Screening in Ovarian Cancer: Any closer to the Holy Grail?

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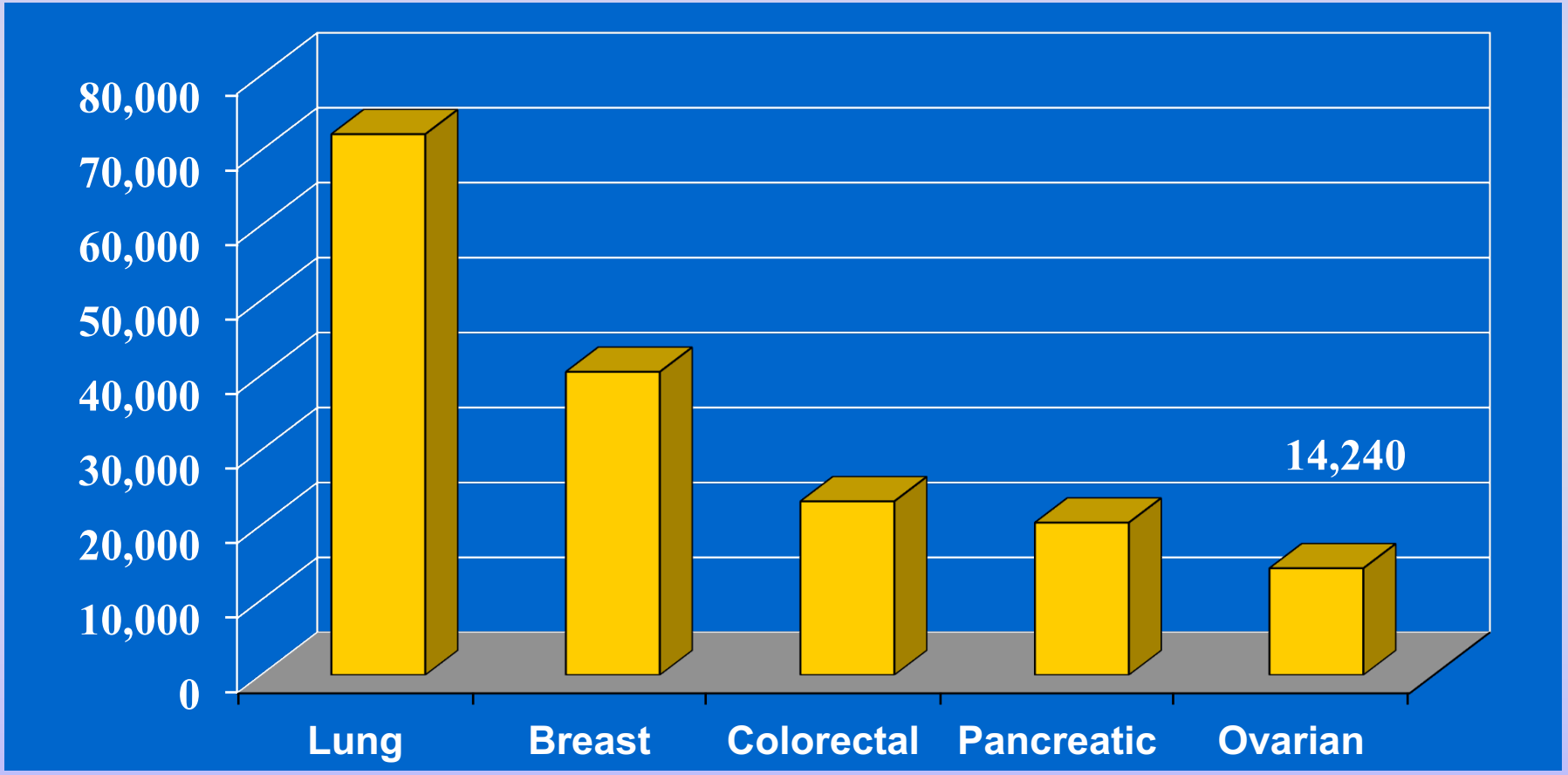
Dialogue For Action® On Cancer Screening and Prevention, April 20, 2017

DISCLOSURES

- **Collaboration with nVision Medical Corp.**
  - **Research support**

Ovarian Cancer

2016 Female Cancer Deaths



Miller, American Cancer Society, 2016

5-year Survival in epithelial cancers 2002-2008

Site	Overall	Localized	Regional	Distant
Prostate	99%	100%	100%	28%
Breast	89%	98%	84%	24%
Endometrial	82%	95%	67%	16%
Bladder	78%	70%	33%	6%
Colorectal	64%	90%	70%	12%
Ovarian	44%	92%	72%	27%
Stomach	24%	62%	22%	3%
Liver / Biliary	15%	28%	10%	3%
Pancreatic	6%	23%	9%	2%

Siegel, Cancer Statistics, 2013

Challenges in Early Detection of Ovarian Cancer

- Low prevalence of disease
  - 1.7% lifetime risk
- Absent or nonspecific symptoms
  - Too much space in IP cavity
  - May mimic more common conditions
  - Heartburn, weight gain, bloating

Traditional Methods of Screening

- Ca125
- Transvaginal Ultrasound
- Patient-reported history

Results - PLCO

Table 4. Follow-Up of Positive Screens of Either Type

	Screening Round			
	T0	T1	T2	T3
Screened				
n	28,746	27,541	26,584	25,423
Positive				
n	1,675	1,341	1,224	1,148
% of screened	5.8	4.9	4.6	4.5
Biopsies				
n	566	264	182	158
% of positive	33.8	19.7	14.9	13.8
Neoplasms*				
n	27	17	15	15
% of biopsies	4.8	6.4	8.2	9.5
% of positive (PPV)	1.6	1.3	1.2	1.3
Yield per 10,000 screened	9.3	6.1	5.6	5.9
Invasive cancers (ovarian or peritoneal)				
n	18	13	14	15
% of biopsies	3.2	4.9	7.7	9.5
% of positive (PPV)	1.1	1.0	1.1	1.3
Yield per 10,000 screened	6.2	4.7	5.2	5.9

PPV, positive predictive value.
* Includes invasive cancers and ovarian cancers of limited malignant potential.

Overall: 34,000 eligible
28,000 screened
3,400 had one positive test
1,170 had a biopsy
60* cancers (29 in the un-screened pts)

20 biopsies for every cancer

Partridge,… Buys, Obstet Gyn (113), 2009

UKCTOCS Design

Inclusion: 50-74 yrs, PMP, no active CA, no increased risk familial Ovarian Cancer

