



Γυναικολογικά νεοπλάσματα

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Κατ' επιλογήν μάθημα Παθολογικής Ογκολογίας 2025

Αθήνα, 19/5/2025

Cancer statistics, 2025



Estimated New Cases

Breast	316,950	32%
Lung & bronchus	115,970	12%
Colon & rectum	71,810	7%
Uterine corpus	69,120	7%
Melanoma of the skin	44,410	4%
Non-Hodgkin lymphoma	35,210	4%
Pancreas	32,490	3%
Thyroid	31,350	3%
Kidney & renal pelvis	28,570	3%
Leukemia	28,170	3%
All sites	988,660	

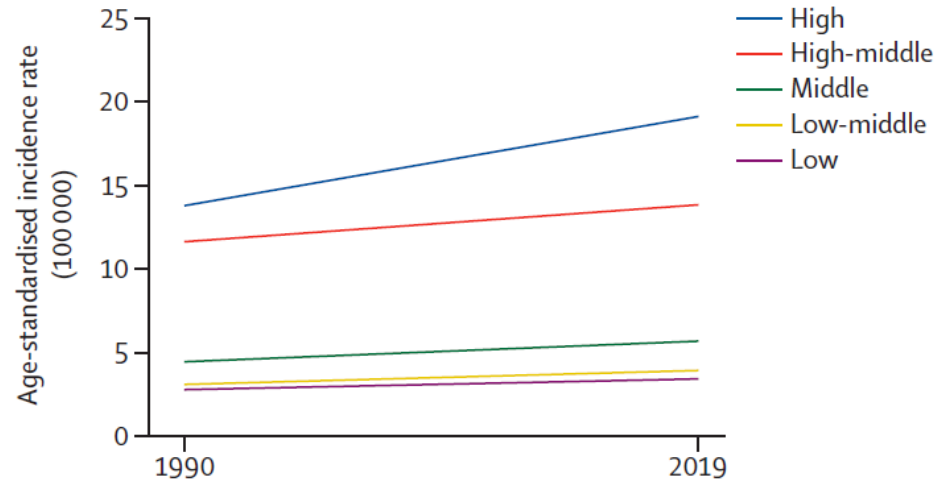
Estimated Deaths

Lung & bronchus	60,540	21%
Breast	42,170	14%
Pancreas	24,930	8%
Colon & rectum	24,000	8%
Uterine corpus	13,860	5%
Ovary	12,730	4%
Liver & intrahepatic bile duct	10,840	4%
Leukemia	10,040	3%
Non-Hodgkin lymphoma	8,330	3%
Brain & other nervous system	8,160	3%
All sites	294,220	

1. Endometrial cancer (EC)

Epidemiology

- The most common gynaecological cancer in high income countries
 - US: 66,200 new cases and 13,030 deaths (2023)
- Its **incidence is increasing annually**, by an estimated 1-2%



- **5-10%** of EC cases are **hereditary**
- The risk of recurrence steadily increases from 5% in StI to 27% in StIII
- For those patients staged **III/IV** → **5y OS: 17%**

Associated risk factors for EC

Characteristic	No. of times risk increased
Obesity	
30-49 lb	3.0
>50 lb	10.0
Nulliparity	2.0
Late menopause	2.4
“Bloody” menopause	4.0
Diabetes mellitus	2.8
Unopposed estrogen	4.0 – 8.0
Complex atypical hyperplasia	29.0
DO NOT forget OLDER AGE !	

Clinical presentation of EC

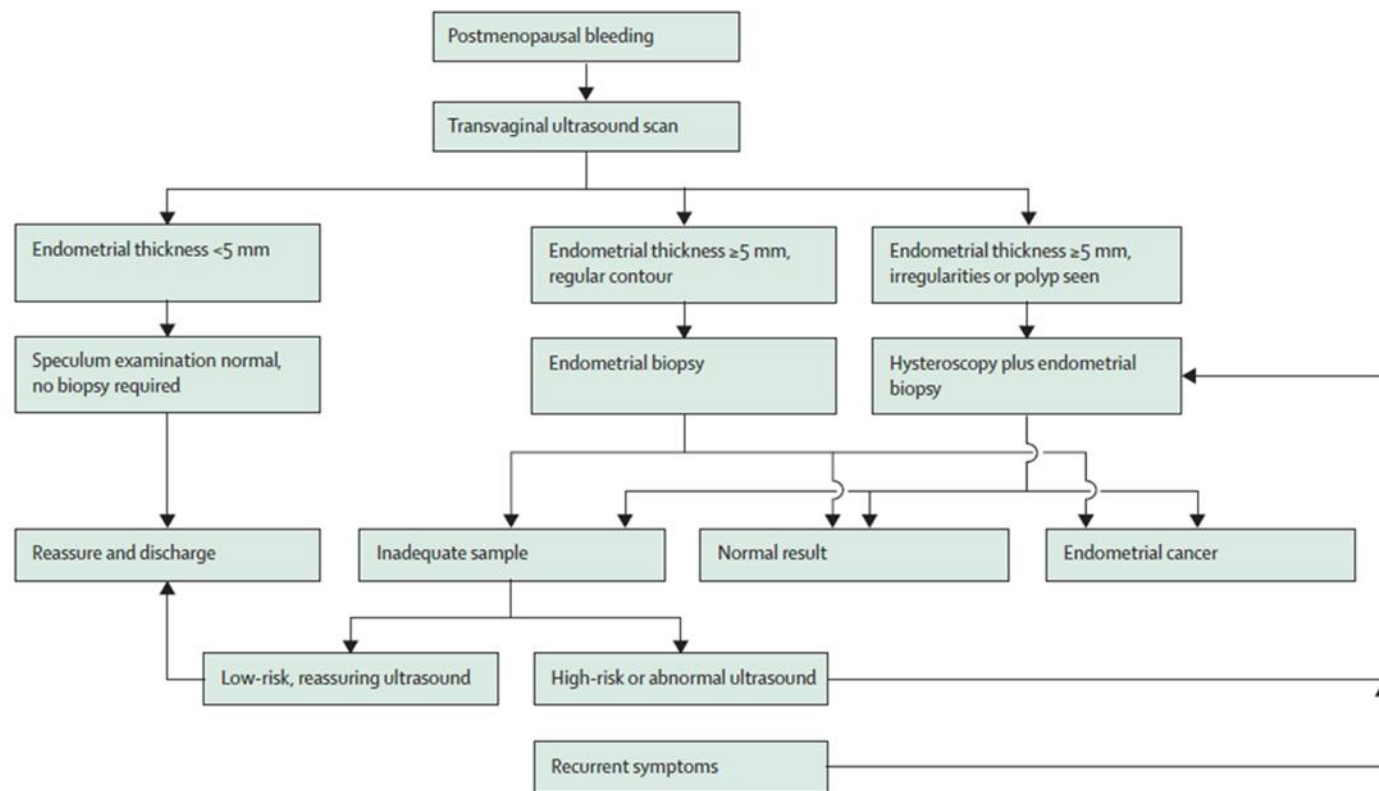


The probability of EC as a cause of postmenopausal bleeding

- <1% in female <50y
- 3% in female aged 55y
- **24% in female >80y**

Diagnosis of EC

Routine investigation of postmenopausal bleeding*

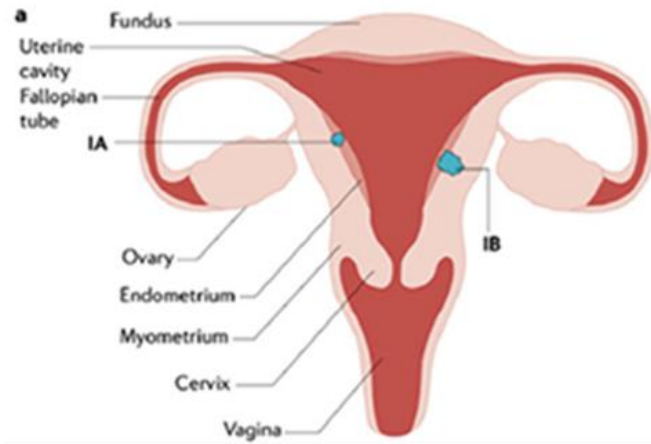


* Decision to **investigate young women** with vaginal bleeding must be guided by **risk factors**:

- family history
- obesity
- polycystic ovary syndrome (PCOS)

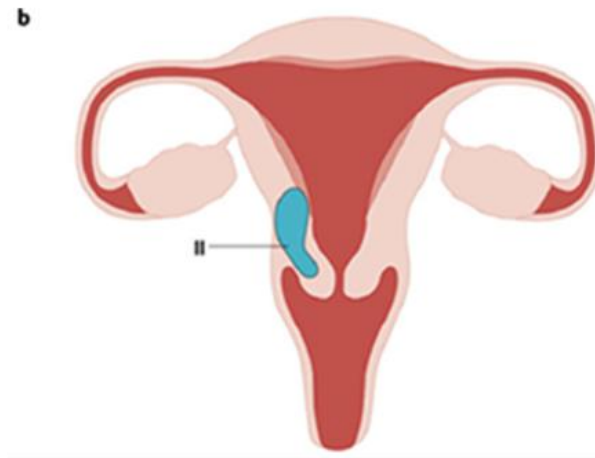
- Histological examination of endometrial tissue sample in those with **thickened (>5mm) endometrium**
- Preoperative assesment includes: **pelvic MRI, chest/abdomen CT**

