THE AVOIDING LATE DIAGNOSIS OF OVARIAN CANCER (ALDO) PROJECT; A PILOT NATIONAL SURVEILLANCE PROGRAM FOR WOMEN WITH PATHOGENIC GERMLINE VARIANTS IN *BRCA1* AND *BRCA2*.

Supplementary Tables, Figures and Information

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Philpott S, *et al. J Med Genet* 2023; 60:440–449. doi: 10.1136/jmg-2022-108741

PARTICIPANT INFORMATION SHEET

Project title: Avoiding Late Diagnosis of Ovarian Cancer (ALDO)

You are being invited to take part in the ALDO project, a one year NHS pilot scheme offering surveillance for ovarian cancer using the ROCA Test. This service is available for women like you, who are at high risk of developing ovarian cancer, and who are unable to or have not yet decided to have their ovaries removed (risk-reducing surgery).

Before you make your decision, it is important for you to understand why this project is being done and what it will involve. Please take your time to read the following information carefully. You may want to talk to your family or friends before taking part.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether you want to take part or not.

What is the purpose of the project?

Women who carry a mutation in the BRCA1 and or BRCA2 gene are at a high risk of developing ovarian cancer. The only way to prevent ovarian cancer is to have risk-reducing surgery (having your ovaries and fallopian tubes removed). However many women delay having surgery for a number of reasons such as wanting to complete their family, avoid early menopause and associated symptoms / problems or because they have other significant health problems which make surgery too risky.

For women who do delay having surgery, surveillance with a 4 monthly blood test could be a reassuring option until they are ready for surgery. Routine surveillance with the ROCA Test does not prevent ovarian cancer, but it does detect the cancer at an earlier stage than if no surveillance is done. The aim of this project is to test surveillance within the NHS and gather evidence to help the NHS decide whether this screening should be adopted as standard practice.

Why have I been invited to take part?

You have been invited to take part because you carry a mutation in the BRCA1 or BRCA2 gene, and as far as we are aware, you have not yet decided to have surgery to remove your ovaries.

Do I have to take part?

It is up to you whether you want to take part in this project. Whatever your decision, the care you currently receive will remain the same. If you agree to this now, you can stop taking part at any time and you don't have to give a reason.

If you decide to have risk-reducing surgery at any time during the project, you can continue with the surveillance until your surgery date.

What will taking part involve?

If you decide to take part, you will have a blood test taken every 4 months. You will be sent a blood taking pack to take to your GP. Once the blood has been taken, you need to post it back to us for analysis in our laboratory. We will supply the pre-paid envelope for this purpose.

Your blood will be tested for CA-125, a protein which increases in cases of ovarian cancer. The result of the CA-125 is then analysed by the ROCA Test, which tells us how likely it is that you currently have an ovarian cancer. The ROCA Test calculates your risk, by looking at your age, your menopause status and previous CA-125 levels if you have any.

Your result will be classified as one of the following:

- Normal
- Mildly Elevated (your current risk of having ovarian cancer is between 1 in a 1000 and 1 in 501)
- Moderately Elevated (your current risk of having ovarian cancer is between 1 in 500 to 1 in 34)
- Significantly Elevated (your current risk of having ovarian cancer is greater than 1 in 33)

You will receive the results within 7 days of the sample reaching the laboratory. In most cases, an elevated result does not mean that you have ovarian cancer, but will mean that you need a repeat blood test and possibly some other investigations such as a scan of your ovaries (done using a small probe placed inside the vagina). If you do need a scan or other investigations you will need to attend one of the following hospitals, depending on where you live: UCLH (University College London Hospital), Barts Hospital London, St George's Hospital London, St Mary's Hospital Manchester, Liverpool Women's Hospital, Princess Ann Hospital, Southampton or Birmingham City Hospital. We will tell you which hospital you will be seen at.
Any results requiring scans and/or hospital appointments will be shared with you, your GP, and the local ALDO project gynaecologist with responsibility for your surveillance.
The surveillance will last for 1 year and after that you will need to discuss your options with your local genetics team or gynaecologist as appropriate.
We will also ask you to complete 2 short questionnaires, one at the start of the project and one at the end. These questionnaires are to find out your views on surveillance.

During the 18 months after the surveillance has ended we may contact you, with a questionnaire and to tell you about other research projects which you may be interested in. We will only do this if you have provided consent for this.

What are the benefits?

This ROCA Test has been tested successfully in several clinical trials over the past 15 years involving over 200,000 women.
In the UK Familial Ovarian Cancer Screening Study (UKFOCSS), screening was offered to women with a strong family history of ovarian or breast cancer, many of whom carried BRCA mutations. Women diagnosed with cancer as a result of screening had less advanced cancers compared to those who presented with symptoms after the end of screening. As a result, their surgery was less complex. Additionally the proportion of women who had all of their tumours removed was very high, which is important in terms of predicting a better outcome.
By taking part in this surveillance you will be monitored closely which you may find reassuring.

What are the limitations?

- The ROCA test will not prevent you from getting ovarian cancer, only risk-reducing surgery can do that.
- The ROCA Test may not detect all women with ovarian cancer. Therefore, it is very important to remain aware of the symptoms of ovarian cancer and speak with your doctor if you are concerned. You can find the symptoms listed at the end of this document.
- If your ROCA Test is elevated, then it will need to be repeated and in some circumstances, other tests (e.g. an ultrasound scan of your ovaries, or an MRI or CT scan) may be needed to help the doctor decide whether surgery is necessary.
- An elevated ROCA Test result does not mean you definitely have ovarian cancer. Your ROCA score could be elevated due to other medical problems. Some women might have a naturally high level of CA-125 which causes a temporary elevated ROCA result until the algorithm learns what your normal level of CA-125 is.
- Although there is evidence that more early stage ovarian cancers can be detected in women who undergo surveillance using the ROCA Test, many women will still be diagnosed after the cancer has spread, when prognosis may be poor.
- Surveillance with the ROCA Test has not yet definitively been shown to save lives. The latest report published in the Lancet[2] provides evidence which some have interpreted as encouraging but this will be clearer when there is longer follow up and a further publication, likely in 2019.

