

Prevention of Gynecologic Malignancies

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Gynecologic cancers in the United States 2023

Endometrial cancer

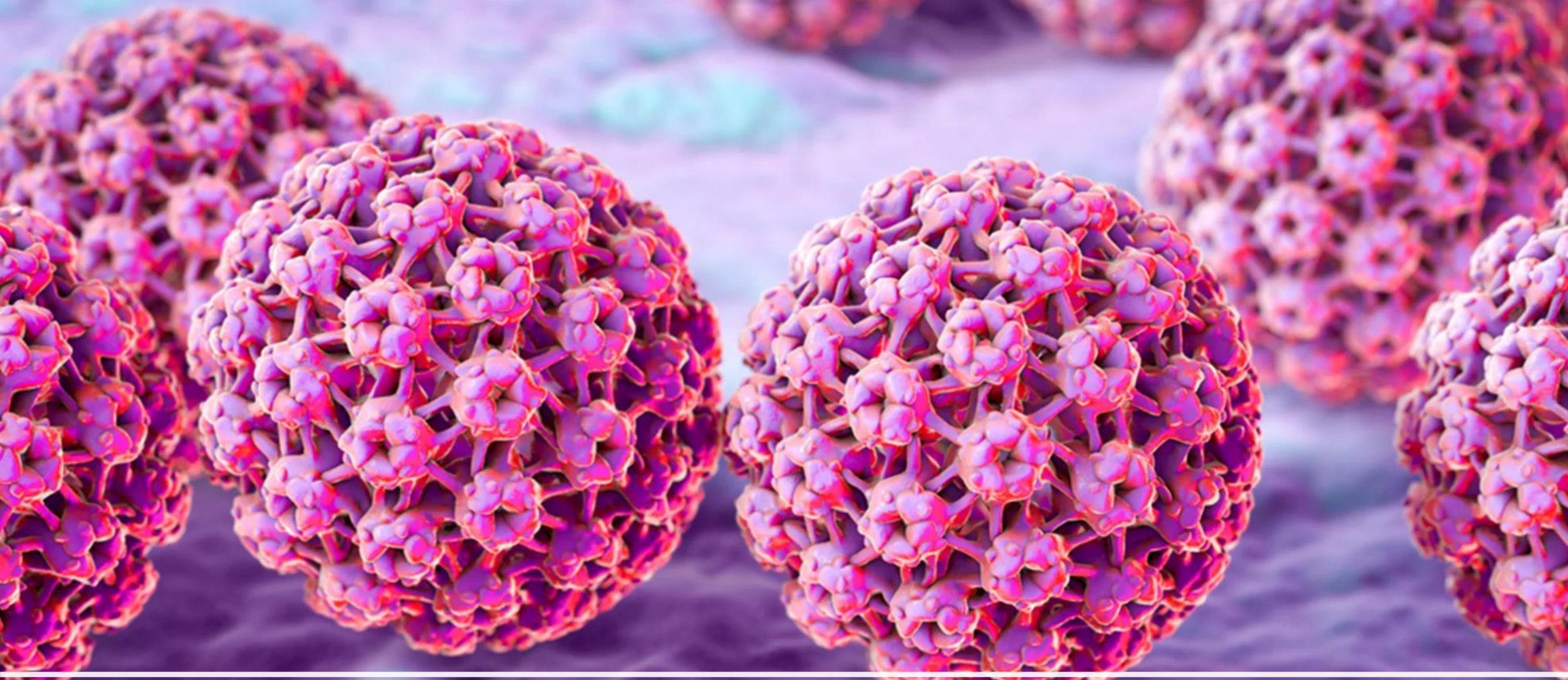
- 66,200 new cases, lifetime risk (general population) 2.8%
- 13,030 deaths

Ovarian cancer

- 19,710 new cases, lifetime risk (general population) 1.3%
- 13,270 deaths

Cervical cancer

- 13,960 new cases, lifetime risk (general population) 0.7%
- 4,310 deaths

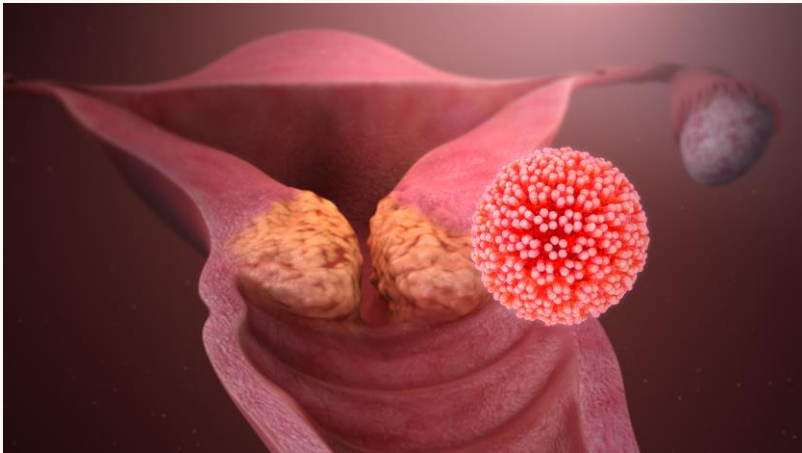


Cervical Cancer

Cervical Cancer Risk Factors

- HPV infection
- Lack of HPV vaccination
- Cervical dysplasia
- Cigarette smoking
- HIV/AIDS
- Other immunosuppressive conditions or medications

HPV and cervical cancer



HPV 16 and 18 cause >70% of all cervical cancers

Putting risk into perspective

- Risk of cervical cancer if HPV 16 positive compared to HPV 16 negative is **434**
- Risk of lung cancer in U.S. white male smoker compared to non-smoker is **10-20**
- Risk of breast cancer with HRT in Women's Health Initiative only **1.3**

Primary Prevention: HPV Vaccines

Bivalent (Cervarix): contains virus-like particles of HPV 16 and 18

Quadrivalent (Gardasil): contains virus-like particles of HPV 6, 11, 16 and 18

9-valent (Gardasil 9): contains virus-like particles of HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58

Vaccination recommendations

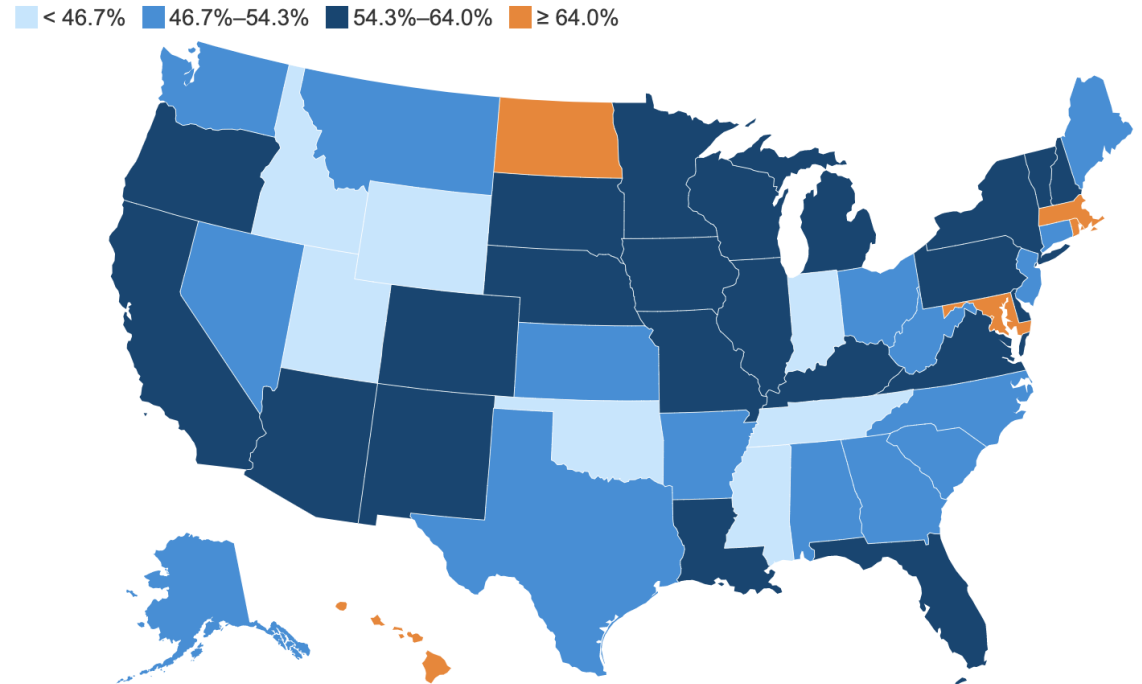
- Routine HPV vaccination for boys and girls should be initiated at age 11 or 12 years
- Vaccination series can be started beginning at age 9 years
- For adolescents and adults aged 13 to 26 years who have not been previously vaccinated or who have not completed the vaccine series, catch-up vaccination is recommended
- The World Health Organization (WHO) recommends that the primary target of HPV vaccination programs be females aged 9 to 14 years and that local public health programs should recommend vaccination of older females only if it is affordable and cost effective and does not divert resources from vaccinating the primary target population or screening for cervical cancer

- _____

Adolescents ages 13-17 with HPV Up-to-Date (UTD) Vaccination Series, 2019

Adolescents ages 13-17 with HPV Up-to-Date (UTD) Vaccination Series, 2019

■ < 46.7% ■ 46.7%–54.3% ■ 54.3%–64.0% ■ ≥ 64.0%



Vaccine Efficacy

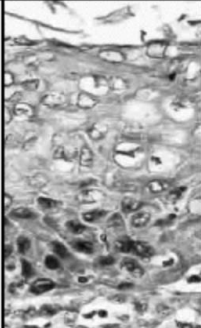
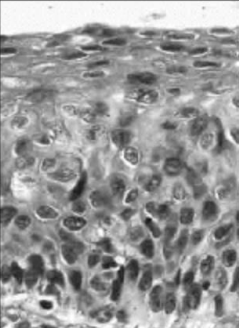
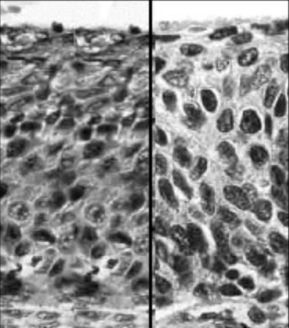
- HPV vaccination is effective in preventing cervical disease, including cervical intraepithelial neoplasia (CIN2 or 3) and adenocarcinoma in situ.
- Vaccine efficacy is greatest in those who do not have prior HPV infection (97-100%)
- Quadrivalent and 9-valent HPV vaccines have been demonstrated to reduce the incidence of vaginal and vulvar intraepithelial neoplasia (VAIN and VIN 1-3).



Secondary Prevention: Screening

- Purpose: find & treat precancerous lesions to prevent invasive cervical cancer
 - Define “**precancerous lesion**”?
- What tests do we have to identify precancerous lesions?
- How to best stratify risk based on these test results?
- Do we need triage testing?

Terminology and histology of cervical intraepithelial neoplasia

LAST System ^[1]	Cytology	LSIL	HSIL	
	Histology	LSIL	p16 staining should be performed*	HSIL
Bethesda Classification System ^[2]	Cytology	LSIL	HSIL	
	Histology	CIN 1	CIN 2	CIN 3
Previous terminology		Mild dysplasia	Moderate dysplasia	Severe dysplasia Carcinoma in-situ
Histologic images				

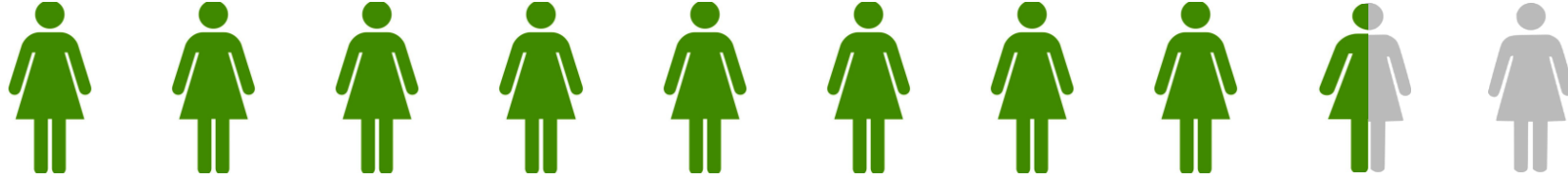
Terminology regarding cytologic and histologic precancerous changes of the uterine cervix. The corresponding terminology from the previous classification systems is shown. Images of the histologic correlates for each category are also shown.



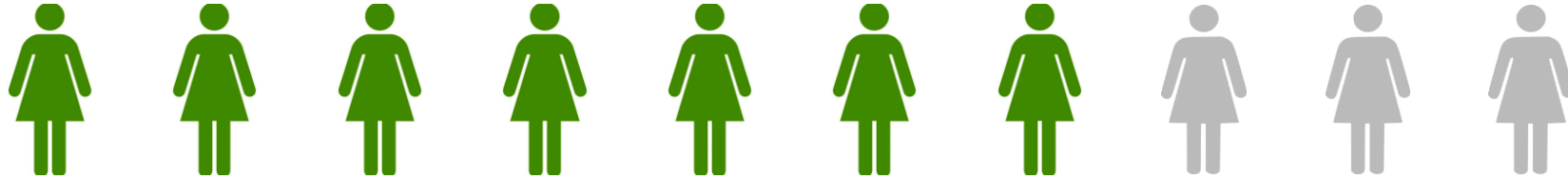
Ovarian cancer

Ovarian cancer is curable at early stages

Stage 1



Stage 2



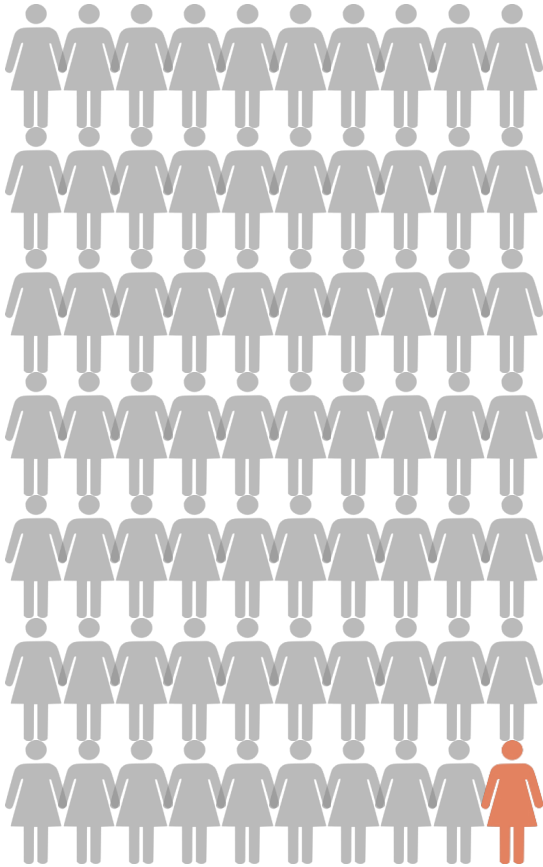
Stage 3



Stage 4




Ovarian cancer is a genetic disease




All women




Women born with DNA repair mutations such as BRCA1/2 (~1% of population)

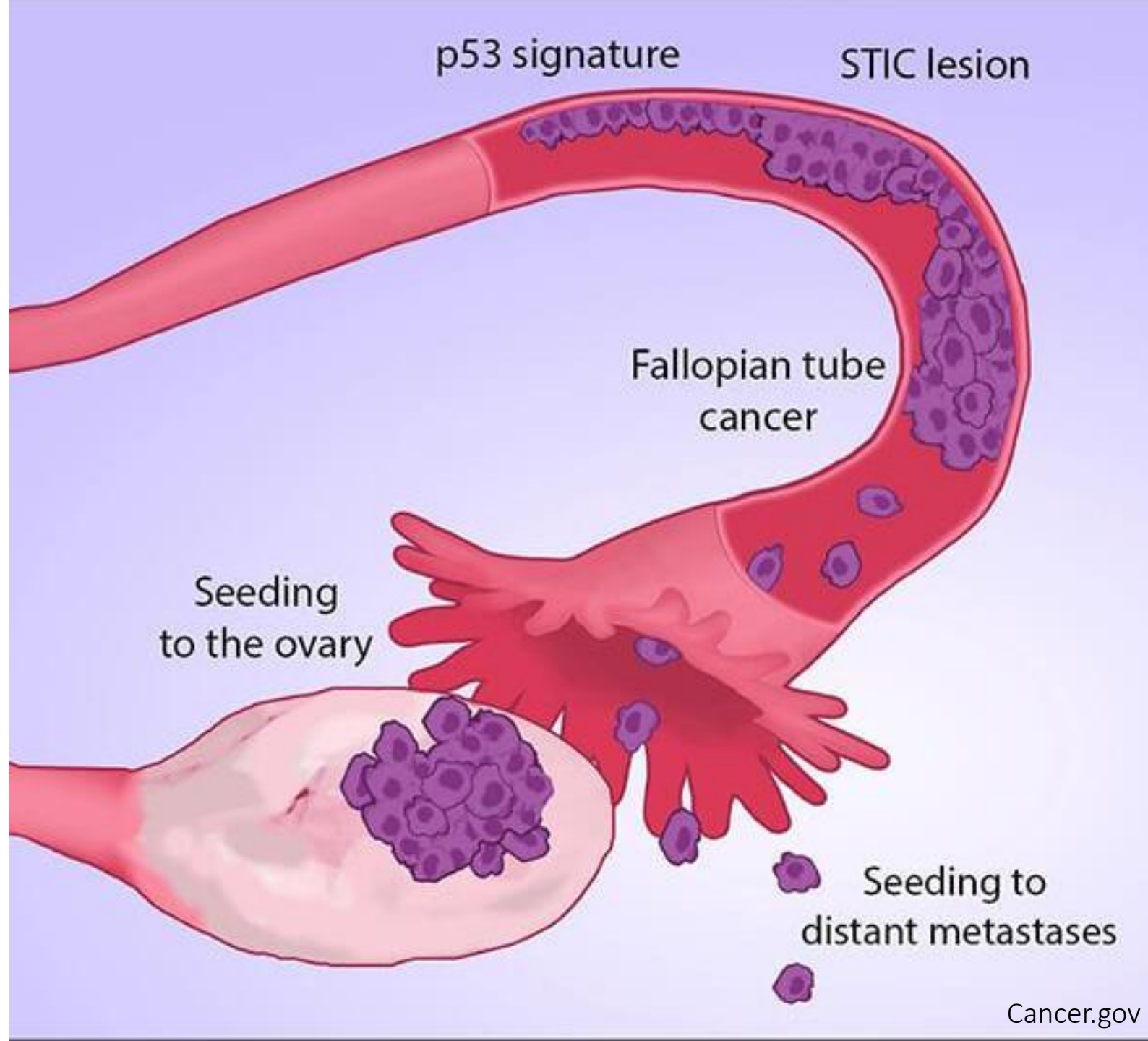


Screening in ovarian cancer?

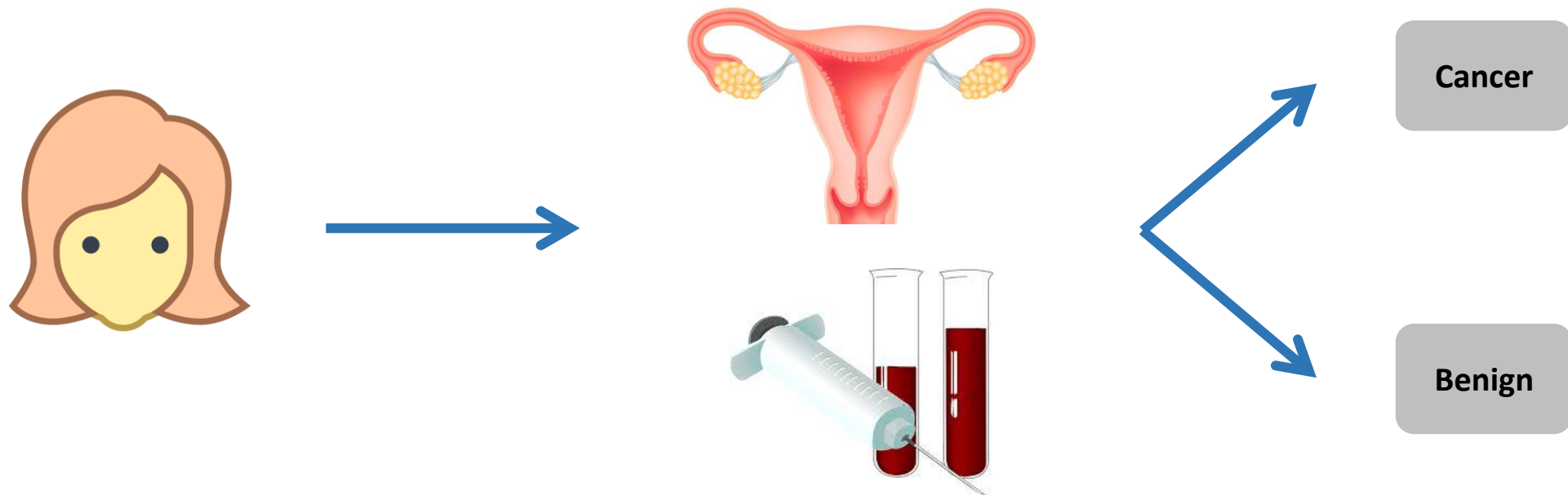


- Challenging because ovarian cancer is rare
 - A screening protocol for ovarian cancer should have a positive predictive value of at least 10 percent
 - A screening program that targets all women over age 50 would require a test with a specificity of at least 99.6 percent (assuming a sensitivity of 80 percent) to achieve a positive predictive value of 10 percent.
 - No such screening exists currently
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Ovarian cancer is hypothesized to start in the Fallopian tubes and is MICROSCOPIC



PRECiSE: PREdiction with Circulating tumor DNA to Screen for Epithelial ovarian cancer



Ovarian
cancer:
other risk
factors

Endometriosis

Hormone replacement
therapy

Obesity and height

Ovarian cancer:
factors
associated with
decreased risk

Oral contraceptive pills (dose-dependent)

Tubal ligation (30% lower risk)

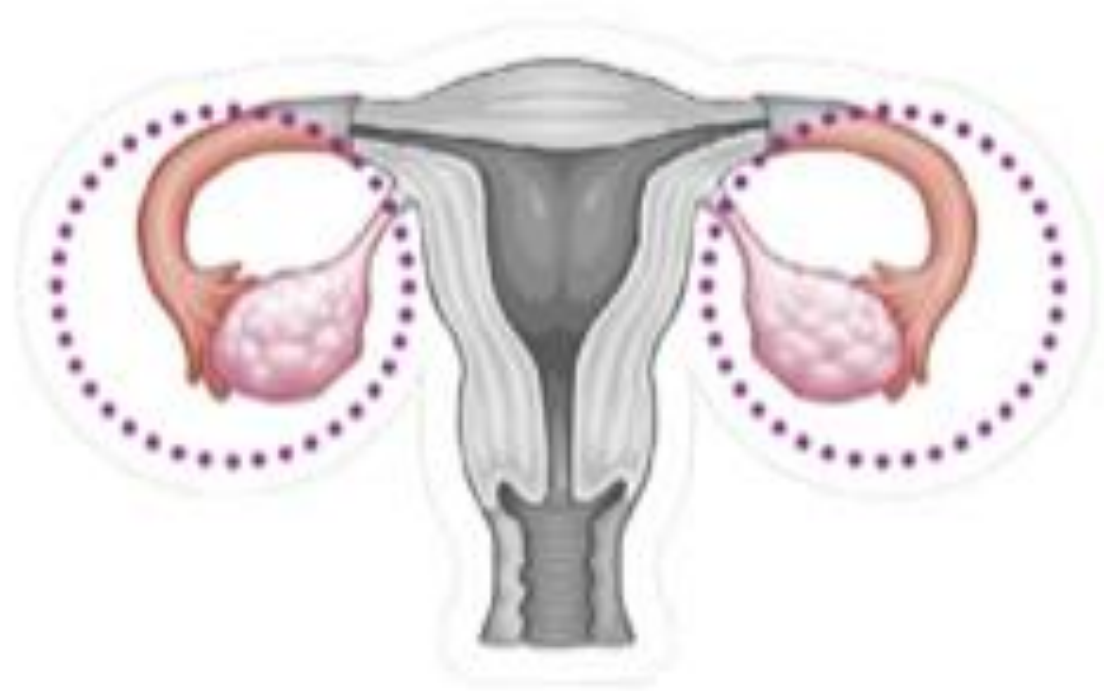
Salpingectomy (50% lower risk)

Multiparity (30% lower risk)

Breastfeeding (dose-dependent)

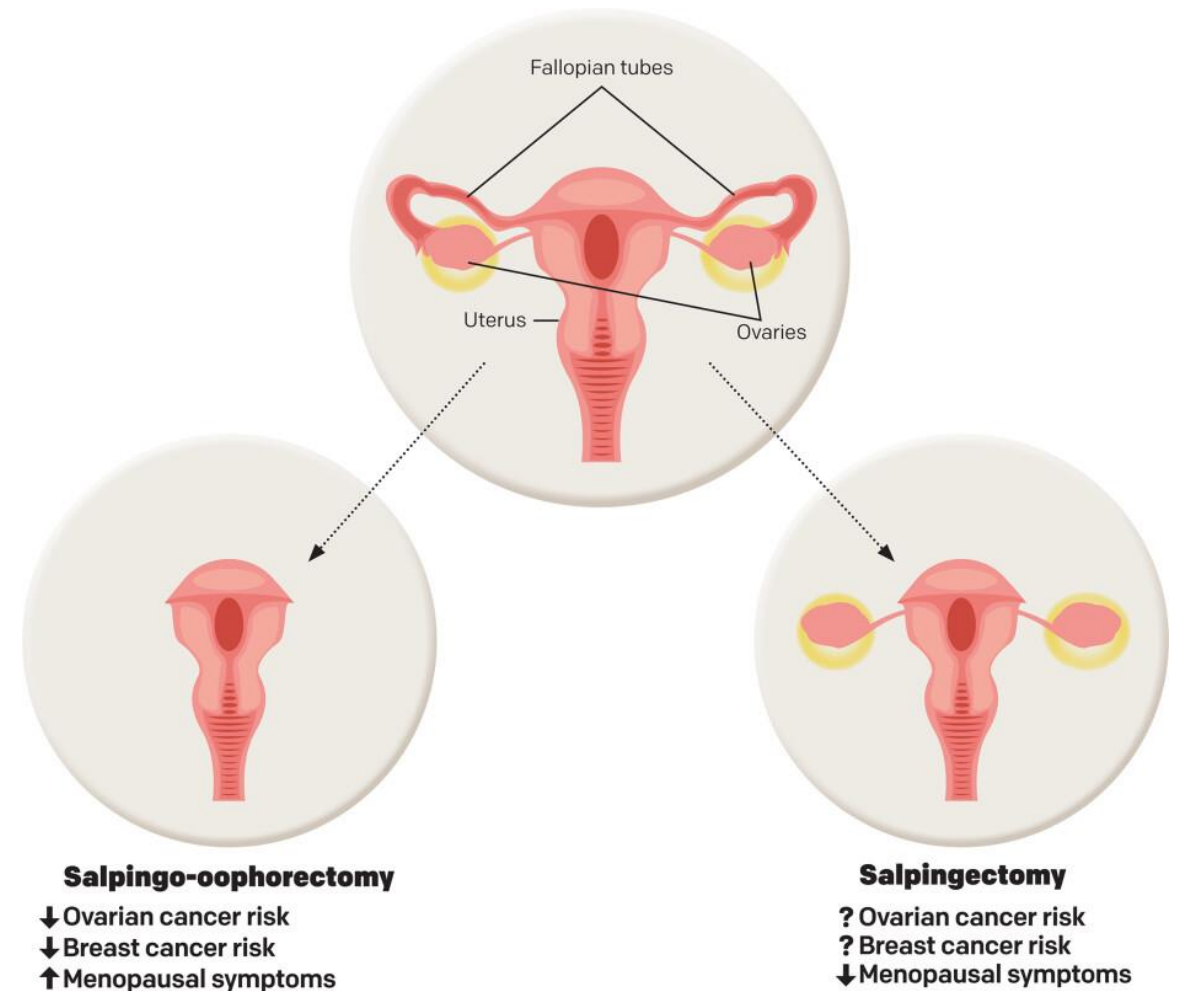
BRCA1 and BRCA2 mutation carriers: opportunity for risk-reduction

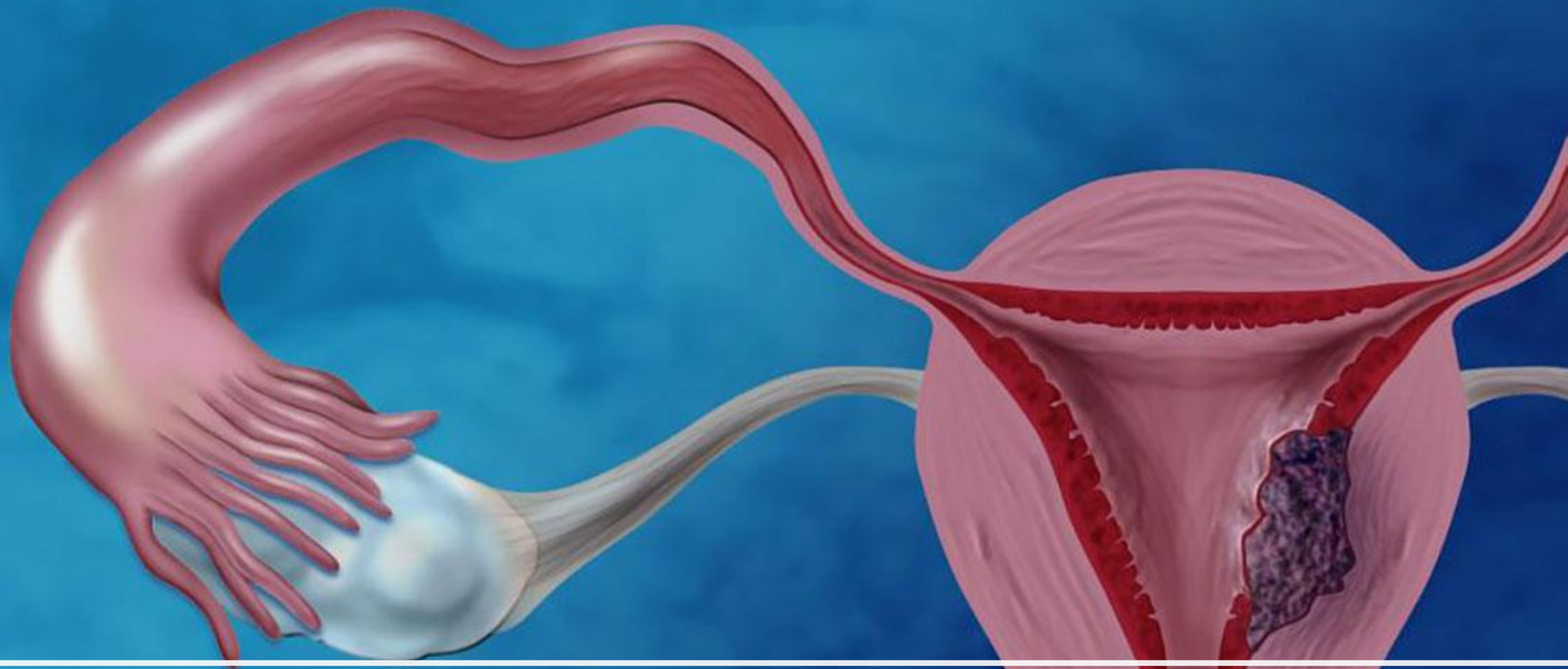
- Risk-reducing bilateral salpingo-oophorectomy associated with 90% reduction in risk of ovarian cancer



What about salpingectomy for BRCA carriers?

- Bilateral salpingectomy alone and bilateral salpingectomy followed by delayed oophorectomy MAY be alternatives to risk-reducing BSO
 - Benefits: avoiding pre-mature menopause and retaining fertility options





Endometrial Cancer

Risk factors for endometrial cancer (grade 1-2 endometrioid)

- Excess estrogen, without the balance of progesterone
 - Exogenous: HRT, tamoxifen
 - Endogenous: chronic anovulation, PCOS, obesity
- Lynch Syndrome (hereditary nonpolyposis colon cancer), a germline mutation in of the DNA mismatch repair genes



Strategies for prevention: endometrioid grade 1-2

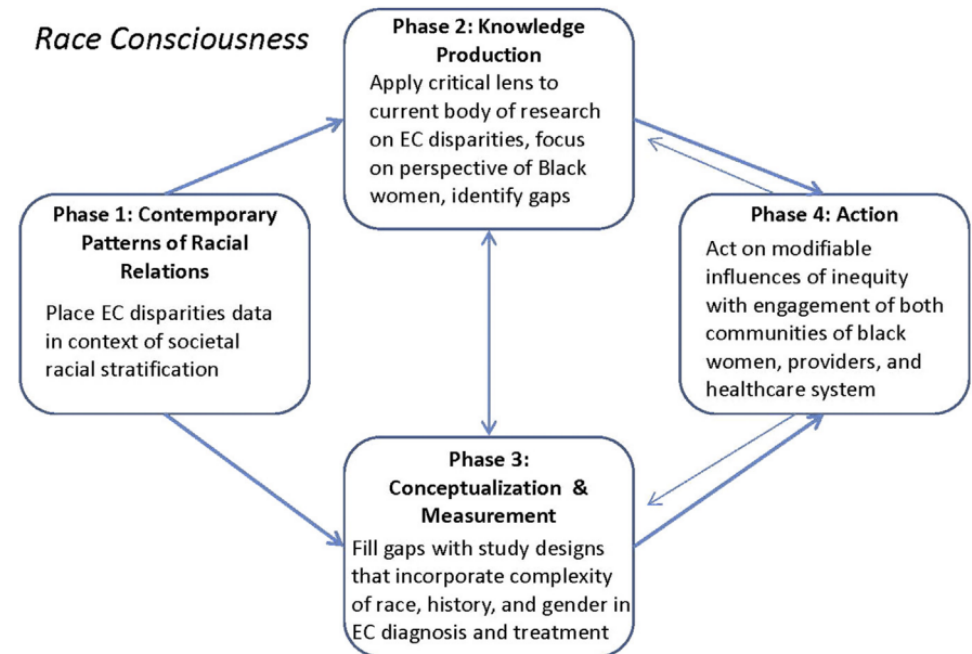


- Lynch Syndrome: birth control pills, risk-reducing hysterectomy after childbearing
- Tamoxifen: ?LNG IUD ?safe in PR+ breast cancer?
- PCOS: birth control pills
- Obesity: weight reduction through lifestyle modifications or bariatric surgery
 - In obese women, bariatric surgery may reduce risk EC to to 50-80%

Racial disparities in endometrial cancer

- Black women are disproportionately affected by endometrial cancer
- Black women (compared to white women) have higher incidence of EC, a higher incidence of aggressive endometrial cancers (clear cell, serous, carcinosarcoma and high-grade endometrioid)
- Black women have higher five-year mortality (compared to white women) for nearly every stage and subtype of EC
- Etiology of these disparities is unknown

FIGURE 1
Public Health Critical Race Praxis¹⁸: Adapted and Applied to Endometrial Cancer Disparities



Public health critical race praxis, adapted from Ford and Airhihenbuwa,²⁷ and applied to endometrial cancer (EC) disparities.

Doll. Endometrial cancer disparities: critiquing literature. Am J Obstet Gynecol 2018.