Our Future Health

Our Future Health Protocol

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Chief Investigator

Raghib Ali, MBBChir, MD
Chief Investigator, Chief Executive Officer & Chief Medical Officer

Co-Principal Investigators

Michael B Cook, PhD
Executive Director of Science

David J Hunter, MBBS, ScD
Chief Science Adviser

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1. Background

1.1. Overall aims

The overarching objective of Our Future Health is to help people live healthier lives for longer through better prevention, earlier detection and improved treatment of diseases. The Our Future Health research programme will speed up the discovery of new methods of early disease detection, and the evaluation of new diagnostic tools, to help identify and treat diseases early when outcomes are usually better.

To achieve these objectives, we will recruit up to 5 million adults from across the UK to create a diverse and inclusive cohort of people who have consented to participate in the research. In addition to being asked for permission to link their personal health data to other health-relevant data, participants will be asked to provide biological samples and complete questionnaires on recruitment; agree to re-contact for ongoing biological sampling and questionnaires and consider taking part in further research studies; and agree to being offered personal health information arising from the research. The specific aims are presented below.

- **Specific Aim 1:** Build a resource linking multiple sources of health and health-relevant information, including genetic data, on millions of people in the UK, to facilitate basic discovery research by academic and commercial researchers on early indicators of disease
- **Specific Aim 2:** Analyse the data in the resource to estimate personal disease risk information for participants, based on genetic and non-genetic information, and offer this estimated personal health information to participants
- **Specific Aim 3:** Re-contact sub-groups of participants generally for additional samples, and additional data collection including linkage to digital data sources
- **Specific Aim 4:** Re-contact participants on a risk-stratified basis (i.e. recall-by-genotype/phenotype or sociodemographic characteristics) over time specifically to enable secondary studies by academic and commercial researchers that are greatly enhanced by being able to identify highly enriched sub-populations/sub-cohorts of participants

Building this large resource with linkage, feedback and re-contact will facilitate a new generation of discovery and translational research that will advance the development and testing of early diagnostic technologies and preventive (or 'personalised precision health') interventions.

The UK is uniquely placed to deliver this programme. We have an exceptional track record in population research, and many outstanding research groups. Our diverse (ethnically/ socioeconomically) population is willing to take part in research. Our government is committed to levelling up the major inequalities in health outcomes seen across the population. The NHS and our comprehensive disease registration systems provide a mechanism for invitation, recruitment and follow-up at an unprecedented size and scale. In addition, a programme of this scale and nature is made possible by the major advances in digital technologies over the past decade. Furthermore, the proportion of the UK public connected to data and devices ('digital health') is substantial and rapidly growing.

The Our Future Health research programme is intended to be both a prospective observational cohort and a platform for future discovery and translational research studies with consent for return of results, risk-stratification, and re-contact. Our Future Health will build on our national

strengths and complement existing prospective cohort resources and translational research efforts in the UK.

1.2. Genesis of Our Future Health

The initial idea to set up a very large cohort in the UK to improve early detection of chronic diseases was first discussed in 2016, when several medical research charities (including Cancer Research UK), the Medical Research Council, and leading public health practitioners and academics started exploring the rationale. The concept was described in the 2017 Life Sciences Industrial Strategy and discussions progressed on possible government funding.

The proposal to establish a 5-million strong volunteer cohort enabling research intended to improve the early detection of chronic diseases was set out in the Accelerating Detection of Disease challenge of the government's Industrial Strategy Challenge Fund (ISCF).

An investment of £79 million was allocated from the ISCF by UK Research and Innovation to test the feasibility of, and establish, the Our Future Health research programme. This was expected to be matched by funding of at least £160 million from industry and charity partners who would work in partnership with Our Future Health to design and deliver the programme.[1]

1.3. Initial planning of Our Future Health

In 2018, a Science Task & Finish Group was convened to make recommendations on the scientific design / scientific protocol of Our Future Health (Successive Chairs: Prof David Hunter; Prof Chris Whitty, Prof Patrick Chinnery). The Science Task & Finish Group concluded its work in early 2020.

An Ethics and Feedback Advisory Group (EFAG) was established in Sept 2019 to provide strategic advice on the development of ethical guidelines and principles for Our Future Health, and to develop an Ethics and Governance Framework to guide its operations (Successive Chairs: Prof Martin Bobrow; Prof Michael Parker). The first draft of this Framework (completed in Oct 2020) provides advice to the Board and Executive, and will be publicly available for funders, partners, researchers, participants and the general public. Building on the work of EFAG, an Ethics Advisory Board has been established as part of the long-term governance of the cohort and is responsible for monitoring the implementation of the Ethics & Governance Framework, and for reviewing and updating it as appropriate.

An Industry Advisory Group and an NHS Advisory Group were established early on in the development of the programme. Further details regarding governance structures being put in place can be found at the end of this document.

In Sept 2019, a not-for-profit company was established to run Our Future Health. The company, initially named Early Disease Detection Research Project UK (EDDRP UK), was registered as a charity in May 2020. The Executive was established in April-May 2020 with Dr Andrew Roddam as the CEO. The programme was subsequently renamed from the placeholder EDDRP UK to Our Future Health in 2021.

[1] https://www.ukri.org/innovation/industrial-strategy-challenge-fund/accelerating-detection-of-disease/

2. Scientific rationale

2.1. Prospective study design

Prospective observational cohort studies are valuable because these real-world studies facilitate the identification of biomarkers and causative factors that contribute to future disease.[2] Prospective study designs are less prone to bias than case-control study designs.

Existing large prospective studies in the UK and Europe include:

- **UK Biobank:** 500,000 participants, UK[3]
- **Million Women Study:** 1.3 million participants, England and Scotland[4]
- **Whitehall I and II Studies:** 17,500 and 10,000 participants respectively, England[5,6]
- **ALSPAC:** Avon Longitudinal Study of Parents and Children, 14,000 families, England[7]
- **Understanding Society:** The UK Longitudinal Household Study, 40,000 households, UK [8]
- **GLAD Study:** Genetics Links to Anxiety and Depression, n=22,000 to date (aim is 40,000), UK[9]
- **EPIC:** European Prospective Investigation of Cancer and Nutrition, 500,000 participants, UK and 9 countries in Europe[10]
- **Genes and Health:** 50,000 participants (aim is 100,000), UK[11]

There are a number of large or influential prospective studies in the US, including:

- **All of Us** (currently have recruited ~350,000 participants; aiming to achieve a final sample size of 1 million, US)[12]
- **Million Veteran Programme** (1 million participants, US)[13]
- **Nurses Health Study** (275,000 participants, US)[14]
- **Framingham Heart Study** (originally 5,000 participants, US)[15]

Prospective studies with East Asian and Hispanic populations have also been set up, including the following which are collaborations with investigators at Oxford University:

- **Kadoorie Study** (500,000 participants, China)[16]
- **Mexico City Prospective Study** (150,000 participants, Mexico)[17]

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[2] Manolio et al (*Nature Reviews Genetics,* 2006) Genes, environment and the value of prospective cohort studies. https://pubmed.ncbi.nlm.nih.gov/16983377/
[3] https://www.ukbiobank.ac.uk/
[4] http://www.millionwomenstudy.org/introduction/
[5] van Rossum et al (*J Epidemiol Community Health*, 2000) Employment grade differences in cause specific mortality. A 25 year follow up of civil servants from the first Whitehall study. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1731642/
[6] https://academic.oup.com/ije/article/34/2/251/746997
[7] http://www.bristol.ac.uk/alspac/about/
[8] https://www.understandingsociety.ac.uk/
[9] https://gladstudy.org.uk/about/
[10] https://epic.iarc.fr/
[11] https://www.genesandhealth.org/
[12] https://allofus.nih.gov/
[13] https://www.research.va.gov/mvp/
[14] https://www.nurseshealthstudy.org/
[15] https://framinghamheartstudy.org/
[16] https://www.ckbiobank.org/site/
[17] https://www.ctsu.ox.ac.uk/research/prospective-blood-based-study-of-150-000-individuals-in-mexico

Other listings include the International HundredK+ Cohorts Consortium (IHCC; www.ihccglobal.org) and the NCI Cohort Consortium (https://epi.grants.cancer.gov/cohort-consortium).

Prospective cohort studies provide important insights into disease aetiology, however they have not traditionally been designed to provide insights on whether or how these basic discoveries can be translated into actual health benefits for individuals and societies. For this, translational research is needed.

2.2. Translational research

Translational research studies are valuable because they aim to establish whether and how basic discoveries about disease aetiology can be translated into positive outcomes for populations.[18] Translational research has been defined as having four phases (T1-T4):[19]

- T1 involves processes that bring ideas from basic research through early testing in humans
- T2 involves the establishment of effectiveness in humans and clinical guidelines
- T3 primarily focuses on implementation and dissemination research
  Implementation research has been defined as the scientific inquiry into questions concerning implementation—the act of carrying an intention into effect, which in health research can be policies, programmes, or individual practices (collectively called interventions); the intent is to understand what, why, and how interventions work in "real world" settings and to test approaches to improve them[20]
- T4 focuses on outcomes and effectiveness in populations

Very recent examples of translational research include studies to develop and assess the outcomes and effectiveness of COVID19 vaccines.[21]

In the US, the NIH-organised and funded Electronic Medical Records and Genomics (eMERGE) Network consortium provides an example of discovery and translational research at a national scale. The eMERGE Network, founded in 2007, brings together US medical research institutions and researchers with a wide range of expertise in genomics, statistics, ethics, informatics, and clinical medicine. The primary goal of eMERGE is to develop, disseminate, and apply approaches to research that combine biorepositories with electronic medical record systems for genomic discovery and genomic medicine implementation research. In addition, the consortium includes a focus on social and ethical issues such as privacy, confidentiality, and interactions with the broader community.[22]

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[18] Woolf SH. The Meaning of Translational Research and Why It Matters. JAMA. 2008;299(2):211–213. doi:10.1001/jama.2007.26 https://jamanetwork.com/journals/jama/article-abstract/1149350?casa_token=udidtTeK55sAAAAA:hLwr1Fm0mlBmfbkjNrxXQCu3IeSAYdhQo_XUZUMgPB7aDbwKvps80SSOqb6Ca86JYajafw7MEA

[19] Fort, D., Herr, T., Shaw, P., Gutzman, K., & Starren, J. (2017). Mapping the evolving definitions of translational research. Journal of Clinical and Translational Science, 1(1), 60-66. doi:10.1017/cts.2016.10 https://doi.org/10.1017/cts.2016.10

[20] Peters, Taghreed, Olakunle, Akua, Nhan. Implementation research: what it is and how to do it BMJ 2013; 347:f6753 https://www.bmj.com/content/347/bmj.f6753.full

[21] Sharpe et al (2020) The early landscape of coronavirus disease 2019 vaccine development in the UK and rest of the world https://onlinelibrary.wiley.com/doi/full/10.1111/imm.13222

[22] https://www.genome.gov/Funded-Programs-Projects/Electronic-Medical-Records-and-Genomics-Network-eMERGE

In the UK, examples of individual translational research studies that are embedded within public health programmes at a national scale include:

- A study examining uptake of colorectal cancer screening over three invitation rounds in the NHS Bowel Cancer Screening Programme among individuals aged 60-64yrs (n=62,000)[23]
- A randomised controlled trial (UK Age trial) investigating the effect of mammogram breast screening from age 40 years on breast cancer mortality involving 23 breast screening units across Great Britain (n=161,000)[24]
- A study of the effectiveness of NHS Health Check programme at reducing cardiovascular disease risk among patient aged 40-74 years after one year (n=3,172)[25]

The intent is that Our Future Health research programme will provide both a:

(1) **Prospective observational dataset** for basic science / epidemiological, discovery and aetiological research e.g. on the causes and early signs of disease; and
(2) **Translational research platform** comprising a cohort of people who can be re-contacted for translational/implementation research to develop and test new diagnostic technologies, prevention strategies and treatments.

Our ambition is to recruit an ethnically and socioeconomically diverse population. We expand further on this important point in the sample frame section below.

2.3. Sample frame

The ambition of Our Future Health is to recruit 5 million participants each of whom will provide consent, complete a baseline questionnaire, donate a blood sample and be eligible for linkage to health-related data. The 5 million number will provide a UK prospective cohort in which, with sufficient statistical precision, it will be possible to study:

- Both common and rare phenotypes and diseases
- Subpopulations based on ethnicity, index of multiple deprivation, geography, risk stratification, genotypes, and precursor conditions
- Statistical interactions between genotypes and environmental factors in relation to disease
- Pre-diagnostic/pre-interventional bloods for studies of subpopulations with specific diseases/phenotypes
- Sub-populations based on their disease-specific genotypes or polygenic risk scores
- Populations invited and consented to ancillary studies.

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[23] Lo SH, Halloran S, Snowball J, et al Colorectal cancer screening uptake over three biennial invitation rounds in the English bowel cancer screening programme. Gut 2015;64:282-291. https://gut.bmj.com/content/64/2/282

[24] Duffy et al (*Lancet Oncology,* 2020) Effect of mammographic screening from age 40 years on breast cancer mortality (UK Age trial): final results of a randomised, controlled trial. https://www.sciencedirect.com/science/article/pii/S1470204520303983

[25] Artac et al (2013) Effectiveness of a national cardiovascular disease risk assessment program (NHS Health Check): Results after one year. https://www.sciencedirect.com/science/article/pii/S0091743513001473?casa_token=2N7-pXNXZBgAAAAA:3mJYFPV7jt7dbdA4LdvD4HNEwl8579DrVQzivVRuplw7wvr0oSRR-JYspHbmSa6QQOr8t3nC2w

After describing the sample frame ambition, the sections that follow provide additional details of the above novel aspects of Our Future Health that are facilitated by the large sample size and the ability to recontact participants.

2.3.1. Sample frame ambition

The 5 million participants we aspire to recruit into Our Future Health will be reflective of the UK population according to the most recent census data available. To inform such, we have drawn on 2011 census data of population counts by age, sex, ethnicity, and index of multiple deprivation for England and Wales, Scotland, and Northern Ireland. We will update our sample frame with census 2021/22 when they become available in late 2022 and 2023.

Table 1. Sample frame ambition

Sex >	**Female**				**Male**			
Ethnicity >	**White**	**Black**	**Asian**	**Mixed/Other**	**White**	**Black**	**Asian**	**Mixed/Other**
Age v								
18–19	68,090	3,360	6,755	3,859	69,687	3,308	7,068	3,968
20–29	354,596	16,074	45,872	16,666	353,073	14,744	47,995	18,184
30–39	347,493	17,760	44,405	12,902	343,187	15,893	44,993	14,818
40–49	416,477	18,376	28,215	9,369	406,695	16,686	27,690	10,168
50–59	356,575	9,130	19,971	4,972	350,377	8,091	19,132	5,337
60–69	331,220	4,114	11,255	2,609	317,787	2,982	9,516	2,639
70–79	229,045	3,419	6,365	1,433	195,353	3,075	6,536	1,384
80–84	85,797	799	1,479	421	59,129	702	1,332	372
85+	92,450	442	953	346	43,752	358	684	242
Totals	**2,281,742**	**73,474**	**165,270**	**52,577**	**2,139,040**	**65,840**	**164,946**	**57,110**
%	**45.6%**	**1.5%**	**3.3%**	**1.1%**	**42.8%**	**1.3%**	**3.3%**	**1.1%**

This sample frame ambition is reflective of the UK population in terms of age, sex, and ethnicity. It will provide large numbers of participants of the primary ethnic minority groups resident in the UK – Indian, Pakistani, Bangladeshi, Chinese, Black African, Black Caribbean, Arab and Mixed – populations that have been underrepresented in health research. Combined with a proportional representation of participants across the nations, this sample frame will provide for a diverse cohort that will be amenable to a variety of studies that have not been possible in a UK prospective cohort before.

Achieving a sample that is reflective of the UK population is an overarching aim of the Our Future Health programme for both ethical and scientific reasons. Ethically, it is important that we make substantial efforts to make participation in Our Future Health equitable and accessible to people regardless of their socioeconomic position, disability, physical health, mental health, sex, age, and ethnicity. Scientifically, it is important that the participants in Our Future Health are sufficiently diverse to facilitate a range of discovery and translational research the resource is intended to support. Related to this, the concept of “representativeness” has been debated at length in the

epidemiologic literature[26,27]. We recognise that our participant sample is unlikely to be fully representative of the UK population in a large range of demographics and risk factors that extend beyond those shown in Table 1. However, the important aspects of representativeness and selection biases are specific to any hypothesis being tested and the external population to which an inference is to be made[28]. By ensuring we recruit a diverse population, we will provide a resource that is amenable to a large range of hypotheses and potential inferences to improve the health of the UK population.

2.3.2. Common and rare phenotypes and diseases

The size of this sample frame ambition will provide the ability to prospectively assess, with strong statistical precision, a wide range of common and rare phenotypes and diseases in a UK population. In addition, it will provide large numbers of prevalent diseases for retrospective, statistically powered case-control and case-cohort studies.

We have estimated incident diagnoses of disease that would accrue in Our Future Health in the initial 2.5-years of follow-up using various population/subpopulation sizes (**Appendix A**), demonstrating the immediacy of the impact that this programme will have on health research.

To interpret the advantages of these estimated incident diagnoses that may accrue in the population that comprises the Our Future Health cohort, we have also calculated minimal detectable odds ratios for aetiologic studies using ranges of case numbers, alpha values (critical p values), and exposure prevalence (**Table 2**). Note that the colour shading of all tables in these sample frame ambition sections indicates 0 cases (pure green), 5,000 cases (yellow), and 10,000 or more cases (red), a scale based on aetiologic odds ratios of ~1.5 for mid-range exposure prevalence and mid-range alphas.

[26] Nohr, E. A. and J. Olsen (2013). "Commentary: Epidemiologists have debated representativeness for more than 40 years--has the time come to move on?" International Journal of Epidemiology 42(4): 1016-1017.
[27] Schooling, C. M. and H. E. Jones (2014). "Is representativeness the right question?" International Journal of Epidemiology 43(2): 631-632.
[28] Huang, J. Y. (2021). "Representativeness Is Not Representative: Addressing Major Inferential Threats in the UK Biobank and Other Big Data Repositories." Epidemiology 32(2): 189-193.

Table 2. Minimal Detectable Odds Ratios by Case Count, Exposure Prevalence, and Critical p-value

Exposure Prevalence[a]	Critical p-value	Minimum detectable odds ratio, by number of cases[b]						
		500	1,000	2,500	5,000	7,500	10,000	25,000
0.5	0.05	1.28	1.19	1.12	1.08	1.07	1.06	1.04
0.5	0.00005	1.62	1.40	1.24	1.16	1.13	1.11	1.07
0.5	0.00000005	1.89	1.56	1.32	1.22	1.17	1.15	1.09
0.25	0.05	1.31	1.22	1.13	1.09	1.08	1.07	1.04
0.25	0.00005	1.65	1.44	1.26	1.18	1.15	1.13	1.08
0.25	0.00000005	1.90	1.59	1.35	1.24	1.19	1.17	1.10
0.1	0.05	1.45	1.31	1.19	1.13	1.11	1.09	1.06
0.1	0.00005	1.92	1.62	1.38	1.26	1.21	1.18	1.11
0.1	0.00000005	2.25	1.83	1.50	1.35	1.28	1.24	1.15
0.025	0.05	1.88	1.60	1.37	1.26	1.21	1.18	1.11
0.025	0.00005	2.83	2.22	1.74	1.51	1.41	1.35	1.22
0.025	0.00000005	3.53	2.66	1.98	1.67	1.54	1.47	1.29
0.01	0.05	2.43	1.97	1.59	1.41	1.33	1.29	1.18
0.01	0.00005	4.08	3.02	2.19	1.82	1.66	1.56	1.35
0.01	0.00000005	5.35	3.78	2.61	2.09	1.87	1.75	1.46
0.0025	0.05	4.21	3.11	2.25	1.85	1.69	1.59	1.36
0.0025	0.00005	8.60	5.70	3.63	2.75	2.39	2.18	1.72
0.0025	0.00000005	12.32	7.76	4.65	3.38	2.88	2.59	1.95
0.001	0.05	6.80	4.67	3.10	2.41	2.12	1.96	1.59
0.001	0.00005	16.14	9.85	5.67	4.00	3.35	2.98	2.18
0.001	0.00000005	24.59	14.28	7.70	5.20	4.24	3.72	2.59

[a] Exposure prevalence among controls.

[b] Calculated at 80% power assuming 4 controls per case.

A variety of scenarios can be deduced from this flexible table set up. For example, the advantages of having a population of 1 million can be clearly seen for diagnoses such as transient ischaemic attack and ischaemic stroke, irritable bowel syndrome, cholecystitis, tinnitus, diabetic eye disease, uterovaginal prolapse, postmenopausal bleeding, septicaemia, migraine, peripheral neuropathy, dementia, and rosacea, all of which accrue 4,000–6,000 cases in this short term period of follow-up – a threshold that provides strong statistical precision for testing aetiologic hypotheses. An increase to 2 million participants sees many other diagnoses surpass a 4,000-case threshold in this short period of follow-up, including lung and bowel cancers, stroke, non-rheumatic mitral valve disorder, anal fissure, Barrett's oesophagus, blindness, obstructive and reflux uropathy, neuropathic bladder, agranulocytosis, spinal stenosis, rheumatoid arthritis, fibromatosis, polymyalgia rheumatica, chronic sinusitis, sleep apnoea, and pulmonary collapse. The diseases that can be researched with strong statistical precision is obviously increased further as the number of participants and thus case numbers increase. At 5 million participants, many rarer diseases accrue to sufficient numbers to provide for strong statistical precision for a range of hypotheses to be investigated. These tables underscore the benefits of progressing towards and reaching 5 million participants in being able to study both common and rare phenotypes and diseases. They also underscore the unique opportunities that Our Future Health will provide to the world research community.

Another important use of the Our Future Health cohort will be in developing and validating predictive models of health and disease status. This includes polygenic/integrative risk scores and biomarkers, which will be generated and returned to consenting participants as a primary objective of the programme. However, with the rapid growth and development of machine learning methods, in step with advances in computing power, there will be a broad interest in using the cohort to develop new predictive models of different types. The case numbers shown in Appendix A demonstrate the potential of Our Future Health for research into predictive models of health and disease as they provide for high precision for estimates of validation statistics such as sensitivity and specificity (**Table 3**).

Table 3. Margins of Error for Estimates of Sensitivity and Specificity by Case or Control Count.

Sensitivity or Specificity (%)	Margin of error[a] (%), by number of cases or controls[b]						
	500	1,000	2,500	5,000	7,500	10,000	25,000
50	4.4	3.1	2.0	1.4	1.1	1.0	0.6
70	4.0	2.8	1.8	1.3	1.0	0.9	0.6
80	3.5	2.5	1.6	1.1	0.9	0.8	0.5
90	2.6	1.9	1.2	0.8	0.7	0.6	0.4
95	1.9	1.4	0.9	0.6	0.5	0.4	0.3

[a] Margin of error is half the width of a 95% confidence interval

[b] Cases for sensitivity; controls for specificity

2.3.3. Subpopulations

We will strive for diversity in our sample frame ambition by aspiring to reflect the UK population in terms of age, sex, ethnicity, socioeconomic status, and geography. Achieving this aim will deliver a variety of subpopulations of interest each of which will accrue sufficient incident disease as to offer aetiologic and diagnostic insights. Subpopulations may be defined by the participant factors stated above, as well as minor allele frequencies, precursor diseases (e.g. colonic polyps, Barrett's oesophagus), genetic disease risk profiles, and blood group subtypes. These examples of potential subpopulations for study provide further underscore the benefits of our sample frame ambition. In terms of ethnic diversity, 5 million participants would be partly comprised of 149,000 Black participants and 330,000 Asian participants, primary ethnic-specific populations of which would include: 100,000 Indian, 68,000 Pakistani, 62,000 Black African, 45,000 Black Caribbean, 31,000 Chinese, and 26,000 Bangladeshi. This will provide a research platform to understand differences in disease risk by ethnicity[29,30,31], providing a levelling-platform with the potential to improve health for all ethnicities in the UK. Statistical interactions

Our Future Health will create new opportunities to investigate how different factors interact to cause disease or alter treatment efficacy. Estimating these interaction effects has previously been challenging; in contrast to the individual effects of specific treatments, environmental factors or

[29] Ali, R., et al. (2021). "Life expectancy by ethnic group in England." BMJ 375: e068537.
[30] Maruthappu, M., et al. (2015). "Incidence of prostate and urological cancers in England by ethnic group, 2001-2007: a descriptive study." BMC Cancer 15: 753.
[31] Shirley, M. H., et al. (2014). "Incidence of breast and gynaecological cancers by ethnic group in England, 2001-2007: a descriptive study." BMC Cancer 14: 979.

genetic variants, estimating interactions requires considerably larger sample sizes[32]. Additional obstacles to the study of interactions include the availability of high-quality and wide-ranging exposure assessments, known temporality of exposures, and ethnically and geographically diverse populations[33].

To examine the potential to estimate gene-environment interactions using the Our Future Health cohort, we have calculated minimum detectable odds ratios under a variety of scenarios. Here we assume a conservative scenario, such as might be found in a pharmacogenetic context, where the environmental exposure is a treatment with a modest effect ($OR_E = 1.25$) and the genetic factor has no effect on the outcome ($OR_G = 1.0$) except in treated individuals. We assume that the minor (risk) allele is dominant. We then estimate the minimum detectable odds ratio for the interaction between the treatment and genotype (OR_{GE}, the effect of the genetic factor in treated individuals) for a range of genotype minor allele frequencies (MAF), treatment prevalence, critical p-values for significance tests, and numbers of cases (**Table 4**).[34] These calculations ignore model misspecification, measurement error and other issues which reduce precision, further underscoring the need for the sample frame ambition of Our Future Health.

[32] Ritz, B. R., et al. (2017). "Lessons Learned From Past Gene-Environment Interaction Successes." American Journal of Epidemiology 186(7): 778-786.
[33] McAllister, K., et al. (2017). "Current Challenges and New Opportunities for Gene-Environment Interaction Studies of Complex Diseases." American Journal of Epidemiology 186(7): 753-761.
[34] Moore, C.M., et al. (2019). “Power and sample size calculations for genetic association studies in the presence of genetic model misspecification.” Human Heredity 84:256-271.

Table 4. Minimal Detectable Interaction Odds Ratios by Case Count, Risk Allele Frequency, Exposure Prevalence, and Critical p-value

Risk allele frequency	Exposure prevalence[a]	Critical p-value	Minimum detectable interaction odds ratio, OR_{GE}, by number of cases[b]			
			2,500	5,000	10,000	25,000
0.25	0.25	0.05	1.30	1.20	1.14	1.09
0.25	0.25	0.00005	1.57	1.38	1.25	1.16
0.25	0.1	0.05	1.44	1.30	1.20	1.12
0.25	0.1	0.00005	1.87	1.56	1.38	1.23
0.25	0.05	0.05	1.64	1.42	1.28	1.17
0.25	0.05	0.00005	2.33	1.83	1.54	1.32
0.1	0.25	0.05	1.38	1.26	1.18	1.11
0.1	0.25	0.00005	1.75	1.49	1.33	1.20
0.1	0.1	0.05	1.57	1.38	1.26	1.16
0.1	0.1	0.00005	2.18	1.74	1.49	1.29
0.1	0.05	0.05	1.84	1.55	1.37	1.22
0.1	0.05	0.00005	2.87	2.12	1.71	1.41
0.05	0.25	0.05	1.53	1.35	1.24	1.15
0.05	0.25	0.00005	2.06	1.68	1.45	1.27
0.05	0.1	0.05	1.81	1.53	1.35	1.21
0.05	0.1	0.00005	2.76	2.06	1.68	1.40
0.05	0.05	0.05	2.22	1.77	1.51	1.30
0.05	0.05	0.00005	4.02	2.67	2.02	1.57
0.01	0.25	0.05	2.39	1.86	1.56	1.33
0.01	0.25	0.00005	4.56	2.91	2.15	1.63
0.01	0.1	0.05	3.40	2.39	1.87	1.49
0.01	0.1	0.00005	9.81	4.59	2.92	1.99
0.01	0.05	0.05	5.50	3.27	2.32	1.72
0.01	0.05	0.00005	63.37	8.97	4.36	2.53

[a] Population prevalence of the exposure.

[b] Calculated at 80% power assuming 4 controls per case.

2.3.4. Pre-diagnostic bloods

The lack of large prospective cohort studies with pre-diagnostic bloods available to researchers has stifled disease interception research[35]. There has been a distinct lack of progression of biomarkers from nested case-control studies to the pre-diagnostic arena for insights on diagnosis and prognosis. The sample size ambition of Our Future Health will reduce pressures of biospecimen retention requirements and enable the possibility of boutique subpopulation research studies using pre-diagnostic blood specimens. Although the Access Board will devise the rules for biospecimen access, any such study proposal will undoubtedly require strong preliminary

[35] Pepe, M. S., et al. (2001). "Phases of biomarker development for early detection of cancer." Journal of the National Cancer Institute 93(14): 1054-1061.

evidence[36,37] that will form the basis of a conservative selection strategy[38,39] to ensure the resource is used appropriately and preserved for the long term. Nevertheless, Our Future Health has the possibility to be the only large-scale UK prospective cohort study to offer the possibility of access to pre-diagnostic biologic samples for biomarker validation.

Broad assays (-omics) are no longer confined to small sample sets – high throughput efficiencies are enabling the ability to deep phenotype the totality of samples in a given resource[40,41,42,43.] Continued gained efficiencies will likely spur the continued movement to big, layered -omics data and Our Future Health will provide an ideal platform for such cohort-wide deep phenotyping which greatly increases the potential for insights into the determinants and causes of disease.

2.4. Participant questionnaires

Participant questionnaires comprise an essential component of any health-related population study. Through questionnaires, we can elicit important health-related information that is not available, is incomplete, or is potentially incorrect in medical records and other health-related linked data that participants consent to donating to Our Future Health when joining the programme. Questionnaire data is also more rapidly obtainable than many health-related linked data and can complement health-record linkage by obtaining repeated measurements or more detailed self-reports than might be possible via the healthcare system. Examples of questionnaire derived health-related information that can supplement and complement health-related linked data include:

- up-to-date health status, exposures, and outcomes (e.g. general health, current cigarette smoker, mental health)
- long-term health or exposure histories that pre-date electronic medical records (e.g. any surgical procedure before 1990, lifetime cigarette smoking history)
- exposures or outcomes that are either poorly or not captured by electronic medical records (e.g. typical alcohol consumption, recent physical activity, over-the-counter medications, mental health)
- Measures that are not regularly repeated or typically available until later in life in medical records (e.g. body weight, alcohol consumption, anxiety, physical activity)
- Health relevant lifestyle factors and personal characteristics that might be unavailable in medical records (e.g. employment status, marital status, type of housing)

[36] Wentzensen, N. and R. C. Eldridge (2015). "Invited Commentary: Clinical Utility of Prediction Models for Rare Outcomes-The Example of Pancreatic Cancer." American Journal of Epidemiology 182(1): 35-38.
[37] Wentzensen, N. and S. Wacholder (2013). "From differences in means between cases and controls to risk stratification: a business plan for biomarker development." Cancer Discov 3(2): 148-157.
[38] Pepe, M. S., et al. (2008). "Pivotal evaluation of the accuracy of a biomarker used for classification or prediction: standards for study design." Journal of the National Cancer Institute 100(20): 1432-1438.
[39] Pepe, M. S., et al. (2015). "Improving the quality of biomarker discovery research: the right samples and enough of them." Cancer Epidemiology, Biomarkers and Prevention 24(6): 944-950.
[40] He, K. Y., et al. (2017). "Big Data Analytics for Genomic Medicine." Int J Mol Sci 18(2).
[41] Rappaport, S. M. (2012). "Biomarkers intersect with the exposome." Biomarkers 17(6): 483-489.
[42] Siroux, V., et al. (2016). "The exposome concept: a challenge and a potential driver for environmental health research." Eur Respir Rev 25(140): 124-129.
[43] Wild, C. P. (2012). "The exposome: from concept to utility." International Journal of Epidemiology 41(1): 24-32.

Thus, self-report questionnaires significantly contribute to a comprehensive assessment of health, enhancing research insights into how we may improve the nation's health.

Questionnaires also allow us to serve certain populations that would otherwise continue to be misclassified and underrepresented in health research. For example, asking about sexual orientation and gender identity will allow us to ensure we are recruiting a sample representative of all peoples in the UK. This in turn will enable research that supports the provision of a health-care system that serves the needs of all, rather than over-generalising research from nonrepresentative populations.

Delivering regular, repeated questionnaires also facilitates the ongoing involvement of participants – reminding them of the important research programme they have consented to be part of, and retaining their interest and attention. We will have the opportunity to further engage participants by using questionnaire responses to formulate feedback and advice that might be of interest and support individual health choices.

In addition to our core participant questionnaire, we will develop a roadmap of future questionnaires built from these principles that underscore the scientific and participant rationales of our programme.

2.5. Physical measurements

We will assess physical measurements when participants provide blood samples for those metrics and in locations where this is feasible and cost-effective. Although height and weight are typically accurately self-reported within a population[44], in-person assessment of these metrics provides individual accuracy which is important for a variety of disease risk estimations as well as participant feedback that incorporates such information[45]. Weight is associated with many diseases including cardiovascular disease and cancer. Height can be used to calculate body mass index (BMI) from weight which has greater predictive accuracy for disease, and height also an independent predictor of certain cancers, vascular disease and all-cause mortality.

Capturing height and weight in-person can easily be extended to measurement of other physical characteristics such as waist circumference[46], bioimpedance[47], and blood pressure. Waist circumference is highly correlated with intra-abdominal fat mass while bioimpendance analysis is a non-invasive, low-cost analysis of body composition. Waist circumference and bioimpedance analysis have each been shown to be associated with a higher risk of diabetes and vascular events independently of BMI. Excessive intra-abdominal fat may be more harmful to health than fat elsewhere due to higher release of free fatty acids into the portal bloodstream which lowers the body's sensitivity to insulin, and alters the balance of blood lipids.

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[44] Celis-Morales et al (*Genes Nutr*, 2015) How reliable is internet-based self-reported identity, socio-demographic and obesity measures in European adults? https://pubmed.ncbi.nlm.nih.gov/26143178/

[45] Newell et al (*Am J Prev Med*, 2017) The accuracy of self-reported health behaviors and risk factors relating to cancer and cardiovascular disease in the general population 1: A critical review. https://pubmed.ncbi.nlm.nih.gov/10987638/

[46] Ross et al (*Nat Rev Endocrinol*, 2020) Waist circumference as a vital sign in clinical practice: a Consensus Statement from the IAS and ICCR Working Group on Visceral Obesity. https://pubmed.ncbi.nlm.nih.gov/32020062/

[47] Böhm et al (*Eur J Clin Nut*, 2017) The use of bioelectrical impedance analysis for body composition in epidemiological studies. https://pubmed.ncbi.nlm.nih.gov/23299875/

Elevated blood pressure or hypertension is a well-established cause of coronary heart disease, stroke and several other vascular diseases. In addition, blood pressure accounts for a large proportion of the effects of obesity on health, such that a proper understanding of the effects of obesity is not possible without a proper understanding of the effects of blood pressure.

Thus, each of these baseline physical measurements provide significant contributions to disease risk predictions and have a strong rationale for being included in the Our Future Health research programme.

2.6. Data linkages

Health-related data linkages are a core component of the UK research infrastructure, made possible by routine data collection that can be safely and securely linked to participants. Our Future Health participants consent to data linkages when joining the programme, and their donation of these data provide important additional information on individual and geographic disease-related exposures as well as individual health outcomes. Examples of each of these are shown below:

- Individual disease-related exposures
    - medication prescriptions
    - coronavirus infection
    - surgical implants
    - radiation therapy

- Geographic disease-related exposures
    - particulate matter from combustion and other sources
    - food choices including distance and accessibility
    - meteorological information including flooding and extreme weather
    - geographic deprivation metrics

- Individual health outcomes
    - diagnoses captured in primary care records, secondary care records, and cancer registration databases
    - survival time following a serious diagnosis or clinical intervention
    - date of death including underlying and contributory causes of death

These participant-level geotemporal health-related data will greatly enrich the Our Future Health programme enabling researchers to assess the success of interventions, how and in who new therapies extend survival from acute disease, and how social determinants contribute to heath inequalities. These examples highlight the strong rationale for data linkages in this research programme.

2.7. Biological samples

A broad variety of biological specimen types could theoretically be collected in a given research study, but most prospective cohort studies have decided to collect blood at baseline on all of their participants. This is because it is a minimally-invasive, cost-effective, and a participant-accepted specimen type that can provide systemic insights on an individual's health-related exposures, disease risk, and disease status. For example, blood can provide information on viral exposures,

pesticide exposures, polycyclic aromatic hydrocarbon exposure, lipid profile including high density and low density lipoproteins, genetic susceptibility, DNA adducts, diabetes metrics, circulating tumour DNA (ctDNA), and circulating proteins indicative of disease. These examples of scientific insights that can be derived from blood provide a strong rationale for the collection of this biospecimen from all Our Future Health participants.

From these baseline blood samples, we plan to assess cholesterol and HbA1c. Hypercholesterolaemia is a well-established cause of coronary heart disease, stroke and several other vascular diseases and its measurement is required to provide an integrated risk score for ischaemic heart disease. HbA1c provides an estimate of blood glucose (sugar) levels and will be conducted for participants who have a diabetes risk score above the recommended test threshold. Vascular diseases and diabetes are major causes of morbidity and mortality in the UK providing the strong rationale for measuring these biomarkers at baseline.

Moreover, blood collection is highly feasible and cost-effective given the facts that phlebotomy services are readily available and deployable, and that high-throughput automated laboratories and biobanks exist for processing and storage. These facts support the selection of blood as the central biological sample that we will collect when a participant joins the programme. However, this does not preclude the collection of additional biological specimen types, and we will continuously monitor the feasibility and cost-effectiveness of such as the programme progresses.

3. Recruitment

3.1. Overall strategy

As described in our sample frame section, our ambition is to recruit up to 5 million people from diverse backgrounds. To achieve this ambition, we plan to engage the public (our potential participants), invite eligible participants by post or email, attain digital consent to participate in the programme, attain a digital baseline health questionnaire, and attain physical measurements and a blood sample at an in-person appointment.

We will deliver local and national communication strategies to make the public aware of the programme, its primary aims and what and how a participant's time, data, and blood sample will be used.

In addition to using post and email for invitations, we will also design and deploy in-person settings to advertise and consent individuals into the programme.

To ensure we do not preclude participation of individuals who cannot or prefer not to use digital tools, we will enable hardcopy and telephone completion of consent and questionnaires.

We will provide flexibility in venues for attaining physical measurements and blood from consented participants, primarily focusing on:

1. Community strategies such as pharmacy collaborations, mobile units, and 'pop-up' clinics.
2. Partnerships with the NHS to use existing appointments such as blood donations and health care phlebotomy.

Schematic summaries of these recruitment workflows are shown in Figures 1, 2, and 3 below.

This primary overarching plan has a strong rationale in that it is flexible, scalable, cost-efficient, and feasible. It will be built with the widely used COM-B Model (Capability, Opportunity, Motivation, Behaviour)[48] of human behaviour in mind, which encourages careful consideration of barriers when designing activities relating to behaviour (in this case, becoming a participant of Our Future Health). Our recruitment strategy will also be aligned with the highest ethical principles, as detailed in our Ethics & Governance Framework (**Appendix B**).

Our recruitment strategy will enable rapid, large-scale recruitment into the programme while simultaneously allowing us to adapt, tailor, and target our methods to ensure inclusion of populations that have been underrepresented in health research. In the following sections, we describe our detailed plans for engagement, invitation, consent, baseline questionnaire, and phlebotomy.

3.2. Engagement

The goals of engagement are to raise awareness of Our Future Health, generate interest in taking part, and to provide opportunities for the public and other stakeholders to share their views.

[48] COM-B Model (Michie et al, 2011) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3096582/

To recruit a cohort that is reflective of the UK population, specific engagement strategies will be designed, tested and deployed. Engagement strategies will be designed to promote equality, diversity, and inclusion in Our Future Health. These engagement strategies will be designed to support our local and region-specific recruitment plans.

3.2.1. Engagement through partnerships

Identifying and building relationships with individuals and organisations who can support participant recruitment to Our Future Health is an essential component of this programme. We will aim to work with partners that can support recruitment by publicising the programme to target audiences and through existing networks, and with partners that are able to support our plans to send invitations to people to take part. This will include local opinion formers in public health, large businesses, community organisations, academia and local government.

Collaborative engagement with delivery partners – such as community pharmacy networks – has the potential to increase awareness and engagement via well-known organisations that have strong local and national footprints. In hospitals, we will work with research ambassadors (volunteers who are Good Clinical Research Practice trained), who will directly support engagement of potential participants. In primary care we will work with patient participation groups and for blood donation recruitment we will be working with donor carers.

To overcome hesitancy within seldom heard/underrepresented groups, we will aim to develop partnerships with trusted voices and community leaders or representatives, including local public health teams, community groups and those who have strong networks in each area.

Engagement strategies will be designed with the support of our Diversity and Inclusion Advisory Board which comprises people with expertise in engaging communities locally and nationally. We will also leverage the expertise on our Ethics Advisory Board, Scientific Advisory Board and our Public Advisory Board, each of which provide additional expertise of the challenges of engaging and recruiting participants into health research studies from diverse backgrounds across the country in culturally appropriate ways.

To achieve engagement with and maintain ongoing support from a range of partners, we are planning to focus on a combination of:

- Clear, motivating partnership proposals, backed up by credible voices from a range of domains (e.g. science, healthcare, charities, politics, celebrities) and working with existing partners to engage others
- Providing feedback on partners' support in driving recruitment, so they can be credited for their efforts and achievements
- Strong, enduring relationships with leaders in partner organisations, particularly in the third sector, and ongoing engagement and outreach
- High quality tools, content and campaign resources to make it easy for partners to promote Our Future Health
- Tailored campaigns, co-created with partners to improve impact
- Supporting national, local and digital PR, to provide a positive ongoing context for partners choosing and continuing to help us

3.2.2. Publicity campaigns and communications

A comprehensive programme of publicity activities will increase awareness and understanding of Our Future Health among the target population. We will deliver regional publicity campaigns in targeted recruitment locations from early Summer 2022. The campaigns will be designed to increase responses to invitations sent to members of the public, and so enable recruitment into the cohort. Activities will include advertising, public relations, social media and community-based events that can effectively reach the target population in each area.

Following the series of regional engagement activities, as we expand the scope of recruitment across the UK from 2023 onwards, we are planning national level awareness engagement and campaign activities. These activities will aim to increase levels of awareness across the target population as a whole, particularly those groups that we anticipate are less likely to engage and respond. We will explore a range of messaging, channels and methods of engagement designed to increase motivations to participate in the programme, including:

- Participant referrals – supported by tools, simple processes and (non-financial) incentives to encourage people to recruit others within their family and communities
- Membership bodies/groups – tapping into the scale of organisations that have a strong connection to or presence within our target audiences. These could be place-based or interest-based opportunities, or a combination of the two (e.g. faith organisations)
- Patients as advocates – exploring routes through patient charities/groups to encourage people with diseases to make the case within their communities and families for participation
- Partnership marketing – working with organisations with significant reach (e.g. charities, consumer brands, sports orgs, large employers) to promote participation across their customers, staff, audiences and supporters
- Social campaigning – adopting a networking approach to increase reach using social media in particular, drawing on the potential to tap into motivations around specific disease areas with the support of relevant charities
- Influencers – engaging and enlisting the support of high profile advocates who have reach and influence across target populations, both geographically and digitally.

We are also exploring ways to influence national and local healthcare decisions by engaging with credible stakeholders/advocates at the regional and national level. These may be a combination of those within the NHS healthcare system (e.g. high profile clinicians, NHS Health Check commissioners, NHS leadership) and across the broader public health arena e.g. medical charities, local authorities, patient groups and researchers.

3.3. Invitation

3.3.1. Invitation methods

We will use NHS DigiTrials as the primary route for postal invitation with the intention to reach most of the U.K.'s adult population through our invitations. NHS DigiTrials provides unparalleled scale, the ability to target invitations based on demographic information, and will help us build trust with potential participants. The NHS DigiTrials application process includes Section 251 support which will enable NHS DigiTrials – on our behalf – to select eligible individuals and send named invitations for participation in Our Future Health. We will dynamically adjust the number of

invites sent to specific population groups based on conversion rates and our ambition to recruit a diverse cohort that is reflective of the UK population.

Invitations may also be sent by collaborations with community pharmacy networks using their existing customer databases. We are also exploring other ways to send invitations, including potential partnerships with existing cohorts such as REACT.

In partnership with NHS bodies, invitations to Our Future Health will be sent by email to blood donors by NHSBT, and through existing patient communication systems – which may include post, email and text message – in primary and secondary care. Text messages are attractive because they are inexpensive, already sent in high volume by the NHS, and can include a link to our participant information sheet and consent process that can be accessed via a patient's smartphone or computer prior to a planned appointment. Our Public Advisory Board members and secondary care PPIE work in 2021 revealed that this was an acceptable and viable format, but with the caveat that it needs to come from a known and trusted source.

NHS primary and secondary care settings offer the opportunity to recruit a diverse cross-section of the UK population in terms of age, ethnicity and deprivation, countering concerns of the healthier, less diverse population that can typically be recruited from the blood donor population. For example, NHS primary care conducts the Health Check programme[49], which is offered every 5-years via postal invite to GP registrants aged 40 to 74 years. The Health Check programme has consistently higher uptake within higher deprived populations as well as within underrepresented ethnicities in health research including Indian, Caribbean and Chinese.[50]

3.3.2. Feasibility of invitation strategy

The invitation methods described above have high feasibility based on past use of the infrastructure by prior studies.

The largest UK example of a successful postal recruitment strategy is UK Biobank. Individuals registered with the NHS were invited by post and able to respond via post, internet, or phone to arrange an appointment at an assessment centre. Consent, questionnaire, baseline measurements, and phlebotomy were all conducted at assessment centres that were specially designed and fitted out for this purpose.