FIGO Staging of EC

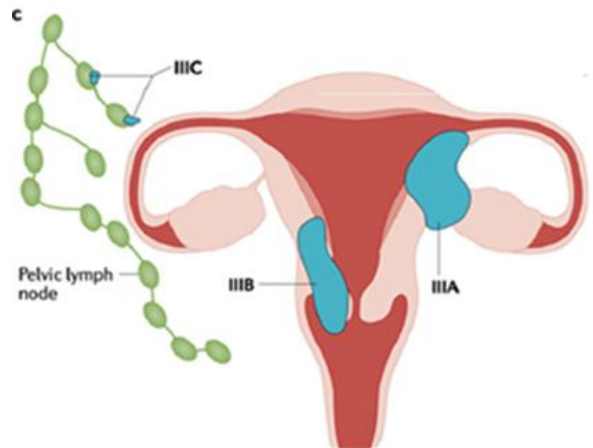


Stage I: tumor confined to the corpus uteri

- IA: <50% myometrial invasion
- IB: ≥50% myometrial invasion

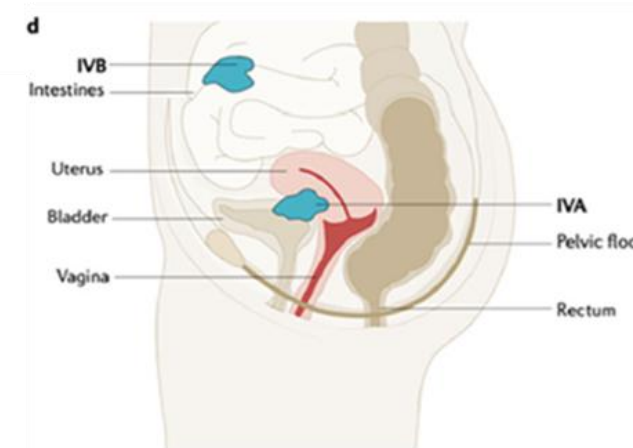


Stage II: tumor invades cervical stroma, but does not extend beyond the uterus



Stage III: local and/or regional spread of the tumor

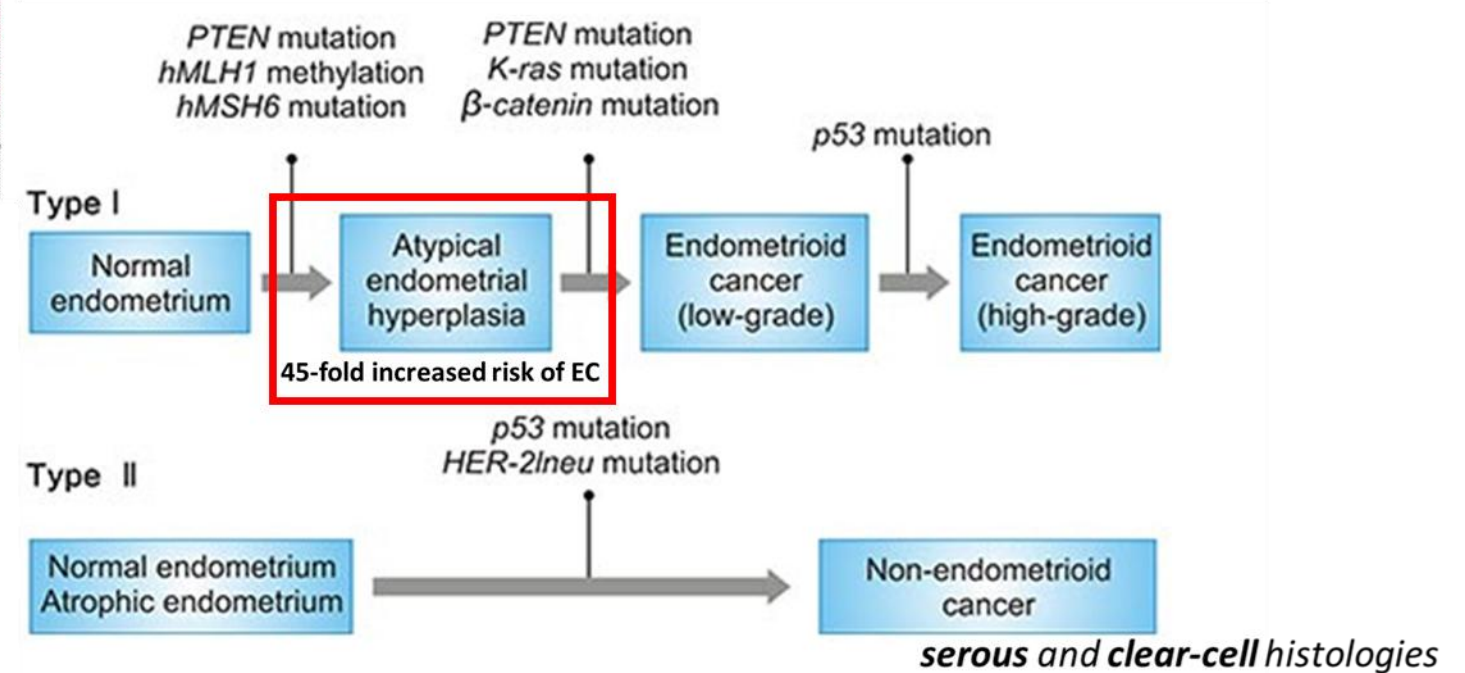
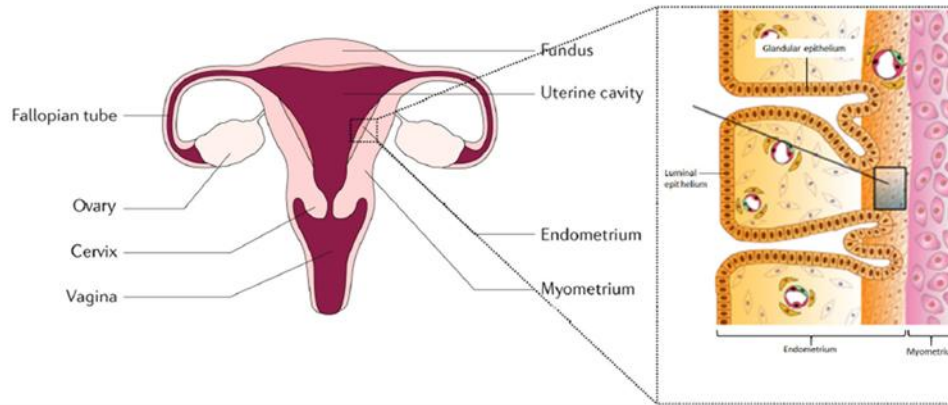
- IIIA: tumor invades the serosa of the corpus uteri *and/or* adnexae
- IIIB: vaginal *and/or* perimetrial involvement
- IIIC1: positive pelvic lymph nodes
- IIIC2: positive para-aortic lymph nodes with *or* without positive pelvic lymph nodes



Stage IV: tumor invades bladder and/or bowel mucosa, and/or distant metastases

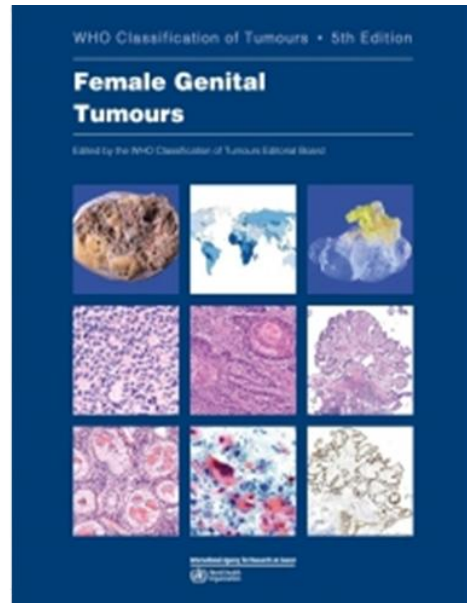
- IVA: bladder and/or bowel mucosa invasion
- IVB: distant metastases, including inguinal lymph nodes

Gene mutations in the carcinogenesis of EC

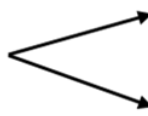


Histological classification of EC

WHO, Female Genital Tumors, 2020

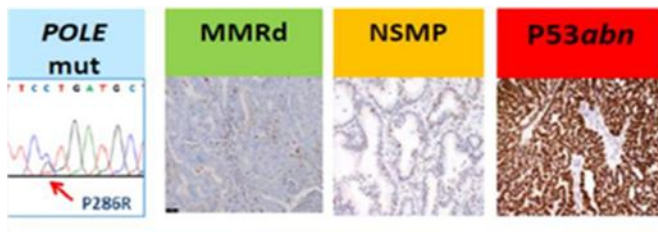
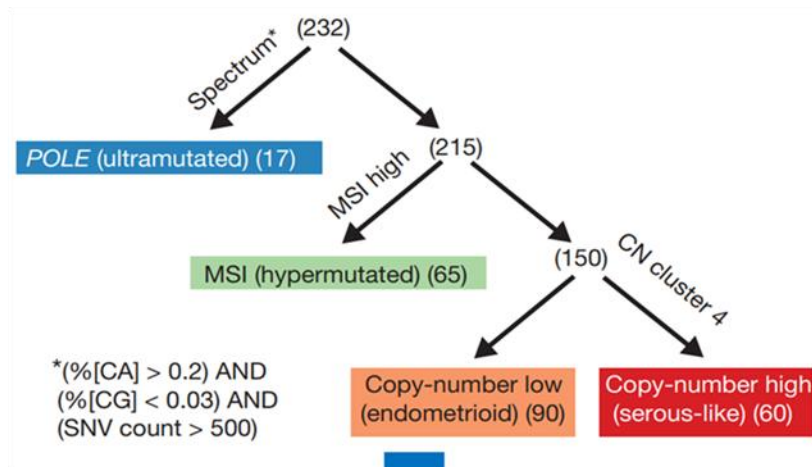


- Endometrioid carcinoma
- Serous carcinoma
- Clear cell carcinoma
- Undifferentiated – Dedifferentiated carcinoma
- Mixed carcinoma
- Other
- Carcinosarcoma
- Neuroendocrine carcinoma

Challenges 
→ **heterogeneity** of some histotypes **regarding prognosis**
→ **poor interobserver reproducibility**, particularly among the high-grade ECs

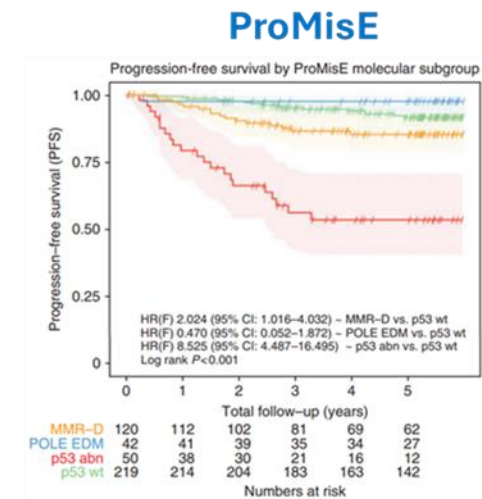
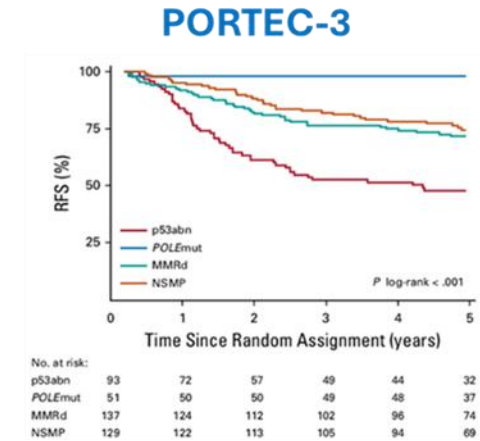
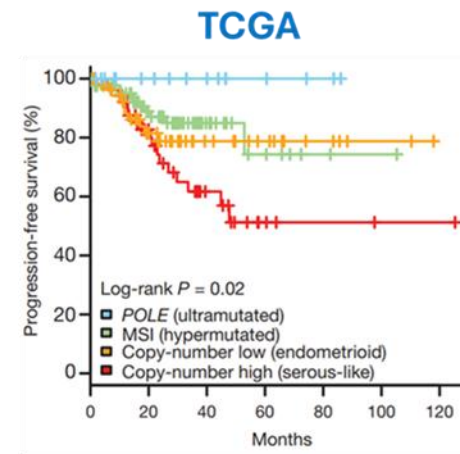
The tipping point

EC molecular biology into the clinic



Best prognosis

Worst prognosis



Kommos S, et al. Ann Oncol. 2018;29(5):1180-1188
 León-Castillo A, et al. J Clin Oncol. 2020 Oct 10;38(29):3388-3397
 Cancer Genome Atlas Research Network. Nature. 2013;497(7447):67-73

Molecular classification of EC

Incorporated into the FIGO staging



Molecular classification is **encouraged in ALL endometrial carcinomas**, especially high-grade tumours [IV, B].



Molecular classification **should be carried out for ALL EC pathology specimens** regardless of histological type [IV, A].

