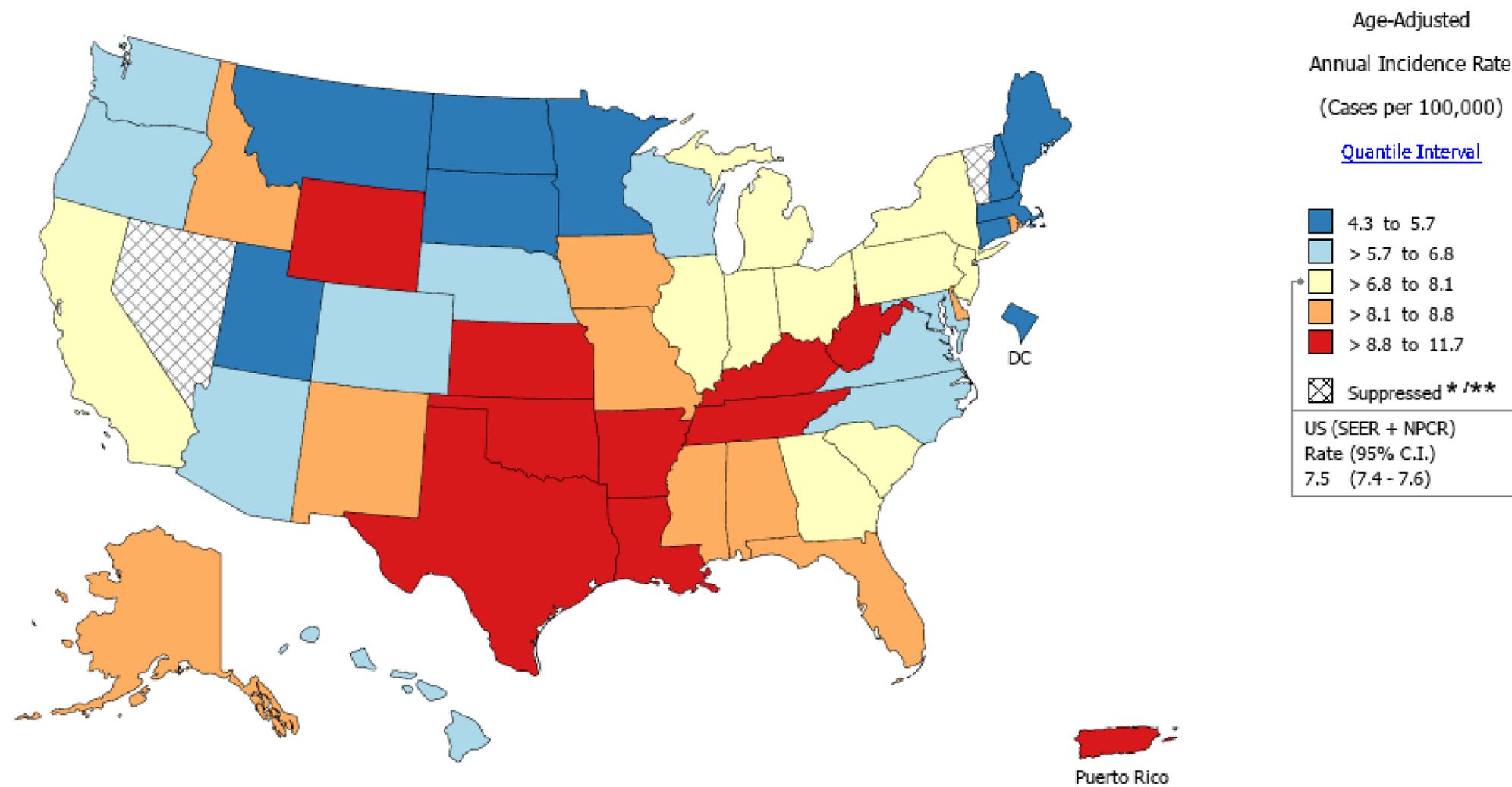# CERVICAL CANCER IN ALABAMA:
## THE PARADOX OF ONGOING DISPARITIES AND EMERGING SUCCESS

Jennifer Young Pierce, MD, MPH
University of South Alabama Mitchell Cancer Institute
Program Leader, Cancer Control and Prevention
Professor, Gynecologic Oncology

October 12, 2021

# Incidence Rates† for United States by State
## Cervix, 2018
## All Races (includes Hispanic), Female, All Ages

Age-Adjusted Annual Incidence Rate (Cases per 100,000)

Quantile Interval

- 4.3 to 5.7
- > 5.7 to 6.8
- > 6.8 to 8.1
- > 8.1 to 8.8
- > 8.8 to 11.7

⊠ Suppressed * /**

US (SEER + NPCR)
Rate (95% C.I.)
7.5  (7.4 - 7.6)

