



**The GHD Reversal Trial**

The Growth Hormone Deficiency Reversal Trial: Effect on final height of discontinuation vs continuation of growth hormone treatment in pubertal children with isolated growth hormone deficiency – A non-inferiority randomised controlled trial

**Young Person 16-18 Years Information Sheet**

1. **Invitation and brief summary**

We would like to invite you to take part in our research study.

Our study is about young people who have been diagnosed with Growth Hormone Deficiency (GHD) as children and so are taking growth hormone medication to help with their growth. When these children enter puberty we think their bodies may produce enough growth hormone naturally, so they may not need to take growth hormone medication for their growth anymore. We want to find out if children who stop taking their growth hormone medication when they are in early puberty still grow as much as children who carry on taking the medication. Joining the study is entirely up to you. Before you decide, we would like you to understand why the research is being done and what it will involve for you.

A member of our team will go through the study with you and answer any questions that you might have. Please take your time to read the information carefully and ask any questions, so that you can make an informed choice about your taking part in the GHD Reversal trial.

Please feel free to talk to others (e.g. members of the research team, family and friends) about the study if you wish, to help you to decide whether or not you would like to take part, and to answer any questions you may have.

1. **Purpose and background to the research**

Growth hormone is a chemical that occurs naturally in the body and that helps to encourage growth. In our research study we are interested in young people who have been diagnosed with Growth Hormone Deficiency (GHD) but who have started to produce a ‘normal’ amount of growth hormone on their own as they start puberty.

Most people with GHD are diagnosed when they are children. To try to make sure that they have enough growth hormone to continue to grow they have daily injections of growth hormone. Recently, research has shown that when some children enter puberty they start to produce a normal amount of growth hormone of their own and so may not need the daily injections to continue to grow.

If our research shows that young people are making enough growth hormone to carry on growing themselves it would be very important as it will free them from the burden of daily injections and from taking a medicine that they don’t need, and this would save money for the NHS.

Our research study will recruit 138 young people from hospitals in the UK and Austria who have previously been diagnosed with GHD, but in whom tests have shown that they are now producing a normal amount of growth hormone of their own. The young people will be put into one of two groups – half will stop taking growth hormone medication, and half will continue taking growth hormone medication. Our trial is a ‘randomised controlled trial’. This means that the group each young person is put into will be chosen at random by a computer, to make sure that the results are fair.

It is up to you if you want to take part in this study. If you choose not to take part in the study it will not affect the care you receive in any way. You will continue to be treated by your doctor as normal.

1. **Why have I been chosen?**

You have been asked to take part in this study as you have been previously diagnosed with GHD. You will have stopped your growth hormone injections temporarily for the growth hormone stimulation test. This test has shown that you are now making a normal amount of growth hormone. This means that you may be producing enough growth hormone to reach your final height without needing more.

1. **What would taking part involve?**

If you agree to take part in this study, you will be put into one of two study groups. One group will stop taking their growth hormone injections whilst the other group will continue taking their growth hormone injections. The group that you are put into is randomly chosen by a computer, so if you are already sure that you want to keep on taking your growth hormone injections, or are already sure that you want to stop taking your growth hormone injections, then you won’t be able to take part in this study.

If you have agreed to take part in the study, we will ask you to sign a form to record this.

Similarly to when you go to hospital for your routine GHD checkups, your height and weight will be measured and blood samples will be taken (to look at the lipids and level of growth hormone in it). To make sure that the height measurement is as accurate as possible, you will be measured repeatedly until 3 measurements in a row are all within 0.5 cm of each other. A blood sample will be taken, approximately 5 ml (1 teaspoon) of blood at each appointment. Additionally, you will be asked to fill in a short questionnaire called the CHU-9D (which will take no longer than five minutes to complete in clinic) so we can estimate how you feel about your life on the day. An X-ray of your hand will be performed. This will be used to tell us about your skeletal growth, which is measured in years and is called your bone age.

