United Kingdom Collaborative Trial of Ovarian Cancer Screening (UKCTOCS)

You are being asked to take part in a research study of screening for ovarian cancer. Invitations are being sent to women in your region who are not known to have ovarian cancer. Before you decide it is important for you to understand why the research is being done and what it will involve. Please read the following information carefully and discuss it with friends, relatives and your GP if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

What is the purpose of the study?
Ovarian cancer is the fourth commonest cause of death from cancer amongst women in the UK. The majority of women who develop this cancer have few symptoms until it has spread outside the ovaries. By then, the cancer is much more difficult to treat and many women will die as a consequence of the cancer. In contrast, treatment is more successful and the outlook can be good for the small proportion of women diagnosed before the ovarian cancer has spread. The purpose of this study is to determine whether screening will detect ovarian cancer at an early stage when treatment is more effective and therefore reduce the number of deaths due to the disease.

Large studies performed by our research team during the last decade have developed and refined two methods of screening. One method uses ultrasound scanning, similar to the scanning used in pregnancy, to check for any enlargement or abnormality of the ovaries. This trial will use a method of ultrasound scanning called transvaginal scan whereby a probe is inserted into the vagina to see the ovaries. This method of scanning gives a much clearer picture of the ovaries than a transabdominal scan, where the probe is placed on the abdomen. Transvaginal scan should be no more uncomfortable than having a smear test. If, however, transvaginal scanning is not possible or acceptable a transabdominal scan will be performed. The second method involves a blood test to measure a substance called CA125, which is released at higher levels into the blood in women with ovarian cancer. Using these tests it seems likely that over 80% of women with ovarian cancer can be identified before they have symptoms. This current very large trial will answer the question whether early detection of ovarian cancer, using these tests can save the lives of women who have ovarian cancer.

The study will also assess the cost implications of the screening methods to the National Health Service (NHS), what anxieties and fears being screened may raise and what complications might arise as a result of screening. This information will be used to make a decision about whether an NHS national screening programme for ovarian cancer should be introduced.

The study will last for 10 years. If you agree to take part you will be followed up for 6 years.

Why have I been chosen?
We need a total of 200,000 women, aged 50-74 years to take part in this study. You have been invited as you belong to this age group. Your details were obtained from the age/sex register of your health authority.

Do I have to fulfil any other criteria to take part?
In order to be eligible to take part you should:

- Be 50-74 years of age.
- Postmenopausal, i.e. you should not have had a period within the past 12 months if you are not taking hormone replacement therapy (HRT). However, if you are taking HRT, you are still eligible to take part, if you have taken it for one year or more.
- Not have had both your ovaries removed at surgery. You can still take part if only one ovary was removed.
- Not have had surgery, chemotherapy or radiotherapy for any type of cancer within the past 12 months.
- Not currently be taking part in any other screening programme for ovarian cancer.
- Not belong a to a family with a high risk of familial ovarian cancer. Such families have:

1. Two or more first degree relatives (mother, sister, daughter) with ovarian cancer.
2. One first degree relative with ovarian cancer and one first degree relative with breast cancer diagnosed under 50 years of age.
3. One first degree relative with ovarian cancer and two first or second degree (grandmother, grandaughter, aunt or niece) relatives with breast cancer diagnosed under 60 years of age.

4. Three first degree relatives with cancer of the large intestine or bowel, with at least one diagnosed before the age of 50 years and at least one first degree relative with ovarian cancer.

"If you do belong to such a family and are a first degree relative of the person with cancer you may be at slightly higher risk of developing ovarian cancer and require regular screening. If you are concerned about your risk of developing ovarian cancer, further information can be obtained from the OVACOME (a support group for ovarian cancer patients and their families, tel: 0207 380 9589), Cancer BACUP (an information service about cancer, tel: 0808-800-1234) or your GP."

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be asked to sign a consent form. If you decide to take part you are free to withdraw at any time and without giving a reason. This will not affect any medical care you receive.

What will happen to me if I take part?

If you agree to take part in this study please attend the appointment that you have been given in the attached letter. If you are unable to make this appointment, please phone to re-arrange to a more convenient time. At the appointment, you will be shown a video about the study and given the opportunity to ask any questions. If you decide to participate you will be asked to fill a datasheet and to sign a consent and data protection form. A blood sample will be taken. Your General Practitioner will be informed of your participation.

