Our Future Health

Ethics and governance framework

Version 2.0
April 2021

Our Future Health

Contents

EXECUTIVE SUMMARY

Improvements in early detection and prevention of disease will enable better provision of care, reduce costs and improve health outcomes. The Our Future Health (Our Future Health) programme aims to enrol up to five million people to a research cohort to help address this need. The success of Our Future Health depends on building and maintaining public trust and confidence. This will require the programme to demonstrate high ethical and governance standards across all its activities. Our Future Health established an Ethics and Feedback Advisory Group (EFAG) to develop an Ethics and Governance Framework to guide its operations**.**

Our Future Health can learn from best practice established by other large cohorts, for example UK Biobank. However, there are some novel aspects of Our Future Health which need particular thought, such as:

- the size of Our Future Health and the practicalities of recruiting such a large and diverse cohort, including the need to communicate with participants largely through a digital platform, with very little opportunity for personal contact;
- the intention to regularly use the cohort to recruit participants for further studies to test diagnostics, treatments or behavioural interventions;
- the proposal to provide participants with individual health-related information, for example their disease risk categorisation.

We set out some key principles that should guide decision making and offer some high-level guidance on the major operational areas of the programme.

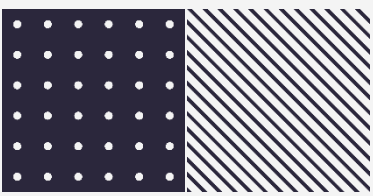
The balance between research and care

In order to ensure clarity in its relationship with participants, we recommend that Our Future Health should be approved and regulated as a research programme. Participants should not expect to receive individual clinical care as a result of taking part. However, Our Future Health should recognise that its relationship with some participants may go beyond that of pure research. Where a participant needs clinical assessment, screening, support or treatment as a result of information discovered through Our Future Health, this must be appropriately resourced and supported.

Public and participant involvement

The success of the Our Future Health cohort critically depends on building and maintaining public trust and confidence. A public and participant involvement strategy must be developed as a priority. Extensive public involvement and significant piloting from the very beginning will be crucial to help answer some of the questions that have been raised and to provide evidence to inform this Framework and the Our Future Health programme.

Involving participants in a meaningful way over the lifetime of the cohort will help strengthen the programme, ensure it meets the expectations of those who contribute their time, data, samples



and information, and help motivate participants to stay engaged. Public engagement and involvement activities must be woven in at all levels of the cohort, and adequately resourced.

Recruitment

Recruiting a cohort of 5 million people has never been attempted before. Our Future Health will need to interact with more than 10 per cent of the adult population of the UK, and responsible use of a digital platform will be essential to help achieve this.

Our Future Health must endeavour to recruit a broad mix of people that reflects the diversity of the UK population, including (but not limited to) a range of ethnic and socioeconomic backgrounds. This will be crucial to ensure discoveries from Our Future Health can be of value across society and to understand differences between different sections of the population. Recruitment methods should be carefully designed in consultation with people from underrepresented and seldom heard groups, to reduce barriers to participation. Specific effort should be made to facilitate both the recruitment and continued involvement of people with limited capacity to consent. (See Section 3.1)

Consent

We recommend that Our Future Health should operate with 2 stages of consent.

- Phase 1: Every participant should be recruited with a single broad consent. This should set out clearly what participation will involve; and give permission for initial assessment, sample collection and analysis, and long-term follow-up through linkage to health and health-related data. Participants should also agree to be re-contacted with requests for further information and samples, or to be invited to take part in additional studies.
- Phase 2: Additional studies will each need supplementary consent, which will provide more detailed information about the details of the individual study. There is no obligation on participants to agree to take part in any phase 2 study – each will be the subject of a separate and independent consent.

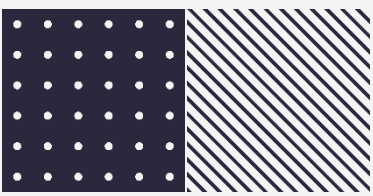
Phase 1 consent will need to be broad, to define the types of research that might be facilitated, and how access will be governed. It should be made clear that the decisions participants may face later could be complex and have significant implications for their lives.

Our Future Health should follow best practice to ensure appropriate standards for valid consent. The way in which information is conveyed is as important as the information itself and Our Future Health should make sure that information resources are available in a range of accessible formats, and try to assess whether participants have understood the information.

Participants have a right to withdraw from the Our Future Health cohort at any time, without having to give a reason. This should be explained as part of the consent process. (See Section 3.2)

Recontact

Participants might be re-contacted for additional studies that require new sampling or clinical assessment, additional data linkage, enrolment in a trial or a new follow-up programme. The



Phase 1 consent process should set expectations for why and how participants might be re-contacted over the lifetime of the cohort.

Initial recontact should always be by the Our Future Health team. Participants should be given the choice whether or not they are willing to provide additional samples or information. A governance mechanism will be needed to assess and approve additional studies, taking care to monitor and avoid recontact fatigue leading to cohort attrition. (See Section 3.3)

Some studies may require that participants are made aware of individual health information, for example if they are being recruited because of their risk of a particular disease, the reason for their selection will need to be explained. However, this could disclose information about their risk profile before they have given consent. Strategies which do not involve selection before consent should be used where possible.

Provision of individual health-related information ("Feedback")

There is significant debate about whether and how participants should be provided with individual health-related information. Providing clinically significant information to participants can be of benefit, if it is valid and leads to better health management but it can also be harmful, if it is misleading, causes distress or results in unnecessary medical procedures.

Our Future Health must take a responsible and cautious approach, based on the following principles:

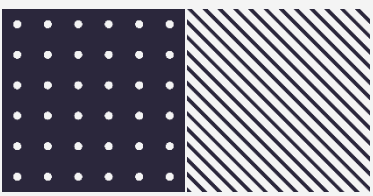
- Participants must be given a choice about receiving individual feedback.
- Our Future Health must have a transparent mechanism to assess potential benefits and harms before any feedback is provided.
- There must be a robust, long-term clinical support system in place for participants who receive individual information in this way.

We distinguish between two types of feedback, which should be treated differently:

1. **Clinically significant information**, which is already used in routine practice to guide clinical management. This type of information may be provided on initial examination when admitted to the study, or on an ongoing basis during the course of the cohort, provided the principles described above are met and the practicalities can be appropriately addressed. However, in practice this is far from straightforward, and we discuss the many problems surrounding the return of clinically relevant information to participants (Section 3.4.4).

2. **Information of unproven clinical validity or utility.** This type of information should only be provided if participants give additional, specific consent as part of a separate research protocol.

Our Future Health must actively engage with the public and participants to understand people's expectations about feedback. The approach to providing feedback must be clearly explained



during the consent process. This should take into account uncertainties, recognising that feedback policies may need to be updated in light of emerging evidence and decisions may change over time.

Our Future Health may consider offering participants information about their risk status for certain diseases. Some risk stratification will be clinically validated (e.g. a QRisk score for cardiovascular risk, or a high cholesterol level) but some will be of unproven clinical validity or utility. Polygenic risk scores (PRS), for example, have not yet been widely used in clinical care**.** Information that is not of proven clinical utility or validity (including, currently, most PRS) should only be provided with separate, specific consent which carefully explains the uncertainties. When providing any information about risk profiling, it is crucial that the inherent complexities and uncertainties are communicated.

Our Future Health should not provide complex information to participants without ensuring ongoing support is available to help them manage and interpret that information. This could have considerable resource implications which must be appropriately addressed from the outset. We would caution strongly against providing a feedback programme, however well intended, without ensuring that a high-quality long-term support system is in place. (See Section 3.4)

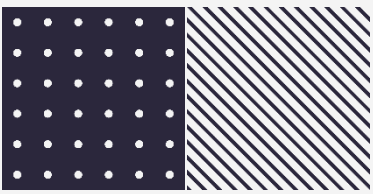
Data stewardship

Our Future Health will collect a vast amount of data over the lifetime of the cohort. In order to build and retain participants' trust, Our Future Health must demonstrate a robust approach to data security and have rigorous processes to control access and use. The initial consent process should set out information about what data is collected, how data will be kept safe, and how data access will be managed. The importance of transparency cannot be overstated. Our Future Health's approach should be grounded in the National Data Guardian's advice that there should be 'no surprises'.

Initially Our Future Health will collect information from NHS records and other health and social care datasets, but there is potential for linkage with other types of dataset over the lifetime of the cohort, including information collected from wearables or social media. There must be a transparent mechanism for making decisions about additional data linkage, with a clear scientific rationale for extending data collection. We anticipate that data linkage beyond health and care datasets will need additional consent.

Our Future Health must develop a robust and transparent policy that sets out detailed information about how data and samples may be accessed and used. There must be an explicit mechanism to ensure appropriate research access to the accumulated cohort data, in order to maximise the value of the resource in the public interest. An appropriately constituted data and sample access committee(s) (DAC), reporting to the Our Future Health Board, should be responsible for access policy and overseeing decisions about access to data and samples.

The resource should be available to all bona fide researchers for all types of health-related research that is in the public interest, in accordance with the participants' consent. The same criteria should be applied to all researchers, whether academic, charitable or commercial companies, and whether from the UK or abroad. No party should be given exclusive access to the



resource. Short term exclusivity for newly generated data may be granted to researchers who generate the data, to allow them to exploit their own research findings before they become widely available, but this should not be an automatic right. The need for, and duration of, data exclusivity must be agreed by the Data Access Committee on a case-by-case basis. (See Section 3.5)

Support for participants

Participants must be given appropriate support throughout the programme, and this must be adequately resourced. Communications must be clear and accessible to ensure participants understand the implications of participation and have help when interpreting feedback. It will be essential to also provide a level of personal support for those who need it, whether by telephone, online or face-to-face.

Governance, advisory and control structures

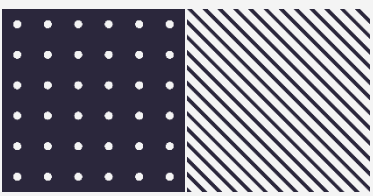
Our Future Health must be governed well and in the public interest. The governance mechanisms should be appropriately constituted, accountable and open to scrutiny. The mechanisms should include a main Board, Scientific Advisory Board(s), an Ethics Advisory Committee and a Participant Advisory Panel. Special advisory committees will also be required, including dedicated Access and Feedback Committees. (See Section 4.2)

External partnerships

The Our Future Health cohort depends on close partnerships between participants, researchers, healthcare professionals, industry, charities, government and international research efforts. The roles of different partners must be transparent, and clearly defined.

Commercial partners: Industry partners will play an important role in achieving Our Future Health's goals and add value to the work, but the public and participants can be uncomfortable about commercial involvement. It is important to address these concerns proactively and openly. A policy on commercial partnerships, including details about oversight and scrutiny, should be developed as a priority, and the involvement of industry partners must be carefully explained in the consent process. We recommend that the Participant Advisory Panel should be involved in the development of this policy, and should also discuss and scrutinize the conditions on which Founding Partners can join. Industry involvement must be on terms which are consistent with the overall aims, objectives and values of Our Future Health, and should be designed to deliver public benefit. (See Section 4.3)

Implications for the NHS: The Our Future Health cohort will be closely associated with the NHS and there must be funding, resource and support to match. Our Future Health must ensure that healthcare professionals are properly prepared, well informed and not overburdened as a result of the programme. It will be essential to ensure appropriate engagement within relevant NHS professionals and structures throughout the lifetime of the cohort. We recommend that Our Future Health should work with NHS bodies and personnel to undertake a detailed analysis of the resource implications of implementation for the NHS. (See Section 4.4)



1. INTRODUCTION

1.1. Background and context

Improvements in early detection and prevention of disease will enable better provision of care, improve outcomes and reduce costs to the health service. The Our Future Health (Our Future Health) programme aims to enrol up to five million people to a research cohort to help address this need. A major role will be to enable the recruitment of targeted sub-populations for trials of diagnostics and therapeutics. The success of the Our Future Health cohort depends on building and maintaining public trust and confidence. This will require the programme to demonstrate high ethical and governance standards across all its activities.

