ENDORISK-I

Patient information for participation in medical scientific research

Personal risk of lymph node metastases in patients with uterine (endometrial) cancer (ENDORISK-I)

Introduction

Dear Madam,

You are receiving this information letter because your doctor has diagnosed you with cancer of the womb and you may soon be scheduled for surgical treatment. With this letter we would like to ask you if you would consider to participate in research to improve care for patients with cancer of the womb. Participation is completely voluntary.

Below, you will read the details of this study, what it entails for you and what the advantages and disadvantages of taking part in this study would be. We realize this is a lot of information. After having read this information sheet you can decide whether you want to participate in this study ? You can also discuss the information with your loved ones before deciding to participate. If you decide to participate, please complete the form with signatures found in Appendix C.

1. What is the purpose of this study?

In this study, we will evaluate whether personalized information in an additional tool can help patients and doctors better decide what kind of surgery is best for patients with cancer of the womb.

Radboud University Medical Centre (Radboudumc) designed this study. Researchers, including doctors/nurses/specialists/research nurses, are also conducting this study at the following hospitals: Canisius Wilhelmina Hospital, Nijmegen, Streekziekenhuis Koningin Beatrix, Winterswijk, Slingeland hospital, Doetinchem, Rijnstate hospital, Arnhem, Bernhoven hospital, Uden, Gelderse Vallei hospital, Ede, Amphia hospital, Breda, Jeroen Bosch hospital, Den Bosch, Catharina hospital, Eindhoven, St Anna hospital, Geldrop, Elkerliek hospital, Helmond, Elisabeth-Tweesteden hospital, Tilburg and Maxima Medisch Centrum, Veldhoven. We aim to include 735 patients in this study.

The medical ethics review committee METC Oost-Nederland approved this study.

2. What is the background to this study?

Cancer of the womb is a malignancy that arises from the inner lining on the inside of the womb.

For most patients, treatment of cancer of the womb involves surgery in which the womb, along with the ovaries and fallopian tubes, is removed. These are subsequently examined under the microscope. In a small proportion of patients, the tumor can spread to other parts of the body, such as the lymph nodes. We call this metastases. Metastases in the lymph nodes can only be found by removing these lymph nodes. If the tumor has spread through the body, additional radiotherapy, chemotherapy or hormone therapy may be advised.

Your risk of lymph node metastasis can be estimated with a number of tests. With a new tool, the ENDORISK model, we can work out together with you to see what the best treatment is in your situation. We also take your personal wishes into account.

In the ENDORISK tool, we combine the results of the various tests and examinations that have already been performed. This gives doctors more information on the likelihood that the cancer has spread to the lymph nodes around the womb. This allows doctors to decide whether surgical removal of the lymph nodes. Besides the lymph nodes, other reasons may play a role in whether or not to opt for additional treatment, such as how fit (?) you are and your preferences.

In patients with a high risk of metastases, lymph nodes in the pelvis are removed during surgery so that they can be evaluated under the microscope. By removing lymph nodes, the pathologist can investigate whether there are actually metastases.

Lymph nodes can be removed in two ways: with a sentinel lymph node procedure, or by removing all lymph nodes in the pelvis. In the sentinel lymph node procedure, only the lymph nodes where possible metastases first appear are removed. These lymph nodes are then examined for the presence of cancer. Because less lymph nodes are remove, the risk of side effects, such as lymphoedema: fluid retention in the legs and/or abdomen, is reduced. Less than 5 out of 100 patients experience lymphoedema after a sentinel lymph node procedure.

In a small proportion of patients, we unfortunately cannot find these sentinel lymph nodes. To be sure about metastases in the lymph nodes, we will then have to remove more lymph nodes. If more lymph nodes are removed, a more extensive surgery is needed and there are more surgical risks. Up to 20 out of 100 patients will suffer from lymphoedema after this more extensive surgery. Lymphoedema can lead to restrictions in daily life, such as difficulty moving.

The gynaecologist will discuss the risk of metastases with you and explain the pros and cons of the sentinel lymph node procedure and possible removal of all lymph nodes. Together, you will decide which treatment is best for you.

With this study, we want to see if the ENDORISK tool helps you and your doctor choose which surgery is best for you.