DC

Puerto Rico

**Notes:**
Note: Alaska, DC, Hawaii and Puerto Rico are not drawn to scale.
State Cancer Registries  may provide more current or more local data.
Data presented on the State Cancer Profiles Web Site may differ from statistics reported by the State Cancer Registries (for more information).
†  Incidence rates (cases per 100,000 population per year) are age-adjusted to the 2000 US standard population (19 age groups: <1, 1-4, 5-9, ... , 80-84, 85+). Rates are for invasive cancer only (except for bladder which is invasive and in situ) or unless otherwise specified. Rates calculated using SEER*Stat. Population counts for denominators are based on Census populations as modified by NCI. The 1969-2018 US Population Data  File is used for SEER and NPCR incidence rates.
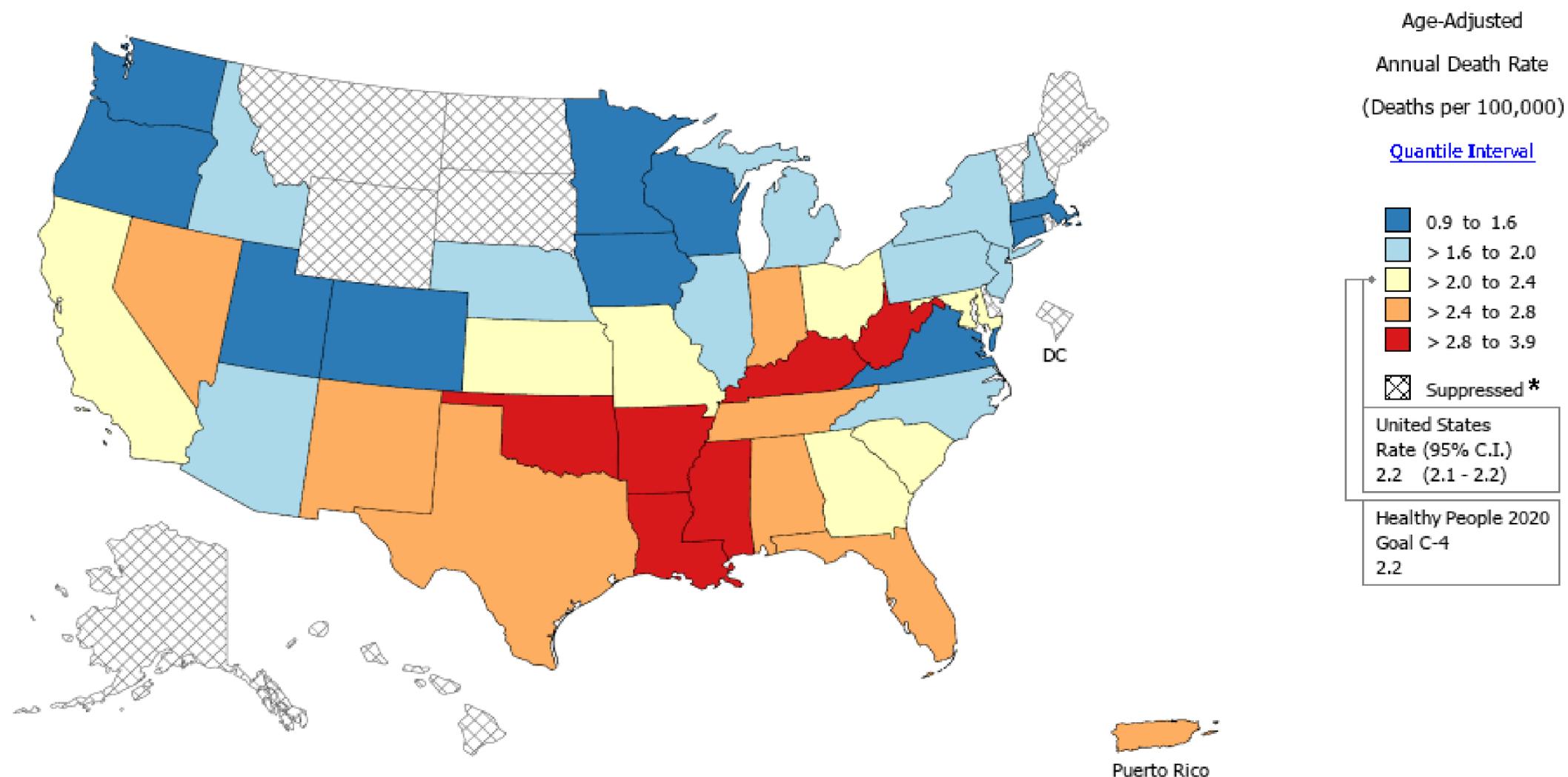   Rates are computed using cancers classified as malignant based on ICD-O-3. For more information see malignant.html
*  Data have been  suppressed  to ensure confidentiality and stability of rate estimates. Data is currently being suppressed if there are fewer than 16 counts for the time period.
◇  Data not available  for this combination of geography, statistic, age and race/ethnicity.
Data for the United States does not include data from Puerto Rico

Presented By:   **Jennifer Young Pierce, MD, MPH**

**Death Rates for United States by State**
**Cervix, 2019**
**All Races (includes Hispanic), Female, All Ages**

Age-Adjusted Annual Death Rate (Deaths per 100,000)

Quantile Interval

- 0.9 to 1.6
- > 1.6 to 2.0
- > 2.0 to 2.4
- > 2.4 to 2.8
- > 2.8 to 3.9
- ⊠ Suppressed *

United States Rate (95% C.I.)
2.2 (2.1 - 2.2)

Healthy People 2020 Goal C-4
2.2

Puerto Rico

**Notes:**
Note: Alaska, DC, Hawaii and Puerto Rico are not drawn to scale.
State Cancer Registries may provide more current or more local data.
Data presented on the State Cancer Profiles Web Site may differ from statistics reported by the State Cancer Registries (for more information).
Source: Death data provided by the National Vital Statistics System public use data file. Death rates calculated by the National Cancer Institute using SEER*Stat. Death rates (deaths per 100,000 population per year) are age-adjusted to the 2000 US standard population (19 age groups: <1, 1-4, 5-9, ... , 80-84, 85+). The Healthy People 2020 goals are based on rates adjusted using different methods but the differences should be minimal. Population counts for denominators are based on the Census 1969-2018 US Population Data File as modified by NCI.
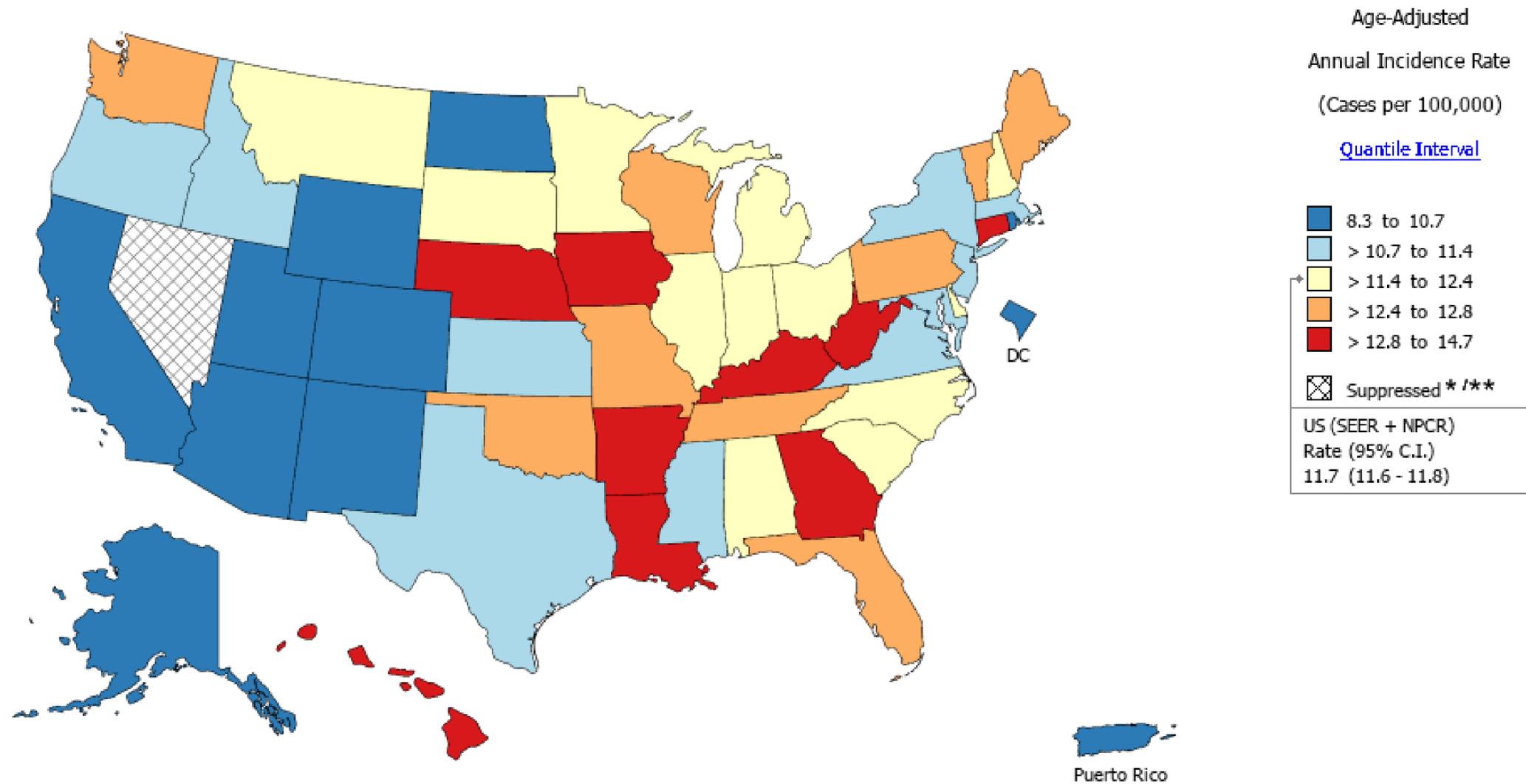* Data have been suppressed to ensure confidentiality and stability of rate estimates. Data is currently being suppressed if there are fewer than 16 counts for the time period.
Healthy People 2020 Goal C-4 : Reduce the death rate from cancer of the uterine cervix to 2.2.
Healthy People 2020 Objectives provided by the Centers for Disease Control and Prevention .
Data for the United States does not include data from Puerto Rico

