PIRU POLICY INNOVATION AND EVALUATION RESEARCH UNIT

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Summary report

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PIRU Publication 2020-26S

For further details, please contact:

Nicholas Mays
Professor of Health Policy and Director
Policy Innovation and Evaluation Research Unit
Department of Health Services Research & Policy
London School of Hygiene and Tropical Medicine
15–17 Tavistock Place
London WC1H 9SH
Email: nicholas.mays@lshtm.ac.uk
www.piru.ac.uk

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Summary report

Sara Ryan[1], Sian Rees[1,2], Elizabeth Holdsworth[3], Jade Howard[1,4], Fauzia Knight[1], Louise Locock[1,4], Melissa Stepney[1], Angela Martin[1] and Nicholas Mays[3]

1 Nuffield Department of Primary Care Health Sciences, University of Oxford

2 now Oxford Academic Health Science Network

3 Policy Innovation and Evaluation Research Unit, Department of Health Services Research and Policy, London School of Hygiene and Tropical Medicine, University of London

4 now Health Services Research Unit, University of Aberdeen

February 2020

Acknowledgements

The authors would like to thank the following:

The participants of the separate studies that made up this research programme; the participants, carers and specialist health professionals who agreed to be interviewed about their experiences of the 100,000 Genomes Project and the public and non-specialist health professionals who took part in focus groups, Thuy Phan, Felix Gille and Carol Dumelow, who collected and analysed some of the data.

Members of the advisory panel, who engaged with the research and acted as 'critical friends', Ruth Sanders who ensured all material for dissemination on the website healthtalk.org was delivered to the DIPEx charity in accordance with the principles of the Information Standard. Also, Adam Barnett and Jo Kidd of the DIPEx charity who produced and published the new resource on healthtalk.org/experiences-participating-100000-genomes-project, and Caroline Jordan who provided editorial assistance.

This report is based on independent research commissioned and funded by the NIHR Policy Research Programme through its core support to the Policy Innovation Research Unit (Project No: 102/0001). The views expressed in the publication are those of the authors and are not necessarily those of the NHS, the NIHR, the Department of Health and Social Care, its arm's length bodies or other Government Departments.

Contents

Background

The 100,000 Genomes Project (the 'Project'), announced in December 2012, was established to:

- develop new capability and capacity in genomic medicine in order to transform the provision of health services in England;
- create new capability for clinical genomics research and
- establish an infrastructure for the protection and analysis of clinical and genomic data.

The primary mechanism to achieve these aims was through sequencing 100,000 genomes from patients with cancers, rare disorders and infectious diseases, linking the resultant sequence data to a standardised, extensible account of diagnosis, treatment and outcomes. The Project achieved its goal of sequencing 100,000 genomes in December 2018.

The Policy Innovation and Evaluation Research Unit (PIRU) at London School of Hygiene and Tropical Medicine (LSHTM) was asked by the then Department of Health to conduct a qualitative study exploring the experiences of those people who donated their DNA to the Project ('participants') and the experiences of health care staff involved in the Project, as well as the public's perceptions of genomic research more generally. Data collection for the current study took place between late 2015 and late 2017.

The aims of this study were to:

- Understand the motivation of people who agreed to take part in the 100,000 Genomes Project; their experiences of receiving information, giving consent and taking part; their attitudes to data sharing, governance and confidentiality and their views about feedback and use of their Project data for research and clinical care.
- Learn about the experiences of clinicians who asked people to take part in the Project.
- Explore the understanding and perceptions of members of the public of genomic research in general.
- Explore the understanding and perceptions of the non-specialist NHS workforce of genomic research in general, and of the 100,000 Genomes Project in particular, and to identify potential training needs related to any roll-out of genomic medicine services in the NHS.
- Draw on the above, in order to make suggestions for improvement, thereby improving the likelihood of the Project achieving its goals.

This summary report complements the full report of the study which sets out the methods and findings in greater detail (Ryan et al., 2020). There is also a related section on the healthtalk website (healthtalk.org/experiences-participating-100000-genomes-project) which draws on this study's interviews with participants. It includes eight educational films covering differing aspects of the experience of taking part in the 100,000 Genomes Project:

- being invited to take part;
- concerns about taking part;
- reasons for wanting to take part;
- deciding to take part;
- sample storage;
- data protection and sharing;
- thoughts on medical research and genomic medicine;
- messages for health professionals and Genomics England.

