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Opinion

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Public and patient involvement in research to support genome services development in the UK

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Abstract

Public and patient involvement (PPI) - the collaboration in research with members of the public and patients with relevant experience - is becoming well established in health service research in the UK. It is supported by funders and academic institutions. Published principles and guidelines for researchers, developed through consultation and consensus building, are available. Meanwhile, as genome sequencing is adopted into routine health care, translational genomics research and research to evaluate new genomic services are growing. Given the ethical and social implications of offering genome sequencing within a national health service, it is important that researchers give full consideration to planning and implementing meaningful PPI. Here we present five case studies of PPI in a variety of clinical genomic studies, including commentary on positive impacts and suggestions for improvements. We call for funders and academic institutions to continue and increase their efforts to enable and promote PPI across genomic and other health service research.

Keywords: PPI, patient involvement, genome sequencing, health service research

INTRODUCTION

"Public and patient involvement" or PPI, is becoming an established feature of health research in the UK. For example, it is mentioned in 12 of the 33 articles published in 2022 by the National Institute for Health Research (NIHR)[1]. It is the practice of working in partnership with people who have life experience relevant to the research - enabling them to inform, influence and actively collaborate in research - and is distinct from recruiting study participants and from "engagement", which focuses on disseminating findings outside academic journals and conferences[2]. Efforts have been made to produce frameworks that capture the variety of strategies developed for effective PPI, activities that PPI participants can undertake, and principles to optimise outcomes[3-6]. Discussion in the literature is expanding into standardised reporting of PPI and the finer points of representation on PPI advisory boards by inviting individuals with and without some level of research experience[7,8].

Two key motivators behind the growth in PPI activity are the ethical and democratic imperative of giving the ultimate beneficiaries of research an opportunity to influence its direction, and the related argument that it can improve research and service development outcomes and relevance. These arguments apply along the pipeline from basic to clinical and translational research, although the benefits arising from PPI for laboratory research may be less tangible[9]. Translating new knowledge into clinical services, however, requires an understanding of a wide range of potential impacts on the users of the services and their families, including those that researchers might not anticipate. It is perhaps easier to comprehend the impact that involving PPI contributors can have on research that aims to design and evaluate new clinical services.

The growing body of literature about measuring the impacts of PPI includes a focus on clinical trials[10] and on those involved in research themselves[11], although the value of quantitative metrics and whether measuring impact per se is the most useful way forward are still debated issues[12,13].

The growing evidence around the practice and outcomes of PPI has gone hand in hand with the development of resources by UK-based organisations which aim to support researchers in establishing meaningful PPI. These take the form of national standards, sets of principles, guidelines and toolkits[14-17] developed through consultation and consensus building exercises, plus mechanisms to link interested participants and researchers with each other[18,19]. Standards and principles focus variously on deciding who to involve and how to involve and support PPI members, good communication and documenting PPI processes and impact. Major UK health research funding organisations now encourage or even require PPI planning to form part of applications for funds[20-24].

In the arena of genomics, the UK continues to be a significant actor in the development of the technology and its application in health services. Large-scale projects such as the UK Biobank, the NIHR BioResource and the 100,000 Genomes Project have generated vast numbers of highly cited publications, and the latter led directly to the establishment of the new Genomic Medicine Service (GMS) in the NHS[25-30]. The GMS aims to promote equity of provision and includes new testing services, such as rapid turnaround exome/genome sequencing for fetal anomalies and for seriously ill children who are in hospital without a diagnosis[31,32]. Still at the research stage but embedded within the NHS is the Newborn Genomes Programme which will evaluate the application of genome sequencing for newborns, its impact on the NHS and the risks and benefits for individuals and families[33].

APPLIED GENOMICS AND MEANINGFUL PPI

The culture of a positive approach to PPI among health researchers, and the mature ethical, legal and social research community in the UK, have facilitated the adoption of PPI within the evaluation of proposed and live pilot genomics services. In many ways, the core principles of good PPI apply as with any other health research - but there are potential conflicts between social and scientific perspectives of genomics, and particular issues for patients such as the benefits and risks of knowing certain types of genomic information, such as variants of unknown significance and secondary findings, which means a particularly attentive approach to PPI is warranted[34,35]. PPI strategies that include a focus on underserved populations are also an important part of helping to address the issue of a lack of diversity among the participants in genomics research to date[36,37].

