

G0 biological sample collection participant information sheets and consent forms post HT Act

Please note

- These samples were collected after the commencement of the HT Act (1st Sept 2006)
- Other versions of the documentation provided may have been used during sample collection
- The request for donation of specific sample types may have changed throughout the course of the collection timepoint

Table of samples collected for G0 post HT Act and their corresponding consent form and participant information sheet

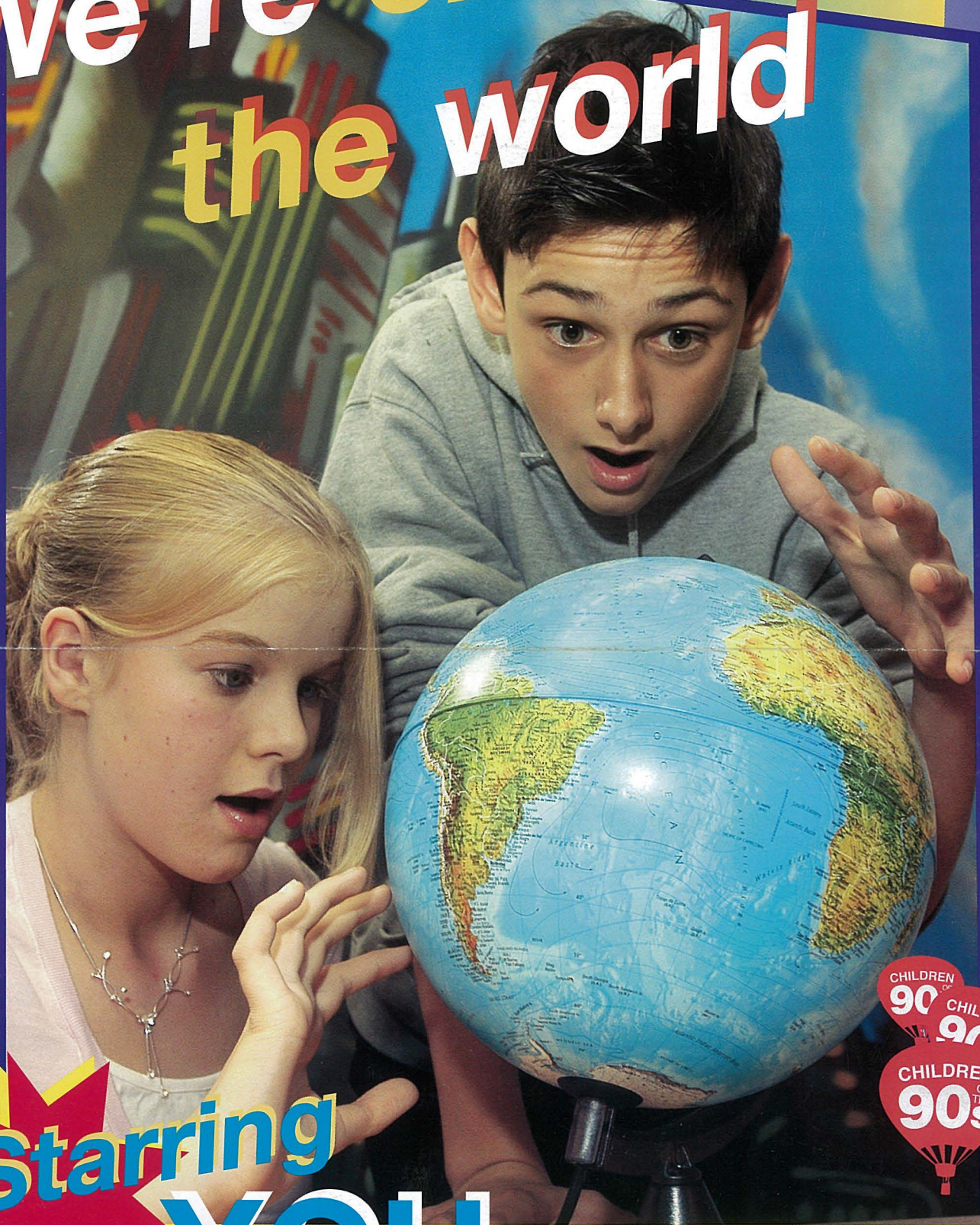
cohort	collection	sample collection dates	sample type	non HTA relevant material	HTA relevant material existing holdings	HTA relevant material post HTAct	copy of PIS provided	copy of consent form provided
G0 mother/father	Carer *	2005-02 to 2008-06	whole blood, blood derivatives, cell line, DNA	Y	Y	Y	1. We're changing the world (pg. 1) 2. DNA, Genes and Cell-Lines (pg. 6)	1. TeenFocus2 Parent Blood Consent (pg. 5) 2. TeenFocus2 Parent Cell line Consent (pg. 8)
G0 mother	Focus on mothers 1	2008-12 to 2011-07	whole blood, blood derivatives, cell line, DNA	Y		Y	1. Focus on Mothers Information Sheet (pg. 9) 2. Focus on Mothers Fasting Blood Additional Information Sheet (pg. 13)	1. Focus on Mothers Combined Consent (pg. 16) 2. Focus on Mothers Blood Consent (pg. 18)
G0 mother	Focus on mothers 2	2011-07 to 2013-06	whole blood, blood derivatives, cell line, DNA	Y		Y	1. FoM2 Participant Information Leaflet (pg. 19) 2. FoM2 Fasting Blood Additional Information Sheet (pg. 27)	1. FoM2 Combined Consent (pg. 31) 2. FoM2 DNA and Cell line consent (pg. 32)
G0 mother	Focus on mothers 3	2013-03 to 2014-03	whole blood, blood derivatives, cell line, DNA	Y		Y	1. FoM3 Participant Information Leaflet (pg. 33)	1. FoM3 Combined Consent (pg. 41) 2. FoM3 DNA and Cell line consent (pg. 42)
G0 mother	Focus on mothers 4	2014-04 to 2015-03	whole blood, blood derivatives, cell line, DNA	Y		Y	1. FoM4 Participant Information Leaflet (pg. 43)	1. FoM4 Combined Consent (pg. 51) 2. FoM4 Cell line consent (pg. 52)
G0 father	Partner	2010-07 to 2012-01	whole blood, blood derivatives, cell line, DNA	Y		Y	1. Partner Enrolment Information Sheet (pg. 53) 2. Parents DNA, Genes and Cell Lines Information Sheet (pg. 57)	1. ALSPAC Enrolment Visit Combined Consent (pg. 56) 2. Enrolment Visit Blood Consent (pg. 59)
G0 father	Focus on fathers	2011-09 to 2013-02	whole blood, blood derivatives, cell line, urine, DNA	Y		Y	1. FoF Participant Information Leaflet (pg. 60) 2. FoF DNA and Cell Line Additional Information Sheet (pg. 69)	1. Focus on Fathers Combined Consent (pg. 68) 2. Focus on Fathers Combined Consent (pg. 71)

NB: Page numbers in table are those labelled as 'G0 participant sample documentation post HT Act page' in document. * The collection includes samples donated pre and post HT Act.

CARERS SAMPLES

Biological samples were collected from a parent/guardian when the G1 participant attended one of the Teen Focus Clinics. If the parent/guardian accompanied the G1 participant at multiple Teen Focus timepoints samples were only collected from the parent/guardian at one timepoint. An example of the information given for the collection of carers samples is provided.

We're changing the world



CHILDREN OF THE 90s
CHILDREN OF THE 90s
CHILDREN OF THE 90s

Starring
YOU

and a cast of thousands....

at **STANBOLUS**

Reception area:
Battle the aliens on our new space invaders machine.

Day in the life

As soon as they arrive, Reuben and Kez can see that Focus is going to be fun



Hmmm.... it's looking good!!!

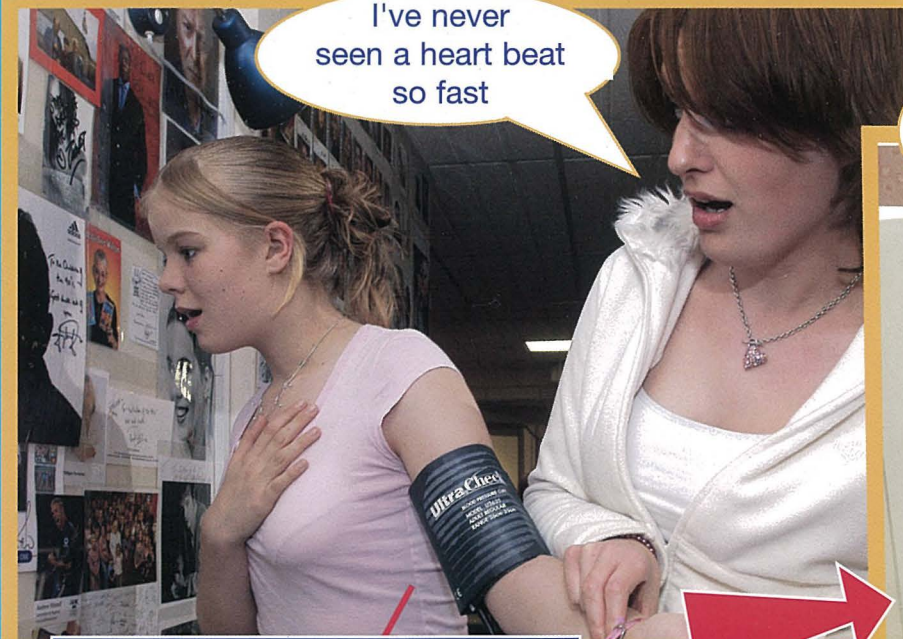
Measuring: You will be able to see how your skeleton. Also, for the first time we will also be looking at h

Kez sees herself in a totally new way



Oh no, they can see right through me!

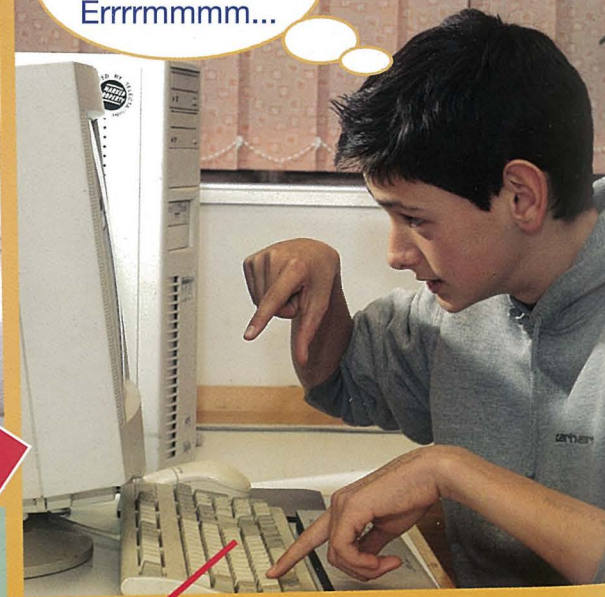
I've never seen a heart beat so fast



but Kez has spotted her heart-throb on the Wall of Fame

It asks, "Are you decisive?" Errrrrrmmmm...

Reuben is determined to beat the computer



Blood pressure:
We'd like to check your blood pressure to see if it is changing as you get older.

Computer sessions:
We will be asking about your life and about your friends on the computer. There are some games to play too.

Diet:
How has what you eat since you were 10+? The you fill in help us to do 13-14 year olds' diets

of TEENFOCUS2

Fitness:
We want to see how fit you are and whether this has changed since you were 9+.

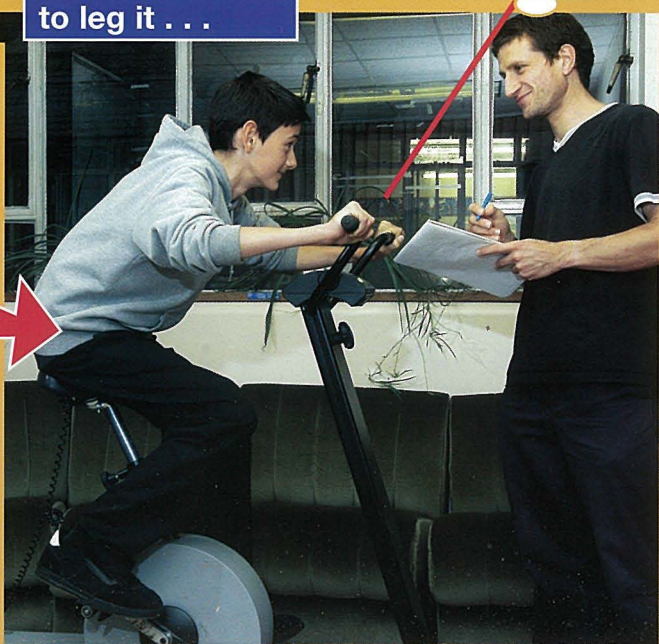
is developing again with our special low dose scanner.
flexible some of your joints are.

Then things get even weirder . . .

Are we going round the bend?

Reuben decides to leg it . . .

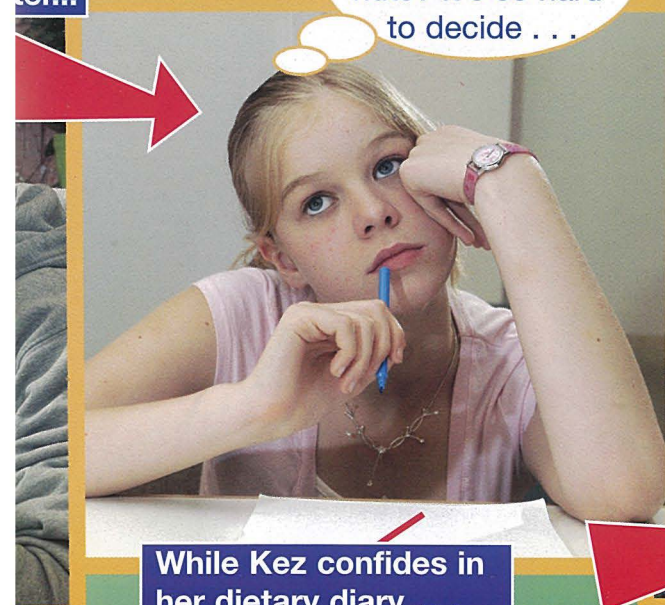
This guy should go in for the Olympics!



ned
ter...

Carrot stick or 6-pack of doughnuts? It's so hard to decide . . .

I've had enough excitement for one day



While Kez confides in her dietary diary . . .



Better not over-do it . . .

. . . and they both test out their activity monitors

Activity monitors:

The monitors that you wore at 11+ are producing excellent information in relation to diet, blood pressure, height, weight and so on. We need to see how these things change as you get older.

NOW! Turn the page

to find out more...

and drink changed dietary diaries over what we like today.



WHAT YOU CAN EXPECT AT...

TeenFocus2



You may feel that lots of things are changing in your life - at school, with your friendships, tastes and attitudes, abilities and interests. We want to monitor those changes and describe, in scientific papers, what it means to be growing towards adulthood in the first decade of the 21st Century.

That's why your visit and the information you give are so important. It's also why some of the

measures and questions are apparently the same as before. The results may be very different this time, because you are older.

You can say no, or stop if there is anything you don't want to do or answer. All the information you give us is stored anonymously. We are sorry that we can't feed back to you all your own results, but we can give you height, weight, and blood pressure measurements.

You're changing the world!

Because of you and all the children of the 90s, people across the globe can look forward to happier and healthier lives. So, as a symbol, we're creating a picture of the world, made up of your faces which will become a poster for the Focus Centre. We'll be sure to have a magnifying glass on hand too so that you can spot your friends.

Measuring

Are you happy for us to measure your height, weight, arm and hip circumferences and the straightness of your back? If so please wear clothes you're happy to be measured in. We'll be doing an additional scan of one hip (see picture). This is something that is usually done when people have a scan of their whole body.



● To contact
TeenFocus2

call: 0117-928 8266

Interview and Computer session

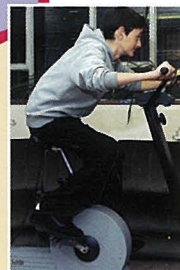
We want to see how things in your life are changing as you get older. We are interested in the moods and feelings that you have and what sort of person you think you are.