This resource will be of interest and of use to healthcare professionals, policy makers and the general public.

Methods

A range of qualitative data was collected as follows:

1. One-to-one interviews with 100,000 Genomes Project participants: rare diseases (n=15) and common cancers (n=19) – December 2015 to September 2017. No people who declined to take part were interviewed.

2. One-to-one interviews with staff involved in the Project: policy makers and managers from NHS England and Genomics England, 'the centre' (n=4), and people working in local Genomics Medicines Centres (GMCs) (n=22 interviews with 19 staff of whom three were interviewed twice) – December 2015 to June 2017.

3. Focus groups with the general public (n=9, each with 5-8 people), including specific Black, Asian and Minority Ethnic (BAME) groups – October 2015 to October 2017.

4. Focus groups with non-specialist (i.e. not involved in the Project or genomics) primary and secondary care clinical staff (n=4, each with 6-8 people) – January to October 2017.

Findings

Participants in the 100,000 Genomes Project

The cancer and rare disease groups were distinctly different in their prior experiences of, and motivation to take part in, the Project. The latter commonly had longstanding experience of their conditions and established relationships with consultants and other health professionals. Most participants in this group had a strong desire to know more about their disease and often had considerable knowledge of genetics and their particular condition. In some respects, they had a 'vested interest' in taking part in the Project to generate greater understanding of their own condition and the implications for other family members and future generations. Cancer participants were mostly at a very early stage in their illness and their focus was necessarily on their immediate care and treatment. Consequently, they typically did not have longstanding relationships with cancer professionals or the same depth of understanding of their condition held by those with rare diseases. Only a few of the cancer participants interviewed expressed an interest in knowing why they, in particular, had developed cancer and what the Project could help them learn about their cancer.

Inevitably, the timing in relation to being asked to participate in the Project was very different between the two groups. Cancer patients typically had relatively little time between being invited to take part, often during their pre-operative assessment, and their surgery when Project samples would be taken. This seems to have been mitigated by the fact that participants were asked to donate a section of tumour for whole genome sequencing (WGS), which was going to be removed regardless of their participation in the Project. The rare disease group was invited via different routes, for example, by email or letter, or at a yearly appointment, and consequently had more time to think about whether or not to take part.

There was general concern about the lack of communication from Genomics England once samples had been donated. This ranged from slight pique about not being contacted soon after donating a sample to have their participation acknowledged (as would be the case, for example, with blood donation), to longer-term disquiet about not hearing anything. Not surprisingly, participants did not differentiate between Genomics England and the NHS GMCs which were responsible for all patient contact, guided by NHS England under the terms of their contracts with NHSE.

At the time of interview, none of the participants in the study had received results (see below for the current cumulative rates of diagnosis being achieved) and there was frustration from some about this delay (our study end date was extended twice to try to interview participants who had received results, but this was not possible given the delays in the process). Being kept informed with a brief newsletter or email was clearly important to many participants and there was some reflection on their part that they had experienced better communication in other medical research, such as bio-banking. Since the data were collected for this study, Genomics England has attempted to address these concerns by instituting a 'Track my sample' process which was launched in December 2017 after data collection in the current study had finished. This was followed by a regular participant newsletter and more information on the Project's website focused on the needs of participants.

Despite these concerns, there was a markedly positive attitude towards taking part in the Project. Some participants described the pride they felt in being part of potentially transformative work. While some direct benefits to participants were mentioned, such as additional screening or the possibility of finding out whether a rare disease was inherited, there was a strong sense of duty related to people's participation, of 'giving back' to the NHS.

There was also a high level of trust demonstrated in the Project which appears to relate to strong confidence in the NHS 'brand' and the fact that the Project was a publicly funded government initiative.

The strength of this trust was demonstrated by the lack of concern or even interest some participants expressed in the consent process, and only slight concern raised about the long-term use of the data. Participants were clearly reassured that their data were in safe hands and had been anonymised effectively. There was generally, if not exclusively, pragmatism about the commercial use of their data. The casual uncertainty, even confusion, some participants expressed about the details of the Project further demonstrates their high level of trust. Participants did not know, or understand, aspects of the Project and appeared comfortable with not knowing. This has potential implications for how much information it is necessary to provide.

