Title of the study: Study of irritable bowel symptoms during ovarian stimulation in PCOS (Polycystic ovarian syndrome) patients compared to women who wish to freeze their eggs.

Sponsor of the study: *VUB*

Research organisation*: UZ Brussel*

Medical Ethics Committee: *Medical Ethics Committee, VUB/UZ Brussel*

Local investigators: *Prof. Dr. Sébastien Kindt, Gastroenterology and Hepatology Department, Prof. Dr. Shari Mackens and Prof. Dr. Michel De Vos, Brussels IVF*

I Information vital to your decision to take part

Introduction

You are invited to participate in an observational clinical study. This study will make use of questionnaires.

Participation in the study may or may not be beneficial for you. There is, however, no guarantee that you will benefit from taking part in this study.

Before you agree to take part in this study, we invite you to take note of its implications in terms of organisation, possible risks and benefits, to allow you to make a decision with full awareness of the implications. This is known as giving “informed consent”.

Please read these few pages of information carefully and ask any questions you want to the investigator or his/her representative. There are 3 parts to this document: the information essential to your decision, your written consent and supplementary information (appendices) detailing certain aspects of the basic information.

If you take part in this clinical study, you should be aware that:

- This clinical study is being conducted after having been reviewed by one ethics committee.
- Your participation is voluntary and must remain free from any coercion. It requires the signature of a document expressing your consent. Even after having signed this document, you can stop taking part by informing the investigator. Your decision not to take part or to stop taking part in the study will have no impact on the quality of your care or on your relationship with the investigator/treating physician(s)
- The data collected on this occasion are confidential and your anonymity is guaranteed during publication of the results.
- Insurance has been taken out in case you should suffer any damage in connection with your participation in this clinical study.
- You will not incur any charges for the visits/consultations, examinations or treatments specific to this study.
- You may contact the investigator or a member of his/her team at any time should you need any additional information.

Further information about your “Rights as a participant in a clinical study” can be found in appendix 2 page 4.

Objectives and course of the study

The aim of this study is to gain insight into the occurrence of irritable bowel symptoms during ovarian stimulation in individuals with PCOS (polycystic ovarian syndrome) and in women who wish to freeze their eggs. Irritable bowel syndrome (IBS) is a condition characterized by constipation or diarrhea or both. Patients with IBS suffer from abdominal discomfort or pain, bloating, and nausea. These symptoms are related to bowel movement patterns.

There are many different subgroups of women undergoing fertility treatment. This study focuses on PCOS and social freezing. Women with PCOS are at greater risk of developing gastrointestinal disorders. Social freezing of eggs is becoming increasingly popular, and this subgroup represents a significant proportion of the women who come to the fertility clinic at UZ Brussel. As this is expected to become even more popular in the future, it would be useful to investigate IBS symptoms during this treatment.

We invite you to participate in this clinical study as part of the group of women with PCOS or as a woman who chooses social freezing.

To participate in this study, you must

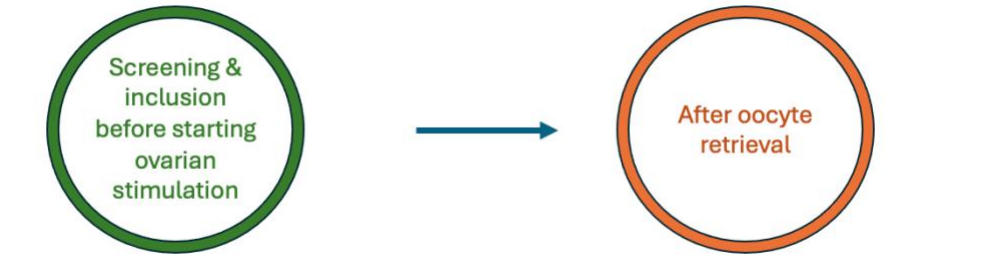
- Have been diagnosed with PCOS or have opted for social freezing
- Be starting your first ovarian stimulation
- Be over 18 years of age
- Have never given birth
- Have sufficient knowledge of Dutch, French, or English

You may not participate if you:

- Have a known gastrointestinal disorder
- Have a systemic or autoimmune disorder that affects the gastrointestinal system
- Have a history of abdominal surgery (appendectomy, gallbladder removal, are permitted if >6 months ago)
- Have had abdominal flu in the past 6 weeks
- Have had previous ovarian stimulation

The duration of this study consists of two visits that coincide with consultations. The first visit coincides with the consultation for ovarian stimulation. During the first visit, you will receive information about the study and it will be determined whether you meet the criteria to participate. If you are eligible to participate, you will complete five questionnaires about your gastrointestinal symptoms, anxiety, and depression. Completing the questionnaires takes approximately 20-30 minutes.

The second visit will coincide with the day of the egg retrieval. During this visit, you will be asked to complete the questionnaires about gastrointestinal symptoms, anxiety, and depression again. This will take approximately 10 minutes.



- Provide study information
- Signing ICF
- Demographics (length, weight)
- Duration of infertility
- Obstetrical history : GPA
- Ethnicity
- If applicable: type of PCOS
- Questionnaires *

- Questionnaires *
- Hormonal profile **
- Number of follicles on last US ** number of COC collected during oocyte retrieval **

* IBS-SSS, Rome IV criteria, GSRS, PHQ-9, GAD-7
** part of standard care

Abbreviations:
ICF = informed consent form
GPA = gravida (number of pregnancies), para (number of births), abortus (number of abortions)
COC = cumulus-oocyte complex

Data collection from patient records

As part of this study, several data will also be collected from your medical records.

The following information will be collected: your age, the type of medication administered for ovarian stimulation, the hormones measured in your blood samples, the number of follicles observed on the last ultrasound, and the number of eggs retrieved during egg retrieval.

Results on the GAD7 and/or PHQ9 questionnaires

"Psychological questionnaire screen for underlying psychological disorders such as anxiety and depression, but do not provide a clinical diagnosis. In case the score on these questionnaires is above the defined threshold, the investigator will contact your treating physician at the fertility clinic to determine if referral for further examination is required."

Risks and benefits

Your participation in this study does not pose any health risks.

Your participation in this study will also help us to better understand irritable bowel symptoms during ovarian stimulation in women with PCOS and in the context of social freezing, enabling us to propose better treatments in the future.

Withdrawal from the study

Your participation is voluntary. You are entitled to withdraw from the study for any reason, without having to justify your decision. Nevertheless, it may be useful for the investigator and for the sponsor of the study to know if you are withdrawing because the constraints of the tests, treatments and investigations are too great (too many uncomfortable side effects, for example).

It is also possible that the investigator withdraws you from the study because he/she thinks it is better for your health or because he/she finds out that you are not following the instructions given to participants.

Finally, the ethics committees that initially approved the study or the sponsor may break off the study because of health reasons.

If you withdraw your consent, the data collected up to the moment of your withdrawal will be retained. This is to ensure the validity of the study. No new data will be provided to the client.

If you take part in this study, we ask you:

- To cooperate fully in the smooth running of this study.
- Not to conceal any information relating to your state of health, the medication you are taking or the symptoms you are experiencing.
- To contact the investigator if you wish to participate in another clinical trial.

Contact

If you need further information, but also if you have problems or concerns, you can contact the investigators (Prof. Dr. Sébastien Kindt, Prof. Dr. Shari Mackens, Prof. Dr. Michel De Vos) or a member of the BIVF study team (02 477 66 48).

If you have any questions relating to your rights as a participant in a study, you can contact the participant rights ombudsman of your institution on this telephone number: 02 477 70 70. If necessary, he/she can put you in contact with the ethics committee.

Title of the study: Study of irritable bowel symptoms during ovarian stimulation in PCOS patients compared to women who wish to freeze their eggs.

II Informed consent

Participant

I declare that I have been informed of the nature of the study, its purpose, its duration, any risks and benefits and what is expected of me. I have taken note of the information document and the appendices to this document.

I have had sufficient time to think about it and discuss it with a person of my choice, such as my GP or a member of my family.

I have had the opportunity to ask any questions that came to mind and have obtained a satisfactory response to my questions.