The starting point for an ethical framework for Our Future Health is the three key principles underpinning most research involving human participants: respect for autonomy, beneficence and justice.[1] Building on these principles, Our Future Health can learn from previous cohorts where appropriate, but some aspects need new deliberation. These include the practicalities of recruiting such a large and diverse cohort, and the proposal to provide individuals with information about their risk categorisation. Our Future Health must make the most of the opportunity to become an exemplar, using new digital technologies in a way that sets the bar high for care and sensitivity.

Ethics and Feedback Advisory Group

Very early in its development, Our Future Health established an independent Ethics and Feedback Advisory Group (EFAG) to provide strategic advice on the development of ethical guidelines and principles for the Our Future Health cohort, and to develop an Ethics and Governance Framework to guide its operations (see Annex A for a list of members of EFAG). **This Framework provides advice to the Our Future Health Board and Executive, and will be publicly available for funders, partners, researchers, participants and the general public**. EFAG, an independent group which reports to the Our Future Health Board, will continue as part of the long-term governance of the cohort and will be responsible for monitoring the implementation of the Framework, and for reviewing and updating it as appropriate.

It will be important to ensure close interaction between EFAG and the emerging scientific strategy as the operating principles and discussions develop. **Extensive public involvement and significant piloting will be crucial to help answer some of the questions that have been raised and to provide evidence to inform the Framework and the Our Future Health programme.**

We envisage the Framework is a living document. It will initially need to be reviewed frequently, as experience accumulates from initial piloting and the impact of the COVID-19 pandemic on health services is clearer. After that, the Framework should be reviewed on a regular basis, at least every five years, to ensure that it remains relevant to current scientific and ethical standards.

[1] The Declaration of Helsinki sets out the defining principles for research involving human participants. https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/

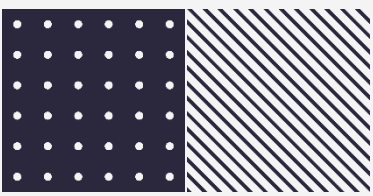
1.2. What is new or different about Our Future Health?

The Our Future Health cohort will learn from and build on best practice established by other cohorts, particularly UK Biobank. However, there are some aspects of Our Future Health which are new or different, and these need particular thought.

- **The size of Our Future Health:** Recruiting a cohort of 5 million people has never been attempted before. While the scale does not necessarily raise new ethical issues, it will be important to consider the practicalities of recruiting such a large and diverse cohort. Our Future Health will be interacting with more than 10% of the adult population of the UK, and it will be particularly important to consider how to ensure appropriate support is available for participants who need it (discussed further in Section 3.1 and 4.4).
- **Digital platform:** Our Future Health will make extensive use of a digital platform to keep in contact with participants and collect information. It will be important to make sure the platform is used transparently and responsibly, with careful and sensitive communications. Our Future Health must also work to ensure this approach does not exclude any groups, making alternative arrangements available if necessary.
- **The proposal to frequently use the cohort to recruit participants for further trials:** Our Future Health will have two elements – Phase 1 will include the recruitment and ongoing follow-up of 5 million people; Phase 2 will involve selected sub-sets of participants being invited to take part in additional studies. It will be important to be very clear about the different consent required for each phase. The need for initial broad consent, with further detailed supplementary consent for Phase 2 studies is discussed further in Section 3.2.2.
- **Feedback:** Our Future Health is still considering making certain health related information available to participants. The nature of some of the additional studies which can be envisaged will make it unavoidable to disclose some individual information of possible clinical relevance, to participants. Return of clinically relevant information could be of benefit to participants, if it is correct and leads to better health management or leaves them better informed about their health. But it can also be harmful, if it is confusing or misleading or leaves them with anxieties and concerns which are not properly managed. This means it will be particularly important for Our Future Health to take a careful and responsible approach to decisions about feedback, as discussed in Section 3.4.

1.3. Boundaries between research and clinical care

Clinical care involving patients has the primary purpose of providing a direct benefit to the patient through diagnosis, prevention, care or treatment. People are also sometimes asked to participate in projects which are purely research, with the primary purpose to test a hypothesis or to generate new generalisable knowledge. These two activities are often seen as separate, with different governance processes and expectations. However, the boundaries can be blurred. For example, a clinical trial of a new treatment involves both research and care; a genome analysed for diagnostic purposes might also provide evidence for research on the association of other genomic variations with particular diseases. Where research is undertaken in a clinical context with an individual patient it can be easily explained, but when it is scaled to involve large numbers of people, it becomes important to be clear what is involved.



There is therefore a spectrum between care and research, and the scope of any related duty of care tracks that spectrum. The patient / clinician relationship creates a duty of care from the clinician to the patient which has been the subject of many years of legal precedent and covers many different facets of the interaction, from consultation to information, consent, treatment and follow up care. At the other end of the spectrum, the participant / researcher duty of care is still a legal duty of care although its nature and scope are less well defined by legal precedent and more influenced by context, expectations and normal practice of biomedical research.

The scope of the duty depends on, amongst other things:

- the nature of the research project;
- the basis on which participants are recruited (do they or should they expect any benefit from participating?); and
- what the participants should be and are told about the project.

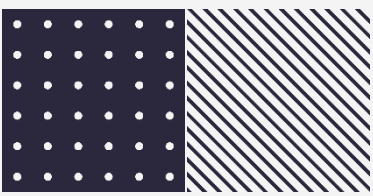
For example, a researcher owes the participant a duty of care which includes:

- the obligation to be clear, transparent and fair about the process;
- the obligation to make the process as safe as possible;
- the obligation to make the process relevant for effective research;
- the obligation to provide certain information back to participants. This is more nuanced and will depend on the nature of the information and how expectations have been set.

For example, UK Biobank was established as a research project. The information provided to participants at the outset made it clear that participants should not expect any personal benefit, including clinical feedback, from taking part. The emphasis was on creating a research resource with the objective of generating discovery about disease in a generalisable manner.

By contrast, the 100,000 Genomes Project was designed as a hybrid between research and clinical care. This is reflected in the information provided to participants, where there is an emphasis on the individual benefit that participants may receive as a result of taking part, including the potential of receiving an individual diagnosis, in addition to the research potential of the genome sequencing information. Participants were recruited as part of their NHS care, and any findings are provided by the clinical team, to ensure that appropriate clinical care and support is available.

Our Future Health is different again. It is intended primarily as a research resource for generalisable discoveries, but participants may be invited to take part in additional trials, to test out diagnostics, treatments or behavioural interventions. This means that participants might receive different clinical care, or have more interaction with the health service, as a result of their involvement. From a participant's perspective, Our Future Health is therefore further along the research-care spectrum than UK Biobank, but it is not as far along as 100,000 Genomes.



In order to ensure clarity in its relationship with participants, **we recommend that Our Future Health should be approved and regulated as a research programme.** Participants should not expect to receive individual clinical care as a result of taking part. However, Our Future Health should recognise that its relationship with some participants may go beyond that of pure research. Where a project includes both research and clinical care, the legal situation and the scope of the duty inevitably becomes more complicated. **Our Future Health should ensure this is appropriately considered and any clinical duty of care required, (for example if an individual needs clinical assessment, screening, preventive measures or treatment as a result of information discovered through participation), will need to be appropriately resourced and supported.**

The implications are particularly relevant when considering consent (Section 3.2), feedback (Section 3.4) and ongoing support for participants (Section 4.4, Box 2).

2. GUIDING PRINCIPLES

In this section, we set out key principles which we believe should underpin the cohort. They are intended to help guide decisions, and to emphasise those issues that are especially important for Our Future Health to get right.

A. **Building an effective research resource:** The principal aim of Our Future Health is to create a cohort that facilitates high quality research in early diagnosis and detection, improved risk prediction and prevention. The outputs of the research should ultimately deliver benefit for the health of the whole population.

B. **Responsive engagement and involvement:** The public and participants should be actively engaged from the very beginning of the Our Future Health planning. Involving participants in a meaningful way over the lifetime of the cohort will help strengthen the programme, ensure it meets the expectations of those who contribute their time, data, samples and information, and help motivate participants to stay engaged.

C. **Inclusive:** Our Future Health must strive to recruit people with broad diversity, for example including a mix of ethnicity and socioeconomic backgrounds, in order to ensure the research results are of value across the UK population and to understand differences between different sections of the population.

D. **Responsible:** This is a complex programme; the nature of the studies based on the cohort will evolve over time. Some related to risk and early diagnosis may not live up to expectations and hypotheses may turn out to be false. There is therefore a potential risk of harm to participants, which Our Future Health must anticipate and avoid. Our Future Health should demonstrate a responsible approach, striving to ensure that it minimises any harm, and maximises benefit, while communicating carefully with participants. Our Future Health must embed flexibility to be able to respond to emerging opportunities.

E. **Support for participants:** Participants must be given appropriate support throughout the programme, and this must be adequately resourced. Communications must be clear and accessible to ensure participants understand the implications of participation, taking care not to overstate the likely clinical benefit for individuals and to manage expectations. Feedback of individual findings, including risk profiling, must be delivered sensitively and with appropriate support.

F. **Collaborative:** The Our Future Health cohort will only succeed if it is built on close partnerships between participants, researchers, healthcare professionals, charities, industry, funders, government and international research efforts. The roles of different partners must be transparent, and fairly defined.

G. **Robust data security:** Our Future Health must demonstrate a robust approach to data security, respecting and protecting participants' privacy and confidentiality throughout everything it does. Our Future Health should embrace the opportunities of innovative uses of digital technology, while minimising any risks for participants.

H. **Working closely with the NHS:** The NHS should be able to derive benefit from new understanding, tools and treatments developed from research engaging the Our Future Health cohort. While linking closely with the NHS, Our Future Health must be careful to ensure that healthcare professionals are not overburdened, and consideration must be given to the appropriate interface between research and care.

I. **Transparent governance and oversight:** Our Future Health must be governed well and in the public interest, with fully accountable governance processes. Our Future Health must be transparent and open to scrutiny across all activities in order to demonstrate trustworthiness and build confidence.

J. **Facilitating access:** A transparent mechanism will be needed to enable appropriate research access to the cohort and accumulated cohort data, in order to maximise the value of the resource in the public interest. The results of research must be open access and as widely shared as possible to contribute to the broader knowledge base.

3. GUIDANCE FOR MAJOR OPERATIONAL THEMES

In this section, we offer high level guidance on the major operational areas of the programme: recruitment, consent, re-contact, feedback of individual findings, and stewardship of data.

3.1. Recruitment

The ethical principle of justice requires that there be fair procedures in the selection of research participants, with different groups of society offered the opportunity to participate.[2] The following guidance should apply for recruitment to Our Future Health:

- **Inclusivity:** To ensure that discoveries can be of value across society, efforts must be made to recruit a broad mix of people that reflects the diversity of the UK population, including (but not limited to) a range of ethnic and socioeconomic backgrounds, and those with underlying physical and mental health conditions. This will help to ensure that, when there is targeted recruitment to further studies, large enough numbers are available from minority populations. Our Future Health should use innovative outreach approaches to engage with, involve, and ensure it is accessible to, diverse populations**. Recruitment methods should be carefully considered, in consultation with people from underrepresented and seldom heard groups, to reduce barriers to participation.** While we appreciate that it may be difficult to have an entirely representative cohort, the aim should be to have a more balanced representation in order for findings to be generalisable[3], and any major gaps should be transparently explained. Recruiting, retaining and involving a diverse sample of the population will require considerable focus and effort, and it is critical that adequate resource is allocated for this part of the programme.[4] It will also be valuable to hear from people who choose not to join or who drop out, to understand their concerns.
- **Mental capacity:** It is a matter of social justice that the recruitment and consent processes, as well as other aspects of the Our Future Health programme, account for the fact that some individuals in society have limited capacity to provide consent, and that some participants will lose (and possibly regain) mental capacity while part of the Our Future Health programme. Although there are obvious hurdles to overcome, we recommend that specific effort should be made to facilitate both the recruitment and continued involvement of such participants. Our Future Health should state explicitly the approach that will be taken if a participant loses capacity during the lifetime of the cohort.