Blood pressure and sample

Would you like to give blood and saliva samples this time? We know we ask you frequently but these samples are so valuable. They answer so many questions especially about things like hormones and antibodies to infection which change over time. Like everything at the visit it's entirely voluntary so you can always say no.

Fitness

To test your fitness, we may ask you to do a basketball task instead of cycling, (pictured).



Parents

Don't feel left out! You often tell us that you want to be involved and we plan to ask if you would be willing to give us a blood sample and if time to have your height, weight and blood pressure measured. As always at these visits everything is voluntary and if you can help us with these things it is a bonus. As you can see from the picture here we had a bit of fun 'sizing up' a 6ft 5in study dad!



... and if you have time to spare at TeenFocus2 there's the Exploratory to explore again - you may find some different things there this time!

◆ Log on to your Children of the 90s website for the latest competitions, games and news
www.alspac.bris.ac.uk/discovery



CHILDREN OF THE 90s

CONSENT FOR EMLA (if applicable)

Have you ever had a bad reaction to local anaesthetics? Y/N

Have you recently used or been given a local anaesthetic? Y/N

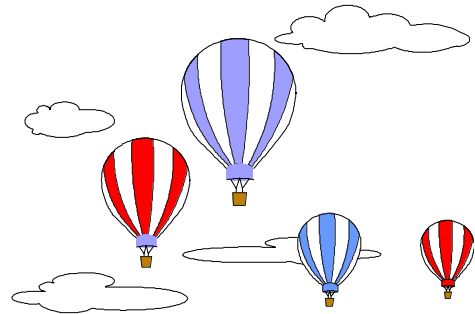
Are you taking any medication containing sulphonamides? Y/N

.....
Are you anaemic? Y/N

Do you suffer from any clotting or bleeding disorders ? Y/N

Signed.....

Date.....



TeenFocus2
24 Tyndall Avenue
Bristol BS8 1TQ
(correspondence only)

Tel: 0117 928 8266 There is an answer phone on this line.
e-mail: focus-admin@bristol.ac.uk

Permission to use blood samples

After the sample below has been taken, you will be informed if it shows that your Haemoglobin is low (below 9g/dl). After that analysis the name will be taken off the blood sample. It will be stored for future analyses. The blood sample will have no name attached to it. Results will be used for statistical purposes only and not linked to named people.

CONSENT

The purposes and possible risks in having blood taken have been explained to me. I understand that donated blood will be considered a gift but I will have the right to withdraw permission for analysis.

I agree to having a sample taken for biochemical analyses by/on behalf of the 'Children of the 90s' study:

Signed:

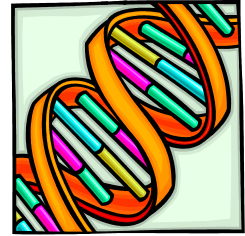
Date:

Name (PLEASE PRINT).....

The University of Bristol holds legal liability insurance in the event that any participant is injured due to any negligence on the part of the University.

DNA, GENES, and CELL-LINES.....

Our genes are important in making us more or less likely to develop many common diseases. We all have a slightly different set of genes in our bodies. DNA from a child's parents (mothers, fathers, partners) can help us in various ways to look at the effects of these differences.



We are therefore asking parents/carers visiting the clinics with their children if they would be prepared to provide a small blood sample which can be treated so that it provides a never-ending supply of cells which can in turn be used to provide DNA and which can also be studied to provide a more detailed description of how some parts of the body work. We would also take the opportunity to save some of the blood so that we could measure other things, like cholesterol.

Question: What are genes?**Answer:** Genes are the instructions which determine growth and development of all living organisms.

Question: What is DNA?

Answer: DNA is the chemical language in which genes are written.

Question: Why do you want to study my DNA?

Answer: Although we all have essentially the same genes as each other, there are many small differences which some of us have and others do not. These different versions of our genes make us more likely or less likely to develop many common diseases, such as allergies (like asthma), or diabetes or heart disease and can affect our character and behaviour.

Question: Is it just genes that cause disease?

Answer: No. We already know that many of our problems are partly caused by genes and partly by our environments.

Question: How will my DNA help?

Answer: Your child's genes are a mixture of your genes and the child's father's genes. By having DNA to study parent's genes we can work out which gene variants are responsible for the way in which your child grows and develops. We will also be able to find out how gene variants have affected parents and compare this with affects on the children.

Question: Why do you need more DNA?

Answer: We each have about 30,000 genes. With your permission, we want to study many of these genes in parents. The DNA we have extracted from blood samples taken during mothers' pregnancies will run out before we can complete this work. This time we would like to collect a blood sample and treat the cells from the sample so that they can be stored indefinitely as 'immortalised' cell-lines. These cells can be used to make more DNA whenever it is needed.

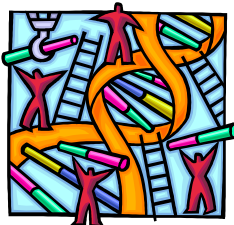
Question: What are *immortalised* cell lines?

Answer: Cells are the building blocks of the body. Skin, muscle, bones, blood, and all the other parts of our body, are made up of millions of cells. Each cell has a copy of all our genes. If we take cells from our bodies we can only keep them alive for a limited time. However if cells are treated with a virus they can be kept alive indefinitely - they become *immortalised*.



Question: Do *immortalised* cell-lines have other uses?

Answer: Yes, our study is unique in its detailed descriptions of its participants gathered over many years (as you have probably realised!). One of the ways in which we may be able to add further important information is by studying *immortalised* cell lines. Cells from cell-lines retain some of the basic features, as well as the DNA, of the people from whom they were derived. For example, cell-lines from people with raised blood pressure grow faster than those from people with normal blood pressure. Studying cells in this way may provide important stepping-stones that will help bridge the gap between genes and people and improve our understanding of how the two are linked.



Question: Will anyone be able to connect the results of tests to me

Answer: No. All the information in the 'Children of the 90s' study is kept separate from your name. No-one who works with samples or answers to questionnaires is allowed to know who they came from. This means that the study is completely confidential.

Question: Would you ever sell my DNA or cell-lines?

Answer: No, we would never sell these, or any of the information you have given us.

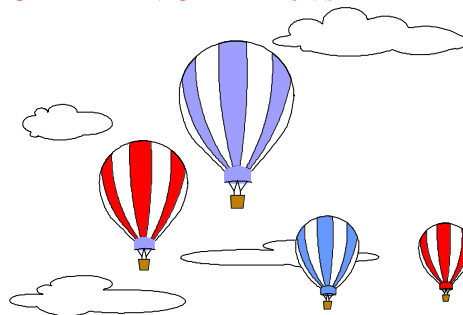
Question: If the 'Children of the 90s' study makes cell-lines from my blood, can I be sure they will not be used for cloning?

Answer: Yes, you can be sure. The use of human tissues, including cell-lines, is strictly controlled. Charities and government organisations which give money for research, Bristol University, and the Children of the 90s study ethics committee, which includes parents of study children, would not allow human cloning.

Question: If I change my mind later and don't want you to keep my DNA or cells, what should I do?

Answer: You can change your mind at any time. Write to us and say you don't want us to keep your DNA or cells. We will remove them and destroy them.

If you would like to know more about the problems we may be able to solve by having parents' DNA, there is a more detailed document available. For more information, Please phone 0117 928 8900, or ask the clinic staff. They will be able to help you, or put you in touch with someone who can.



Focus on Mothers

Oakfield House, Oakfield Grove
Clifton Bristol BS8 2BW
(correspondence only)
Tel: 0117 928 8900 (answer phone)
e-mail: focus-admin@bristol.ac.uk

Focus on Mothers

We are inviting you to the first FOCUS ON MOTHERS visit. This leaflet explains the measurements that will be undertaken at the visit, why these measurements are being done and what they will involve. Please take time to read the following information, which will help you decide whether or not you wish to complete any of them. Please ask us if there is anything that is not clear.

What is the purpose of the study?

The purpose of undertaking this study is to determine what factors are related to body size, bone density, blood pressure, arterial thickness (an indicator of hardening of the arteries “atherosclerosis”), diabetes and abnormal blood lipids (cholesterol) in women in early adult life. It is important to take these measures now before many of you will have changes related to the aging process and before large proportions of you might be taking medications that affect these measures (e.g. blood pressure tablets are taken by about one-third of people over 65 but very few people in their 40s and early 50s). If we take these measures now we will be able to examine the factors that affect natural (not altered by treatment) differences between women in these health related measurements. We hope that this work will provide important information on how we might prevent age related decline in health in the future. From your earlier participation in the study we already have a lot of information on your health and lifestyle. We would like to combine this information with the measurements that we will take at the Focus on Mothers visit in order to answer important questions about obesity, diabetes, heart disease and bone thinning in women.

What measurements are planned?

We would like to ask you to undertake all of the following:

- **DXA scan to measure your lean (muscle) and fat mass and bone density.**
- **Weight, height (standing and seated), waist, hip and arm size.**
- **Ultrasound scan of your neck arteries.**
- **Blood pressure and pulse pressure.**
- **Take a fasting blood sample.**

In addition to completing these measurements in women aged 48 and older we will also ask for:

- **Consent from you to get a copy of your first mammogram (breast scan) from the NHS breast cancer screening programme when you have this done (some time after your 50th birthday)**

You will be familiar with many of these measurements because they are ones that we have undertaken on your children at previous focus visits. The ultrasound scan of neck arteries is a new focus measurement, though this has been done on a sub-sample of your children who attended *Teen Focus 3* as part of the GRACE study. Some, e.g. blood pressure and DXA scan, we have already measured on some of you when you accompanied your children to the Focus visits. **Even if you have had one of these measurements recently at a focus visit we would like to take a further measurement at the Focus on Mothers visit.**

Where can I find out more about each of these measurements?

We have written more detailed information sheets that explain in more detail the reasons and methods for each of the DXA scan, ultrasound scan of your neck arteries, taking of a fasting blood sample and consent for obtaining a copy of your first NHS mammogram (for women aged 48 and older). These are available on the 'Children of the 90s' website (www.alspac.bris.ac.uk) or we can mail or email a copy to you – contact details for requesting these are at the bottom of this sheet.

Do I have to take part?

Not at all. It is up to you to decide whether or not to take part. If you decide to do so you will be asked to sign a consent form. You are still free to withdraw from the study or any of the individual measures at any time.

What will happen if I take part – are there any advantages?

Some of the measurements that we take in the visit might indicate increased risk for some health problems. In those situations where you have provided consent and a test result indicates a possible health risk we would like to tell you about this and give you a letter to take to your GP. Other measurements that we will take are very useful for research but currently they cannot tell us about any health problems. We would not tell you about the results of these tests since their meaning is not clear and there are no recommended actions or treatments. At the start of the visit we will go through all of the measurements with you and answer any questions that you might have. We will then ask you to complete and sign a consent form. This will also ask you about whether or not you want us to feedback certain results to you. If you indicate you do not want this feedback we will not provide it. It is very important to be aware that the visit is run for research purposes and should not be considered to be a 'health screen' or to replace any aspect of your usual health care. If we do inform you that one of the measurements suggests increased risk you should not be alarmed. Your GP will need to talk to you and examine you further and after this might conclude that you are not at increased risk. Similarly, if we do not feedback any results to you, you should not conclude that this means you have a clean bill of health. If you have any symptoms that cause you concern you should contact your GP in the way that you normally would.

The following describes the test results were we plan to provide feedback:

If we note that your blood pressure is high we will tell you and give you a letter to take to your GP so that they can test this again. A single high measure does not mean that you have hypertension or that you need to worry, but it does need to be checked again by your doctor.

If we note that your bone density is low we will tell you and give you a letter to take to your GP so that they can discuss this with you and do further tests if necessary. A single low bone density measure does not mean that you have osteoporosis, but it would be useful to talk to your GP if we note that your measure is low and they may wish to complete further tests.

If we note that you may be at risk of anaemia, have high blood sugar (an indicator of diabetes), high levels of total cholesterol, low density lipoprotein cholesterol or triglyceride levels (all 'bad' cholesterols) or low levels of high density lipoprotein cholesterol ('good' cholesterol) we will send you a letter, with a letter enclosed within it, to take to your GP. The measurement related to anaemia is easy to perform and we will do this in our laboratory and therefore would be able to send a letter (if the measure is low) within a maximum of 4 weeks of your focus visit. For blood sugars and cholesterol the samples are initially stored in deep freezers and then sent in batches for testing to a laboratory in Glasgow that specialises in these measurements when completed in large studies. For these measurements it could be up to 12 months before the results are fed-back to you. However, because people often have no way of knowing that they have high blood sugar or cholesterol problems (there are usually no symptoms), it can be valuable to have this information even after this time.

Are there any disadvantages to taking part?

Other than sparing us your time, we do not see any major disadvantages in taking part. We do need you to come to the visit 'fasted' for the blood sample. This means having nothing but water to eat or drink since the previous night for those of you with morning appointments and for the previous 8 hours for those of you coming to afternoon or evening visits. Once the fasting sample has been taken we will provide you with food and drink before doing any further measurements. Some people are left with bruising after a blood sample has been taken and in a small proportion of people this can be quite marked. All of our staff are fully trained and any difficulties with blood taking will be kept to a minimum. If you do not want to have a blood sample taken then this is OK. We would still very much value your participation in the other measurements. Ultrasound scans do not emit x-rays or gamma-rays and are completely safe. DXA scans emit a very small dose of x-rays but this is smaller than the amount we are all exposed to from our surrounding environment every day. DXA scans are safe. The visit will take approximately 2 hours.

What do I have to do now?

Please complete and return both sides of the 'Your Details and Your Availability' form in the stamped and addressed envelope

Confidentiality and data protection

Any data collected will be stored with individual ID numbers but with no personal data attached. Files that link this ID number to your personal details will be securely stored with only two senior ALSPAC (Children of the 90s) staff having access to these. The data will be used for research purposes only and will be analysed by ALSPAC study researchers and ALSPAC research collaborators. None of these researchers will have access to your personal data.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask the staff when you attend who will do their best to answer your questions. You can also contact Professor Debbie Lawlor, Research Director, about any problems of participating in the study, or the Executive group.

Who is organising and funding the research?

This research is organised by the ALSPAC study team. The Research Director for the mother's study in ALSPAC is Professor Debbie Lawlor. The Mother's study has been funded by the British Heart Foundation. In addition, ALSPAC has core funding from the University of Bristol, the UK Medical Research Council and the Wellcome Trust.

Who has reviewed this study?

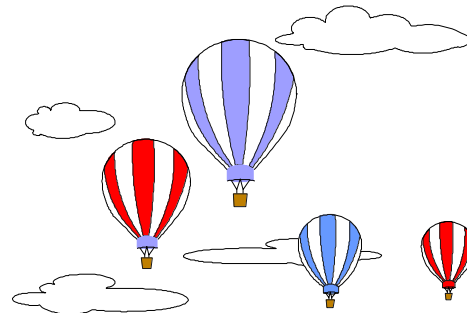
The ALSPAC Ethics & Law committee (which includes parent members) & the North Somerset & South Bristol Research Ethics Committee. Scientifically the study proposal was reviewed by anonymous reviewers and grant board members for the British Heart Foundation.

Contact for further information

Please contact **0117 9288900** to speak to the Focus team if you require more information. There is an answer phone on this line. If you wish to discuss the study further please contact Professor Debbie Lawlor **0117 9287267** (email: d.a.lawlor@bristol.ac.uk) or a member of the ALSPAC executive group **0117 331 1711** (email: alspac-exec@bris.ac.uk)

Thank you for your time in reading about our proposed Focus on Mothers visit and for your ongoing support of Children of the 90s.

CHILDREN OF THE 90s



Focus on Mothers

Oakfield house, Oakfield Grove
Clifton, Bristol BS8 2BW
(correspondence only)

Tel: 0117 928 8900 There is an
answerphone on this line.

e-mail: focus-admin@bristol.ac.uk

DETAILS ABOUT FASTING BLOOD SAMPLES AT FOCUS ON MOTHERS

This leaflet provides additional details on the fasting blood samples that will be undertaken at the Focus on Mothers visit. It is available on request from focus staff and should be used as an addition to the participant information leaflet that was mailed to you. The information leaflet that we mailed to you provides key information about the study that we would like all participating mothers to read.

