Research study checklist

1. Samples from affected child and parents

DNA (5-10ug) ☐

OR

Blood - EDTA ☐

2. Clinical information

Completed Clinical data sheet including pedigree ☐

Photos ☐

3. Consent

Consent obtained using Scottish MREC forms, enclosed ☐

(give patient copy of study information sheet and GDPR transparency document)

OR

Consent obtained under local research ethics approval and

Copy of research ethics committee approval enclosed.* ☐

4. Transportation:

No risk factors for blood-borne viral infections (HIV/Hepatitis B,C)

Commercial invoice, 6 copies (International samples) ☐

Where required by your national law, authorisation for sending patient DNA/samples should be obtained and a *copy of the authorisation sent with the samples*** ☐

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*As a requirement of our European Research Council funding we are asked to submit a copy of your local research ethics committee approval before starting work on samples consented using local ethics forms. If this is not possible, we have approval by the Scottish NHS Multicentre Research Ethics Committee for use of research samples from international collaborators who have used our research consent forms and information sheets. All consent should be taken in accordance with local professional and regulatory standards.

**not required for EU countries.

Clinical Data Sheet
Microcephalic Primordial Dwarfism

INSTITUTE OF GENETICS & CANCER

Name: _____

Date of birth: _____ **Male / Female**

Hospital record/Pedigree Number _____

Clinician (to send report to):_____

Email: _____

UK only: DDD study ref:_____ **GEL ref:**_____

Required Information: Please note we are unable to commence sequencing until growth information is provided.

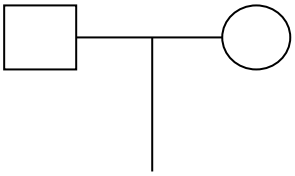
		Date	Weight/kg	OFC/cm	Height/cm
At Birth	**Gestation:**				
At Recent assessment	**Age:**				

MENTAL RETARDATION	None/Mild/Moderate/Severe, or IQ:
CONSANGUINITY	Yes/No Degree:.....
PATELLA SMALL OR ABSENT?	Yes/No Examination: Palpation/USS/Xray Please note patella are not visable on Xray prior to 6 years of age
EARS	Normal/Small Please provide photo if abnormal

Additional Information (please continue overleaf if required)

MEDICAL HISTORY (Please circle or tick box if present)	Teratogen Exposure/Drug Use Yes/No Skin/Hair/Teeth/Nails Normal/Abnormal Deafness ☐ Cytopenia ☐ Recurrent Infections ☐ Diabetes ☐ Seizures ☐ Details.....
EXAMINATION	Malformations ☐ Neurological Deficit ☐ Details.....
INVESTIGATIONS	**Array-CGH Y/N/In progress** MRI/MRA ☐ Skeletal Survey ☐ Results.....

PLEASE SUPPLY COPY OF PEDIGREE OR DRAW OVERLEAF



Consent Form (12/06/23, Version 4)

INSTITUTE OF GENETICS & CANCER

Genetic disorders of growth, development and the brain

Adult Consent Form

Name: **Date of Birth:**

Please keep a copy of this signed form in the patient record

I have read *Information for families: Genetic disorders of growth, development and the brain*: **Yes / No**

I give permission**:**

To: (name of clinician or genetic counsellor)
Of: (insert Departmental address)

To perform genetic tests on our DNA samples to try to establish a cause for my condition (specify name/description of condition):
Yes / No

I would like to receive the result of any genetic finding relating to my genetic condition via the referring clinician:
Yes / No

I understand that:

- My name will not be published.
- Any clinical information and photographs relating to me will be stored securely in the MRC Human Genetics Unit and will be used only for research purposes
- Only genetic information likely to relate directly to the cause of your condition will be reported back to your doctor.
- Anonymised clinical and genetic data from you/your family may be made accessible to other researchers.

Signature of patient ..... Date .....

Signature of clinician ..... Date .....

Thank you for taking the time to read and complete this form. Please return it to your doctor.

