PATHWAYS TRIAL 'Easy Read' Study Description

Who is this article for?

This plain language study description is for anyone who would like to find out more about PATHWAYS TRIAL and what taking part in the study involves. This 'Easy Read' document is a simplified version of the scientific protocol for PATHWAYS TRIAL. PATHWAYS TRIAL, CONNECT and HORIZON INTENSIVE were approved together under the same protocol, so we created separate Easy Read documents - one for each part of the PATHWAYS programme. You are currently reading the Easy Read study description for PATHWAYS TRIAL.

The Easy Read study description for PATHWAYS CONNECT can be found here: https://www.kcl.ac.uk/ioppn/assets/pathways/connect/pathways-connect-easy-read.pdf

The Easy Read study description for PATHWAYS HORIZON INTENSIVE can be found here: https://www.kcl.ac.uk/ioppn/assets/pathways/horizon/pathways-horizon-intensive-easy-read.pdf

What is PATHWAYS TRIAL?

PATHWAYS TRIAL is a research study that will explore how puberty suppressing hormones (medicines that pause puberty) impact the physical, social, and emotional wellbeing of young people with gender incongruence.

Right now, there isn't enough information about the possible benefits or risks that young people with gender incongruence may experience when taking puberty suppressing hormones. PATHWAYS TRIAL aims to help fill this gap in the evidence about what we know.

Why is this important?

Gender incongruence is when someone's gender doesn't match the sex they were registered at birth. Puberty can be a difficult time for young people with gender incongruence. This is because their body starts to change in ways that don't match how they feel inside.

Puberty suppressing hormones may help some young people with gender incongruence explore their gender identity more comfortably without feeling rushed or distressed about their body changing. This might also help them feel more comfortable at school, with friends, and in everyday life.

However, doctors and researchers don't yet know for sure what the benefits or risks of this treatment are. We don't know whether improvements in emotions and well-being are due to puberty suppressing hormones or other care that young people receive for gender incongruence. There may be risks from puberty suppressing hormones as they might affect brain and bone development. Again, there isn't enough research to understand whether these changes happen, how much they change, or if they return to normal after treatment stops.

Because of this uncertainty, a law was introduced in the UK which says that doctors can only offer this treatment to young people with gender incongruence as part of a research study.

PATHWAYS TRIAL is the first randomised controlled trial to explore the effects of puberty suppressing hormones among young people with gender incongruence. The findings will help young people, their families, and doctors make better-informed decisions in the future.

How will PATHWAYS TRIAL be done?

PATHWAYS TRIAL will use a randomised controlled trial design. This means that everyone taking part will be randomly placed in one of two groups - by chance, like

flipping a coin. One group will start the treatment straight away, and the other group will start the treatment after 12 months. No one in the study will decide which group they are in.

This approach helps researchers understand how treatment works, by comparing what happens in both groups. It can show whether starting the treatment earlier is more helpful for young people, or if delaying the treatment might lead to fewer unwanted side effects for example.

Who can take part in PATHWAYS TRIAL?

To take part in PATHWAYS TRIAL, a young person must be attending the NHS Gender Service and have a clinical diagnosis of gender incongruence.

The young person will have a series of tests and scans to check whether they can take part in the trial. These include bone scans, blood and urine tests, and something called a Tanner stage assessment, which is when a doctor looks at their body to know which stage of puberty they are at.

The young person must be in puberty – between early and later puberty. This is checked on examination by a doctor. The young person must also be younger than 15 years and 11 months to take part in PATHWAYS TRIAL.

To join the trial, young people cannot have previously taken puberty suppressing hormones or cross-sex hormones.

Who decides whether a young person can take part in PATHWAYS TRIAL?

The young person's care team at the Gender Service and a National Multidisciplinary Team (NMDT) will look at lots of information about the young person to decide whether they think there is a reasonable chance young people might benefit from puberty suppressing hormones.