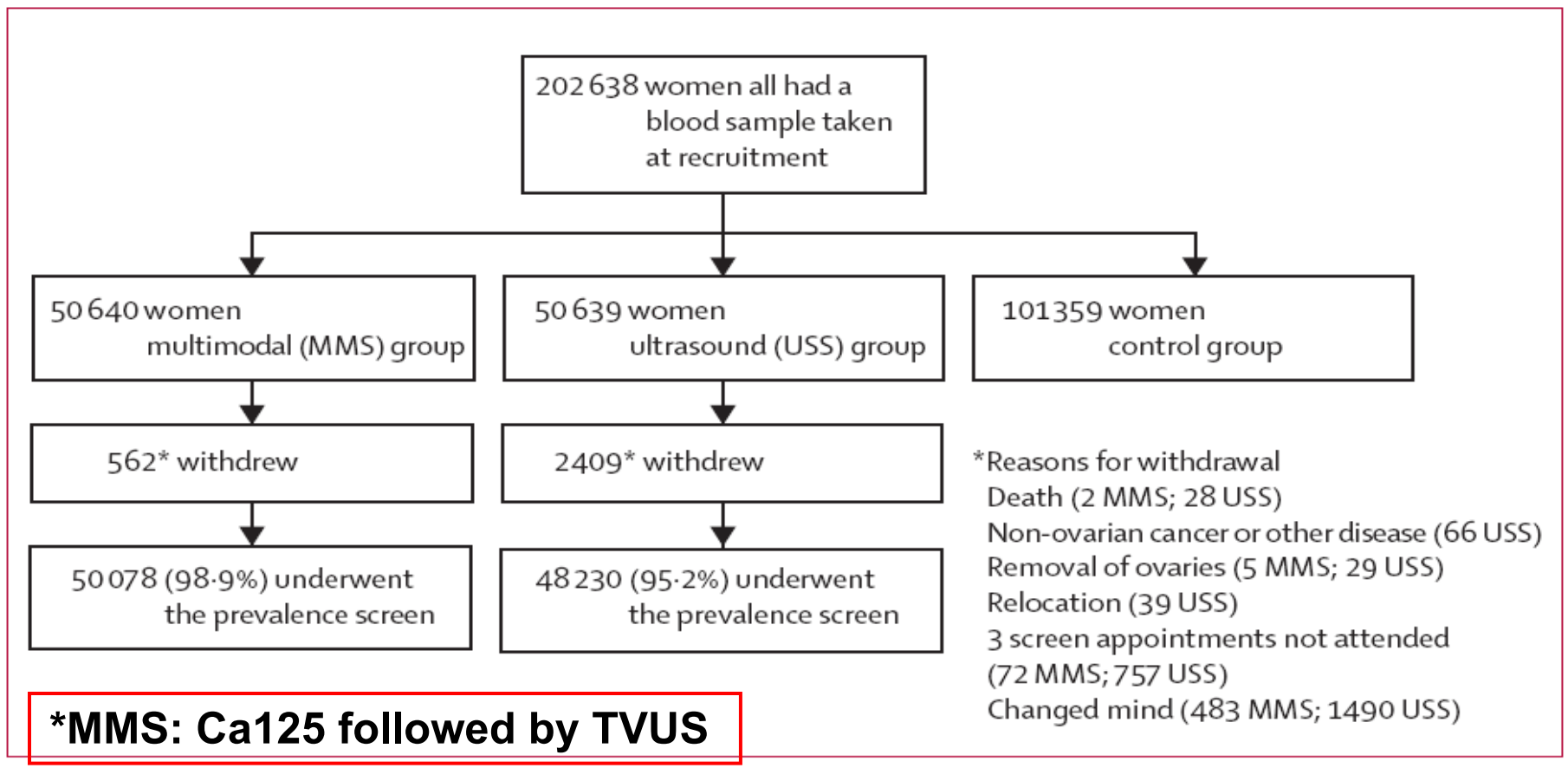


Figure 1: Randomisation and initial (prevalence) screen

Menon,… Jacobs, Lancet Oncology (10), 2009

UKCTOCS Results: Surgical Outcomes

	MMS	USS	Overall
Total surgeries	97	845*	942
Denied access to notes	0	1	1
Diagnostic laparoscopy, ovary normal, not removed	6	34†	40
Normal ovaries	0	15	15
Benign ovarian neoplasm	40	732	772
Ovarian neoplasm of uncertain behaviour (ICD-10 D39.1)	1‡	5	6
Primary peritoneal cancer (ICD-10 C48.2)	1	1	2
Other non-ovarian cancer	4§	7¶	11
Metastatic ovarian cancer	3‖	5**	8
Non-epithelial neoplasm of ovary (ICD-10 C56)	0	1	1
Primary borderline epithelial neoplasm of ovary (ICD-10 C56)	8	20	28
Primary invasive epithelial neoplasm of ovary (ICD-10 C56)	32	23	55
Primary invasive epithelial neoplasm of fallopian tube (ICD-10 C57.0)	2	1	3
Total malignant neoplasms of ovary (ICD-10 C56) and fallopian tube (ICD-10 C57.0)	42	45	87
Screen-negative cancers within 1 year of screen			
Borderline epithelial neoplasm of ovary (ICD-10 C56)	1	0	1
Primary invasive epithelial neoplasm of ovary (ICD-10 C56)	4	8	12
Total malignant neoplasm of ovary (ICD-10 C56) and fallopian tube (ICD-10 C57.0)	5	8	13

*One participant refused access to notes, at the time of writing there is no ONS registration of a cancer for this case. †One woman was diagnosed with ovarian cancer at a second operation undertaken 22 months after the prevalence screen. ‡Patient developed postmenopausal bleeding while waiting for a repeat CA125 test and was diagnosed to have synchronous endometrial cancer and ovarian granulosa cell tumour. §Two endometrial cancers, one stomach cancer, one follicular lymphoma. ¶Three endometrial cancers, one cervical cancer, one anal cancer, one lymphoma, and one multiple myeloma. ‖One pancreatic cancer, one colorectal cancer, and one cancer of the appendix. **Three breast cancers, one endometrial cancer, and one cancer of the appendix.

Table 3: **Histology in women who underwent surgery as a result of screening (screen positives)**

	Screen positive			Screen negative		
	MMS	USS	Overall	MMS	USS	Overall
Stage						
I	14	10	24	3	0	3
II	2	2	4	0	0	0
III	18	10	28	1	7*	8
IV	0	2	2	0	1	1
Early (I/II) stage cancers (%)	47·1%	50·0%	48·3%	75·0%	0·0%	25·0%
Lower 95% CI	29·8%	29·1%	35·0%	19·4%	0·0%	5·5%
Upper 95% CI	64·9%	70·9%	61·8%	99·4%	41·0%	57·2%
Morphology						
Serous	21	14	35	0	2	2
Endometrioid	5	3	8	1	0	1
Clear cell	0	5	5	1	0	1
Carcinosarcoma	1	0	1	1	0	1
Adenocarcinoma	7	2	9	1	6	7
Grade						
1	3	2	5	0	0	0
2	6	2	8	2	0	2
3	24	14	38	2	6	8
Not graded	1	6	7	0	2	2

*In two cases a diagnosis was made on the basis of ascitic fluid cytology, omental biopsy, and imaging: primary surgery was not undertaken.

Table 4: **Characteristics of primary invasive epithelial ovarian and tubal cancers (ICD-10 C56 and C57.0)**

Menon,… Jacobs, Lancet Oncology (10), 2009

UKCTOCS Results: Cancer Statistics

	MMS	USS	Overall	p value*
Total				
Number of women	50 078	48 230	98 308	..
Number of surgeries	97	845	942	..
Primary ovarian and tubal malignancies (ICD-10 C56 and C57.0) within 1 year of prevalence screen†				
Screen positives	42	45	87	..
Screen negatives	5	8	13	..
Sensitivity	89·4%	84·9%	87·0%	0·564
95% CI	76·9–96·5	72·4–93·3	78·8–92·9	..
Specificity	99·8%	98·2%	99·0%	<0·0001‡
95% CI	99·8–99·8	98·1–98·4	99·0–99·1	..
Positive-predictive value	43·3%	5·3%	9·2%	..
95% CI	33·3–53·8	3·9–7·1	7·5–11·3	..
Number of operations per screen positive	2·3	18·8	10·8	..
Primary invasive epithelial ovarian and tubal malignancies within 1 year of prevalence screen§				
Screen positives	34	24	58	..
Screen negatives	4	8	12	..
Sensitivity	89·5%	75·0%	82·9%	0·126
95% CI	75·2–97·1	56·6–88·5	72·0–90·8	..
Specificity	99·8%	98·2%	99·0%	<0·0001‡
95% CI	99·8–99·8	98·1–98·4	99·0–99·1	..
Positive-predictive value	35·1%	2·8%	6·2%	..
95% CI	25·6–45·4	1·8–4·2	4·7–7·9	..
Number of operations per screen positive	2·9	35·2	16·2	..

*Fisher's exact test. †Includes borderline and ovarian neoplasm of uncertain behaviour. ‡Due to very large sample sizes the p values tend to imply statistically significant difference where clinically meaningful difference is minimal. §Borderline epithelial ovarian cancers and ovarian neoplasms of uncertain behaviour treated as false positives.

Table 6: **Performance characteristics for detection of malignant ovarian and tubal neoplasms (ICD-10 C56 and C57.0) in the prevalence screen**

*** Long-term follow-up needed to asses any survival advantage to screening**

Menon,… Jacobs, Lancet Oncology (10), 2009

UKCTOCS mortality

Ovarian cancer screening and mortality in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS): a randomised controlled trial

Ian J Jacobs, Usha Menon*, Andy Ryan, Aleksandra Gentry-Maharaj, Matthew Burnell, Jatinderpal K Kalsi, Nazar N Amso, Sophia Apostolidou, Elizabeth Benjamin, Derek Cruickshank, Danielle N Crump, Susan K Davies, Anne Dawnay, Stephen Dobbs, Gwendolen Fletcher, Jeremy Ford, Keith Godfrey, Richard Gunu, Mariam Habib, Rachel Hallett, Jonathan Herod, Howard Jenkins, Chloe Karpinskyj, Simon Leeson, Sara J Lewis, William R Liston, Alberto Lopes, Tim Mould, John Murdoch, David Oram, Dustin J Rabideau, Karina Reynolds, Ian Scott, Mourad W Seif, Aarti Sharma, Naveena Singh, Julie Taylor, Fiona Warburton, Martin Widschwendter, Karin Williamson, Robert Woolas, Lesley Fallowfield, Alistair J McGuire, Stuart Campbell, Mahesh Parmar†, Steven J Skates†*

