

Lynch Syndrome

Uterine & Ovarian Cancer

current issues in diagnosis,
management and research
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Terminology

- HNPCC - hereditary nonpolyposis colorectal cancer >> misleading
- Risk of endometrial cancer: 27% to 71% (exceeds the risk of bowel cancer)
- Risk of ovarian cancer: 3% to 14%
- Genetic defect in 1 of 3100 people [1]
- Criteria to identify women based on family history

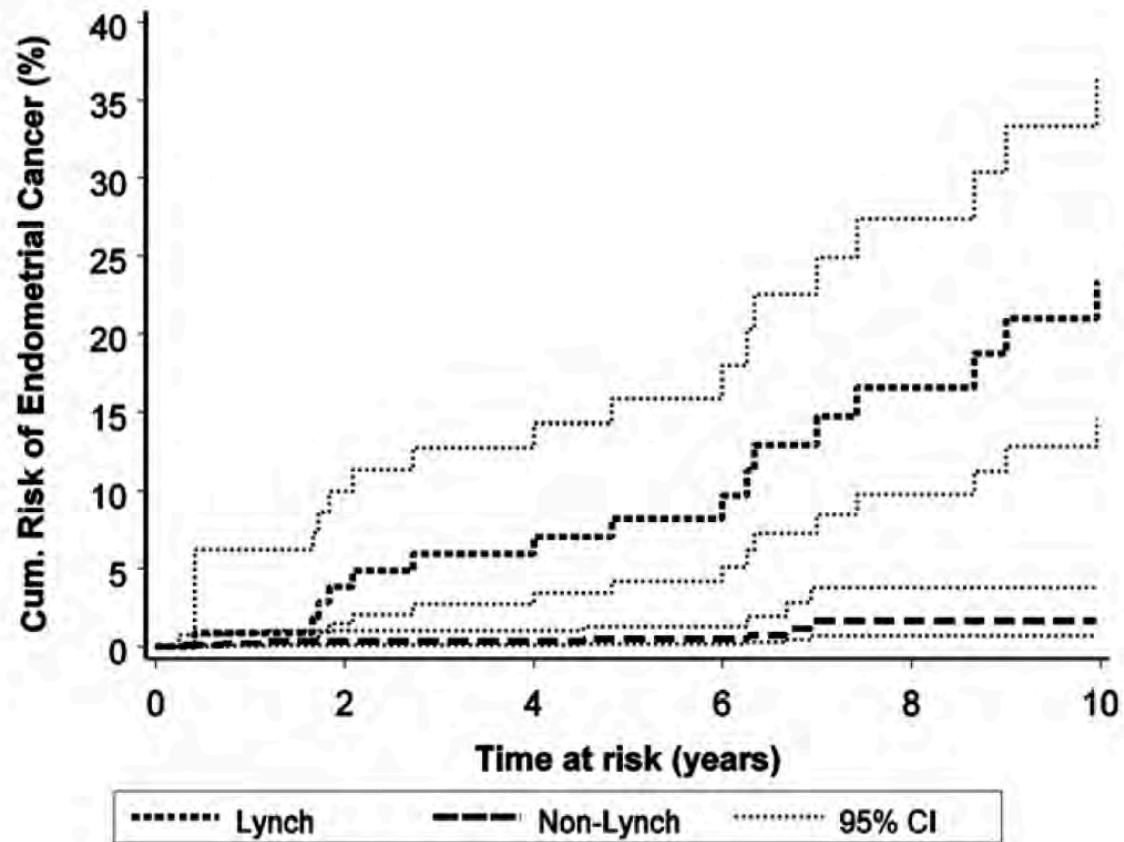
Lifetime cancer risk related to Lynch genotypes