3. How does this study work?

You can participate in this study if you are going to be operated because of cancer of the womb. Your gynaecologist has asked you if you would like to participate in this study. Therefore, you will receive this envelope with a leaflet about this study and a consent form. In this leaflet, on page 3 you can find a link to a video with additional explanation. This video is about your diagnosis, treatment and using ENDORISK in your treatment. You can read the leaflet and watch the video at home. You can also talk to others before making a decision.

If you want to participate, please fill in the consent form and put your signature. You can give the form to your gynaecologist or send it with the enclosed envelope.

When you go over your treatment plan with your gynaecologist, your gynaecologist will enter the results of your tests in the ENDORISK tool. The ENDORISK tool then shows your personal risk of lymph node metastases. The gynaecologist will discuss this score with you. He or she will also explain the pros and cons of removing the lymph nodes.

You will decide together with the gynaecologist whether you want to have your lymph nodes removed during surgery. The types of surgery you can choose from are the same as those if you do not take part in this study.

If you participate in this study, you are giving permission to the researchers to collect your medical data related to your treatment for cancer of the womb. You also consent to receive questionnaires at two times: the first within 4 to 12 weeks of your surgery, the second 1 year after your surgery.

You will receive the questionnaires by e-mail or on paper, depending on your preference. You can indicate this in appendix C. The questions in the questionnaire are about your symptoms, your quality of life and the care you received up to the operation. It will take you about 20 to 30 minutes at a time to complete this questionnaire.

We collect data from your medical record and the Dutch Cancer Registry (NKR) about your cancer of the womb treatment up to five years after your operation. You do not have to do anything yourself for this.

For additional information and explanations about cancer of the womb and ENDORISK, you can watch our information video via the following link: https://www.endorisk.eu/patient

Or via scanning the QR code below by pointing the camera of your phone or tablet at the QR code. The camera will then recognize the code and direct you to our website with the video.