NHS DigiTrials is a similar, more formalised process to invite NHS-registered individuals to research studies, which is already demonstrating success with recruitment to the Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial and the Platform Randomised trial of Interventions against COVID-19 In older people (PRINCIPLE) Trial.[51]

We have already demonstrated the feasibility of NHSBT email invitations sent to blood donors in joining Our Future Health and this pilot study is summarised in **Appendix D**. In addition, INTERVAL[52] and COMPARE[53] studies have already successfully demonstrated recruitment of blood

[49] https://www.nhs.uk/conditions/nhs-health-check/
[50] Cook et al (*Int J Equity Health*, 2016) Who uses NHS health checks? Investigating the impact of ethnicity and gender and method of invitation on uptake of NHS health checks. https://pubmed.ncbi.nlm.nih.gov/26791963/
[51] https://digital.nhs.uk/features/nhs-digitrials-already-saving-lives
[52] https://www.intervalstudy.org.uk/
[53] https://www.comparestudy.org.uk/

donors for research studies that use the first 35 ml of blood that would otherwise be discarded for infection control, while the STRategies to Improve Donor ExperienceS (STRIDES) study[54] is also currently successfully recruiting blood donors.

With regards to NHS primary and secondary care, we are conducting discovery work to establish optimal ways in which to recruit from existing hospital outpatient lists, while Born in Bradford[55] successfully recruited participants in NHS GP practices. Our work to date has included PPIE work comprising a series of multi-disciplinary consultations with patients, public, health care professionals and healthcare research delivery teams to understand how Our Future Health would be received and adopted alongside existing research portfolios. We have also had discussions with Genes and Health to identify commonalities in recruitment strategies and optimise invitations to attract a wider cohort of participants.

3.3.3. Invitation development

We will take a theory- and evidence-based approach to the development of our invitation content. Specifically, we will conduct user research to assess comprehension and acceptability of invitations and use randomised online experiments to identify content that maximises response.

For digital invitations, where possible, we will send a limited number of pre-invitation notifications and invite reminders to optimise response rates. This has been validated in the findings from our PPIE work in primary and secondary care and via input from our Public Advisory Board.

To avoid excluding individuals who do not own a smartphone or have lower digital literacy, in addition to postal invites, we will develop the ability to enable hardcopy and telephone completion of the consent form and questionnaires.

3.4. Reimbursement

Our Future Health is committed to the principle of equity in participation and widening access as substantially as possible. One such initiative is offering reimbursement to compensate for the time and costs incurred to participate in Our Future Health. We intend reimbursement to reduce practical barriers to participation, increasing response rates in those who may otherwise be less likely to participate.

Participants joining Our Future Health through via the community route will be offered reimbursement in the form of a £10 voucher once they have completed all the steps to becoming a full participant. In order to be eligible for reimbursement, participants must register, consent, attend a clinic appointment to donate a blood sample, and complete an on-line questionnaire. Once eligible, participants will be required to claim the £10 voucher within a set period, and to then digitally redeem this voucher from the provider within 28 days.

[54] https://www.strides-study.org.uk/
[55] https://borninbradford.nhs.uk/

3.5. Consent

The primary method of consent in Our Future Health will be digital. The consent process starts with information provision which comprises the consent form and the participant information sheet, opportunities for potential participants to have their questions answered, and a formal recording that the individual consents to participate in the Our Future Health research programme. Participants register an account with their contact details either before or at the time of consent so we know who the consent belongs to, and so we can contact that person as part of their involvement in the programme.

We designed the consent and participant information sheet in alignment with the principles set out in our Ethics & Governance Framework, namely that valid consent comprises three components: information, comprehension, and voluntariness. For further details, please see the Ethics & Governance Framework (**Appendix B**).

The consent form and participant information sheet were rigorously co-developed with members of the public in the following forums:

- 18 focus groups with 82 members of the public.
- 4 meetings with a co-design group comprised of 8 members of the public (a different group to the two that informed the design of the leaflet and video scripts).
- 21 user testing interviews with members of the public (who had previously participated in one of the 18 focus groups).

We worked with Claremont and digital agency Kainos on three rounds of user testing (total n=36) of the participant information sheet (along with other parts of the digitally-delivered process including registration form, consent form, and questionnaire completion). We also had input to the first version of the participant information sheet from the Ethics & Feedback Advisory Group as well as other external stakeholders and advisers including national and international experts in consent from academia. The consent form and participant information sheet were approved by the REC and used in the pilots studies. We recently revised these forms again, after feedback from our participants and with consultation and re-review by our governance Boards, including the Public Advisory Board and the Ethics Advisory Board. We also conducted individual user testing interviews with nine members of the public.

The consent includes the ability to recontact participants, so we can invite them to complete additional questionnaires, provide further samples, receive personal health-related information, and consider invitations to enrol in future (stage 2) studies that will have separate REC-approved study protocols with their own consents and participant information sheets. Some stage 2 studies may recruit participants based on their risk of specific diseases calculated from their self-reported, genetic and/or other health-related information.

We will continue to use our Participant-Reported Experiences Survey (**Appendix C**), which over 900 participants have completed to date, to obtain feedback on the ease and acceptability of the consent process, and as part of our evaluation/analytics and insights.

Individuals with queries can call or email the Our Future Health support centre, which will expand in capacity as our recruitment scales. The support centre will be operated by specially trained staff using an integrated computer system developed for, and dedicated to, Our Future Health. The main functions of the support centre are to:

- Answer questions about consent procedures and the scope of Our Future Health
- Allow questions from potential participants (and their GPs) to be addressed either by the trained call centre staff or, if not possible, by more senior members of the Our Future Health team
- Administer the questionnaire to visually impaired participants, and those who do not or cannot access the questionnaire via the website/digitally

Continued interactions with our participants and the public through the Participant-Reported Experiences Survey and the support centre, respectively, will ensure we can iterate the consent and participant information sheet further, if required, with updates sent to the REC for review and approval prior to deployment.

3.5.1. Participants without capacity to consent

After a participant has consented to be part of Our Future Health, they may subsequently lose capacity (e.g. due to dementia). In such situations we need to balance the ethical requirements to enable access to research participation, as well as protecting vulnerable participants from intrusive or interventional research.

There are two situations where we may become alert to potential changes in capacity:

1. Directly contacted by a representative of the participant
2. From our regular updating of the health information though linkage with national data controllers

For option 1, we will establish a process where we verify the identity of the participant and the legal status of the reporting individual. Once verified we will proceed to our loss of capacity process detailed below.

Option 2 is complex since there are no codes in the medical record which indicate loss of capacity either temporarily or permanently. There are some medical conditions in which loss of capacity is more common and these include: strokes, dementias, and traumatic brain injury. Using only diagnosis codes can be misleading since this is not the same as loss of capacity. Studies have reported that individuals diagnosed with stroke, mild-moderate dementia, and traumatic brain injury results in a 2%[56], 26%[57] and 47%[58] likelihood, respectively, of lacking capacity to consent within a year of diagnosis.

We do not yet know if it is possible to develop an algorithm that can accurately predict who has lost capacity using clinical codes due to the following points:

1. Discovery and validation of an algorithm requires formal assessments of capacity in identified participants.

[56] Pendlebury ST. Stroke-related dementia: Rates, risk factors and implications for future research. Maturitas. 2009;64(3):165-71.
[57] Guarino PD, Vertrees JE, Asthana S, Sano M, Llorente MD, Pallaki M, et al. Measuring informed consent capacity in an Alzheimer's disease clinical trial. Alzheimers Dement (N Y). 2016;2(4):258-66.
[58] Thornhill S, Teasdale GM, Murray GD, McEwen J, Roy CW, Penny KI. Disability in young people and adults one year after head injury: prospective cohort study. BMJ. 2000;320(7250):1631-5.

2. Capacity is a temporal and decision-specific assessment with considerable heterogeneity between patients with the same diagnosis, which increases the risk of any algorithm of inappropriately excluding individuals from research.

We therefore propose that, once we have obtained linked healthcare data, we collaborate with other research programmes to propose a research study to develop a loss of capacity algorithm. This algorithm would be based on broad clinical codes (ICD, Read, SNOMED) and would require formal capacity assessments to be conducted. If a validated algorithm with high positive predictive value and sensitivity in identifying individuals who have lost capacity can be developed, we will explore the appropriateness of using it to identify participants who should proceed through our loss of capacity process. This will require careful interpretation of the Mental Capacity Act, and engagement with participant representatives.

3.6. Baseline questionnaire

We have developed a baseline questionnaire to capture health and lifestyle factors that would be difficult or impossible to obtain from data linkages. This questionnaire was developed largely by a core scientific advisory team and was intended to align closely to existing large epidemiological cohorts, such as the UK Biobank. We went through a process of cognitive testing with Our Future Health participants to refine how questions are asked and understood. The baseline questionnaire collects information on demographics, socioeconomics, physical activity, lifestyle exposures, family history, medical history, depression and anxiety, medications, and supplements. It takes, on average, 35 minutes to complete. This initial version of the baseline questionnaire was previously approved by the REC and was used in pilots conducted in 2021, in which we collected complete questionnaire data on over 1,500 people (report of pilots attached as **Appendix D**).

Piloting, additional cognitive testing, and internal scientific review has enabled us to identify and design improvements to the baseline questionnaire as well as expand slightly on health and family history sections. The changes have been reviewed by the Scientific Advisory Board and are included in **Appendix E**.

From our pilot studies, we know that 95% of participants who start the baseline questionnaire complete it. During early phase recruitment, we will test whether deploying the questionnaire before or after phlebotomy has significant effects on attaining full recruitment of an individual, defined as provision of consent, completion of the baseline questionnaire, and donation of a blood sample.

3.7. Short baseline questionnaire

We will develop a short version of the questionnaire. This will be a shortened list of the already-approved questions from our baseline questionnaire. There will be no additional items or new question types.

The items that comprise the short questionnaire will be selected by:

1. Data reduction approaches
   Where several items have been included to measure the same underlying phenotype, we will identify cardinal items for inclusion in short questionnaire using data reduction approaches.

We will use pilot data to examine the internal validity (Cronbach alpha) of any related items. We will establish inter-item correlations and perform factor analyses to establish the overall fit, factor scores and item loadings. We will iteratively drop less well performing items and re-evaluate internal validity using Cronbach alpha and factor analyses until we find the minimum number of items that can be used to index the underlying outcome.

2. Stakeholder input
   We will review the results from this data driven approach with stakeholders including our scientific advisory board and participant advisory board. We will collect input from stakeholders on priorities for retention and outcomes or items that do not represent immediate priorities for healthcare research.

3. Testing and piloting
   We will pilot the resultant shorter questionnaire with members of the public to establish whether the time taken to complete meets our length criteria (<10minutes) and to ensure it is being understood and is generally acceptable to participants.

When we have a satisfactory short questionnaire, we will test it against the longer baseline questionnaire to establish whether rates of conversion to full participant (consent + blood sample + questionnaire) are improved. The short form questionnaire may enable a streamlined, in-person, full participant recruitment model to be deployed in the field, if desired or required. Any participants who complete a short core questionnaire will be asked to provide responses to the remaining questions from the primary baseline questionnaire after recruitment.

3.8. Phlebotomy and physical measurements

We will record physical measurements and collect a blood sample from each consented participant at an in-person appointment in one of the following settings:

1. Community covering pharmacies, mobile units, and 'pop-up' clinics
2. Existing NHSBT appointments for blood donations
3. Existing NHS appointments for health care phlebotomy

Participants will have a choice in where they donate their blood and undergo a brief physical assessment. Location choice will largely be within the community route (pharmacy collaborations, Our Future Health mobile units and 'pop-up' clinics). If the participant has been recruited through an NHS route, then they will likely automatically be in an existing phlebotomy route such as blood donation, or primary or secondary health care.

As general practice, two vials of blood will be drawn from participants. However, up to five vials of blood could be taken for purposes such as quality control or where samples may be unusable. Blood samples will be used to extract DNA and conduct genotyping, as well as conduct baseline assessments of cholesterol and HbA1c and will be sent to our biobank for long-term storage. At all opportunities the blood collection time and date, and time of last significant meal will be collected at the time of blood draw. Physical measurements will also be taken at this time including blood pressure, height, weight, and waist circumference.

Point of care testing (POCT) for cholesterol will also be offered to participants at their clinic appointment. The cholesterol test will be performed using a finger-prick blood test with the Mission POCT device, which is approved for use by the NHS. Whilst all participants will have the

option of receiving the results of their POCT on a proforma, alongside other physical measurements taken at the appointment, these measurements are taken for research purposes only –not clinical or diagnostic purposes and are not a personal health check/substitute for the NHS Health Check.
Advice to participants about their cholesterol reading will be explained in the proforma given to them at the clinic appointment, with their result recorded. For participants who receive a cholesterol reading greater than 9 in the first test (or greater than 7.5 if under the age of 30), a repeat test using the same device will be performed. Participants will only be directed to inform their GP if the measurement of their total cholesterol (after a repeat test in the same appointment) is greater than 9.0 (and they are over 30) or greater than 7.5 (and they are under 30), to enable further work-up for a possible diagnosis of familial hypercholesterolaemia unless any of the following apply:

- They have had an NHS Health Check in the last 5 years.
- They are having yearly checks for heart disease, stroke or diabetes.
- They remember having their cholesterol measured in the last 2 years.

In each of the above cases, participants will be informed that there is no need to inform their GP, regardless of their measurement.

Participants will also be directed to visit the following page on the British Heart Foundation website: bhf.org.uk/informationsupport/risk-factors/high-cholesterol, in order to learn more about cholesterol levels and how these can be reduced through lifestyle changes.

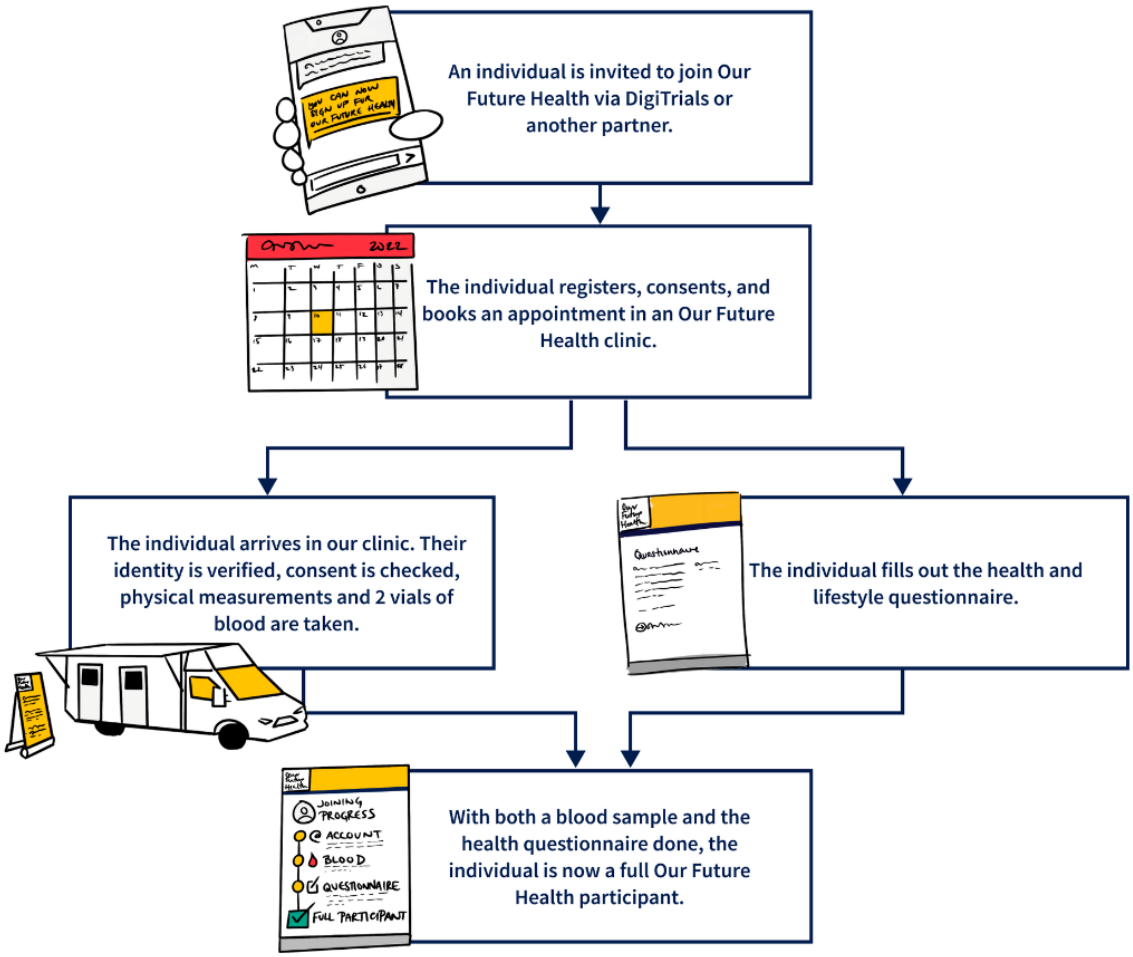
3.8.1. Community routes

We have conducted extensive market research and a viability assessment from which we are confident of being able to conduct phlebotomy and physical measurements outside of the NHS in a cost-efficient manner using pharmacy collaborations, mobile units, or ‘pop-up’ clinics.

Through a booking system, consented participants will be able to book, online or by telephone, an appointment location and time for phlebotomy and physical measurements. By establishing Our Future Health community collection sites, we will have greater control over locations, the participant experience and how we manage consent relative to limitations of working solely within the NHS.

We have benefited from information shared by GRAIL which has recently operationalised the Galleri study, and this has allowed us a greater understanding of, for example, cancellation rates, no shows, and other aspects of user behaviour. Based on our research, our approach is to phase the roll out of the venues, with a lower capacity for the first two months of deployment, which will allow us to learn and adapt the service according to behaviour.

Figure 1. Flowchart of recruitment in community settings

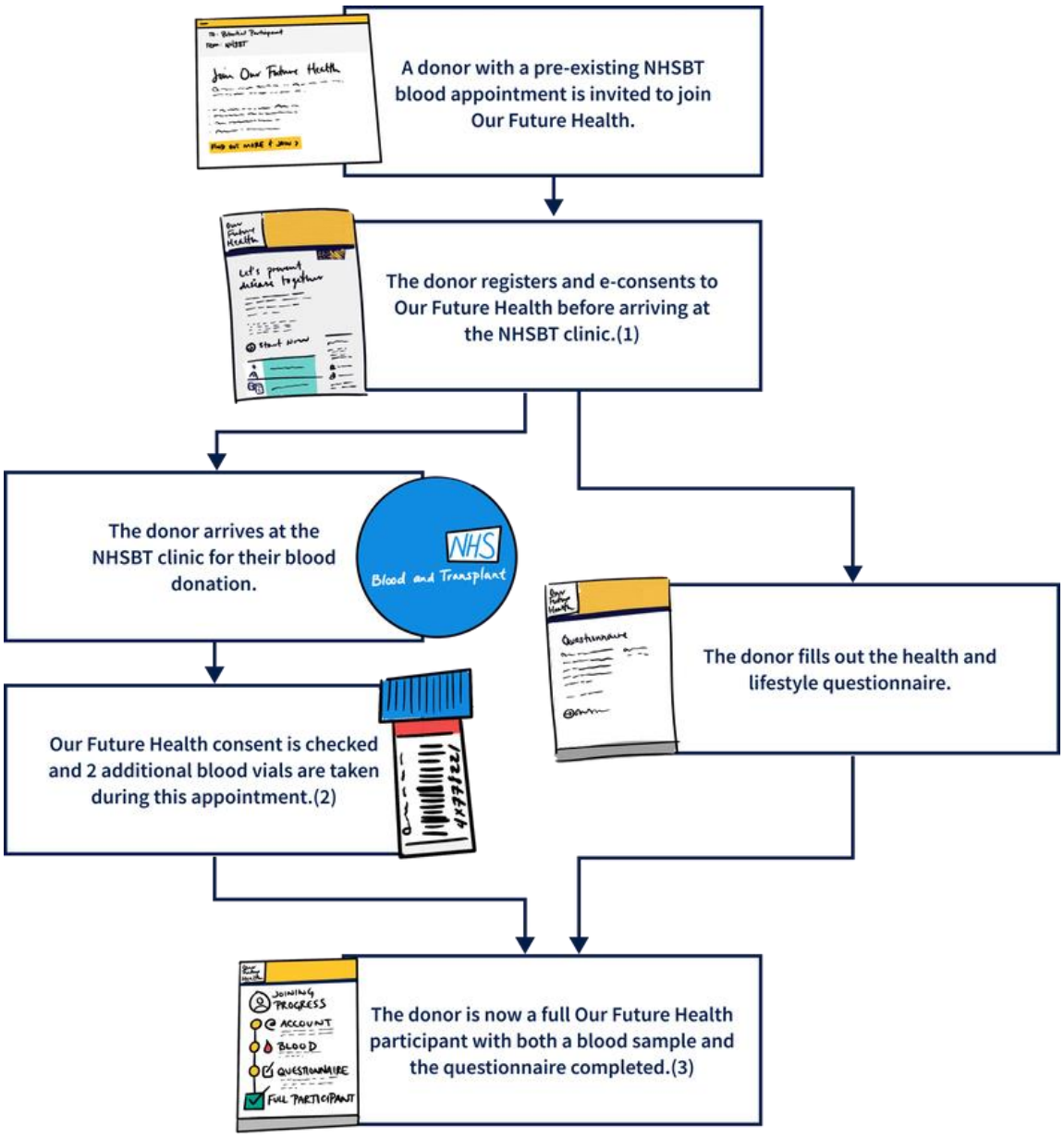


We are also working with community pharmacy groups and the NIHR 'research ready community programme for community pharmacies.' Community pharmacies are an attractive venue with 89% of the UK population being able to access a community pharmacy within a 20-minute walk, with access being greater in areas of highest deprivation. Community pharmacists can also access harder to reach patient populations.

3.8.2. NHS blood donor route

For the NHS blood donor route, following a donor consenting online to Our Future Health, we are now working with NHSBT to optimise the process by which participants are linked with their future blood samples. The goal is to maximise efficiency and minimise friction for both NHSBT and Our Future Health. A flag is created in the NHSBT system to notify phlebotomists of blood donors who have consented to participate in Our Future Health and wish to provide a blood sample at their next donor appointment. Our Future Health regional leads (senior NHSBT research nurses) will support donor carers in implementing this phlebotomy route in the main phase of the programme.

Figure 2. Flowchart of NHSBT recruitment



The participant information materials inform participants that Our Future Health will share specific genetic information about them from their blood sample with NHSBT. This includes red blood cell types, platelet types, HLA subtypes and white blood cell groups. NHSBT will use this information to provide better matched blood and stem-cells for patients. The genetic information will also help NHSBT improve their services. Participants are also informed that Our Future Health will share personal identifiable information about them with NHSBT in order for their genetic information to be linked with their NHSBT donor record.

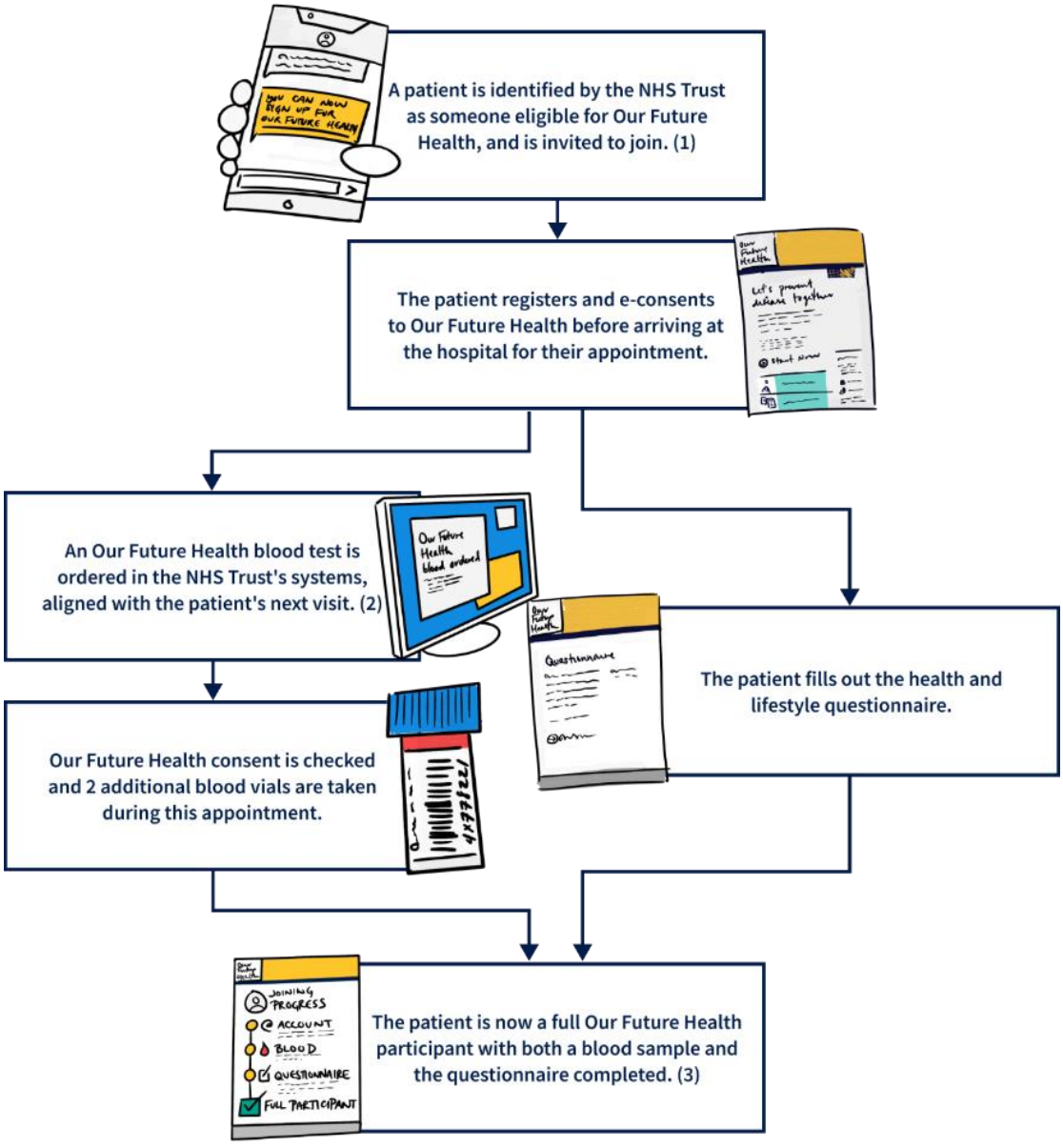
3.8.3. NHS routes

For NHS hospitals, we will utilise existing phlebotomy service infrastructure as a cost-effective and scalable solution for Our Future Health participants to provide a blood sample. For many outpatient department appointments, there is a requirement for patients to give a blood sample for diagnostic or monitoring purposes. There is an opportunity to invite patients scheduled to

attend phlebotomy to consider becoming a participant of Our Future Health and then donating their blood sample during their scheduled medical phlebotomy appointment.

In conjunction with the hospitals, we will develop a specific Our Future Health blood test request within the pathology ordering system. This has been done for other research projects within NHS trusts such as Leeds Teaching Hospital Trust (LTHT). Our Future Health bloods will be requested for all consenting participants and will be collected at the same time as their next routine clinical blood draw. This will minimise any additional burden on NHS phlebotomy services.

Figure 3. Flowchart of the recruitment steps in the context of working with NHS hospitals



We will also have pop-up clinics in NHS hospitals whereby staff, visitors and patients who are not having a routine blood draw can take part in the programme. This is effectively 'the community route in hospitals' and participants will also be able to have physical measurements taken in these pop-up clinics.

4. Blood sample logistics, processing and genotyping

Each participant blood sample will have a unique barcode label which will be linked in Our Future Health's system to participant ID and personal data. Blood samples will be sent overnight at ambient temperature and centrifuged within 24–30 hours at the country-specific processing facility to fractionate the blood. DNA will be extracted from buffy coat before being genotyped using a custom genotype array. Aliquots of plasma, buffy coat and residual DNA will be sent to our ultra-low temperature biobank for long-term storage.

We will design the blood sample logistics, processing, and genotyping pipeline with flexibilities, redundancies, and integrations throughout. Quality management, quality control and data security will be embedded in this pipeline with a variety of security standards and ISOs requiring certification or self-declared conformity. This pipeline will deliver the real-time throughput needs of Our Future Health and will provide quality-checked, called genotype data that will flow back to Our Future Health via a secure API.

We will conduct imputation on the genotyping data to expand the number of genetic markers using UK reference panels. Imputed genotypes will help us to deliver each of our programme's four specific aims, providing a resource for basic and translational research, as well as the basis for generating integrated risk scores and other genetic information which may be returned to participants. To ensure that this information can be generated, offered and delivered to participants who choose to receive it in a timely manner, this bioinformatics pipeline will include the calculation of polygenic/integrated risk scores. This will enable the programme to be able to offer such information to participants as well part of the ways in which participants can be identified and subsequently invited to join additional studies, each of which will have their own REC approvals and materials.

4.1. Repeat blood samples

There are strong scientific rationales for collecting repeat blood samples. These include the ability to investigate:

- Age-specific biomarker thresholds to improve risk prediction or provide individualised baseline levels
- Age-specific biomarker changes to improve risk prediction or provide for proxy endpoints
- Specific time-windows proximal to disease when the likelihoods of earlier detection and improved intervention are high
- More accurate classification through correction of regression-dilution bias
- Random variation and patterns of variation (e.g. seasonal, menstrual, etc.) of biomarkers in healthy, asymptomatic and symptomatic patients
- Natural history of disease
- Discover biomarkers in a disease course that are predictive of treatment response

We are committed to collecting repeat blood samples to cover this research gap. Repeat blood samples will enhance the resource, broaden scientific opportunities, and help future-proof the scientific utility of the Our Future Health programme by enabling diversity and evolution of the types of blood samples collected.

We will continue to work with all stakeholders – including our participants and all of our boards outlined in the attached Governance Manual (**Appendix F**) – to design and deliver a programme of repeat blood samples.

5. Data linkage

Linkage to health-related data is a central component of the Our Future Health programme, forming part of the core cohort dataset. We will link to and/or store data that is controlled by third parties, and provide that data in de-identified form to researchers. Agreeing to link to data held by third parties will be a requirement of joining the programme.

5.1. NHS data linkages

We will link all Our Future Health participants to the country-specific central demographic register. This will confirm electronic identification of the participant and enable the first high priority set of data linkages that will include primary care, secondary care, cancer data, and death data.

Demographic registers for the UK include the Personal Demographics Service (PDS; England), the NHS Central Register (NHSCR; Scotland), the Welsh Demographic Service Dataset (WDSD; Wales), and the Health and Social Care Northern Ireland (HSCNI; Northern Ireland). Once a participant is linked with the demographic register this will enable us to search priority linkage datasets for any records each participant may have.

High-priority NHS datasets for the Our Future Health programme include:

a. **Primary care data:** General practice data are an essential component of our programme to provide a detailed picture of a participant's health. These data include exposures, phenotypes, diagnoses, and prescriptions/dispensing of medicines.
b. **Secondary care data including hospital admissions:** Secondary care data provide detailed records of hospital outpatient and inpatient visits, surgeries, and procedures that are an essential component of understanding a participant's health status, diagnoses, and progression/regression of disease.
c. **Cancer registration data:** Cancer registration provides almost complete capture of cancer diagnoses in the UK. These datasets provide patient and tumour level information including pathology reports, molecular testing results, treatment records, and hospital activity records.
d. **Death registration data:** Vital status, date of death, underlying cause of death, and contributory causes of death are essential data for any study within the Our Future Health programme.

We anticipate that following these high priority NHS data we will also explore linking to disease/service specific registries (e.g. cardiac disease, kidney disease, intensive care), coronavirus infection, coronavirus vaccination, imaging (e.g. Diagnostic Imaging Data Set [DID]), costings, pre-cancers (e.g. UK National Barrett's Oesophagus Registry [UKBOR]), and maternity (e.g. Maternity Services Data Set [MSDS]) amongst others.

5.2. Other linked data sets

Once the initial high priority set of linkages have been completed, we will further explore additional linkages to datasets such as census, education, welfare, employment, environment etc. Our ambition is to build a complete picture of health in our programme to enable comprehensive research studies to be conducted.

6. Feedback of health-related information to participants

6.1. Background to issues around feedback

In any new longitudinal cohort study, decisions need to be made about whether and how any personal results or data are to be made available to participants. These may include lifestyle-based findings, results from physical measurements, imaging, analysis of biological samples or genetic results, or indeed all the (raw) data that is obtained about a participant.

Debates around whether and how personal genetic results should be returned to research participants is not new. In 2013, the American College of Medical Genetics (ACMG) released its recommendation that secondary findings from a list of (at the time) 56 genes should be offered to research participants having clinical exome or genome sequencing.[59] In 2014, the Clinical Sequencing Exploratory Research (CSER) Consortium and the Electronic Medical Records and Genomics (eMERGE) Network in the US agreed that, in most circumstances, if results meet an actionability threshold for return and the research participant has consented to return, genomic results, along with referral for appropriate clinical follow-up, should be offered to participants.[60]

In recent years, it has also been argued, in the context of clinical trials, that research participants should be empowered to have ownership of their own data.[61]

6.2. Rationale for participant feedback

We will offer participants feedback of personal health-related results (including lifestyle and genetic results) if they wish to receive them and consent to feedback. The rationale for offering feedback is that:

1. It is useful for participants to have received some specific personal disease risk results if they are to be approached for risk-stratified enrolment in deep phenotyping and/or risk-stratified prevention trials.

2. It will provide the opportunity to provide much-needed empirical evidence on the delivery and outcomes of novel types of risk information that will provide valuable insights to inform healthcare delivery and policy.

3. It may be a reasonable 'value exchange' for at least some participants who might see feedback as a personal benefit from taking part.

[59] Green et al (*AJHG*, 2013) ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. https://www.nature.com/articles/gim201373.
[60] Jarvik et al (*AJHG*, 2014) Return of genomic results to research participants: the floor, the ceiling, and the choices in between. https://www.sciencedirect.com/science/article/pii/S0002929714001815
[61] S Terry & P Terry (*Science Translational Medicine,* 2011) Power to the people: participant ownership of clinical trial data. https://stm.sciencemag.org/content/3/69/69cm3.short?casa_token=Fxcu6zimlKcAAAAA:BJdgYy7NtgZc18chJ-nTpFOhfW7KYaR5sCcV49j8XB7eLv5qO9FLr-jJlVmlZhHEwLvEWe9xr3X_iw

6.3. Framework for participant feedback

The Ethics and Feedback Advisory Group (EFAG) considered the issue of feedback in considerable detail. They highlighted a number of important considerations which form a framework for how we will develop a feedback policy:

1. It is good practice that there should be immediate feedback of key results from measurements at recruitment, for example, BMI or blood pressure. However, while the concept of providing clinically significant feedback on an ongoing basis to participants may initially be attractive, the practicalities should not be underestimated.

2. Providing personal health information of uncertain clinical validity or utility should be approached with caution, and recommends it should only be provided if participants give additional, specific consent to receive it.

3. There needs to be consideration of any feedback offered to participants on the resource implications for the NHS (GPs in particular) and that even a few cases of confusion or anxiety could lead to a damaging public impression of Our Future Health.

4. Providing access to the raw data about themselves (either on request, or routinely) can appear attractive, though can be problematic and care should be taken in considering interpretation. Providing access to vast amounts of uninterpreted information creates a risk that erroneous medical implications will be deduced, and leave participants overwhelmed and vulnerable.

5. It should not be assumed that everyone will be motivated by receiving individual feedback and therefore the offering should be carefully piloted and revisited and refined over the course of the cohort.

Guided by the Ethics and Feedback Advisory Group, our founding principles for how we approach all individual-level information access, including genomic information, include: providing participants with a choice; assessing the benefits and harms; having an explicit purpose for providing feedback which can be clearly explained to participants; careful communication; and ensuring adequate long-term clinical support for those receiving individual-level genomic results.

We recognise the challenges and complexities associated with providing information to participants. It will require extensive consultation, exploration, and discovery with our governance boards and members of the public to formulate a policy and procedure. It will need to be pilot tested before being widely deployed and be shown to contribute to the health maintenance of participants, while not contributing unsustainably to primary or secondary care workloads.

We will submit a future amendment detailing our approach to providing individual-level genomic information to participants.

6.4. Examples of participant feedback

Below are some examples of the types of feedback that are being considered:

(a) Questionnaire insights are under development and may include comparisons to healthy recommendations, comparisons to the population, as well as resources participants may wish to consult.

(b) Baseline physical measurements (blood pressure, height, weight, waist circumference) as well as baseline blood measures of cholesterol. These measurements are not intended to be a 'health check' and are not, for now, shared with their GP or the NHS. However, we are working with the NHS and the Office for Health Improvement and Disparities to explore potential options for sharing these data with the NHS in the future. We will provide written feedback to participants about their blood pressure, heart rate, and cholesterol (from a POCT/ 'finger-prick' test) on a proforma with advice to contact NHS 111, a Pharmacist or GP in the rare circumstances where that is necessary or if they have e(i.e measurements that warrant medical attention immediately or within days e.g. a very low heart rate). For the vast majority of results, we will also direct participants to the NHS website on blood pressure, and the British Heart Foundation website on cholesterol where they can obtain further information and advice.

(c) Being approached by NHSBT if their genotypes suggest that they have less common minor blood group antigens that are underrepresented among NHSBT blood donors. This may be particularly beneficial for minority groups for whom NHSBT sometimes has difficulty providing optimally matched blood products.

(d) Providing participants with increased access to information stored in their NHS health care records.

(e) Integrated risk scores that provide disease risk estimates. Leading integrated risk score candidates that may initially be feedback to participants include cardiovascular disease,[62] age-related macular degeneration, glaucoma, and type II diabetes. Each of these integrated risk scores provides good risk prediction and are clinically actionable.

(f) Other examples include risk predictions based on common genetic variants associated with risk of iron overload, deep venous thrombosis, or that influence the efficacy or side effects of prescription drugs.

6.5. Assessment of outcomes of participant health-related feedback

One of the key rationales providing participants with health-related feedback is to provide valuable insights into the delivery and outcomes that can inform healthcare delivery and policy. As the Ethics and Feedback Advisory Group noted in the Ethics & Governance Framework (page 27), there has been very little research to explore the implications or value of receiving research findings, and Our Future Health has an opportunity to provide evidence and set best practice.

[62] Natarajan et al (*Circulation*, 2017) Polygenic Risk Score Identifies Subgroup With Higher Burden of Atherosclerosis and Greater Relative Benefit From Statin Therapy in the Primary Prevention Setting https://www.ahajournals.org/doi/full/10.1161/circulationaha.116.024436

In the genomics field, examples of the limited research in this area include the Mi-Genes study in the US[63] and the FinnGen study in Finland.[64]

We are developing a plan for the assessment of participant-reported outcomes and experiences of receiving individual-level information (e.g. distress, anxiety, comprehension, medication initiation/adherence, 'lifestyle' behaviours) as well as for assessment of health care recorded outcomes (e.g. medication prescribing, hospital appointments, cholesterol levels).

[63] Kullo et al (2016) Incorporating a Genetic Risk Score Into Coronary Heart Disease Risk Estimates Effect on Low-Density Lipoprotein Cholesterol Levels (the MI-GENES Clinical Trial. https://www.ahajournals.org/doi/full/10.1161/CIRCULATIONAHA.115.020109

[64] Widen et al… Ripatti (18 September 2020, medRxiv) Communicating polygenic and non-genetic risk for atherosclerotic cardiovascular disease - An observational follow-up study. https://www.medrxiv.org/content/10.1101/2020.09.18.20197137v1

7. Re-contacting participants for future research

7.1. Background on re-contact

Many previous prospective cohorts, including UK Biobank, allow for participants to be re-contacted for further sampling, questionnaires and other activities such as additional studies. However, most previous cohorts have not been set up in a way that allow for participants to be re-contacted on a risk-stratified basis.

For example, although 1% of UK Biobank access applications are to re-contact participants into third-party studies, UK Biobank participants "consented on the understanding that no results would be fed back to them following their assessment visits" and so "care is taken to ensure that re-contact does not represent implicit feedback of which participants are not aware".[65] UK Biobank further states that "recruitment based on genotype or on phenotype that is not explicitly self-reported by the participant is highly restricted".[66]

There is however some precedent for risk-stratified recontact (recall-by-genotype/phenotype) approaches to re-contact, for example in East London Genes and Health (ELGH)[67] (for specific example see ELGH familial hypercholesterolemia 'genotype-first recall' study[68]), and in NIHR BioResource[69] (for specific example see the IBD BioResource Protocol[70]).

7.2. Rationale for re-contacting participants

The development of new diagnostic tests and approaches is often limited by the lack of availability of samples from people with and without a specific disease. Different technologies require different types of samples; standardised, quality-assured processes for sample collection and storage can be critical to evidence generation, yet are rarely assured. In addition, samples collected and processed for one application or technology are often not suitable for others.

The need to establish studies at the scale required, tracking participants and data over long timeframes, whilst maintaining adequate levels of follow-up, limits industry and academic engagement in early detection research. Disease-specific cohorts are difficult to scale and are often not available for a range of other conditions. This is highly inefficient in its use of participants and samples.

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[65] Conroy et al (2019) The advantages of UK Biobank's open-access strategy for health research. https://onlinelibrary.wiley.com/doi/full/10.1111/joim.12955

[66] UK Biobank's re-contact procedures for third party researchers. https://www.ukbiobank.ac.uk/wp-content/uploads/2018/05/ukb-recontactprocs-14.3.2018-item-5b-2.pdf

[67] Finer et al… & van Heel (2019) Cohort Profile: East London Genes & Health (ELGH), a community-based population genomics and health study in British Bangladeshi and British Pakistani people. https://academic.oup.com/ije/article/49/1/20/5555939

[68] ELGH genotype-first recall to study extreme genetic risk of atherosclerotic cardiovascular disease. http://www.genesandhealth.org/research/research-studies-approved/s00013-genotype-first-recall-study-extreme-genetic-risk-atherosclerotic

[69] https://bioresource.nihr.ac.uk/

[70] https://www.ibdbioresource.nihr.ac.uk/wp-content/uploads/2017/01/protocol-V6.pdf

There are two key reasons why a risk-stratified approach to re-contacting participants based on genotype or phenotype will substantially increase the value of Our Future Health as a research resource:

1. Having the cohort risk-stratified for a wide variety of diseases and consented for re-contact based on risk profiles will open up the possibility of enrolling participants at high risk in more detailed secondary protocols involving additional biological samples collection, imaging or other detection methods. This will substantially help improve the potential success of research on early detection, diagnosis, prevention and treatment of disease.

2. Being able to re-contact cohort participants on a risk stratified basis will allow researchers to test hypotheses regarding the benefits of early detection and early diagnosis. Enabling researchers to re-contact participants based on their risk will support research on whether focusing early detection methods such as screening on those at high risk increases their efficiency and cost-effectiveness. Research will also be supported exploring whether preventive measures could be applied before early signs, symptoms or diagnoses of advanced disease.

7.3. Planned approach for re-contact

Our Future Health will recontact participants to invite them to further sampling, questionnaires and other activities such as additional studies which enhance the cohort and are being organised by the programme.

7.3.1. Inviting participants to third party research studies

We are currently developing our Access Process and this includes the specifics of our strategy for re-contact of participants with particular reference to the invites to third party studies. We are working with our Public Advisory Board members to write and define the re-contact policy.

The Access Board will manage applications for researchers (academic or industry) to re-contact participants eligible for further studies e.g. deep phenotyping or prevention trials. A model for this for some genetic disease predisposition variants has been pioneered through the NIHR BioResource with respect to referral to Clinical Pathways.

8. Participant communication and withdrawal

Following recruitment, participants will be able to set preferences related to how they are contacted by the research programme. Participants will be able to decide how they are contacted: by email, by text message or by letter. Participants will be able to choose:

- "Yes, you may contact me"
    - Participants decide how to be contacted (text message, email, letter).
- "No, you may not contact me"
    - Our Future Health will no longer contact participants with the exception of essential service messages (a partial withdrawal).

At the time of consenting, participants will be informed that they can withdraw from the programme at any time without providing a reason. If a user chooses to withdraw from Our Future Health, they will be given two options:

- "No further access"
    - Our Future Health will no longer contact the participant and delete all identifiable data from the participant record
    - Our Future Health will retain permission to use de-identified information and samples provided previously
    - Our Future Health will unlink external datasets, but will retain historical data in a de-identified form
- "No further use"
    - Our Future Health will no longer contact the participant
    - Our Future Health will not obtain any further information on the participant and will destroy all data and samples related to this participant (with the exception of existing models or analyses that were created using their de-identified records)*
    - Data and samples for the participant will not be made available for new research projects.**
    - It won't be possible to remove their data from any research that took place before the withdrawal.

*Participants are told that it may not be possible to trace all distributed sample remnants for destruction. Such a withdrawal will prevent information about them from contributing to further analyses, but it would not be feasible to remove their data from analyses that had already been done.

** Participants are also told that this may not happen immediately as data is made available to researchers in a series of releases; we anticipate that new releases will be made on a quarterly basis. Their data will not be included in new releases but there could be a period of up to three months when their data are included in the current release of the data.

Participants who do not have internet access will contact the Our Future Health support team by telephone to request a withdrawal form. Once received and verified, an approved member of the team will make the required changes in the database and, where appropriate, initiate data deletion and sample destruction.

9. Data access

9.1. General approach and principles

Researchers will apply to the Our Future Health Access Board to access data, samples or to re-contact participants recruited through the research programme. The principles detailed below have been developed with public members of our Access Board, the Ethics Advisory Board and the Founders Board.

Further information about the Access Board, including all of the relevant documents (once approved by the Access Board when it is appointed) will be available on the Our Future Health website.