After this, you will continue with your regular 6 monthly visits to your hospital’s Endocrine clinic where your growth will be monitored until you reach your near ‘final height’ – defined in this study as growing at less than 2 cm per year, and a bone age of 14 (for females) and 16 (for males). At this point you will have another hand X-ray to measure your bone age, which is an extra X-ray compared to what would be your usual standard care. With your permission we will send a copy of these X-rays to Great Ormond Street Hospital in London (if you are based in the UK) or to Kepler Universitätsklinikum in Linz (if you are based in Austria), so they can determine your skeletal growth (bone age). This information will be passed onto the GHD Reversal Trial team at the University of Birmingham.

At the 6 monthly visits your height and weight will be measured, and blood samples (approximately 5 ml, 1 teaspoon, per appointment) will be taken to look at the levels of growth hormone in it. In addition, the blood sample will also be used to measure lipids at the final assessment. You will be asked to complete another questionnaire so we can measure your quality of life. We will also collect information on any other medication that you have taken, and other healthcare visits that you may have had, such as GP visits, outpatient appointments, A&E visits, and hospital admissions.

If you are in the group that has stopped taking growth hormone and your doctors find that you are growing at a slower rate and blood tests show that your growth hormone level is low, another growth hormone stimulation test will be arranged. If this confirms that your production of growth hormone is low then you will restart your growth hormone injections. Similarly, if your doctor feels that you need to restart growth hormone for any reason, you will be able to do this.

If you become pregnant whilst you are in the trial, we will ask you to sign a form to allow us to collect details of the pregnancy and its outcome. You will have access to pregnancy and contraception advice in line with standard care and this will not be affected by your participation in this trial.

We expect most people to be in the study for around three years, but as this is determined by when the growth rate has slowed to less than 2 cm per year and the relevant bone age is reached, some people may be in the study for different times.

1. **What are the possible benefits of taking part?**

You may not directly benefit from taking part in the study, however the information we get from the study may help us to improve the treatment of young people with growth hormone deficiency in the future.

1. **What are the possible disadvantages and risks of taking part?**

Taking part in this study is very unlikely to cause you any unusual discomfort or side-effects. Blood samples will be taken, so it is possible that discomfort, bleeding or bruising may happen because of this procedure, which is standard for all blood samples that are taken for any purpose. The blood samples would be taken as part of GHD standard care whether you were in the study or not.

You will have two X-rays during the trial. You would usually have one X-ray as part of standard care. As X-rays use ionising radiation, this means that you will be exposed to more radiation than you would if you were not taking part in the trial. The X-ray use in this trial has been reviewed by two independent experts who have confirmed that the additional risk of any negative effects is extremely low. Ionising radiation can cause cancer which can develop after many years or decades. The added risk of developing cancer due to taking part in this trial is estimated as about 1 in 45 million (0.000002%). For comparison, the risk of developing cancer in the general population is about 50%.

If you are put in the group who stop the injections of growth hormone then your growth will be monitored closely. At the first sign that you might be developing another shortage of growth hormone you will be retested and growth hormone treatment restarted. Your doctor can also restart growth hormone at any time they feel there is a need for it.

1. **Who is organising and funding the research?**

The GHD Reversal Trial is being run by the Chief Investigator Professor Mehul Dattani at University College London. The study is being funded by the National Institute for Health Research Health Technology Assessment Programme (NIHR HTA) and Sponsored by University College London. The GHD Reversal Trial is being co-ordinated by the Birmingham Clinical Trials Unit at the University of Birmingham.

Your doctor will not be paid for including you in this trial.

1. **How have patients and the public been involved in this study?**

Children who are receiving injections for growth hormone deficiency and their parents have helped develop the research questions that should be asked. A member of this group is also a co-applicant and will continue to be involved in the study.