Jacobs, IJ,…Skates SJ, Lancet 387(10022), 2016

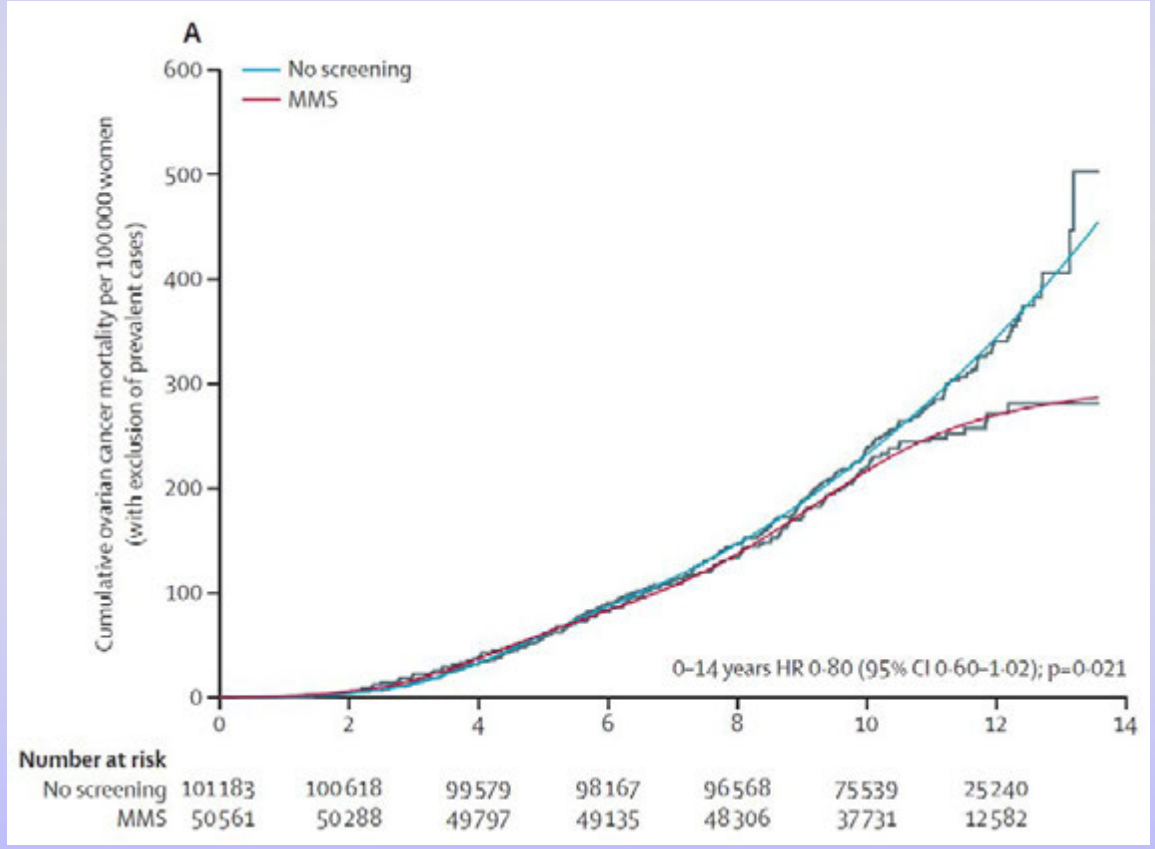
UKCTOCS mortality

	Number of women (n)	Deaths (n)	Mortality reduction 0–14 years (%)	p value	Mortality reduction 0–7 years (%)	Mortality reduction 7–14 years (%)
Ovarian cancer (primary analysis)						
Cox model						
MMS	50 624	148	15% (–3 to 30)	0·10	..	..
USS	50 623	154	11% (–7 to 27)	0·21	..	..
No screening	101 299	347	..	..	..	..
Royston-Parmar model						
MMS	50 624	148	16% (–1 to 33)	0·11	8% (–20 to 31)	23% (1 to 46)
USS	50 623	154	12% (–6 to 29)	0·18	2% (–27 to 26)	21% (–2 to 42)
No screening	101 299	347	..	..	..	..
Royston-Parmar model (excluding prevalent cases)						
MMS	50 561	120	20% (–2 to 40)	0·021	8% (–27 to 43)	28% (–3 to 49)
No screening	101 183	281	..	..	..	..
Weighted log-rank (post-hoc)						
MMS	50 624	148	22% (3 to 38)*	0·023	..	..
USS	50 623	154	20% (0 to 35)*	0·049	..	..
No screening	101 299	347	..	..	..	..

- **Overall Non-significant reduction in mortality with screening**
- **Significant (20% reduction) if you exclude prevalent cases**

Jacobs, IJ,…Skates SJ, Lancet 387(10022), 2016

UKCTOCS mortality



- **Cumulative mortality begins to decline after 7 years**
- **This is expected when you consider median mortality is 5 years, plus exclusion of prevalent cases that would appear for about 2 years into screening**

Jacobs, IJ,…Skates SJ, Lancet 387(10022), 2016

Limitations in Traditional Methods of Screening

- Ca125 – poor sensitivity
  - Normal in 50% of Stage I cancers
- TV Ultrasound – poor specificity
  - >99% of abnormalities are benign

A 2-Stage Ovarian Cancer Screening Strategy Using the Risk of Ovarian Cancer Algorithm (ROCA) Identifies Early-Stage Incident Cancers and Demonstrates High Positive Predictive Value

Karen H. Lu, MD[1]; Steven Skates, PhD[2]; Mary A. Hernandez, MSN[3]; Deepak Bedi, MD[4]; Therese Bevers, MD[5]; Leroy Leeds, MD[6]; Richard Moore, MD[7]; Cornelius Granai, MD[7]; Steven Harris, MD[8]; William Newland, MD[9]; Olasunkanmi Adeyinka, MD[10]; Jeremy Geffen, MD[11]; Michael T. Deavers, MD[12]; Charlotte C. Sun, DrPH[1]; Nora Horick, MS[2]; Herbert Fritsche, PhD[3]; and Robert C. Bast Jr, MD[3]

Cancer October 1, 2013

- **Risk of Ovarian Cancer Algorithm**
  - **Serial Ca125 values from 22,000 women in prior longitudinal studies used to determine "change point" for her own baseline**
  - **Ca125 annually if "low risk (less then 1 in 2,000)**
  - **Repeat in 3 months if "intermediate risk" (1:500 to 1:2,000)**
  - **If risk great than 1:500, TVUS and gyn onc referral**