Finally, two ethical concerns were raised: the potential increase in prenatal testing for genetic disorders leading to an increase in the termination of foetuses with genetic abnormalities; and concern about receiving results related to familial genetic risk and what this might mean for family members who had not consented to finding out this information.

Members of the public

There was considerable enthusiasm for the Project among the wider public. Most focus group participants began with little or no knowledge of genomic research or the Project. They raised more concerns than were raised in the interviews with Project participants. These were largely about data protection and ownership of the data more generally. Some people, particularly from black and minority ethnic (BAME) groups, expressed greater caution about privacy and control over the uses to which their data might be put.

Professionals involved in the Project

There was considerable excitement about the Project from many of those interviewed. However, the opportunities and challenges were often seen differently by those working at the centre and those in GMCs. GMC staff were more likely to have negative experiences of implementation, relating to a range of issues including:

- the target culture, the speed of implementation and resultant workload in an already pressured system with few extra resources;
- delays and changes in requirements, particularly around informatics and
- the inability to feed back results to participants, given the delays in sequencing.

There were also shared views on successes, for example, changes to pathology process, improving the profile of genetics services generally and engaging with patients and public around genomics.

The hybrid nature of the Project was also raised, it being a mix between a research study and a transformation project. This resulted in perceived tension between the generation of knowledge, and achieving targets and realising actual patient benefit.

Interviewees recognised that there were significant workforce, training and development needs, alongside the need for more public information and debate.

Non-specialist NHS clinical staff

These staff had very little awareness of the Project and knowledge about WGS. There were positive views about its potential, but also worries that it might lead to unnecessary treatment, with uncertain benefit for individual patients. Generally, these staff were more sceptical about the potential of genomic medicine than those directly involved. The resource and training implications for an already stretched NHS were a source of anxiety, with a fear that future access to genomic services might widen inequalities, favouring those who could pay outside the NHS.

Interpreting the findings

Despite low levels of knowledge about genomics among the general public and non-specialist clinicians, we found broad support for the overall aims of the Project. However, there were some concerns about genomics in general, and the Project's implementation, in particular. Discussions with those who had little knowledge of genomics, or of the Project, were characterised by seeking more information through questioning, and drawing on their prior knowledge of other areas of health care or what they had learned from mainstream media to discuss the topic at hand. These groups included the general public, and, perhaps more surprisingly, non-specialist health care staff. These groups speculated on the potential benefits of genomic medicine, the concerns it raises and the role it could play in the future of healthcare. The public were generally optimistic about the potential societal benefits of genomic medicine. They speculated that future generations might have a lower disease burden as the result of genomic technology.

Non-specialist health care staff were more reserved and sceptical about the benefits of genomic medicine. They did not believe that WGS would necessarily offer benefit without concomitant major advances in disease-specific cures. Non-specialist staff also had concerns that receiving uncertain results could drive patients to seek further information, pushing health care professionals to carry out a multitude of further tests, often unnecessarily. They also questioned the impact on their own workload if there was widespread roll-out of genomic testing.

There were some concerns in the public focus groups related to data ownership and protection. However, this was set against an understanding that people regularly gave personal data to retailers via loyalty cards with little anxiety. Non-specialist staff also raised these issues in discussion, on behalf of the public and patients. People from BAME groups expressed more concern about data protection and ownership, with strong views that the data had to remain within the control of the NHS as a trusted data custodian. Genomics England has subsequently undertaken in-depth work to understand the views of people and patients from BAME backgrounds (see: www.genomicsengland.co.uk/about-genomics-england/how-we-work/patient-and-public-involvement).

Interviews and discussions with people more familiar with genomic medicine, and the 100,000 Genomes Project specifically, inevitably demonstrated greater depth of knowledge about issues such as the potential impact of secondary findings on patients and their families. These groups included the focus groups with a rare disease support group (Cardiomyopathy UK) and a cancer activist group (Independent Cancer Patient Voices), as well as interviews with staff involved in the Project. The two focus groups expressed strong views about the need for sensitivity if feeding back secondary findings, owing to the potential for harm to patients or their relatives.

Support for the Project was commonly found amongst professionals directly involved in it. However, many concerns were raised about the way in which it had been implemented. These concerns were particularly expressed by those working in the GMCs, where the focus on targets, the changing requirements and a sense that they were not listened to caused frustration in many, and, in some, disillusionment.