Potential participants were involved in reviewing this Participant Information Sheet. We also had input from the Young Persons Advisory Group and from members of the Trial Management Group, some of whom are members of the Child Growth Foundation (CGF).

In designing this study, we have taken into account patient opinions on the frequency of participant visits and the tests that we will carry out.

1. **Who has reviewed the study?**

To protect participant’s safety and dignity all research in the UK is approved by an independent group of people, called a Research Ethics Committee (REC). This study has been reviewed and given a favourable opinion by Wales Research Ethics Committee 3 (Wales REC 3).

1. **Will my taking part in this study be kept confidential?**

If you decide to take part in the GHD Reversal Trial all information which is collected about you during the course of the research will be kept strictly confidential in the same way as your medical records. Information about your condition and progress will be sent by your care team to the GHD Reversal Trial office at the University of Birmingham Clinical Trials Unit, on paper and electronically, where it will be securely stored under the provisions of the General Data Protection Regulation and Data Protection Act 2018.

Copies of your hand X-rays will be sent to Great Ormond Street Hospital in London if you are based in the UK, or to Kepler Universitätsklinikum in Linz if you are based in Austria, so that your skeletal growth (bone age) can be measured. The results of these bone age measurements will be sent to the GHD Reversal Trial office at the University of Birmingham Clinical Trials Unit, on paper and electronically, where it will be securely stored under the provisions of the General Data Protection Regulation and Data Protection Act 2018.Your relevant medical records may be inspected by authorised individuals from the Birmingham Clinical Trials Unit or your hospital. They may also be looked at by the study team, the Sponsor and regulatory authorities. The purpose of this is to check that the study is being carried out correctly. All these parties have a duty of confidentiality to you.

You will be asked will be asked to confirm if you would be happy to be contacted to take part in future research studies. If you do decide to take part in these additional studies then you will need to formally consent to this.

You can find out more about how we use your information

* at [www.hra.nhs.uk/information-about-patients/](https://www.hra.nhs.uk/information-about-patients/)
* on Sponsor website <https://www.ucl.ac.uk/legal-services/privacy>
* on University of Birmingham website <https://www.birmingham.ac.uk/privacy/index.aspx>
* by asking one of the research team
* by sending an email to the sponsor’s office at data-protection@ucl.ac.uk

Further information can also be found at; <http://www.hra.nhs.uk/patientdataandresearch> (if you are unable to access the internet and/or would prefer a paper copy, please ask us and we can provide a print out).

1. **Involvement of General Practitioner/other healthcare practitioner**

With your consent, your GP or other healthcare practitioner (such as community paediatrician) will be notified of your participation in the GHD Reversal Trial and kept informed of your progress.

1. **What will happen to the samples I give?**

The blood samples taken from you will not be stored. Any biochemical data will be stored as part of your clinical records in the hospital in which your care is primarily based. All X-rays will be stored at your hospital as part of your clinical records. X-rays transferred to Great Ormond Street Hospital or Kepler Universitätsklinikum for estimation of your skeletal growth (bone age), will be securely deleted 60 days after their receipt at Great Ormond Street Hospital (London) or Kepler Universitätsklinikum (Linz).

1. **What if something goes wrong?**

We do not expect any problems to occur as a result of your participation in the trial. However, all participants are covered for negligent harm according to NHS indemnity guidelines.

If you have concerns about any aspect of this trial, you should ask to speak to a member of the research team who will do their best to answer your questions.

If this hasn’t resolved your concern and you wish to complain about any aspect of the way you have been approached or treated during the course of this trial, the normal National Health Service complaints mechanisms will be available to you. Your hospital PALs team will be able to help you with this.

Tel: *<insert local PALS contact number(s)>*Email: *<insert local PALS email address>*

However, if you remain unhappy or have a complaint about any aspect of this study and wish to speak to someone independent of the research team/hospital, please contact the Head of Research Governance and Compliance, UCL/UCLH Joint Research Office, University College London, Gower Street, London WC1E 6BT email: research-incidents@ucl.ac.uk.

