NUFFIELD COUNCIL ON BIOETHICS

TOWARDS A GOLD STANDARD OF ETHICS ACROSS GENOMIC HEALTHCARE & RESEARCH: WHERE ARE WE?

PROJECT REPORT

JANUARY 2024

Contents

Executive Summary

Key points

- **Individuals and organisations across the genomic healthcare and research field should work together to share thinking, embed existing work and, where possible, reach consensus.**
- **This will require engagement from all those involved across genomics including patients, research participants, researchers, clinicians, policymakers and funders.**
- **We conclude that a UK-wide co-ordination role will be required to ensure that these actions can be taken forward.**

In the 2020 Genome UK Strategy, the UK Government committed to establishing a 'gold standard UK model' for how to apply strong and consistent ethical standards in genomic healthcare and research. The Nuffield Council on Bioethics first partnered with the Office for Life Sciences (OLS) and genomic healthcare leads in Scotland, Wales and Northern Ireland to support the delivery of this commitment in 2022. The summary report of this work 'Ethics in Genomics and Research: Building Connections and Sharing Best Practice' and a summary of associated case studies was published in July 2023.

Following the publication of the summary report, the Nuffield Council on Bioethics continued its partnership with the OLS to address one of the report's recommendations. The recommendation identified a need to create a comprehensive map of existing ethics resources in order to understand what information and guidance is already available and identify areas where further work may be needed. We have engaged with relevant stakeholders and undertaken desk-based research to inform this document.

Existing resources were identified across many relevant topics including (but not limited to) consent and confidentiality, data use, data protection and data governance, prenatal testing and synthetic genomics. Our intention is that the resources included in this document can begin to help establish the 'gold standard UK model' for how to apply strong and consistent ethical standards, while recognising ethics can be embedded in multiple other ways too. These resources will serve as a tangible starting point for genomic healthcare and research bodies to begin learning from existing ethics resources and avoid unnecessary duplication in future work.

By mapping current resources, and hearing from people across the genomic healthcare and research field, we have also identified gaps where further resources could be useful. Some of these gaps overlap with topics where there are some existing resources. Although these resources are valuable, they may not be sufficient to meet the entirety of stakeholder needs.

Individuals and organisations across the genomic healthcare and research field should work together to share thinking, embed existing work and, where possible, reach consensus. This includes developing new resources that address the gaps identified, as well as building on and providing consistency across existing resources (if inconsistencies arise). Collaboration must be dynamic and responsive to ensure that issues can be addressed as they arise. This will require engagement from all those involved across genomics including patients, research participants, researchers, clinicians, policymakers and funders. Here, we conclude that a UK-wide co-ordination role will be required to ensure that these actions can be taken forward.

If the commitment set out in Genome UK to reach a 'gold standard UK model' for ethics is to be achieved, ethics needs to be better embedded across genomics. Individuals and organisations should be encouraged to learn about the importance of ethics, how to promote (consistent) ethical practice and how to use ethics effectively to shape the future of genomics. As a result, we hope that a gold standard UK model for ethics would ensure patients and participants have more consistent and equitable experiences of genomics; and the promises of genomics can be realised.

This report is accompanied by a 'resource bank.' This 'resource bank' will include the resources mentioned throughout the report. The bank will be amendable over time at the request of external stakeholders who may have identified or developed missing or future resources. Similarly, resources can be removed on request if they are no longer relevant or appropriate. Requests can be made by emailing the Nuffield Council on Bioethics at: bioethics@nuffieldbioethics.org

Glossary

Artificial intelligence (AI)	AI describes the use of computers and digital technology to perform complex tasks in an intelligent way, sometimes autonomously (without human direction). AI has enabled genomic discoveries, for example, due to the increased amount of data it can analyse.
Broad consent	Broad consent means that an individual gives informed consent once, for their data to be used and shared for a wide range of purposes. They are only asked to re-consent when a new potential use for their data does not fit within the original scope.
Carrier status	Carrier status means that an individual has a genetic variant associated with a condition but may not show symptoms of this condition. Their status means they may pass the variant on to biologically related children.
Data access agreement	Data access agreements oversee conditions for data access and data sharing. For example, they may include where the data are stored, what purposes the data can be used for, and how long the data can be accessed.
Data access committee	Data access committees oversee data access requests. They often apply rules to ensure that data are accessed and shared in an ethically and legally permissible way.

Dynamic consent	Dynamic consent provides an individual with the opportunity to give informed consent each time there is a request for their data to be used or shared, over time.
Ethics committee	Ethics committees vary in purpose and composition. They may review clinical cases or research proposals and practice. They may then provide ethics advice and/or give denial and approval of a certain practice.
Federated data systems	A federated data system is a software platform which allows multiple databases to function as one.
Genomics	Genomics is an encompassing term which covers the study of an individual's DNA (the 'genome'). For example, the characterisation of genes and how genes and their products interact with each other and the wider environment.
Genetics	Genetics looks at one gene or genomic region. This can include studying the structure and function of the gene, and how it is passed on from one generation to the next. For example, some genetic conditions are due to mutations in a single gene, such as Cystic Fibrosis and Huntington's Disease.
Genetic/Genomic counsellors	Genetic/genomic counsellors work with patients and families to provide information and support related to genomics. This information and support is intended to help them to make informed health decisions.

Genomic healthcare and research	Genomic healthcare and research covers genomics related activities that are focused on human genomes and human health. This includes the clinical utilisation of genomics, as well as research, and new technologies aimed at advancing our understanding of genomics and health.
Polygenic scores	Polygenic scores (PGS), sometimes referred to as 'polygenic risk scores' or 'polygenic indexes,' aim to make calculations about an individual's genetic susceptibility to a certain outcome. PGS exist for health and non-health outcomes.
Secure data environments	Secure data environments (sometimes known as 'trusted research environments') are data and research platforms which provide remote access to data for approved researchers.
Synthetic data	Synthetic data are artificial data which are designed to mimic real data. Use of these data has been proposed as an alternative to traditional genomic data.

Introduction

In the 2020 Genome UK Strategy, the UK Government committed to establishing a 'gold standard UK model' for how to apply strong and consistent ethical standards in genomic healthcare and research. The Government's 2022 UK-wide shared commitments plan recognised the need for further discussion and collaboration to enable the meaningful implementation of the commitment on ethics.

In 2022 the Nuffield Council on Bioethics partnered with the Office for Life Sciences (OLS) and genomic healthcare leads in Scotland, Wales and Northern Ireland to support the delivery of this commitment. This included collecting case studies gathered via a 'call for evidence' on approaches to ethics across genomic healthcare and research, as well as two UK-wide workshops with people from within the field of human genetics and genomics (including researchers, clinicians, ethicists, patient representatives and policymakers). The summary report of this work 'Ethics in Genomics and Research: Building Connections and Sharing Best Practice' and a summary of the case studies was published in July 2023.

Following the publication of the summary reports, the Nuffield Council on Bioethics continued its partnership with the OLS to undertake research recommended by this previous work. This report outlines our findings.

What is meant by genomic healthcare and research?

For our purposes, 'genomic healthcare and research' covers genomics related activities that are focused on human genomes and human health. This includes the clinical utilisation of genomics, as well as research, and new technologies aimed at advancing our understanding of genomics, health and disease.

'Genomics' is an encompassing term which covers the study of an individual's DNA (the 'genome'). This includes the characterisation of genes and how genes and their products interact with each other and the wider environment. Techniques range from genome sequencing (a technique that is used to 'read' DNA, allowing for the discovery of disease associated variants and research advancements) to emerging practices such gene editing (a technique which can change the composition of a gene). 'Genomics' can also include comparisons with other individuals within and across populations.

‘Genetics’, which is sometimes used interchangeably, or in tandem with ‘genomics’ means something slightly different. ‘Genetics,’ more specifically, looks at one gene or genomic region. This can include studying the structure and function of the gene and whether any variation will be passed on from one generation to the next. For example, some genetic conditions are due to mutations in a single gene, such as Cystic Fibrosis and Huntington’s Disease.

Why genomics?

Advances in human genomics promise to further our understanding of how genomes influence health and disease, with the aim of helping to improve diagnosis, treatment and support for patients with certain conditions. Genomics may also support the prevention of disease. However, to reach this potential, stakeholders across genomic healthcare and research must address many ethical considerations. This is essential to ensure that research and healthcare using genomics can maintain the trust of the public, patients and participants and encourage them to engage. Stakeholders include the researchers who collect, access and use genomic data, the clinicians who interpret and translate this data for their patients, as well as the policymakers and governance bodies who oversee genomic research and its application, among others.

Findings from our previous call for evidence and UK-wide workshops

Through the call for evidence and our subsequent workshops, numerous ethics questions pertinent to genomic healthcare and research were identified. These included considerations around:

- Weighing the potential benefits and harms of genomics initiatives, such as biobanks and research programmes.
- What needs to happen to ensure that patients and participants are able to provide informed consent for genomic and genetic testing and screening, and make decisions about this testing in children and people who are not able to give consent themselves.
- Deciding what findings should be returned to patients and participants and their families, how to do this and whose responsibility it is.
- Resolving the tension between respecting data privacy and facilitating the sharing and use of data for research and diagnosis.