Implications of the research for future policy and practice

Building on widespread support for the Project

Our findings support the argument that the 'social unease' concerning the collection, storage and use of human tissue in medical research widely discussed in the existing literature may be overstated. It has been argued that it is largely based on theoretical debate among experts or single case analyses (Dixon-Woods et al, 2008). This qualitative study of participants in the 100,000 Genomes Project and of members of the public reveals a generally supportive attitude towards genomics, though it needs to be recognised that the study was not able to interview those who had been approached but chosen not to participate in the Project. It seems reasonable to hypothesise that non-participants would have been somewhat more sceptical about the value of genomics and more critical of the Project than those who chose to take part. The positive attitude among participants was accompanied by a willingness to participate in related research, and a strong trust in science, researchers and institutional governance, especially in the NHS (Lipworth et al (2011). Indeed, this study revealed a remarkable acceptance by participants of long waits for results and, in some cases, even discomfort while providing samples. For example, while recounting problematic experiences during the process of giving samples, participants offered only mild rebukes or suggestions for change rather than expressing serious concern with the Project.

There was also evidence within the public focus groups that unease could be generated in the minds of participants as a result of the discussion itself, rather than by the nature of genomics per se. As Hoeyer (2003) found:

> *"The very act of questioning people or involving them in a hypothetical deliberative process may plant a seed of doubt that their judgements have been under-informed and they 'ought' to think differently as responsible citizens."*

Learning for further implementation of genomic medicine in the NHS

The 100,000 Genomes Project was, as its name suggests, a 'project'. This meant that it was managed separately from the routine activity of the NHS with its own structure and system of accountability. It was also time-limited and, as its title indicated, there were clear, ambitious, centrally set targets related to the number of genomes that were to be collected within the life of the Project. The Project was initiated by, and strongly associated with, central government and had a deliberately high public and political profile. The then Prime Minister, David Cameron, was closely associated with it and led the launch. While the Project was implemented through a new special purpose vehicle – Genomics England, a company owned by, the now, Department of Health and Social Care (DHSC) – and a network of regional GMCs, there was relatively little additional funding for the GMCs in relation to the tasks and responsibilities given to them. Also, much of the work fell to NHS staff who had to accommodate the Project in addition to their existing commitments. This was partly because the Project was initiated during the lengthy period of public sector financial austerity instituted after the 2008 financial crisis, but also because there was a relative dearth of staff with genomics expertise available to implement the Project locally. As a result, specialist staff reported that they were being stretched uncomfortably between their existing work and the additional requirements of the Project.

The endeavour itself was novel. Nothing on this scale had been undertaken in genomics, in the UK or elsewhere. Planning the Project inevitably involved significant uncertainty. The Project was also a hybrid; it was neither very large-scale research nor a health service transformation project. It had characteristics of both. Its task was to build a large genomic databank with potential for long-term research, as well as learning how to develop genomics as a service that would be more routinely offered across the NHS. Genomics England officially described the Project as an NHS 'transformation service'.

Research-related aspects of the Project meant an intense focus on informed consent, data anonymity and data security. The Project recruited 'participants' rather than 'patients', and participants might be past, current or never patients. Whilst Project participants were asked to consent for their data to be used over the long-term, the Project was not set up to engage with them as participants over the long-term. This contrasts with, for example, bio-banking projects which return to their participants to collect further data and to report on emerging research findings. Some participants were told by their recruiting consultant, appropriately as it happens, that they might never be contacted by the Project again. This study suggests that the rare disease participants would have welcomed more communication after donating a sample. It is less clear whether this holds true for cancer patients as well.

This combination of high expectations from central government, novelty (with related technical and logistical challenges), multiple goals and constrained additional funding produced a stressful environment for implementation. This appeared to be felt especially at GMC level where staff reported a lack of involvement in the Project and a sense that their expertise was not listened to. This meant that initial enthusiasm had to compete over time with some disillusionment. The first highly publicised targets were not met because it took considerably longer to undertake each stage in the process; identifying potential participants, analysing samples and making them ready for research and/or feedback to participants. Our analysis suggests that the Project could have been implemented more effectively and there may be value in learning from the Project to inform similar initiatives in future.

Evidence suggests that successful implementation of service transformation depends on a range of interdependent processes. The report of a recent WHO expert meeting on health system transformation (WHO, 2018) highlighted the following as potentially critical:

- reconciling and managing tensions between 'bottom-up' and 'top-down' approaches to policy implementation;
- developing a coherent vision of the desired end-state;
- ensuring ongoing political support;
- appropriate leadership across all the agencies involved;
- adequate resources and
- supportive information and other technology.