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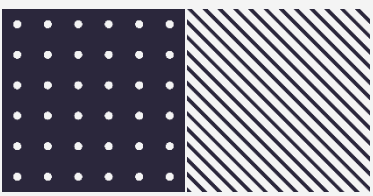
[2] The Belmont Report, page 9 (Part D: Applications – Selection of Subjects)

[3] For example, a cohort of two thirds women and one third men would not be representative but would still be generalisable if the numbers in both groups are large enough to support robust comparisons between the two groups. It may be necessary to have over-representation of some minority groups in order to have sufficient numbers for valuable and robust research.

[4] In addition to *standard* materials, some *tailored* materials for some groups will be needed, e.g. easy-to-read documents for people with learning difficulties, translation into the five most dominant languages in the UK, videos are all but essential for certain groups of people with certain forms of impairment.



- **Digital platform:** Since the main route for recruitment, consent and ongoing engagement will of necessity be via a digital platform, it will be important to ensure that this does not unnecessarily exclude any groups from participation in Our Future Health.
- **Reimbursement:** Participants should not have to meet any costs of taking part in the cohort and so recompense for expenses should be made available. In situations which make unusual demands on participants' time, compensation for time spent can be considered.
- **Association with the NHS:** It is possible that recruitment will take place within an NHS setting, for example close to Health Check clinics.[5] This could be a useful way to help recruit a diverse population at a moment where they are already thinking about their health.[6] However it will be important to manage expectations to avoid confusion between recruitment for a research programme and the delivery of healthcare. It must be made clear that participants should not expect to receive individual clinical care as a result of taking part in Our Future Health. The approach should also ensure that those who do not want to participate in research are not deflected from receiving clinical care. **The significant resource implications for the NHS** are addressed in Section 4.4.

3.2. Consent

The ethical principle of respect for autonomy requires that people should be given the opportunity to choose what will or will not happen to them, which means that adequate standards of valid consent must be met during all recruitment processes.[7] **We recommend that Our Future Health should seek initial broad consent for all participants at recruitment (Phase 1 consent), with further detailed supplementary consent as required for additional studies (Phase 2)** (see Section 3.2.2 for further discussion).

3.2.1. Ensuring adequate standards for valid consent

Valid consent comprises three components: (a) information, (b) comprehension and (c) voluntariness.

a) Information: At the time of recruitment into Our Future Health, potential participants must be given sufficient detail about the programme which they are being invited to join to make an informed decision.

- **Information about the implications of taking part.** Individuals should be adequately informed about the nature and purpose of the cohort, what is involved, what will be required at entry, and what type of information will be collected on an ongoing basis. Potential

[5] There is an opportunity to embed social and behavioural science research that examines experiences around recruitment in a medical setting as part of the Our Future Health cohort. This could be particularly relevant given the very different contexts of the NHS Health Check and blood donation, where one begins with an expectation of receiving health information while the other is solely altruistic.

[6] We note that the current shift to remote consultation as a result of COVID-19 may lead to some practical difficulties.

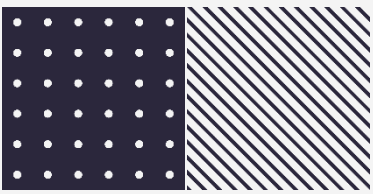
[7] UK Policy Framework for Health and Social Care Research, Health Research Authority (2017).

participants must be given a sense of what is reasonable for them to expect from participation. A list of information that should be provided, based on Health Research Authority (HRA) guidance, is given in Box 1.

- **Broad consent.** The consent requested at Phase 1 should be broad (described as generic by the HRA) because it will not be possible to anticipate all future research at the time of consent. Consent should enable research into human health and disease and factors that may influence them, and strategies for improving health care.
- **Setting expectations about research-care boundaries.** People should be asked to consent to Our Future Health on the understanding that this is a research project, rather than raising expectations that participants will receive individual clinical care. Although there may also be clinical or behavioural interventions that arise from their participation, the personal clinical benefit of participation should not be overstated. Providing, or raising the expectation of personally useful clinical information can lead to therapeutic misconception – the individual believes that they are taking part in the project because of the personal clinical information it will provide them, rather than for the purpose of furthering knowledge of disease and treatment for everyone.
- **Ongoing engagement.** Beyond the information provided during consent, Our Future Health should continue to communicate regularly with participants, to remind them about the nature of the cohort study as a whole, what is involved and what they might expect, and to update them on progress of the work.

b) Comprehension: the way in which information is conveyed is as important as the information itself.

- **Scalability.** The Our Future Health programme will need to provide information in a way that is scalable, i.e. leveraging online approaches rather than one-to-one in-person methods; however, the information must still be presented in a way that supports adequate comprehension and meets all the usual standards of informed consent.
- **Proportionality.** The amount and nature of information and support provided to potential participants should be proportionate to the scale and complexity of the Our Future Health programme. It will be important to strike a balance between providing adequate information while avoiding 'information overload'.
- **Adequate time.** Participants should not face the decision about participation in Our Future Health 'out of the blue', but should be given adequate time to think about their decision; this should include time to discuss participation with others who may be affected by their involvement (e.g. family members).
- **Multiple formats.** Information should be offered to potential participants in multiple formats (e.g. videos, animations, audio, interactive website) in order to make it as accessible as possible. The information provided must be consistent across formats.
- **Plain accessible language.** All information provided should be clear, concise and avoid jargon. Written information should be readable to people with a wide range of literacy levels,



consistent with HRA guidance[8] and the Plain English Campaign "Crystal Mark".[9] Information will need to be available in a range of languages to reach diverse groups.

- **Opportunity to ask questions.** Potential participants must have the opportunity to ask questions and have these answered both initially and over time by an appropriately trained individual; this does not need to be done in-person, but can be done via telephone, email, online etc.
- **Ascertaining comprehension.** Our Future Health should endeavour to assess whether participants have understood the information. We do not recommend the use of a quiz or test as a formal requirement during the consent process, because it is challenging to define quantitatively whether an individual has 'adequate' knowledge, and such tests may present unnecessary barriers to participation in the Our Future Health programme. However, it will be important to explore all available ways to ensure participants understand the information and innovative alternatives, such as the use of decision aids[10], should be explored instead.

c) Voluntariness: consent is valid only if voluntarily given.

- **Ensuring consent is valid.** Ensuring consent is valid involves making all reasonable efforts to assess whether appropriate information is given so that participants understand what they are signing up for, in addition to ensuring they are doing so free of coercion and undue influence. In the Our Future Health programme, ensuring valid consent will require a range of activities, including making sure that information resources are available in a range of accessible formats for different cultures (e.g. different languages, versions for visually impaired individuals).
- **Well-recorded documentation of consent.** It is vital that there is a well-documented electronic record of an individual's consent, including clarity about which secondary (phase 2) studies they have consented to and which they have refused, in order to ensure that subsequent users of data know that participants did give consent, and what constraints there are on the uses of data. Appropriate mechanisms will be needed to ensure that consent is given by the participant themselves when it is given via a digital platform (in line with the HRA guidance on e-consent).[11]
- **Values as well as comprehension.** Potential participants will want to be comfortable that they are taking part in something which accords with their values. The consent process should reflect that an informed decision is one that is not only informed by adequate knowledge but also an understanding of whether the programme is consistent with the individual's personal values. Some research studies have used web-based tools that include 'values clarification exercises' as part of helping individuals make decisions about participation.[12]

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[8] http://www.hra-decisiontools.org.uk/consent/style.html
[9] http://www.plainenglish.co.uk/
[10] Decision aids for people facing health treatment or screening decisions: Cochrane Review 2017. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD001431.pub5/abstract
[11] HRA statement on eConsent (2018) https://www.hra.nhs.uk/about-us/news-updates/hra-and-mhra-publish-joint-statement-seeking-and-documenting-consent-using-electronic-methods-econsent/
[12] https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-017-4889-0

Box 1: Information that should be provided as part of consent

The consent information should set expectations of what participation will involve and include the following details.

- **The purpose of the cohort** and why the research is taking place: this needs to be very clear about what type of research is acceptable and / or if anything is excluded.
- **What participation will involve**, including the initial collection of samples and long-term follow-up of participations throughout the lifetime of the cohort (see Section 3.2.3).
- **The use of data:** The information provided should set out what data about individuals will be collected or linked, and from what types of sources, who will have access to it and for what purposes, how decisions will be made, and how confidentiality and anonymity will be protected. This should include clear red lines, setting out what Our Future Health will never do with data (see Section 3.5).
- **Re-contact:** The initial consent process should set expectations for how participants might be re-contacted, including that some participants may be invited to take part in additional studies over the lifetime of the cohort, which would need further consent (see Section 3.3).
- **Feedback:** Potential participants must be informed about how communication of individual findings will be handled, both at initial examination and subsequently. This should explain the types of information that may be provided, the process and likely timeframe, and the choices that participants will have. It should also include explanation about the uncertainty around the interpretation of some information and how decisions about feedback will be made (see Section 3.4).
- **Withdrawal:** The approach that will be taken if participants choose to withdraw at any stage, should be set out in the initial consent (see Section 3.2.3).
- **The funding and governance of the project, including the role of commercial partners**, and the expectation that commercial companies will be able to access the data for research purposes, or apply to Our Future Health to invite participants to take part in phase 2 studies (see Section 4.3). This should also include clarification that participants will not receive financial gain from any commercial exploitation.
- **Implications for insurance:** HRA guidance states that potential participants should be told if participation might affect any insurance cover that they may have. Since Our Future Health is a research project, and much of the work done on the cohort will be governed by separate embedded research projects, those participating will not need to declare any findings to their insurers. However, this is less clear if Our Future Health provides individual findings (e.g. Polygenic Risk Scores for specific diseases) to participants, outside of any research protocol. This is discussed further in Box 5.
- The fact that **participation is voluntary**
- The **implications for a participant's individual care.**

3.2.2. Initial and supplementary consent

Our Future Health will have two elements: Phase 1 will involve the recruitment, enrolment and long-term follow-up of 5 million people, and then sub-sets of participants could be invited to take part in additional studies during Phase 2. **Our Future Health should use initial broad consent for Phase 1, with further detailed supplementary consent as required for additional studies in Phase 2.**

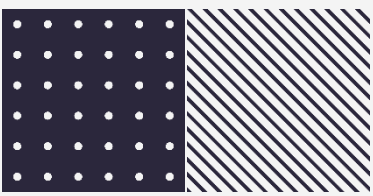
a) Initial (Phase 1) consent
This should allow:

1. Initial assessment at recruitment, including clinical examination, sample collection and survey completion;
2. Analyses including DNA studies, from collected samples;
3. Long-term follow-up, through ongoing access and linkage to health and care records (and other specified relevant datasets);
4. Long-term storage of samples and health-related data (in compliance with GDPR);
5. Use of stored samples and data for studies by external researchers, if approved through Our Future Health governance structures;
6. Re-contact by Our Future Health to ask for further information or samples, with no obligation to accept;
7. Re-contact by Our Future Health to invite participation in additional studies, which may be undertaken by external researchers or Our Future Health, with no obligation to accept (see Section 3.3);
8. Feedback of individual 'clinically significant findings', if participants have opted to receive feedback (as discussed further in Section 3.4).

This consent will need to be broad, define the types of research that might be facilitated, and how access will be governed. It should set expectations about what participation will involve, as set out in Box 1, and **about why, how and when participants could be invited to give consent for additional studies.**

b) Supplementary (Phase 2) consent
This will need to be sought for additional studies that require new sampling or clinical assessment, additional data linkage, enrolment in a trial or a new follow-up programme. Additional studies must be approved by Our Future Health and relevant research governance structures. **Initial recontact should always be by the Our Future Health team** (see Section 3.3). The additional consent will need to explain the new study, set out what is involved, and provide details about feedback where relevant. The process should be kept as efficient as possible, so as to minimise burden on participants while at the same time allowing them to understand the new study and make an informed decision about participation. Where further consent is for a clinical trial, the consent processes and information required are likely to be more detailed, following specific HRA guidance.