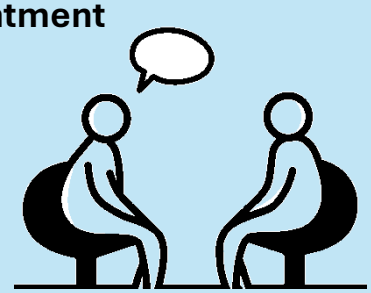
The National Multidisciplinary Team is a group of specialist doctors from the NHS Children and Young People's Gender Service. They make sure that decisions about who can join the trial are made fairly and in the same way for everyone, no matter which doctor or gender service a young person sees.

The National Multidisciplinary Team looks carefully at information about each young person's physical and mental health, how they're doing at school, and whether they are safe and well at home. This helps them get a full picture of the young person's wellbeing before deciding if they think this treatment is suitable.

The young person's parent or legal guardian also needs to agree for the young person to take part, and the young person needs to agree for themselves.

What will happen if someone takes part?

Finding out about the treatment



The young person and their parent/legal guardian will receive detailed information about the possible benefits and risks of puberty suppressing hormones, including information about fertility preservation. They will then talk to the young person's care team at the Gender Service, as both the young person and their parent/legal guardian need to be able to show that they have a good understanding of what the treatment involves and the possible benefits and risks of the treatment.

Agreeing to take part

Once doctors have agreed that the young person might benefit from puberty suppressing hormones, the young person and their parent/legal guardian will be told more about the research and what will happen. If they want to take part, they will be asked to give their consent (agreement) by signing a consent form.

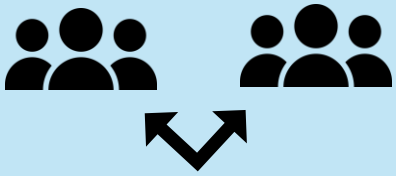
They can take as long as they want to make up their minds.

Finding out which group the young person is in

A computer programme will randomly pick which group the young person is in.

Group 1: This group will start the treatment straight away.

Group 2: This group will wait 12 months before starting the treatment.



A doctor at the Gender Service will tell the young person and their parent/legal guardian which group they are in.

Safety checks and scans

Before starting the treatment, a doctor will ask the young person and their parent/caregiver some questions about how the young person is feeling.

To make sure it is safe for the young person to take part, they will need to have some tests and measurements taken. This will include checking their:

- Blood and urine
- Height and weight
- Blood pressure
- Heart rate and heart activity

If they were registered female at birth, they will also need to take a pregnancy test.

Bone scans

The young person will be asked to have 2 types of bone scan, one to check how strong their bones are, and the other to check how their bones are growing.

Stage of puberty

If the young person is in the group starting treatment after 12 months, they will have a Tanner stage (puberty) assessment again when they are about to start the treatment. This is when a doctor or specialist nurse looks at their body to check what stage of puberty they are at. All young people taking part in the trial will have also had this assessment before joining the trial.

Starting the treatment

If the tests and scans show that it is safe for the young person to start treatment, the young person will be given the puberty suppressing hormone by an injection.

Continuing the treatment

The treatment lasts for 6 months, so the young person will have the injection once every 6 months from when they start the treatment.

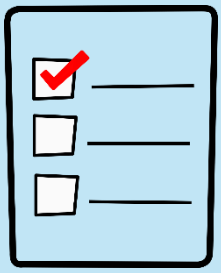
The young person will repeat some of the safety checks and scans, including the height, weight and blood pressure measurements and a pregnancy test (if applicable) every time they are due to have the treatment, to check that it is still safe for them.
A doctor will also ask them if there are any other medications they are taking and if they have experienced any side effects of the treatment.

A doctor may suggest the young person changes to an injection that lasts for 3 months or 1 month, depending on how the young person feels and how their body responds.

