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The long-term impact on deaths and cost-effectiveness of screening for ovarian cancer using a blood test and ultrasound

Submission date
06/04/2000

Recruitment status
No longer recruiting

Registration date
06/04/2000

Overall study status
Completed

Last Edited
14/03/2025

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-at-screening-the-general-population-for-ovarian-cancer

Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT00058032

Protocol serial number
Current Version 9.0

Study information

Scientific Title
UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) and the long-term impact of screening on ovarian cancer mortality in UKCTOCS

Acronym
UKCTOCS and LTFU UKCTOCS

Study objectives
Current hypothesis as of 24/08/2020:
Hypothesis 1 – Preclinical detection by screening can reduce mortality from ovarian cancer (OC).
Hypothesis 2 – OC mortality can be reduced without unacceptable physical and psychological morbidity.
Hypothesis 3 – OC mortality can be reduced at an acceptable economic cost to the health service.
Hypothesis 4 – If population screening for OC were introduced compliance would be high enough for an impact on overall mortality from OC to be achievable.

Previous hypothesis as of 01/10/2015:
Hypothesis 1 – Preclinical detection by screening can reduce mortality from Ovarian Cancer (OC).
Hypothesis 2 - OC mortality can be reduced without unacceptable physical and psychological morbidity.
Hypothesis 3 - OC mortality can be reduced at an acceptable economic cost to the health service.
Hypothesis 4 - If population screening for OC were introduced compliance would be high enough for an impact on overall mortality from OC to be achievable

Original hypothesis:
1. To establish the impact of preclinical detection of ovarian cancer by screening on ovarian cancer mortality
2. To determine the physical morbidity of ovarian cancer screening
3. To determine the resource implications of screening and the interventions which result from

screening
4. To record the psychological consequences of screening in the subgroups of true negative, true positive, false negative and false positive screening results
5. To assess the feasibility of population screening for ovarian cancer as reflected by uptake of invitations and compliance rates with annual screening
6. To compare the performance of two screening strategies for ovarian cancer
7. To establish a serum bank for future assessment of novel tumour markers

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West Medical Research and Ethics Committee (renamed to North West – Haydock), 21/06/2000, ref: 00/8/034

Study design
Part 1: Randomised controlled trial
Part 2: Observational longitudinal follow up study

Primary study design
Interventional

Study type(s)
Screening

Health condition(s) or problem(s) studied
Tubo-ovarian cancer

Interventions
Current intervention as of 24/08/2020:
Three groups:
1. A control group (no screening)
2. A multimodal group (annual screening with serum CA125 interpreted using the Risk of Ovarian Cancer Algorithm (ROCA) as the primary test and CA125/ROCA and ultrasound as the secondary test)
3. An ultrasound group (annual screening with ultrasound as the primary test and repeat ultrasound in 6-8 weeks as the secondary test)

Participants will be followed up through national cancer and death registries and hospital administrative databases via data linkage using their NHS number and follow-up questionnaires.

Quality of life questionnaires will be sent to women newly diagnosed with ovarian cancer.

Previous intervention:
Randomised controlled trial:
Three groups:
1. A control group (no screening)
2. A multimodal group (annual screening with serum CA125 interpreted using the Risk of Ovarian Cancer Algorithm (ROCA) as the primary test and CA125 and ultrasound as the

secondary test)
3. An ultrasound group (annual screening with ultrasound as the primary test and repeat ultrasound in 6 - 8 weeks as the secondary test)

Observational longitudinal follow up study:
Eligible women will be followed up through national cancer and death registries and hospital administrative databases via data linkage using their NHS number till 31st June 2019. Quality of life questionnaires will be sent to women newly diagnosed with ovarian cancer

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
Current primary outcome measure as of 24/08/2020:
UKCTOCS:
Ovarian cancer mortality at 7 years after randomisation. Death due to ovarian cancer, defined by WHO 2003 criteria, as determined by independent outcomes committee review of patient notes of all women identified through data linkage and postal follow-up to have a 'possible ovarian cancer' (pre-specified list of International Classification of Disease codes) up to 31st December 2014.

