Subject information for participation in medical research – FOil study

The FOil study: Does hysterosalpingography (HSG) lead to more pregnancies than hysterosalpingo-foam sonography (HyFoSy) in infertile women, and does it save costs?

Official title: *Is, in infertile women undergoing a basic fertility work-up, tubal flushing with oil-based contrast medium during hysterosalpingography cost-effective compared to tubal flushing via hysterosalpingo-foam sonography?*

Dear Madam,

You have received this letter because you are in the process of a fertility work-up. With this letter, we would like to ask you to participate in a medical study. Your participation is voluntary.

This information letter explains the rationale of the study, what participation entails, and the possible benefits and disadvantages. Please read the information and decide if you want to take part.

If you want to take part, please complete the forms in Appendix B and C.

Ask your questions

You can make your decision based on the information in this letter. But we also suggest that you

- Ask questions you may have to the researcher who gave you this letter.
- Talk to your partner, family or friends about this study.
- Ask questions you may have to an independent expert. For contact details, see Appendix A.
- Read information on taking part in medical research on www.rijksoverheid.nl/mensenonderzoek (in Dutch) or https://www.government.nl/documents/leaflets/2020/06/03/medical-research-information-for-human-subjects (in English).

1. General information

The Department of Reproductive Medicine of the Amsterdam University Medical Center, location VUmc has set up this study. Below, we refer to Amsterdam UMC as the 'sponsor'.

Researchers may be gynecologists, clinicians and research staff. They conduct this study in different hospitals in the Netherlands.

For this study, a total of 1102 participants are required. This study has been approved by the Medical Ethics Committee (METC) Amsterdam UMC.

2. Purpose of the study

The aim of this scientific study is to compare two different methods of tubal patency testing: hysterosalpingography (HSG; an X-ray picture of the uterus and fallopian tubes) and hysterosalpingo-foam sonography (foam ultrasound). Both methods can be used to assess the patency of the fallopian tubes (both are called a tubal patency test), but it is still unclear whether they lead to the same number of pregnancies. In this study, we aim to find out which method gives the highest chance of getting pregnant and having a healthy baby.

3. Background of the study

Hysterosalpinogograpgy (HSG) and hysterosalpingo-foam sonography (foam ultrasound) are two diagnostic methods used to assess the patency of the fallopian tubes. Nowadays, both methods are used in fertility care.

1. HSG: during a HSG, a contrast medium is injected into the uterine cavity via the cervix. X-ray images follow the contrast fluid as it moves through the uterus and fallopian tubes.
2. Foam ultrasound: during a foam ultrasound, foam is injected into the uterine cavity, via the cervix. An internal (vaginal) ultrasound is then made, showing the foam in the uterus and the fallopian tubes.

When the fallopian tubes are open, the contrast medium or foam will pass through the fallopian tubes. We call this flushing of the fallopian tubes. Flushing of the fallopian tubes may increase the chance of getting pregnant.

From a previous Dutch study (H2Oil study), we know that flushing the fallopian tubes with an oil-based contrast medium during a HSG increases the chances of a pregnancy by 10% compared to flushing the tubes with a water-based contrast agent. Currently, it is not known whether flushing the fallopian tubes with foam during a foam ultrasound also increases the chances of an ongoing pregnancy. However, women report that the foam ultrasound is less painful than HSG. In addition, foam ultrasound does not expose the patient to X-rays and an iodinated contrast medium as HSG does.

It is important for patients and clinicians to investigate if flushing the fallopian tubes by HSG and foam ultrasound results in comparable chances of an ongoing pregnancy. The results of this study will help patients and clinicians make an informed decision between both tubal patency test methods.

4. What does participation mean?

How long will it take to complete the study?

The appointment for either a HSG or a foam ultrasound takes approximately 30 minutes.

To collect the information we need to answer our research questions, we will first try to obtain the data from your medical records. If data is missing, we will send you a questionnaire on any fertility treatments and pregnancies six months after participation. If you get pregnant within six months of your participation, we will send you an additional questionnaire.