Cancer site	MLH1		MSH2		MSH6	
	Men	Women	Men	Women	Men	Women
Any Lynch cancer	76 percent*		80 percent*		73 percent*	
Colorectal	58 to 65 percent	50 to 53 percent	54 to 63 percent	39 to 68 percent	36 to 69 percent	18 to 30 percent
Endometrial	NA	27 percent	NA	40 percent	NA	71 percent
Ovarian	NA	6 percent	NA	12 percent	?	
Upper urologic tract	2.1 percent	0.4 percent	20 percent	9 percent	?	
Gastric	6 percent*		5 percent*		?	
Small bowel*	3 percent	6 percent	3 percent	6 percent	?	
Biliary/pancreatic	4 percent*				?	
Brain tumors (gliomas)	1.7 percent		2.5 percent		?	
Sebaceous gland tumors	42 percent of families ^Δ		44 percent of families ^Δ		0 percent of families ^Δ	

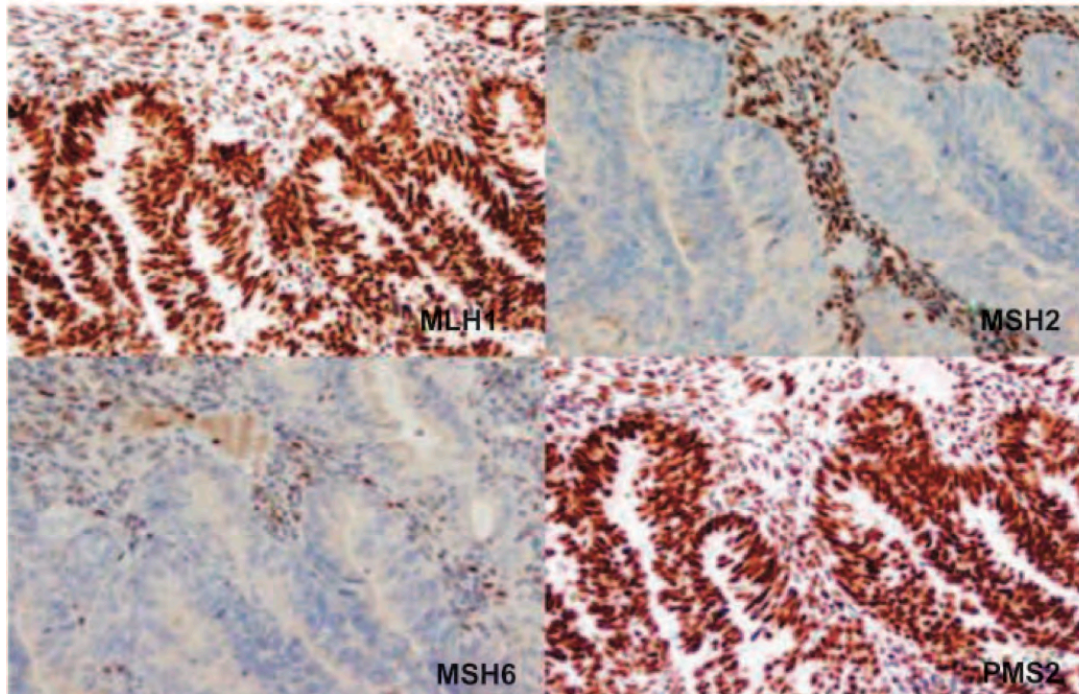
Endometrial Cancer

- Majority of EC are non-Lynch related
- Lynch in only 2% to 5%
- A Lynch carrier very high risk of EC
- Mean age ~ 50 years (62 years in Non-Lynch)
 - 18% were diagnosed under the age of 40 years
- Cell types: majority are endometrioid cancers
- Location of tumour: Lower uterine segment
 - 10 of 35 patients

Endometrial cancer risk (Lynch)