A key point is that **although initial consent will be broad and general, the decisions that participants may face later could be complex and have significant implications for their lives.**



The initial consent process, while high level, will therefore need to set expectations clearly while supplementary consent will be essential to ensure participants are appropriately informed to make more specific choices. Issues arising in these subsequent (Phase 2) studies might be sufficiently complex that more traditional face-to-face consenting is deemed necessary, but the numbers of people recruited to individual sub-studies is likely to be far smaller than the whole cohort.

Our Future Health should avoid having a menu of different options within the initial consent. In dealing with so many participants, many of whom will be recruited to a variety of separate specific sub-studies, it will be critically important that the Our Future Health consent records show clearly what each participant has agreed to.

3.2.3. Right to withdraw

Participants have a right to withdraw from the Our Future Health cohort at any time, without having to give a reason. This should be explained as part of the consent process. The approach that will be taken if participants choose to stop taking part should be clearly set out, with information about what will happen to their data and samples.

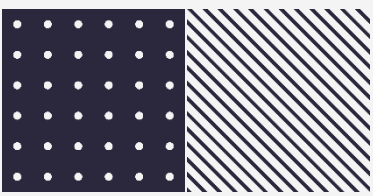
Three options for withdrawal should be offered[13]:

- **'No further contact':** Our Future Health would no longer contact the participant, but would have their permission to retain and use information and samples collected previously, and to continue to obtain and use further information from health records.
- **'No further access':** Our Future Health would no longer contact the participant or obtain further information from their health records, but would still have their permission to retain and use information and samples collected previously.
- **'No further use':** Our Future Health would no longer contact the participant or obtain further information, and any information and samples collected previously would no longer be available to researchers. Our Future Health would destroy samples (although it may not be possible to trace all distributed sample remnants) and would only hold information for archival audit purposes.

It should be made clear that, with any of these options, it would not be possible to remove data from research that had already taken place. Our Future Health may need to retain minimal personal data for archival audit purposes, and to assess any impact on research findings, but this administrative record should not be part of the main database that is available to researchers.

Some participants will die while still part of the cohort. In line with the Human Tissue Act 2004 (in England, Wales and Northern Ireland) and HTA Code of Practice on Consent (2017) the participant's consent to join Our Future Health would remain valid even after their death and data would continue to be retained. This provision maximises the potential for increased medical knowledge from information about the participant. Although the participant's consent extends

[13] These options are modelled on the approach taken by UK Biobank and Genomics England



beyond their death, the participant's relatives may sometimes have a different opinion after the participant has died. This view should be handled sensitively by the Our Future Health team, with relatives being encouraged to respect their deceased relative's wishes.

3.3. Re-contact

Ongoing communication with participants will be a key feature of Our Future Health. **The initial consent process at the time of recruitment should set expectations for why, how and when participants might be re-contacted over the lifetime of the cohort.** These include:

- To provide general updates about the cohort, recent news and developments, for example through newsletters and bulletins.
- To provide feedback of individual health-related findings to participants (see Section 3.4 below).
- To ask for additional samples or further information as part of the cohort follow-up, for example to complete a new survey or to collect data from a wearable.
- To invite participants to take part in further research, which may be conducted by third parties (although contact should initially come from Our Future Health); this may require the provision of feedback, for example of individual risk categorisation.

Participants should always be contacted first by the Our Future Health team; this is likely to be through the digital platform (except for those participants who do not use the digital platform). **Participants should be given the choice whether or not they are willing to provide additional samples or information, or whether they want to receive feedback.** Participants have a clear right to refuse. Detailed records of consent or refusal must be kept accessible to guide decisions on data usage.

Participation in Our Future Health is a long-term endeavour. It should be made clear to participants that, although they will be kept regularly updated about the cohort's progress, they should not necessarily expect to be re-contacted, either with information about individual findings or an invitation to an additional study, within the first few years. Such re-contact may not come until many years after the study began. Some sub-groups of participants found to have particular risk status may be more likely to be re-contacted sooner, but the information gathered about all participants as part of initial Phase 1 consent alone will be of considerable value to medical research.

Where re-contact is to invite participants to take part in a further study, the following guidance should apply:

- **Mechanism for assessing studies.** Our Future Health will need a formal mechanism to assess and approve additional studies, for example a dedicated committee (see Section 4.2.2). The decision process will need to consider the science and ethics, but also issues such as burden on participants, the costs and resource required, and the depletion of limited samples. The tolerance of many participants to frequent re-contact should not be taken for granted, particularly for groups with uncommon but "interesting risk profiles". This committee will need to establish criteria for selecting acceptable studies, and whether there should be a limit

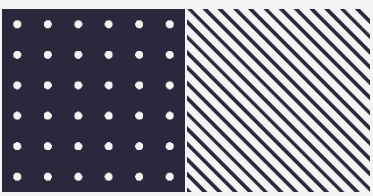
on the number of times a participant can be approached to take part in additional studies. The safety of the proposed research, and issues such as whether they will involve disclosure of personal predictive health information and how that will be managed, will be very important. Our Future Health is likely to be exploring new territory in this area. **Care will need to be taken to monitor and avoid recontact fatigue leading to cohort attrition.** Participants views will be important in helping to inform these decisions, particularly when assessing whether the level of burden on participants is appropriate.

- **Supplementary consent for additional (Phase 2) studies.** The participant will be re-contacted, and the nature of the new study and the implications of taking part will be explained. Participants must be given the choice whether to participate and have a clear right to refuse. This process should be kept as efficient and concise as possible, so as to minimize burden on participants while at the same time allowing them to fully understand the role they are being asked to play in the research programme. It should be made clear that, once participants agree to take part in a specific additional study, they may then be contacted directly by the study organisers.
- **Risk stratification.** If selected participants are invited to take part in additional studies on the basis of their risk of particular disorders, the basis of their selection will need to be explained to them and this will disclose information about their risk profile. The decision-making mechanism will therefore also need to take into account whether providing such information is appropriate (see Section 3.4 below), and how to manage the disclosure process. Participants must be given a choice as to whether they would like to learn this information. This leads to a dilemma: if only at-risk groups are approached, there is a risk that information would be divulged before consent is obtained. The mechanism for recontact will therefore need careful thought on a case-by-case basis. This is likely to be a particular issue when dealing with chronic conditions for which no validated clinical action is available. **Strategies which do not involve selection before consent should be developed wherever practicable.**

3.4. Provision of individual health-related information ("Feedback")

Providing **general feedback** on the progress of a project, including aggregate findings, to all participants is recognised as good practice. This should be given to all participants in lay language and accessible formats, for example through a regular newsletter. Our Future Health should explore ways to make the most of the digital platform to maintain engagement with participants, while not being overly intrusive.

There is significantly more debate about whether and how participants should be provided with individual health-related feedback. In theory, where findings relating to an individual participant are of known clinical validity and utility, it is possible to make the case that information should be given, because they might benefit from knowing the information clinically; and for reasons of reciprocity, respect and transparency. However, **providing access to complex information without appropriate support may be of limited benefit or even harmful**, e.g. if it results in unnecessary medical procedures or causes distress.



It will be crucial to understand more about what participants might want in the way of feedback, and particularly to explore the implications of feedback as a motivation for people to take part in Our Future Health. Initial small focus groups suggested that the promise of providing feedback may encourage some people to participate and foster long-term engagement with the cohort, but this needs more testing and evaluation in practice and at scale. Not everyone will be motivated by receiving individual feedback. Participants are being asked to be altruistic, and for some people being provided with thanks, encouragement and information about the progress of their collective endeavour will be enough. For others, the possibility of receiving feedback might even deter them from taking part. Our Future Health must actively engage with the public and participants to understand people's expectations about feedback, with a programme of deliberative work to develop the most appropriate approach. This will need to address views about providing feedback both during Phase 1 and as part of Phase 2 studies, and whether people might be interested in receiving comparative information about the cohort as a whole. **These discussions must be structured to enable participants to see and come to a judgement about both the benefits and the hazards as well of receiving individual information. Without appropriate understanding, feedback may simply be seen as a risk-free benefit.** The protocols will need to be carefully piloted and revisited and refined over the course of the cohort.

3.4.1. Principles for the provision of feedback

Deciding whether individual health-related information should be given to participants is a balance between its value and the undoubted potential for harm. The approach must be responsible and cautious. We set out some basic principles to help Our Future Health in guiding decisions about feedback of information of proven clinical significance.

- **Participants must have a choice:** Participants should be able to choose (both during the initial consent process, and for subsequent Phase 2 studies) whether or not to receive feedback about their individual findings.[14] We recognise that if participants do not want to receive feedback at any stage of the study, it may limit their ability to be invited to take part in Phase 2 studies, but we see choice as essential.[15] (see Section 3.4.3)
- **Assessment of benefits and harms:** Communication of clinically significant information to participants can be of benefit to them, if it is correct, robust and leads to better health management or leaves them better informed about their health. It can also be harmful, if it is confusing or misleading or leaves them with anxieties and concerns which are not properly managed. **An assessment of potential good versus harm must precede any attempt to provide such information to participants.** (see Section 3.4.4)
- **There must be an explicit purpose for providing feedback which can be clearly explained to participants:** There are different responsibilities depending on whether feedback is being provided to inform clinical care, or as part of research, including recruiting participants to an

[14] Knoppers et al (2013). The NASEM report also concluded that when individual research results are offered, participants have the right to decide whether to receive their results.
[15] We note that there may be legal implications if a participant chooses not to receive information about clinically relevant information that might need to be explored in more detail.

additional research study. **We recommend that an explicit decision is taken in each case, as to whether the feedback proposed is predominantly "clinical" or "research", as this will guide the way it is managed and the responsibilities which Our Future Health takes on itself in providing the information.**

- **Careful communication:** Findings must be communicated clearly, responsibly and with care, especially given the potential complexity of the information. (see Section 3.4.3)
- **There must be adequate long-term clinical support for those receiving individual feedback:** Our Future Health should not provide complex information to participants without ensuring ongoing support is available to help them manage and interpret that information. **We would caution strongly against providing a feedback programme, however well intended, without ensuring that a high-quality, tailored and long-term support system is in place.** It should not be assumed that the NHS will simply be able to provide this ongoing support without prior agreement. Failure to ensure specific and properly resourced support risks causing harm to some participants and bringing the entire programme into disrepute. The provision of proper support may have significant resource implications. (see Section 3.4.4)

3.4.2. Types of feedback

a) Providing feedback about clinically significant information

'Clinically significant' information is information that is already accepted and used in routine clinical practice to guide clinical management. Such a finding, whether physical, imaging or laboratory results (e.g. selected DNA mutations or biochemical abnormalities) would, if discovered during a normal clinical interaction, require discussion, further investigation or treatment. To be clinically significant, a finding must meet two criteria:

i) **Be clinically valid:** this refers to how well the variant being analysed is related to the presence, absence, or risk of a specific disease.[16] The findings must have been accepted as clinically valid on the basis of satisfactory evidence by relevant health authorities and health professionals.

ii) **Have clinical utility:** this refers to whether the finding can provide information about diagnosis, treatment, management or prevention of a disease that will be helpful to a participant.[17] The finding must be accepted by informed clinicians as being actionable or appropriate to guide clinical decision-making.

Where feedback is clinically significant, of both proven clinical validity and utility, it could be justifiable to provide the information to participants, provided all the principles described above (Section 3.4.1) are met. In particular, there must be careful assessment of the benefits and harms, consent must be given (see Section 3.4.3), and there must be a robust support system in place (see Section 3.4.4).