To what extent did the Project demonstrate these features in the period 2015-17 and what can be learned from the experience? It appears that the Project largely succeeded in developing a coherent vision of the desired end-state, ensuring ongoing political support and having appropriate leadership. However, it is less clear whether support from Ministers and the top-down imperatives to deliver the 100,000 genomes were effectively informed by, and reconciled with, bottom-up feedback on the practical realities of achieving this. The speed of planned implementation was not realistic and the Project could have benefitted from more effective interaction between officials at the centre and the GMCs. The central government culture of 'can do' and emphasis on 'delivery' means that there was a tendency for officials to avoid raising awkward details of implementation for fear of being seen as obstructive of activist ministers (King and Crewe, 2014: 337-42). For example, necessary changes in laboratory processes had not been identified fully before the Project started. During the pilot and initiation phases of the Project, experimental work still had to be undertaken to adapt the DNA extraction process from cancer samples to minimise DNA damage. This work concluded that fresh tissue was required for optimal WGS and thus a new process had to be implemented across the GMCs.

The high level of ambition announced at the start of the Project does not seem to have been informed by a thorough feasibility assessment of what could be

done within a particular period of time. Staff at all levels had to locate and solve implementation problems as they arose. Many GMC staff perceived the Project as highly, and possibly excessively, target-driven. The high level political support and level of ambition was a two-edged sword; it both maintained the profile of the Project and a sense of urgency to generate 100,000 genomes, while demanding unrealistic recruitment targets.

GMC staff further described feeling that insufficient attention had been given to their expertise or experience in the planning and evolution of the Project. This meant that the Project implementation was insufficiently grounded in the realities of local health care systems from the perspective of GMC staff. Communication was experienced as largely uni-directional, with staff from the 'centre' seen as being in control, while GMC staff were 'peripheral'. These leadership and communication challenges are additional evidence of unmanaged tensions between 'top-down' and 'bottom-up' approaches.

Information technology systems played a major role in implementation, but were highly problematic. The speed of initial planning and setting of ambitious milestones, perhaps understandable in the context of high priority, politically led, policy developments, did not fit with the practicalities of implementing a new system of data collection and storage. This does not seem to have been identified as a significant risk at the outset, nor does it seem that there was contingency built into the Project for such unexpected eventualities. Given the novelty and scale of what was being attempted, this was risky.

These findings resonate with those of a more detailed evaluation of the implementation of the West Midlands GMC undertaken entirely separately, but over approximately the same period as the current study, December 2015 to January 2017 (Brown and Exworthy, 2017). The West Midlands study, which included interviews with national level stakeholders, core GMC staff and recruiters, but also staff in Local Delivery Partner (LDP) organisations in the West Midlands, identified a similar tension between the Project as a research enterprise and a service transformation initiative. Similarly, participants grappled with the dissonance between having a strong vision of how the Project might benefit patients and the NHS in the future, and the current reality of practical challenges, delays in processes and in results reaching participants, and the length of time before findings would be likely to benefit patients. Interviewee staff in the West Midlands reported how delays were de-motivating staff in LDPs and beyond, a finding reflected in this study. LDP staff similarly complained that the GMC did not understand, or take adequately into account, the constraints under which they were operating. This mirrors the way GMC staff in the current study complained about how staff at 'the centre' failed to appreciate the challenge of local environments and capacity. In the West Midlands, there were similar concerns about the capacity within the GMC and the LDPs of already busy staff to cope with the extra work demanded by the Project within the timescales required to meet centrally determined targets. Similarly, GMC and LDP staff reported that work on the Project was having negative consequences for other pre-existing areas of their work and particular groups of staff (e.g. phlebotomists) due to insufficient additional resources being available. As with interviewees in our study, informants in the West Midlands were also able to identify positive effects of involvement in the Project, for example, when it was possible to recruit more staff (e.g. from charitable sources as well as from Project funds) and when front-line staff became more knowledgeable and confident in approaching patients to recruit them to the Project. Although relationship building took longer than Project timescales allowed, staff did report how the GMC's activities had initiated the development of networks of relationships across services.