Step 1. Eligibility criteria

You can participate in this study if:

- You have been trying to conceive for at least one year;
- You are between 18 and 42 years old;
- You have been told that you will be scheduled for tubal patency testing (HSG or foam ultrasound).

If your partner or sperm donor has impaired semen quality, we may exclude you from participation in this study .

Step 2. HSG or foam ultrasound

If you decide to participate, you will be randomly allocated to one of the two groups:

- Group 1: HSG with an oil-based contrast medium.
- Group 2: foam ultrasound.

Step 3. Examinations and measurements

- Before the HSG or foam ultrasound, you will be asked to complete a questionnaire about your experienced anxiety regarding the tubal patency test. Immediately after a HSG or foam ultrasound, we will ask you to indicate how painful you found the HSG or foam ultrasound on a scale of 0 to 10.
- Approximately six months after your participation, you will receive a questionnaire about fertility treatments and pregnancies (if this information is missing from your medical record). If you get pregnant within six months of the tubal patency test, you will receive a second questionnaire on the outcome of your pregnancy. These questionnaires take around ten minutes to complete.
- Approximately six months after your participation, you will receive another questionnaire about your health, work and health care use. We use this information to assess the costs of both methods. This questionnaire will take about fifteen minutes to complete.

We use a secure and private server for the online questionnaires. We ask your permission to use your email address to send you the questionnaires.

5. Agreements

We want the study to go well. So, if you participate in the study, you agree to contact the researcher in these situations:

- You are admitted to a hospital;
- You suddenly develop any health problems;
- You no longer want to participate in the study;
- Your phone number, address or email address changes.

6. What are the possible side effects, adverse reactions or discomforts of HSG and foam ultrasound?

Both tubal patency tests are currently used in fertility care and are considered safe procedures.

HSG uses an oil-based contrast medium which contains iodine. This may cause adverse effects if you are allergic to or have an iodine sensitivity. If you have an allergy or sensitivity to iodine, you cannot participate in this study.

Due to the use of iodinated contrast, there is a very small chance that you may develop a temporary decrease in thyroid function. In most cases, this will resolve without any treatment. Previous studies have shown that a temporary reduced thyroid gland function does not affect the development of the thyroid gland of your child.

7. What are the benefits and disadvantages if you take part in the study?

It is important that you weigh up the potential benefits and disadvantages before deciding to take part in the study.

If you take part in the study, you will be randomly allocated one of the two tubal patency tests (HSG or foam ultrasound). Research shows that flushing the fallopian tubes with an oil-based contrast medium during HSG increases the chance of an ongoing pregnancy. However, this has not yet been researched for foam ultrasound. Foam ultrasound is thought to be less painful and it does not expose women to an iodinated contrast medium or radiation (X-rays).

Choosing not to participate in the study

It is up to you to decide whether you want to take part in the study. If you do not want to participate, you will be treated according to the local protocol at your hospital. This may be either tubal flushing by HSG or foam ultrasound.

8. When does the study end?

The researcher will inform you if there is any new information about the study that is important for you. The researcher will then ask you if you want to continue participating in the study.

In these situations, the study will end for you:

- You have completed all the visits and questionnaires (as described in section 4).
- You want to stop taking part in the study. You can stop at any time. Report this to the researcher immediately. You do not have to explain why you want to stop.
- If your physician decides it is better for you to stop.
- If the researcher, the government, or the reviewing medical ethics committee decides to stop the study.

Overall, the end of the study is when all participants have completed the study.

What happens when you stop participating?

The researchers use the data that has been collected up until the moment that you decide to stop participating in the study.

9. Usage and storage of your data

Your personal data will be collected, used and stored for this study. This includes information such as your name, address, date of birth and information about your health. The collection, use and storage of this data is necessary to answer the questions asked in this study and to publish the results. We will ask for your and your partner's permission to use this information.