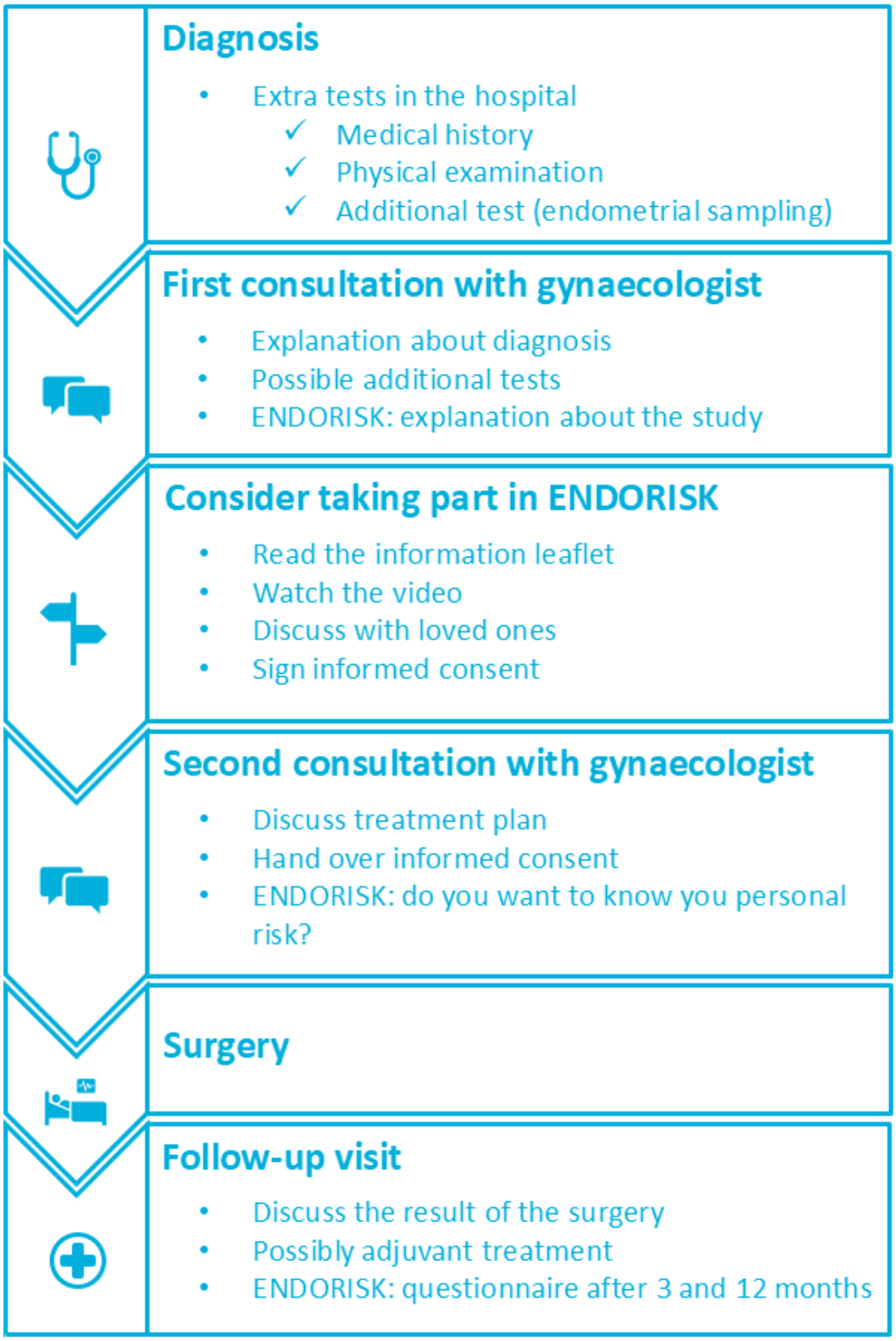

Figure 1: ENDORISK-I study workflow

4. What arrangements will we make with you?

You will contact the researcher in the following cases:

- You no longer want to take part in this study. You can tell us this at any time during this study. The researchers will then use your data collected up to the time of stopping.
- Your telephone number, address or e-mail address changes.

5. What side effects, adverse effects or discomforts may you experience?

Not applicable in this study.

6. What are the advantages and disadvantages of taking part in this study?

If you take part in this study, we can use ENDORISK to estimate your risk of cancer spreading in the lymph nodes. This does not mean that we will know for sure whether or not you have metastases in the lymph nodes. It may be nice to have more information about your risk of metastases in the lymph nodes, but it is also understandable if you prefer not to know this information. You have the choice to indicate to your doctor that you do not want to receive the information from the ENDORISK tool yourself, even though you are participating in this study. In that case, only the doctor will look at the ENDORISK score. However, the doctor will then include the information from the ENDORISK model in the treatment choice.

With your participation, you will help the researchers to see what the use of the ENDORISK tool means in everyday care. This will allow us to help patients like you in the future by improving care around cancer of the womb. Taking part in research will cost you extra time, by completing the two questionnaires. In total, this is usually 40 to 60 minutes.

Don't want to participate?

You decide whether to take part in this study. Don't want to participate? Then you and your doctor will also decide which treatment is best for you. However, you will not receive any information from the ENDORISK tool for this decision.

7. When will this study stop?

The researcher will let you know if there is any new information about this study that is important to you. The researcher will then ask you if you want to continue participating.

In these situations, this study stops for you:

- You want to stop this study yourself. You can do this at any time. In that case, report this immediately to the researcher. You do not have to say why you are stopping. You will still receive the standard care for cancer of the womb.
- The researcher thinks it is better for you to stop.

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- One of the following bodies decides that this study should stop:
    - Radboud university medical centre / Participating hospitals,
    - the government, or
    - The medical ethics committee reviewing this study.
- The endpoint of the whole study has been reached

What happens if you stop this study?
The researchers use the data collected up to the time of stopping.

The whole study ends when all participants finish.

8. What happens after this study?

Will you receive the results of this study?
In Appendix C, you have the option to sign up for the ENDORISK newsletter. This newsletter will keep you informed about the progress of our study. As soon as you subscribe, you will receive the newsletter by e-mail, so you will not miss any developments. You can unsubscribe at any time by sending an e-mail to endorisk@radboudumc.nl .

9. What do we do with your data?

Are you participating in this study? Then you also give us permission to collect, use and store your data.

What data do we save?
We keep this data: your name, your address, your date of birth, data about your health, and (medical) data we collect during this study.

Why do we collect, use and store your data?
We collect, use and store your data to answer the questions in this study. And to publish the results.

How do we protect your privacy?
To protect your privacy, we encode your data. On all your files, we put only this code. We keep the decryption key in a secure place in the hospital. When we process your data, we always use only this code. Even in reports and publications about this study, no one can uncover that it was about you.