9.1.1. Key principles guiding access

1. The access procedures will be as simple as possible, and the decisions will emerge in a timely fashion. The objective is to maximise responsible use of the dataset, not to unduly guard it for the benefit of a restricted user group.
2. The key principles underpinning these Access Procedures are the granting of data, samples and/or re-contacting of participants i.e. the Our Future Health 'Resource' to suitable research projects and to ensure that in this manner, the Resource is used extensively, in a responsible and useful way to benefit society as widely as possible.
3. Access to the Resource will be underpinned by the principles of the "Five Safes": safe data, safe projects, safe people, safe settings, safe outputs.
4. The Our Future Health Access Board is responsible for access to the data, samples, and participants. All data policies, access policies, and information relating to how the data is managed and accessed has been made publicly available to ensure transparency and disclosure.
5. These Access Procedures reflect the value of the Resource and the undertakings given to the participants when they joined the programme.
6. Our Future Health will continue to interact with participants, researchers, and society in general to maximise engagement and interest throughout the Resource's lifetime (which is intended to be some decades) and ensure that the research projects that are taking place as well as the findings that result from those projects are publicised with a view to generating further interest and maintaining the initiative's momentum.
7. Researchers who are granted access to the Resource for an approved research project will be required to return their results to Our Future Health and to publish their findings so that other researchers can use and build on this knowledge to further benefit the public interest (public health benefit). Full details will be included in the Our Future Health Publication Policy.
8. In order for a research project to be approved, the Researcher will need to demonstrate that their research will provide knowledge, further scientific understanding and that it meets our definition of public health benefit.
9. The process for applying to use the Resource has been designed to be efficient but robust. Data and/or samples will be provided in an expeditious manner once projects are awarded and the required documentation has been signed and approved, to enable research to begin in a timely manner.
10. Our Future Health will maintain an up-to-date list of Registered Researchers and their affiliations. Organisations conducting research studies will ensure compliance with security and information governance accreditations, as determined by Our Future Health over time.

9.2. Researchers and organisations

The registered researcher process is modelled on 'safe people': researchers are trained and authorised to use data safely. Our Future Health will maintain an up-to-date list of registered researchers and their affiliations. Organisations conducting research studies will ensure compliance with security and information governance accreditations as determined by Our Future Health over time, such as the NHS Data Security and Protection Toolkit. Researchers must not attempt to re-identify individual participants.

Researchers can only undertake their research in a trusted research environment. The results of studies run using Our Future Health will be returned to the Resource.

We will maintain an up-to-date list of registered researchers and their affiliation. Organisations conducting research studies will ensure compliance with security and information governance accreditations as determined by Our Future Health over time, such as the NHS Data Security and Protection Toolkit

9.3. Dissemination of results

Researchers who use Our Future Health will be required to disseminate the results of their research as rapidly and widely as possible, subject to ethics and confidentiality considerations. They will be encouraged to discuss their research findings with other scientists and the public, and to share relevant data and materials as openly as possible. Researchers who have had access to samples will be required to provide details of the assay techniques used and return the results to the Our Future Health resource within 9 – 36 months of approval. A limited delay prior to the return of findings to the Our Future Health TRE will be permitted (depending on the party's membership status, the exclusivity period will be between 9-36 months and will require review by the Access Board) in order to e.g. enable a paper to be published; a patent to be filed; or other competitive advantage to be pursued. Users will be required to undertake to notify Our Future Health in advance of publishing such findings, to acknowledge the contribution of the resource, and to provide a copy of any published reports. In addition, researchers will be required to provide Our Future Health with a copy of all of the results of their research based on the resource (including any negative findings and relevant supporting data) for incorporation into the central database.

9.4. Access agreements and fees

As a condition of access to relevant data (i.e. assay results, physical measures, or questionnaire responses) from the resource, the approved researcher would be required to enter into an access agreement with Our Future Health. Researchers will need to detail the purposes for which they want to use the data, this includes hypothesis-driven and non-hypothesis driven research studies, and standard terms relating to exploitation and dissemination of results.

Similarly, when samples are provided to a laboratory for assays, a materials transfer agreement will require that the samples are used for the agreed purposes only and that the results of the assays are returned to the Our Future Health platform within specified time limits.

Information identifying participants will be removed before any data or samples are released, and the agreements will include an undertaking not to attempt to identify participants. We will generally permit exclusive use of the relevant data set for a limited period from its release in order

to allow time for the approved researcher to conduct and report the agreed analyses. Subsequently, the results will be incorporated into the resource database for use by other approved researchers.

Access to the resource will not be permitted for police use, except where required by court order, and the Our Future Health platform will resist access for this use (in particular by seeking to be represented in all court applications for such access). A system for monitoring compliance with the terms of the access agreement will be put in place before the resource becomes available for access, and a policy developed for dealing with non-compliance (e.g. restrictions on future access).

It is anticipated that a data access fee will generally be charged for access to the Our Future Health platform. This fee will differ between commercial users and academics or charities. The chief aim of this fee will be to cover the costs of any sample and/or data retrieval, preparation and analysis required for the particular research use and to help cover the costs of maintaining the resource for future users. This fee may be waived for initial funders of the programme and will be scaled to ensure those who have contributed are at a financial advantage when accessing the resource compared to those who have not participated in the funding round. The Board will determine a fee structure which, is in keeping with Our Future Health's charitable status. In addition, researchers will be billed their own cloud computing and storage costs within the TRE, as is happening with new TREs set up by UK Biobank and Genomics England. This allows for more intensive research techniques such as machine learning but leaves the choice to the researcher as to how much to spend.

9.5. Trusted research environments

The success of Our Future Health rests on the research and science that is conducted with the data and the cohort, but this must be balanced with strict security and confidentiality commitments we will be making. The best way to balance these needs will be to provide a trusted research environment within which to access de-identified data.

The evolving policy landscape in the UK is moving towards the use of trusted research environments (TREs) as safe shared spaces for data analytics that prevent the data from leaving. The UK Health Data Research Alliance (representing 33 major health data organisations in the UK including UK Biobank, the NIHR BioResource, NHS England, NHS Digital, NHSX, Public Health England, Genomics England and many key hospitals and charities) "is committed to an approach to data access based primarily around trusted (trustworthy) research environments; with appropriate robust and independent TRE accreditation, monitoring and auditing,"[71] and this commitment is echoed in the new UK genomics strategy.[72] NHS Digital have committed to shifting 80% of data access to their Data Access Environment (or other NHS Digital accredited secure data environments) by 2022,[73] and Genomics England have launched a trusted environment for all their researchers to use.[74]

All research will therefore be conducted within an appropriate accredited TRE, and each study will have a separate allocated workspace within the TRE. During the pilot phases we have been

[71] Trusted Research Environments (TRE), A strategy to build public trust and meet changing health data science needs, Health Data Research UK Green Paper, July 2020
[72] Genome UK: the future of healthcare, UK Government Office for Life Sciences, Sep 2020
[73] Improving our Data Processing Services (DPS), NHS Digital, Feb 2020
[74] Genomics England launches next-generation research platform central to UK COVID-19 response, Jun 2020

working with the NHS Digital Data Access Environment as a TRE accessible just to a small number of Our Future Health staff, but we aim to launch our main TRE for approved studies at the end of 2022, with a beta period beforehand. The TRE is the subject of a procurement in 2022, and will be a significant part of our technology stack, providing a wide variety of computation and data storage resources as well as analysis tools for clinical, genetic and other data types, to serve the needs of researchers from many disciplines.

The technical architecture and systems are explained in following sections, but here we illustrate the main approach to enabling research access to data. This must be read in conjunction with the Ethics and Governance Framework.

- Research data will be accessible **within accredited trusted research environments.** A trusted research environment is a secure online environment that allows researchers to access data and perform analysis or computation. No participant-level data can be exported from a trusted research environment.
- Accreditation of a trusted research environment will be **reviewed periodically** by Our Future Health. The accreditation criteria will apply **equally to all research environments**, and will include security, data governance, operational, technical, confidentiality and access control requirements as well as data licensing provisions from data controllers. Trusted research environment accreditation will include requirements and controls from accreditations such as ISO27001 Annex A, and from relevant UK data protection regulations such as UK General Data Protection Regulation (UK GDPR). Controls will assure the environment and its boundary; operational, technical and scientific staff; and organisational processes.
- Access to data held in trusted research environments will be limited to **registered researchers**
- Data will be made available within accredited trusted research environments for research projects that are approved for **fixed and agreed periods of time**
- Trusted research environments will maintain end-to-end verifiable logs of all aspects of their operation, including researcher access and activity; cloud and data usage; and data imports and exports.
- The Our Future Health trusted research environment will be **flexible** in providing a wide range of researcher-friendly tools for data science and analysis, including the ability for researchers to bring **additional datasets, libraries and code,** and scale their use of **chargeable cloud computing and storage**
- Researchers may export **results** from trusted research environments such as aggregate data, summary level statistics, visualisations, parameters and trained models.
- The TRE will have controlled ways to import code, tools, libraries and additional datasets, and to export code, tools and libraries. The export of individual level data is not permitted, but aggregate data, summary level statistics, visualisations, parameters and trained models can be exported. In order to manage this export in a safe way (the “safe outputs” principle from the “Five Safes”), we will initially create an “airlock” process with an airlock manager role to perform manual review, and during 2023 we will be investigating how to create a process that can scale up appropriately.
- We will accredit registered research or healthcare organisations which will enable researchers who are employed or contracted by these institutions to become registered researchers subject to them being verified as a bona fide researcher.

9.6. Data to be shared for research

- All data made available will be robustly **de-identified** to protect the privacy of participants while maintaining its scientific and research value
- Comprehensive **data dictionaries** and metadata will be maintained by Our Future Health and made available for researchers to use. **Provenance** & traceability of all data items will be recorded and made available for researchers
- Wherever possible data will be structured and coded using commonly used **standards to allow for broadest use of the data, in the public interest**
- Participants can choose to **withdraw** from the programme at any time. Ongoing use of their data will be dependent on their individual consent at the point of withdrawal.

9.7. Accreditation of TREs

We are undertaking detailed design work to inform the procurement of our own TRE and the accreditation process for all TREs that will be authorised to hold a copy of the Our Future Health data. As part of this, we are:

- Researching existing accreditation standards and frameworks
- Receiving expert input from data governance, cyber security, and legal experts
- Conducting a consultation exercise with: relevant industry and charity organisations who may wish to apply for accreditation; organisations such as HDRUK and the NHSX Data Strategy team to ensure that we are informed by emerging policy and standards for TREs; other research programmes such as Genomics England and UK Biobank; and other NHS organisations
- Engaging with the public via our Public Advisory Board and through a public consultation
- Working with regulatory and statutory bodies such as the Information Commissioner's Office (ICO) as part of our involvement in the "regulatory sandbox" programme
- Working with our advisory and governance boards
- Engaging with a range of researchers to co-develop functionality and usability to ensure the Our Future Health TRE and tooling delivers against their needs and requirements

We have committed to publishing an initial version of our accreditation criteria in June 2022, and publishing a final version in September 2022.

10. Digital data and platform

10.1. Overview

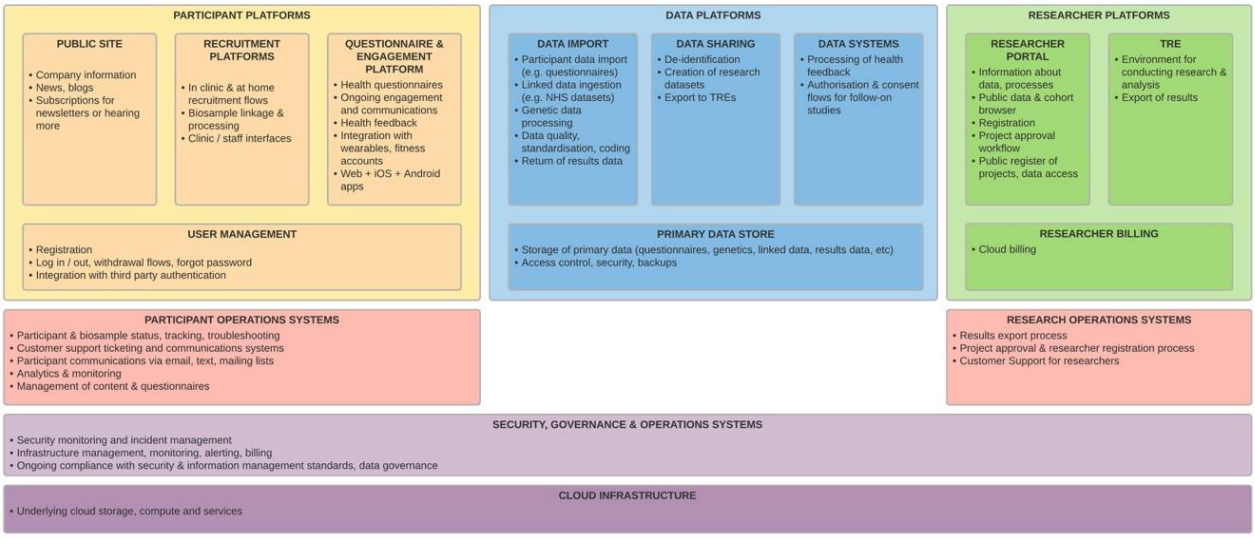
The data that are to be used by Our Future Health are of the highest sensitivity and, as such, need to be handled with the greatest care. Security is a prime concern. It is essential that Our Future Health is compliant with the requirements of relevant legislation, such as the Data Protection Act and the UK GDPR. We will not be able to gain access to the broad range of third-party datasets required, or be able to provide validated research data, if these external requirements are not considered. Key aspects of the controls required include identity and identifier management, ensuring the accuracy of the data collected, inclusion of comprehensive audit data (such as the staff and equipment involved in data collection) and strict controls on data access.

The following sections describe the first post-pilot iteration of the system as envisaged, but do not include the technical design for providing feedback to participants or for recruitment into stage 2 studies. The functionality for these future iterations will be developed during discovery and design phases over 2022-2023.

10.2. Systems architecture

The Our Future Health system is designed to meet the needs of participants, researchers and operational Our Future Health staff, and as such it comprises a number of primary components. The diagram below (**Figure 4**) shows a high-level system map of the components within the Our Future Health architecture (it does not include any partner or external components).

Figure 4. High level system architecture – primary components



10.2.1. Participant platforms

The participant platforms are all the systems facing our participants. They will be scaled as participant numbers grow, and will need to serve the needs of a diverse community. We will aim for an AA standard of accessibility according to the Web Content Accessibility Guidelines (WCAG 2.1) to

ensure we can serve the needs of people with disabilities, and we will be adding an internationalisation layer to allow translations into common UK languages. To quote from the gov.uk Service Manual[75], the WCAG guidelines explain how to make digital services, websites and apps accessible to everyone, including users with impairments to their:

- Vision - like severely sight impaired (blind), sight impaired (partially sighted) or colour blind people
- Hearing - like people who are deaf or hard of hearing
- Mobility - like those who find it difficult to use a mouse or keyboard
- Thinking and understanding - like people with dyslexia, autism or learning difficulties

As per the prior section on freephone information service, we will also offer the ability to complete the questionnaire via telephone.

The recruitment platforms manage the first contact with participants including registration, consent, booking of appointments and sample processing. This will be a flexible set of components to manage multiple recruitment routes with differing flows and requirements (for example, consent could be in a clinic or on a participant's device prior to a visit; there will be different ways to link a sample to a participant in a hospital compared to an NHSBT centre). As well as managing interactions with participants, the Recruitment Platforms will include interfaces for nurses, health assistants and staff in clinics. There will be multiple integrations with recruitment partner systems as well as sample processing labs. These platforms will continue to evolve building on the work we have done in our pilot studies during 2021, and will remain a bespoke set of web applications and outsourced services.

Our public site is our main organisational website and will serve a variety of needs for participants, researchers and stakeholders, providing information about the programme as well as news, and pointers to services for participants or researchers.

The questionnaire & engagement platform will be the long-term system for participants to engage with Our Future Health. It will include comprehensive health questionnaire functionality, ongoing communication with participants via web or app interfaces, the delivery of information or feedback. Any front-end integrations, such as with services for wearable or fitness tracking data, will be via this platform. Over time more modules will be added such as cognitive function testing. This platform is likely to be a customisation of a system we procure during 2022. We expect this platform to include both iOS and Android apps as well as an accessible mobile web experience.

Serving the needs of the platforms above will be a range of user management services including authentication and authorisation, common flows such as email verification and forgotten passwords. This includes the main store of participant login information. It will be connected to other systems using standard API protocols such as OAuth.

The participant operations systems include all of the platforms used by our staff in monitoring and operating the programme. Currently this comprises:

- The Customer Relationship Management (CRM) system can be used to communicate with participants and interested parties, to track the status of sample processing, and to provide operational analytics (it does not contain health data). Currently this is Microsoft Dynamics.

[75] https://www.gov.uk/service-manual/helping-people-to-use-your-service/understanding-wcag

- The Customer Support system is used by the support team to handle incoming questions and requests from participants via phone and email. Currently this is Freshdesk.
- There will be multiple analytics systems to understand metrics and progress. We use Matomo for web analytics at the moment, that maintains participant privacy as information does not leave our cloud environment.
- The Questionnaire & Engagement Platform it will include interfaces for staff to manage content and questionnaires. In addition, our public site includes a Content Management System (CMS) that is currently Wordpress.

10.2.2. Data platforms

The data platforms form the core of our systems, where data is ingested, processed, stored and shared out. None of these systems are accessible to participants or researchers or our own analytics staff – all interfaces are via other platforms. We anticipate that these systems will remain under our control rather than being outsourced, although we will likely procure specific tools or systems as needed.

The primary data store is the storage for participant data: both the data we originate (like questionnaires and genetic data) and linked data we bring in from elsewhere. This component will see a great focus on security and resilience. The primary data store will separately store identifiable participant data and the participant health data, so that the identity of a participant is not stored together with their health data. A unique Participant ID will be allocated for every participant, although this will be purely for internal usage. There will be no access to this data store other than time-limited and audited access by technical systems administration. All data will be stored encrypted and securely backed up to storage considered off-line, within the UK, using public cloud services.

The data import systems will be a number of pipelines that process incoming data from our participant platforms (such as newly consented participants joining the programme, or questionnaire completions), genetic and operational / quality data from our lab partners, connected to linked NHS datasets, results returned from research studies. Our data engineering and software teams will be working on data cleaning, quality, standardisation, coding within these systems.

The data sharing systems will be created to manage important processes used to provision datasets for research for approved studies within TREs, including robust de-identification. A freshly generated Research Participant ID will be created for each participant, with the linkage back to the original Participant IDs only stored within the secure Our Future Health data store and only available to secure internal systems. Further data systems manage participant withdrawals, and will handle flows such as the processing of health feedback, polygenic risk scores or other personalized information for participants, the authorisation and consent needed for stage 2 studies.

10.2.3. Researcher platforms

The researcher platforms are the systems for the research community to learn about Our Future Health, manage registration and study approvals, and gain access and use the TRE.
The researcher portal will be a public web site and set of services with information about the data we have available, documentation about the TRE, the processes for registering and project approval. We anticipate there will be a public version of a high-level cohort browser, to allow researchers to see how many participants could be in a defined cohort (only showing aggregate

data such as participant counts). The process of registering as a researcher and managing the workflow of project approval will happen within this portal. Researchers will be able to log in to this portal to manage their project and gain access to the TRE. The workflow around stage two studies will likely be managed from within this portal. In addition here is where we will be able to show information about approved projects and how data is being used. Finally we will have the environment to support a growing community of researchers, and ways for them to interact with and learn from one another.

Within the TRE, researchers will pay for their own usage of cloud compute and any additional storage they choose to use within their own workspaces. The cloud consumption of all of the users of the TRE will likely dwarf that of the Our Future Health central systems, so this creates a sustainable way for the community of researchers and scientists to grow, and use whichever combination of tools they need to. The researcher billing service will be procured, and we require the supplier to manage the tracking of researcher cloud usage, invoicing, payment processing, and the resulting liability.

The research operations systems are used by Our Future Health staff to operate the research platforms and processes. These will include the management of researcher registration, the approval workflow for studies working with the Access Board, the airlock. There will be a customer support system for researchers, likely through the same platform as used for participant queries, and likely further systems as the research usage of Our Future Health scales.

10.3. Security, governance and operations systems

This layer of the architecture represents systems used by Our Future Health technical staff to operate the various platforms. These will include monitoring, logging, alerting, incident management, billing. In governance terms, this will include policies and processes ensuring compliance with security and data governance standards. We describe our security posture below (section 10.8).

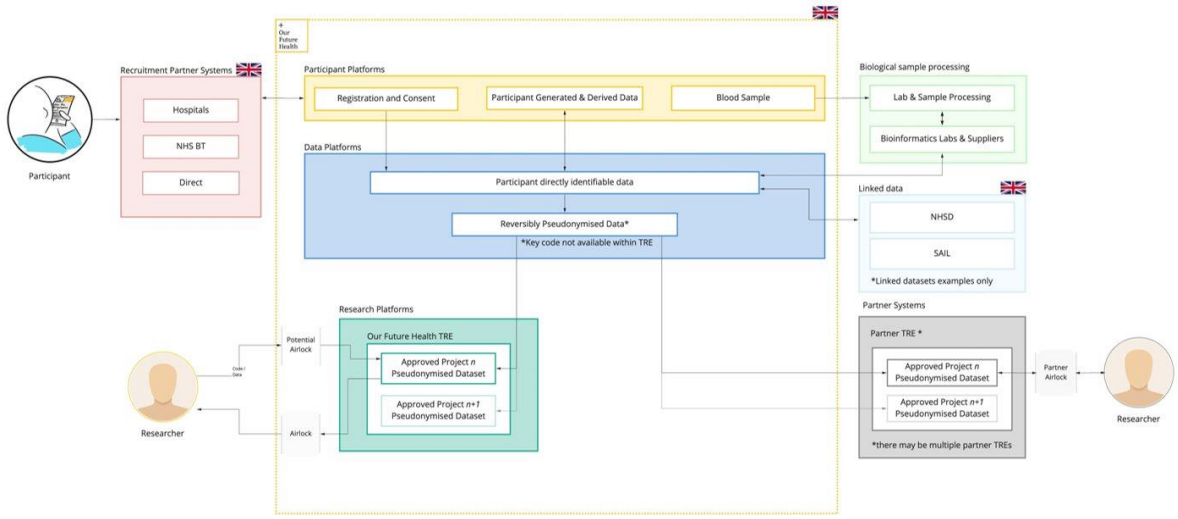
10.4. Cloud infrastructure

This is the cloud compute and storage infrastructure that underlies all of the other services, including the hosting of the primary data store. We will be procuring a provider of public cloud infrastructure during 2022, that will become one of our major technology partners. There will be additional services here such as domain name registration, email sending, certificate management.

10.5. Primary data flows

The figure below (**Figure 5**) illustrates the primary flows of data between the various system components described above and including the journey of blood samples.

Figure 5. High level data flows



10.6. Consent and participant withdrawal

Participant consent is described above (Section 3.4). From a technical perspective the consent functionality is designed to collect and store:

- Date and time of consent
- Site of consent, if at a physical location
- Details of the device, if known (device type, operating system, browser version, IP address)
- Version of the Participant Information Sheet (PIS) provided to the participant at the time of consenting
- Identifying and contact information provided by the individual
- Level of ID verification performed, if at a physical location

A copy of the consent form and participant information sheet will be sent to the participant. Once consent is provided, the participant will be assigned a unique participant ID which will be stored within the system.

Participants will be able to withdraw from the programme at any time as explained in Section 8 above. In the case of the fullest withdrawal option, where a participant has asked that their data and samples be removed, the system will be able to process deletion of participant data from all relevant systems across the architecture. We will commit to remove their pseudonymised data from all future research dataset releases, but it will be retained in research datasets that have already been distributed for approved studies.

System and operational logs will not contain identifiable information and web analytics will be anonymous.

An operational record will be retained of a participant's previous consent and subsequent withdrawal, for audit purposes, only accessible to very limited technical staff.

The deletion process will take place in batches on at least a monthly basis.

10.7. Data linkage

Section 5 above describes the data sets that Our Future Health will be linking with.

From a technical viewpoint, the linking component comprises multiple systems:

- Linkage to central NHS data from England will likely happen within an NHS Digital environment, as part of a pipeline of processes prior to data being loaded into a trusted research environment
- Linkage to other government or NHS data will happen either directly in the Our Future Health cloud environment, within the NHS Digital environment or even within other NHS or government environments, depending on the data sharing agreements and restrictions in place

In either case there will be a partial and iterative process to attempt matching where there is incomplete data, and a procedure for manual intervention and quality control. Over time there will be significant data cleaning and standardisation effort required to deal with differing identity systems across the UK, both different government data sources and the NHS across the devolved nations.

10.8. Security and resilience

Information security is a key concern for the programme. The Our Future Health baseline for cyber security utilises the current ISO27001, Annex A controls across the following domain areas:

- **Information security policies**
  Information security is led from upper management, and clearly communicated across the organisation through policy and process documentation that is regularly updated.
- **Organisation of information security**
  Information security is led and championed by Senior Management.
- **Human resource security**
  Robust Joiners, Movers and Leavers processes, that are linked to appropriate levels of vetting and contractual controls for all staff.
- **Asset management**
  Detailed understand of all applicable business information assets and their owners. Clear guidance in place showing appropriate classification and handling of assets based on sensitivity levels.
- **Access control**
  All access management processes, are based on the concept of least privilege, with systems including Role Based Access Control and detailed audit trails and access review processes in place.
- **Cryptography**
  Where sensitive data is processed, transmitted or stored, appropriately strong cryptography is in place to protect data in transit and at rest.
- **Physical and environmental security**
  Appropriate physical security to protect operational environments, and environmental protection to mitigate threats such as power failure and flooding. Where responsibility is outsourced to third parties such as hosting partners, there should be clear minimum requirements set.

- **Operations security**
  Security controls are built into standard operational processes and Business as Usual, across end user computing, back-office systems and management of online services.
- **Communication security**
  All internal and public network communications are appropriately protected based on their sensitivity, including email and collaboration services.
- **System acquisition, development and maintenance**
  Where services include bespoke development, scripting or customisation a robust development lifecycle is used that includes security at all stages.
- **Supplier relationships**
  Use of supply chain is carefully managed and monitored for all vendors, partners, contractors that are utilised in service delivery.
- **Information security incident management**
  All security incidents are managed through formal process, that includes investigation, root cause analysis and remediation where needed. Learning from incidents will be fully shared to enhance the security program.
- **Business continuity management**
  Business continuity that considers people, processes, systems and locations will be designed, implemented and tested regularly to ensure it is fit for purpose.
- **Compliance**
  All applicable compliance requirements will be monitored and updated based on contractual and regulatory changes, and monitoring of the threat landscape that may identify new requirements.

Our Future Health will achieve Cyber Essentials Plus certification and meet NHS Data Security and Protection Toolkit standards in 2022.

11. Public and participant involvement and engagement (PPIE)

11.1. Rationale for PPIE

Involving the public and participants of Our Future Health in the design and delivery of the programme is vitally important to its success. PPIE is important to Our Future Health as it helps us to:

a) Design recruitment pathways that are feasible, relevant, accessible, and inclusive for the UK public
b) Improve the process of informed consent for participants
c) Improve the experience of participating in Our Future Health
d) Improve the communication of research findings and discoveries to participants, the public and stakeholders and our funding partners
e) Include the voice of people and communities that have traditionally been excluded or omitted from health research.

11.2. PPIE strategy

We are committed to upholding best practice in PPIE, in accordance with the UK Standards for Public Involvement (NIHR 2021). We will do this by adopting the following principles as part of our PPIE strategy:

Clarity:

- Being clear about our definition of PPIE and what it means to Our Future Health.

Oversight:

- Ensuring that important decisions about the participants of Our Future Health are overseen by our PPIE representatives through our Public/Participant Advisory Boards and wider PPIE contributor networks.
- Ensuring that the public/participant voice is represented throughout Our Future Health, with nominated PPIE representatives on advisory boards with additional public/participant representatives invited to help shape our public/participant facing processes.

Transparency:

- Publishing our PPIE charter on our website including details of our PPIE Advisory Board representatives.
- Regularly measuring and evaluating the scale, impact, and value of PPIE activity within Our Future Health.

Opportunity:

- Adopting an inclusive approach to PPIE as an organisation by sharing PPIE opportunities widely on a variety of accessible platforms.
- Supporting our PPIE representatives by providing training and encouraging continuous feedback on our PPIE activities.

11.3. Summary of PPIE work

In 2020-2021, we involved over 200 members of the public in the design and development of the public-facing materials as well as in other aspects of the programme design. Much of this work was carried out with Claremont, a behaviour change communications agency with considerable experience in the health care and health research sectors. Activities included:

- 4 focus groups, 2 co-design meetings and 21 interviews with the public to develop the scientific protocol
- 12 interviews with a variety of stakeholders from charities and existing cohort studies
- 2 focus groups with 11 NHS primary care staff
- 18 focus groups, 10 co-design meetings, 21 interviews with the public to co-develop the participant information sheet, consent form & other public-facing videos & materials
- 21 interviews to understand the role of industry in health research
- 4 focus groups to explore insights around recruitment methods
- 3 focus groups to explore public motivators and feedback preferences
- 1 member of the public attended a REC meeting with a member of Our Future Health staff

Outputs from this work included:

- Co-designed and REC approved PIS and Consent form
- Co-designed explainer videos for Our Future Health (YouTube)
- Public Engagement Strategy (Claremont 2021)

During 2021 we have continued to demonstrate our commitment to PPIE with the following activities:

- 3 focus groups and 4 interviews with members of the public and health care professionals, providing insights into research recruitment in hospitals.
- In-person observations and interviews with patients and staff working in primary care and blood donation sites at NHSBT to learn more about their lived experiences and preferences for invitation into the programme. This work also helped to identify key national PPIE groups and representatives that we needed to build relationships with.
- We have appointed and trained 22 members of the public to our advisory boards and working groups (11 PPIE representatives for the Public Advisory Board, 2 representatives for the Secondary Care Working Group, 2 representatives for the Primary Care Working Group, 2 representatives for the Ethics Advisory Board, 2 representatives for the Technology Advisory Board, and 3 representatives for the Access Board), with a further list of over 40 volunteers for future user testing and PPIE activities.
- Commissioning of a public consultation (with research agency Kohlrabi Consulting) with 34 members of the public. This work helped to provide insights for our communication of access and storage of participant data.
- A PPIE training package for new public representatives

11.4. Development of public-facing materials

We will ensure that public-facing materials for Our Future Health are developed and co-designed with members of the public. As noted above, the written text and scripts for our existing materials were tested and reviewed as part of our PPIE programme. We previously sought REC approval for all the first versions of these written materials (January 2021):

- A short introductory video designed to reach a broad range of mainstream audiences
- Posters to increase awareness of Our Future Health in public spaces including in NHS sites and across a range of community locations
- A short leaflet about Our Future Health designed to be distributed to members of the public
- Invitation letters
- Five 'explainer' videos to support the consent process and make the information provided in the participant information sheet more accessible to potential participants, particularly those with lower reading ages or lower interest in reading written text
- The participant information sheet

11.5. Participant-reported experiences

We will administer a quantitative survey instrument/questionnaire to assess participant-reported experiences (PREs) to understand key indicators such as satisfaction, attitudes and understanding. The participant-reported experience measure (PREM) survey instrument will include the following measures:

- Satisfaction
    - e.g. with the information provided, website, consent process
- Informed choice
    - Attitudes/values
    - Knowledge/understanding
    - Decision
- Communication about the programme to others
    - e.g. family members, friends, GP, other healthcare professional
- Motivation
    - Reasons for taking part and completing various elements of the programme
    - Reasons for booking blood appointments

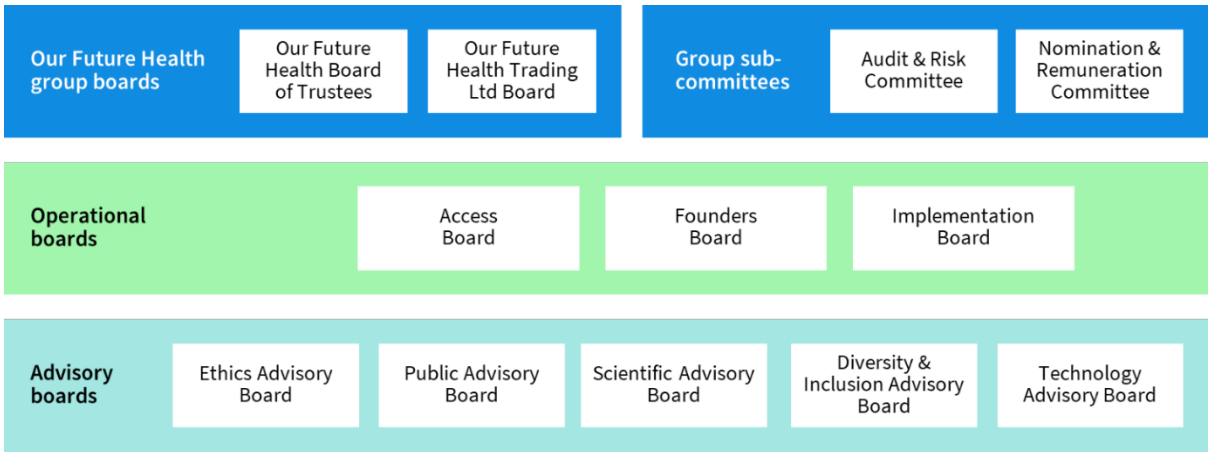
The PREM questionnaire was developed in 2021. We collected participant-reported experiences using the PREM during our 2021 pilot phase. We also conducted in-depth interviews with a subset of participants and active/passive decliners to provide complementary rich qualitative insights on their experiences. The current version of this measure is attached (**Appendix C**). Minor additions may be made to ensure we are accurately capturing participant reported experiences during 2022 recruitment activities. We will continue to conduct qualitative interviews on subsets of PREM questionnaire responders to ensure we complement quantitative findings with a deeper understanding of the participant experience.

12. Governance

The Our Future Health research programme is organisationally complex, receives funding and income through a range of sources and is required to work in partnership with various aspects of the NHS and across all nations of the UK. As such, it is critical that we have an appropriate governance and management structure that enables the programme to take effective and timely decisions, but also provides opportunities for consultation with stakeholders, which requires us to have agile approaches to programme governance. Given the pace of developments both in the genomic, digital, data and analytics areas, the programme must have the flexibility to respond to emerging opportunities and capitalise on innovations and novel research, as well as respond rapidly to new and emergent threats to data security, integrity and participants' wishes.

The programme also requires robust governance to ensure legal compliance, the security of data and privacy of participants, and to meet and exceed the expectations of the participants in order that we create long term relationships with the programme which are built on a bedrock of trust. It is also vital that we build into our plans the ability for participants to have meaningful interactions through the digital interfaces and provide effective support, information and reassurance where required. See **Figure 6**, below:

Figure 6. Our Future Health Governance structure



The governance model comprises a number of advisory and implementation boards. The function of these groups is to advise the Our Future Health Executive Team and the Our Future Health Board. The Access Board will be responsible for access to data, samples and participants and will report to the main Board. From time to time the programme may also establish task-focussed and time-limited working groups, as required. An overview of the governance structure can be found in the Governance Manual (**Appendix F**).

To promote coordination there will be some cross membership between the different governance structures, where this is appropriate; for example, the views of the public and participants will be intrinsic to the skills profile of a number of advisory boards and the Access Board.

Our Future Health

Our Future Health is a company limited by guarantee registered in England and Wales (number 12212468) and a charity registered with the Charity Commission for England and Wales (charity number 1189681) and OSCR, Scottish Charity Regulator (charity number SC050917). Registered office: 2 New Bailey, 6 Stanley Street, Manchester M3 5GS.

Our Future Health

Appendix A: Estimated Numbers of Incident Diagnoses in Initial 2.5-year Follow-up Period of Our Future Health

Appendix A: Estimated Numbers of Incident Diagnoses in Initial 2.5-year Follow-up Period of Our Future Health

Condition	Category	1M	2M	3M	4M	5M
Primary Malignancy – Skin	Cancers	8,050	16,100	24,150	32,200	40,250
Primary Malignancy – Prostate	Cancers	3,620	7,240	10,860	14,480	18,100
Primary Malignancy – Breast	Cancers	3,370	6,740	10,110	13,480	16,850
Primary Malignancy – Lung	Cancers	2,790	5,580	8,370	11,160	13,950
Primary Malignancy – Bowel	Cancers	2,770	5,540	8,310	11,080	13,850
Primary Malignancy – Bladder	Cancers	1,360	2,720	4,080	5,440	6,800
Primary Malignancy – Melanoma	Cancers	1,190	2,380	3,570	4,760	5,950
Non Hodgkins Lymphoma	Cancers	920	1,840	2,760	3,680	4,600
Leukaemia	Cancers	710	1,420	2,130	2,840	3,550
Primary Malignancy – Kidney	Cancers	710	1,420	2,130	2,840	3,550
Primary Malignancy – Oesophageal	Cancers	670	1,340	2,010	2,680	3,350
Primary Malignancy – Pancreas	Cancers	610	1,220	1,830	2,440	3,050
Primary Malignancy – Uterus	Cancers	590	1,180	1,770	2,360	2,950
Primary Malignancy – Oropharyngeal	Cancers	540	1,080	1,620	2,160	2,700
Primary Malignancy – Stomach	Cancers	520	1,040	1,560	2,080	2,600
Primary Malignancy – Ovary	Cancers	500	1,000	1,500	2,000	2,500
Monoclonal Gammopathy of Unknown Significance	Cancers	440	880	1,320	1,760	2,200
Plasma Cell Malignancy	Cancers	430	860	1,290	1,720	2,150
Primary Malignancy – Brain	Cancers	390	780	1,170	1,560	1,950
Myelodysplastic Syndrome	Cancers	330	660	990	1,320	1,650
Primary Malignancy – Liver	Cancers	260	520	780	1,040	1,300
Polycythaemia vera	Cancers	220	440	660	880	1,100
Primary Malignancy – Biliary	Cancers	220	440	660	880	1,100
Primary Malignancy – Mesothelioma	Cancers	190	380	570	760	950
Primary Malignancy – Thyroid	Cancers	130	260	390	520	650
Primary Malignancy – Cervix	Cancers	65	130	195	260	325
Primary Malignancy – Testis	Cancers	60	120	180	240	300

Hypertension	Cardiovascular	49,730	99,460	149,190	198,920	248,650
Atrial Fibrillation	Cardiovascular	13,820	27,640	41,460	55,280	69,100
Stable Angina	Cardiovascular	8,600	17,200	25,800	34,400	43,000
Heart Failure	Cardiovascular	8,580	17,160	25,740	34,320	42,900
Myocardial Infarction	Cardiovascular	7,590	15,180	22,770	30,360	37,950
Transient Ischaemic Attack	Cardiovascular	4,360	8,720	13,080	17,440	21,800
Ischaemic Stroke	Cardiovascular	4,150	8,300	12,450	16,600	20,750
Peripheral Arterial Disease	Cardiovascular	3,920	7,840	11,760	15,680	19,600
Unstable Angina	Cardiovascular	3,750	7,500	11,250	15,000	18,750
Coronary Heart Disease	Cardiovascular	3,580	7,160	10,740	14,320	17,900
Venous thrombolism	Cardiovascular	3,190	6,380	9,570	12,760	15,950
Non-rheumatic Aortic valve disorder	Cardiovascular	3,080	6,160	9,240	12,320	15,400
Pulmonary Embolism	Cardiovascular	3,000	6,000	9,000	12,000	15,000
Multiple valve disorder	Cardiovascular	2,490	4,980	7,470	9,960	12,450
Stroke – not otherwise specified	Cardiovascular	2,420	4,840	7,260	9,680	12,100
Non-rheumatic Mitral valve disorder	Cardiovascular	2,400	4,800	7,200	9,600	12,000
Left Bundle Branch Block	Cardiovascular	2,050	4,100	6,150	8,200	10,250
Right Bundle Branch Block	Cardiovascular	1,980	3,960	5,940	7,920	9,900
Abdominal Aortic Aneurysm	Cardiovascular	1,830	3,660	5,490	7,320	9,150
Raynauds Disease	Cardiovascular	1,770	3,540	5,310	7,080	8,850
Supraventricular Tachycardia	Cardiovascular	1,490	2,980	4,470	5,960	7,450
Atrioventricular Block, first degree	Cardiovascular	1,230	2,460	3,690	4,920	6,150
Intracerebral Haemorrhage	Cardiovascular	930	1,860	2,790	3,720	4,650
Cardiomyopathy – other	Cardiovascular	890	1,780	2,670	3,560	4,450
Pericardial Effusion	Cardiovascular	740	1,480	2,220	2,960	3,700
Secondary Pulmonary Hypertension	Cardiovascular	700	1,400	2,100	2,800	3,500
Rheumatic Valve Disorder	Cardiovascular	680	1,360	2,040	2,720	3,400
Ventricular Tachycardia	Cardiovascular	660	1,320	1,980	2,640	3,300
Primary Pulmonary Hypertension	Cardiovascular	630	1,260	1,890	2,520	3,150
Atrioventricular Block, third degree	Cardiovascular	620	1,240	1,860	2,480	3,100
Dilated cardiomyopathy	Cardiovascular	480	960	1,440	1,920	2,400

Subarachnoid Haemorrhage	Cardiovascular	450	900	1,350	1,800	2,250
Atrioventricular Block, second degree	Cardiovascular	440	880	1,320	1,760	2,200
Sick Sinus Syndrome	Cardiovascular	350	700	1,050	1,400	1,750
Subdural haematoma	Cardiovascular	340	680	1,020	1,360	1,700
Hypertrophic cardiomyopathy	Cardiovascular	130	260	390	520	650
Trifascicular Block	Cardiovascular	110	220	330	440	550
Bifascicular Block	Cardiovascular	90	180	270	360	450
Gastro-oesophageal Reflux Disease	Digestive	21,280	42,560	63,840	85,120	106,400
Diverticular Disease	Digestive	15,440	30,880	46,320	61,760	77,200
Gastritis	Digestive	14,220	28,440	42,660	56,880	71,100
Diaphragmatic Hernia	Digestive	12,670	25,340	38,010	50,680	63,350
Abdominal Hernia	Digestive	11,590	23,180	34,770	46,360	57,950
Oesophageal Ulcer	Digestive	11,410	22,820	34,230	45,640	57,050
Cholelithiasis	Digestive	8,310	16,620	24,930	33,240	41,550
Irritable Bowel Syndrome	Digestive	5,690	11,380	17,070	22,760	28,450
Cholecystitis	Digestive	4,360	8,720	13,080	17,440	21,800
Peptic Ulcer	Digestive	3,640	7,280	10,920	14,560	18,200
Anal Fissure	Digestive	2,570	5,140	7,710	10,280	12,850
Barrett's Oesophagus	Digestive	2,010	4,020	6,030	8,040	10,050
Fatty Liver	Digestive	1,810	3,620	5,430	7,240	9,050
Peritonitis	Digestive	1,790	3,580	5,370	7,160	8,950
Appendicitis	Digestive	1,670	3,340	5,010	6,680	8,350
Pancreatitis	Digestive	1,370	2,740	4,110	5,480	6,850
Cirrhosis	Digestive	1,170	2,340	3,510	4,680	5,850
Alcoholic Liver Disease	Digestive	1,050	2,100	3,150	4,200	5,250
Ulcerative Colitis	Digestive	930	1,860	2,790	3,720	4,650
Liver Failure	Digestive	740	1,480	2,220	2,960	3,700
Anorectal Prolapse	Digestive	680	1,360	2,040	2,720	3,400
Cholangitis	Digestive	650	1,300	1,950	2,600	3,250
Anorectal Fistula	Digestive	610	1,220	1,830	2,440	3,050
Coeliac Disease	Digestive	600	1,200	1,800	2,400	3,000

Portal Hypertension	Digestive	590	1,180	1,770	2,360	2,950
Oesophageal Varices	Digestive	560	1,120	1,680	2,240	2,800
Crohns Disease	Digestive	530	1,060	1,590	2,120	2,650
Volvulus	Digestive	410	820	1,230	1,640	2,050
Angiodysplasia of colon	Digestive	350	700	1,050	1,400	1,750
Autoimmune liver disease	Digestive	150	300	450	600	750
Deafness	Ear	15,010	30,020	45,030	60,040	75,050
Tinnitus	Ear	6,190	12,380	18,570	24,760	30,950
Meniere's Disease	Ear	470	940	1,410	1,880	2,350
Raised Total Cholesterol	Endocrine	36,530	73,060	109,590	146,120	182,650
Raised LDL-C	Endocrine	24,180	48,360	72,540	96,720	120,900
Obesity	Endocrine	16,180	32,360	48,540	64,720	80,900
Type 2 Diabetes Mellitus	Endocrine	13,940	27,880	41,820	55,760	69,700
Raised Triglycerides	Endocrine	13,780	27,560	41,340	55,120	68,900
Low HDL-C	Endocrine	9,740	19,480	29,220	38,960	48,700
Thyroid Disease	Endocrine	7,730	15,460	23,190	30,920	38,650
Diabetes Mellitus – other or not specified	Endocrine	1,030	2,060	3,090	4,120	5,150
Hyperparathyroidism	Endocrine	670	1,340	2,010	2,680	3,350
Polycystic Ovarian Syndrome	Endocrine	370	740	1,110	1,480	1,850
Syndrome of Inappropriate AntiDiuretic Hormone	Endocrine	210	420	630	840	1,050
Type 1 Diabetes Mellitus	Endocrine	100	200	300	400	500
Cataract	Eye	20,500	41,000	61,500	82,000	102,500
Diabetic Eye Disease	Eye	5,700	11,400	17,100	22,800	28,500
Glaucoma	Eye	3,640	7,280	10,920	14,560	18,200
Macular Degeneration	Eye	3,610	7,220	10,830	14,440	18,050
Blindness	Eye	2,030	4,060	6,090	8,120	10,150
Retinal Detachment	Eye	1,080	2,160	3,240	4,320	5,400
Retinal Vascular Occlusion	Eye	940	1,880	2,820	3,760	4,700
Anterior Uveitis	Eye	850	1,700	2,550	3,400	4,250
Ptosis	Eye	810	1,620	2,430	3,240	4,050
Keratitis	Eye	730	1,460	2,190	2,920	3,650