One aspect of the Project which appears to have been particularly effective in terms of implementation was the consent process. There was upfront commitment to evaluate consent materials and process at an early stage on the grounds that

this was a crucial part of the Project, particularly given the demanding time-related targets for participant recruitment. The evaluation led to prompt action to simplify the materials given to potential participants (NW Coast NHS Genomic Medicine Centre, 2016). In this case, experience of similar research programmes did appear to have been used in the planning process.

The evidence of past successes and failures of UK Governments indicates that setting up the Project as a 'project' with dedicated central management rather than as part of the routine work of government or the NHS was also a definite advantage. A number of past failures of innovative, centrally-led, initiatives have been associated with inadequate attention to the complexity and ambition of innovations and the resultant need for dedicated expert management (King and Crewe, 2014: 376-7). By contrast, the 100,000 Genomes Project had strong scientific leadership in place at the national level. In this regard, it conformed to the third of the ten 'lessons' or principles of effective policy implementation in the UK context contained in the Institute for Government's report, *Doing them justice: lessons from four cases of policy implementation* (Norris et al., 2014) (see below).

Where the Project was perhaps on less secure ground relates to the points made above on time pressures and the extent to which the perspectives of those at local level, on whom implementation to time ultimately depended, were considered in planning. The full list of the Institute for Government's ten 'lessons' for effective policy implementation which cover these aspects, among others, is given below. The Project exhibited some of these principles much more strongly than others, as follows:

1. **Be clear about the problem and the outcomes that matter most** – this was a strong point of the Project and was conveyed consistently to all parties in terms of the long-term vision for genomics in the UK;

2. **Think about implementation while still developing the policy** – the Project worked hard to integrate policy design and implementation, though not always entirely successfully, at least from the perspective of local implementers who felt that more could have been done to take their perspectives and experience into account (see above);

3. **Get the right capability** – already mentioned above and a strong point of the Project, particularly in relation to its research and scientific aspects;

4. **Be aware of, and ready to respond to, the wider system** – while the assets in the NHS were clearly built upon, it is less clear that the constraints of a health care system under immense pressure were fully taken into account in the implementation planning. In this sense, the timing of the Project during a period of unprecedented slowdown in the growth of NHS resources was a limitation;

5. **Stay close to the implementers** – this principle encourages creation of short feedback loops between implementers and the policy 'centre' which was certainly a feature of the Project enabling information about progress to flow easily upwards. However, GMC staff perceived that this led to increased pressure to deliver against overly demanding performance targets (see 'lesson 2, above);

6. **Be clear about where and how decisions are made** – the use of project terminology, organization and management made decision making responsibilities very clear;

7. **Invest in routines to keep implementation on track** – this relates to regular scrutiny of progress both by officials and Ministers which was strongly evident in the Project;

8. **Use junior Ministers to drive progress** – this is the lesson that policy areas where junior ministers are closely involved tend to have the best prospects for being successfully implemented. Since Genomics England was set up as a company with its own board, outside the DH, specifically to deliver the Project, this aspect of the implementation process was much less apparent;

9. **Allow for and learn from variation** – GMC staff tended to report that the target setting and reporting process on a very regular basis allowed little space for this lesson to be applied;

10. **Build in long-term focus** – this was an explicit aspect of the Project. The website states that the Project will 'create a new genomic medicine service for the NHS – transforming the way people are cared for and bringing advanced diagnosis and personalised treatments to all those who need them.' www.genomicsengland.co.uk/about-genomics-england/the-100000-genomes-project

One question to ask of the 100,000 Genomes Project is whether some of the implementation problems discussed above could have been identified in advance had there been greater deliberation (King and Crewe, 2014; 386) which is not traditionally an activity associated with fast-moving central government policy-making in the UK. There is inevitable uncertainty in putting in place a novel system for the collection, storage and use of genomic samples on a large scale. However, a longer planning period and better engagement with local staff with expertise might have led to the earlier identification of technical stumbling blocks, the resolution of these problems more efficiently, and at less cost. It might also have been advantageous from the outset to have adopted the approach taken in related types of enterprise, such as bio-banking, where participants enter into a long-term relationship with the research team in which typically they are continuously kept informed about the ways in which their data are being used and with what results.

