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HEALTHY ARIZONA WORKSITES PROGRAM (HAWP) PRESENTS:

WHAT EVERY EMPLOYER AND WOMAN SHOULD KNOW ABOUT GYNECOLOGIC CANCERS

Presented by:

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WEBINAR HOUSEKEEPING

WELCOME

All lines have been muted.

Please type any questions into the chat or Questions panel and we will do our best to answer them all at the end.

All handouts and a copy of the presentation slides are available in the Handouts panel.

Please complete the survey that will be emailed out after the presentation

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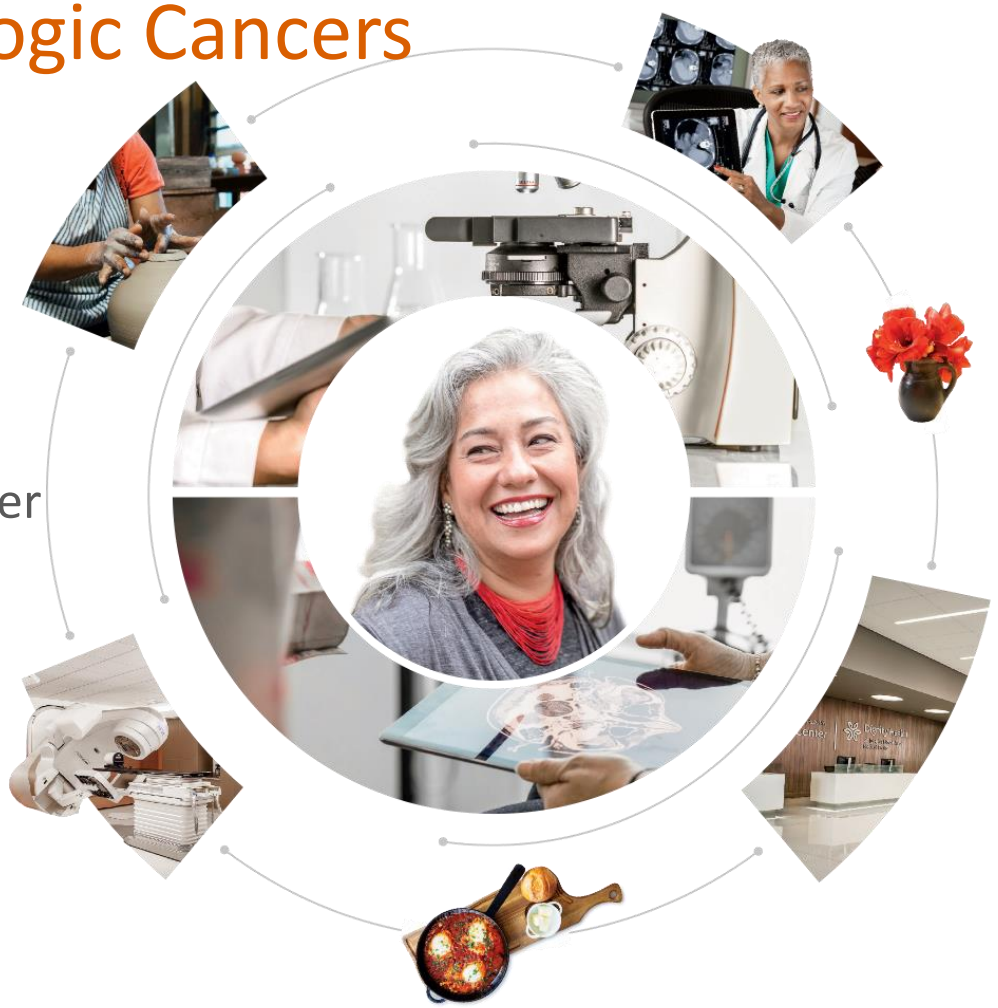
Special thanks to our supporting partner Dignity Health for their generous support in making this webinar possible.

What Every Employer And Woman Should Know About Gynecologic Cancers



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Division of Gynecologic Oncology
January 23, 2020

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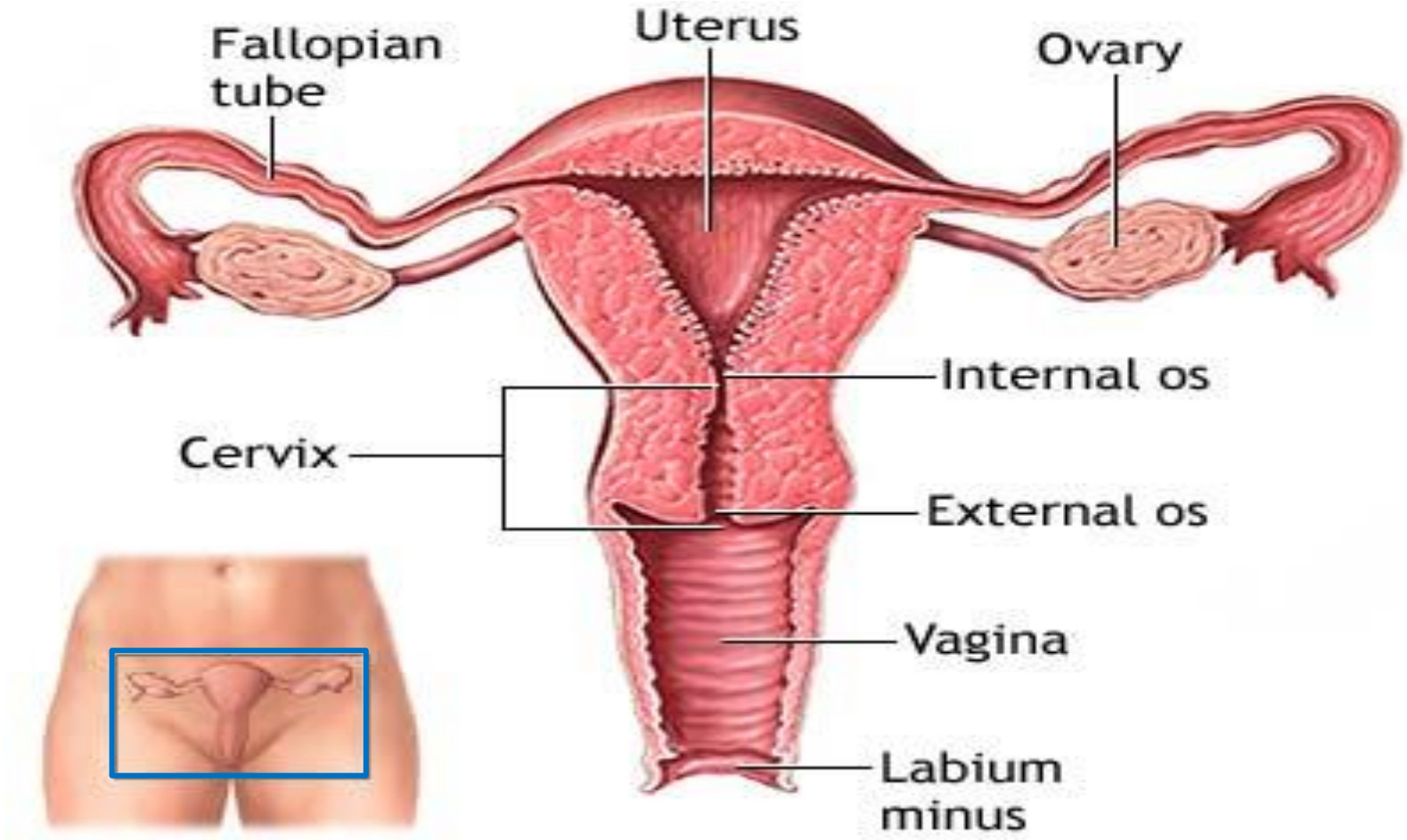
Key Objectives

1. Understand the scope and types of gynecologic (GYN) cancers.
2. Incidence and mortality GYN cancer rates in the United States.
3. Staging of gynecologic cancers.
4. Surgical options for treating GYN cancers.
5. Adjuvant therapy options for gynecologic cancers.
6. Understand the anatomy in gynecologic cancers.
7. Understand the basic outcomes of treatment in gynecologic cancers.

Scope of Gynecologic Region



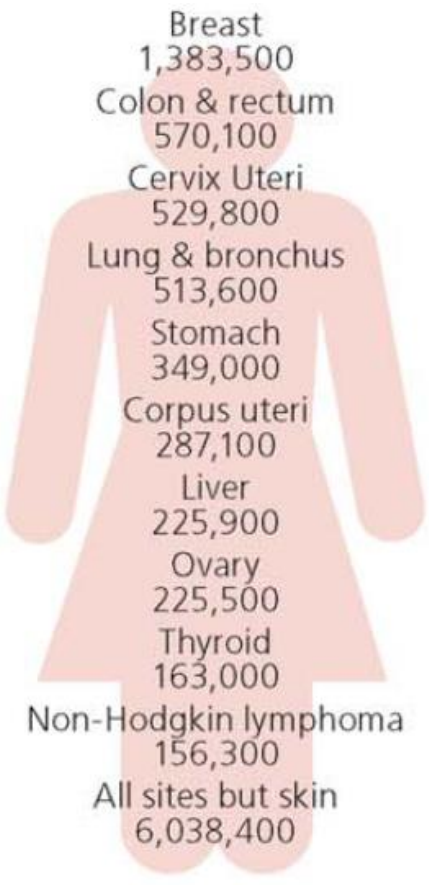
Anatomy Female Pelvic Region

Types of Gynecologic Oncology (Cancers)

- Pre-invasive vulvar, vaginal, & cervical disease
- Vulvar cancer
- Cervical cancer
- Endometrial cancer
- Uterine sarcoma
- Fallopian tube cancer
- Ovarian cancer
- Gestational trophoblastic disease (pregnancy-related tumors)

