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Abstract

Patient and public involvement and engagement (PPIE) can provide valuable insights into the experiences of those living with and affected by a disease or health condition. Inclusive collaboration between patients, the public and researchers can lead to productive relationships, ensuring that health research addresses patient needs. Guidelines are available to support effective PPIE; however, evaluation of the impact of PPIE strategies in health research is limited. In this Review, we evaluate the impact of PPIE in the Therapies for Long Covid in non-hospitalised individuals (TLC) Study, using a combination of group discussions and interviews with patient partners and researchers. We identify areas of good practice and reflect on areas for improvement. Using these insights and the results of a survey, we synthesise two checklists of key considerations for PPIE — and we propose that research teams use these checklists to optimize the impact of PPIE for both patients and researchers in future studies.

Editors summary: By evaluating the impact of patient and public involvement and engagement (PPIE) in the TLC study – which evaluated therapies for long-COVID – the authors generate a checklist of key considerations to guide PPIE in future research.

[H1] Introduction

Insights from patient and public involvement and engagement (PPIE) can ensure that research is more relevant to the needs of patients, caregivers, and service users.(1-4) The UK's National Institute for Health and Care Research (NIHR) has been a pioneer in promoting an understanding of PPIE and facilitating its implementation and evaluation in research. The organisation has produced several guidance documents including a handbook on PPIE and the UK Standards for Public Involvement in Research, which researchers can use to review their plans for PPIE in research projects.(5, 6) In addition, there are guidelines on diversity and inclusion in public involvement (7, 8), reimbursement for PPIE (9) and co-production of research.(10) Globally, there is increasing recognition of the importance of PPIE with new initiatives at national and international levels.(11)

However, despite enthusiastic support from policymakers and researchers, the reporting of PPIE in study reports is often absent or minimal; where present, it is usually focused on the mechanics of how patient and public input to the study was obtained. Robust evidence of the

impacts of PPIE in research is limited.(12, 13) It should be acknowledged that evaluating impact can be challenging. Researchers may be less inclined to undertake a formal evaluation of PPIE impact as the pathways to impact are often convoluted, and attribution is not always straightforward.(14) Furthermore, researchers may be uncertain about which approaches to adopt for the evaluation of PPIE impact and the utilisation of available guidelines might be challenging in practice.(15) These issues create a relative evidence void for PPIE and a barrier to the efficient development and sharing of best practice. For PPIE to be meaningful, we need to understand what works and what does not; just as in any other area of science, we need to evaluate it robustly and report it transparently. As a research community, we recognise that all clinical research provides an opportunity to evaluate the impact of PPIE to support a cycle of innovation and improvement.

The ongoing 'Therapies for Long COVID in non-hospitalised individuals' (TLC) Study was set up to investigate the burden of long COVID on patients.(16) Patient partners were actively involved in the various stages of the study and provided vital input that led to tangible outcomes and impact. Here, we discuss the lessons learned from conducting PPIE for the TLC study which are applicable to health research beyond long covid. We identify areas of good practice and reflect on areas for improvement. Finally, we provide two checklists of considerations for PPIE to guide the planning and implementation of PPIE in future health research. **Box 1** provides the definitions of key terms.

[H1] PPIE and long COVID: the TLC study

The World Health Organisation (WHO) defines long covid as a "Post covid-19 condition that occurs in individuals with a history of probable or confirmed SARS CoV-2 infection, usually 3 months from the onset of covid-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis." (17) People with long covid experience a variety of symptoms that affect their physical and mental health leading to impaired quality of life and difficulties with employment.(17-20) While our understanding of the pathogenesis, symptoms and complications of long covid has improved, the long-term effects are yet to be fully understood. It is therefore essential that individuals with lived experiences of long covid are actively involved and contribute meaningfully (through high-quality PPIE) to research projects investigating the condition.(21) Indeed, the term 'long covid' was itself coined by patients, further demonstrating how PPIE can frame discussions in health research.(22)

In response to the challenge posed by long covid, the NIHR funded several studies – including the TLC Study(23) – to provide a better understanding of the condition and to explore potential interventions. Most of these long COVID studies involved substantial PPIE (summarized in ref (24)). **Figure 1** illustrates the aims and the work packages of the TLC Study. Work packages 1 and 3 have been completed;(25-28) for work package 2, the literature review and retrospective cohort study are completed(18, 19), while the Bio-Wear sub-study is currently being set-up. The results of the feasibility trial as part of work package 4 are being written up for publication while the economic evaluation is ongoing. A summary of the PPIE methodology used in the TLC study can be found in **Box 2**.

