



Princess Margaret Hospital

University Health Network

Can Ovarian Cancer be Prevented?

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Ovarian Cancer: When I started at PMH

- **Surgery**
- **Adriamycin and cisplatin x 9 cycles**
- **CAP**
- **Second look laparotomy**
- **Second line therapy ... Melphalan**

- **Screening??? Possible**
- **Prevention ... Not on the radar screen**



Cancer Prevention in Cervix Cancer

- Screening followed by colposcopy is one of the best examples of a cancer prevention program:
- Rates of cervical cancer dropped dramatically mid 50's to late 80's when the rates stopped falling
- The current cohort of patients with Cx Ca are women who do not get screened, or screening failures
- Screening works



Screening: Ovarian Cancer could work

	% Presentation	% Survival
Stage 1 & 2	30%	70-80%
Stage 3 & 4	70%	10-15%



Screening for Ovarian Cancer

- **General population: Incidence is 40/100,000 (women >50 yrs.)**
- **Most optimistic outcome would be to screen 100K women to cure an additional 10 women**
- **Complicated: High grade serous ca rarely if ever detected in early stage. Therefore to detect curable disease detection of a cancer 5mm or less will be required.**
- **Screening could be targeted to a high risk population: those with hereditary BR/OV ca**



Cancer Risk with BRCA Gene Mutations:

Mutation	Breast Cancer Risk	Ovarian Cancer Risk
BRCA 1	60-80%	20-40%
BRCA 2	60-80%	20-25%
General Population	11%	1.5%



SCREENING

- **CA125** **Low sensitivity**
- **Ultrasound** **Low specificity**
- **LPA**
- **Proteomics** **Low specificity**



SCREENING

- The combination of
- 1. Lack of effective screening tests to detect early stage ovarian cancer and
- 2. The mortality of advanced stage ovarian cancer

**Provides the rationale for preventative strategies even if the best option for prevention is surgery.
(Prophylactic oophorectomy)**



Definition:PO

- Surgery to remove all normal ovarian tissue to prevent development of Ovarian Cancer
- It is not surgery for symptoms or abnormal finding (Ultrasound,CA125,Pelvic exam)



Cancer Prevention Rebbeck NEJM 346:1618 2002

	Prophylactic Oophorectomy	Observation
N=	259	292
BRCA 1	219 (84.6%)	240 (82.2%)
BRCA 2	42	52
Follow-up	8.2 yrs	8.8yrs
Cancer at PO	6 (2.3%)	-
Cancer post PO	2 (0.8%)	58 (20%) p<.001



Cancer Prevention Rebbeck NEJM 346:1618 2002

- **Risk of Ovarian /Peritoneal Serous Carcinoma following PO vs observation**

– **0.04 (0.01-0.16) p <0.001**



Cancer Prevention: N. Kauff NEJM 346:1609 2002

	Prophylactic Oophorectomy	Observation
N=	98	72
BRCA 1	56	48
BRCA 2	42	24
Cancers at PO	3 (3.1%)	
Proportion OV CA disease free at 5 yr	98%	83% p=.04
Proportion Breast CA disease free 5 y	94%	79% p=.07
Proportion Both disease free at 5 yr	94%	69% p=.006



Risk of Breast Cancer Following PO

	Risk of Breast Cancer	Risk of Breast or Gyn Cancer
Kauff (98)	0.32 (0.08-1.2)	0.25 (0.08-0.74)
Rebbeck (292)	0.47 (0.29-0.77)	



Prophylactic Oophorectomy in BRCA1 and BRCA2 Carriers



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Amy Finch

**Familial Ovarian Cancer Clinic, Princess Margaret
Hospital**

Objectives

- To determine the optimal age for oophorectomy
- To estimate the rate of occult ovarian and fallopian tube cancer at the time of prophylactic oophorectomy and risk of peritoneal cancer post surgery
- To determine women's overall satisfaction with their decision to undergo prophylactic oophorectomy
- To determine the impact of oophorectomy on sexual functioning



Occult cancers BRCA1 vs. BRCA2

- BRCA1

- 94 women

- 6 occult cancers*

- Rate of **7.1%**

- *includes one tubal *in situ*

- BRCA2

- 65 women

- 1 occult cancer

- Rate of **1.6%**



Primary peritoneal cancer post oophorectomy

- Of 159 women that underwent prophylactic oophorectomy one peritoneal cancer diagnosed to date
- 51 Years of age at time of PO
- Diagnosis of metastatic primary peritoneal serous carcinoma 6 years after oophorectomy
- BRCA1 5382insC mutation