Scleritis	Eye	590	1,180	1,770	2,360	2,950
Erectile Dysfunction	Genitourinary	23,340	46,680	70,020	93,360	116,700
Benign Prostatic Hyperplasia	Genitourinary	9,645	19,290	28,935	38,580	48,225
Acute Kidney Injury	Genitourinary	9,100	18,200	27,300	36,400	45,500
Chronic Kidney Disease	Genitourinary	8,350	16,700	25,050	33,400	41,750
Menorrhagia	Genitourinary	7,780	15,560	23,340	31,120	38,900
Urinary Incontinence	Genitourinary	7,780	15,560	23,340	31,120	38,900
Uterovaginal Prolapse	Genitourinary	5,585	11,170	16,755	22,340	27,925
Postmenopausal Bleeding	Genitourinary	4,055	8,110	12,165	16,220	20,275
Urolithiasis	Genitourinary	3,750	7,500	11,250	15,000	18,750
Obstructive and reflux uropathy	Genitourinary	2,350	4,700	7,050	9,400	11,750
Neuropathic Bladder	Genitourinary	2,330	4,660	6,990	9,320	11,650
Glomerulonephritis	Genitourinary	1,800	3,600	5,400	7,200	9,000
Postcoital Bleeding	Genitourinary	1,580	3,160	4,740	6,320	7,900
Dysmenorrhoea	Genitourinary	1,475	2,950	4,425	5,900	7,375
Endometriosis	Genitourinary	1,250	2,500	3,750	5,000	6,250
End Stage Renal Disease	Genitourinary	950	1,900	2,850	3,800	4,750
Hydrocele	Genitourinary	925	1,850	2,775	3,700	4,625
Endometrial Hyperplasia	Genitourinary	760	1,520	2,280	3,040	3,800
Female Infertility	Genitourinary	730	1,460	2,190	2,920	3,650
Tubulo-interstitial Nephropathy	Genitourinary	700	1,400	2,100	2,800	3,500
Chronic Cystitis	Genitourinary	530	1,060	1,590	2,120	2,650
Male infertility	Genitourinary	250	500	750	1,000	1,250
Anaemia – other	Haem/Imm	13,030	26,060	39,090	52,120	65,150
Iron Deficiency Anaemia	Haem/Imm	9,520	19,040	28,560	38,080	47,600
Agranulocytosis	Haem/Imm	2,230	4,460	6,690	8,920	11,150
Secondary Thrombocytopaenia	Haem/Imm	1,470	2,940	4,410	5,880	7,350
Vitamin B12 deficiency anaemia	Haem/Imm	1,030	2,060	3,090	4,120	5,150
Hypersplenism	Haem/Imm	500	1,000	1,500	2,000	2,500
Aplastic Anaemia	Haem/Imm	490	980	1,470	1,960	2,450
Folate Deficiency Anaemia	Haem/Imm	480	960	1,440	1,920	2,400

Secondary Polycythaemia	Haem/Imm	320	640	960	1,280	1,600
Primary thrombocytopaenia	Haem/Imm	250	500	750	1,000	1,250
Hyposplenism	Haem/Imm	200	400	600	800	1,000
Sarcoidosis	Haem/Imm	200	400	600	800	1,000
Thrombophilia	Haem/Imm	200	400	600	800	1,000
Other haemolytic anaemia	Haem/Imm	110	220	330	440	550
Immunodeficiency	Haem/Imm	90	180	270	360	450
Sickle Cell Trait	Haem/Imm	60	120	180	240	300
Thalassaemia Trait	Haem/Imm	40	80	120	160	200
Bacterial Infection	Infections	24,590	49,180	73,770	98,360	122,950
Infection – Other organisms	Infections	23,180	46,360	69,540	92,720	115,900
Infection – Lower Respiratory Tract	Infections	18,680	37,360	56,040	74,720	93,400
Urinary Tract Infection	Infections	12,360	24,720	37,080	49,440	61,800
Infection – Digestive System	Infections	8,790	17,580	26,370	35,160	43,950
Infection – Skin	Infections	7,040	14,080	21,120	28,160	35,200
Infection – Other organs	Infections	5,370	10,740	16,110	21,480	26,850
Septicaemia	Infections	4,800	9,600	14,400	19,200	24,000
Pelvic Inflammatory Disease	Infections	3,100	6,200	9,300	12,400	15,500
Viral Infection	Infections	3,090	6,180	9,270	12,360	15,450
Fungal Infection	Infections	2,710	5,420	8,130	10,840	13,550
Infection – Ear/Upper Respiratory Tract	Infections	2,460	4,920	7,380	9,840	12,300
Infection – Bone	Infections	860	1,720	2,580	3,440	4,300
Rheumatic Fever	Infections	670	1,340	2,010	2,680	3,350
Infection – Male Genitourinary	Infections	635	1,270	1,905	2,540	3,175
Infection – Anorectal	Infections	540	1,080	1,620	2,160	2,700
Infection – Liver	Infections	500	1,000	1,500	2,000	2,500
Infection – Eye	Infections	350	700	1,050	1,400	1,750
Chronic Hepatitis	Infections	320	640	960	1,280	1,600
Infection – Other Genitourinary	Infections	320	640	960	1,280	1,600
Infection – Other nervous system	Infections	320	640	960	1,280	1,600
Tuberculosis	Infections	310	620	930	1,240	1,550

Parasitic Infection	Infections	220	440	660	880	1,100
Infection – Heart	Infections	150	300	450	600	750
Meningitis	Infections	70	140	210	280	350
Enthesopathy	Musculoskeletal	36,420	72,840	109,260	145,680	182,100
Osteoarthritis	Musculoskeletal	31,380	62,760	94,140	125,520	156,900
Osteoporosis	Musculoskeletal	8,180	16,360	24,540	32,720	40,900
Spondylosis	Musculoskeletal	7,200	14,400	21,600	28,800	36,000
Gout	Musculoskeletal	6,770	13,540	20,310	27,080	33,850
Carpal Tunnel Syndrome	Musculoskeletal	6,490	12,980	19,470	25,960	32,450
Intervertebral Disc Disorder	Musculoskeletal	6,170	12,340	18,510	24,680	30,850
Fracture – Wrist	Musculoskeletal	3,160	6,320	9,480	12,640	15,800
Spinal Stenosis	Musculoskeletal	2,930	5,860	8,790	11,720	14,650
Fracture – Hip	Musculoskeletal	2,840	5,680	8,520	11,360	14,200
Rheumatoid Arthritis	Musculoskeletal	2,650	5,300	7,950	10,600	13,250
Fibromatosis	Musculoskeletal	2,500	5,000	7,500	10,000	12,500
Polymyalgia Rheumatica	Musculoskeletal	2,360	4,720	7,080	9,440	11,800
Scoliosis	Musculoskeletal	1,140	2,280	3,420	4,560	5,700
Collapsed Vertebra	Musculoskeletal	970	1,940	2,910	3,880	4,850
Spondylolisthesis	Musculoskeletal	930	1,860	2,790	3,720	4,650
Giant Cell Arteritis	Musculoskeletal	450	900	1,350	1,800	2,250
Psoriatic Arthritis	Musculoskeletal	420	840	1,260	1,680	2,100
Sjogren Syndrome	Musculoskeletal	240	480	720	960	1,200
Ankylosing Spondylosis	Musculoskeletal	210	420	630	840	1,050
Lupus Erythematosus	Musculoskeletal	210	420	630	840	1,050
Reactive Arthritis	Musculoskeletal	30	60	90	120	150
Migraine	Neurological	5,700	11,400	17,100	22,800	28,500
Peripheral Neuropathy	Neurological	5,510	11,020	16,530	22,040	27,550
Epilepsy	Neurological	1,640	3,280	4,920	6,560	8,200
Chronic Fatigue Syndrome	Neurological	1,600	3,200	4,800	6,400	8,000
Parkinson's Disease	Neurological	1,280	2,560	3,840	5,120	6,400
Diabetic Neuropathy	Neurological	1,260	2,520	3,780	5,040	6,300

Trigeminal Neuralgia	Neurological	1,080	2,160	3,240	4,320	5,400
Bell's Palsy	Neurological	970	1,940	2,910	3,880	4,850
Essential Tremor	Neurological	720	1,440	2,160	2,880	3,600
Autonomic Neuropathy	Neurological	590	1,180	1,770	2,360	2,950
Multiple Sclerosis	Neurological	230	460	690	920	1,150
Motor Neurone Disease	Neurological	170	340	510	680	850
Congenital Septal Defect	Perinatal	290	580	870	1,160	1,450
Depression	Psychiatric	20,000	40,000	60,000	80,000	100,000
Anxiety	Psychiatric	15,610	31,220	46,830	62,440	78,050
Dementia	Psychiatric	5,850	11,700	17,550	23,400	29,250
Alcohol Misuse	Psychiatric	5,740	11,480	17,220	22,960	28,700
Delirium	Psychiatric	1,960	3,920	5,880	7,840	9,800
Substance Misuse	Psychiatric	1,330	2,660	3,990	5,320	6,650
Schizophrenia	Psychiatric	740	1,480	2,220	2,960	3,700
Bipolar Affective Disorder	Psychiatric	620	1,240	1,860	2,480	3,100
Intellectual Disability	Psychiatric	420	840	1,260	1,680	2,100
Personality Disorder	Psychiatric	390	780	1,170	1,560	1,950
Obsessive Compulsive Disorder	Psychiatric	270	540	810	1,080	1,350
Autism	Psychiatric	90	180	270	360	450
Eating Disorders	Psychiatric	60	120	180	240	300
Chronic Obstructive Pulmonary Disease	Respiratory	11,680	23,360	35,040	46,720	58,400
Allergic/chronic Rhinitis	Respiratory	11,130	22,260	33,390	44,520	55,650
Asthma	Respiratory	8,770	17,540	26,310	35,080	43,850
Pleural Effusion	Respiratory	6,610	13,220	19,830	26,440	33,050
Respiratory Failure	Respiratory	4,310	8,620	12,930	17,240	21,550
Chronic Sinusitis	Respiratory	2,740	5,480	8,220	10,960	13,700
Sleep apnoea	Respiratory	2,710	5,420	8,130	10,840	13,550
Pulmonary Collapse	Respiratory	2,470	4,940	7,410	9,880	12,350
Bronchiectasis	Respiratory	1,840	3,680	5,520	7,360	9,200
Aspiration Pneumonitis	Respiratory	1,560	3,120	4,680	6,240	7,800
Nasal Polyps	Respiratory	1,290	2,580	3,870	5,160	6,450

Pulmonary Fibrosis	Respiratory	1,220	2,440	3,660	4,880	6,100
Pleural Plaque	Respiratory	920	1,840	2,760	3,680	4,600
Pneumothorax	Respiratory	800	1,600	2,400	3,200	4,000
Asbestosis	Respiratory	370	740	1,110	1,480	1,850
Hypertrophic Nasal Turbinates	Respiratory	370	740	1,110	1,480	1,850
Dermatitis	Skin	23,300	46,600	69,900	93,200	116,500
Actinic keratosis	Skin	7,760	15,520	23,280	31,040	38,800
Seborrheic Dermatitis	Skin	5,290	10,580	15,870	21,160	26,450
Urticaria	Skin	4,560	9,120	13,680	18,240	22,800
Rosacea	Skin	4,040	8,080	12,120	16,160	20,200
Psoriasis	Skin	3,470	6,940	10,410	13,880	17,350
Acne	Skin	1,850	3,700	5,550	7,400	9,250
Lichen Planus	Skin	1,000	2,000	3,000	4,000	5,000
Pilonidal cyst/sinus	Skin	440	880	1,320	1,760	2,200
Vitiligo	Skin	330	660	990	1,320	1,650
Hidradenitis	Skin	310	620	930	1,240	1,550
Alopecia Areata	Skin	300	600	900	1,200	1,500

Calculations conducted by Ralph Goldacre (University of Oxford) based on Kuan et al (2019) A chronological map of 308 physical and mental health conditions from 4 million individuals in the English National Health Service. The Lancet Digital Health 2019 Vol. 1 Issue 2 Pages e63-e77. Calculations are based on Clinical Practice Research Datalink (CPRD) data using harmonised Read, International Classification of Diseases (tenth revision), and Office of the Population Censuses and Surveys Classification of Interventions and Procedures version 4 codes across primary-care and secondary-care records. Calculations assume a uniform distribution over 5 ten-year age groups (30–79 years) and an equal number of men and women.

Our Future Health

Appendix B: Ethics and Governance Framework

Our Future Health

Ethics and governance framework

Version 2.0
April 2021

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.

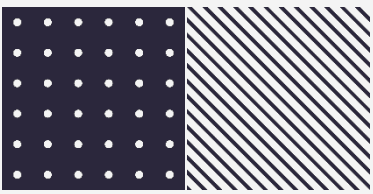
The balance between research and care

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.

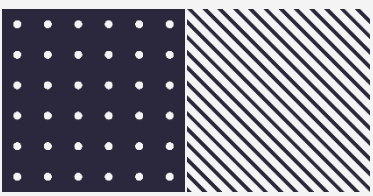
Phase 1 consent will need to be broad, to define the types of research that might be facilitated, and how access will be governed. It should be made clear that the decisions participants may face later could be complex and have significant implications for their lives.

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)

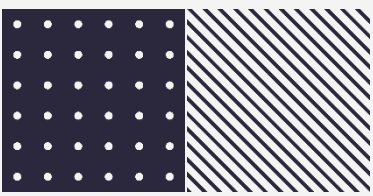
Data stewardship

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

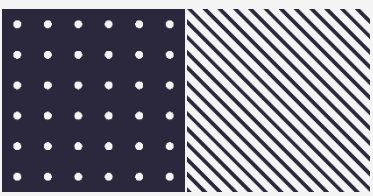
Our Future Health must be governed well and in the public interest. The governance mechanisms should be appropriately constituted, accountable and open to scrutiny. The mechanisms should include a main Board, Scientific Advisory Board(s), an Ethics Advisory Committee and a Participant Advisory Panel. 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/

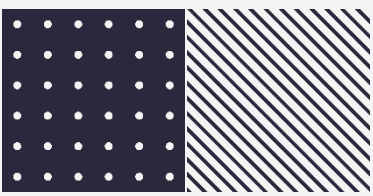
1.2. What is new or different about Our Future Health?

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.

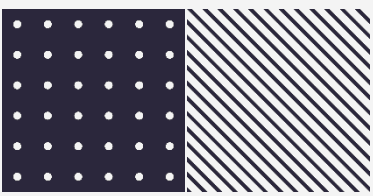
For example, a researcher owes the participant a duty of care which includes:

- 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 participants

[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.

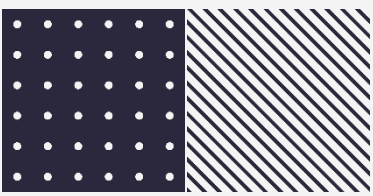
[7] UK Policy Framework for Health and Social Care Research, Health Research Authority (2017).

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.**

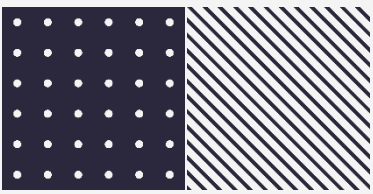
a) Initial (Phase 1) consent
This should allow:

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

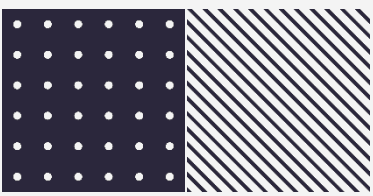
on the number of times a participant can be approached to take part in additional studies. The safety of the proposed research, and issues such as whether they will involve disclosure of personal predictive health information and how that will be managed, will be very important. Our Future Health is 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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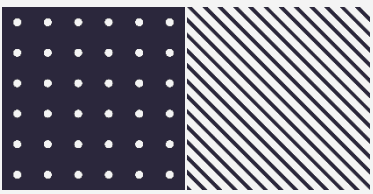
[16] A Thorogood (2019) Return of individual genomic research results: are laws and policies keeping step? European Journal of Human Genetics 27, 535–546 (2019)

[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:

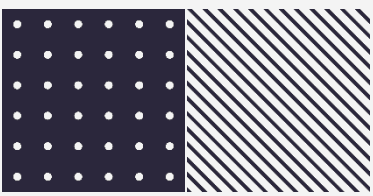
- **On initial examination when admitted to the study.** We consider it good practice that there should be immediate feedback of key results of measurements on recruitment, for example, BMI or blood pressure. Usually only abnormal measurements would be reported, but this may need to be reconsidered if 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

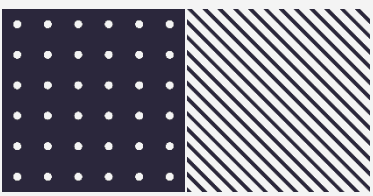
Information about an individual which may potentially be significant to the individual's health, but which has not been validated to the extent of being generally recognised or accepted for clinical use, must be treated with extreme caution. It would not usually be appropriate to give participants individual 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?

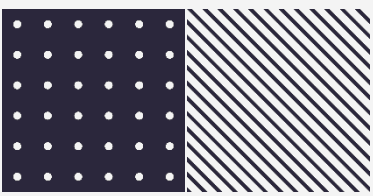
- Is there valid consent? Is the feedback proposed within the boundaries of the expectations for feedback set during the initial (or most recent) consent process?
- What support or interpretation will be needed?
- Who will provide feedback, and how will it be given?
- Will a GP or other healthcare provider 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.

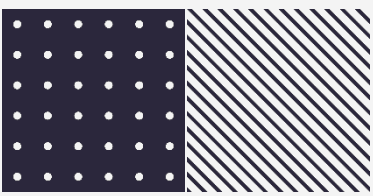
3.5.1. Confidentiality

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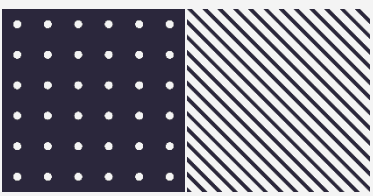
[22] See work by Health Data Research UK: https://ukhealthdata.org/projects/aligning-approach-to-trusted-research-environments/

[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.

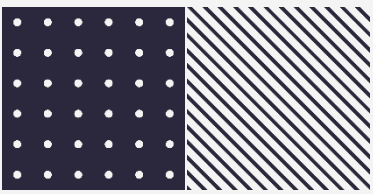
Over the course of the lifetime of the cohort, there is also the potential that the Our Future Health programme might want to link other types of data, for example to add social and lifestyle information that could help build a more comprehensive picture of health or risk of disease. Types of data that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

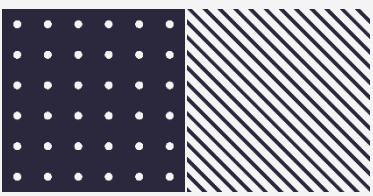
- Where access to data is approved, data must be de-identified and only the minimum amount of data required for the successful completion of the relevant research should be made available.
- Access to biological samples that are limited and depletable should be carefully controlled and coordinated, according 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.

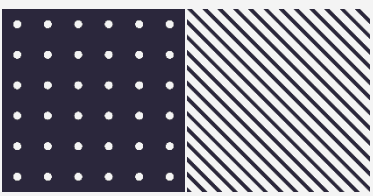
Decisions about limited elements of exclusivity are complex and need careful thought. The public have shown that they understand the need to reward effort but are suspicious of health data being unduly locked away from general research use, particularly by commercial entities. **We recommend that Our 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.

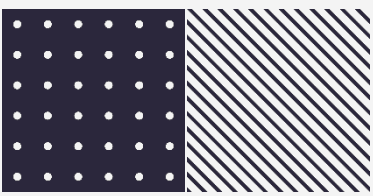
4.2.2. Governance, advisory and control structure

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:

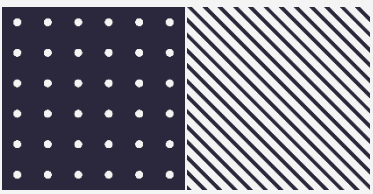
- **Main Board:** Our Future Health is a Charity, established as a company limited by guarantee. The Board establishes the ethos and broad operating principles of the Charity, which is perceived as a public-private partnership providing a resource for researchers to improve health, particularly by developing 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.

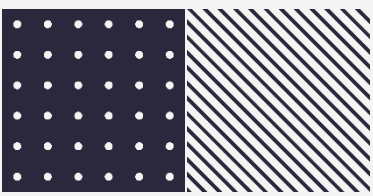
The Access Committee works in the best interests of the participants, and the charity. The skills needed on the committee are determined by the nature of its work. It must make assessments of science quality, probable health impact, and of likely participant views. People with broad experience across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

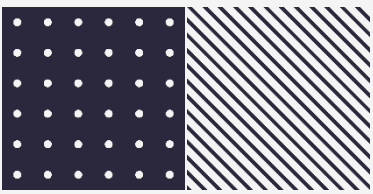
UK biomedical research charities will be approached to become founding partners of Our Future Health. Charities are likely to have a number of different roles, for example: provision of funding, identifying research priorities, supporting researchers seeking access to data for research studies, or funding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

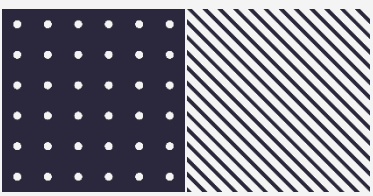
- Industry partners will play an important role in achieving Our Future Health's goals and add value to the work. Commercial involvement should be welcomed, provided it is on terms which are consistent with the overall aims, objectives and values of Our Future Health.

  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.

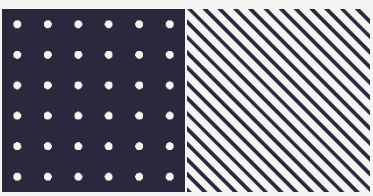
[30] https://www.gov.uk/government/publications/creating-the-right-framework-to-realise-the-benefits-of-health-data/creating-the-right-framework-to-realise-the-benefits-for-patients-and-the-nhs-where-data-underpins-innovation

- 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

***Professor Martin Bobrow, CBE FRS FMedSci – Chair**
University of Cambridge; Wellcome Trust Sanger Institute

Dr Jo Ellins
Senior Fellow at the Health Services Management Centre and Deputy Director of the BRACE Rapid Evaluation Centre, University of Birmingham

Professor Bobbie Farsides, BSc, PhD
Professor of Clinical and Biomedical Ethics at Brighton and Sussex Medical School

Anna Gill, OBE
PPI rep

Professor Anneke Lucassen BMedSci, MBBS, DPhil(Oxon), FRCP
Professor of Clinical Genetics, University of Southampton

Professor Azeem Majeed
Professor of Primary Care and Head of the Department of Primary Care & Public Health at Imperial College London

Dr Richard Milne
Society and Ethics Research Group, Wellcome Genome Campus

Professor Mike Parker
Director of the Wellcome Centre for Ethics and Humanities and Director of the Ethox Centre at the University of Oxford

***Nicola Perrin, MBE**
Founder of Understanding Patient Data, Secretariat to EFAG

Dr Imran Rafi
Chair of the Royal College of GPs Clinical Innovation and Research Centre (CIRC)

***Dr Saskia Sanderson**
Chief Behavioural Scientist, Our Future Health

Jonathan Sellors
Legal counsel, UK Biobank

Dr Fiona Walter
Principal Researcher in Primary Care Cancer Research, Department of Public Health and Primary Care, at the University of Cambridge

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

Our Future Health

Our Future Health is a company limited by guarantee registered in England and Wales (number 12212468) and a charity registered with the Charity Commission for England and Wales (charity number 1189681) and OSCR, Scottish Charity Regulator (charity number SC050917). Registered office: New Bailey, 4 Stanley Street, Manchester M3 5JL.

Our Future Health

Appendix C: Participant reported experience measures

Our Future Health Participant-Reported Experience Measures (PREM) 6-week Follow-Up Survey V2

Summary

The primary aim of the Participant Reported Experience Measures (PREM) surveys is to measure participants' satisfaction with and acceptability of the Our Future Health recruitment process overall, with focus on the consent process and information materials, providing a biological sample and completing the baseline questionnaire. The PREM surveys will provide a key source of quantitative data on acceptability which is a key outcome measure in the pilot studies.

The 6-week follow-up PREM survey measures participants' experiences in 4 modules: 1) Consent process and Information materials; 2) Biological samples; 3) Baseline questionnaire; 4) Overall experience. Each module contains closed-ended questions (depending on level of completion of process) to assess satisfaction with and acceptability of each of these processes in Our Future Health at baseline, plus one open-ended question per module to allow participants to describe their experiences in more detail. There is an additional question at the end to invite individuals to take part in a follow-up interview if they are happy to share their experience in-depth.

The PREM survey will be triggered to be sent via email 6 weeks after consent is gained. The survey will become available for participants on their OFH Dashboard 6 weeks after they consent.

This survey will be revised for the main phase: qualitative interviews, validation testing and the PPI advisory committee/co-design team will help to do this.

Table summary of modules

Module	Who is shown the module	Skip logics/exceptional questions
1. Consent process	All participants	
2. Biological Sample	All participants	
3. Questionnaire	All participants	Q10. ONLY *If answered Q1. Yes response options (yes all of it),(yes most of it),(yes some of it)*
4. Overall	All participants	

[All participants to be invited to complete]

[PREM EMAIL]

Dear [first name],

Recently, you joined Our Future Health, the UK's largest health research programme. We also asked you to complete a questionnaire and give a sample of your blood or saliva.

We are constantly trying to improve the experience of our participants. We would like to ask you some questions about your experiences of being involved in Our Future Health so far. Your feedback will be used to improve Our Future Health for future participants. This survey should take less than 5 minutes to complete.

Click here to start the survey

If you have any further questions, please email our Support Team at support@ourfuturehealth.org.uk or call us on 0808 501 5634 between 9am and 5pm Monday to Friday.

Thank you

[Introduction] Note: Text in square brackets not shown to participants

Recently, you joined Our Future Health, the UK's largest health research programme. We also asked you to complete a questionnaire and give a sample of your blood or saliva.

We are constantly trying to improve the experience of our participants. We would like to ask you some questions about your experiences of being involved in Our Future Health so far. Your feedback will be used to improve Our Future Health for future participants. This survey should take less than 5 minutes to complete.

Consent process and Information materials

1) At the start of Our Future Health, I was told what was going to happen and what to expect
   a) Strongly agree
   b) Agree
   c) Neither agree nor disagree
   d) Disagree
   e) Strongly disagree

2) The information I was given was easy to understand
   a) Strongly agree
   b) Agree
   c) Neither agree nor disagree
   d) Disagree
   e) Strongly disagree

3) I had enough information to make an informed choice about whether or not to take part in Our Future Health
   a) Yes
   b) Partly
   c) No
   d) I didn't have a choice
   e) Not sure

4) Overall, I am satisfied with the information I received before taking part in Our Future Health
   a) Strongly agree
   b) Agree
   c) Neither agree nor disagree
   d) Disagree
   e) Strongly disagree

5) On the following screens, please choose the option on the scale that best reflects your current view of participating in the Our Future Health research programme.

a) Please choose the option that best reflects how negative or positive you found the experience of signing up to Our Future Health.

Negative						Positive
1	2	3	4	5	6	7
○	○	○	○	○	○	○

b) Please choose the option that best reflects how confusing or straightforward you found the experience of signing up to Our Future Health.

Straightforward						Confusing
1	2	3	4	5	6	7
○	○	○	○	○	○	○

c) Please choose the option that best reflects how boring or interesting you found the experience of signing up to Our Future Health.

Boring						Interesting
1	2	3	4	5	6	7
○	○	○	○	○	○	○

d) Please choose the option that best reflects how easy or hard you found the experience of signing up to Our Future Health.

Easy						Hard
1	2	3	4	5	6	7
○	○	○	○	○	○	○

e) Please choose the option that best reflects how slow or quick you found the experience of signing up to Our Future Health.

Slow						Quick
1	2	3	4	5	6	7
○	○	○	○	○	○	○

6) Do you have any other thoughts or comments about signing up for Our Future Health? If so, please use the space below to share your thoughts:
a) free text box

Providing a sample of your saliva or blood

7) Did you book an appointment to provide a sample of your blood (at a pharmacy or mobile clinic for example)?

    - Yes, I did book an appointment
    - No, I did not book an appointment
    - Don't know

[The next question is for those who answered 'Yes, I did book an appointment' or "Don't know' to the question above]

8) Did you provide a sample of your blood?
    - Yes, I did provide a blood sample
    - No, I did not provide a blood sample
    - Don't know

[The next question is for those who answered 'No, I did provide a blood sample' to the question above]

9) Can you tell us why you did not provide a sample of your blood?
    - I was not able to attend my appointment
    - I attended my appointment but was not able to provide a blood sample
    - I don't remember

[The next question is for those who answered 'No, I did not book an appointment' to the question above]

10) Can you tell us why you did not book an appointment to provide a sample of your blood?

    - I was not able to find a time or location that I could attend
    - I forgot to book an appointment
    - I am afraid of needles and donating blood
    - I decided I did not want to provide a blood sample
    - Prefer not to say
    - Don't know
    - Other [free text]

[The next question is for those who answered 'Yes, I did book an appointment' to the question above]

11) On the following screens, please choose the option on the scale that best reflects your experience of booking an appointment to provide a blood sample.

    a) Please choose the option that best reflects how negative or positive you found the experience of booking an appointment to provide a blood sample.

Negative						Positive
1	2	3	4	5	6	7
○	○	○	○	○	○	○

b) Please choose the option that best reflects how confusing or straightforward you found the experience of booking an appointment to provide a blood sample.

Straightforward						Confusing
1	2	3	4	5	6	7
○	○	○	○	○	○	○

c) Please choose the option that best reflects how boring or interesting you found the experience of booking an appointment to provide a blood sample.

Boring						Interesting
1	2	3	4	5	6	7
○	○	○	○	○	○	○

d) Please choose the option that best reflects how easy or hard you found the experience of booking an appointment to provide a blood sample..

Easy						Hard
1	2	3	4	5	6	7
○	○	○	○	○	○	○

e) Please choose the option that best reflects how slow or quick you found the experience of booking an appointment to provide a blood sample.

Slow						Quick
1	2	3	4	5	6	7
○	○	○	○	○	○	○

[The next question is for those who answered 'Yes, I did provide a blood sample' to the question above]

12) On the following screens, please choose the option on the scale that best reflects your experience of providing a blood sample for Our Future Health.

a) Please choose the option that best reflects how negative or positive you found the experience of providing a blood sample.

Negative						Positive
1	2	3	4	5	6	7
○	○	○	○	○	○	○

a) Please choose the option that best reflects how confusing or straightforward you found the experience of providing a blood sample.

Straightforward						Confusing
1	2	3	4	5	6	7
○	○	○	○	○	○	○

b) Please choose the option that best reflects how boring or interesting you found the experience of providing a blood sample.

Boring						Interesting
1	2	3	4	5	6	7
○	○	○	○	○	○	○

b) Please choose the option that best reflects how easy or hard you found the experience of providing a blood sample.

Easy						Hard
1	2	3	4	5	6	7
○	○	○	○	○	○	○

c) Please choose the option that best reflects how slow or quick you found the experience of providing a blood sample.

Slow						Quick
1	2	3	4	5	6	7
○	○	○	○	○	○	○

2) Do you have any further thoughts or comments about the process of booking an appointment for blood collection in Our Future Health? If so, please provide them in the box below:
    - o *free text box*

2. Do you have any further thoughts or comments about the process of providing a blood sample in Our Future Health? If so, please provide them in the box below:
    - o *free text box*

Filling out the questionnaire about your health and lifestyle

As part of Our Future Health you are asked to fill out a questionnaire about your health and lifestyle.

3) Have you completed the questionnaire?
    - o Yes all of it
    - o Yes most of it
    - o Yes some of it
    - o No and I don't intend to
    - o No but I do intend to
    - o Not sure / don't know
    - o Choose not to answer

[The next question is shown ONLY *If answered Q1. Yes options (yes all of it),(yes most of it),(yes some of it); ask*]

4) Choose an option on the scale that best reflects your experience of filling out the questionnaire:

Hard 1 ○	2 ○	3 ○	4 ○	5 ○	6 ○	Easy 7 ○
Short 1 ○	○	○	○	○	○	Long 7 ○
Confusing 1 ○	○	○	○	○	○	Straightforward 7 ○

Interesting 1 ○	○	○	○	○	○	Boring 7 ○
Negative 1 ○	○	○	○	○	○	Positive 7 ○

5) Do you have any further thoughts or comments about the Our Future Health questionnaire? If so, please provide them in the box below:
    - o *free text box*

Your overall experience of being a part in Our Future Health so far

6) Why did you decide to take part in Our Future Health?
    Select all options that apply
    - o I want to help improve the health of future generations
    - o I want to help tackle common diseases
    - o I want to help tackle rare diseases
    - o I want to help tackle diseases that affect me or my family
    - o I want to help tackle diseases that affect my community
    - o I am interested in taking part in health research
    - o I agree with the aims of this research
    - o I want to receive personal results about my health in the future
    - o I want to make sure people like me are represented in health research
    - o Not sure / don't know
    - o Other [free text]

7) If you had a question about Our Future health, were you able to get an answer?
    - o I didn't have a question
    - o Yes, my question was answered fully
    - o Yes, my question was answered partially
    - o No, I didn't get an answer

8) [*Only if DID NOT respond "I didn't have a question" in Q13*] Where did you go to find answers to your questions? Tick all that apply
    a) I emailed the Our Future Health support team
    b) I called the Our Future Health support team
    c) I read the Frequently Asked Questions on the website
    d) I read the participant information or consent documents
    e) I wasn't sure where to go to find answers
    f) Other [Please specify]

9) Choose an option on the scale below that best reflects your experience of taking part in Our Future Health so far

Not demanding 1 ○	2 ○	3 ○	4 ○	5 ○	6 ○	Demanding 7 ○
Slow 1 ○	2 ○	3 ○	4 ○	5 ○	6 ○	Quick 7 ○
Straightforward 1 ○	2 ○	3 ○	4 ○	5 ○	6 ○	Confusing 7 ○
Boring 1 ○	2 ○	3 ○	4 ○	5 ○	6 ○	Interesting 7 ○
Positive 1 ○	2 ○	3 ○	4 ○	5 ○	6 ○	Negative 7 ○

10) Choose an option on the scale below that best reflects your opinions about Our Future Health.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
I think it's a good idea	1 ○	2 ○	3 ○	4 ○	5 ○
I think it is important	1 ○	2 ○	3 ○	4 ○	5 ○
I would recommend friends and family take part	1 ○	2 ○	3 ○	4 ○	5 ○

11) Do you have any further thoughts or comments about your overall experience of being a part of Our Future Health so far? If so, please provide them in the box below:
    - *free text box*

12) We would like to invite some people to take part in a 30-minute telephone interview to tell us more about their experiences of Our Future Health. Would you be happy for us to invite you to an interview about your experiences?
    - Yes
    - No

13) Can we use the answers you have provided in the public domain? We will never use your name or anything that would identify you.

    - Yes
    - No

Our Future Health

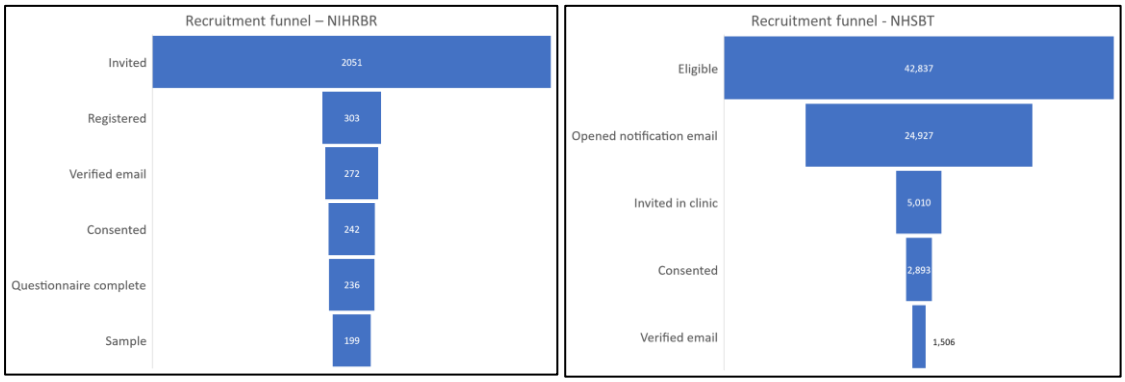
Appendix D: Evaluation of and insights from the first two live end-to-end recruitment pilots

Appendix D: Evaluation of and insights from the first two live end-to-end recruitment pilots

Between May and October 2021, Our Future Health conducted a series of end-to-end recruitment pilot studies with NIHR BioResource (NIHR BioResource, May-Aug) and NHS Blood and Transplant (June-Oct). Participants from across the 13 NIHR BioResource centres across England were approached via email and asked to consent remotely. Participants approached via NHS Blood and Transplant (NHSBT) were made aware of the research programme via email, and then approached in clinic and taken through the consent process by one of five Our Future Health research nurses working with six units.

Across the two pilot studies, 3,135 participants were recruited. In the pilot with NIHR BioResource, 2,051 individuals were invited to participate in Our Future Health, of whom 242 consented (12%). In the pilot with NHSBT, around 58% of donors approached to participate agreed to do so (N=2,893); this represents 7% of donors with appointments to give blood in a participating clinic.

The recruitment funnels below indicate where potential participants were lost in the recruitment journey. For NIHR BioResource, most participants who registered with Our Future Health went on to provide a biological sample, but there is work required to optimise the invite. For NHSBT, recruitment in clinic meant that a small proportion of eligible donors were able to be approached in clinic.



We conducted a wide range of qualitative and qualitative research to understand these recruitment figures further and learned the following lessons:

- We need to collect better data on responses to invites when approaching individuals remotely. For example, email open rates were not available for NIHR BioResource, limiting our interpretation of the low conversion rate from invite to consent. We were able to obtain good data on why donors chose not to participate when approached in person.

- Moving consent online may overcome several challenges identified in NHSBT. As noted above, time constraints limited the number of donors who could be approached in person, suggesting that a remote approach to invitation would maximise the number of people eligible

- to consent. The most commonly reported reason for not taking part was ‘not having enough time’. Moving consent online would allow greater flexibility in when someone

could consent. Finally, the research nurses and senior management reported that consent in clinic introduced a level of disruption that was too much to sustain alongside a well-functioning donation clinic.

- Our sample collection and questionnaire procedures worked extremely well. Over 80% of NIHR BioResource and over 90% of NHSBT participants provided a sample. In addition, over 90% of eligible individuals completed the questionnaire. We obtained useful feedback on the type of information individuals were willing to tell us in the survey. We also confirmed that our approach to mirror existing sample-taking processes maximises the number of samples we can obtain.

- We were able to collect, record and evaluate key metrics regarding the diversity of our recruited sample in line with our recruitment targets, including age, gender, deprivation and ethnicity. At present, we are only able to collect data on gender and ethnicity during our baseline questionnaire, which means that we cannot tell if there is any difference in the demographic composition of those who consent and register for the study, but do not go on to finish the questionnaire.

- Our recruited sample to date represents a broad range of adult age groups and indices of deprivation, and our gender ratio is well balanced between those who identify as male and female. However, over 90% of our sample are White. This is >10% more than proportion of the UK population who identify as White in the 2011 census. This indicates that our initial approach to recruitment is not effective at recruiting an ethnically diverse cohort and we need to proactively develop recruitment material and approaches that address this limitation.

Our Future Health

Appendix E: Baseline Questionnaire

Key

[Anything in square brackets is not shown to participants]
[CAPITAL SQUARE BRACKETS INDICATE VARIABLE NAME (BRACKETED TEXT INDICATES QUESTION SOURCE)]

Text in square boxes indicates help text

About you and your household [SECTION 1]

[SECTION INTRO]
This section is where we gather most of our data.
This is the information that will help researchers make discoveries to improve the health of people in the UK. It will be the largest and most diverse research project that has been done in the UK. We are grateful that you and many others are donating their information to help future generations live in good health for longer.
[INTRO1D(UKB)]

If you do not wish to answer a question you can select 'Prefer not to answer'.
If you want to see previous questions and change your answers, use the BACK button.
If you have any difficulties with completing this, you can use the HELP button or ask a staff member for assistance.
Remember, if you cannot find an exact answer, please select the closest response.

- Please touch NEXT to continue

(H3) How to complete the questionnaires or get help

- If you do not wish to answer a question you can select 'Prefer not to answer'.
- If you want to see previous questions and change your answers, use the BACK button
- If you have any difficulties with completing this, you can use the Help button on the top right of every page.
- Remember, if you cannot find an exact answer, please select the closest response
- You can complete all the questions for each section now or save your progress and continue at a later time

The HELP button will provide you with some additional information to help you answer each question. If you still need help after reading the information provided, do not hesitate to press the HELP button.

[SEX (ONS 2021)]

What sex was assigned to you at birth?
A question about gender identity will follow later in the questionnaire

SELECT 1 from

1 Female
2 Male
3 Intersex
-3 Prefer not to answer

We ask about your sex at birth because it can help researchers make new discoveries about how the sex you were born with affects health and risk of disease. It is also important when processing your biological sample in the lab

[GENDER]

Select the option that best describes your current gender identity

SELECT 1 from

1 Gender-fluid
2 Man
3 Nonbinary
4 Woman
5 I don't identify with any option provided
-3 Prefer not to answer

[GENDER_B (OXFORD_EDI)]

Do you identify as trans or do you have a trans history?

SELECT 1 from

1 Yes
2 No
-3 Prefer not to answer

[SEXUAL_ORIENTATION (CENSUS 2021)]

Which of the following best describes your sexual orientation?

SELECT 1 from

1 Asexual
2 Bisexual
3 Gay
4 Heterosexual/Straight
5 Lesbian
6 Pansexual
7 Queer
8 Other sexual orientation not listed
-3 Prefer not to answer

This question is voluntary, so you can respond "prefer not to answer" if you prefer

"Straight/Heterosexual" means that you're only attracted to people of the opposite sex

"Gay or Lesbian" means that you're attracted to people of the same sex

"Bisexual" means that you're attracted to more than one sex

"Pansexual" means that you're attracted to people regardless of their sex or gender identity

"Asexual" means that you're not attracted to any sex

We realise we have not listed every sexual orientation. If your sexual orientation is not described by any of these categories, please select the "other sexual orientation not listed" option.

[HEIGHT_M (STRIDES)]

We are now going to ask you to tell us how tall you are.
How would you prefer to enter your height?

SELECT 1 from

1 Feet/inches **-> GO TO HT_FT**

2 Metres/centimetres **-> GO TO HT CM**

3. I do not want to report my height -> GO TO WEIGHT_M

[HT_FT]

What is your height (Without shoes)?
If you don't know, please provide a best guess

Enter INTEGER

[Require]:

3ft0– 7ft 11 as given

OR

-3 Prefer not to answer

[HT_CM]

What is your height (Without shoes)?
If you don't know, please provide a best guess

Enter INTEGER

[Require]:

90cm - 2m 99cm as given]

OR

-3 Prefer not to answer

[WEIGHT_M (STRIDES)]

We are now going to ask you to tell us how much you weigh.
How would you prefer to enter your weight?

SELECT 1 from

1 Stones/pounds **-> GO TO WT_ST**

2 Kilograms **_-> GO TO WT_CM**

3 I do not want to report my weight -> GO TO Language

[WT_ST (STRIDES)]

What is your weight (Without shoes/heavy clothing)?
If you don't know, please provide a best guess

Enter INTEGER
[Require min value
3 stones
max value
63 stones
OR
-3 Prefer not to answer

[WT_KG (STRIDES)]

What is your weight (Without shoes/heavy clothing)?
If you don't know, please provide a best guess

Enter INTEGER
[Require min value
20kg
max value
400kg]
OR
-3 Prefer not to answer

[LANGUAGE (PSE UK)]

What is your main language?

SELECT 1 from

1 English

2 Welsh

3 (Scottish) Gaelic

4 Punjabi

5 Gujarati

6 Bengali
7 Urdu
8 Hindi
9 Cantonese
10 Mandarin
11 Polish
12 Arabic
13 Other (extended drop down list. Includes BSL and ASL. See excel)
14 Prefer not to answer

[ETHNICITY (PSE UK)]

What is your ethnic group? Choose one option that best describes your ethnic group or background?

1 White - English / Welsh / Scottish / Northern Irish / British
2 White – Irish
3 White - Gypsy or Irish Traveller
4 White – Polish
5 Any other white background
6 Mixed - White and Black Caribbean
7 Mixed - White and Black African
8 Mixed - White and Asian
9 Any other mixed multiple ethnic background
10 Asian or Asian British – Indian
11 Asian or Asian British – Pakistani
12 Asian or Asian British – Bangladeshi
13 Chinese
14 Any other Asian/Asian British background
15 Black or Black British – African
16 Black or Black British – Caribbean
17 Any other Black / African / Caribbean background
18 Arab
19 Other
20 Prefer not to answer

[MARITAL STATUS (CENSUS 2021)]

What is your current legal marital or registered civil partnership status?

SELECT 1 from

1 Never married and never registered a civil partnership
-> GO TO D4 (UKB)
2 Married **-> GO TO MARITAL_STATUS_A**
3 In a registered civil partnership **-> GO TO MARITAL_STATUS_B**
4 Separated, but still legally married **-> GO TO MARITAL_STATUS_A**
5 Separated, but still legally in a civil partnership **-> GO TO MARITAL_STATUS_b**

6 Divorced **-> GO TO MARITAL_STATUS_C**

7 Formerly in a civil partnership which is now legally dissolved **-> GO TO MARITAL_STATUS_D**

8 Widowed **-> GO TO MARITAL_STATUS_C**

9 Surviving partner from a registered civil partnership **-> GO TO MARITAL_STATUS_D**

10 Other **-> GO TO D4 (UKB)**

-3 Prefer not to answer **-> GO TO D4 (UKB)**

[MARITAL_STATUS_A (CENSUS 2021]

Who is your legal marriage to?

SELECT 1 from

1 Someone of the opposite sex

2 Someone of the same sex

4 Other

-3 Prefer not to answer

➔ **GO TO D4**

[MARITAL_STATUS_B (CENSUS 2021]

Who is your registered civil partnership to?

SELECT 1 from

1 Someone of the opposite sex

2 Someone of the same sex

3 Other

-3 Prefer not to answer

➔ **GO TO D4**

[MARITAL_STATUS_C (CENSUS 2021]

Who was your legal marriage to?