[H2] Impacts and outcomes of PPIE in the TLC study

PPIE, whether at the level of consultation or collaboration, has influenced the design and conduct of every aspect of the TLC study, from the earliest stages of grant proposals right through to the dissemination of study findings.

[H3] Development of grant proposal and project set up

The grant application for the TLC study was co-developed with individuals with long covid and caregivers, and had a patient co-applicant. The application was successful and the reviewing panel noted '…strong patient and public involvement (PPI) and links with other relevant covid-19 research...'

Initially, the researchers and patient partners did not consider the core PPIE group to be sufficiently representative in terms of ethnicity and gender — characteristics identified in literature as being closely linked to the incidence of long covid.(18) Patient partners addressed this by recruited additional individuals from ethnic minority groups via their personal networks and links to national long covid support groups, thus improving the diversity of the core PPIE group. Our record of the socio-demographic characteristics of patient partners (kept with their consent) and log of PPIE activities has enabled us to actively monitor diversity/inclusion throughout the study.

[H3] Study design

Patient partners highlighted the fact that our initial eligibility criteria did not include patients who visited hospital Accident and Emergency (A&E) units due to covid symptoms but were not subsequently admitted as in-patients. In response, we widened the inclusion criteria in the study protocol. Based on their lived experiences, patient partners considered the original

6 months follow up for the Biowear sub-study (Figure 1; WP2) too long and felt it risked a high dropout rate; after further discussions, we reduced it to 3 months. At a PPIE meeting, patient partners stressed the importance of non-pharmacological interventions that directly improved physical function and work capability. For them, inability, or reduced ability to work due to their symptoms was a major impact of long covid. This feedback shaped the focus of our systematic review of these interventions.(27, 28)

[H3] Undertaking research

Development of the Symptom Burden Questionnaire for Long Covid™ (SBQ™)-LC

According to patient partners, existing tools for symptom burden measurement did not fully address the breadth of long covid symptoms — highlighting an unmet need which led to the development of the SBQ-LC. Patient partners' first-hand reports of long covid verified the literature review findings and informed the early design of the questionnaire. Their valuable feedback on the long list of symptoms helped refine the wording of individual questionnaire items, which improved clarity. Patient partners identified issues with the functionality of the Atom 5™ study platform (which enabled video assessments and questionnaires via a smartphone application) during the usability testing of the questionnaire prototype, which were subsequently addressed. They assisted with the recruitment of individuals who field-tested the draft questionnaire through links with long covid patient support groups — namely Long Covid SOS, Long Covid Scotland, and Long Covid Support. As a result, 330 responses were received of which there were 274 complete responses.

Over-the-counter medication (OTC) survey

We were alerted by a patient partner to the fact that some individuals with long COVID were spending substantial sums of money on OTC medications or alternative therapies to manage symptoms — with little or no evidence of efficacy and potential risks of harm. As a result, we co-designed a survey to assess the situation. Patient partners suggested several treatments being used by the long covid community that researchers were previously unaware of; this meant that the final survey was more comprehensive and relevant.

Co-production of a non-pharmacological virtual intervention

We held a consensus meeting with six individuals with long covid, 10 healthcare professionals, four researchers and three other experts to discuss the design of a non-pharmacological virtual intervention for people with long covid.(25) A co-production team including patient partners was formed to select a virtual intervention and design a feasibility study.

Patient partners trialled heart rate monitoring using a Smart Watch but expressed concerns over its potential to cause anxiety and harm among participants by encouraging physical exertion and risking post-exertional malaise. As a result, this was excluded from the feasibility study. Recruitment to this feasibility study was then facilitated by patient partners, to ensure diversity in terms of ethnicity, sex, and geographical location. This was achieved through their links with churches, the Caribbean African Health Network, Long Covid Warrington group, Long Covid Manchester group, Covid Aid Support Community, and Covid-19 Research Support group.