FASTING BLOOD SAMPLES

We want to take a fasting blood sample from you and measure haemoglobin (a marker of anaemia), fasting blood glucose (sugar), insulin (the hormone that controls blood glucose levels in the body) and lipids (forms of cholesterol). The reasons that we want to do these tests is that they are related to risk of diabetes and heart disease and, also, because changes that occur during pregnancy (for example how much weight a woman puts on in a particular pregnancy or what time of pregnancy most weight is gained) can affect levels of these chemicals in the blood later in life. Measuring these will help us with important research questions about what causes diabetes and heart disease in women.

If you agree to provide a fasting blood sample this will mean that you have to come to the focus visit without having had anything to eat or drink (except water) since the night before if you come to a morning visit (before 2pm) or for the previous 8 hours if you come to an appointment in the afternoon or early evening (any appointment after 2pm). Once we have taken the fasting sample we will provide you with food and drinks before doing any other measurements.

Many of you will have had blood tests before – for example when you were pregnant. At the focus visit we will ask you to lie down on a couch whilst we take the sample. We realise that samples are often taken in the sitting position in general practice visits and hospital clinics. However, because you will have been fasting we will only take samples with participants lying on a couch at the focus visit.

Once you are lying on the couch in a comfortable position the focus tester will apply a tourniquet to your upper arm to make the veins in the space on your inner arm where the forearm meets the upper

arm more visible. The tester may gently tap on the area where blood will be taken to make the veins stand out. Once the tester is confident they have located a vein they will tell you that they are going to insert the needle to take blood. Once they have completed taking the sample the focus tester will release the tourniquet, remove the needle and apply pressure with a piece of cotton wool over the area where blood has been taken.

All of the staff are fully trained to take blood samples. Nonetheless sometimes it is difficult to take a blood sample from an individual. Sometimes the focus tester will feel that it is better to take a sample from the back of your hand rather than your arm. Sometimes an initial attempt to collect blood will fail and the tester will ask you if they can try again. These are rare events and we would never allow more than 3 attempts at getting blood. If you felt uncomfortable at any time during the procedure or you wanted the test to stop for any other reason we will stop it immediately.

Is taking a blood sample safe?

It is likely that most of you will have had a blood sample taken before and will therefore know that it can be a little uncomfortable and can result in bruising. Our trained staff will minimise the likelihood of marked bruising. Some individuals faint when they are having a blood test. This can occur 'out of the blue' in people who have had previous tests with no problems. For this reason we only take blood samples at the focus visit with you lying on a couch. If you do faint this should prevent any serious injury. In the rare event that you do faint we will make sure that you are fully recovered before we discuss any further measurements.

Will you let me know my blood test results?

As with the other measurements we will first ask you for consent to let you know the results of test that are clinically meaningful. With your consent we will let you know if you have a low haemoglobin level (indicator of anaemia) or a very high haemoglobin level (which can mean that your blood flows too slowly) and also if you have high fasting blood glucose (indicator of diabetes), high levels of total cholesterol, low density lipoprotein cholesterol or triglyceride levels (all 'bad' cholesterol) or low levels of high density lipoprotein cholesterol ('good' cholesterol).

We will let you know about these results via a letter after the focus visit. The letter will also include a letter for you to take to your GP.

We will know the results of the haemoglobin test within 1-2 week of you coming to the focus visit and would send a letter to you if your level is low or very high so that it reached you at the latest within 4 weeks of your visit. The result will not necessarily mean you are anaemic but you should talk to your GP. They might want to repeat the test, examine you and do some additional tests. Depending upon the results of these they might suggest you take an iron supplement or discuss other treatments.

The results of the glucose and cholesterol tests will not be available for some months after you come to the focus visit. These tests are done by one of our collaborators in Glasgow and we will send batches of samples to Glasgow at approximately 6 month intervals. This will mean that it will be possible to let you know if you have high (or low, as relevant) levels for any of these tests at between 3-18 months since the time you attended the focus visit. Because diabetes and cholesterol problems do not have symptoms and therefore you would not know if you had a problem, it can be important to let you know any results that are outside the normal range even if it is several months since we took the sample. If you give us consent to do so we will send you a letter and a letter to take to your GP if the results suggest you have high glucose or cholesterol problems. The results would not mean that you definitely had diabetes or were at increased risk of heart disease. Your GP would most likely want to repeat the test. They would also talk to you about other risk factors and most likely examine you (e.g. test your blood pressure and look at the back of your eyes) and possibly ask for some

additional blood tests. Depending on the results of these they might reassure you that there are no problems or they might ask you to make changes to your lifestyle or they might talk to you about treatments.

Will you be doing anything else with my blood sample?

Yes. With your permission we would like to store some of your blood sample so that we can use it for future research that arises. One of the important strengths of the *Children of the 90s* study (ALSPAC) is that it is able to respond very quickly to important research questions about health and well-being as they arise. Storing some of your blood sample will help us to be able to do this. For example, disease research often begins in animal and 'test-tube' research. If this research were to suggest that different levels of a chemical that circulates in human blood might predict risk of diabetes or heart disease or cancer in humans, we would be able to use stored blood samples to measure this chemical and test this new research hypothesis. We have stored blood (both fasting and non-fasting) in a similar way from samples taken from your children at the focus visit (when you have given us consent). The samples are stored with unique IDs that allow us to link any test results to other data but that would never allow someone working in a laboratory to be able to link these results to your personal data.

We only need to do one blood test to obtain extra blood for storage so allowing us to do this will not mean that you have to have 2 separate blood tests.

Will you be taking more blood for genes and DNA?

Many of you will be aware that over the last 3 years we have been collecting extra blood samples for DNA and immortalised cell-lines for those ALSPAC mothers on whom we do not already have these samples. We now have these samples on the majority of you. However, we will use the opportunity of this focus on mothers visit to ask any of you for whom we do not have such a sample whether you would be willing for us to take some additional blood and use it for extraction of DNA or establishing immortalised cell-lines. This will not require us to do a separate blood test; we will simply take a little bit more blood when we do the fasting blood test. A separate information sheet that describes the importance of having DNA and immortalised-cell lines and how we use these in ALSPAC is enclosed (this is the same as a leaflet many of you will have already seen).

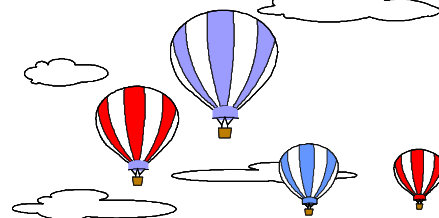
Contact for further information

Please contact **0117 9288900** to speak to the Focus team if you require more information. There is an answer phone on this line. If you wish to discuss the study further please contact Professor Debbie Lawlor **0117 9287267** (email: d.a.lawlor@bristol.ac.uk) or a member of the ALSPAC executive group **0117 331 1711** (email: alspac-exec@bris.ac.uk)

Thank you for your time in reading about our proposed Focus on Mothers visit and for your ongoing support of Children of the 90s.

Visit No.

CHILDREN OF THE 90s



FOCUS ON MOTHERS

Oakfield house, Oakfield Grove
Clifton, Bristol BS8 2BW
(correspondence only)

Tel: 0117 928 8266 There is an answer phone on this line.
e-mail: focus-admin@bristol.ac.uk

Permission to complete and use clinic data

We would like to ask you to undertake all of the following measurements/procedures:

Please cross the boxes and initial to indicate that you consent, or leave blank if you do not consent. Also cross and initial to indicate whether you would like us to inform you, and give you a letter to give to your GP, if the results of tests marked * give cause for concern.

- (a) DXA scan of bone density*, fat and muscle mass
- (b) Weight, height, waist, hip and arm circumference
- (c) Blood pressure* and pulse pressure
- (d) Ultrasound scan of arteries in your neck (Carotid artery intima media thickness)

	1. Consent to test		2. Consent to inform	
	Cross box	Initial	Cross box	Initial
(a)	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
(b)	<input type="checkbox"/>	<input type="text"/>		
(c)	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
(d)	<input type="checkbox"/>	<input type="text"/>		

I understand that donated blood will be considered a gift but I will have the right to withdraw permission for analysis.

Fasting blood sample for:

- (e) Haemoglobin (test for anaemia)*
- (f) Glucose (sugar)*
- (g) Lipids (forms of cholesterol)*
- (h) Storage for other tests relevant to health

(e)	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
(f)	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
(g)	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
(h)	<input type="checkbox"/>	<input type="text"/>		

Signature

Date signed

<input type="text"/>	<input type="text"/>	/	<input type="text"/>	<input type="text"/>	/	2	0	<input type="text"/>	<input type="text"/>
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Initial

Last Name

<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
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PLEASE TURN OVER

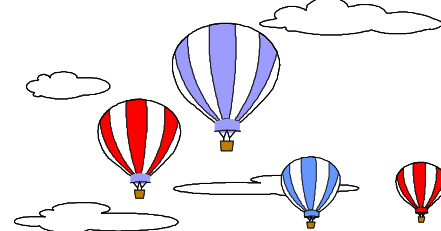
The University of Bristol holds legal liability insurance in the event that any participant is injured due to any negligence on the part of the University.

Draft



Permission to obtain a copy of your first mammogram (breast scan)

CHILDREN OF THE 90s



FOCUS ON MOTHERS

Oakfield house, Oakfield Grove
Clifton, Bristol BS8 2BW
(correspondence only)

Tel: 0117 928 8266 There is an answer phone on this line.
e-mail: focus-admin@bristol.ac.uk

If you are aged 48 years or older, we would like permission to take a copy of your first mammogram taken as part of the NHS breast screening programme. If you are older than 50 you may already have had a screening mammogram and we would use this permission to obtain a copy of your first mammogram now. If you are younger than 50 you will be invited for a mammogram in the future and we would like to obtain permission to obtain a copy of your first mammogram in the future.

We consider that this consent form will be valid for 2-3 years only (the invitation for your first mammogram will be sent within 12 months of your 50th birthday). Therefore if you are under 48 years of age we will not ask you to sign this consent form now, but may contact you some time in the future for this permission.

(i) Have you already had at least one mammogram? Yes No

(j) If yes, what year was your first mammogram completed?

(k) If no, have you received an invitation for your screening mammogram? Yes No

(l) If you have received an invitation, could you tell us approximately when your appointment is? / /

Please cross the box and initial to indicate that you consent, or leave blank if you do not consent.

Consent to test

Cross box Initial

(m) I give permission for ALSPAC researchers to obtain a copy of my first mammogram

Signature

Date signed / / 2 0

Initial Last Name

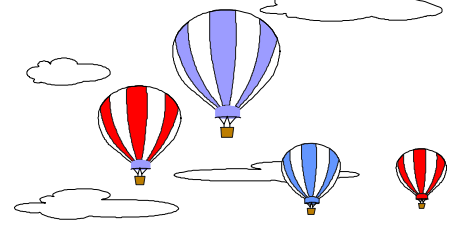
Draft

The University of Bristol holds legal liability insurance in the event that any participant is injured due to any negligence on the part of the University.



Visit No.

CHILDREN OF THE 90s



FOCUS ON MOTHERS

Oakfield house, Oakfield Grove
Clifton, Bristol BS8 2BW
(correspondence only)

Tel: 0117 928 8266 There is an answer phone on this line.
e-mail: focus-admin@bristol.ac.uk

Permission to use blood sample for cell lines

After processing the name will be taken off the blood samples. The cell lines and DNA samples will be stored with no names attached to them. Results will be used for statistical purposes only and not linked to named people.

CONSENT

The purposes and possible risks in having blood taken have been explained to me. I understand that donated blood will be considered a gift but I will have the right to withdraw permission for analysis.

I understand that the main stocks of DNA and/or cell lines will be stored in Bristol, but that the DNA/cell lines (with an anonymous number only), or information about the sequence of my DNA, may be sent to specialist research laboratories in the UK and abroad for analyses, and the results returned to Children of the 90s. Researchers at these laboratories have no access to personal information about study participants.

I agree that information about my genes can be analysed together with information about my health, disease and life style factors in order to undertake research into biological or genetic factors affecting the risk of developing a range of common medical conditions. I understand that any such analyses will only be undertaken on data from which all personal information has been removed and replaced with an anonymous code.

I agree to having the following blood samples taken for analyses for the 'Children of the 90s' study: (If you consent, please cross **one** of the boxes below)

A sample for cell lines ('immortalised' DNA) 1

OR

A sample for DNA only 2

Signature

Date signed

		/			/	2	0		
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Initial

Last Name

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The University of Bristol holds legal liability insurance in the event that any participant is injured due to any negligence on the part of the University.

Draft





Focus on Mothers 2 Participant Information Leaflet

We are inviting you to the second **FOCUS ON MOTHERS** visit.

Participation in the visit is completely voluntary and if you do decide not to participate this will not affect future invitations to you or your child to participate in Children of the 90s research. The visit is for research purposes and consent to take part will be obtained.

Many of the measurements at this second visit will be similar to those that were undertaken at the first focus on mothers visit. The visit will take approximately 2 hours.

This leaflet explains the measurements that will be undertaken at the visit, why these measurements are being done and what they will involve. Please take time to read the following information, which will help you decide whether or not you wish to complete any of them.

Please ask us if there is anything that is not clear.



**Avon Longitudinal Study
of Parents and Children**

**Oakfield House
Oakfield Grove, Bristol
BS8 2BN, UK**

T +44 (0)117 331 0010

E info@childrenofthe90s.ac.uk

W childrenofthe90s.ac.uk

What is the purpose of the study?

The purpose of this study is to understand how measurements such as bone density, body size and blood pressure change as women go through mid-life. We want to understand whether changes in these characteristics are caused by changes in hormones, changes in lifestyle, genetic factors or a mixture of these.

What measurements are planned?

We would like to ask you to undertake all of the following:-

a) Informed consent: At the start of the visit we will go through all of the measurements answering any questions you may have. We will ask you to complete and sign a consent form.

b) Fasting blood sample: We will collect blood in the usual way. We will test your blood for haemoglobin (a measure of anaemia), fasting cholesterol, glucose (sugar), insulin (the hormone that controls glucose) and hormones related to reproduction and going through the menopause (oestrogen, follicular stimulating hormone, luteinizing hormone, anti-müllerian hormone and sex hormone binding globulin). All staff are fully trained to take blood. At any time during the sample taking you can ask for the procedure to stop.

Will you be doing anything else with my blood sample? Yes. With your consent we would like to store some of your blood sample so we can use it for answering future research questions that arise. The samples are stored with unique ID numbers allowing test results to be linked to other data, but that would never allow someone working in a laboratory to be able to link these results to your personal information such as your name, age or date of birth.

Will you be taking blood for DNA and genetics? Yes, with your consent we would like to take a sample that we can use to extract DNA. Many of you have already provided us with a sample that we have used to extract DNA and that we have used for genetic research. The genetic research that we have done has contributed to understanding how genes and non-genetic risk factors work together to affect how healthy someone is. We would now like to conduct research into understanding how these relationships happen.

Although genes do not change over life there is evidence that how they work does. Processes called epigenetics involve molecules (such as a methyl molecule) being attached to part of an individual's DNA and these molecules affect how the gene works. Factors such as smoking, diet and exercise might influence how many of these molecules are attached to someone's DNA and

which genes they are attached to at different times in a person's life. We would like to do further research in this area and in particular would like to see how patterns of methylation of DNA change during mid-life in women. Thus, we would like a new sample of your DNA so that we can compare methylation patterns in it to those that were on your earlier DNA sample.

c) Weight, height (standing and seated), waist, arm and hip size.

d) DEXA scan to measure your lean (muscle) and fat mass and bone density: We would like to scan your whole body to measure muscle mass, fat mass and bone density. We use a machine called a Lunar Prodigy narrow fan beam DEXA scanner.

Your clothes must not have any metal fastenings; watches, piercings and other metal objects should be removed if possible, since these can interfere with the result. You will be asked to lie on a couch and remain very still for 6 to 10 minutes. The machine's arm will pass over you twice; first to scan the whole skeleton, second to scan your hip in more detail. The second scan is similar to the first, except that your foot is positioned against a rest to rotate the hip to a 45-degree angle.