Risk of Peritoneal Carcinomatosis

- low.
- Streuwing 4.6%
- Piver 1.9%
- Rebbeck 4.0%
- Kauff 2.0%



Optimal Surgery: P O

- Most important technical aspect to surgery is the need to remove the entire ovary
- This requires identification of the ureter and clamping the infundibulopelvic ligament well above the ovary
- **BSO vs TAH BSO**



Results I

Population Characteristics

Patients (n)	192
Age (years)	46 (32-76)
BRCA 1 (n)	112
BRCA 2 (n)	70
Hysterectomy and BSO (n)	165
BSO (n)	17
BSO with previous TAH (n)	10
Follow up months (months)	37 (1-179)

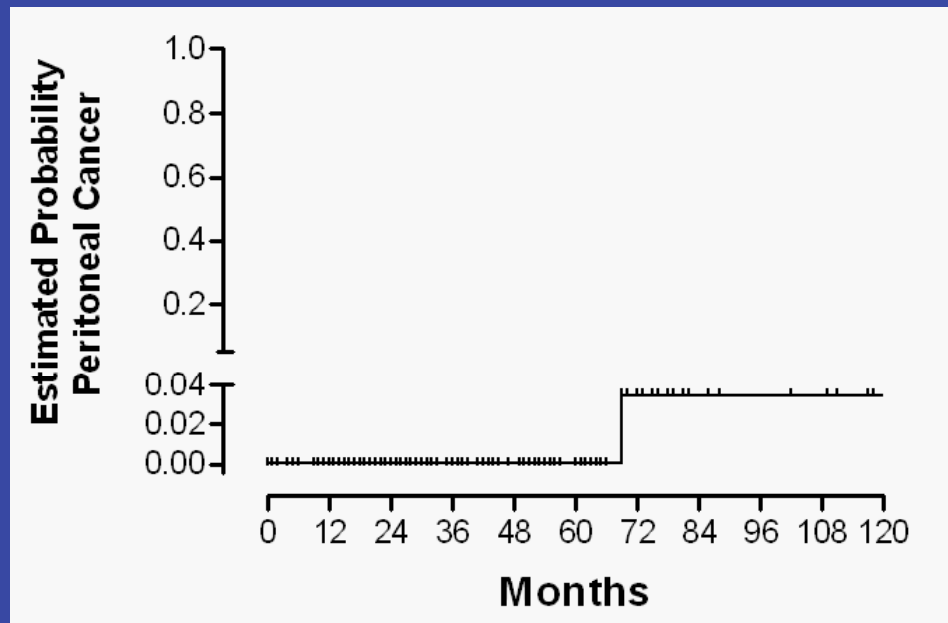


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Results II

- **Post surgery peritoneal cancer**
 - One single case during follow up (0.52%)
 - 568 person-years
 - Incidence 176 per 100,000/yr



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PREVENTION:

- OCP
- Tubal Ligation
- **Surgery:** Prophylactic Oophorectomy



Reproductive Risk Factors for Ovarian Cancer in Carriers of BRCA 1 or BRCA 2 mutations: a case control study

McLaughlin et al and The Hereditary Ovarian Cancer Group
Lancet Oncology 8:26-34 2007

	Cases	Controls
numbers	799	2424
BRCA 1	670	2043
BRCA 2	128	380
Both	1	1
Median age at Diagnosis	49 yrs	



OCP use and risk of Ovarian Cancer in Carriers

Use of OCP	Cases 799 (%)	Controls 2424 (%)	Multivariate (CI)	P value
Never	432 (54%)	995 (41%)		
0 – 1 yr	118 (15%)	358 (15%)	0.67 (0.5 – 0.89)	p = 0.006
1.1 – 3 yrs	86 (11%)	278 (11%)	0.63(0.46 – 0.86)	p = 0.004
3.1 – 5 yrs	48 (6%)	231 (10%)	0.36 (0.25 – 0.53)	p < 0.0001
> 5 yrs	113 (14%)	541 (22%)	0.47 (0.35 – 0.62)	P < 0.0001
missing	2 (0.3%)	21 (.9%)		
Ever use			0.56 (0.45 – 0.71)	P < 0.0001