[H3] Dissemination of study findings

Patient partners contributed to the content of study newsletters and press releases, ensuring they were patient-friendly. They shared study updates and publications within their support groups (Long Covid SOS & Long Covid Scotland) and broader networks. Several patient partners spoke to the media about study findings, and one spoke about PPIE at an NIHR long covid event on 1st Nov 2021. Patient partners suggested and produced patient-focused content for the study webpage which are publicly available via YouTube. These include a series of videos in which they talked about living with long covid and shared their tips on how they are adapting to their new life. Patient partners also led a long covid webinar where they shared their experiences of the condition and described their input to the TLC project. Despite having little or no prior experience of academic writing, as co-authors patient partners provided comments on intellectual content of this and other manuscripts(19, 24, 26) and ensured that the wording in manuscripts was acceptable from a patient perspective.

[H2] Successes

We believe patient partners should provide their reflections on what they consider a successful implementation of PPIE in addition to the activity/impact logs kept by researchers. This section incorporates the feedback obtained from our patient partners on the successes and challenges for PPIE in the TLC study.

Patient partners confirmed that their early involvement with the study provided the opportunity for them to identify important issues, including those related to study design, that the researchers had missed. They acknowledged that their feedback led to changes in the study design and the text of manuscripts. Patient partners and researchers stated that one of the strengths of the study's PPIE approach was the flexibility in terms of giving them the option of contributing as a group and/or on a one-to-one basis. This meant that those who were not able to attend meetings due to health or work demands or personal preference were still able to contribute substantially to the study. The introduction of breaks during PPIE

meetings worked well and allowed patient partners to rest as they often became fatigued over time.

The training we provided to patient partners was targeted to anticipate and respond to their needs at each stage of the study. An alternative approach would have been to deliver a pre-planned full curriculum of relevant material. However, patient partners indicated that they preferred our more agile, responsive approach. For instance, during the co-production of the feasibility trial the researchers spent time explaining trial processes and key terms during weekly meetings. The approach was less formal, more bespoke, and perhaps not always identified as 'training'. We recommend that approaches to training and support for PPIE group members should be carefully considered and tailored to the needs of the individuals and the programme of work.

Patient partners in the co-production team reported unforeseen positive impacts; working on the project gave them a sense of purpose whilst coping with the daily challenges of their condition. They also reported benefiting from the peer support that developed between them as a result of working closely together.(25)

[H2] Challenges

The biggest challenge - especially in the early stages - was balancing public engagement against time and resource constraints. The TLC study was set up against a background of urgent population-level medical need, a demanding project timeline and a need to provide answers that would inform national policy. The study also aimed to support and partner with individuals whose lives had been recently turned upside down by long covid, and who often experienced symptoms that were a direct barrier to their ability to contribute to research. A key learning from the set-up period is the need to prioritise communication not only with patient partners but with the wider patient communities. This is important even when logistical demands of a study (e.g., ethics applications) are extremely pressing, and there are no results to share. A practical response is to recognise and obtain resources that may be required at this key pressure point, to ensure patient and public communities are adequately supported.

The pressured timeline also made it difficult to provide as much time as we would have liked to our patient partners to review study documents. This was a particular concern where individuals were affected by long covid symptoms such as fatigue. However, by adopting a flexible approach to involvement, patient partners were able to provide feedback verbally or in writing. We continually provided other opportunities to contribute if they were unable to input to a particular aspect due to time constraints or their health at the time. This way, we maximised their involvement in the study within the overall constraints of the study timeline.

Some challenges arose directly from new insights that patient partners provided. For instance, they identified the need to conduct research into OTC and alternative therapy medication use, which was not part of the original work plan submitted for funding. While we encourage and support such contributions, it is important to note that these may come with resource implications. Furthermore, resource needs for facilitating and reimbursing PPIE may not be fully known and budgeted for when grant applications are made. This may later determine the extent of PPIE that is undertaken during a project. Including additional budget for patient-led initiatives in future bids could support such activities.

We found that some patient partners felt external pressure to respond to queries about TLC's research on social media which ideally should be routed to the researchers. It is therefore important to clarify how social media will be managed as part of the terms of reference. This is particularly important for research with considerable public interest so that patient partners are not burdened. As co-authors on publications, patients are required to provide an email address for the online submission systems. However, some patient partners did not feel comfortable sharing personal accounts and so we offered generic study email addresses as an option. We would recommend this approach for future studies.