- Addressing inequalities in how people experience and benefit from genomic healthcare and research and mitigating the potential for genetic discrimination.
- Understanding and aligning genomics initiatives with public values, for example in response to changing societal perceptions of disability and impairment.
- Managing the expectations of participants and patients, and avoiding hype around genomics.
- Considering the implications of genomics beyond health, such as in the field of education and employment.[1]

Our research also indicated that the way individuals and organisations across genomic healthcare and research embedded ethics within their work varied. Ethics related activities undertaken included patient, participant and public engagement exercises, the appointment of ethics leads and ethics committees and the provision of professional education and training with an ethics component.

Despite this, our research found that participants faced the challenge that there was "a lack of awareness about what ethics can offer and a reluctance on the part of others to think about ethical issues."[2] For example, 'ethics' was often seen as a barrier to progress, rather than an essential consideration in any decision-making or policy development (that should be embedded from the beginning of any use of genomics across healthcare and research).

There was also uncertainty on how to reach consensus and move forward to promote ethics in practice. The perception of ethics, and lack of consistency in its application can make it difficult for those working in this space to clearly identify, address and navigate ethical issues. For patients and participants whose data are being used, this may result in inequitable experiences of 'good practice' relating to genomics. For example, some organisations may have clearly embedded ethics in practice, including clear informed consent mechanisms, transparent data-sharing governance and established ethics committees and/or personnel which can ensure a person's data are being used appropriately, while other organisations may have less stringent mechanisms in place.

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1 Nuffield Council on Bioethics (2023) Ethics in Genomics Healthcare and Research: Building Connections and Sharing Best Practice. Summary Report, available at: https://www.nuffieldbioethics.org/assets/pdfs/FINAL-version-Genomics-workshop-summary-and-analysis.pdf

2 Nuffield Council on Bioethics (2023) *Ethics in Genomics Healthcare and Research: Building Connections and Sharing Best Practice. Summary Report,* available at: https://www.nuffieldbioethics.org/assets/pdfs/FINAL-version-Genomics-workshop-summary-and-analysis.pdf

Many of the ethical considerations identified are not dissimilar to those across other areas of healthcare and research. However, in our workshop deliberations it was agreed that genomics merits independent focus due to the number of ethical considerations identified, the pace of development within genomics and its prominent positioning within UK policy.

In our conclusions from this previous research, we identified that the development of a 'gold standard UK model' for establishing ethics would be useful for those working in the field to help negotiate ethical issues, promote consistency and ultimately create better practice for all those interacting with genomics. This approach would need to incorporate different components, such as ethical principles, professional guidance, discussion fora and practical toolkits, which would need to remain flexible to allow for interpretation in different contexts over time. We also acknowledged that it is not appropriate for the UK to aspire to lead the world in ethics across genomics healthcare and research. Instead, we need to be sensitive to the international context of genomics, while remaining UK-specific. Questions remain around whether some elements of a best practice approach should be purely advisory, or a requirement (e.g. by law).

To begin working towards a 'gold standard UK model' for ethics across genomic healthcare and research our work identified the following:

(1) a need to create a comprehensive map of existing resources relating to ethics across genomic healthcare and research in order to understand what is already available and identify areas where further work is needed; and

(2) the potential need for a network (or similar) as a useful way to engage those working across genomics in healthcare and research to encourage the development of an ethics 'gold standard' approach. What such a network might look like and how to move this next step forward needs further discussion.[3]

3 Nuffield Council on Bioethics (2023) *Ethics in Genomics Healthcare and Research: Building Connections and Sharing Best Practice. Summary Report,* available at: https://www.nuffieldbioethics.org/assets/pdfs/FINAL-version-Genomics-workshop-summary-and-analysis.pdf

Current work

Following the publication of our previous work in July 2023, the Nuffield Council on Bioethics continued its partnership with the OLS to address the recommendation aimed at mapping existing resources that address ethics across genomic healthcare and research in the UK.

The mapping has been informed by engagement with relevant stakeholders and desk-based research aimed at:

(1) identifying publicly available resources;

(2) understanding which resources are currently being developed; and

(3) recognising where there are current gaps that require attention.

The resources in our mapping include practical tools, guidelines, guidance, documentation, recommendations, ethics reviews and policy reports developed in the last 10 years.[4] The resources also had to be genomic-specific, have a UK focus and be centred around ethics, or how to achieve practice that had considered ethics. These could be developed by any stakeholder across genomic healthcare and research.

Our intention is that the resources we have identified can begin to help establish a 'gold standard UK model' for ethics across genomic healthcare and research. These resources can act as a tangible starting point for organisations to begin learning from existing ethics resources and promote collaboration in future work. We heard from some respondents to our engagement work that they did not know where to start when seeking to embed ethics and developing practical ethics resources, especially when the issue is controversial. Sharing ethics resources, even when they have been produced for internal use, can help support others in multiple ways. They may encourage others to begin thinking about ethics in areas of similar work and promote accountability for decision-making and/or practice. Accessible resources can avoid unnecessary duplication, maintain a consistent approach and enable challenge or support in future consensus building where there is uncertainty.

The resources will be provided in the text of this report and will also be published separately as a 'resource bank.' This 'resource bank' will be a live document, amendable over time at the request of external stakeholders who may have identified

4 This does not include academic papers.

or developed missing or future resources. Similarly, resources can be removed on request if they are no longer relevant or appropriate.[5]

By identifying current resources, and hearing from people across the genomic healthcare and research field, we have outlined the gaps where further resources could be useful. It is clear that current resources, although valuable, are not sufficient. Collaboration is required between individuals and organisations to embed existing work and address the areas where further work and consensus is needed. In doing so, important future steps towards a 'UK gold standard' model for ethics can be taken.

Ethics across genomics

We recognise that ethics can be embedded in genomic policy and practice in other ways, beyond genomic-specific ethics resources. Resources related to wider research and the provision of healthcare more generally may also have a genomics application, such as those on consent and confidentiality in a clinical and/or research context. As mentioned in our previous work, ethics committees, the appointment of ethics staff and the provision of education and training with an ethics component, are all ways in which ethics can be addressed and embedded in practice. For example, NHS England's Genomic Education Programme provides information and training modules for healthcare professionals on ethics.[6] Ethics may also be implicit in governance mechanisms adopted by organisations. Similar to introducing ethics committees and the appointment of ethics personnel, organisations can adopt practical mechanisms/ frameworks to ensure ethics is, and continues to be, prioritised. For example, data access committees, data access agreements and the way data are stored (e.g. secure data environments and federated data systems) are all ways ethics can be built into governance mechanisms to ensure genomic data is handled responsibly and appropriately, and complies with data regulation and law.

Discussion groups and ethics forums can also facilitate the consideration of ethical issues in genomic practice across healthcare and research. Such groups and fora can provide support for a range of individuals grappling with situations that raise ethical dilemmas including patients and their families, research participants, researchers and practitioners. The Genethics forum, established in 2001, is one example of such a group.[7] The forum provides an environment for healthcare professionals, lab staff and

5 Requests can be made by emailing the Nuffield Council on Bioethics at: bioethics@nuffieldbioethics.org

6 NHS England *Genomics Education Programme,* available at: https://www.genomicseducation.hee.nhs.uk/

7 Genethics Forum, available at: http://genethicsforum.ning.com/

patient groups to discuss ethical issues and, where possible, draw conclusions and reach a consensus.

Ensuring that patient, research participant and public voices are heard and embedded as part of the development and application of genomics may also help to promote ethics. It is well recognised that practice can be improved when public engagement is done well and the findings are properly embedded in healthcare and research activities.[8] Positive outcomes from good public engagement include building public trust in genomics, increasing diversity across those willing to engage with genomics, improvements in science and fairer outcomes.[9] This engagement ensures that decisions align as much as possible with the values of the individuals whose data are being used.[10] There are organisations, such as Genetic Alliance UK and the Sickle Cell Society,[11] which support public engagement in genomics by representing and providing support to patients living with genetic conditions and their families.

Many aspects of genomic healthcare and research are also subject to professional and statutory regulation. Existing regulation addresses a range of areas relevant to genomics which also have an ethical dimension. These include consent, data protection and human rights. As such, regulation can act as a mechanism for implementing ethical considerations by ensuring responsible practice. The UK Government and Association of British Insurers' (ABI) Code on Genetic Testing and Insurance plays a similar role.[12] This Code aims to provide reassurance to the public about how and whether genetic testing could affect their access to life, critical illness and income protection insurance in the UK, and sets 'best practice' for insurance companies using genomic data. Reassurance may be required due to ethical concerns held by some that the use of genetic and genomic data for insurance purposes could potentially lead to genetic discrimination.

