



THE UNIVERSITY OF
TENNESSEE
HEALTH SCIENCE CENTER.

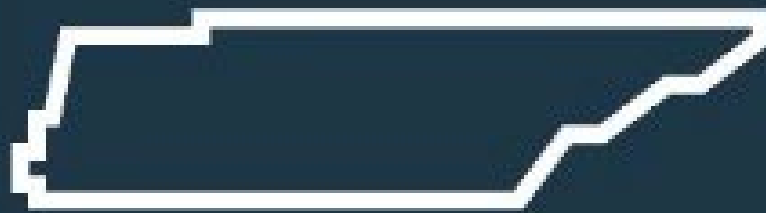
Cervical Cancer: The Road to Perdition

John O Schorge, MD, FACS

Cancer survival has improved since the mid-1970s for all of the most common cancers except uterine cervix and uterine corpus, largely reflecting the absence of major treatment advances for these cancers.'

CA Cancer J Clin 2023



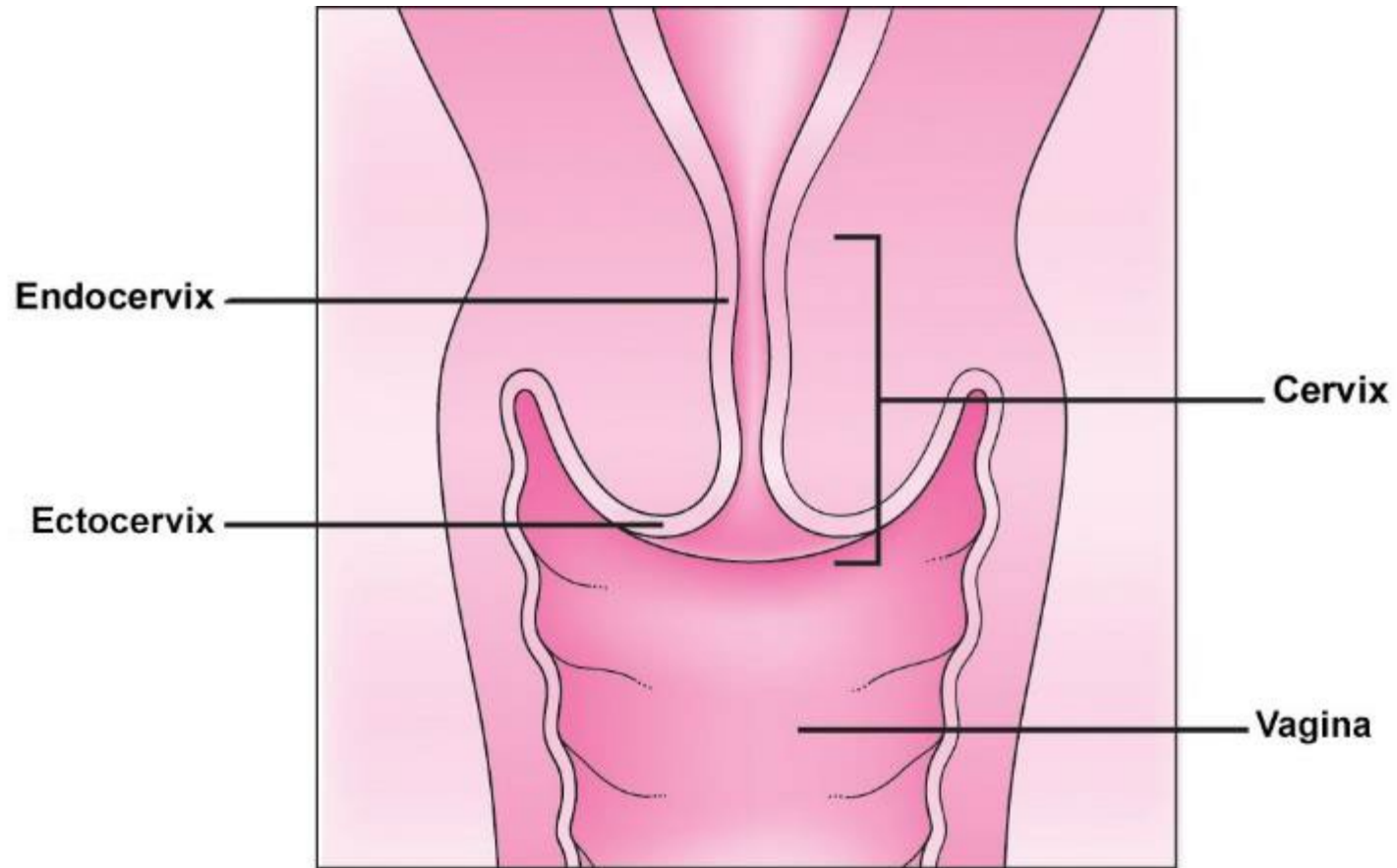


RATES IN TENNESSEE

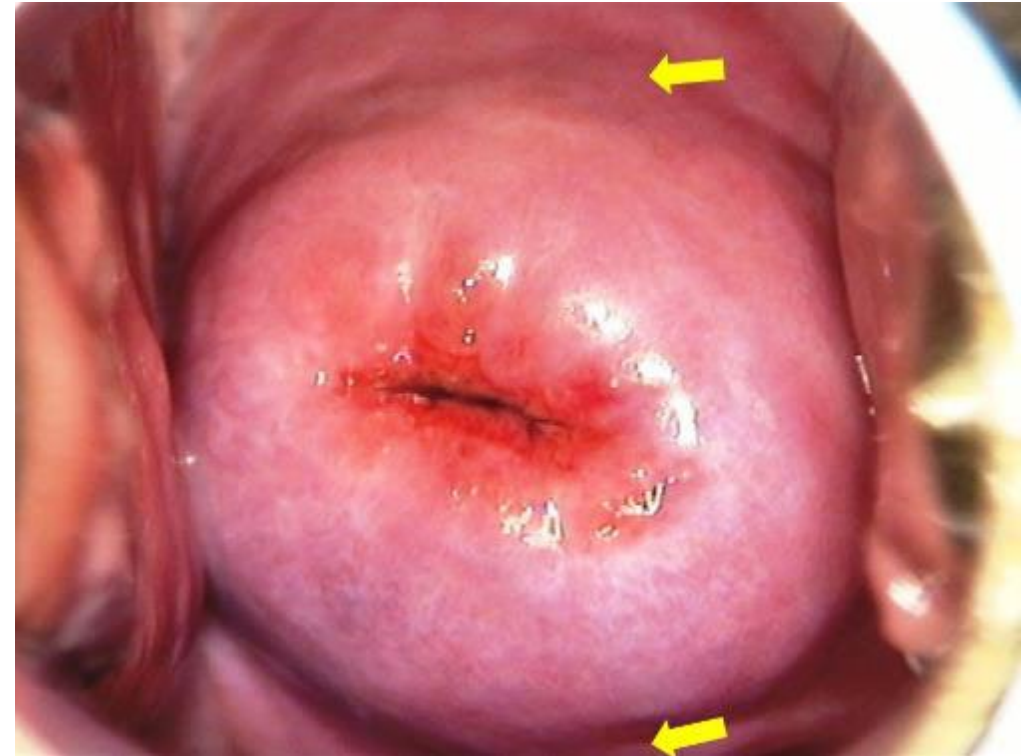
Every day in Tennessee, a woman is diagnosed with cervical cancer, and every 3 days one dies from the disease.

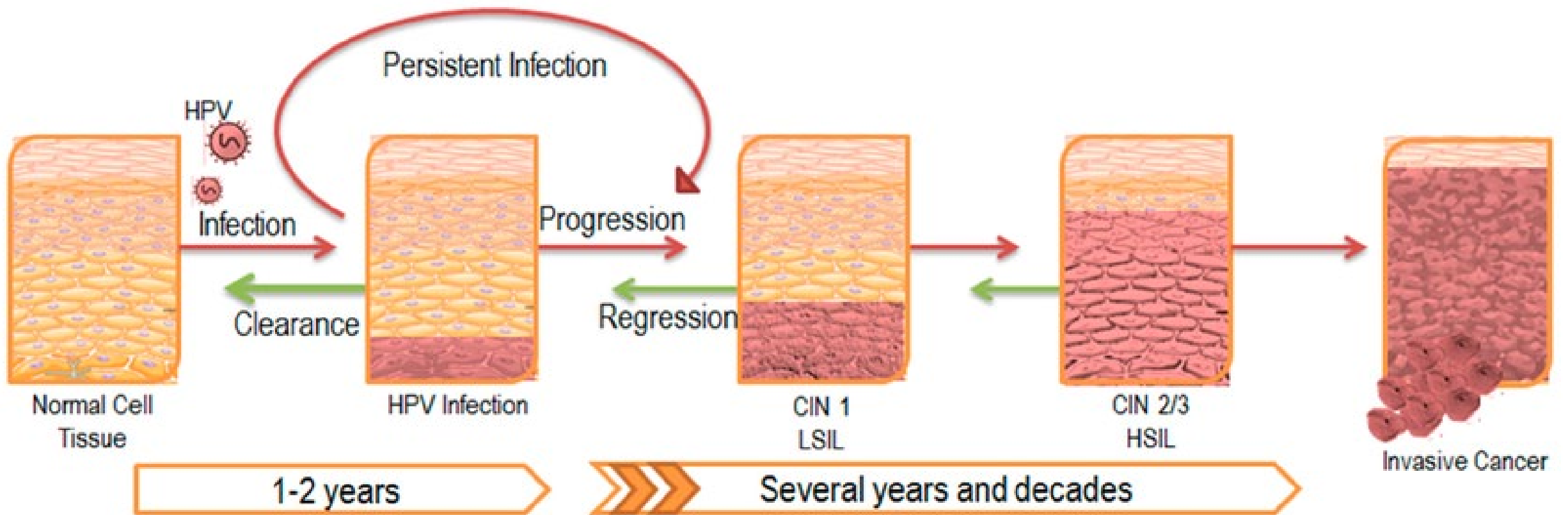
ROAD TO
PERDITION

Features of the cervix



© Jo's Cervical Cancer Trust







CANCER OF THE CERVIX

The cervix connects the vagina to the upper part of the uterus. Any individual with a cervix can develop cervical cancer; however, those with some risk factors have a higher chance of developing cervical cancer.

Did you know that cervical cancer is one of the few cancers that has pre-cancerous cells (cells that are not yet cancerous) that can be treated to prevent the development of cervical cancer?



Risk Factors



Cervical cancer risk factors^[17-19]

Genital Infection with high risk human papillomavirus

HIV infection

Smoking

Younger age at first sexual intercourse

Greater number of sexual partners

Oral contraceptives use greater than 5 yr

Having 4 or greater full-term pregnancies

History of sexual transmitted diseases

HIV: Human immunodeficiency virus.

RISK FACTORS FOR CERVICAL CANCER



SMOKING

Did you know that smoking and tobacco use increase your risk of developing cervical cancer? If you quit smoking or using tobacco products, you can reduce your risk.

To get more information on quitting, please call 800-QUIT-NOW or go to <https://www.tn.gov/health/health-program-areas/fhw/tobacco.html>



HPV INFECTION

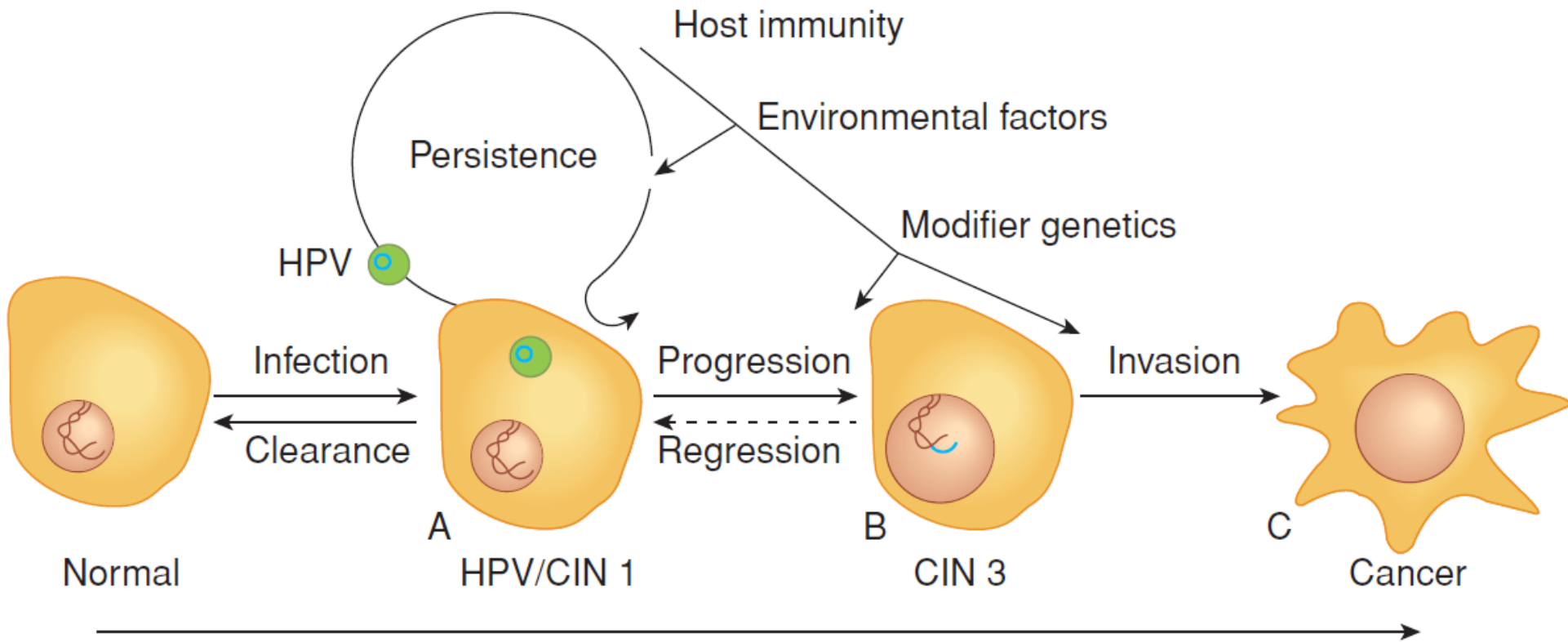
Did you know that the Human Papillomavirus (HPV) causes over 90% of all cervical cancers? By getting vaccinated against HPV, you can reduce your risk.

