RIUNIONE ANNUALE SCREENING CERVICALE

REGIONE DEL VENETO

IL TUMORE EREDO-FAMILIARE NELL'ENDOMETRIO E NELL'OVAIO

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Università degli Studi di Padova


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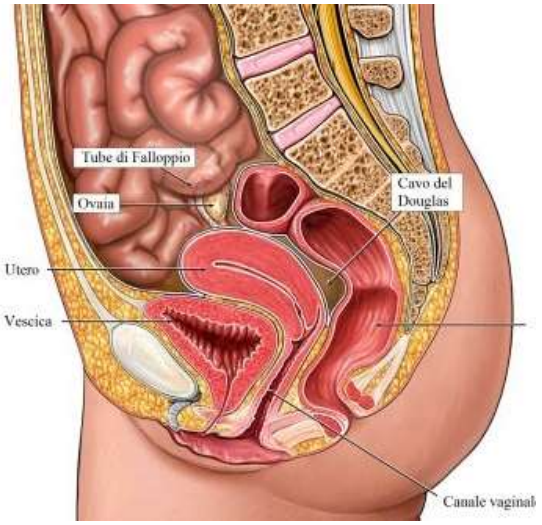
OVAIO: *organo pari e simmetrico nella pelvi , diametri 2,5 – 3 cm*

CARCINOMA OVARICO: *forte tendenza a diffondere a livello pelvico e addominale, anche con lesione primitiva molto piccola*



Tumori più frequentemente causa di morte per età

Rango	Maschi			Femmine		
	Età			Età		
	0-49	50-69	70+	0-49	50-69	70+
1°	Polmone (14%)	Polmone (30%)	Polmone (26%)	Mammella (29%)	Mammella (22%)	Mammella (15%)
2°	Sistema nervoso centrale (10%)	Colon-retto (10%)	Colon-retto (11%)	Polmone (9%)	Polmone (14%)	Colon-retto (13%)
3°	Colon-retto (8%)	Fegato (8%)	Prostata (10%)	Colon-retto (7%)	Colon-retto (10%)	Polmone (10%)
4°	Leucemie (8%)	Pancreas (7%)	Fegato (7%)	Ovaio (6%)	Pancreas (7%)	Pancreas (8%)
5°	Fegato (7%)	Stomaco (6%)	Stomaco (7%)	Sistema nervoso centrale (6%)	Ovaio (7%)	Stomaco (7%)

I numeri del cancro in Italia 2017

Ministero della Salute – Roma
15 Settembre 2017

Fattori che impattano sull'andamento dell'incidenza e della mortalità

- Prevenzione primaria in particolare per i tumori fumo-correlati e per gli stili di vita
- Programmi di screening (mammella, cervice uterina, colon-retto)
- Miglioramenti diagnostici

Table 5. Recommendations for Ovarian-Cancer Screening.*

Professional Group	Recommendation
U.S. Preventive Services Task Force[45]	Does not recommend routine screening, concluding that "the potential harms outweigh the potential benefits"
American Cancer Society[46]	Does not recommend routine screening; possible screening for women with a family history of ovarian cancer, although "it is not known how helpful" the tests will be in improving survival
American College of Obstetricians and Gynecologists[47]	Does not recommend routine screening; suggests evaluation of signs and symptoms of ovarian cancer (e.g., pelvic mass, pelvic or abdominal pain, urinary frequency or urgency, increased abdominal size or bloating, or difficulty eating or feeling of fullness)
National Comprehensive Cancer Network[36]	Does not recommend routine screening; recommends screening of high-risk women (i.e., those with either a family history of ovarian or breast cancer or a documented *BRCA* mutation) with transvaginal ultrasonography and CA-125 measurements every 6 mo, starting at the age of 35 years or 5 to 10 years before the earliest age at diagnosis of ovarian cancer in relatives; recommends strong consideration of risk-reducing prophylactic salpingo-oophorectomy at the completion of childbearing in women with a *BRCA* mutation