SELECT 1 from

3 Someone of the opposite sex

4 Someone of the same sex

4 Other

-3 Prefer not to answer

➔ **GO TO D4**

[MARITAL_STATUS_D (CENSUS 2021]

Who was your registered civil partnership to?

SELECT 1 from

5 Someone of the opposite sex
6 Someone of the same sex
5 Other
-3 Prefer not to answer

➔ **GO TO D4**

[D4 (UKB)]

What type of accommodation do you live in?

SELECT one of 7 from

1 A house or bungalow
2 A flat, maisonette or apartment
3 Mobile or temporary structure (i.e. caravan)
4 Sheltered accommodation **-> GO TO D5A**
5 Care home **-> GO TO D5A**
-7 None of the above
-3 Prefer not to answer

Please select:

-A house or bungalow for any whole, detached, semi-detached or terraced (including end-terrace) house or bungalow.

-A flat, maisonette, or apartment for any purpose-built block of flats or tenement, part of a converted or shared house (including bed-sits) or within a commercial building (for example in an office building, or hotel, or over a shop).

-If none of the options apply, select 'None of the above'.

[D5 (UKB)]

Do you own or rent the accommodation that you live in?

SELECT one of 8 from

1 Own outright (by you or someone in your household)
2 Own with a mortgage
3 Rent - from local authority, local council, housing association, student accommodation
4 Rent - from private landlord or letting agency
5 Pay part rent and part mortgage (shared ownership)
6 Live in accommodation rent free
-7 None of the above

-3 Prefer not to answer

Please select:

- Own outright if you or someone in your household owns the accommodation that you live in.

- Own with mortgage if you or someone in your household has a mortgage on the accommodation that you live in.

[D5A (UKB)]

Do you have any of the following in your home? (You can select more than one answer)

TOGGLE of 6 choices
[Require >1 response]

1 A gas hob or gas cooker
2 A gas fire that you use regularly in wintertime
3 An open solid fuel fire that you use regularly in wintertime
-7 None of the above **[EXCLUSIVE]**
-1 Do not know [**EXCLUSIVE]**
-3 Prefer not to answer **[EXCLUSIVE]**

Select the answer which best describes how your home is mainly heated. If you use more than one type of heating equally, you can choose multiple answers. Solid fuel refers to wood or coal. Regular use is when you use this for most days of the week in the winter time.

[D5A1 (UKB)]

How many years have you lived at your current address?

Enter INTEGER
[Require ≥ 1, ≤ current age,
Units: years]
OR
-10 Less than a year
OR
-1 Do not know
OR
-3 Prefer not to answer

If you have lived there for less than one year select 'Less than a year'.

If you are unsure, please provide an estimate or select 'Do not know'.

If you have lived at your current address at different times, add up the total number of years you lived there. For instance, if you lived at your current address for 3 years, moved overseas for one year and returned to your current address for another 5 years, then you would enter 8 years.

[D7 (UKB)]

Including yourself, how many people are living together in your household? (Include those who usually live in the house such as students living away from home during term, partners in the armed forces or professions such as pilots)

Enter INTEGER
[Require ≥ 1, ≤ 100
Units: people]
OR
-1 Do not know
OR
-3 Prefer not to answer

➔ **IF ANSWER = 1, GO TO D8**

If you live alone, enter 1.

Include those who usually live in the house such as students living away from home during term, partners in the armed forces or professions such as pilots.

[D7A (UKB)]

How are the other people who live with you related to you? (You can select more than one answer)

TOGGLE of 9 choices
[Require ≥1 choices]
1 Husband, wife, or partner
2 Son and/or daughter (include step-children)
3 Brother and/or sister
4 Mother and/or father
5 Grandparent
6 Grandchild
7 Other related
8 Other unrelated
-3 Prefer not to answer **[EXCLUSIVE]**

Answer this question considering all the people who you counted in the household in response to the previous question.

[D8 (UKB)]

How many cars or vans are owned, or available for use, by you or members of your household? (Please include company vehicles if available for private use)

SELECT one of 7 from
1 None

2 One
3 Two
4 Three
5 Four or more
-1 Do not know
-3 Prefer not to answer

Do not include motorcycles.

----------END OF SECTION 1 ----------

Work And Education [SECTION 2]

This section is about work and education. Different physical Requirements of us at work can result in different illnesses and issues. Examining and understanding different levels of work and education can also help us examine inequalities which can result in poor health and other social issues. Your work may have changed during the COVID-19 pandemic. Please answer the questions as accurately as you can based on your current situation.

[D9 (UKB)]

Which of the following describes your current situation? (You can select more than one answer)

TOGGLE of 10 choices
[Require ≥1 choices]

1	In paid employment or self-employed	
2	Retired	**-> GO TO D12**
3	Looking after home and/or family	
4	Unable to work because of sickness or disability	
5	Unemployed	**-> GO TO D12**
8	On paid leave (furlough)	
6	Doing unpaid or voluntary work	
7	Full or part-time student	
-7	None of the above **[EXCLUSIVE]**	
-3	Prefer not to answer **[EXCLUSIVE]**	

If more than one situation applies, select all that are appropriate.

[D9AA (UKB)]

How many years have you worked in your current role? (If you have more than one job please answer this, and the following questions on work, for your MAIN role only. Looking after home and/or family should be considered as a job/work)

Enter INTEGER
[Require ≥1, ≤ Current age,
Units: years]
OR
-10 Less than a year
OR
-1 Do not know
OR
-3 Prefer not to answer

If you have more than one 'current job' then answer this question for your MAIN job only (ie: the job that you spend most of your time doing).

If you have been with the same employer, but have changed jobs whilst you have worked for them, then only give the number of years that you have been in your current job (not the number of years that you have been employed by the same company).

For instance, if you have worked as mail-room sorter but then been promoted to manager of the mail-room, please give the number of years you have worked as the mail-room manager only.

If you have changed employers, but have had the same job, please give the total number of years that you have worked in
that job. For instance, if you have worked as a cleaner for 3 different companies, please give the total number of years working as a cleaner.

[D9A (UKB)]

In a typical WEEK, how many hours do you spend at work? (Do not include hours travelling to and from work)

Enter INTEGER
[Require ≤ 168,
Units: hours]
OR
-1 Do not know
OR
-3 Prefer not to answer

If you have more than one 'current job' then answer this question for your MAIN job only.

Please round up or down to the nearest hour.

[D9G (UKB)]

How many times a WEEK do you travel from home to your main work? (count outward journeys only)

Enter INTEGER
[Require ≥0, ≤ 999,
Units: times]
OR
-10 Less than once a week
OR
-1 Do not know
OR
-3 Prefer not to answer

If the number of times varies each week, take an average over the last 4 weeks.

If you only work from home please enter 0.

[D9E (UKB)]

What types of transport do you use to get to and from work? (You can select more than one answer)

TOGGLE of 6 choices
[Require ≥1 choices]
1 Car/motor vehicle
2 Walk
3 Public transport
4 Cycle
-7 None of the above **[EXCLUSIVE]**
-3 Prefer not to answer **[EXCLUSIVE]**

If you have more than one 'current job' then answer this question for your MAIN job only.

If you use more than one form of transport then select all that apply.

[D9F (UKB)]

About how many miles is it between your home and your work?

Enter INTEGER
[Require ≥0, ≤ 999,
Units: miles]
OR
-10 Less than one mile
OR
-1 Do not know
OR
-3 Prefer not to answer

If you have more than one 'current job' then answer this question for your MAIN job only.

If you are unsure, please provide an estimate or select 'Do not know'.

If you only work from home please enter 0.

[D9B (UKB)]

Does your work involve walking or standing?

SELECT one of 6 from
1 Never/rarely
2 Sometimes
3 Usually
4 Always
-1 Do not know

-3 Prefer not to answer

If you have more than one 'current job' then answer this question your MAIN job only.

[D9C (UKB)]

Does your work involve heavy manual or very physical work?

1 Never/rarely

SELECT one of 6 from

2 Sometimes

3 Usually

4 Always

-1 Do not know

-3 Prefer not to answer

If you have more than one 'current job' then answer this question for your MAIN job only. Physical work includes work that involves handling of heavy objects and use of heavy tools.

[D9D (UKB)]

Does your work involve shift work?

SELECT one of 6 from

1 Never/rarely **-> GO TO D12 (UKB)**

2 Sometimes

3 Usually

4 Always

-1 Do not know

-3 Prefer not to answer"

Shift work is a work schedule that falls outside of the normal daytime working hours of 9am-5pm. This may involve working afternoons, evenings or nights or rotating through these kinds of shifts.

[D9DA (UKB)]

Does your work involve night shifts?

SELECT one of 6 from

1 Never/rarely

2 Sometimes

3 Usually

4 Always

-1 Do not know.

-3 Prefer not to answer

If you have more than one 'current job' then answer this question for your MAIN job only. Night shifts are a work schedule that involves working through the normal sleeping hours, for instance working through the hours from 12am to 6am.

[D12 (UKB)]

Which of the following qualifications do you have? (You can select more than one)

TOGGLE of 8 choices

[Require ≥1 choices]

1 College or University degree

2 A levels/AS levels/BTEC or equivalent

3 O levels/GCSEs or equivalent

4 CSEs or equivalent

5 NVQ or HND or HNC or equivalent

6 Other professional qualifications e.g., nursing, teaching

-7 None of the above **[EXCLUSIVE]**

-3 Prefer not to answer **[EXCLUSIVE]**

A levels/AS levels and equivalent includes the Higher School Certificate O levels/GCSEs and equivalent includes the School Certificate. If your education was in another country please choose the category(ies) that best fits with your educational qualifications.

[D11 (UKB)]

At what age did you complete your continuous full-time education?
If you stopped your studies with no intention of returning, please give the age at which you stopped even if you began studying again later in life.

Enter age in years

[Require ≥ 5, ≤ current age,

Expect ≤ 40,

Units: years]

OR

0 Still in full time education

OR

-2 Never went to school

OR

-1 Do not know

OR

-3 Prefer not to answer

Please give the age that you completed 'continuous' full time education.
For example, if you stopped your studies when you were 17 years old with the intention that you had completed your studies but then returned to full time studies when you were 24, enter 17. However if you only temporarily stopped your studies at 17 with the intention that you would return to studies (for instance a gap year) and then completed your full time education at 21, enter 21

[D10 (UKB)]

What is the average total income before tax received by your HOUSEHOLD?

SELECT one of 7 from

1 Less than £18,000
2 £18,000 to £30,999
3 £31,000 to £51,999
4 £52,000 to £100,000
5 Greater than £100,000
-1 Do not know
-3 Prefer not to answer

Add up the incomes of everyone in your household for your answer.

The information you provide is confidential and won't be shared with any tax authorities.

----------END OF SECTION 2 ----------

Your lifestyle [SECTION 3]

Note: square brackets are not seen
Help and hint text is presented in boxes where available

[SECTION INTRO]

In this section we ask you about your day-to-day physical activity.

This will help our researchers look at how exercise is tied to overall health, but also things like how healthy your bones, lungs, and heart as well as diseases such as type 2 diabetes.

We'll also ask about driving habits, sleep patterns and the use of tobacco, vaping and alcohol if relevant.

Aspects of your lifestyle may have changed during the COVID-19 pandemic. Please answer the questions as accurately as you can based on your current situation.

[WP1 (UKB)]

Thinking about the last 4 weeks, in a typical WEEK, on how many days did you walk for at least 10 minutes at a time?
(Include walking that you do at work, travelling to and from work, and for sport or leisure)

Enter INTEGER
[Require ≥ 0, ≤ 7
Units: days]
OR
-1 Do not know
OR
-2 Unable to walk **-> GO TO WP2**
OR
-3 Prefer not to answer

[WP1A (UKB)]

Thinking about the last 4 weeks, , how many minutes did you usually spend walking on a typical DAY?

Enter INTEGER
[Require ≥ 0, ≤ 1440
Units: minutes]
OR
-1 Do not know
OR
-2 Unable to walk
OR
-3 Prefer not to answer

Count the number of minutes that you usually spend walking in one day.

If the time you usually spend walking on each day of the week varies a lot, give an average of the time you spend walking. For instance, if on one day of the week you usually walk for 4 hours but on the other day you walk 2 hours then give the average - that is 3 hours.

[WP2 (UKB)]

Thinking about the last 4 weeks, in a typical WEEK, on how many days did you do 10 minutes or more of moderate physical activities like carrying light loads, cycling at normal pace? (Do not include walking)

Enter INTEGER
[Require ≥ 0, ≤ 7
Units: days]
OR
-1 Do not know
OR
-3 Prefer not to answer

Count the number of days in a week that you do moderate physical activities for at least 10 minutes continuously at a time.

Remember to include activities that you do for work, leisure, travel and around the house.

[WP2A (UKB)]

Thinking about the last 4 weeks, how many minutes did you usually spend doing moderate activities on a typical DAY?

Enter INTEGER
[Require ≥ 0, ≤ 1440
Units: minutes]
OR
-1 Do not know
OR
-2 Unable to walk
OR
-3 Prefer not to answer

If the time you usually spend doing moderate physical activity on each day of the week varies a lot, give an average of the time you spend doing moderate physical activity.

[WP3 (UKB)]

Thinking about the last 4 weeks, in a typical WEEK, how many days did you do 10 minutes or more of vigorous physical activity?
(These are activities that make you sweat or breathe hard such as fast cycling, aerobics, heavy lifting)

Enter INTEGER

[Require ≥ 0, ≤ 7
Units: days]
OR
-1 Do not know
OR
-3 Prefer not to answer

Count the number of days in a week that you do vigorous physical activities for at least 10 minutes continuously at a time.

Remember to include activities that you do for work, leisure, travel and around the house.

[WP3A (UKB)]

Thinking about the last 4 weeks, how many minutes did you usually spend doing vigorous activities on a typical DAY?

Enter INTEGER
[Require ≥ 0, ≤ 1440
Units: minutes]
OR
-1 Do not know
OR
-2 Unable to walk **-> GO TO WP4AA**
OR
-3 Prefer not to answer

If the time you usually spend doing vigorous physical activity on each day of the week varies a lot, give an average of the time you spend doing vigorous physical activity.

[WP4 (UKB)]

How would you describe your usual walking pace?

SELECT one of 5 from
1 Slow pace
2 Steady average pace
3 Brisk pace
-7 None of the above
-3 Prefer not to answer

Slow pace is defined as less than 3 miles per hour. Steady average pace is defined as between 3-4 miles per hour. Fast pace is defined as more than 4 miles per hour.

[WP4A (UKB)]

At home, during the last 4 weeks, about
how many times a DAY do you climb a flight of stairs? (approx 10 steps)

SELECT one of 8 from

0 None
1 1-5 times a day
2 6-10 times a day
3 11-15 times a day
4 16-20 times a day
5 More than 20 times a day
-1 Do not know
-3 Prefer not to answer

If you are unsure, please provide an estimate or select 'Do not know'.

[WP4AA (UKB)]

In the last 4 weeks, which forms of transport have you used most often to get about? Not including travel to and from work; you can select more than one answer

TOGGLE of 6 choices
[Require ≥1 choices]

1 Car/motor vehicle
2 Walk
3 Public transport
4 Cycle
-7 None of the above **[EXCLUSIVE]**
-3 Prefer not to answer **[EXCLUSIVE]**

Remember not to include journeys to and from work.

[WP4B1 (UKB)]

In the last 4 weeks did you spend any time doing the following?
(You can select more than one answer)

TOGGLE of 7 choices
[Require ≥1 choices]

1 Walking for pleasure (not as a means of transport)
2 Other exercises (e.g., swimming, cycling, keep fit, bowling)
3 Strenuous sports
4 Light DIY (e.g., DIY that does not require a lot of physical effort)
5 Heavy DIY (e.g., DIY that requires a lot of physical effort)
-7 None of the above **[EXCLUSIVE]** **-> GO TO WP11**
-3 Prefer not to answer **[EXCLUSIVE]** **-> GO TO WP11**

➔ **If ANSWER = 1 GO TO WP4C1 (UKB)**
➔ **If ANSWER = 2 GO TO WP4C2 (UKB)**
➔ **If ANSWER = 3 GO TO WP4C3 (UKB)**

➔ **If ANSWER = 4 GO TO WP4C4 (UKB)**

➔ **If ANSWER = 5 GO TO WP4C5 (UKB)**

➔ **IF ANSWER INCLUDES MULTIPLE RESPONSES 1-5 SHOW EACH APPLICABLE WP4C1-5 IN ORDER**

Strenuous sports include sports that make you sweat or breathe hard. Heavy DIY includes chopping wood, home or car maintenance, lifting heavy objects or using heavy tools.

[WP4C1 (UKB)]

How many times in the last 4 weeks did you go walking for pleasure?

SELECT one of 8 from 1

1 Once in the last 4 weeks
2 2-3 times in the last 4 weeks
3 Once a week
4 2-3 times a week
5 4-5 times a week
6 Every day
-1 Do not know
-3 Prefer not to answer

If the time you spent walking for pleasure varied, please give an average over the past 4 weeks.

[WP4E1 (UKB)]

Each time you went walking for pleasure, about how long did you spend doing it?

SELECT one of 9 from

1 Less than 15 minutes
2 Between 15 and 30 minutes
3 Between 30 minutes and 1 hour
4 Between 1 hour and 1½ hours
5 Between 1½ hours and 2 hours
6 Between 2 and 3 hours
7 Over 3 hours
-1 Do not know
-3 Prefer not to answer

➔ **If WP4B1 ANSWER DID NOT INCLUDE 2 OR 3 OR 4 OR 5 GO TO WP11**

If the time you spent walking for pleasure varied, please give an average over the past 4 weeks.

[WP4C2 (UKB)]

How many times in the last 4 weeks did you do other exercises such as swimming, cycling, keep fit?

SELECT one of 8 from

1 Once in the last 4 weeks
2 2-3 times in the last 4 weeks
3 Once a week
4 2-3 times a week
5 4-5 times a week
6 Every day
-1 Do not know
-3 Prefer not to answer

[WP4E2 (UKB)]

Each time you did other exercises such as swimming, cycling, keep fit, about how long did you spend doing them?

SELECT one of 9 from

1 Less than 15 minutes
2 Between 15 and 30 minutes
3 Between 30 minutes and 1 hour
4 Between 1 hour and 1½ hours
5 Between 1½ hours and 2 hours
6 Between 2 and 3 hours
7 Over 3 hours
-1 Do not know
-3 Prefer not to answer

➔ **If WP4B1 ANSWER DID NOT INCLUDE 3 OR 4 OR 5 GO TO WP11**

[WP4C3 (UKB)]

How many times in the last 4 weeks did you do strenuous sports?

SELECT one of 8 from

1 Once in the last 4 weeks
2 2-3 times in the last 4 weeks
3 Once a week
4 2-3 times a week
5 4-5 times a week
6 Every day
-1 Do not know
-3 Prefer not to answer

[WP4E3 (UKB)]

Each time you did strenuous sports, about how long did you spend doing it?

SELECT one of 9 from

1 Less than 15 minutes
2 Between 15 and 30 minutes

3 Between 30 minutes and 1 hour
4 Between 1 hour and 1½ hours
5 Between 1½ hours and 2 hours
6 Between 2 and 3 hours
7 Over 3 hours
-1 Do not know
-3 Prefer not to answer

➔ **If WP4B1 ANSWER DID NOT INCLUDE 4 OR 5 GO TO WP11**

[WP4C4 (UKB)]

How many times in the last 4 weeks did you do light DIY?

SELECT one of 8 from

1 Once in the last 4 weeks
2 2-3 times in the last 4 weeks
3 Once a week
4 2-3 times a week
5 4-5 times a week
6 Every day
-1 Do not know
-3 Prefer not to answer

[WP4E4 (UKB)]

Each time you did light DIY, about how long did you spend doing it?

SELECT one of 9 from

1 Less than 15 minutes
2 Between 15 and 30 minutes
3 Between 30 minutes and 1 hour
4 Between 1 hour and 1½ hours
5 Between 1½ hours and 2 hours
6 Between 2 and 3 hours
7 Over 3 hours
-1 Do not know
-3 Prefer not to answer

➔ **If WP4B1 ANSWER DID NOT INCLUDE 5 GO TO WP11**

[WP4C5 (UKB)]

How many times in the last 4 weeks did you do heavy DIY?

SELECT one of 8 from

1 Once in the last 4 weeks
2 2-3 times in the last 4 weeks
3 Once a week
4 2-3 times a week
5 4-5 times a week

6 Every day
-1 Do not know
-3 Prefer not to answer

[WP4E5 (UKB)]

Each time you did heavy DIY, about how long did you spend doing it?

SELECT one of 9 from

1 Less than 15 minutes
2 Between 15 and 30 minutes
3 Between 30 minutes and 1 hour
4 Between 1 hour and 1½ hours
5 Between 1½ hours and 2 hours
6 Between 2 and 3 hours
7 Over 3 hours
-1 Do not know
-3 Prefer not to answer

[WP11 (UKB)]

How often do you visit friends or family or have them visit you?

SELECT one of 9 from

1 Almost daily
2 2-4 times a week
3 About once a week
4 About once a month
5 Once every few months
6 Never or almost never
7 No friends/family outside household
-1 Do not know
-3 Prefer not to answer

If this varies, please give an average of how often you visit or have had visits in the last year. Include meeting with friends or family in environments outside of the home such as in the park, at a sports field, at a restaurant or pub.

[WP12 (UKB)]

Which of the following do you attend once a week or more often?
If this varies, please think about activities in the last year.
(You can select more than one)

TOGGLE of 7 choices

1 Sports club or gym
2 Pub or social club
3 Religious group
4 Adult education class
5 Other group activity
-7 None of the above

-3 Prefer not to answer

You can include online activities.

[WP12A (UKB)]

In a typical DAY in summer, how many hours do you spend outdoors?

Enter INTEGER

OR

-10 Less than an hour a day

OR

-1 Do not know

OR

-3 Prefer not to answer

If the time you spend outdoors in summer varies a lot, give the average time per day. For example, if you spend 1 hour a day on each weekday and 4 hours a day on the weekend, the total hours in a week are 13 (5 + 8), so you spend approximately 2 hours a day.

[WP12B (UKB)]

In a typical DAY in winter, how many hours do you spend outdoors?

Enter INTEGER

OR

-10 Less than an hour a day

OR

-1 Do not know

OR

-3 Prefer not to answer

If the time you spend outdoors in winter varies a lot, give the average time per day. For example, if you spend 1 hour a day on each weekday and 4 hours a day on the weekend, the total hours in a week are 13 (5 + 8), so you spend approximately 2 hours a day.

[WP5 (UKB/NSCH)]

In a typical DAY, how many hours do you usually spend in front of a TV watching TV programs, videos, or playing video games??

Enter INTEGER

OR

-10 Less than an hour a day

OR

-1 Do not know

OR

-3 Prefer not to answer

If the time you spend in front of the TV varies a lot, give the average time for a 24-hour day in the last 4 weeks.

[WP5A (UKB/NSCH)]

In a typical DAY, how many hours do you usually spend with computers, cell phones, handheld video games, and other electronic devices?
(Do not include using a computer at work; put 0 if you do not spend any time doing it)

Enter INTEGER
OR
-10 Less than an hour a day
OR
-1 Do not know
OR
-3 Prefer not to answer

If the time you spend on the computer or other handheld devices varies a lot, give the average time for a 24-hour day in the last 4 weeks. Remember not to include time spent on a computer at work.

[WP7 (UKB)]

In a typical DAY, how many hours do you spend driving?

Enter INTEGER
OR
-10 Less than an hour a day
OR
-1 Do not know
OR
-3 Prefer not to answer

If the time you spend driving varies a lot, give the average time for a 24-hour day in the last 4 weeks.

Include driving a car, bus, motorcycle, boat, truck etc.

Include all the driving that you do as part of work, getting to work or outside of work. If you do not drive, please enter 0.

[SL1 (UKB)]

About how many hours sleep do you get in every 24 hours? (please include naps)
Enter INTEGER
OR
-1 Do not know

OR

-3 Prefer not to answer

If the time you spend sleeping varies a lot, give the average time for a 24 hour day in the last 4 weeks.

[SL1AA (UKB)]

On an average day, how easy do you find getting up in the morning?

SELECT one of 6 from

1 Not at all easy
2 Not very easy
3 Fairly easy
4 Very easy
-1 Do not know
-3 Prefer not to answer

If this varies a lot, answer this question in relation to the last 4 weeks.

[SL1AB (UKB)]

Do you consider yourself to be?

SELECT one of 6 from

1 Definitely a 'morning' person
2 More a 'morning' than 'evening' person
3 More an 'evening' than a 'morning' person
4 Definitely an 'evening' person
-1 Do not know
-3 Prefer not to answer

If this varies a lot, answer this question in relation to the last 4 weeks.

[SL1A (UKB)]

Do you have a nap during the day?

SELECT one of 4 from

1 Never/rarely
2 Sometimes
3 Usually
-3 Prefer not to answer

If this varies a lot, answer this question in relation to the last 4 weeks.

[SL4 (UKB)]

How likely are you to doze off or fall asleep during the daytime when you don't mean to? (e.g. when working, reading or driving)

SELECT one of 5 from

0 Never/rarely
1 Sometimes
2 Often
-1 Do not know
-3 Prefer not to answer

If you are unsure, please provide an estimate or select 'Do not know'.

[SL2 (UKB)]

Do you have trouble falling asleep at night or do you wake up in the middle of the night?

SELECT one of 4 from

1 Never/rarely
2 Sometimes
3 Usually
-3 Prefer not to answer

If this varies a lot, answer this question in relation to the last 4 weeks.

[SL3 (UKB)]

Does your partner or a close relative or friend complain about your snoring?

SELECT one of 4 from

1 Yes
2 No
-1 Do not know
-3 Prefer not to answer

If you are unsure, please provide an estimate or select 'Do not know'.

[TOBACCO_A (CONNECT)]

Have you ever used any of these **tobacco** products, even once?
Select all that apply.

TOGGLE of 8 choices

[Require ≥1 choices]

0 Cigarettes (manufactured or hand-rolled) -> **GO TO S3A**
1 Electronic delivery devices that can be vaped, such as e-cigarettes (e.g., UWELL, Vype, Vuse, Vapouriz, WizMix). -> **GO TO V2**
2 Cigars, cigarillos, or little filtered cigar (e.g., Montecristo, Romeo Y Julieta, Cohiba, Davidoff, Neos red)

3 Chewing tobacco, snus, snuff, Gutkha**,** or dip (e.g., Skruf, Tulsi, Sikandar, conwood, Al Capone powder)
4 Shisha, hookah or water pipe
5 Tobacco pipe
6 I have **not** used any of these tobacco products **[EXCLUSIVE]** → **GO TO S11**
-3 Prefer not to answer **[EXCLUSIVE]**

IF RESPONSE != 0 OR 1 OR 6 GO TO TOBACCO_B

[S3A (CONNECT/UKB)]

How old were you when you **first** smoked a cigarette?

Enter INTEGER
OR
-1 Do not know
OR
-3 Prefer not to answer

If you do not remember when you had your first cigarette, please enter your best guess.

[V2 (NHS3)]

How old were you when you first used an e-cigarette (vaping)?

Enter INTEGER
OR
-1 Do not know
OR
-3 Prefer not to answer

[V3 (NHS3)]

When you used your first e-cigarette (vaping)

SELECT one of 6 from
1 I had never smoked tobacco cigarettes
2 I was a current smoker of tobacco cigarettes and had no plans to quit
3 I was a current smoker of tobacco cigarettes and was planning to quit
4 I was a current smoker of tobacco cigarettes and was planning to reduce smoking
5 I had stopped smoking tobacco cigarettes
-3 Prefer not to answer

[TOBACCO_B (CONNECT)]

Have you ever **regularly** used any of these **tobacco** products?

Select all that apply.

TOGGLE of 8 choices
[Require ≥1 choices]

0 Cigarettes (manufactured or hand-rolled)
1 Electronic delivery devices that can be vaped, such as e-cigarettes (e.g., UWELL, Vype, Vuse, Vapouriz, WizMix). → **GO TO V2**
2 Cigars, cigarillos, or little filtered cigar (e.g., Montecristo, Romeo Y Julieta, Cohiba, Davidoff, Neos red) → **GO TO S11**
3 Chewing tobacco, snus, snuff, **Gutkha,** or dip (e.g., Skruf, Tulsi, Sikandar, conwood, Al Capone powder) → **GO TO S11**
4 Shisha, hookah or water pipe → **GO TO S11**
5 Tobacco pipe → **GO TO S11**
6 I have **not** used any of these tobacco products **[EXCLUSIVE]** → **GO TO S11**
-3 Prefer not to answer **[EXCLUSIVE]** → **GO TO S11**

We understand that the meaning of "regular basis" might be different for different people. When you answer this question, please think about what "regular basis" means to you.

[S3B (UKB/CONNECT)]

How old were you when you first started smoking **on a regular basis**?

Enter INTEGER
OR
-1 Do not know
OR
-3 Prefer not to answer

We understand that the meaning of "regular basis" might be different for different people. When you answer this question, please think about what "regular basis" means to you.

If you don't know, please give us your best estimate

[S2AA (CONNECT]

On how many occasions have you smoked cigarettes in your life?

SELECT one of 5 from

0 10 or less → **GO TO S11**
1 11—49 → **GO TO S11**
2 50—99
3 100 or more
-3 Prefer not to answer → ***GO TO S11***

[S4(UKB/CONNECT)]

What type of cigarettes have you mainly smoked?

SELECT one of 6 from

1 Manufactured cigarette
2 Hand-rolled cigarettes
-7 None of the above
-3 Prefer not to answer

If you smoke both hand-rolled, and manufactured cigarettes select the one that you smoke more of.

If you still currently smoke, report the type you smoke most frequently

[S1 (UKB/CONNECT)]

Do you smoke cigarettes now?

SELECT one of 4 from

1 Yes, every day
2 Yes, some days
3 Yes, but rarely

0 No, not at all **-> S2 (UKB)**
-3 Prefer not to answer **-> S2 (UKB)**

[S1A (CONNECT)]

On the days that you smoke, how many cigarettes do you smoke **per day on average?** Please provide the number of cigarettes, not the number of packs.

Enter INTEGER
OR
-10 Less than one a day
OR
-1 Do not know

➔ **GO TO S5A**

Count the total number of cigarettes (including both hand-rolled and manufactured cigarettes)

For hand-rolled cigarettes:
- One ounce of tobacco makes about 30 cigarettes.
- One gram of tobacco makes about 1 cigarette.

[S2 (UKB/CONNECT)]

In the past, how often have you smoked cigarettes?

SELECT one of 4 from

1 Smoked every day **-> S2B**

2 Smoked some days

3 Smoked rarely

-3 Prefer not to answer

[S4AA (UKB/CONNECT)]

Did you ever smoke cigarettes on **most or all days**?

SELECT one of 3 from

0 No → **GO TO S5A**

1 Yes

-3 Prefer not to answer → **GO TO S5A**

[S4AB (CONNECT)]

On the days that you smoked how many cigarettes did you smoke **per day on average?** Please provide the number of cigarettes, not the number of packs.

Enter INTEGER

OR

-10 Less than one a day

OR

-1 Do not know

Count the total number of cigarettes (including both hand-rolled and manufactured cigarettes if both are smoked)

For hand-rolled cigarettes:
- One ounce of tobacco makes about 30 cigarettes.
- ONE GRAM OF TOBACCO MAKES ABOUT 1 CIGARETTE.

[S8 (UKB)]

How old were you when you last smoked cigarettes on most days? S11

Enter INTEGER

OR

-1 Do not know

OR

-3 Prefer not to answer

[S5A (UKB)]

Compared to 10 years ago do you smoke...

SELECT one of 4 from

1	More nowadays?	**-> GO TO S9**
2	About the same?	**-> GO TO S9**
3	Less nowadays?	**-> GO TO S5B (UKB)**
-3	Prefer not to answer	**-> GO TO S9**

[S5B (UKB)]

SHOW IF (S5A = 3) OR (S1 > S1A AND S1 != 0 AND S1 != -3)

Why did you reduce your smoking?
(You can select more than one answer)

TOGGLE of 19 choices

[Require ≥1 choices]

1	Advice from a GP/Health professional
2	TV advert for a nicotine replacement product
3	Government TV/radio/Press advert
4	Hearing about a new stop smoking treatment
5	A decision that smoking was too expensive
6	Being faced with smoking restrictions
7	I knew someone else who was stopping
8	Seeing a health warning on a cigarette pack
9	Being contacted by my local NHS Stop Smoking Services
10	Health problems I had at the time
11	A concern about future health problems
12	Attending a local stop smoking activity or event
13	Something said by family/friends/children
14	A significant birthday
15	The coronavirus outbreak
16	Restrictions on where I could smoke
-7	None of the above [**EXCLUSIVE**]
-1	Do not know [**EXCLUSIVE**]
-3	Prefer not to answer [**EXCLUSIVE**]

➔ **GO TO S9**

[S9 (UKB)]

In the time that you smoked, did you ever stop for more than 6 months?

SELECT one of 4 from

1 Yes **-> GO TO S10**

0 No **-> IF (S1 == 0 AND S3 != -3) GO TO S10 ELSE GO TO S11**

-1 Do not know **-> IF (S1 == 0 AND S3 != -3) GO TO S10 ELSE GO TO S11**

-3 Prefer not to answer **-> IF (S1 == 0 AND S3 != -3) GO TO S10 ELSE GO TO S11**

[S10 (TOOLKIT)]

Why did you stop smoking?
(You can select more than one answer)

TOGGLE of 19 choices

[Require ≥1 choices]

1 Advice from a GP/Health professional

1 TV advert for a nicotine replacement product

1 Government TV/radio/Press advert

1 Hearing about a new stop smoking treatment

5 A decision that smoking was too expensive

6 Being faced with smoking restrictions

7 I knew someone else who was stopping

8 Seeing a health warning on a cigarette pack

9 Being contacted by my local NHS Stop Smoking Services

10 Health problems I had at the time

11 A concern about future health problems

12 Attending a local stop smoking activity or event

13 Something said by family/friends/children

14 A significant birthday

15 The coronavirus outbreak

16 Restrictions on where I could smoke

-7 None of the above [**EXCLUSIVE**]

-1 Do not know [**EXCLUSIVE**]

-3 Prefer not to answer [**EXCLUSIVE**]

[V4 (NHS3)]

How often, on average, did you use e-cigarettes (vaping) during the past 12 months?

SELECT one from 12

1 Never
2 Less than 1 time/mo
3 2-3 times/mo
4 1-2 times /week
5 3-6 times /week
6 1-4 times /day
7 5-14 times /day
8 15-24 times /day
9 25– 34 times /day
10 35 – 44 times /day
11 More than 45 times /day
-3 Prefer not to answer

[V5 (NHS3)]

What type of e-liquids/cartridges do you or did you use in your e-cigarettes?

CHOOSE ALL THAT APPLY

1 Fruit/dessert flavour WITHOUT nicotine
2 Fruit/dessert flavour WITH nicotine
3 Menthol flavour WITHOUT nicotine
4 Menthol flavour WITH nicotine
5 Tobacco flavour WITHOUT nicotine
6 Tobacco flavour WITH nicotine
7 Marijuana or THC concentrate
8 Alcohol
9 Other:
-3 Prefer not to answer

[S11V2 (CONNECT)]

In **the past year**, about how often were you around tobacco smoke from other people smoking in your home or at work?

SELECT one of 8 from

1 Every day
1 Most days of the week
2 A few days per week
3 One day per
4 A few days per month
5 One day per month
6 A few days per
0 Never → **GO TO A1**
-3 Prefer not to answer → **GO TO A1**

[S12 (UKB)]

On days you were around other people's tobacco smoke in **the past year** in your home or work, about how many hours per day were you around it?

SELECT one of 6 from

0 Less than 1 hour per day
1 1 to 2 hours per day
2 3 to 5 hours per day
3 6 to 9 hours per day
4 10 to 15 hours per day
5 More than 15 hours per day
-3 Prefer not to answer

IF TOBACCO _B = 1 GO TO V2 ELSE GO TO A1

[A1 (UKB)]

About how often do you drink alcohol?

SELECT one of 7 from

1	Daily or almost daily	
2	Three or four times a week	
3	Once or twice a week	
4	One to three times a month	**-> GO TO A2B (UKB)**
5	Special occasions only	**-> GO TO A2B UKB)**
6	Never	**-> GO TO A1A (UKB)**
-3	Prefer not to answer	**-> GO TO END SECTION 3**

If this varies a lot, please provide an average considering your intake over the last year

[A1A (UKB)]

Did you previously drink alcohol?

SELECT one of 3 from

1	Yes	**-> GO TO A7A (UKB)**
0	No	**-> GO TO END SECTION 3**
-3	Prefer not to answer	**-> GO TO END SECTION 3**

[A2B (UKB)]

In an average MONTH, how many glasses of RED wine would you drink?
(There are six glasses in an average bottle)

Enter INTEGER

OR

-1 Do not know

OR

-3 Prefer not to answer

Please include sparkling red wine here.

[A2C (UKB)]

In an average MONTH, how many glasses of WHITE wine or champagne would you drink? (There are six glasses in an average bottle)

Enter INTEGER
OR
-1 Do not know
OR
-3 Prefer not to answer

Please include sparkling white wine, prosecco and rosé here.

[A2E (UKB)]

In an average MONTH, how many pints of beer or cider would you drink?
(Include bitter, lager, stout, ale, Guinness)

Enter INTEGER
OR
-1 Do not know
OR
-3 Prefer not to answer

[A2A (UKB)]

In an average MONTH, how many measures of spirits or liqueurs would you drink?
(there are 25 standard measures in a normal sized bottle; spirits include drinks such as whisky, gin, rum, vodka, brandy)

Enter INTEGER
OR
-1 Do not know
OR
-3 Prefer not to answer

[A2F (UKB)]

In an average MONTH, how many glasses of fortified wine would you drink? (There are 12 glasses in an average bottle) (Fortified wines include drinks such as sherry, port, vermouth)

Enter INTEGER
OR
-1 Do not know
OR
-3 Prefer not to answer

Fortified wines include: Sherry, Port, Vermouth, Muscat,Madeira, Malaga, Tokay, Frontignan, Frontignac.

[A2G (UKB)]

In an average MONTH, how many glasses
of other alcoholic drinks (such as alcopops) would you drink?

Enter INTEGER

OR

-1 Do not know

OR

-3 Prefer not to answer

[A3B (UKB)]

In an average WEEK, how many glasses of RED wine would you drink?
(There are six glasses in an average bottle)

Enter INTEGER

OR

-1 Do not know

OR

-3 Prefer not to answer

Please include sparkling red wine here.

[A3C (UKB)]

In an average WEEK, how many glasses of WHITE wine or champagne would you drink?
(There are six glasses in an average bottle)

Enter INTEGER

OR

-1 Do not know

OR

-3 Prefer not to answer

Please include sparkling white wine, prosecco and rosé here.

[A3E (UKB)]

In an average WEEK, how many pints of beer or cider would you drink?
(Include bitter, lager, stout, ale, Guinness)

Enter INTEGER

OR

-1 Do not know

OR

-3 Prefer not to answer

[A3A (UKB)]

In an average WEEK, how many measures of spirits or liqueurs would you drink?

(there are 25 standard measures in a normal sized bottle; spirits include drinks such as whisky, gin, rum, vodka, brandy)

Enter INTEGER

OR

-1 Do not know

OR

-3 Prefer not to answer

For mixed drinks that contain spirits or liqueurs, count one bottle as one measure. There is a question later on alcopops

[A3F (UKB)]

In an average WEEK, how many glasses of fortified wine would you drink?
(There are 12 glasses in an average bottle; Fortified wines include drinks such as sherry, port, vermouth)

Enter INTEGER

OR

-1 Do not know

OR

-3 Prefer not to answer

Fortified wines include: Sherry, Port, Vermouth, Muscat,Madeira, Malaga, Tokay, Frontignan, Frontignac.

[A3G (UKB)]

In an average WEEK, how many glasses of other alcoholic drinks (such as alcopops) would you drink?

Enter INTEGER

OR

-1 Do not know

OR

-3 Prefer not to answer

[A5 (UKB)]

When you drink alcohol is it usually with meals?

SELECT one of 5 from

1 Yes

0 No

-6 It varies

-1 Do not know

-3 Prefer not to answer

[A6 (UKB)]

Compared to 10 years ago, do you drink?

SELECT one of 5 from

1 More nowadays
2 About the same
3 Less nowadays **-> GO TO A7 (UKB)**
-1 Do not know
-3 Prefer not to answer

➔ **GO TO END SECTION 3**

[A7 (TOOLKIT)]

Which of the following, if any, do you think contributed to you reducing the amount you drank?

TOGGLE of 14 choices
[Require ≥1 choices]

1 Advice from a doctor/health worker
2 Government TV/radio/press article
3 A decision drinking was too expensive
4 I knew someone else who was cutting down
5 Health problems I had at the time
6 A concern about future health problems
7 Something said by family/friends/children
8 A significant birthday or event
9 Improve my fitness
10 Help with weight lows
11 Detox (e.g., Dry January)
12 Other reason
-1 Do not know **[EXCLUSIVE]**
-3 Prefer not to answer **[EXCLUSIVE]**

[A7A (TOOLKIT)]

Which of the following, if any, do you think contributed to you stopping drinking alcohol?

TOGGLE of 14 choices
[Require ≥1 choices]

1 Advice from a doctor/health worker
2 Government TV/radio/press article
3 A decision drinking was too expensive
4 Financial reasons I knew someone else who was cutting down
5 Other reason Health problems I had at the time

6 A concern about future health problems
7 Something said by family/friends/children
8 A significant birthday or event
9 Improve my fitness
10 Help with weight lows
11 Detox (e.g., Dry January)
12 Other
-1 Do not know **[EXCLUSIVE]**
-3 Prefer not to answer **[EXCLUSIVE]**

----------END OF SECTION 3----------

Family health history [SECTION 4]

We ask about your family history because some diseases and health issues can be passed down generations.

In a long-term study like ours, this helps us identify when this is happening, with who and why and helps us work toward solving these issues for future generations.
Now, some questions about you and your family.

[D2 (UKB)]

Where were you born?

SELECT one of 12 from

1	England	**-> GO TO Y1 (UKB)**
2	Wales	**-> GO TO Y1 (UKB)**
3	Scotland	**-> GO TO Y1 (UKB)**
4	Northern Ireland	**-> GO TO Y1 (UKB)**
5	UK (don't know country)	**-> GO TO Y1 (UKB)**
6	Republic of Ireland	
7	India	
8	Pakistan	
9	Poland	
10	Other (extended drop down list. See excel)	
-1	Do not know	**-> GO TO Y1 (UKB)**
-3	Prefer not to answer	**-> GO TO Y1 (UKB)**

[D2A (UKB)]

What year did you first come to live in the United Kingdom?
Please enter a date in the following format: dd/mm/yyyy

Enter INTEGER

OR

-1 Do not know

OR

-3 Prefer not to answer

Please give the year that you FIRST came to live in the United Kingdom. Do not count years if you came to holiday or visit friends or family.

[Y1 (UKB)]

Were you adopted as a child?

SELECT one of 4 from

1 Yes

0 No

-1 Do not know

-3 Prefer not to answer

[Y13 (UKB)]

Is your biological father still alive?

SELECT one of 4 from

1	Yes	
0	No	**-> GO TO Y13B (UKB)**
-1	Do not know	**-> GO TO Y13D (UKB)**
-3	Prefer not to answer	**-> GO TO Y13D (UKB)**

[Y13A (UKB)]

What is his age now?

Enter INTEGER
[Require > current age, ≤ 122
Units: years]
OR
-1 Do not know
OR
-3 Prefer not to answer

[Y13B (UKB)]

What was his age when he died?

Enter INTEGER
[Require ≥ 10, ≤ 122
Units: years]
OR
-1 Do not know
OR
-3 Prefer not to answer

[Y13D (UKB)]

Has/did your biological father ever suffer from?
You can select more than one answer
We will ask more details for any type of disorder that you select here

TOGGLE
[Require ≥1 choices]

0 Autoimmune disorder **-> GO TO AUTO_A**
1 Blood disorders (Anaemia) **-> GO TO BLOOD_A**
2 Cancer **-> GO TO CANC_A**

4 Digestive system or liver problems **-> GO TO DIG_A**

5 Endocrine, nutritional and metabolic disorders (e.g., diabetes, thyroid disorder, vitamin deficiencies) **-> GO TO EN_A**

6 Eye or visual problems **-> GO TO EYE_A**

7 Fractures, breaks, or joint problems **-> GO TO FRAC_A**

8 Heart or circulatory disease (e.g., high blood pressure or stroke) **-> GO TO HEART_A**

9 Kidney or urinary system disorders **-> GO TO KIDN_A**

10 Lung or respiratory problems **-> GO TO LUNG_A**

11 Mental health conditions (e.g.depression, bipolar disorder) **-> GO TO MH_A**

12 Neurodevelopmental conditions (e.g., Autism spectrum disorder, ADHD) **-> GO TO ND_A**

13 Neurological disorders (things that affect that brain or nervous system) **-> GO TO NEU_A**

14 Reproductive system problems **-> GO TO REPRO_A**

15 Other not listed **-> GO TO Y16 (UKB)]**

16 None of these **-> GO TO Y16 (UKB)]**

-1 I don't know **[EXCLUSIVE]** **-> GO TO Y16 (UKB)]**

-3 Prefer not to answer **[EXCLUSIVE]** **-> GO TO Y16 (UKB)]**

Answer this question for blood relations only. If you are not sure if your father suffered from any of the listed illnesses, please select 'Do not know'. If you know your father suffered from certain listed illnesses but are unsure about others, only select the ones you are sure about.

[AUTO_A_DAD]

Has your father ever been diagnosed with any of the following autoimmune disorders?

0 Rheumatoid arthritis

1 Lupus

2 Inflammatory Bowel Disease (IBD)

3 Multiple Sclerosis (MS)

4 Graves' disease

5 Guillain-Barre syndrome

6 Psoriasis

7 Other (not listed)

-1 I don't know

-3 Prefer not to answer

[BLOOD_A_DAD]

Has your father ever been diagnosed with any of the following types of anaemia?