Presented By: **Jennifer Young Pierce, MD, MPH**

# Incidence Rates† for United States by State
## Oral Cavity & Pharynx, 2018
## All Races (includes Hispanic), Both Sexes, All Ages



Age-Adjusted

Annual Incidence Rate

(Cases per 100,000)

Quantile Interval

- 8.3 to 10.7
- > 10.7 to 11.4
- > 11.4 to 12.4
- > 12.4 to 12.8
- > 12.8 to 14.7
- ⊠ Suppressed * / **

US (SEER + NPCR)
Rate (95% C.I.)
11.7 (11.6 - 11.8)

DC

Puerto Rico

**Notes:**
Note: Alaska, DC, Hawaii and Puerto Rico are not drawn to scale.
State Cancer Registries may provide more current or more local data.
Data presented on the State Cancer Profiles Web Site may differ from statistics reported by the State Cancer Registries (for more information).
† Incidence rates (cases per 100,000 population per year) are age-adjusted to the 2000 US standard population (19 age groups: <1, 1-4, 5-9, ... , 80-84, 85+). Rates are for invasive cancer only (except for bladder which is invasive and in situ) or unless otherwise specified. Rates calculated using SEER*Stat. Population counts for denominators are based on Census populations as modified by NCI. The 1969-2018 US Population Data File is used for SEER and NPCR incidence rates.
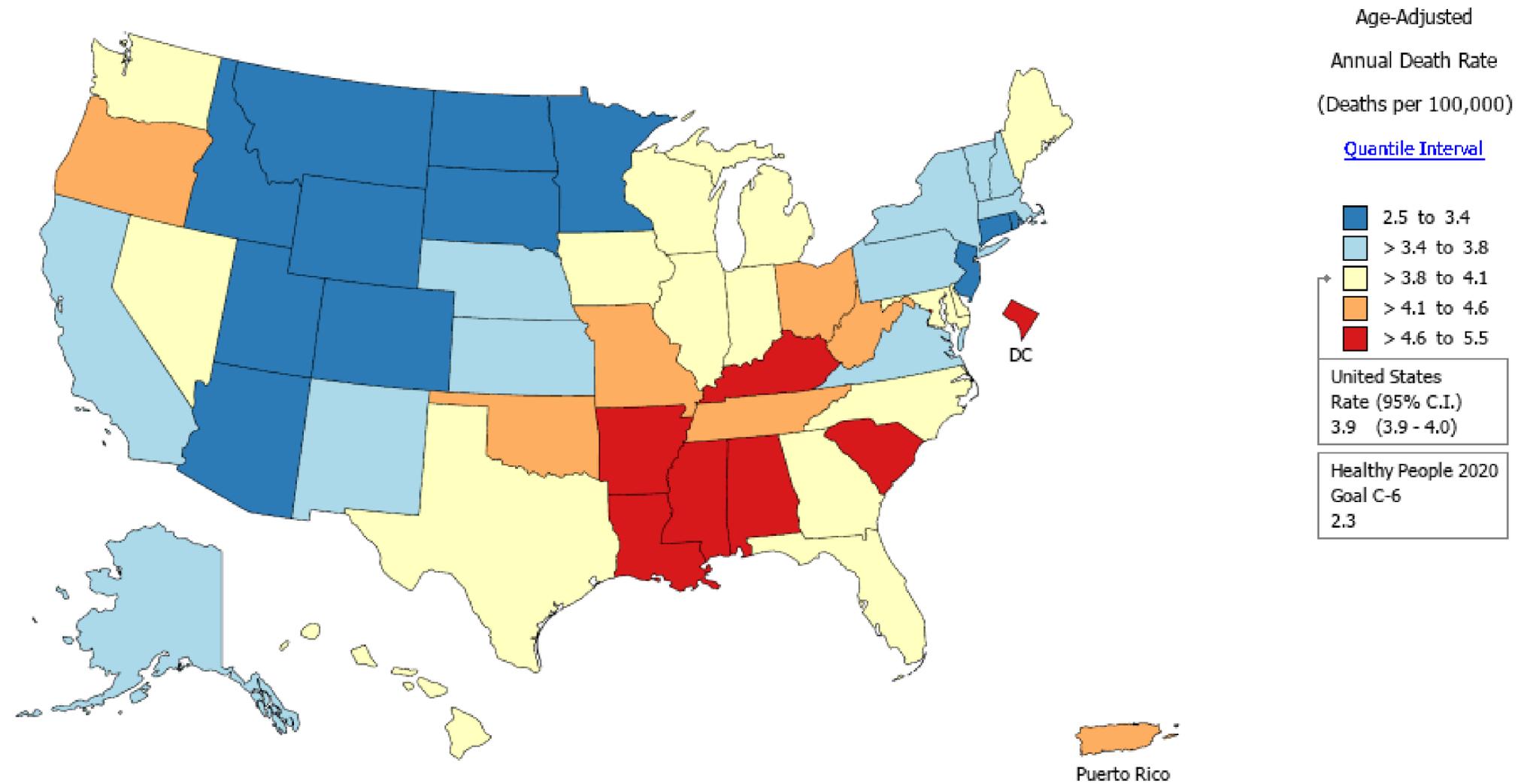Rates are computed using cancers classified as malignant based on ICD-O-3. For more information see malignant.html
* Data have been suppressed to ensure confidentiality and stability of rate estimates. Data is currently being suppressed if there are fewer than 16 counts for the time period.
◇ Data not available for this combination of geography, statistic, age and race/ethnicity.
Data for the United States does not include data from Puerto Rico

Presented By: **Jennifer Young Pierce, MD, MPH**

# Death Rates for United States by State
## Oral Cavity & Pharynx, 2015 - 2019
## All Races (includes Hispanic), Male, All Ages