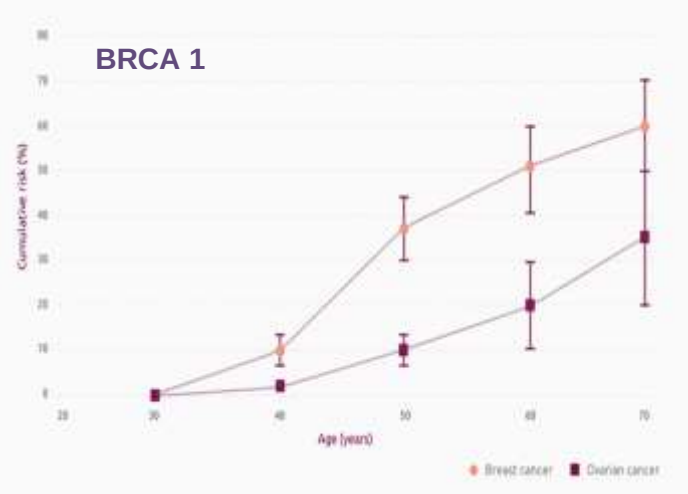
* CA-125 denotes cancer antigen 125.

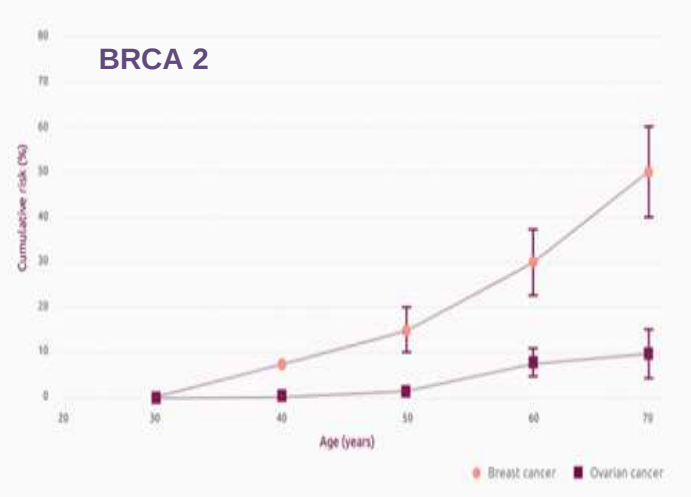
DL Clarke-Pearson, NEJM 2009

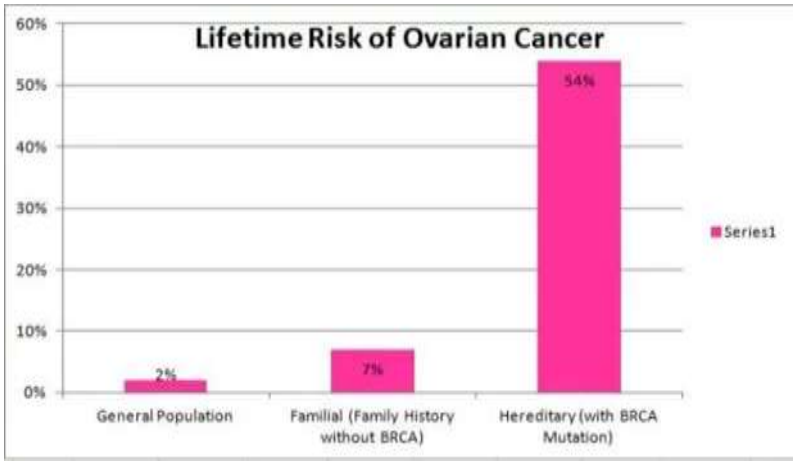
Il rischio di sviluppare un carcinoma ovarico in donne portatrici di mutazione BRCA *supera il 50 % nel corso della vita*

