

Information Event for BRCA Carriers
Best Western Epping Forrest, London, 24th March 2018

The ALDO Project, Risk-Reducing Surgery and Management of Menopausal Symptoms

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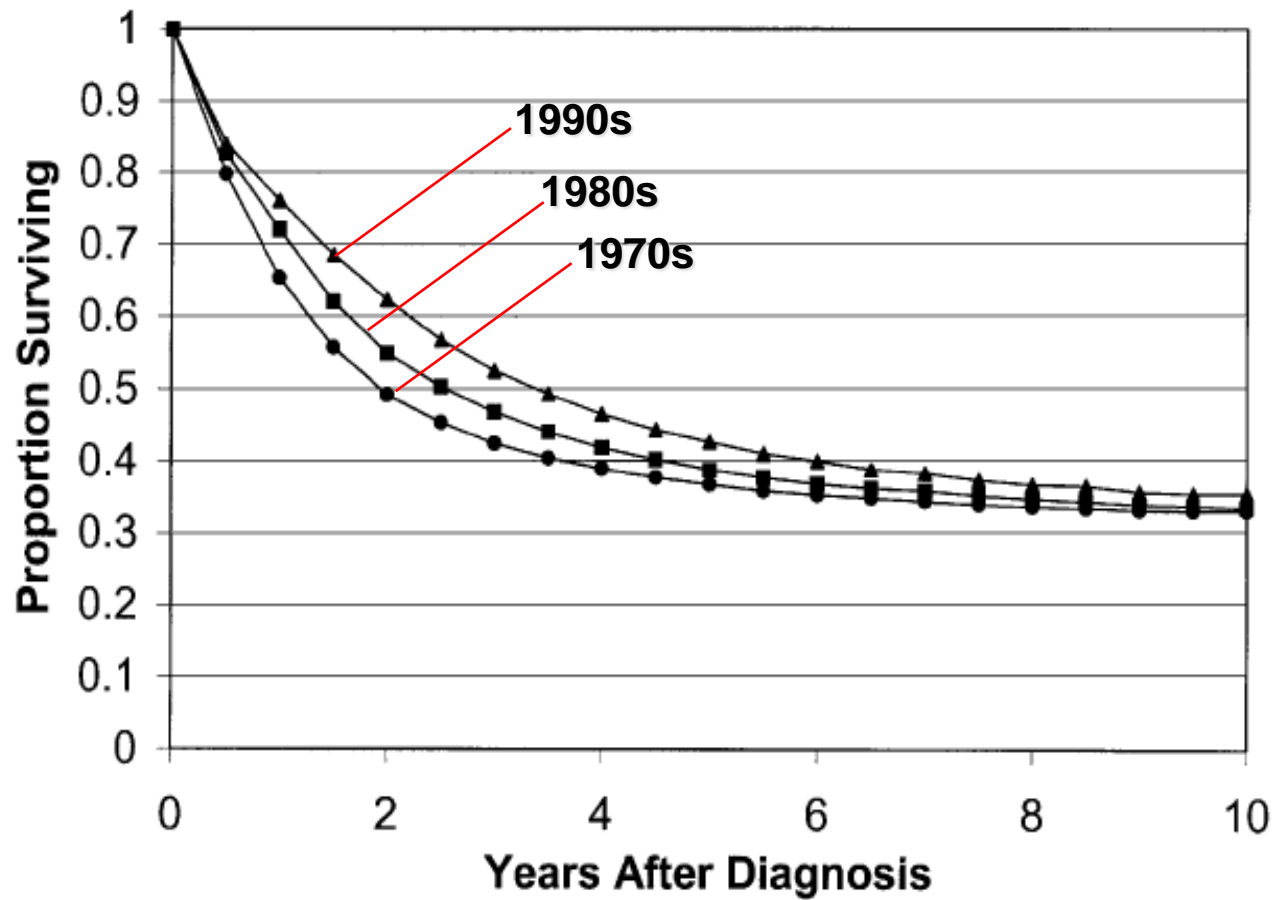
Relevant Disclosures

Consultancy work with:

Abcodia (ROCA test)

Everything Genetic Ltd (Color BRCA and gene panel testing in UK)