Risk of endometrial cancer finding Lynch

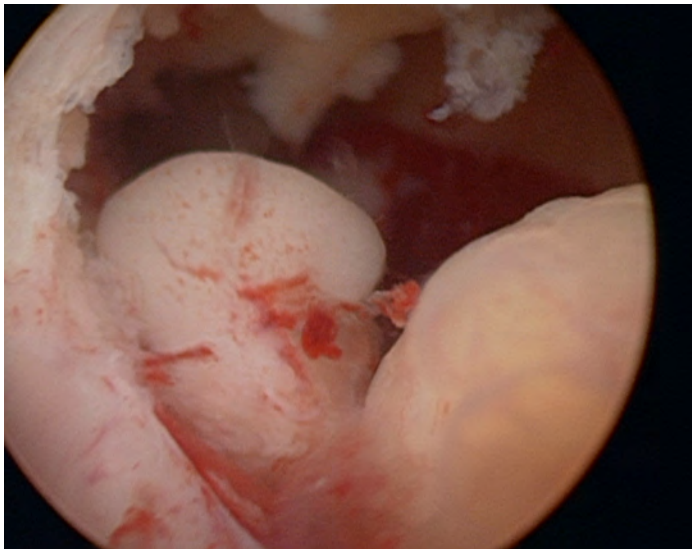


18% of patients who were 50 years of age or younger and were diagnosed with endometrial cancer had presumptive Lynch.

Diagnosis of Endometrial Cancer

- Abnormal bleeding = WARNING SIGN!
- Requires investigation:

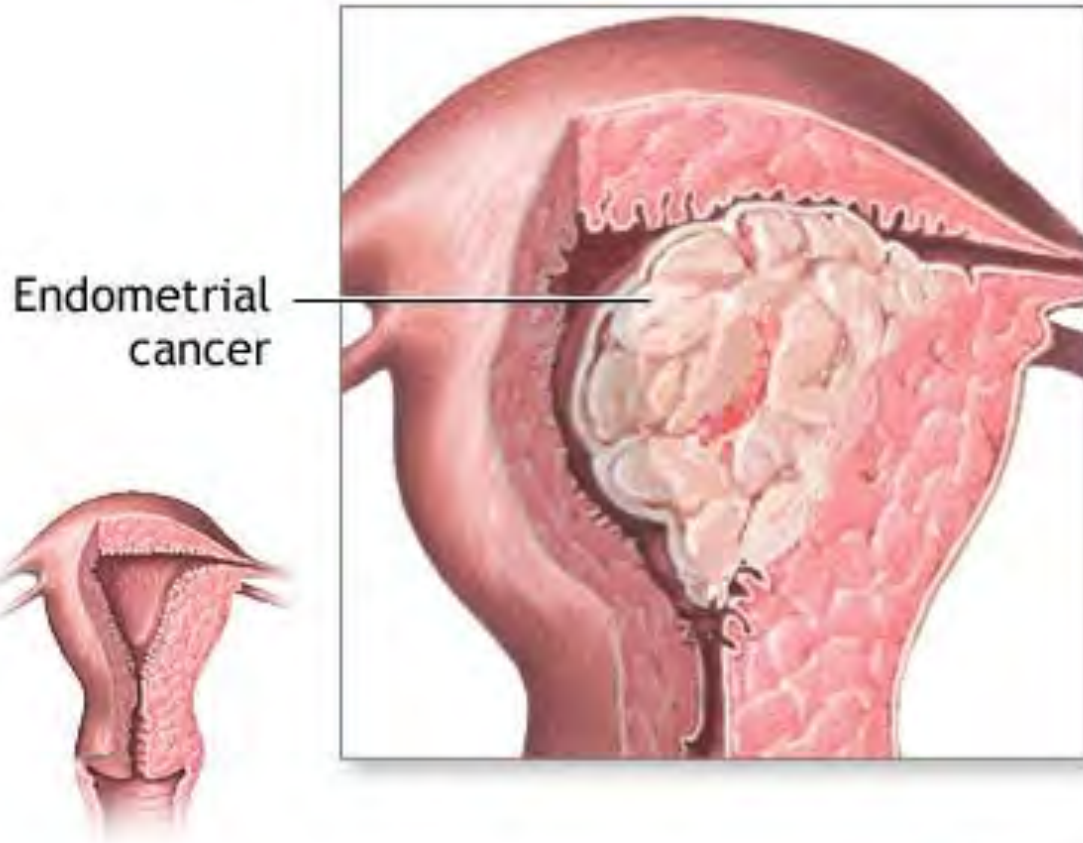
Hysteroscopy D&C



Pipelle endometrial sampling



Endometrial Cancer



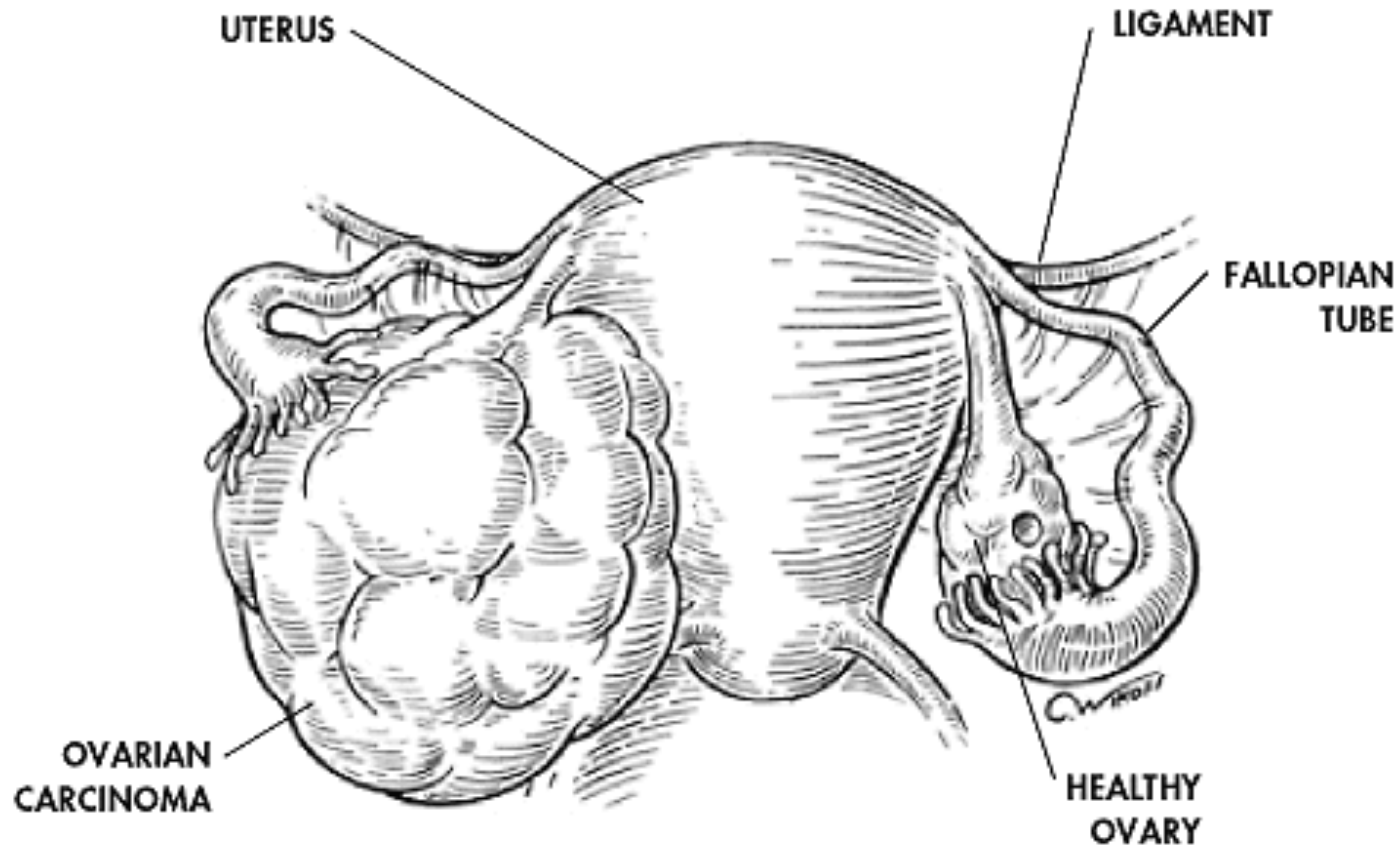
Treatment

- Hysterectomy
- Removal of ovaries
- ± Lymph nodes
- ± Radiation
- ± Chemotherapy