Age-Adjusted

Annual Death Rate

(Deaths per 100,000)

Quantile Interval

- 2.5 to 3.4
- > 3.4 to 3.8
- > 3.8 to 4.1
- > 4.1 to 4.6
- > 4.6 to 5.5

United States
Rate (95% C.I.)
3.9 (3.9 - 4.0)

Healthy People 2020
Goal C-6
2.3

DC

Puerto Rico

**Notes:**
Note: Alaska, DC, Hawaii and Puerto Rico are not drawn to scale.
State Cancer Registries may provide more current or more local data.
Data presented on the State Cancer Profiles Web Site may differ from statistics reported by the State Cancer Registries (for more information).
Source: Death data provided by the National Vital Statistics System public use data file. Death rates calculated by the National Cancer Institute using SEER*Stat. Death rates (deaths per 100,000 population per year) are age-adjusted to the 2000 US standard population (19 age groups: <1, 1-4, 5-9, ... , 80-84, 85+). The Healthy People 2020 goals are based on rates adjusted using different methods but the differences should be minimal. Population counts for denominators are based on the Census 1969-2018 US Population Data File as modified by NCI.
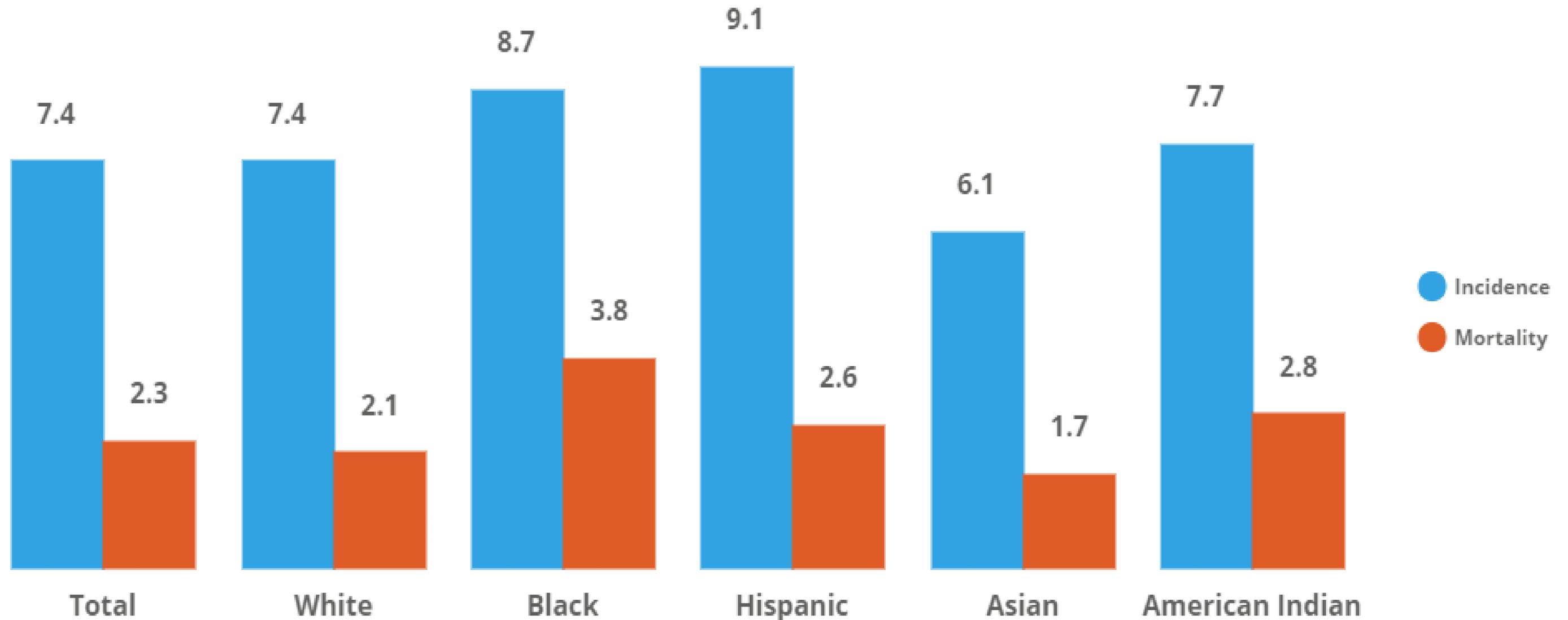Healthy People 2020 Goal C-6 : Reduce the oropharyngeal cancer death rate to 2.3.
Healthy People 2020 Objectives provided by the Centers for Disease Control and Prevention .
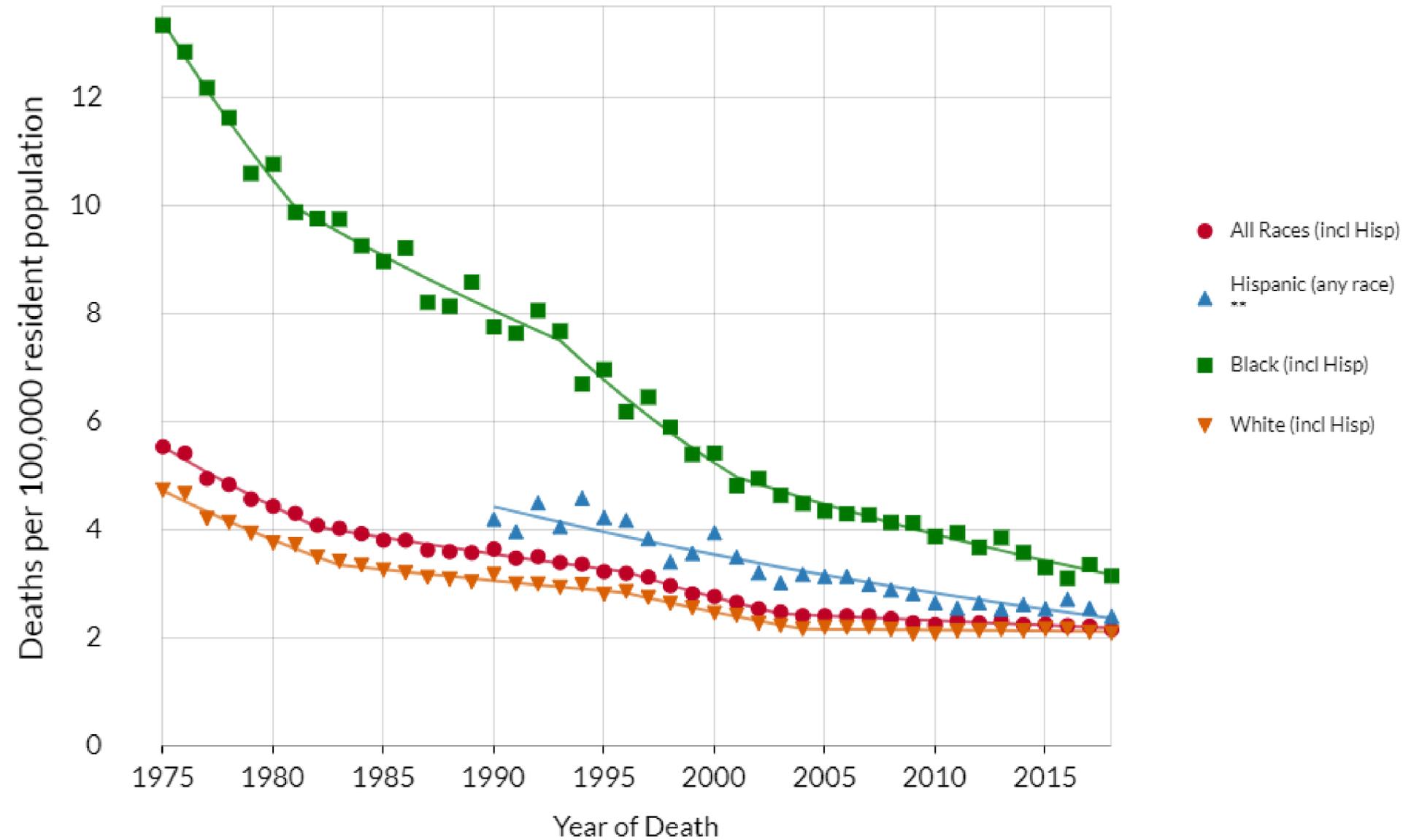Data for the United States does not include data from Puerto Rico