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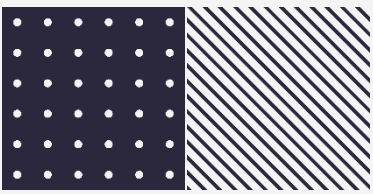
[16] A Thorogood (2019) Return of individual genomic research results: are laws and policies keeping step? European Journal of Human Genetics 27, 535–546 (2019)

[17] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4084965/



There are two different situations in which Our Future Health might consider providing such feedback:

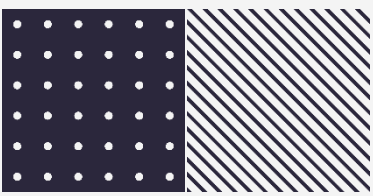
- **On initial examination when admitted to the study.** We consider it good practice that there should be immediate feedback of key results of measurements on recruitment, for example, BMI or blood pressure. Usually only abnormal measurements would be reported, but this may need to be reconsidered if some recruitment is via the NHS Health Check (or something similar), where the expectation is that all results will be provided.
- **On an ongoing basis during the course of the cohort.** The concept of providing clinically significant feedback on an ongoing basis to participants may initially be attractive, but the practicalities should not be underestimated. While in principle it might be possible to define a list of clinically significant findings that could be provided during the lifetime of the cohort, experience has shown that this is not easy in practice, particularly in rapidly evolving areas such as genetics/genomics.[18] Thought also needs to be given as to how often the list would be revised, and whether feedback for any one individual would be provided as a one-off activity or on an ongoing basis as new knowledge accrues. The criteria that should be taken into consideration are discussed further in Section 3.4.4 and Box 3. We believe such feedback could sometimes be justified but, because of the complexity of these issues, we do not at this stage recommend it without detailed further consideration.

b) Providing feedback about information of unproven clinical validity or utility

Information about an individual which may potentially be significant to the individual's health, but which has not been validated to the extent of being generally recognised or accepted for clinical use, must be treated with extreme caution. It would not usually be appropriate to give participants individual information of unproven clinical validity or utility, because the information may be misleading and could lead to unnecessary harm or distress. However, there are two reasons why Our Future Health may want to consider giving such feedback:

- **For the purposes of research:** Our Future Health could have the opportunity to assess the impact of providing feedback about risk information, to understand more about whether or how patients manage their risks, and to explore how to provide information about risk appropriately and sensitively.
- **For transparency:** If a sub-group is invited to an additional trial on the basis of risk categorisation (using a method that is not yet fully clinically validated), the researchers inviting participants to these studies will know they are considered to be at increased risk. In order to ensure the enrolment process for those studies is transparent, and consent is valid, individual participants will also need to know why they are considered eligible.

[18] it can be extremely difficult to clearly define what is clinically significant, particularly in rapidly evolving areas such as genetics/genomics, where it is difficult to prove both the clinical validity and utility on an individual basis. This difficulty may be exacerbated where the findings are detected as part of a population screen rather than through clinical presentation.



Our Future Health must exercise caution before providing such information. We recommend it should only be provided if participants give additional, specific consent as part of a separate research protocol. This separate consent (usually when sub-groups of participants are invited to join additional Phase 2 studies) should include more detailed information about the nature of the proposed study, the information which will be fed back and the uncertainties relating to it, and allow participants to decide specifically whether or not to receive the information. The principles set out above (Section 3.4.1) must also apply, including a thorough assessment of benefits and harms, and the provision of robust long-term support for participants (discussed further in Section 3.4.4 below).

Box 2: Why should Our Future Health not routinely provide all genomic information to participants?

It could be argued that people have an absolute right to their own personal information. It is possible for people to access direct-to-consumer genetic tests and receive information about their genome and possible disease susceptibilities from a number of commercial organisations, although these tests are not without problems. *

We do not recommend Our Future Health should take a similar approach, for a number of reasons. Participants are agreeing to take part in a research project, and being offered what could be perceived as diagnostic information risks confusing some people about the purpose of the cohort. The clinical validity and utility of much of the information from such tests is not yet fully established, and it risks undermining trust in Our Future Health if such information is given without due care and responsibility. This is particularly so since Our Future Health is a large national programme, with considerable support from public funds, and closely associated with the NHS which has a strong reputation for evidence-based health care. Although some people may be attracted by the idea of receiving such information and appreciate its limitations, others may become confused or anxious, may turn to their clinical carers for support, and a few such cases could lead to a damaging public impression of the Our Future Health programme.

There would be significant resource implications for the NHS, if 5 million participants visit their GPs to seek advice and help with interpretation of the information they have received. Healthcare professionals will be particularly cautious about participants receiving information where there is not sufficient evidence for implementation in clinical practice, or clear, agreed clinical management guidelines. Many of them may feel unable to give proper advice.

We are extremely cautious about whether it would be appropriate to provide participants with access to all raw data about themselves (either on request, or routinely). Providing access to vast amounts of uninterpreted information creates a risk that erroneous medical implications will be deduced, and leave participants overwhelmed and vulnerable. Such information should only be safely divulged if there are adequate support facilities to help interpret and utilise the information appropriately.

In either case, this should only be considered if Our Future Health provided the resource for a long term robust clinical genetic support for participants.

*See for example the position statement on Direct-to-Consumer genetic testing by the Royal College of GPs and the British Society for Genetic medicine

3.4.3. Setting and managing expectations about feedback

Information during initial consent: The approach to providing feedback must be explained during the consent process.[19] This should include information about the types of feedback that might be provided, the process, a realistic timeframe, and the choices that participants will be given. Care must be taken to ensure the study is not viewed as a likely source of diagnostic information for individual participants, to explain the potential uncertainties and to set expectations appropriately. It should be made very clear what types of information will be provided initially. For example, if participants are invited to undertake a memory test as part of recruitment, should they expect to be given the results?

Recognising uncertainties: The nature of the science conducted with the Our Future Health cohort will evolve, and findings that are not initially of proven validity or utility might be viewed differently as evidence accumulates. Our Future Health should recognise that feedback policies may well need to be updated and decisions may change over time. This approach should be communicated to participants during initial consent.

3.4.4. Delivering feedback

Addressing the practical implications of providing feedback is an essential part of ensuring any feedback is responsible. Our Future Health's approach to providing feedback must take into account the following points:

- **Making decisions about the provision of feedback:** There will need to be a formal, transparent and accountable mechanism to provide ongoing advice to the Board on different feedback situations. One option would be a standing expert advisory committee. This group would need to agree overarching policies, keep them under review as evidence evolves, and make decisions about specific instances of feedback and recontact. An indicative list of questions that the committee would need to consider in each case is set out in Box 3. This includes assessment of the utility and validity of the information being provided, the implications for individuals and the practicalities of providing the information. The committee should be appropriately constituted with expertise to consider the scientific and clinical evidence, ethical issues, the resource implications, participant views and communication strategies. The decisions of this committee, and the reasonings, should be publicly accessible.
- **Providing support and advice:** When people receive results from direct-to-consumer testing, they frequently turn to their GP for advice and support in interpreting this information. The same is likely to apply for Our Future Health participants given information about their health, and care must be taken not to become a burden on the NHS. Participants will need expert advice about what to do with health information they receive. Our Future Health will need to consider how to ensure appropriate support is available, and the role of the GP. Feedback should only proceed if long-term arrangements are in place to manage any issues which may

[19] Knoppers BM, Deschênes M, Zawati MH, *et al.* Population studies: return of research results and incidental findings Policy Statement. *Eur J Hum Genet* 2013;**21**:245–7. doi:10.1038/ejhg.2012.152)

arise for the participants who receive such information, whether they relate to accessing further medical care and treatment or to the resolution of uncertainties and anxieties.

- **Ensuring appropriate resource:** Providing adequately supported feedback could have considerable resource implications, both for Our Future Health and for the health service, which must be appropriately addressed from the outset. There are likely to be significant implications for healthcare professionals, including the need for training and support, and this must be taken into account as part of the decision-making process about the provision of feedback. The impact on the UK health system of large numbers of participants taking risk information back to their GP is not trivial. If these issues are not properly dealt with in advance, they risk damaging the reputation of the study and derailing its capacity to function effectively.
- **Analytical quality:** Any feedback provided should meet the technical quality and other criteria applicable to clinical results, which often differ from the standards applied to research data. Laboratory results must be performed to clinical standards, or confirmed in a clinically accredited laboratory.
- **Improving the evidence base:** There has been very little research to explore the implications of receiving such research findings, the value of receiving such information, and the most appropriate ways to provide information about risk status as part of research. There is significant potential to conduct research using the Our Future Health cohort to provide an evidence base about good feedback models, with an opportunity to set best practice. Such research should be carefully scrutinised as part of the access process to ensure it is of high quality, and participants should be asked to consent, as part of a Phase 2 study.

Box 3: Questions to consider when assessing the provision of feedback

What is the nature of the information being provided?

- What is the evidence for the finding? Is the clinical validity known, or is the information still unproven or at research stage? Is this a 'clinical' or a 'research' finding?
- What is the potential severity of the condition? What impact does it have on quality of life?
- What is the utility of the information? What interventions are available? Can the condition, or the risk of developing a condition, be prevented, reduced or managed through an available intervention? Is the intervention a treatment, screening or lifestyle change?
- With information about risk categorisation, what are the certainty bounds of the estimate? Do other known factors influence whether or not the risk manifests?
- Is the effect the same for different populations? For example, polygenic risk scores have so far been developed on the basis of predominantly European white ancestry samples, which means that feedback could be much less accurate for participants from ethnic minorities. Are the results still useful across populations?

What are the implications for individuals?

- What are the potential benefits or harms to individual participants, or particular populations, of knowing, or not knowing, the information? Are there specific psychological, social or behavioural benefits or harms?
- Are there implications for insurance (see Box 5)
- Is there a potential for stigmatisation as a result of the return of this information?
- Are there implications for family members? Are there implications for those of child-bearing age?
- What is the motivation for feedback? Is feedback primarily being given for clinical benefit, or as part of research purposes? Is this clear to the recipient?
- Is feedback being given as part of recruitment to a further research study? If so, is it to trial an intervention? Is a control group being approached as well as those in a high-risk group, to facilitate learning from the intervention?

What are the practicalities of providing the information?

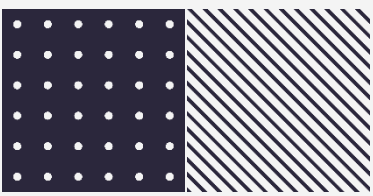
- Is there valid consent? Is the feedback proposed within the boundaries of the expectations for feedback set during the initial (or most recent) consent process?
- What support or interpretation will be needed?
- Who will provide feedback, and how will it be given?
- Will a GP or other healthcare provider be involved and, if so, have they agreed to be involved and what are the implications?
- What are the resource implications for the cohort and for the NHS? Where relevant, what would be the implications of providing the feedback at scale? What is the chance of false positives, and are there any implications that need to be considered?
- What is the timeframe? How long after initial (or most recent relevant) contact will the feedback be given?

3.4.5. Other issues to consider

Providing feedback as part of recruitment to an additional study. Where the purpose is for recruitment to an additional study, there will need to be a mechanism to decide whether a proposed trial and associated disclosure of information is appropriate. Researchers will have to provide specific reasons to justify any feedback. The mechanism for recontact will need careful thought, recognising that if only at-risk groups are approached, information would be implicitly divulged before consent is obtained. As with any feedback, findings must be communicated clearly and responsibly, and appropriate support must be provided to help participants interpret the information. For Phase 2 studies, Our Future Health's responsibility will be to ensure that proper care is in place, but it may be the responsibility of the researchers or their sponsors to actually provide it.

Providing information about risk profiles. Our Future Health may consider offering participants information about their risk status for certain diseases. It is important to recognise that methods of risk stratification could fall into two different categories: some will be clinically validated (for example a QRisk score for cardiovascular risk, or a high cholesterol level) but some will be of unproven clinical validity or utility. Polygenic risk scores (PRS), for example, have not yet been widely used in clinical care. As discussed above (Section 3.4.2), information that is not of proven clinical utility or validity (including, currently, most PRS) should only be provided with separate, specific consent which carefully explains the uncertainties. It is probable than an increasing number of PRS will become adopted into clinical care during the lifetime of the cohort, as validating studies are completed, and so this will need to be kept under review. When providing any information about risk profiling, it is crucial that the inherent complexities and uncertainties are carefully managed and communicated responsibly.[20] Providing this, whether or not through the NHS, would require careful planning and adequate ongoing resource and could be very challenging.