DEXA scans measure how much calcium and other minerals are in the bone being looked at. The result is called the 'bone mineral density' (BMD). Denser bones have more calcium and minerals. They are stronger and less likely to break. We will measure your total body and hip BMD. If you have a low hip BMD (which might indicate risk of osteoporosis) and you have consented to be informed about this, we will give you an information sheet and a letter to take to your GP.

e) pQCT scan of the arm and wrist: A Peripheral Quantitative Computerised Tomography (pQCT) scan looks at the strength and quality of bones. We scan the lower arm and wrist with the pQCT and it gives us a cross-section showing the internal structure. The pQCT scan tells us about the internal structure of bones and the way it varies between people. This internal structure may be important in predicting who is at risk of breaking bones and of osteoporosis in later life. Part of our research will be to look at whether pQCT scans pick up early changes in bones that identify women at future risk of osteoporosis more accurately than does DEXA scan.

Are the DEXA and pQCT scans safe? Yes. These scans use x-rays but the level of radiation is tiny, e.g. the x-ray dose of 5 micro Sieverts is less than the average daily natural radiation dose we get from the environment around us and does not carry any measurable risk at all.

f) Blood pressure and pulse.

g) Physical capability:

i) **Hand-grip strength** will be assessed using a digital spring dynamometer. This tests muscle strength. The picture shows one of these machines. You will be asked to grip the machine (as shown in the picture), and pull the two parts as tightly together as possible. We will ask you to repeat the test 4 (2 with your right hand and 2 with your left hand) times and will record all four measurements.



ii) The **Chair rise test**, examines strength in your legs and your motor fitness. You will be asked to stand up from sitting on a chair, without using your hands and with your feet remaining in a similar place on the floor in front of the chair. After a practice, we will time how long it takes you to complete 10 chair rises.

iii) The **static balance test** involves asking you to stand on one leg, with your hands at your side and your eyes facing forward, and stay like this for as long as you can. We will time how long you can balance on one leg, up to a maximum of 30 seconds (after 30 seconds if you are still holding the balance we will ask you to stop). The test will be done with your eyes open and then you will be asked to repeat it with your closed. For this test it is important that you **wear flat comfortable shoes, such as trainers**. Please come to the test in a pair of shoes that are flat and comfortable or bring a pair of pumps or trainers with you for doing this test.

iv) **Timed three metre walk** involves asking you to walk (but not run) as fast as you can from one line to a second one that is 3 metres away. We will time how long this walk takes you. For this test it is important that you **wear flat comfortable shoes, such as trainers**. Please come to the test in a pair of shoes that are flat and comfortable or bring a pair of pumps or trainers with you for doing this test.

h) Assessments of thought processes: We would like to do separate tests of your memory, how you process new information and how your brain uses that information:-

i) Verbal episodic memory – you will be asked to listen to a brief story (played from a tape). You will then be asked to repeat key facts from the story immediately and again 10 minutes later. A score is allocated for the number of key facts that are correctly remembered from the paragraph at each time point.

ii) Working memory – our staff will read out 5 numbers to you and ask you to repeat them backwards; if you do this accurately the test is repeated with 6 numbers and so on. The result is the highest number of numbers you can correctly repeat backwards.

iii) Speed of information processing – you will be shown several numbers paired with geometric symbols (e.g. 5 = a square). You will then be given 90 seconds to pair specific numbers to their geometric symbols. The number correctly assigned in the given time is the score allocated.

iv) Executive function – you will be asked to list as many words beginning with certain letters that you can think of. The number of words (without repeats) is the test score.

v) Word recognition – you will be provided with a list of pairs of words. One will be a real word, the other will be a made-up word. You will be asked to indicate which is the made-up word for each pair.

Do I have to take part?

Not at all. It is up to you to decide whether or not to take part. If you decide to take part, you are still free to withdraw from the study or any of the individual measures at any time.

What will happen if I take part – are there any advantages?

The Focus visit is not a health check and we are asking you to help us with research that we hope will help people in the future. Some of the measurements that we take might indicate increased risk for some health problems (see below). Where you have given us written consent for us to feedback any results for these tests, we will advise you about your result and give you a letter to take to your GP. Other measurements taken are useful for research but their results have no clear medical meaning at the moment. Therefore we will not tell you about those results.

If we do not feedback any results to you, you should not conclude this means you have a clean bill of health. If you have any symptoms that cause you concern you should contact your GP in the way that you normally would.

The following describes the test results where we plan to provide feedback (if you have given us consent to do so):-

- If your **blood pressure** is high we will tell you at the clinic and give you a letter to take to your GP so that they can test this again, discuss this with you, and do further tests if necessary.
- If your **hip bone density** is low we will tell you at the clinic and give you a letter to take to your GP so that they can discuss this with you and do further tests if necessary.
- If you have low haemoglobin (risk of **anaemia**) or very high haemoglobin (this can mean your blood flows too slowly), have high **blood sugar** (an indicator of diabetes) or high levels of total cholesterol you will be sent a letter along with a letter for you to take to your GP.

The assays for anaemia will be done in our laboratory and a result will be available within 4 weeks (maximum) of your visit. If you have values outside the normal range and have given consent for feedback, you will receive a letter at the latest 4 weeks after your visit for this test. For cholesterol and blood sugar the samples are sent away in batches for testing. Therefore, it could be up to 12 months before the results are fed-back to anyone with levels outside of the normal range. If your levels are outside the normal range for these and you have given written consent, we will send you a letter about this between 4 to 12 months following your visit.

Are there any disadvantages to taking part?

Other than sparing us your time, we do not see any major disadvantages in taking part. We do need you to come to the visit 'fasted' for the blood sample, i.e. having nothing to eat or drink (except water) since the previous night for morning appointments and for the previous 8 hours for afternoon or evening visits. Once the fasting sample has been taken we will provide you with food and drink before doing any further measurements. Some people are left with bruising after a blood sample has been taken and in a small number this can be quite marked.

DEXA and pQCT scans emit a very small dose of x-rays but this is smaller than the amount we are all exposed to from our surrounding environment every day. Both scans, and all of the other tests we will undertake with your consent, are safe. The visit will take approximately 2 hours and we will cover travel expenses and also provide you with a £10 shopping-gift token to compensate you for your time spent at the clinic.

Where does the visit take place?

The visit will be at the same place as the first visit – Oakfield House in Clifton, Bristol. We really do appreciate you giving up your time to come to this visit. If you are unable to come to Oakfield House, but would like to take part in the research, we will be offering home visits towards the end of the study. We will be able to do all of the measurements and tests at your home except the bone scans – it is not possible to carry the machines needed to do these outside of the clinic.

If I attend this Focus assessment am I committed to future Focus on Mother assessments?

Not at all. The recent Wellcome Trust grant that is funding this study provides funds for two follow-up Focus on Mothers visits (Focus on Mothers 2 and Focus on Mothers 3), but there is no obligation for you to attend both of these. This is a very interesting time in your lives and one that has been relatively under researched and we are keen to improve our understanding of what things support women living a long and healthy life and what put them at greater risk of diseases as they become older. BUT we would always start any new Focus visit with letters of invite and information about the visit. You can decide whether you want to take part or not. If at any time you would like us to stop contacting you completely, you just need to let us know and we will respect that wish.

What do I have to do now?

Please complete and return both sides of the “Focus on Mothers 2 Appointment” form in the stamped and addressed envelope.

Confidentiality and data protection

Any data collected will be stored with individual ID numbers but with no personal information, for example names, addresses or dates of birth, attached. Files that link this ID number to your personal details will be securely stored with only two senior ALSPAC (Children of the 90s) staff having access to these. The data will be used for research purposes only and will be analysed by ALSPAC study researchers. None of these researchers will have access to your personal information.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask the staff when you attend who will do their best to answer your questions. You can also

contact the visit team or the ALSPAC Executive Group about any problems of participating in the study.

Who is organising and funding the research?

This research is organised by the ALSPAC study team. The Research Director for the Focus on Mothers 2 in ALSPAC is Professor Debbie Lawlor. The Focus on Mothers 2 has been funded by the Wellcome Trust.

In addition, ALSPAC has core funding by the Wellcome Trust, the UK Medical Research Council and the University of Bristol.

Who has reviewed this study?

The ALSPAC Ethics & Law Committee (which includes parent members) and the South West Central Bristol Research Ethics Committee.

Scientifically, the study proposal was reviewed by anonymous reviewers and grant board members for the Wellcome Trust.

Contact for further information

Please contact **0117 3310012** to speak to the Visit team if you require more information (there is an answerphone on this line).

If you wish to discuss the study further, please email the ALSPAC Executive Group at research@childrenofthe90s.ac.uk.

Thank you for your time in reading about our proposed Focus on Mothers 2 visit and for your ongoing support of Children of the 90s.



ALSPAC

Avon Longitudinal Study of Parents and Children

Oakfield House
Oakfield Grove
Clifton
Bristol BS8 2BN
Tel: 0117 3310012
E-mail: focus-admin@bristol.ac.uk

Focus on Mothers 2

www.alspac.bris.ac.uk

DETAILS ABOUT FASTING BLOOD SAMPLES AT FOCUS ON MOTHERS

This leaflet provides additional details on the fasting blood samples that will be undertaken at the Focus on Mothers 2 visit. It is available on request from focus staff and should be used as an addition to the participant information leaflet that was mailed to you. The information leaflet that we mailed to you provides key information about the study that we would like all participating mothers to read.

FASTING BLOOD SAMPLES

We want to take a fasting blood sample from you and measure haemoglobin (a marker of anaemia), fasting blood glucose (sugar), insulin (the hormone that controls blood glucose levels in the body), lipids (forms of cholesterol) and hormones. The reasons that we want to do these tests is that they are related to risk of diabetes and heart disease and, also, because changes that occur during pregnancy (for example how much weight a woman puts on in a particular pregnancy or what time of pregnancy most weight is gained) can affect levels of these chemicals in the blood later in life. Lastly, some of these measures can change as women start to go through the menopause. Measuring these will help us with important research questions about what causes diabetes and heart disease in women and to understand why some women have few or no symptoms as they go through the menopause whereas others have a very difficult time.

If you agree to provide a fasting blood sample this will mean that you have to come to the focus visit without having had anything to eat or drink (except water) since the night before if you come to a morning visit (before 2pm) or for the previous 8 hours if you come to an appointment in the afternoon or early evening (any appointment after 2pm). Once we have taken the fasting sample we will provide you with food and drinks before doing any other measurements.

Many of you will have had blood tests before – for example when you were pregnant. At the focus visit we will ask you to lie down on a couch whilst we take the sample. We realise that samples are often taken in the sitting position in general practice visits and hospital clinics. However, because you will have been fasting we will only take samples with participants lying on a couch at the focus visit.

Once you are lying on the couch in a comfortable position the member of staff will apply a tourniquet to your upper arm to make the veins in the space on your inner arm where the forearm meets the upper arm more visible. Once the tester is confident they have located a vein they will tell you that they are going to insert the needle to take blood. Once they have

completed taking the sample the member of staff will release the tourniquet, remove the needle and apply pressure with a piece of cotton wool over the area where blood has been taken.

All of the staff are fully trained to take blood samples. Nonetheless sometimes it is difficult to take a blood sample from an individual. Sometimes the member of staff will feel that it is better to take a sample from the back of your hand rather than your arm. Sometimes an initial attempt to collect blood will fail and the tester will ask you if they can try again. These are rare events and we would never allow more than 3 attempts at getting blood. If you felt uncomfortable at any time during the procedure or you wanted the test to stop for any other reason we will stop it immediately.

Is taking a blood sample safe?

It is likely that most of you will have had a blood sample taken before and will therefore know that it can be a little uncomfortable and can result in bruising. Our trained staff will minimise the likelihood of marked bruising. Some individuals faint when they are having a blood test. This can occur 'out of the blue' in people who have had previous tests with no problems. For this reason we only take blood samples at the focus visit with you lying on a couch. If you do faint this should prevent any serious injury. In the rare event that you do faint we will make sure that you are fully recovered before we discuss any further measurements.

Will you let me know my blood test results?

As with the other measurements we will first ask you for consent to let you know the results of test that are clinically meaningful. With your consent we will let you know if you have a low haemoglobin level (indicator of anaemia) or a very high haemoglobin level (which can mean that your blood flows too slowly), if you have high fasting blood glucose (indicator of diabetes) or high levels of total cholesterol.

We will let you know about these results via a letter after the focus visit. The letter will also include a letter for you to take to your GP.

We will know the results of the haemoglobin test within 4 weeks of you coming to the focus visit and would send a letter to you if your level is low or very high so that it reached you at the latest within 4 weeks of your visit. The result will not necessarily mean you are anaemic but you should talk to your GP. They might want to repeat the test, examine you and do some additional tests. Depending upon the results of these they might suggest you take an iron supplement or discuss other treatments.

The results of the glucose and cholesterol tests will not be available for some months after you come to the focus visit. These tests are done by one of our collaborators in Glasgow and we will send batches of samples to Glasgow at approximately 6 month intervals. This will mean that it will be possible to let you know if you have high (or low, as relevant) levels for any of these tests at between 4-12 months since the time you attended the focus visit. Because diabetes and cholesterol problems do not have symptoms and therefore you would not know if you had a problem, it can be important to let you know any results that are outside the normal range even if it is several months since we took the sample. If you give us consent to do so we will send you a letter and a letter to take to your GP if the results suggest you have high glucose or cholesterol problems. The results would not mean that you definitely had diabetes or were at increased risk of heart disease. Your GP would most likely want to repeat the test.

They would also talk to you about other risk factors and most likely examine you (e.g. test your blood pressure and look at the back of your eyes) and possibly ask for some additional blood tests. Depending on the results of these they might reassure you that there are no problems or they might ask you to make changes to your lifestyle or they might talk to you about treatments.

Will you be doing anything else with my blood sample?

Yes. With your permission we would like to store some of your blood sample so that we can use it for answering any future research questions that arise. One of the important strengths of the *Children of the 90s* study (ALSPAC) is that it is able to respond very quickly to important research questions about health and well-being as they arise. Storing some of your blood sample will help us to be able to do this. For example, disease research often begins in animal and 'test-tube' research. If this research were to suggest that different levels of a chemical that circulates in human blood might predict risk of diabetes or heart disease or cancer in humans, we would be able to use stored blood samples to measure this chemical and test this new research hypothesis. We have stored blood (both fasting and non-fasting) in a similar way from samples taken from you/your child at the focus visit (when you/your child has given us consent). The samples are stored with unique IDs that allow us to link any test results to other data but that would never allow someone working in a laboratory to be able to link these results to your personal data such as your name, age or date of birth.

We only need to do one blood test to obtain extra blood for storage so allowing us to do this will not mean that you have to have 2 separate blood tests.

Will you be taking more blood for DNA and genetics?

Yes, with your consent we would like to take a sample that we can use to extract DNA. Many of you have already provided us with a sample that we have used to extract DNA and that we have used for genetic research. The genetic research that we have done has contributed to understanding how genes and non-genetic risk factors work together to affect how healthy someone is. We would now like to conduct research into how these relationships happen.

Although genes do not change over life there is evidence that how they work does. Processes called epigenetics involves molecules (such as a methyl molecule) being attached to part of an individual's DNA and these molecules affect how the gene works. Factors such as smoking, diet and exercise might influence how many of these molecules are attached to someone's DNA and which genes they are attached to at different times in a person's life. We would like to do further research in this area and in particular would like to see how patterns of methylation of DNA change during mid-life in women. Thus, we would like a new sample of your DNA so that we can compare methylation patterns in it to those that were on your earlier DNA sample.

A separate information sheet that describes the importance of having DNA and immortalised-cell lines and how we use these in ALSPAC is enclosed (this is the same as a leaflet many of you will have already seen).

Contact for further information

Please contact **0117 3310012** to speak to the Focus team if you require more information. If you wish to discuss the study further please email a member of the ALSPAC executive group email: alspac-exec@bris.ac.uk.

Thank you for your time in reading about our proposed Focus on Mothers 2 visit and for your ongoing support of Children of the 90s.



Focus on Mothers 2

Visit Number _____

 Oakfield House, Oakfield Grove
 Clifton, Bristol BS8 2BN

Tel: 0117 331 0012

E-mail: focus-admin@bristol.ac.uk

Permission to complete and use clinic data

We would like to ask you to undertake all of the following measurements/procedures:

Please cross the boxes and initial to indicate that you consent, or leave blank if you do not consent. Also cross and initial to indicate whether you would like us to inform you, and give you a letter to give to your GP, if the results of tests marked * give cause for concern.