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SPECIAL ARTICLE



FIGO staging of endometrial cancer: 2023

Jonathan S. Berek¹ | Xavier Matias-Guiu² | Carien Creutzberg³ | Christina Fotopoulou⁴ | David Gaffney⁵ | Sean Kehoe⁶ | Kristina Lindemann⁷ | David Mutch⁸ | Nicole Concin^{9,10} | Endometrial Cancer Staging Subcommittee, FIGO Women's Cancer Committee

Stage designation	Molecular findings in patients with early endometrial cancer (Stages I and II after surgical staging)
Stage IA _m ^{POLEmut}	POLEmut endometrial carcinoma, confined to the uterine corpus or with cervical extension, regardless of the degree of LVSI or histological type
Stage IIC _m ^{p53abn}	p53abn endometrial carcinoma confined to the uterine corpus with any myometrial invasion, with or without cervical invasion, and regardless of the degree of LVSI or histological type

Concin N, et al. Int J Gynecol Cancer. 2021;31(1):12-3

Oaknin A, et al. Ann Oncol. 2022;33(9):860-877

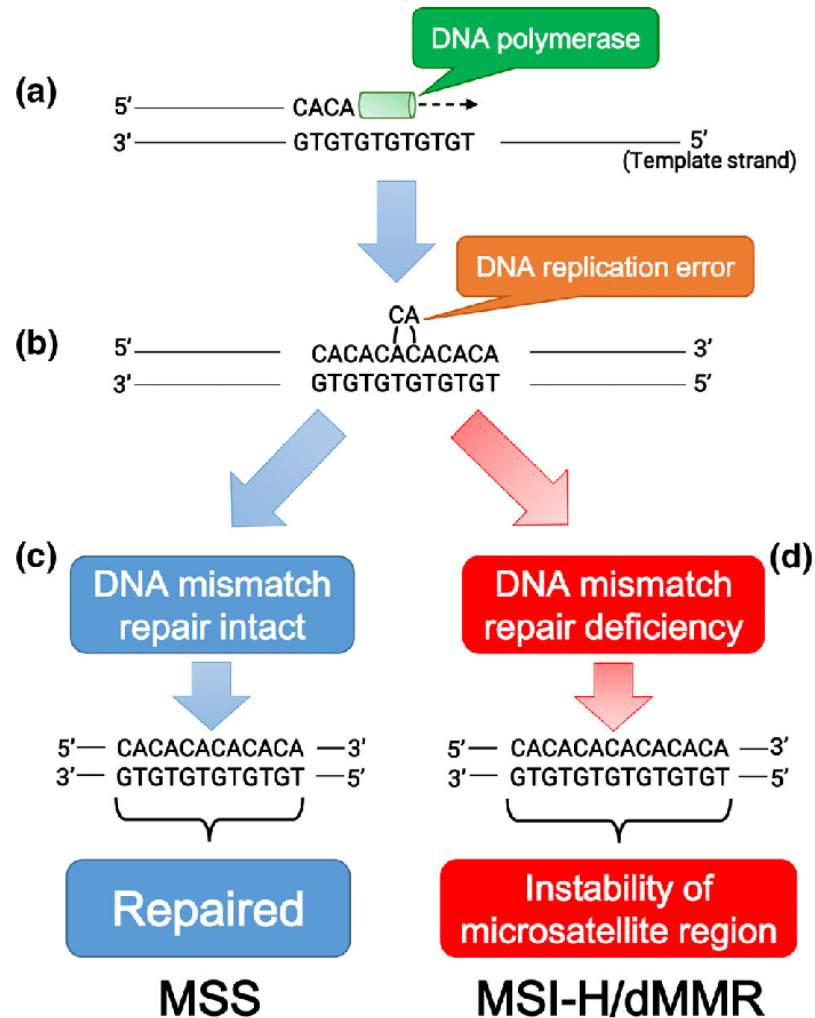
Berek JS, et al. Int J Gynaecol Obstet. 2023;162(2):383-394

Basic principles for EC treatment

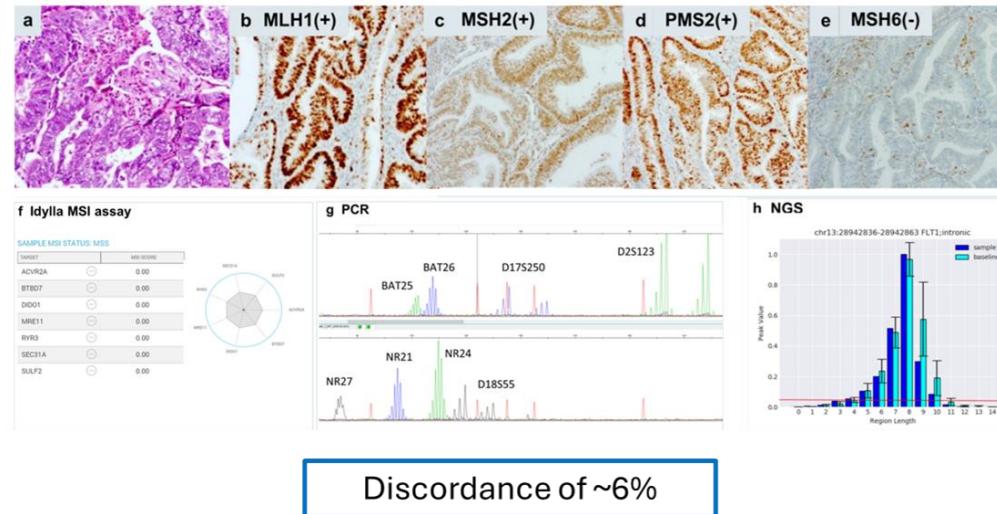
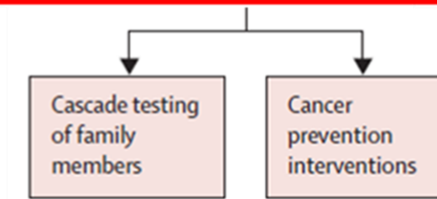
- Surgery
- Radiation therapy (external beam RT, brachytherapy)
- Systemic therapy
 - Chemotherapy
 - Immunotherapy
 - Targeted therapies (multi-targeted TKIs, hormone therapy, PARP inhibitors etc.)

NO screening tools are available for EC

Mismatch repair (MMR)/Microsatellite instability (MSI) status



- Lynch syndrome (inherited dMMR) accounts for 2-5% of all cases



2. Ovarian cancer (OC)

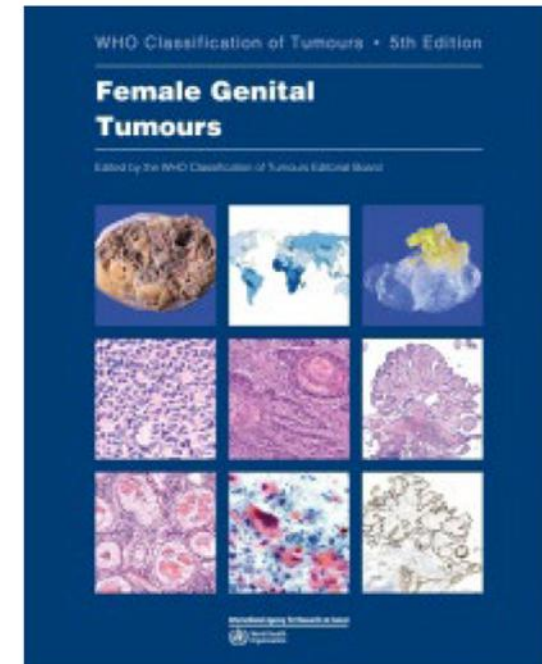
Epidemiology

- The most lethal gynecological cancer in high income countries
 - 313,000 new cases and 208,000 deaths (2020)
- Its **incidence is slowly decreasing** (since 2000s)
- >70% of patients present with late-stage (III-IV) OC
- 5-year survival rates
 - Stage I: 93% → Stage IV: **30%**

Histological classification of OC

WHO, Female Genital Tumors, 2020

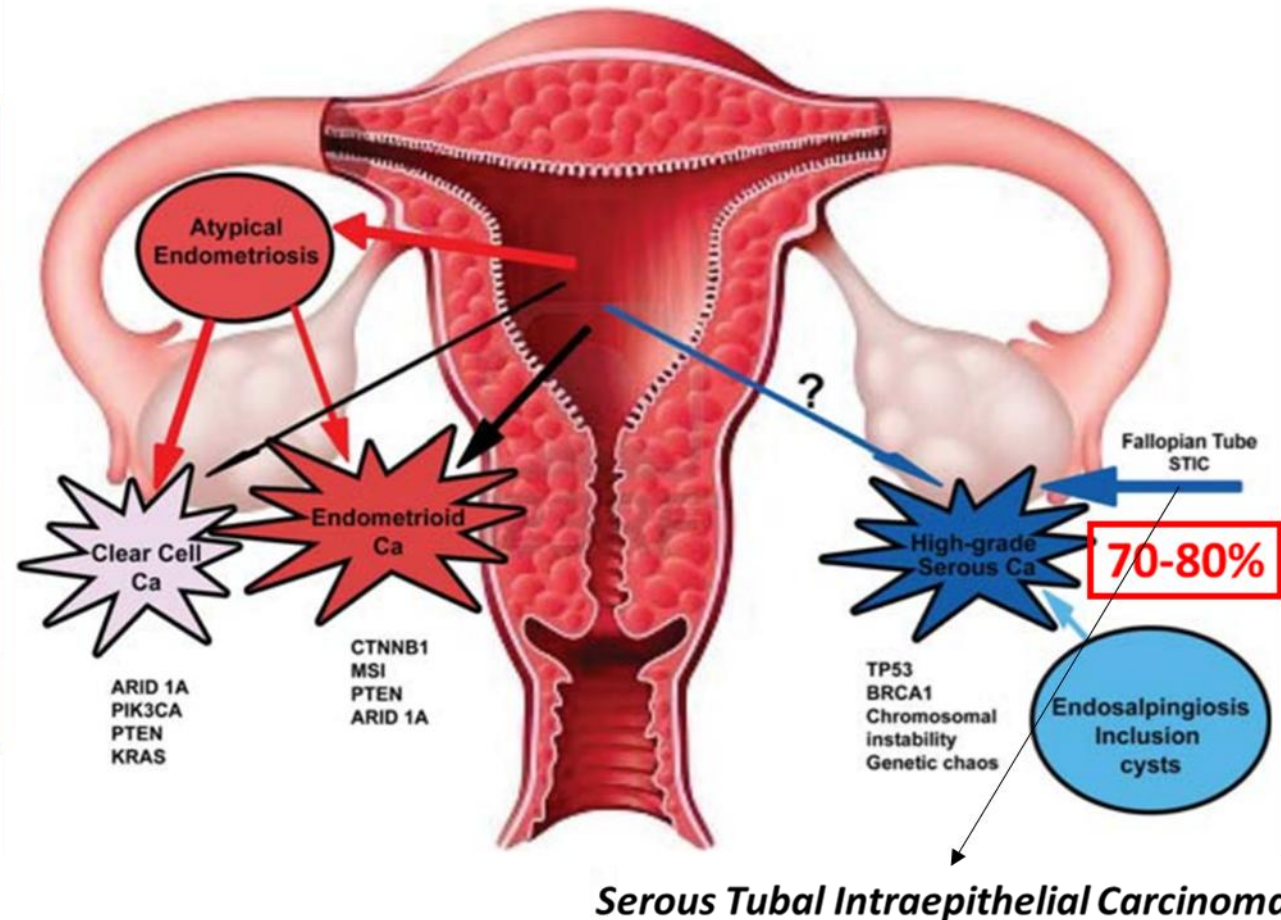
		All tumors	Malignant tumors
1.	Epithelial	55%	80%
2.	Sex-cord stromal	8%	
3.	Germ cell	30%	2%
4.	Mesenchymal (leiomyoma, hemangioma)		
5.	Mixed epithelial/mesenchymal (adenosarcoma)		very uncommon
6.	Miscellaneous (FATWO, small cell carcinoma hypercalcemic type)		
7.	Metastases	6-10%	