Long term impact of screening on ovarian cancer mortality in UKCTOCS (LTFU UKCTOCS):
Death due to ovarian cancer, defined by WHO 2014 criteria as determined by independent outcomes committee review of patient notes of all women identified through data linkage to have a 'possible ovarian cancer' (pre-specified list of International Classification of Disease codes) up to 30th June 2020.

Previous primary outcome measure as of 04/01/2017:
Randomised controlled trial:
Ovarian cancer mortality at 7 years after randomisation. Death due to ovarian cancer, defined by WHO 2003 criteria, as determined by independent outcomes committee review of patient notes of all women identified through data linkage and postal follow-up to have a 'possible ovarian cancer' (pre-specified list of International Classification of Disease codes) till 31st December 2014.

Observational longitudinal follow up study:
Death due to ovarian cancer, defined by WHO 2014 criteria as determined by independent outcomes committee review of patient notes of all women identified through data linkage to have a 'possible ovarian cancer' (pre-specified list of International Classification of Disease codes) till 31st December 2018.

Key secondary outcome(s))
Current secondary outcome measures as of 24/08/2020:
UKCTOCS:
1. Performance characteristics: Sensitivity, specificity, positive predictive values of the two screening strategies (multimodal and ultrasound) for detection of ovarian cancer diagnosed within 1 year of last screen. Ovarian cancer diagnosis is based on outcomes review of medical notes of all women who developed ovarian cancer during the trial.

2. Surgical complications in women who underwent false positive surgery and were found to have benign or normal adnexae. This is assessed through central medical note review and assigned by designated trial gynaecological oncologist.
3. Cost-effectivenesss of the multimodal (MMS) and ultrasound screening (USS) strategies separately comparing them to a no-screening arm:
3.1. Incremental cost-effectiveness analysis over the 14-year period of the trial (censorship 31st Dec 2014)
3.2. Incremental cost-effectiveness analysis for the cumulative mortality estimated over a 25-year period by extrapolating beyond the 14 years of the trial
4. Compliance with annual screening: The proportion of women who attended all tests that formed part of an annual screening episode of the total who were eligible for that annual screening episode. Psychological morbidity related to screening - assessed in a separate MRC funded study, UKCTOCS Psychosocial study, PI Prof Dame Lesley Fallowfield.

LTFU UKCTOCS:
Cost-effectiveness of ovarian cancer screening: This will be assessed using individual patient datafrom English (Hospital Episodes Statistics), Welsh (Patient Episode Database for Wales) and Northern Ireland hospital administrative databases. The data will be augmented with resource data collected on individual diagnostic tests and treatment through medical record review. All unit costs will be based on NHS Reference Costs with additional costs as reported by the relevantPersonal Social Services Research Unit Cost exercise.

Previous secondary outcome measures as of 04/01/2017:
Randomised controlled trial:
1. Performance characteristics: Sensitivity, specificity, positive predictive values of the two screening strategies (multimodal and ultrasound) for detection of ovarian cancer diagnosed within one year of last screen. Ovarian cancer diagnosis is based on outcomes review of medical notes of all women who developed ovarian cancer during the trial.
2. Surgical complications in women who underwent false positive surgery and were found to have benign or normal adnexae. This is assessed through central medical note review and assigned by designated trial gynaecological oncologist.
3. Cost-effectivenesss of the multimodal (MMS) and ultrasound screening (USS) strategies separately comparing them to a no-screening arm:
3.1. Incremental cost-effectiveness analysis over the 14 year period of the trial (censorship 31st Dec 2014)
3.2. Incremental cost-effectiveness analysis for the cumulative mortality estimated over a 25-year period by extrapolating beyond the 14 years of the trial
4. Compliance with annual screening: The proportion of women who attended all tests that formed part of an annual screening episode of the total who were eligible for that annual screening episode. Psychological morbidity related to screening - assessed in a separate MRC funded study, UKCTOCS Psychosocial study, PI Prof Dame Lesley Fallowfield.