What personal data do we store?

- Your name;
- Your email address to send the questionnaires;
- Your date of birth;
- Your medical history;
- Information about your pregnancy and subsequent childbirth;
- Date of birth of your child(ren);
- (Medical) data that we collect during the study;
- Results of the semen analysis of your partner. We collect this information because the semen quality influences your chance to get pregnant. Therefore, we ask your partner to sign a consent form as well.

We also ask your permission to request information from your general practitioner, clinician or midwife about any fertility treatments and pregnancies.

Why do we collect, use and store your data?

We collect, use and store your data to answer the research questions and publish the results.

How do we protect your privacy?

To protect your privacy, your data is encrypted. Your data can only be traced back to you via the encryption key. This key is securely stored at the local research facility. We will only use it to process your data. The data cannot be traced back to you in reports and publications about the study.

Who will have access to my data?

Certain people have access to all the data at the study site, including unencrypted data. This is necessary to check that the study is being conducted according to standards in a good and reliable way. Those with access to your data for review include:

- Members of the committee that monitors the safety of the trial;
- A monitor appointed by the sponsor (Amsterdam UMC);
- National and international regulatory authorities. They will keep your information confidential. We ask you to give your permission for this access. The Inspectorate for Health and Youth Care (IGJ) can access your data without your permission.

How long will your data be stored?

We keep your records stored in the hospital and at the sponsor for 15 years.

Can we use your data for other research?

After this study, your data may also be important for other scientific research in the field of infertility. For this purpose, your data will be stored at the hospital for 15 years. You can indicate on the consent form whether you agree to this. If you do not agree, you can still take part in the current study. This will not affect the care you receive.

Can you withdraw your consent to the use of your personal data?

You can withdraw your consent to the use of your personal data at any time. This applies to the use of your data for this study as well as for storage and use for future research. Please note that if you withdraw your consent, the data collected up until you withdraw consent may still be used in the research.

More information about your rights in relation to data processing:

- Would you like to know more about your rights in relation to the processing of personal data? Then please visit the following website: www.autoriteitpersoonsgegevens.nl.
- Do you have a question about your rights? Or do you have a complaint about the processing of your personal data? Please contact the person responsible for the processing of your personal data. For this study: Amsterdam UMC. See Appendix A for the contact details and website.
- If you have questions or complaints about the processing of your personal data, we advise you to contact the research team first. You can also contact the Data Protection Officer of Amsterdam UMC or the Dutch Data Protection Authority.

Where can you find additional information on the study?

This website provides more information about the study: https://www.zorgevaluatienederland.nl. You can find the study by searching 'FOil study'. Once the study has ended, a summary of the results will be available on this website.

10. No compensation for participation

There is no financial compensation for participating in this study.

11. Are you insured during the study?

You are not additionally insured for this study, as the risks are the same as those involved with standard tubal patency testing. That is why the Sponsor of the Medical Ethics Committee Amsterdam UMC does not have to take out additional insurance.

12. Do you have any questions?

You can ask questions about the study to the researchers involved in this study. Would you like advice from an independent expert? If so, contact details can be found in appendix A. If you have any complaints about the study, you can discuss these with the researcher or your treating specialist. If you prefer not to do so, you may contact the complaints' officer at your hospital. All the relevant details can be found in Appendix A.

13. How do you give consent for the study?

After you have had sufficient time to consider your participation, you will be asked to decide whether you want to participate in this study. If you agree, you and your partner will be asked to sign the enclosed consent form. Your written consent indicates that you have understood the information and agree to participate in the study. Both you and the researcher will receive a signed copy of the consent form.

Thank you for your time.