8 See: Genetic Alliance *Patient Involvement,* available at: https://geneticalliance.org.uk/information/research-and-innovation/patient-involvement/

9 Murtagh MJ, Machirori M, Gaff CL et al (2022) Engaged Genomic Science Produces Better and Fairer Outcomes *Wellcome Open Research* **6:311** available at: https://doi.org/10.12688/wellcomeopenres.17233.1

10 Hastings Ward J, Middleton R, McCormick, et al (2022), Research Participants: Critical Friends, Agents for Change *European Society of Human Genetics* **30**, 1309-13.

11 Genetic Alliance UK, available at: https://geneticalliance.org.uk/ and Sickle Cell Society, available at: https://www.sicklecellsociety.org/

12 HM Government and Association of British Insurers (2018) *Code on Genetic Testing and Insurance* available at: https://www.gov.uk/government/publications/code-on-genetic-testing-and-insurance

We recognise that further work to map these additional routes and resources would be useful to ensure that we have a full picture of how ethics is being embedded across the UK. We have begun to identify some of this work while undertaking our mapping of resources. Please see:

(1) Annex 1 for discussion groups, ethics forums and patient support groups;

(2) Annex 2 for public engagement outputs; and

(3) Annex 3 for relevant regulation.

The international context

The international context of genomics is another area that needs consideration. Genomics institutes and the sharing of data and knowledge often span jurisdictional borders. Humanity is also interconnected by our genomes and so any genomic healthcare and research in the UK may have consequences elsewhere. Any 'gold standard UK model' should therefore be sensitive to and aware of the global nature of genomics and open to diverse viewpoints, while also maintaining applicability to UK practice and regulation.

There is international work that can be drawn upon in developing best practice for the UK. The Global Alliance for Genomics and Health (GA4GH) is an organisation which develops international standards to ensure the responsible use of genomic data, within a human rights framework.[13] Its regulatory and ethics workstream develops a range of internationally applicable tools and resources that can be adapted for UK purposes.[14] Topics addressed to date include consent, data access, genetic discrimination and return of research results to research participants, among others. Further work to understand the entirety of international resources that could be adapted for UK purposes, may be of value.

We recognise that our mapping is the beginning of a wider piece of work to establish a 'gold standard UK model' for ethics across genomic healthcare and research. Our focus on genomic-specific resources in the UK acts as a tangible starting point.

13 The Global Alliance for Genomics and Health, available at: https://www.ga4gh.org/

14 See: Global Alliance for Genomics and Health *Regulatory and Ethics Works Stream,* available at: https://www.ga4gh.org/work_stream/regulatory-ethics/

Which topics do current resources address?

Our research identified resources across the following topics:

- Consent and confidentiality
- Data use, data protection and data governance
- Direct-to-consumer testing
- Equitable collaboration
- Gene editing
- Genetic relatedness
- Genomics and artificial intelligence
- Genomic/genetic research and medicine
- Genetic testing in newborns and childhood
- Incidental findings
- Patient/participant engagement
- Polygenic scores
- Prenatal testing
- Synthetic genomics

The resources

The resources identified and a summary of their contents can be found below. Each resource is listed by topic in alphabetical order. Within each area, resources are listed by date, from most recent to least recent (within 10 years).

Although separated by the topics outlined above, there may be overlap between the content of each. For example, consent is an area that is critical and is thus mentioned across many of these resources.

The resources mentioned in this report are captured and accurate as of December 2023. Genomics and its applications will continue to develop, as will understanding, attitudes and ethical approaches. There is likely to be variation in how people will approach ethics in the future and have approached ethics in the past. The regulatory background in which each resource was developed will also be relevant. It is therefore

recommended that time is taken to review each document through this contextual lens before utilising any listed resources in practice.

Consent and confidentiality

Consent must be given before genomic data can be used for healthcare and/or research. For adults, valid consent is achieved when it is given voluntarily, is informed and when the person has capacity. Capacity is measured by an individual's ability to understand the information given to them, weigh it up and make an informed decision on that basis.[15]

Confidentiality aims to ensure that an individual's identifiable personal information is protected from being shared and accessed by others, where consent has not been given to share it. However, this is not absolute. There may be instances where disclosing an individual's personal information to others may be necessary (e.g. if required by law or court order) or deemed appropriate (e.g. if justified on 'public interest' grounds).

How to achieve valid consent and determine when confidential information can be disclosed without consent can be a challenge in practice.

Resource	Summary
Health Research Authority (HRA) and the Medical Research Council (MRC) Consent and Participant Information Guidance (2023)	This tool provides guidance for researchers and ethics committees on consenting participants for research, and how to prepare materials to support this process. The section 'Content: Participation Information Sheet – What's Involved' includes a sub-section specific to 'Genetic Research'.

15 Adults are presumed to have capacity in the UK, but there will be different considerations when seeking consent in relation to children, or an adult who lacks capacity, to make the decision.

British Medical Association (BMA) Confidentiality Toolkit: A Toolkit for Doctors (2021)	This toolkit provides answers to doctors (dealing with adult patients) on commonly asked questions about when confidential information can be disclosed to third parties. Sections 7 and 9 specifically reference genomics. • Section 7 focuses on 'Public Interest Disclosures'. • Section 9 focuses on 'Requests from Third Parties'.
Joint Committee on Genomics in Medicine (Royal College of Physicians, The Royal College of Pathologists and the British Society for Genomic Medicine) Consent and Confidentiality in Genomic Medicine – Guidance on the Use of Genetic and Genomic Information in the Clinic 3rd edition (2019)	This report provides guidance to enable healthcare professionals in all specialties to consider and understand how consent and confidentiality issues may arise in genomic medicine.
General Medical Council (GMC) Confidentiality: Good Practice in Handling Patient Information (2017)	This guidance sets out the principles of confidentiality and respect for patient's privacy that is expected to be understood and followed by healthcare professionals in the UK. This includes a framework for considering when to disclose patients' personal information and sets out responsibilities for all doctors managing and protecting patient information. Sections 73-76 of this guidance refers to 'Disclosing Genetic and Other Shared Information'.

Data use, data protection and data governance

Genomic data are collected, stored and used to inform healthcare and/or research. Mechanisms should ensure that this is done appropriately. This includes methods of governance and data protection so that data are secure, safe from misuse and shared only for approved purposes. For example, this may include ensuring that an individual's data are not identifiable to others and that they are not shared with malicious third parties. In the UK, the use of data are largely governed by legislation and regulation, namely the Data Protection Act 2018 and the General Data Protection Regulation.[16]

Resource	Summary
The British Society for Genetic Medicine The Retention of Genetic Family Records: Guidance for Clinical Practice (2023)	This report provides guidance and recommendations around the retention of genetic family information and genomic test data in health records in clinical practice.
Medical Research Council (MRC) Guidance on Identifiability, Anonymisation and Pseudonymisation (2019)	This guidance discusses the concept of identifiability and the controls that can be used to minimise the risk of identifiability of data within research. Section 5.3 specifically addresses 'Genetic (Sequence) Information'.

16 General Data Protection Regulation, *Complete Guide to GDPR Compliance*, available at: https://gdpr.eu/

PHG Foundation The GDPR and Genomic Data (2018) [Funded by the Information Commissioner's Office]	This report explores how genomic data in healthcare and health research is impacted by the General Data Protection Regulation (GDPR) and the UK Data Protection Act 2018. The report includes challenges, potential mitigations and makes recommendations for genomics professionals, policymakers and regulators.
Nuffield Council on Bioethics The Collection, Linking and Use of Data in Biomedical Research and Health Care: Ethical Issues (2015)	This report explores the ethical issues raised by the collection and use of data in biomedical research and healthcare. The report includes principles for the design and governance of data initiatives and identifies examples of good practice relevant to anyone approaching a data initiative.

Direct-to-consumer genomic testing

Direct-to-consumer (DTC) companies offer genomic testing to individuals outwith the public UK healthcare system. These tests offer to inform customers about their genes, including their chance of developing certain conditions. However, there are concerns that some DTC tests provide misleading and/or inaccurate results to users.[17]

Resource	Summary
UK Parliament [Science and Technology Committee] Direct to Consumer Genomic Testing (2021)	This report discusses the main opportunities and risks of direct-to-consumer genomic tests. The report includes recommendations directed at the government to address the identified risks.
Royal College of General Practitioners and the British Society for Genetic Medicine Position Statement on Direct to Consumer Testing (2019)	This position statement provides recommendations for healthcare professionals who are asked to provide clinical expertise about the results of direct-to-consumer genomic or genetic testing.

17 Genomics Education Programme (2020) *Consumer genetic testing: expectation and reality*, available at: https://www.genomicseducation.hee.nhs.uk/blog/direct-to-consumer-genetic-testing-expectation-and-reality/

Equitable collaboration

Genomic healthcare and research often involves collaboration between individuals, organisations, and across countries. This includes partnerships between stakeholders based in high-income countries (like the UK) and low-and-middle income countries. These partnerships should embed principles of equity, ensuring that exploitation is avoided, potential benefits are shared and contributions from all partners are enabled and acknowledged.