I understand that my participation in this study is voluntary and that I am free to end my participation in this study without this affecting my relationship with the therapeutic team in charge of my health).

I understand that data about me will be collected throughout my participation in this study and that the investigator and the sponsor of the study will guarantee the confidentiality of these data in accordance with applicable European and Belgian legislation.

I agree to my personal data being processed as described in the section dealing with confidentiality guarantees (page 5). I also consent to these data being transferred to and processed in countries other than Belgium.

I agree/do not agree (delete as appropriate) to the study data collected for the purposes of this study being processed at a later date provided this processing is limited to the context of the present study

I agree to my GP or other specialists in charge of my health being informed of my participation in this clinical study.

I have received a copy of the information to the participant and the informed consent form.

Surname, first name, date and signature of the volunteer.

Investigator

I, the undersigned, , investigator, confirm that I have verbally provided the necessary information about the study and have given the participant a copy of the information document.

I confirm that no pressure was applied to persuade the participant to agree to take part in the study and that I am willing to answer any additional questions if required.

I confirm that I operate in accordance with the ethical principles set out in the latest version of the “Helsinki Declaration”, the “Good Clinical Practices” and the Belgian Law of 7 May 2004 related to experiments on humans.

Surname, first name, date and signature of the investigator’s representative	Surname, first name, date and signature of the investigator

III Supplementary information

1: Supplementary information on the organisation of the study

Once it has been confirmed that you are eligible for the study, you will be asked to complete several questionnaires. An overview of these questionnaires can be found in a table on page 2 of this document.

You will be given sufficient time to complete the questionnaires during your consultation at the fertility clinic.

2: Supplementary information on the protection and the rights of the participant in a clinical study

Ethics Committee

This study has been reviewed by an independent Ethics Committee, namely the Ethics Committee of VUB/UZ Brussel, which has issued a favourable opinion. It is the task of the Ethics Committees to protect people who take part in a clinical trial. They make sure that your rights as a participant in a clinical study are respected, that based on current knowledge, the balance between risks and benefits remains favourable to the participants, that the study is scientifically relevant and ethical.

The ethics committees issue an opinion on this matter in accordance with the Belgian law of May 7, 2004.

You should not under any circumstances take the favourable opinion of the Ethics Committee as an incentive to take part in this study.

Voluntary participation

Before signing, do not hesitate to ask any questions you feel are appropriate. Take the time to discuss matters with a trusted person if you so wish.

Your participation in the study is voluntary and must remain free of any coercion: this means that you have the right not to take part in the study or to withdraw without giving a reason, even if you previously agreed to take part. Your decision will not affect your relationship with the investigator or the quality of your future therapeutic care.

However, it is advisable to inform the investigator if you have decided to stop taking part in the study.

If you agree to take part, you will sign the informed consent form. The investigator will also sign this form to confirm that he/she has provided you with the necessary information about the study. You will receive a copy of the form.

Costs associated with your participation

The sponsor has agreed to reimburse the hospital for the time that the physician-researcher and his team spend on this study. You will not receive any compensation for your participation in this study. However, your participation will not entail any additional costs for you.

Guarantee of confidentiality

Your participation in the study means that you agree to the investigator collecting data about you and to the study sponsor using these data for research purposes and in connection with scientific and medical publications.

The processing of your personal data in this study is authorised because it is necessary for scientific research purposes.

Your data will be processed in accordance with the European General Data Protection Regulation (GDPR) and with the Belgian legislation on the protection of natural persons with regard to the processing of personal data. UZ Brussel shall act as data controller for your data.

You are entitled to ask the investigator what data are being collected about you and what is their use in connection with the study. This data concerns your current clinical situation but also some of your background, the results of examinations carried out within the context of care of your health in accordance with the current standards and obviously the results of examinations required by the protocol. You have the right to inspect these data and correct them if they are incorrect[1].

The investigator has a duty of confidentiality vis-à-vis the data collected.

This means that he/she undertakes not only never to reveal your name in the context of a publication or conference but also that he/she will pseudonymise (your identity will be replaced by an ID code in the study) your data before sending them to the manager of the database of collected data (Prof. Dr. Sébastien Kindt, Gastro-enterology and Hepatology department, UZ Brussel, Laarbeeklaan 101, 1090 Jette).

The investigator and his/her team will therefore be the only ones to be able to establish a link between the data transmitted throughout the study and your medical records[2].

The personal data transmitted will not contain any combination of elements that might allow you to be identified[3].

For the study data manager designated by the sponsor, the data transmitted will not allow you to be identified. The latter is responsible for collecting the data gathered by all investigators taking part in the study, processing them and protecting them in accordance with the requirements of the Belgian law on the protection of privacy.

To verify the quality of the study, it is possible that your medical records will be examined by persons subject to professional secrecy and designated by the ethics committee, the sponsor of the study or an independent audit body. In any event, this examination of your medical records may only take place under the responsibility of the investigator and under the supervision of one of the collaborators designated by him/her.

The (pseudonymised) study data will be able to be sent to Belgian or other regulatory authorities, to the relevant ethics committees, to other investigators and/or to organisations working in collaboration with the sponsor.

They will also be able to be sent to other sites of the sponsor in Belgium and in other countries where the standards in terms of the protection of personal data may be different or less stringent[4]. As explained above, the transmitted data are pseudonymised.

Your consent to take part in this study therefore also implies that you agree the use of your pseudonymised medical data for the purposes described in this information form and to their transmission to the aforementioned people and authorities.

The sponsor undertakes only to use the data collected within the context of the study in which you are taking part.

The sponsor will use the data collected within the context of the study in which you are taking part, but would also like to be able to use them in connection with other research concerning the same disease as yours. Any use of your data outside the context described in this document is only possible with the approval of the ethics committee.

[1] These rights are guaranteed by the European Data Protection Regulation (GDPR), by the Belgian legislation of 18 July 2018 on the protection of natural persons with regard to the processing of personal data and by the Law of 22 August 2002 on patient rights.

[2] For clinical trials, the law requires this link with your records to be retained for 20 years.

[3] The database containing the results of the study will therefore not contain any combination of elements such as your initials, your gender and your full date of birth (dd/mm/yyyy).

[4] The client undertakes to comply with the conditions set out in the European General Data Protection Regulation (GDPR) and Belgian legislation on the protection of natural persons with regard to the processing of personal data.

If you withdraw your consent to take part in the study, to guarantee the validity of the research, the data pseudonymised up to the point at which you withdraw will be retained. No new data may be sent to the sponsor.

If you have any questions relating to how your data are being processed, you may contact the investigator. The data protection officer in your hospital can be contacted as well : gegevensbescherming@uzbrussel.be or dpo@vub.be.

Finally, if you have a complaint concerning the processing of your data, you can contact the Belgian supervisory authority who ensures that privacy is respected when personal data are processed.

The Belgian supervisory authority is called:
Data Protection Authority (DPA)
Drukpersstraat 35,
1000 Brussels
Tel. +32 2 274 48 00
e-mail: contact@apd-gba.be
Website: https://www.dataprotectionauthority.be

Insurance

Any participation in a clinical study involves a risk, however small it is. Even if there is no fault, the sponsor accepts responsibility for damage caused to the participant (or in the event of death, his/her dependants) and directly or indirectly linked to his/her participation in the study. The sponsor has taken out insurance for this responsibility[5].

If the investigator believes that a link with the study is possible (the insurance does not cover the natural progression of your disease or the known side effects of your normal treatment), he/she will inform the study sponsor, which will initiate the declaration procedure to the insurance company. The latter will appoint an expert - if it considers it necessary - to assess whether there is a link between your new health problems and the study.

In the event of disagreement either with the investigator or with the expert appointed by the insurance company and also whenever you feel it is appropriate, you or - in case of death - your dependants may bring proceedings against the insurer directly in Belgium (Ethias, Prins-Bisschopssingel 73, 3500 Hasselt).

The law provides that the insurer may be summoned to appear either before the judge of the location where the event giving rise to the damage occurred, or before the judge of your domicile, or before the judge of the insurer's registered offices.

[5] In accordance with Article 29 of the Belgian Law related to experiments on humans (7 May 2004)