Classification of epithelial ovarian tumors: Degree of **proliferation** ± **stromal invasion**

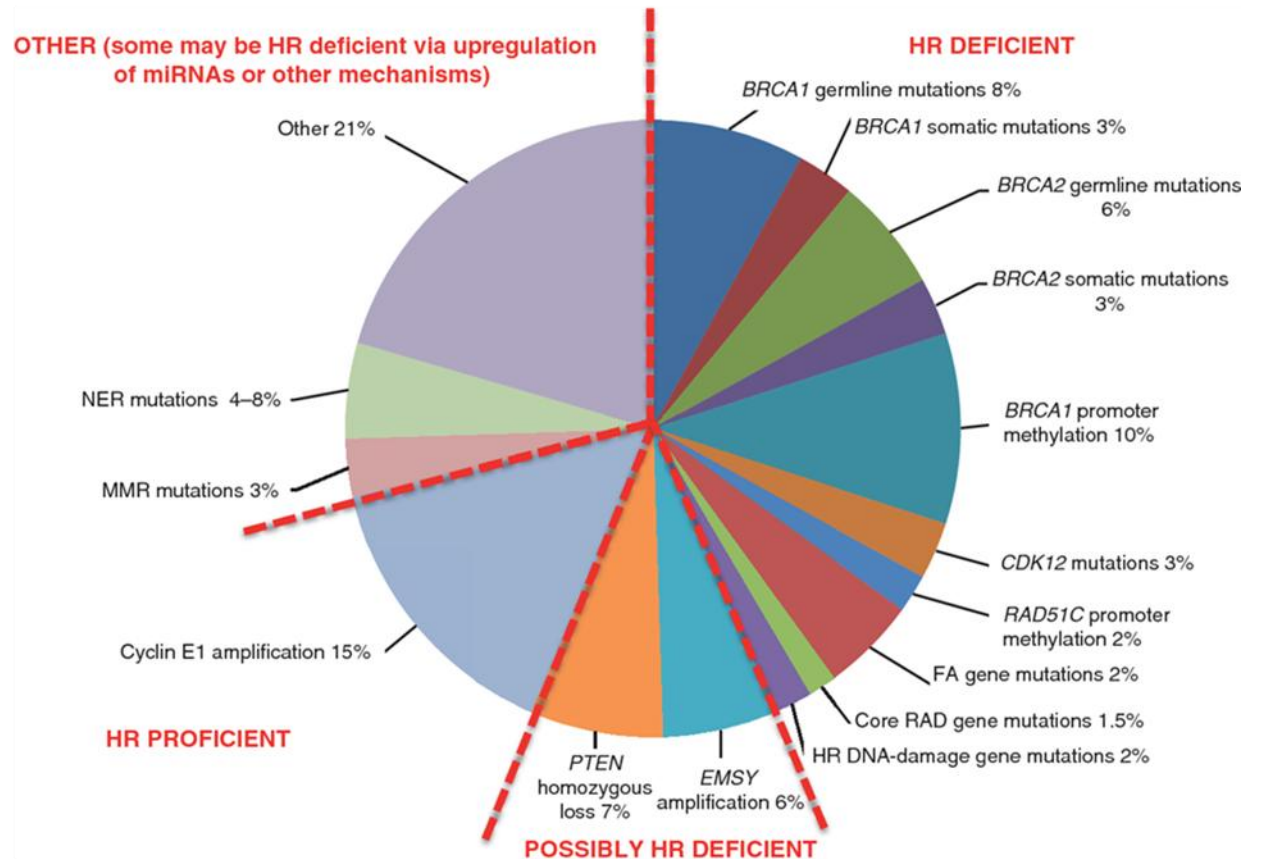
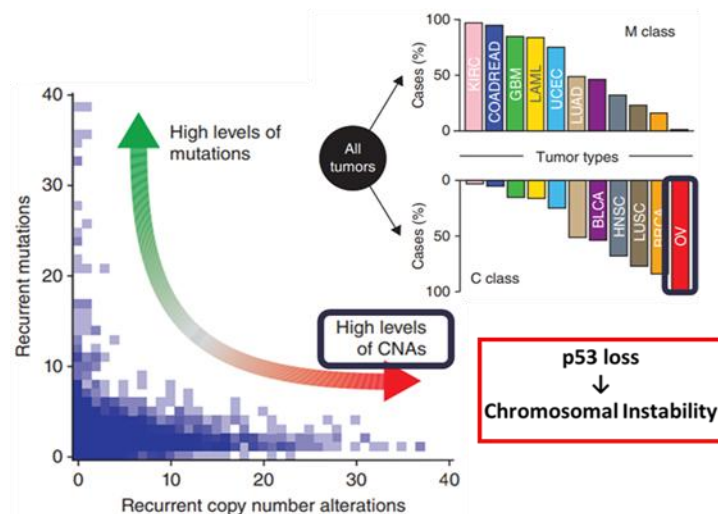
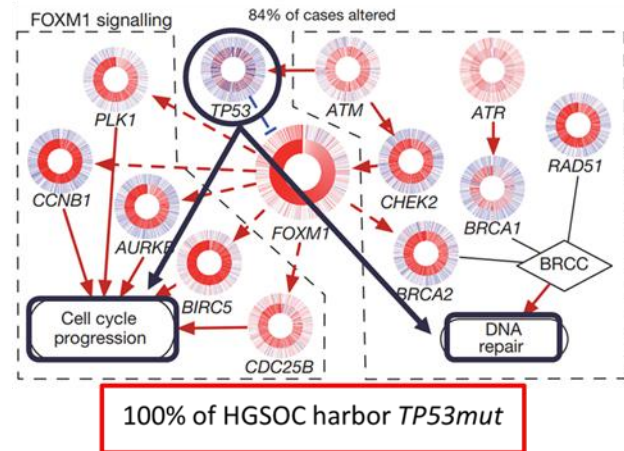
High-grade serous ovarian cancer (HGSOC) is the most common

	Serous	Endometrioid	Mucinous	carcinosarcoma
PAX8	+++	+92%	+40%	+ epi - sarcoma
CK7	+++	+++	+++	+ epi - sarcoma
CK20	-	-	+focal	-
ER/PR	+	+	-	-
WT1	+	- + 4%	-	+ epi serous - sarcoma
NapsinA	-	- +5%	- +3%	+ epi clear c -sarcoma
P53	Abnl (mt) HG NI (wt) LG	NI (wt) +/-Abnl HG	NI (wt) Abnl(mt)	Abnl (mt) epi and sarc

