Category 1 enhanced phenotyping at baseline assessment visit in last 200,000 participants and subsequent invitation to complete web-based diet questionnaire

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Addendum to main study protocol (9 April, 2009)

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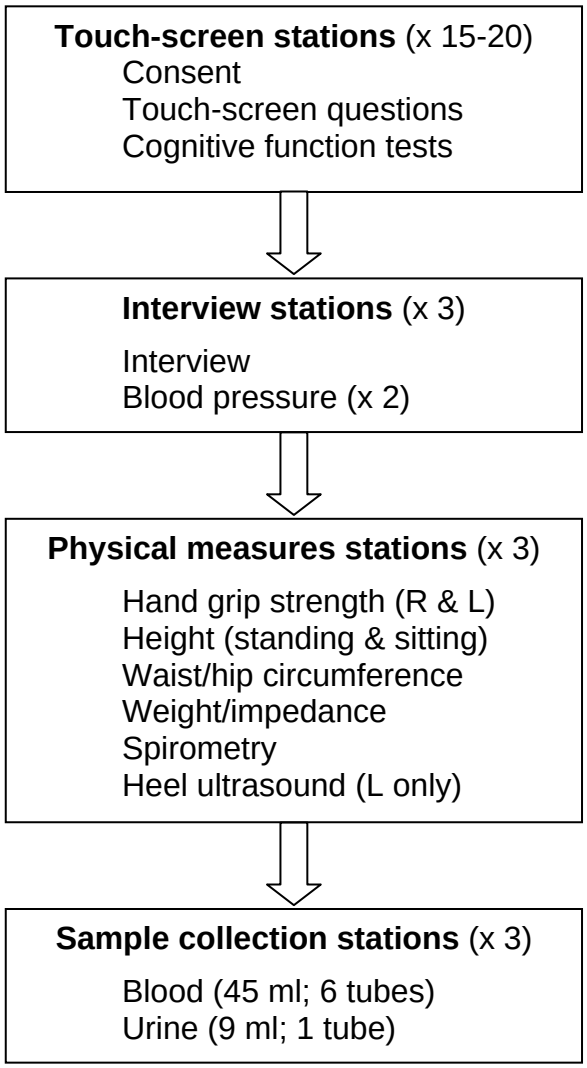
1.0 Introduction

Following piloting in 2005-2006, the UK Biobank protocol was endorsed by an International Peer Review Panel, and full-scale recruitment started in April 2007. By late 2010, UK Biobank will have recruited 500,000 men and women from the UK general population who are aged 40-69 at their baseline assessment visit. A number of questions and measures potentially associated with various health outcomes were excluded from the baseline assessment of the whole cohort for reasons of feasibility (in particular, constraints imposed by the available funding). It was, however, recognised that there were opportunities for enhancement by adding extra phenotyping in large subsets of the cohort. For, as follow-up becomes more prolonged and more cases of different conditions occur, more detailed assessments in a substantial proportion of the whole study population would become increasingly informative. This would be the case especially if such measures were more precise and more strongly related to health outcomes than those that are being made in the whole cohort. Consequently, the International Peer Review Panel endorsed, with the support of the funders, UK Biobank's proposal that a wide range of possible enhancements be investigated and this work has been taken forward by a Working Group on Enhancements (chair: Professor Paul Elliott, Imperial College, London: Appendix 1), which has consulted with a wide range of experts both in this country and beyond.

Now that UK Biobank is running smoothly, with 275,000 people recruited by March 2009, it is timely to consider introducing such enhancements. The proposed strategy for enhanced phenotyping involves the initial introduction of a limited number of "Category 1" enhancements that can be accommodated within the time and budget constraints of the current assessment visit without disruption to the recruitment process (although they will still be introduced in a gradual fashion and their impact monitored closely). Introduction of these enhancements in mid-2009 should allow them to be undertaken in the last 200,000 participants. (More extensive enhancements to the current assessment visit ["Category 2"] or at subsequent re-assessment visits ["Category 3"] will be the subject of subsequent research ethics applications provided that additional funding is obtained.)

