Information Sheet for Research Participants

You will be given a copy of this Information Sheet and a signed copy of your consent form to keep, should you decide to participate in the study.

Study title:
Physiological study of kisspeptin in post-menopausal health

We'd like to invite you to take part in our 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 friends, relatives, and your GP if you wish, before deciding if you would like to take part. Please do ask us if there is anything that is not clear or if you would like more information. **You are free to withdraw at any time without explanation.**

What is the purpose of the study?

Menopause is a natural process that marks the end of menstrual periods, and typically occurs between the ages of 45 and 55 years. It affects nearly 13 million women in the UK, one third of the total UK female population. It happens when the body stops producing reproductive hormones (oestrogen and progesterone).

Menopause can increase the risk of conditions that affect the liver e.g., excess fat build-up in the liver, the bone e.g., osteoporosis (thin bones which are more likely to break) and the brain e.g., mood or memory problems.

Kisspeptin, a naturally occurring hormone already present in our bodies. Previous research suggest that it could have positive effects on the liver, bone, mood, and memory. However, its effects on these functions have not previously been studied in women after the menopause. Therefore, we plan to study how giving kisspeptin to women after the menopause for 12 weeks affects these aspects of health.

In this study, we will be using the natural occurring form of the kisspeptin hormone, and not a drug approved by the Medicines and Healthcare Products Regulatory Agency. Therefore, this study is not a clinical trial. Instead, it is a research study that will help us understand the effects of this natural hormone on the health of postmenopausal women.

Why have I been chosen?

You have been asked to take part in this study because you are a woman who has gone through the menopause and could have abnormal liver function. As we anticipate that kisspeptin will improve liver function, we intend to include women who have abnormal liver function at the start of the study.

We are looking for up to 36 women

- who are post-menopausal (i.e. absence of menstruation in the preceding 12 months with follicle stimulating hormone levels in the postmenopausal range) with abnormal liver function test.
- who are not taking medication or stable on medication for 3 months (i.e. no significant changes in dose, formulation or route of administration).
- who are at the stable weight (i.e. up to ±6kg change in weight) for 3 months if you have not had bariatric surgery or stable weight for 12 months if you have had bariatric surgery in the preceding 24 months

A full list of inclusion and exclusion criteria will be reviewed at a screening visit.

Do I have to take part?

Your participation in the study is entirely voluntary. If you decide to take part, you will be given this information sheet to keep and be asked to sign a consent form at a screening visit. If you decide to take part you are still free to withdraw at any time and without giving a reason, and your usual healthcare will not be affected.
If you withdraw from the study, any samples already collected from you will be stored and will only be identifiable to the medical investigators involved in this study. These samples will then be analysed by us at a later date.

What will happen to me if I take part?

1. Screening and pre-study tests

If you are interested in the study, you will be invited to the Clinical Research Unit in Charing Cross Hospital for a screening visit which will last up to one hour. You will be seen by a member of the research team who will explain the study and answer any queries. If you are happy to proceed with the study, you will be asked to sign a consent form. If you agree to take part in the study and provide consent, one of the doctors will perform a full clinical assessment, which will include a medical history, a physical examination and blood tests to ensure that there are no abnormalities that will affect your ability to participate in the study. If you have not had an ultrasound of your liver during the last 6 months, we will arrange for you to have one before you start the study. During the screening visit, you will also be taught how to give yourself an injection using a mannequin. A researcher will watch you practise and will provide any further training you may need.

After the screening visit, within 1 week, we will inform you if you can join the study. If you join the study, you will be randomly assigned to receive either kisspeptin, or a similar looking injection that has no medical effects (called placebo), for 12 weeks. Neither you nor the research team will know which injection you are taking until after you have completed the study. An independent researcher will have this information which can be shared with you at the end of the study and can be provided in the unlikely event that urgent medical care is needed.

Prior to starting the injections at home, we will organise a visit during which you will complete some questionnaires and tasks assessing brain function, including cognition and mood (this visit will take up to 5 hours), as well as visits where several scans are carried out. These scans include an MRI and a Fibroscan (special ultrasound scan) to look at your liver, and a 'DEXA scan' which will assess the density of your bones. These scans will take place in one of the hospitals at Imperial College Healthcare NHS Trust.

2. Study visits

You will be asked to attend the Clinical Research Unit at Charing Cross Hospital every other week from the start of the injections (i.e. weeks 1, 2, 4, 6, 8, 10, 12 – exact dates will be provided to you following the screening visit) and once after stopping the injections (i.e. week 24). On weeks 1, 6, 12, 24 you will attend longer study visits (up to 5 hours long). You will be reimbursed £125 for each longer study visit for your time and expenses. The rest of the study visits will be much shorter (up to 3 hours long) and you will receive £50 per study visit.