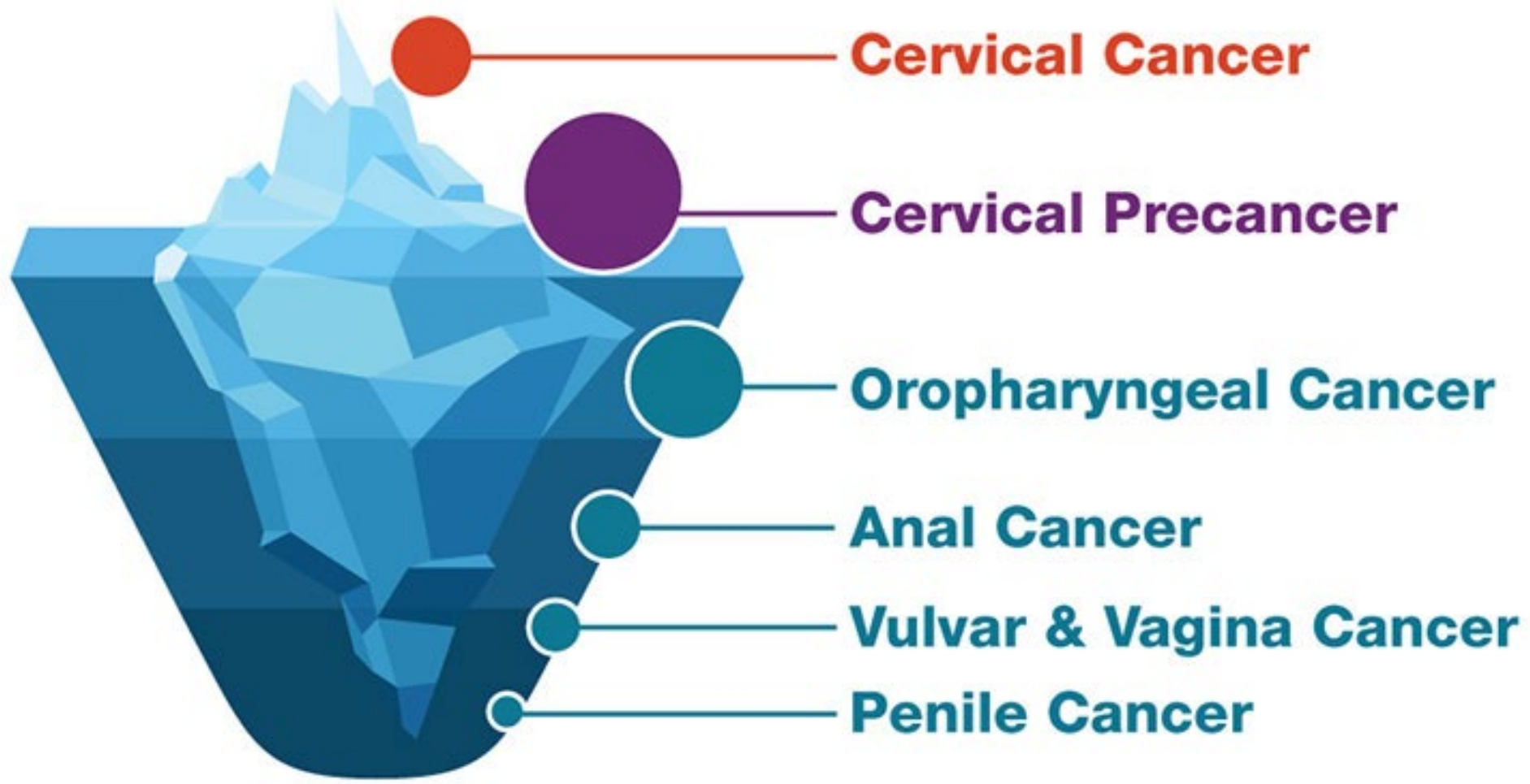
For more information on the HPV Vaccine visit <https://www.cdc.gov/hpv/>



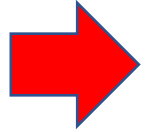
TO LEARN ABOUT OTHER RISKS TALK TO YOUR HEALTHCARE PROVIDER

The path to cervix cancer





Educational objectives



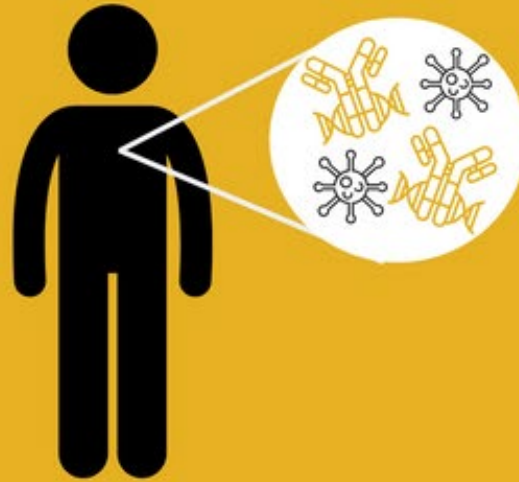
1. Gain knowledge of the current status of prevention strategies in the Mid-South region & across the country.
2. Become more aware of the most updated developments in screening for cervix cancer.
3. Describe the impact of health care disparities on outcomes and potential solutions.
4. Learn about novel therapies that are changing the paradigm of care for women with advanced disease.

preventable

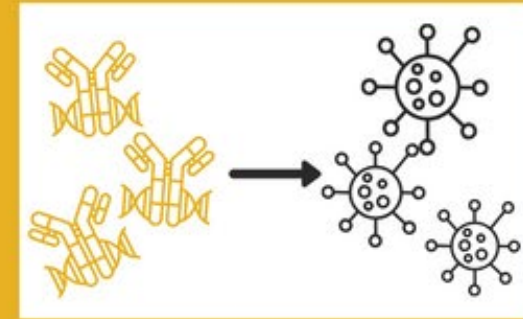
HOW THE HPV VACCINE WORKS



Vaccine introduces VLPs into body



The body produces antibodies to attack the VLPs



If HPV enters the body, the immune system produces those same antibodies and removes the infection

Learn more at www.nomancampaign.org

HPV VACCINE FACTS:



90%

Prevents 90% of HPV Cancers.



HPV vaccine can prevent at least 6 types of cancers.

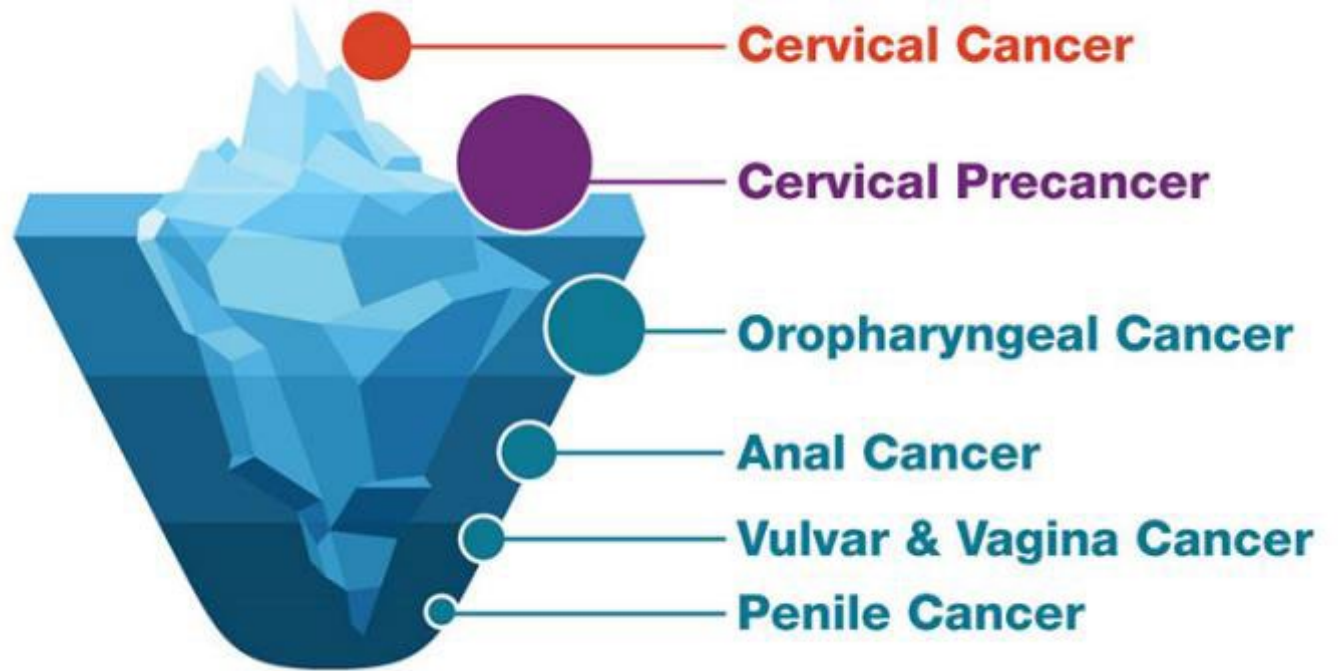


4 out of 5 people will get HPV in their lives.

ALABAMA
PUBLIC
HEALTH

IMM
IMMUNIZATION DIVISION

HPV vaccine is cancer prevention!



ORIGINAL ARTICLE

HPV Vaccination and the Risk of Invasive Cervical Cancer

Jiayao Lei, Ph.D., Alexander Ploner, Ph.D., K. Miriam Elfström, Ph.D.,
Jiangrong Wang, Ph.D., Adam Roth, M.D., Ph.D., Fang Fang, M.D., Ph.D.,
Karin Sundström, M.D., Ph.D., Joakim Dillner, M.D., Ph.D.,
and Pär Sparén, Ph.D.

ABSTRACT

BACKGROUND

The efficacy and effectiveness of the quadrivalent human papillomavirus (HPV) vaccine in preventing high-grade cervical lesions have been shown. However, data to inform the relationship between quadrivalent HPV vaccination and the subsequent risk of invasive cervical cancer are lacking.

METHODS

We used nationwide Swedish demographic and health registers to follow an open population of 1,672,983 girls and women who were 10 to 30 years of age from 2006 through 2017. We assessed the association between HPV vaccination and the risk of invasive cervical cancer, controlling for age at follow-up, calendar year, county of residence, and parental characteristics, including education, household income, mother's country of birth, and maternal disease history.

- Sweden
- 1.7 million
- 10 to 30 yrs

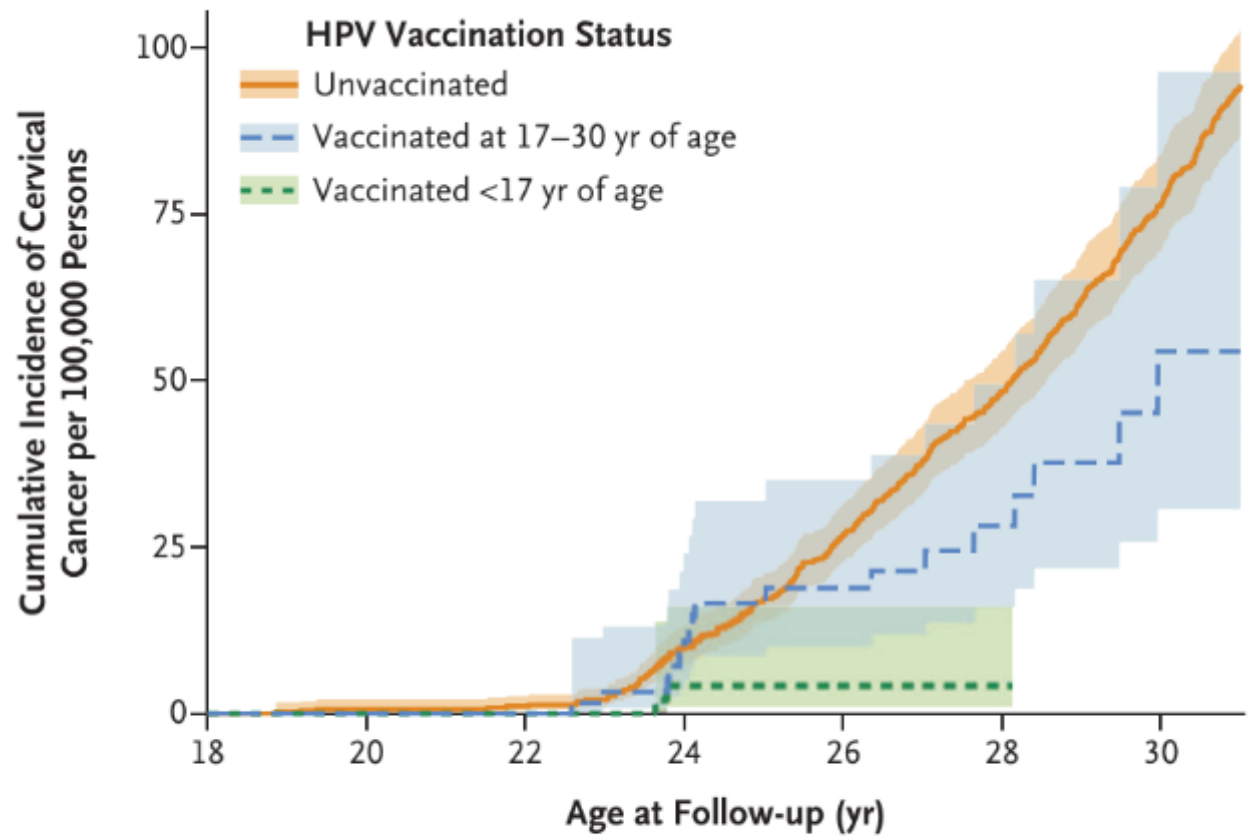
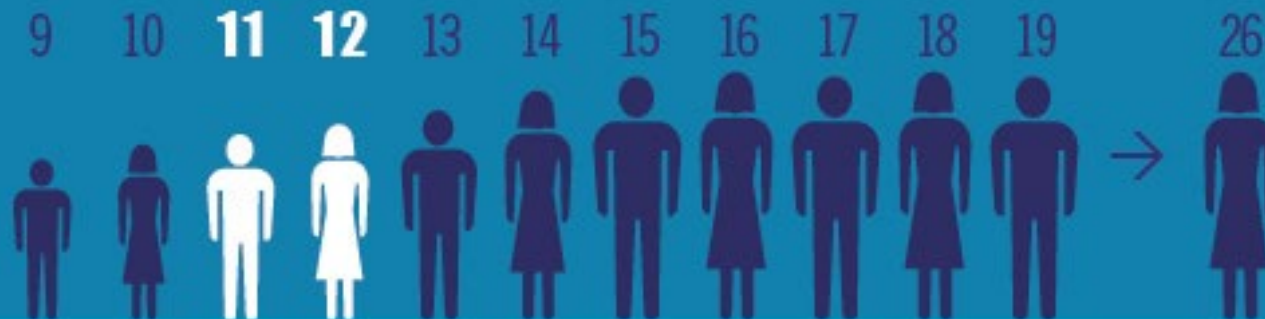


Figure 2. Cumulative Incidence of Invasive Cervical Cancer According to HPV Vaccination Status.