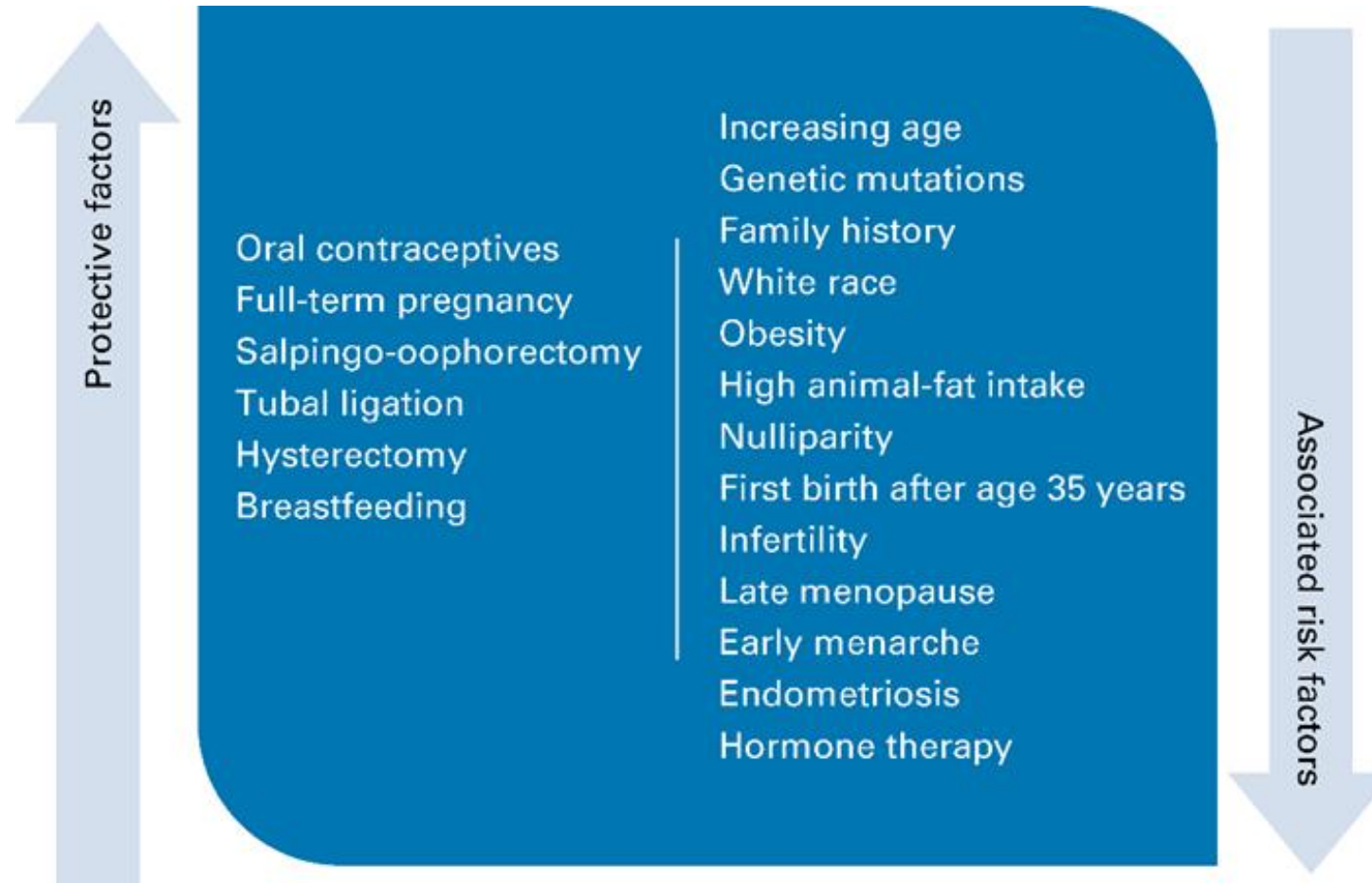


HGSOC

A disease of DNA repair and Copy Number Alterations



Protective and associated risk factor for OC



- Carriers of a g*BRCA1/2* pathogenic variant have a high lifetime risk of HGSOC

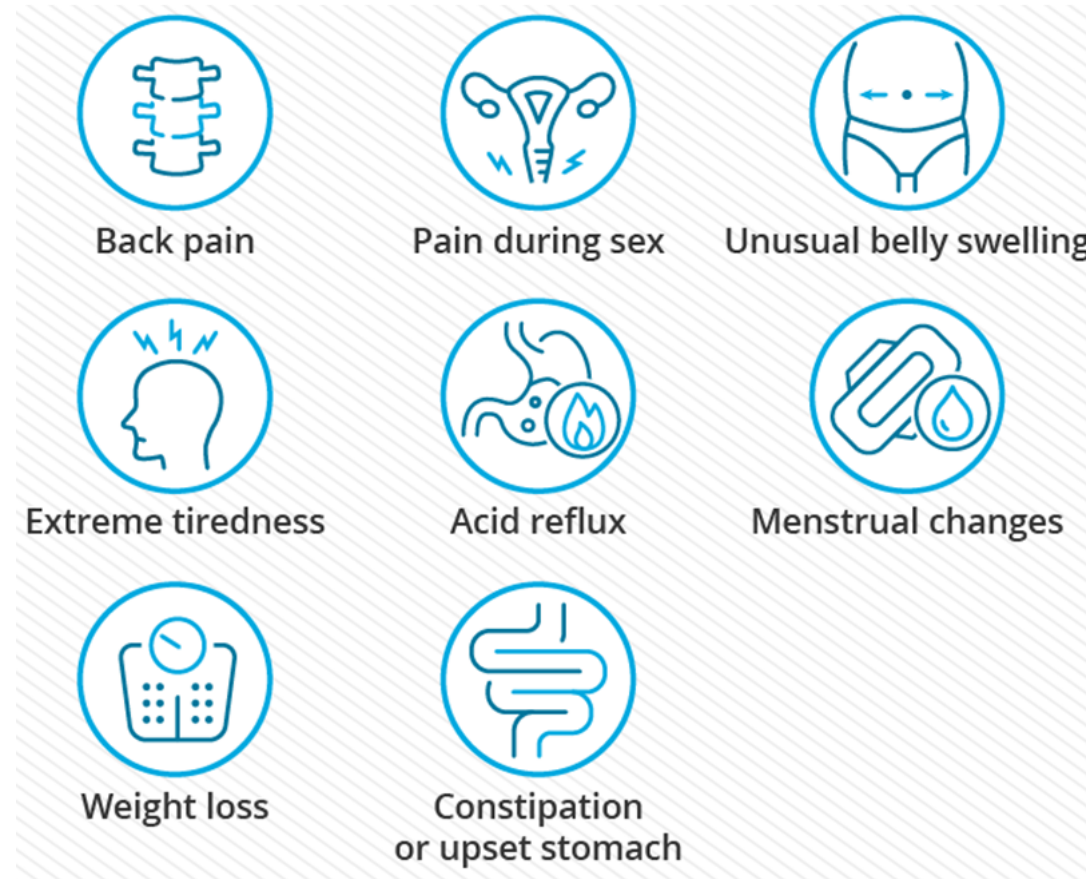
- *BRCA1* PV: **44%**
 - *BRCA2* PV: **17%**
- } Vs general population: 1.3% (80 years of age)

- Risk does not start to increase above that of the general population until:

- *BRCA1* PV: **mid-30s**
 - *BRCA2* PV: **50 years of age**
- } between age 35-40 years
between age 40-45 years

*Risk-Reducing Bilateral
Salpingo-Oophorectomy
(rrBSO)*

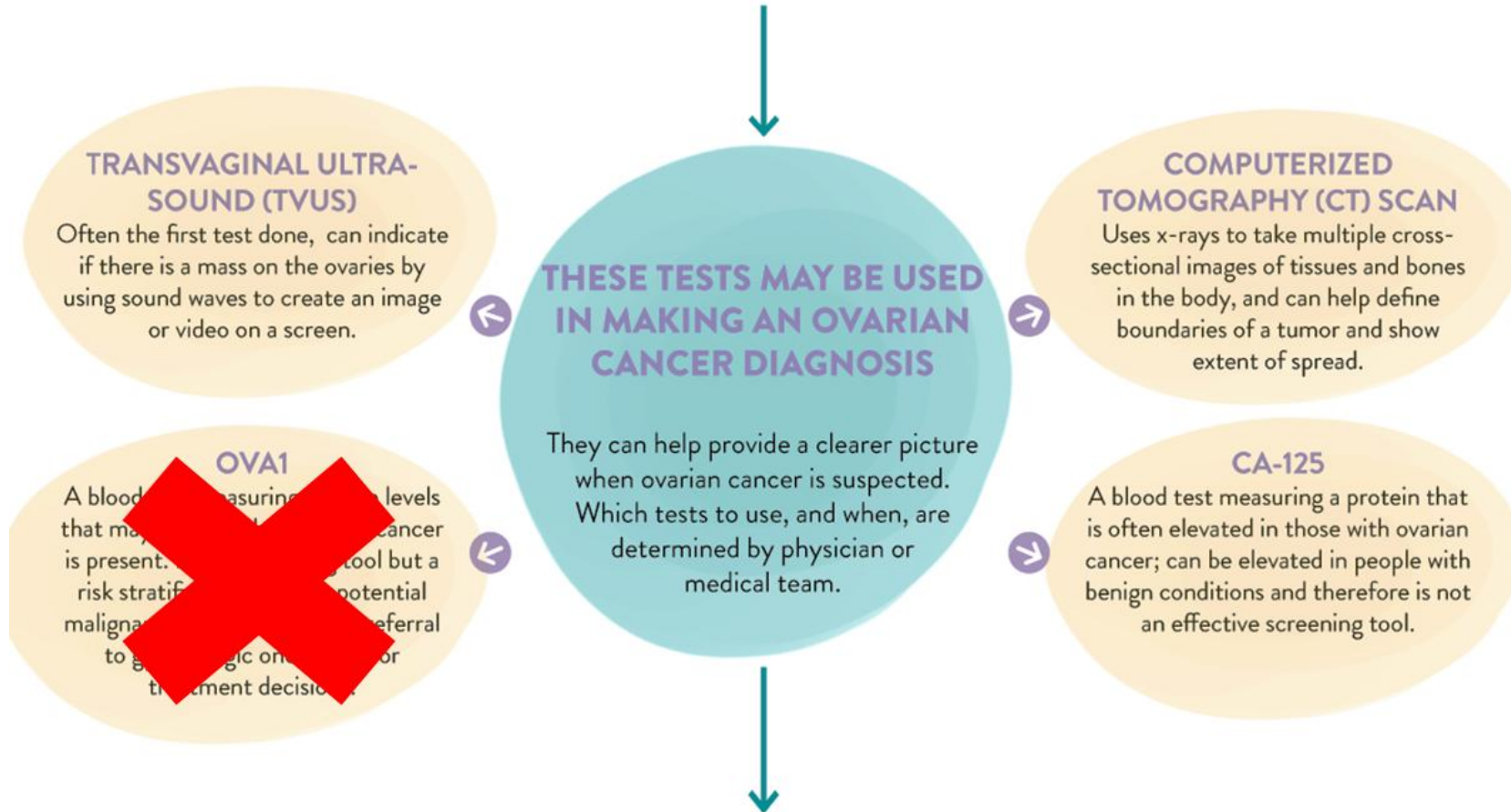
Clinical presentation of OC



NO screening tools are available!

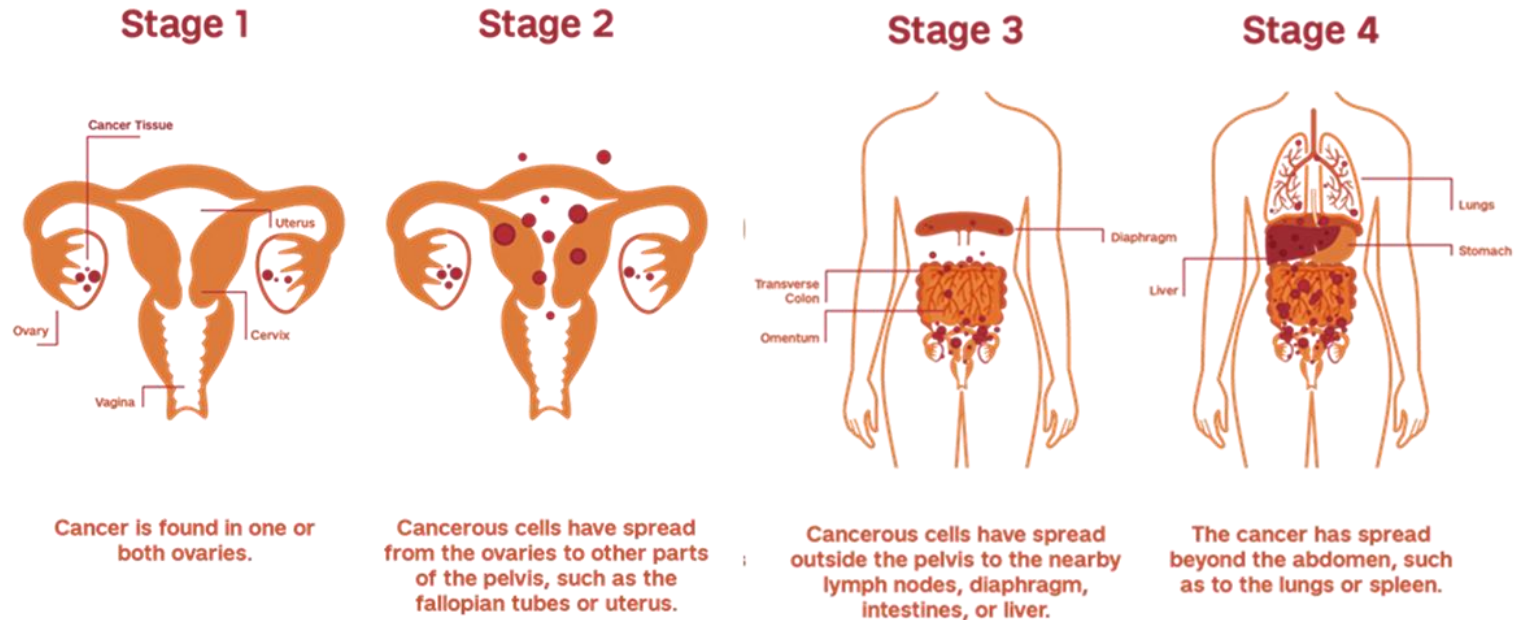
Diagnosis of OC

THERE IS NO EARLY DETECTION TEST OR SCREENING TOOL FOR OVARIAN CANCER.



SURGERY IS THE ONLY WAY TO DEFINITELY DIAGNOSE AND STAGE OVARIAN CANCER.

AJCC/FIGO Staging of OC



AJCC stages	Number of cases annually	Proportion of all cases diagnosed	Vital status at 10 years		10-year survival
			Alive (proportion of all survivors)	Dead (proportion of all deaths)	
I and II	1,716	13%	944 (35.4%)	772 (7.3%)	55%
III and IV	11,484	87%	1,723 (64.6%)	9,761 (92.7%)	15%

Basic principles for OC treatment

Early stage (IA-IC) OC

Summary of recommendations	LoE	Go R	Consensus
Laparotomy is the standard surgical approach to treat and stage patients with apparent early stage ovarian carcinoma	V	A	Yes: 100% (40 voters)
Whatever the approach used, rupture of an intact tumour with spillage of cancer cells at the time of surgery must be avoided	IV	A	Yes: 100% (40 voters)
For patients with early stage disease requiring adjuvant chemotherapy, acceptable treatment regimens are: • carboplatin alone or • carboplatin /paclitaxel	I II	A A	Yes: 100% (40 voters) Yes: 100% (40 voters)

Can advanced-stage OC be cured?