32,845 women with OC



OC Statistics for UK

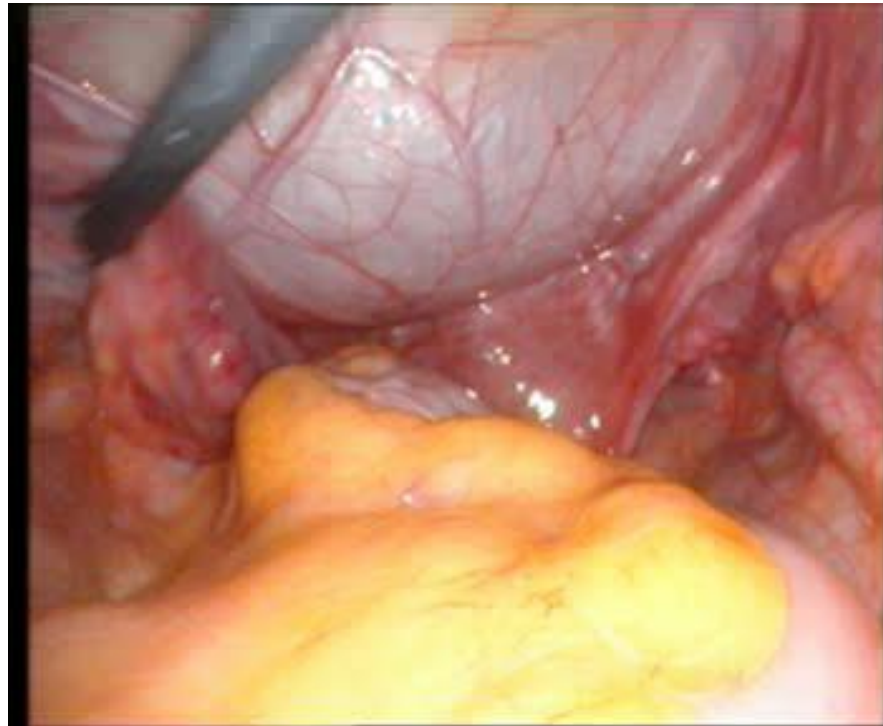
- 6th commonest women's cancer in UK
- 7,270 cases in 2015 - 20 women every day
- 4,128 deaths in 2014 - 11 women every day – most lethal gynae cancer
- Only 35% survive >10 yr (2010-11)
- At least 10% due to inherited predisposition

If I was a BRCA-carrier....

What would I want to know?

What questions should I ask?

Where are my tubes and ovaries and what do they look like?



Is there anything I can do to reduce my risk of ovarian cancer other than surgery?

- Contraceptive choices (pill protective but avoid <25 yr due to increased breast cancer risk)
- Breastfeeding protective
- Pregnancies (esp at later ages) are protective

None of these are guaranteed to prevent OC

1. Do I really need to have risk-reducing surgery (RRSO)?

Yes

It may save your life

We know that in the medium term (approx. 5 yr),
'all-cause mortality' is reduced (2 large well-conducted studies)

2. When should I have the surgery?

It depends.....

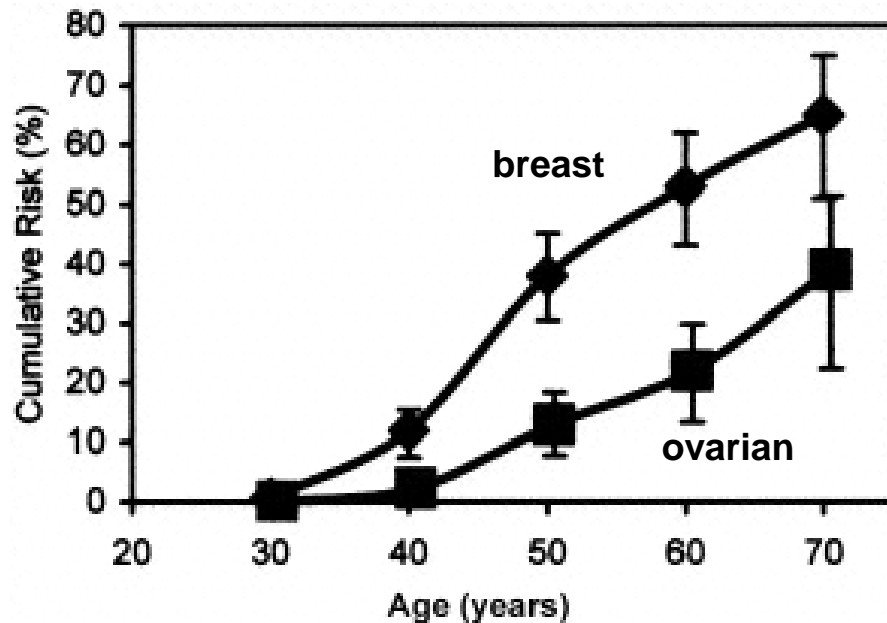
BRCA1 or BRCA2?