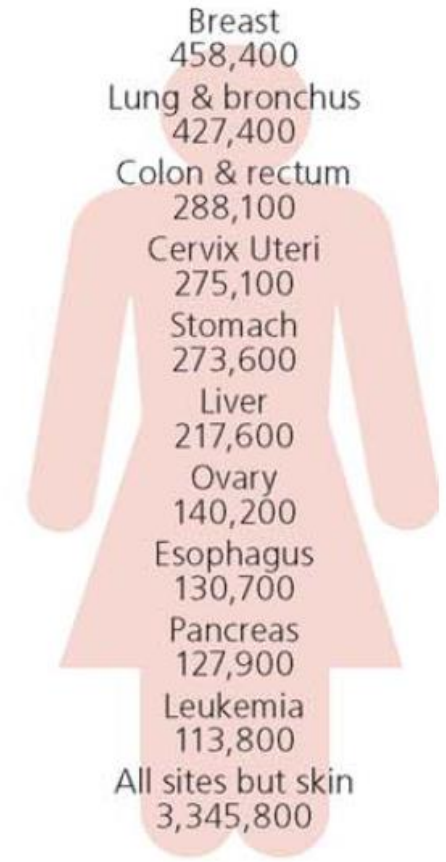
The Global Burden of Cancer In Women Worldwide

New Cases Annually



- 9% of all new cancer cases
- 8% of total cancer deaths
- 85% of deaths occur in developing countries

Deaths Annually



Quick Introduction to GYN Oncology

What you should know…

- Cancer Biology
- Cancer Therapeutics
- **Cancer Screening***
- Early Diagnosis
- **Cervical Cancer***
- **Uterine Cancer***
- **Ovarian Cancer***
- Vulvar/Vaginal Cancer
- Gestational Trophoblastic Neoplasm/Disease

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**Content we will review today, due to limited time*

Cervical Cancer

Brief Introduction

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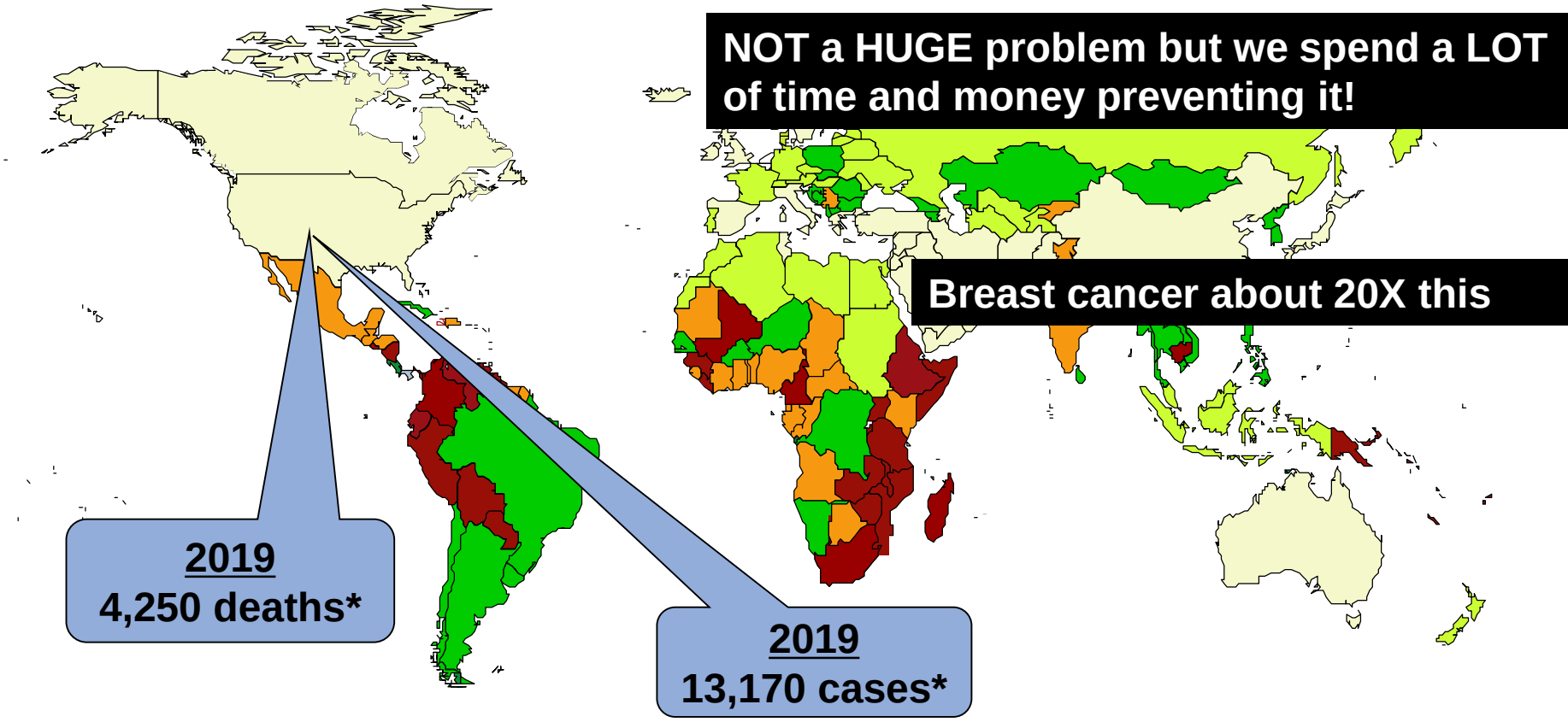
Incidences of Cervical Cancer (Estimates)



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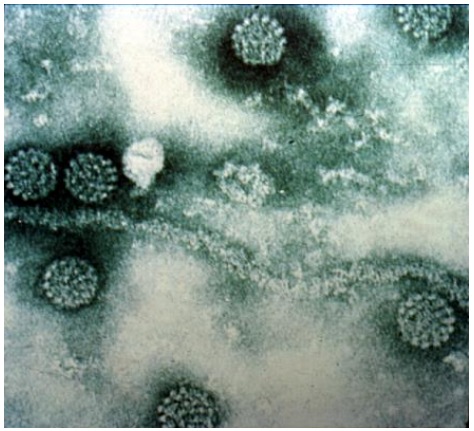
Source: American Cancer Society Facts and Figures 2019

Cervical screening and abnormal Pap management have been changing.

Why?

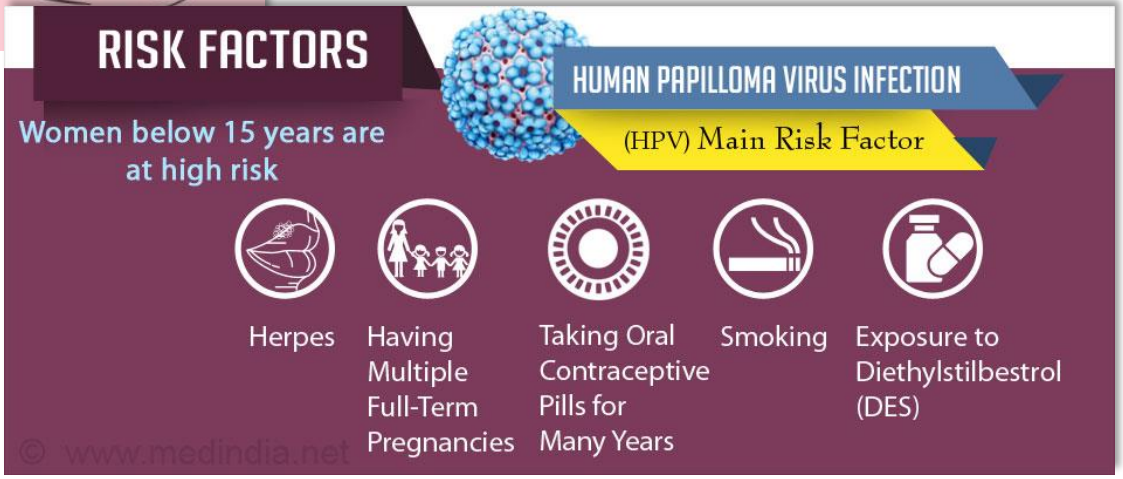
- Concern that an **occasional woman gets cervical cancer despite adherence** to recommended cervical screening guidelines.
- **Adolescents are often over treated** leading to early pregnancy loss and/or infertility.



Current State of Science

- Data appears to be in favor of any **Pap plus HPV Test offers women the best protection against cervical disease.**
- Also in favor of **HPV genotyping and maybe primary screening** (ATHENA TRIAL).

Signs and Risk Factors of Cervical Cancer



Human papillomavirus DNA testing for the detection of cervical intraepithelial neoplasia grade 3 and cancer: 5-year follow-up of a randomised controlled implementation trial

N W J Bulkmans, J Berkhof, L Rozendaal, F J van Kemenade, A J P Boeke, S Bulk, F J Voorhorst, R H M Verheijen, K van Groningen, M E Boon, W Rutinga, M van Ballegooijen, P J F Snijders, C J L M Meijer

Published Online October 4, 2007 DOI:10.1016/S0140-6736(07)61450-0

See Online/Comment DOI:10.1016/S0140-6736(07)61480-9

Department of Pathology (N W J Bulkmans MD, L Rozendaal MD, F J van Kemenade MD, S Bulk MD, F J Voorhorst MD, Prof P J F Snijders PhD, Prof C J L M Meijer MD), Department of Clinical Epidemiology and Biostatistics (J Berkhof PhD), Institute for Research in Extramural Medicine (A J P Boeke MD), and Department of Obstetrics and Gynaecology (Prof R H M Verheijen MD), VU University Medical Centre, Amsterdam, Netherlands; Department of Pathology, Spaarne Ziekenhuis, Hoofddorp, Netherlands (K van Groningen MD); Leiden Cytology and Pathology Laboratory, Leiden, Netherlands (M E Boon MD); Department of Pathology, Kennemer Gasthuis, Haarlem, Netherlands (W Rutinga MD); and Department of Public Health and Social Medicine, Erasmus University, Rotterdam, Netherlands (M van Ballegooijen MD)

Correspondence to: Prof C J L M Meijer, Department of Pathology, VU University Medical Centre, PO box 7057, 1007 MB Amsterdam, Netherlands
cjlm.meijer@vumc.nl

Background DNA of high-risk types of human papillomavirus (HPV) have a higher sensitivity for cervical ... or worse (CIN3+) than does cytological testing, but the necessity of such testing in ... Our aim was to determine whether the effectiveness of cervical screening ...ished.