Age at follow-up is truncated in the graph because no cases of cervical cancer were observed in girls younger than 18 years of age.

HPV VACCINE IS BEST AT 11-12 YEARS

Preteens have a higher immune response to HPV vaccine than older teens.



While there is very little risk of exposure to HPV before age 13, the risk of exposure increases thereafter.

- 65% drop in cervical cancer incidence during 2012 through 2019 among women in early 20s
- 1st group to receive HPV vaccination series
- Foreshadows steep reductions in burden of HPV-associated cancer



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NATIONWIDE

**6^{OUT}
OF 10**

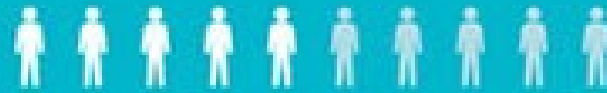
**GIRLS HAVE STARTED
THE HPV VACCINE SERIES**

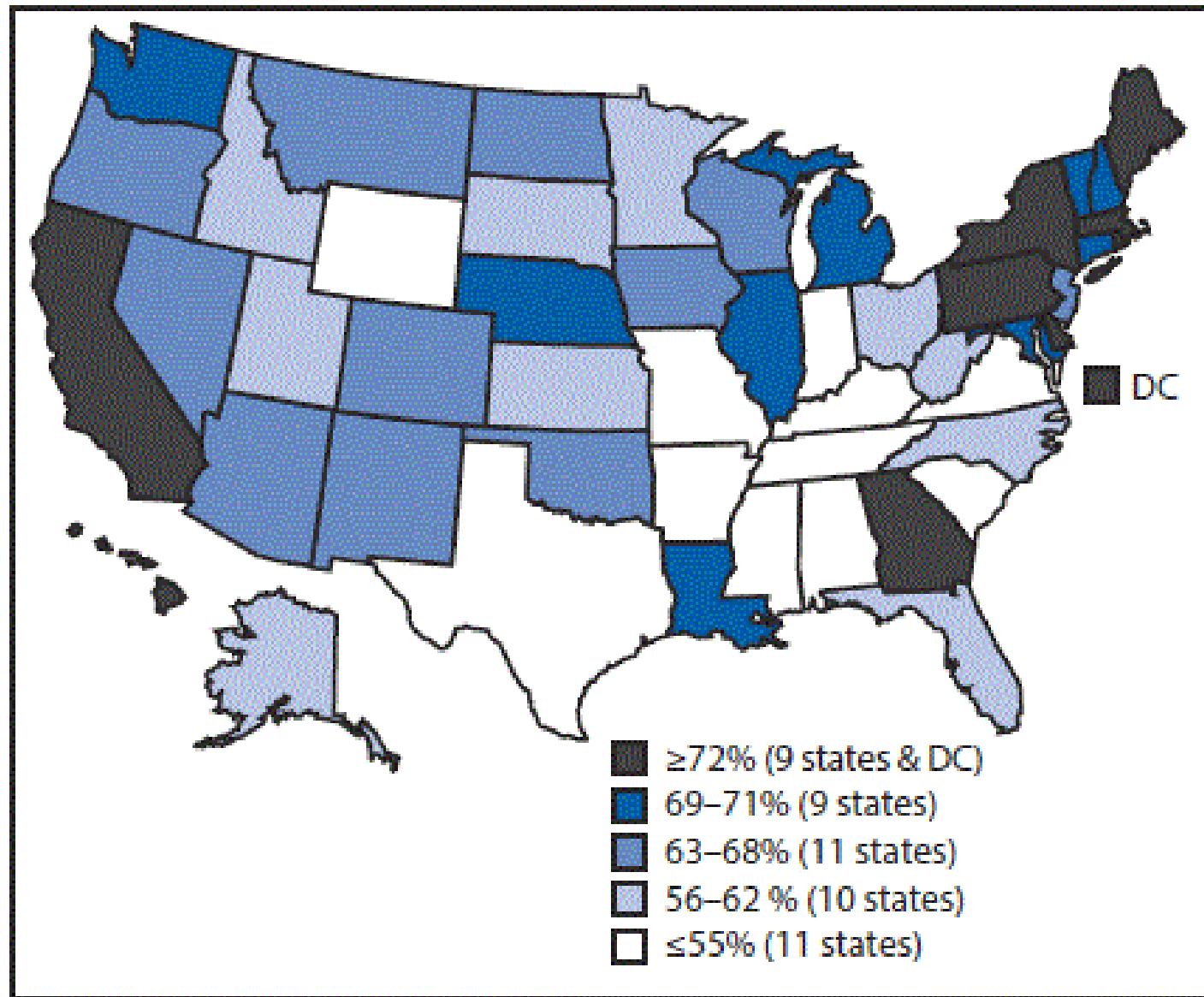


NATIONWIDE

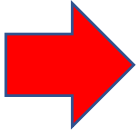
**5^{OUT}
OF 10**

**BOYS HAVE STARTED
THE HPV VACCINE SERIES**





Educational objectives

1. Gain knowledge of the current status of prevention strategies in the Mid-South region & across the country.
-  2. Become more aware of the most updated developments in screening for cervix cancer.
3. Describe the impact of health care disparities on outcomes and potential solutions.
4. Learn about novel therapies that are changing the paradigm of care for women with advanced disease.

SCREENING FOR CERVICAL CANCER

WHO SHOULD GET SCREENED

21-65

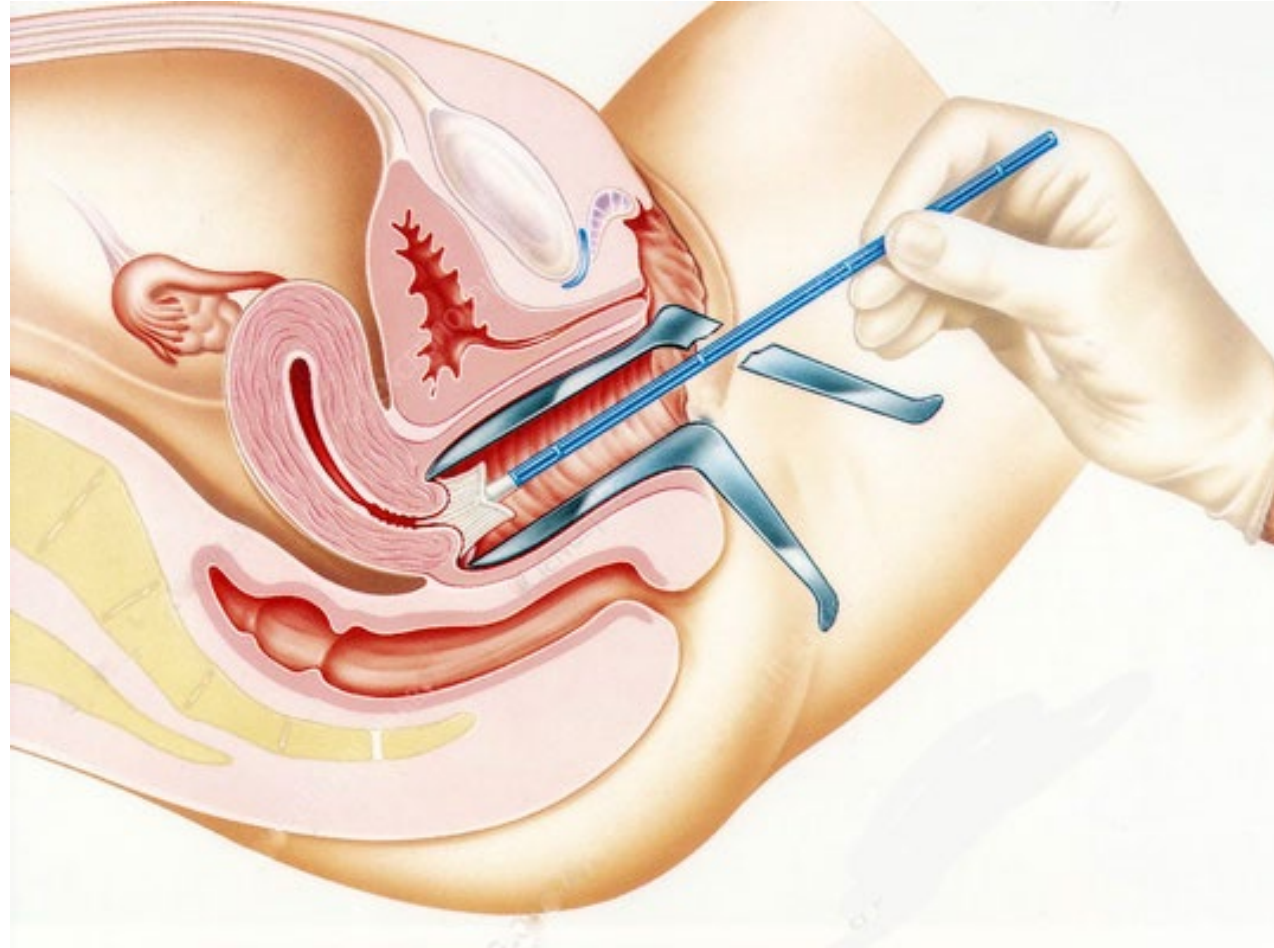
21-65 YEARS OLD

If you are 21-65 years old you should get a cervical cancer screening. This may include a cytology test (or a pap smear), an HPV test, or both.

Talk with your healthcare provider about what screening is right for you!