- Ovarian cancer surveillance using the ROCA Test may create anxiety in some women if there are elevated results even when no cancer is present. In some women, these results will lead to surgery even when no cancer is present and occasionally the surgery will cause complications. All women undergoing surveillance should understand these risks.

What are the risks?
In addition to the above limitations, you may experience some bruising from having blood samples taken. If your ROCA scores are moderately or significantly elevated, you will be required to attend a named hospital for a transvaginal ultrasound scan. Some women may find this procedure uncomfortable.

Who is organising and funding this project?
The project was conceived as part of the national Cancer Vanguard's challenge to industry in 2017, to work with the NHS on projects to improve the early diagnosis of cancer. UCLH Cancer Collaborative is leading the project on behalf of its two partners in the former Cancer Vanguard – Greater Manchester Cancer Vanguard Innovation and RM Partners. Abcodia is a private company dedicated to improving early cancer diagnosis. They own the rights to the ROCA Test and are funding this project.

What will happen to my blood samples?
Your blood samples will be analysed in the laboratories used by UCLH (run by Health Services Laboratories (HSL)). The blood samples will be labelled with your initials, date of birth and study ID number. Your blood sample will be stored for 3 months before being destroyed.
If you agree to your blood samples being used for future ethically approved research projects, including projects run by commercial companies worldwide, your samples, will be stored indefinitely. These samples will be stored anonymously (your initials, date of birth and study ID will be removed).

What data will you collect and who will have access to my data?
We will store a limited amount of your personal data on a secure database held on the UCLH NHS system. This will include the personal data that you submit to us on the enclosed form, your blood results over the course of the project and results of any further investigations you may need (such as scans). If you decide to have surgery at any time during the project then we will request some details about your surgery from the hospital where you are treated. At the start of the project, we will also ask your genetics centre for a copy of your BRCA test result for our records.
In order to run the ROCA Test, we will need to transfer some anonymised data outside of the NHS to another secure database. This data will include your blood results, your age and your menopause status. We will not transfer any identifiable data such as your name or address.
Only NHS staff working on this project will have access to these secure databases. Your GP and genetics team will be informed about your participation in this project and we will share any abnormal results with them, as well as a summary of your results at the end of the project.
UCLH will act as the Lead Data Controller for this project and if you consent to take part in this project, you will be asked to provide your consent to UCLH as the Lead Organisation.

Who is involved in managing my data and how will my information be kept confidential?
All data we collect on you will be stored in a secure database within the NHS.
At the end of this document you can find a list of the organisations that are involved in this project and their roles in the management of your data.

What happens to my data at the end of the project?
At the end of the project, the data that has been collected will be anonymised and an evaluation will be carried out to assess whether the project has been successful. No personally identifiable data will be used in this evaluation or be shared outside the NHS. It will not be possible to identify you or your data in the information used for the evaluation.

An anonymised copy of the data collected as part of the project will be shared with Abcodia, to support future developments in ovarian cancer surveillance. This will include the type of BRCA1 or BRCA2 mutation, ROCA test scores and CA-125 levels for each participant, and where additional investigations or surgery have been carried out it will also include information about these. It will not include your personal details, such as your name or address. It will not be possible to identify you from this information.
We will keep all of your personal data in the secure database within the NHS for 10 years after the project. This is in line with the standard practice for research studies. If the clinical team would like to use this data for any purpose other than described here for this project, then they will make contact with you to ask for your permission for this. They will not use your data without your permission.

What will happen to the results of this project?
The results of the evaluation will be shared with NICE and other NHS Clinical Commissioners so that they can assess whether this service is beneficial to NHS patients. We hope also to publish the results of the evaluation so that a wider audience can benefit from the learning from this project.

Who has reviewed this project?
This project has been reviewed and approved by an independent NHS ethics committee and by the HRA (Health Research Authority).

Who has sponsored this project?
This project is being sponsored by University College London (reference number 17/0841).
What happens next?
If you agree to take part in this surveillance project, you will need to sign the consent form and send it back to us. If we do not hear back from you, then your recruiting site may send out a reminder letter. We will then send you a blood pack to take to your GP to have your first blood test taken. We will send you the result within 7 days of receiving the blood sample.

Who can I speak to about the project?
If you have any questions about the project, then you can speak to your genetics team or you can contact the Project Manager at uclh.aldo@nhs.net or via telephone on 07773572706.
You can also speak to your local hospital PALS service on [insert tel no] or for more independent advice you can speak to a nurse at Cancer Research UK (CRUK) on 0808 800 4040 or via a webpage https://www.cancerresearchuk.org/about-us/contact-us/talk-to-our-nurses?wssl=1.

If you decide to take part in the project, but later decide that you do not wish to continue to take part, then you can opt out by contacting the Project Manager, as detailed above.
If you wish to exercise your rights under Data Protection Laws please contact the Project Manager, as detailed above, who will direct you appropriately.

What if there is a problem?
If you have a concern about any aspect of this project, please contact the project team who will do their best to answer your questions [contact number]. If you remain unhappy and wish to complain formally, you can do this [insert local PALS number].