Consent Form (12/06/23, Version 4)

INSTITUTE OF GENETICS & CANCER

Genetic disorders of growth, development and the brain

Adult (unable to consent for themselves) Consent Form

Patient's Name: **Date of Birth:**

Please keep a copy of this signed form in the patient record

I have read *Information for families: Genetic disorders of growth, development and the brain*: **Yes / No**

I give permission**:**

To: (name of clinician or genetic counsellor)
Of: (insert Departmental address)

To perform genetic tests on _____'s DNA sample to try to establish a cause for his/her condition (specify name/description of condition):
Yes / No

I would like to receive the result of any genetic finding relating to his/her genetic condition via the referring clinician: **Yes / No**

I understand that:

- _____'s name will not be published.
- Any clinical information and photographs relating to him/her will be stored securely in the MRC Human Genetics Unit and will be used only for research purposes
- Only genetic information likely to relate directly to the cause of his/her condition will be reported back to his/her doctor.
- Anonymised clinical and genetic data from his/her family may be made accessible to other researchers.

Signature of person consenting* ..... Date .....

Signature of clinician ..... Date .....

Thank you for taking the time to read and complete this form. Please return it to your doctor.

* This should be the patient's legal proxy or equivalent in your country. (eg. Scotland:- welfare guardian/attorney or nearest relative).

Consent Form (12/06/23, Version 4)

INSTITUTE OF GENETICS & CANCER

Genetic disorders of growth, development and the brain

Parent/Guardian Consent Form

Please keep a copy of this signed form in the patient record

I/We have read *Information for families: Genetic disorders of growth, development and the brain*: **Yes / No**

I/We give permission on behalf of my/our child

Named: **Date of Birth:**

And myself/ourselves:

Mother (Full Name):

Father (Full Name):

To: (name of clinician or genetic counsellor)
Of: (insert Departmental address)

To perform genetic tests on our DNA samples to try to establish a cause for my/our child's condition (specify name/description of condition):
Yes / No

I would like to receive the result of any genetic finding relating to my child's genetic condition via the referring clinician: **Yes / No**

I/We understand that:

- My child's name will not be published.
- Any clinical information and photographs relating to my child will be stored securely in the MRC Human Genetics Unit and will be used only for research purposes
- Only genetic information likely to relate directly to the cause of your child's condition will be reported back to your doctor.
- Anonymised clinical and genetic data from your family may be made accessible to other researchers.

Signature of mother ..... Date .....

Signature of father ..... Date .....

Signature of legal guardian ..... Date .....

Signature of clinician ..... Date .....

Thank you for taking the time to read and complete this form. Please return it to your doctor.

INSTITUTE OF GENETICS & CANCER

STUDY TITLE: Genetic disorders of growth, development and the brain
Family information sheet (primordial dwarfism)
(Version 6, date 12/06/23)

We would like to invite you to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

The aim of this study is to identify genes that cause reduced growth. In particular we are studying conditions in which growth is reduced from early on in development. The conditions we are studying include diagnosis such as Microcephalic Dwarfism, MOPD II, MOPD I/III, Seckel syndrome, Meier Gorlin syndrome and Dubowitz syndrome. Finding such genes will help make genetic testing possible for these disorders. This knowledge may eventually help in the management and treatment of these or other illnesses. Our research can also help understand how these genes normally work in the human body and brain.

Why has my family been chosen?

You have been approached about this research because you have a family member/relative whose reduced growth could be caused by changes in such a gene.

Do we have to take part?

It is up to you to decide whether or not to take part. If you decide to take part you are free to withdraw from the study at any time and without giving a reason. This will not affect the standard of care you receive in any way.

What will happen to me if our family takes part?

If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. Your doctor will also take into consideration children's views, according to their age and intellectual ability, in the consent process. We will ask your doctor to take a sample of blood from your affected family member. We may also ask for samples from unaffected family members. Occasionally, it could be helpful to also have a very small piece of skin, and if so this will be discussed with you. Likewise, very occasionally, it may be useful to study a spare tissue left over from an operation or medical procedure, and if so this will be discussed with you.