Methods ...in the regular cervical screening programme in the ...PV DNA testing or to conventional cytological ...ere done in both groups. The primary ...re done by intention to treat. This trial is ...ber ISRCTN20781131.

...trol group were recruited, followed up for ... More CIN3+ lesions were detected at baseline ...0, 70% increase, 95% CI 15–151; p=0·007). The ...er in the intervention group than in the control ...l). The number of CIN3+ lesions over the two ...

...rvical screening leads to earlier detection of CIN3+ ...sion of the screening interval.

THE NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 18, 2007 VOL. 357 NO. 16

Human Papillomavirus DNA versus Papanicolaou Screening Tests for Cervical Cancer

Marie-Hélène Mayrand, M.D., Eliane Duarte-Franco, M.D., Isabel Rodrigues, M.D., Stephen D. Walter, Ph.D., James Hanley, Ph.D., Alex Ferenczy, M.D., Sam Ratnam, Ph.D., François Coutlée, M.D., and Eduardo L. Franco, Dr.P.H., for the Canadian Cervical Cancer Screening Trial Study Group*

ABSTRACT

BACKGROUND To determine whether testing for DNA of oncogenic human papillomaviruses (HPV) is superior to the Papanicolaou (Pap) test for cervical-cancer screening, we conducted a randomized trial comparing the two methods.

METHODS We compared HPV testing, using an assay approved by the Food and Drug Administration, with conventional Pap testing as a screening method to identify high-grade cervical intraepithelial neoplasia in women ages 30 to 69 years in Montreal, St. John's, Canada. Women with abnormal Pap test results or a positive HPV ... least 1 pg of high-risk HPV DNA per milliliter) underwent colposcopy and bi... did a random sample of women with negative tests. Sensitivity and specificity ... were corrected for verification bias.

RESULTS A total of 10,154 women were randomly assigned to testing. Both ... on all women in a randomly assigned sequence at the same ses... HPV testing for cervical intraepithelial neoplasia of grade 2 or ... fidence interval [CI], 84.2 to 100), whereas the sensitivity ... (95% CI, 33.6 to 77.2; P=0.01). The specificity was 94.1% ... testing and 96.8% (95% CI, 96.3 to 97.3; P<0.001) for ... unaffected by the sequence of the tests. The sensitivity ... 100%, and the specificity was 92.5%. Triage procedure ... in fewer referrals for colposcopy than did either ... adverse events were reported.

CONCLUSIONS As compared with Pap testing, HPV ... tion of cervical intraepithelial ... ISRCTN57612064.)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Human Papillomavirus and Papanicolaou Tests to Screen for Cervical Cancer

Pontus Naucler, M.D., Ph.D., Walter Ryd, M.D., Sven Törnberg, M.D., Ph.D., Anders Strand, M.D., Ph.D., Göran Wadell, M.D., Ph.D., Kristina Elfgren, M.D., Ph.D., Thomas Rådberg, M.D., Björn Strander, M.D., Ola Forslund, Ph.D., Bengt-Göran Hansson, Ph.D., Eva Rylander, M.D., Ph.D., and Joakim Dillner, M.D., Ph.D.

ABSTRACT

BACKGROUND Screening for cervical cancer based on testing for human papillomavirus (HPV) increases the sensitivity of detection of high-grade (grade 2 or 3) cervical intraepithelial neoplasia, but whether this gain represents overdiagnosis or protection against future high-grade cervical epithelial neoplasia or cervical cancer is unknown.

METHODS In a population-based screening program in Sweden, 12,527 women 32 to 38 years of age were randomly assigned at a 1:1 ratio to have an HPV test plus a Papanicolaou (Pap) test (intervention group) or a Pap test alone (control group). Women with a positive HPV test and a normal Pap test result were offered a second HPV test at least 1 year later, and those who were found to be persistently infected with the same high-risk type of HPV were then offered colposcopy with cervical biopsy. A similar number of double-blinded Pap smears and colposcopies with biopsy were performed in randomly selected women in the control group. Comprehensive registry data were used to follow the women for a mean of 4.1 years. The relative rates of grade 2 or 3 cervical intraepithelial neoplasia or cancer detected at enrollment and at subsequent screening examinations were calculated.

RESULTS At enrollment, the proportion of women in the intervention group who were found to have lesions of grade 2 or 3 cervical intraepithelial neoplasia or cancer was 51% greater (95% confidence interval [CI], 13 to 102) than the proportion of women in the control group who were found to have such lesions. At subsequent screening examinations, the proportion of women in the intervention group who were found to have grade 2 or 3 lesions or cancer was 42% less (95% CI, 4 to 64) and the proportion with grade 3 lesions or cancer was 47% less (95% CI, 2 to 71) than the proportions of control women who were found to have such lesions. Women with persistent HPV infection remained at high risk for grade 2 or 3 lesions or cancer after referral for colposcopy.

CONCLUSIONS The addition of an HPV test to the Pap test to screen women in their mid-30s for cervical cancer reduces the incidence of grade 2 or 3 cervical intraepithelial neoplasia or cancer detected by subsequent screening examinations. (ClinicalTrials.gov number, NCT00479375.)

From the Department of Medical Microbiology, Malmö University Hospital, Lund University (P.N., O.F., B.-G.H., J.D.); the Department of Pathology and Clinical Cytology (W.R.), the Department of Obstetrics and Gynecology (T.R., B.S.), and the Oncology Center (B.S.), Sahlgrenska University Hospital, Gothenburg; the Cancer Screening Unit, Oncology Center (S.T.) and the Department of Obstetrics and Gynecology (K.E.), Karolinska University Hospital, and the Division of Gynecology, Department of Women's and Children's Health, Karolinska Institutet, Stockholm; the Department of Medicine, Dermatology, and Venereology, University Hospital, Uppsala (A.S.); and the Department of Virology, University of Northern Sweden, Umeå (G.W.) — all in Sweden. Address reprint requests to Dr. Naucler at the Department of Medical Microbiology, Lund University, Malmö University Hospital, Malmö S-20502, Sweden.

N Engl J Med 2007;357:1589-97.

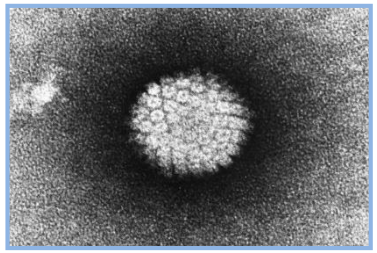
Methods

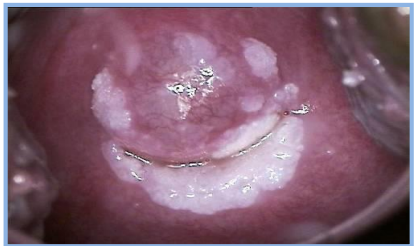
Patients and procedures

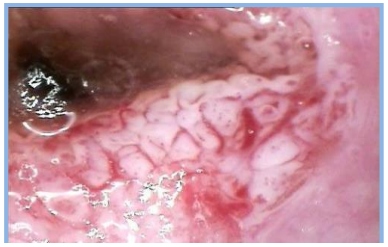
POBASCAM is a population-based randomised controlled implementation trial to assess the effectiveness of cervical screening with HPV DNA testing combined with cytological testing (intervention group) compared with conventional cytological testing only (control group, HPV DNA test results blinded). The trial was done within the regular Dutch nationwide screening programme that invites women aged 30–60 years to be screened every 5 years. The design, methods, and baseline results of the trial have been described previously.[21] Briefly, between January, 1999, and September, 2002, women invited for

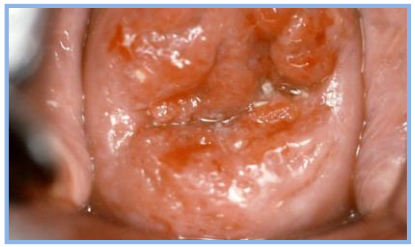
Detecting Cancer from Screening Pap smear

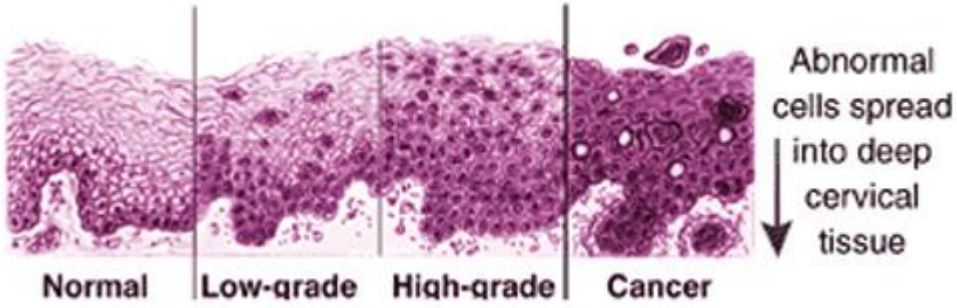
Transient Infection		Persistent Infection	
Normal → Precancerous, possible regress or persist to severe disease → Invasive			
HPV Infection	CIN 1,2	CIN 2,3[1]	Cervical Cancer[2]











Colposcopy demonstrates abnormal vasculature and angiogenesis dependent progression

TABLE 1

Screening for Cervical Cancer: Clinical Summary of the USPSTF Recommendations

Population	Women aged 21 to 29 years	Women aged 30 to 65 years	Women younger than 21 years, women older than 65 years with adequate prior screening, and women who have had a hysterectomy
Recommendations	Screen for cervical cancer every 3 years with cytology alone. Grade: A	Screen for cervical cancer every 3 years with cytology alone, every 5 years with hrHPV testing alone, or every 5 years with cotesting. Grade: A	Do not screen for cervical cancer. Grade: D
Risk assessment	All women aged 21 to 65 years are at risk for cervical cancer because of potential exposure to hrHPV types through sexual intercourse and should be screened. Certain risk factors further increase risk for cervical cancer, including HIV infection, a compromised immune system, in utero exposure to diethylstilbestrol, and previous treatment of a high-grade precancerous lesion or cervical cancer. Women with these risk factors should receive individualized follow-up.		
Screening tests	Screening with cervical cytology alone, primary testing for hrHPV alone, or both at the same time (cotesting) can detect high-grade precancerous cervical lesions and cervical cancer. Clinicians should focus on ensuring that women receive adequate screening, appropriate evaluation of abnormal results, and indicated treatment, regardless of which screening strategy is used.		
Treatment and interventions	High-grade cervical lesions may be treated with excisional and ablative therapies. Early-stage cervical cancer may be treated with surgery (hysterectomy) or chemotherapy.		