14. Appendices to this information

A. Contact details
B. Informed Consent Form madam
C. Informed Consent Form partner

Appendix A: Contact details – Amsterdam UMC

For more information about this study, you can contact one of the investigators:

Principal investigator: Prof. dr. V. Mijatovic, gynaecologist Amsterdam UMC. Contact through Reproductive Medicine secretary office: 020 444 3269

Researcher: Drs. J. Huijser. FOil@amsterdamumc.nl | 020 444 4567

Independent expert:

If you have any doubts about participation, you can consult an independent expert who is not involved in the study himself, but knows a lot about this study. Also if you have questions before or during the study that you would rather not ask your doctor, you can contact the independent expert: Dr. M.G.A.J. Wouters. He can be reached by telephone via the secretariat of the women's clinic: 020-5663754 on working days during office hours

Complaints:

E-mail: klachten@amsterdamumc.nl

Data Protection Officer of AmsterdamUMC:

E-mail: privacy@amsterdamumc.nl

Appendix B: Informed consent form FOil study - Madam

Belonging to FOil study: 'Does hysterosalpingography (HSG) lead to more pregnancies than hysterosalpingo-foam sonography (HyFoSy) in infertile women and does this save costs?'

- I was able to read the information letter. I was also able to ask questions. My questions have been answered to my satisfaction. I have had enough time to decide whether to participate.
- I know that participation is voluntary. I know that I may decide at any time not to participate after all or to withdraw from the study. I do not need to give a reason for this.
- I give permission that the researcher can request additional information from my midwife, gynecologist, general practitioner or specialist about any fertility treatments, pregnancy and birth.
- I consent to the collection and use of my data in the manner and for the purposes set out in the information letter.
- I know that some people may have access to all my data to verify the study. These people are listed in this information letter. I consent to the inspection by them.
- I give permission to keep my data for 15 years after the end of this research.
- I give permission to forward my contact details (address and telephone number) to the research team at Amsterdam UMC so that they can approach me for possible follow-up research and sending the questionnaires.
- I want to take part in this study.

Please fill out yes or no in the following table.

I give permission to store my data to use it for other research, as stated in the information letter.	Yes ☐	No ☐
I give permission to be asked if I want to participate in a follow-up study after this study.	Yes ☐	No ☐

My name is (subject): .....

My email address:

My telephone number:

Signature: .....

Date: __/__/__

I declare that I have fully informed this subject about this study. If information comes to light during the course of the study that could affect the study subject's consent, I will inform him/her of this in a timely fashion. The study subject will receive the full information letter, together with a signed copy of the consent form.

Investigator name (or their representative): .....

Signature:

Date: __/__/__

Appendix C: Informed consent form FOil study - Partner

Belonging to FOil study: 'Does hysterosalpingography (HSG) lead to more pregnancies than hysterosalpingo-foam sonography (HyFoSy) in infertile women and does this save costs?'

- I was able to read the information letter. I was also able to ask questions. My questions have been answered to my satisfaction. I have had enough time to decide whether to participate.
- I know that participation is voluntary. I know that I may decide at any time not to participate after all or to withdraw from the study. I do not need to give a reason for this.
- I consent to the collection and use of my data in the manner and for the purposes set out in the information letter.
- I know that some people may have access to all my data to verify the study. These people are listed in this information sheet. I consent to the inspection by them.
- I give permission to keep my data for 15 years after the end of this research.
- I give permission to forward my contact details (address and telephone number) to the research team at Amsterdam UMC so that they can approach me for possible follow-up research and sending the questionnaires.
- I want to take part in this study.

Please fill out yes or no in the following table.

I give permission to keep my data to use it for other research, as stated in the information letter.	Yes ☐	No☐
I give permission to be asked if I want to participate in a follow-up study after this study.	Yes ☐	No ☐

My name is (subject): .....

My email address:

My telephone number:

Signature: .....

Date: __/__/__

I declare that I have fully informed this subject about this study. If information comes to light during the course of the study that could affect the study subject's consent, I will inform him/her of this in a timely fashion. The study subject will receive the full information letter, together with a signed copy of the consent form.

Investigator name (or their representative): .....

Signature: ……

Date: __/__/__