These samples will provide us with DNA which can then be used to identify and test genes. Cells from these samples will be stored in the laboratory and may be used to create cell lines. Cell lines provide a renewable supply of DNA and a source of cells for study. Studying cells will help with understanding how these conditions occur as well as the normal role of these genes in the body. We may also convert cell lines into other cell types to grow cells and small amounts of tissue most relevant to the disorder being studied.

The sample will be used for research purposes only and will be stored indefinitely. The sample will be treated as a gift from you, and will be under the custodianship of the MRC Human Genetics Unit at the University of Edinburgh.

We will also ask your doctor for clinical information about your family member, relevant to their condition (that may include photos, if these are part of their clinical record). Any personal data and information given to us will be kept confidential.

What are the possible benefits of taking part?

A gene change could be identified in your family during the research which would provide an explanation for the reduced growth and make gene testing for family members possible. However, there may be no direct benefit from this research to you or your family. There would not be any financial benefit to you if this research led to the development of a new treatment or medical test.

What are the possible disadvantages and risks of taking part?

There is a risk of some minor discomfort and bruising from the blood or skin sample. Your doctor will make sure that any distress caused to children is kept to a minimum, for instance by using local anaesthetic cream to numb the area, before the sample is taken. For those with needle-phobia samples of saliva, can be taken instead to obtain DNA.

How will my information be kept confidential?

Names and dates of birth along with clinical information will be stored securely at the MRC Human Genetics Unit. Each individual in the study is given a unique code number which is held securely at the Human Genetics Unit, and is used to label all samples stored.
DNA samples and cell lines will be stored and analysed in the MRC Human Genetics Unit. Anonymised (coded) samples and cell lines may also be sent to other research labs for analysis (such as the Wellcome Trust Sanger Institute, Cambridge for high throughput genome sequencing).
Anonymised data generated from the analyses may also be shared with other research teams performing similar work, to increase the chance of important discoveries. Likewise, results of whole genome sequencing will be shared with the wider research community by storing the information in an archive called EGA (www.ebi.ac.uk/ega). The genetic data that is deposited will be identified only by a code number and will only be accessible to bona fide researchers who have agreed to use the data for research and to keep the data confidential and safe.

What if new information becomes available?

Information relevant to the condition being studied in your family may be discovered. This may mean that gene testing became possible for your family. You will be given the option on the consent form to say if you would like to be re-contacted in that case. A diagnostic test would require discussion with your doctor. A new DNA sample might be needed for the diagnostic test that is then arranged.

Will any genetic tests be done for any other diseases?

No. The analyses that are done during the project will examine the DNA at very high resolution to determine the cause of condition being studied. Because the approaches are genome-wide, these techniques could also identify other genetic problems that are not related to this condition, but only in rare cases. This would be termed an incidental finding. We will NOT look for or follow up on such possible changes in the DNA sequence.

What happens when the research study finishes?

DNA and tissue samples will continue to be stored at the MRC HGU after the study is ended. These samples may be used for future related research studies. Every care will be taken to prevent misuse of your sample by other researchers, and such future studies will require approval by an Ethics Committee. If a future study will provide information useful to you the samples will be anonymised by coding. Otherwise, such samples will be completely anonymised. Completely anonymous cell lines may be deposited at the end of the research in a European or International cell-line bank so that they could be available to other qualified researchers to increase the possibility of future important discoveries. Such researchers would generally be academic researchers at other Universities, but could possibly include those working for companies.

How long will the study take and what will happen to the results of the research study?

The study is currently funded until 31/03/2028. Gene sequencing of an already identified gene(s), may identify the cause your condition in 6-12 months, however, it may take much longer to identify the responsible gene, and we plan to continue working on your sample until we do so. The results from the study will be published in scientific medical journals during the study and after its completion.

Who is funding the research?

The Medical Research Council and European Research Council are funding this research.