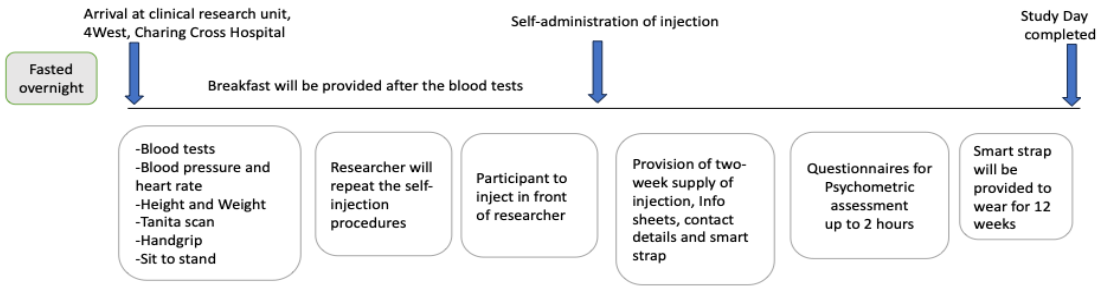
What will happen during the long study visits?

The study will start with a long study visit (up to 5 hours long), which will take place at the Clinical Research Unit in Charing Cross Hospital (first study visit; week 1). You will be asked to attend in the morning (before 10am) having fasted from the previous night. You will be asked not to have anything to eat or drink after 10pm the night before the study visit, but you can drink water and take your usual medicines.
During this visit:

1) We will carry out blood tests whilst you are fasted. Breakfast will be provided after completing these blood tests. This will take approximately 10 minutes.
2) Following the blood tests, you will be provided with breakfast and refreshment. Then you will be given the opportunity to practise the injection technique on the mannequin again. This will take approximately 30 minutes.
3) We will record your blood pressure, height, weight, hip and waist measurements. This will take approximately 5 minutes.

4) We will assess your body composition and muscle function by asking you to stand on a special scale that estimates the amount of muscle, fat and water in your body, asking you perform hand squeezing tests and asking you to sit and stand several times. This will take approximately 15 minutes.
5) You will be asked to give yourself the first injection of kisspeptin or placebo whilst a researcher observes to make sure that you are able to administer the injection independently (as you will be doing this at home). If you need help with anything or have any questions, the researcher will be there to assist you.
6) You will be given a secure box with a 2-week supply of kisspeptin or placebo and all the things you will need for the injections, along with an information sheet with instructions and contact details for any queries.
7) Following the supervised injection, you will be asked to complete a series of tests and questionnaires. This phase will take up to two hours. These questionnaires will assess various aspects of your behaviour (mood, anxiety), cognition (memory, concentration) and general wellbeing (menopause related and sexual function related).
8) You will be provided with refreshments and lunch during this visit (which will take approximately 20 minutes).
9) At the end of the study visit (before you go home), you will also be given a smart strap and asked to wear it for 12 weeks throughout the study period and bring it with you to the Clinical Research Unit when you come for the week 12 study visit. This smart strap will measure the levels of your physical activity.

Figure 1 - Summary of first study visit



Subsequent long day study visits (weeks 6, 12, 24) will also last up to 5 hours and will take place at the same location (i.e. the Clinical Research Unit in Charing Cross Hospital). During these study visits, we will carry out a welfare check, answer any questions you might have, check your injection sites, and carry out blood tests. You will also complete questionnaires that assess your memory, concentration, general wellbeing and sexual function because these can be affected following menopause.

Short visits will take place in the same location in weeks 2, 4, 8, 10 and will take up to 3 hours. During these visits, we will carry out a welfare check, answer any questions you might have, check your injection sites, carry out blood tests and give you a new supply for 2 weeks of injections.