	1. Consent to test		2. Consent to inform	
	Cross box	Initial	Cross box	Initial
(a) DXA scan of bone density*, fat and muscle mass	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
(b) Weight, height, waist, hip and arm circumference	<input type="checkbox"/>	<input type="text"/>		
(c) Blood pressure* and pulse pressure	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
(d) pQCT of arm and wrist	<input type="checkbox"/>	<input type="text"/>		
(e) Physical capability tasks	<input type="checkbox"/>	<input type="text"/>		
(f) Assessment of thought processes	<input type="checkbox"/>	<input type="text"/>		
I understand that donated blood will be considered a gift but I will have the right to withdraw permission for analysis.				
Fasting blood sample for:				
(g) Haemoglobin (test for anaemia)*	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
(h) Glucose (sugar)*	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
(i) Lipids (forms of cholesterol)*	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
(j) Storage for future research	<input type="checkbox"/>	<input type="text"/>		
(k) Hormones related to reproduction and menopause	<input type="checkbox"/>	<input type="text"/>		

Signature

Date signed

 / / 20

Initial

Last Name

8646

The University of Bristol holds legal liability insurance in the event that any participant is injured due to any negligence on the part of the University.





Focus on Mothers 2

Oakfield House, Oakfield Grove
Clifton, Bristol BS8 2BN

Tel: 0117 331 0012

E-mail: focus-admin@bristol.ac.uk

Visit Number _____

Permission to use blood sample for cell lines

After processing the name will be taken off the blood samples. The cell lines and DNA samples will be stored with no names attached to them. Results will be used for statistical purposes only and not linked to named people.

CONSENT

The purposes and possible risks in having blood taken have been explained to me. I understand that donated blood will be considered a gift but I will have the right to withdraw permission for analysis.

I understand that the main stocks of DNA and/or cell lines will be stored in Bristol, but that the DNA/cell lines (with an anonymous number only), or information about the sequence of my DNA, may be sent to specialist research laboratories in the UK and abroad for analyses, and the results returned to Children of the 90s. Researchers at these laboratories have no access to personal information about study participants.

I agree that information about my genes can be analysed together with information about my health, disease and life style factors in order to undertake research into biological or genetic factors affecting the risk of developing a range of common medical conditions. I understand that any such analyses will only be undertaken on data from which all personal information has been removed and replaced with an anonymous code.

I agree to having the following blood samples taken for analyses for the Children of the 90s study: (If you consent, please cross **one** of the boxes below)

A sample for cell lines ('immortalised' DNA) 1

OR

A sample for DNA only 2

Signature

Date signed

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Initial

Last Name

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The University of Bristol holds legal liability insurance in the event that any participant is injured due to any negligence on the part of the University.





Focus on Mothers 3 Participant Information Leaflet

You are invited to the third **FOCUS ON MOTHERS** visit.

Participation in the visit is completely voluntary and if you decide not to participate this will not affect future invitations to you or your child to participate in Children of the 90s research. The visit is for research purposes and consent to take part will be obtained.

Many of the measurements at this third visit will be identical to those that were undertaken at the second focus on mothers visit. The visit will take approximately 2 and a half hours.

This leaflet explains the measurements that will be undertaken at the visit, why these measurements are being done and what they will involve. Please take time to read the following information, which will help you decide whether or not you wish to complete any of them.

Please ask us if anything is not clear.



**Avon Longitudinal Study
of Parents and Children**

**Oakfield House
Oakfield Grove, Bristol
BS8 2BN, UK**

T +44 (0)117 331 0010

E info@childrenofthe90s.ac.uk

W childrenofthe90s.ac.uk

What is the purpose of the study?

The purpose of this study is to understand how measurements such as bone density, body size and blood pressure change as women go through mid-life. We want to understand whether changes in these characteristics are caused by changes in hormones, changes in lifestyle, genetic factors or a mixture of these.

What measurements are planned?

We would like you to undertake all of the following:-

a) **Informed consent:** At the start of the visit we will explain all the measurements and answer any questions you may have. We will ask you to complete and sign a consent form.

b) **Fasting blood sample:** We will collect blood in the usual way. We will test your blood for haemoglobin (a measure of anaemia), fasting cholesterol, glucose (sugar), insulin (the hormone that controls glucose) and hormones related to reproduction and going through the menopause (oestrogen, follicular stimulating hormone, luteinizing hormone, anti-müllerian hormone and sex hormone binding globulin). All staff are fully trained to take blood. At any time during the sample taking you can ask for the procedure to stop.

Will you be doing anything else with my blood sample? Yes. With your consent we would like to store some of your blood sample so we can use it to answer future research questions that arise. The samples are stored with unique ID numbers allowing test results to be linked to other data, but that would never allow someone working in a laboratory to be able to link these results to your personal information such as your name, age or date of birth.

Will you be taking blood for DNA and genetics? Yes, with your consent we would like to take a sample that we can use to extract DNA. You may have already provided us with a sample from which we have extracted DNA and used for genetic research. The genetic research that we have done has contributed to understanding how genes and non-genetic risk factors work together to affect how healthy someone is. We would now like to conduct research into understanding how these relationships happen.

Although genes do not change over life there is evidence that how they work does. Processes called epigenetics involve molecules (such as a methyl molecule) being attached to part of an individual's DNA and these molecules affect how the gene works. Factors such as smoking, diet and exercise might influence how many of these molecules are attached to someone's DNA and which genes they are attached to at different times in a person's life. We would like to do further research in this area and in particular would like to see

how patterns of methylation of DNA change during mid-life in women. Thus, we would like a new sample of your DNA so that we can compare methylation patterns in it to those that were on your earlier DNA sample.

c) Weight, height (standing and seated), waist, arm and hip size.

d) DEXA scan to measure your lean (muscle) and fat mass and bone density: We would like to scan your whole body to measure muscle mass, fat mass and bone density. We use a machine called a lunar prodigy narrow fan beam DEXA scanner.

Your clothes must not have any metal fastenings; watches, piercings and other metal objects should be removed if possible, since these can interfere with the result. You will be asked to lie on a couch and remain very still for 6 to 10 minutes. The machine's arm will pass over you twice; first to scan the whole skeleton, second to scan your hip in more detail. The second scan is similar to the first, except that your foot is positioned against a rest to rotate the hip to a 45-degree angle.

DEXA scans measure how much calcium and other minerals are in the bone being looked at. The result is called the 'bone mineral density' (BMD). Denser bones have more calcium and minerals. They are stronger and less likely to break. We will measure your total body and hip BMD. If you have a low hip BMD (which might indicate risk of osteoporosis) and you have consented to be informed about this, we will give you an information sheet and a letter to take to your GP.

e) pQCT scan of the arm and wrist: A Peripheral Quantitative Computerised Tomography (pQCT) scan looks at the strength and quality of bones. We scan the lower arm and wrist with the pQCT and it gives us a cross-section showing the internal structure. The pQCT scan tells us about the internal structure of bones and the way it varies between people. This internal structure may be important in predicting who is at risk of breaking bones and of osteoporosis in later life. Part of our research will be to look at whether pQCT scans pick up early changes in bones that identify women at future risk of osteoporosis more accurately than does DEXA scan.

Are the DEXA and pQCT scans safe? Yes. These scans use x-rays but the level of radiation is tiny, e.g. the x-ray dose of 5 micro Sieverts is less than the average daily natural radiation dose we get from the environment around us and does not carry any measurable risk at all.

f) 3D whole body scan: A whole-body three-dimensional photonic scan provides a three-dimensional image of your whole body, using laser scanners and computer software. This image can provide information on size, shape and posture that is not available from the more conventional measures such

as weight and height or the DEXA scan. Things like age and how many children a woman has affect body shape. Body shape in turn is possibly associated with conditions such as diabetes and heart disease but this needs further research.

The results from this scanner are best if they are done with all of your clothing removed. The scanner is inside a private room where you can undress and no one else will enter. If you wish we can do scans with **grey or skin-coloured underwear without underwire**, so if you think you would prefer this option please make sure to wear these.

g) **Blood pressure and pulse.**

h) **Physical capability:**

i) **Hand-grip strength** will be assessed using a digital spring dynamometer. This tests muscle strength. The picture shows one of these machines. You will be asked to grip the machine (as shown in the picture), and pull the two parts as tightly together as possible. We will ask you to repeat the test 4 times (twice with your right hand and twice with your left hand) and will record all four measurements.



ii) The **chair rise test**, examines strength in your legs and your motor fitness. You will be asked to stand up from sitting on a chair, without using your hands and with your feet remaining in a similar place on the floor in front of the chair. After a practice, we will time how long it takes you to complete 10 chair rises.

iii) The **static balance test** involves asking you to stand on one leg, with your hands at your side and your eyes facing forward, and stay like this for as long as you can. We will time how long you can balance on one leg, up to a maximum of 30 seconds (after 30 seconds if you are still holding the balance we will ask you to stop). The test will be done with your eyes open and then you will be asked to repeat it with your eyes closed. For this test it is important that you **wear flat comfortable shoes, such as trainers**. Please come to the test in a pair of shoes that are flat and comfortable or bring a pair of pumps or trainers with you for doing this test.

iv) **Timed three-metre walk** involves asking you to walk at your normal speed from one line to a second one that is 3 metres away. We will time how

long this walk takes you. For this test it is important that you **wear flat comfortable shoes, such as trainers**. Please come to the test in a pair of shoes that are flat and comfortable or bring a pair of pumps or trainers with you for doing this test.

i) **Assessments of thought processes:** We would like to do separate tests of your memory, how you process new information and how your brain uses that information:-

i) **Verbal episodic memory** – you will be asked to listen to a brief story (played from a tape). You will then be asked to repeat key facts from the story immediately and again 10 minutes later. A score is allocated for the number of key facts that are correctly remembered from the paragraph at each time point.

ii) **Working memory** – our staff will read out 5 numbers to you and ask you to repeat them backwards; if you do this accurately the test is repeated with 6 numbers and so on. The result is the highest number of numbers you can correctly repeat backwards.

iii) **Speed of information processing** – you will be shown several numbers paired with geometric symbols (e.g. 5 = a square). You will then be given 90 seconds to pair specific numbers to their geometric symbols. The number correctly assigned in the given time is the score allocated.

iv) **Executive function** – you will be asked to list as many words beginning with certain letters that you can think of. The number of words (without repeats) is the test score.

v) **Word recognition** – you will be provided with a list of pairs of words. One will be a real word, the other will be a made-up word. You will be asked to indicate which is the made-up word in each pair.

j) **Assessment of physical activity:** We will ask you to wear a motion sensor (CSA accelerometer) for 7 days and then return it to us in a prepaid envelope. The accelerometer records your movements and therefore provides objective information about your habitual physical activity and will allow us to study these patterns of physical activity in relation to health outcomes.

Do I have to take part?

Not at all. It is up to you to decide whether or not to take part. If you decide to take part, you are still free to withdraw from the study or any of the individual measures at any time.

What will happen if I take part – are there any advantages?

The Focus visit is not a health check and we are asking you to help us with

research that we hope will help people in the future. Some of the measurements that we take might indicate increased risk for some health problems (see below). Where you have given us written consent for us to feed back any results for these tests, we will advise you about your result and give you a letter to take to your GP. Other measurements taken are useful for research but their results have no clear medical meaning at the moment. Therefore we will not tell you about those results.

If we do not feed back any results to you, you should not conclude this means you have a clean bill of health. If you have any symptoms that cause you concern you should contact your GP in the way that you normally would. The following describes the test results where we plan to provide feedback (if you have given us consent to do so):-

- If your **blood pressure** is high we will tell you during your visit and give you a letter to take to your GP so that they can test this again, discuss this with you, and do further tests if necessary.
- If your **hip bone density** is low we will tell you during your visit and give you a letter to take to your GP so that they can discuss this with you and do further tests if necessary.
- If you have low haemoglobin (risk of **anaemia**) or very high haemoglobin (this can mean your blood flows too slowly), have high **blood sugar** (an indicator of diabetes) or high levels of total cholesterol you will be sent a letter along with a letter for you to take to your GP.

The tests for anaemia will be done in our laboratory and a result will be available within 4 weeks (maximum) of your visit. If you have values outside the normal range and have given consent for feedback, you will receive a letter at the latest 4 weeks after your visit for this test. For cholesterol and blood sugar the samples are sent away in batches for testing. Therefore, it could be up to 12 months before the results are fed back to anyone with levels outside of the normal range. If your levels are outside the normal range for these and you have given written consent, we will send you a letter about this between 4 to 12 months following your visit.

Are there any disadvantages to taking part?

Other than giving us your time, we do not see any major disadvantages in taking part. We do need you to come to the visit 'fasted' for the blood sample, i.e. having nothing to eat or drink (except water) since the previous night for morning appointments and for the previous 8 hours for afternoon or evening visits. Once the fasting sample has been taken we will provide you with food and drink before doing any further measurements. Some people are left with

bruising after a blood sample has been taken and in a small number this can be quite marked.

DEXA and pQCT scans emit a very small dose of x-rays but this is smaller than the amount we are all exposed to from our surrounding environment every day. Both scans, and all of the other tests we will undertake with your consent, are safe. The visit will take approximately 2 and a half hours and we will cover travel expenses and also provide you with a £10 shopping-gift token to compensate you for your time spent at the clinic.

Where does the visit take place?

The visit will be at the same place as the first visit – Oakfield House, Oakfield Grove in Clifton, Bristol, BS8 2BN. We really appreciate you giving up your time to come to this visit. If you are unable to come to Oakfield House, but would like to take part in the research, we will be offering home visits towards the end of the study. We will be able to do all of the measurements and tests at your home except the bone scans – it is not possible to carry the machines needed to do these outside of the Focus Centre.

If I attend this Focus assessment am I committed to future Focus on Mother assessments?

Not at all. The recent Wellcome Trust grant that is funding this study provided funds for two follow-up Focus on Mothers visits (Focus on Mothers 2 and Focus on Mothers 3), but there is no obligation for you to attend Focus on Mothers 3. This is a very interesting time in women's lives and one that has been relatively under researched. We are keen to improve our understanding of what things support women to live a long and healthy life and which ones put them at greater risk of diseases as they become older. We always start any new Focus visit with a letter of invitation and information about the visit. You can decide whether you want to take part or not. If at any time you would like us to stop contacting you completely, you just need to let us know and we will respect that wish.

What do I have to do now?

Please complete and return both sides of the "Your Details and Your Availability" form in the stamped addressed envelope.

Confidentiality and data protection

Any data collected will be stored with individual ID numbers but with no personal information, for example names, addresses or dates of birth, attached. Files that link this ID number to your personal details will be securely stored. The data will be used for research purposes only and will be analysed

by Children of the 90s study researchers. None of these researchers will have access to your personal information.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask the staff when you attend who will do their best to answer your questions. You can also contact the Admin team or the Children of the 90s Executive Group about any problems of participating in the study using the contact details on page 1 of this leaflet or the bottom of your invite.

Who is organising and funding the research?

This research is organised by the Children of the 90s study team and is funded by the Wellcome Trust. The Research Director for Focus on Mothers 3 is Professor Debbie Lawlor.

In addition, Children of the 90s receives core funding from the Wellcome Trust, the UK Medical Research Council and the University of Bristol.

Who has reviewed this study?

The Children of the 90s Ethics and Law Committee (which includes parent members) and the South West Central Bristol Research Ethics Committee.

Scientifically, the study proposal was reviewed by anonymous reviewers and grant board members for the Wellcome Trust.

Contact for further information

Please contact **0117 3310012** to speak to the Admin team if you require more information.

If you wish to discuss the study further, please email the Children of the 90s Executive Group at research@childrenofthe90s.ac.uk.

Thank you for reading about your proposed Focus on Mothers 3 visit and for your ongoing support of Children of the 90s.