Resource	Summary
Wellcome Sanger Institute Embedding Equity in International Research Collaboration (2023)	This document is **internal policy** at the Wellcome Sanger Institute to support research teams to collaborate equitably with international partners based in low-and-middle income countries. This includes guidelines for collaboration and areas that require further exploration.

Gene editing

Human genome editing is a method that can make specific changes to DNA.[18] Editing can be done somatically (which means any changes made cannot be passed down to future biologically related generations. Germline cells (which, when used for reproduction, would have impacts for future, biologically related generations) can also be edited. Through gene therapies, or other mechanisms, changes could be made on both physical traits and health-related conditions.[19]

Resource	Summary
Nuffield Council on Bioethics Genome Editing and Human Reproduction: Social and Ethical Issues (2018)	This report explores the range of ethical issues related to the prospect of genome editing becoming a reproductive option in the future. The report provides two overarching principles that must be met for 'heritable genome editing interventions' to be ethically acceptable.
Nuffield Council on Bioethics Genome Editing: An Ethical Review (2016)	This review considers genome editing. This includes where it may have a use and the potential impact that future advances may have.

18 World Health Organisation, *Human Genome Editing,* available at: https://www.who.int/health-topics/human-genome-editing#tab=tab_1

19 National Human Genome Research Institute, *What is Genome Editing?* Available at: https://www.genome.gov/about-genomics/policy-issues/what-is-Genome-Editing

Genetic relatedness

Humans pass down their DNA over genetically related generations. This means that we share genetic information with our biologically related family and relatives. Looking at DNA can tell us whether individuals are full siblings, for example. Similarly, genomic information related to disease may be shared by genetic relatives. Deciding when and how this information should be shared, if at all, is not always straightforward.

Resource	Summary
British Medical Association (BMA) Consent in Paternity Testing (2020)	This guidance sets out doctors' legal and ethical responsibilities when asked to assist with paternity testing.

Genomics and artificial intelligence

Genomics, as a field, has developed in tandem with the growth of artificial intelligence (AI). Over time, both technologies have become progressively intertwined.[20] AI capabilities have enabled genomic discoveries due to the increased volume of data that can be analysed. As such, advances in AI have focused on developing AI-powered genomic research and technologies.[21] Ethical considerations have been applied to both AI and genomics separately, however, there is some uncertainty about the ethical considerations of both, when utilised together.

20 Ada Lovelace Institute and Nuffield Council on Bioethics (2023) *DNA.I* available at: https://www.adalovelaceinstitute.org/wp-content/uploads/2023/08/Ada-Lovelace-Institute-NCOB-DNAI-genomics.pdf

21 Ada Lovelace Institute and Nuffield Council on Bioethics (2023) DNA.I available at: https://www.adalovelaceinstitute.org/wp-content/uploads/2023/08/Ada-Lovelace-Institute-NCOB-DNAI-genomics.pdf

Resource	Summary
PHG Foundation Artificial Intelligence for Genomic Medicine (2020)	This report examines the intersection between AI and genomics. It investigates the limitations and challenges of realising its full potential for health. The report includes a practical set of recommendations for policymakers.

Genomic research and medicine

Genomics, in practice, is undertaken in different ways depending on the individual or organisation and their focus within healthcare and/or research. Some organisations have developed resources to enshrine 'best practice' across healthcare and research activities to ensure ethics is promoted in practice.

Resource	Summary
The Association of Genetic Nurses and Counsellors Code of Ethics (2021)	This code provides guidance for the ethical and professional conduct of genetic counsellors working in the UK.
Wellcome Sanger Institute Good Research Practice Guidelines (2021)	These guidelines are **internal policy** on good research practice at the Wellcome Sanger Institute, including ethics.

Our Future Health Ethics and Governance Framework (2021)	This **internal framework** outlines the key principles for guiding programme decision-making and provides ethical and governance input on the major operational areas of the Our Future Health research programme.
Health Education England The Topol Review: Preparing the Healthcare Workforce to Deliver the Digital Future (2019)	This review explores the deployment of digital healthcare technologies, including genomics, throughout the NHS. Ethical considerations and recommendations to support for the citizen and the patient, healthcare professionals and the health system throughout this deployment are included. Chapter 4 focuses specifically on genomics, but genomics is also mentioned throughout.

Genomic testing in newborns, babies and children

Genomics can help provide insights into the current and future health of newborns, babies and children. Currently, newborns can undergo a 'heel prick' test which looks for nine genetic conditions. Babies and children may then also undergo further genomic testing if they present symptoms that indicate a genetic condition.

In 2023 Genomics England, in partnership with the NHS, launched a new research programme called the Generation Study. This research programme aims to evaluate the utility and feasibility of broadening newborn screening of newborns to include childhood-onset rare genetic conditions using whole genome sequencing.[22] This will be piloted in 100,000 newborns in the UK. This programme will sequence the newborn's entire genome and will include children who are asymptomatic and (seemingly) healthy.

22 Genomics England, *Newborn Genomes Programme*, available at: https://www.genomicsengland.co.uk/initiatives/newborns

Consent is required for this genomic testing. There are different ways in which these data can be stored and findings can be communicated. Ensuring this is done appropriately requires ethical navigation.

Resource	Summary
Royal College of Physicians, The Royal College of Pathologists and British Society of Genetic Medicine Genetic Testing in Childhood – Guidance for Clinical Practice (2022) [Report of the Joint Committee on Genomics in Medicine]	This report provides guidance to healthcare professionals in the UK on best practice for genetic testing in childhood.
Nuffield Council on Bioethics Whole Genome Sequencing of Babies (2018)	This briefing note explores the ethical issues raised by whole genome sequencing of babies.

Incidental findings

Genomic research or testing may reveal unexpected findings that have potential health implications for an individual. These findings could hold importance for the participant or patient, but may not fall within the scope of research or testing that they consented to. Whether or not these findings should be disclosed can be difficult to ascertain.

Resource	Summary
Medical Research Council (MRC) and Wellcome Trust Framework on the Feedback of Health-Related Findings in Research (2014)	This framework aims to help researchers identify and consider the relevant issues when designing and implementing policy relating to the feedback of health-related findings.

Patient and participant engagement

Engaging with patients and participants, if done appropriately, can shape a practice that individuals are willing to engage with and help build public trust in the acquisition and use of genomic data. Patient and participant interaction with genomics can help ensure that benefits and advancements can be achieved. Without this, there will be a lack of data and understanding to inform discovery. Engagement should be undertaken with ethical considerations in mind.

Resource	Summary
Genomics England [Participant Panel] Language and Terminology (2022)	This guide has been developed by the Participant Panel at Genomics England to recommend how Genomics England and their partner organisations should talk about people participating in genomics research. This includes a set of general principles and advice about terminology relating to disability, genetics and genomics.
PHG Foundation The Ethical and Legal Framework for a Genomics England and Sano Genetics Participant Engagement Programme (2021) [Commissioned by Genomics England]	This report examines the legal and ethical implications of an online platform for patient engagement in precision medicine research. Overarching ethical and legal issues that apply to the development of any digital participant engagement platform – regardless of the features the application enabled – are included, as well as project specific considerations. Mitigation suggestions that could be adopted to address challenges are provided.

Polygenic scores

Polygenic scores (PGS), sometimes referred to as 'polygenic risk scores' or 'polygenic indexes,' aim to make calculations about an individual's genetic susceptibility to a certain outcome, and may have applications in research and prediction. PGS exist for health (e.g., cardiovascular disease) and non-health (e.g., how long one spends

in education)[23] outcomes. PGS should be carefully constructed and interpreted, depending on the condition and population.[24]

Research and development of PGS are ongoing, with some clinical trials underway.[25] In the UK, PGS are most commonly available on a commercial DTC basis.[26] PGS are not currently used by the NHS, however, some early evaluation pilot studies have taken place. Further research is required to evaluate their validity and potential use across healthcare.[27]

Resource	Summary
PHG Foundation Evaluation of Polygenic Score Applications (2023)	This report explores the application of medical test evaluation methods and their principles relating to polygenic score-based products.
PHG Foundation Implementing Polygenic Scores for Cardiovascular Disease into NHS Health Checks (2021)	This report considers the implementation and delivery of polygenic score analysis for cardiovascular disease risk assessment as part of the NHS Health Check Programme. It explores the implications arising from the implementation and delivery and the changes needed to implement and deliver polygenic score analysis within existing practice.