Contacts for further information

In this leaflet we have tried to answer any questions you may have about the project. If you have more questions, please ask your clinical geneticist or specialist for further explanation. If you still have queries after speaking with them, please contact:

Prof Andrew Jackson
MRC Programme Leader and Hon. Consultant Clinical Geneticist
MRC Human Genetics Unit
Institute of Genetics and Cancer, University of Edinburgh
Western General Hospital
Edinburgh EH4 2XU
Tel: 0131 651 8500

If you have any concerns or complaints arising from this research study please contact:
Stephen Lissaman, IGC Business Manager, MRC Human Genetics Unit, IGC, University of Edinburgh, Edinburgh, EH4 2XU.

INSTITUTE OF GENETICS & CANCER

STUDY TITLE: Genetic disorders of growth, development and the brain
Child information sheet (primordial dwarfism)
(Version 4, date 12/06/23)

We would like to invite you to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and talk to your family about it. Ask us if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

We are trying to identify the genes that cause people to be much smaller than average. We hope that our research will help explain how your condition occurred. Finding these genes will help make gene tests possible. It could also help us to understand how these genes normally work in the body.

Why has my family been chosen?

You have been approached about this research because your doctor thinks your small size could be caused by a gene change.

Do we have to take part?

It is up to you and your parents to decide whether or not to take part. If you decide not to take part, this will not affect the care you get from your doctors in any way.

What will happen to me if our family takes part?

If you do decide to take part you will be given this information sheet to keep. Your parents will be asked to sign a consent form. Your doctor will also check with you that you agree as well. Your doctor will also take a small blood sample for you. (If you don't like needles he may instead ask you to provide a spit sample). This will provide us with DNA which can then be used to look at your genes. We may also look at the cells in your blood and study how these grow and divide.

The samples that you give will only be used for research. They will be treated as a gift from you. They will be looked after by the MRC Human Genetics Unit at the University of Edinburgh.

We will also ask your doctor for medical information about your condition. Your personal information will be kept confidential by us.

What are the possible benefits of taking part?

We may be able to identify the gene that is causing your condition during our research. This would help us explain why you are smaller than other children of your age. This will also make gene testing for your family. This could help with diagnosis and your medical care. However, we may not be able to find the gene and so there may also be no direct benefit to you or your family

What are the possible disadvantages of taking part?

Like any blood sample, taking the blood might hurt a little, but your doctor may use cream to numb the skin to stop this happening. Also sometimes you could end up with a small bruise from the blood sample, but this would go away in a few days.

Contacts for further information

In this leaflet we have tried to answer any questions you may have about the project. If you have more questions, please ask your doctor for more explanation. If you still have questions after speaking with them, you can write to or phone me:

Professor Andrew Jackson
MRC Programme Leader and Hon. Consultant Clinical Geneticist
MRC Human Genetics Unit
Institute of Genetics and Cancer, University of Edinburgh
Western General Hospital
Edinburgh EH4 2XU
Tel: 0131 651 8500

June 2023

DNA and Blood Sample Sending Instructions

Blood samples

Please send 5-10ml EDTA blood sample from the affected child and parents. For small children please send 5ml, or no more than 1ml/kg body weight. DNA samples (or blood) from unaffected siblings are also appreciated where available.

Send samples at room temperature, ideally to arrive within 48 hours. So that we can receive and process samples during weekdays, we would prefer samples to be collected and shipped as early in the week as possible (i.e. Monday/Tuesday).

DNA samples

Please send 5-10ug DNA from affected child and parents.

Please send to:

Andrea Robertson/Maggie MacDonald
Andrew Jackson Lab
MRC Human Genetics Unit, IGC
University of Edinburgh
Crewe Road
Edinburgh
EH4 2XU
UK
Tel: +44 (0) 131 651 8500

For blood samples, please notify us of the expected arrival date and the parcel tracking number - email:
andrea.robertson@ed.ac.uk, m.e.macdonald@ed.ac.uk

Sending samples from abroad, please complete and enclose 5 copies of the commercial invoice form (also in the information pack) with the blood samples to ensure clearance through customs into the UK. Blood and skin samples should be shipped at room temperature. With longhaul flights, samples may be exposed to very low temperatures. Therefore, insulation by wrapping the blood sample tubes in tissue/paper, and if at all possible placing them in a polystyrene box, will ensure they are preserved as well as possible.