ROCA screening results

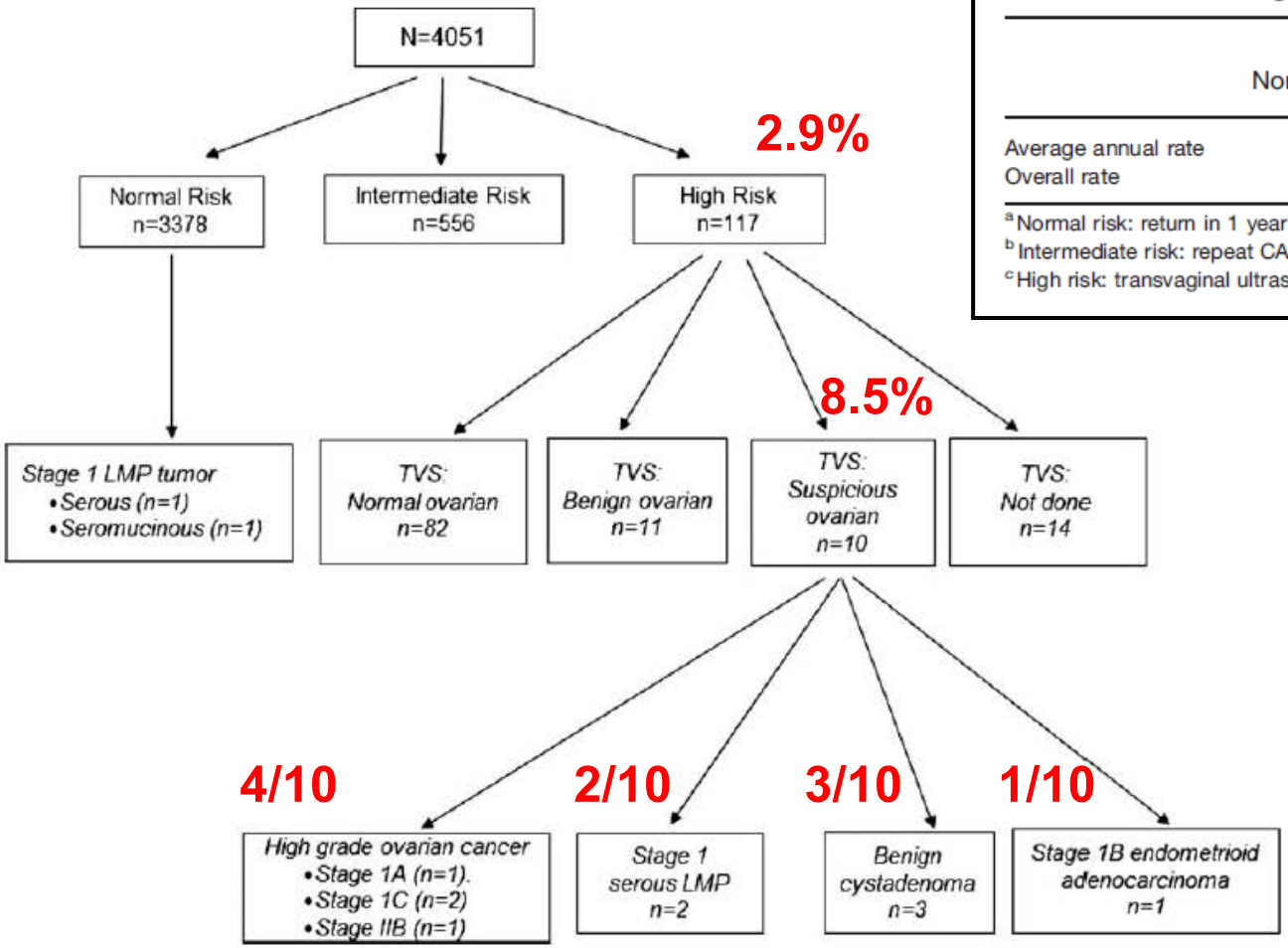


Figure 1. Overall flow diagram for participants through December 1, 2011, shows the number of patients by most acute ROCA (Risk of Ovarian Cancer Algorithm) category. Abbreviations: LMP, low malignant potential; TVS, transvaginal ultrasound.

TABLE 2. Screening Rates for Risk Groups

	Normal risk[a]	Intermediate risk[b]	High risk[c]
Average annual rate	93.3%	5.8%	0.9%
Overall rate	83.4%	13.7%	2.9%

[a] Normal risk: return in 1 year for CA125.
[b] Intermediate risk: repeat CA125 in 3 months.
[c] High risk: transvaginal ultrasound and referral to gynecologic oncologist.

Lu,… Bast, Cancer (119), 2013

ROCA Ca125 profiles

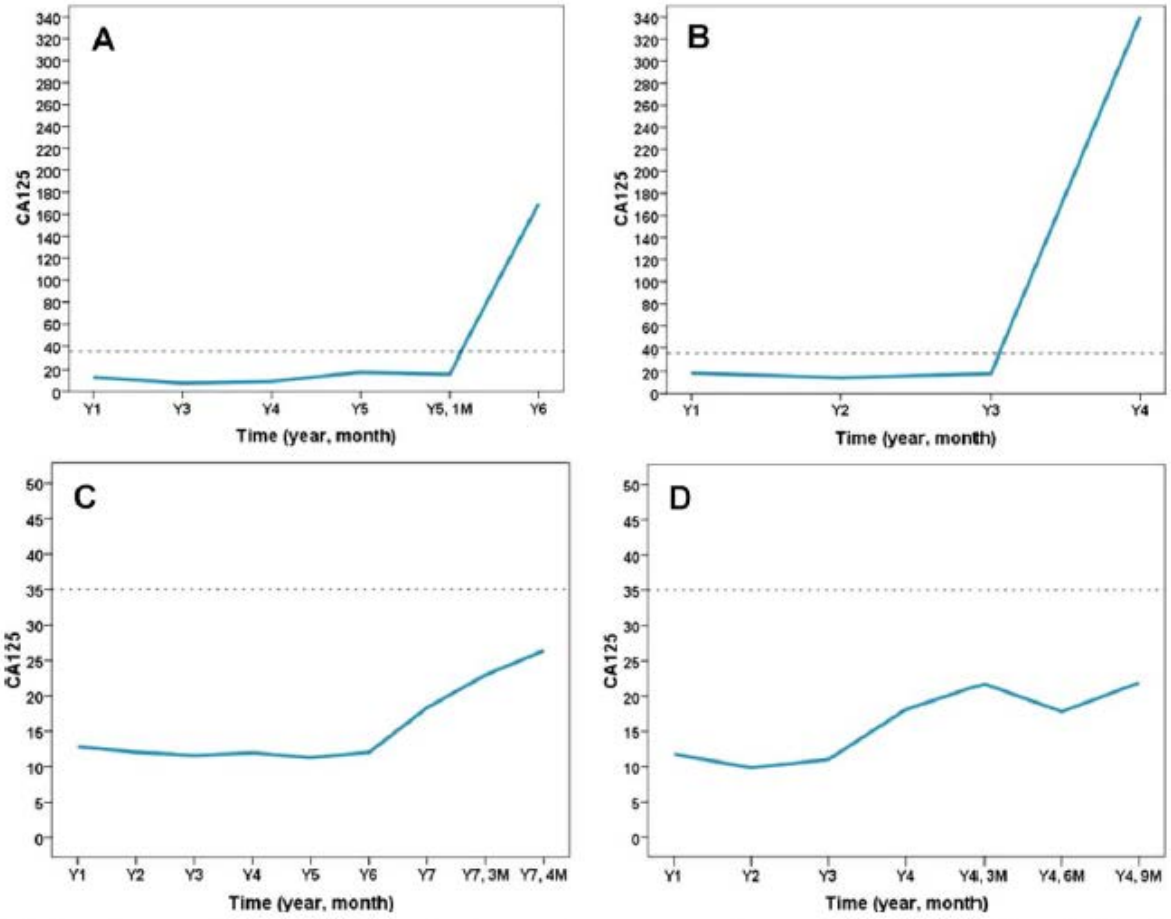


Figure 2. CA125 values are shown over time for invasive ovarian cancers. (A) Stage IC mixed-grade endometrioid and clear cell carcinoma; (B) stage IC high-grade mixed mucinous and endometrioid type with clear cell carcinoma; (C) stage IA high-grade serous carcinoma; (D) stage IIB high-grade serous carcinoma and high-grade endometrioid.

Lu,… Bast, Cancer (119), 2013

Prevention: Salpingectomy to Prevent "Ovarian" Cancer

- **Retrospective review procedures from 1973-2009 (Sweden)**
  - **Prior surgery (n=251,465) versus unexposed popn (n=5,449,119)**

Procedure	HR (95% CI)
Salpingectomy	0.65 (0.52 to 0.81)
Hysterectomy	0.79 (0.70 to 0.88)
Tubal Sterilization	0.72 (0.64 to 0.81)
Hyst/BSO	0.06 (0.03 to 0.12)

Procedure	HR (95% CI)
Unilateral Salpingectomy (n=472,263)	0.71 (0.56 to 0.91)
Bilateral Salpingectomy (n=70,566)	0.35 (0.17 to 0.73)

Falconer H et al, Ovarian cancer risk after salpingectomy: a nationwide population-based study. J Natl Cancer Inst. 2015 Jan 27;107(2).