1.1 Current baseline assessment visit

The main protocol describes in detail the current assessment visit, but in summary it involves participants moving through a fixed sequence of dedicated stations:



The current invitation letter that the visit is expected to be **about 90 minutes**, but experience to date has shown that the actual visit duration is an average of **73 minutes** (interquartile range: 64-99 minutes; see table below). Early experience has also shown that the wait time is increased when more than 120 participants per day are seen, so the invitation mailing and appointment systems have been refined (and are now running smoothly) in order to ensure that the daily throughput does not exceed 110 per day.

Visit stage	Average process time (mins)	Average elapsed time (mins)
Wait for Consent	1	1
Touchscreen questionnaire	37	43
Wait for interview	3	46
Interview and blood pressure	8	54
Wait for physical measures	3	57
Physical measures station	9	66
Wait for venepuncture	2	68
Venepuncture station	4	72
Exit	1	73
Total process time (mins)	63	
Total waiting time (mins)	10	

The Category 1 enhancements proposed below are expected to take an extra 20 minutes to undertake, which would be expected to increase the total visit duration to about 90 minutes (although total visit duration and wait times will continue to be monitored closely). North West REC previously approved an optional heart health check by a British Heart Foundation (BHF) nurse at the end of the assessment visit. This BHF assessment (now ended) took an extra 20-30 minutes and was taken up by about two-thirds of participants, which indicates that participants are likely to be willing to stay for about 90 minutes.

2.0 Category 1 enhancements to baseline assessment visit

The following Category 1 enhancements are proposed for inclusion from Q2 2009 to end of recruitment in late 2010, allowing them to be undertaken on the last 200,000 participants recruited:

1. Additional questions on the touchscreen questionnaire to assess cognitive function and psychological status further, and a small number of additional questions suggested by relevant experts (expected time to complete: about 4 minutes; see Section 2.1 below);

2. Inclusion of a hearing test using the touchscreen questionnaire while wearing headphones (expected time to complete: about 4 minutes; see Section 2.2 below);

3. Measurement of pulse wave velocity using a non-invasive infra-red finger probe during the interview station (expected time to complete: 1-2 minutes; see Section 2.3 below);

4. Measurement of heel bone ultrasound on both heels (currently only left heel is measured) during the measurements station in order to improve

the precision of the bone density estimates by reducing random error (expected time to complete: 1-2 minutes);

5. Detailed web-based diet questionnaire (expected time to complete: 10-15 minutes; see Section 2.4)

About 2-3 minutes is expected to be saved from the interview section of the current visit by removing questions on parents' first names and their month and year of birth (which were originally included to allow probabilistic linkage of siblings, but have now been removed because there was poor participant recall and recent data indicate that genetic analysis will be a much more reliable method for such linkage).

2.1 Additional questions on the touchscreen questionnaire

Experience to date has shown high levels of participant acceptability with both the content of the current questionnaire and the method of administration using a touchscreen format. Currently, 200-300 questions and some simple cognitive function tests are completed in about 30-40 minutes. Cognitive function is currently assessed on the touchscreen system by a paired-associated learning test to assess global cognition and by a reaction time test. Psychological state is currently assessed in terms of psychological traits (neuroticism) and mood using standardised questions, and by recording medical presentations for psychological symptoms and serious life events. These assessments take about 10 minutes to complete and have been found to have high levels of participant acceptability.