Samples should be packed in accordance with IATA regulations.

Infection Risk

Finally, for our lab workers, please ensure there are no risk factors in the family for blood-borne viral infections (ie. HIV/hepatitis B, C). We can not accept high risk samples.

Do please let us know if you need any further information or clarification - andrea.robertson@ed.ac.uk, m.e.macdonald@ed.ac.uk, andrew.jackson@ed.ac.uk.

June 2023

Skin Biopsy Sample Sending Instructions

Skin biopsies should be taken using standard aseptic technique, eg. using a 3mm punch biopsy. Prior to biopsy the site should be thoroughly washed with an antiseptic soap (eg chlorhexidine) and this washed off with PBS (or wiped with 70% ethanol, which is allowed to dry before the biopsy is taken). Iodine and Mercurochrome-like antiseptics (eg Betadine) should be avoided.

The skin biopsy sample should be placed in a sterile tube containing cell culture media or PBS. This should be shipped immediately to us at room temperature. We would prefer samples to be collected and shipped as early in the week as possible to ensure they arrive as quickly as possible. Ideally we would like to receive samples within 2-3 days. Please use a tracked-delivery method (ie courier) and notify us of the tracking number on sending the sample. Our FedEx number is: 5412 7866 4

Disposable biopsy punches and sterile sample containers with culture media can be provided if needed.

Please send to:
Andrea Robertson/Maggie MacDonald
Andrew Jackson Lab
MRC Human Genetics Unit, IGC
University of Edinburgh
Crewe Road
Edinburgh
EH4 2XU
UK
Tel: +44 (0) 131 651 8500

Please email us with the expected arrival date and parcel tracking number: andrea.robertson@ed.ac.uk, m.e.macdonald@ed.ac.uk

Sending samples from abroad, please complete and enclose 5 copies of the commercial invoice form (also in the information pack) with the skin samples to ensure clearance through customs into the UK. Skin samples should be shipped at room temperature. With longhaul flights, samples may be exposed to very low temperatures. Therefore, insulation by wrapping the sample tubes in tissue/paper, and if at all possible placing them in a polystyrene box, will ensure they are preserved as well as possible. Samples should be packed in accordance with IATA regulations.

Infection Risk
Finally, for our lab workers, please ensure there are no risk factors in the family for blood-borne viral infections (ie. HIV/hepatitis B, C). We can not accept high risk samples.

Do please let us know if you need any further information or clarification – andrea.robertson@ed.ac.uk, m.e.macdonald@ed.ac.uk, andrew.jackson@ed.ac.uk.

INSTITUTE OF GENETICS & CANCER

Medical Research Council

THE UNIVERSITY of EDINBURGH

CANCER RESEARCH UK

Commercial Invoice

From:

To:

Andrea Robertson/Maggie MacDonald
Andrew Jackson Lab
MRC Human Genetics Unit
University of Edinburgh
Crewe Road
Edinburgh
EH4 2XU

Tel: +44 (0) 131 651 8500

AWB # -

VAT No: 592950700

The Shipment contains:

Human Blood Samples- for medical research purposes only.

The sample is being supplied free of charge with no commercial transaction involved to be used for medical research and laboratory use only.

Value for custom purposes only £1.00

I can confirm –

1. That this material is not known or suspected to contain an etiological agent, host, or vector of human disease.
2. The material is non-hazardous, non-contagious and non-toxic.
3. The material does not come from a facility where work with exotic viruses affecting livestock and avian species is conducted.
4. The material is not recombinant.
5. The contents are for research purposes only.
6. Being supplied free of charge with no commercial transaction involved for medical research purposes only.

I hereby certify that the contents of this consignment are fully and accurately described above by the proper shipping name and are classified, packed, marked and labelled, and in proper condition for carriage by air according to applicable national regulations and IATA regulations.

Certified true and correct,

Height and Head circumference charts
Primary Microcephaly and Primordial Dwarfism research projects

Research Use Only

Derived from British Birth Cohort data, using LMSgrowth and
With thanks to Prof Tim Cole and Huiqi Pan for their help.