Observational longitudinal follow up study:
Cost-effectiveness of ovarian cancer screening: This will be assessed using individual patient data from English (Hospital Episodes Statistics), Welsh (Patient Episode Database for Wales) and Northern Ireland hospital administrative databases. The data will be augmented with resource data collected on individual diagnostic tests and treatment through medical record review. All unit costs will be based on NHS Reference Costs with additional costs as reported by the relevant Personal Social Services Research Unit Cost exercise.

Previous secondary outcome measures as of 01/10/2015:
1. Performance characteristics of the two screening strategies (serum CA125 versus ultrasound)

2. Physical morbidity resulting from surgical intervention attributable to screening
3. Psychological consequences of screening
4. Resource implications of screening and the resulting interventions
5. Feasibility of screening, as reflected by compliance rates with annual screening
6. Establish a serum bank for future assessment of novel tumour markers

Completion date
31/12/2024

Eligibility

Key inclusion criteria
1. Aged 50 - 74 years
2. Postmenopausal: either
2.1. Greater than 12 months amenorrhoea following a natural menopause or hysterectomy, or
2.2. Greater than 12 months of hormone replacement therapy (HRT) commenced for menopausal symptoms

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
50 years

Upper age limit
74 years

Sex
Female

Total final enrolment
202638

Key exclusion criteria
1. History of bilateral oophorectomy
2. Currently active non-ovarian malignancy. Women who have a past history of malignancy will only be eligible if:
2.1. They have no documented persistent or recurrent disease, and
2.2. They have not received treatment for more than 12 months
3. Women who have had an ovarian malignancy in the past
4. Women at high risk of ovarian cancer due to familial predisposition as defined by the eligibility criteria for the UK Familial Ovarian Cancer Screening Study (UKFOCSS)
5. Women participating in other ovarian screening trials

Date of first enrolment
17/04/2001

Date of final enrolment
29/09/2005

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Wales

Study participating centre
UKCTOCS Coordinating Centre - UCL (2001-2018
Gynaecological Cancer Research Centre
Department of Women's Cancer
Institute for Women's Health, UCL
London
United Kingdom
W1T 7DN

Study participating centre
University College London - Tumour Marker Laboratory (2001-2012)
London
United Kingdom
WC1E 6BT

Study participating centre
Belfast City Hospital
Belfast
United Kingdom
BT9 7AB

Study participating centre
St Michael's Hospital
Bristol
United Kingdom
BS2 8EG

Study participating centre
University of Wales College of Medicine
Cardiff
United Kingdom
CF14 4XN

Study participating centre
Derby City General Hospital
Derby
United Kingdom
DE22 3NE

Study participating centre
Queen Elizabeth Hospital
Gateshead
United Kingdom
NE9 6SX

Study participating centre
Liverpool Women's Hospital
Liverpool
United Kingdom
L8 7SS

Study participating centre
Royal Free Hospital
London
United Kingdom
NW3 2QG

Study participating centre
St Bartholomew's Hospital
London
United Kingdom
EC1A 7BE

Study participating centre
Manchester Royal Infirmary
Manchester
United Kingdom
M13 9WL

Study participating centre
James Cook University Hospital
Middlesbrough
United Kingdom
TS4 3BW

Study participating centre
Llandudno General Hospital
Gwynedd
United Kingdom
LL30 1LB

Study participating centre
Nottingham City Hospital
Nottingham
United Kingdom
NG5 1PB

Study participating centre
St Mary's Hospital
Portsmouth
United Kingdom
W2 1NY

Study participating centre
UKCTOCS Coordinating Centre - MRC CTU at UCL (since 2018)
Institute of Clinical Trials & Methodology
University College London
London
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WC1V 6LJ