Who can see your data?
Your gynaecologist and the research staff supporting this study in your hospital can see your name and other personal data without a code. This may include data collected specifically for this study, as well as data from your medical record. If the research team in your hospital is supported by the ENDORISK research team from the Radboudumc, at the end of this study, all personal data will be sent back to the

hospital in which you are participating. At the end of this study, the ENDORISK research team will only keep anonymized data and questionnaires. This data does not contain your name, only the code associated with you.

How long do we keep your data?
We keep your data in the hospital for 15 years. All data collected are stored at a secure location. Only your hospital's research team has access to this data. Your collected data may also be relevant and used for other scientific research in the field of cancer of the womb and/or of the further development of the ENDORISK model.

May we use your data and body material for other research?
Your collected data may also be relevant for other scientific research in the field of cancer of the womb. Only anonymous data, without patient number, date of birth or name, can be shared for other scientific research. For this purpose, your data will be kept at the hospital for 15 years. In the consent form, you indicate whether you agree to this. Do you not give permission? Then you can still take part in this study. You will receive the same care.

Can you withdraw your consent to the use of your data?
You can withdraw your consent to the use of your data at any time. Just tell the researcher. But beware: do you withdraw your consent, and have researchers already collected data for a study? Then they may still use this data.

Want to know more about your privacy?

- Would you like to know more about your rights when processing personal data? Then take a look at Rights and duties - Radboudumc or www.autoriteitpersoonsgegevens.nl.
- Do you have questions about your rights? Or do you have a complaint about the processing of your personal data? If so, please contact the person responsible for processing your personal data. For your research this is: Radboud University Medical Centre. See Appendix A for contact details, and website.
- If you have complaints about the processing of your personal data, we recommend that you first discuss these with the research team. You can also go to Radboud university medical centre's Data Protection Officer. Or you can file a complaint with the Personal Data Authority.

Where can you find more information about this study?
You can find more information about this study on the following website: www.endorisk.eu.

10. Will you get reimbursed if you take part in this study?

Using the ENDORISK model for this study does not cost you anything. You will also not receive any compensation if you take part in this study.

11. Are you insured during this study?

Insurance has been arranged for everyone taking part in this study. The insurance pays for damage caused by this study. But not for all damages. In **Appendix D** you will find more information about the insurance and the exceptions. It also says who you can report damage to.

12. We inform your treating specialist

Not applicable in this study.

13. Any questions?

You can ask the research team questions about this study. Do you have a complaint? Please discuss this with the researcher or the doctor treating you. Do you want advice from someone who has no interest in this? Then contact the independent expert, contact details are in Appendix A. The independent expert knows a lot about this study but is not involved in it. Would you rather not? Then go to your hospital's complaints committee. All contact details are in Appendix A.

14. How do you consent to this study?

You can first think about this research calmly. Then tell the researcher if you understand the information and whether or not you want to take part. Do you want to participate? Then fill in the consent form that you will find enclosed with this information letter. We ask you to do this before or during the consultation in which your treatment is discussed. Thank you for your time.

Thank you in advance for your time.

Kind regards, also on behalf of the rest of the ENDORISK research team,

Anna Schoenaker (researcher), Ruben Koek (physician-researcher), Marike Lombaers (physician-researcher) and Hanny Pijnenborg (gynaecologist)

15. Appendices to this information

A. Contact details
B. Consent form for study participation
C. Consent form to send questionnaire
D. Insurance information

Appendix A: contact details for [name of participating centre].

ENDORISK research team [Participating centre name]:

[Name], gynaecologist

Phone number:

Email:

Facility Data Protection Officer:

Independent expert: dr. Bertho Nieboer, Gynaecologist, bertho.nieboer@radboudumc.nl

ENDORISK Radboudumc research team:

Marike Lombaers, physician-researcher

Anna Schoenaker, researcher

Ruben Koek, physician-researcher

Hanny Pijnenborg, gynaecologist

ENDORISK telephone number: 06 31 01 51 09

Email: endorisk@radboudumc.nl

Contact details for complaints about this study:
Radboudumc
Attn: Klachtenbemiddeling
Mailbox 348
Reply number 540
6500 VC NIJMEGEN
Tel: 024-3613191
Website Complaints Mediation: https://www.radboudumc.nl/patientenzorg/uw-afspraak/meer-informatie/klachten