In order to characterise cognition better (in particular, cognitive reserve and executive function), it is planned to include tests for numerical and verbal reasoning and for working memory. The additional questions proposed for assessing psychological state should provide better characterisations for depression (according to Diagnostic & Statistical Manual of Mental Disorders [DSM] IV criteria) and bipolar disorder. For depression, two extra screening questions are to be included (with two follow-up questions for those who screen positive) and, for bipolar disorder, two extra questions are to be included (with six follow-up questions for those who screen positive). These questions have been selected following consultation with experts (e.g. Prof Kenneth Kendler, US, for depression; Prof Nick Craddock, Cardiff, for bipolar disorder) who have analysed large patient datasets to identify those questions most strongly associated with the particular disorders. An additional six questions have also been included to assess self-reported happiness in relation to various life domains (such as health, friendship and financial situation). These tests have been piloted for UK Biobank in about 160 adults aged 20-65 (Dr John Gallacher, Cardiff), and take up to 3-4 minutes depending on the answers given to the screening questions.

In addition, a few extra questions (e.g. domestic heating, private healthcare, claudication, sudden death) that various experts recommended be included were accepted by the Enhancements Working Group (see Appendix 2).

2.2 Hearing assessment using the touchscreen questionnaire

It is estimated that about 20% of UK adults have some degree of hearing loss and the prevalence increases rapidly with age (Department of Health. 2007). Noise exposure at work and leisure appears to be the major preventable risk factor for hearing loss under the age of 50, but the causes in older people are less clear (Health & Safety Executive. 2001). Currently, hearing is assessed in UK Biobank only by three questions on the touchscreen questionnaire about perceived difficulties with hearing and use of a hearing aid. Consultation with leading experts (led by Professor David Moore, MRC Institute of Hearing Research, Nottingham) identified extra questions on occupational and leisure noise exposure to include on the touchscreen system (see Appendix 2).

It is also proposed that an automated hearing test developed by a European consortium of audiometry experts (Speech-in-Noise Screening Test; Smits & Houtgast 2005]) be conducted to assess hearing thresholds at different frequencies. Such audiometry tests do not require sound-proof facilities and have been used successfully in "field" settings in other studies. This test can also be administered over the internet and by telephone (Hearcom website), which would allow re-assessment of hearing in participants to be conducted during follow-up. The Speech-in-Noise test has been adapted for use on the touchscreen system. Participants would be advised to put on the headphones provided and, when, ready, the following information would be displayed:

"The hearing test will determine how well you can hear three spoken numbers played with a rushing noise in the background. Each ear will be tested separately and each sound will consist of the words "The digits…" followed by three spoken numbers that will be played with a rushing noise in the background. After listening to each sound, you should enter the three numbers you have heard using the number pad on the screen. When ready to begin the test, select Next."

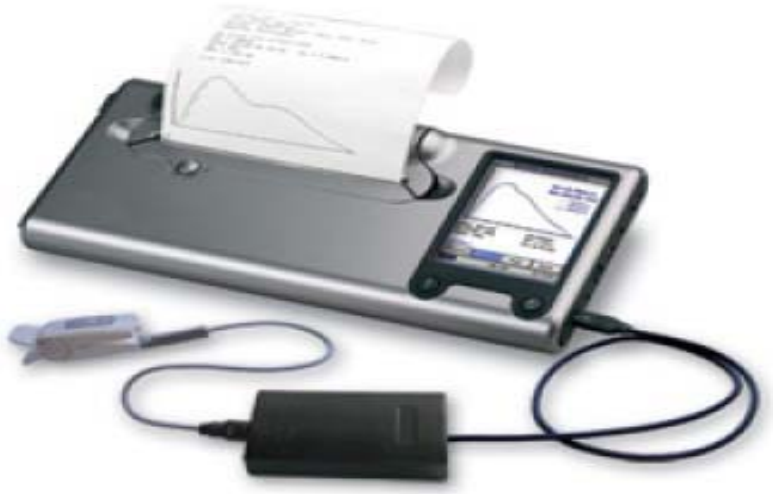
The test is expected to take about 4 minutes to complete.

