, Elston L, et al. Patient and public perspectives on cell and gene therapies: a systematic review. *Nature Communications* 2020; **11**(1): 6265.
6. NIHR. Briefing notes for researchers - public involvement in NHS, health and social care research. 2021. https://www.nihr.ac.uk/documents/briefing-notes-for-researchers-public-involvement-in-nhs-health-and-social-care-research/27371 (accessed 27/06/2024.
7. NIHR. Patient and public involvement in health and social care research: A handbook for researchers2014. https://www.rds-yh.nihr.ac.uk/wp-content/uploads/2015/01/RDS_PPI-Handbook_2014-v8-FINAL-11.pdf (accessed 15/11/2022).
8. NIH. Translational Science Principles. https://ncats.nih.gov/about/about-translational-science/principles (accessed 23/07/2024.
9. NHMRC. Consumer and community engagement. https://www.nhmrc.gov.au/about-us/consumer-and-community-involvement/consumer-and-community-engagement#download (accessed 23/07/2024.
10. SFA. Public Engagement with Science (PES) Programme. https://scienceforafrica.foundation/programmes/public-engagement-with-science23/07/2024).
11. Public Engagement. https://www.indiaalliance.org/public-engagement (accessed 23/07/2024.
12. ACCELERATE. Why is stakeholder engagement important for translational research? . https://www.ucl.ac.uk/school-life-medical-sciences/sites/school-life-medical-sciences/files/why_engage_resource_final.pdf (accessed 27/06/2024.
13. Redman S, Greenhalgh T, Adedokun L, Staniszewska S, Denegri S. Co-production of knowledge: the future. *BMJ (Clinical research ed)* 2021; **372**: n434.
14. Simons G, Birch R, Stocks J, et al. The student patient alliance: development and formative evaluation of an initiative to support collaborations between patient and public involvement partners and doctoral students. *BMC Rheumatol* 2023; **7**(1): 36.
15. NIHR BTRU in Precision Cellular Therapeutics. https://www.rdm.ox.ac.uk/about/our-clinical-facilities-and-units/nihr-btru-in-precision-cellular-therapeutics (accessed 27/06/2024.
16. Shaw K, Aiyegbusi, O. L., Calvert, M. . Patient and Public Involvement and Engagement Strategy, 2022-2027: University of Birmingham, 2022.
17. CIHR. Strategy for Patient-Oriented Research - Patient Engagement Framework. https://cihr-irsc.gc.ca/e/48413.html (accessed 23/07/2024.
18. Shaw K, Aiyegbusi, O. L., Calvert, M. . Public and Patient Involvement and Engagement (PPIE). A Practical Planning Guide for BTRU Researchers: University of Birmingham, 2023.
19. Shaw K, Calvert, M., Aiyegbusi, O. L. . Patient and Student Partnership: A Guide for Patients, Students and Supervisors: University of Birmingham, 2023.
20. WHO Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing: report of the sixth meeting, 25-26 March 2021. Geneva: World Health Organization, 2021.
21. UN. Transforming our world: the 2030 Agenda for Sustainable Development. https://sdgs.un.org/2030agenda (accessed 27/06/2024.
22. NIHR. Community engagement and involvement. https://www.nihr.ac.uk/researchers/i-need-help-funding-my-research/tips-for-making-your-application/community-engagement-and-involvement (accessed 27/06/2024.
23. Public Involvement in Research Impact Toolkit (PIRIT). https://www.cardiff.ac.uk/marie-curie-research-centre/patient-and-public-involvement/public-involvement-in-research-impact-toolkit-pirit (accessed 27/06/2024.

24. Aiyegbusi OL, McMullan C, Hughes SE, et al. Considerations for patient and public involvement and engagement in health research. *Nature Medicine* 2023.