Radboudumc Data Protection Officer contact details:
Radboudumc
Attn: Functionaris voor Gegevensbescherming
Mailbox 630
P.O. Box 9101
6500 HB NIJMEGEN
Website Privacy: https://www.radboudumc.nl/patientenzorg/rechten-en-plichten/privacy
E-mail: gegevensbescherming@radboudumc.nl

Appendix B: consent form trial subject

Belonging to **" Personal risk of lymph node metastases in cancer of the womb (ENDORISK-I)"**

- I read the information letter. I was also able to ask questions. My questions were answered well enough. I had enough time to decide whether to participate.
- I know that participating is voluntary. I also know that I can decide to stop at any time. I do not then have to say why I want to stop.
- I give the researchers permission to collect and use my data for the purposes stated in the written information.
- I know that for monitoring/controlling this study, some people will be able to see all my data. Those people are listed in this information letter. I give these people permission to see my data for this monitoring.
- I know that my data will be used for (further) scientific research and made available to researchers for statistical analysis, without being traceable to me personally.
- I consent to my data being linked to my disease and treatment data as recorded in the Dutch Cancer Registry and to data from the medical record.
- Please tick yes or no in the table below.

I give permission that, if I die during the term of this study, my official cause of death data will be requested from the Central Bureau for Statistics Netherlands.	Yes ☐	No☐
I consent to the sharing of my anonymised data with other parties as part of scientific research, as stated in the written information.	Yes ☐	No☐
I consent to being asked to participate in a follow-up study if necessary after this study.	Yes ☐	No☐
I want to receive my personal ENDORISK score from my treating gynaecologist	Yes ☐	No ☐

- I want to participate in this study.

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

Signature: ..... Date : __ / __ / __

I declare that I have fully informed this subject about the said study. Will any information become known during this study that may affect the subject's consent? If so, I will let this subject know in good time.

Investigator's name (or representative):.....

Signature:..... Date:__ / __ / __

Appendix C: consent form to send questionnaire

Accompanying **" Personal risk of lymph node metastasis in cancer of the womb (ENDORISK-I)"**

By entering your name and address in the field below, you indicate your consent to the use of your address data for sending the questionnaire. This data will be processed with the utmost care. Under no circumstances will we give these data to third parties. To ensure that your answers remain anonymous, this form will be separated from the questionnaire immediately upon receipt. We adhere to the relevant laws and regulations.

First name:…….

Last name:……

Address: ……

Postal code: ……. City……..

Phone number: ……

(If your details are unclear)

E-mail address to receive the questionnaire:

……@.....

□ I do not have an e-mail address (you will receive the questionnaire on paper)

Would you like to be kept informed about the survey via our digital newsletter? Then also enter your email address. You will then receive the newsletter by email. You can unsubscribe at any time by sending an email to endorisk@radboudumc.nl .

Yes ☐ No ☐

Appendix D: insurance information

Accompanying **" Personal risk of metastases in the lymph nodes in cancer of the womb (ENDORISK-I)"**

The Radboud University Medical Centre has arranged insurance for everyone taking part in this study. The insurance will pay for any damage you have as a result of taking part in this study. It covers damage you suffer during this study, or within 4 years of the end of your participation in this study. You must report damage to the insurer within 4 years.

Do you have damage due to this study? Then report this to this insurer:

The insurer of this study is: Name insurer: Centramed Address: P.O. Box 7374, 2701 AJ Zoetermeer Telephone number: 070 301 70 70 E-mail: info@centramed.nl Policy number: 624.100.021

The insurance pays a maximum of €650,000 per person and €5,000,000 for the entire investigation and €7,500,000 per year for all investigations by the same client.

Please note that the insurance **does not** cover the following damages:

- Damage due to a risk about which we have given you information in this letter. But this does not apply if the risk turned out to be greater than we thought in advance. Or if the risk was very unlikely.
- Damage to your health that would have occurred even if you had not participated in this study.
- Damage that occurs because you did not follow directions or instructions or did not follow them properly.
- Damage caused by a treatment method that already exists. Or by research into a treatment method that already exists.
- Damage to the health of your children or grandchildren.

These provisions are in the 'Decree on compulsory insurance in medical scientific research with humans 2015'. This decree can be found in the Government Law Database (https://wetten.overheid.nl).