23 For more information see: Social Science Genetic Association Consortium, *FAQs about Polygenic Prediction Within and Between Families From a 3-Million Person GWAS of Educational Attainment,* available at: https://www.thessgac.org/faqs

24 PHG Foundation (2023) *Unpacking Polygenic Scores,* available at: https://www.phgfoundation.org/briefing/unpacking-polygenic-scores

25 PHG Foundation (2023) *Application of Polygenic Scores in Healthcare,* available at: https://www.phgfoundation.org/briefing/application-of-polygenic-scores-in-healthcare

26 See: 23 and Me, *Health and Ancestry Service*, available at: https://www.23andme.com/en-gb/dna-health-ancestry/

27 PHG Foundation (2023) *The Path to Using Polygenic Scores in Healthcare,* available at: https://www.phgfoundation.org/briefing/the-path-to-using-polygenic-scores-in-healthcare

Prenatal and pre-implantation genetic testing

Prenatal testing is available for pregnant people to provide insights into the genetics of the fetus they are carrying. These tests vary in invasiveness, from a blood test to inserting a needle into the person's abdomen to obtain a sample of amniotic fluid or through the cervix to obtain a small placental biopsy.

Embryos can also be tested for genetic information where prospective parents are using in vitro fertilisation (IVF). This testing is often offered to people known to carry serious genetic conditions. Test results can be used to inform decisions about which embryo is selected for insertion into the womb.

Resource	Summary
UK Cancer Genetics Group, Fetal Genomics Group and the British Society for Genomic Medicine Prenatal Diagnosis and Pre-Implantation Genetic Testing for Germline Cancer Susceptibility Gene Variants: Guidance for Clinical Practice (2023)	This report provides guidance to healthcare professionals to facilitate equitable access to prenatal diagnosis and preimplantation genetic testing for individuals and couples with a germline cancer susceptibility gene variant.
Royal College of Physicians, The Royal College of Pathologists and the British Society for Genetic Medicine Ethical Issues in Prenatal Genetic Diagnosis – Guidance for Clinical Practice (2022) [A report on the Joint Committee on Genomics in Medicine]	This report considers the ethical issues that can arise in prenatal genetic testing and provides guidance on decision-making processes for professionals and patients.

Nuffield Council on Bioethics Non-Invasive Prenatal Testing: Ethical Issues (2017)	This report considers the ethical issues Non-Invasive Prenatal Testing (NIPT) may pose and how we can address these through a series of recommendations.

Synthetic data

Synthetic data are artificial data which are designed to mimic real data. Utilising these data has been proposed as an alternative to traditional genomic data. Traditional genomic data requires consent and secure data governance, among other things. Synthetic data may minimise privacy risks and have fewer legal barriers for use.[28] It could also fill gaps in the datasets that are currently available. Utilisation and testing of synthetic data is at the very early stages of being implemented and so there is uncertainty around the application and relevant ethical considerations.

Resource	Summary
PHG Foundation Are Synthetic Health Data 'Personal Data'? (2023)	This report analyses whether the use of synthetic data, such as synthetic human data, potentially mitigates some of the data processing challenges associated with the use of personal data.

28 PHG Foundation (2023) *Are Synthetic Health Data 'Personal Data?* available at: https://www.phgfoundation.org/report/are-synthetic-health-data-personal-data

Summary

These resources are aimed at a range of groups including healthcare professionals, researchers, regulators and policymakers. Some of the resources provide practical guidance for their target audience, while others explore the ethical considerations a particular topic invokes and/or suggests recommendations for governance and/or practice. Most resources are externally facing, meaning that their content has been drafted for others to learn from and adopt their content. Others have been developed for internal purposes and would need to be adapted for other settings.

Publicly available resources from for-profit companies and other prominent organisations that hold and use considerable amounts of data were not found. Although it is often publicly claimed that ethics is being undertaken, the outputs from this work do not seem to be in the public domain. This may be because organisations believe their ethics work is only relevant for internal use. For our purposes, this makes it harder to establish where there are gaps and identify best practice.

It is also important to acknowledge that even where an area has been identified as having ethics resources, this does not mean that the resources included cover all bases. Some of the identified resources are context specific and serve particular audiences (e.g. resources for clinicians only). As can be seen in the following section, we have identified gaps which overlap with some of these categories.

These resources provide a starting point for a ‘gold standard UK model’ of ethics to be established. Further work may be required to review the identified resources in more detail to identify any overlap, inconsistencies and/or where the output may have become outdated.

Where are there gaps and where would additional future resources would be useful?

By mapping current resources and speaking to stakeholders we have identified gaps that it would be useful to address. These gaps are topics where resources were not identified, or where further resources would be beneficial.

The topics identified include novel and/or contentious areas, as well as areas that are already covered by some existing resources. For these topics, there is often divergence or uncertainty on how to take ethical considerations into account in practice.

There may be existing ethics resources that are not publicly available which begin to address some of the gaps we identify. We encourage individuals and organisations to share these publicly.[29] This is important to ensure practice is transparent, so that others can learn from them and/or challenge existing ethics resources to ensure consistency and accountability.

Filling these gaps will require collaboration and consensus building across everyone involved in genomic healthcare and research if the UK Government's commitment to establishing a 'gold standard UK model' is to be achieved.

The gaps

Consent

Consent is one topic where we both identified existing resources in our mapping but also identified gaps via our stakeholder engagement work.

Standardised consent guidelines and generic consent forms that can be used by anyone regardless of their jurisdiction (within the UK), or their financial and workforce constraints, were identified by stakeholders as potentially useful resources. Seeking valid consent can require sophisticated discussions around the potential benefits and disadvantages of gaining information as a result of genomic testing and on what will happen to the data collected. This requires transparency about the degree of certainty and uncertainty of tests. Ideally, this would be provided by genetic counsellors and other trained healthcare professionals.

29 Contributions can be made by emailing the Nuffield Council on Bioethics at: bioethics@nuffieldbioethics.org

Specific issues around consent included how to approach informed consent for:

(1) incidental findings (findings that are not the primary purpose of undertaking genomic analysis);

(2) findings where treatment is not available;

(3) reuse/reanalysis (where data is repurposed to answer a new question); and

(4) familial disclosure (where results for one individual have relevance to other genetically related family members).

Different 'models' of consent are also being explored in practice. This includes 'broad consent' and 'dynamic consent.' These vary in the amount of interaction participants and/or patients have with their data and what they are used for. Guidance on which 'model' is most appropriate in different settings could be an area to explore in future resources.

Uncertainty in this area could be due to a lack of awareness of current resources. However, it could also be due to the expanding nature of genomics and associated technologies. How to obtain valid consent for emerging practice across genomics and healthcare may be difficult to navigate. It may be challenging to provide clear up-to-date information, especially when healthcare professionals and researchers are still considering if and how these developments will impact practice.

Data use, data protection and data governance

Data use, data protection and data governance are other areas where we identified resources, but where gaps were also noted. Some specific questions remain about how to store data over a lifetime (and beyond). This includes what data should be included, who should be able to access it and how to remain adequately transparent about the uses of data.

Alongside data protection legislation and regulation, there are often mechanisms in place across institutions to govern data and mitigate against concerns such as re-identification and misuse. These include mechanisms such as data access agreements, data access committees and secure research environments. However, these mechanisms often vary between institutions, which means ethics may be embedded inconsistently.

Data sharing between the NHS and for-profit commercial and/or tech companies, as they become more intertwined, is another area which was highlighted to us as requiring attention.

Direct-to-consumer genomic testing

There is currently insufficient regulation, standardised information and ethics guidance regarding direct-to-consumer (DTC) tests. A variety of genomic tests are currently offered by DTC companies, with varying degrees of clinical and scientific utility. Information about the presence of variants relating to rare and serious diseases may be provided to users. Other examples include genetic ancestry testing (which provides information on where an individual's DNA might have been present, over time), and polygenic scores for common diseases such as heart disease and breast cancer, as well as non-health-related traits such as educational attainment.[30]

Without adequate information or support from professionals to interpret DTC test results there are concerns that people, and potentially their families, may be left more anxious or more relaxed about a result than they should be. Questions around the validity of consent also exist if users do not have a proper understanding of what the tests can realistically offer.

As these tests become more widely used, individuals may rely on this information as 'healthcare.' There may be societal consequences of this that need to be explored. For example, this may put pressure on the NHS to confirm DTC test results through validated testing; and trust in genomics may be impacted when results provided by DTC tests are misleading.

We identified the following resource which is currently being developed to address DTC testing:

Royal College of General Practitioners	An updated version of their existing 2019 statement on direct-to-consumer genomic testing.

30 See: 23 and Me, *Health and Ancestry Service*, available at: https://www.23andme.com/en-gb/dna-health-ancestry/ and Genome Link, *Could your DNA reveal your Educational Attainment,* available at: https://genomelink.io/traits/educational-attainment

Diversity and genomics

The current lack of diversity in genomic healthcare and research is a well-known issue and there is a clear need to increase diversity across genomics.[31] However, no UK resources relating to diversity and genomics were identified in our mapping.

This applies to the lack of diversity:

(1) within the data used to generate and inform research findings and health outcomes;

(2) in the genomic workforce; and

(3) accessibility of genomic services.