***BRCA1**, raggiunge il 10-20 % a 50 anni*

***BRCA 2** a 50 anni è di circa il 3%*







MANCANZA DI PROTOCOLLI ED INTERVENTI DIAGNOSTICI DI PROVATA EFFICACIA

SALPINGO-OVARIECTOMIA BILATERALE PROFILATTICA

Meglio se laparoscopica, + citologia peritoneale

Efficacia superiore al 90 %

Se prima della menopausa, riduce il rischio di K mammella di circa il 50%

***BRCA1**, tra i 35 ed i 40 anni*

***BRCA 2** tra i 40 ed i 50 anni*

Table 1. Recommendations for Ovarian Cancer Screening in High-Risk Women

Organization	Recommendation
American Cancer Society	Women may be screened, but it is not known how helpful the screening tests are.[12]
American College of Obstetricians and Gynecologists	If appropriate, these women may be offered ovarian cancer screening. Screening with CA-125 measurement and TVUS every 6 mo has been recommended by the National Comprehensive Cancer Network, although evidence is insufficient to demonstrate that current screening methods improve survival rates for these women.[13]
Canadian Task Force on Preventive Health Care	Insufficient evidence to recommend for or against screening, but expert opinion suggests that these women be referred to an academic health center for regular combination screening.[14]
National Comprehensive Cancer Network	Screen with TVUS and CA-125 every 6 mo starting at age 35 y or 5-10 y before the youngest relative received an ovarian cancer diagnosis.[15]
United States Preventive Services Task Force	The positive predictive value of an initially positive screening test would be more favorable for women at higher risk; if ongoing clinical trials show that screening has a beneficial effect on mortality rates, then women at higher risk are likely to experience the greatest benefit.[16]

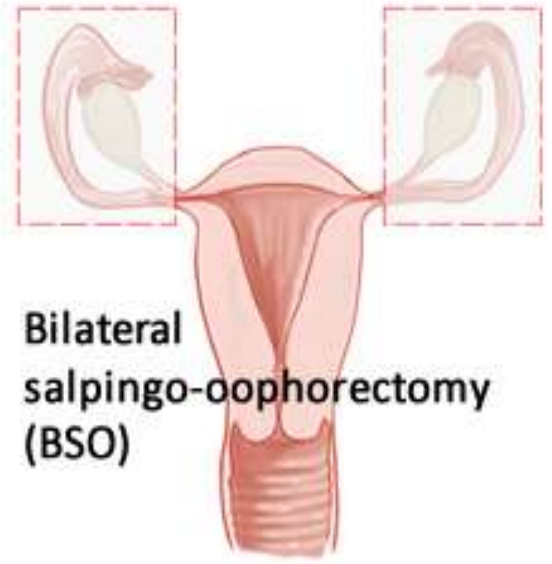
Abbreviations: CA-125, cancer antigen 125; TVUS, transvaginal ultrasonography.

JAMA INTERN MED/VOL 173 (NO. 2), JAN 28, 2013

SALPINGO-OVARIECTOMIA BILATERALE PROFILATTICA

TECNICA SPECIFICA:

richiede **la completa rimozione dell'ovaio e della salpinge**, con sufficiente quantità di tessuto peritoneale circostante comprendente il mesoovaio ed il mesosalpinge.
Arteria e vena ovarica devono essere coagulate e sezionate almeno 2 cm distalmente all'ovaio per ottenere una rimozione completa e per poter verificare un eventuale interessamento vascolo-linfatico.
La salpinge ed il ligamento utero-ovarico devono essere sezionati tangenzialmente all'utero, per garantire la completa rimozione delle strutture.
Ovaio e salpinge devono essere asportati mediante sacchetto (endobag) per evitare disseminazione endoperitoneale di eventuali lesioni



MA… *l'asportazione delle ovaie comporta la menopausa*

- *Possibilità di terapia ormonale sostitutiva fino ai 50 anni*
- *Salpingectomia bilaterale, seguita in un secondo momento da ovariectomia (?)*

SORVEGLIANZA GINECOLOGICA

A partire dai 30 anni
o 10 anni prima del caso più giovane in famiglia

- **Ecografia pelvica (TV)**
- **Dosaggio sierico CA-125**

OGNI 6 MESI

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CARCINOMA DELL'ENDOMETRIO

Il tumore dell'endometrio si esprime biologicamente ed istologicamente in due distinti gruppi di neoplasie, caratterizzati da una **diversa patogenesi**