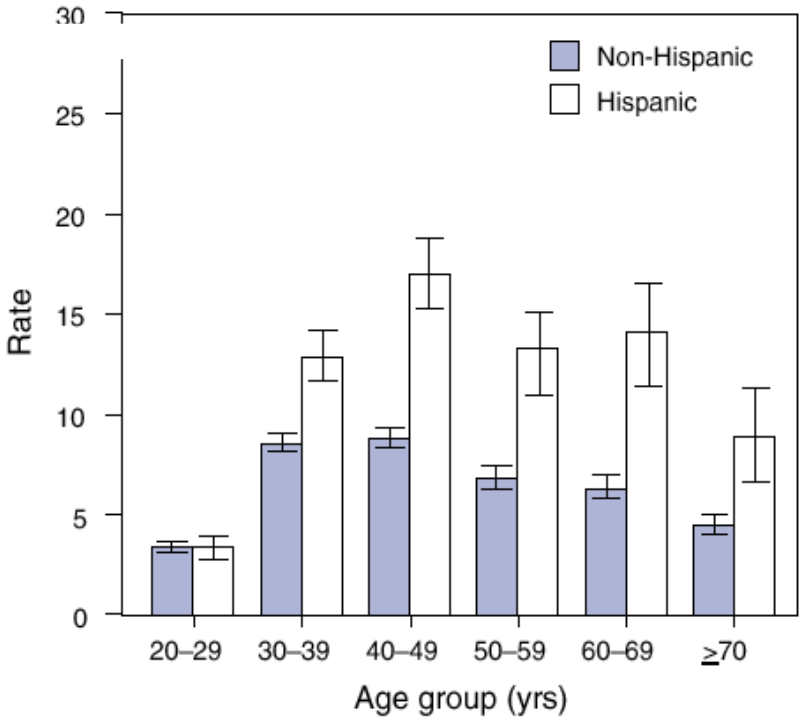
Note: These recommendations apply to individuals who have a cervix, regardless of their sexual history or HPV vaccination status. These recommendations do not apply to individuals who have been diagnosed with a high-grade precancerous cervical lesion or cervical cancer, those with in utero exposure to diethylstilbestrol, or those who have a compromised immune system (e.g., individuals living with HIV).

Note: For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, go to https://www.uspreventiveservicestaskforce.org/.

HIV = human immunodeficiency virus; hrHPV = high-risk HPV; USPSTF = U.S. Preventive Services Task Force.

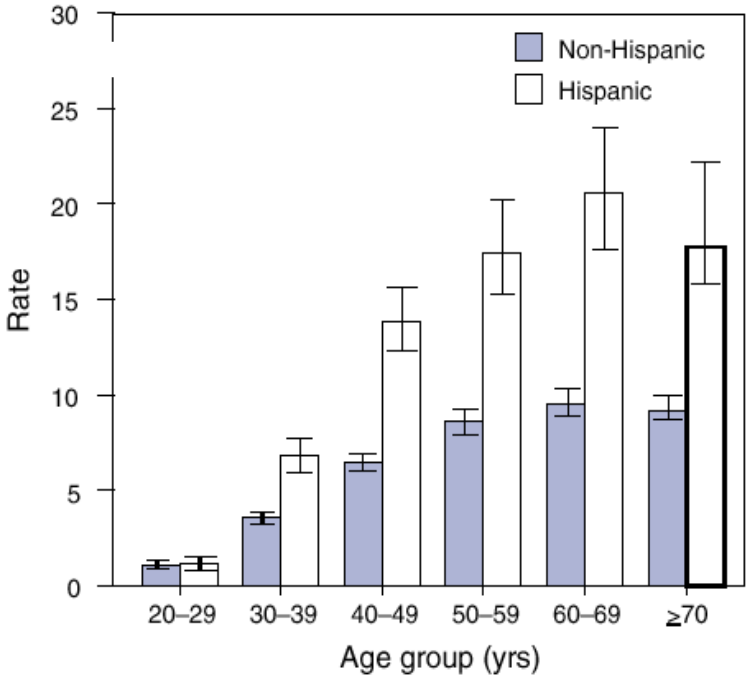
FIGO Stage Depends on Age and Ethnicity

FIGURE 1. Incidence* and 95% confidence intervals of localized† invasive cervical cancer among Hispanic and non-Hispanic women, by age group — Surveillance, Epidemiology, and End Results Program, United States, 1992–1999



* Per 100,000 women.
† Localized-stage cancer is confined to the cervix.

FIGURE 2. Incidence* and 95% confidence intervals of advanced† invasive cervical cancer among Hispanic and non-Hispanic women, by age group — Surveillance, Epidemiology, and End Results Program, United States, 1992–1999



* Per 100,000 women.
† Advanced-stage cancer (includes regional and distant) requires direct extension to corpus uteri or any site beyond the cervix, lymph node involvement, or metastasis.

Pre-Treatment Staging of Cervical Cancer

- FIGO system is clinical
- Cystoscopy and proctoscopy if suspect bladder or rectal involvement
- MRI superior to CT in evaluating local extension
- MRI or CT for hydronephrosis and retroperitoneal spread (pelvic and aortic nodes)
- CXR or CT to evaluate thoracic involvement
- PET if no evidence of extrapelvic spread

- CXR
- MRI or CT of abdomen and pelvis with and without contrast
- PET if MRI/CT and CXR show no metastases

Monk et al J Clin Oncol 25:2952-2965. 2007

Treatment for Cervical Cancer

- Surgery
  - Fertility Sparing Surgery
    - Cone biopsy
    - Trachelectomy
  - Surgical Staging
  - Radical Hysterectomy
- Radiation Therapy (External beam or Brachytherapy)
- Chemotherapy (Medical Oncology)
- Immunotherapy??

Fertility Sparing (Cone Biopsy)

- Why chose this option?
  - Stage IA1 disease (squamous and glandular)
  - Clear margins including CIN 3 on cone
  - Desire for future fertility

- Expected Recovery Time

- Side Effects or Complications

Radical Hysterectomy

Why chose this option?

- Used to treat cervical cancers with invasion > 3mm but confined to the cervix and vagina < 4 cm (Stage IA2 –IB1)
- Removal of parametrium (cervical stroma) and upper vagina
- Good surgical candidate
- Completed child baring or refuses the increased risks associated with fertility sparing approach
- Small chance for adjuvant therapy (FIGO stage IA2 – IB1)

Expected recovery time

- **Robotic** – Recovery rate varies, but staying in the hospital only one night is typical, depending on complications. Surgery takes 3-4 hours and recovery is faster than other surgical methods.
- **Laparoscopic** – Recovery varies, hospital stay is 2-3 days with 1- 6 weeks recovery, depending on complications and extent of surgery

Good questions to ask your provider

- **Your Alternatives**: Radiation +/- chemotherapy or surgery
- **Your Risks**: Surgical complications, sterility
- **Your Benefits**: Potential cure

Uterine Cancer

Brief Introduction

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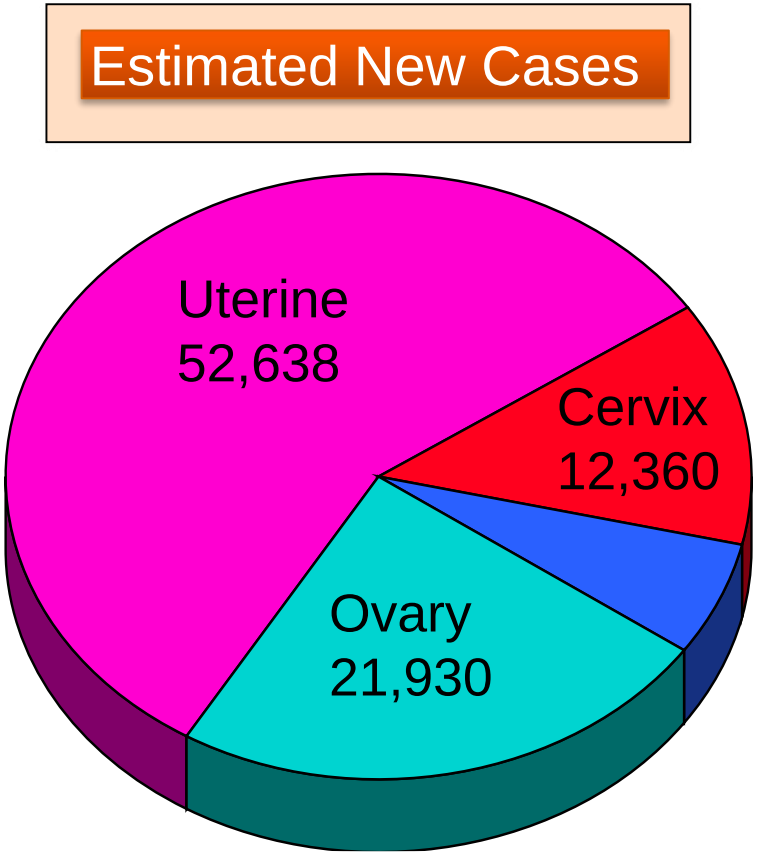
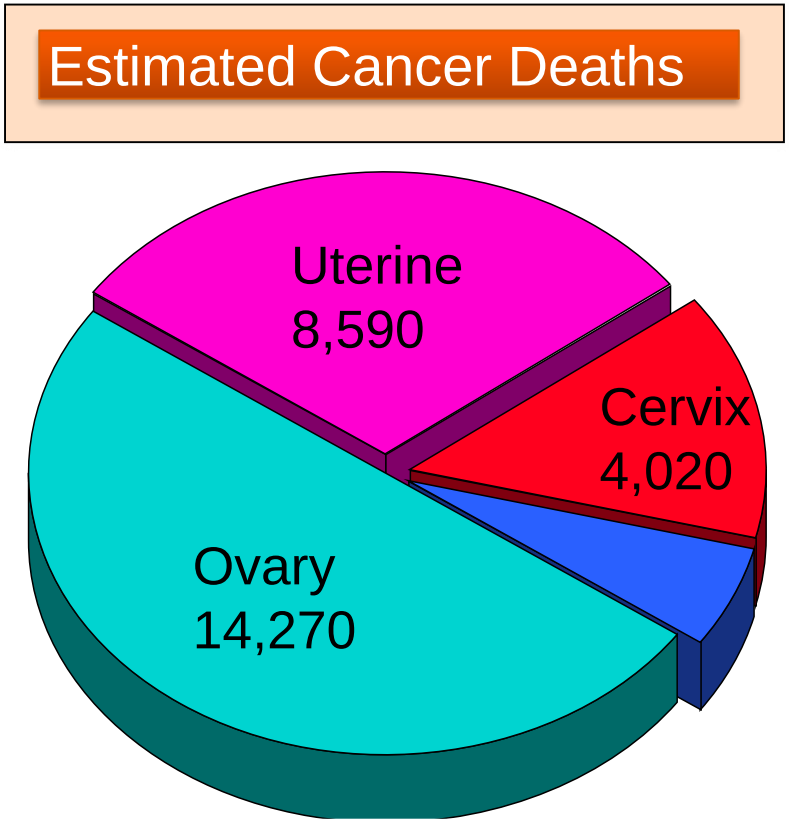
Female Genital Cancer Incidence 2014 USA





Cancer Facts & Figures ACS 2014

Uterine Cancer Subtypes

- Endometrial Origin
  - Endometrioid Adenocarcinoma
  - (Papillary) Serous Carcinoma
  - Clear Cell Carcinoma
- Sarcoma
  - Leiomyosarcoma
  - Carcinosarcoma
  - Endometrial Stromal Sarcoma

Risk Factors

- Age
- Obesity
- Unopposed Estrogen
  - Nulliparity (condition in a woman of never having given birth)
  - Late menopause
  - Estrogen-only HT
  - Tamoxifen (used to treat hormone-receptor positive early, locally advanced and metastatic breast cancers.)
- Hereditary Nonpolyposis Colorectal Cancer Syndrome
  - <10% of uterine cancers, RR 20-60x

Endometrial Cancer

Brief Introduction

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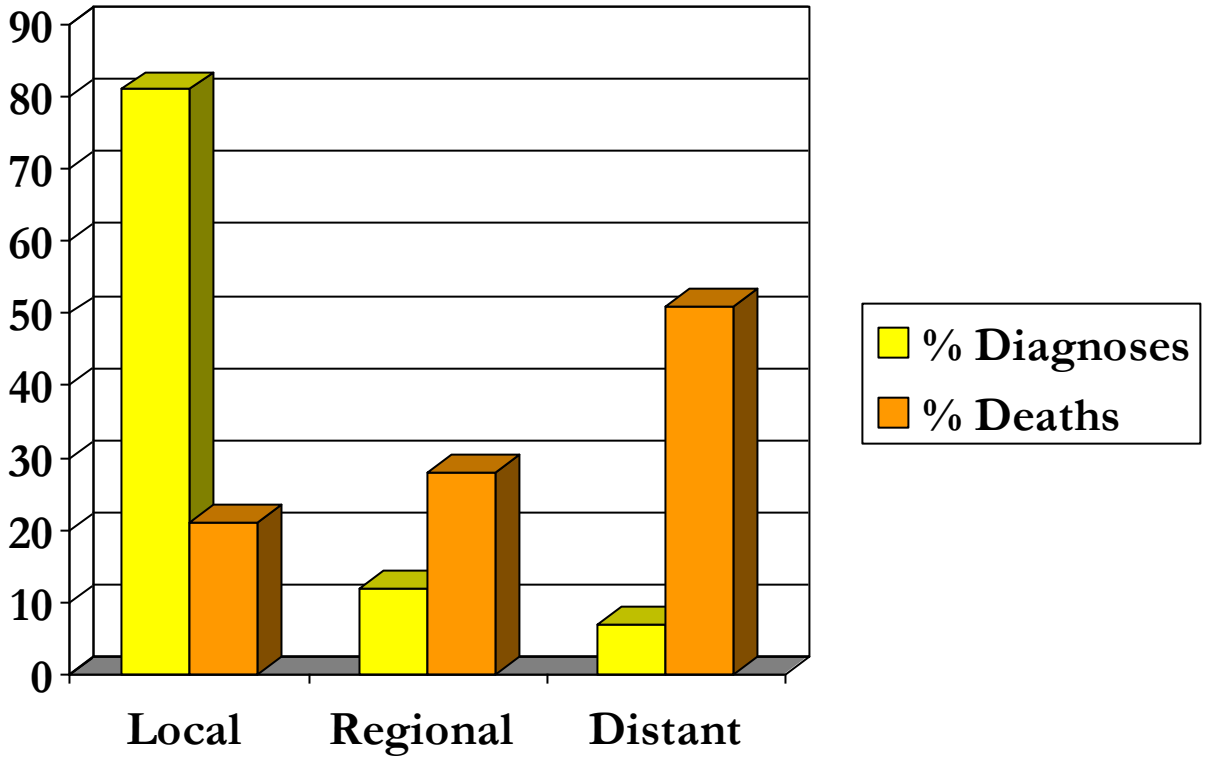
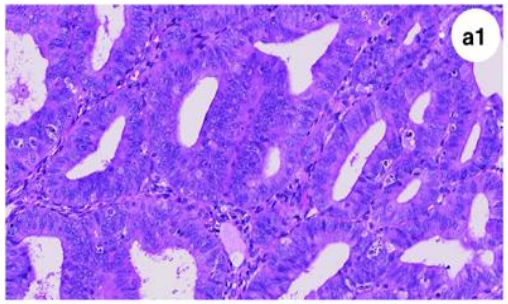
Endometrial Cancer Statistics

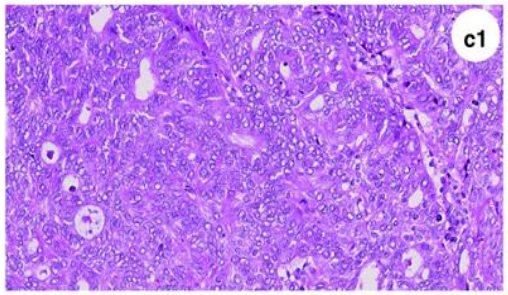


SEER 1996-2002, NCI 2006

Endometrial Cancer Grading

- Grade 1 <5% solid component
- Grade 2 5-50% solid component
- Grade 3 >50% solid component





Benedet, et al. International Journal of Gynecology and Obstetrics 2000;70:207-312

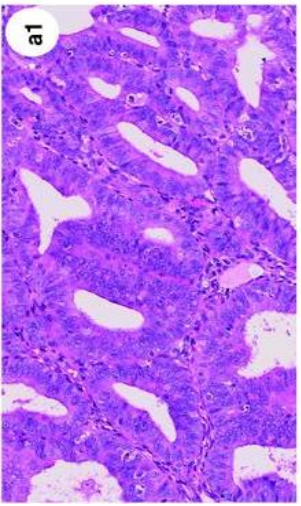
Histology in GOG Advanced and Recurrent Endometrial Cancer Chemotherapy Trials

1. Endometrioid = 52%
2. Serous = 18%
3. Mixed = 9%
4. Clear Cell = 4%
5. Other = 18%

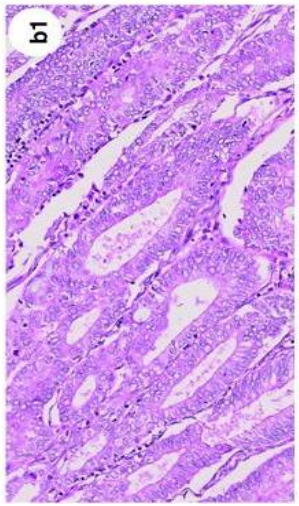
McMeekin DS et al Gynecol Oncol. 2007 Jul;106(1):16-22.

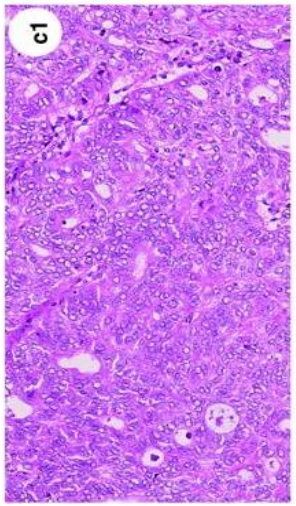
Endometrial Cancer Histologies

Normal endometrium

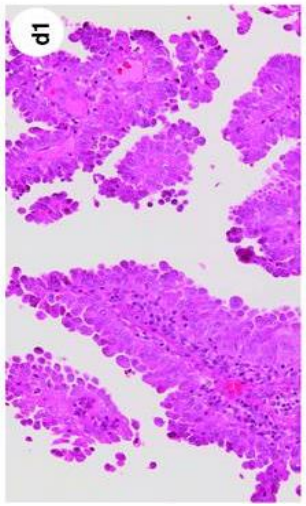


Grade 1 endometrioid

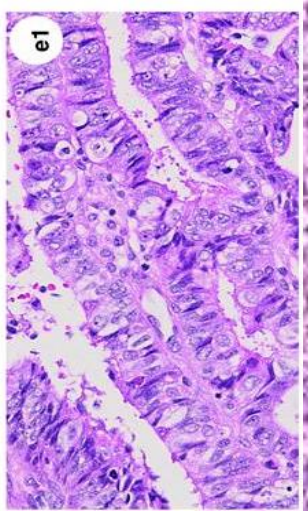


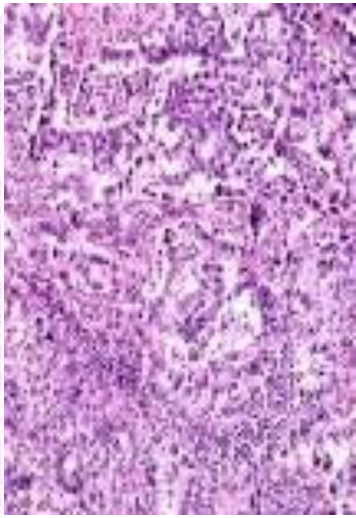


Grade 3 endometrioid



Serous





Clear Cell

Type I vs. Type II Endometrial Cancer

	Type I	Type II
Hormonal Impact	ER Dependent	ER Independent
Histology	Endometrioid	Serous, Clear Cell, Carcinosarcoma
Patient	Younger, Obese, Peri-menopausal	Older, Thin, Postmenopausal
Distribution	85%	15%
Mutations	Kras, PTEN, MLH1	P53, erbB2