Ovarian Cancer

- Life time risk is 3% to 14% in Lynch carriers
 - :: 1.3% in general population
- Patients are younger: 45 years
 - :: 62 years in general population
- Histological cell types: no difference between Lynch and Non-Lynch patients
- Risk groups: not identifiable

Ovarian Cancer



Diagnosis of Ovarian Cancer

- No early warning signs
- Symptoms are late
 - Bowel problems
 - Urinary frequency
 - Increased abdominal girth
- Most patients are diagnosed at stage 3 or 4



Treatment of Ovarian Cancer

- Epithelial Ovarian Cancers
 - Surgery + Chemotherapy
- Non-Epithelial Ovarian Cancer
 - Limited surgery + chemotherapy
- Borderline tumours
 - Surgery only

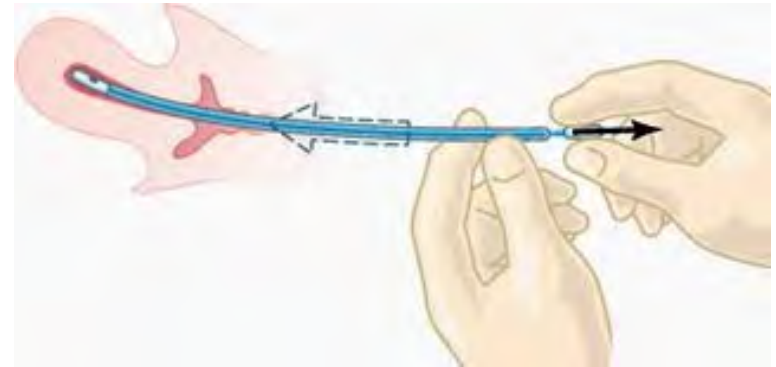


Synchronous + metachronous cancers

- Timing:
 - At the same time (14%)
 - Before (50%)
 - After (50%)
- Ovarian cancer (n=80)
 - Endometrial cancer (n=21)
 - Colorectal cancer (n=28)
 - Gastric, small bowel, urinary tract (n=6)