Do you already have menopausal symptoms?
(age/tamoxifen/chemo)

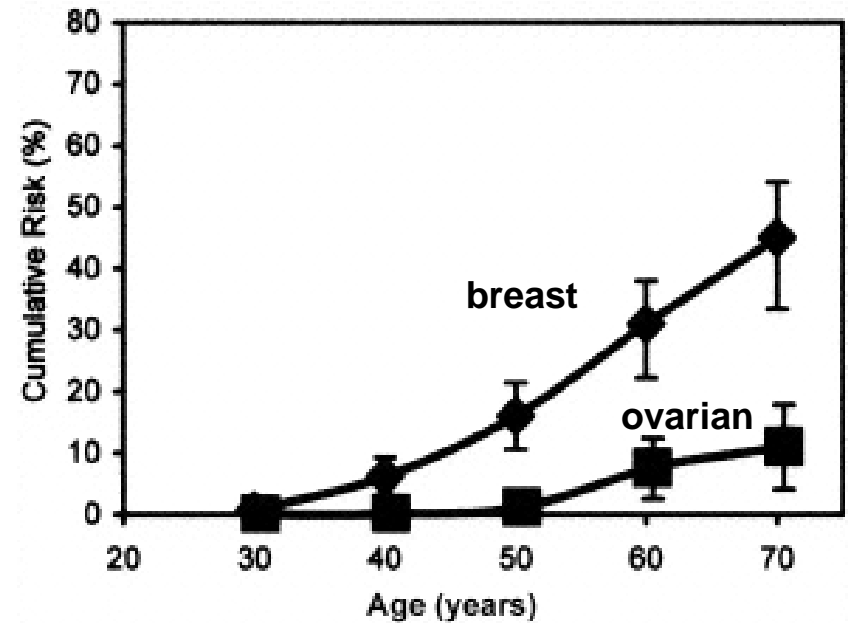
When did your mother/aunt/grandmother go through her
menopause?

Age of onset of cancers in your family?

Age-related cancer risks



BRCA1



BRCA2

RRSO before risk-reducing mastectomy?

Do RRSO at younger age if early-onset OC in family?

Age-related cancer risks

Age group (yr)	BRCA1-carrier	BRCA2-carrier
20-24	0.001	0.001
25-29	0.002	0.002
30-34	0.18	0.004
35-39	0.28	0.01
40-44	0.87	0.08
45-49	1.49	0.14
50-54	0.96	0.60
55-59	1.19	0.75

Annual % incidence of OC in BRCA-carriers according to age

Adapted from Antoniou et al *AJHG*, 2003

3. Will having RRSO reduce my risk of breast cancer?

- Not yet known for certain
- Some studies suggest up to 50% reduction in breast cancer risk if oophorectomy in 40s
- No benefit if done postmenopausally
- Recent re-analysis suggests previous studies may be flawed
- One large better-designed study suggests only prevention is breast cancer before age 50 yr in BRCA2 carriers (very small number so may not be reliable)
- Await new data (EMBRACE)
- Would it stop you having Risk-reducing mastectomy?

4. If I have RRSO, should I have HRT?

Depends on age and presence of menopausal symptoms

Have you had breast cancer?

If yes – discuss with oncologist

- triple negative breast cancer
- intractable menopausal symptoms

4. If I have RRSO, should I have HRT?

If no prior breast cancer, then HRT is needed until age of natural menopause (average 51 yr) to reduce risks:

- osteoporosis
- cardiovascular disease
- dementia

5. If I have RRSO, how will I feel?

Are you already postmenopausal?

Are you taking tamoxifen?

Depends on if you are able to take HRT

Even if you can take HRT, it may not alleviate all symptoms
(but it is likely to alleviate most of them)

5. If I have RRSO, how will I feel?

Options if you can't take HRT:

Flushes/sweats – clonidine/SSRIs (type of anti-depressant)

Vaginal dryness – various moisturising agents (e.g. Sylk/Yes)

Mood problems – exercise/CBT/Agnus Castus/SSRIs

Osteoporosis – exercise/Calcium + Vit
D/bisphosphonates/raloxifene/strontium ranelate

Cardiovascular disease – diet/exercise/statins

Dementia – diet/exercise/keeping mentally active

6. Can I get away with removing tubes only?

Evidence suggests majority of BRCA-associated cancers start at end of Fallopian tube

Limited clinical and animal data suggests at least some OC start outside fallopian tube in BRCA-carriers

Evidence from general population suggests removing tubes approximately halves risk of OC

There is currently NO evidence of safety of this approach in BRCA-carriers

6. Can I get away with removing tubes only?

Potential problems:

- May offer less protection than salpingo-oophorectomy
- May result in premature menopause (probably not big effect)
- Will you return to have your ovaries removed once you've gone through menopause?
- Second op exposes you to x2 risks of surgery
- Second op may be technically more difficult –adhesions

7. Should I be screened until I'm ready to have my ovaries removed?

- Screening will not prevent OC
- No conclusive evidence as yet that it saves lives

Data from UKFOCSS phase 2 screening (4-monthly CA125 blood tests analysed by ROCA test and annual ultrasound):

- Detected most OC before it causes symptoms
- Detected OC at earlier stages
- Associated with a high rate of complete cytoreduction despite less complex surgery
- Did not detect microscopic cancers found following RRSO
- Most cancers have spread at point they were detected

Consequently....

Safest option in 2018 is to undergo RRSO once you are old enough, have completed your family and are prepared to take HRT

But until you are ready for RRSO, surveillance using 4-monthly ROCA screening is safest option