What are the symptoms of ovarian cancer?
The main symptoms to look out for include:

- feeling constantly bloated
- a swollen tummy
- discomfort in your tummy or pelvic area

- feeling full quickly when eating, or loss of appetite
- needing to pee more often or more urgently than normal

Other symptoms can include:

1. persistent indigestion or nausea
2. pain during sex
3. a change in your bowel habits
4. back pain
5. vaginal bleeding – particularly bleeding after the menopause
6. feeling tired all the time
7. unintentional weight loss

Please see your GP if:

- you've been feeling bloated most days for the last three weeks
- you have other symptoms of ovarian cancer that won't go away

Your GP can do some simple tests for ovarian cancer to see if you might have it.
If you've already seen your GP and your symptoms continue or get worse, go back to them and explain this.

Data Management
The following organisations will play a role in the management of your data as part of this project. Their role is detailed in this table:

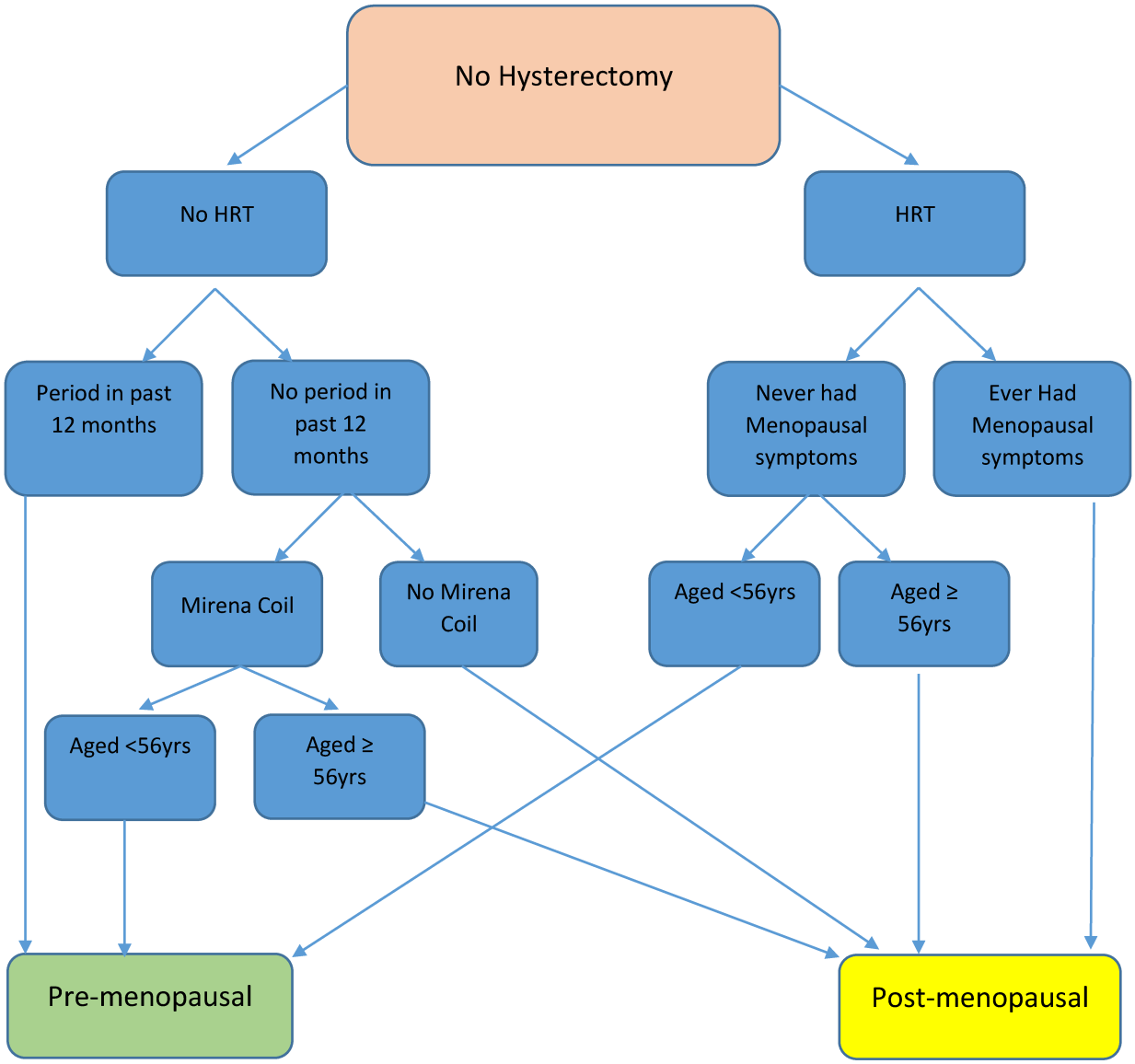
University College London (UCL)	Lead Data Controller
UCLH	Data Processor
Health Services Laboratories (HSL)	Data Processor
Your genetics or familial cancer service, including: • North East Thames Regional Genetics service (Great Ormond Street Hospital NHS Foundation Trust) • Manchester Centre for Genomic Medicine, Saint Mary's Hospital (Manchester University NHS Foundation Trust) • Barts Health NHS Trust • Guys and St Thomas's NHS Foundation Trust • Royal Marsden NHS Foundation Trust	Data Controller

A Data Processing Agreement is in place between UCLH and Abcodia, and between UCLH and HSL to govern the appropriate management of your personal information.