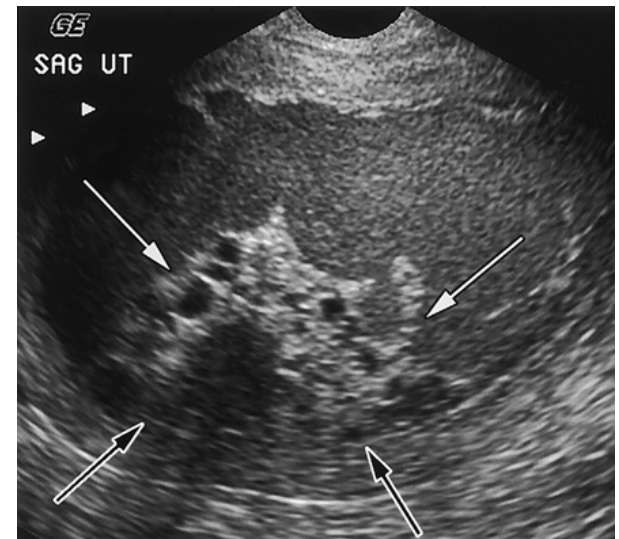
Surveillance – Endometrial Cancer

- Premenopausal women:
 - Endometrial sampling



??? RELIABLE **???**

- Postmenopausal women:
 - Transvaginal ultrasound



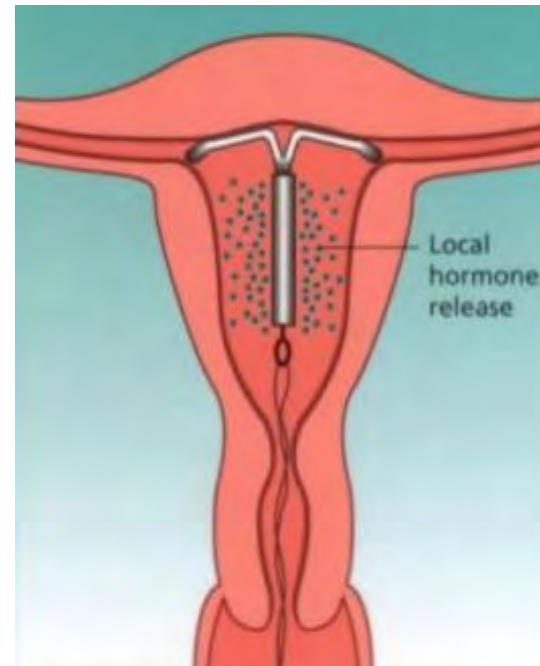
Surveillance - Ovarian Cancer

- UNRELIABLE – UNPROVEN
- Nevertheless sometimes recommended by professional societies