This article describes recent and current PPI case studies [Tables 1-5] from research focused on delivery of genomics in the NHS, and what lessons can be learned. The case studies are presented following Donabedian's three components approach, originally designed for evaluating the quality of care[51]. The components are: structure (attributes of the case study), process (the systems and processes adopted to deliver the desired outcome) and outcome (impact on the project, researchers, and PPI participants themselves).

PPI in the evaluation of new genomics services [Tables 1-3]

PPI in new applications of genomics [Tables 4 and 5]

CONCLUSION

The five case studies presented illustrate that PPI can bring significant and beneficial influence to research that addresses sensitive and ethically-challenging topics in genomics service development. The case studies point to PPI advisors directly impacting study protocols, budgets and materials, refining recruitment approaches for parents who may be bereaved or traumatized and improving diversity, and giving invaluable contextual information to support the interpretation of findings. Integrating PPI contributors in this way has provided invaluable insight to the research teams, which should also benefit their future research work.

Some limits to the benefits of PPI can be directly linked to the existence of barriers or the lack of enablers, which can reduce the effectiveness of PPI activities undertaken by researchers[52]. The case studies explore a range of both organisational enablers (such as resourcing and training) and those at a personal level (such as a collaborative approach that involves PPI contributors at every stage, with clarity around roles and expectations). Further, greater awareness of the imbalances of power inherent in the way PPI partnerships are established could lead to better quality outcomes. For example, we recognise in our case studies the tendency for researchers to set meeting agendas and make decisions about how PPI contributors will engage, and that a more flexible collaborative approach, such as inviting PPI contributors to lead PPI groups, can be very valuable. Our case studies also clearly illustrate challenges in achieving equality and diversity in recruitment and involvement -careful planning and resourcing, and early consultation with patient or community groups, are important to address this. Finally, long-term partnerships with individuals over the course of several studies might lead to a narrowing of the viewpoints being offered - conversely, PPI teams will always be too small to be representative of the study population, and their input must be sought and valued in that context.

Table 1. Case study 1 - reflections on PPI structure, process and outcome

PPI in "evaluation of the NHS Genomic Medicine Service for paediatric rare diseases"
Structure
Research aim: • To understand how genome sequencing for paediatric rare diseases is being delivered in the new Genomic Medicine Service (GMS)[38], with a focus on barriers and enablers to successful delivery. PPI team: • Representatives from Genetic Alliance UK and Unique, and three parent representatives recruited through SWAN UK (Syndromes without a name)[39-41], who sit on the study advisory board
Process
Recruitment: • By advertisement distributed through the patient groups' social media channels explaining the role, who the researchers were looking for (parents with experience of an undiagnosed child, and experience of genetic or genomic testing), and what the expectations of the PPI group would be. The lead researcher spoke to potential participants by phone, and both were recruited. • Diversity: the researchers stated in recruitment advertisements that they were keen to include representation from different ethnic groups, and from fathers. One mother with South Asian heritage applied and joined, but no fathers applied. It was important to recruit individuals with lived experience to complement the patient organisation representatives who may not be representative of the wider community. Supporting involvement: • Expectations of the PPI team set out clearly by the PI in the terms of reference: support development of the study protocol, information sheets and ethics application; assist in developing topic guides and questionnaires to ensure the topics covered are important and relevant to patients and families; develop strategies to troubleshoot any problems, e.g., with recruitment; assist in data analysis, in particular interpreting how the findings may be of relevance to patients and families, and to support translating the findings into recommendations for practice for clinicians and policy makers; and develop plain language summaries and support other effective methods of communicating findings to a wider audience. • The PPI team was integrated into the main advisory group which meets twice each year, but the initial meeting was limited to parent members of the PPI team to build rapport, discuss the study and air questions and concerns. Parent participants were generally contacted by phone after advisory group meetings to discuss the feedback that they did not feel able to share during the meeting. • Meetings have been virtual, and ad hoc phone or email contact is made between meetings to ensure relationships are maintained. • Plans are in place to deliver online training for those wanting to upskill (to be determined by the PPI team but could include data analysis, writing and presenting)
Outcome
Positive impacts on PPI contributors and on the study: • The feedback from parent participants during post-meeting phone calls is that they feel able to ask questions and participate in the discussions about the study. • The PPI team has reviewed and commented on study documents and provided input into which measures to include in a survey for parents of children having WGS. As a result of their feedback, the survey includes a measure of parental health and family functioning which was seen as an important outcome of testing. • A number of the PPI team were co-authors on the published research protocol[38] and they will be invited to co-author further academic publications from the project. There will also be the opportunity to co-present some of the research findings at conferences. Limitations of PPI in this study: • Two parent participants had to drop out due to other commitments. One has been replaced, but it would have been preferable to recruit more participants at the start to allow for this possibility. • It would have been beneficial to build training and support into the grant application to allow one of the parents to act as a lay co-researcher on the team ("an expert by experience"), to access the parent interview transcripts and provide a counter-perspective to analysis by the social scientist