Supplementary Table 1: ALDO Menopause Questions:

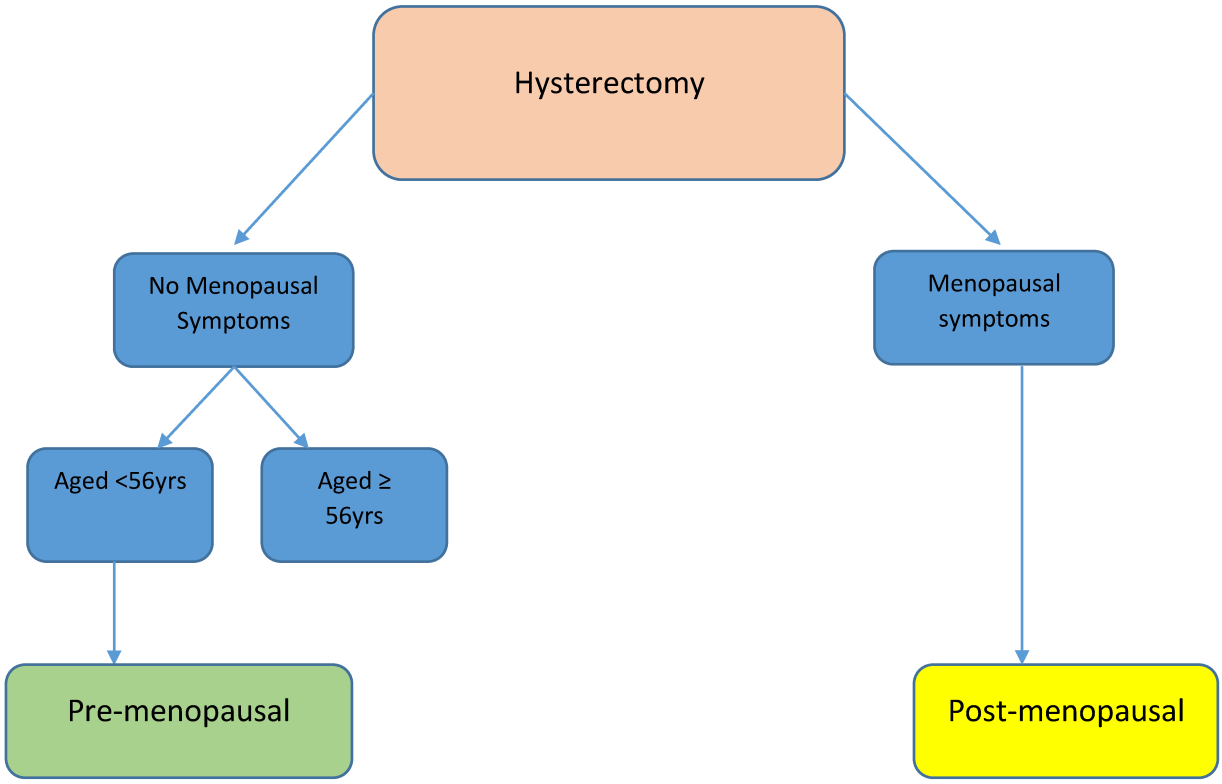
1. Have you had a period in the past year?
a. If yes, date of last period
2. Have you had a hysterectomy (an operation to remove your womb)?
3. Have you had surgery to remove both your ovaries?
4. Do you have a Mirena® coil fitted?
a. If yes, is this part of Hormone Replacement Therapy (HRT)
5. Have you ever had hot flushes and/or night sweats for more than 1 month?
6. Are you taking Hormone Replacement Therapy (HRT)?

Supplementary Figure 1: Flow Chart to Determine Menopausal Status for someone who has not had a hysterectomy



This algorithm is based on the principal that 12 months' amenorrhoea in women with an intact uterus and no Mirena(trademark) intra-uterine system (IUS) *in situ* indicates probable menopause. However, in those with a prior hysterectomy, or those with an IUS, or in those with an intact uterus on HRT, amenorrhoea is an unreliable sign of menopause. Therefore, a pragmatic cut-off age of 56 yr in such women was chosen, as >80% of such women would be menopausal at this age (Shadyab et al. Ages at menarche and menopause and reproductive lifespan as predictors of exceptional longevity in women: the Women's Health Initiative. Menopause. 2017 Jan;24(1):35-44) irrespective of the above factors.

Supplementary Figure 2: Flow Chart to Determine Menopausal Status for someone who has had a hysterectomy



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Supplementary Table 2: ALDO modifications to the UKFOCSS protocol	
1	The term 'screening' was replaced by 'surveillance' in keeping with NICE guidelines for surveillance for early detection of breast cancer in high-risk women[1].
2	We did not offer annual Transvaginal ultrasound scans
3	Based on the results from UKFOCSS, the ROCA cut-offs for determining the categories for repeating surveillance tests were adjusted.
4	The risk level at which women were referred direct to gynaecology rapid access clinics (without waiting for a repeat blood test or scan) was set at 1 in 33, which is the National Institute for Health and Care Excellence risk threshold for automatic 2 week wait referral for suspected cancer.
5	Following discussions with BRCA-carriers, the terms for classifying ROCA results were changed from 'Normal', 'Low Intermediate', 'High Intermediate' and 'Elevated' to 'Normal', 'Mildly Elevated', 'Moderately Elevated' and 'Significantly Elevated', respectively.
6	CA125 samples could be analysed up to 7 days post the blood being drawn (based on a stability study which found samples remained stable during that time).
7	The algorithm to determine menopause status was improved to include women with a Mirena® intra-uterine system.