We recruited fewer men to the PPIE group despite approaching several men throughout the course of the study. It is unclear why men have been reluctant to participate, but it is worth mentioning that women are more likely to develop long covid. Furthermore, maintaining adequate numbers of patient partners was a challenge as patients' symptoms improved over time and several returned to work either full time or part-time. As a result, some were unable to participate further in the study. For those still able and interested in contributing, our flexible approach was found to be helpful.

[H1] Key considerations for PPIE

We generated an initial long-list of 'key considerations' for PPIE based on the group discussions, interviews with patient partners and researchers, and the log of PPIE activities (**Box 2**). The list was discussed with patient partners and revised based on their suggestions for edits and additional items. This list was used to create a survey (in SmartSurvey™) which was sent to patient partners and researchers involved in the TLC Study.

The survey consisted of 32 items, organised under eight sections, including six which coincided with stages of research, namely: (i) Development of grant proposal (ii) Project set-up (iii) Study design (iv) Undertaking research (v) Dissemination of study findings and engagement (vi) Evaluation of PPIE. Two other important aspects of PPIE were also

included, namely (i) Practical considerations for PPIE and (ii) Membership of PPIE group, as well as a free text box for suggestions and comments.

The survey was completed by 34 individuals: 20 (58.2%) patient partners and 14 (41.2%) researchers. Of the 20 patient partners, 18 (90.0%) were female, there were 9 (45.0%) in both 30-49 and 50-69 (years) age categories, and thirteen (65.0%) had 1-3 years of PPIE experience. Fifteen (75.0%) of the patient partners were White; four (20.0%) were of Black and 1 (5%) of Asian descent. Of the 14 researchers, 9 (64.3%) were female and 9 (64.3%) were aged 30-49 years old; 8 (57.1%) were White and 6 (42.9%) from various ethnic minority groups. Half of the researchers had 5+ years of PPIE experience and 4 (28.6%) had 1-3 years of PPIE experience.

Respondents rated each item in the survey on a scale of importance. Most of the items were considered as ‘very important’ or important’ considerations for PPIE in research. Even items with the lowest rankings still had high endorsement from survey respondents — possibly reflecting the fact that the survey items, co-developed with patient partners and researchers, adequately captured the values of the respondent group. The item ‘Enough time should be given to obtain and collate patient feedback, and modify the application as required’ had the highest overall rating, with 100% of respondents considering it an important/very important consideration. On the other hand, the item ‘Patients should be involved as co-applicants on grant applications’ had the lowest overall rating as important or very important (67.7%); the raw data shows that it was considered as important/very important by 85.7% of researchers and only 55.0% of patient partners.

23 items rated as important/very important by 80% or more survey respondents (pre-specified threshold), formed our checklist of key considerations for PPIE for all studies (**Table 1**). We strongly recommend that research teams endeavour to incorporate these in their PPIE work as appropriate. The 9 items rated as important/very important by less than 80% of respondents were grouped together as a checklist of additional, desirable considerations for PPIE in research (**Table 2**). While these have not made it to our checklist of key considerations, they still had high endorsement from patient partners. We still believe they are important and should be discussed with patient partners when conducting clinical or health research.

Discussion

This article outlines the tangible benefits and impacts of PPIE on the various work packages of the TLC Study. The invaluable contributions of our patient partners to the codesign and dissemination of study findings have enabled us to tailor our research to address patient needs and engage with a wider audience. Unforeseen benefits such as peer support and a sense of purpose that patient partners derived by actively contributing to the study further highlight the wider value of PPIE in research. Funders and researchers generally consider the inclusion of patient partners as co-applicants and co-authors on grant applications and peer reviewed articles as important. While patients still value these types of involvement, these might not be their top priority. It is therefore necessary to explore with patients and the public how they wish to engage in research.