Presented By:
**Jennifer Young Pierce, MD, MPH**

# Racial and Ethnic Disparities in Cervical Cancer
## Cervical Cancer Incidence and Mortality Rates per 100,000 people

| | Total | White | Black | Hispanic | Asian | American Indian |
|---|---|---|---|---|---|---|
| Incidence | 7.4 | 7.4 | 8.7 | 9.1 | 6.1 | 7.7 |
| Mortality | 2.3 | 2.1 | 3.8 | 2.6 | 1.7 | 2.8 |

● Incidence
● Mortality

KFF.org

Presented By: Jennifer Young Pierce, MD, MPH

# Historical trends in Cervical Cancer Mortality by Race in US



Notes:
Created by statecancerprofiles.cancer.gov on 05/13/2021 5:20 pm.
Regression lines calculated using the Joinpoint Regression Program (Version 4.8.0.0)

The following group(s) are suppressed due to insufficient counts:

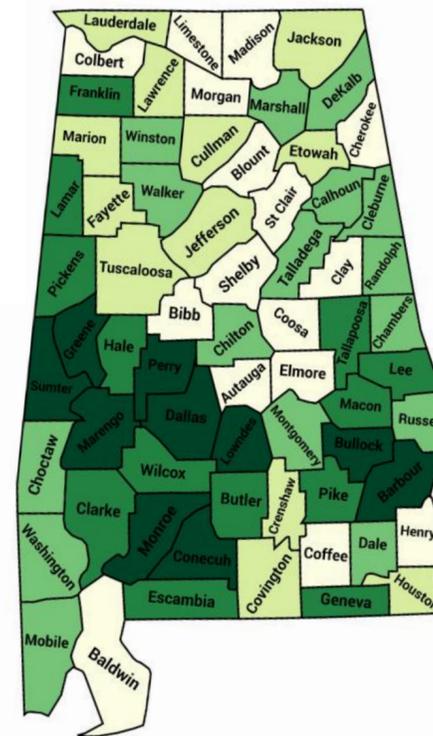Mortality United States Cervix White Non-Hispanic Female All Ages

Presented By:

**Jennifer Young Pierce, MD, MPH**

# HPV-Associated cancers in US highlight areas of ongoing disparity

*Vickers et al 2020*

**Rurality and Poverty by County in Alabama (2018)**
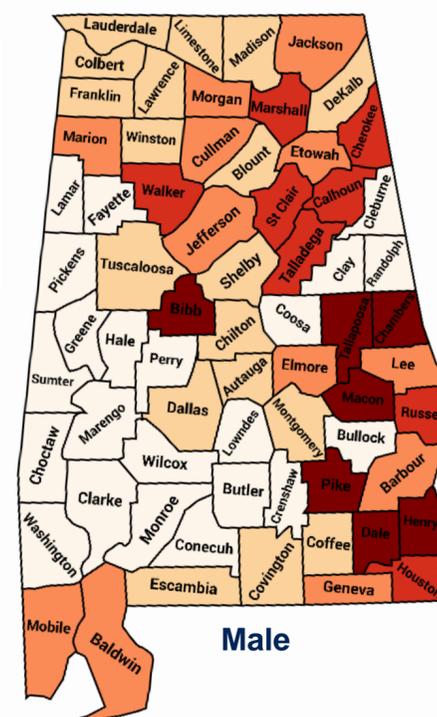
RUCC 9
RUCC 8
RUCC 7
RUCC 6
RUCC 4
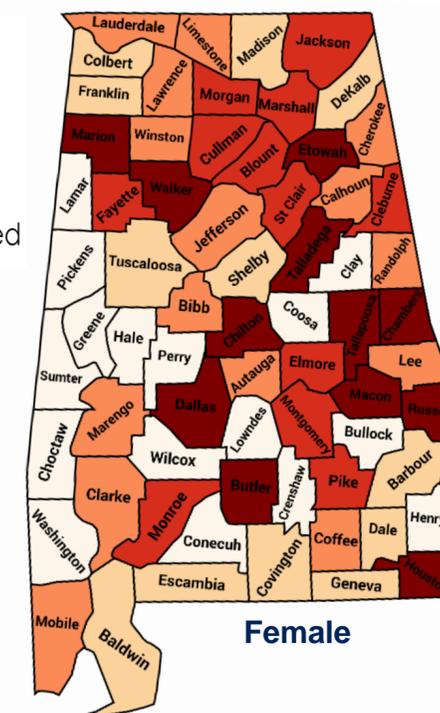RUCC 1, 2, and 3
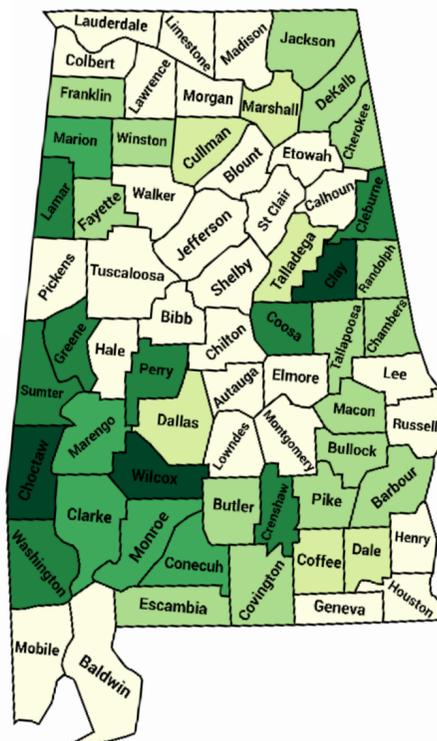
26.1-40
22.1-26
19.1-22
17.1-19
8.5-17