1. https://www.nice.org.uk/guidance/cg164/chapter/Recommendations#surveillance-and-strategies-for-early-detection-of-breast-cancer

Supplementary Table 3. Surgical complexity scoring on ALDO[1]	
Procedure	**Points**
TAHBSO	1
Omentectomy	1
Pelvic lymphadenectomy	1
Paraaortic lymphadenectomy	1
Pelvic peritoneum stripping	1
Abdominal peritoneum stripping	1
Large bowel resection	2
Diaphragm stripping/resection	2
Splenectomy	2
Liver resection/s	2
Small bowel resection/s	2
Rectosigmoidectomy with anastomosis	3

1. Aletti GD et al. Relationship among surgical complexity, short-term morbidity, and overall survival in primary surgery for advanced ovarian cancer. Am J Obstet Gynecol. 2007 Dec;197(6):676.e1-7. doi: 10.1016/j.ajog.2007.10.495. PMID: 18060979. https://doi.org/10.1016/j.ajog.2007.10.495

Key

TAHBSO = total abdominal hysterectomy and bilateral salpingo-oophorectomy

To calculate total score per patient, simply add scores from individual procedures undertaken during surgery and allocate to complexity group as follows:

Total score 1-3 = low complexity

Total score 4-7 = intermediate complexity

Total score >7 = high complexity

Supplementary Figure 3: Markov model used for cost effective analysis

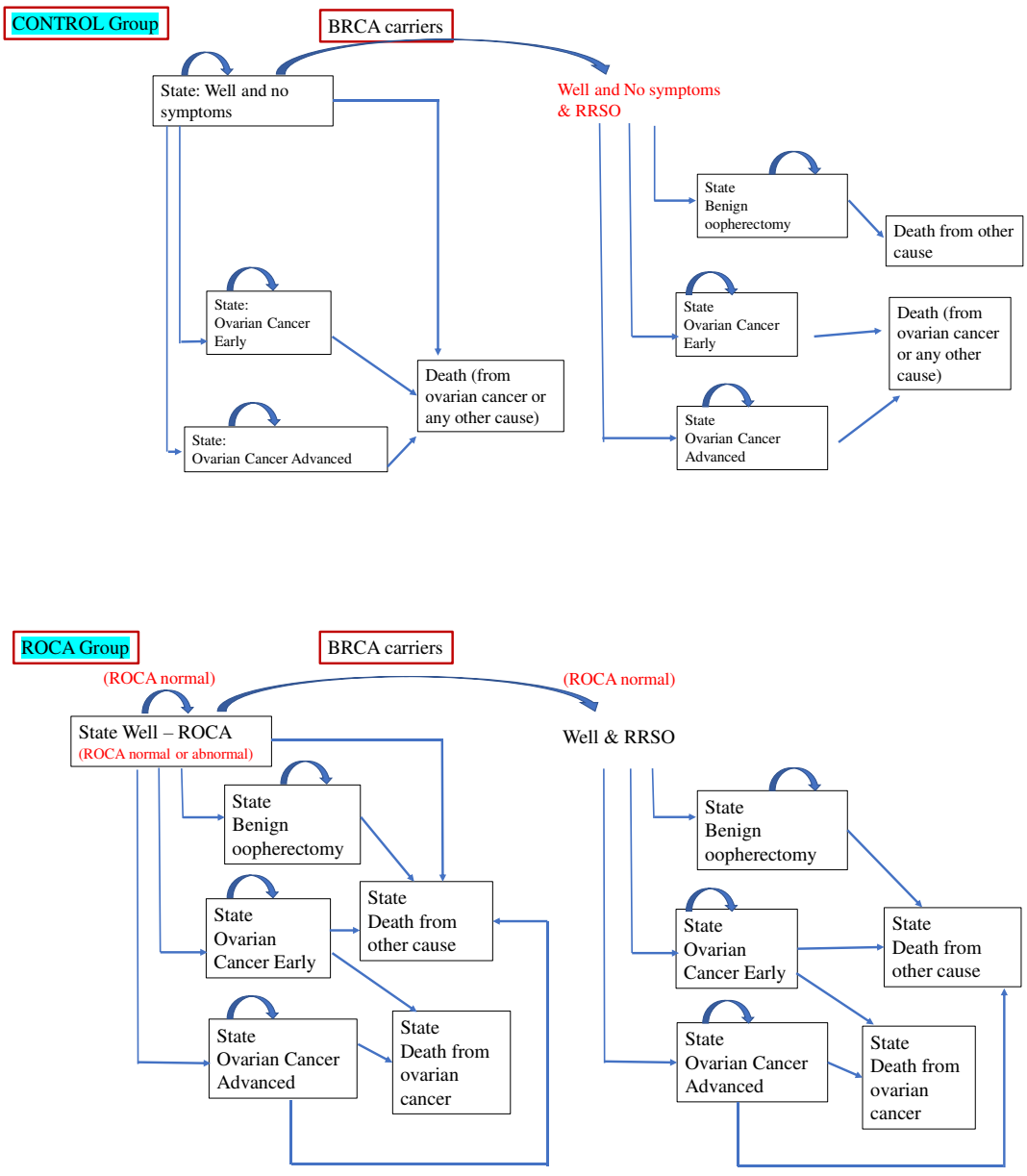
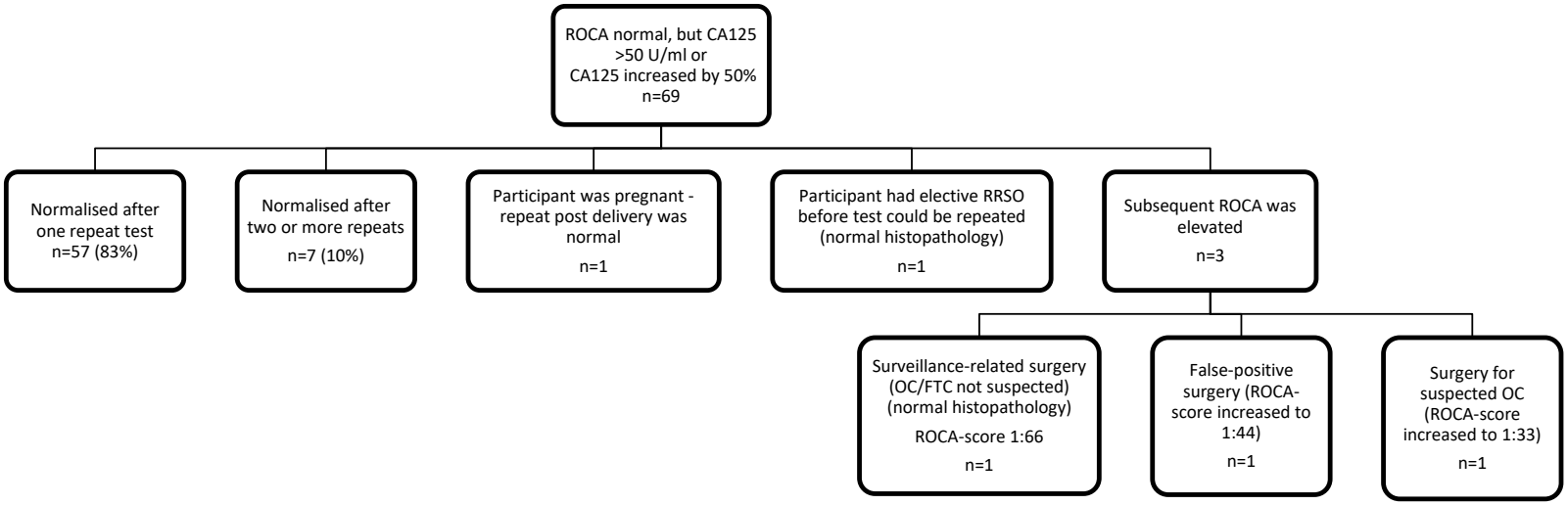