Online questionnaires

The young person and their parent/caregiver will be asked to complete some questionnaires. These will ask about:

- The young person's emotions and behaviours
- How they feel about their gender and body (young person only)
- Their relationships with others (young person only)
- Their daily life with friends, family, education and other activities



They can answer the questionnaires on a phone, tablet or laptop, either on their own, or with a researcher via phone, or video call, or in-person when they visit the clinic.

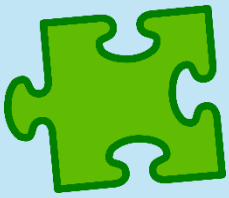
They will complete most of these questionnaires once a year and they will take around an hour to complete.

They will be asked to complete some of the questionnaires more often (every 3 months) for the first 2 years of the trial.

Measuring thinking, learning and memory (cognitive assessments)

The cognitive assessments are short puzzles and tasks that tell us about how the young person learns, thinks and solves different problems. For example, they might be shown some pictures and after a short break be asked to tell the researchers what they saw, to see what they can remember.

These take about two hours, and the young person can take breaks.



Young people taking part will be asked to complete cognitive assessments in the clinic, once a year whilst on the treatment. They will get a voucher worth £30 every time they complete cognitive assessments.

How long will young people be followed up during the trial?

Young people will complete questionnaires and have safety checks and scans regularly for 2 years during the trial. After the first 2-years, all participants will be asked to complete questionnaires and have a bone scan once a year, whilst the PATHWAYS research study is running.

Follow-up into adult life is important; people taking part will also be asked whether they agree to take part in longer-term follow-up including linking information about them through the NHS and national health registries to understand how they are doing long-term.

What will happen when a young person finishes their treatment in PATHWAYS TRIAL?

When the young person finishes their treatment in the trial, their doctor at the Gender Service will talk to them and their parent/caregiver about how they have found the treatment. The doctor will ask about the young person's quality of life, their mental and physical health, and how they feel about their gender and body. The doctor will then explain their options and what may happen next. This may include continuing puberty suppressing hormones, stopping the treatment, or starting another treatment.

If the young person wants to stay on puberty suppressing hormones or start gender affirming hormones, then their decision will be reviewed by the National Multidisciplinary Team that also agreed for the young person to start the trial.

What if someone wants to stop taking part?

Anyone taking part can decide to stop taking puberty suppressing hormones and leave PATHWAYS TRIAL at any time, and they do not need to give a reason. If they decide to stop taking part in PATHWAYS TRIAL, they will be asked whether it is ok to continue collecting information about them to help make the study results useful for others.

If a young person decides to stop taking puberty suppressing hormones, their care in the Gender Service or anywhere else in the NHS will not change in any other way, and their doctors will talk to them and their parents/ guardians about the different treatment choices they have.

How will researchers analyse the data?

After 12 months, the researchers can compare the two groups to see what difference the treatment has made, because only one group will have had the treatment at this point.

After 24 months, both groups will have had the treatment, but for different lengths of time. By comparing the groups again, the researchers can see whether it is more helpful to have had the treatment for longer, or to have it for less time and to start the treatment later in puberty.

Who is funding the trial?

The research is funded by the National Research Collaboration Programme (NRCP), a partnership between NHS England and the National Institute for Health and Care Research (NIHR).

Who is monitoring the trial?

The research is led by King's College London and co-sponsored by King's College London and the South London and Maudsley NHS Foundation Trust.

The study has been carefully checked by independent scientists who advise the National Institute for Health and Care Research (NIHR). These include independent academic peer reviewers and NIHR funding committee consideration.

It has also been carefully checked by the Medicines and Healthcare products Regulatory Agency and received approval from a Research Ethics Committee.

The research is overseen by two groups of people who are independent from the research team and the funders. A Data Monitoring Committee will check the data and highlight any concerns they have about the quality of the data (such as the amount of missing information) and any concerns about the safety or wellbeing of people taking part.

The Programme Steering Committee will include at least two people with lived experience of being a gender diverse young person, or a parent/caregiver of a gender diverse young person, as well as scientists. The Programme Steering Committee will advise on the study's progress overall.