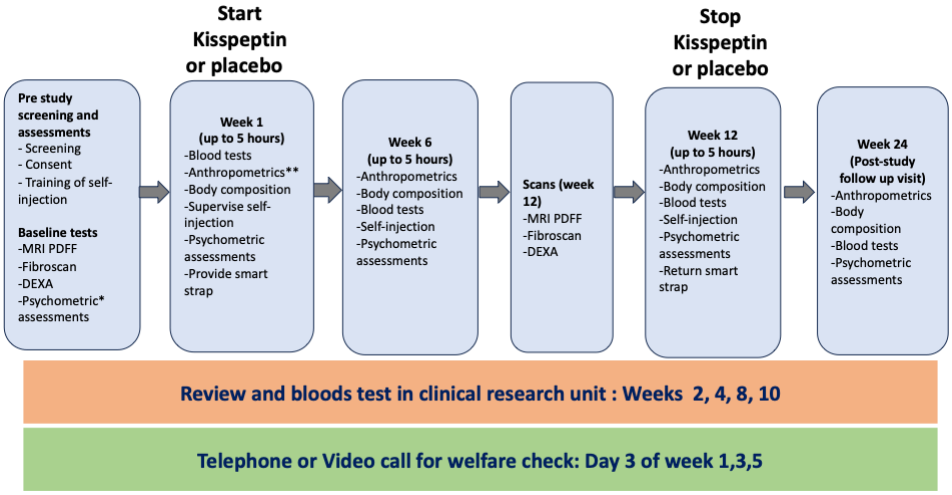
3. What will happen throughout the 12-week study period?

You will give yourself an injection every day for 12 weeks. You will be asked to administer this injection in the morning. You should keep all the vials and bring the used vials back to the Clinical Research Unit whenever you come for a study visit (both long and short study visits). The follow-up visits will alternate weekly between phone/video calls and in-person appointments at the Clinical Research Unit at Charing Cross Hospital. The phone/video calls will be arranged at a time that is convenient for you. On the 3rd day of your injection, you will be given the option of a video call or an in-person visit to the clinical research unit for this follow-up. The purpose is to make sure that you can give yourself the injections correctly, have the injection sites inspected by a member of the research team, and address any questions you may have. The fortnightly calls (weeks 3, 5) should not last longer than 10 minutes. In the event of any significant issues, you will be promptly scheduled for an in-person visit at the research unit.

In Week 12, you will have appointments to repeat the MRI, Fibroscan and bone mineral density scans. At the end of Week 12, you will stop giving yourself injections. A short study visit will take place in Week 24 (i.e. 12

weeks after you have stopped the injections), which will be for welfare checks, clinical assessments and blood tests. A summary of all of the study visits is shown in figure 2.

Figure 2 Study protocol



*Psychometric assessments- Standardised tests to measure person's mind and behaviour
** Anthropometric – measurement of body dimension including height, weight and waist circumference etc

What do I have to do?

The only restrictions on your lifestyle are that you will be asked not to have anything to eat or drink after 10pm the night before the long day study visits at week 1, 6, 12 and 14, but you can drink water and take your usual medicines.

What are the possible benefits of taking part?

We anticipate that kisspeptin could have beneficial effects whilst you are taking the injections, but we will not know if this is the case until the study is completed. The information we will collect during the study (including the blood tests and scan results) may provide some additional information about your health. If any significant abnormalities are detected, we will discuss them with you and discuss them with senior members of the research team who are also experienced senior doctors at Imperial College London Healthcare NHS Trust. If you consent, we will inform your GP if significant abnormalities are detected so that they can arrange appropriate further assessments and/or referral to a specialist. Furthermore, the information that we get from this study will help us to better understand the role of kisspeptin in the health of post-menopausal women, which may lead to beneficial treatments in the future.

What are the possible disadvantages and risks of taking part?

Kisspeptin is a naturally occurring hormone that is produced by our bodies. Low levels of kisspeptin are present in the blood of men and women who are not pregnant (including post-menopausal women). Very high levels of kisspeptin are found throughout pregnancy in women and this does not have harmful effects. Additionally, kisspeptin has been administered to hundreds of people without any side effects. The placebo injections are salty water only and therefore they are not expected to cause any effects in the body.

We have given kisspeptin to hundreds of patients without encountering any side effects to date. However, you may experience some discomfort related to the injections. The most frequently encountered side-effects include slight pain, minor bruises and minimal bleeding related to the injection. We can be contacted via email (imperial.kisspeptin@nhs.net) if you have any questions related to the injections.

DEXA scan
If you take part in this study, you will have a DEXA scan of your Hips, Lumbar Spine and Total Body composition. All of these will be extra to those that you would have if you did not take part. These procedures use ionising radiation to form images of your body and provide your doctor with other clinical information. Ionising radiation may cause cancer many years or decades after the exposure. We are all at risk of developing cancer during our lifetime. 50% of the population is likely to develop one of the many forms of cancer at some stage during our lifetime. Taking part in this study will add only a very small chance of this happening to you.