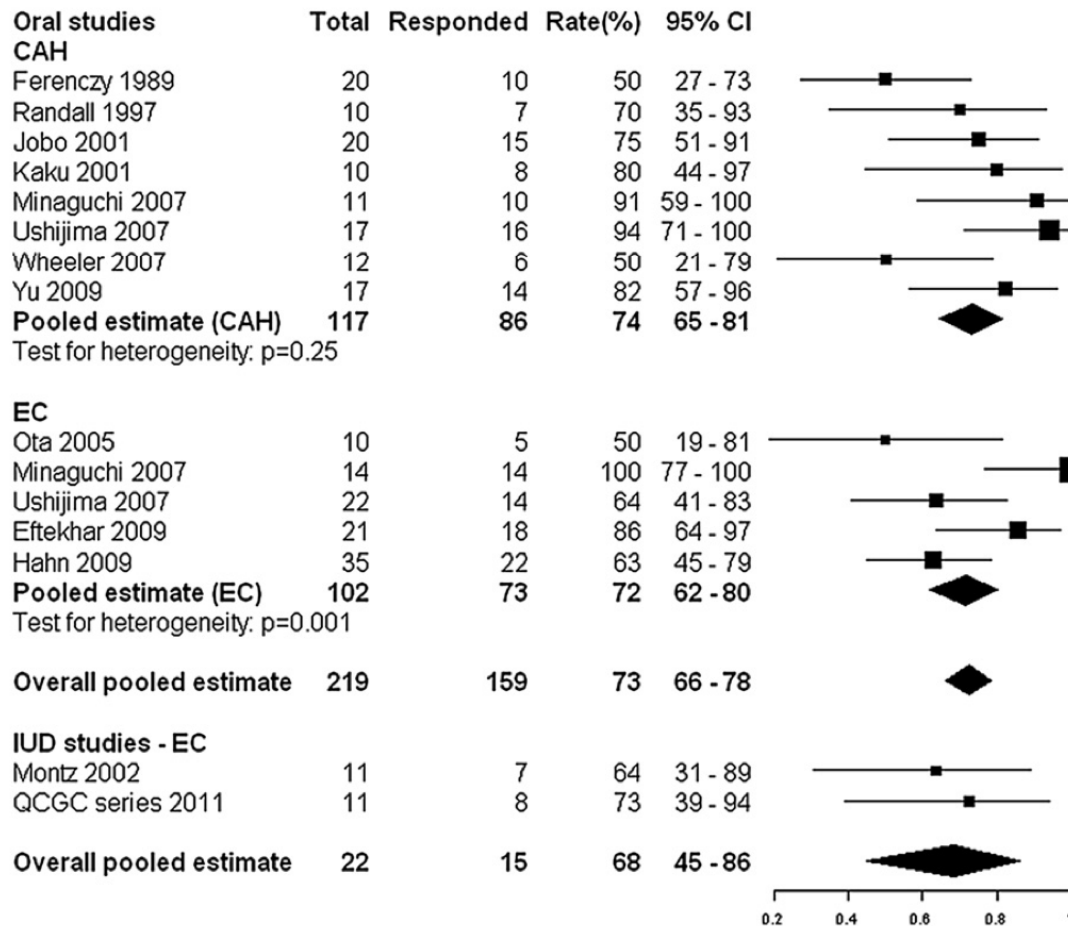
Chemoprevention

- Ovarian Cancer:
 - Oral contraceptive pill – Risk reduction by 50%
- Endometrial Cancer:
 - Mirena
 - Endometrial polyps -90%*
 - Endometrial cancer ??



*Wong et al: Obstet Gynecol 2013

Mirena to treat endometrial carcinoma



Prophylactic Surgery for Ovarian Cancer

- Remove Ovaries + Fallopian Tubes
 - Majority of women have uterus removed at the same time
- Label them correctly
- Collect samples from peritoneal lining



Prophylactic Surgery for Endometrial cancer

- Remove uterus = hysterectomy
- **Hysterectomy** is the most common gynaecological surgical procedure (~30,000 women in AUS every year)
 - 2,000 for cancer
 - 28,000 for abnormal bleeding, pain
- **Ovaries** can be preserved in young women or removed.
 - **Lynch**: Ovaries should be removed



Prevention & Screening

	Uterine Ca	Ovarian Ca
Chemoprevention Risk reduction	Unknown (Mirena)	50% (OCP)
Screening*	unreliable	unreliable
Prophylactic surgery (Risk reduction in %)	100%	90%

* Screening still recommended by some because of lack of effective alternatives

Pre-surgical assessment

- Medical check up
- Stop blood thinners + herbs/supplements (10 d)
- Gynaecological examination
- PAP smear
- Ultrasound
- Blood tests
- Bowel Prep is not required

Surgical Approach*

- Avoid laparotomy
 - Surgical complication rate is too high
- Avoid vaginal surgery
 - Ovaries cannot be removed
 - Unsafe in women who had previous surgery (cesarean section)
- Laparoscopic approach is recommended
 - Hospital stay 1 or 2 days

Risks of surgery

- Conversion from laparoscopic to open
- Medical and anaesthetic risks
- Risk of organ injury (bowel, bladder, ureter, bleeding, nerves)
- Deep vein thrombosis, Pulmonary embolus
- Infection
- Shoulder tip pain
- Postoperative pain
- Vaginal discharge for 6 weeks
- Sexual dysfunction (?)

Summary & Recommendations

- Lynch is autosomal dominant inherited
- Endometrial cancer: 27% to 71%
- Ovarian cancer: 3% to 14%
- Women who have completed childbearing
 - Prophylactic surgery
 - 100% effective to prevent endometrial cancer
 - 90% effective to prevent ovarian cancer
- Young women who have completed childbearing
 - Prophylactic surgery
 - Screening

Summary – cont'd

Screening

– Endometrial cancer:

- Chemoprevention: Mirena
- Young women: endometrial sampling (yearly) from age 30 years (or 5 years prior to earliest age of cancer)
- Menopausal women: TVUS

– Ovarian cancer:

- Chemoprevention (OCP)
- TVUS (very unreliable)
- Serum CA125 every 6 to 12 months (very unreliable)

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REFERRAL
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Prof. Obermair specializes in surgery for gynaecological cancer and complex pelvic surgery for benign conditions.

<http://obermair.info/information/gynaecological-cancer/>