2.3 Measurement of pulse wave velocity

Arterial stiffness increases with age and is associated with other risk factors for vascular disease (such as diabetes, blood pressure, cholesterol and end-stage renal failure; Sutton-Tyrrell *et al* 2005). It has also been suggested that arterial stiffness may be an independent predictor of vascular disease risk. Decreased arterial elasticity may have unfavourable vascular consequences, including increased aortic and left ventricular systolic pressure, and decreased capacity for myocardial perfusion during diastole. As elevated arterial stiffness can be detected before cardiovascular disease becomes clinically apparent, it may act as a marker for the development of future vascular events (Duprez *et al* 2001). Arterial stiffness can be estimated using a variety of different methods, although all are based on the assumption that the distensibility of the artery is inversely proportional to the speed of the pulse wave along the artery on which it is measured. The most widely accepted method for

measuring pulse wave velocity uses the SphygmoCor device, which is too complicated and time-consuming (about 30-40 minutes) for large-scale epidemiological studies.

Recent technological developments have now made the assessment of arterial stiffness feasible in UK Biobank using systems that have been validated against the SphygmoCor device (Prof Phil Chowienczyk, London). One of these systems is the PulseTrace PCA2 (see picture below), which estimates arterial stiffness from a pulse waveform measured using an infra-red sensor clipped on to the end of the index finger. The shape of this waveform is directly related to the time it takes for the pulse wave to travel through the arterial tree. This measure only takes about 2 minutes, and the device is extremely easy to use, non-invasive, well accepted by patients, operator-independent and inexpensive. A single pulse wave will be recorded at the end of the interview station after completion of the second blood pressure reading, and the entire procedure takes about 1-2 minutes.



2.4 Dietary assessment using a web-based questionnaire

Turning to the assessment of diet, previous studies have provided conflicting evidence about the relevance of various dietary components to disease outcomes (Bingham et al 2003; Beresford et al 2006; Howard et al 2006; Willett 2008), which may relate to differences in the methods used to assess diet (Day et al 2001; Willett 2008). The availability of biological samples in UK Biobank will allow the direct measurement of many biomarkers related to diet (e.g. lipids, vitamins, red cell fatty acids: Bingham et al 2008). But, since such biomarkers do not necessarily reflect intake (Cade et al 2002) and are not available for many dietary items, questions about diet also need to be asked. Currently, the assessment visit involves self-completion of a relatively short (average of about 5 minutes to complete) set of food frequency-type questions

at the touchscreen station. These were selected in order to allow the ranking of participants according to commonly eaten food groups based on the expected distribution in the British population, as well as seeking information about some common sources of various nutrients (Hoare et al 2004). It is recognised that this approach does not allow assessment of total energy intake or of some specific nutrient intakes, but alternative approaches (such as multiple-day food diaries) involve significant time and cost to complete and code, and are not feasible for the repeated measures needed to take account of variation over time.

In piloting for UK Biobank, about two-thirds of study participants indicated that they regularly used, and would be happy to be contacted via the internet, in order to answer additional questions. Hence, UK Biobank commissioned the development of a validated web-based diet questionnaire (Prof Valerie Beral, Oxford; in consultation with the US National Institutes of Health, International Agency for Research on Cancer and UK Foods Standards Agency) for participants to complete repeatedly during follow-up. This web-based questionnaire, which is based on recall of food and drink consumption on the previous day, only takes about 10-15 minutes to complete and (by contrast with diet diaries) involves automatic coding of the quantity of reported food items, allowing estimation of the intake of various nutrients. The advantages of such an instrument for a study as large as UK Biobank include ease of administration, timely access to data, and the ability to obtain repeat measurements (which is particularly important for measuring exposures such as diet: Schatzkin et al 2003; Willett 2008). Initial validation studies have involved comparison of nutrient estimates from this web-based diet questionnaire to estimates from 100 coded food diaries completed previously by participants in EPIC, and has shown close agreement for nutrient intake between food diaries and the web-based questionnaire. Further validation studies comparing the web questionnaire to a 24 hour dietary recall collected by a trained interviewer in 116 volunteers has resulted in further refinement of the questionnaire, including the addition of example pictures of food types, provision of more options to pick from a list rather than giving free text answers, and inclusion of a summary at the end that can be checked and changed if necessary. Validation studies using biomarkers and assessing energy intake will double labeled water will be completed shortly.