What are the side effects of taking part?

From our previous studies we do not expect any side effects, but the unexpected can occur. During each study visit, at least one experienced doctor will monitor you closely. If you suffer from any ill effects during the visit, you should report them to the doctors monitoring you immediately. If you suffer from any ill effects afterwards you should report them to one of the research doctors on the contact number below, by email (imperial.kisspeptin@nhs.net) or when you next see them. All adverse effects will be recorded in an adverse event form and placed in your personal research file. You may ask for the study to stop at any time without prejudice and if there are any significant side effects, the study will be stopped.

What if new information becomes available?

Sometimes during the course of a research project, new information becomes available. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to continue in the study, you will be asked to sign an updated consent form. Also, on receiving new information your research doctor might consider it to be in your best interests to withdraw you from the study.
If you lose the capacity during the study, you will be withdrawn from the study. However, any data that we had already collected when you were able to give consent may be used in the study. We will seek your informed consent for this at the screening visit. If you do not consent to this and you lose capacity during the study, your samples would be disposed of in accordance with the Human Tissue Authority's Code of Practice following completion of the study and not kept for use in future ethically approved research.

What happens when the research study stops?

Once the study has finished, the results of the study can be made available to you and/or your GP should you wish. If you have any problems immediately following the study, then you should contact the research team via email (imperial.kisspeptin@nhs.net).
Kisspeptin will not be available to you after the end of the trial. There are additional stages of development and approval required before it becomes readily available.
With your consent, the blood samples that are taken from you during the study may be kept in secure storage after initial analysis at Imperial College London for analysis in future research, after the study finishes. If this is not required, we will dispose of your samples safely and securely in keeping with NHS clinical codes of practice. Your samples will be always pseudonymised and only accessed by authorised study researchers. We will ask for your written consent to keep your samples at the initial screening visit. However, if you decide not to give permission for this, you can still take part in the study.

What if something goes wrong?

Imperial College London holds insurance policies which apply to this study. If you experience harm or injury as a result of taking part in this study, you will be eligible to claim compensation without having to prove that Imperial College is at fault. This does not affect your legal rights to seek compensation.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study, then you should immediately inform the Investigator (Prof Waljit Dhillo 02083833242). The normal National Health Service mechanisms are also available to you. If you are still not satisfied with the response, you may contact the Imperial College, Research Governance and Integrity Team.

Will my taking part in this study be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential. Any information about you which leaves the hospital will have your name and address removed so that you cannot be recognised from it. It is a requirement that your GP is informed, with your consent, of your participation in this study.

Who is organising and funding the research?

This study is being organised by the Section of Endocrinology and Investigative Medicine at Imperial College London. The study will be funded by the National Institute for Health Research (NIHR).

Expenses

To cover expenses including travel costs, time off work and lost earnings, participants will receive a total of £1055 (i.e., £125 per long study visit in weeks 1, 6, 12 & 24, £50 for each short study visit (weeks 2, 4, 8, 10), £10 for telephone/video calls (day 3, weeks 3 and 5), £200 for baseline scans and assessments in week 1 and £125 for scans in week 12 on completion of the study. This will not cover the costs of carer needs. Participants should be aware that as this study involves provision of expenses, entitlement to benefits paid by the government may be affected. Participants will be asked to fill in an expense claim form with bank details so that the money can be transferred following completion of study visits.

Who has reviewed the study?

This study has been reviewed by the East of England - Cambridgeshire and Hertfordshire Research Ethics Committee. This study was given a favourable ethical opinion for conduct in the NHS by XXXX REC.

Contact for Further Information

If you experience any problems during the study, you may withdraw at any stage without requiring any explanation. You can also contact the Chief Investigator, Professor Dhillo's personal secretary (02083833242) or the hospital switchboard (02083831000) which has home and mobile numbers for all the doctors involved in the study. The study team can be reached by email at imperial.kisspeptin@nhs.net.

Thank you for reading and for your interest in our study.

GDPR

HOW WILL WE USE INFORMATION ABOUT YOU?
Imperial College London is the sponsor for 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 appropriately. Imperial College London will keep your personal data for:

- 10 years after the study has finished in relation to data subject consent forms.
- 10 years after the study has completed in relation to primary research data.

The study is expected to finish in 01/11/2029.

For more information / confirmation regarding the end date please contact the study team, see '**WHERE CAN YOU FIND OUT MORE ABOUT HOW YOUR INFORMATION IS USED'** for contact information.