• ***Tipo I (80-85%)*** : **estrogeno-dipendente -** basso grado di malignità e frequentemente legati ad una storia di **iperplasia endometriale** a cui fanno capo tutte le condizioni di **iperestrogenismo non adeguatamente bilanciato dal progesterone**

• ***Tipo II (15-20%):*** non sembra legato all'iperestrogenismo e non riconosce nell'iperplasia con atipie il suo precursore morfologico

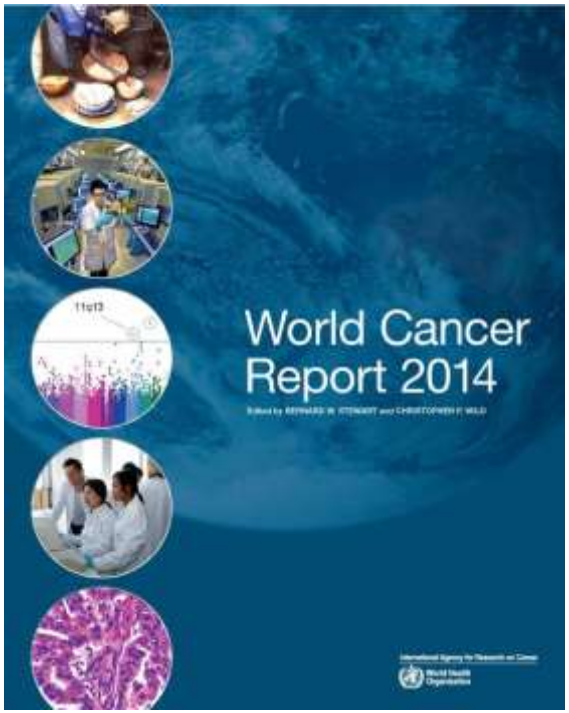
La maggior parte dei casi si verifica in **perimenopausa e menopausa**

-75 % in perimenopausa e menopausa

- 25% in premenopausa

-10-15 % età < 50 anni

- 3-5% età < 40 anni



- ✓ Nuovi casi: 320.000 donne in tutto il mondo
- ✓ Morti per K endometrio: 76.000 donne in tutto il mondo
- ✓ **Sesto** tumore più frequente nel genere femminile
- ✓ **Nord Europa, l'Est Europa e Nord America** hanno i più alti tassi di tumore dell'endometrio, mentre Africa e Asia Occidentale i più bassi

Più frequente nei ***paesi sviluppati*** rispetto ai paesi in via di sviluppo

Incidenza in Italia: 24/100.000 anno

American Cancer Society Guidelines for the Early Detection of Cancer:

Update of Early Detection Guidelines for Prostate, Colorectal, and Endometrial Cancers