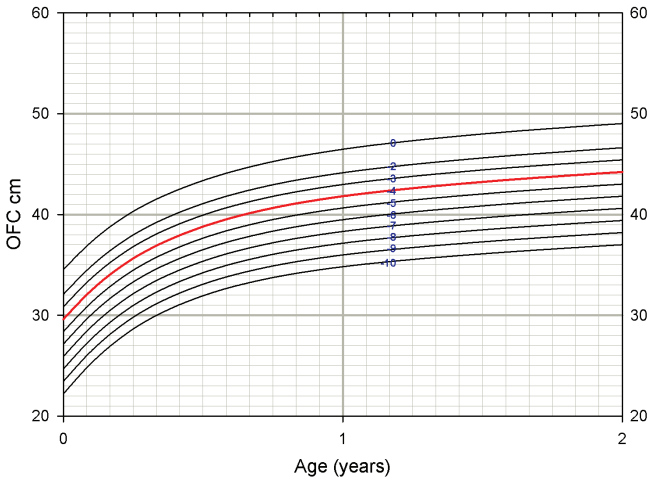
These charts have not been extensively validated, and so to be used at the user's own risk. Please let me know if there are any improvements I can make.

Andrew Jackson

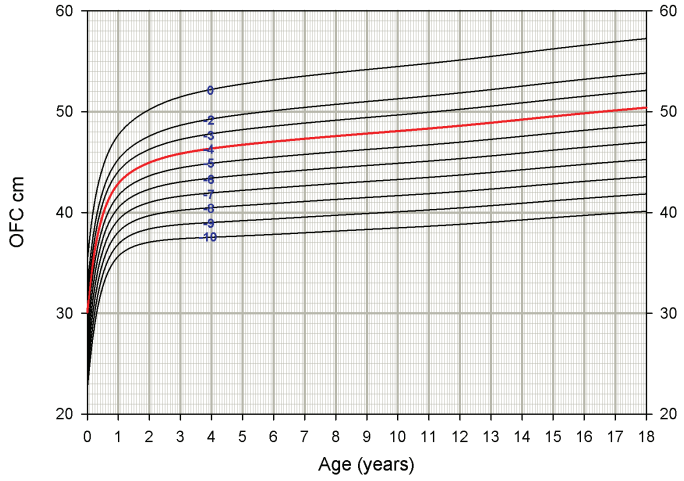
November 2009

Male HC- standard deviations below mean

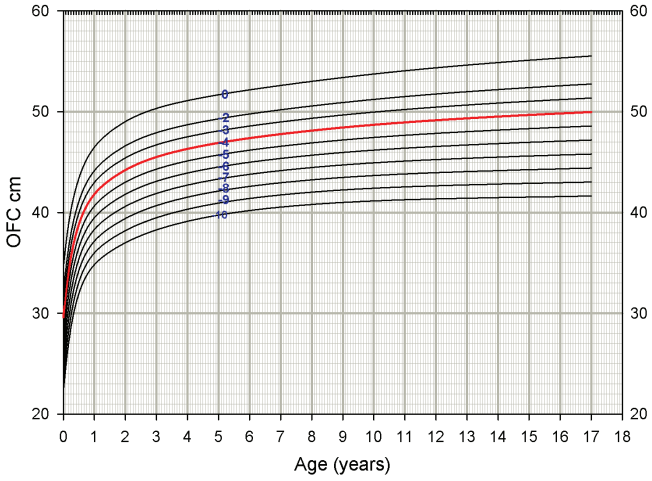
Female HC- standard deviations below mean