0 Iron deficiency anaemia

1 Vitamin deficiency anaemia

2 Sickle cell anaemia
3 Aplastic anaemia
4 Thalassaemia
5 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[CANC_A_DAD (CONNECT)]

Which type(s) of cancer specifically was your father diagnosed with?
Please indicate where the cancer originated, even if it spread to other body areas

0 Anal
1 Bladder
2 Brain
3 Breast
4 Cervical
5 Colon/rectal
6 Oesophageal
7 Head and neck (Including cancers of the mouth, sinuses, nose, or throat. Not including brain or skin cancers.)
8 Gastric
9 Kidney
10 Leukaemia (blood and bone marrow)
11 Liver
12 Lung or bronchial
14 Lymphoma
15 Ovarian
16 Pancreatic
17 Prostate
18 Skin. -> GO TO DAD_CANC_B
19 Stomach
20 Testicular
21 Thyroid
22 Uterine (endometrial)
23 Another type of cancer
24 I know they had cancer, but don't know what type
-1 I don't know
-3 Prefer not to answer

[CANC_B_DAD (CONNECT)]

What type of skin cancer specifically was your father diagnosed with?

0 Melanoma
1 Basal cell

2 Squamous cell
-1 I don't know
-3 Prefer not to answer

[DIG_A_DAD (CONNECT)]

Has your father ever been diagnosed with any of the following digestive system problems?

0 Gastro-oesophageal Acid Reflux (GORD)
1 Barrett's Oesophagus
2 Irritable bowel syndrome
3 Inflammatory Bowel Disease
4 Diverticulitis or Diverticulosis
5 Ulcerative Colitis
6 Crohn's Disease
7 Coeliac Disease (also known as Gluten-Sensitive Enteropathy)
8 Gallstones (Biliary Stones)
9 Fatty liver disease
10 Liver Cirrhosis
11 Hepatitis
12 Pancreatitis
5 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[EN_A_DAD]

Has your father ever been diagnosed with the following conditions?

0 Type 1 diabetes
1 Type 2 diabetes
2 overactive thyroid
3 underactive thyroid
4 Cushing syndrome
5 Lactose intolerance
6 Vitamin A deficiency
7 Thiamine deficiency
8 Vitamin D deficiency
3 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[EYE_A_DAD]

Has your father ever been diagnosed with any of the following eye or visual problems?

0 Glaucoma
1 Visual impairment including blindness
2 Double vision
3 Night blindness
4 Colour blindness
5 Macular degeneration
6 Cataracts
7 Retinal detachment
8 Diabetic retinopathy
9 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[FRAC_A_DAD]

What type of fractures, breaks, joint or bone problems have your father experienced?

0 Hip fracture
1 Osteoporosis
2 Osteoarthritis (arthritis)
3 Gout
4 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[HEART_A_DAD (CONNECT)]

Has your father ever been diagnosed with any of the following heart or circulatory diseases?

0 B-12 Deficiency (Pernicious Anaemia)
1 Coronary Artery/Coronary Heart Disease
2 Congestive Heart Failure
3 High Cholesterol
4 Heart Attack (Myocardial Infarction)
5 Abnormal Heart Rhythm (Arrhythmia)
6 Chest Pain (Angina)
7 Heart Valve Problems
8 High Blood Pressure (Hypertension) [Please do **not** include hypertension during pregnancy.]
9 Blood Clots (Deep Vein Thrombosis, Pulmonary Embolism)
10 Stroke
11 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[KIDN_A_DAD (CONNECT]

Has your father ever been diagnosed with any of the following kidney or urinary tract problems?

0 Kidney stones
1 Chronic kidney disease (or chronic kidney failure)
2 Other (not listed)
-1 I don’t know
-3 Prefer not to answer

[LUNG_A _DAD (CONNECT)]

Has your father ever been diagnosed with any of the following lung or respiratory conditions?

0 Chronic Obstructive pulmonary disease, COPD (including emphysema and chronic bronchitis)
1 Lung fibrosis
2 Bronchiectasis
3 Asthma
4 Hay Fever (Allergic to pollen or Allergic Rhinitis)
5 Other (not listed)
-1 I don’t know
-3 Prefer not to answer

[ND_A_DAD]

Has your father ever been diagnosed with one or more of the following conditions by a professional, even if your father don't have it currently?

Please include disorders even if your father did not need treatment for them or if your father did not agree with the diagnosis. Select ALL that apply

0 Autism spectrum disorder
1 Developmental learning disorders
2 Attention deficit hyperactivity disorder (ADHD)
3 Disorder of intellectual development
4 Developmental motor coordination disorder
5 Developmental speech or language disorders
6 Stereotyped movement disorder
7 Other (not listed)
8 None of the above
-1 I don’t know
-3 Prefer not to answer

[MH_A_DAD]

Has your father ever been diagnosed with one or more of the following conditions by a professional, even if your father don't have it currently?

Please include disorders even if your father did not need treatment for them or if your father did not agree with the diagnosis. Select ALL that apply

1	Anxiety	**-> GO TO ANX_B**
2	Bipolar disorder	
3	Body dysmorphia	
4	Depression	**-> GO TO DEP_B**
5	Premenstrual dysphoric disorder	
6	Post Traumatic Stress Disorder	
7	Obsessive Compulsive Disorder	
8	Eating disorder	**-> GO TO EATD_B**
9	Psychosis	
10	Schizophrenia	
11	Schizoaffective disorder	
12	Personality disorder	
13	Other (not listed)	
14	None of the above	
-1	I don’t know	
-3	Prefer not to answer	

[ANX_B_DAD]

Which anxiety disorder(s) specifically has your father been diagnosed with in their lifetime?

0	Generalised anxiety disorder
1	Agoraphobia
2	Social anxiety disorder
3	Panic disorder
4	Panic attacks
5	Specific phobia
6	Other (not listed)
7	None of the above
-1	I don’t know
-3	Prefer not to answer

[DEP_B_DAD]

Which depressive disorder(s) specifically has your father been diagnosed with in their lifetime?

0	Major Depressive Disorder
1	Perinatal depression
2	Postnatal depression

3 Other (not listed)
4 None of the above
-1 I don't know
-3 Prefer not to answer

[EATD_B_DAD]

Which eating disorder(s) specifically has your father been diagnosed with in their lifetime?

0 Anorexia nervosa
1 Atypical anorexia nervosa
2 Bulimia nervosa
3 Binge eating disorder
4 Other (not listed)
5 None of the above
-1 I don't know
-3 Prefer not to answer

[NEU_A_DAD]

Has your father ever been diagnosed with any of the following neurological or brain disorders?

0 Epilepsy
1 Parkinson's disease
2 Alzheimer's disease/dementia
3 Early onset Alzheimer's disease/dementia
4 Vascular dementia
5 Migraine with aura
6 Migraine without aura
7 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[REPRO_A_DAD (CONNECT)]

Has your father ever been diagnosed with any of the following conditions?

0 Endometriosis
1 Polycystic Ovary Syndrome (PCOS)
2 Enlarged prostate
3 Fibrocystic Breast, or another Benign Breast Disease (such as proliferative Benign Breast Disease or LCIS)
4 Ductal Carcinoma in situ (DCIS)
5 Uterine Fibroids
6 Other (not listed)

-1 I don't know
-3 Prefer not to answer

[Y16 (UKB)]

Is your biological mother still alive?

SELECT one of 4 from

1	Yes	
0	No	**-> GO TO Y16B (UKB)**
-1	Do not know	**-> GO TO Y16D (UKB)**
-3	Prefer not to answer	**-> GO TO Y16D (UKB)**

[Y16A (UKB)]

What is her age now?

Enter INTEGER
[Require > current age, ≤ 122
Units: years]
OR
-1 Do not know
OR
-3 Prefer not to answer

[Y16B (UKB)]

What was her age when she died?

Enter INTEGER
[Require > current age, ≤ 122
Units: years]
OR
-1 Do not know
OR
-3 Prefer not to answer

[Y16D (UKB)]

Has/did your mother ever suffer from? (You can select more than one answer)

TOGGLE
[Require ≥1 choices]

2 Autoimmune disorder **-> GO TO AUTO_A**
3 Blood disorders (Anaemia) **-> GO TO BLOOD_A**
2 Cancer **-> GO TO CANC_A**
3 Complications or difficulties in pregnancy or childbirth **-> GO TO PREG_A**
4 Digestive system or liver problems **-> GO TO DIG_A**

5 Endocrine, nutritional and metabolic disorders (e.g., diabetes, thyroid disorder, vitamin deficiencies) **-> GO TO EN_A**

6 Eye or visual problems **-> GO TO EYE_A**

7 Fractures, breaks, or joint problems **-> GO TO FRAC_A**

8 Heart or circulatory disease (e.g. high blood pressure or stroke) **-> GO TO HEART_A**

9 Kidney or urinary system disorders **-> GO TO KIDN_A**

10 Lung or respiratory problems **-> GO TO LUNG_A**

11 Mental health conditions (e.g.depression, bipolar disorder) **-> GO TO MH_A**

12 Neurodevelopmental conditions (e.g., Autism spectrum disorder, ADHD) **-> GO TO ND_A**

13 Neurological disorders (things that affect that brain or nervous system) **-> GO TO NEU_A**

14 Reproductive system problems **-> GO TO REPRO_A**

15 Other not listed **-> GO TO Y17 (UKB)]**

16 None of these **-> GO TO Y17 (UKB)]**

-1 I don't know **[EXCLUSIVE]** **-> GO TO Y17 (UKB)]**

-3 Prefer not to answer **[EXCLUSIVE]** **-> GO TO Y17 (UKB)]**

Answer this question for blood relations only. If you are not sure if your mother suffered from any of the listed illnesses, please select 'Do not know'. If you know your mother suffered from certain listed illnesses but are unsure about others, only select the ones you are sure about.

[AUTO_A_MOM]

Has your mother ever been diagnosed with any of the following autoimmune disorders?

0 Rheumatoid arthritis

1 Lupus

2 Inflammatory Bowel Disease (IBD)

3 Multiple Sclerosis (MS)

4 Graves' disease

5 Guillain-Barre syndrome

6 Psoriasis

7 Other (not listed)

-1 I don't know

-3 Prefer not to answer

[BLOOD_A_MOM]

Has your mother ever been diagnosed with any of the following types of anaemia?

0 Iron deficiency anaemia

1 Vitamin deficiency anaemia

2 Sickle cell anaemia

3 Aplastic anaemia

4 Thalassaemia
5 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[CANC_A_MOM (CONNECT)]

Which type(s) of cancer specifically was your mother diagnosed with?
Please indicate where the cancer originated, even if it spread to other body areas

0 Anal
1 Bladder
2 Brain
3 Breast
4 Cervical
5 Colon/rectal
6 Oesophageal
7 Head and neck (Including cancers of the mouth, sinuses, nose, or throat. Not including brain or skin cancers.)
8 Gastric
9 Kidney
10 Leukaemia (blood and bone marrow)
11 Liver
12 Lung or bronchial
14 Lymphoma
15 Ovarian
16 Pancreatic
17 Prostate
18 Skin
19 Stomach
20 Testicular
21 Thyroid
22 Uterine (endometrial)
23 Another type of cancer
24 I know they had cancer, but don't know what type
-1 I don't know
-3 Prefer not to answer

[CANC_B_MOM (CONNECT)]

What type of skin cancer specifically was your mother diagnosed with?

3 Melanoma
4 Basal cell
5 Squamous cell
-1 I don't know

-3 Prefer not to answer

[PREG_A_MOM (CONNECT+ICD)]

What type of complication or difficulties with pregnancy or childbirth has your mother experienced?

0 Miscarriage (pregnancy loss before 20 weeks)
1 Stillbirth (pregnancy loss after 20 weeks)
2 Live birth and still birth (loss of one or more multiples)
3 Ectopic or tubal pregnancy
4 Trying to get pregnant for more than a year but not getting pregnant during that time
5 hyperemesis gravidarum
6 Gestational diabetes
7 Preterm labour and delivery
8 Complicated labour and delivery
9 Traumatic labour or delivery
10 Pre-eclampsia
11 Eclampsia
12 Gestational hypertension
13 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[DIG_A_MOM (CONNECT)]

Has your mother ever been diagnosed with any of the following digestive system problems?

0 Gastro-oesophageal Acid Reflux (GORD)
1 Barrett's Oesophagus
2 Irritable bowel syndrome
3 Inflammatory Bowel Disease
4 Diverticulitis or Diverticulosis
5 Ulcerative Colitis
6 Crohn's Disease
7 Coeliac Disease (also known as Gluten-Sensitive Enteropathy)
8 Gallstones (Biliary Stones)
9 Fatty liver disease
10 Liver Cirrhosis
11 Hepatitis
12 Pancreatitis
5 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[EN_A_MOM]

Has your mother ever been diagnosed with the following conditions?

0	Type 1 diabetes
1	Type 2 diabetes
2	overactive thyroid
3	underactive thyroid
4	Cushing syndrome
5	Lactose intolerance
6	Vitamin A deficiency
7	Thiamine deficiency
8	Vitamin D deficiency
3	Other (not listed)
-1	I don’t know
-3	Prefer not to answer

[EYE_A_MOM]

Has your mother ever been diagnosed with any of the following eye or visual problems?

1	Glaucoma
1	Visual impairment including blindness
2	Double vision
3	Night blindness
4	Colour blindness
5	Macular degeneration
6	Cataracts
7	Retinal detachment
8	Diabetic retinopathy
9	Other (not listed)
-1	I don’t know
-3	Prefer not to answer

[FRAC_A_MOM]

What type of fractures, breaks, joint or bone problems have your mother experienced?

15	Hip fracture
1	Osteoporosis
2	Osteoarthritis (arthritis)
3	Gout
4	Other (not listed)
-1	I don’t know
-3	Prefer not to answer

[HEART_A_MOM (CONNECT)]

Has your mother ever been diagnosed with any of the following heart or circulatory diseases?

0 B-12 Deficiency (Pernicious Anaemia)
1 Coronary Artery/Coronary Heart Disease
2 Congestive Heart Failure
3 High Cholesterol
4 Heart Attack (Myocardial Infarction)
5 Abnormal Heart Rhythm (Arrhythmia)
6 Chest Pain (Angina)
7 Heart Valve Problems
8 High Blood Pressure (Hypertension) [Please do **not** include hypertension during pregnancy.]
9 Blood Clots (Deep Vein Thrombosis, Pulmonary Embolism)
10 Stroke
11 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[KIDN_A_MOM (CONNECT]

Has your mother ever been diagnosed with any of the following kidney or urinary tract problems?

0 Kidney stones
1 Chronic kidney disease (or chronic kidney failure)
2 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[LUNG_A _MOM (CONNECT)]

Has your mother ever been diagnosed with any of the following lung or respiratory conditions?

0 Chronic Obstructive pulmonary disease, COPD (including emphysema and chronic bronchitis)
1 Lung fibrosis
2 Bronchiectasis
3 Asthma
4 Hay Fever (Allergic to pollen or Allergic Rhinitis)
5 Other (not listed)
-1 I don't know

-3 Prefer not to answer

[ND_A_MOM]

Has your mother ever been diagnosed with one or more of the following conditions by a professional, even if your mother don't have it currently?

Please include disorders even if your mother did not need treatment for them or if your mother did not agree with the diagnosis. Select ALL that apply

9 Autism spectrum disorder
10 Developmental learning disorders
11 Attention deficit hyperactivity disorder (ADHD)
12 Disorder of intellectual development
13 Developmental motor coordination disorder
14 Developmental speech or language disorders
15 Stereotyped movement disorder
16 Other (not listed)
17 None of the above
-1 I don't know
-3 Prefer not to answer

[MH_A_MOM]

Has your mother ever been diagnosed with one or more of the following conditions by a professional, even if your mother don't have it currently?

Please include disorders even if your mother did not need treatment for them or if your mother did not agree with the diagnosis. Select ALL that apply

16 Anxiety **-> GO TO ANX_B**
17 Bipolar disorder
18 Body dysmorphia
19 Depression **-> GO TO DEP_B**
20 Premenstrual dysphoric disorder
21 Post Traumatic Stress Disorder
22 Obsessive Compulsive Disorder
23 Eating disorder **-> GO TO EATD_B**
24 Psychosis
25 Schizophrenia
26 Schizoaffective disorder
27 Personality disorder
28 Other (not listed)
29 None of the above
-1 I don't know
-3 Prefer not to answer

[ANX_B_MOM]

Which anxiety disorder(s) specifically has your mother been diagnosed with in their lifetime?

8	Generalised anxiety disorder
9	Agoraphobia
10	Social anxiety disorder
11	Panic disorder
12	Panic attacks
13	Specific phobia
14	Other (not listed)
15	None of the above
-1	I don't know
-3	Prefer not to answer

[DEP_B_MOM]

Which depressive disorder(s) specifically has your mother been diagnosed with in their lifetime?

5	Major Depressive Disorder
6	Perinatal depression
7	Postnatal depression
8	Other (not listed)
9	None of the above
-1	I don't know
-3	Prefer not to answer

[EATD_B_MOM]

Which eating disorder(s) specifically has your mother been diagnosed with in their lifetime?

6	Anorexia nervosa
7	Atypical anorexia nervosa
8	Bulimia nervosa
9	Binge eating disorder
10	Other (not listed)
11	None of the above
-1	I don't know
-3	Prefer not to answer

[NEU_A_MOM]

Has your mother ever been diagnosed with any of the following neurological or brain disorders?

8	Epilepsy
9	Parkinson's disease

10 Alzheimer's disease/dementia
11 Early onset Alzheimer's disease/dementia
12 Vascular dementia
13 Migraine with aura
14 Migraine without aura
15 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[REPRO_A_MOM (CONNECT)]

Has your mother ever been diagnosed with any of the following conditions?

0 Endometriosis
1 Polycystic Ovary Syndrome (PCOS)
2 Enlarged prostate
3 Fibrocystic Breast, or another Benign Breast Disease (such as proliferative Benign Breast Disease or LCIS)
4 Ductal Carcinoma in situ (DCIS)
5 Uterine Fibroids
6 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[Y17 (UKB)]

How many brothers do you have?

(Please include those who have died, and twin brothers. Do not include half-brothers, stepbrothers or adopted brothers)

Enter INTEGER
[Require ≥ 0, ≤ 25]
OR
-1 Do not know
OR
-3 Prefer not to answer

➔ **IF ANSWER > 0, GO TO Y19**

[Y18 (UKB)]

How many sisters do you have?
(Please include those who have died, and twin sisters. Do not include half-sisters, stepsisters or adopted sisters)

Enter INTEGER

[Require ≥ 0, ≤ 25]

OR

-1 Do not know

OR

-3 Prefer not to answer

➔ **IF Y17 > 0 OR IF ANSWER > 0, GO TO Y19**

➔ **IF (ANSWER = 0 OR -1 OR -3) AND Y17 (ANSWER = 0 OR -1 OR -3), GO TO END SECTION**

[Y19 (UKB)]

Have any of your brothers or sisters suffered from any of the following illnesses?
Please select all that apply
We will ask more details for any type of disorder that you select here

TOGGLE

[Require ≥1 choices]

4 Autoimmune disorder **-> GO TO AUTO_A**

5 Blood disorders (Anaemia) **-> GO TO BLOOD_A**

2 Cancer **-> GO TO CANC_A**

3 Complications or difficulties in pregnancy or childbirth **-> GO TO PREG_A**

4 Digestive system or liver problems **-> GO TO DIG_A**

5 Endocrine, nutritional and metabolic disorders (e.g., diabetes, thyroid disorder, vitamin deficiencies) **-> GO TO EN_A**

6 Eye or visual problems **-> GO TO EYE_A**

7 Fractures, breaks, or joint problems **-> GO TO FRAC_A**

8 Heart or circulatory disease (e.g. high blood pressure or stroke) **-> GO TO HEART_A**

9 Kidney or urinary system disorders **-> GO TO KIDN_A**

10 Lung or respiratory problems **-> GO TO LUNG_A**

11 Mental health conditions (e.g.depression, bipolar disorder) **-> GO TO MH_A**

12 Neurodevelopmental conditions (e.g., Autism spectrum disorder, ADHD) **-> GO TO ND_A**

13 Neurological disorders (things that affect that brain or nervous system) **-> GO TO NEU_A**

14 Reproductive system problems **-> GO TO REPRO_A**

15 Other not listed **-> GO TO END SECTION**

16 None of these **-> GO TO END SECTION**

-1 I don't know **[EXCLUSIVE]** **-> GO TO END SECTION**

-3 Prefer not to answer **[EXCLUSIVE]** **-> GO TO END SECTION**

Answer this question for blood relations only. Include any sisters or brothers who have died. If you are not sure if your sisters or brothers suffered from any of the listed illnesses, please select 'Do not know'.

If more than one sister or brother has suffered from any of the listed illnesses, you only need to select the illness once.

[AUTO_A_SIB]

Has your brother or sister ever been diagnosed with any of the following autoimmune disorders?

0 Rheumatoid arthritis
1 Lupus
2 Inflammatory Bowel Disease (IBD)
3 Multiple Sclerosis (MS)
4 Graves' disease
5 Guillain-Barre syndrome
6 Psoriasis
7 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[BLOOD_A_SIB]

Has your brother or sister ever been diagnosed with any of the following types of anaemia?

0 Iron deficiency anaemia
1 Vitamin deficiency anaemia
2 Sickle cell anaemia
3 Aplastic anaemia
4 Thalassaemia
5 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[CANC_A_SIB (CONNECT)]

Which type(s) of cancer specifically were your brother or sister diagnosed with?
Please indicate where the cancer originated, even if it spread to other body areas

0 Anal
1 Bladder
2 Brain
3 Breast
4 Cervical
5 Colon/rectal
6 Oesophageal
7 Head and neck (Including cancers of the mouth, sinuses, nose, or throat. Not including brain or skin cancers.)
8 Gastric

9 Kidney
10 Leukaemia (blood and bone marrow)
11 Liver
12 Lung or bronchial
14 Lymphoma
15 Ovarian
16 Pancreatic
17 Prostate
18 Skin
19 Stomach
20 Testicular
21 Thyroid
22 Uterine (endometrial)
23 Another type of cancer
24 I know they had cancer, but don't know what type
-1 I don't know
-3 Prefer not to answer

[CANC_B_SIB (CONNECT)]

What type of skin cancer specifically were your brother or sister diagnosed with?

6 Melanoma
7 Basal cell
8 Squamous cell
-1 I don't know
-3 Prefer not to answer

[PREG_A_SIB (CONNECT+ICD)]

What type of complication or difficulties with pregnancy or childbirth has your sister experienced?

0 Miscarriage (pregnancy loss before 20 weeks)
1 Stillbirth (pregnancy loss after 20 weeks)
2 Live birth and still birth (loss of one or more multiples)
3 Ectopic or tubal pregnancy
4 Trying to get pregnant for more than a year but not getting pregnant during that time
5 hyperemesis gravidarum
6 Gestational diabetes
7 Preterm labour and delivery
8 Complicated labour and delivery
9 Traumatic labour or delivery
10 Pre-eclampsia
11 Eclampsia
12 Gestational hypertension

13 Other (not listed)
-1 I don’t know
-3 Prefer not to answer

[DIG_A_SIB (CONNECT)]

Has your brother or sister ever been diagnosed with any of the following digestive system problems?

0 Gastro-oesophageal Acid Reflux (GORD)
1 Barrett’s Oesophagus
2 Irritable bowel syndrome
3 Inflammatory Bowel Disease
4 Diverticulitis or Diverticulosis
5 Ulcerative Colitis
6 Crohn’s Disease
7 Coeliac Disease (also known as Gluten-Sensitive Enteropathy)
8 Gallstones (Biliary Stones)
9 Fatty liver disease
10 Liver Cirrhosis
11 Hepatitis
12 Pancreatitis
5 Other (not listed)
-1 I don’t know
-3 Prefer not to answer

[EN_A_SIB]

Has your brother or sister ever been diagnosed with the following conditions?

0 Type 1 diabetes
1 Type 2 diabetes
2 overactive thyroid
3 underactive thyroid
4 Cushing syndrome
5 Lactose intolerance
6 Vitamin A deficiency
7 Thiamine deficiency
8 Vitamin D deficiency
3 Other (not listed)
-1 I don’t know
-3 Prefer not to answer

[EYE_A_SIB]

Has your brother or sister ever been diagnosed with any of the following eye or visual problems?

2 Glaucoma
1 Visual impairment including blindness
2 Double vision
3 Night blindness
4 Colour blindness
5 Macular degeneration
6 Cataracts
7 Retinal detachment
8 Diabetic retinopathy
9 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[FRAC_A_SIB]

What type of fractures, breaks, joint or bone problems have your brother or sister experienced?

30 Hip fracture
1 Osteoporosis
2 Osteoarthritis (arthritis)
3 Gout
4 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[HEART_A_SIB (CONNECT)]

Has your brother or sister ever been diagnosed with any of the following heart or circulatory diseases?

0 B-12 Deficiency (Pernicious Anaemia)
1 Coronary Artery/Coronary Heart Disease
2 Congestive Heart Failure
3 High Cholesterol
4 Heart Attack (Myocardial Infarction)
5 Abnormal Heart Rhythm (Arrhythmia)
6 Chest Pain (Angina)
7 Heart Valve Problems
8 High Blood Pressure (Hypertension) [Please do **not** include hypertension during pregnancy.]
9 Blood Clots (Deep Vein Thrombosis, Pulmonary Embolism)
10 Stroke

11 Other (not listed)
-1 I don’t know
-3 Prefer not to answer

[KIDN_A_SIB (CONNECT]

Has your brother or sister ever been diagnosed with any of the following kidney or urinary tract problems?

0 Kidney stones
1 Chronic kidney disease (or chronic kidney failure)
2 Other (not listed)
-1 I don’t know
-3 Prefer not to answer

[LUNG_A _SIB (CONNECT)]

Has your brother or sister ever been diagnosed with any of the following lung or respiratory conditions?

0 Chronic Obstructive pulmonary disease, COPD (including emphysema and chronic bronchitis)
1 Lung fibrosis
2 Bronchiectasis
3 Asthma
4 Hay Fever (Allergic to pollen or Allergic Rhinitis)
5 Other (not listed)
-1 I don’t know
-3 Prefer not to answer

[ND_A_SIB]

Has your brother or sister ever been diagnosed with one or more of the following conditions by a professional, even if your brother or sister don't have it currently?

Please include disorders even if your brother or sister did not need treatment for them or if your brother or sister did not agree with the diagnosis. Select ALL that apply

18 Autism spectrum disorder
19 Developmental learning disorders
20 Attention deficit hyperactivity disorder (ADHD)
21 Disorder of intellectual development
22 Developmental motor coordination disorder
23 Developmental speech or language disorders
24 Stereotyped movement disorder
25 Other (not listed)

26 None of the above
-1 I don’t know
-3 Prefer not to answer

[MH_A_SIB]

Has your brother or sister ever been diagnosed with one or more of the following conditions by a professional, even if your brother or sister don't have it currently?

Please include disorders even if your brother or sister did not need treatment for them or if your brother or sister did not agree with the diagnosis. Select ALL that apply

31 Anxiety **-> GO TO ANX_B**
32 Bipolar disorder
33 Body dysmorphia
34 Depression **-> GO TO DEP_B**
35 Premenstrual dysphoric disorder
36 Post Traumatic Stress Disorder
37 Obsessive Compulsive Disorder
38 Eating disorder **-> GO TO EATD_B**
39 Psychosis
40 Schizophrenia
41 Schizoaffective disorder
42 Personality disorder
43 Other (not listed)
44 None of the above
-1 I don’t know
-3 Prefer not to answer

[ANX_B_SIB]

Which anxiety disorder(s) specifically has your brother or sister been diagnosed with in their lifetime?

16 Generalised anxiety disorder
17 Agoraphobia
18 Social anxiety disorder
19 Panic disorder
20 Panic attacks
21 Specific phobia
22 Other (not listed)
23 None of the above
-1 I don’t know
-3 Prefer not to answer

[DEP_B_SIB]

Which depressive disorder(s) specifically has your brother or sister been diagnosed with in their lifetime?

10	Major Depressive Disorder
11	Perinatal depression
12	Postnatal depression
13	Other (not listed)
14	None of the above
-1	I don't know
-3	Prefer not to answer

[EATD_B_SIB]

Which eating disorder(s) specifically has your brother or sister been diagnosed with in their lifetime?

12	Anorexia nervosa
13	Atypical anorexia nervosa
14	Bulimia nervosa
15	Binge eating disorder
16	Other (not listed)
17	None of the above
-1	I don't know
-3	Prefer not to answer

[NEU_A_SIB]

Has your brother or sister ever been diagnosed with any of the following neurological or brain disorders?

16	Epilepsy
17	Parkinson's disease
18	Alzheimer's disease/dementia
19	Early onset Alzheimer's disease/dementia
20	Vascular dementia
21	Migraine with aura
22	Migraine without aura
23	Other (not listed)
-1	I don't know
-3	Prefer not to answer

[REPRO_A_SIB (CONNECT)]

Has your brother or sister ever been diagnosed with any of the following conditions?

0	Endometriosis
1	Polycystic Ovary Syndrome (PCOS)

2 Enlarged prostate
3 Fibrocystic Breast, or another Benign Breast Disease (such as proliferative Benign Breast Disease or LCIS)
4 Ductal Carcinoma in situ (DCIS)
5 Uterine Fibroids
6 Other (not listed)
-1 I don't know
-3 Prefer not to answer

----------END OF SECTION 4 ----------

Your health history [SECTION 5]

This section includes questions about:
-Your general health and any illnesses you may have had in the past.
-Screening tests that you may have had done.
-Details on your reproductive health, covering areas such as children you have had and puberty.
-Medications you might be taking.
-Your mental wellbeing.
All the information you give us is treated confidentially.
Now some questions about your health.

[H3 (UKB)]

In general how would you rate your overall health?

SELECT one of 6 from

1 Excellent
2 Good
3 Fair
4 Poor
-1 Do not know
-3 Prefer not to answer

[H4 (UKB)]

Do you have any physical or mental health conditions or illnesses lasting or expected to last 12 months or more?

SELECT one of 4 from

1 Yes
0 No **-> GO TO H4B**
-1 Do not know
-3 Prefer not to answer

[H4A (UKB)]

Do you receive any of the following? (You can select more than one answer)

TOGGLE of 6 choices
[Require ≥1 choices]

1 Attendance allowance
2 Personal independence payment (previously disability living allowance)
3 Blue badge
-7 None of the above **[EXCLUSIVE]**
-1 Do not know **[EXCLUSIVE]**
-3 Prefer not to answer **[EXCLUSIVE**

Only select a response if you personally receive the benefit. Do not include if your spouse or someone in your household receives one of these benefits.

[H4B (UKB)]

Do you use private healthcare?

SELECT one of 6 from

1 Yes, all of the time
2 Yes, most of the time
3 Yes, sometimes
4 No, never
-1 Do not know
-3 Prefer not to answer

If you have access to private healthcare but always use the NHS, select No, never.

[COVID (WT Q)]

Do you think that you have or have had COVID-19?

1 Yes, confirmed by a positive test
2 Yes, suspected by a doctor but not tested
3 Yes, my own suspicions
4 No
-1 Do not know
-3 Prefer not to answer

[Y6AB (UKB)]

Do you wear sun protection (e.g., sunscreen lotion, hat) when you spend time outdoors in the summer?

SELECT one of 7 from

1 Never/rarely
2 Sometimes
3 Most of the time
4 Always
5 Do not go out in sunshine
-1 Do not know
-3 Prefer not to answer

If you are unsure, please provide an estimate or select 'Do not know'.

[H7C (UKB)]

Have you had any of the following in the past year?

(You can select more than one answer)

TOGGLE of 8 choices
[Require ≥1 choices]

1 Mouth ulcers
2 Painful gums
3 Bleeding gums
4 Loose teeth
5 Toothache
6 Dentures
-7 None of the above **[EXCLUSIVE]**
-3 Prefer not to answer **[EXCLUSIVE]**

[H8 (UKB)]

In the last year have you had any falls?

SELECT one of 4 from

1 No falls
2 Only one fall
3 More than one fall
-3 Prefer not to answer

Do not include falls while playing sport or exercising.

[H9 (UKB)]

Compared with one year ago, has your weight changed?

SELECT one of 5 from

0 No - weigh about the same
2 Yes - gained weight
3 Yes - lost weight
-1 Do not know
-3 Prefer not to answer

[SY2 (UKB)]

In the last year have you ever had wheeze or whistling in the chest?

SELECT one of 4 from

1 Yes
0 No
-1 Do not know
-3 Prefer not to answer

➔ **IF WP1 = -2 GO TO SY4I**

[SY3 (UKB)]

Do you get short of breath walking with people of your own age on level ground?

SELECT one of 4 from

1 Yes
0 No
-1 Do not know
-3 Prefer not to answer

[SY4 (UKB)]

Do you get a pain in either leg on walking?

SELECT one of 4 from

1 Yes
0 No
-1 Do not know
-3 Prefer not to answer

This includes hip, knee, ankle, or muscle pain.

[SY4I (UKB)]

Have you ever had surgery to remove any of the following?

SELECT one of 6 from

0 No
1 Yes, toes
2 Yes, leg below the knee
3 Yes, leg above the knee
-1 Do not know
-3 Prefer not to answer

[SY5 (UKB)]

In the **last month** have you experienced any of the following that **interfered with your usual activities?**
(You can select more than one answer)

TOGGLE of 10 choices
[Require ≥1 choices]

1 Headache
2 Facial pain
3 Neck or shoulder pain
4 Back pain
5 Stomach or abdominal pain
6 Hip pain
7 Knee pain
8 Premenstrual pains
9 Pain all over the body

-7 None of the above **[EXCLUSIVE]**

-3 Prefer not to answer **[EXCLUSIVE]**

[SY6]

Have you ever experienced any of the following that i**nterfered with your usual activities regularly for more than 3 months**?

(You can select more than one answer)

TOGGLE of 10 choices

[Require ≥1 choices]

1 Headache

2 Facial pain

3 Neck or shoulder pain

4 Back pain

5 Stomach or abdominal pain

6 Hip pain

7 Knee pain

8 Premenstrual pains

9 Pain all over the body

-7 None of the above **[EXCLUSIVE]**

-3 Prefer not to answer **[EXCLUSIVE]**

Think about whether you have ever in your lifetime had a period of three or more consecutive months where you experienced significant pain that made it difficult for you to take part in your usual activities.

[SY1 (UKB)]

Do you ever have any pain or discomfort in your chest?

SELECT one of 4 from

1	Yes	**-> SY1A**
0	No	**-> H10 (UKB)**
-1	Do not know	**-> H10 (UKB)**
-3	Prefer not to answer	**-> H10 (UKB)**

[SY1A (UKB)]

Do you get this pain or discomfort when you walk at an ordinary pace on the level?

SELECT one of 4 from

1	Yes	**-> SY1C**
0	No	**-> SY1B**
-1	Unable to walk on the level	**-> H10 (UKB**
-3	Prefer not to answer	**-> H10 (UKB**

[SY1B (UKB)]

Do you get this pain or discomfort when you walk uphill or hurry?

SELECT one of 4 from

1	Yes	**-> SY1C**
0	No	**-> H10 (UKB**
-1	Unable to walk up hills or to hurry	**-> H10 (UKB**
-3	Prefer not to answer	**-> H10 (UKB**

[SY1C (UKB)]

Does this chest pain go away when you stand still?

SELECT one of 4 from

1	Yes
0	No
-1	Do not know
-3	Prefer not to answer

[H10 (UKB)]

Have you ever had a screening test for bowel (colorectal) cancer?
(Please include tests for blood in the stool/faeces or a colonoscopy or a sigmoidoscopy)

SELECT one of 4 from

1	Yes	**-> H10A**
0	No	
-1	Do not know	
-3	Prefer not to answer	

➔ **IF SEX = Female GO TO FH7 (UKB)**

➔ **IF SEX = (Male OR Prefer not to answer) GO TO MH2 (UKB)**

Screening tests for bowel or colorectal cancer include:
- FOBT (faecal occult blood test) - this is when you are given a set of cards and asked to smear a part of your stool on three separate occasions onto the cards and then return the cards to be tested for blood.
- Sigmoidoscopy - a tube is used to examine the lower bowel. This is usually done in a doctor's office without pain relief.
- Colonoscopy - a long tube is used the examine the whole large bowel; you would usually have to drink a large amount of special liquid to prepare the bowel, and you would be given a sedative medication for the procedure.

[H10A (UKB)]

How many years ago was the most recent one of these tests?

Enter INTEGER

[Require ≥ 0, ≤ current age
Units: years]
OR
-10 Less than 1 year ago
OR
-1 Do not know
OR
-3 Prefer not to answer

➔ **IF SEX = Female GO TO FH7 (UKB)**
➔ **IF SEX = (Male OR Prefer not to answer) GO TO MH2 (UKB)**

If you are unsure, please provide an estimate or select 'Do not know'.

[MH2 (UKB)]

Have you ever had a blood test for prostate cancer (prostate specific antigen or PSA test)?

SELECT one of 4 from

1	Yes	
0	No	**-> MH7 (UKB)**
-1	Do not know	**-> MH7 (UKB)**
-3	Prefer not to answer	**-> MH7 (UKB)**

If you are unsure, select 'Do not know'.

[MH3 (UKB)]

How many years ago was your last test?

Enter INTEGER
[Require ≥ 0, ≤ current age
Units: years]
OR
-10 Less than a year ago
OR
-1 Do not know
OR
-3 Prefer not to answer

[MH7 (UKB)]

How many biological children have you had?

Enter INTEGER
[Require ≥ 0, ≤ 200]
OR

-1 Do not know

OR

-3 Prefer not to answer

➔ **IF ANSWER = 0 AND SEX = Male GO TO L1 (UKB)**

➔ **IF ANSWER = 0 AND SEX = Prefer not to answer GO TO FH7 (UKB)**

➔ **IF ANSWER = 1 GO TO FH3D (UKB)**

[FH3C (UKB)MM]

How old were you when you had your FIRST child?

Enter INTEGER
[Require ≥ 8, ≤ current age
Units: years]

OR

-4 Do not remember

OR

-3 Prefer not to answer

[FH3D (UKB)MM]

How old were you when you had your LAST child?

Enter INTEGER
[Require ≥ 8, ≤ current age
Units: years]

OR

-4 Do not remember

OR

-3 Prefer not to answer

➔ **IF SEX = Male GO TO L1 (UKB)**

➔ **IF SEX = Prefer not to answer GO TO FH7 (UKB)**

[FH7 (UKB)]

Have you ever been for breast cancer screening (a mammogram)?

SELECT one of 4 from

1	Yes	
0	No	**-> FH8**
-1	Do not know	**-> FH8**
-3	Prefer not to answer	**-> FH8**

[FH7A (UKB)]

How many years ago was your last screen?

Enter INTEGER
[Require ≥ 0, ≤ current age]
OR
-10 Less than 1 year ago
OR
-1 Do not know
OR
-3 Prefer not to answer

If you are unsure, please provide an estimate or select 'Do not know'.

[FH8 (UKB)]

Have you ever had a cervical smear test?

SELECT one of 4 from
1 Yes
0 No **-> FH1**
-1 Do not know **-> FH1**
-3 Prefer not to answer **-> FH1**

[FH8B (UKB)]

How many years ago was your last cervical smear test?

Enter INTEGER
[Require ≥ current age]
OR
-10 Less than a year ago
OR
-1 Do not know
OR
-3 Prefer not to answer

If you are unsure, please provide an estimate or select 'Do not know'.

[FH1 (UKB)]

How old were you when your periods started?

Enter INTEGER
[Require ≥ 5, ≤ current age
Units: years]
OR
-1 Do not know
OR

-3 Prefer not to answer

If you are unsure, please provide an estimate or select 'Do not know'.

[FH2 (UKB)]

Have you had your menopause (periods stopped for more than 12 months)?

SELECT one of 5 from

1	Yes	**-> FH2A (UKB)**
0	No	**-> FH2B (UKB)**
2	Not sure - had a hysterectomy	
3	Not sure - other reason	**-> FH2B (UKB)**
-3	Prefer not to answer	

➔ **IF (ANSWER = 2 OR ANSWER = -3) AND MH7 > 0 GO TO FH5 (UKB)**
➔ **IF (ANSWER = 2 OR ANSWER = -3) AND MH7 < 0 GO TO FH3 (UKB)**

[FH2A (UKB)]

How old were you when you had your last period?

Enter INTEGER
[Require ≥ FH1 integer, ≤ current age]
OR
-1 Do not know
OR
-3 Prefer not to answer

➔ **IF MH7 > 0 GO TO FH5 (UKB)**
➔ **ELSE GO TO FH3**

If you are unsure, please provide an estimate or select 'Do not know'.

[FH2B (UKB)]

How many days since your last menstrual period?

Enter INTEGER
[Require ≥ 0, ≤ 365,
Units: days]
OR
-10 More than one year
OR
-1 Do not know
OR
-3 Prefer not to answer

Please count from the first day of your last menstrual period. If you are unsure, please provide an estimate or select 'Do not know'.

[FH2C (UKB)]

How many days are there usually between your periods? (This is the time from the first day of one period, to the day before the start of the next)

Enter INTEGER
[Require ≥ 7, ≤ 365,
Units: days]

OR
-6 Irregular cycle
OR
-1 Do not know
OR
-3 Prefer not to answer

➔ **IF MH7 > 0 GO TO FH5 (UKB)**
➔ **ELSE GO TO FH3**

[FH3 (UKB)]

How many children have you given birth to?

Enter INTEGER
[Require ≥ 0, ≤ 25,
Units: children]
OR
-3 Prefer not to answer

➔ **IF ANSWER = 0 GO TO FH5 (UKB)**
➔ **IF ANSWER = 1 GO TO FH3D (UKB)**

[FH3C (UKB)]

How old were you when you had your FIRST child?

Enter INTEGER
[Require ≥ 0, ≤ current age,
Units: years]
OR
-4 Do not remember
OR
-3 Prefer not to answer

[FH3D (UKB)]

How old were you when you had your LAST child?

Enter INTEGER
[Require ≥ 8, ≤ current age,
Units: years]
OR
-4 Do not remember
OR
-3 Prefer not to answer

[FH5 (UKB)]

Have you **ever used a medical or implant method of contraception?** Please do not respond about condom, diaphragm or natural family planning.

SELECT one of 4 from

1	Yes	**-> FH5AA**
0	No	**-> FH6 (UKB)**
-1	Do not know	**-> FH6 (UKB)**
-3	Prefer not to answer	**-> FH6 (UKB)**

[FH5AA]

What have you used for contraception? Please note we are only asking about medication or implant methods of contraception. Please do not respond about condom, diaphragm or natural family planning.
Select all that apply.

0	Combined pill	-> GO TO FH5A
1	Injection	
2	Implant	
3	IUD (coil)	
4	IUS (hormonal coil)	
5	Progesterone only pill (mini pill)	-> GO TO FH5A
6	Patch	
7	Vaginal ring	
8	Other not listed	
-1	I don't know	
-3	Prefer not to answer	

[FH5A (UKB)]

About how old were you when you first went on the contraceptive pill?

Enter INTEGER
[Require ≥ 5, ≤ current age]
OR
-1 Do not know

OR

-3 Prefer not to answer

If you are unsure, please provide an estimate or select 'Do not know'.

[FH5B (UKB)]

How old were you when you last used the contraceptive pill?

Enter INTEGER

[Require ≥ FH5A response, ≤ current age]

OR

-1 Do not know

OR

-3 Prefer not to answer

OR

-11 Still taking the pill

If you are currently taking the pill, select 'Still taking the pill'. If you are unsure, please provide an estimate or select 'Do not know'.

[FH6 (UKB)]

Have you **ever** used hormone replacement therapy (HRT)?

SELECT one of 4 from

1 Yes

0 No **-> GO TO FH9**

-1 Do not know **-> GO TO FH9**

-3 Prefer not to answer **-> GO TO FH9**

[FH6A (UKB)]

How old were you when you first used HRT?

Enter INTEGER

[Require ≥ 16, ≤ current age]

OR

-1 Do not know

OR

-3 Prefer not to answer

If you are unsure, please provide an estimate or select 'Do not know'.

[FH6B (UKB)]

How old were you when you last used HRT?

Enter INTEGER

[Require ≥ FH6A, ≤ current age]
OR
-1 Do not know
OR
-11 Still taking HRT
OR
-3 Prefer not to answer

If you are currently using HRT, select 'Still taking HRT'. If you are unsure, please provide an estimate or select 'Do not know'.

[FH9 (UKB)]

Have you had a hysterectomy (womb removed)?

SELECT one of 4 from

1	Yes	
0	No	**-> GO TO FH10**
-5	Not sure	**-> GO TO FH10**
-3	Prefer not to answer	**-> GO TO FH1**

[FH9A (UKB)]

How old were you when you had your hysterectomy?

Enter INTEGER
[Require ≥ 0, ≤ current age]
OR
-1 Do not know
OR
-3 Prefer not to answer

If you are unsure, please provide an estimate or select 'Do not know'.

[FH10 (UKB)]

Have you had BOTH ovaries removed?

SELECT one of 4 from

1	Yes	
0	No	**-> GO TO L1(UKB)**
-5	Not sure	**-> GO TO L1(UKB)**
-3	Prefer not to answer	**-> GO TO L1(UKB)**

Only enter 'Yes' if you have had both ovaries removed If you are unsure of whether both ovaries have been removed, select 'Do not know'.

[FH10A (UKB)]

How old were you when you had BOTH ovaries removed?