All three have implications that will continue to perpetuate and amplify health inequalities if they are not addressed.

(1) Diverse Data

Increased diversity in genomic data would enable the benefits of genomics to apply to people more equitably. Research would have accurate findings for more people and there would be applicable (and safe) clinical options for everyone.

In 2021, 86% of genomic studies were conducted in populations of 'European descent.'[32] This highlights the stark areas of underrepresentation in our current research and genomic databases. Other dimensions of diversity, such as sex, age, socio-economic and environmental factors (such as geography) are also not often captured. Although humans are 99.9% genetically identical, variation in the 0.1% can have important consequences for our health. Understanding this variation and the interaction with our environment is important so that all populations can benefit equally from advances in genomics.

Efforts need to be made to both engage with (and include) individuals who are not represented in current datasets and encourage researchers and clinicians to be cognisant of this problem and subsequently make changes to practice. The former

31 The need has been recognised by many calls to increase diversity. See CMS and Wellcome Trust (2023) *Data Diversity in Human Genomics Global Landscaping,* available at: https://cms.wellcome.org/sites/default/files/2023-01/RFP-Data-Diversity-Genomics-Global-Landscaping.pdf, Our Future Health *Why Diversity is Essential to Our Mission*, available at: https://ourfuturehealth.org.uk/our-research-mission/why-diversity-is-essential-to-mission/ and Genomics England *Diverse Data,* available at: https://www.genomicsengland.co.uk/initiatives/diverse-data

32 Fatumo S, Chikowore T, Choudhury A, et al (2022) A Roadmap to Increase Diversity in Genomic Studies Nature Medicine **28**, 243-250.

requires acknowledgement of the valid reasons individuals might not have engaged with genomics in the past, due to instances of exclusion or exploitation.[33] The latter includes awareness of the language being used to categorise people and the potential ramifications this could have. Efforts by researchers and clinicians should involve being transparent about defining what 'diversity' means for a research project, why this matters, and how research has taken account of this.

In the UK, the Genomics England's website indicates that their Diverse Data Initiative are developing some resources that could begin to address some of these issues:[34]

Genomics England	Lost in Translation: A flexible guide for using context-appropriate language in diversity in genomics. A code to conduct sensitivity analyses in Genomics' England's data within your own research to explore whether any ancestral biases exist. A handbook for how to collaboratively come to a shared understanding and definition of where to prioritise efforts and attention in data diversification projects.

33 For example, in 2003 members of the Havasupai tribe found out their genetic data, which had been collected for Type 2 diabetes studies had been used in studies relating to schizophrenia, migration and inbreeding without their knowledge or consent.

34 Genomics England, *Diverse Data: Products, Tools and Behaviours*, available at: https://www.genomicsengland.co.uk/initiatives/diverse-data/tools

International resources have also been developed, or are in development which address this issue:

The National Academies of Sciences, Engineering and Medicine	Using Population Descriptors in Genetics and Genomics Research: A New Framework for an Evolving Field (2023) This report focuses on understanding the current use of population descriptors in genomics research, examining best practice for researchers, and identifying processes for adopting best practices within the biomedical and scientific communities.
The Global Alliance for Genomics and Health (GA4GH)	Considerations for how Genetic and Genomic Researchers Should Approach Thinking About Diversity in Data. The policy is awaiting approval and is aiming to become an official GA4GH policy in 2024.

(2) Workforce

Diversity (e.g. based on ethnicity, sex, disability) within the genomics workforce is also lacking. This not only means priorities are likely to be set by those already served by genomics, but also that recruitment of participants is likely to suffer. It has been demonstrated that diverse research staff helps with diverse enrolment.[35]

Changes need to be set for inclusive recruitment and priority setting within genomics that can support crucial improvements being made. There should also be pressure on funders to ensure they equitably distribute funding to diverse researchers, research areas and training programmes.

35 George S, Duran N and Norris K (2014) A Systematic Review of Barriers and Facilitators to Minority Research Participation Among African Americans, Latinos, Asian Americans, and Pacific Islanders *American Journal of Public Health* **104(2)** 16-31.

(3) Access

Access to genomics is another area which needs addressing. As with wider healthcare provision across the UK, there are stark inequalities in access, especially for those who need to access care the most.[36] For genomics to deliver on the promised benefits, it not only needs to serve everyone equitably, it also needs to be accessible to all.

Familial disclosure

There is a need to expand good practice around disclosing genomic information where these findings could also impact an individual's family members. Unanswered questions include what are healthcare professional's responsibilities, how to balance a duty of disclosure and the right not to know, and how to support families and communities to live with this information, especially when findings may be uncertain.

This can become increasingly complex when individuals do not provide consent that their genetic findings can be shared with others that could benefit from this knowledge.[37] When genomic testing is being undertaken in children, ensuring parents and guardians understand the impact some findings may have on their own lives when providing consent is pertinent.

Efforts are required to establish how to ensure ethics is promoted in practice, and researchers and clinicians understand their responsibilities and roles. Individuals undergoing genomics testing should also understand how their genetic information relates to family members and what this means in terms of genetic testing.

Genomics and artificial intelligence

As the intersection between genomics and artificial intelligence (AI) continues to grow, the relevant ethical issues and how they can be addressed across healthcare and research need attention. Questions remain about how these new advancements should be developed and deployed, as well as the implications that using these technologies together might have.

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36 See: Best S, Vidic N, An K, Collins F and White SM (2022) A Systematic Review of Geographical Inequities for Accessing Clinical genomic and Genetic Services for Non-Cancer Related Rare Disease *European Journal of Human Genetics* **30** 645-652.

37 See: *ABC v St George's NHS Trust* (and other NHS defendants) [2020] EWHC 455 (QB). This legal case has established a legal duty to do this where there is a close relationship between the professional and at-risk relatives, and when disclosure could reduce or prevent a risk of serious harm.

In the UK, a collaboration between the Ada Lovelace Institute and the Nuffield Council on Bioethics has begun to address this area:

Ada Lovelace Institute and the Nuffield Council on Bioethics	The interim report DNA.I - Early Findings and Emerging Questions on the Use of AI in Genomics (2023) illustrates progress to date investigating the ethical, social and political and economic issues arising from the application of artificial intelligence and genomics. A final report is due to be published Spring 2024. This report will illustrate recommendations related to the development of AI powered genomic health prediction technology.

Gene editing

As advances in gene editing continues, we need to ensure that consensus of what is ethically acceptable is built in tandem.

One area that may require further deliberation is heritable genome editing. Heritable genome editing happens where changes are made to the genetic material of eggs, sperm or cells that lead to their development for reproductive purposes (e.g. to be used to establish a pregnancy). Following the Third International Summit on Human Genome Editing in early 2023, the organising committee identified that 'governance frameworks and ethical principles for the responsible use of heritable human genome editing are not in place.'[38] Heritable genome editing is illegal in the UK. However, a recent Citizen's Jury undertaken by Wellcome Connecting Science identified that participants agreed (17-4) that 'the government should consider changing the law to allow intentional genome editing of human embryos for serious genetic conditions.'[39] This is a step that would require significant ethical debate.

38 The Royal Society (2023) Statement from the Organising Committee on the Third International Summit on Human Genome Editing, available at: https://royalsociety.org/news/2023/03/statement-third-international-summit-human-genome-editing/

39 Wellcome Connecting Science (2023) *UK Citizens' Jury on Genome Editing,* available at: https://societyandethicsresearch.wellcomeconnectingscience.org/project/uk-citizens-jury-on-genome-editing/

The organising committee of the Summit also identified that mechanisms are required for human genome editing to ensure research with proven, legitimate findings. Additional areas requiring attention include ensuring that the cost and access of gene therapies utilising gene editing techniques are affordable and accessible.

Some international work has been developed in this area:

World Health Organisation (WHO) [Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing]	Human Genome Editing: A Framework for Governance (2021).

Insurance and genomics

Current rules around insurance and genomics are covered by the UK Government and Association of British Insurers' (ABI) Code on Genetic Testing and Insurance.[40] The Code outlines that insurers who have signed up to adhere to the Code will not require individuals to undertake a predictive or diagnostic test, and will only consider the result of a predictive test where the condition being tested for is specified under the Code.[41] The only test that can currently be requested to be disclosed is a predictive test for Huntington's Disease, when an applicant is seeking life insurance over £500,000.