Every care will be taken in the course of this research study to ensure your safety. However in the unlikely event that you are injured in the course of the study, compensation may be available.

If you suspect that the injury is the result of the Sponsor’s (University College London) or the hospital's negligence then you may be able to claim compensation. After discussing with your study doctor, please make the claim in writing to Professor Mehul Dattani who is the Chief Investigator for the studyand is based at University College London (UCL). The Chief Investigator will then pass the claim to the Sponsor’s Insurers, via the Sponsor’s office. If you have a claim then it might be helpful to consult a lawyer.

1. **What if I do not want to take part?**

Your decision to take part in this study is entirely voluntary. You can change your mind at any point and you don’t have to give a reason why.

If you choose to stop taking part in the study, we will keep the information about you that we have already collected.

If you choose to stop taking part in the study, we would like to continue collecting information about your health from your routine hospital notes. If you do not want this to happen, tell us and we will stop.

We need to manage your information about you in specific ways for the research to be reliable. This means that we won’t be able to let you see or change the data we hold about you. Research could go wrong if data is removed or changed.

GDPR stands for the General Data Protection Regulation. In the UK we follow the GDPR rules and have a law called the Data Protection Act. All research using patient data must follow UK laws and rules. Universities, NHS organisations and companies may use patient data to do research to make health and care better. As universities and the NHS are funded from taxes they are expected to do research as part of their job. They still need to be able to prove that they need to use patient data for the research. In legal terms this means that we are using patient data as part of ‘a task in the public interest’.

In the unlikely event that you lose the capacity to consent during the study you will be withdrawn, and we will use any data already collected.

Should you wish to withdraw from the study, but do not let the study staff or study office know of the type of withdrawal you want, then we will assume that you are happy for us to continue using the data we have collected on you, as well as linking your information with any NHS or central government bodies for measuring any long-term outcomes. We will also assume that you do not want the study office to contact you in the future.

If you wish to find more about how we use your information, please contact Legal Services at the address below.

The Data Protection Officer, Legal Services, The University of Birmingham, Edgbaston, Birmingham B15 2TT
Email: dataprotection@contacts.bham.ac.uk
Telephone: +44 (0)121 414 3916

If you would like more information on your rights, would like to exercise any right or have any queries relating to our processing of your personal data, or if you wish to make a complaint about how your data is being or has been processed, please contact the Sponsor’s (University College London) Data Protection Officer at data-protection@ucl.ac.uk

1. **What happens if new information becomes available?**

Sometimes we get new information about the treatment being studied. If this happens, a member of the research team will tell you and discuss whether you should continue in the study.

If your doctor is happy for you to continue in the study, you will have the option to decide whether to continue or not. A member of the research team may ask you to re-sign a consent form if you decide you want to continue.

If you decide not to carry on, your standard clinical care will continue. This will be arranged by your doctor.

1. **What happens when the research study stops?**

At the end of the study you will have a further growth hormone stimulation test to see if you need to keep taking growth hormone as an adult. Any future care will be discussed with you by the doctors who are looking after you.

1. **What will happen to the results of the research study?**

The results and conclusions will be published in peer reviewed medical journals and presented at academic meetings.

The research team will provide you with a summary of the trial results once the trial is complete and published.

At the end of the study, an anonymised dataset will be produced and made available for other researchers to use. Any personal data will not be made available but securely stored for 25 years after which the personal information will be securely destroyed.

1. **Where can I get further information?**

For queries about the trial or for further information please contact:

<Insert local PI name>, Telephone <insert local PI contact details>, GHD Reversal Trial Principal Local Investigator.

The GHD Reversal Trial coordinating centre is located at the Birmingham Clinical Trials Unit, Institute of Applied Health Research, University of Birmingham, B15 2TT.

Tel: 0121 415 9131, Email: GHDReversal@trials.bham.ac.uk