**HPV-associated Cancers by County in Alabama (2018)**

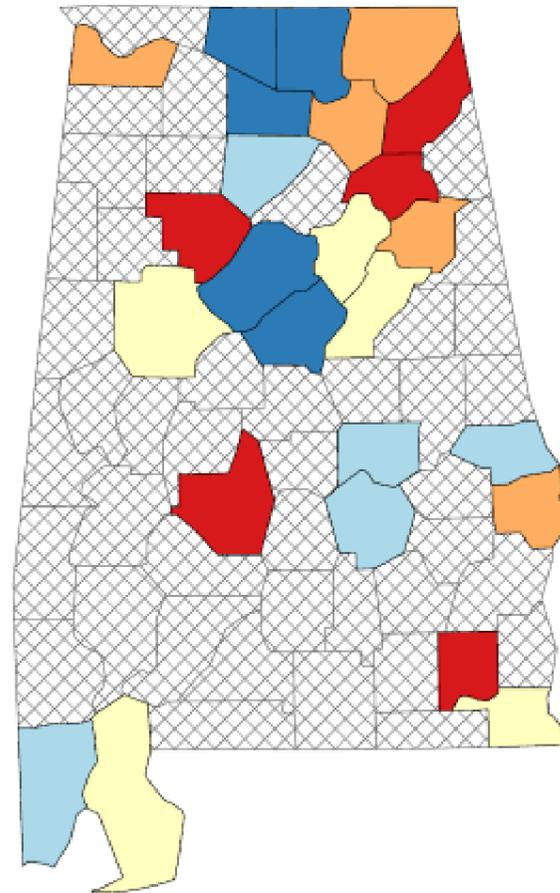13.0 - 17.6
12.0 - 12.9
11.0 - 11.9
7.9 - 11.0
Data suppressed

**Male**

19.1-26.4
15.7-19
14.1-15.6
11.3-14
Data suppressed

**Female**

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2021 ASCO® ANNUAL MEETING

# Incidence Rates[†] for Alabama by County
## Cervix, 2014 - 2018
## All Races (includes Hispanic), Female, All Ages



Age-Adjusted

Annual Incidence Rate

(Cases per 100,000)

Quantile Interval

- ■ 5.6 to 8.1
- ■ > 8.1 to 10.0
- ■ > 10.0 to 11.0
- ■ > 11.0 to 12.9
- ■ > 12.9 to 18.6
- ⊠ Suppressed * /**

US (SEER + NPCR)
Rate (95% C.I.)
7.7   (7.6 - 7.8)

Alabama
Rate (95% C.I.)
9.4   (8.8 - 9.9)

**Notes:**
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[†]  Incidence rates (cases per 100,000 population per year) are age-adjusted to the 2000 US standard population (19 age groups: <1, 1-4, 5-9, ... , 80-84, 85+). Rates are for invasive cancer only (except
     for bladder which is invasive and in situ) or unless otherwise specified. Rates calculated using SEER*Stat. Population counts for denominators are based on Census populations as modified by NCI.
     The 1969-2018 US Population Data  File is used for SEER and NPCR incidence rates.
     Rates are computed using cancers classified as malignant based on ICD-O-3. For more information see malignant.html
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Data for the United States does not include data from Puerto Rico

Presented By:
**Jennifer Young Pierce, MD, MPH**

# Social determinants of health

| Economic Stability | Neighborhood and Physical Environment | Education | Food | Community and Social Context | Health Care System |
|---|---|---|---|---|---|
| Employment | Housing | Literacy | Hunger | Social integration | Health coverage |
| Income | Transportation | Language | Access to healthy options | Support systems | Provider availability |
| Expenses | Safety | Early childhood education | | Community engagement | Provider linguistic and cultural competency |
| Debt | Parks | Vocational training | | Discrimination | |
| Medical bills | Playgrounds | Higher education | | | Quality of care |
| Support | Walkability | | | | |

## Health Outcomes
Mortality, Morbidity, Life Expectancy, Health Care Expenditures, Health Status, Functional Limitations