SCREENING FOR CERVICAL CANCER

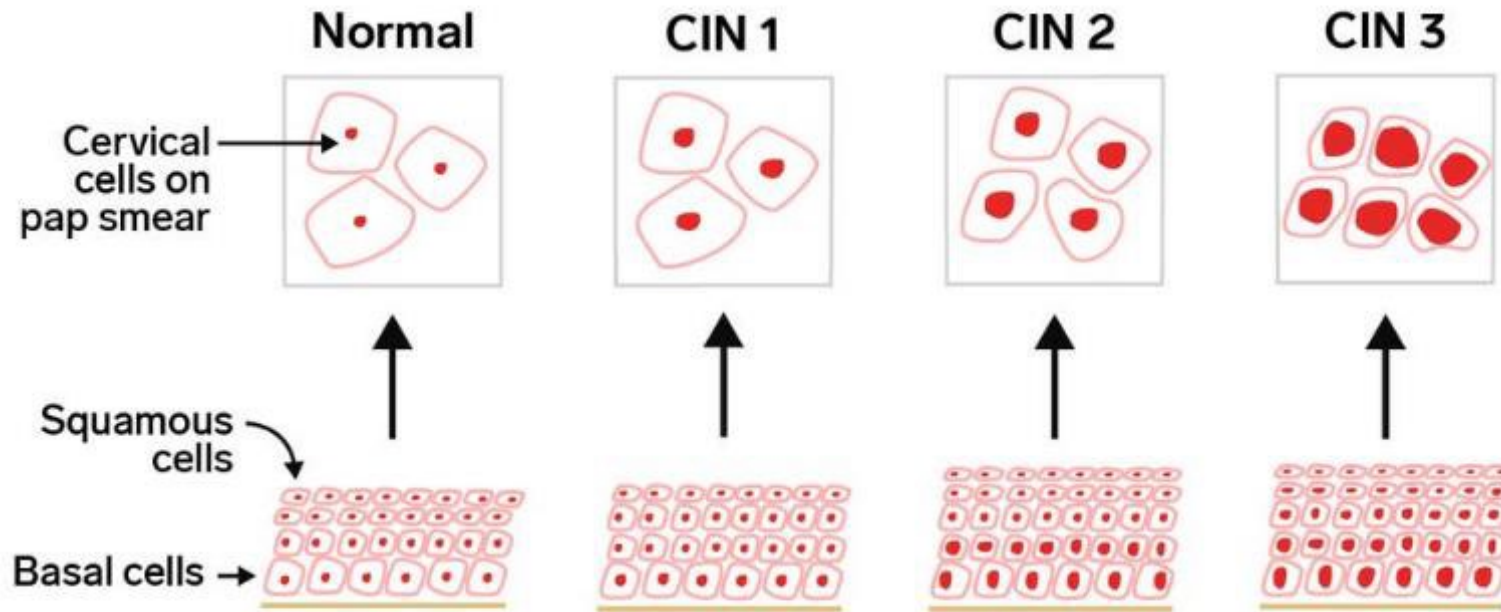


SCREENING FOR CERVICAL CANCER



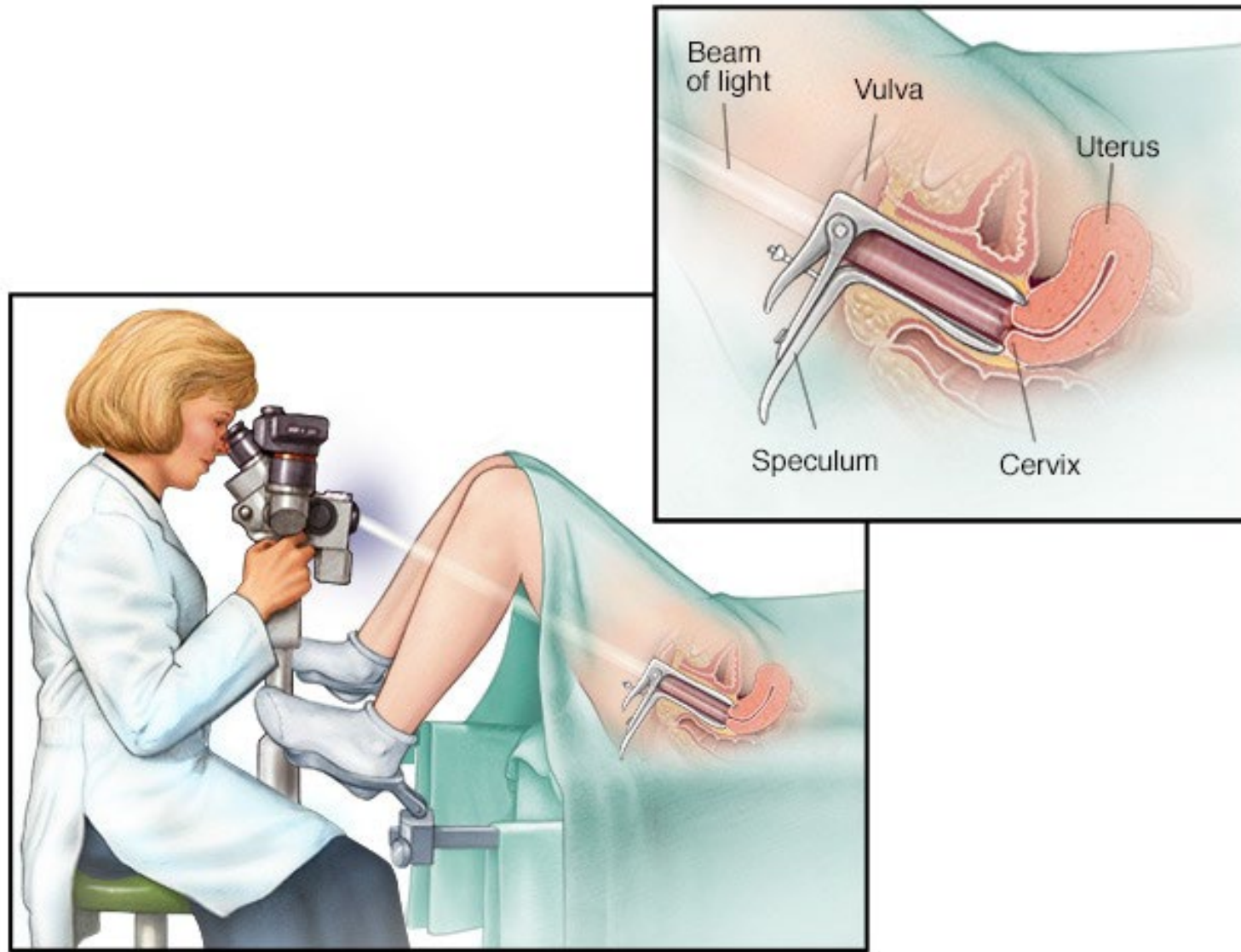
SCREENING FOR CERVICAL CANCER

Normal v.s. abnormal cervical cells

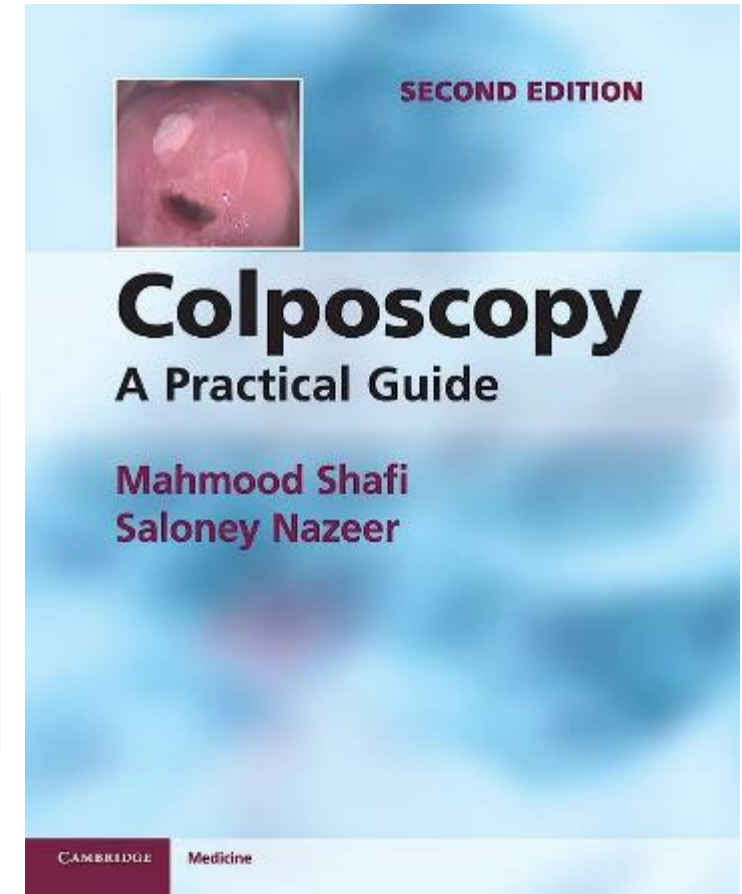


Source: Los Angeles Obstetricians & Gynecologists

INSIDER



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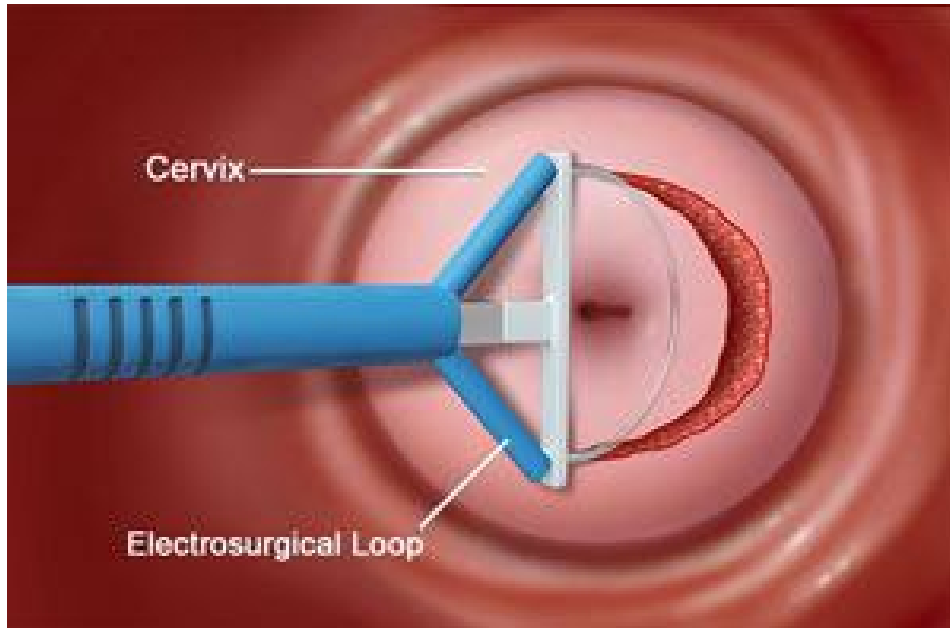


Center for HPV And Dysplasia (aka CHAD)

Linda Moses, MD & Marina Santa Cruz, MD



LEEP v CKC (Cold Knife Conization)



Squamous lesions (CIN3)



Figure 2. Fixation sutures are used at both sides, at 3 and 9 o'clock

Glandular lesions: (AIS – adenoca in situ)

ASCCP

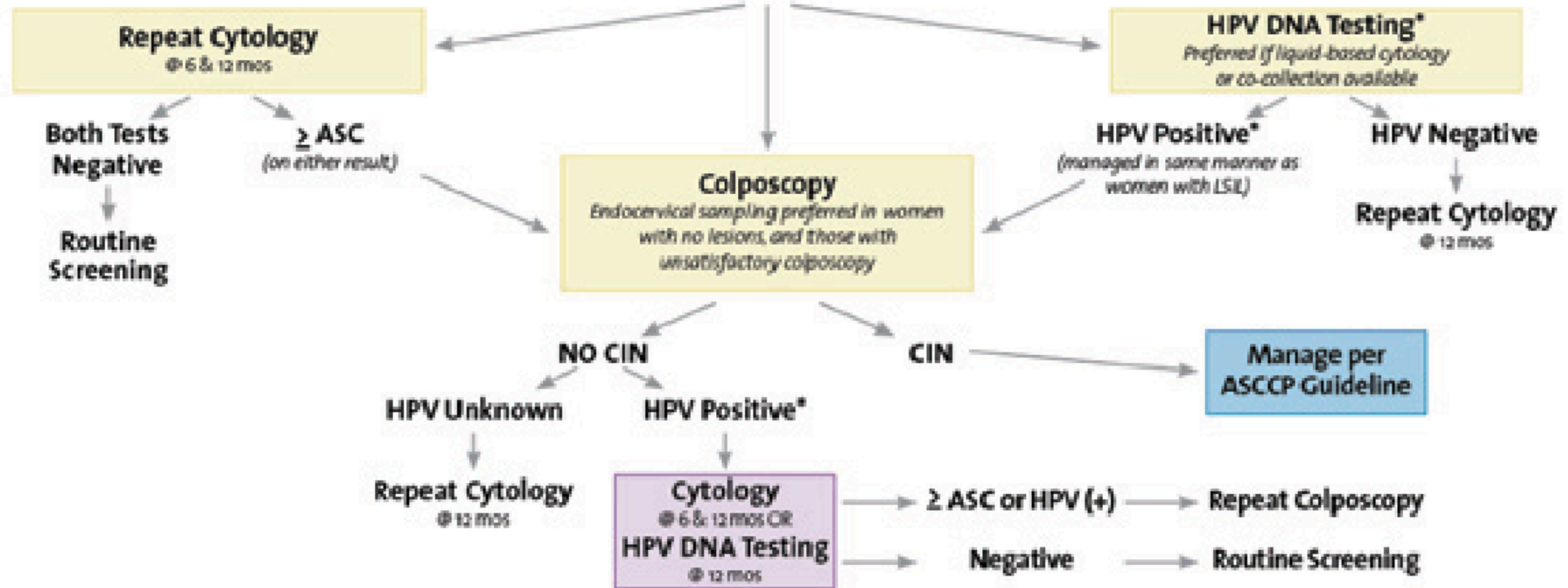
The society for lower genital tract disorders since 1964.

Algorithms

Updated Consensus Guidelines for
Managing Abnormal Cervical Cancer
Screening Tests and Cancer Precursors

American Society for Colposcopy and Cervical Pathology

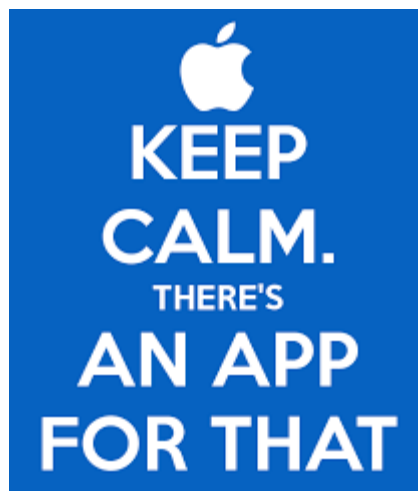
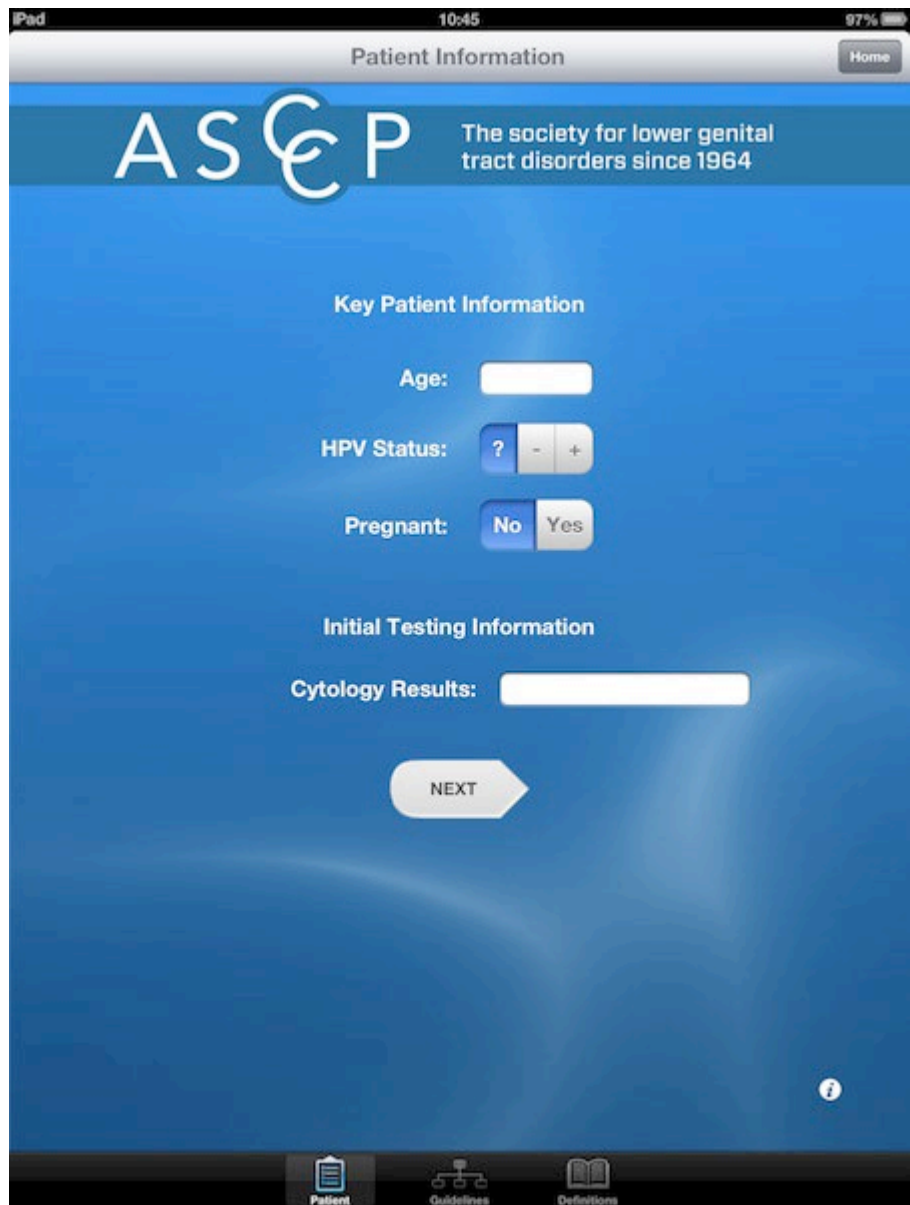
Management of Women with Atypical Squamous Cells of Undetermined Significance (ASC-US)



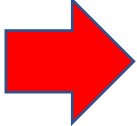
Copyright 2006, 2007, American Society for Colposcopy and Cervical Pathology. All rights reserved.