[20] Uncertainties about many types of clinically used risk scores include: questions about the confidence intervals around risk estimates; the validity of the findings for different population groups; varying perceptions about the clinical utility of the information; the role of other unknown factors, including environment, generational effects or other genetic factors; public perceptions of genetic information (for example that it might be viewed as more 'deterministic' than other risk factors); and public understanding of risk.



Box 4: Ongoing support for participants

At various stages such as initial recruitment, when results are returned for whatever reason, and at recruitment to sub-studies, individuals may experience issues which are difficult for them and which may cause them confusion, anxiety or stress. A programme of this size must predominantly depend on electronic means of communication, but in our view **it will be essential to also provide a level of personal support for those who need it, whether by telephone, online or face-to-face.** This could be provided by dedicated programme staff, by some part of the NHS or in other ways, but those providing the support will need to be properly equipped and trained for the task and resourced accordingly.

Box 5: Implications of the provision of feedback for insurance

Life and health insurers have an obvious interest in methods of early detection of disease. Improving the overall health of the population is to their and societies' advantage; but they are concerned that people who learn of a disease propensity and do not disclose that to their insurers may take out more insurance than they would have done, at rates which do not reflect the extra risk that they incur. A default assumption of most insurance is that the client is obliged to disclose all relevant known facts to the insurer at the time of taking out or renewing the insurance, and failure to do so may invalidate the policy. Some decades ago the UK Government came to agreement with the Association of British Insurers (ABI) (who represent many but not all UK insurance companies) as to how to fairly manage this potential conflict between the commercial interests of the companies and the interest of the Public health.

This is now regulated by a Code on Genetic Testing and Insurance.*

> *"The Code is a voluntary agreement between Government and the Association of British Insurers, whereby insurers signed up to the Code will never require or pressure any applicant to undertake a predictive or diagnostic genetic test, and only consider the result of a predictive genetic test for a very small minority of cases."*

For the purposes of Our Future Health, this clause is important:

> *"Any predictive genetic test result obtained exclusively in the context of scientific research does not need to be disclosed to an insurer, regardless of the test or the level of cover."*

Since Our Future Health is a research project, and much of the work done on the cohort will be governed by separate embedded research projects, those participating will not need to declare any findings to their insurers.

If Our Future Health proceeds to release individual test results (e.g. Polygenic Risk Scores for specific diseases) to participants, outside of any research protocol, the situation becomes more ambiguous, in that the participants will have been recruited to the project under a general research consent but the results returned would not have any specific research goal associated with them.

We recommend that the Our Future Health executive should, if need be, contact the ABI to seek clarification of how they would treat Our Future Health participants. If there is any question of participants incurring extra scrutiny in the insurance market, this will need to be clearly indicated in the consent and information documents.

3.5. Stewardship of data and samples

Our Future Health will collect a vast amount of data over the lifetime of the cohort. In order to build and retain participants' trust, Our Future Health must demonstrate a robust approach to data security, and must have rigorous and transparent governance processes to control access and use. These should be set out clearly in a detailed data management policy, which should address three aspects:

- protecting confidentiality and keeping data safe (see Section 3.5.1);
- how data will be added to the resource (see Section 3.5.2); and
- how data will be accessed and used (see Section 3.5.3).

The **importance of transparency cannot be overstated.** Our Future Health should explain clearly to participants how data will be used and for what purposes, who will have access, what protections will be in place, and the accountability mechanisms. **This should be grounded in the National Data Guardian (NDG)'s advice that there should be 'no surprises'.** This is particularly important given the involvement of industry partners and researchers. As discussed in Section 4.3.3, evidence suggests the public are often particularly concerned about commercial access to health data, and Our Future Health should address these concerns openly and proactively.

The initial consent process should set out information about what data is collected, how data will be kept safe, and how data access will be managed. In addition to explaining how data might be used, the consent information should also set out "red lines", providing clear information about uses of data that will never be allowed, for example participant's data will never be passed to third parties for marketing purposes without consent.

Information provided during the consent process should be kept broad and high-level, to enable people to understand properly what they are consenting to. This should then be followed by the provision of further detail about data access as part of an ongoing conversation with participants. Given changing attitudes to uses of data across society, it will be particularly important to regularly engage with participants over the lifetime of the cohort to ensure the approach to data use is trustworthy.

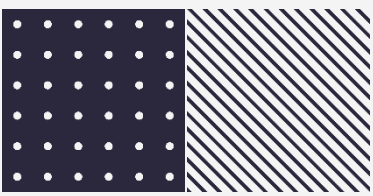
3.5.1. Confidentiality

Protecting patient privacy and confidentiality, and ensuring robust security safeguards is fundamental.

a) Data security

Our Future Health must have robust IT systems and appropriate security measures in place to protect data and reduce the risk of cyber threats. These should meet both the National Data Guardian's data security standards and the Department of Health and Social Care's Information Governance requirements.[21] Our Future Health should make use of industry-standard technical

[21] See, for example, the NHS Data Security and Protection Toolkit: https://www.dsptoolkit.nhs.uk/



controls to prevent unauthorised use of data, including a programme of risk assessment and regular testing and review. There should be verifiable audit trails, and a transparent process in place in the event of any data breach. Our Future Health should publish information about how data will be stored and de-identified.

Given the need to build confidence in data security, Our Future Health should undertake work to explore the most appropriate approach to allow access and analysis of data. For example, the model of a Trusted Research Environment could be used to ensure that data can only be used within a 'safe setting', with remote access strictly controlled and monitored, rather than allowing researchers to download data. [22] Once approved, researchers should only be given access to the specific information they need for their study.

b) Meeting data protection requirements

Our Future Health must be fully compliant with the latest data protection legislation, including the Data Protection Act 2018. In line with the GDPR requirement for transparency, Our Future Health should have an easily accessible privacy policy, which meets best practice standards for accessibility and plain language.[23] This should set out:

- The purpose and legal basis on which Our Future Health will process both personal data, and 'special category data' (including ethnic origin and genetic data). [24]
- How the data minimisation principles will be met, including information about how data will be cleaned and de-identified.
- Information about data retention. Because Our Future Health is a long-term resource, data will need to be kept for a significant time period but it will still be important to have a clear retention schedule.
- The rights that are, and are not, available to participants in respect to Our Future Health's use of data. Where rights do not apply, Our Future Health must be clear about the reasons for any exemptions.[25]
- The approach that will be taken to Subject Access Requests.
- The sanctions that will apply for any organisation or individual who attempts to breach a participant's confidentiality or for any misuse of data.
- The approach that will be taken if police or other law enforcement agencies request access to the data.

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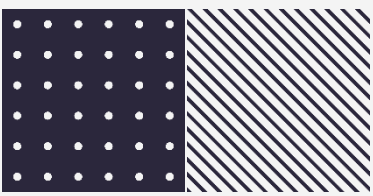
[22] See work by Health Data Research UK: https://ukhealthdata.org/projects/aligning-approach-to-trusted-research-environments/

[23] See for example the Genomics England Privacy Policy: https://www.genomicsengland.co.uk/privacy-policy/

[24] It is likely that Our Future Health will process personal data using Article 6(1)(f) - legitimate interests as the lawful basis, rather than consent, but this must be clearly explained to participants.

[25] Genomics England's privacy policy, for example, explains that the right to portability does not apply because Genomics England relies on a lawful basis of legitimate interests. The right to erasure does not apply because Genomics England relies on the exception in GDPR Article 17(3)(d) to allow them to keep data to inform a research programme.



Our Future Health should also undertake a Data Protection Impact Assessment (DPIA), to help identify the potential impact on individuals and minimise the data protection risks. There must be a named Data Protection Officer and Our Future Health might also consider identifying a Caldicott Guardian. Given the sensitive nature of the data that will be collected and stored, Our Future Health should discuss the proposals from an early stage with the Information Commissioner's Office to ensure appropriate measures are being implemented. Our Future Health will also need to comply with the common law duty of confidentiality, and it will therefore also be important to engage the NDG.

3.5.2. Adding new data into the resource

Our Future Health will initially collect information from NHS records and other health and social care datasets, and this must be clearly set out in the Phase 1 consent process. Particular thought should be given to the types of social care data that might be collected, recognising that this may be a cause of concern to some participants. Any linkage will need to have the necessary approvals in place (for example from the HRA Confidentiality Advisory Group, or from NHS Digital's IGARD[26]), and must be clearly explained to participants.

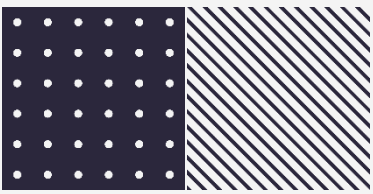
Over the course of the lifetime of the cohort, there is also the potential that the Our Future Health programme might want to link other types of data, for example to add social and lifestyle information that could help build a more comprehensive picture of health or risk of disease. Types of data that Our Future Health might consider linking include:

- administrative data, for example information about education, household, income and employment;
- social media data; and
- information collected from wearables or self-generated data.

Careful thought must be given as to how any additional datasets might be added to the resource. **There must be a clear mechanism for making decisions about additional data linkage.** This should be responsible, open and transparent, with criteria set out in advance. Each additional linkage must be justified, with an explicit reason and scientific rationale for extending data collection beyond conventional health data, which can be clearly explained to participants. The process should also consider issues of representation and potential bias in datasets. Different groups may be over or under-represented in different datasets, and it will be important to proactively consider this for each dataset, and consider ways to mitigate any bias in advance.

We recommend that additional data linkage beyond health and care datasets will need additional consent. This is important to ensure that participants have a choice about the addition of further information that goes beyond health and care data. It may also be necessary when third party data providers are involved, which may have restrictions on what data can be released. One possibility might be to consider having an opt-out approach to allow linkage of a few specific

[26] https://digital.nhs.uk/about-nhs-digital/corporate-information-and-documents/independent-group-advising-on-the-release-of-data



additional data sets but this principle would need significant further discussion by EFAG and consultation with participants.

3.5.3. Access to data and samples

Our Future Health must develop a robust and transparent policy that sets out detailed information about how data and samples may be accessed and used. **There must be an explicit mechanism to ensure access to any data generated in or utilising the resource is responsible and in the public interest.** Decisions should be subject to careful scrutiny by an appropriately constituted and accountable governance process such as a Data Access Committee. Given the nature of access requests is expected to evolve over time, the criteria used will need to be flexible enough to be futureproof, while giving participants confidence in the process by which access decisions will be taken.

Building on existing principles of best practice for access to the data and samples, Our Future Health should adopt the following approach:

- The resource should be available to all bona fide researchers for all types of health-related research that is in the public interest, in accordance with the participants' consent.
- All researchers, whether in universities, charities, government agencies or commercial companies, and whether based in the UK or abroad, should be subject to the same application process and approval criteria.
- An appropriately constituted access committee, reporting to the Our Future Health Board, should be responsible for the access policy and for overseeing individual decisions about applications to access data and samples, following a transparent process. Application summaries and decisions should be made public. The mechanics of the access procedures should be as simple as possible, and the decisions should emerge in a timely fashion and at reasonable cost. **The objective is to maximise responsible use of the dataset, not to unduly guard it for the benefit of a restricted user group.** The role of the Access Committee is discussed further in Section 4.2.2.
- For data use only, the assessment should take into account the following questions:
    - Is this appropriate research within the context of the participant consent?
    - Is the research feasible and sensible? There is no intention of setting a high scientific quality bar, but approving work which, for example, cannot be carried out on this dataset is wasting time for both Our Future Health and the researcher
    - Is the research likely to be very controversial (to society, rather than scientifically)? This is not necessarily a bar, but the Access Committee must guard against bringing the Charity into disrepute.
- Because data are not depletable, it is appropriate to approach data-only applications with the intention of approving them unless there is a reason not to.