Sponsor information

Organisation
University College London (UK)

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (UK)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Cancer Research UK

Alternative Name(s)
CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
Department of Health (UK)

Funder Name
The Eve Appeal (UK)

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The individual participant data that underlie the results reported in The Lancet May 2021 article, after de-identification will be available upon request beginning 12 months after publication from the MRC CTU at UCL (mrcctu.datareleaserequest@ucl.ac.uk). Researchers will need to state the aims of any analyses and provide a methodologically sound proposal. Data requestors will need to sign a data access agreement, cover administrative costs and in keeping with patient consent for secondary use, obtain ethical approval for any new analyses.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/08/2006		Yes	No
Results article	results	01/05/2007		Yes	No
Results article	results	13/11/2008		Yes	No
Results article	results	01/04/2009		Yes	No
	results	10/08			

Results article		/2010	Yes	No
Results article	results	01/01 /2011	Yes	No
Results article	results	01/03 /2011	Yes	No
Results article	results	01/11 /2011	Yes	No
Results article	results	01/01 /2012	Yes	No
Results article	results	10/04 /2012	Yes	No
Results article	results	05/06 /2012	Yes	No
Results article	results	01/09 /2012	Yes	No
Results article	results	01/11 /2012	Yes	No
Results article	results	01/01 /2013	Yes	No
Results article	results	15/01 /2013	Yes	No
Results article	results	28/05 /2013	Yes	No
Results article	results	01/10 /2013	Yes	No
Results article	results	26/11 /2013	Yes	No
Results article	results	03/03 /2014	Yes	No
Results article	results	01/05 /2014	Yes	No
Results article	results	30/05 /2014	Yes	No
Results article	results	27/06 /2014	Yes	No
Results article	results	01/08 /2014	Yes	No
Results article	results	24/09 /2014	Yes	No
Results article	results	01/12 /2014	Yes	No
Results article	results	15/01 /2015	Yes	No
Results article	results	01/02 /2015	Yes	No
Results article	results	17/03 /2015	Yes	No
Results article	results	01/04 /2015	Yes	No
Results article	results	01/04 /2015	Yes	No
Results article	results	20/06 /2015	Yes	No
Results article	results	01/07 /2015	Yes	No
Results article	results	01/07 /2015	Yes	No

Results article	results	14/07/2015		Yes	No
Results article	results	01/10/2015		Yes	No
Results article	results	10/01/2016		Yes	No
Results article	results	01/02/2016		Yes	No
Results article	Key results discussing primary analysis	05/03/2016		Yes	No
Results article	results	01/04/2016		Yes	No
Results article	results	01/06/2016		Yes	No
Results article	results	15/06/2016		Yes	No
Results article	results	25/06/2016		Yes	No
Results article	results	09/11/2016		Yes	No
Results article	results	03/01/2017		Yes	No
Results article	results	06/03/2017		Yes	No
Results article	results	11/04/2017		Yes	No
Results article	results	01/06/2017		Yes	No
Results article	results	28/06/2017		Yes	No
Results article	results	27/03/2018		Yes	No
Results article	results	15/04/2020	16/04/2020	Yes	No
Results article	results	01/10/2019	22/07/2020	Yes	No
Results article	results	25/01/2021	27/01/2021	Yes	No
Results article	results on ultrasound strategy performance	18/02/2021	08/03/2021	Yes	No
Results article	Key long term follow up results	05/06/2021	13/08/2021	Yes	No
Results article	Exploratory analysis	01/09/2023	04/09/2023	Yes	No
Results article	Ovarian cancer symptoms in pre-clinical invasive epithelial ovarian cancer	17/11/2023	20/11/2023	Yes	No
Results article	Key primary and secondary outcome results	11/05/2023	14/03/2025	Yes	No
Other publications	update	01/03/2021	03/03/2021	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Plain English results				No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes