Title of the study: Gynecologists' feedback on ART-Pregnancy rates: a randomized controlled trial (GAP-RCT)

Sponsor of the study: UZ Leuven

Clinics: Leuvens Universitair Fertiliteitscentrum, Herestraat 49, 3000 Leuven; Fertiliteitscentrum, Gasthuis Zusters Antwerpen (GZA) Ziekenhuizen campus Augustinus, Oosterveldlaan 22, 2610, Wilrijk

Medical Ethics Committee: Ethische commissie onderzoek UZ / KU Leuven (central); Commissie Medische Ethiek (local)

GZA Local investigators: Prof. Dr. Karen Peeraer, UZ Leuven; Prof. Dr. De Loecker, GZA Augustinus; Dr. Eline Dancet, KU Leuven; Johanna Devroe, UZ Leuven; Dr. Geysenbergh Brecht, GZA Augustinus; Louise Dias, GZA Augustinus.

I. Information vital to your decision to take part (3 pages)

You are being invited to take part in a clinical study, in which you are randomised between two different type of doctor-patient communication. This means that the treatment you have been offered was prescribed in the usual manner, in accordance with the conditions of good medical practice and independently of your possible participation in this study.

We are simply asking you whether we can collect data from your medical records to be able to combine them with those of other patients receiving the same treatment and to process them statistically for research purposes. Apart from a few questionnaires we will ask you to complete, no additional diagnostic or monitoring procedure will be proposed.

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.

<u>If you take part in this study, you should be aware that:</u>

- The treatment offered to you by the investigator in accordance with current recommendations will not be altered if you take part in the study.
- This clinical study is being conducted after having been reviewed by one or more ethics committees.
- 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.
- 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 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 III

<u>Objectives of the study</u>

Interviewed couples going through IVF have indicated that they want a personalized prognosis. The personalized prognosis of a couple is the IVF-cycle specific couple's chance on the live birth of a child and can be calculated with a mathematical model that takes account of data from that couple's medical chart. So far, no study has examined giving couples their personalized IVF-prognosis influences couple's expected IVF-success rates and couple's wellbeing.

This study will divide couples in two groups: an intervention group and a control group. Couples from the control group will receive a photo of your transferred embryo(s) and the number of cryopreserved embryos.

Couples from the study group will receive the following extra feedback: the quality rating of your transferred embryo's and your personalized IVF-prognosis for this cycle.

This study will examine the expected IVF-live birth rates in both groups. Furthermore, we will explore whether the IVF-live birth rates expected by patients are associated with patient characteristics en if the personalized IVF-prognosis influences couple's distress and their decision to discontinue IVF.

Course of the study

We are inviting you to take part in this study because you are having an IVF (with or without ICSI) treatment with an oocyte aspiration and embryo transfer.

This clinical study would like to include approximately 160 couples.

To be able to take part in this study you must have had at least one previous IVF cycle (with or without ICSI). Couples meeting the following criteria can not take part: pre-implantation genetic diagnosis (PGD), donated oocytes/sperm/ embryos, spermatozoa obtained by testicular extraction (ICSI-CRYO-TESE), HIV-positive patients and/or embryo transfer on day 2.

if you decide to participate in this study, you and your partner will be asked to sign the informed consent **on the day of your oocyte aspiration**. We will also ask you to complete a short questionnaire on general optimism and on your expected success rate. In addition we ask your permission to extract data from your medical chart.

In case your gynaecologist decides not to perform an embryo transfer between day of oocyte aspiration and day of embryo transfer no prognosis can be calculated and your study participation will have to be discontinued.

On the day of your 'fresh' embryo transfer, a specially designed computer program will allocated you to a control group or a study group. Your chance of being allocated to the control group is 50% and your chance of being allocated to the intervention group is also 50%. Neither you nor your physician will be able to influence this division in groups. Couples from the control group will receive a photo of their transferred embryo(s) and will be informed on the number of cryopreserved embryos. Couples in the study group will receive the following extra feedback: the quality rating of their transferred embryo's and their personalized cycle-specific IVF-prognosis. Immediately after the embryo transfer you and your partner will be asked to fill out a questionnaire on your expected chance on a child, the received information and on your anxiety (5 minutes).

If you unfortunately do not happen to conceive after the transfer of the last (fresh or cryopreserved) embryo of the studied IVF-cycle, you and your partner will receive a text message with a link to an online questionnaire on infertility specific stress within two days of the conclusive **pregnancy test**.

Your active participation ends after completing the questionnaires. But we ask your permission to follow-up clinical and compliance outcomes in your medical chart 12-18 months after the oocyte aspiration.

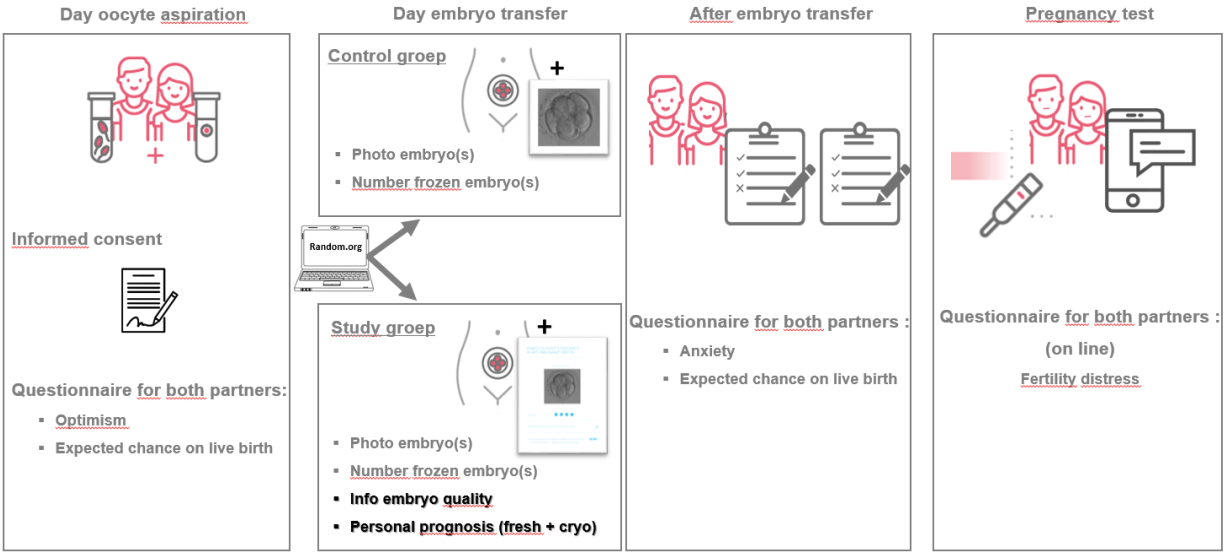

Figure 1: Course of the GAP-RCT

Description of risks and benefits

As indicated above, neither the treatment that has been proposed nor the diagnostic and monitoring procedures for your clinical situation go beyond good medical practice. No risk, in terms of health, can be linked to your participation in this study. It will offer you a picture of your embryo and if you are in the study group, standardized information on embryo quality and a personalized prognosis will be communicated. Completing questionnaires at 3 different time points may be inconvenient.

Withdrawal of consent

Your participation is voluntary and you are entitled to withdraw your consent to take part in the study for any reason, without having to justify your decision.

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

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

- To cooperate fully in the smooth running of this study.
- Not to conceal anything such as information relating to your state of health, the medication you are taking or the symptoms you are experiencing.
- To inform your doctor if you are asked to take part in another study to discuss with him/her the possibility of taking part in this study and to see whether you should then stop taking part in the present study.

Contact

If you need further information, but also if you have problems or concerns, you can contact the investigator Prof. Dr. Karen Peeraer or Prof. Dr. Peter De Loecker, a member of his/her research team Johanna Devroe (016 34 08 31 or johanna.devroe@uzleuven.be) or head nurse of the Sint Augustinus Fertility clinic, Louise Dias (03 443 41 76 or Louise.dias@gza.be).

If you have any questions relating to your rights as a participant in a clinical study, you can contact the patient rights ombudsman of your institution on this telephone number: 016/ 34 48 18. If necessary, he/she can put you in contact with the ethics committee.

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II Informed consent

Participant

I declare that I have been informed of the nature of the study, its purpose, its duration, the possible side effects 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 (GP, relative).

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

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. 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 research 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 (better understanding of the disease and its treatment).

I agree/do not agree (delete as appropriate) to my GP or other specialists in charge of my health being contacted if required to obtain additional information about my health.

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

Initials	**date**	**signature of the volunteer (woman)**
_____	_____	_____
Initials	**date**	**signature of t he volunteer (partner)**
_____	_____	_ _____

Investigator

I, the undersigned, Prof. Dr. Karen Peeraer, investigator, and Johanna Devroe, representative of the investigator confirm that the necessary information about the study was verbally provided and the participant was given a copy of the information document.

I confirm that no pressure was applied to persuade the patient 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

We will ask you to complete 3 questionnaire. The questionnaires relate to your expected success rates, your general optimism and your fertility related stress and anxiety. You will receive one questionnaire on the day of your oocyte aspiration, one on the day of your fresh embryo transfer and one on the day of your pregnancy test. Each questionnaire will only take 5 minutes.

2. Supplementary information on the risks associated with participation in the study: not applicable

Not applicable.

3: Supplementary information on the protection and 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 UZ / KU Leuven, which has issued a favorable opinion after consulting the "Commissie Medische Ethiek GZA". 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 patient and as a participant in a clinical study are respected, that based on current knowledge, the study is scientifically relevant and ethical.

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.

If you agree to take part in this study, 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

You will not receive any compensation for your participation in this study. Furthermore, the study will not involve 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.

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 Leuven 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 current standards. 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.

1 These rights are guaranteed by the European Data Protection Regulation (GDPR), by the Belgian legislation 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.

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 encode your data before sending them to the manager of the database of collected data KU Leuven

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 despite everything 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 third parties (ethics committee, representatives of the study sponsor, external auditors). In any event, this may only take place under the responsibility of the investigator or of one of his/her colleagues and by persons subject to the obligation of professional secrecy.

These (encoded) data will be able to be sent to Belgian or other regulatory authorities, to the relevant ethics committees, to other doctors 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].

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

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 and its treatment. Any use of your data outside the context described in this document is only possible with the approval of the ethics committee.

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

At UZ Leuven, an archiving period of 25 years applies to study documents of experiments that fall within the scope of the Belgian law of 7 May 2004. The Clinical trial master File is therefore archived for at least 25 years after the end of the study ("Last Patient last Visit").

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: DPO - UZ Leuven, Herestraat 49, 3000 Leuven, e-mail dpo@uzleuven.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

Even without fault, the sponsor accepts responsibility for damage caused to the participant (or his/her dependants) and linked directly or indirectly to participation in this study. In this context, the sponsor has taken out an insurance contract (Amlin Europe via Vanbreda Risks & Benefits NV, contractnummer: 299.053.700; contactgegevens: Vanbreda Risks & Benefits NV, Plantin Moretiuslei 297, 2140 Antwerpen)[5].

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[2] For clinical studies, 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 sponsor then undertakes to respect the constraints of the European General Data Protection Regulation (GDPR) and the Belgian legislation on the protection of natural persons with regard to the processing of personal data.

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