Some of the impacts we have described here have also been reported by others.(24, 29) For instance, the meta-analysis by Crocker et al found that the involvement of people with lived experience of a condition under study (in PPI interventions) was significantly associated with improved enrolment (odds ratio 3.14 *vs* 1.07; P=0.02).(29) For the TLC study, patient partners assisted with recruitment for the field-testing of the SBQ-LC and the feasibility study for the non-pharmacological intervention by promoting these via their networks. Patient partners also played key roles in the dissemination of our study findings, similar to other long covid studies described by Routen et al.(24)

There is a need for PPIE to be embedded in research at an organisational level and not just conducted ad-hoc for each project.(30) There is growing recognition that PPIE should occur at all levels in the delivery, research, and regulation of healthcare interventions. International regulatory agencies including the Medicines and Healthcare products Regulatory Agency (MHRA), U.S Food and Drug Administration (FDA), and European Medicines Agency (EMA) have produced guidance and strategy documents for PPIE.(31-33) They also acknowledge that there is an opportunity for greater PPIE in drug development and regulation.(34) Increasingly, funding organisations such as the NIHR expect that patient and public input is obtained and plans for this are detailed in grant applications. Some journals have introduced policies requiring authors to report if, and how, patients and the public were involved in their research and/or the drafting of manuscripts. While these are welcomed advances, care should be taken that they do not become tick-box exercises.

Further research on the evaluation of PPIE is required. Reflection and evaluation are key for progress towards developing ever more meaningful, effective PPIE. The potential to learn from advancing experience in PPIE will be lost if it is not reported. The contributions of the TLC study patient partners provide an example of how PPIE may positively impact all stages

of health research, even in an urgent public health context. Other researchers may draw on our experience to better plan, implement, and evaluate PPIE for other long covid research as well as research related to other health conditions.

Figure 1. Patient and public involvement in the TLC study. The aims of the TLC study were firstly, to evaluate the symptom burden and underlying pathophysiology of long COVID syndromes in non-hospitalized individuals and the impact on quality-of-life and work capability and, secondly, to identify potential therapies and co-produce a remotely delivered non-pharmacological support intervention. To achieve these aims, four work packages (WP) – each with substantial PPIE elements – were designed and initiated.

Box 1: Definition of key terms

The **'involvement'** component of PPIE refers to activities and research carried out 'with' or 'by' members of the public or patients, rather than 'to', 'about' or 'for' them. Patients and members of the public are actively involved in the development, running and management of research projects or activities.(35, 36)

The **'engagement'** element of PPIE focuses on the dissemination of information and outcomes from research to patients and the public, so that they are informed of developments while providing them the opportunity to share their insights and input.(35, 36)

Coproduction is "an approach in which researchers, practitioners and the public work together, sharing power and responsibility from the start to the end of the project, including the generation of knowledge." Patients, members of the public and other stakeholders are equal partners in research with joint ownership of key decisions during the project.(10)

Box 2. Methodological approach to PPIE in the TLC study

We consider PPIE in research as a methodological activity to improve research quality.(15) Our overarching approach was collaborative; there was patient representation on the project management group to provide strategic oversight.

Recruitment

For the grant application, we approached individuals from acute care and outpatient and day (OPD) services and through leaflets distributed across NHS Trusts. 14 people with long covid and four caregivers provided feedback on the application.

The PPIE group for the study was established and operated in accordance with UK Standards for Public Involvement in Research and the NIHR INVOLVE guidelines on diversity and inclusion.(6, 7) We recruited patient partners with long covid through the following channels:

- Individuals who reached out directly to the research team.

- Members of Long Covid SOS, and Long Covid Scotland through group coordinators.
- GPs based in Birmingham.

Formation of PPIE group

(i) A broader group of 40 individuals who helped with aspects of the project including the cognitive and usability testing of the SBQ^{TM}-LC.

(ii) The core group of 15 individuals who worked closely with the researchers throughout the research.

(iii) A team of 5 who co-produced the non-pharmacological intervention/feasibility study.

(iv) A few individuals preferred to liaise one-to-one with the researchers.

Evaluation of PPIE

- We used the Public Involvement Impact Assessment Framework (PiiAF) Guidance and the Research Contributions Framework (37, 38) to develop our evaluation plans.
- A log of PPIE input was used in the assessments.
- Furthermore, six patient partners participated in a group discussion and six researchers were interviewed. Content analysis of the transcripts of the audio recordings was performed. Insights from this analysis facilitated the development of the survey.
- We used the stages of research described in the NIHR Handbook for Researchers as a framework for reporting the outcomes/impacts of PPIE complying with the stipulations of the Guidance for Reporting Involvement of Patients and the Public (GRIPP2) checklist.(5, 39)
- The feedback from the patient partners informed the findings we have reported in this article.