* Test only for high-risk (oncogenic) types of HPV

Figure 2 Management of women with atypical squamous cells of undetermined significance



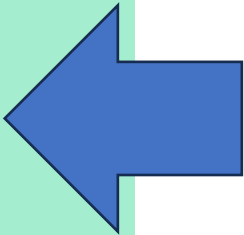
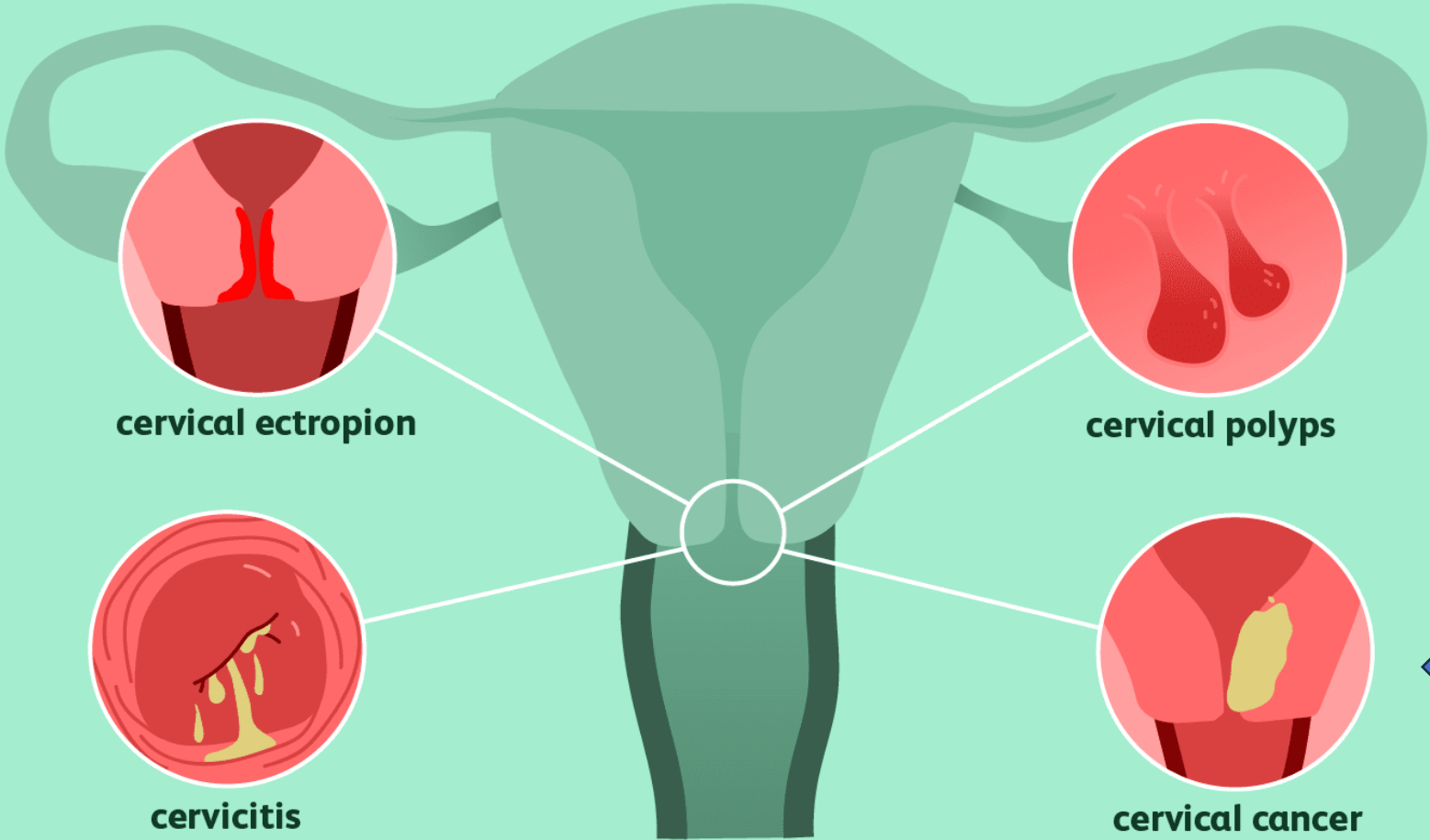
Educational objectives

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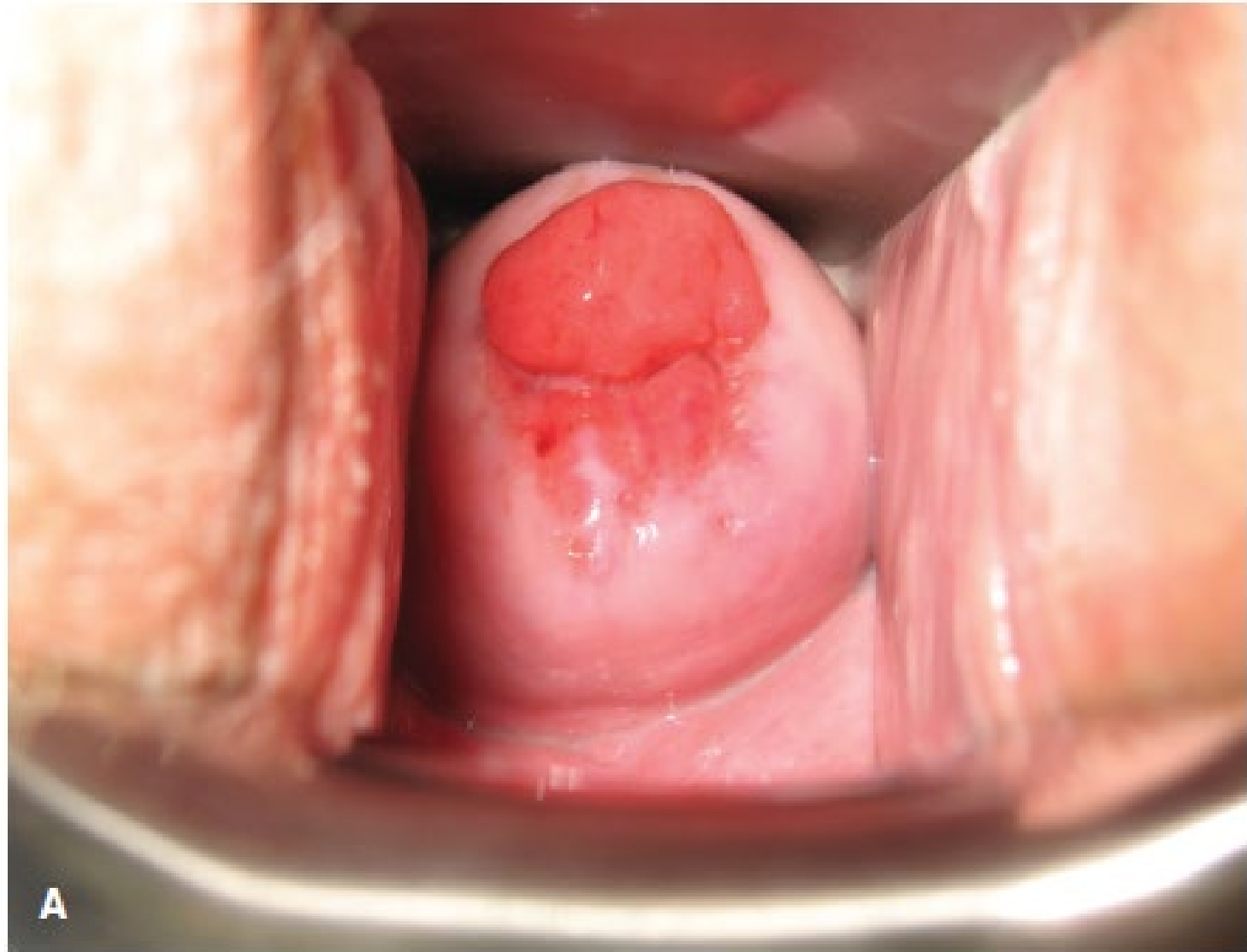
Survival rates are **lower** for Black patients than for White for every cancer type

Siegel RL, et al. Cancer statistics, 2022
CA Cancer J Clin 2022;72:7-33.

Causes of Cervical Bleeding After Sex



verywell

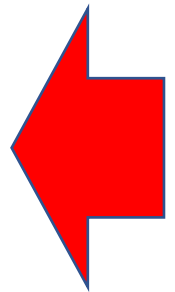
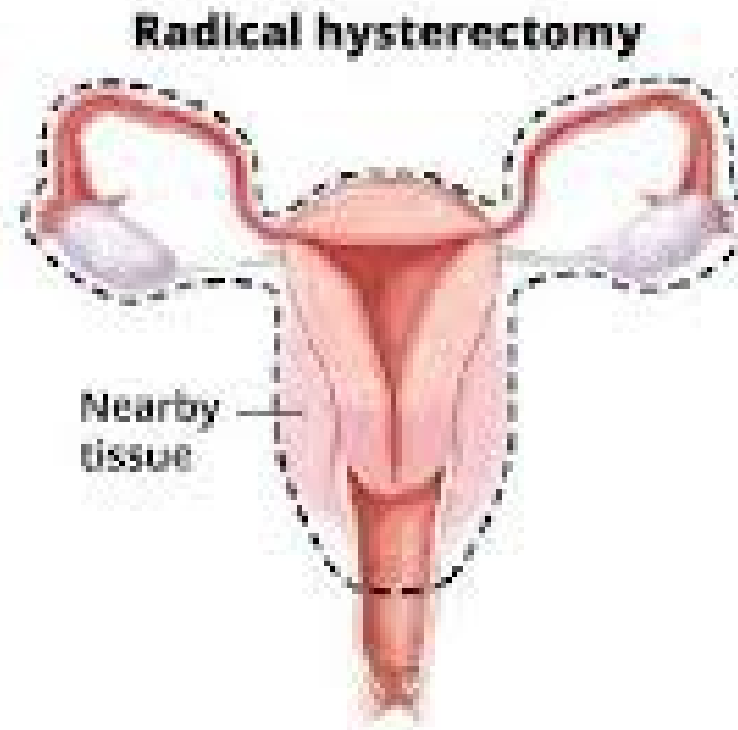
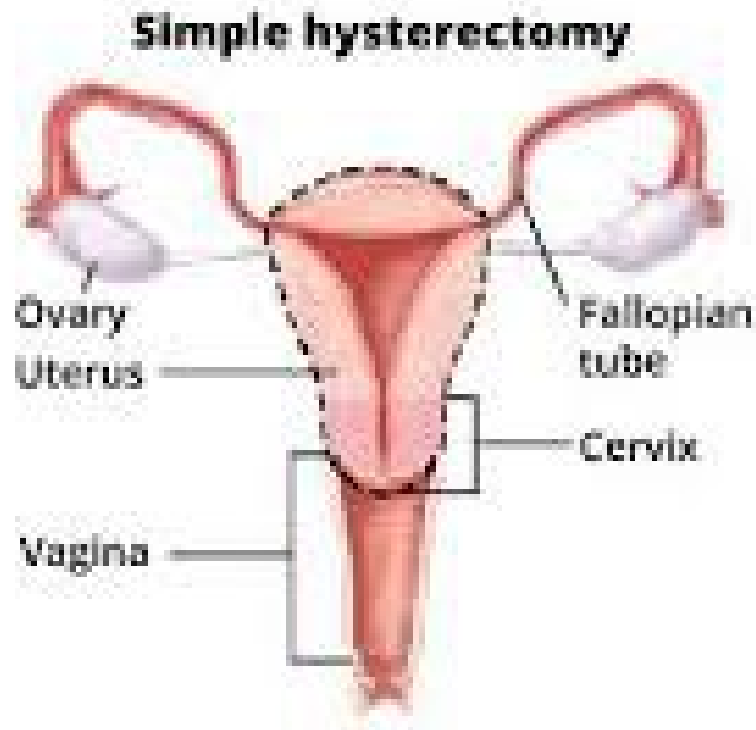


A

Types of cervical cancer



Cervix cancers require negative margins



Radical hysterectomy

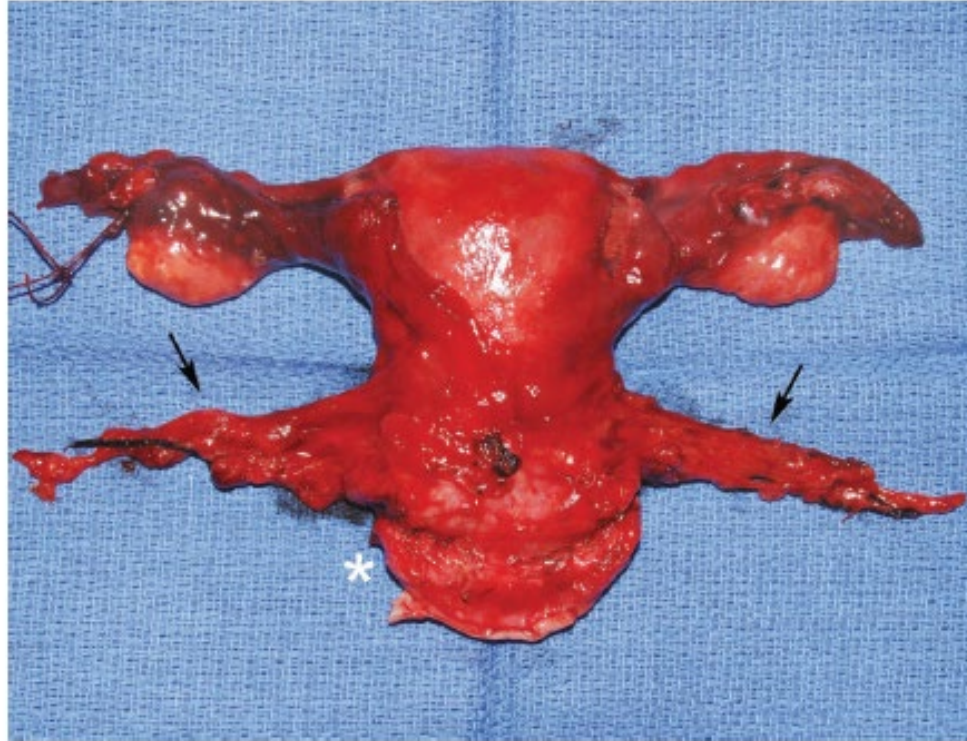


FIGURE 30-11 Gross surgical specimen following radical hysterectomy. The specimen includes the adnexa, uterus, parametria (*arrows*), and segment of proximal vagina (*asterisk*).