Enter INTEGER
[Require ≥ 0, ≤ current age]
OR
-1 Do not know
OR
-3 Prefer not to answer

[L1 (UKB)]

Have you ever been diagnosed with any of the following by a doctor or other health professional?
Please select all that apply
We will ask more details for any type of disorder that you select here

TOGGLE
[Require ≥ 1 choices]

6 Autoimmune disorder **-> GO TO AUTO_A**
7 Blood disorders (Anaemia) **-> GO TO BLOOD_A**
2 Cancer **-> GO TO CANC_A**
3 Complications or difficulties in pregnancy or childbirth **-> SHOW IF FEMALE; GO TO PREG_A**
4 Digestive system or liver problems **-> GO TO DIG_A**
5 Endocrine, nutritional and metabolic disorders (e.g., diabetes, thyroid disorder, vitamin deficiencies) **-> GO TO EN_A**
6 Eye or visual problems **-> GO TO EYE_A**
7 Fractures, breaks, or joint problems **-> GO TO FRAC_A**
8 Heart or circulatory disease (e.g. high blood pressure or stroke) **-> GO TO HEART_A**
9 Kidney or urinary system disorders **-> GO TO KIDN_A**
10 Lung or respiratory problems **-> GO TO LUNG_A**
11 Mental health conditions (e.g.depression, bipolar disorder) **-> GO TO MH_A**
12 Neurodevelopmental conditions (e.g., Autism spectrum disorder, ADHD) **-> GO TO ND_A**
13 Neurological disorders (things that affect that brain or nervous system) **-> GO TO NEU_A**
14 Reproductive system problems **-> GO TO REPRO_A**
15 Other not listed **-> GO TO L5DF**
16 None of these **-> GO TO L5DF**
-1 I don't know **[EXCLUSIVE]** **-> GO TO L5DF**
-3 Prefer not to answer **[EXCLUSIVE]** **-> GO TO L5DF**

If the diagnosis was for cancer, please select cancer. We will ask more about the type of cancer in a subsequent question.

[AUTO_A]

Have you ever been diagnosed with any of the following autoimmune disorders by a doctor or other health professional?

0 Rheumatoid arthritis
1 Lupus
2 Inflammatory Bowel Disease (IBD)
3 Multiple Sclerosis (MS)
4 Graves' disease
5 Guillain-Barre syndrome
6 Psoriasis
7 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[BLOOD_A]

Have you ever been diagnosed with any of the following types of anaemia by a doctor or other health professional?

0 Iron deficiency anaemia
1 Vitamin deficiency anaemia
2 Sickle cell anaemia
3 Aplastic anaemia
4 Thalassaemia
5 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[CANC_A (CONNECT)]

Which type(s) of cancer specifically were you diagnosed with?
Please indicate where the cancer originated, even if it spread to other body areas

0 Anal
1 Bladder
2 Brain
3 Breast
4 Cervical
5 Colon/rectal
6 Oesophageal

7 Head and neck (Including cancers of the mouth, sinuses, nose, or throat. Not including brain or skin cancers.)
8 Gastric
9 Kidney
10 Leukaemia (blood and bone marrow)
11 Liver
12 Lung or bronchial
14 Lymphoma
15 Ovarian
16 Pancreatic
17 Prostate
18 Skin
19 Stomach
20 Testicular
21 Thyroid
22 Uterine (endometrial)
23 Another type of cancer
24 I know I had cancer, but don't know what type
-1 I don't know
-3 Prefer not to answer

[CANC_B (CONNECT)]

What type of skin cancer specifically were you diagnosed with?

9 Melanoma
10 Basal cell
11 Squamous cell
-1 I don't know
-3 Prefer not to answer

[PREG_A (CONNECT+ICD)]

What type of complication or difficulties with pregnancy or childbirth have you experienced?

0 Miscarriage (pregnancy loss before 20 weeks)
1 Stillbirth (pregnancy loss after 20 weeks)
2 Live birth and still birth (loss of one or more multiples)
3 Ectopic or tubal pregnancy
4 Trying to get pregnant for more than a year but not getting pregnant during that time
5 hyperemesis gravidarum
6 Gestational diabetes
7 Preterm labour and delivery
8 Complicated labour and delivery
9 Traumatic labour or delivery
10 Pre-eclampsia

11 Eclampsia
12 Gestational hypertension
13 Other (not listed)
-1 I don’t know
-3 Prefer not to answer

[DIG_A (CONNECT)]

Have you ever been diagnosed with any of the following digestive system problems by a doctor or other health professional?

0 Gastro-oesophageal Acid Reflux (GORD)
1 Barrett’s Oesophagus
2 Irritable bowel syndrome
3 Inflammatory Bowel Disease
4 Diverticulitis or Diverticulosis
5 Ulcerative Colitis
6 Crohn’s Disease
7 Coeliac Disease (also known as Gluten-Sensitive Enteropathy)
8 Gallstones (Biliary Stones)
9 Fatty liver disease
10 Liver Cirrhosis
11 Hepatitis
12 Pancreatitis
5 Other (not listed)
-1 I don’t know
-3 Prefer not to answer

[EN_A]

Have you ever been diagnosed with the following conditions by a doctor or health professional?

0 Type 1 diabetes
1 Type 2 diabetes
2 overactive thyroid
3 underactive thyroid
4 Cushing syndrome
5 Lactose intolerance
6 Vitamin A deficiency
7 Thiamine deficiency
8 Vitamin D deficiency
3 Other (not listed)
-1 I don’t know
-3 Prefer not to answer

[EYE_A]

Have you ever been diagnosed with any of the following eye or visual problems by a doctor or other health professional?

3 Glaucoma
1 Visual impairment including blindness
2 Double vision
3 Night blindness
4 Colour blindness
5 Macular degeneration
6 Cataracts
7 Retinal detachment
8 Diabetic retinopathy
9 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[FRAC_A]

What type of fractures, breaks, joint or bone problems have you experienced?

45 Hip fracture
1 Osteoporosis
2 Osteoarthritis (arthritis)
3 Gout
4 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[HEART_A (CONNECT)]

Have you ever been diagnosed with any of the following heart or circulatory diseases by a doctor or other health professional?

0 B-12 Deficiency (Pernicious Anaemia)
1 Coronary Artery/Coronary Heart Disease
2 Congestive Heart Failure
3 High Cholesterol
4 Heart Attack (Myocardial Infarction)
5 Abnormal Heart Rhythm (Arrhythmia)
6 Chest Pain (Angina)
7 Heart Valve Problems
8 High Blood Pressure (Hypertension) [Please do **not** include hypertension during pregnancy.]
9 Blood Clots (Deep Vein Thrombosis, Pulmonary Embolism)

10 Stroke
11 Other (not listed)
-1 I don’t know
-3 Prefer not to answer

[KIDN_A (CONNECT]

Have you ever been diagnosed with any of the following kidney or urinary tract problems by a doctor or other health professional?

0 Kidney stones
1 Chronic kidney disease (or chronic kidney failure)
2 Other (not listed)
-1 I don’t know
-3 Prefer not to answer

[LUNG_A (CONNECT)]

Have you ever been diagnosed with any of the following lung or respiratory conditions by a doctor or other health professional?

0 Chronic Obstructive pulmonary disease, COPD (including emphysema and chronic bronchitis)
1 Lung fibrosis
2 Bronchiectasis
3 Asthma
4 Hay Fever (Allergic to pollen or Allergic Rhinitis)
5 Other (not listed)
-1 I don’t know
-3 Prefer not to answer

[ND_A]

Have you ever been diagnosed with one or more of the following conditions by a professional, even if you don't have it currently? By professional we mean: any doctor, nurse, or person with specialist training.

Please include disorders even if you did not need treatment for them or if you did not agree with the diagnosis. Select ALL that apply

27 Autism spectrum disorder
28 Developmental learning disorders
29 Attention deficit hyperactivity disorder (ADHD)
30 Disorder of intellectual development
31 Developmental motor coordination disorder
32 Developmental speech or language disorders

33 Stereotyped movement disorder
34 Other (not listed)
35 None of the above
-1 I don’t know
-3 Prefer not to answer

[MH_A]

Have you ever been diagnosed with one or more of the following mental health conditions by a professional, even if you don't have it currently? By professional we mean: any doctor, nurse, or person with specialist training.

Please include disorders even if you did not need treatment for them or if you did not agree with the diagnosis. Select ALL that apply

46 Anxiety **-> GO TO ANX_B**
47 Bipolar disorder
48 Body dysmorphia
49 Depression **-> GO TO DEP_B**
50 Premenstrual dysphoric disorder
51 Post Traumatic Stress Disorder
52 Obsessive Compulsive Disorder
53 Eating disorder **-> GO TO EATD_B**
54 Psychosis
55 Schizophrenia
56 Schizoaffective disorder
57 Personality disorder
58 Other (not listed)
59 None of the above
-1 I don’t know
-3 Prefer not to answer

[ANX_B]

Which anxiety disorder(s) specifically have you been diagnosed with in your lifetime?

24 Generalised anxiety disorder
25 Agoraphobia
26 Social anxiety disorder
27 Panic disorder
28 Panic attacks
29 Specific phobia
30 Other (not listed)
31 None of the above
-1 I don’t know
-3 Prefer not to answer

[DEP_B]

Which depressive disorder(s) specifically have you been diagnosed with in your lifetime?

15 Major Depressive Disorder
16 Perinatal depression
17 Postnatal depression
18 Other (not listed)
19 None of the above
-1 I don't know
-3 Prefer not to answer

[EATD_B]

Which eating disorder(s) specifically have you been diagnosed with in your lifetime?

18 Anorexia nervosa
19 Atypical anorexia nervosa
20 Bulimia nervosa
21 Binge eating disorder
22 Other (not listed)
23 None of the above
-1 I don't know
-3 Prefer not to answer

[NEU_A]

Have you ever been diagnosed with any of the following neurological or brain disorders by a doctor or other health professional?

24 Epilepsy
25 Parkinson's disease
26 Alzheimer's disease/dementia
27 Early onset Alzheimer's disease/dementia
28 Vascular dementia
29 Migraine with aura
30 Migraine without aura
31 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[REPRO_A (CONNECT)]

Have you ever been diagnosed with any of the following conditions by a doctor or other health professional?

0 Endometriosis **[validation show if question refers to female]**

1 Polycystic Ovary Syndrome (PCOS) **[validation show if question refers to female]**
2 Enlarged prostate [**validation show if question refers to male]**
3 Fibrocystic Breast, or another Benign Breast Disease (such as proliferative Benign Breast Disease or LCIS)
4 Ductal Carcinoma in situ (DCIS)
5 Uterine Fibroids
6 Other (not listed)
-1 I don't know
-3 Prefer not to answer

[L5DF]

DO YOU REGULARLY TAKE ANY OF THE FOLLOWING TYPES OF MEDICATIONS? (YOU CAN SELECT MORE THAN ONE ANSWER)

0 Medication for autoimmune disorders **> GO TO AUTO_MEDS_A**
1 Medication for bone health **-> GO TO BONE_MED_A**
2 Treatment for Cancer **-> GO TO CANC_MED_A**
3 Medication for diabetes or diabetic health **-> GO TO DIA_MED_A**
4 Medications for Digestive problems (including acid reflux and liver problems)**-> GO TO DIG_MED_A**
5 Medications for Endocrine disorder (e.g., under or over-active thyroid) **-> GO TO ENDO_MED_A**
6 Medications for heart or circulatory health (e.g., high blood pressure or stroke) **-> GO TO HEART_MED_A**
7 Medication for lung or breathing problems (including asthma) **-> GO TO LUNG_MED_A**
8 Medication for mental health conditions and insomnia (e.g., Depression, bipolar disorder) **-> GO TO MH_MED_A**
9 Medication for neurological disorders (e.g., Alzheimer's, epilepsy, Parkinson's)**-> GO TO NEURO_MED_A**
10 Pain relief medication **-> GO TO PAIN_MED_A**
11 Medication for reproductive or sexual health (including contraception, erectile dysfunction, menopause or hormone medication) **-> GO TO REPRO_MED_A**
12 Supplements, vitamins, or nutritional health **-> GO TO SUPP_MED_A**
13 Herbal remedies **-> GO TO HERBAL_MED_A**
14 I take medication but I don't know what they're for **-> GO TO OTHER_MEDS_A**
15 None of these **-> GO TO PHQ_TRIG**

-1 I don't know **[EXCLUSIVE]** **-> GO TO PHQ_TRIG**
-3 Prefer not to answer **[EXCLUSIVE]** **-> GO TO PHQ_TRIG**

By regularly we mean something you take on a fixed schedule, or on most days of the week for the last four weeks. Please also tell us about implants or slow release injections that you have or regularly receive

[AUTO_MED_A]

Do you regularly take any of the following medication? (You can select more than one answer)

0 Amino salicylates (5-ASAs, mesalazine)
1 Azathioprine
2 Corticosteroids (e.g., prednisolone)
3 Disease-modifying ani-rheumatic drugs (DMARDs, e.g., methotrexate, leflunomide, hydroxychloroquine, sulfasalazine)
4 Tacrolimus
5 JAK inhibitors
6 Tumour Necrosis Factor (TNF) inhibitors
7 Tocilizumab
8 Rituximab
9 Mycophenolate
10 Cyclosporine
11 Other not listed
-1 I don't know
-3 Prefer not to answer

By regularly we mean something you take on a fixed schedule, or on most days of the week for the last four weeks.

If you know you take a medication regularly, but don't recognise these names, please check the packaging. Sometimes the brand names on the packaging will not be the same as the key ingredients.

[BONE_MED_A]

Do you regularly take any of the following medication? (You can select more than one answer)

0 Bisphosphonates (e.g., alendronic acid, ibandronic acid, risendronic acid, zoledronic acid)
1 Selective oestrogen receptor modulators (SERMs, Raloxifene)
2 Strontium Ranelate
3 Monoclonal antibodies (Denosumab, Romosozumab)
4 Parathyroid hormone (e.g., teriparatide)

5 Vitamin D and/or Calcium supplements
6 Hormone Replacement Therapy (HRT)
7 Testosterone treatment
8 Other not listed
-1 I don't know
-3 Prefer not to answer

By regularly we mean something you take on a fixed schedule, or on most days of the week for the last four weeks.

If you know you take a medication regularly, but don't recognise these names, please check the packaging. Sometimes the brand names on the packaging will not be the same as the key ingredients.

[CANC_MED_A]

Are you currently receiving any of the following treatments? (You can select more than one answer)

0 Chemotherapy
1 Hormone therapy
2 Immunotherapy / Targeted therapy
4 Radiotherapy
-1 I don't know
-3 Prefer not to answer

[DIA_MED_A]

Do you regularly take any of the following medication? (You can select more than one answer)

0 Acarbose (Glucobay)
1 DPP-4 Inhibitors (Gliptins, e.g., Sitagliptin, Vildagliptin, Saxagliptin, Alogliptin)
2 GLP-1 (incretin memetics, e.g., Exenatide, Liraglutide, Lixisenatide)
3 Insulin
4 Metformin
5 Prandial glucose regulator (e.g., Repaglinide, Nateglinide)
6 SGLT2 inhibitors (e.g., Dapagliflozin, Canagliflozin, Empagliflozin, Ertuglflozin)
7 Statins
8 Sulphonylureas (e.g., Glibenclamide, Gliclazide, Glipizide Tolbutamide)
9 Thiazolidinediones (e.g., Pioglitazone; Actos)
10 Other not listed
-1 I don't know

-3 Prefer not to answer

By regularly we mean something you take on a fixed schedule, or on most days of the week for the last four weeks.

If you know you take a medication regularly, but don't recognise these names, please check the packaging. Sometimes the brand names on the packaging will not be the same as the key ingredients.

[DIG_MED_A]

Do you regularly take any of the following medication? (You can select more than one answer)

0 Proton pump inhibitors (e.g., omeprazole, esomeprazole, lansoprazole, rabeprazole, pantoprazole, dexlansoprazole)
1 Other indigestion medicine (e.g., ranitidine, famotidine, nizatidine, cimetidine)
2 Laxatives (e.g., Dulcolax, Senokat)
3 Aminosalicylates (5-ASAs, mesalazine)
4 Azathioprine
5 Corticosteroids (e.g., prednisolone)
6 Mercaptopurine
7 Methotrexate
8 JAK inhibitors
9 Tumour Necrosis Factor (TNF) inhibitors
10 Pancreatin (e.g., Creon, Pancrex)
11 Other not listed
-1 I don't know
-3 Prefer not to answer

By regularly we mean something you take on a fixed schedule, or on most days of the week for the last four weeks.

If you know you take a medication regularly, but don't recognise these names, please check the packaging. Sometimes the brand names on the packaging will not be the same as the key ingredients.

[ENDO_MED_A]

Do you regularly take any of the following medication? (You can select more than one answer)

0 Levothyroxine
1 Carbimazole
2 Propylthiouracil
3 Beta Blocker
4 Hydrocortisone

5 Prednisolone
6 Growth hormone
7 Desmopressin
8 Dopamine agonists (cabergoline, bromocriptine)
9 Other not listed
-1 I don't know
-3 Prefer not to answer

By regularly we mean something you take on a fixed schedule, or on most days of the week for the last four weeks.

If you know you take a medication regularly, but don't recognise these names, please check the packaging. Sometimes the brand names on the packaging will not be the same as the key ingredients.

[HEART_MED_A]

Do you regularly take any of the following medication? (You can select more than one answer)

0 Aspirin (low dose)
1 Anticoagulant (blood thinners, e.g., warfarin, Rivaroxaban, dabigatran, apixaban and edoxaban)
2 Antiarrhythmic (e.g., flecainide, digoxin)
3 Calcium channel blocker (e.g., verapamil, diltiazem)
4 Cholesterol lowering medication/statins -> GO To HEART_MD_B
5 Blood pressure medication (e.g., enalapril, lisinopril, perindopril, ramipril, candesartan, irbesartan, losartan, valsartan and Olmesartan)
6 Beta blocker (e.g., bisoprolol, atenolol)
7 Diuretic (e.g., Furosemide, Fendroflumethiazide, Amiloride, Bumetanide, Metalozone, Spironolactone)
8 Glyceryl trinitrate (GTN)
9 Nicorandil
10 Anti-platelet (Clopidogrel)
11 Other not listed
-1 I don't know
-3 Prefer not to answer

By regularly we mean something you take on a fixed schedule, or on most days of the week for the last four weeks.

If you know you take a medication regularly, but don't recognise these names, please check the packaging. Sometimes the brand names on the packaging will not be the same as the key ingredients.

[HEART_MED_B]

What type of medications do you regularly take to lower your cholesterol?
(You can select more than one answer)

1 Statins (e.g., atorvastin (Lipitor),fluvastin (Lescol), pravastin (Lipostat), rosuvastin (Crestor), simvastin (Zocor))
2 Clofibrate (e.g., atromid)
3 Cholesterol-lowering injection (e.g., Inclisiran, evolocumab, alirocumab)
4 Ezetimibe
5 Bempedoic acid (e.g., Nilemdo)
6 Other not listed
-1 I don't know
-3 Prefer not to answer

By regularly we mean something you take on a fixed schedule, or on most days of the week for the last four weeks.

If you know you take a medication regularly, but don't recognise these names, please check the packaging. Sometimes the brand names on the packaging will not be the same as the key ingredients.

[LUNG_MED_A]

Do you regularly take any of the following medication? (You can select more than one answer)

0 Asthma reliver inhaler (usually blue)
1 Asthma preventer inhaler (containing steroid medicine)
2 Asthma combination inhaler
3 Anticholinergic inhaler (for COPD or asthma, e.g., Tiotropium or Spiriva)
4 Leukotriene receptor antagonist (LTRAs) tablets (e.g., Montelukast)
5 Tablet bronchodilator (e.g., theophylline)
6 Corticosteroids (e.g., prednisolone)
7 Other not listed
-1 I don't know
-3 Prefer not to answer

By regularly we mean something you take on a fixed schedule, or on most days of the week for the last four weeks.

If you know you take a medication regularly, but don't recognise these names, please check the packaging. Sometimes the brand names on the packaging will not be the same as the key ingredients.

[MH_MED_A]

Do you regularly take any of the following medication? (You can select more than one answer)

0	antidepressant - Selective serotonin reuptake inhibitor (SSRI, e.g., Fluoxetine, citalopram, escitalopram, paroxetine, sertraline)
1	antidepressant - Tricyclic a (e.g., amitriptyline, clomipramine)
2	antidepressant - other (e.g., mirtazapine, venlafaxine, duloxetine)
3	"Typical" Antipsychotic (e.g., chlorpromazine, haloperidol, promazine, sulpride)
4	"Atypical" Antipsychotic (e.g., amisulpiride, Aripiprazole, clozapine, risperidone, olanzapine, quetiapine)
5	Beta-blocker (e.g., atenolol, bisoprolol, metoprolol, propranolol)
6	Benzodiazepine (e.g., alprazolam, diazepam, halazepam, prazepam, clonazepam, clorazepate)
7	Lithium
8	Sleeping pills (e.g., Antihistamines, melatonin, zopiclone, barbituates)
9	Pregabalin
10	Valproic acid/Sodium valproate
11	Other mood stabilising medication (e.g., Depakote, carbamezapine)
12	Other not listed
-1	I don't know
-3	Prefer not to answer

Please indicate whether you take an antidepressant, even if it is prescribed for a different mental health disorder such as anxiety

By regularly we mean something you take on a fixed schedule, or on most days of the week for the last four weeks.

If you know you take a medication regularly, but don't recognise these names, please check the packaging. Sometimes the brand names on the packaging will not be the same as the key ingredients.

[NEURO_MED_A]

Do you regularly take any of the following medication? (You can select more than one answer)

0	Anti-epileptic drugs (AEDs, e.g., Sodium valproate, carbamazepine, lamotrigine, levetiracetam, topiramate)

1 Acetylcholinesterase (AChE) inhibitors (e.g., Donepezil, galantamine, rivastigmine)
2 Amantadine
3 Amitriptyline for migraines
4 Catechol-O-methyltransferase (COMT) inhibitors (e.g., entacapone, opicapone)
5 Levodopa (e.g., co-beneldopa, co-careldopa)
6 Dopamine agonists (e.g., pramipexole, ropinirole)
7 Memantine
8 Monoamine oxidase-B inhibitors (e.g., selegiline, rasagiline, safinamide)
9 Pregabalin or Gabapentin
10 Propranolol for migraines
11 Riluzole
12 Triptans
13 Other not listed
-1 I don't know
-3 Prefer not to answer

By regularly we mean something you take on a fixed schedule, or on most days of the week for the last four weeks.

If you know you take a medication regularly, but don't recognise these names, please check the packaging. Sometimes the brand names on the packaging will not be the same as the key ingredients.

[PAIN_MED_A (CONNECT/UKB)]

Do you regularly take any of the following medication? (You can select more than one answer)

0 Aspirin
1 Ibuprofen (e.g., Neurofen)
2 Paracetamol
3 Naproxen (e.g., Naprosyn, Stirlescent, Feminax Ultra, Period Pain Reliever, Boots Period Pain Relief)
4 Diclofenac
5 Opioids (e.g., codeine, tramadol, morphine, fentanyl, oxycodone, buprenorphine diamorphine)
6 Oher not listed
-1 I don't know
-3 Prefer not to answer

By regularly we mean something you take on a fixed schedule, or on most days of the week for the last four weeks.

If you know you take a medication regularly, but don't recognise these names, please check the packaging. Sometimes the brand names on the packaging will not be the same as the key ingredients.

[REPRO_MED_A (NHS)]

SHOW IF SEX = FEMALE | GENDER = FEMALE

Do you regularly take any of the following medication? (You can select more than one answer)

0	Contraceptive medication, coil, implant or patch **-> GO TO CONTRA_MED_B**
1	Medication to treat erectile dysfunction (e.g., Sildenafil (Viagra), Tadalafil (Cialis), Vardenafil (Levitra), Avanafil (Spedra))
2	Combined Hormone Replacement Therapy (HRT)
3	Oestrogen-only HRT
4	Oestrogen treatment (Pessary, cream or vaginal ring)
5	Testosterone HRT
6	Oestrogen or testosterone blockers (e.g., clomifene)
7	Other not listed
-1	I don't know
-3	Prefer not to answer

By regularly we mean something you take on a fixed schedule, or on most days of the week for the last four weeks.

If you know you take a medication regularly, but don't recognise these names, please check the packaging. Sometimes the brand names on the packaging will not be the same as the key ingredients.

[CONTRA_MED_B (NHS)]

What do you regularly or currently use for contraception? Please note we are only asking about medication or implant methods of contraception. Please do not respond about condom, diaphragm or natural family planning.

9	Combined pill
10	Injection
11	Implant
12	IUD (coil)
13	IUS (hormonal coil)
14	Progesterone only pill (mini pill)
15	Patch
16	Vaginal ring
17	Other not listed
-1	I don't know
-3	Prefer not to answer

[SUPPL_MED_A]

Do you regularly take any of the following supplements? (You can select more than one answer)

0 Vitamin A
1 Vitamin B
2 Vitamin C
3 Vitamin D
4 Vitamin E
5 Folic acid or Folate (Vit B9)
6 Multivitamins +/- minerals
7 Fish oil (including cod liver oil)
8 Glucosamine
9 Calcium
10 Zinc
11 Iron
12 Selenium
13 Other not listed
-1 I don't know
-3 Prefer not to answer

By regularly we mean something you take on a fixed schedule, or on most days of the week for the last four weeks.

If you know you take a supplement regularly, but don't recognise these names, please check the packaging. Sometimes the brand names on the packaging will not be the same as the key ingredients.

[HERBAL_MED_A]

Do you regularly take any of the following herbal remedies? (You can select more than one answer)

0 Black cohosh
1 Chamomile
2 Echinacea
3 Ephedra
4 Feverfew
5 Garlic
6 Ginger
7 Ginseng
8 Gingko
9 Goldenseal
10 Guarana
11 Kava

12 Kalms
13 St John's Wort
14 Salvian
15 Senna
16 Valerian
17 Bespoke herbal preparations made for me
18 Other not listed
-1 I don't know
-3 Prefer not to answer

You might take these remedies as tablets, drops, powders, or teas. Please select any herbal remedies you take regularly, regardless of how you administer them.

If you know you take a herbal medication or remedy, but don't recognise these names, please check the packaging. Sometimes the brand names on the packaging will not be the same as the key ingredients.

[PHQ_TRIG]

➔ **IF select opt out, SKIP to end of section 5**
➔ **ELSE [PHQ9_1]**

[PHQ9_1]

Over the last two weeks, how often have you been bothered by any of the following problems: [Little interest or pleasure in doing things

TOGGLE of 6 choices:

1 Not at all
2 Several days
3 More than half the days
4 Nearly every day
-1 Do not know
-3 Prefer not to answer

[PHQ9_2]

Over the last two weeks, how often have you been bothered by any of the following problems: Feeling down, depressed, or hopeless?

TOGGLE of 6 choices:

1 Not at all
2 Several days
3 More than half the days
4 Nearly every day
-1 Do not know
-3 Prefer not to answer

[PHQ9_3]

Over the last two weeks, how often have you been bothered by any of the following problems: Trouble falling or staying asleep, or sleeping too much?

TOGGLE of 6 choices:

1 Not at all
2 Several days
3 More than half the days
4 Nearly every day
-1 Do not know
-3 Prefer not to answer

[PHQ9_4]

Over the last two weeks, how often have you been bothered by any of the following problems: Feeling tired or having little energy?

TOGGLE of 6 choices:

1 Not at all
2 Several days
3 More than half the days
4 Nearly every day
-1 Do not know
-3 Prefer not to answer

[PHQ9_5]

Over the last two weeks, how often have you been bothered by any of the following problems: Poor appetite or overeating?

TOGGLE of 6 choices:

1 Not at all
2 Several days
3 More than half the days
4 Nearly every day
-1 Do not know
-3 Prefer not to answer

[PHQ9_6]

Over the last two weeks, how often have you been bothered by any of the following problems: Feeling bad about yourself – or that you are a failure or have let yourself or your family down?

TOGGLE of 6 choices:

1 Not at all
2 Several days
3 More than half the days

4 Nearly every day
-1 Do not know
-3 Prefer not to answer

[PHQ9_7]

Over the last two weeks, how often have you been bothered by any of the following problems: Trouble concentrating on things, such as reading the newspaper or watching television?

TOGGLE of 6 choices:

1 Not at all
2 Several days
3 More than half the days
4 Nearly every day
-1 Do not know
-3 Prefer not to answer

[PHQ9_8]

Over the last two weeks, how often have you been bothered by any of the following problems: Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual?

TOGGLE of 6 choices:

1 Not at all
2 Several days
3 More than half the days
4 Nearly every day
-1 Do not know
-3 Prefer not to answer

[PHQ9_9]

Over the last two weeks, how often have you been bothered by any of the following problems: Thoughts that you would be better off dead or of hurting yourself in some way

TOGGLE of 6 choices:

1 Not at all
2 Several days
3 More than half the days
4 Nearly every day
-1 Do not know
-3 Prefer not to answer

More on suicidal thoughts

If you have had thoughts of self-harming or are feeling suicidal contact someone immediately.

- See your GP or the out-of-hours GP service. If you have already taken an overdose or cut yourself badly, dial 999.

- There are helplines with specially trained volunteers who will listen to you, understand what you are going through, and help you through the immediate crisis.

- Contact a friend, family or someone you trust.

The Samaritans operate a service 24 hours a day, 365 days a year, for people who want to talk in confidence. Call 116123.

[PHQ9_IMPAIR]

[DISPLAY IF ANY PHQ9 > 1)

How difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

TOGGLE of 6 choices:

1 Not difficult at all
2 Somewhat difficult
3 Very difficult
4 Extremely difficult
-1 Do not know
-3 Prefer not to answer

[GAD7_1]

Over the last two weeks, how often have you been bothered by any of the following problems: Feeling nervous, anxious or on edge?

TOGGLE of 6 choices:

1 Not at all
2 Several days
3 More than half the days
4 Nearly every day
-1 Do not know
-3 Prefer not to answer

[GAD7_2]

Over the last two weeks, how often have you been bothered by any of the following problems: Not being able to stop or control worrying?

TOGGLE of 6 choices:

1 Not at all
2 Several days
3 More than half the days
4 Nearly every day
-1 Do not know
-3 Prefer not to answer

[GAD7_3]

Over the last two weeks, how often have you been bothered by any of the following problems: Worrying too much about different things?

TOGGLE of 6 choices:

1 Not at all
2 Several days
3 More than half the days
4 Nearly every day
-1 Do not know
-3 Prefer not to answer

[GAD7_4]

Over the last two weeks, how often have you been bothered by any of the following problems: Trouble relaxing?

TOGGLE of 6 choices:

1 Not at all
2 Several days
3 More than half the days
4 Nearly every day
-1 Do not know
-3 Prefer not to answer

[GAD7_5]

Over the last two weeks, how often have you been bothered by any of the following problems: Being so restless that it is hard to sit still?

TOGGLE of 6 choices:

1 Not at all
2 Several days
3 More than half the days
4 Nearly every day
-1 Do not know
-3 Prefer not to answer

[GAD7_6]

Over the last two weeks, how often have you been bothered by any of the following problems: Becoming easily annoyed or irritable?

TOGGLE of 6 choices:

1 Not at all
2 Several days
3 More than half the days

4 Nearly every day
-1 Do not know
-3 Prefer not to answer

[GAD7_7]

Over the last two weeks, how often have you been bothered by any of the following problems: Feeling afraid as if something awful might happen?

TOGGLE of 6 choices:

1 Not at all
2 Several days
3 More than half the days
4 Nearly every day
-1 Do not know
-3 Prefer not to answer

[GAD7_IMPAIR]

[DISPLAY IF ANY GAD7 > 1)

How difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

TOGGLE of 6 choices:

1 Not difficult at all
2 Somewhat difficult
3 Very difficult
4 Extremely difficult
-1 Do not know
-3 Prefer not to answer

----------**End of Section 5**----------

Our Future Health

Appendix F: Governance Manual

+
Our
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Our Future Health Governance Manual

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1. Introduction

1.1 Governance

1.1.1 Our Future Health, a company established to govern the Our Future Health research programme, is a company limited by guarantee (Number 12212468), incorporated in England on 17th September 2019. The registered office address is 2 New Bailey, 6 Stanley Street, Salford, Greater Manchester, United Kingdom, M3 5GS. The Articles of Association were last amended on 10th December 2019. Our Future Health is also registered as a charity registered with the Charity Commission for England and Wales (Charity Number 1189681) and OSCR, Scottish Charity Regulator (Charity Number SC050917).

1.1.2 Our Future Health Trading Limited is a private limited company (Number 12599493) which is wholly owned by Our Future Health. It was incorporated in England on 13th May 2020 and has the same registered office as Our Future Health. The Articles of Association have not been amended since incorporation. The relationship between Our Future Health and Our Future Health Trading Limited is set out in an Intercompany Agreement. Details of the current trustees and directors of both entities can be found in Appendix A.

1.1.3 The Our Future Health research programme is solely governed by Our Future Health.

1.2 Our Board of Trustees

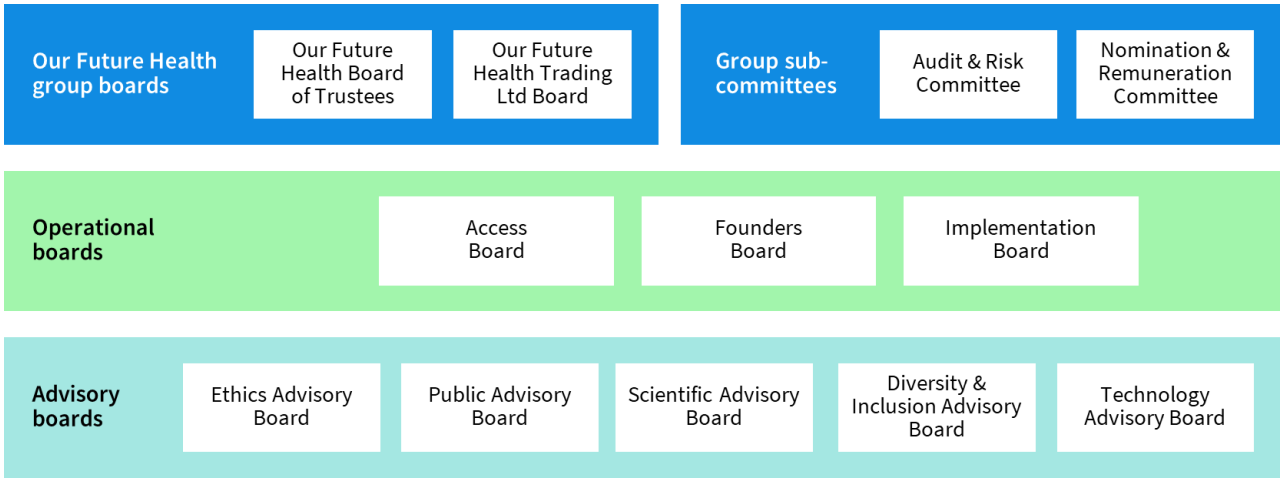
1.2.1 The Board of Trustees of Our Future Health ("Board") is responsible for the governance and strategy of Our Future Health. The Board currently comprises of 4 trustees, comprising a mix of medical and scientific expertise. The trustees have full legal responsibility for the actions of Our Future Health. The trustees are appointed for a renewable term of 3 years and are the directors of the company for the purposes of the Companies Act 2006. Details of the current trustees and directors can be found in Appendix A.

1.2.2 The Board meets at least four times a year. They delegate day to day responsibility for the running of Our Future Health to the Executive Team. The Executive Team of Our Future Health and Our Future Health Trading Limited consists of the Chief Executive Officer and their direct reports, all of whom are employees of Our Future Health.

1.2.3 The Board has approved and adopted a Conflicts of Interest Policy.

1.3 Our governance structures

1.3.1 The Board also delegates specific responsibilities either directly to a sub-committee of the Board – for example, Audit & Risk – or to the Executive Team which has overall responsibility day to day for the delivery of the Our Future Health research programme and shall manage all operations and logistics of establishing and making the Resource available to researchers. The "Resource" (when used in this document) means the data and samples which will be provided via the Our Future Health research programme along with access to the same via related tools including the Our Future Health Trusted Research Environment. The governance committees are delegated certain tasks required of the Board and these committees are accountable for them. For the Executive Team to operate effectively, they have established operational and advisory boards to support them in delivering the research programme. The operational boards work with the Executive Team to review and make recommendations to the Board on operational matters, while the advisory boards provide additional external expertise into strategic and operational aspects of the research programme either directly via the Executive Team and/or via the operational boards.



In addition to the boards noted above, Our Future Health will shortly establish, in consultation with the Founders Board, a Data Privacy & Information Security Committee/Board for the research programme and Resource.

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2. Audit & Risk Committee

2.1 Purpose

2.1.1 The purpose of the Audit and Risk Committee ("Committee") is to provide formal and transparent arrangements for applying financial reporting internal control principles and to maintain an appropriate relationship with the Charity's auditors.

2.2 Constitution and membership

2.2.1 The Committee has been established as a committee of the Board by resolution of the Board.

2.2.2 The members of the Committee will be appointed by the Board, on the recommendation of the Nomination and Remuneration Committee and in consultation with the chair of the Committee and the following paragraphs will govern the constitution of the Committee:

2.2.2.1 The Committee will comprise at least three members;

2.2.2.2 The Chair of the Charity will not be a member of the Committee;

2.2.2.3 At least one member of the Committee should have recent and relevant financial experience with competence in accounting and/or auditing; and

2.2.2.4 The Committee as a whole must have competence relevant to the health sector.

2.2.3 The chair of the Committee will be appointed by the Board, on the recommendation of the Nomination and Remuneration Committee. In the absence of the Chair of the Committee, the members present will select one of their number present to chair the meeting.

2.2.4 Appointments to the Committee will be for a period of up to three years, which may be extended by no more than two further periods of up to three years, provided the person still meets the criteria for membership of the Committee.

2.2.5 The Governance Manager will act as the secretary of the Committee.

2.3 **Attendance**

2.3.1 The Committee will invite a representative of the auditors to attend meetings of the Committee on a regular basis. The Committee should have at least one meeting, or part of a meeting, annually with the auditors without management being present.

2.3.2 The Committee may request the Chair of the Charity, the Chief Executive Officer, the Chief Operating Officer and any relevant senior management to attend meetings of the Committee, either regularly or by invitation, but such invitees have no right of attendance.

2.4 **Meetings**

2.4.1 The Committee will meet at least four times each year having regard to the Charity's financial reporting and audit cycle, and at such other times as the chair of the Committee thinks fit.

2.4.2 Meetings of the Committee will be arranged to tie in with the publication of the Charity's financial statements.

2.4.3 Meetings of the Committee will be called by the Governance Manager at the request of the chair of the Committee, or at the request of auditors if they consider it necessary.

2.4.4 Unless otherwise agreed by all members of the Committee, notice of meetings, confirming the venue, time and date together with an agenda and all relevant papers, should normally be circulated to each member of the Committee, to any other person required to attend, and to all other Trustees, at least five working days prior to the date of the meeting.

2.4.5 The quorum for meetings of the Committee will be two members.

2.4.6 Decisions of the Committee will be made by majority vote. In the event of an equality of votes, the chair of the Committee will have a second or casting vote.

2.5 **Reporting**

2.5.1 Sufficient time should be allowed after Committee meetings for the Committee to report to the Board on the nature and content of discussion, on recommendations, and on actions to be taken. The Governance Manager will minute the proceedings and resolutions of all meetings of the Committee, including recording the names of those

present and in attendance, and will ascertain, at the beginning of each meeting, the existence of any conflicts of interest and minute them accordingly. Draft minutes of Committee meetings will be circulated promptly to all members of the Committee and, once agreed, to all members of the Board.

2.5.2 The chair of the Committee will report formally to the Board on its proceedings after each meeting on all matters within its duties and responsibilities and will also formally report on how it has discharged its responsibilities.

2.5.3 The Committee will make whatever recommendations to the Board that it deems appropriate on an area within its remit where action or improvement is needed.

2.6 **Duties of the Committee**

2.6.1 The Committee should carry out the duties below for the Charity, Our Future Health Trading Limited (company number 12599493) and the group as a whole, as appropriate.

2.6.2 Financial reporting

2.6.2.1 The Committee will monitor the integrity of the financial statements of the Charity, and any formal announcements relating to the Charity's financial performance, reviewing and reporting to the Board on significant financial reporting issues and judgements contained in them having regard to matters communicated to it by the auditor.

2.6.2.2 In particular, the Committee will review and challenge where necessary:

(a) Financial and cash flow forecasts for upcoming financial period(s);"

(b) The consistency of, and any changes to, significant accounting policies both on a year on year basis and across the charity/group;

(c) The methods used to account for significant or unusual transactions where different approaches are possible;

(d) Whether the Charity has followed appropriate accounting standards and made appropriate estimates and judgements, taking into account the views of the auditor;

(e) The clarity of disclosure in the Charity's financial reports and the context in which statements are made; and

(f) All material information presented with the financial statements, such as the strategic report and the corporate governance statement relating to the audit and to risk management.

2.6.2.3 The Committee shall review any other statements requiring Board approval which contain financial information first, where to carry out a review prior to Board approval would be practicable and consistent with any prompt reporting requirements under any law or regulation.

2.6.2.4 Where the Committee is not satisfied with any aspect of the proposed financial reporting by the Charity it will report its views to the Board.

2.6.3 Narrative reporting

2.6.3.1 Where requested by the Board, the Committee should review the content of the annual report and accounts and advise the Board on whether, taken as a whole, it is fair, balanced and understandable.

2.6.4 Internal control and risk assessment systems

2.6.4.1 The Committee will keep under review the adequacy and effectiveness of the Charity's internal financial reporting and internal control policies and systems, covering all material controls, including financial, operational and compliance controls, and the Charity's procedures for the identification, assessment, management and reporting of risks.

2.6.4.2 The Committee will review the major existing and emerging risks facing the charity and strategies in place to mitigate them, reporting to the Board.

2.6.5 Compliance, whistleblowing and fraud

2.6.5.1 The Committee will:

(a) Review the adequacy and security of the Charity's arrangements for its employees and contractors to raise concerns, in confidence, about possible wrongdoing in

financial reporting or other matters. The Committee will ensure that these arrangements allow proportionate and independent investigation of such matters and appropriate follow up action;

(b) Review the Charity's procedures for detecting fraud;

(c) Review the Charity's systems and controls for the prevention of bribery and receive reports on non-compliance.

2.6.6 Audit

The Committee will:

2.6.6.1 Consider and make recommendations to the Board in relation to the appointment, re-appointment and removal of the Charity's auditor;

2.6.6.2 If an auditor resigns investigate the issues leading to this and decide whether any action is required;

2.6.6.3 Oversee the relationship with the auditor including (but not limited to):

(a) Recommendations on their remuneration;

(b) Approval of their terms of engagement, including any engagement letter issued at the start of each audit and the scope of the audit;

2.6.6.4 Assess annually the auditor's independence and objectivity taking into account relevant UK law, regulation, and other professional requirements and the group's relationship with the auditor as a whole, including any threats to the auditor's independence and the safeguards applied to mitigate those threats including the provision of any non-audit services;

2.6.6.5 Satisfy itself that there are no relationships (such as family, employment, investment, financial or business) between the auditor and the Charity (other than in the ordinary course of business) which could adversely affect the auditors independence and objectivity;

2.6.6.6 Monitor the auditor's processes for maintaining independence, its compliance with relevant UK law,

regulation, other professional requirements including the guidance on the rotation of audit partner and staff;

2.6.6.7 Assess annually the qualifications, expertise and resources of the auditor and the effectiveness of the audit process, which will include a report from the auditor on their own internal quality procedures;

2.6.6.8 Discuss the audit or the factors that could affect audit quality and review and approve the annual audit plan and ensure that it is consistent with the scope of the audit engagement, having regard to the seniority, expertise and experience of the audit team; and

2.6.6.9 Review the findings of the audit with the auditor. This will include but not be limited to, the following:

(a) A discussion of any major issues which arose during the audit;

(b) The auditor's explanation of how risks to audit quality were addressed;

(c) Key accounting and audit judgements;

(d) The auditor's view of their interactions with senior management; and

(e) Levels of errors identified during the audit.

2.6.6.10 The Committee will also review the effectiveness of the audit process, including an assessment of the quality of the audit, the handling of key judgements by the auditor, and the auditor's response to questions from the Committee.

2.7 **Other matters**

The Committee will:

2.7.1 Have access to sufficient resources in order to carry out its duties;

2.7.2 Give due consideration to laws and regulations and any applicable rules, as appropriate;

2.7.3 Oversee any investigation of activities which are within its terms of reference;

2.7.4 Work and liaise as necessary with all other board committees, taking particular account of the impact of risk management and internal controls being delegated to different committees; and

2.7.5 Arrange for periodic reviews of its own performance and, at least annually, review its constitution and terms of reference to ensure it is operating at maximum effectiveness and recommend any changes it considers necessary to the Board.

2.8 **Authority**

The Committee is authorised to:

2.8.1 Seek any information it requires from any employees in order to perform its duties;

2.8.2 Obtain, at the Charity's expense, expert independent legal, accounting or other professional advice on any matter it believes it necessary to do so; and

2.8.3 Call any employee to be questioned at a meeting of the Committee as and when required.

3. Nomination & Remuneration Committee

3.1 Purpose

3.1.1 The purpose of the Nomination and Remuneration Committee ("Committee") is to:

3.1.1.1 Establish a formal, rigorous and transparent procedure for the appointment of new Trustees to the Board; and

3.1.1.2 Establish a formal and transparent procedure for developing policy on senior management remuneration.

3.2 Constitution and membership

3.2.1 The Committee has been established as a Committee of the Board by resolution of the Board.

3.2.2 The members of the Committee shall be appointed by the Board. The Committee shall comprise at least **three** members, the majority of whom shall be Trustees.

3.2.3 The chair of the Committee shall be appointed by the Board and should be a Trustee. In the absence of the chair of the Committee, the members present shall elect one of their number present to chair the meeting from those who would qualify under these terms of reference to be appointed to that position by the Board. The Chair of the Charity should not chair the Committee when it is dealing with the appointment of a successor to the Chair.

3.2.4 Appointments to the Committee shall be for a period of up to three years, which may be extended for up to two further periods of up to three years, provided the member still meets the criteria for membership of the Committee.

3.2.5 Only members of the Committee have the right to attend Committee meetings. However, other individuals such as the Chief Executive Officer, the Chief Operating Officer and external advisers may be invited to attend for all or part of any meeting, as and when appropriate.

3.2.6 The governance manager shall act as the secretary of the Committee and will ensure that the Committee receives information and papers in a timely manner to enable full and proper consideration to be given to issues.

3.3 **Meetings**

3.3.1 The Committee will meet at least twice each year and at such other times as the chair of the Committee shall think fit.