Presented By: **Jennifer Young Pierce, MD, MPH**

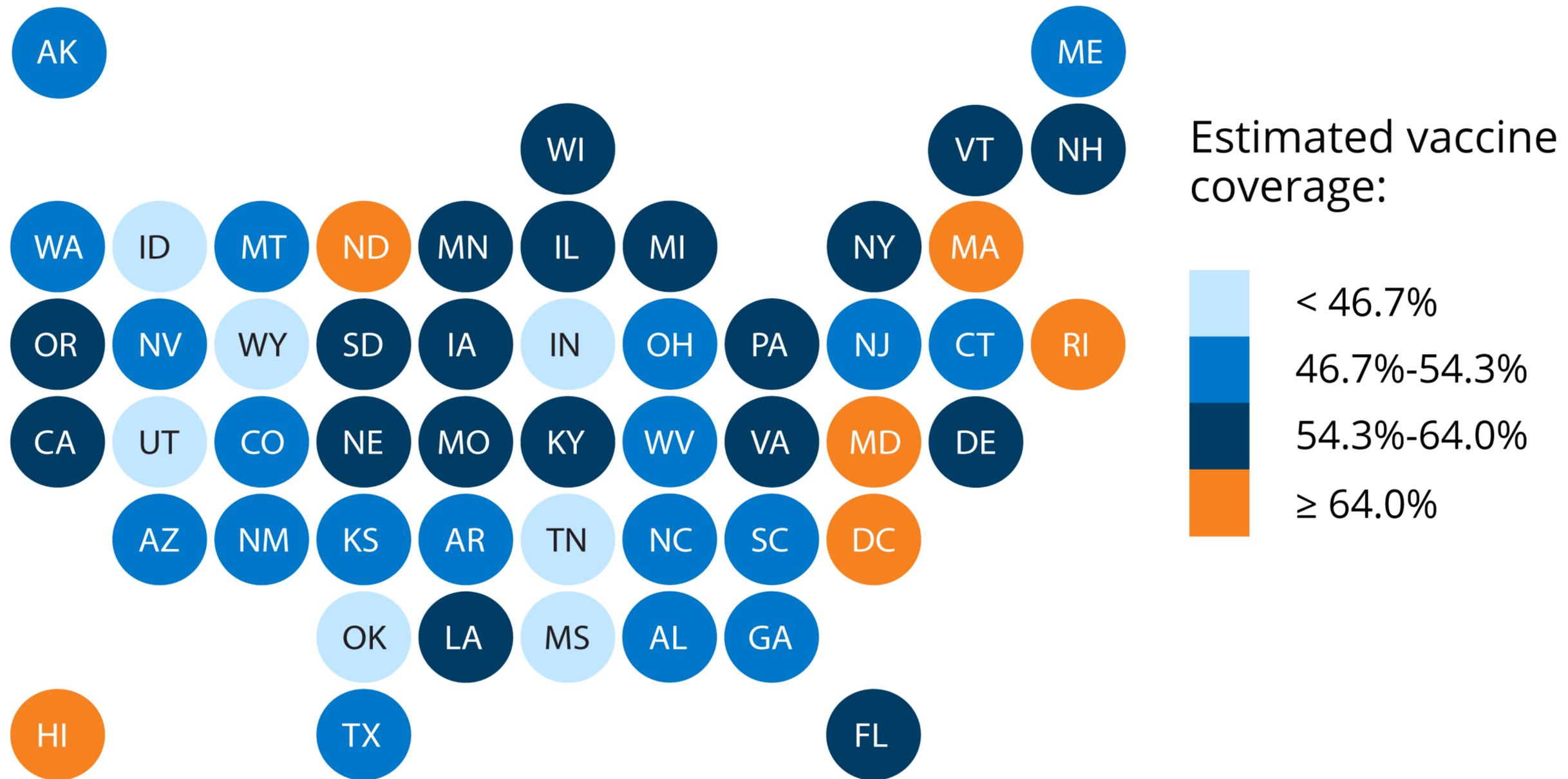# Health disparities in Gyn cancers multifactorial
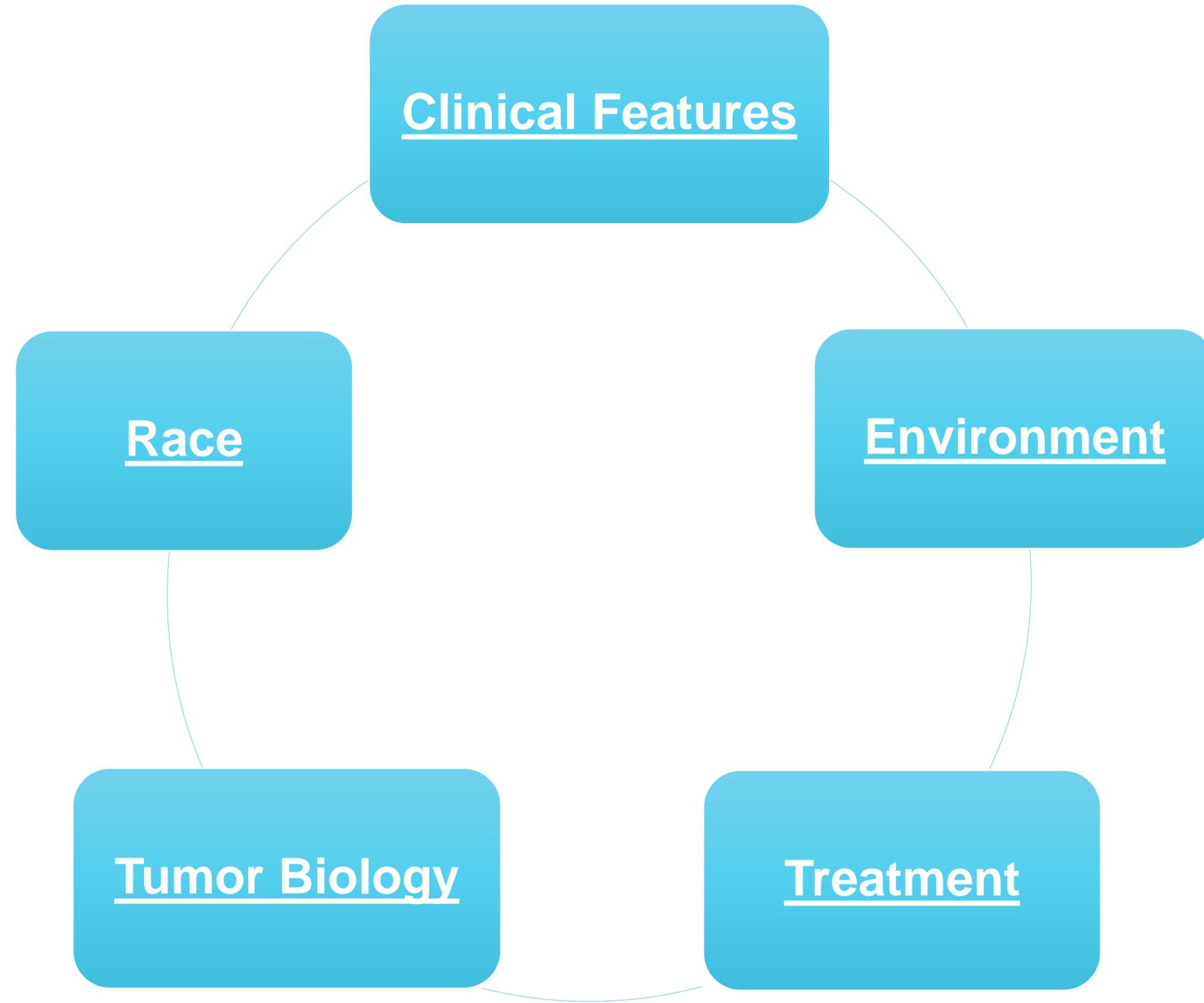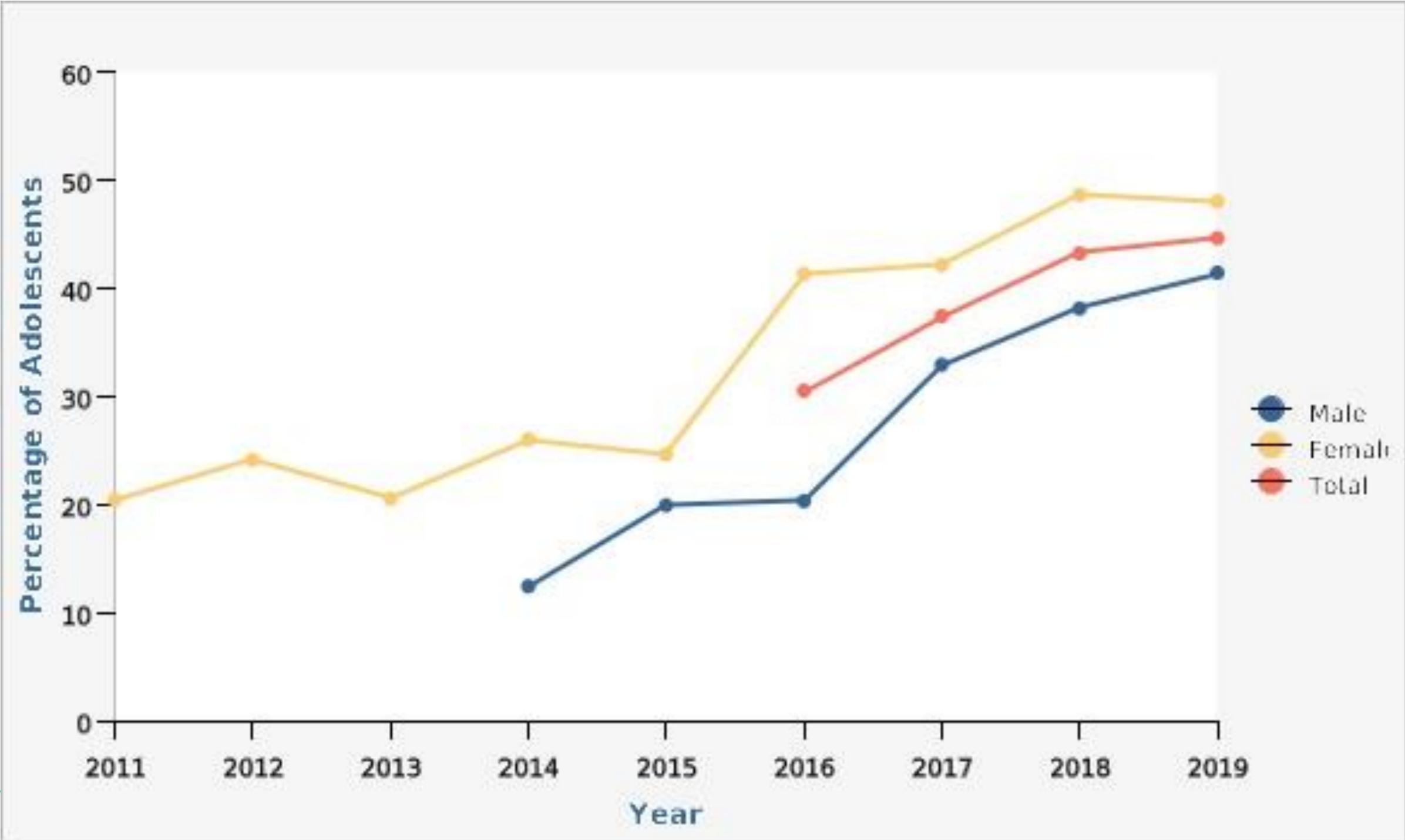
# Cervical cancer management in US