CA Cancer J Clin 2001:51:38-75

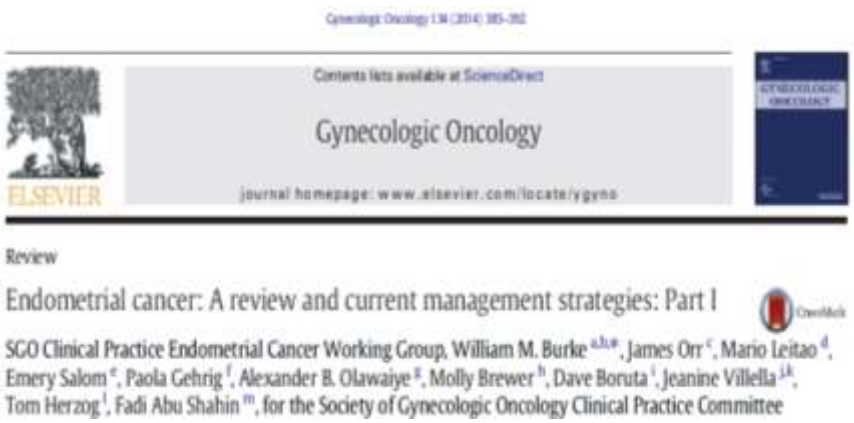
Risk factors for endometrial cancer

Risk factor	Relative risk (RR) (other statistics are noted when used)
Increasing age	Women 50- to 70-years-old have a 1.4 percent risk of endometrial cancer
Unopposed estrogen therapy	2 to 10
Tamoxifen therapy	2
Early menarche	NA
Late menopause (after age 55)	2
Nulliparity	2
Polycystic ovary syndrome (chronic anovulation)	3
Obesity	2 to 4
Diabetes mellitus	2
Estrogen-secreting tumor	NA
Lynch syndrome (hereditary nonpolyposis colorectal cancer)	22 to 50 percent lifetime risk
Cowden syndrome	13 to 19 percent lifetime risk
Family history of endometrial, ovarian, breast, or colon cancer	NA

NA: RR not available.

DIAGNOSI: clinica e strumentale

- **Nel 95% dei casi perdite ematiche vaginali anomale (AUB)**


Contents lists available at ScienceDirect
Gynecologic Oncology
journal homepage: www.elsevier.com/locate/ygyno
ELSEVIER

Review

Endometrial cancer: A review and current management strategies: Part I

SGO Clinical Practice Endometrial Cancer Working Group, William M. Burke [a,b,*], James Orr [c], Mario Leitao [d], Emery Salom [e], Paola Gehrig [f], Alexander B. Olawaiye [g], Molly Brewer [h], Dave Boruta [i], Jeanine Villella [j,k], Tom Herzog [l], Fadi Abu Shahin [m], for the Society of Gynecologic Oncology Clinical Practice Committee

- ✓ Suspicion of the presence of endometrial neoplasia (neoplastic endometrial hyperplasia or carcinoma) depends upon **symptoms, age, and the presence of risk factors**.
- ✓ **Abnormal uterine bleeding** is present in approximately 75 to 90 percent of women with endometrial carcinoma .
- ✓ *The amount of bleeding does not correlate with the risk of cancer*.

ECOGRAFIA PELVICA TV

con misurazione rima endometriale (+/- 4 mm)

Ultrasound Obstet Gynecol 2004; 24: 558–565
Published online 14 September 2004 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/uog.1704

How thick is too thick? When endometrial thickness should prompt biopsy in postmenopausal women without vaginal bleeding

R. SMITH-BINDMAN*†, E. WEISS‡ and V. FELDSTEIN*
*Departments of *Radiology, †Epidemiology and Biostatistics and ‡Obstetrics and Gynecology, University of California, San Francisco, CA, USA*

In postmenopausal women without vaginal bleeding, the risk of cancer is approximately 6.7% if the endometrium is thick (> 11 mm) and 0.02% if the endometrium is thin (≤ 11 mm)

Ultrasound Obstet Gynecol 2012; 40: 621–629
Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.12306

Capacity of endometrial thickness measurement to diagnose endometrial carcinoma in asymptomatic postmenopausal women: a systematic review and meta-analysis

M. C. BREIJER*†, J. A. H. PEETERS‡, B. C. OPMEER§, T. J. CLARK¶, R. H. M. VERHEIJEN**, B. W. J. MOL* and A. TIMMERMANS*

*The results from this systematic review **do not justify the use of endometrial thickness as a screening test for endometrial carcinoma and atypical endometrial hyperplasia** in asymptomatic postmenopausal women*

SOGC CLINICAL PRACTICE GUIDELINE

Recommendations

1. Transvaginal ultrasound should not be used as screening for endometrial cancer. (II-1E)
2. Endometrial sampling in a postmenopausal woman without bleeding should not be routinely performed. (II-1E)
3. Indications for tissue sampling of the endometrium in bleeding postmenopausal women with an endometrial thickness of greater than 4 to 5 mm should not be extrapolated to asymptomatic women. (II-2E)
4. A woman who has endometrial thickening and other positive findings on ultrasound, such as increased vascularity, inhomogeneity of endometrium, particulate fluid, or thickened endometrium over 11 mm, should be referred to a gynaecologist for further investigations. (II-1A)
5. Decisions about further investigations should be made on a case-by-case basis in asymptomatic women with increased