Table 1. Key consideration(s) for PPIE for all studies

Stage/aspect of research	Key consideration(s)	
Development of grant proposal	Enough time should be given to obtain and collate patient feedback and modify applications as required.	☐
	Patients should be consulted throughout the grant writing process and provide their lived experience to help shape the proposal.	☐
	Patients should be involved in the early discussions before the formulation of research question(s).	☐
	Patients should input into development of the research question(s).	☐
	Patients should co-produce the Lay Summary (this is a patient-friendly summary of research aims, research plan and potential benefits).	☐
Project set-up	There should be early PPIE meetings that focus on providing patient partners in depth but jargon free information about work packages.	☐
	An initial PPIE meeting should be scheduled to introduce the patients to each other and the research team and outline the study plans.	☐
	An early meeting should be held which explains and clarifies participation as a PPIE member as distinct from being a study participant.	☐
	Training and information needs should be considered and provided as required.	☐
Study design	Feedback from patients should be obtained even if incorporating this might alter research plans and timelines.	☐

Undertaking research	When asking for patient feedback on technical documents such as protocols, it might be useful to highlight which specific jargon-free areas you need them to review. Alternatively, provide additional information and support to enable them to understand more technical content.	☐
	Patients should be given enough time (at least a week for an hour's work) to review and provide feedback on documents.	☐
Dissemination of study findings and engagement	Patients should be actively involved in the dissemination of study findings if they would like to do so (e.g., posting on patient forums, participating in media interviews).	☐
	Patients should review and provide feedback on study findings.	☐
Practical considerations	Consider the needs of the group to ensure accessibility for attendance to PPIE meetings (e.g., work commitments, childcare, and seen and unseen disabilities).	☐
	There should be flexibility in the timing of dates and times for meetings.	☐
	Research team should be in regular communication with the PPI group to update on activities, planned activities and timelines (e.g., newsletters and regular meetings).	☐
	There should be flexibility in the mode of obtaining patient feedback (i.e., face to face or online videoconferencing, telephone, or email).	☐
	There should be flexibility in the method of obtaining patient feedback (i.e., group or one-to-one meetings).	☐
	Include sufficient funding to support PPI team with emerging ideas during the grant.	☐
	Research team should arrange timely payment for activities (vouchers or fee).	☐
Membership of PPIE group	The target population should be considered, and efforts made to recruit a diverse group from different backgrounds and via different recruitment routes (e.g., through social media, community groups and traditional links like GPs).	☐
	Follow recommendations and guidelines such as the NIHR Standards for PPIE.	☐

Table 2. Desirable consideration(s) for PPIE in research

Stage/aspect of research	Desirable consideration(s)	
Development of grant proposal	Patients should be involved as co-applicants on grant applications.	☐
Project set-up	Less experienced members might benefit from matching with a more experienced 'buddy'.	☐
	Patient input on aspects of project set-up such as design of study logo and website should be sought.	☐
Study design	Patients should be asked specifically for feedback on eligibility criteria.	☐
	Patients should be asked specifically for feedback on recruitment strategies.	☐
Dissemination of study findings and engagement	Patients should provide input on the communication strategy for the project.	☐
	Patients should be co-authors on study publications.	☐

Evaluation of PPIE	Patients should collaborate with researchers to evaluate their contributions to research studies.	☐
Practical considerations	A generic email account should be set up for patient affiliations (to ensure their privacy).	☐

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Competing interests

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Author contributions

OLA, MJC conceptualised the study. OLA, MJC, YA, LA, LB, JC, AC, FJ, SK, KLM, PM, GP, MSC, and DS provided input on the survey design. OLA analysed the survey results and drafted the manuscript. CM created the figures. SEH, CM, GMT, AS, RH, EHD, CF, SH, MJC, YA, LA, LB, JC, AC, FJ, SK, KLM, PM, JO, GP, MSC, DS, OLA and members of the TLC Study Group read, revised, and approved the final manuscript. The views expressed in this article are those of the author(s) and not necessarily those of the NIHR, or the Department of Health and Social Care or Merck.

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