Figure 4: Results of failsafe repeat samples

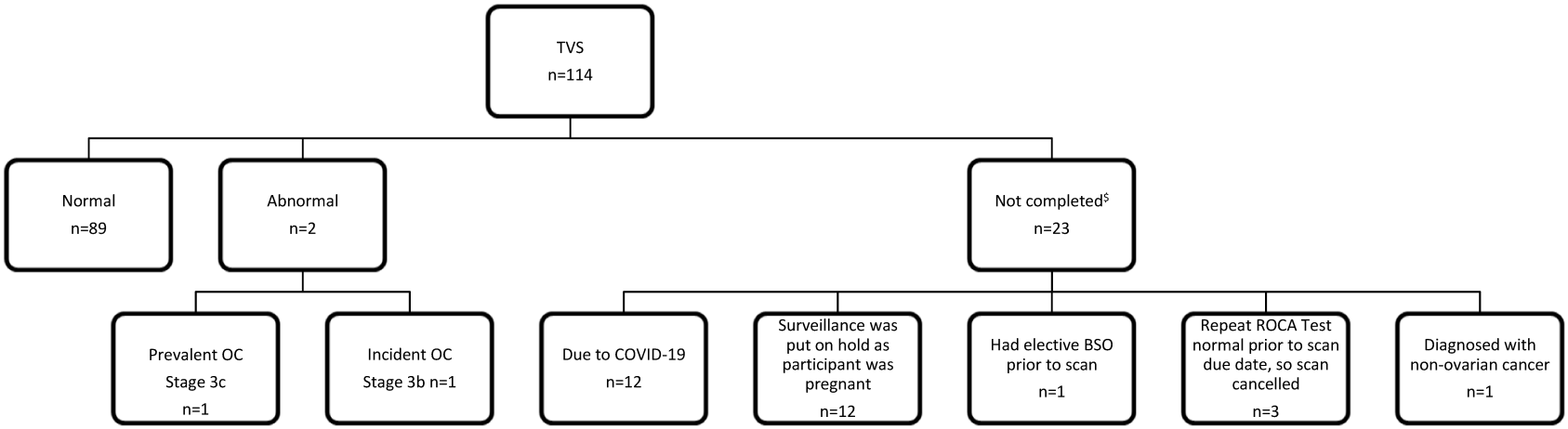


Key

RRSO = Risk Reducing Salpingo-oophorectomy

OC = Ovarian Cancer

Figure 5: Outcomes of scans done for moderately elevated ROCA results



Key:
*Requested in 104 women
$ All repeat tests where indicated were normal
TVS = Trans Vaginal Ultrasound Scan
OC =Ovarian Cancer

Supplementary Table 4: Reasons for not providing blood samples

Never returned a sample n=67	
Reason	**Number**
Reason not ascertained	40
Too busy to provide sample	9
Planning RRSO imminently	5
Difficulty getting an appointment for blood sample	4
Health issues	4
Moved away	2
Sample lost in transit	2
Did not receive blood packs	1
Returned 1 or more sample n=44	
Reason	**Number**
Reason not ascertained	24
Difficulty getting an appointment for blood sample	6
Too busy to provide sample	6
Health issues	3
Moved away	2
Did not receive blood packs	1
Pregnancy	1
Found result letters stressful	1

Supplementary information on the cost-effectiveness analysis of the ALDO surveillance programme

Methods

This supplementary information outlines the model used to estimate the cost-effectiveness of the ALDO surveillance programme for women with a pathogenic BRCA variant, who are at high risk of developing ovarian cancer (OC) as based on the reported ALDO clinical results. We perform a simulated incremental cost-effectiveness analysis of the ALDO surveillance screening programme compared to a no-screening arm over the lifetime period of a modelled population cohort of 1,000 at risk women using a Markov cohort approach. The analysis is based on individual patient level data collected during the ALDO study for the surveillance arm, and collected from relevant literature for the control, no-surveillance arm. The cost-effectiveness perspective adopted in this study is the UK National Health Service (NHS). The NHS is the major provider of all cancer services within the UK. We consequently use the UK National Institute of Health and Care Excellence (NICE) recommended discount rate of 1.5% per annum for public health interventions[1].