It is proposed that participants would be invited to spend 10-15 minutes at the end of their assessment visit completing this web-based diet questionnaire (Appendix 3) on one of a bank of computers connected to the internet (while having refreshments at the end of their visit). A member of staff would be available to introduce participants to this web-based system (which it is intended be repeated subsequently: see below) and to answer questions about it. This process would provide more detailed dietary information on these participants at the baseline visit and would introduce them to the system so that repeat measures can be obtained more readily during follow-up (see below), while allowing further assessment of the web-based questionnaire in a controlled environment. The written consent given by all participants at the baseline assessment visit includes agreement to be *“re-contacted by UK*

Biobank (e.g. to answer some more questions and/or attend another assessment visit), but this is optional". At about 1, 3, 6, 9 and 12 months after their baseline visit, participants who complete the diet questionnaire at their assessment visit would be sent an email or SMS text message (with no reminder for non-responders) asking them to complete it again:

"Message from UK Biobank: Please could we invite you to spend 10-15 minutes today completing a web-diet questionnaire to record what you ate and drank yesterday? If you are willing to help, please log on at www.ukbiobank.ac.uk, enter the following number ##########, and follow the instructions. If you have any questions, please call 0800-0-276-276. Thank you."

When this approach has been shown to work, it would be extended to those participants who had attended their baseline visit prior to the introduction of these Category 1 enhancements. Depending upon the response rate to the email/text invitation, the invitation may be extended to participants who did not provide such details by sending a similar message by mail.

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Appendix 1: Membership of the Enhancements Working Group

Professor Paul Elliott; Imperial College, London (Chair)

Professor Mark Caulfield; Queen Mary, University of London
Dr John Gallacher; University of Cardiff
Professor Alan Silman; University of Manchester
Professor Nick Wareham; University of Cambridge
Dr Ioanna Tzoulaki; Imperial College, London
Professor Rory Collins; University of Oxford & UK Biobank
Dr Tim Sprosen; UK Biobank

Appendix 2: Additional questions on the touchscreen questionnaire

Additional questions on depression & bipolar disorder

Qu. No	Question	Responses	Allowable values	Action branches
P6	Looking back over your life, have you ever had a time where you were feeling depressed or down for at least seven days in a row?	Select from - YE Yes - NO No - UN Do not know - DA Prefer not to answer	Not null	If yes go to P6A. Otherwise go to P6C
P6A	How many days was the longest period where you were feeling depressed or down?	Enter number OR UN Do not know OR DA Prefer not to answer	Minimum value of 7 requiredl	Go to P6B
P6B	How many periods have you had where you were feeling depressed or down for at least seven days in a row?	Enter number OR UN Do not know OR DA Prefer not to answer	Minimum value of 1 required	Go to E1
P6C	Have you ever had a time when you were uninterested in things or unable to enjoy the things you used to?	Select from - YE Yes - NO No - UN Do not know - DA Prefer not to answer	Not null	If yes go to P6D. Otherwise go to P7
P6D	How many days was the longest period when you were uninterested in things or unable to enjoy the things you used to?	Enter number OR UN Do not know OR DA Prefer not to answer	Not null	Go to P6E
P6E	How many period have you had when you were uninterested in things or unable to enjoy the things you used to?	Enter number OR UN Do not know OR DA Prefer not to answer	Not null	Go to P7
P7	Have you ever had a period of time lasting at least two days when you were feeling so good, “high”, excited or “hyper” that other people thought you were not your normal self or you were so “hyper” that you got into trouble?	Select from - YE Yes - NO No - UN Do not know - DA Prefer not to answer	Not null	Go to P8
P8	What about a period of time lasting at least two days when you were so irritable that you found yourself shouting at people or starting fights or arguments?	Select from - YE Yes - NO No - UN Do not know - DA Prefer not to answer	Not null	If yes to P7 and/or P8 go to P8A. If no go to E1
P8A	Please try to remember a period when you were in a “high” or “irritable” state and select which of the following apply	Select: - I was more active than usual - I was more talkative than usual - I needed less sleep than usual - I was more creative or had more ideas than usual - All of the above - None of the above	Not null-	Go to P8B