The three phases of OC treatment

- **Resectability**

- Aim to achieve a status of **no (visible) residual disease**

- **Eradication**

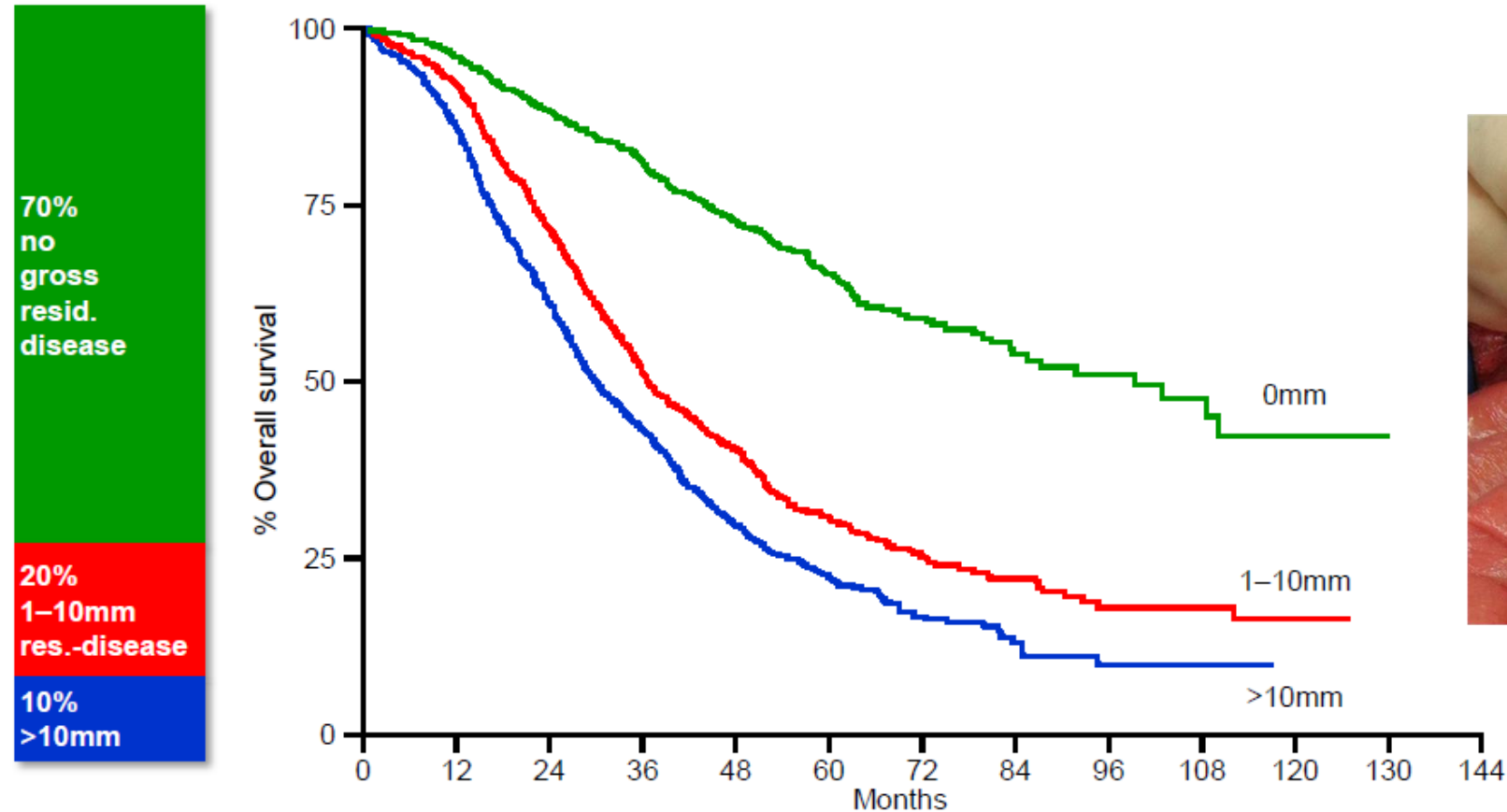
- Aim to eliminate all cancer cells present after debulking surgery with **(neo)adjuvant chemotherapy**

- **Prevention of recurrence**

- Aim to prevent or delay recurrence after surgery and chemotherapy with **maintenance therapy**

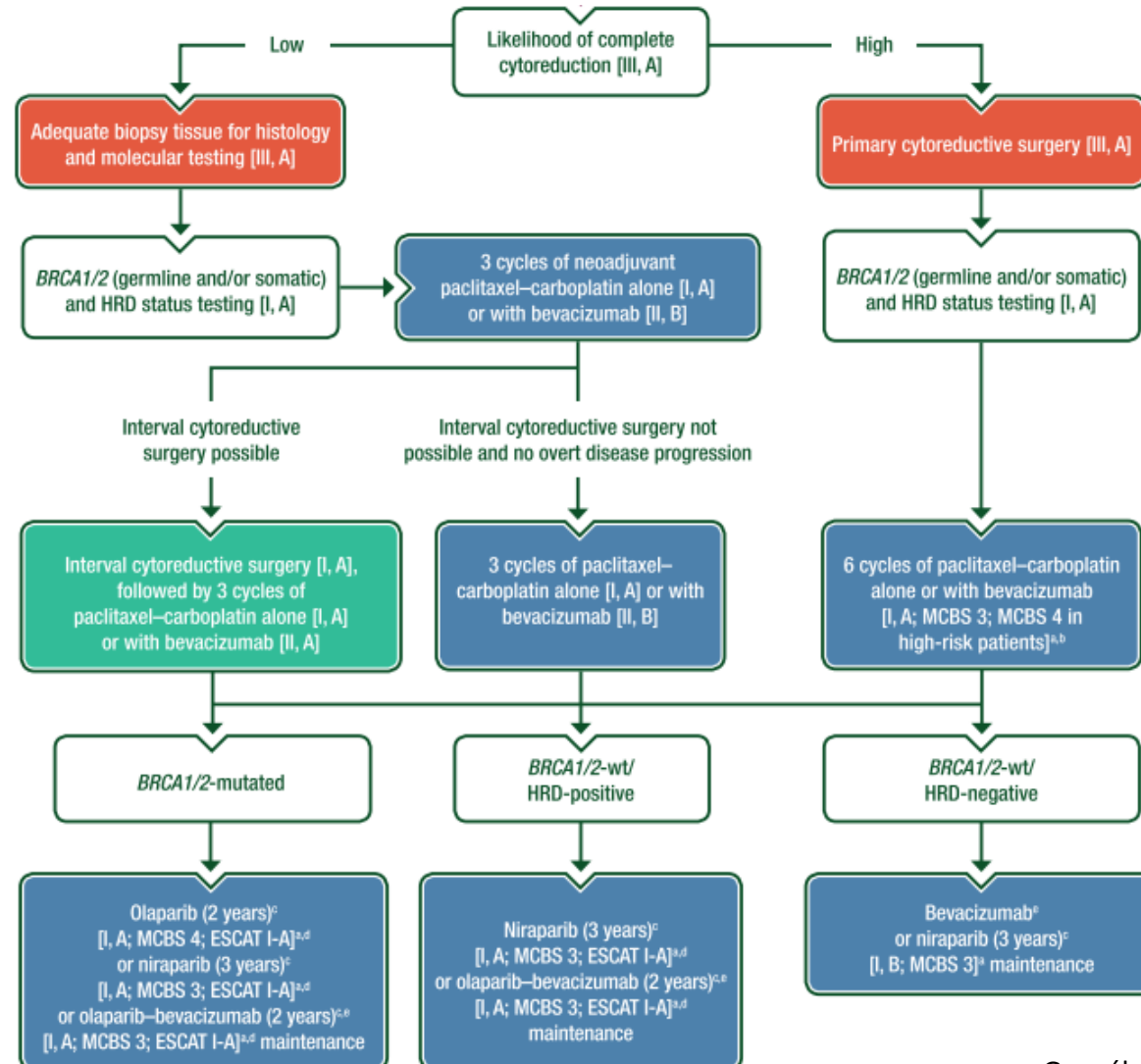
R0 cytoreduction

The most significant prognostic factor in advanced EOC



Basic principles for OC treatment

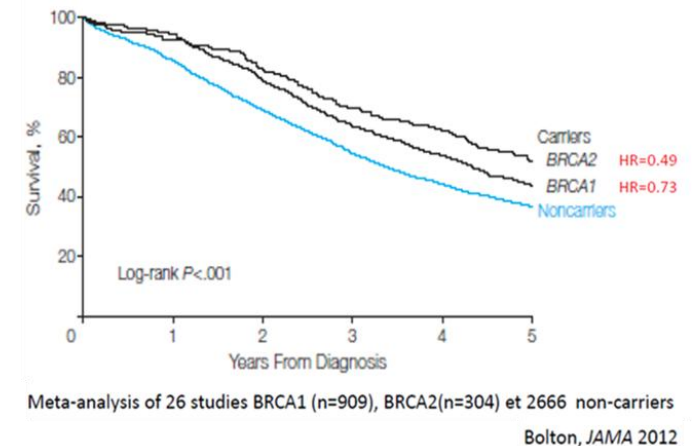
Advanced stage (II-IV) OC



Basic principles for OC treatment

Maintenance therapy in advanced stage (II-IV) OC

- **All HGSOC patients**, regardless of stage and/or age, should be referred for **genetic counseling**
 - *BRCA1/2mut* in ~**25%** of cases
 - *BRCA1/2mut* OC is associated with **better prognosis**
 - *BRCAmut* OC patients derive unprecedented **benefit from PARP inhibitors**



Konstantinopoulos PA, et al. Cancer Discov. 2015
DiSilvestro P. ESMO 2022
González-Martín A. ESMO 2019
Ray-Coquard I.L. ESMO 2022

Basic principles for OC treatment

Recurrent disease

Assessment of the following factors [I-II, A]:

- Histotype
- *BRCA1/2* status
- Number of prior lines
- Exposure and response to prior treatment
- TFIp
- Potential for surgery
- Residual toxicity
- Patient's general condition
- Patient preference

Platinum resistant disease

Platinum-free interval <6 months
(mOS <9-12 months)

Early palliative care [I, A]
Single agent (non-platinum)^c [I, B]
+ bevacizumab, if not contraindicated
or previously exposed [I, A; MCBS 4]^d
Trabectedin–PLD (if TFIp >6 months
and platinum intolerant) [II, C; MCBS 2]^d

Platinum sensitive disease

Platinum-free interval >6 months
(mOS: 24-36 months)

Platinum-based doublet^e (PLD preferred) + PARPi maintenance^{f,g},
if responsive and PARPi-naïve [I, A]
(preferred option if *BRCA1/2*-mutated)
or platinum-based doublet^e (PLD preferred) + bevacizumab^f [I, A]
(if no contraindication or previous exposure to bevacizumab)