THE UNIVERSITY OF ARIZONA Cancer Center

Dignity Health. St. Joseph's Hospital and Medical Center

Dinkelspiel H et al Ob Gyn Intl 2014

Endometrial Cancer Symptoms

- Irregular Vaginal Bleeding
- Postmenopausal Bleeding
- Uterine mass or Adnexal Mass
- Abdominal/pelvic Discomfort

Endometrial Cancer Risk Factors

- Changes or fluctuations in the balance of hormones
- Irregular ovulation patterns
- Taking hormones after menopause that contain estrogen but not progesterone
- A rare type of ovarian tumor that secretes estrogen
- Starting menstruation at an early age — before age 12 — or beginning menopause later
- Never having been pregnant
- Older age
- Obesity
- Hormone therapy for breast cancer
- An inherited colon cancer syndrome, known as Lynch syndrome or Hereditary nonpolyposis colorectal cancer (HNPCC)

Detecting Endometrial Cancer

- Surgical Risk Assessment
- Review of Systems
- Physical Exam
  - Abdominal
  - Pelvic
  - Nodal survey
- Imaging

Screening

- Not cost-effective
  - Low incidence
  - Invasive test (EMB)
  - Poor sensitivity
  - Symptoms in early stages

- Recommended only for HNPCC patients
  - Education
  - TVUS (EML <5 mm, <5% chance cancer)
  - Endometrial biopsy

Endometrial Cancer
Surgical Staging

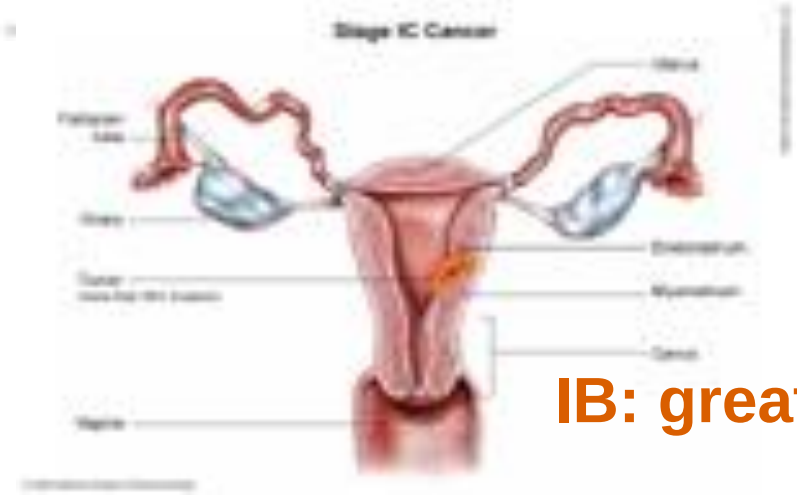
- Minimum Procedure
  - Total hysterectomy (Radical advocated, cervical dz)[1]
  - Bilateral salpingoophorectomy
  - +/- pelvic lymph node dissection
- Approach-open vs laparoscopic (standard or robotic)

1. Mariani, et al. Gynecol Oncol. 2001 Oct;83(1):72-80

Endometrial Cancer
Stage I-confined to corpus

5-Year Survival Percentage
81-91% Survival Rate

IA: less than 50% myometrial invasion



IB: greater than 50% myometrial invasion

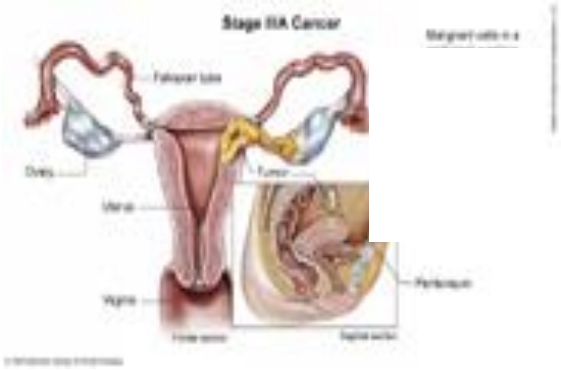
Endometrial Cancer
Stage II -Cervical involvement

5-Year Survival Percentage
71-79% Survival Rate

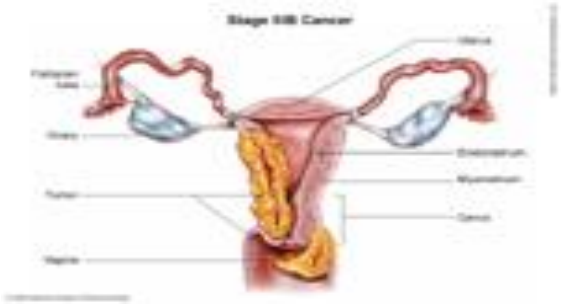
II: cervical stromal involvement

Endometrial Cancer
Stage III -Pelvic/nodal spread

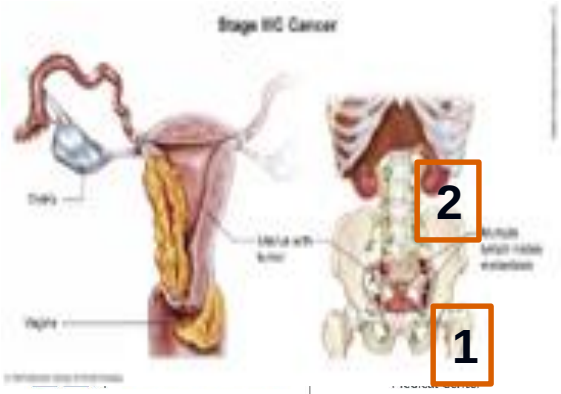
5-Year Survival Percentage
30 - 60 % Survival Rate



IIIA: serosal spread
adnexal metastases



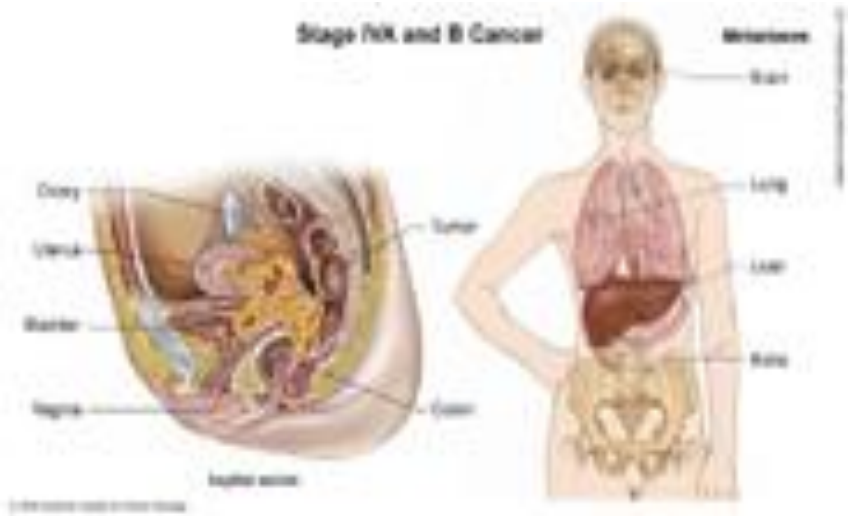
IIIB: vaginal metastases
parametrial involvement



IIIC1: pelvic nodal metastases
IIIC2: para-aortic nodal metastases

Endometrial Cancer
Stage IV -Metastatic Disease

5-Year Survival Percentage
15-17% Survival Rate



IVA=direct extension
- **anterior: bladder**
- **posterior: rectum**

IVB=distant metastasis
- **upper abdomen**
- **omentum**
- **bone, lung, brain**
- **groin lymph nodes**

Low-Risk, Early-Stage Treatment Options

- IA Grade 1 or 2
- IB Grade 1 or 2
- Considered cured with surgery
- 5-year survival=95%
- No further treatment required

Early-Stage, High-Risk Treatment Options

- Outer-third myometrial invasion
- Grade 2 or 3
- Cervical involvement
- Lymphvascular invasion
- Age ≥ 50
- Age ≥ 70

Ovarian Cancer

Brief Introduction

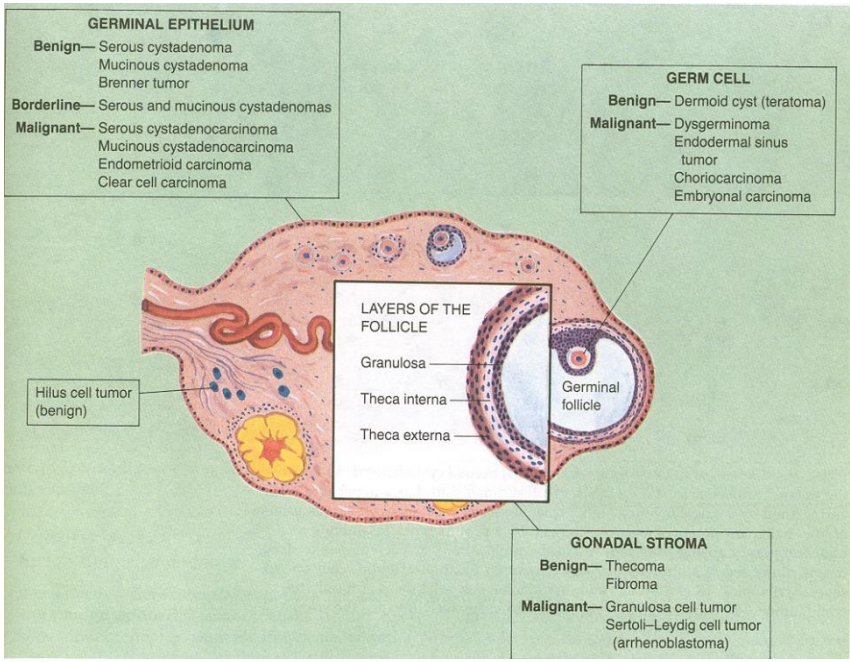
THE UNIVERSITY OF ARIZONA Cancer Center
Dignity Health. St. Joseph's Hospital and Medical Center

What is Ovarian Cancer?