Novel Opportunities for Screening

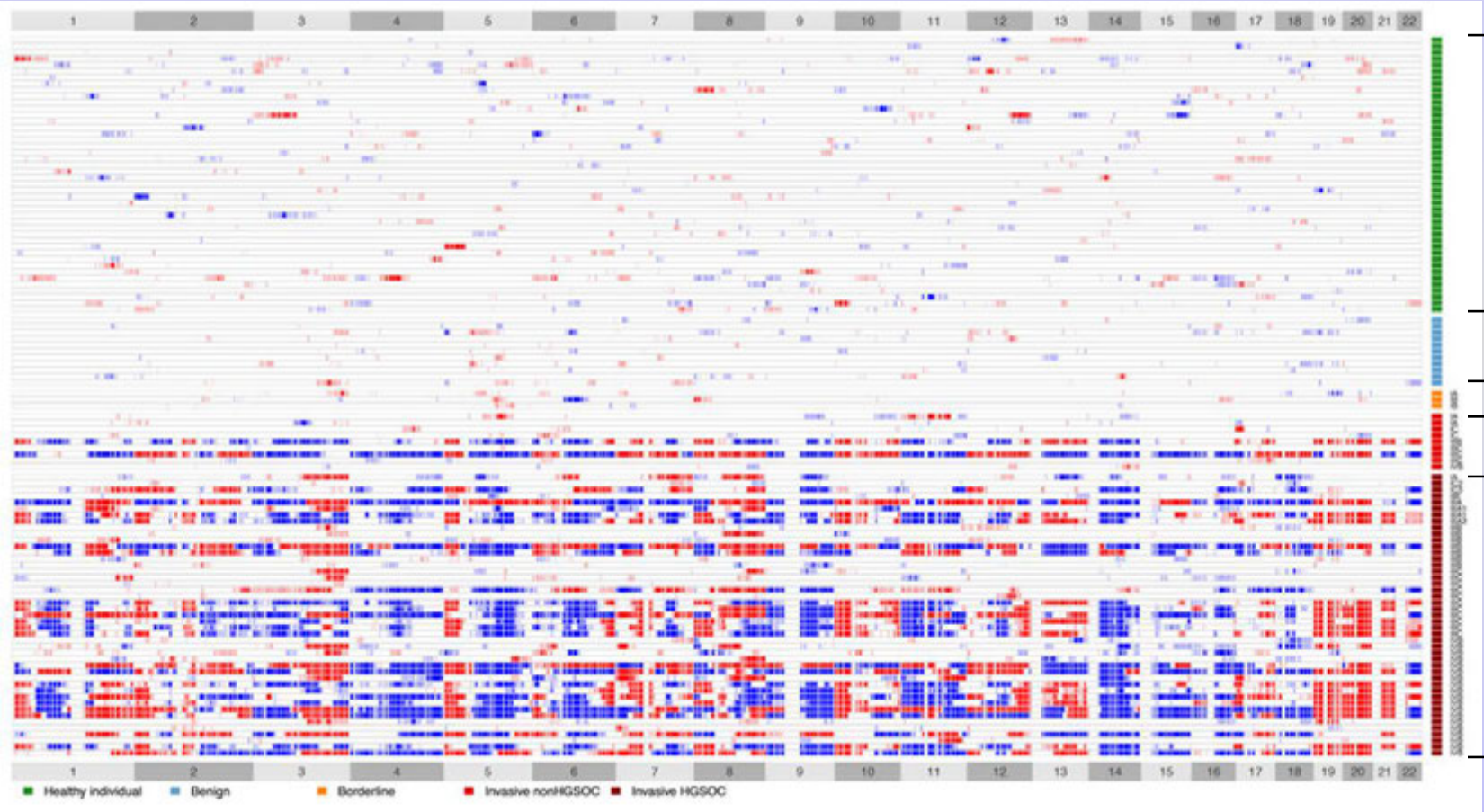
- Serum biomarkers
  - Cell-free DNA
  - Molecules beyond Ca125
  - Circulating Tumor Cells
- Proximal fluid testing
  - Pap smears, tampon collection
  - Fallopian tube sampling
  - Cytology, DNA or other molecules

Cell-Free DNA

- Anecdotally identified women with ovarian cancer during prenatal testing for aneuploidy
  - Tumor-specific mutations are uncommon in ovarian cancer
- Compared 57 cancers, 11 benign, and 44 healthy women
  - Enriched for high prevalence
- Assigned genome-wide z-scores based on chromosome instability
- Achieved specificity of 99.6%
- Reduced efficacy in early-stage disease, but low numbers

Vanderstichele A, …. Vergote. Clin Can Res Nov 14, 2016.

Cell-Free DNA



Healthy

Benign

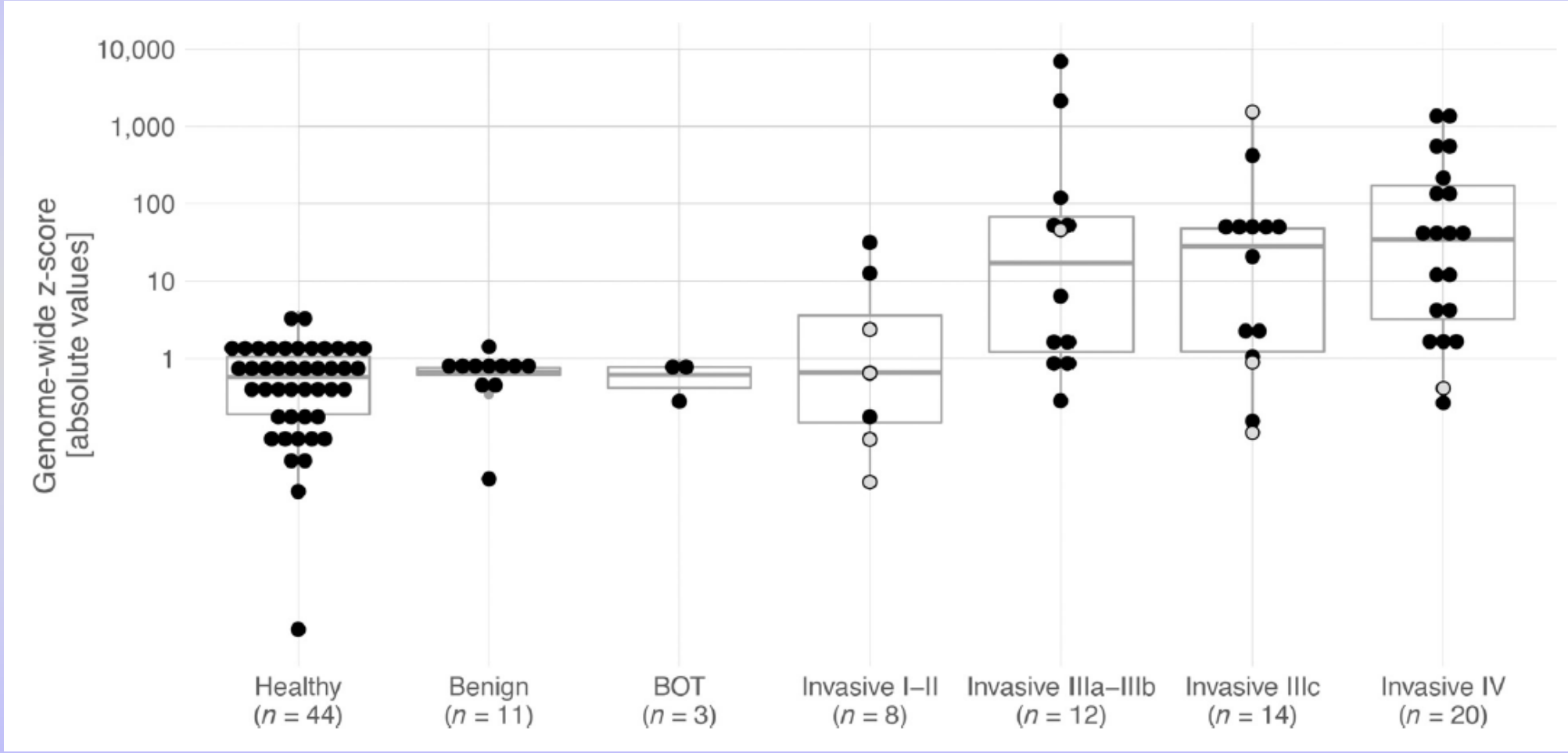
Borderline (LMP)

Non-HGSOC

HGSOC
- 8 Stage I-II
- 26 Stage III
- 20 Stage IV

Vanderstichele A, …. Vergote. Clin Can Res Nov 14, 2016.

Cell-Free DNA



Vanderstichele A, …. Vergote. Clin Can Res Nov 14, 2016.

Proximal Fluids: TP53 mutations in vaginal secretions

- Kinde et al, developed SafeSeq technology, allowing detection of rare mutations
  - Retrospective analysis of pap smears, detected DNA from ovarian cancer patients in 40% of cases
- Overnight tampon placement, detected tumor DNA in 60% of cases when patients had tubes intact

Table 2. Mutational Analysis of Tumor and Vaginal Tampon DNA

Patient No.	Histologic Percentage of Malignant Cells	Tissue Mutation(s) (Percentage of Template Molecules With Mutation)	Mutation Detected in Tampon DNA	Percentage of Mutant Tumor DNA in Tampon
1	70	TP53 g.chr17:7577538C>T, c.743 G>A, p.R248Q (32%)	TP53 g.chr17:7577538C>T, c.743 G>A, p.R248Q	0.01
2	90	TP53 g.chr17:7579707delT, c.89delA, p.N30fs (69%)	Not detected	
3	80	TP53 g.chr17:7577559 G>T, c.722C>A, p.S241Y (21%)	Not detected	
4	80	TP53 g.chr17:7578190T>C, c.659A>G, p.Y220C (39%)	TP53 g.chr17:7578190T>C, c.659A>G, p.Y220C	0.02
5	70	TP53 g.chr17:7578234_7578235delAT, c.614_615delAT, p.Y205fs (36%)	Not detected	
6	70	TP53 g.chr17:7578394T>C, c.536A>G, p.H179R (86%)	Not detected	
7	90	TP53 g. chr17:7577115A>G, c.823T>C, p.C275R (59%)	TP53 g. chr17:7577115A>G, c.823T>C, p.C275R	0.07
8	50	TP53 g.chr17:7577120C>T, c.818 G>A, p.R273H (66%)	Not detected	

Kinde I, … Diaz LA Jr. Sci Transl Med. 2013 Jan 9;5(167):167

Erickson BK, … Landen CN, Obstet Gynecol. 2014 Nov;124(5):881-5.