BIOPSIA ENDOMETRIALE

The development of equipment and techniques for office-based endometrial biopsy has generally replaced the need for diagnostic dilation and curettage (D&C) performed in the operating room

- ✓ Pipelle
- ✓ Vabra
- ✓ Novak
- ✓ Citobrus

ISTEROSCOPIA DIAGNOSTICA

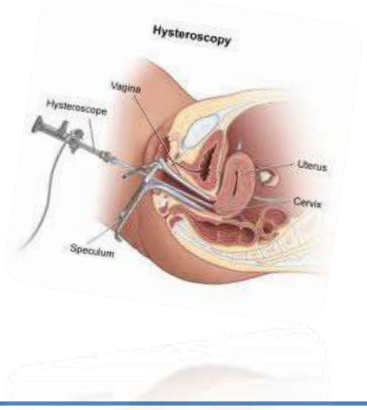
+/- biopsia endometrio

Role of hysteroscopy with endometrial biopsy to rule out endometrial cancer in postmenopausal women with abnormal uterine bleeding

Pietro Litta[a], Federica Merlin[a], Carlo Saccardi[a], Chiara Pozzan[a], Giuseppe Sacco[a], Mara Fracas[a], Giampiero Capobianco[b], Salvatore Dessole[b,*]

Maturitas 50 (2005) 117–123

Hysteroscopy provides direct visualization of the endometrial cavity, thereby allowing targeted biopsy or excision of lesions identified during the procedure.



The genetic prediction of risk for gynecologic cancers☆

Leslie M. Randall [a,*], Bhavana Pothuri [b]

Gynecologic Oncology 141 (2016) 10–16

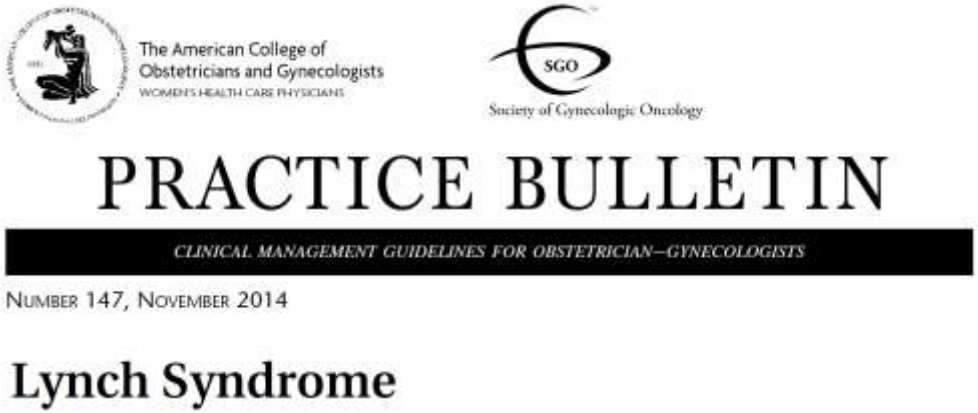
Lifetime risk of Lynch associated cancers in women based on MMR gene mutation.

	MLH1	MSH2	MSH6	PMS2
Endometrial cancer	20-54%	21-49%	16-71%	15%
Colon cancer	50-53 %	39-68%	18-30%	15%
Ovarian cancer	4–20%	7.5–24%	0–13.5%	
Upper urologic	0.4%	9%	0.7%	
Gastric	6%	2%	4%	
Small Bowel	6%	6%		
Biliary/pancreatic	4%	4%		
Brain tumors	1.7%	2.5%		

Although much attention has been shed on colon cancer since it is more common, it is reported that **women with HNPCC have a lifetime risk of up 71% of developing endometrial cancer**. This risk may equal or exceed a woman's risk of developing colon cancer which is 25-50%. In addition, **women with Lynch syndrome have a lifetime risk of developing ovarian cancer of 4-24%.**