Three types of cancer
- Epithelial
- Germ cell
- Stromal

Epithelial tumors are of mesodermal origin
- Same as primary peritoneal cancer

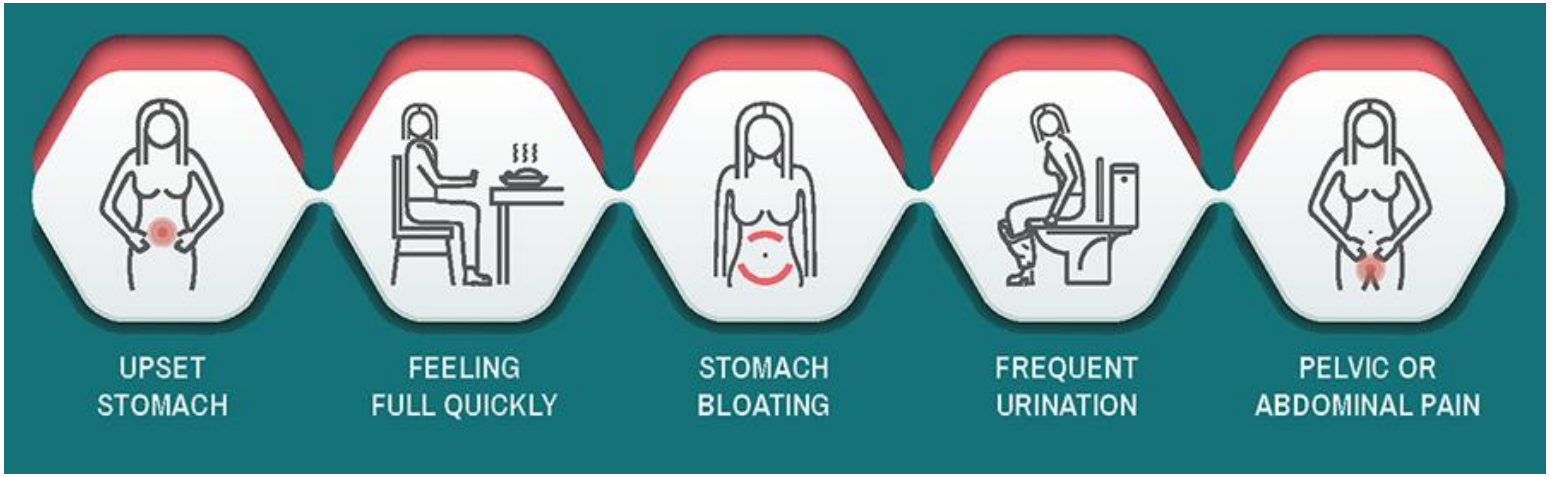
Epithelial cancers related to ovulatory events which increase mutation frequency
- Reduced by OCPs, Pregnancy or Lactation



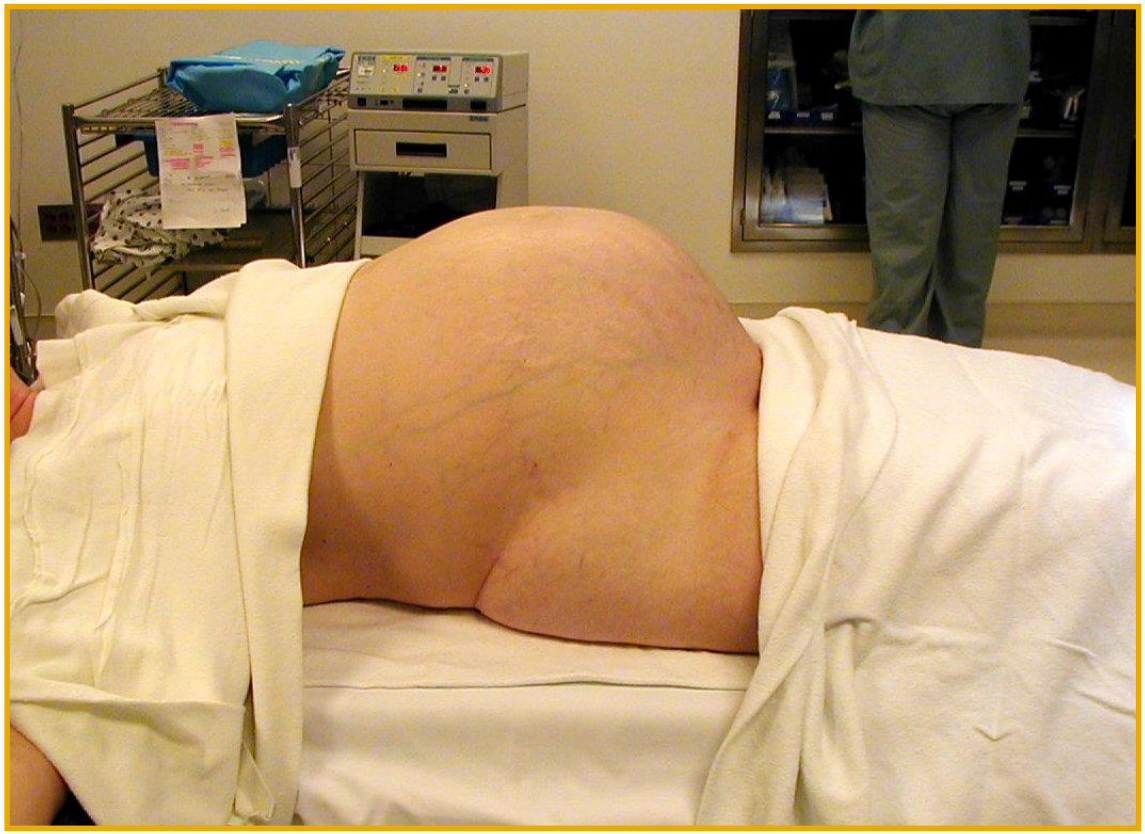
Ovarian Cancer Symptoms

CONSENSUS STATEMENT:

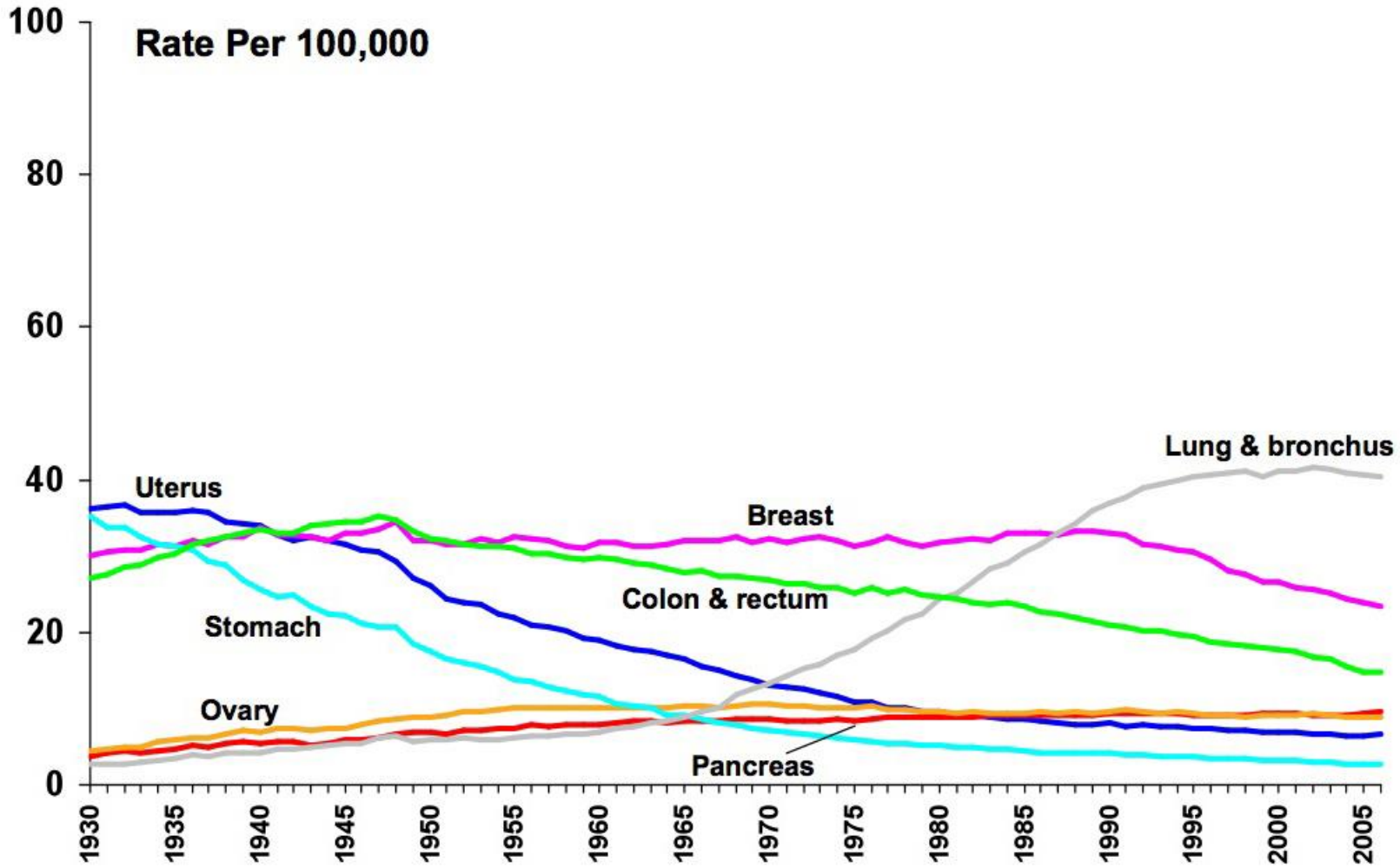
Some can have no symptoms in the early stages, but the following symptoms are more likely to occur in women with ovarian cancer than the general population:



Patient with Ovarian Cancer



Cancer Death Rates* Among Women, US,1930-2006



*Age-adjusted to the 2000 US standard population.
Source: US Mortality Data 1960-2006, US Mortality Volumes 1930-1959,
National Center for Health Statistics, Centers for Disease Control and Prevention, 2009.