Tubal Ligation vs Ovarian Cancer Risk

Tubal Ligation		Cases	Controls	Multivariate (CI)	P value
BRCA 1	never	482 (73%)	1508(74%)		
	yes	94 (14%)	274 (13%)	0.80 (0.59 – 1.08)	P = 0.15
	missing	89 (13%)	261 (13%)		
BRCA 2	never	86 (67%)	243 (64%)		
	yes	26 (20%)	89 (23%)	0.63 (0.34– 1.15)	P = 0.13
	missing	16 (12%)	48 (13%)		



Ovarian Cancer Prevention

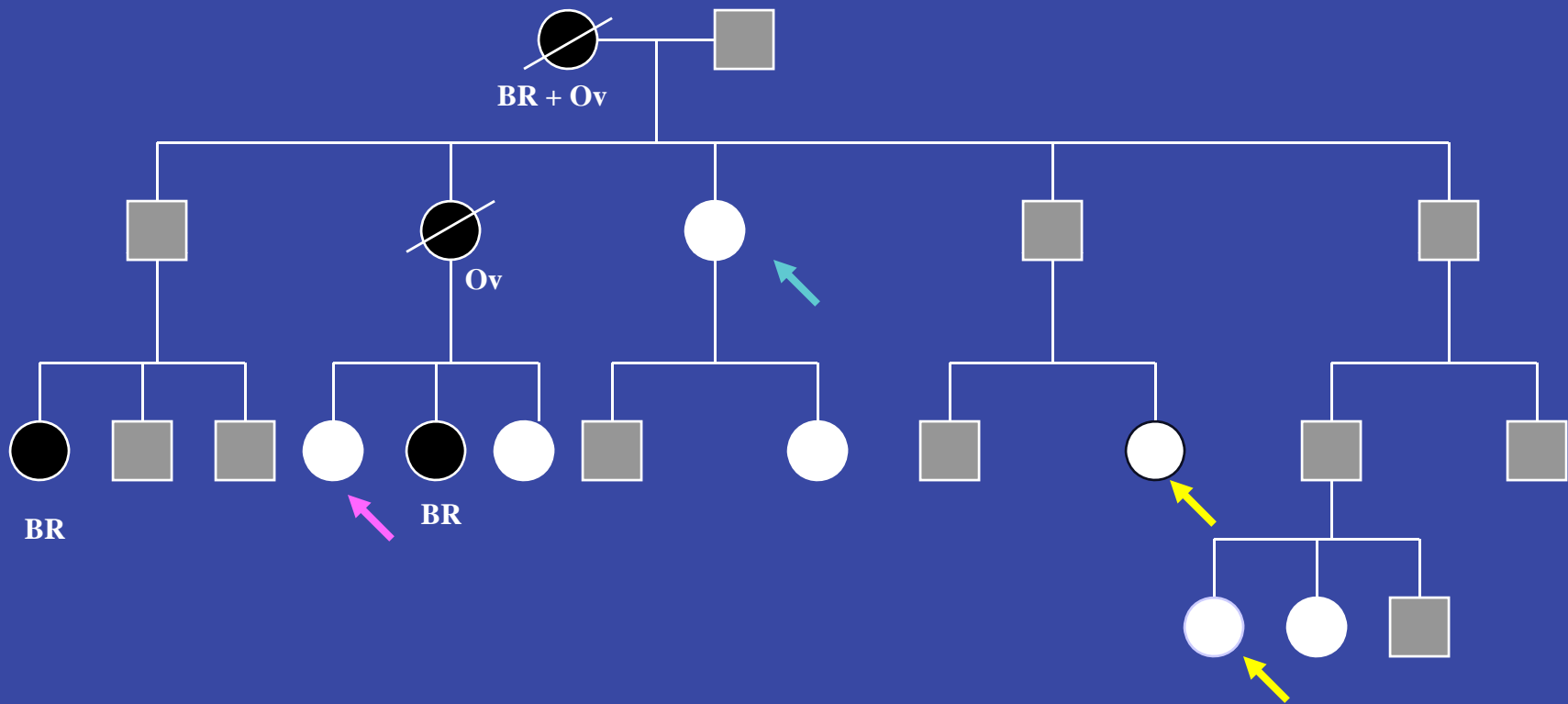
- Identification of hereditary population can be an effective way to prevent Ov Ca and ultimately reduce the overall incidence of ovarian cancer



Histology Vs BRCA Mutations

Histology	BRCA1	BRCA2	Either
Invasive	39(7.6%)	21(4.1%)	53(11.7%)
Serous	37(10.9%)	19(5.6%)	49(16.4%)
Endometrioid	2(2.1%)	2(2.1%)	4(4.3%)
Mucinous	0	0	0
Other	0	0	0
Borderline	0	0	0





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