P8B	What is the longest time period that these “high” or “irritable” periods have lasted?	Select from - At lease two days, but less than a week - Less than a week - A week or more - UN Do not know - DA Prefer not to answer	Not null	Go to P8C
P8C	How much of a problem have these ‘high,’ or ‘irritable’ periods caused you?	Select from - No Problems - Needed treatment or caused problems with work, relationships, finances, the law or other aspects of life. - UN Do not know - DA Prefer not to answer	Not null	Go to E1

Questions on self-reported happiness

P31	In general how happy are you?	Select from - Extremely happy - Very happy - Moderately happy - Moderately unhappy - Very unhappy - Extremely unhappy - UN Do not know - DA Prefer not to answer	Not null	Go to P31A
P31A	In general how satisfied are you with the WORK that you do?	Select from - 01 Extremely happy - 02 Very happy - 03 Moderately happy - 04 Moderately unhappy - 05 Very unhappy - 06 Extremely unhappy - 07 I am not employed - UN Do not know - DA Prefer not to answer	Not null	Go to P31B
P31B	In general how satisfied are you with your HEALTH?	Select from - 01 Extremely happy - 02 Very happy - 03 Moderately happy - 04 Moderately unhappy - 05 Very unhappy - 06 Extremely unhappy - UN Do not know - DA Prefer not to answer	Not null	Go to P31C
P31C	In general how satisfied are you with your FAMILY RELATIONSHIPS?	Select from - 01 Extremely happy - 02 Very happy - 03 Moderately happy - 04 Moderately unhappy - 05 Very unhappy - 06 Extremely unhappy - UN Do not know - DA Prefer not to answer	Not null	Go to P31D
P31D	In general how satisfied are you with your FRIENDSHIPS?	Select from - 01 Extremely happy - 02 Very happy - 03 Moderately happy - 04 Moderately unhappy - 05 Very unhappy - 06 Extremely unhappy - UN Do not know - DA Prefer not to answer	Not null	End of section

Question on domestic heating

D5A1	How is your home mainly heated? (You can select more than one answer)	Select from: - 01 Gas Central Heating - 02 Electric Storage Heaters - 03 Oil (Kerosene) central heating - 04 Portable gas or paraffin heaters - 05 Solid fuel central heating - 06 Open fire without central heating - NN None of the above - UN Do not know - DA Prefer not to answer	If 06 do not allow 01, 02, 03, 05. If 01, 02, 03, 04, 05 do not allow 06. NN, UN, DA can only occur by themselves.	End of section

Question on use of private healthcare

Qu. No	Question	Responses	Allowable values	Action branches
H4B	Do you use private healthcare?	- 01 Yes, all of the time - 02 Yes, most of the time - 03 Yes, sometimes - 04 No, never - UN Do not know - DA Prefer not to answer	Not null	Go to H5