We initiate the ROCA surveillance testing programme in woman of 35 years of age and adopt a Markov population cohort model to examine the incremental cost-effectiveness of the programme and compare it to a control arm where women are assumed to have the self-determined choice of undertaking risk-reducing salpingo-oophorectomy (RRSO) or that they may develop symptoms due to an OC and enter associated therapy. The Markov model uses a simulation of 1,000 women who face progression through a number of health states to death, either from OC or a competing risk (these are given in Figure S3). The model follows the individuals from the point they undergo gene testing for their BRCA status until death using annual cycles.

The effectiveness measures used are life years gained (LYG) and quality adjusted life years (QALY) gained. These are based on extrapolations of the detection of OC in the surveillance arm and the development of OC in the control arm, taking into account the choice to undergo RRSO in both arms. The extrapolations are made, in the normal Markov cohort manner, through allocating transition probabilities to the population to move them through various health states.

In any given year (model cycle) an individual can decline or defer RRSO or opt for RRSO. For individuals who do not opt for RRSO the model assumptions and the data sources used to populate

the model are detailed below. Estimates of the annual risk of OC by age for BRCA-carriers are taken from Kotsopoulos et al (2018)[2] for both arms, and the breakdown into early (stages 1 and 2) and late (stages 3 and 4) cancer from the ALDO data for the surveillance arm and from Rosenthal et al (2017)[3] for the control arm.

The probabilities of the transition from healthy (i.e. no cancer) to death for both arms are based on BRCA-carrier specific death rates given in Mai (2009)[4] up to age 55 years after which the probabilities are assumed equal to the ONS mortality, again for both arms. The probability of transition from the state of advanced cancer to death for the first 12 years is based on Rubin et al (1996)[5] and these are then adjusted by the relative risk (hazard ratios) reported by Lavie et al (2019)[6] to give the probabilities of transition from the early cancer state to death. Beyond 12 years individuals are assigned the same probabilities of transition from both advanced and early cancer state to death as given by the ONS for the general UK population[7], given that after 12 years they are considered to be in complete remission. This assumption is based on expert opinion and supported by the lack of BRCA-carrier specific life tables and holds for both arms.

For individuals who opt for RRSO the model assumptions and the data sources used to populate the model follow. To determine the number of individuals who decide to undergo RRSO, age- and time from genetic test- dependent estimates of the proportion of individuals opting for RRSO are taken from Evans et al (2009)[8] and applied to both arms. Following RRSO an individual can be diagnosed free of OC, with early OC or with advanced OC. The estimates for the above prevalence figures at the time of RRSO were obtained from Kotsopoulos et al (2018)[2]. The corresponding probabilities from transition to death from any of the above health states were obtained from the same sources as for the individuals in the same health states who had not opted for RRSO described above. This approach was adopted for both arms.

We use quality of life (QoL) data taken from Edwards, Barton, Thurgar et al. (2015)[9] who reviewed 187 papers reporting QoL data relating to OC, of which 27 provided data suitable for use in economic evaluations. While their concern was with advanced recurrent and refractory OC, the study reported QoL tariffs for stable and progressive disease, estimated at 0.718 and 0.649 respectively. These values were based on a sample population of over 600 patients and were generally representative of values used for similar states in other studies. We take these values to proxy the QoL tariffs for early-stage OC (0.718) and advanced OC (0.649) within the Markov model.

We analyse only direct health service costs covering the surveillance and control populations and the subsequent treatment costs. Resource usage was based on the identification of surveillance visits, blood tests, clinic visits, surgery and follow-up clinical assessment. In addition, chemotherapy agents and the number of cycles were identified for those treated for OC as based on NICE Guidance Ovarian Cancer Overview 2019.[10]

For the early cancer state all women are assumed to receive surgery and chemotherapy of 6 cycles of paclitaxel and carboplatin. Following this, 80% (platinum-sensitive relapse) receive a further 6 cycles of paclitaxel and carboplatin and the remaining 20% (platinum-resistant relapse) receive a further 6 cycles of weekly paclitaxel. For the advanced cancer state all women are assumed to receive surgery and chemotherapy (6 cycles of carboplatin and paclitaxel) followed by maintenance therapy with Olaparib alone (80% of patients) or Olaparib and Bevazicumab (20% of patients). Following this, 80% (platinum-sensitive relapse) receive a further 6 cycles of paclitaxel and carboplatin and the remaining 20% (platinum-resistant relapse) receive a further 6 cycles of weekly paclitaxel and Best Supportive Care (BSC). No overall survival benefit from use of maintenance Olaparib was assumed.[11] The resulting overall annual per patient surgery and chemotherapy (including maintenance) cost is £48,309 for these individuals and £21,515 for the individuals in the early cancer state.