The authors of the case studies have identified improvements that could have been made in their approaches. There is scope for funders and academic institutions to take steps to further embed good practices across genomic and other health service research. Concrete actions are important in themselves, such as communicating clearly about what funders and academic institutions expect researchers to do, signposting to existing PPI resources, and providing financial and practical support - but these steps are also necessary if we are to create and sustain an academic culture where effective PPI is a given.

Table 6 provides the key recommendations identified by the authors for fellow investigators in health service research, arising directly from the case studies presented.

Table 2. Case study 2 - reflections on PPI structure, process and outcome

PPI in "evaluation of rapid genomic sequencing for critically ill children (rGS Study)"
Structure
Research aim: • Rapid genomic testing can offer faster diagnoses and much earlier decisions about care for babies and children when they are critically ill and a monogenic condition is suspected[42]. This mixed-methods study is looking at the delivery of this test in the NHS from the perspective of parents and professionals to facilitate optimal care and support for children and their parents[39]. PPI team: • There are four arms to the PPI Team. ○ 1. Two of the co-applicants are from patient organisations (Genetic Alliance UK and Alstrom Syndrome UK)[39,43] and sit in the research team, bringing experience with a range of research projects and in setting up PPI advisory groups, and a broad perspective on rare disease. The Genetic Alliance UK representative leads on the PPI elements of the evaluation. ○ 2. There is a social science researcher based at a patient organisation (Genetic Alliance UK). ○ 3. A PPI Advisory Group with patient organisation representatives and individual parents. The individual parents offer their lived experience of having a child who was cared for in intensive care and/or offered exome or genome sequencing. ○ 4. A representative of a patient organisation, who is not part of the PPI Advisory Group, sits on the main study steering group alongside clinicians and researchers to bring a patient voice to those meetings
Process
Recruitment for the PPI Advisory Group: • Parent members (of children with a developmental disorder, or a suspected/diagnosed rare condition) were recruited through advertisements and completed a short application form to allow for selection based on diversity as well as experience in genome sequencing and/or neonatal or paediatric intensive care. A father was recruited after additional calls were made through support groups for fathers, and a mother with South Asian heritage was recruited by invitation. Five parents in total were recruited. • Relevant patient organisations were approached and invited to suggest a representative who could join the PPI advisory group. Supporting involvement: • PPI members of the core research team have contributed to funding applications, study design and development from the outset. • Because of the sensitive nature of the topic area, and to help members feel comfortable sharing their experiences, a separate PPI advisory group was set up rather than only including PPI members within the wider study advisory group (including researchers and clinicians). • The PPI Advisory Group meets on an ad hoc basis when feedback is needed. Members are paid for their time. • One of the social science researchers is based at Genetic Alliance UK to further strengthen the links between PPI input and research processes
Outcome
Positive impacts on PPI contributors and on the study: • PPI input into study materials and recruitment planning is particularly important for this research due to (1) the sensitive nature of the planned interviews with parents whose child has been very unwell or may have died; and (2) the need to consider diversity in the study when exploring parent experiences and equity of access to testing. • The PPI advisory group has given detailed feedback on the wording and images for an online parents' survey and the participant information sheets. The diverse experiences of the group have been especially helpful in alerting the researchers to wording that can impact, for example, bereaved parents, those not biologically related to their child and same-sex couples. • The group has helped find meaning in the survey results and given advice on topics to include in the parent interviews. They will be invited to give feedback on themes and quotes from the interview analyses to inform interpretation. • In the future, it is hoped that this group will help with the preparation of publications and the development of recommendations for practice that are focused on parent and patient priorities and needs. • Having PPI co-applicants ensured PPI input from the initial design of the study, and informed budget decisions such as funding for translation of study materials and options for other formats such as audio and video. They are part of the research team, which means that there is iterative feedback between the PPI and research teams throughout the study. Limitations of PPI in this study: • Within the PPI advisory group, it was not possible to find representatives of all parent experiences that are relevant to the study. For example, very few fathers put themselves forward to be involved. • The researchers tend to direct the PPI input, setting the meeting agenda, setting questions and drafting materials for comment. It may be helpful to be less prescriptive and allow the PPI input to be more iterative and open

Table 3. Case study 3 - reflections on PPI structure, process and outcome

PPI in "optimising exome prenatal sequencing services (EXPRESS study)"
Structure
Research aim: • EXPRESS is a mixed-methods research project studying the roll-out of prenatal exome sequencing as part of the NHS Genomic Medicine Service[44]. Prenatal exome sequencing is offered when ultrasound scans show a baby is not developing as expected and doctors suspect a monogenic condition. Expectant parents who are offered the test will have been faced with uncertain scan findings and will then be asked to make decisions about further testing and the future management of their pregnancy. They may be offered the option to terminate their pregnancy. PPI Team: • There are three arms to the PPI Team. 1. Two funding co-applicants and core members of the research team are from the patient organisations (Alstrom Syndrome UK and Antenatal Results and Choices (ARC))[43,45]. The Director of ARC leads the PPI elements of the research. 2. There is a social science researcher based at a patient organisation (ARC).

3. A PPI Advisory Group was established with representatives of parent organistations and an individual member with relevant experience

Process

Recruitment:
- ARC provided guidance on appropriate recruitment of parents to the study PPI: the group's members include representatives from a number of parent and patient support organisations, and a researcher who has personal experience in prenatal testing and bereavement.

Supporting involvement:
- The group has been asked to focus on the qualitative arm that is investigating parents' views and experiences of prenatal exome sequencing, and the ethics workstream that aims to explore associated ethical issues.
- The group meets quarterly and members are paid for their time.
- One of the researchers is embedded at ARC and received training to work on the charity's helpline to gain an in-depth understanding of what parents face when making decisions around testing, diagnosis and termination of pregnancy

Outcomes

Positive impacts on PPI contributors and on the study:
- Including patient group representatives as co-applicants ensured that they helped inform the overall study design.
- The PPI group gave feedback on interview topics and questions, recruitment methods, the design of multiple formats of patient information, and the creation of a newsletter about the research for patients to make sure they are clear and inclusive.
- The PPI group gave feedback on themes arising during interview analysis to inform interpretation and are co-authors on the published research protocol[44].
- Embedding the researcher at ARC allowed them to fully focus on parents' experiences and provide an active link between the research team and the patient organisation, which in turn helps the wider research team to maintain a focus on parent priorities.

Limitations of PPI in this study:
- English-speaking white middle-class participants are overrepresented at the time of writing. PPI involvement in designing a specific budget and plan for targeted methods of recruitment, e.g., using community groups, may have helped us reach potential participants from underrepresented demographics

Table 4. Case study 4 - reflections on PPI structure, process and outcome

PPI in "genomics england newborn genomes programme"
Structure
Research aim: • Genomics England's Newborn Genomes Programme will launch in 2023 and is a co-designed research study, i.e., it develops the PPI approach such that patients and public partners actively influence decision-making in the project design and operation. The programme will explore the benefits, challenges, and practicalities of sequencing newborns' genomes[33]. An in-depth and early phase of consultation with stakeholders as part of the research design has been carried out to focus on how to "choose conditions", i.e., determining which rare genetic conditions, out of the many potential options, should be looked for as part of the study. A six-month process was designed to establish a set of underpinning principles. Note: This case study illustrates an approach to PPI that is "modular" - in addition to integrating PPI advisors for the lifetime of a project (drawing on the long-standing Genomics England Participant Panel - a key advisory group for Genomics England consisting of patients, family members and carers who have had genome sequencing)[46], the scale of this work requires additional consultation with distinct (and relatively large) groups of people at discrete stages of the study as part of the co-design. As there are over 6000 known rare conditions with varying levels of impact on health and quality of life, it was important to capture as wide a range of views as possible. It was also critical to include the perspectives of those who do not have experience in rare conditions, as most babies who take part in the study will not receive a positive result
Process
• First, a working group was established comprising healthcare professionals, scientists, ethics and policy researchers, and representatives from patient groups and the public. A member of Genomic England's standing Participant Panel was included. • Principles were proposed by the group, then tested at online workshops with members of the public, people with experience in rare conditions, and healthcare professionals. Each principle was debated in order to capture participants' concerns and interests. • A series of explanatory materials, including presentations and videos, was generated to support workshop participants, and a member of the programme team was available to answer questions at each workshop. • Deliberations were led by expert facilitators from a public participation charity[47]. The Participant Panel at Genomics England was also consulted about the principles in an additional session
Outcome
Benefits of PPI in this study: • Four final principles emerged from the workshops, which will underpin the design of the programme. They relate to validity of the test, severity of the condition, benefits of intervention and equity of access to interventions (e.g., through the UK's NHS)[33]. • Carrying out these workshops early in the programme means that participants' diverse views are integral to the design phase of the work. Limitations of PPI in this study: • PPI endeavours correspond to a moment in time with a wide variety of participants who might all have different views. When making decisions such as which conditions will be looked for in this research study, it is difficult to achieve consensus, and inevitably it is impossible to incorporate some individuals' views. For this reason, decisions that incorporated PPI input should be revisited in light of changing practices. This revisiting is something that the Newborn Genomes Programme is committed to throughout the duration of its study

Table 5. Case study 5 - reflections on PPI structure, process and outcome

PPI in "The secondary cardiac findings evaluation (SCARFE) study"
Structure Research aim: • The SCARFE study was developed to understand the benefits and risks of informing people about a secondary genomic finding, specifically in an inherited heart condition[48]. Secondary findings are genomic changes that are not related to a patient's known health condition but might indicate a risk of a separate serious condition[49]. It is not yet clear whether looking for secondary findings is beneficial. For example, informing a patient about a secondary finding might enable healthcare actions that would detect a health condition early, allowing medical intervention - but being told about a secondary finding might cause people long-term anxiety, and if the risk of disease development is very low, people might undergo tests and treatment they do not need. Inherited heart conditions are a group of disorders that can occasionally lead to sudden cardiac death; if people are genetically at risk because they carry a variant associated with an inherited heart condition, screening tests such as echocardiogram and ECG can identify people whose hearts are affected, and measures can be taken to manage their risk
Process Recruitment: As a new area of study with the potential to inform people about a serious health risk, it was important to involve patients and the public from the outset. PPI members were recruited from an existing Genomics PPI group based in Oxford, including people who had a rare disease or cancer, and their relatives and carers. Supporting involvement: • The research team presented the study aims to the PPI participants, and invited questions and discussion during an informal round-table; all PPI participants were encouraged to voice opinions
Outcome Benefits of PPI to this study: • A key question was how best to contact participants eligible for the study from the NIHR BioResource Rare Disease Study[27] (who had agreed to be contacted about future studies). Potential participants would need enough information to make a decision about taking part in SCARFE without causing alarm or breaching their right not to know unexpected genomic information. Through discussion with the PPI group, the research team was prompted to explore the use of a pre-invitation opt-out letter that would be sent to all BioResource participants. • The resulting letter was based on other stakeholders' deliberation[50] and advised BioResource participants that if they did not wish to be contacted about studies which might tell them about their risk of other health conditions, they could decline the approach [Supplementary Material]. The PPI group was invited to review the document, and the opt-out process was included in the SCARFE protocol submitted for research ethics committee approval

Table 6. Key recommendations for PPI in health service research

Planning
• Researchers should keep in mind that PPI in health research is an active collaboration and two-way process for mutual benefit. PPI teams should find the experience both enjoyable and rewarding, and their impact/influence should be made clear to the whole study team, including the PPI contributors. • Plan for early training opportunities to ensure PPI contributors feel comfortable with technical aspects of the research, and for the research team to learn about lived experiences. • Perform evaluation from the start of the project: what approaches could be used to evaluate the benefit to the PPI contributors, the research team and the study itself? Document and share learnings. • It is helpful both for PPI participants and researchers to set out clear criteria for membership of the PPI group or for PPI members of a study advisory group, along with a clear outline of what is being asked of them and how the group will operate - everyone should be assured that meetings are interactive with an emphasis on the ability to ask questions and on listening and respecting all views. • To facilitate effective planning for PPI, include people with PPI expertise as co-applicants on the initial funding application and include a budget for PPI activities. To improve diversity and representation from underserved groups, a budget is also needed to support targeted methods of recruitment to advisory groups, e.g., through community groups. • Where possible, embed researchers in patient/parent support organisations to gain in-depth experience of the research context. This is particularly valuable when doing research on sensitive topics, for example, prenatal testing or seriously ill children
Recruitment • Consider involving both individuals with lived experience (not necessarily patients) and representatives of patient groups. The latter can bring a broad perspective that complements individuals' experiences, and access to networks of affected individuals. If patient group representatives have experience in academic research, they may be able to advise on what PPI can bring to a study, what is involved in setting up a PPI advisory group within the processes and constraints of research, and what worked and what did not in previous projects. In addition, they may be well placed to support PPI members of advisory groups new to research. • Researchers and patient organisations can build close relationships over time - this, plus the "small world" nature of rare conditions, means that the same people are often invited to take part in PPI for multiple studies. The case studies presented illustrate this. Researchers should always consider which are the most relevant organisations that could contribute (and which staff), and whether "new" organisations could be approached in order to optimise the independent perspective that PPI can bring. Think about the size of the PPI advisory group: there is no one "patient voice", so the group should be large enough to represent a suitable diversity of opinion and experience but small enough to allow full and open discussions. Plan meetings according to the needs of the PPI participants: many find remote meetings convenient, but face-to-face meetings can build rapport. Consider informal settings and what practical support might be needed for face-to-face meetings
Involvement • Involve PPI participants as far as possible in all stages of the study, from planning the grant application to interpreting findings (not just at the manuscript review stage) to helping develop recommendations for practice. Early consultation with PPI participants will facilitate consideration of the ethical and practical issues that studies can raise, and will improve protocol development.

• Keep in touch with PPI participants, both between meetings (e.g., by email) to ensure their continued interest, and immediately after meetings (offer phone calls to discuss issues that might have been too difficult to bring up in a group, and signposting to independent support organisations).

• Provide opportunities for the PPI team to co-author papers or co-present research at meetings. Not only does this ensure they are acknowledged for their role in the study and have some ownership of the results, but it can also support parents/the public to develop new skills.

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REFERENCES

1. NIHR open research. Available from: https://openresearch.nihr.ac.uk/ [Last accessed on 3 Feb 2023].
2. NIHR. What is patient and public involvement and public engagement? Available from: https://www.spcr.nihr.ac.uk/PPI/what-is-patient-and-public-involvement-and-engagement [Last accessed on 3 Feb 2023].
3. Shippee ND, Domecq Garces JP, Prutsky Lopez GJ, et al. Patient and service user engagement in research: a systematic review and synthesized framework. *Health Expect* 2015;18:1151-66. DOI PubMed PMC
4. Hoekstra F, Mrklas KJ, Khan M, et al. A review of reviews on principles, strategies, outcomes and impacts of research partnerships approaches: a first step in synthesising the research partnership literature. *Health Res Policy Syst* 2020;18:51. DOI PubMed PMC
5. Greenhalgh T, Hinton L, Finlay T, et al. Frameworks for supporting patient and public involvement in research: systematic review and co-design pilot. *Health Expect* 2019;22:785-801. DOI PubMed PMC
6. Baines RL, Regan de Bere S. Optimizing patient and public involvement (PPI): identifying its "essential" and "desirable" principles using a systematic review and modified Delphi methodology. *Health Expect* 2018;21:327-35. DOI PubMed PMC
7. Staniszewska S, Brett J, Simera I, et al. GRIPP2 reporting checklists: tools to improve reporting of patient and public involvement in research. *BMJ* 2017;358:j3453. DOI
8. Knowles SE, Walkington P, Flynn J, Darley S, Boaden R, Kislov R. Contributors are representative, as long as they agree: how confirmation logic overrides effort to achieve synthesis in applied health research. *Health Expect* 2022;25:2405-15. DOI PubMed PMC
9. Hanley B, Amjad A, Ratcliffe N, Smith AL, Yu R. Workshop report. Patient and public involvement in laboratory based research: reflections on six studies. Available from: https://drive.google.com/file/d/1Vejrg9Oa3dURUrI4fHydQSsZGSdmBNG2/view [Last accessed on 3 Feb 2023].
10. Crocker JC, Ricci-Cabello I, Parker A, et al. Impact of patient and public involvement on enrolment and retention in clinical trials: systematic review and meta-analysis. *BMJ* 2018;363:k4738. DOI PubMed PMC
11. Brett J, Staniszewska S, Mockford C, et al. A systematic review of the impact of patient and public involvement on service users, researchers and communities. *Patient* 2014;7:387-95. DOI PubMed
12. Staley K. "Is it worth doing? *Res Involv Engagem* 2015;1:6. DOI PubMed PMC
13. Russell J, Fudge N, Greenhalgh T. The impact of public involvement in health research: what are we measuring? *Res Involv Engagem* 2020;6:63. DOI PubMed PMC
14. NHS Health Research Authority public involvement web resource. Available from: https://www.hra.nhs.uk/planning-and-improving-research/best-practice/public-involvement/ [Last accessed on 3 Feb 2023].
15. National Institute for Health and Care Research public involvement web resource. UK standards for public involvement. Available from: https://sites.google.com/nihr.ac.uk/pi-standards/home [Last accessed on 3 Feb 2023].
16. Parkinson's disease UK public involvement web resources. patient and public involvement in research. Available from: https://www.parkinsons.org.uk/research/patient-and-public-involvement-research [Last accessed on 3 Feb 2023].
17. Brett J, Staniszewska S, Simera I, et al. Reaching consensus on reporting patient and public involvement (PPI) in research: methods and lessons learned from the development of reporting guidelines. *BMJ Open* 2017;7:e016948. DOI PubMed PMC
18. National Institute for Health and Care Research public involvement opportunities web resource. Opportunities for public involvement in NHS, public health and social care research. Available from: https://www.peopleinresearch.org/ [Last accessed on 3 Feb 2023].
19. National Institute for Health and Care Research INVOLVE directory. Charity Involvement Directory. Available from: https://www.invo.org.uk/charity-involvement-directory/ [Last accessed on 3 Feb 2023].
20. National Institute for Health and Care Research web guide for applicants. A brief guide to public involvement in funding applications. Available from: https://www.nihr.ac.uk/documents/a-brief-guide-to-public-involvement-in-funding-applications/24162 [Last accessed on 3 Feb 2023].
21. Great Ormond Street Hospital Charity grant funding web resource. GOSH charity and sparks national funding call 2022/23 FAQs. Available form: https://www.gosh.org/what-we-do/grant-funding/apply-grant-funding/joint-national-funding-call-supporting-information/ [Last accessed on 3 Feb 2023].
22. Wellcome grant funding web resource. Research involving human participants policy. Available from: https://wellcome.org/grant-funding/guidance/research-involving-human-participants-policy [Last accessed on 3 Feb 2023].
23. UK Research and Innovation, Medical Research Council applicant guidance. Guidance for Applicants 2022. Available from: https://www.ukri.org/wp-content/uploads/2022/08/MRC-15082022-Guidance-for-Applicants-22.3-FINAL.pdf [Last accessed on 3 Feb 2023].
24. UK Research and Innovation, Economic and Social Research Council applicant guidance. ESRC Research Funding Guide August 2022. Available from: https://www.ukri.org/wp-content/uploads/2021/11/ESRC-150822-ResearchFundingGuide.pdf [Last accessed on 3 Feb 2023].
25. Tan VY, Timpson NJ. The UK BioBank: a shining example of genome-wide association study science with the power to detect the murky complications of real-world epidemiology. *Ann Rev Genom Genet* :569-589. DOI