The incidence of Lynch syndrome in patients presenting with endometrial cancer is approximately 2.3%, However, in younger patients the incidence is much greater: *in women less than 50 years of age, 5-9% of women with endometrial cancer, had a mismatch repair gene mutation.*

LYNCH SYNDROME


The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS
SGO
Society of Gynecologic Oncology

PRACTICE BULLETIN

CLINICAL MANAGEMENT GUIDELINES FOR OBSTETRICIAN–GYNECOLOGISTS

NUMBER 147, NOVEMBER 2014

Lynch Syndrome

The estimated **endometrial cancer** risk **by age 40 years** in women with Lynch syndrome is approximately *2–4%*, and the estimated **ovarian cancer** risk is *approximately 1–2%*;
by age 50 years, this risk increases to *8–17% and 3–7%, respectively*

LYNCH SYNDROME

REVIEW

Hereditary gynaecological malignancies: advances in screening and treatment

Ann K Folkins & Teri A Longacre

Histopathology 2013, 62, 2–30.

Box 2. Screening and Surveillance Recommendations for Women With Lynch Syndrome

- Colonoscopy every 1–2 years, beginning at age 20–25 years, or 2–5 years before the earliest cancer diagnosis in the family, whichever is earlier
- Endometrial biopsy every 1–2 years, beginning at age 30–35 years
- Keeping a menstrual calendar and evaluating abnormal uterine bleeding

Prophylactic hysterectomy and bilateral salpingo- oophorectomy is a risk-reducing option for *women with Lynch syndrome who have completed childbearing*.

…the incidence of **endometrial cancer** was significantly reduced by hysterectomy **(33% to 0%)** after a mean follow-up time of 7 years. Similarly, after an 11-year mean follow-up, the risk of **ovarian cancer** after bilateral salpingo-oophorectomy was **0% compared with 5.5% in the control group**

TUMORI EREDITARI DEL COLON RETTO E DELL'ENDOMETRIO
PERCORSO OPERATIVO CLINICO-DIAGNOSTICO PER L'IDENTIFICAZIONE, DIAGNOSI, SORVEGLIANZA E PREVENZIONE DEI SOGGETTI AD ALTO RISCHIO

SORVEGLIANZA E PROFILASSI GINECOLOGICA IN DONNE CON SINDROME DI LYNCH

La letteratura internazionale riguardo la sorveglianza endometriale ed ovarica nelle donne con sindrome di Lynch è concorde nel ritenere la sola ecografia pelvica transvaginale non efficace nella prevenzione e diagnosi precoce dell'adenocarcinoma endometriale e del carcinoma ovarico.
Tutte le maggiori linee guida delle società internazionali concordano con l'utilità di eseguire una biopsia endometriale annuale a partire dai 30-35 anni di età.
Per questi motivi si consiglia l'esecuzione di una **ecografia pelvica transvaginale + isteroscopia diagnostica e biopsia endometriale annuali a partire dai 30-35 anni**.
Il rischio stimato di adenocarcinoma endometriale a 40 anni è del 2-4% ed il rischio stimato di carcinoma ovarico è di circa 1-2%. All'età di 50 anni il rischio stimato di adenocarcinoma endometriale aumenta a 8-17% e quello di carcinoma ovarico raggiunge il 3-7%.
Perciò si ritiene utile eseguire un **counselling relativo alla possibilità di sottoporsi ad isterectomia e annessiectomia bilaterale profilattiche (preferibilmente laparoscopiche) tra i 45 ed i 50 anni. L'età di 50 anni appare più adeguata bilanciando il rischio oncologico con quello della menopausa precoce**.