Additional approaches under investigation

- Mass spec analysis of vaginal secretions
  - Collaboration with Larry Maxwell, MD and Tom Conrads, PhD at INOVA
- Hysteroscopic sampling of Fallopian tube
  - Collaboration with nVision, FDA-approved MAKO device
- Identification of circulating tumor cells
  - Collaboration with Axon Dx, Charlottesville VA

Conclusions

- There is no current accepted method for screening the general population for ovarian cancer
  - New algorithms for following changes in Ca125 are promising
- A detailed family history should be taken to identify patients at high risk
  - Have a low threshold for referral to genetic counselor
- Salpingectomy reduces risk by 65% and should be considered in operative patients electing for ovarian preservation
- Novel detection methods of detection using proximal fluids and peripheral blood are under investigation

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Landen Lab

Robbie Cornelison, MS, PhD candidate (UVA)
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Zack Dobbin, MD/PhD (UAB, U Chicago)
Yulia Petrova, PhD (UVA)
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Surbhi Sarna, MD (nVision)

Dongquan Chen, PhD (UAB Biostatistics)
David Schneider, PhD (UAB Biochemistry)

Ken Nephew (Indiana U)
Ernst Lengyel (U of Chicago)

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Katie Terry (Harvard)

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DoD Ovarian Cancer Academy

FOUNDATION FOR WOMEN'S CANCER
Gynecologic Cancer Awareness • Research • Education

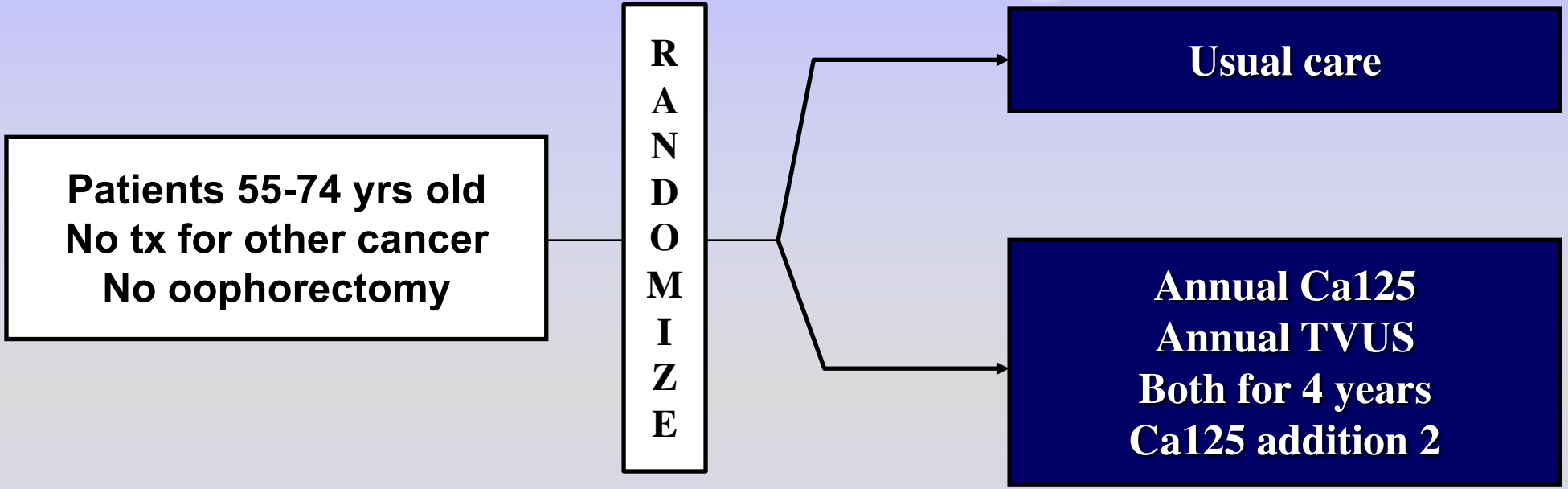
Tina's Wish
Know Early. Know Hope.™

RSDP Reproductive Scientist Development Program

THE OVARIAN CANCER RESEARCH FUND, INC.

Congressionally Directed Medical Research Programs
CDMRP
Department of Defense

PLCO design



- Results delivered to both patients and physician in 3 wks
- Management at discretion of physician
- 3 categories of cancer:
  - Screen-detected cancer
  - Interval cancer (CA in previously screened pt)
  - CA in never screened patient

Primary end point:
Reduction in mortality

Prorok et al, Contol Clin Trials (21), 2000

Results – PLCO

Table 2. Compliance With Screening Tests

	Screening Round			
	T0	T1	T2	T3
Total eligible	34,261	33,319	32,707	32,114
% Compliant				
TVU	83.1	81.2	79.6	77.7
CA 125 compliant	83.9	82.4	81.0	79.0
Either compliant	83.9	82.4	81.0	79.1
Both compliant	83.1	81.1	79.5	77.6

TVU, transvaginal ultrasonography.

Table 3. Transvaginal Ultrasonography and CA-125 Screening Results

	Screening Round			
	T0	T1	T2	T3
n (receiving at least one screening test)	28,746	27,541	26,584	25,423
% Positive				
Either test	5.8	4.9	4.6	4.5
TVU	4.6	3.4	2.9	2.9
CA 125	1.4	1.6	1.8	1.7
Both tests	0.12	0.08	0.08	0.05
First positive TVU	–	1.9	1.3	1.3
First positive CA 125	–	0.9	0.9	0.6

TVU, transvaginal ultrasonography.