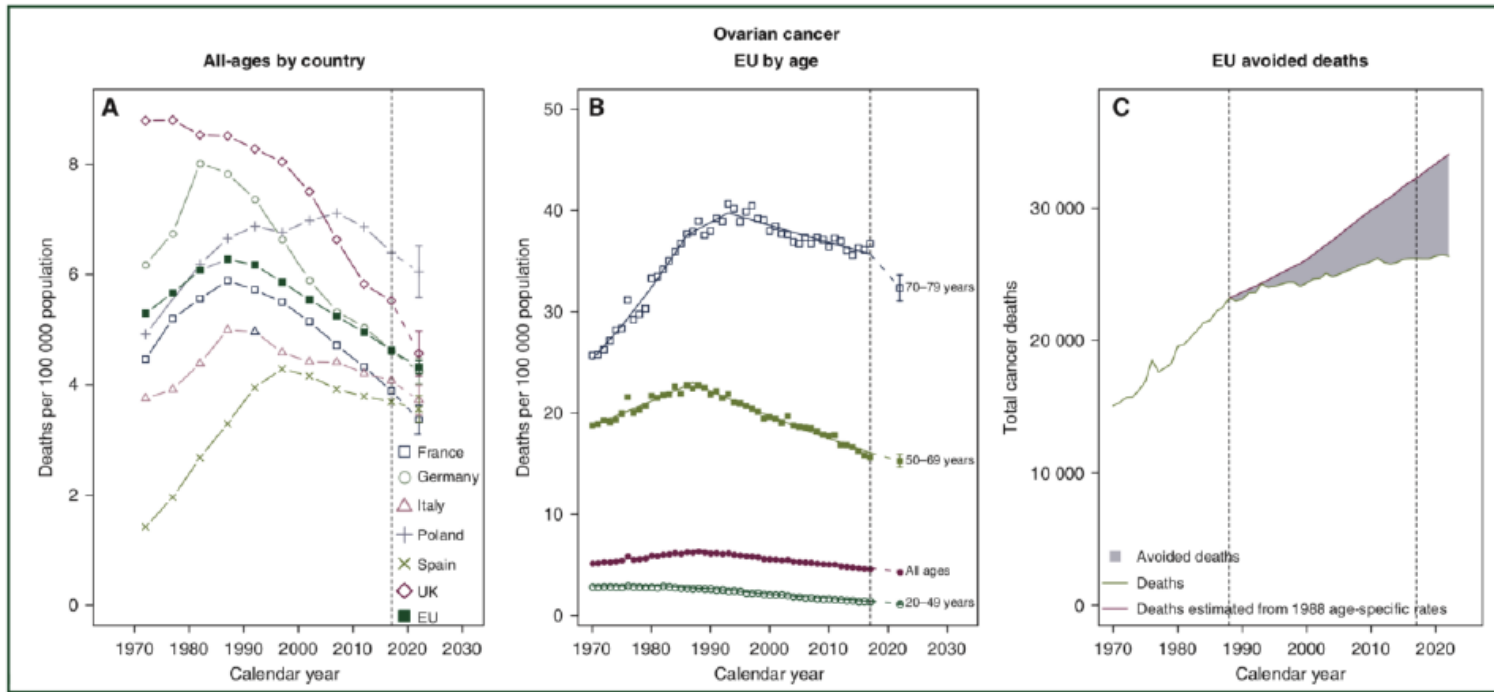
Do NOT forget the feasibility of Secondary Cytoreductive Surgery (CRS)

European cancer mortality predictions for the year 2022 with focus on ovarian cancer

M. Dalmartello¹, C. La Vecchia^{1*}, P. Bertuccio¹, P. Boffetta^{2,3}, F. Levi⁴, E. Negri^{1,3,5} & M. Malvezzi¹

111 000 cancer deaths have been avoided (during a period of 34 years).
In 2022 alone, 8000 are predicted to be avoided

Main driving factors
(by Dalmartello et al)

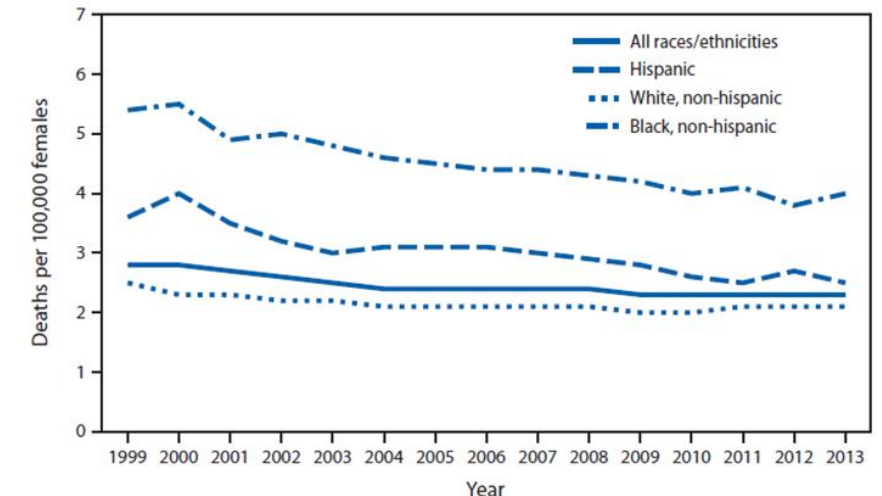


- Use of oral contraceptives
- Early diagnosis ?
- Improved surgery
- Platinum in the 80s
- Taxanes in the 90s
- ~~Gemcitabine~~
- ~~Intraperitoneal CT~~
- Possibly bevacizumab ?
- Prophylactic BSO in BRCAmut carriers
- PARPi

3. Cervical cancer (CC)

Epidemiology

- The 4th most common malignancy in female, worldwide
 - 604,000 new cases and 342,000 deaths (2020)
- Its **incidence is decreasing** (>25% since the early 1990s)
 - Global HPV vaccine uptake
- 5-year survival rates
 - Stage I: 92% → Stage IV: **18%**

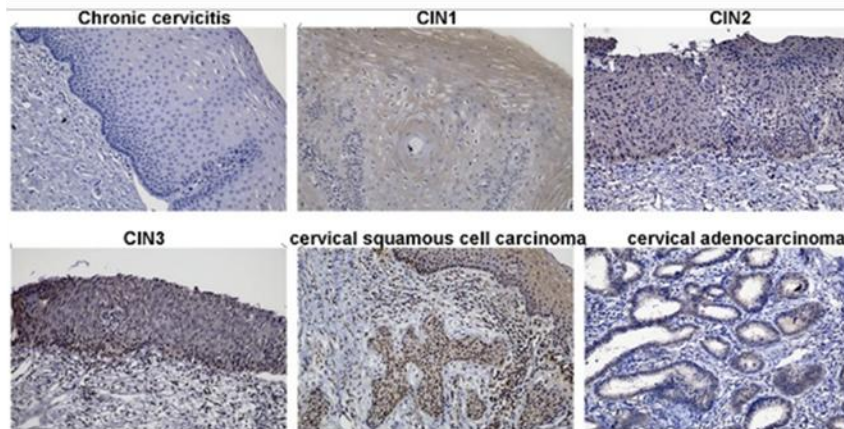


Pathogenesis of CC

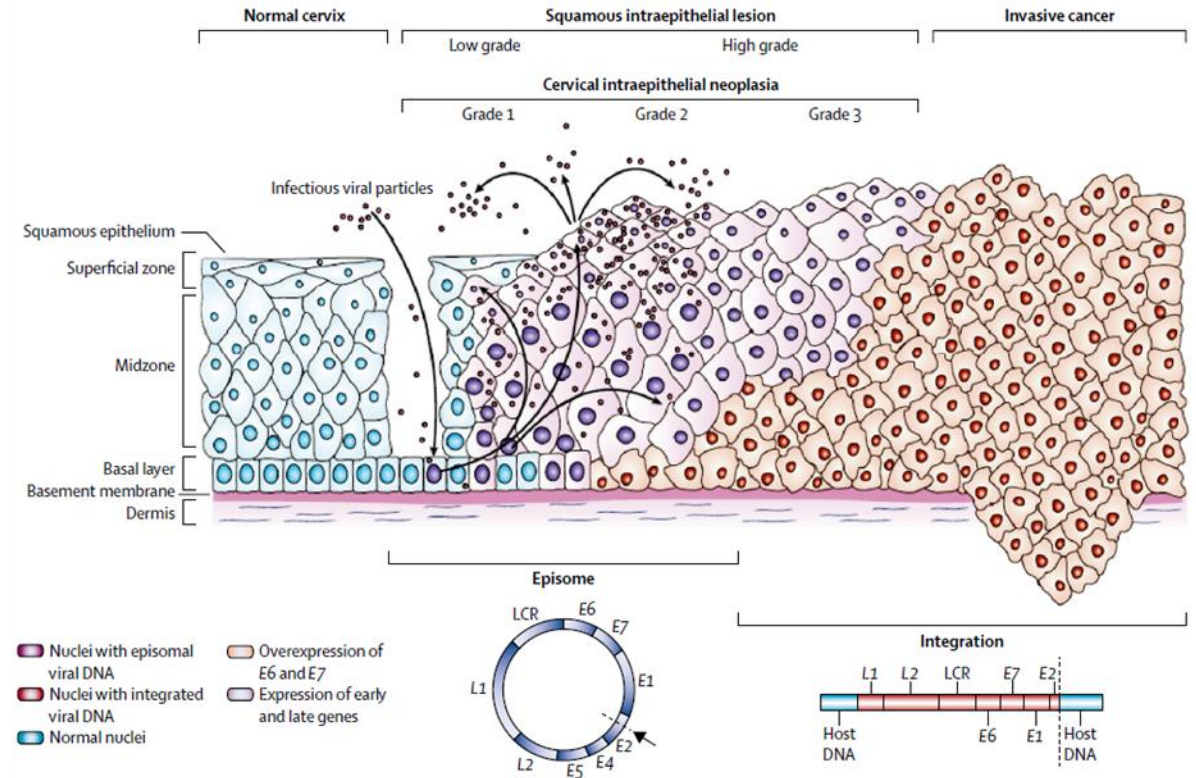
Chronic HPV infection causes almost all cases