You will be given a further questionnaire to complete at home and return by post to assess the psychological implications of screening and the acceptability of the screening methods. This should not take more than 10 minutes of your time. A small number of women including those who have abnormal results on screening will be sent repeat questionnaires to complete at home in the course of the study.

Because we do not know if either of the screening methods are able to save lives from ovarian cancer we need to compare both methods of screening with a group of women who will not be screened. This will tell us whether screening can save lives and which method is most effective. This is called a randomised trial. The groups are selected by a computer and cannot be influenced by you or us. Of the 200,000 women who agree to participate half will be screened every year for 6 years and half will be in the control group and followed up with questionnaires without screening. Overall the study will take 10 years to complete. Of the 100,000 women who will be screened 50,000 will be screened with ultrasound and 50,000 with the CA 125 blood test.

Travel expenses (for visits due to the research study) cannot be guaranteed as they are not provided by the research funders. In the event of hardship, you may wish to discuss travel costs with the research team at your regional centre who will do their best to help you.

Control / Questionnaire Group

If you are allocated to the group not to be screened you will be asked to complete health related questionnaires 4 and 7 years after you are recruited. The questionnaires will be sent to your home for you to complete and you will not be required to attend any further appointments. We will request your GP to refer you to the same specialist at the regional centre as women who are allocated to the screened groups if at anytime you develop symptoms that raises the possibility of ovarian cancer. You will not be asked to have further blood tests or an ultrasound scan. The blood test taken at your registration visit will not be tested at this time but will be stored to be used at some stage in the future to assess potential tests for cancer. As these will be tests in the initial phases of being researched, the results will not be conclusive and therefore you will not be notified of the results. If you are allocated to this group your contribution is vital to the outcome of the study.

Blood test for CA125 group (multimodal group)

If you are allocated to the CA125 group the blood taken at your registration visit will be tested. Your potential risk of developing ovarian cancer (ROC) in the year following the blood test will be calculated. Your ROC will be recalculated after each blood test. The ROC calculation is looking for changes in your blood results over time. For this reason your recommended follow-up may vary during the course of the study but will be one of the following:

- If your ROC is within normal limits you will be asked to return for a further blood test in one year. Most women will fall into this group and be recalled annually throughout the study.
- If there is a slight change in the levels of your blood test your ROC will be classified as intermediate and you will be asked to return for a repeat blood test 3 months later.

- If your ROC is higher than would be expected (elevated) you will be sent an appointment for a further blood test and an ultrasound scan of your ovaries. It is important to note that most women who require an ultrasound scan will not have an abnormality of their ovary and will not require surgery. If the ultrasound scan does reveal an abnormality of the ovaries, you will be referred to a specialist at the regional centre for further tests and surgery to remove your ovaries. This will be arranged in consultation with yourself and your General Practitioner. Only 1 in 5 of the women who have an abnormal test and have surgery will have ovarian cancer. The others will usually have less serious conditions of the ovary.

Ultrasound group
If you are allocated to the ultrasound group you will be sent an appointment for a scan of your ovaries. If no abnormalities are detected on the scan you will be sent an appointment for a further scan in one year. If an abnormality is seen, you will be sent an appointment for a repeat scan in 6-8 weeks. This is because many of the abnormalities will disappear on their own and need no treatment. If the repeat scan is normal you will be recalled in one year. If the repeat scan shows that the changes seen in the first scan persist, you will be referred to a specialist at the regional centre for further tests and surgery to remove your ovaries. This will be arranged in consultation with yourself and your General Practitioner. Only 1 in 15 of the women who have an abnormality detected at ultrasound and have surgery will have ovarian cancer. The others will usually have non cancerous conditions of the ovary.

You will be notified by post of your recommended follow-up after every blood test or investigation.

Samples storage and future use
We will store a portion of all blood taken during the course of the trial. These samples will be stored indefinitely under the custodianship of University College London. Some of these stored samples will be used for future research studies. The focus of this research will be the early detection and treatment of disease. Researchers will have to get permission from the Ethics Committee before using any samples. If this happens, all the samples you donated will be used anonymously. As the samples will not have your name or identification, it will not be possible to trace them back to you or to inform you of the results. It is possible that collaborative research may include researchers working for commercial companies. If you are concerned about any future research please do discuss this with the UKCTOCS team. It is still possible for you to take part in the screening study if you do not wish the blood taken for analysis in this study to be used for future research.