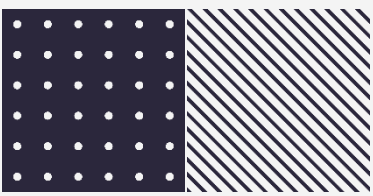
- Where access to data is approved, data must be de-identified and only the minimum amount of data required for the successful completion of the relevant research should be made available.
- Access to biological samples that are limited and depletable should be carefully controlled and coordinated, according to a transparent policy. The focus must be much more competitive – only a limited number of uses are available over the lifetime of the resource, and only the highest quality applications should be supported. Judging both the quality of the science, and the importance of the issue being addressed, should be the responsibility of the Access Committee.
- Requests for subject re-contact need detailed scrutiny, as discussed in Section 3.4. This work should be probably undertaken by a special Feedback advisory committee (see Section 4.4.5) working closely with the Access Committee.
- Any researcher accessing data or samples will be required to sign a binding data access agreement, which includes a clause prohibiting the unauthorised re-identification of participants and setting out sanctions that will apply for any attempt to breach a participant's privacy.
- Researchers will be required to publish their findings and deposit their results within the Our Future Health resource so that the knowledge gained can be widely disseminated.

3.5.4. Exclusive access

The interests of participants are served by making the resource as accessible as possible to as many high-quality researchers as possible. **No party should be given exclusive access to the whole resource.** However, there may need to be some arrangements for limited elements of exclusivity where a user has generated new data using the cohort. For example, where a company (or any other researchers) provide intellectual effort or funding to develop new data for the resource, they may be allowed exclusive access to that newly developed data for a time-limited period (the exclusivity period) to enable them to capitalize on their contribution and discoveries. After the exclusivity period is complete, the data must then be made available for other researchers to use. This is the approach that other research programmes have taken to partnerships for major additions to the dataset.

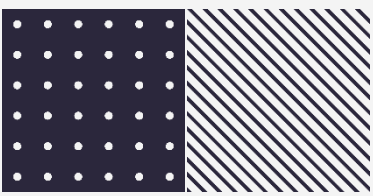
Decisions about limited elements of exclusivity are complex and need careful thought. The public have shown that they understand the need to reward effort but are suspicious of health data being unduly locked away from general research use, particularly by commercial entities. **We recommend that Our Future Health should not accept limited exclusivity as an automatic right. Its existence and duration must be justified on a case-by-case basis.**

The Data Access Committee should help to develop a process to guide future discussions, and agree who will be involved in decisions. It will be important to include the Participants Advisory Panel in discussions. The process should take into account the following aspects:



- Arrangements for limited elements of exclusivity should apply equally to academic, charity-funded and industry researchers. Academics will want to publish and stake priority, industry researchers will want to get IP protection. They all make important contributions and may deserve time to capitalise on their discoveries.
- The nature of the research and the need for a period of exclusivity
- How to define the exclusivity period, including the start and end points, which may also depend on the type of research.
- What the time period should be. There may be some push towards setting a standard time period for exclusivity, for example current practice is for about a year. However, despite its simplicity, we would urge caution because of the complexities of the issues involved and the variation in types of application that will be received.
- There must be a clear justification for any exclusivity period, which should be openly explained and published.

The implications of preferential terms of access for industry partners are considered further in the discussion about commercial partnerships below (see Section 4.3.3).



4. STRUCTURAL AND GOVERNANCE ISSUES

4.1. Public and participant involvement, engagement and communications

With 5 million adult recruits, Our Future Health will be interacting with more than 10 per cent of the adult population of the country. Keeping these people engaged and enthusiastic will require a dedication to regular, careful communication of the highest and most active standard, above anything that most scientific projects have attempted. **The success of the Our Future Health cohort depends on building and maintaining public trust and confidence.**

Participants and the public must be actively engaged from the beginning, and public involvement should be woven in at all levels of the cohort, rather than being siloed or seen as an 'add-on'. This has a number of functions: first, to inform the development and design of the cohort to ensure the approach is acceptable to participants; secondly, to improve the quality and accessibility of specific material and information provided; and, thirdly, to continue to motivate participants to stay engaged. It is also an important way of demonstrating that the contribution participants make is recognised and reciprocated.

A public and participant involvement strategy must therefore be developed as an early priority. This is likely to include a number of elements:

- Establishing a public (and subsequently, participant) advisory panel to provide ongoing input into the design and development of Our Future Health.
- Creating a much larger 'user testing group' (or groups) to trial consent materials and the digital platform to ensure they are fit-for-purpose.[27]
- Public dialogue activities to explore specific issues in more detail, for example expectations relating to feedback or access to data.
- Tailored engagement with 'seldom-heard' and 'harder to reach' groups to ensure Our Future Health is able to reach diverse communities in culturally appropriate ways.
- In discussion with participants, thought should also be given as to how best to represent participants' views on advisory groups, from Board-level down, to provide input into ongoing decision-making. Establishing a panel of members of the public initially, and participants subsequently, will be valuable to provide advice for the cohort long-term but, on its own, is not enough.
- The digital platform is also likely to provide a route to consult participants quickly, efficiently and in new ways about proposed developments to the cohort.

Public engagement and involvement activities must be adequately resourced. Our Future Health should become an exemplar of best practice, making use of Our Future Health's digital platform and trialling innovative approaches for engagement. A one-size-fits-all approach will not be suitable, because engagement and involvement activities and information will need to be tailored and appropriate for diverse populations.

[27] The HRA states the following: "the best way to make sure your consent documentation is fit for purpose is to test it with patient groups or other members of the public."

Involvement and engagement activities should be monitored and evaluated during the life of the cohort, to examine their impact on decision-making and the development of Our Future Health, and to refine the Our Future Health approach. In addition, given that Our Future Health is intended to be a population health resource, there should also be a mechanism to ensure that discussions reflect the wider public interest.

4.2. Oversight and governance

4.2.1. Regulation and approval

The final Our Future Health protocol will need to be approved by the Health Research Authority (HRA). Its review will include the core scientific proposals, the operational procedures, detail of recruitment invitations, participant information and consent materials. The approval will cover consent for Phase 1, as set out in Section 3.2.2. If Our Future Health has Research Tissue Bank status[28], projects using data or samples acquired and linked as part of Phase 1 would not need further Research Ethics Committee (REC) approval, provided they have gone through Our Future Health's internal approval mechanism. Phase 1 consent will also include agreeing to receive invitations to join Phase 2 projects, but separate REC approval is likely to be needed for at least some of these new projects, which will have separate protocols, information and consent forms.

The cohort will also need to meet the requirements of the GDPR, the Human Tissue Act and other relevant research governance frameworks.

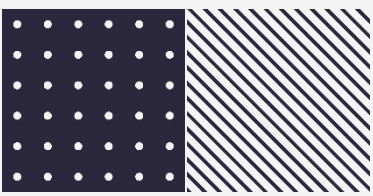
4.2.2. Governance, advisory and control structure

Ensuring the right mechanisms for oversight and governance will be essential to ensure appropriate accountability for the programme, and to help build public trust and confidence. The governance mechanisms should be appropriately constituted, accountable, and open to scrutiny.

Our recommendations for the structure of Our Future Health are as follows:

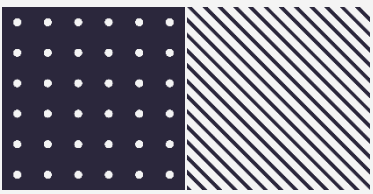
- **Main Board:** Our Future Health is a Charity, established as a company limited by guarantee. The Board establishes the ethos and broad operating principles of the Charity, which is perceived as a public-private partnership providing a resource for researchers to improve health, particularly by developing better early diagnostics and preventative interventions. This explicitly involves industrial partners. We believe this is the basis on which consent is being sought from the public. If this were to change, for example if it evolved over time to an industry-dominated programme with much more prominent commercial motives, **we think it may jeopardise the consent which has been obtained.** We do not anticipate this as a likely eventuality, but would urge that legal advice is sought on how the future status of the project can be protected from such a change.

[28] https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/research-tissue-banks-and-research-databases/



- **Scientific Advisory Board/s:** Our Future Health is a very large, ambitious and state-of-the-art concept. As a research platform, it has to collect and curate massive amounts of data in a way which will enable unpredictable numbers and types of future research projects. The design of protocols and of further research projects will require extensive scientific knowledge in many different fields. It would be expected that the CEO and Board of such an extensive programme would be supported by a very high-quality SAB. Disciplines which may be required include epidemiology, genetics and genomics, biostatistics, behavioural and other social sciences, public health, medicine, data management and handling. It may be necessary to divide the workload between more than one SAB. A separate International SAB is also recommended to ensure Our Future Health maintains work to the highest international standards. SABs usually are organised by, and report to, the CEO with provision for the Chair of the SAB to report directly to the Board as required.
- **Ethics Advisory Committee:** EFAG is already well established. It has drawn up an ethical and governance framework for the project, with specific concentration on the issues arising from return of clinically relevant results to participants. An Ethics Advisory Committee (EAC) will be needed to monitor the development of the Our Future Health project, to react to new issues arising and to advise the CEO and the Board as the project progresses. EAC should be an advisory committee to the Executive and the Board. It sets its own agenda in consultation with the Board and the Executive. To ensure it can act as an independent voice, particularly in representing participants' views, it must have the right to publish its recommendations and to speak publicly about its findings, although it would not expect to do this without prior notification to the Our Future Health Board. The Chair should have a place at a high level of the Project management structure, preferably on the project Board.
- **A participant advisory panel:** As discussed in Section 4.1, there must be a mechanism for participants to provide ongoing input into the design and development of Our Future Health with a dedicated participant panel as part of the advisory structures of Our Future Health.
- **Access committee(s):** As Our Future Health reaches maturity, it is hoped that it will facilitate research by many researchers from diverse backgrounds. The Access Committee must ensure that each researcher, and each project, is properly assessed before approval to access the resource. The mechanics of releasing appropriate data in a controlled fashion for approved projects is the responsibility of the Executive – the Access Committee sets policy, and then inspects and approves each application for use (although much of this can be delegated once a system is in place and running). It works closely with the Executive, and reports to the Board.

  The Access committee should develop clear policies on which to base its decisions, which should be as explicit as possible and should be publicly available e.g. on the Our Future Health website. It will monitor each application in order to ensure that both the applicant, and the proposed research, fit the access policies. The questions to be considered are discussed above in Section 3.5.1.



The Access Committee/s will inform Our Future Health's decision-making on the following issues:

- requests for access to data and samples
- requests to re-contact sub-groups of the cohort to take part in Phase 2 studies
- decisions about the provision of feedback
- collection of data from new sources, such as wearables or social media.

Although they raise some specific issues, these are all adjudicated by the access committee. In the case of Our Future Health, it may well be that the number of re-contact applications, and their potential complexity, will eventually necessitate more than one access committee.

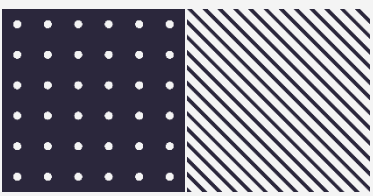
The Access Committee works in the best interests of the participants, and the charity. The skills needed on the committee are determined by the nature of its work. It must make assessments of science quality, probable health impact, and of likely participant views. People with broad experience across different fields will be particularly valuable as members.

- **Feedback Advisory Committee:** The nature of Our Future Health makes issues relating to the provision of health-related information to participants a central issue, and one which has not previously been as intensively explored. As discussed in Section 3.4, it may be necessary to have a dedicated committee to provide advice on the detailed policy. There will also be an ongoing need to consider and monitor individual research programmes which may wish to return information to participants, either because it is part of the research design or because the selection of participants on basis of risk makes it likely that they will be made aware of their risk status. Exactly how work should be divided between Access and Feedback committees will have to be worked through once the groups are established, and kept under review as the project develops.
- **Special Advisory Committees:** Our Future Health has established Advisory committees in relation to Industrial partners, and to the NHS. These are both critical areas of Our Future Health engagement, and this enables close contact with them.