Partridge,… Buys, Obstet Gyn (113), 2009

UKCTOCS Screening Results: U/S

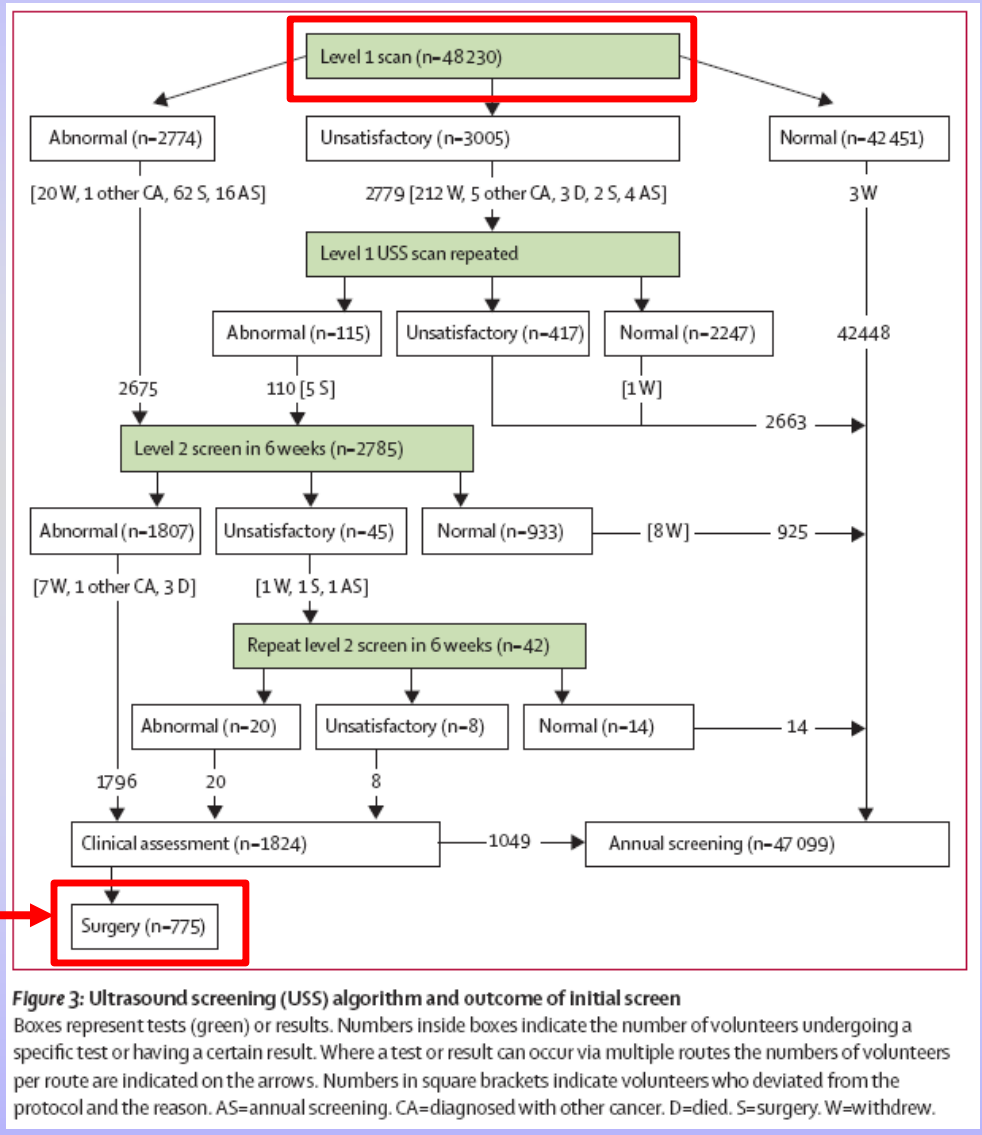
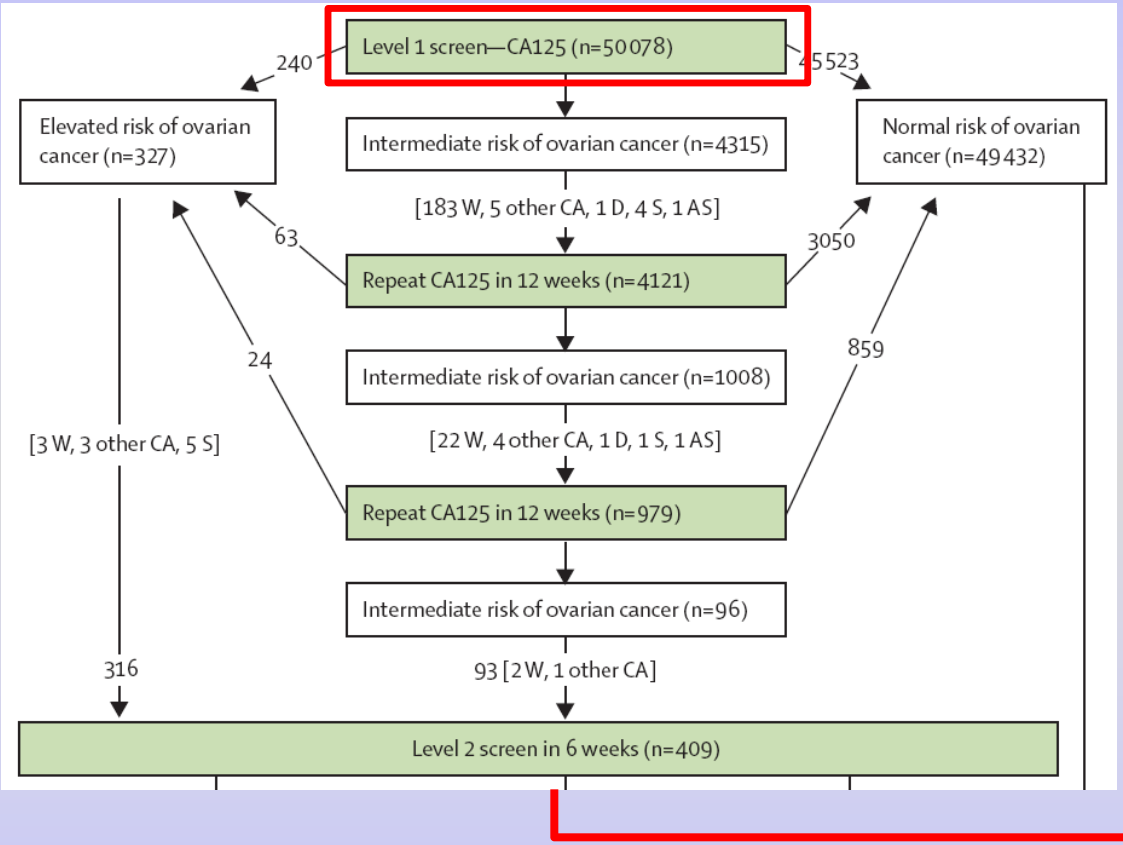
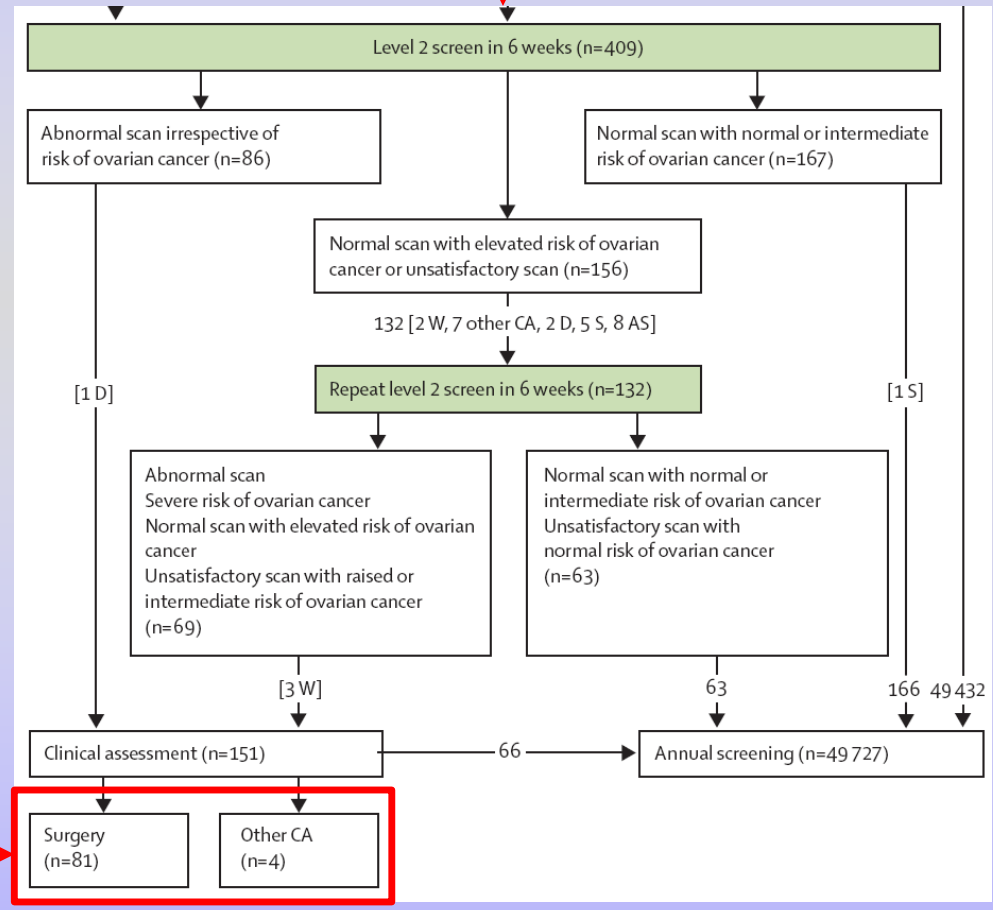


Figure 3: **Ultrasound screening (USS) algorithm and outcome of initial screen**
Boxes represent tests (green) or results. Numbers inside boxes indicate the number of volunteers undergoing a specific test or having a certain result. Where a test or result can occur via multiple routes the numbers of volunteers per route are indicated on the arrows. Numbers in square brackets indicate volunteers who deviated from the protocol and the reason. AS=annual screening. CA=diagnosed with other cancer. D=died. S=surgery. W=withdrew.