3.3.2 Meetings of the Committee shall be called by the secretary of the Committee at the request of the chair of the Committee.

3.3.3 Unless otherwise agreed by all members of the Committee, notice of meetings, confirming the venue, time and date together with an agenda and all relevant papers, should normally be circulated to each member of the Committee, to any other person required to attend, and (unless it would be inappropriate to do so) to all other Trustees, at least five working days prior to the date of the meeting.

3.3.4 The quorum for meetings of the Committee shall be two members, both of whom must be Trustees.

3.3.5 Decisions of the Committee will be made by majority vote. In the event of an equality of votes the chair of the Committee will have a second or casting vote.

3.4 **Reporting**

3.4.1 Sufficient time should be allowed after Committee meetings for the Committee to report to the Board on the nature and content of discussion, on recommendations, and on actions to be taken. The governance manager shall minute the proceedings and resolutions of all meetings of the Committee, including recording the names of those present and in attendance. Draft minutes of Committee meetings shall be circulated promptly to all members of the Committee and, once agreed, to all Trustees unless it would be inappropriate to do so.

3.4.2 The Committee chair shall report to the Board on its proceedings after each meeting on the nature and content of its discussion, recommendations and action to be taken.

3.4.3 The Committee shall make whatever recommendations to the Board that it deems appropriate on an area within its remit where action or improvement is needed, and adequate time should be made available for Board discussion where necessary.

3.5 **Duties of the Committee**

3.5.1 The Committee should carry out the duties below for the Charity, Our Future Health Trading Limited (company number 12599493) and the group as a whole, as appropriate. The Committee shall:

3.5.2 Nomination function

3.5.2.1 Regularly review the structure, size and composition (including the skills, knowledge, experience and diversity) of the Board and make recommendations to the Board with regard to any changes;

3.5.2.2 Ensure plans are in place for orderly succession to Board and senior management positions, and oversee the development of a diverse pipeline for succession, taking into account the challenges and opportunities facing the Charity, and the skills and expertise needed on the Board in future;

3.5.2.3 Keep under review the leadership needs of the Charity, both at executive and at board level;

3.5.2.4 Keep up to date and fully informed about strategic issues affecting the Charity and the sector in which it operates;

3.5.2.5 Be responsible for identifying and nominating for the approval of the Board, candidates to fill Trustee vacancies as and when they arise;

3.5.2.6 Before any appointment is made by the Board, evaluate the balance of skills, knowledge, experience and diversity on the Board, and, in the light of this evaluation prepare a description of the role and capabilities required for a particular appointment. In identifying suitable candidates the Committee shall (if appropriate):

(a) Use open advertising or the services of external advisers to facilitate the search;

(b) Consider candidates from a wide range of backgrounds; and

(c) Consider candidates on merit and against objective criteria and with due regard for the benefits of diversity on the Board, including gender, taking care that appointees have enough time available to devote to the position;

3.5.2.7 Prior to the appointment of a Trustee, other significant time commitments should be disclosed. The proposed appointee should also be required to disclose any other interests that may result in a conflict of interest;

3.5.2.8 Ensure that on appointment to the Board, Trustees receive a role description setting out clearly what is expected of them in terms of time commitment, Committee service and involvement outside Board meetings;

3.5.2.9 Review the results of the Board performance evaluation process that relate to the composition of the Board and succession planning; and

3.5.2.10 Review annually the time required from Trustees. Performance evaluation should be used to assess whether the Trustees are spending enough time to fulfil their duties.

The Committee shall also make recommendations to the Board concerning:

3.5.2.11 Any changes needed to the succession planning process if its periodic assessment indicates the desired outcomes have not been achieved;

3.5.2.12 Suitable candidates for new Trustees and succession for existing Trustees;

3.5.2.13 Membership of the Audit and Risk Committee, and any other board committees as appropriate, in consultation with the chairs of those committees;

3.5.2.14 The re-appointment of any Trustee at the conclusion of their specified term of office having given due regard to their performance and ability to continue to contribute to the Board in the light of the knowledge, skills and experience required; and

3.5.2.15 Any matters relating to the continuation in office of any Trustee at any time.

3.5.3 Remuneration function

3.5.3.1 Have delegated responsibility for determining the policy for setting remuneration for senior management;

3.5.3.2 Design remuneration policies and practices to support strategy and promote long-term sustainable success, with executive remuneration aligned to the Charity's purposes and values, clearly linked to the successful delivery of the Charity's long-term strategy;

3.5.3.3 Ensure that no senior manager will be involved in any decisions as to their own remuneration outcome;

3.5.3.4 In determining remuneration policy take into account all other factors which it deems necessary including relevant legal, regulatory requirements and any relevant charity commission guidance. The objective of such policy shall be to attract, retain and motivate executive management of the quality required to run the Charity successfully without paying more than is necessary;

3.5.3.5 Review the ongoing appropriateness and relevance of the remuneration policy;

3.5.3.6 Within the terms of the agreed policy and in consultation with the Charity chair and/or Chief Executive Officer, as appropriate, determine the total individual remuneration of senior managers; and

3.5.3.7 Have full authority to appoint remuneration consultants and to commission or purchase any reports, surveys or information which it deems necessary at the Charity's expense. However, the Committee should avoid designing pay structures based solely on benchmarking to the market or on the advice of remuneration consultants.

3.6 **Other matters**

3.6.1 The Committee shall:

3.6.1.1 Work and liaise as necessary with all other board committees, ensuring the interaction between committees and the Board is reviewed regularly;

3.6.1.2 Have access to sufficient resources in order to carry out its duties as required;

3.6.1.3 Give due consideration to laws and regulations as appropriate; and

3.6.1.4 Arrange for periodic reviews of its own performance and, at least annually, review its constitution and terms of reference to ensure it is operating at maximum effectiveness and recommend any changes it considers necessary to the Board for approval.

3.7 **Authority**

3.7.1 The Committee is authorised by the Board to obtain, at the Charity's expense, outside legal or other professional advice on any matters within its terms of reference.

4. Ethics Advisory Board

4.1 Purpose

4.1.1 The Ethics Advisory Board (EAB) will monitor the development of the Our Future Health programme and respond to ethical issues that arise, including those related to data privacy, security and regulatory compliance. It will set its own agenda in consultation with the Executive and the Board.

4.1.2 It will seek to develop and establish its ways of working and reporting in the public interest, with an appropriate level of openness to public scrutiny and a focus on public trust. It will work with Our Future Health to create a culture of transparency, whilst taking into account commercial and/or NHS sensitivities to public disclosure.

4.2 Membership

4.2.1 Members of the EAB are invited based on their personal expertise and to contribute to the combined balance of expertise needed to advise the programme.

4.2.2 Members of the EAB shall be appointed for a period of two years. Such appointment may then be extended by up to two years at a time by re-invitation and mutual agreement, provided the member continues to meet the criteria for membership of the EAB.

4.2.3 In addition to core members, others may be invited to attend as appropriate according to the agenda in order to bring additional expertise and experience to the group as needed.

4.2.4 The secretariat for the EAB will be provided by Our Future Health.

4.3 Meetings

4.3.1 The EAB will meet three to four times a year as required. Ad hoc meetings can be arranged with the Chair's agreement as needed.

4.3.2 Advice may be also sought from the EAB in correspondence where a view is needed and it is not practical to schedule a meeting in time.

4.3.3 The agenda, supporting papers and details of each meeting will be circulated at least five working days in advance.

4.3.4 Minutes will be circulated promptly after each meeting and will be agreed at the subsequent EAB meeting.

4.3.5 Members will declare any conflicts of interest in accordance with the Our Future Health Conflict of Interest Policy. The secretary or their nominee should ascertain whether any other conflicts exist based on the agenda at the beginning of each meeting and minute them accordingly.

4.4 Reporting

4.4.1 The EAB will report formally to the Board of Trustees on its activities after each meeting via a written summary; the Chair of the EAB will report to the Board in person twice a year. Working with the Our Future Health Head of Ethics, Compliance & Governance and the Our Future Health Executive, the EAB will keep the Board informed about relevant developments in the public and professional discussion of ethical issues affecting the programme.

4.5 Duties of the Board

The Ethics Advisory Board will:

4.5.1 Identify, respond to, define and examine relevant ethical issues to inform the success and ethical delivery of the Our Future Health programme in the public interest, including consideration of the interests of participants;

4.5.2 Act as a responsive ethics resource, providing timely advice, guidance and recommendations on ethical issues, as requested by the Board and Our Future Health;

4.5.3 Provide timely ethical review and advice on policies and documents under development by Our Future Health;

4.5.4 Carry out a timely review of the ethical aspects of the pilot phase of the programme and taking this into consideration, make recommendations to the Board for the ethical conduct of the main phase of the initiative;

4.5.5 Ensure that the programme is informed and guided by the Our Future Health Ethics and Governance Framework and periodically review the framework document so it remains up-to-date.

4.5.6 Provide general advice on the interests of research participants and the general public in relation to Our Future Health.

4.6 Other matters

4.6.1 The EAB will work closely with a number of the other advisory boards and the Access Board.

4.6.2 The Our Future Health Governance Manager will work closely with the chairs of all advisory boards and relevant Our Future Health team leads to ensure appropriate connections are made between issues raised at the groups. This will allow other Boards to refer issues to the EAB for consideration as needed; the EAB Chair can refer issues to other advisory boards for consideration in the same way.

4.6.3 The EAB shall review its own performance and these terms of reference annually to ensure it is operating at maximum effectiveness and recommend any changes it considers necessary to the Board for approval.

4.6.4 EAB members shall refer to the Our Future Health communications team if they are asked to talk about Our Future Health publicly or are approached by the media about the programme.

4.6.5 A Deputy Chair will be appointed to the EAB after 12 months to support the Chair in their role.

4.6.6 Members will receive a small honorarium and will be reimbursed for all reasonable costs for attending EAB meetings.

5. Founders Board

5.1 Purpose

5.1.1 The Founders Board will advise Our Future Health on, and assist Our Future Health with, certain key aspects regarding the development and delivery of the Our Future Health research programme.

5.1.2 The Founders Board shall be comprised of:

(a) Representatives of Our Future Health and Our Future Health Trading Limited including the Chief Executive Officer and other Executive Team members;

(b) A representative from each Founding Industry Member;

(c) A representative from each Founding Member Charity;

(d) A representative from UKRI

5.1.3 The Founders Board will be designed to ensure that scientific and public interest expertise is represented and available for assisting the Our Future Health research programme, and will be the forum for advising Our Future Health on and providing the input into, co-ordination, review and agreement of the following activities:

5.1.3.1 establishing and amending, as necessary, the Scientific Protocol for the Resource for data and sample collection, recruitment and serial sampling;

5.1.3.2 monitoring the progress against goals, roadmaps and timelines with respect to the implementation of the Resource;

5.1.3.3 ensuring the Access Process under which Registered Researchers who have gained study approval may run Stage 1 Studies and Stage 2 Studies, is conducted as contemplated, and is regularly reviewed to address any updates that may be recommended;

5.1.3.4 creating an accreditation process through which Founding Members will be able to apply for accreditation of their own Trusted Research Environments;

5.1.3.5 the review of and recommendation on the admission of new or additional Founding Members;

5.1.3.6 reviewing and advising on the creation and application of any charging model applied by Our Future Health for use of the Resource;

5.1.3.7 reviewing and advising on the creation of further Our Future Health policies which directly impact the implementation and usability of the Resource; and

5.1.3.8 matters which may require advisory input, remedy or escalation.

In all situations, decisions of the Founders Board must be undertaken considering the overall scientific objectives and goals of the Our Future Health research programme and the budget it is operating under. All supporting information required by the Founders Board shall be provided by the Executive Team.

5.2 **Meetings of the Founders Board**

5.2.1 Unless otherwise agreed at the Founders Board, the Founders Board shall meet at least monthly or more regularly if required during 2022. Thereafter the Founders Board may decide to reduce the meetings to a quarterly interval.

5.2.2 The Founders Board may convene an extraordinary meeting at the request of a Founding Member or the Executive Team.

5.2.3 A minimum quorum of at least seventy five percent (75%) of representatives from Founding Industry Members and at least seventy five percent (75%) of representatives from Founding Member charities and at least one representative from the Executive Team.

5.2.4 No later than five (5) Business Days in advance of a scheduled Founders Board meeting, the Founders Board will receive an operational report from the Executive Team which will include details on:

5.2.4.1 updates on development of the Resource, related recruitment/enrolment and progress against (and proposed deviations from) any related plans, timelines and milestones;

5.2.4.2 cohort diversity reporting and review in line with the then current Scientific Protocol, including target age ranges, eligible populations, ethnic diversity, gender diversity and socioeconomic status;

5.2.4.3 minutes and if appropriate metrics from the other governance boards, subject to relevant confidentiality measures;

5.2.4.4 Our Future Health's and Our Future Health Trading Limited's budget position versus plan, including expenditure and budgeting;

5.2.4.5 status of any proposed studies received by the Access Board, subject to appropriate confidentiality restrictions, which may benefit from a consortium of Founding Members to perform;

5.2.4.6 any matters which may require advisory input, remedy or escalation;

5.2.4.7 other scientific, strategic or budgetary topics as reasonably requested in advance by the Founders Board.

5.2.5 Meeting minutes of the Founders Board shall be recorded and stored in a secure portal for general access by all Founding Members.

5.2.6 There shall be one vote for each representative of the Founding Industry Members and Founding Charity Members that are present at the relevant quorate Founders Board meeting. Items being considered by the Founders Board will be voted on and decisions reached subject to the following voting thresholds (dependent on the item):

5.2.6.1 A unanimous vote in favour from all representatives of Founding Industry Members and Founding Charity Members present at the meeting

5.2.6.2 A super majority vote where super majority means at least seventy five percent of the votes cast by representatives from Founding Industry Members present at the meeting and at least seventy five percent of votes cast by representatives from Founding Member charities present at the meeting

5.2.6.3 A simple majority vote (i.e. more than 50%) from both the Founding Industry Members and the Founding Charity Members present at the meeting (along with more than 50% of votes cast by all representatives with voting rights present at the meeting)

5.2.7 In the situation where there is a deadlock in the voting, there is a process through which matters can be escalated in an attempt to resolve the issues.

5.2.8 The members of the Founders Board will nominate a chairperson who will serve as chairperson of the Founders Board for a period of twelve (12) months, with the chairperson to then rotate between representatives from the Founding Industry Members and Founding Charity Members.

5.2.9 Only members of the Founders Board have the right to attend and vote at the Founders Board meetings (except the representatives of Our Future Health and Our Future Health Trading Limited on the Founders Board who have no voting rights). However, other individuals such as members of other Our Future Health advisory boards, alliance or project managers from Founding Industry Members or Founding Charity Members, can be invited to attend as observers for all or part of the meetings.

5.2.10 The Founders Board, in consultation with the Executive Team, may choose to establish time-limited working sub-groups who would be charged with specific deliverables. These sub-groups would be established jointly between the Founders Board, relevant members of the Executive Team and/or other relevant experts.

5.2.11 Our Future Health through the Executive Team shall provide to the Founders Board all information and documentation necessary for the Founders Board to fulfil and carry out its roles, responsibilities and activities including in relation to matters referred to in this Founders Board section.

5.3 **Remediation process**

5.3.1 If the development of the Resource and/or related recruitment/enrolment are materially behind schedule, and/or if progress is not consistent with (or deadlines may be or are missed for) related plans, timelines and milestones the Executive Team shall:

5.3.1.1 provide full details of and reasons for the issue which has triggered the remediation process as soon as possible to the Founders Board, including convening an extraordinary meeting of the Founders Board where required;

5.3.1.2 provide detailed proposed solutions for discussion including any consequences to the Resource operation; and

5.3.1.3 the Founders Board shall discuss the matter at a meeting and agree next steps and potential solutions including any update to the planned timelines and goals, taking into account scientific quality and the overall goals of the Our Future Health research programme.

5.4 Secretariat

5.4.1 The secretariat will be provided by Our Future Health.

5.4.2 The secretariat is responsible for ensuring that the board receives relevant information and papers in a timely manner to enable full and proper consideration to be given to issues.

5.4.3 The secretariat will also provide logistical support, if needed, to progress work undertaken in the period between meetings of the Founders Board.

5.4.4 The secretariat shall minute the meetings of the Founders Board, including recording the names of those present and in attendance. Once approved by the chairperson, minutes shall be distributed to the relevant board / committee for its next meeting.

5.4.5 Founders Board members will declare any Conflicts of Interest in accordance with the Our Future Health Conflict of Interest Policy.

6. Implementation Board

6.1 Purpose

6.1.1 Our Future Health Board maintains the overall responsibility and decision-making authority for the programme and delegates the day-to-day implementation and management of it to the Our Future Health Executive Team. The Executive Team shall manage all operations and logistics of establishing and making the Resource available to researchers.

6.1.2 The Implementation Board will be a forum for the input into, co-ordination, review and agreement of the following activities:

6.1.2.1 Operational delivery plan to include recruitment planning and processes, sample logistics and handling

6.1.2.2 Conducting the recruitment, consenting and follow-up of cohort participants pursuant to the scientific protocol, including obtaining all necessary informed consents

6.1.2.3 Collecting core cohort data including linked NHS records and wider linkage across government administrative data

6.1.2.4 Return of 'results' to participants and NHS clinical systems

6.1.2.5 Establishing, maintaining, hosting and operating the Our Future Health trusted research environment (TRE) to enable registered researchers to use, access and analyse the core cohort data

6.1.3 The Implementation Board will comprise members of partner organisations who are involved in or support the delivery of the Our Future Health programme. This includes representatives from:

6.1.3.1 UK nations supporting health & social care

6.1.3.2 NHS blood & transplant

6.1.3.3 NHS England (incorporating NHS Digital and NHS-X)

6.1.3.4 NIHR

6.1.3.5 NHS Accelerated Access Collaborative

6.1.3.6 Office for Health Improvement and Disparities

6.1.3.7 Health Data Research UK

6.1.3.8 Professional Medical Society & Colleges

6.1.3.9 In addition to these members, the Chief Executive Officer and the Chief Operating Officer will also be members and the Board shall be chaired by the Chief Executive Officer. Other members of the Our Future Health Executive Team may be invited to attend as appropriate.

6.1.4 The Implementation Board is a strategic group aimed at providing Our Future Health with advice and challenge in order to deliver the programme in the most effective way. Members of the group are acting purely as representatives of their organisations, and any necessary approvals and regulatory steps will still need to be followed.

6.1.5 The Implementation Board shall meet at least quarterly or more regularly if required. At each quarterly meeting, the Board will receive an operational report which will include at a minimum the following matters:

6.1.5.1 Updates on development of the Resource, related recruitment/enrolment and progress against (and proposed deviations from) any related plans, timelines and milestones. This shall include reporting on matters related to recruitment/enrolment figures (by reference to specific 'recruited' criteria, and status (including whether a cohort participant is 'active', which means they have not partially or fully withdrawn any consent));

6.1.5.2 Cohort diversity reporting and review;

6.1.5.3 Minutes from the other advisory boards;

6.1.5.4 Our Future Health's budget position versus plan;

6.1.5.5 Any proposed amendments to the core protocol;

6.1.5.6 Any matters which may require remedy or escalation;

6.1.5.7 Other topics as reasonably requested in advance by the Board.

6.1.6 In all situations, the Implementation Board must consider the overall scientific objectives and goals of the Our Future Health programme and the budget it is operating under.

6.1.7 Following initial review and alignment with the core materials described above, should the Our Future Health programme materially

change, the Implementation Board would be asked to consider and report upon the impact of such changes.

6.1.8 Meeting minutes of the Implementation Board shall be recorded and stored in a secure portal or Sharepoint for general access by all members.

6.1.9 Our Future Health shall provide to the Implementation Board all information and documentation necessary for the Implementation Board to fulfil and carry out its roles, responsibilities and activities.

6.1.10 The Implementation Board can propose representatives who could be participants at other advisory boards established by Our Future Health in support of the programme.

6.1.11 Members will declare any conflicts of interest in accordance with the Our Future Health Conflict of Interest Policy.

7. Access Board

7.1 Purpose

7.1.1 The Access Board (AB) will be responsible for the implementation of the access process summarised herein and for overseeing decisions about applications to access data, samples, and participants. Application summaries and decisions will be made public. The overarching objective of the Access Board is to maximise responsible use of the Resource. The Access Board will review applications requesting data or biological samples or seeking permission to approach participants for secondary studies. At all times consideration of the best interests of the participants will be paramount.

7.2 Membership

7.2.1 The Access Board will be comprised of sector nominees. Sector nominees should include broad representation from across industry, charities and academia sectors, and be sufficiently skilled in the field, including ethics expertise, and capable of applying the terms of reference of the Access Board consistently.

7.2.2 Access Board representatives must not be from the Founding Members, with the exception of any representative nominated by the Founders Board to sit on the Access Board.

7.2.3 The Access Board will establish rules for representation from across the sectors outlined above, and voting and quorum requirements to be used at each Access Board meeting, to ensure appropriate voting rights across the sectors.

7.3 Meetings

7.3.1 The Access Board supports the Executive Team by developing and operationalising the Resource access process. It should maintain close working arrangements with the Founders Board, Ethics Advisory Board and other boards as required and can request expertise when required, e.g. from the Scientific Advisory Board. The Access Board will have to ensure that the Resource access process enables timely decisions on all types of applications.

7.3.2 The Access Board shall conduct its activities under strict confidentiality to protect the interests of the applicant. To provide appropriate transparency to the general public, a lay summary is required for each approved application (the wording of which will be agreed between the Access Board and the applicant) and will be made available within the

Our Future Health public register of studies, which shall be updated regularly by Our Future Health. Such public register shall not contain or disclose Founding Industry Member's Confidential Information, any Personal Information or other proprietary information including biological target information in an approved study.

7.4 **Reporting**

7.4.1 The Access Board will provide regular reports to the Our Future Health Executive Team and other Our Future Health boards as required including the Founders Board.

7.5 **Duties of the Board**

7.5.1 Specifically, the Access Board will:

7.5.1.1 Undertake the review of all applications for studies which require access to the Resource and establish clear policies and procedures for accessing participants' data, samples and for re-contact with the participants themselves consistent with paragraph 7.6 below.

7.5.1.2 Establish a definition of a "depleting" study and an overall depletion framework, along with related examples and principles. This definition and depletion framework will be consistently applied in the Access Board's decision process, taking into account the need to conserve the Resource for the long term and promote maximal value from the Resource.

7.5.1.3 Ensure applications are:

(a) In the best interests of, and acceptable to, the participants and consistent with the consent provided

(b) Led by registered researchers

(c) Ethical and feasible

(d) Aligned with the overarching objectives of Our Future Health (i.e. are aimed at improving human health) and are not likely to bring the study into disrepute or stigmatise any of its participants.

7.5.1.4 Regularly review the access procedures to ensure they are acceptable to participants and meeting the needs of Our Future Health's user communities.

7.5.1.5 Always apply the depletion framework when assessing applications and shall reject applications for any study that may be depleting as per the agreed definition and depletion framework.

7.6 The Access Board has overall responsibility for ensuring that access to, and usage of, the Resource is consistent with:

7.6.1 the undertaking given to and the specific Informed Consent given by the Cohort Participants;

7.6.2 (and in compliance with) all laws and regulations including respect for human rights;

7.6.3 the conditions placed on Our Future Health in the ethical approval granted by the Health Research Authority;

7.6.4 the principles of the Our Future Health research programme to advance early disease diagnosis and detection for the benefit of the public, disease discovery and making innovation available;

7.6.5 the Our Future Health Ethics Framework; and

7.6.6 the Resource Access Process and its objective to facilitate access to the Core Cohort Data, Cohort Participants and Samples and other aspects of the Resource to enable high quality studies. Studies submitted to the Access Board may be broad (such as data mining) or narrow (such as a discrete research question) in their objectives.

7.7 **Other matters**

7.7.1 The Access Board shall conduct its activities under strict confidentiality to protect the interests of the applicant.

7.7.2 Members will receive a small honorarium and will be reimbursed for all reasonable costs for attending meetings.

7.7.3 Members will declare any conflicts of interest in accordance with the Our Future Health Conflict of Interest Policy.

8. Scientific Advisory Board

8.1 Purpose

8.1.1 The Scientific Advisory Board (SAB) will provide advice to the Our Future Health Executive Team to ensure that the programme is able to achieve its goals in a scientifically rigorous and robust way, considering the changing landscape of population health research in the UK and new scientific opportunities as they arise.

8.1.2 Specifically, the SAB will provide advice on:

8.1.2.1 The scientific priorities for the research programme

8.1.2.2 Key aspects of Resource design and delivery including measurements and sample analyses

8.1.2.3 How best to maximise scientific utility and impact, given the resources available

8.1.2.4 Identify and prioritise enhancements to the Resource that will improve utility and impact

8.1.2.5 Identify scientific issues that require detailed evaluation by time-limited expert subgroups and to advise on the membership and remit of such

8.1.2.6 Areas where Our Future Health has made/is making a significant scientific contribution to the field

8.1.3 As required, the SAB will delegate specific 'deep-dive' tasks (e.g. questionnaire or microarray design) to ad hoc working groups.

8.2 Expertise

8.2.1 There will be a need for broad expertise covering the following key areas: public health; longitudinal population studies; biosample processing, analysis and biobanking; population genetics/genomics; primary care; social/behavioural science; wearables and remote monitoring; statistics and study design; visualisation and analysis of large complex datasets; data linkage (both health and other administrative data).

8.3 Method of working and frequency of meetings

8.3.1 The SAB will meet quarterly and possibly more frequently in the early years of the study. It is envisaged that members will also be called upon

between meetings to provide advice on specific scientific issues as they emerge.

8.4 **Other matters**

8.4.1 Members will receive a small honorarium and will be reimbursed for all reasonable costs for attending meetings.

8.4.2 Members will declare any conflicts of interest in accordance with the Our Future Health Conflict of Interest Policy.

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9. Technology Advisory Board

9.1 Purpose

9.1.1 The Technology Advisory Board (TAB) provides insights into the main platform technology solutions and decisions. This Board will comprise experts and technical leaders who can provide advice on the key decisions related to the main platform and digital interfaces to ensure long-term sustainability, anticipate change and deliver value to the project.

9.1.2 Specifically, the TAB will cover:

9.1.2.1 Privacy-preserving, anonymisation and de-identification technologies; data ethics

9.1.2.2 Cybersecurity and cyber resilience

9.1.2.3 The architecture and scalability of the Our Future Health technology platform

9.1.2.4 Systems engineering and software development

9.1.2.5 Integrating and linking clinical data drawn from NHS and other healthcare data systems

9.1.2.6 Health data and genomics analytics, including the application of artificial intelligence, machine learning and federated techniques

9.1.2.7 Data standards and best practice in the representation, access and sharing of health data consistent with the fair (findable, accessible, interoperable, and reusable) principles

9.1.2.8 Accessibility of the systems to a diverse audience

9.1.2.9 Growth and scaling of Our Future Health systems; working across technology suppliers and partners

9.1.3 The TAB will collaborate with other governing bodies where appropriate and if required it will set up working groups to address specific issues.

9.2 Proposed membership

9.2.1 The following key competencies will be represented: expertise in personal data and data ethics; cybersecurity; data infrastructure and engineering including scaling of cloud systems and the storage and processing of large volumes of health data; software engineering; experience of NHS and health data across the UK system; clinical data standards; accessibility; application of AI/ML to health data; data analytics; data processing for genomics; growth and scaling of large-scale platforms; commercial and strategic issues working with it and technology suppliers.

9.3 **Method of working and frequency of meetings**

9.3.1 The TAB will meet quarterly. It is envisaged that members will also be called upon between meetings to provide advice on specific scientific issues as they emerge.

9.4 **Other matters**

9.4.1 Members will receive a small honorarium and will be reimbursed all reasonable costs for attending TAB meetings.

9.4.2 Members will declare any conflicts of interest in accordance with the Our Future Health Conflict of Interest Policy.

10. Public Advisory Board

10.1 Purpose

10.1.1 To provide public oversight and an ongoing consultation resource for the design and delivery of, and production of new materials for, the Our Future Health research programme. The Public Advisory Board will act as an intermediary between the relevant Our Future Health governance boards and the public voice.

10.2 Responsibilities

10.2.1 Members will already be familiar with the aims of the project due to prior involvement and co-design work. Therefore, its members will not represent a true objective public insight. Rather, the group will be convened with the purpose to provide ongoing consultation and oversight of the project. The Public Advisory Board will provide advice and guidance for the following areas:

10.2.1.1 Participant recruitment strategies

10.2.1.2 Community and public engagement initiatives

10.2.1.3 Proposed amendments to the project that directly affect participants or public perceptions of the research programme

10.2.1.4 Submitted consultation proposals from Our Future Health teams

10.2.1.5 Feedback on public- and participant-facing materials as required

10.2.1.6 Advice regarding feedback of information to participants

10.2.1.7 Advice on governance arrangements and issues of public trust

10.3 Membership

10.3.1 Members will be recruited from a pool of 24 individuals who have previously taken part in co-design groups. Membership of the previous co-design groups were selected based on specific criteria to ensure diverse representation across the groups; therefore, members of the Public Advisory Board will be representative in terms of gender, age, ethnicity, and geographical location in the UK.

10.3.2 Membership will be voluntary but will for a period of 12 months.

10.4 **Method of working and frequency of meetings**

10.4.1 The chair of the Public Advisory Board will be the public engagement and involvement lead for the first 12 months, after which members will elect the chair and additional roles for the group. Elected representatives will hold their role for 12 months unless they wish to step down.

10.4.2 The Public Advisory Board will meet four times a year, or as required (for example if a submitted proposal needs immediate consultation). Members will work closely with the public engagement and involvement lead and will produce a written response to all proposals submitted to the group within 7 working days.

10.4.3 Members will sign a confidentiality agreement document and all meetings may be recorded for internal purposes only. It may be possible for members of Our Future Health team to be an 'observer' at one of the meetings (with prior agreement).

10.4.4 Members may also be asked to be a public representative on additional governance boards within Our Future Health, such as the Scientific Advisory Board and members will be asked to express an interest for the role. Membership on additional governance boards will be in addition to the requirements of the Public Advisory Board and members will be reimbursed in accordance with our honorarium policy.

10.4.5 As Our Future Health grows and recruits participants into the programme, the Public Advisory Board will become the public and participant advisory Board. Further details of this transition will be circulated to members in advance of any changes and will be approved internally before members are asked to join.

10.5 **Working principles**

10.5.1 Members will agree to:

10.5.1.1 Make every effort to attend all meetings and come prepared to ask questions and contribute fully

10.5.1.2 Give apologies in advance if unable to attend for any reason

10.5.1.3 Respect the views of other members of the group, even if they disagree

10.5.1.4 Respect the confidentiality of any material shared

10.6 **Other matters**

10.6.1 Members will receive a small honorarium and will be reimbursed for all reasonable costs for attending meetings.

10.6.2 Members will declare any conflicts of interest in accordance with the Our Future Health Conflict of Interest Policy.

11. Diversity and Inclusion Advisory Board

11.1 Purpose

11.1.1 Our Future Health is committed to building a research programme that truly reflects the UK population, so that we can identify differences in how diseases begin and progress in people from different backgrounds. The purpose of the Diversity & Inclusion Advisory Board (DAB) is to advise and provide strategic support to the Our Future Health research programme regarding involvement, engagement, recruitment and retention of communities who are often under-represented in health research, including Black, Asian and other minority ethnic groups, and people from lower socioeconomic backgrounds.

11.1.2 The DAB will provide expert advice to Our Future Health on equality, equity, diversity, and inclusion in relation to issues including participant recruitment, retention and engagement with and evaluation of the programme.

11.1.3 The DAB will advise the Our Future Health Leadership Team, and where appropriate the Our Future Health Board of Trustees via the Our Future Health Leadership Team or the Our Future Health Executive Team.

11.2 Membership

11.2.1 Members of the DAB will represent groups that possess experience and networks in communities that are classified as under-represented. Members will have extensive experience of influencing and motivating communities to engage in both national and local strategic projects.

11.2.2 The DAB will comprise 20-25 members drawn from the following groups:

Community engagement leaders and workers

Individuals who have led and/or worked on community engagement projects for harder-to-reach audiences – their experience does not have to be specifically health related and it will be important that they can provide tactical advice on national engagement strategies

Public health, social & health care

Individuals with experience working with patients from diverse backgrounds in the public health or health care contexts, including from organisations with similar objectives in engaging harder-to-reach groups

Communications, PR, and media

Individuals from communications, PR or media backgrounds with experience of engaging with harder-to-reach groups – health experience is not essential, but they will understand how to deliver successful targeted campaigns

Academic research

Experienced and respected research leaders who have a professional background that includes targeting of under-represented groups in health research

Faith leaders

National-level faith leaders with significant influence across their communities – experience in working with third parties as a conduit to under-represented communities would also be desirable

11.2.3 Members will either be directly invited to be a part of the DAB, or will respond to a national-level advertisement. In the latter case, members will be selected via an assessment process comprising a written application and panel interview. Efforts will be made to create a board that includes people from a broad range of backgrounds and communities.

11.2.4 The secretariat will be provided by Our Future Health.

11.3 **Meetings**

11.3.1 The DAB will begin by meeting quarterly, with the ongoing meeting frequency to be determined by the Chair, in consultation with the Secretariat, and based on Our Future Health requirements.

11.3.2 Unless otherwise agreed, notice of each meeting date and time, venue confirmation, agenda of items to be discussed, and any supporting papers, will be forwarded to each member of the Board no less than 5 working days before the date of the meeting.

11.3.3 The Chair will assume responsibility for determining the frequency, timing and agenda for the meetings, with support from the Secretariat and a nominated Our Future Health Leadership Team representative.

11.3.4 The Chair (or representative) will be responsible for liaison with the Our Future Health Leadership Team and others as required.

11.3.5 The Chair will ensure that equal and proper consideration is given to issues arising and may be asked to communicate with other DAB

members on behalf of Our Future Health in the period between meetings. The Chair will also be part of the Chairs Group, enabling networking with other Our Future Health advisory groups.

11.3.6 The Secretariat will ensure that DAB members receive relevant pre-reads and papers in a timely manner, to enable sufficient time for full and proper consideration before the meeting. The Secretariat will also provide logistical support, if needed, to progress work undertaken by/on behalf of the DAB in the period between meetings.

11.3.7 The Secretariat will be responsible for minuting the meetings, including recording the names of those present and in attendance. Once approved by the Chair, minutes will be distributed to the DAB members before the next meeting.

11.4 **Reporting**

11.4.1 The Our Future Health Leadership and Executive Teams will receive the minutes of meetings, as well as a short verbal report from the Leadership Team representative shortly after the meeting.

11.5 **Duties of the Board**

11.5.1 Specifically, the DAB will advise on:

11.5.1.1 aspects of programme design and delivery that relate to engaging, recruiting and retaining under-represented groups;

11.5.1.2 how to maximise diversity of the cohort and ability to recruit and retain under-represented groups, given the resources available;

11.5.1.3 addressing motivators and barriers to taking part in health research among under-represented groups;

11.5.1.4 facilitating communication, awareness building and networking with key community, academic, religious, and professional organisations and groups aligned to the aims of Our Future Health;

11.5.1.5 evaluating the programme to identify and prioritise enhancements that will further improve diversity and ability to reach under-represented groups over time.

11.6 **Other matters**

11.6.1 Membership will be for one year in the first instance.

11.6.2 The DAB will have access to sufficient resources to carry out its duties, including access to assistance for the Chair as required. Members may be invited to take part in external consultation activities at the discretion of Our Future Health, depending on availability and relevant expertise or interests.

11.6.3 Members will receive a small honorarium and will be reimbursed for all reasonable costs for attending meetings.

11.6.4 Members will declare any conflicts of interest in accordance with the Our Future Health Conflict of Interest Policy.

12. Working Groups

In addition to the main advisory boards, there will be a number of working groups/task forces which are established by the Executive Team to address key issues. Charters for these groups are included here.

12.1 Technology Task Force

12.1.1 Purpose

12.1.1.1 The Technology Task Force (TTF) is established by the Executive Team and shall report to that team through the Chief Technology Officer. The TTF will help with development of the Our Future Health Trusted Research Environment (TRE) specification and the accreditation process for 3rd party TREs. Additionally, the TTF will ensure that the programme is able to achieve its goals by contributing to discussion in relation to the design and delivery of the TRE platform and data tools, data security and data flows required to support the project, considering the changing data and technology landscape in the UK and internationally.

12.1.1.2 The TTF provides a direct route for Founding Members (charity and industry) to contribute to discussion which will influence the technology solutions for the programme.

12.1.2 Membership

12.1.2.1 Membership of the Technology Task Force will comprise Founding Industry Members and Founding Charity Members who have signed a partnership agreement. These entities may nominate appropriately qualified personnel to attend meetings of the Technology Task Force based on the agenda rather than having a fixed standing member, so as to facilitate robust and detailed discussions on a range of topics that will vary over time.

12.1.2.2 The Technology Task Force may nominate up to two (2) representatives (one (1) representative from Founding Industry Members and one (1) representative from Founding Member charities) to attend the Technology Advisory Board to represent the Technology Task Force.

12.1.2.3 The Chair of the Technology Task Force will be selected by the Technology Task Force and approved by Our Future Health, such approval shall not be unreasonably withheld.

12.1.3 Secretariat

12.1.3.1 The secretariat will be provided by Our Future Health.

12.1.3.2 The secretariat is responsible for ensuring that the task force receives relevant information and papers in a timely manner to enable full and proper consideration to be given to issues.

12.1.3.3 The secretariat will also provide logistical support, if needed, to progress work undertaken in the period between meetings of the Technology Task Force.

12.1.3.4 The secretariat shall minute the meetings of the Technology Task Force, including recording the names of those present and in attendance. Once approved by the chairperson, minutes shall be distributed to the relevant board / committee for its next meeting.

12.1.4 Other matters

12.1.4.1 The Technology Task Force shall have access to sufficient resources in order to carry out its duties, including access to the Secretariat for assistance as required.

12.1.4.2 Representatives on the Technology Task Force will declare any conflicts of interest prior to a meeting and recuse themselves from discussions as necessary.

12.2 **Primary Care Working Group**

12.2.1 Purpose

12.2.1.1 Our Future Health will be the UK's largest ever health research programme, designed to enable the discovery and testing of more effective approaches to prevention, earlier detection and treatment of diseases. It will collect and link multiple sources of health and health-relevant information, including genetic data, across a cohort of 5 million people that truly reflects the UK population. This will create a world-leading resource for academic and commercial researchers to undertake discovery research on early indicators of disease, plus the opportunity to re-

contact participants on a risk-stratified basis for secondary studies.

12.2.1.2 Since large-scale recruitment of the cohort will be conducted in primary care, effective collaboration with Our Future Health will be integral to the success of the Resource. If appropriate consent is received, clinical data from physical measurements and genomic analyses may be shared with participants directly by the study or via primary care. In either case, the challenges of delivering complex information on clinical risk (e.g., using polygenic risk scores) in community settings must be understood and any impacts to citizens and local healthcare systems mitigated.

12.2.1.3 Our Future Health Primary Care Working Group is the new name for Our Future Health Clinical Liaison Group.

12.2.2 Responsibilities

12.2.2.1 To provide advice and guidance on design and implementation of the study protocol in all four nations of the UK, particularly in relation to recruitment in primary care and the feedback of clinical (including genomic) data

(a) To give insights on procedures and policies in primary care and make best use of routinely stored information

(b) To help maximise the utility of feedback to participants (e.g., improved risk stratification of cardiovascular disease using polygenic risk scores) and minimise any unwarranted impact on clinical services, especially primary care

(c) To mediate between Our Future Health and organisations representing the interests of primary care, e.g., the Royal College of General Practitioners (RCGP), the British Medical Association (BMA)

12.2.2.2 The Primary Care Working Group has been assembled to assist the Executive Team in addressing the issues described in the remit. Its function will be time-limited (initially to 2 years) and task-focused, with meeting agendas agreed prior to circulation by Executive Team and Board.

12.2.2.3 Our Future Health is the legal entity established to administer the research platform.

12.2.3 Secretariat

12.2.3.1 The Chair shall act as the secretary of the Primary Care Working Group and is responsible for ensuring that it receives relevant information and papers in a timely manner to enable full and proper consideration to be given to issues. The Chair will also provide logistical support, if needed, to progress work undertaken by/on behalf of the Group in the period between meetings.

12.2.4 Frequency and duration of meetings

12.2.4.1 The Primary Care Working Group will meet approximately monthly in the first instance with ongoing frequency of meetings to be determined by the Chair, in consultation with the Executive Team. Meetings will normally be less than two hours in duration with timings to be indicated in the agenda.

12.2.5 Other matters

12.2.5.1 The Primary Care Working Group shall have access to sufficient resources in order to carry out its duties, including access to the Chair for assistance as required. Members of the Primary Care Working Group may be invited to join other advisory or operational groups in the Our Future Health research programme, depending on relevant expertise and/or interest. Members will be reimbursed for meeting attendance plus travel expenses where applicable. The level of reimbursement will be reviewed in line with the duration of meetings. Members will declare any Conflicts of Interest in accordance with guidance outlined in the Code of Conduct for Our Future Health.

12.3 **Secondary Care Working Group**

12.3.1 Purpose

12.3.1.1 Our Future Health will be the UK's largest ever health research programme, designed to enable the discovery and testing of more effective approaches to prevention, earlier detection, and treatment of diseases. It will collect

and link multiple sources of health and health-relevant information, including genetic data, across a cohort of 5 million people that truly reflects the UK population. This will create a world-leading resource for academic and commercial researchers to undertake discovery research on early indicators of disease, plus the opportunity to re-contact participants on a risk-stratified basis for secondary studies.

12.3.1.2 Secondary care settings offer the opportunity for ease in recruitment pathways in an environment that is well equipped to assisting with research. Effective collaboration with clinicians and academics working in secondary care research will be crucial, ensuring maximal benefit to Our Future Health, while safeguarding against undue negative impact on care delivery.

12.3.2 Responsibilities

12.3.2.1 To provide advice and guidance on potential secondary care recruitment routes in conjunction with the secondary care discovery group.

12.3.2.2 To advise on the acceptability, translatability and scalability of recruitment pathways developed by our collaborators, including (but not limited to) Leeds Teaching Hospitals and NHS Scotland.

12.3.2.3 To collaborate on secondary care main study plans and pilots (should they take place).

12.3.2.4 To advise on future plans for recruitment via Biomedical Research Centres (BRCs).

12.3.2.5 To mediate between Our Future Health and organisations representing the interests of secondary care, e.g., the Royal College of Physicians (RCP), the British Medical Association (BMA).

12.3.2.6 The Secondary Care Working Group has been assembled to assist the Executive Team in addressing the issues described in the remit. Its function will be time-limited (initially to 1 year) and task-focused, with meeting agendas agreed prior to circulation by Executive Team and Board.

12.3.3 Secretariat

12.3.3.1 The Chair shall act as the secretary of the Secondary Care Working Group (with support from the Our Future Health Business Operations team) and is responsible for ensuring that it receives relevant information and papers in a timely manner to enable full and proper consideration to be given to issues.

12.3.3.2 The Chair will also provide logistical support, if needed, to progress work undertaken by/on behalf of the Group in the period between meetings.

12.3.4 Frequency and duration of meetings

12.3.4.1 The Secondary Care Working Group will meet approximately monthly in the first instance with ongoing frequency of meetings to be determined by the Chair, in consultation with the Executive Team. Meetings will normally be less than two hours in duration with timings to be indicated in the agenda.

12.3.5 Other matters

12.3.5.1 The Secondary Care Working Group shall have access to sufficient resources to carry out its duties, including access to the Chair for assistance as required.

12.3.5.2 Members of the Secondary Care Working Group may be invited to join other advisory or operational groups in the Our Future Health research programme, depending on relevant expertise and/or interest.

12.3.5.3 Members will be reimbursed at a rate of £100 per meeting attendance plus travel expenses where applicable. The level of reimbursement will be reviewed in line with the duration of meetings.

12.3.5.4 Members will declare any Conflicts of Interest in accordance with guidance outlined in the Code of Conduct for Our Future Health.

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Appendix A

Our Future Health

Our Future Health is a company limited by guarantee (company number 12212468). It is registered as a charity with the Charity Commission for England and Wales (charity number 1189681) and with OSCR, the Scottish Charity Regulator (charity number SC050917).

The directors (also known as trustees) are: Professor Sir John Bell; Professor Fiona Watt; Dr Sir Harpal Singh Kumar; and Dr Tim Peakman.

Our Future Health operates the foundation model of governance whereby the only members of Our Future Health are the directors from time to time. This governance model is common in the charity sector.

Our Future Health Trading Limited

Our Future Health Trading Limited (company number 12599493) is a company limited by shares; its sole shareholder is Our Future Health.

Its directors are: Professor Sir John Bell; Professor Fiona Watt; Dr Sir Harpal Singh Kumar; and Dr Andrew Roddam.

Appendix B

Draft ToR for Data Privacy & Information Security Board/Committee

13. Data Privacy & Information Security Board/Committee

13.1 Purpose

The Data Privacy & Information Security Board brings together expertise across scientific, regulatory, legal, ethical, and technology domains to provide expert advice to the research programme on the awareness and adoption of data protection technology and on all matters related to the protection and privacy of data including protecting a participant's privacy / rights.

In this context, data protection is defined as the assurance that data is usable and accessible for authorized purposes only, with acceptable performance and in compliance with applicable laws and regulations. As well as the technology associated with data protection, there is also a wider context which is being driven by increasing legislation to keep personal data private.

13.2 Proposed membership

The committee will be made up of representatives from the other Advisory Boards to reflect the breadth of expertise required for this group. Additionally, this board will be strengthened through additional members with particular expertise in data privacy & governance, legal, data security and data trust.

13.3 Method of working and frequency of meetings

13.3.1 The board will meet quarterly. It is envisaged that members will also be called upon between meetings to provide advice on any urgent or emerging issues as they emerge.

13.4 Other matters

13.4.1 Members will receive a small honorarium and will be reimbursed all reasonable costs for attending meetings.

13.4.2 Members will declare any conflicts of interest in accordance with the Our Future Health Conflict of Interest Policy.