COWDEN SYNDROME

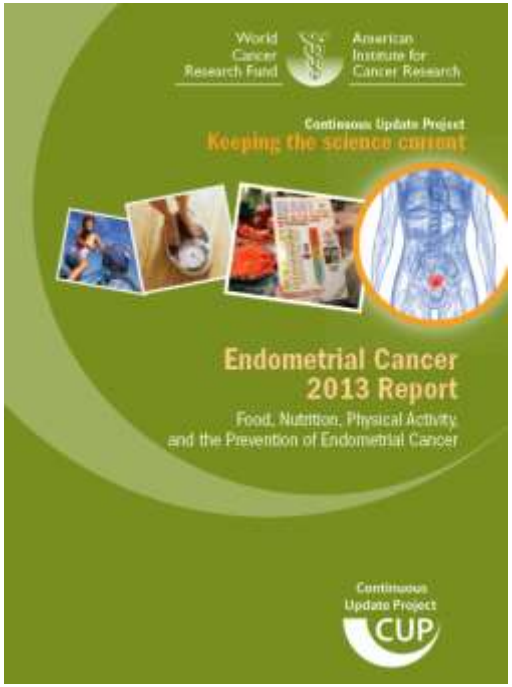
is characterized by a mutation in the PTEN tumour-suppressor gene, which leads to uncontrolled cell division and the formation of hamartomatous neoplasms and certain cancers (breast, thyroid), **representing an increased lifetime risk of endometrial carcinomas of 13–19 %**

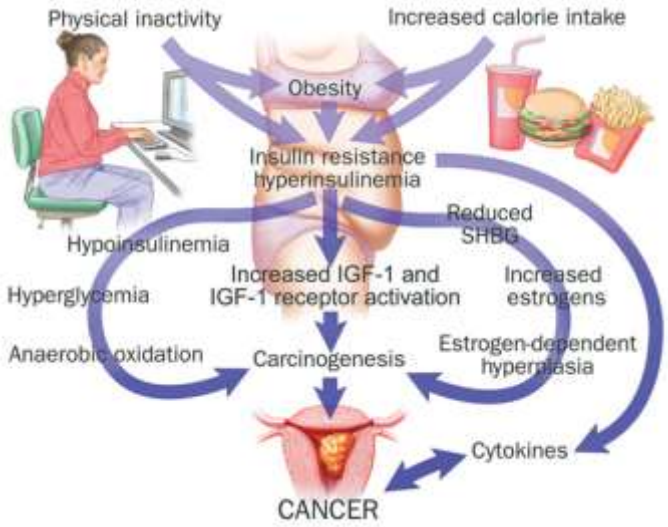
Do hereditary syndrome-related gynecologic cancers have any specific features?

Nelson Neto [1] · Teresa Margarida Cunha [2]

Insights Imaging (2015) 6:545–552

Although still not validated, **the adoption of the screening guidelines for LS**, including annual endometrial biopsies beginning at age 30 to 35 has already proposed





The **Continuous Update Project** Panel judged that there was convincing evidence that ***body fatness (reflected by BMI, measures of abdominal girth and adult weight gain) increases the risk of endometrial cancer***. Glycaemic load is probably a cause of endometrial cancer, and *physical activity and coffee both probably protect against this cancer*.

Using the new findings from the Continuous Update Project show that **about 31% of cases of endometrial cancer can be prevented by being physically active and maintaining a healthy weight**.

Stay Healthy

Alimentazione

Attività fisica

Chirurgia profilattica

Screening

Sorveglianza

Contraccettivi combinati

Management of Genetic Syndromes Predisposing to Gynecologic Cancers

Susan Miesfeldt, MD[1,2,3,*]
Amanda Lamb, ScM[1]
Christine Duarte, PhD[2]

Current Treatment Options in Oncology (2013) 14:34–50

There is incomplete information on the impact of diet and other lifestyle factors on cancer penetrance among those with or at risk for hereditary gynecologic cancers. However, *the widely recognized benefits of a healthy diet that is rich in fruits and vegetables, optimum weight control, regular physical activity, and avoidance of known carcinogens, such as cigarettes, are considered important for quality of life and longevity*. Therefore, **it is recommended that HBOC and LS-affected women be advised of the potential benefits of dietary and lifestyle modifications as they relate to overall health and potentially to cancer risk**.


"The best interest
of the patient
is the only interest
to be considered"
William J. Mayo, MD
The Needs of the patient come first
MAYO CLINIC


not all
That's Folks!