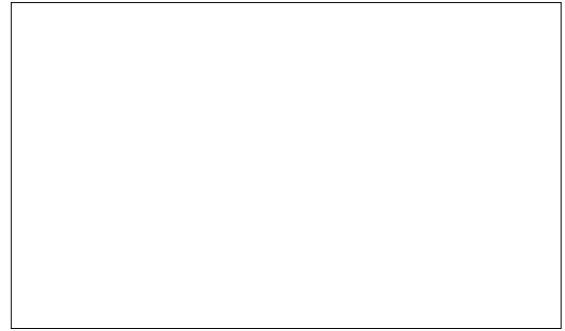


Focus on Mothers 3

Oakfield House, Oakfield Grove
Clifton, Bristol BS8 2BN

Tel: 0117 331 0012
There is an answer phone on this line

E-mail: admin@childrenofthe90s.ac.uk



Permission to use blood sample for cell lines

After processing the name will be taken off the blood samples. The cell lines and DNA samples will be stored with no names attached to them. Results will be used for statistical purposes only and not linked to named people.

CONSENT

The purposes and possible risks in having blood taken have been explained to me. I understand that donated blood will be considered a gift but I will have the right to withdraw permission for analysis.

I understand that the main stocks of DNA and/or cell lines will be stored in Bristol, but that the DNA/cell lines (with an anonymous number only), or information about the sequence of my DNA, may be sent to specialist research laboratories in the UK and abroad for analyses, and the results returned to Children of the 90s. Researchers at these laboratories have no access to personal information about study participants.

I agree that information about my genes can be analysed together with information about my health, disease and life style factors in order to undertake research into biological or genetic factors affecting the risk of developing a range of common medical conditions. I understand that any such analyses will only be undertaken on data from which all personal information has been removed and replaced with an anonymous code.

I agree to having the following blood samples taken for analyses for the Children of the 90s study: (If you consent, please cross **one** of the boxes below)

A sample for cell lines ('immortalised' DNA) 1

OR

A sample for DNA only 2

Signature

Date signed

		/			/	2	0		
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Initial

Last Name

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The University of Bristol holds legal liability insurance in the event that any participant is injured due to any negligence on the part of the University.

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Focus on Mothers 4 Participant Information Leaflet

We are inviting you to the fourth **FOCUS ON MOTHERS** visit.

Participation in the visit is completely voluntary and if you do decide not to participate this will not affect future invitations to you or your child to participate in Children of the 90s research. The visit is for research purposes and consent to take part will be obtained.

All of the measurements at this fourth visit will be identical to those that were undertaken at other focus on mothers' visits. The visit will take approximately 2 and a half hours.

This leaflet explains the measurements that will be undertaken at the visit, why these measurements are being done and what they will involve. Please take time to read the following information, which will help you decide whether or not you wish to complete any of them.

Please ask us if there is anything that is not clear.



**Avon Longitudinal Study
of Parents and Children**

**Oakfield House
Oakfield Grove, Bristol
BS8 2BN, UK**

T +44 (0)117 331 0012

E info@childrenofthe90s.ac.uk

W childrenofthe90s.ac.uk

What is the purpose of the study?

The purpose of this study is to understand how measurements such as bone density, body size and blood pressure change as women go through mid-life. We want to understand whether changes in these characteristics are caused by changes in hormones, changes in lifestyle, genetic factors or a mixture of these.

What measurements are planned?

We would like to ask you to undertake all of the following:-

a) Informed consent: At the start of the visit we will go through all of the measurements and answer any questions you may have. We will ask you to complete and sign a consent form.

b) Fasting blood sample: We will collect blood in the usual way. We will test your blood for haemoglobin (a measure of anaemia), fasting cholesterol, glucose (sugar), insulin (the hormone that controls glucose) and hormones related to reproduction and going through the menopause (oestrogen, follicular stimulating hormone, luteinizing hormone, anti-müllerian hormone and sex hormone binding globulin). All staff are fully trained to take blood. At any time during the sample taking you can ask for the procedure to stop.

Will you be doing anything else with my blood sample? Yes. With your consent we would like to store some of your blood sample so we can use it for answering future research questions that arise. The samples are stored with unique ID numbers allowing test results to be linked to other data, but that would never allow someone working in a laboratory to be able to link these results to your personal information such as your name, age or date of birth.

Will you be using my blood for DNA and genetics? Yes, with your consent we would like to use your fasting blood sample to extract DNA for genetic studies. Many of you have already provided us with a sample that we have used to extract DNA and that we have used for genetic research. The genetic research that we have done has contributed to understanding how genes and non-genetic risk factors work together to affect how healthy someone is. We would now like to conduct research into understanding how these relationships happen.

Although genes do not change over life there is evidence that how they work does. Processes called epigenetics involve molecules (such as a methyl molecule) being attached to part of an individual's DNA and

these molecules affect how the gene works. Factors such as smoking, diet and exercise might influence how many of these molecules are attached to someone's DNA and which genes they are attached to at different times in a person's life. We would like to do further research in this area and in particular would like to see how these patterns of methylation in DNA change during mid-life in women. This is why we need a new sample of your DNA so that we can compare methylation patterns in it to those that were on your earlier DNA sample.

c) Weight, height (standing and seated), waist, arm and hip size.

d) DEXA scan to measure your lean (muscle) and fat mass and bone density: We would like to scan your whole body to measure muscle mass, fat mass and bone density. We use a machine called a Lunar Prodigy narrow fan beam DEXA scanner.

Your clothes must not have any metal fastenings; watches, piercings and other metal objects should be removed if possible, since these can interfere with the result. You will be asked to lie on a couch and remain very still for 6 to 10 minutes. The machine's arm will pass over you twice; first to scan the whole skeleton, second to scan your hip in more detail. The second scan is similar to the first, except that your foot is positioned against a rest to rotate the hip to a 45-degree angle.

DEXA scans measure how much calcium and other minerals are in the bone being looked at. The result is called the 'bone mineral density' (BMD). Denser bones have more calcium and minerals. They are stronger and less likely to break. We will measure your total body and hip BMD. If you have a low hip BMD (which might indicate risk of osteoporosis) and you have consented to be informed about this, we will give you an information sheet and a letter to take to your GP.

e) pQCT scan of the arm and wrist: A Peripheral Quantitative Computerised Tomography (pQCT) scan looks at the strength and quality of bones. We scan the lower arm and wrist with the pQCT and it gives us a cross-section showing the internal structure. The pQCT scan tells us about the internal structure of bones and the way it varies between people. This internal structure may be important in predicting who is at risk of breaking bones and of osteoporosis in later life. Part of our research will be to look at whether pQCT scans pick up early changes in bones that identify women at future risk of osteoporosis more accurately than does a DEXA scan.

Are the DEXA and pQCT scans safe? Yes. These scans use x-rays but the level of radiation is tiny, e.g. the x-ray dose of 5 micro Sieverts is

less than the average daily natural radiation dose we get from the environment around us and does not carry any measurable risk at all.

f) Ultrasound scan of the carotid artery (in your neck): At the Focus on Mothers 1 visit, we asked to complete an ultrasound scan of the carotid artery in your neck in order to measure how thick the wall of the artery was. The artery wall thickness is a measure of atherosclerosis. We would like to repeat this measure in the Focus on Mothers 4 visit in order to study potential changes in this measure.

h) Blood pressure and pulse.

i) Physical capability:

i) **Hand-grip strength** will be assessed using a digital spring dynamometer. This tests muscle strength. You will be asked to grip the machine and pull the two parts as tightly together as possible. We will ask you to repeat the test 4 (2 with your right hand and 2 with your left hand) times and will record all four measurements.

ii) **Chair rise test**, examines strength in your legs and your motor fitness. You will be asked to stand up from sitting on a chair, without using your hands and with your feet remaining in a similar place on the floor in front of the chair. We will time how long it takes you to complete 10 chair rises.

iii) **Static balance test** involves asking you to stand on one leg, with your hands at your side and your eyes facing forward, and stay like this for as long as you can. We will time how long you can balance on one leg, up to a maximum of 30 seconds (after 30 seconds if you are still holding the balance we will ask you to stop). The test will be done with your eyes open and then you will be asked to repeat it with your closed. For this test it is important that you **wear flat comfortable shoes, such as trainers**. Please come to the test in a pair of shoes that are flat and comfortable or bring a pair of pumps or trainers with you for doing this test.

iv) **Timed three metre walk** involves asking you to walk (but not run) as fast as you can from one line to a second one that is 3 metres away. We will time how long this walk takes you. For this test it is important that you **wear flat comfortable shoes, such as trainers**. Please come to the test in a pair of shoes that are flat and comfortable or bring a pair of pumps or trainers with you for doing this test.

j) Assessments of thought processes: We would like to do separate tests of your memory, how you process new information and how your brain uses that information:-

i) Verbal episodic memory – you will be asked to listen to a brief story (played from a tape). You will then be asked to repeat key facts from the story immediately and again 10 minutes later. A score is allocated for the number of key facts that are correctly remembered from the paragraph at each time point.

ii) Working memory – our staff will read out 3 numbers to you and ask you to repeat them backwards; if you do this accurately the test is repeated with 4 numbers and so on. The result is the highest number of numbers you can correctly repeat backwards.

iii) Speed of information processing – you will be shown several numbers paired with geometric symbols (e.g. 5 = a square). You will then be given 2 minutes to pair specific numbers to their geometric symbols. The number correctly assigned in the given time is the score allocated.

iv) Executive function – you will be asked to list as many words beginning with certain letters that you can think of. The number of words (without repeats) is the test score.

v) Word recognition – you will be provided with a list of pairs of words. One will be a real word, the other will be a made-up word. You will be asked to indicate which is the real word for each pair.

k) BCG scar size: We will ask you some questions about a scar you may have developed following the standard BCG immunisation you had at school and measure it (if you have a scar) using a ruler. Our aim is to discover more about the genetics linked to scarring. Trying to better understand the development of scars should help to develop more effective treatments to prevent scarring. This is important as scarring can occur not only on the skin but also inside of the body and can lead to complications after surgery or heart attacks.

Do I have to take part?

Not at all. It is up to you to decide whether or not to take part. If you decide to take part, you are still free to withdraw from the study or any of the individual measures at any time.

What will happen if I take part – are there any advantages?

The Focus visit is not a health check and we are asking you to help us with research that we hope will help people in the future. Some of the measurements that we take might indicate increased risk for some health problems (see below). Where you have given us written consent for us to feedback any results for these tests, we will advise you about your result and give you a letter to take to your GP. Other measurements taken are useful for research but their results have no clear medical meaning at the moment. Therefore we will not tell you about those results.

If we do not feedback any results to you, you should not conclude this means you have a clean bill of health. If you have any symptoms that cause you concern you should contact your GP in the way that you normally would.

The following describes the test results where we plan to provide feedback (if you have given us consent to do so):-

- If your **blood pressure** is high we will tell you at the clinic and give you a letter to take to your GP so that they can test this again, discuss this with you, and do further tests if necessary.
- If your **hip bone density** is low we will tell you at the clinic and give you a letter to take to your GP so that they can discuss this with you and do further tests if necessary.
- If you have low haemoglobin (risk of **anaemia**) or very high haemoglobin (this can mean your blood flows too slowly), have high **blood sugar** (an indicator of diabetes) or high levels of total **cholesterol** you will be sent a letter along with a letter for you to take to your GP.

The assays for anaemia will be done in our laboratory and a result will be available within 4 weeks (maximum) of your visit. If you have values outside the normal range and have given consent for feedback, you will receive a letter at the latest 4 weeks after your visit for this test. For cholesterol and blood sugar the samples are sent away in batches for testing. Therefore, it could be up to 12 months before the results are fed-back to anyone with levels outside of the normal range. If your levels are outside the normal range for these and you have given written consent, we will send you a letter about this between 4 to 12 months following your visit.

Are there any disadvantages to taking part?

Other than sparing us your time, we do not see any major disadvantages in taking part. We do need you to come to the visit 'fasted' for the blood sample, i.e. having nothing to eat or drink (except water) since the previous night for morning appointments and for the previous 8 hours for afternoon or evening visits. Once the fasting sample has been taken we will provide you with food and drink before doing any further measurements. Some people are left with bruising after a blood sample has been taken and in a small number this can be quite marked.

DEXA and pQCT scans emit a very small dose of x-rays but this is smaller than the amount we are all exposed to from our surrounding environment every day. Both scans, and all of the other tests we will undertake with your consent, are safe. The visit will take approximately 2 and a half hours and we will cover travel expenses and also provide you with a £10 shopping-gift token to compensate you for your time spent at the clinic.

Where does the visit take place?

The visit will be at the same place as the first visits – Oakfield House in Clifton, Bristol. We really do appreciate you giving up your time to come to this visit.

If I attend this Focus assessment am I committed to any future Focus on Mother assessments?

Not at all. This is a very interesting time in your lives and one that has been relatively under researched and we are keen to improve our understanding of what things support women living a long and healthy life and what put them at greater risk of diseases as they become older. BUT we would always start any new Focus visit with letters of invite and information about the visit. You can decide whether you want to take part or not. If at any time you would like us to stop contacting you completely, you just need to let us know and we will respect that wish.

What do I have to do now?

Please complete and return both sides of the "Focus on Mothers 4 Appointment" form in the stamped and addressed envelope.

Confidentiality and data protection

Any data collected will be stored with individual ID numbers but with no personal information, for example names, addresses or dates of birth, attached. Files that link this ID number to your personal details will be

securely stored with only two senior ALSPAC (Children of the 90s) staff having access to these. The data will be used for research purposes only and will be analysed by ALSPAC study researchers. None of these researchers will have access to your personal information.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask the staff when you attend who will do their best to answer your questions. You can also contact the visit team or the ALSPAC Executive Group about any problems of participating in the study.

Who is organising and funding the research?

This research is organised by the ALSPAC study team. The Research Director for the Focus on Mothers 4 in ALSPAC is Professor Debbie Lawlor. The Focus on Mothers 4 has been funded by the Lifelong Health and Wellbeing programme (LLHW).

In addition, ALSPAC has core funding by the Wellcome Trust, the UK Medical Research Council and the University of Bristol.

Who has reviewed this study?

The ALSPAC Ethics & Law Committee (which includes parent members) and the South West Central Bristol Research Ethics Committee.

Scientifically, the study proposal was reviewed by anonymous reviewers and grant board members for the Wellcome Trust.

Contact for further information

Please contact **0117 3310012** to speak to the Visit team if you require more information (there is an answerphone on this line).

If you wish to discuss the study further, please email the ALSPAC Executive Group at research@childrenofthe90s.ac.uk.

Thank you for your time in reading about our proposed Focus on Mothers 4 visit and for your ongoing support of Children of the 90s

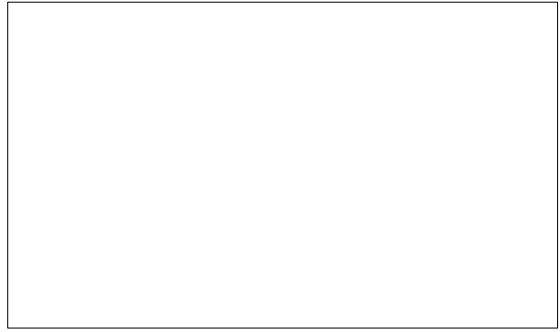


Focus on Mothers 4

Oakfield House, Oakfield Grove
Clifton, Bristol BS8 2BN

Tel: 0117 331 0012
There is an answer phone on this line

E-mail: admin@childrenofthe90s.ac.uk



Permission to complete and use clinic data

We would like to ask you to undertake all of the following measurements/procedures:

Please cross the boxes and initial to indicate that you consent, or leave blank if you do not consent. Also cross and initial to indicate whether you would like us to inform you, and give you a letter to give to your GP, if the results of tests marked * give cause for concern.

	1. Consent to test		2. Consent to inform	
	Cross box	Initial	Cross box	Initial
(a) DXA scan of bone density*, fat and muscle mass	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
(b) Weight, height, waist, hip and arm circumference	<input type="checkbox"/>	<input type="text"/>		
(c) Blood pressure* and pulse pressure	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
(d) pQCT of arm and wrist	<input type="checkbox"/>	<input type="text"/>		
(e) Physical capability tasks	<input type="checkbox"/>	<input type="text"/>		
(f) Assessment of thought processes	<input type="checkbox"/>	<input type="text"/>		
(g) Ultrasound scan of the carotoid artery	<input type="checkbox"/>	<input type="text"/>		
(h) Wound Healing (BCG scar)	<input type="checkbox"/>	<input type="text"/>		
<div style="border: 1px solid black; padding: 5px;"> I understand that donated blood will be considered a gift but I will have the right to withdraw permission for analysis. </div>				
Fasting blood sample for:				
(i) Haemoglobin (test for anaemia)*	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
(j) Glucose (sugar)*	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
(k) Lipids (forms of cholesterol)*	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
(l) Storage for future non genetic research	<input type="checkbox"/>	<input type="text"/>		
(m) Storage for future genetic research	<input type="checkbox"/>	<input type="text"/>		
(n) Hormones related to reproduction and menopause	<input type="checkbox"/>	<input type="text"/>		

Signature

Date signed

		/			/	2	0		
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Initial

Last Name

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The University of Bristol holds legal liability insurance in the event that any participant is injured due to any negligence on the part of the University.



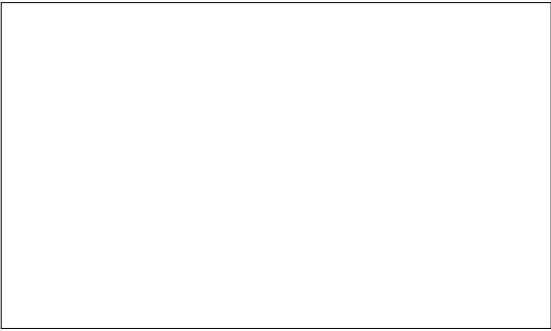


Focus on Mothers 4

Oakfield House, Oakfield Grove
Clifton, Bristol BS8 2BN

Tel: 0117 331 0012
There is an answer phone on this line

E-mail: admin@childrenofthe90s.ac.uk



Permission to use blood sample for cell lines

After processing the name will be taken off the blood samples. The cell lines and DNA samples will be stored with no names attached to them. Results will be used for statistical purposes only and not linked to named people.

CONSENT

The purposes and possible risks in having blood taken have been explained to me. I understand that donated blood will be considered a gift but I will have the right to withdraw permission for analysis.

I understand that the main stocks of DNA and/or cell lines will be stored in Bristol, but that the DNA/cell lines (with an anonymous number only), or information about the sequence of my DNA, may be sent to specialist research laboratories in the UK and abroad for analyses, and the results returned to Children of the 90s. Researchers at these laboratories have no access to personal information about study participants.

I agree that information about my genes can be analysed together with information about my health, disease and life style factors in order to undertake research into biological or genetic factors affecting the risk of developing a range of common medical conditions. I understand that any such analyses will only be undertaken on data from which all personal information has been removed and replaced with an anonymous code.

I agree to having the following blood samples taken for analyses for the Children of the 90s study: (If you consent, please cross the box below)

A sample for cell lines ('immortalised' DNA)	1 <input type="checkbox"/>
--	----------------------------

Signature

Date signed / / 2 0

Initial Last Name

The University of Bristol holds legal liability insurance in the event that any participant is injured due to any negligence on the part of the University.





ALSPAC www.bristol.ac.uk/alspac

Avon Longitudinal Study of Parents and Children

Oakfield House
Oakfield Grove
Clifton
Bristol BS8 2BN
Tel: 0117 3310010
Email: alspac-project@bristol.ac.uk

Partner Enrolment Information Sheet

Your son / daughter has been taking part in the Children of the 90s (ALSPAC) study for the last 18 years. The enclosed information sheet is a reminder about the study and an update on its progress since their birth.

You and your partner have probably completed several (possibly many!) questionnaires about your study child since they were born. We are now focusing in more detail on your health. We hope the question and answer section below will explain why we are doing this now.

Why do you want to enrol me now? The study has been going on for many years.

Partners/fathers have always been part of the study and we recognise their vital impact and influence on the health and development of the children. Until now we have relied on the mother to pass on information to their partner but we would now like to approach you directly.

Some fathers have already said how keen they are to be involved on an equal footing with the mothers.

In the course of the Children of the 90s project, parents have provided information about themselves as well as about their children. This not only enables us to look at how family life affects the development of the children, but also to study parents themselves. We have specific funding in place to look at fathers in more detail.

If I enrol, what happens then?

Filling in the enrolment form just gives us permission to contact you or send you mail directly. You will be asked separately at each point about taking part in different areas of the study.

What will taking part involve?

Within the next year or so:

We will send you a fathers/partners questionnaire about yourself. This will include questions about your health and well-being, life events and activities.

We will ask you to consider letting us take a small sample of your blood for DNA analysis, if you have not already given us one.

Why do you want my DNA?

Learning more about parents and partners themselves

There has been little research on father's genes and how they affect their parenting behaviour. Looking at your DNA will help us to study how your genes affect your behaviour and lifestyle, and how this affects the family environment.

Your DNA will also enable us to investigate factors affecting your own health and help us to focus on the genetic aspects of men's health within the ALSPAC study.

Whether a parent is a biological parent of the study child or not does not affect the value of their DNA to this part of the study.

Parent and children's genes



One of the main aims of the Children of the 90s study is to look at children's genes and their environment to see how they interact to affect health and development.

Each child's genes come from both mother and father, so the value of the genetic information is increased greatly if we are able to look at both parents.

The effect of genes can be altered depending on whether they come from mother or father. DNA from parents will enable us to see how particular genes work in the child depending on which parent they came from.

It is for this reason that studies looking at complex conditions such as asthma, obesity or diabetes need to look at DNA from parents as well as children.

Many parents have already kindly donated a small blood sample, including over 1400 fathers and partners. We would like to increase the numbers of parents taking part in these vital areas of our research.

We will send out further information about the various studies so you can decide if you want to take part. Everything is completely voluntary and we will always ask your consent for relevant areas.

What are the possible disadvantages and risks of taking part?

The main disadvantage is giving up your time to fill in the questionnaire or travelling to our centre to give us a blood sample. We will try to make it as easy as possible for you to visit us by being flexible about appointment times and covering your travelling expenses.

There is a risk of minor discomfort or bruising in giving a blood sample, and there is a slight risk that you will feel faint during or after giving the sample. Our staff are trained how to minimise these events and to look after you if they do. The small amount of blood we are taking will not affect your health. We will check before taking a sample that you are able to do so safely.

What are the possible benefits of taking part?

It is not intended that there will be any direct benefit to your health by taking part in our research.

However, if you attend our centre to give a blood sample, we will give you a letter to give to your GP if your haemoglobin, cholesterol, glucose or blood pressure are outside the normal ranges.

How secure will my information be?

The information we collect from you will be stored for use only by researchers from Children of the 90s and their approved research colleagues. The research data is labelled with a study number only, so it cannot be linked to you. Your personal details are stored separately and securely and not available to those looking at the data. This means you can be sure all your information will be held confidentially.

Will anyone else know that I am taking part?

Any communication between you and the study would be confidential, we would not tell anyone else, including your partner or study child(ren).

Who has approved this study?

- The ALSPAC Executive Committee, a group of the senior researchers and managers who work in Children of the 90s
- The Children of the 90s Law & Ethics Committee, an advisory group with researchers, lawyers and study parents who are there to protect your interests as study members
- All research connected to the NHS is looked at by an independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed and approved by the North Somerset and South Bristol Research Ethics Committee.

What happens if I enrol and then change my mind in the future?



You are free to withdraw any time. Just let us know and we will make the necessary changes. Your decision will not affect the participation of anyone else in the study.

What plans do you have for fathers in the future?

We hope to obtain more research funds to collect clinical measures from fathers/partners just as we have been doing for the study children for a long time now. Study mothers are currently being invited to take part in similar clinics. The measurements we might record include blood pressure and other measures of your heart and circulation.

We hope to send you a further questionnaire in a few years time to collect information on changes in your health and life events, subject to funding being available.

We do hope you will help us continue our research by enrolling in the study and by taking part in the different areas. The Children of the 90s families are unique and irreplaceable.

If you would like more information or have any questions, please look at the study website

<www.bristol.ac.uk/alspac>

or contact:

Jennie Cross (Family Liaison Manager)

Email: alspac-project@bristol.ac.uk

Phone: (0117) 33 10010

address:

Children of the 90s

Oakfield House

Oakfield Grove

Clifton

Bristol BS8 2BN



Enrolment Visit

Visit Number _____

Oakfield House, Oakfield Grove
Clifton, Bristol BS8 2BN

Tel: 0117 331 0012

There is an answer phone on this line

E-mail: focus-admin@bristol.ac.uk

Permission to complete and use clinic data

We would like to ask you to undertake all of the following measurements/procedures:

Please cross the boxes and initial to indicate that you consent, or leave blank if you do not consent. Also cross and initial to indicate whether you would like us to inform you, and give you a letter to give to your GP, if the results of tests marked * give cause for concern.

(a) Weight and height

(b) Blood pressure* and pulse pressure

1. Consent to test		2. Consent to inform	
Cross box	Initial	Cross box	Initial
<input type="checkbox"/>	<input type="text"/>		
<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
<input type="checkbox"/>	<input type="text"/>		

I understand that donated blood will be considered a gift but I will have the right to withdraw permission for analysis.

Blood sample for:

(c) Haemoglobin (test for anaemia)*

(d) Glucose (sugar)*

(e) Cholesterol*

(f) Storage for future research

Signature

Date signed

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DNA, Genes, and Cell Lines

Our genes play an important role in defining many characteristics about individuals and some can make us more or less likely to develop many common diseases. We all have a slightly different set of genes in our bodies. DNA from a child's parents can help us in various ways to look at the effects of these differences. To help us look at these differences and understand varying characteristics and the causes of diseases, we are asking fathers to provide a small blood sample we can use to purify DNA for genetic studies. We are also able to treat the sample to produce a cell line which can provide a never-ending supply of DNA. These cells can also be studied to provide a more detailed description of how some parts of the body work.

What are genes?

Genes are the instructions, which determine growth and development of all living organisms.

What is DNA?

DNA is the chemical language in which genes are written.

Why do you want to study my DNA?

Although we all have essentially the same genes as each other, there are many small differences which some of us have and others do not. These different versions of our genes can make us more likely or less likely to develop many common diseases, such as allergies (like asthma), or diabetes or heart disease and can affect our character and behaviour. This is why studying the genes of non-biological parents is also important, as their genes influence the way they behave, and therefore the environment of the children.

Is it just genes that cause disease?

No. We already know that many of our common health problems are partly caused by genes and partly by our environments.

How will my DNA help?

A child's genes are a mixture of its parents' genes. By having DNA to study parent's genes we can work out which gene variants are responsible for the way in which your child grows and develops. We will also be able to find out how gene variants have affected parents and compare this with affects on the children.

Why do you need cell lines to make DNA?

We each have about 30,000 genes. With your permission, we want to study many of these genes, but the DNA from a single blood sample would run out before we can complete this work. We would like to collect a blood sample from you and treat the cells from the blood so that they can be stored indefinitely as 'immortalised' cell lines. These cells can be used to make more DNA whenever it is needed.

What are immortalised cell lines?

Skin, muscle, bones, blood, and all the other parts of our body, are made up of millions of cells. Each cell has a copy of all our genes. If we take cells from our bodies we can only keep them alive for a limited time. However if cells are treated with a special safe virus they can be kept alive indefinitely - they become *immortalised*.

Do immortalised cell lines have other uses?

Yes they do. Cells from cell lines retain some of the basic features, as well as the DNA, of the people they came from. We can look for changes over time in the way the cells behave and for certain markers. For example, one study found that cell lines from people with raised blood pressure grow faster than those from people with normal blood pressure. Studying cells in this way may provide important stepping-stones that will help bridge the gap between genes and the whole person and improve our understanding of how the two are linked.



Where are my DNA and/or cell lines kept?

The main stocks of DNA and cell lines are stored here in Bristol. They will be kept indefinitely. Small portions of the samples (with an anonymous number) are also sent to specialist research laboratories in the UK and abroad for analysis, and the results are returned to us. Outside researchers who work with Children of the 90's data or samples are bound by a strict code of conduct and have no access to information that would identify study participants.



Will anyone be able to connect the results of genetic tests to me?

No. All the information in the 'Children of the 90s' study is kept separate from your name. No one who works with samples is allowed to know who they came from. This personal information is completely confidential.

Would you ever sell my DNA or cell lines?

No, we would never sell these, or any of the information you have given us.

If the 'Children of the 90's' study makes cell lines from my blood, can I be sure they will not be used for cloning?

Yes, you can be sure. The use of human tissues, DNA, and cell lines is strictly controlled. Charities and government organisations which give money for research, Bristol University, and the Children of the 90s study ethics committee, which includes parents of study participants, would not allow human cloning.

If I change my mind later and don't want you to keep my DNA or cells, what should I do?

You can change your mind at any time. Write to us and say you don't want us to keep your DNA or cells. We will remove the main stocks and destroy them.



What are the possible disadvantages and risks of taking part?

The main disadvantage is giving up your time to visit our centre to give us a blood sample. We will try to make it as easy as possible for you to visit us by being flexible about appointment times and covering your travelling expenses. There is a risk of minor discomfort or bruising in giving a blood sample, and there is a slight risk that you will feel faint during or after giving the sample. Our staff are trained how to minimise these events and to look after you if they do. The small amount of blood we are taking will not affect your health. We will check before taking a sample that you are able to do so safely.

What are the possible benefits of taking part?

It is not intended that there will be any direct benefit to your health by taking part in our research. However, if you attend our centre to give a blood sample, we will give you a letter to give to your GP if your haemoglobin, cholesterol, glucose or blood pressure are outside the normal ranges.

Who has approved this study?

- The ALSPAC Executive Committee, a group of the senior researchers and managers who work in Children of the 90s
- The Children of the 90s Law & Ethics Committee, an advisory group with researchers, lawyers and study parents who are there to protect your interests as study members
- All research connected to the NHS is looked at by an independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed and approved by the North Somerset and South Bristol Research Ethics Committee.

For more information about DNA, genes and cell lines, contact us (details at the top of this sheet) and ask to be put in contact with Dr Sue Ring.



Enrolment Visit

Visit Number _____

Oakfield House, Oakfield Grove
Clifton, Bristol BS8 2BN

Tel: 0117 331 0012

There is an answer phone on this line

E-mail: focus-admin@bristol.ac.uk

Permission to use blood sample for cell lines

After processing the name will be taken off the blood samples. The cell lines and DNA samples will be stored with no names attached to them. Results will be used for statistical purposes only and not linked to named people.

CONSENT

The purposes and possible risks in having blood taken have been explained to me. I understand that donated blood will be considered a gift but I will have the right to withdraw permission for analysis.

I understand that the main stocks of DNA and/or cell lines will be stored in Bristol, but that the DNA/cell lines (with an anonymous number only), or information about the sequence of my DNA, may be sent to specialist research laboratories in the UK and abroad for analyses, and the results returned to Children of the 90s. Researchers at these laboratories have no access to personal information about study participants.

I agree that information about my genes can be analysed together with information about my health, disease and life style factors in order to undertake research into biological or genetic factors affecting the risk of developing a range of common medical conditions. I understand that any such analyses will only be undertaken on data from which all personal information has been removed and replaced with an anonymous code.

I agree to having the following blood samples taken for analysis for the 'Children of the 90s' study: (If you consent, please cross **one** of the boxes below)

A sample for cell lines ('immortalised' DNA) 1

OR

A sample for DNA only 2

Signature

Date signed

<input type="text"/>	<input type="text"/>	/	<input type="text"/>	<input type="text"/>	/	2	0	<input type="text"/>	<input type="text"/>
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The University of Bristol holds legal liability insurance in the event that any participant is injured due to any negligence on the part of the University.

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Fathers Information Leaflet

We are inviting you to the first **FOCUS ON FATHERS** visit.

Participation in the visit is completely voluntary and if you do decide not to participate this will not affect future invitations to you or your child to participate in Children of the 90s research. The visit is for research purposes and consent to take part will be obtained.

This leaflet explains the measurements that will be undertaken at the visit, why these measurements are being done and what they will involve. Please take time to read the following information, which will help you decide whether or not you wish to complete any of them.

Please ask us if there is anything that is not clear.



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What is the purpose of the study?