Questions on intermittent claudication

Qu. No	Question	Responses	Allowable values	Action branches
SY3	Do you get short of breath walking with people of your own age on level ground?	Select from - YE Yes - NO No - UN Do not know - DA Prefer not to answer	Not null	Go to SY4
SY4	Do you get a pain in either leg on walking?	Select from - YE Yes - NO No - UN Do not know - DA Prefer not to answer	Not null	If yes go to SY4A. If no go to SY5
SY4A	Does this pain ever begin when you are standing still or sitting?	Select from - YE Yes - NO No - UN Do not know - DA Prefer not to answer	Not null	Go to SY4B
SY4B	Do you get this pain in your calf (calves)?	Select from - YE Yes - NO No - UN Do not know - DA Prefer not to answer	Not null	Go to Sy4C
SY4C	Do you get pain when you walk uphill or hurry?	Select from - YE Yes - NO No - UN Do not know - DA Prefer not to answer	Not null	Go to SY4D
SY4D	Do you get pain when you walk at an ordinary pace on the level?	Select from - YE Yes - NO No - UN Do not know - DA Prefer not to answer	Not null	If yes go to SY4E. Otherwise go to SY4F
SY4E	Does the pain ever disappear when you are still walking?	Select from - YE Yes - NO No - UN Do not know - DA Prefer not to answer	Not null	Go to SY4F

SY4F	What you do if you get pain when you are walking?	Select from - 01 Stop - 02 Slow down - 03 Continue at same pace - UN Do not know - DA Prefer not to answer	Not null	Go to SY4G
SY4G	What happened to the pain if you stand still?	Select from - 01 Pain usually continues for more than 10 minutes - 02 Pain usually disappears in less than 10 minutes - UN Do not know - DA Prefer not to answer	Not null	Go to SY4H
SY4H	Have you ever had surgery on the arteries of your legs (other than for varicose veins)?	Select from - YE Yes - NO No - UN Do not know - DA Prefer not to answer	Not null	Go to Sy4I
SY4I	Have you ever had surgery to remove any of the following?	Select from - 01 Toes - 02 Leg below the knee - 03 Leg above the knee - UN Do not know - DA Prefer not to answer	Not null	Go to SY5

Question on sudden death

Y22	Have any of your mother, father, brothers or sisters died suddenly from a non-accidental cause? (Do not include half-, step- or adopted brothers and sisters)	Select from - YE Yes - NO No - UN Do not know - DA Prefer not to answer	Not null	

Additional questions on hearing

H7A	Do you use a hearing aid most of the time?	Select one from - YE Yes - NO No - DA Prefer not to answer	Not null	Go to H7B
H7B	Do you have a cochlear implant?	Select one from - YE Yes - NO No - DA Prefer not to answer	Not null	Go to H11
H11	Do you get or have you had noises (such as ringing or buzzing) in your head or in one or both ears that lasts for more than five minutes at a time?	Select one from - 11 Yes, now most or all of time - 12 Yes, now a lot of the time - 13Yes, now some of the time - 14 Yes, but not now, but have in the past - NO No, never - UN Do not know - DA Prefer not to answer	Not null	If yes go to H11A. Otherwise go to H12
H11A	How much do these noises worry, annoy or upset you when they are at their worst?	Select one from - 11 Severely - 12 Moderately - 13 Slightly - 04 Not at all - UN Do not know - DA Prefer not to answer	Not null	Go to H12

H12	Have you ever worked in a noisy place where you had to shout to be heard?	Select one from - 11 Yes, for more than 5 years - 12 Yes, for around 1-5 years - 13Yes, for less than a year - NO No - UN Do not know - DA Prefer not to answer	Not null	Go to H13
H13	Have you ever listened to music for more than 3 hours per week at a volume which you would need to shout to be heard or, if wearing headphones, someone else would need to shout for you to hear them?	Select one from - 11 Yes, for more than 5 years - 12 Yes, for around 1-5 years - 13 Yes, for less than a year - NO No - UN Do not know - DA Prefer not to answer	Not null	Go to F1