26. Turnbull C, Scott RH, Thomas E, et al. The 100,000 genomes project: bringing whole genome sequencing to the NHS. *BMJ* 2018;361:k1687. DOI
27. NIHR BioResource website. Rare Diseases BioResource. Available from: https://bioresource.nihr.ac.uk/rare-diseases/rare-diseases/ [Last accessed on 3 Feb 2023].
28. Biobank UK publication list. Available from: https://www.ukbiobank.ac.uk/enable-your-research/publications [Last accessed on 3 Feb 2023].
29. National Institute for Health and Care Research, BioResource publications list. Available from: https://bioresource.nihr.ac.uk/publications/ [Last accessed on 3 Feb 2023].
30. Genomics England publications list. Available from: https://www.genomicsengland.co.uk/research/publications?ged=1 [Last accessed on 3 Feb 2023].
31. NHS service guidance. Rapid exome sequencing service guidance: fetal anomalies testing. Available from: https://www.england.nhs.uk/wp-content/uploads/2021/07/B0179_Guidance-rapid-exome-sequencing-service-for-fetal-anomalies_July21.pdf [Last accessed on 3 Feb 2023].
32. Stark Z, Ellard S. Rapid genomic testing for critically ill children: time to become standard of care? *Eur J Hum Genet* 2022;30:142-9. DOI PubMed PMC
33. Genomics England newborn genomes web resource. Newborn Genomes Programme. Available from: https://www.genomicsengland.co.uk/initiatives/newborns [Last accessed on 3 Feb 2023].
34. Murtagh MJ, Machirori M, Gaff CL, et al. Engaged genomic science produces better and fairer outcomes: an engagement framework for engaging and involving participants, patients and publics in genomics research and healthcare implementation. *Wellcome Open Res* 2021;6:311. DOI PubMed PMC
35. Burke K, Clarke A. The challenge of consent in clinical genome-wide testing. *Arch Dis Child* 2016;101:1048-52. DOI PubMed
36. Sharif SM, Blyth M, Ahmed M, et al. Enhancing inclusion of diverse populations in genomics: A competence framework. *J Genet Couns* 2020;29:282-92. DOI PubMed
37. Fatumo S, Chikowore T, Choudhury A, Ayub M, Martin AR, Kuchenbaecker K. A roadmap to increase diversity in genomic studies. *Nat Med* 2022;28:243-50. DOI PubMed
38. Lewis C, Buchanan J, Clarke A, et al. Mixed-methods evaluation of the NHS Genomic Medicine Service for paediatric rare diseases: study protocol [version 2; peer review: 3 approved, 1 approved with reservations]. *NIHR Open Res* 2022;1:23. DOI
39. Genetic Alliance UK. Available from: https://geneticalliance.org.uk/ [Last accessed on 3 Feb 2023].
40. Unique. Available from: https://rarechromo.org/ [Last accessed on 3 Feb 2023].
41. SWAN UK. Available form: https://www.undiagnosed.org.uk/ [Last accessed on 3 Feb 2023].
42. Video summary explaining our research. Available from: https://vimeo.com/718758712 [Last accessed on 3 Feb 2023].
43. Alstrom Syndrome UK. Available from: https://www.alstrom.org.uk/ [Last accessed on 3 Feb 2023].
44. Hill M, Ellard S, Fisher J, et al. Optimising exome prenatal sequencing services (EXPRESS): a study protocol to evaluate rapid prenatal exome sequencing in the NHS Genomic Medicine Service [version 2; peer review: 2 approved]. *NIHR Open Res* 2022;2:10. DOI PubMed PMC
45. Antenatal Results and Choices (ARC) website. Available from: https://www.arc-uk.org/ [Last accessed on 3 Feb 2023].
46. Hastings Ward J, Middleton R, McCormick D, et al. Research participants: critical friends, agents for change. *Eur J Hum Genet* 2022;30:1309-13. DOI PubMed PMC
47. Involve. Available from: https://involve.org.uk/ [Last accessed on 3 Feb 2023].
48. Ormondroyd E, Harper AR, Thomson KL, et al. Secondary findings in inherited heart conditions: a genotype-first feasibility study to assess phenotype, behavioural and psychosocial outcomes. *Eur J Hum Genet* 2020;28:1486-96. DOI PubMed PMC
49. Green RC, Berg JS, Grody WW, et al. ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. *Genet Med* 2013;15:565-74. DOI
50. Beskow LM, Fullerton SM, Namey EE, Nelson DK, Davis AM, Wilfond BS. Recommendations for ethical approaches to genotype-driven research recruitment. *Hum Genet* 2012;131:1423-31. DOI PubMed PMC
51. Donabedian A. Evaluating the quality of medical care. *Milbank Q* 2005;83:691-729. DOI PubMed PMC
52. Ocloo J, Garfield S, Franklin BD, Dawson S. Exploring the theory, barriers and enablers for patient and public involvement across health, social care and patient safety: a systematic review of reviews. *Health Res Policy Syst* 2021;19:8. DOI PubMed PMC