Male HC- standard deviations below mean



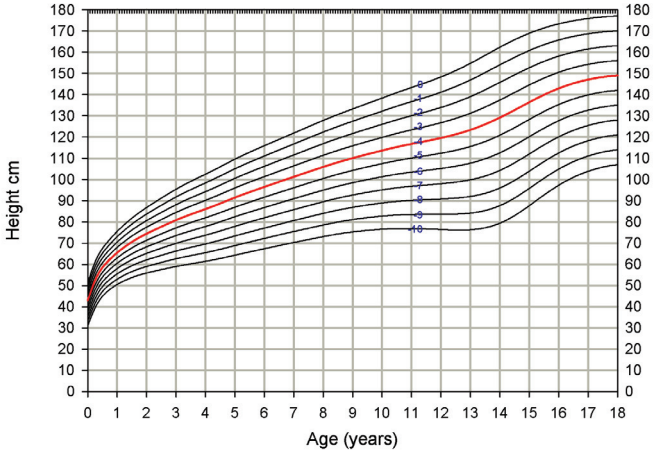
Female HC- standard deviations below mean



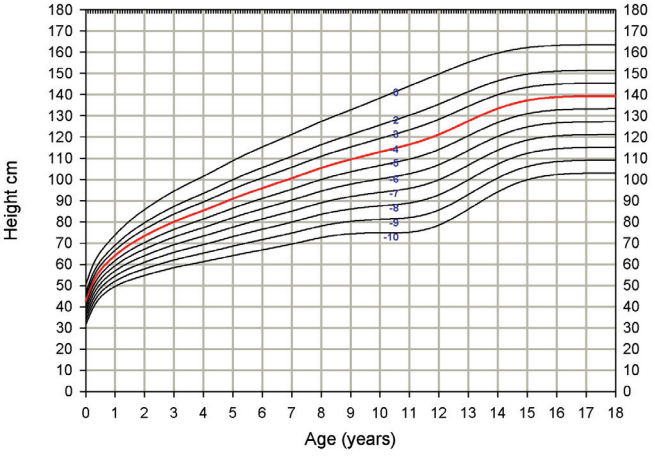
Male height - standard deviations below mean

Female height - standard deviations below mean

Male height - standard deviations below mean



Female height - standard deviations below mean



General Data Protection Regulation (GDPR) Participant Information

Genetic disorders of growth, development and the brain

20th August 2018. Version 1

The EU General Data Protection Regulation (GDPR), along with the new UK Data Protection Act, will govern the processing (holding or use) of personal data in the UK.

You are receiving this as you/your child is a participant in this clinical research study. The information below details what data is held about you and who holds or stores this.

University of Edinburgh and NHS Lothian are the co-sponsors for this study based in the United Kingdom. We will use information from you/your child's medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. The University of Edinburgh will keep identifiable information about you/your child for 20 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

Providing personal data directly e.g. verbally, in a questionnaire or from your care provider

The University of Edinburgh will use your/your child's name, hospital number(s), and date of birth to contact your clinician(s) about the research study, and make sure that relevant information about the study is recorded, and to oversee the quality of the study. Individuals from the University of Edinburgh and official regulatory organisations may look at your medical and research records to check the accuracy of the research study. The only people in University of Edinburgh who will have access to information that identifies you will be members of the research team who are clinicians and/or staff members who need this information to encode (anonymise) samples received and to generate reports for your clinician(s).

Providing personal data indirectly e.g. from your medical records

The University of Edinburgh will also receive information about you for this research study from your/your child's own doctors' records. This information may include your/your child's name, address, hospital number(s) and date of birth and health information, which is regarded as a special category of information. We will use your/your child's health information in the research project.

Contact for further information

You can find out more about how we use your information and our legal basis for doing so in our Privacy Notice at www.accord.scot.

For further information on the use of personal data by NHS sites, please link to the Health Research Authority (HRA) website; https://www.hra.nhs.uk/information-about-patients/.

If you wish to raise a complaint on how we have handled your personal data, you can contact our Data Protection Officer who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO) at https://ico.org.uk/.

Data Protection Officer contact information:

University of Edinburgh
Data Protection Officer
Governance and Strategic Planning
University of Edinburgh
Old College
Edinburgh
EH8 9YL
Tel: 0131 651 4114
dpo@ed.ac.uk

NHS Lothian
Data Protection Officer
NHS Lothian
Waverley Gate
2-4 Waterloo Place
Edinburgh
EH1 3EG
Tel: 0131 465 5444
Lothian.DPO@nhs.net