All surveillance and treatments were recorded within NHS settings. The 2019-2020 NHS tariff prices associated with relevant hospital episodes (in-patient, day case and out-patient), procedures, blood tests and clinics were attached to these visits (UK Dept. of Health, 2020).[12] The unit costs arising from treatment of OC with chemotherapy agents were gained from a number of secondary sources, primarily reports from NICE (UK)[13] and the British National Formulary (BNF) prices 2020,[14] as reported by NHS England, and for BSC at end of life.[15]

The unit cost of the CA125-ROCA test used to predict the likelihood of the presence of OC was based on the current price of £150.[16] Although the blood tests forming the basis of the ROCA were administered through GPs in the ALDO study, we make the conservative assumption that an out-patient visit is incurred in testing. This estimate was used in the base-case analysis and subjected to sensitivity analysis to account for the uncertainty surrounding the estimated value.

On the basis of the data and assumptions outlined above we find that the ROCA surveillance testing programme is cost saving to the NHS. The number of life years gained by the surveillance

programme is 0.046 and the number of QALYs gained is 0.179. The control arm incurs a cost of £220,677 per patient over lifetime while the ROCA surveillance arm incurs a cost of £202,337 per patient over lifetime. As such the ROCA surveillance arm provides health benefit at lower cost and is deemed cost saving for the base-case analysis (the calculated ICER is estimated to be -£102,496 per QALY gained).

Various sensitivity analyses were undertaken. First, a threshold ROCA price was established through sensitivity analysis where the ALDO surveillance arm, given the baseline assumptions would no longer be considered cost saving. This threshold for the ROCA price is established at £585. If the ROCA algorithm were priced at £585, the incremental cost-effectiveness for the ALDO surveillance arm becomes £987 per QALY over a lifetime. This means the ALDO surveillance remains highly cost-effective, given current NHS England guidance, at this price.

In a separate sensitivity analysis we considered the impact on the ICER if the surveillance was stopped for women in older age groups, specifically, if the ALDO surveillance algorithm was not extended beyond ages 80, 75, 70, or 50. In all cases the ALDO surveillance remained cost saving. Further sensitivity analyses considered the impact on the ICER of different cancer detection rates. In the base-case analysis the detection of early stage cancers was set at 33.3% and that of advanced cancers at 66.7% as based on the ALDO programme results. In this set of sensitivity analyses, given the small numbers in ALDO, the detection rate of early cancers was increased by an absolute 10% and then decreased by an absolute 10% from the detection rate used in the base-case analysis. In both cases the ALDO surveillance remained cost saving. Finally, at a detection rate of 11.5% for early stage cancer, the ALDO surveillance programme reverted from being cost-saving to being cost-effective.

References

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2. Kotsopoulos, J., Rosen, B., Fan, I., et al, 2016, Ten-year survival after epithelial ovarian cancer is not associated with BRCA mutation status, Gynecologic Oncology 140 (2016) 42–47.
3. Rosenthal, A.N., Fraser L. S.M., Philpott, S., et al, 2017, Evidence of Stage Shift in Women Diagnosed With Ovarian Cancer During Phase II of the United Kingdom Familial Ovarian Cancer Screening Study, Journal of Clinical Oncology, 35, 1411-1420.

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Table A9: ALDO Collaborators, Project Steering Committee, Outcomes Committee members

Centre	Collaborators
St Bartholomew's Hospital, London, UK	Ranjit Manchanda
Birmingham Women's Hospital, UK	Jonathon Hoffman
Birmingham City Hospital, UK	Janos Balega
All Wales Medical Genomics Service, Swansea, UK	Alex Murray
Cardiff and Vale University Health Board, UK	Aarti Sharma
Clinical Genetics, Great Ormond Street Hospital, London, UK	Munaza Ahmed
Clinical Genetics, Guy's and St Thomas' NHS Foundation Trust, London, UK	Louise Izatt, Anju Kulkarni and Vishakha Tripathi
Yorkshire Regional Clinical Genetics Service, The Leeds Teaching Hospitals NHS Trust, Leeds, UK	Julian Adlard
The Leeds Teaching Hospitals NHS Trust, Leeds, UK	Tim Broadhead
Clinical Genetics, Liverpool Women's NHS Foundation Trust, UK	Lynn Greenhalgh
Liverpool Women's NHS Foundation Trust, UK	Sian Taylor
Manchester Centre for Genomic Medicine, UK	Gareth Evans
Saint Mary's Hospital, Manchester	Richard Edmondson
North Tees and Hartlepool Foundation Trust, UK	Mary George
The North West Thames Regional Genetics Service, UK	Angela Brady
Oxford Centre for Genomic Medicine, UK	Joyce Solomons
South west Thames Centre for Genomics, St George's University Hospitals NHS Foundation Trust, London, UK	Helen Hanson and Katie Snape
St George's University Hospitals NHS Foundation Trust, London, UK	Kevin Hayes
Clinical Genetics, University Hospital Southampton NHS Foundation Trust, UK	Lucy Side
University Hospital Southampton NHS Foundation Trust, UK	Richard Hadwin
Familial Cancer Clinic Department of Gynaecology, University College London Hospitals NHS Foundation Trust, UK	Adam Rosenthal

Project Steering Committee	Usha Menon, Gareth Evans, Richard Edmondson, Emma Woodward, Munaza Ahmed, Ranjit Manchanda, Nasa Turabi (chair), Adam Rosenthal, Sue Philpott, Caroline Presho (Patient representative), Athena Lamnisos (CEO, The Eve Appeal), Helga Laszlo (NCL Cancer Alliance), Julie Barnes (CEO, Abcodia Ltd.)
Outcomes Committee	Adam Rosenthal, Naveena Singh, Malcolm Scott