Follow up
All study participants will be mailed a health questionnaire in years 3 and 7. In addition, the Office of National Statistics will be provided with the name, address and NHS number of all the study participants.

What do I have to do before the tests?
There is no special preparation for either the blood test or the ultrasound scan.

What is the procedure being tested?
Two screening procedures are being tested to find out whether ovarian cancer can be detected in the early stage.

The blood test for CA125
Most women who develop ovarian cancer have high levels of the protein called CA125 in their blood. The CA125 test is therefore currently used to diagnose ovarian cancer in women with symptoms and to monitor women after treatment. It has been shown that the CA125 test can be elevated in the early stage of many ovarian cancers. In addition, the research team believes that it may be possible to identify those women with early ovarian cancer where the CA125 blood test is not elevated by looking for changes i.e. increases in a woman's blood results over time.

Ultrasound scans
Ultrasound is currently widely used for diagnosing ovarian cancer in women with symptoms. It has been shown that the ultrasound test can be abnormal in the early stage of many ovarian cancers.

What are the possible disadvantages of taking part?
- Some women may have ovarian cancer that has not been identified by the test and thus be falsely reassured. If you develop any symptoms that you are concerned about, you should see your doctor as soon as possible.
- CA125 is not a test for all types of cancer. You should continue with all routine screening e.g. smear tests and breast screening, as advised by your GP surgery.
- Women taking part in the study have a 1 in 70 chance of being referred for surgery on the basis of abnormal screening results.

- Of every 1,000 women who undergo screening, 20-30 will have a positive screening test leading to surgery but only 2-3 of these women will actually have ovarian cancer. Most of the other women will be found to have other less serious abnormalities at surgery (e.g. ovarian cysts, endometriosis, scar tissue or infection). In a small number of women who undergo surgery no abnormality will be found at all.
- Not all women with ovarian cancer who are identified by the screening test will have early disease, the disease may be more advanced. The screening test may therefore not make a difference to the type of treatment a woman may receive or the outcome of the treatment.
- Having a screening test can create anxiety in some women.

What are the possible benefits of taking part?

- The only direct benefit of taking part for the women allocated to the questionnaire group is that we will request that they are referred to the specialist at the regional centre if their GP suspects that they may have an ovarian cancer. The participation of these women is however vital to the outcome of the study. Their participation will help decide whether either screening method is of benefit and whether a national screening programme should be implemented.
- If a woman allocated to the screened groups does have ovarian cancer, but no symptoms, there is at least an 80% chance that she would be identified by the test.
- If a woman allocated to the screened groups does not have cancer there is at least a 99.5% chance that the test will be negative and provide reassurance.

What if new information becomes available?

There is an independent Data Monitoring and Ethics committee that will assess the trial on an ongoing basis. If any information should become available that makes this study unethical, then this committee will recommend to the Trial Steering Committee which also has an independent chairman and non medical representatives that the study be stopped.

What if something goes wrong?

You will always be able to contact a research nurse or doctor at your regional centre to discuss your concerns and we will give you an emergency telephone number. We will take every care in the course of this trial. If through our negligence any harm to you results, you will be compensated. However, a claim may have to be pursued through legal action. Even if the harm is not our fault, the Trusts will consider any claim sympathetically. If you are not happy with any proposed compensation you may have to pursue your claim though legal action.

Will 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. Occasionally the research documentation and results will be looked at by the people funding the research programme to check that the study is being carried out properly. Any information about you which is viewed by people not directly related to the research team will have your name and address removed so that you cannot be recognised from it.

What will happen to the results of the research study?

The results will be reviewed by other medical professionals and published in the medical press. Results will probably only be available within a 12 year period. Should either screening method prove to be of benefit the results will be presented to the government as a case for a national screening programme to be implemented. You will be notified in writing that the study has been completed and of the outcome. Individuals will not be identified in any publications.

Who is organising and funding the research?

The study is being organised by the Gynaecological Cancer Research Centre at the Institute of Women's Health, University College London. It is being funded jointly by the Medical Research Council (MRC), Cancer Research UK and the NHS Research and Development.

For further information please write to:

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