Ovarian Cancer — Current Landscape[1]

- **Ovarian cancer is the 8th most common cancer among US women and 3rd most common female cancer in Arizona**
  - Accounts for ~3% of all cancers in women
  - Median age at diagnosis is 63[2]
- Highest mortality rate of all gynecologic cancers
  - Ranks 5th in cancer-related deaths among US women
    - 1-year survival (after diagnosis): ~76%
    - 5-year survival (after diagnosis): ~45%
- **Early diagnosis and treatment lead to much-improved outcomes**
  - 5-year survival if treated before cancer has spread outside the ovary (stage IA, IB): 93%
  - However, only 19% of all cases are detected at this stage

1. *Cancer Facts & Figures 2008.* American Cancer Society; 2008:4-16.
2. SEER Cancer Statistics Review. 1975-2004.

Treatment Options for Ovarian Cancer

Surgery

- Staging (early stage lesions) followed by biopsies of peritoneum and lypmphadenectmy)
- Debulking (advanced lesions) with possible bowel resection

Intraperitoneal Chemotherapy (acceptable but uncommon)

- Administering more than 6 cycles
- Weekly dosing
- Docetaxel instead of paclitaxel
- Adding a targeted agent (e.g. bevacizumab)
- Reassessment surgery (e.g. second look laparotomy)
- Maintenance or consolidation chemotherapy after complete remission
- Growth factors

Strategies for Cancer Risk-Reduction

- Screening
- Chemoprevention
  - Oral contraceptives
    - Risk reduction proportional to duration of use
    - Large cohort, n=103,551
      - Ever-users RR=0.6 (95% CI 0.5-0.7)
      - Long-term users (≥15 years) RR=0.1 (95% CI 0.01-0.6)
    - Lesser protection with progestin-only methods
- Preventive Surgery
  - Prophylactic oophorectomy
  - Tubal ligation (Not for BRCA1/2 carriers)

Kumle, Br J Cancer; 2004.

Importance of Family History in Ovarian Cancer

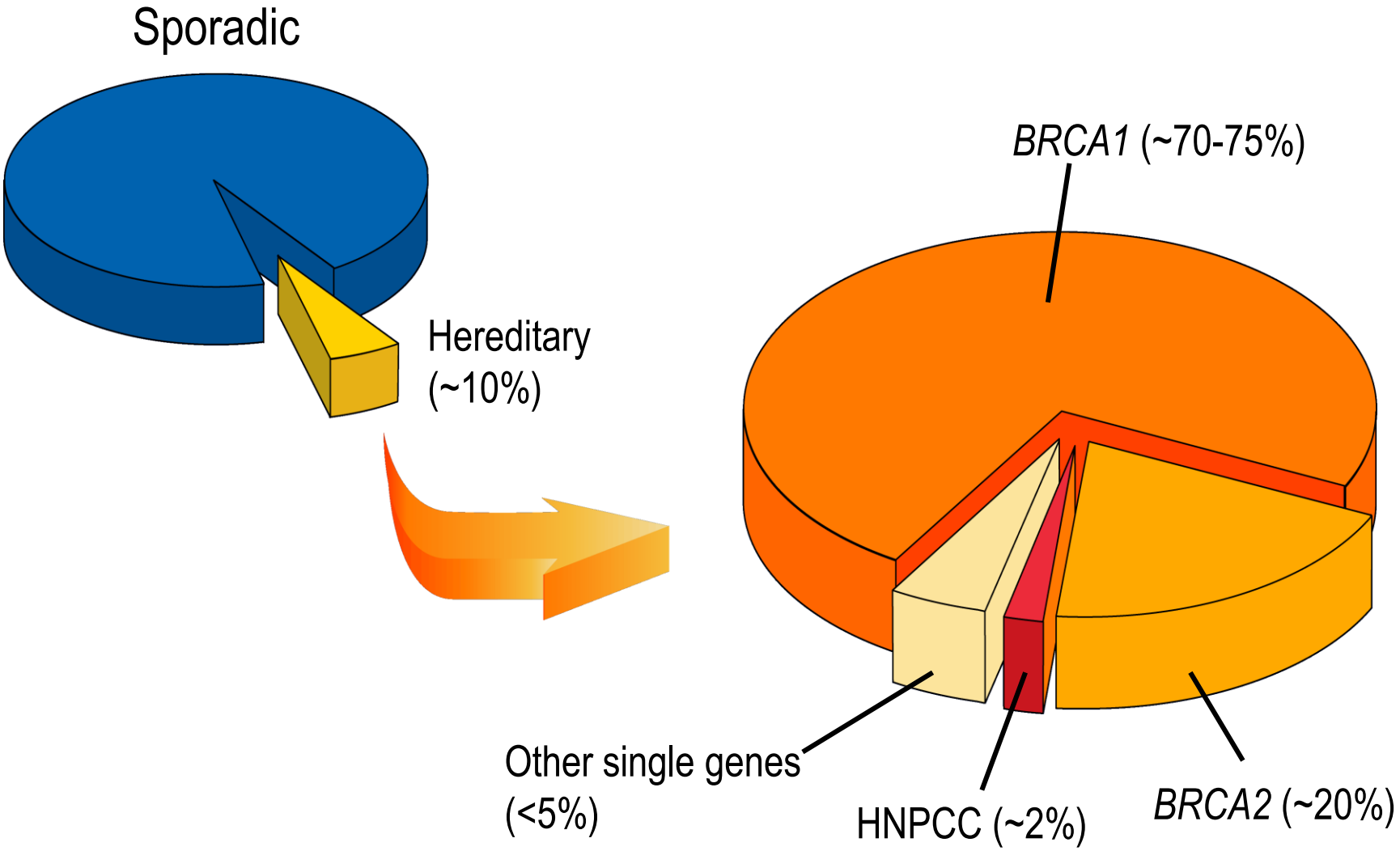
"By far the most important risk factor [in ovarian cancer] is family history"

Weissman et al, 2012

However, younger age? Histology? Mutations?

- *1 first-degree relative →*
  - *Risk increases from 1.4% lifetime risk to 5%*
- *2+ → 7%*

Causes of Hereditary Susceptibility to Ovarian Cancer



Ovarian Cancer Heterogeneity (in mutations and genetics)

2 types or 5 types (*Kurman versus Prat*)

1. **5 types**: low grade, high grade, endometrioid, clear cell, mucinous
2. **Type I**: low grade, clear cell, endometrioid
   - Mutations = KRAS, BRAF, PTEN, PIK3CA, ERBB2

   Type II: high grade, undifferentiated
   - Genomic instability

– P53 mutation, inactivation of BRCA ½, CCNE1 amplification

Genetic Syndromes Associated with Ovarian Cancer

1. BRCA 1 and 2
2. Li Fraumeni
3. Lynch
4. Peutz-Jegher
5. Others?

SGO Guidelines:
Patients Who Should Be Referred For Genetic Counseling

- Women with a personal history of both breast and ovarian cancer
- Women with ovarian cancer and a close relative with breast cancer at ≤ 50 years or ovarian cancer at any age
- Women with ovarian cancer at any age and Ashkenazi ancestry
- Women with breast cancer at ≤ 50 years and a close relative with ovarian or male breast cancer at any age
- Women of Ashkenazi ancestry and breast cancer at ≤ 40 years
- Women with a first or second degree relative with a known *BRCA1* or *BRCA2* mutation

Lancaster et al. Gynecol Oncol 2007

Ovarian Cancer Screening: Exam

- Non-invasive test
- Requires rectal and vaginal examination
- Inefficient
- Hasn’t proved to reduce cancer-related mortality
- High-risk women require 2 per year
- PLCO study recently dropped this as an aspect of screening

Ovarian Cancer Screening—CA-125

- Conditions that elevate CA-125:

Cancers	Diseases	Conditions
Ovarian Cancer	Uterine Fibroids	Pregnancy
Uterine Cancer	Endometriosis	Mid menstrual cycle
Colon Cancer	Pelvic Inflammatory Disease	
Breast Cancer	Liver failure	
Stomach Cancer	Kidney failure	
Liver Cancer	Alcoholism	
	Peritonitis	
	Pancreatitis	

Challenges for the Future - Physicians

- Can we better identify individuals who will benefit from risk-reducing surgery as well as individuals for whom novel risk-reduction approaches are needed?
- Can we make improvements in gynecologic cancer screening to allow this to become a viable alternative to risk-reduction surgery?
- Can we use germline genetic information to better target therapies and minimize toxicities in women with gynecologic cancers?
- Will advances in chemoprevention as well as our basic understanding of the molecular progression of hereditary gynecologic cancer ultimately allow us to eliminate the burden of these inherited cancers entirely?

Challenges for You

1. **Increase employer-sponsored programs and access to resources** so more and more women and men are aware of gynecologic cancers, symptoms, and novel treatment options, i.e., robotic surgery
2. **Invite expert speakers** to talk about GYN cancers during the awareness months, i.e., January is cervical cancer awareness month and September is ovarian cancer
3. **Provide options for genetic testing** through health plans for employees
4. **Continue to sustain a health conscious workplace** by encouraging healthy lifestyles
5. **Support employees and loved ones** going thru treatment or surgical procedures

Thank You!

For more information about gynecological cancers or to request a speaker for your worksite or organization on any cancer-related topic **Call: 602.699.3366**

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