The membership, responsibilities, operating principles, and records of decisions for all of these groups should be publicly available, for example through the project website. It will be important to have clear Terms of Reference for each group to ensure there are no gaps or unnecessary duplication. Some mechanism will also be needed to ensure that these various groups are kept informed about each other's activities. This will make the whole process more efficient, and will create a better sense of a corporate enterprise. We assume there will also need to be special sub-committees relating to audit, remuneration, nominations and appointments etc, which should be set up to meet best practice requirements.

4.2.3. Intellectual property, income generation and royalties

Our Future Health will need a clear statement to explain its approach to Intellectual Property, income generation and royalties. This should make clear who owns the data, and the approach that will be taken to any intellectual property generated from the data. The initial consent



information should make clear that participants will not receive any financial gain from commercial exploitation. EFAG has not yet discussed these issues and should consider general principles and advice to Our Future Health in the near future.

4.3. External partnerships

The Our Future Health cohort will interact closely with a number of important external sectors: UK society (see Section 4.1), healthcare professionals and the NHS (see Section 4.4), government agencies, industry, and charities. Funding is expected to come from a consortium including government, charities and industry. It will be important to build close partnerships and to be transparent and open about these relationships.

4.3.1. Government agencies

The Government has provided start-up funding for the project, through UK Research and Innovation (UKRI), and will provide continuing central support. UKRI may also fund independent researchers to use the resource, thus helping it to realise its full potential as a source of beneficial new information for society at large.

4.3.2. Charities

UK biomedical research charities will be approached to become founding partners of Our Future Health. Charities are likely to have a number of different roles, for example: provision of funding, identifying research priorities, supporting researchers seeking access to data for research studies, or funding research using sub-groups of the cohort in additional studies.

UK charities have excellent links to patient groups, strong brand recognition and are generally regarded as trustworthy by members of the public. Being associated with charities is therefore likely to enhance the standing and acceptability of the project and could help with recruitment. It will be crucial for Our Future Health to work to maintain this trust.

4.3.3. Commercial partnerships

A range of commercial companies, including pharmaceutical, biotechnology, diagnostics and technology companies, are likely to be involved in the Our Future Health cohort. Commercial companies have expertise in discovering, developing and producing new diagnostics and methods for improving the early detection and treatment of chronic disease. Industry involvement is therefore essential if Our Future Health is to achieve its aims.

We know that the public are sometimes uncomfortable about commercial involvement in health data projects and, in a number of surveys, people have expressed concerns about companies using

patient data.[29] It is important to address these concerns openly and proactively. Evidence suggests that there are two main causes. First, people worry about the risk to the individual or their family, with particular concern about data being used for marketing purposes. And secondly, there is unease about the impact for society, with concern that profit motives will override public benefits. There is particular resistance to the use of patient data by the insurance industry, for example. Evidence suggests that people are much more likely to accept commercial involvement if there is an explicit purpose and public benefit.

It will therefore be particularly important to set out fully the nature of any commercial participation in Our Future Health. Like the charitable and government sectors, it is anticipated that companies will have several different roles, including as:

- Founding investors
- Researchers, accessing cohort data to answer research questions
- Funders of Phase 2 studies, inviting sub-groups of the cohort to take part in additional studies
- Suppliers, including developing and maintaining the digital platform for the cohort.

These are different types of involvement which raise different issues and should be treated in distinct ways. **A policy on commercial partnerships, including details about oversight and scrutiny, should be developed as a priority.** This policy should explicitly include the set of ethical principles listed below. Given the importance of maintaining participant confidence, we recommend that it should be discussed with the Participant Advisory Panel as early as possible.

There are inevitable stresses between the public good benefits that will motivate most Our Future Health participants, and the needs of industry; but there are also many points on which these groups have common interests and goals. Project success requires that any significant conflicts of interest are openly acknowledged and appropriately managed. We set out some basic principles to help Our Future Health in guiding decisions about commercial partnerships.

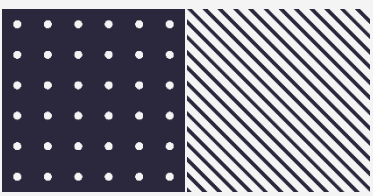
- Industry partners will play an important role in achieving Our Future Health's goals and add value to the work. Commercial involvement should be welcomed, provided it is on terms which are consistent with the overall aims, objectives and values of Our Future Health.

  Transparency is essential to build confidence. It will be important to clearly define different industry roles and Our Future Health must be explicit, both with participants and the wider public, about what partners receive in return for their investment. All contributors to and users of the project and its dataset should be publicly displayed on the website.
- **The involvement of industry partners must be clearly set out in the consent process.** Many other cohorts allow industry access to the cohort for research, but Our Future Health industry partners are likely to be involved as co-funders from the beginning. It is also likely that many

[29] See for example, 'The One-Way Mirror: Public attitudes to commercial access to health data', Wellcome (2015) https://wellcome.ac.uk/sites/default/files/public-attitudes-to-commercial-access-to-health-data-wellcome-mar16.pdf

Phase 2 studies will be industry-led and funded. The nature and extent of industry involvement should be made clear to participants from the outset, with information about the likely role of commercial partners explained in an open and transparent way. Details of industry involvement should be kept up-to-date, with information available both on the website and as part of ongoing communication with participants. Participants must be able to see the reasons and benefits for industry involvement, and the measures put in place to protect their interests.

- **Participants should be given clear commitments that their privacy will be protected,** including:
    - No individual's identifiable data will be disclosed to any partner, academic or industry, without the explicit consent of the individual concerned.
    - No individual's identifiable data will be shared for marketing purposes.
    - All approaches for further contact will be made by Our Future Health itself, to explain what is required and to seek consent, before any data is disclosed. No individual approaches will be made to participants without their consent.
- Industry involvement should be designed to further Our Future Health's aims and to deliver public benefit, for example by speeding the discovery and development of diagnostics and treatments. Given that the interests of participants are served by making the resource as accessible as possible, no industry partner should be given exclusive access to the full resource. Where an industry partner provides intellectual effort or funding to develop new data using the cohort, there may need to be a limited element of exclusivity, allowing exclusive access to that specific newly developed data for a time-limited period. This should not be an automatic right for industry partners and must be justified on case-by-case basis. The same rules and bases for judgement should apply to academic or charity partners, although the needs and motivations may be different. For further discussion about arrangements for limited exclusivity, see Section 3.5.3.
- Our Future Health is expected to have a small number of founding industry partners. These partners will have a key role in providing essential funding to set up the cohort, and without their support Our Future Health would not be feasible. There may, therefore, be good reason for them to have preferential terms of access for a time-limited period, but the details of any such arrangement will need careful thought. Terms that are seen to be not fair or appropriate could significantly undermine confidence in Our Future Health, and make recruitment more difficult. Care should be taken, for example, to ensure that academic, charity and SME-researchers are not excluded from accessing the full resource in any way. **We recommend that the Participant Advisory Panel should discuss and scrutinize the conditions on which founding partners can join.** Absolute transparency will be crucial. Founding partners should also commit to an agreed code of conduct, set out in the commercial partnerships policy.
- When considering any partnership model, Our Future Health should take account of the Principles that the Department of Health and Social Care has developed to ensure appropriate



benefit sharing when patient data is used by companies.[30]

4.4. Implications for healthcare professionals and the NHS

The Our Future Health cohort will be closely associated with the NHS throughout its existence. The proposed scale of the cohort means that there will be few GP practices that do not have participants on their patient lists. The implications for the NHS of recruitment strategies, the provision of feedback about health or risk status, and ongoing support for participants all need careful planning. Our Future Health will also be dependent on linking to NHS datasets to acquire ongoing updated medical information about participants.

As discussed in Section 1.3, Our Future Health is a research resource. However, primary care practices and other NHS related bodies may be involved in facilitating recruitment. There are likely to be occasions where a participant may need clinical assessment, screening, preventive measures or treatment as a result of information discovered through Our Future Health, and occasionally for ongoing support. They may also turn to the NHS for help and advice interpreting information they have received. The key issues for Our Future Health to consider are at what point the NHS can be expected to take on responsibility for this care and how this transition can be most effectively organised and managed. **Our Future Health must be careful to ensure that healthcare professionals are properly prepared, well informed and not overburdened as a result of the programme.**

Our Future Health cannot assume that clinical support for participants will simply materialise from the NHS without proper preparation. It is unrealistic to think that GPs will not notice the impact of 5 million people receiving information about their health or risk status. Indeed, the numbers could be higher because family members may also be affected and seek advice. The following guidance should therefore apply:

- **Ongoing engagement:** It will be essential to ensure appropriate engagement with relevant NHS structures, both from the early stages of planning and throughout the lifetime of the cohort. This should be at high-level and also on the frontline, including both primary and secondary care and other healthcare professionals that may be affected (e.g. Blood Transfusion Service may be involved in recruitment; clinical geneticists in ongoing support and clinical management). If people in the NHS are not adequately prepared, Our Future Health risks rapidly losing the engagement of both GPs and participants. **Unhappy doctors and unhappy participants could soon damage the credibility of Our Future Health and its ability to achieve its mission.** These relationships must be meticulously prepared and cultivated before they can be relied on.

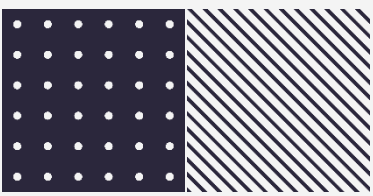
[30] https://www.gov.uk/government/publications/creating-the-right-framework-to-realise-the-benefits-of-health-data/creating-the-right-framework-to-realise-the-benefits-for-patients-and-the-nhs-where-data-underpins-innovation

- Early engagement with NHSX and NHS Digital will also be important to ensure the processes for data linkage can be streamlined as far as possible. (See Section 3.5)
- **Training and support:** Because of the nature of the work that Our Future Health will facilitate, many GPs will find themselves unable to properly advise without help, on issues that arise from participation. Our Future Health will need to consider how to provide the tools and training to inform both participants and NHS staff. There may be existing models that could be built on, for example regional genomics centres, if appropriately engaged, may be able to help provide local expertise.
- **Ensuring appropriate resource:** If Our Future Health is to be closely engaged in the NHS, there must be funding, resource and support to match. For example, there cannot be an expectation that overstretched NHS staff should be involved in recruitment activities in addition to their existing roles, without additional support and possibly resource. Any clinical duty of care required will also need to be appropriately resourced. One possibility might be to consider having trained ancillary staff, operating between the research programme and primary care, to help provide support to participants, either at recruitment or when feedback is provided.

As a first step, we recommend that **Our Future Health should work with NHS to undertake a detailed analysis of how various aspects of the programme, including recruitment and the provision of feedback, will be implemented in practice.** This should work through a number of examples to consider and evaluate the potential implications for healthcare professionals, to understand the potential challenges and barriers, and to assess what support may be required. It will be important to learn from previous examples, including the 100,000 Genomes Project, and to agree together what tangible support mechanisms may be required to deliver the programme effectively.

Implementation research will also be needed to explore how new innovations resulting from Our Future Health might be embedded into routine healthcare practice. This should consider if and how that innovation might be normalized within particular settings and will need to examine the different actors (including organizational infrastructure) that need to be involved in making the innovation work (or not work).

Our Future Health has the potential to provide evidence that informs the delivery of healthcare services in the future. For example, studies may reveal how information about risk could be provided to people most effectively, or how best to target screening programmes. While the research may take some time to mature, the outputs from Our Future Health should ultimately deliver benefit for the health of the whole population.



ANNEX A Membership of the Ethics and Feedback Advisory Group

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**The Framework document was written by Nicola Perrin and Martin Bobrow, with assistance from Saskia Sanderson, on behalf of EFAG.*

Our Future Health

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