We will need to use information from you for this research project. This information will include your NHS number, name and contact details.

People within the College and study team (see section sharing your information with others) will use this information to do the research or to check your records to make sure that research is being done properly and the information held (such as contact) details is accurate**.** We will keep all information about you safe and secure. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

As a university we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study. Our legal basis for using your information under the General Data Protection Regulation (GDPR) and the Data Protection Act 2018, is as follows:

• Imperial College London - "performance of a task carried out in the public interest"); Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research

Where special category personal information is involved (most commonly health data, biometric data and genetic data, racial and ethnic data etc.), Imperial College London relies on "scientific or historical research purposes or statistical purposes.

INTERNATIONAL TRANSFERS
There may be a requirement to transfer information to countries outside the United Kingdom (for example, to a research partner, either within the European Economic Area (EEA) or to other countries outside the EEA. Where this information contains your personal data, Imperial College London will ensure that it is transferred in accordance with data protection legislation. If the data is transferred to a country which is not subject to a UK adequacy decision in respect of its data protection standards, Imperial College London will enter into a data sharing agreement with the recipient research partner that incorporates UK approved standard contractual clauses or utilise another transfer mechanism that safeguards how your personal data is processed.

SHARING YOUR INFORMATION WITH OTHERS
We will only share your personal data with certain third parties for the purposes referred to in this participant information sheet and by relying on the legal basis for processing your data as set out above.

- Other Imperial College London employees (including staff involved directly with the research study or as part of certain secondary activities which may include support functions, internal audits, ensuring

accuracy of contact details etc.), Imperial College London agents, contractors and service providers (for example, suppliers of printing and mailing services, email communication services or web services, or suppliers who help us carry out any of the activities described above). Our third party service providers are required to enter into data processing agreements with us. We only permit them to process your personal data for specified purposes and in accordance with our policies.

POTENTIAL USE OF STUDY DATA FOR FUTURE RESEARCH

When you agree to take part in a research study, the information collected either as part of the study or in preparation for the study (such as contact details) may, if you consent, be provided to researchers running other research studies at Imperial College London and in other organisations which may be universities or organisations involved in research in this country or abroad. Your information will only be used to conduct research in accordance with legislation including the GDPR and the UK Policy Framework for Health and Social Care Research.

This information will not identify you and will not be combined with other information in a way that could identify you, used against you or used to make decisions about you.

WHAT ARE YOUR CHOICES ABOUT HOW YOUR INFORMATION IS USED?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have because some research using your data may have already taken place and this cannot be undone.

- We need to manage your records 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 if this could affect the wider study or the accuracy of data collected.

WHERE CAN YOU FIND OUT MORE ABOUT HOW YOUR INFORMATION IS USED

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team
- by sending an email at imperial.kisspeptin@nhs.net

COMPLAINT

- If you wish to raise a complaint about how we have handled your personal data, please contact the research team first by sending an email to imperial.kisspeptin@nhs.net
- Following our response, if you are not satisfied please contact Imperial College London's/Imperial College Healthcare NHS Trust's Data Protection Officer via email at dpo@imperial.ac.uk / imperial.dpo@nhs.net via telephone on 020 7594 3502 / 020331304001 and/or via post at Imperial College London, Data Protection Officer, Faculty Building Level 4, London SW7 2AZ./8th Floor of Salton House, ICT Division, St Mary's Hospital, Praed Street, London, W2 1NY
- If you remain unsatisfied 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)- via www.ico.org.uk. Please note the ICO does recommend that you seek to resolve matters with the data controller (us) first before involving them.

What will happen to the results of the research study?

The results are likely to be published in scientific journals several months following the study. Your confidentiality will be ensured at all times and you will not be identified in any publication. At the end of the study, the results of the study can be made available to you and/or your GP should you wish.

Who is organising and funding the research?

This study is organized by Imperial College London and is funded by the NIHR Imperial BRC and an NIHR Senior Clinician and Practitioner Research Award who will pay Imperial College for the costs of this study.

Who has reviewed the study?

This study has been reviewed by the East of England – Cambridgeshire and Hertfordshire Research Ethics Committee. This study was given a favourable ethical opinion for conduct in the NHS by XXXX REC.

Contact for Further Information

If you experience any problems during the study, you may withdraw at any stage without requiring any explanation. You can also contact the Chief Investigator, Professor Dhillo's personal secretary (02083833242) or the hospital switchboard (02083831000) which has home and mobile numbers for all the doctors involved in the study. The study team can be reached by email at imperial.kisspeptin@nhs.net.