- Risk factors include:
 - early age of sexual debut
 - multiple sexual partners
 - history of sexually-transmitted infection
 - tobacco smoke

p16-immunostaining pattern



IHC stains of the HPV16 E7 protein in cervical lesions



Clinical presentation of CC



Vaginal bleeding between periods or after menopause



Menstrual bleeding that is longer than usual



Bleeding after intercourse



Pain during sexual intercourse



Persistent pelvic and/or back pain



Pain during urination



Needing to urinate more often



Vaginal discharge that may be heavy and have a foul odor

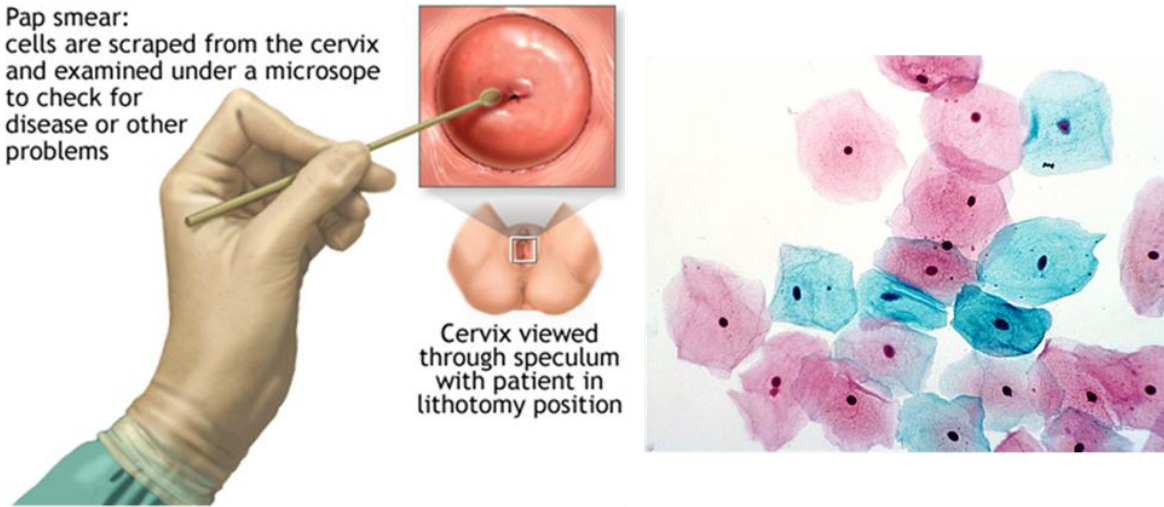


Weight loss

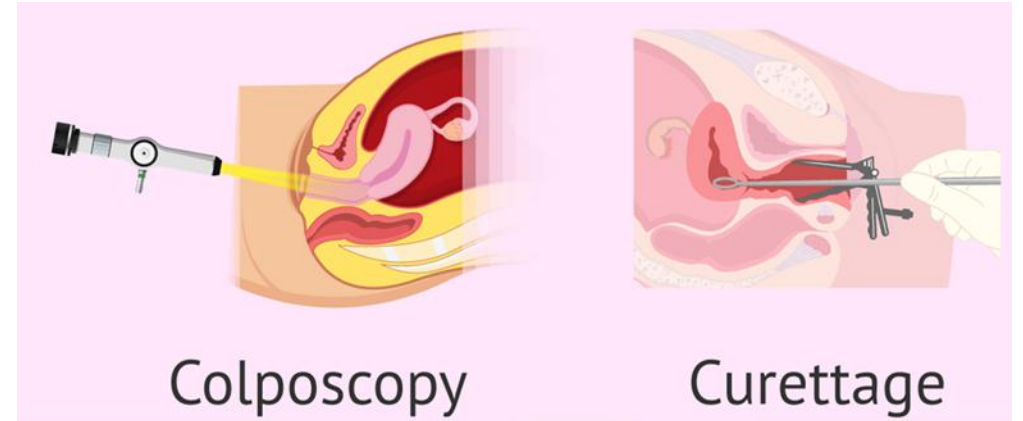
- In its early stages, CC is often **asymptomatic**
- The trial of lower limb oedema, flank pain, and sciatica suggest pelvic sidewall invasion

Diagnosis of CC

Pap smear:
cells are scraped from the cervix
and examined under a microscope
to check for
disease or other
problems

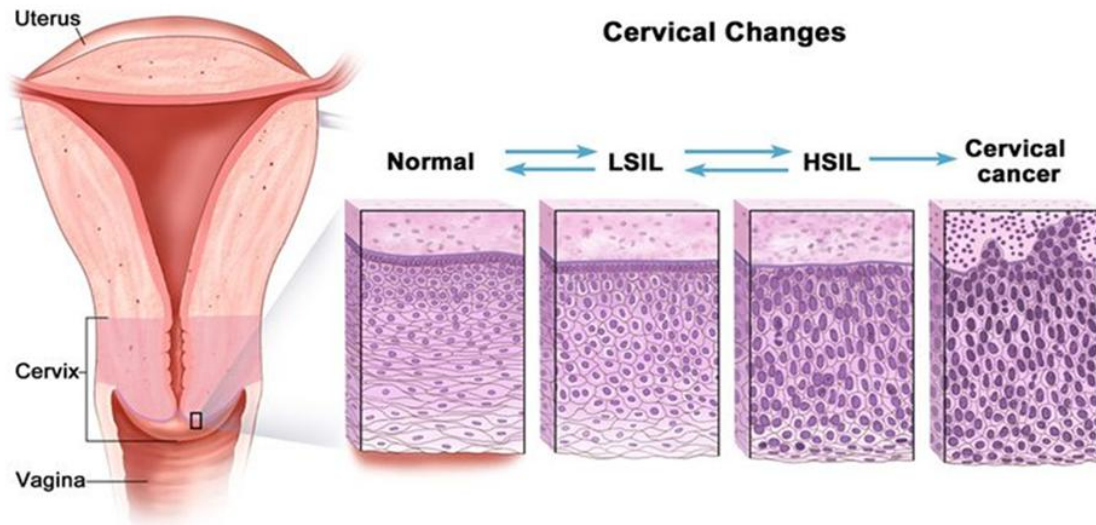


Cervix viewed
through speculum
with patient in
lithotomy position



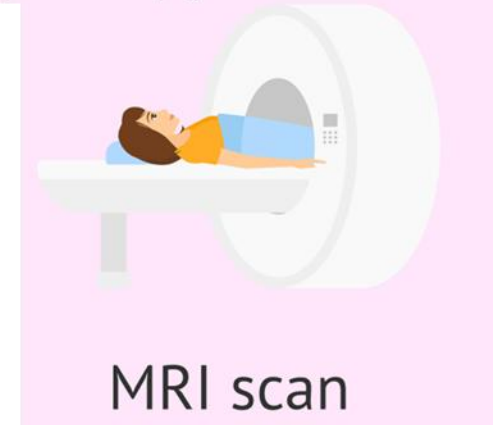
Colposcopy

Curettage



Cervical Changes

Normal ↔ LSIL ↔ HSIL → Cervical cancer



MRI scan

Who should be screened?!

- Women **aged 21-29** should receive **PAP smear screening every 3 years**, with the choice to continue until 65

OR

- Women **aged 30-65** should receive combination **high-risk HPV testing plus PAP smear every 5 years**



Who should NOT be screened?!

- Women **under 21 years**
- Women **older than 65** who have had **three consecutive negative cytology results** *or* **two consecutive negative HPV tests**

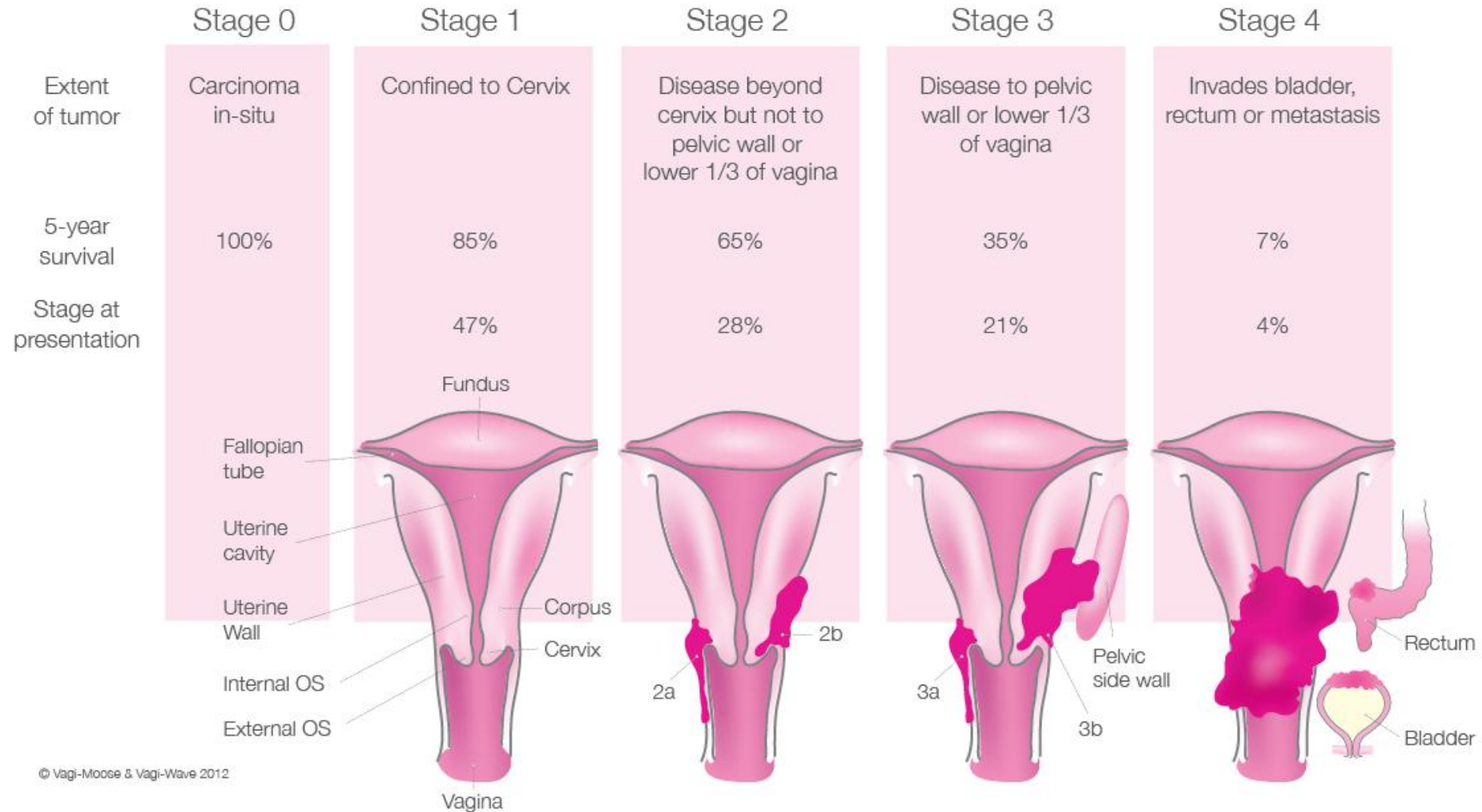


Has your teen had both doses
of the HPV vaccine?

Δ. Η γνωμοδότηση της Εθνικής Επιτροπής Εμβολιασμών

Με βάση τη διεθνή βιβλιογραφία και συνεκτιμώντας τα παραπάνω δεδομένα, η γνωμοδότηση της Εθνικής Επιτροπής Εμβολιασμών περιλαμβάνει τις ακόλουθες αλλαγές στο εμβολιαστικό σχήμα έναντι του HPV: (α) σύσταση για γενικό εμβολιασμό αγοριών και κοριτσιών, (β) το ενδεικνυόμενο διάστημα εμβολιασμού και για τα δύο φύλα είναι η ηλικία 9 έως 11 ετών, (γ) σε περίπτωση που ο εμβολιασμός και για τα δύο φύλα δεν πραγματοποιηθεί στη συνιστώμενη ηλικία, μπορεί να γίνει αναπλήρωση (catch-up) του εμβολιασμού, (δ) επισημαίνεται ότι το εμβόλιο HPV θα αποζημιώνεται πλήρως σε αγόρια και κορίτσια ηλικίας 15-18 ετών μέχρι 31.12.2023, και (ε) ο περιορισμός στην αποζημίωση μετά τις 31.12.2023 δεν αφορά τις ομάδες αυξημένου κινδύνου.

FIGO Staging of CC



Basic principles for CC treatment