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

NOVEMBER 15, 2018

VOL. 379 NO. 20

Minimally Invasive versus Abdominal Radical Hysterectomy for Cervical Cancer

Pedro T. Ramirez, M.D., Michael Frumovitz, M.D., Rene Pareja, M.D., Aldo Lopez, M.D., Marcelo Vieira, M.D., Reitan Ribeiro, M.D., Alessandro Buda, M.D., Xiaojian Yan, M.D., Yao Shuzhong, M.D., Naven Chetty, M.D., David Isla, M.D., Mariano Tamura, M.D., Tao Zhu, M.D., Kristy P. Robledo, Ph.D., Val GebSKI, M.Stat., Rebecca Asher, M.Sc., Vanessa Behan, B.S.N., James L. Nicklin, M.D., Robert L. Coleman, M.D., and Andreas Obermair, M.D.

ABSTRACT

BACKGROUND

There are limited data from retrospective studies regarding whether survival outcomes after laparoscopic or robot-assisted radical hysterectomy (minimally invasive surgery) are equivalent to those after open abdominal radical hysterectomy (open surgery) among women with early-stage cervical cancer.

METHODS

In this trial involving patients with stage IA1 (lymphovascular invasion), IA2, or IB1 cervical cancer and a histologic subtype of squamous-cell carcinoma, adenocarcinoma, or adenosquamous carcinoma, we randomly assigned patients to undergo minimally invasive surgery or open surgery. The primary outcome was the rate of disease-free survival at 4.5 years, with noninferiority claimed if the lower boundary of the two-sided 95% confidence interval of the between-group difference (minimally invasive surgery minus open surgery) was greater than -7.2 percentage points (i.e., closer to zero).

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Ramirez at the Department of Gynecologic Oncology and Reproductive Medicine, Unit 1362, University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030, or at peramire@mdanderson.org.

This article was published on October 31, 2018, at NEJM.org.

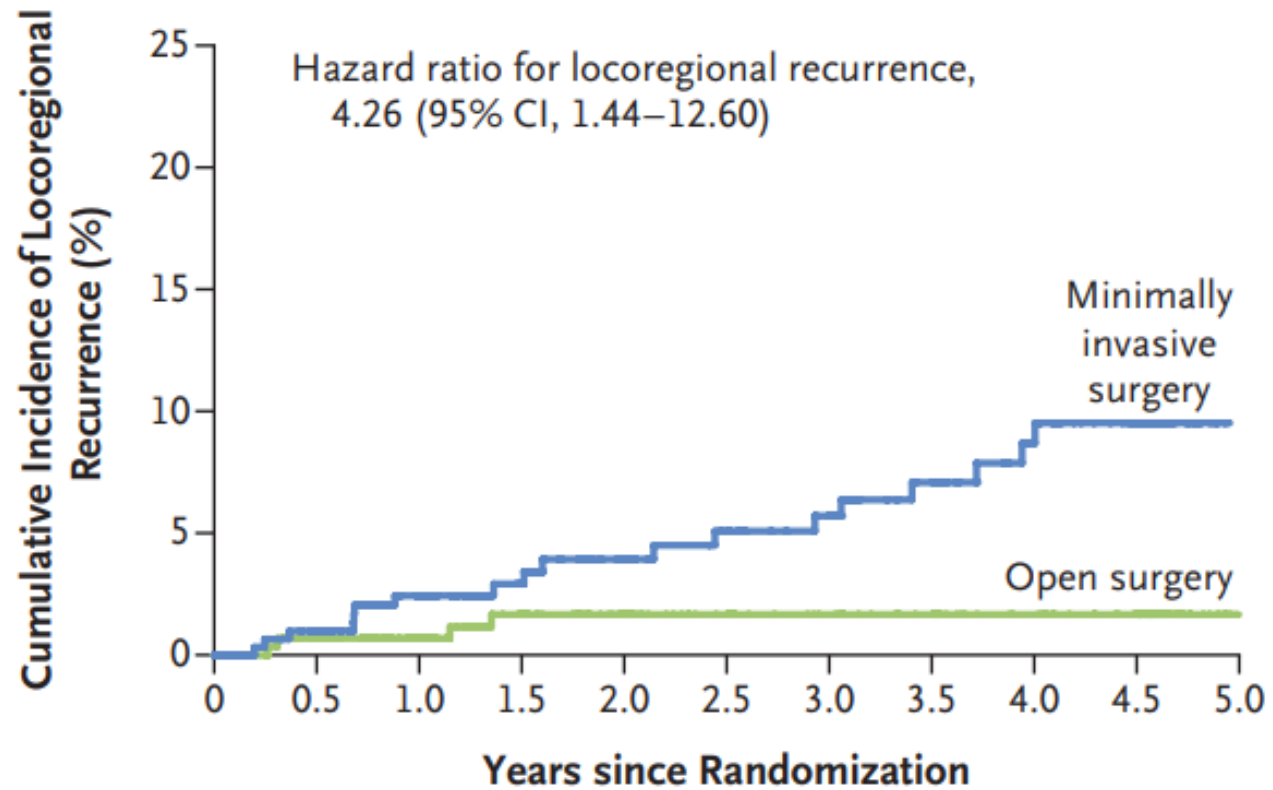
N Engl J Med 2018;379:1895-904.

DOI: 10.1056/NEJMoa1806395

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- 319 patient RCT
- Stage IA1 – IB1
- International trial

C Locoregional Recurrence

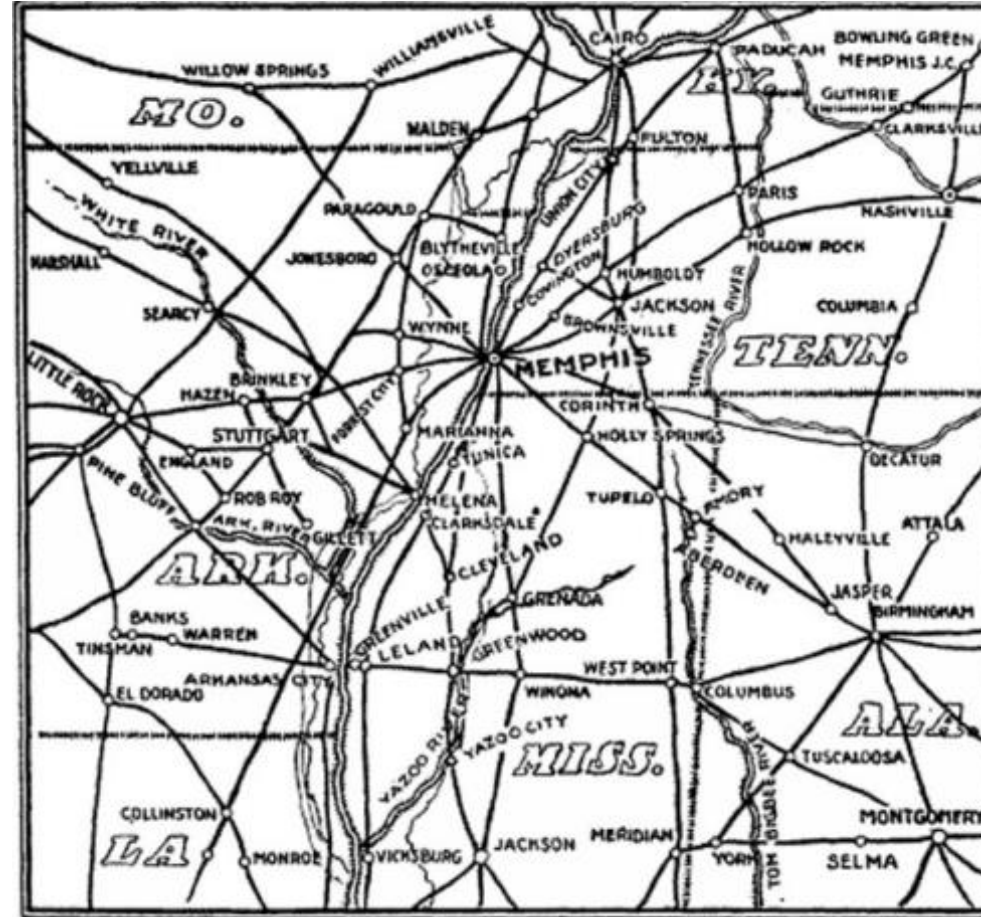


No. at Risk

| | | | | | | | | | | | |
|----------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|---|
| Open surgery | 312 | 280 | 236 | 187 | 163 | 144 | 134 | 123 | 104 | 90 | 7 |
| Minimally invasive surgery | 319 | 292 | 244 | 192 | 167 | 155 | 142 | 121 | 102 | 80 | 5 |

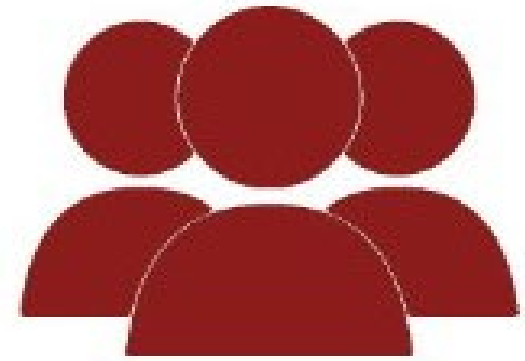
Health disparities in our region

Memphis metropolitan area anchors Mid-South: the very epicenter of disparities of care in the USA



CERVICAL CANCER DOES NOT AFFECT EVERYONE THE SAME

Compared to white women, Blacks and Hispanics are more likely to be diagnosed with cervical cancer and are also more likely to die from the disease.



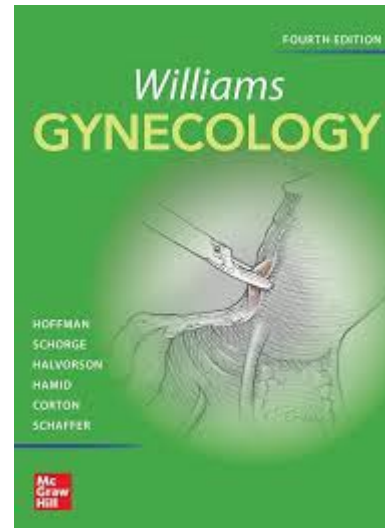
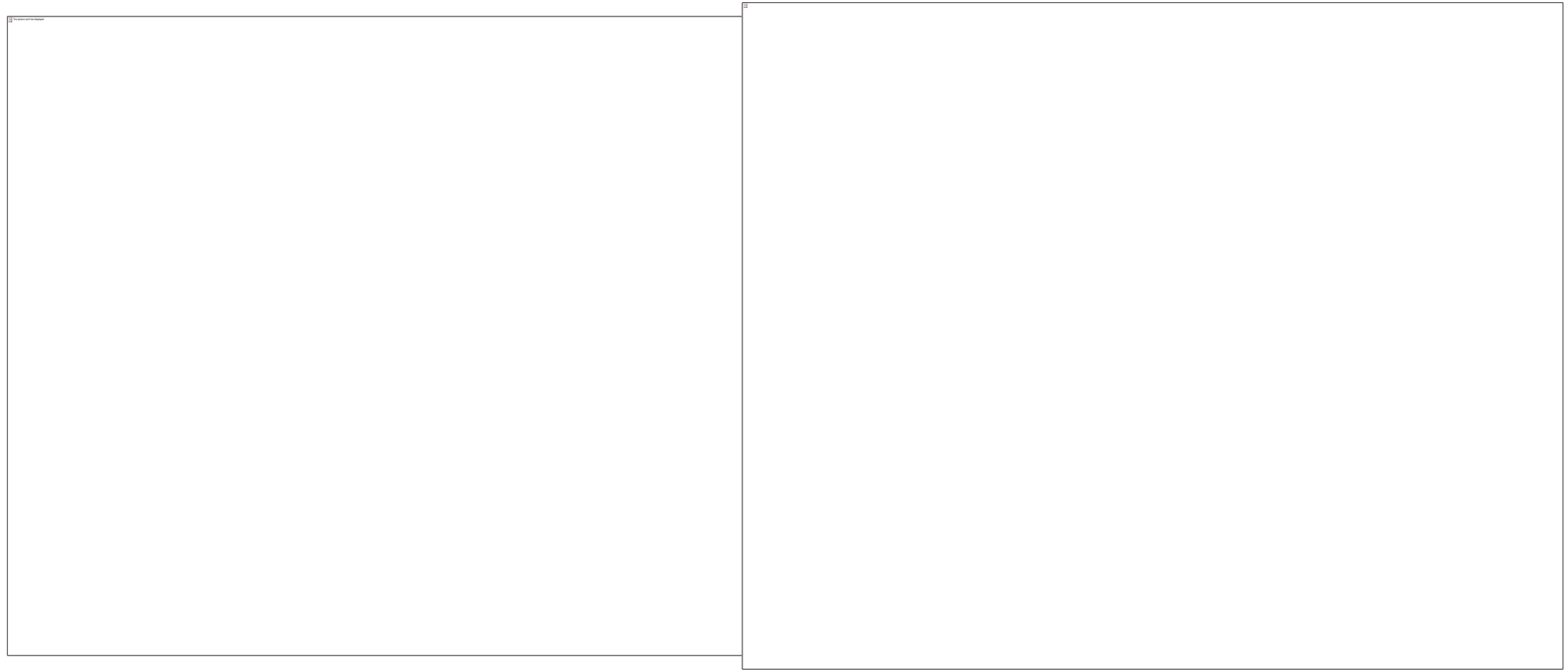


TABLE 30-1. Cervical Cancer Age-Adjusted Incidence and Death Rates (per 100,000 women per year)

| | All Races | White | Black | Asian American & Pacific Islander | American Indian & Alaskan Native | Hispanic |
|-----------|-----------|-------|-------|-----------------------------------|----------------------------------|----------|
| Incidence | 7.3 | 7.2 | 8.7 | 6.4 | 7.9 | 9.3 |
| Death | 2.3 | 2.2 | 3.5 | 1.7 | 1.8 | 2.6 |

Based on cases diagnosed during 2012 through 2016 from 21 geographic areas in the Surveillance, Epidemiology and End Results (SEER) Program.