Predictive test results can be disclosed voluntarily by the applicant and will only be taken into consideration if the result is in the applicants favour and would result in a lower premium. As more people are exposed to predictive genomic testing, due to it becoming more affordable and widely available through direct-to-consumer tests, people may begin to voluntarily disclose predictive results more frequently. However, there are concerns amongst some that despite the current protections, genetic discrimination may become an issue in the future. Inequitable access to genomic testing and a lack of diversity in genomic research may mean that certain groups are prevented from disclosing 'healthy' findings. As more research findings in this field

40 HM Government and Association of British Insurers (2018) *Code on Genetic Testing and Insurance* available at: https://www.gov.uk/government/publications/code-on-genetic-testing-and-insurance

41 UK Government (2022) *Code on Genetic Testing and Insurance: 3-Year Review 2022* available at: https://www.gov.uk/government/publications/code-on-genetic-testing-and-insurance-3-year-review-2022/code-on-genetic-testing-and-insurance-3-year-review-2022

emerge and are translated into diagnostic and predictive testing approaches, the relationship between genomic testing and insurance and associated governance may evolve over time.[42]

Our stakeholder engagement revealed that further guidance might be helpful in this area. This may also be pertinent following a recent call for evidence by the UK government (closed October 2023), which sought views on revising the Code to ensure it remains beneficial to consumers and insurers.[43]

Patient, participant and public engagement

Further guidance on how to embed patient, research participant and public engagement into practice should be developed. Engagement should not be 'tokenistic' and participants should feel like their involvement has mattered and shaped practice. How to best engage can be difficult to determine.

We identified the following international resources which begins to address these issues:

EURORDIS Rare Disease Europe	Patient Partnership Framework for the European Reference Networks (2023).
Global Alliance for Genomics and Health (GA4GH)	Framework for Involving and Engaging Participants, patients and Publics in Genomics Research and Health Implementation (2021).

Good engagement should encourage future participation and trust in clinical practice and research, as those whose data are being used, or will need to be used, will have shaped the way research and healthcare is undertaken.

There are questions about whether research participants should be rewarded and/or incentivised for their engagement in some way, and in what contexts. Some examples include the return of clinically relevant results or through monetary remuneration.

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42 Rodriguez-Rincon D, Parkinson S, Hocking L et al (2022) Assessing the Impact of Developments in Genetic Testing on Insurers' Risk Exposure *Rand Health Quarterly* **9(4):5**.

43 UK Government (2023) *Code on Genetic Testing and Insurance: Call for Evidence*, available at: https://www.gov.uk/government/calls-for-evidence/code-on-genetic-testing-and-insurance-call-for-evidence

International work was identified that explores the return of clinically actionable genomic research results:

Global Alliance for Genomics and Health (GA4GH)	Policy on Clinically Actionable Genomic Research Results (2021).

Public engagement studies are another way in which practice can be informed. We have included a list of some recent public engagement studies in Annex 2.

Polygenic Scores (PGS)

There are currently a limited number of guidelines addressing ethics and the use of PGS in healthcare. This applies to their potential application in research and clinical practice, as well as their current utilisation by direct-to-consumer (DTC) tests.

PGS may support 'preventative healthcare', by indicating an individual's susceptibility towards certain conditions. The potential use of PGS could raise awareness, support early intervention and enable individuals to take control of their own healthcare, to some extent, by making lifestyle changes to mitigate their likelihood of disease.' For example, an individual who has a higher chance of developing heart disease may choose to adopt a healthier, more active lifestyle.[44]

Their potential capabilities need to be further evaluated, however, due to a lack of sufficient evidence on their current validity and positive impact for any given individual. There are other factors that are also important for health outcomes, such as lifestyle, postcode and socio-economic status. As this evaluation is undertaken, it is essential that the ethical considerations related to PGS are explored and that users are fully informed about what a PGS does and does not tell them. This is particularly important not only due to the developing methodology, but also because much of the data used to inform an individual's PGS currently remains biased towards those with European genetic ancestry and may not generalise to other populations.

Individuals may also not want to know about their chance of developing a certain condition and ways to ensure that the 'right not to know' is protected are important.

44 This is already presented to people who are at a higher risk of heart disease due to family history. See: Heart Foundation *Know your Risk: Family History and Heart Disease*, available at: https://www.heartfoundation.org.au/bundles/your-heart/family-history-and-heart-disease >

As these tests are already being offered by some DTC companies, and their use is being piloted in clinical settings, the ethical implications must be addressed.

Additionally, what is meant by 'PGS' is not aways clear. Similar terminology, including 'polygenic risk scores' and 'integrated risk scores' are sometimes used. Clarity is required on what different terms mean, and which ones are the most appropriate to use in specific contexts.

Some international work in this area was identified:

American College of Medical Genetics	Three 'points to consider' documents in relation to polygenic scores: The Clinical Application of Polygenic Risk Scores: A Points to Consider Statement of the American College of Medical Genetics and Genomics (2023) Laboratory Perspectives in the Development of Polygenic Risk Scores for Disease: A Points to Consider Statement of the American College of Medical Genetics and Genomics (2023) Direct-to-Consumer Prenatal Testing for Multigenic or Polygenic Disorders: A Position Statement of the American College of Medical Genetics and Genomics (2021).

Prenatal testing

Prenatal testing for genomic information remains an issue of contention across the UK. There are many ethical issues associated with prenatal testing, which may grow over time as new technologies are developed (e.g. PGS). Important ethical issues to consider were identified in the Nuffield Council on Bioethics' 2017 briefing note

'Non-Invasive Prenatal Testing: Ethical Issues',[45] including how to ensure autonomy in decision-making, accuracy and implications for people with positive tests for genetic conditions.

Screening for carrier status

Any assessment of whether individuals should be screened to establish their 'carrier status' for certain conditions was not identified in our mapping. Individuals who carry a genetic variant associated with a condition may not show symptoms of this condition. Their status means they may pass the variant on to biologically related children. This child may also be a 'carrier' or they may be at risk of being affected if their other biological parent is also a carrier of a variant in the same gene. For autosomal recessive diseases, there is a 25% chance in each pregnancy of a child being affected if both biologically related parents are carriers of an alteration in the same gene.[46] Most people are unaware that they are carriers, unless they have a positive family history or have already had an affected child.

Screening can be used to identify whether individuals have a chance of having a disease or health condition, so that action (e.g. treatment) can be taken and/or they can make informed decisions.[47] In the UK, individuals can be screened for a range of conditions determined by conditions of viability, effectiveness and appropriateness, outlined by the UK National Screening Committee.[48] Screening to establish carrier status for autosomal recessive conditions is not included.

However, expanded carrier screening (ECS) is being offered by some DTC tests to screen individuals for carrier status.[49] This indicates that it is technically possible to screen individuals or prospective parents for variants in genes causing some autosomal recessive conditions. However, there are many considerations necessary in the UK before introducing a new population-based screening programme through the NHS, such as benefits versus harms and the consideration of opportunity cost.[50]

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45 Nuffield Council on Bioethics (2017) *Non-Invasive Prenatal Testing: Ethical Issues,* available at: https://www.nuffieldbioethics.org/assets/pdfs/NIPT-ethical-issues-full-report.pdf

46 National Human Genome Research Institute (2023) *Carrier*, available at: https://www.genome.gov/genetics-glossary/Carrier

47 National Health Service *NHS Screening,* available at: https://www.nhs.uk/conditions/nhs-screening/

48 UK National Screening Committee (2022) *Criteria for a Population Screening Programme,* available at: https://www.gov.uk/government/publications/evidence-review-criteria-national-screening-programmes/criteria-for-appraising-the-viability-effectiveness-and-appropriateness-of-a-screening-programme

49 PRECAS *Reproduction in the Age of Genomic Medicine: The Emergence, Commercialization and Implications of Preconception Expanded Carrier Screening,* available at: https://precas.dmu.ac.uk/index.php/about-the-project/

50 UK National Screening Committee (2022) *Criteria for a Population Screening Programme,* available at: https://www.gov.uk/government/publications/evidence-review-criteria-national-screening-programmes/criteria-for-appraising-the-viability-effectiveness-and-appropriateness-of-a-screening-programme

Providing carrier screening could shift testing for conditions that happens from post-conception (e.g. non-invasive prenatal testing) to pre-conception. However, the number of carrier couples (where both are carriers of alterations in the same gene) would likely be very small. Assessment of whether providing screening for carrier status is ethically appropriate (in both commercial and non-commercial environments) could therefore be explored further.

We identified one social science research project, PRECAS,[51] which is looking to explore the emergence, commercialisation and implications of pre-conception expanded carrier screening.

PRECAS	Research project - Reproduction in the age of genomic medicine: the emergence, commercialisation and implications of preconception expanded carrier screening. This project is investigating the emergence of carrier screening for preconception use among the general population and its wider implications.

51 PRECAS Reproduction in the Age of Genomic Medicine: The Emergence, Commercialization and Implications of Preconception Expanded Carrier Screening, available at: https://precas.dmu.ac.uk/index.php/about-the-project/

Support for healthcare professionals

Guidance and support for healthcare professionals in implementing good practice was noted as a resource gap. Whilst not the focus of the report, we recognise this gap would be of benefit to fill. Support and training in the communication of genetic information is essential as genomics continues to be at the interface of clinical care and health research, but there is a lack of people with relevant specialised training.