Additional questions to assess cognitive function

12	Display: "In this next test we will show you a number to remember and then hide it. After a short wait, we will ask you to enter the number in reverse using the number pad on the screen. The numbers will grow longer as the test continues. When ready press Next to begin test!" Begin check I am unable to try this	Select: Next I am unable to try this		
14	Display: "In this next test you will have a maximum of two minutes to answer as many questions as possible. Don't spend too long on any one question and you can skip any question if you wish. Select next when you are ready to begin! Begin check I am unable to try this	Select Next I am unable to try this	Go to touchscreen questions below: Go to 15	14
IQ1	Add the following numbers together: 1 2 3 4 5 – is the answer? Show "Abandon" button	Select from: - 13 - 14 - 15 - 16 - 17 - Do not know - Prefer not to answer	Not null	Go to IQ2 unless 2 minutes have elapsed in which case go to step 15 Abandon selected go to step 15

IQ2	Which number is the largest? Show “Abandon” button	Select from: - 642 - 308 - 987 - 714 - 253 - Do not know - Prefer not to answer	Not null	Go to IQ3 unless 2 minutes have elapsed in which case go to step 15 Abandon selected go to step 15
IQ3	Bud is to flower as child is to? Show “Abandon” button	Select from: - Grow - Develop - Improve - Adult - Old - Do not know - Prefer not to answer	Not null	Go to IQ4 unless 2 minutes have elapsed in which case go to step 15 Abandon selected go to step 15
IQ4	11 12 13 14 15 16 17 18 Divide the sixth number to the right of twelve by three. Is the answer? Show “Abandon” button	Select from: - 5 - 6 - 7 - 8 - Do not know - Prefer not to answer	Not null	Go to IQ5 unless 2 minutes have elapsed in which case go to step 15 Abandon selected go to step 15
IQ5	If Truda’s mother’s brother is Tim’s sister’s father, what relation is Truda to Tim? Show “Abandon” button	Select from: - Aunt - Sister - Niece - Cousin - No relation - Do not know - Prefer not to answer	Not null	Go to IQ6 unless 2 minutes have elapsed in which case go to step 15 Abandon selected go to step 15
IQ6	If sixty is more than half of seventy-five, multiply twenty-three by three. If not subtract 15 from eighty-five. Is the answer? Show “Abandon” button	Select from: - 68 - 69 - 70 - 71 - 72 - Do not know - Prefer not to answer	Not null	Go to IQ7 unless 2 minutes have elapsed in which case go to step 15 Abandon selected go to step 15
IQ7	Stop means the same as? Show “Abandon” button	Select from: - Pause - Close - Cease - Break - Rest - Do not know - Prefer not to answer	Not null	Go to IQ8 unless 2 minutes have elapsed in which case go to step 15 Abandon selected go to step 15

IQ8	If David is twenty-one and Owen is nineteen and Daniel is nine years younger than David, what is half their combined age? Show “Abandon” button	Select from: - 25 - 26 - 27 - 28 - 29 - Do not know - Prefer not to answer	Not null	Go to IQ9 unless 2 minutes have elapsed in which case go to step 15 Abandon selected go to step 15
IQ9	Age is to years as height is to? Show “Abandon” button	Select from: - Long - Deep - Top - Metres - Tall - Do not know - Prefer not to answer	Not null	Go to IQ10 unless 2 minutes have elapsed in which case go to step 15 Abandon selected go to step 15
IQ10	150…137…125…114…104… What comes next? Show “Abandon” button	Select from: - 96 - 95 - 94 - 93 - 92 - Do not know - Prefer not to answer	Not null	Go to IQ11 unless 2 minutes have elapsed in which case go to step 15 Abandon selected go to step 15
IQ11	Relaxed means the opposite of? Show “Abandon” button	Select from: - Calm - Anxious - Cool - Worried - Tense - Do not know - Prefer not to answer	Not null	Go to IQ12 unless 2 minutes have elapsed in which case go to step 15 Abandon selected go to step 15
IQ12	100…99…95…86…70… What comes next? Show “Abandon” button	Select from: - 50 - 49 - 48 - 47 - 46 - 45 - Do not know - Prefer not to answer	Not null	Go to IQ13 unless 2 minutes have elapsed in which case go to step 15 Abandon selected go to step 15

Appendix 3: Web-based diet questionnaire