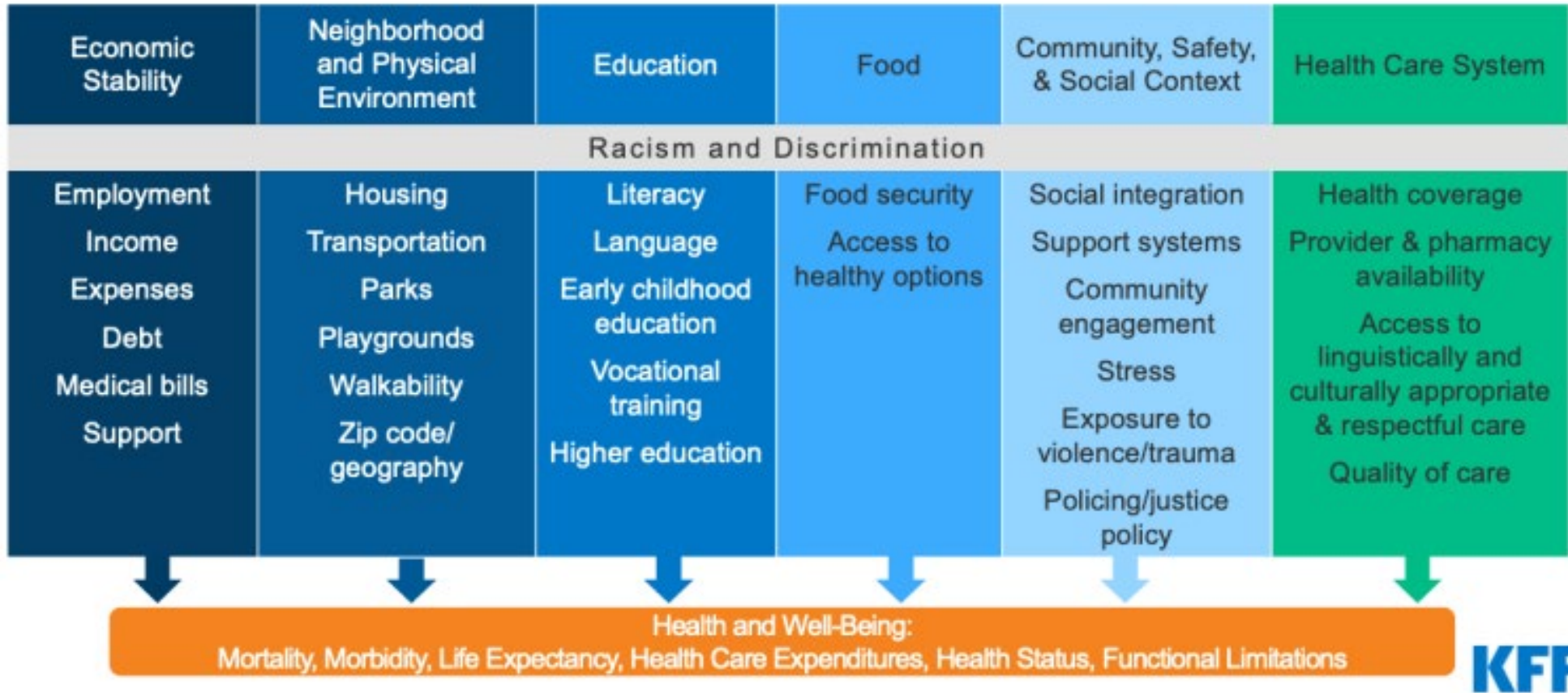


We serve an inner-city community with significant challenges due to poor health literacy and high rates mental illness



Figure 1

Health Disparities are Driven by Social and Economic Inequities



Committee Opinion Dec 2015

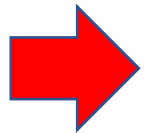
Causes of health disparities in OB/GYN



1. Patient-level factors (genetics, environment, preferences, diet, medical co-morbidities, activity, adherence to treatment plan)
2. Health care system level factors (insurance status, geographic access to care)
3. Practitioner factors (stereotyping and implicit bias)

Educational objectives

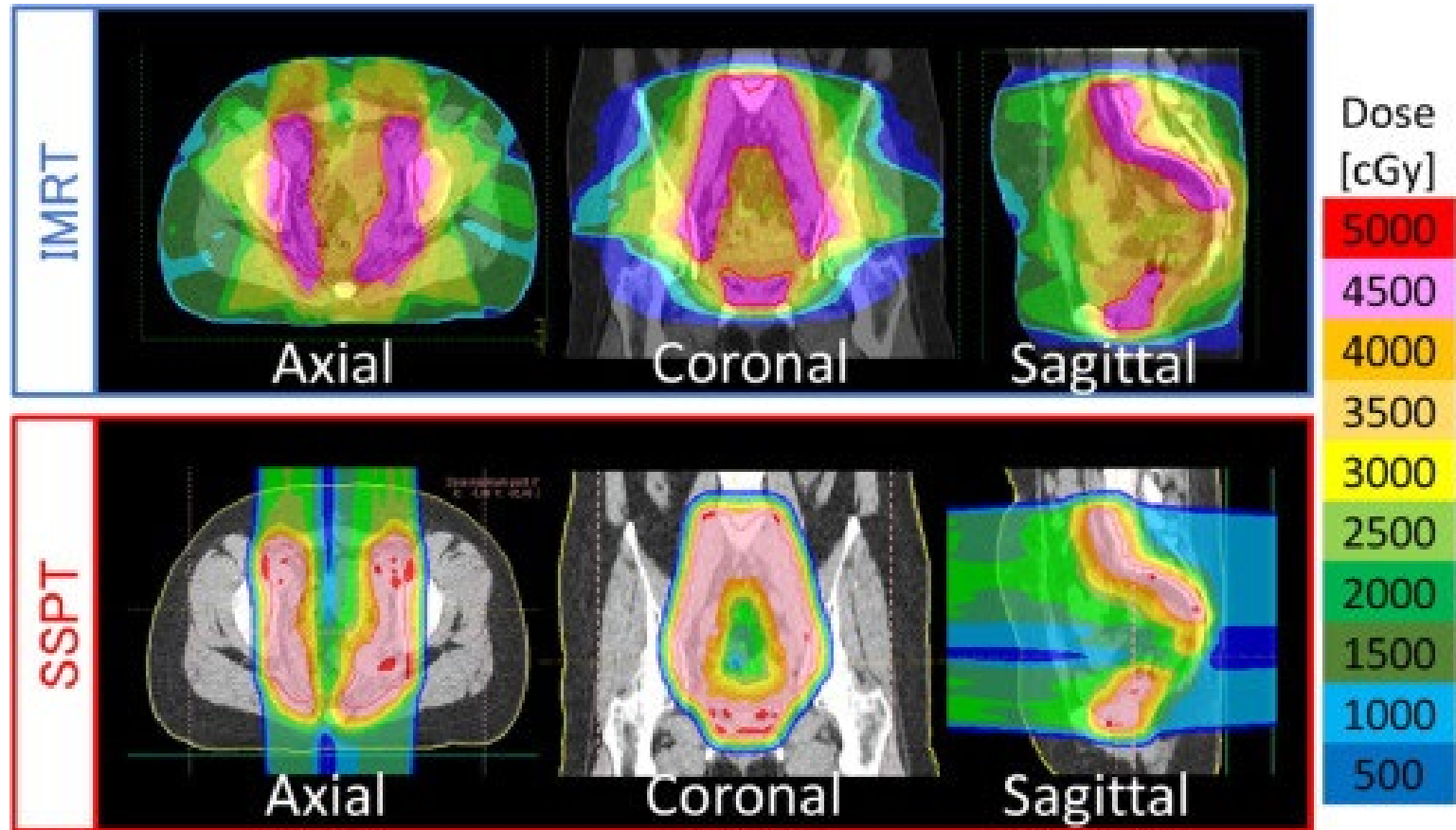
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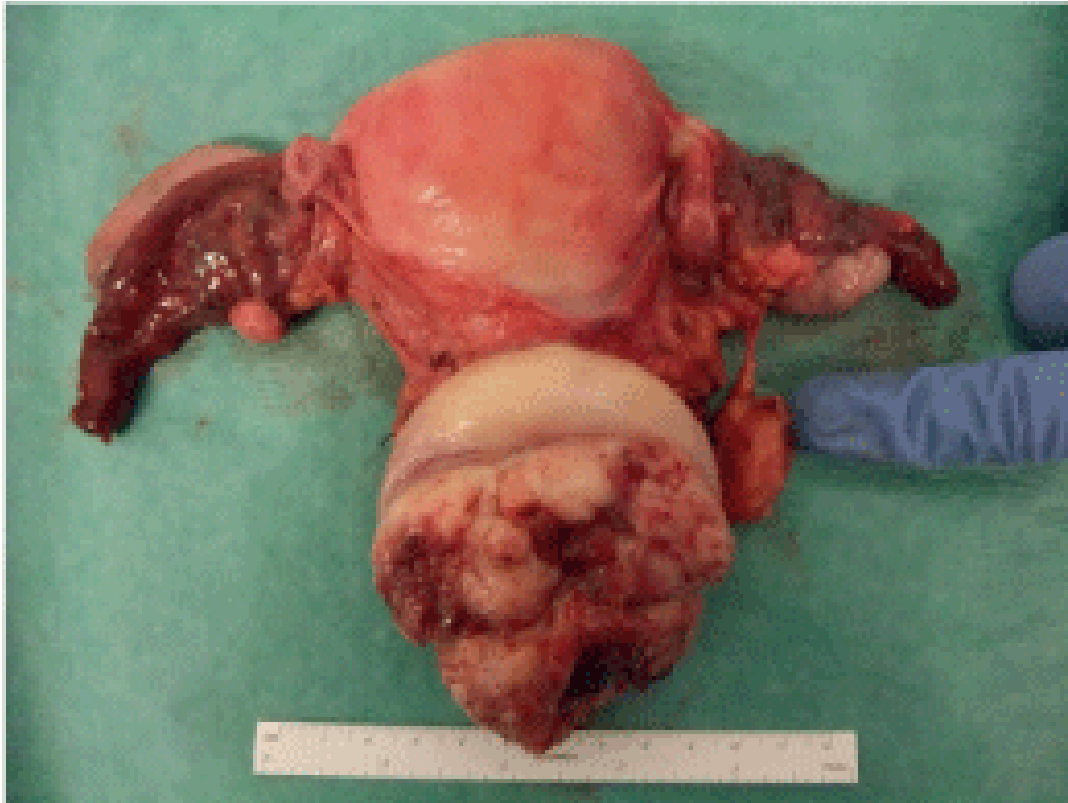


Cervix cancers that are too big to get negative margins require radiation



Dosing = 4500 cGy



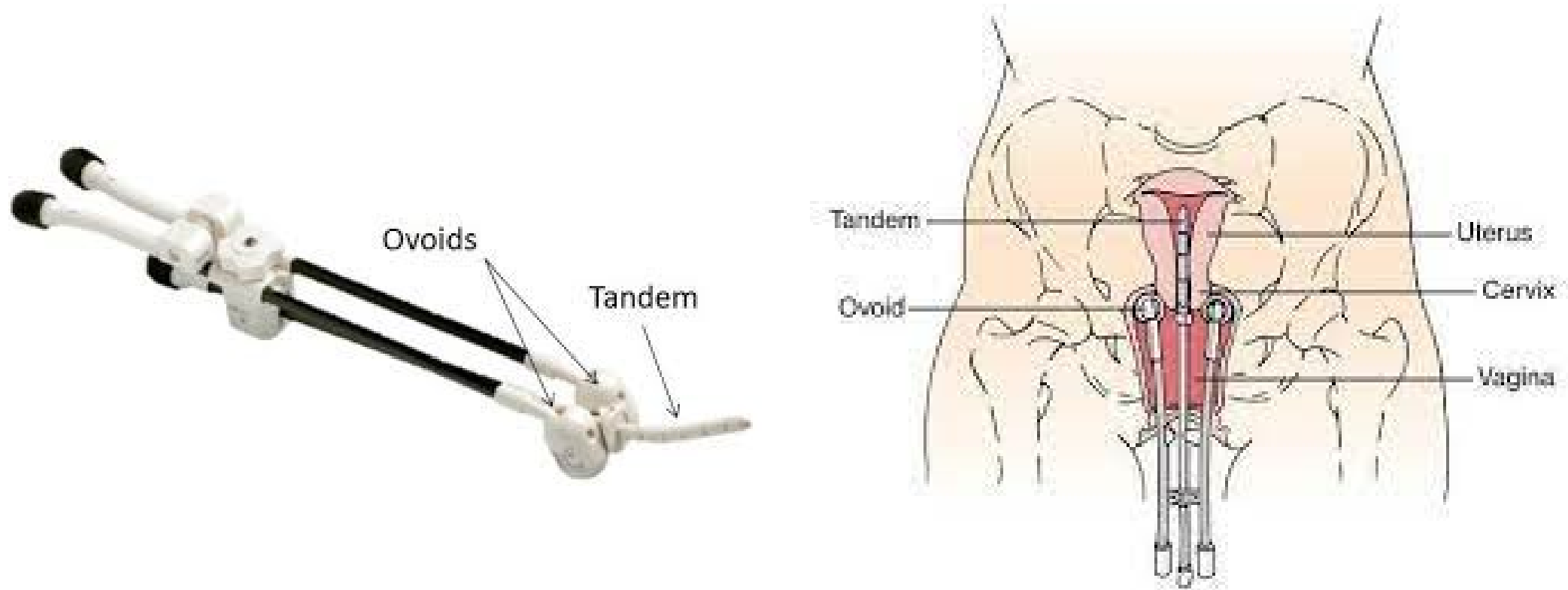


Big cervical cancer

Fact: the higher the dose of radiation, the more curative

- Bladder fistula = 5000 cGy
- Rectal fistula = 6000 cGy

Advanced stage: tandem & ovoid brachytherapy





Appraising the Role of Immunotherapy
in Cervical Cancer Management

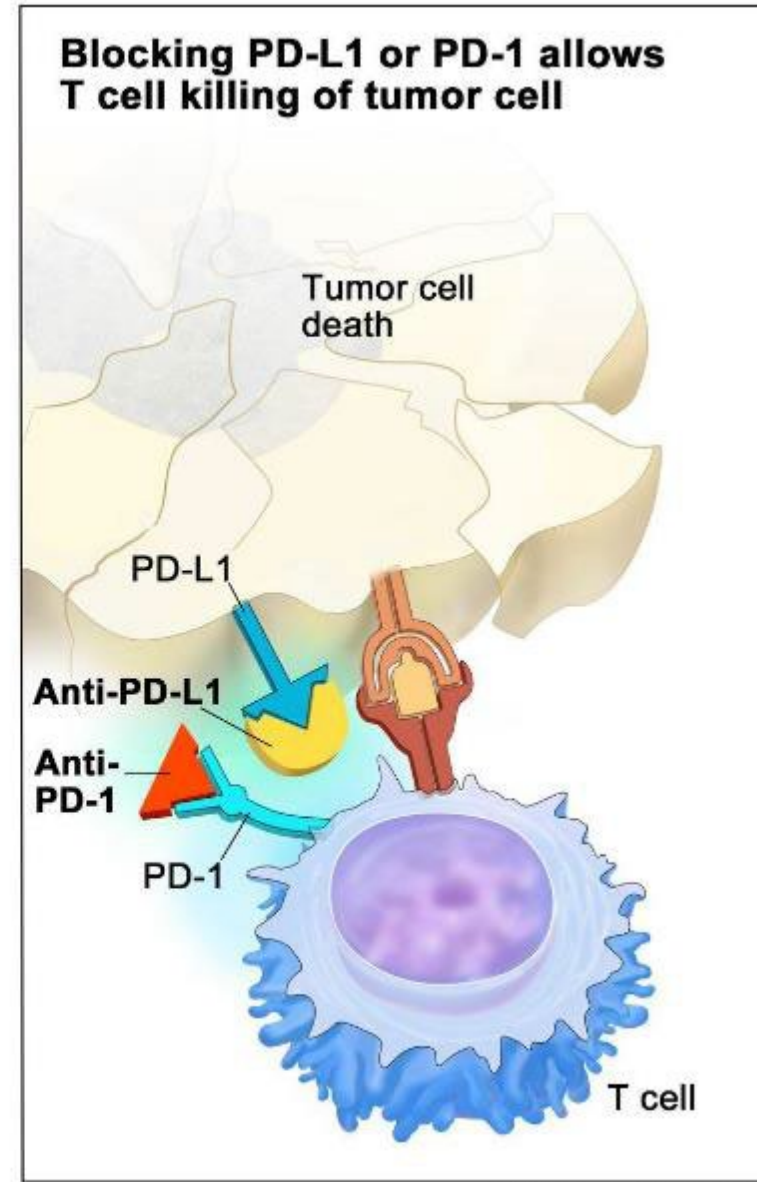
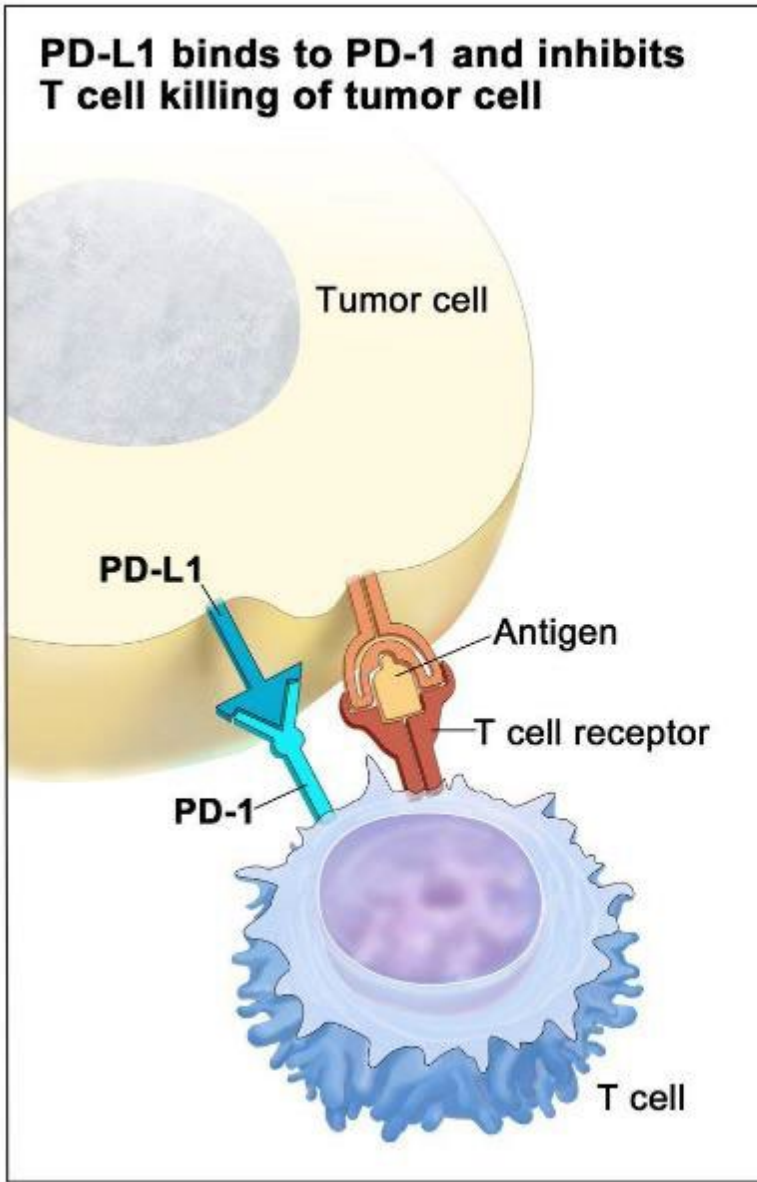
Immunotherapy in Cervical Cancer: What's New?

Provided by K200 Medical Education, LLC



MEDICAL EDUCATION
FOR INTERIM BOARD

This activity is supported by independent medical education
grants from Regeneron Pharmaceuticals, Inc and
Sanofi Genzyme and Merck Sharp & Dohme Corp.



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ORIGINAL ARTICLE

Pembrolizumab for Persistent, Recurrent, or Metastatic Cervical Cancer

N. Colombo, C. Dubot, D. Lorusso, M.V. Caceres, K. Hasegawa, R. Shapira-Frommer, K.S. Tewari, P. Salman, E. Hoyos Usta, E. Yañez, M. Gümüş, M. Olivera Hurtado de Mendoza, V. Samouëlian, V. Castonguay, A. Arkhipov, S. Toker, K. Li, S.M. Keefe, and B.J. Monk, for the KEYNOTE-826 Investigators*

ABSTRACT

BACKGROUND

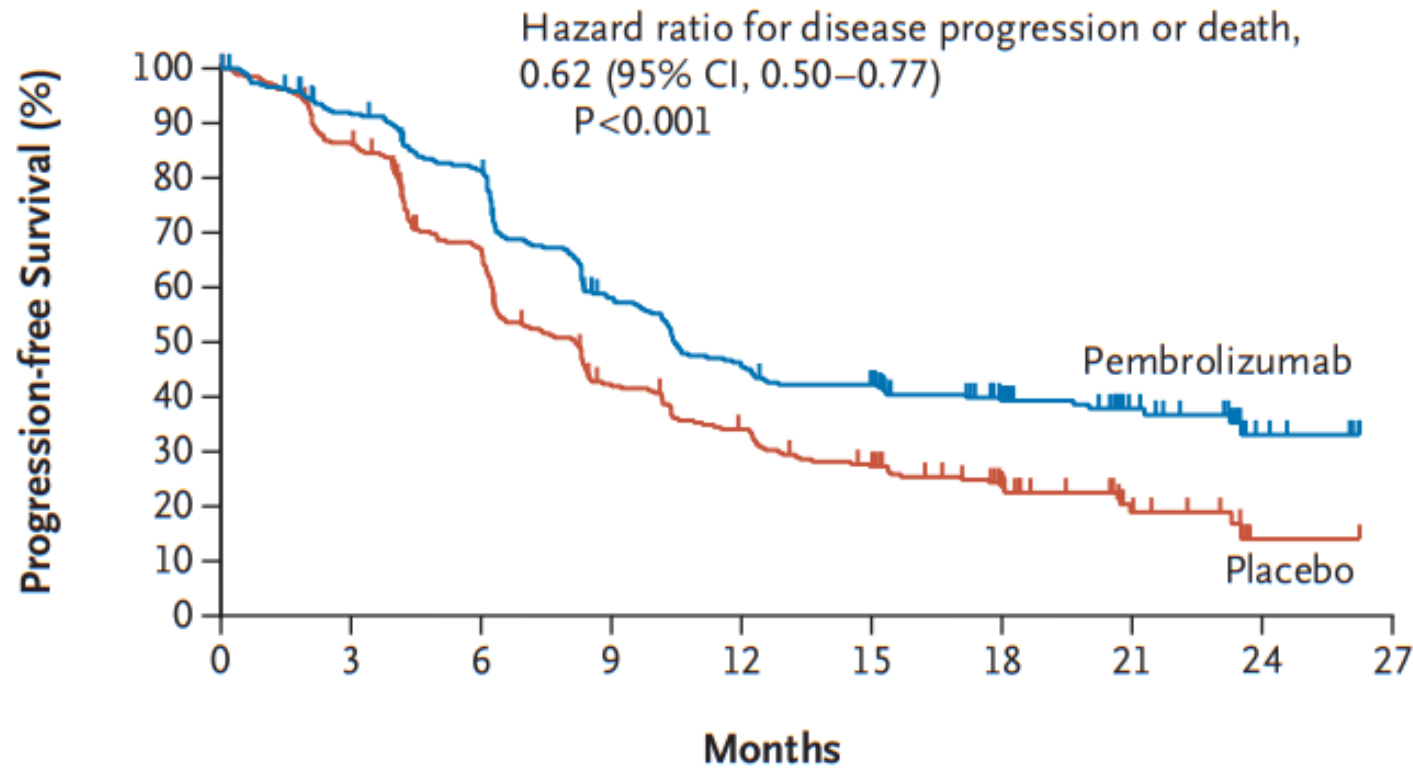
Pembrolizumab has efficacy in programmed death ligand 1 (PD-L1)-positive metastatic or unresectable cervical cancer that has progressed during chemotherapy. We assessed the relative benefit of adding pembrolizumab to chemotherapy with or without bevacizumab.

METHODS

In a double-blind, phase 3 trial, we randomly assigned patients with persistent, recurrent, or metastatic cervical cancer in a 1:1 ratio to receive pembrolizumab

- 548 patients
- Double-blind RCT
- PD-L1 CPS 1+

Patients with a PD-L1 Combined Positive Score of ≥ 1



No. at Risk

| | | | | | | | | | | |
|---------------|-----|-----|-----|-----|-----|-----|----|----|----|---|
| Pembrolizumab | 273 | 238 | 208 | 143 | 112 | 101 | 66 | 34 | 10 | 0 |
| Placebo | 275 | 229 | 170 | 103 | 81 | 63 | 38 | 13 | 1 | 0 |



SYSTEMIC THERAPY FOR CERVICAL CANCER^a

| Squamous Cell Carcinoma, Adenocarcinoma, or Adenosquamous Carcinoma | | |
|--|---|---|
| Chemoradiation ^b | Recurrent or Metastatic Disease | |
| | First-line Therapy ^{b,f} | Second-line or Subsequent Therapy ^j |
| <p>Preferred Regimens</p> <ul style="list-style-type: none"> • Cisplatin^{c,d,1} • Carboplatin if patient is cisplatin intolerant^{c,d} <p>Other Recommended Regimens^e (if cisplatin and carboplatin are unavailable)</p> <ul style="list-style-type: none"> • Capecitabine/mitomycin² • Gemcitabine³ • Paclitaxel^{4,5} | <p>Preferred Regimens</p> <ul style="list-style-type: none"> • PD-L1–positive tumors <ul style="list-style-type: none"> ▶ Pembrolizumab + cisplatin/paclitaxel ± bevacizumab (category 1)^{d,g,h,i,6} ▶ Pembrolizumab + carboplatin/paclitaxel ± bevacizumab (category 1)^{d,g,h,i,6} • Cisplatin/paclitaxel/bevacizumab^{d,g,7} (category 1) • Carboplatin/paclitaxel/bevacizumab^{d,g} <p>Other Recommended Regimens</p> <ul style="list-style-type: none"> • Cisplatin/paclitaxel (category 1)^{8,9} • Carboplatin/paclitaxel^{10,11} (category 1 for patients who have received prior cisplatin therapy) • Topotecan/paclitaxel/bevacizumab^{d,g,7,12} (category 1) • Topotecan/paclitaxel¹² • Cisplatin/topotecan¹² • Cisplatin⁹ • Carboplatin^{13,14} | <p>Preferred Regimens</p> <ul style="list-style-type: none"> • Pembrolizumab for TMB-H tumors^{h,k} or PD-L1–positiveⁱ or MSI-H/dMMR tumors^{h,15} • Tisotumab vedotin-tftv¹⁶ • Cemiplimab^{h,17} <p>Other Recommended Regimens</p> <ul style="list-style-type: none"> • Bevacizumab⁹ • Paclitaxel^{14,18} • Albumin-bound paclitaxel • Docetaxel • Fluorouracil • Gemcitabine • Pemetrexed • Topotecan • Vinorelbine • Irinotecan <p>Useful in Certain Circumstances</p> <ul style="list-style-type: none"> • PD-L1–positive tumors <ul style="list-style-type: none"> ▶ Nivolumab^{h,i,19} • HER2-positive tumors (IHC 3+ or 2+) <ul style="list-style-type: none"> ▶ Fam-trastuzumab deruxtecan-nxki²⁰ • RET gene fusion-positive tumors <ul style="list-style-type: none"> ▶ Selpercatinib • NTRK gene fusion-positive tumors <ul style="list-style-type: none"> ▶ Larotrectinib ▶ Entrectinib |