Genetic counsellors can provide support to individuals and families who are given a genomic test result, however, they are few in number. Resources would be helpful to ensure that other healthcare professionals feel equipped to navigate genomics with patients and participants. They need to have confidence and the competence to discuss appropriate genetic testing and to communicate results. A good understanding of the ethical issues associated with genomics is required to do this successfully. The requirement for an appreciation of the importance of ethics affects not only clinical staff at the interface of genomics and healthcare (e.g. practitioners) but also clinical laboratory staff. Further work to identify necessary and appropriate resources is needed.

This toolkit, developed by the Royal College of General Practitioners and the Health Education Genomics Education Programme pulls together resources to support increasing understanding and awareness of genomic medicine and its incorporation into primary care:

Royal College of General Practitioners and Health Education Genomics Education Programme	Genomics Toolkit

Sustainability and genomics

As the generation, storage and processing of genomic data continues to grow, the importance of minimising the climate change impact, while improving advances in human health, will need to be addressed. Additionally, the clinical response to genomic testing is also likely to have climate-related impacts. This could include increased use of non-reusable test swabs and other unsustainable treatment options. Exploration is required to understand how genomics and climate change may be in tension, in order to resolve and address this in practice.

Whole genome sequencing of newborns

There are limited current, publicly available resources to ensure whole genome sequencing of asymptomatic newborn babies is undertaken ethically. Unanswered questions overlap with the other gaps identified, such as consent, data use, data governance and familial disclosure.

There are also additional considerations such as which conditions to test for, why, and how to relay this to families. Added challenges and questions exist, such as:

- whether and how long the genomic data of 'future populations' should be stored;
- how to protect clinical resources for pre-existing affected individuals (if there is an influx of asymptomatic babies requiring clinical review as a result of sequencing);
- whether to relay results indicating conditions that cannot be treated (due to a lack of resources or options); and
- the practicalities of ensuring respect for children's growing autonomy and ability to make decisions for themselves.

Clinicians responsible for liaising with parents will need to be trained to interpret and convey results and guide parents down an appropriate management pathway.

These are matters of consideration for the Genomics England Generation Study.[52]

Some UK focused work that is 'in progress' may begin to address this:

PHG Foundation	The Genomics England website references that they have commissioned the PHG Foundation to undertake a report on the regulation and governance of genomic data held over the course of newborns' lifetime.

52 Genomics England, *Newborn Genomes Programme*, available at: https://www.genomicsengland.co.uk/initiatives/newborns

What else?

Throughout our mapping we also identified some other resources that are currently in development across the UK. These may also begin to deliver on some of the gaps identified in the previous section. These include:

The British Society for Genetic Medicine	Developing guidance on the interpretation and reporting of large areas of absence of heterozygosity/ large regions of homozygosity (AOH/ ROH).
The British Society for Genetic Medicine and the Royal College of General Practitioners	Developing guidance for healthcare professionals on direct-to-consumer genomic testing, including advice for pharmacy teams and prescribers.
Joint Committee on Genomics in Medicine (with the British Society for Genetic Medicine)	Review of their consent and confidentiality guidance.
Royal College of Obstetricians and Gynaecologists	Green-Top guideline on Cell-Free Fetal DNA Testing. Good Practice Paper on best practice in supporting women who decline antenatal screening, testing, or who choose to continue their pregnancy following detection of a feta anomaly (title to be developed).

We encourage the sharing of these resources once they have been completed.

What does all this mean?

The gaps identified illustrate a significant number of areas where ethical consideration is required across genomics healthcare and research stakeholders in order to reach consensus on 'best practice.' Notably, many of these findings overlap with those identified in our 2022 work. Some of the existing resources we have identified may act as a starting point to cover some of these gaps, where there is overlap.[53] This overlap could illustrate the complexity of these areas, especially where practice is emerging/advancing on a fast-paced basis.

Genomic healthcare and research organisations may already be addressing some of these areas but some of this work is not currently publicly available and/or may still be in development. To promote a 'gold standard UK model' we encourage the sharing of work, even if it is internally facing in nature, to encourage transparency, accountability and shared knowledge exchange.

These gaps are not static. New resources will be developed over time that hopefully address these areas, and new gaps will emerge as genomics continues to develop. We need to be equipped to identify and deal with these as they arise, and build consensus effectively.

53 Further work will be required to untangle any duplication or inconsistencies in the identified resources.

What should be done?

Individuals and organisations across the genomic healthcare and research field should work together to share thinking and, where possible, reach consensus. This includes developing new resources that address the gaps identified, as well as building on and providing consistency across existing resources (if inconsistencies arise). This collaboration needs to be dynamic and responsive to ensure that new and unforeseen issues can be addressed if they arise. This will require engagement from all those involved across genomics including patients, participants, researchers, clinicians, policymakers and funders.

If the commitment set out in Genome UK to reach a 'gold standard UK model' for ethics is to be achieved, ethics needs to be embedded across genomics. Individuals and organisations should be encouraged to learn about the importance of ethics, how to promote consistent ethical practice and how to shape the future of genomics. This could include the development of guidance on how best to embed ethics across genomic healthcare and research. In turn, patients and participants should have more equitable experiences of genomics and the benefits of genomics can be realised.

Given the large number of initiatives and organisations involved across genomic healthcare and research we conclude that a UK-wide co-ordination role will be required to ensure that these actions can be taken forward in a consistent and effective manner.

Annexes

Annex 1: Law and Regulation

Legislation:

- Data Protection Act 2018
- General Data Protection Regulation (GDPR) and associated Information Commissioner's Office Codes of Practice
- Human Fertilisation and Embryology Act 1990 (as amended) and associated Code of Practice
- Human Rights Act 1998
- Human Tissue Act 2004, Explanatory Notes (2004) and associated Codes of Practice
- Mental Capacity Act 2005 and Code of Practice (2007)

Government Codes/Guidance:

- UK Government and Association of British Insurers: Code on Genetic Testing and Insurance
- UK Government, UK National Screening Committee: Criteria for a Population Screening Programme

Annex 2: Public Opinion Reports

[Listed in date order from 2023]

Resource	Summary
Wellcome Connecting Science and The Global Alliance for Genomics and Health Your DNA Your Say Infographics (2023)	A series of infographics disseminating the findings from the Your DNA Your Say study. Although an international study, the study includes findings from the UK.
Progress Education Trust Fertility, Genomics and Embryo Research: Public Attitudes and Understanding (2022)	Section 2 of this report provides data on what the UK public thinks and knows about various aspects of genomics.
Wellcome Connecting Science and Involve Should the UK Consider Changing the law to Allow Intentional Genome Editing of Human Embyros for Serious Genetic Conditions? (2022)	This report outlines findings from the UK Citizens Jury on Human Embryo Editing, including their recommendations for what needs to happen before intentional genome editing of human embryos occurs.
Hopkins Van Mil, Genomics England, UK National Screening Committee, Sciencewise and UK Research and Innovation Implications of Whole Genome Sequencing for Newborn Screening: A Public Dialogue (2021)	This report provides a summary of findings from public engagement around Whole Genome Sequencing in Newborns. The report outlines which considerations need to be taken into account.

National Data Guardian, Understanding Patient Data, Sciencewise, UK Research and Innovation and Hopkins Van Mil Putting Good into Practice: A Public Dialogue on Making Public Benefit Assessments when Using Health and Care Data (2021)	This report provides findings from a public dialogue aimed at understanding how people assess public benefit in the use of health data (and social care data) for purposes beyond individual care. It also provides policy advice or guidance to support making public benefit assessments.
Ipsos Mori, Genomics England, Sciencewise and UK Research and Innovation A Public Dialogue on Genomic Medicine: Time for a New Social Contract? (2019)	This report presents the results of a public dialogue aimed at considering members of the public's opinions on how genomic medicine should best be 'mainstreamed' into the NHS.
Human Tissue Authority and Health Research Authority Consent to Use Human Tissue and Linked Health Data in Health Research (2018)	This report presents the fundings from a public dialogue undertaken to understand views of consent to use patient data linked to human tissue in health research. Section 5 explicitly discusses views of genome sequencing and hybrid consent.
Progress Education Trust Basic Understanding of Genome Editing (2017)	This report provides findings on what people think and know about genome editing and its implications.
Genetic Alliance UK Genome Editing Technologies: The Patient Perspective (2016)	This report presents research findings of a survey focused on exploring the patient perspectives on the ethical use and regulation of genome editing technologies.

Annex 3: Patient and Ethics Groups

Patient Support Group	Ethics Group
Antenatal Results and Choices	Genethics Forum
Genetic Alliance UK	Genetics Society
The Gene People	Link 23
Royal Mencap Society	Moral and Ethics Advisory Group
Sickle Cell Society	SERG Network
UNIQUE	

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Acknowledgements: Thank you to everyone who reviewed and contributed to this report.

This report was written by the Nuffield Council on Bioethics, in partnership with the Office for Life Sciences.

This work was funded by the Office for Life Sciences.

Published by Nuffield Council on Bioethics
100 St John Street, London, EC1M 4EH

January 2024

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