We would like to study the fathers or partners of the Children of the 90s (ALSPAC) participants as this will allow us to have a better understanding whether the way families' function has any influence on men's health. We have used the term father for any man who has the role of a father figure regardless of whether they are the biological father of the young person. Up to now this sort of research has really only looked at women's health but this new study puts the focus firmly on health issues relevant to men.

In addition, by learning more about the health of the fathers, we can add the data we collect to existing information on the mothers in order to study the influence of both parents on the health of their children.

We already have some information on fathers through questionnaires and obtained a few measures on around 1,570 fathers when they accompanied their children to their visits. Now, for the first time, we have been able to set up a fully equipped clinic for the fathers similar to one which the mothers have been taking part in over the last two years. The visit will help determine what factors are related to body size, bone density, blood pressure, arterial thickness (an indicator of hardening of the arteries or "atherosclerosis"), diabetes and abnormal blood cholesterol. It is important to take these measures now, as in the coming years some of you may experience changes related to ageing, and might take medications which would affect these measures, e.g. blood pressure tablets. In the long term, this information may help us better understand why some people experience more health problems than others or age more rapidly and what can be done to improve the population's health.

What measurements are planned?

We would like to ask you to undertake all of the following:-

a) Before you attend the clinic: We will send you a short questionnaire which we will ask you to complete and bring with you. This will cover your home life, mood and any events you may have recently experienced.

b) Informed consent: At the start of the visit we will go through and explain all of the measurements, answering any questions you may have. We will ask you to complete and sign a consent form which indicates that you agree to these measures.

c) Fasting blood sample and questionnaire: We would like you to come to the Focus centre, if possible not having eaten or drunk anything except water

for at least eight hours. This will allow us to measure your fasting sugar and blood fats known as lipids (e.g cholesterol). Don't worry if you are not able to fast before your visit, your blood sample will still be valuable for research, and we would very much like you to take part.

We will take a blood sample in the usual way. This may be a little uncomfortable and bruising may result, though our staff aim to minimise this. Some people faint when having a blood test; this can occur 'out of the blue' when previously someone had had no problems. We only take blood samples with you lying on a couch to reduce the risk of any injury. In case you do faint, we will make sure you are fully recovered before discussing whether you wish to continue or not. All our staff are fully trained to take blood. After this we will provide you with some food and drink (free of charge) and ask you to fill in a questionnaire about your lifestyle which should take between 10-15 minutes.

Will you be doing anything else with my blood sample? Yes. We will also measure your red blood cells (haemoglobin) and with your consent we would like to store some of your blood sample so we can use it for future research that arises. One of the strengths of the *Children of the 90s* is that it is able to respond quickly to newly recognised questions about health and well-being and this will help us do so.

The samples are stored with unique ID numbers allowing test results to be linked to other data, but that would never allow someone working in a laboratory to be able to link these results to your personal information, i.e. your name, address and date of birth.

Will you be taking blood for genes and DNA? You may be aware that over the last few years we have been collecting extra blood samples from fathers for DNA and 'immortalised' cell-lines. We will ask if you are willing for us to take some additional blood to use for extraction of DNA or establishing 'immortalised' cell-lines. This does not require a separate blood test. A separate information sheet describing the importance of DNA, what immortalised cell-lines are, and their use within *Children of the 90s* is enclosed.

d) Body size and dimensions (anthropometry)

We will measure your weight, height (standing and seated), waist, head, arm circumference and hip size.

e) DEXA scan to measure your lean (muscle) and fat mass, and bone density: We would like to scan your whole body to measure muscle mass, fat mass and overall bone density. We use a machine called a Lunar Prodigy narrow fan beam absorptiometer.

Your clothes must not have any metal fastenings; watches, piercings and other metal objects should be removed if possible, since these can interfere with the result. You will be asked to lie on a couch and remain very still for 6 to 10 minutes.

The machine's arm will pass over you twice; first to scan the whole skeleton, second scan your hip in more detail. The second scan is similar to the first, except that your foot is positioned against a rest to rotate the hip to a 45-degree angle.

The following tells you a little bit more about the DEXA scan and how it measures bone density: DEXA scans measure how much calcium and other minerals are in the bone being looked at. The result is called the 'bone mineral density' (BMD). Denser bones have more calcium and minerals. They are stronger and less likely to break.

Your child will have had a DEXA scan at their previous visits and we are keen to compare your results with theirs.

Are the DEXA scans safe? Yes. The machine uses x-rays but the level of radiation is tiny, e.g. the x-ray dose of 5 micro Sieverts is less than the average daily natural radiation dose we get from the environment around us and does not carry any measurable risk at all.

f) Ultrasound scan of your neck arteries: We would like to take ultrasound scans of your neck arteries, so we can measure the thickness of the artery walls. This measurement is the 'carotid artery intima-media thickness (CIMT)'. The CIMT is related to stiffening of the arteries and to atherosclerosis (fatty deposits inside the arteries) in the whole body.

The scans are done using an ultrasound scanner and scan probe. Scans will be taken on both sides of the neck. Ultrasonic gel is applied to the neck with the probe (the gel is not known to cause any hypersensitivity). The probe is moved to the correct position on one side and held steady while the scanner saves a film of the scan. The procedure is repeated on the other side of the neck. It takes approximately 20 minutes.

Is the ultrasound scan safe? Yes. An ultrasound scan does not use x-rays or gamma-rays. It uses sound waves that have a frequency beyond human hearing. Ultrasound scans have been used widely in clinical practice and research for over 30 years and there are no known risks. It is considered to be very safe.

Will I be told the results of my scan? No, because the results are not useful for telling us if your doctor needs to recommend a particular treatment or lifestyle change. CIMT is a very useful measure for research purposes but is not used by doctors for diagnosing illnesses, e.g. a heart attack or stroke. For this reason we will not be feeding back the results of this test to you.

g) Blood pressure and other cardiovascular measures: We will measure your blood pressure and heart rate in the usual way that you may have had done at your doctor's clinic. In addition, to the normal peripheral blood pressure, we will also use a special machine that calculates "central pressure" which is the resistance that the heart experiences when it has to pump the blood around the body. We will also measure how quickly your blood travels along the arteries as a measure of arterial stiffness (pulse wave velocity); stiffer arteries make the pulse wave go faster.

h) Face shape: We have previously measured your child's face shape using special computer software that produces a three dimensional image and is therefore able to measure things like how prominent are the cheeks or chin and whether the face is symmetrical or not. We would also like to do this on you so that with information from you and the mothers we can see to what degree face shape is influenced by maternal or paternal factors. This would be a unique scientific resource. In addition, we believe that how a baby develops in the womb influences subtle differences in face shape and therefore we want to see if there is a link between this and diseases such as high blood pressure and diabetes.

i) Computer-based questions: We will also ask you to complete some questions about your health in a confidential booth using a computer touch-screen. This will include some questions concerning sexual health which some people find sensitive or embarrassing and which you can omit if you so wish. This should take around 10 minutes.

j) Urine sample: Before you leave the clinic, we would like you to give us a small urine sample (about a 1/3rd of a cup). This will be stored in our freezers for future research that can look at how the body breaks down various proteins and removes them from the body in the urine ("metabolomics")

The visit will take approximately 2 hours and we will cover travel expenses and also provide you with a £10 shopping-gift token to compensate you for your time spent at the clinic.

Do I have to take part?

Not at all. It is up to you to decide whether or not to take part. If you decide to do so you will be asked to sign a consent form. You are still free to withdraw from the study or any of the individual measures at any time.

What will happen if I take part – are there any advantages?

The focus visit is not a health check and we are asking you to help us with research that we hope will help people in the future. Some of the measurements that we take might indicate increased risk for some health problems. Where you have consented for us to feedback any results outside the normal range we will advise you and give you a letter to take to your GP. Other measurements taken are useful for research but their results have no clear clinical meaning, they cannot tell us about any health problems and there are no recommended actions or treatments; therefore we will not tell you about those results.

If we do not feedback any results to you, you should not conclude this means you have a clean bill of health. If you have any symptoms that cause you concern you should contact your GP in the way that you normally would.

The following describes the test results where we plan to provide feedback:-

- If your blood pressure is high we will tell you and give you a letter to take to your GP so that they can test this again.
- If you have low haemoglobin (risk of anaemia) or very high haemoglobin (this can mean your blood flows too slowly), have high blood sugar (an indicator of diabetes), or high levels of total cholesterol, you will be sent a letter along with a letter for you to take to your GP.

The assays for anaemia will be done in our laboratory and a result will be available within 4 weeks (maximum) of your visit. If you have values outside the normal range and have given consent for feedback, you will receive a letter at the latest 4 weeks after your visit for this test. For cholesterol and blood sugar the samples are sent away in batches for testing. Therefore, it could be up to 12 months before the results are fed-back to anyone with levels outside of the normal range. If your levels are outside the normal range for these, and you have given written consent we will send you a letter about this between 4 to 12 months of your visit.

Are there any disadvantages to taking part?

Other than sparing us your time, we do not see any major disadvantages in taking part. We do need you to come to the visit 'fasted' for the blood sample, if at all possible, i.e. having nothing to eat or drink (except sips of water) since the previous night for morning appointments and for the previous 8 hours for afternoon or evening visits. Once the fasting sample has been taken we will provide you with food and drink before doing any further measurements. If it is difficult for you to fast do then let us know and we can still see you and take a blood sample.

Some people are left with bruising after a blood sample has been taken and in a small number this can be quite marked. If you do not want to have a blood sample taken, we would still very much value your participation in the other measurements.

The visit will take approximately 2 hours and we will cover travel expenses.

What do I have to do now?

Please complete and return both sides of the Focus on Fathers appointment form in the stamped and addressed envelope.

Confidentiality and data protection

Any data collected will be stored with individual ID numbers but with no personal information attached. Files that link this ID number to your personal details will be securely stored with only two senior Children of the 90s staff having access to these. The data will be used for research purposes only and will be analysed by our study researchers and research collaborators. None of these researchers will have access to your personal data (i.e. your name, address and date of birth).

What if there is a problem?

If you have a concern about any aspect of this study, you should ask the staff when you attend who will do their best to answer your questions. You can also contact the Children of the 90s Executive Group about any problems of participating in the study.

Who is organising and funding the research?

This research is organised by the Children of the 90s study team and led by Professor George Davey Smith. The Focus on Fathers is funded by the

Wellcome Trust, the UK Medical Research Council and the University of Bristol.

Who has reviewed this study?

The ALSPAC (Children of the 90s) Ethics & Law Committee (which includes parent members) and the North West Haydock NHS Research Ethics Committee.

Contact for further information

Please contact **0117 3310030** to speak to the Visit team if you require more information (there is an answerphone on this line).

If you wish to discuss the study further, please email the ALSPAC (Children of the 90s) Executive Group at alspac-exec@bristol.ac.uk.

Thank you for your time in reading about Focus on Fathers and for your ongoing support of Children of the 90s.



ALSPAC www.bristol.ac.uk/alspac

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DNA, Genes, and Cell Lines

Our genes are important in making us more or less likely to develop many common diseases. We all have a slightly different set of genes in our bodies. DNA from a child's parents can help us in various ways to look at the effects of these differences.

We are therefore asking fathers visiting clinics if they would be prepared to provide a small blood sample which can be treated so that it provides a never-ending supply of cells, which can in turn, be used to provide DNA. These cells can also be studied to provide a more detailed description of how some parts of the body work. We would also take the opportunity to save some of the blood so that we could measure other things, like cholesterol.

What are genes?

Genes are the instructions which determine growth and development of all living organisms.

What is DNA?

DNA is the chemical language in which genes are written.

Why do you want to study my DNA?

Although we all have essentially the same genes as each other, there are many small differences which some of us have and others do not. These different versions of our genes can make us more likely or less likely to develop many common diseases, such as allergies (like asthma), diabetes or heart disease, and can affect our character and behaviour. This is why studying the genes of non-biological parents is also important, as their genes influence the way they behave, and therefore the environment of the children.

Is it just genes that cause disease?

No. We already know that many of our common health problems are partly caused by genes and partly by our environments.

How will my DNA help?

A child's genes are a mixture of its parents' genes. By having DNA to study parent's genes we can work out which gene variants are responsible for the way in which your child grows and develops. We will also be able to find out how gene variants have affected parents and compare this with affects on the children.

Why do you need more DNA?

We each have about 30,000 genes. With your permission, we want to study many of these genes, but the DNA from a single blood sample (if you have already provided one) would run out before we can complete this work. Therefore, we would like to collect a blood sample from you and treat the cells from the blood so that they can be stored indefinitely as 'immortalised' cell lines. These cells can be used to make more DNA whenever it is needed.

What are immortalised cell lines?

Cells are the building blocks of the body. Skin, muscle, bones, blood, and all the other parts of our body, are made up of millions of cells. Each cell has a copy of all our genes. If we take cells from our bodies we can only keep them alive for a limited time. However if cells are treated with a special safe virus they can be kept alive indefinitely - they become *immortalised*.

Do immortalised cell lines have other uses?

Yes, our study is unique in its detailed descriptions of its participants gathered over many years (as you have probably realised!). One of the ways in which we may be able to add further important information is by studying *immortalised* cell lines. Cells from cell lines retain some of the basic features, as well as the DNA, of the people from whom they were derived. For example, one study



found that cell lines from people with raised blood pressure grow faster than those from people with normal blood pressure. Studying cells in this way may provide important stepping-stones that will help bridge the gap between genes and the whole person and improve our understanding of how the two are linked.

Will anyone be able to connect the results of genetic tests to me?

No. All the information in the 'Children of the 90s' study is kept separate from your name. No one who works with samples is allowed to know who they came from. This personal information is completely confidential.

Where are my DNA and/or cell lines kept?

The main stocks of DNA and cell lines are stored here in Bristol. They will be kept indefinitely. Small portions of the samples (with an anonymous number) are also sent to specialist research laboratories in the UK and abroad for analysis, and the results are returned to us. Outside researchers who work with Children of the 90's data or samples are bound by a strict code of conduct and have no access to information that would identify study participants.



Would you ever sell my DNA or cell lines?

No, we would never sell these, or any of the information you have given us.

If the 'Children of the 90's' study makes cell lines from my blood, can I be sure they will not be used for cloning?

Yes, you can be sure. The use of human tissues, DNA, and cell lines is strictly controlled. Charities and government organisations which give money for research, Bristol University, and the Children of the 90s study ethics committee, which includes parents of study participants, would not allow human cloning.

If I change my mind later and don't want you to keep my DNA or cells, what should I do?

You can change your mind at any time. Write to us and say you don't want us to keep your DNA or cells. We will remove the main stocks and destroy them. Your samples will not be used for any further tests, and we will not use the results of any analysis being carried out at the time of your withdrawal of consent.



If you would like to know more about the problems we may be able to solve by having parents' DNA, there is a more detailed document available.

For more information, please phone 0117 3310030, or ask the clinic staff. They will be able to help you, or put you in touch with someone who can.



Focus on Fathers

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Tel: 0117 331 0012

There is an answer phone on this line

E-mail: focus-admin@bristol.ac.uk

**PLEASE ENSURE
BARCODE LABEL IS
ON OTHER SIDE**

Permission to use blood sample for cell lines

After processing the name will be taken off the blood samples. The cell lines and DNA samples will be stored with no names attached to them. Results will be used for statistical purposes only and not linked to named people.

CONSENT

The purposes and possible risks in having blood taken have been explained to me. I understand that donated blood will be considered a gift but I will have the right to withdraw permission for analysis.

I understand that the main stocks of DNA and/or cell lines will be stored in Bristol, but that the DNA/cell lines (with an anonymous number only), or information about the sequence of my DNA, may be sent to specialist research laboratories in the UK and abroad for analyses, and the results returned to Children of the 90s. Researchers at these laboratories have no access to personal information about study participants.

I agree that information about my genes can be analysed together with information about my health, disease and life style factors in order to undertake research into biological or genetic factors affecting the risk of developing a range of common medical conditions. I understand that any such analyses will only be undertaken on data from which all personal information has been removed and replaced with an anonymous code.

I agree to having the following blood samples taken for analyses for the 'Children of the 90s' study: (If you consent, please cross **one** of the boxes below)

A sample for cell lines ('immortalised' DNA) 1

OR

A sample for DNA only 2

Signature

Date signed

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The University of Bristol holds legal liability insurance in the event that any participant is injured due to any negligence on the part of the University.