Menon,… Jacobs, Lancet Oncology (10), 2009

UKCTOCS Screening Results: MMS





Menon,… Jacobs, Lancet Oncology (10), 2009

	Total*	Screen positives	Cancers not detected by screening			
			Screen negatives <1 year from last test of screening episode†	Screen negatives >1 year after last test of screening episode	After screening phase‡	Never attended screening
MMS (50 624 women, 548 533 women-years)						
Primary ovarian cancer	338 (100%)	199 (59%)	38 (11%)	41 (12%)	57 (17%)	3 (1%)
Primary non-epithelial neoplasm of ovary (ICD C56)	11 (100%)	7 (64%)	2 (18%)	2 (18%)	0	0
Primary borderline epithelial neoplasm of ovary (ICD C56)	44 (100%)	24 (55%)	10 (23%)	5 (11%)	5 (11%)	0
Primary invasive epithelial neoplasm of ovary (ICD C56)	244 (100%)	147 (60%)	21 (9%)	29 (12%)	44 (18%)	3 (1%)
Primary invasive epithelial neoplasm of fallopian tube (ICD C57.0)	19 (100%)	13 (68%)	2 (11%)	0	4 (21%)	0
Undesignated (unable to delineate if primary site ovary or fallopian tube or peritoneum)	20 (100%)	8 (40%)	3 (15%)	5 (25%)	4 (20%)	0
Primary peritoneal cancer	16 (100%)	13 (81%)	3 (19%)	0	0	0
USS (50 623 women, 548 825 women-years)						
Primary ovarian cancer	314 (100%)	161 (51%)	60 (19%)	46 (15%)	34 (11%)	13 (4%)
Primary non-epithelial neoplasm of ovary (ICD C56)	12 (100%)	11 (92%)	0	1 (8%)	0	0
Primary borderline epithelial neoplasm of ovary (ICD C56)	53 (100%)	48 (91%)	2 (4%)	1 (2%)	0	2 (4%)
Primary invasive epithelial neoplasm of ovary (ICD C56)	220 (100%)	93 (42%)	48 (22%)	37 (17%)	31 (14%)	11 (5%)
Primary invasive epithelial neoplasm of fallopian tube (ICD C57.0)	13 (100%)	4 (31%)	3 (23%)	3 (23%)	3 (23%)	0
Undesignated (unable to delineate if primary site ovary or fallopian tube or peritoneum)	16 (100%)	5 (31%)	7 (44%)	4 (25%)	0	0
Primary peritoneal cancer	10 (100%)	3 (30%)	3 (30%)	4 (40%)	0	0
No screening (101 299 women, 1 097 089 women-years)						
Primary ovarian cancer	630 (100%)	..	501 (80%)	..	129 (20%)	..
Primary non-epithelial neoplasm of ovary (ICD C56)	8 (100%)	..	7 (88%)	..	1 (13%)	..
Primary borderline epithelial neoplasm of ovary (ICD C56)	62 (100%)	..	50 (81%)	..	12 (19%)	..
Primary invasive epithelial neoplasm of ovary (ICD C56)	493 (100%)	..	392 (80%)	..	101 (20%)	..
Primary invasive epithelial neoplasm of fallopian tube (ICD C57.0)	28 (100%)	..	21 (75%)	..	7 (25%)	..
Undesignated (unable to delineate if primary site ovary or fallopian tube or peritoneum)	38 (100%)	..	30 (79%)	..	8 (21%)	..
Primary ovarian neoplasm (histology not available)	1 (100%)	..	1 (100%)	..	0	..
Primary peritoneal cancer	15 (100%)	..	15 (100%)	..	0	..

- **Similar number of cancers found in screened and non-screened groups**

Overcoming prevalence: Can we screen high-risk populations?

Risk Factors:

- Increasing age
- Nulliparity
- Infertility (not due to infertility treatment)
- Endometriosis
- PCOS
- Environmental factors not yet defined
- Hereditary ovarian cancer syndromes (BRCA gene mutations, HNPCC)

Inheritable Gene Mutations

- Make up 20-25% of EOC
- BRCA1: 35-46% Ovarian Cancer risk
- BRCA2: 13-23% Ovary Cancer risk
- Lynch Syndrome (HNPCC)
  - 10-15% risk of developing ovarian cancer
  - 60% risk of developing endometrial cancer
- Other inheritable mutations*
  - 4-7% of BRCA-negative patients
  - CHEK2, BRIP1, ATM, PALB2, Lynch

*Desmond A et al., Clinical Actionability of Multigene Panel Testing for Hereditary Breast and Ovarian Cancer Risk Assessment. JAMA Oncol. 2015 Aug 13.

Criteria for Genetic Testing

- All patients diagnosed with ovarian cancer
- Two or more relatives with ovarian cancer
- Three or more relatives with breast CA at any age
  - Two if one of them was diagnosed at age <50
- A first degree relative with bilateral breast CA
- A relative with both breast and ovarian cancer
- A MALE relative with breast cancer
- Ashkenazi Jewish women with just a 1st degree relative of breast or ovarian cancer

Basically, need 2 indices or risk traits for a referral, except breast cancer >50, when you need 3

- Qualify for Lynch Syndrome: 3, 2, 1

ACOG Practice Bulletin #89, reaffirmed 2014

Screening in High-risk populations

- ACOG recommends screening women with BRCA mutations, starting at age 30 to 35 years or 5 to 10 years before the earliest diagnosis in a family member
  - CA 125 and ultrasound every 6 to 12 months although improved survival has not been proven
- RRSO (maybe salpingectomy) when completing childbearing
  - Be aware 3-5% risk of cancer at RRSO

Salpingectomy w/hysterectomy: safety

ONCOLOGY

Opportunistic salpingectomy: uptake, risks, and complications of a regional initiative for ovarian cancer prevention

Jessica N. McAlpine, MD; Gillian E. Hanley, MA, PhD; Michelle M. M. Woo, PhD; Alicia A. Tone, PhD; Nirit Rozenberg; Kenneth D. Swenerton, MD; C. Blake Gilks, MD; Sarah J. Finlayson, MD; David G. Huntsman, MD; Dianne M. Miller, MD; for the Ovarian Cancer Research Program of British Columbia

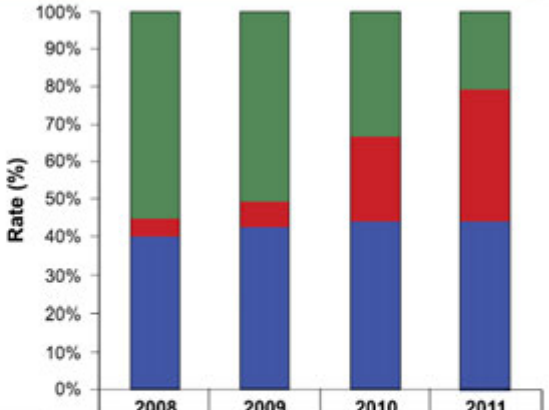
No compromise in safety:

- **Blood transfusion: 2.4% v 2.6%**
- **Readmission: HR 0.91**

McAlpine et al, Am J Obstet Gynecol 2104: 210:47

FIGURE 1

Specific procedures that were performed from 2008-2011 in British Columbia

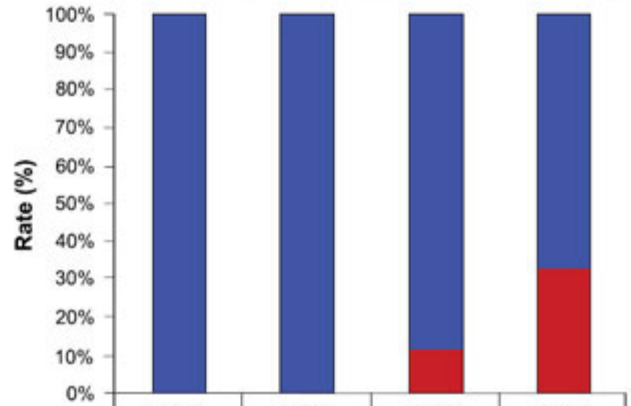


	2008	2009	2010	2011
Hysterectomy alone	55% (n = 2950)	50% (n = 2610)	33% (n = 1762)	21% (n = 1040)
Hysterectomy with bilateral salpingectomy	5% (n = 267)	7% (n = 378)	23% (n = 1240)	35% (n = 1785)
Hysterectomy with bilateral salpingo-oophorectomy	40% (n = 2147)	42% (n = 2197)	44% (n = 2341)	44% (n = 2219)

Proportion of women who underwent hysterectomy alone (*green*), hysterectomy with bilateral salpingectomy (*red*), and hysterectomy with bilateral salpingo-oophorectomy (*blue*).

FIGURE 2

Procedures with a diagnosis code that indicated the encounter was for sterilization that were performed from 2008-2011 in British Columbia



	2008	2009	2010	2011
Tubal ligation	99.6% (n = 3931)	99.7% (n = 3846)	88.6% (n = 3304)	66.7% (n = 2236)
Salpingectomy as sterilization	0.4% (n = 17)	0.3% (n = 11)	11.4% (n = 426)	33.3% (n = 1115)

Proportion of women who underwent isolated bilateral salpingectomy (*red*) or tubal ligation (*blue*).

McAlpine. Uptake and risks of opportunistic salpingectomy. Am J Obstet Gynecol 2014.