Conclusions and implications for the future

Overall, there was support for, and trust in, the 100,000 Genomes Project from participants, members of the public, and specialist and non-specialist staff. However, this research has helped identify a number of issues that should be considered in the future roll-out of genomic medicine in the NHS, as follows:

1. It is clear that non-specialist clinicians' knowledge about genomic medicine and its potential is limited and, in general, such clinicians are wary of claims that genomics will transform their work and patient care. This suggests that professional bodies and Health Education England have a considerable task ahead to inform the wider NHS clinical workforce about genomics and how they should engage with the evolving ability of the NHS to provide genomic medicine services to support a range of different specialties and services. It also suggests that the pace of any roll-out of genomic medicine in the wider NHS will depend on successfully communicating the proof of the potential and actual value of genomics to a dispersed clinical community which has many other competing interests and pressures. Currently, Genomics England reports that the Project is providing a diagnosis in 20-25% of its rare diseases cases and in 50% of cancer cases the data are judged as containing the potential for a therapy or a clinical trial (www.genomicsengland.co.uk/about-genomics-england/the-100000-genomes-project accessed 3 February 2020). This was not the case during most of the period of this research but indicates that more positive messages can now be communicated to the wider NHS workforce.

2. Participants in the 100,000 Genomes Project expressed strong support for its goals and demonstrated a high level of trust in the NHS to implement the Project in a way that would protect their interests. However, there was a desire for more information from the Project after the initial DNA samples had been collected, even among those who had been clearly told that they might not hear anything again from the Project. Participants appeared to appreciate being updated periodically as to what the Project was achieving so that they could see what they had contributed to and as a marker of appreciation for their involvement. Since the data were collected for this study, Genomics England has introduced a 'Track my sample' process and a regular participant newsletter. Similar procedures would be valuable more widely in future. Participants in any new NHS service could be sent a brief annual report summarising the highlights of what had been achieved in the past year, with a particular emphasis on actual or potential benefits to different types of patients. This would be especially helpful in relation to participants who had expected some, or more, follow-up contact from the service. This sort of communication may also benefit the NHS workforce, highlighting the utility of whole genome sequencing and so increasing the likelihood of their embedding genomics in their future practice.

3. The 100,000 Genomes Project was a very challenging venture for the NHS. It straddled the worlds of basic biomedical and clinical research, bio-banking and management of large-scale databases of human samples. It also established testing and reporting of findings at the individual and family level, in services ranging from extremely rare conditions through to common cancers. The implementation of this hybrid was not helped by its timing during a period of major austerity and restraint in NHS funding. There were also very ambitious timescales set at every stage in the Project with stretching targets in terms of collection and preservation of samples as well as delivery of findings to participants and relevant clinicians. Furthermore, the Project had a high political profile as it was a priority of the then Prime Minister, David Cameron. Those involved in implementing the Project at GMC level reported feeling pressurised to deliver, sometimes they felt unfairly so, and commented on the extent to which the Project's management revolved around targets and league tables of the samples collected by each GMC. This was reflected in the title of the Project which was expressed as a target. While none of the implications of the experience of implementing the 100,000 Genomes Project

are especially new, they show that there are opportunities to learn for future similar ventures. In particular, our analysis demonstrates a need for more engagement from the very start of planning with those who would be delivering the Project. Given that Project milestones were routinely missed, it is possible that more realistic plans might have resulted from such a process. In turn, this might have reduced the odds of local implementers feeling disillusioned with the process. There is a fine balance between setting ambitious, collective targets and encouraging healthy competition between sites to deliver these targets, and onerous performance management which can be perceived at a local level as bullying. This should be considered when designing and developing the new NHS genomic medicine service.

4. This study was not able to interview people who had declined to take part in the 100,000 Genomes Project. Given that these people presumably thought carefully about this, it would seem useful to know why they made this decision. Though declining to participate is not necessarily the result of any weakness in the consent process, it might help improve the way that the NHS approaches patients in the future to maximise their engagement with genomics services and/or related research to know more about non-participants' attitudes, preferences and views about genomic medicine. A simple way of doing this would be to include in any future consent form an option for non-participant follow-up.

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The Unit is funded by the National Institute for Health Research (NIHR) Policy Research Programme.

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CPEC CARE POLICY AND EVALUATION CENTRE Research at LSE

Imperial College Business School

Policy Innovation and Evaluation Research Unit
Department of Health Services Research & Policy
London School of Hygiene & Tropical Medicine
15–17 Tavistock Place, London WC1H 9SH

Tel: +44 (0)20 7927 2784
www.piru.ac.uk