- **Primary Prevention** ➡ **Vaccination**

- **Secondary Prevention** ➡ **Screening and Treatment**

- **Early Diagnosis** ➡ **Surgery**

- **Advanced Disease** ➡ **Chemoradiation**

- **Metastatic Disease** ➡ **Combination chemotherapy**

Presented By: **Jennifer Young Pierce, MD, MPH**

# HPV Vaccination Rates of Adolescents, by State

## Adolescents ages 13-17 with HPV Up-to-Date Vaccination Series, 2019



Estimated vaccine coverage:

< 46.7%

46.7%-54.3%

54.3%-64.0%

≥ 64.0%

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Jennifer Young Pierce, MD, MPH

# HPV Vaccine Up to date – NIS Teen 2019

# In Alabama and US private insurance = lower vaccination



$r_P = -0.34$, p<0.001

HPV Vaccination Rate (Female)

Percentage with Private Insurance

$r_P = -0.36$, p=0.003

HPV Vaccination Rate (Male)

Percentage with Private Insurance

$r_P = -0.40$, p=0.001

HPV Vaccination Rate (Total)

Percentage with Private Insurance

*Pierce et al 2019*

Presented By: Jennifer Young Pierce, MD, MPH
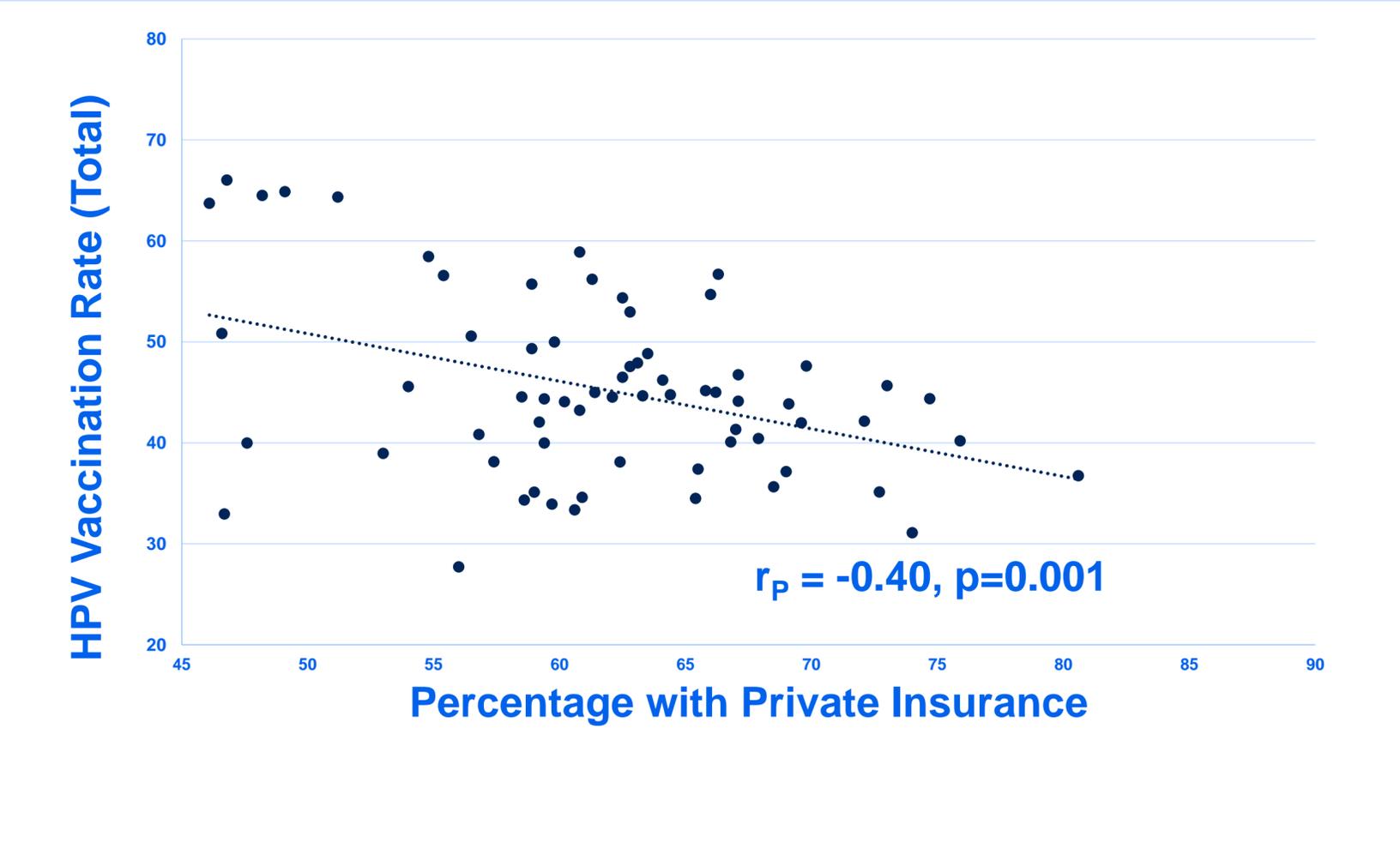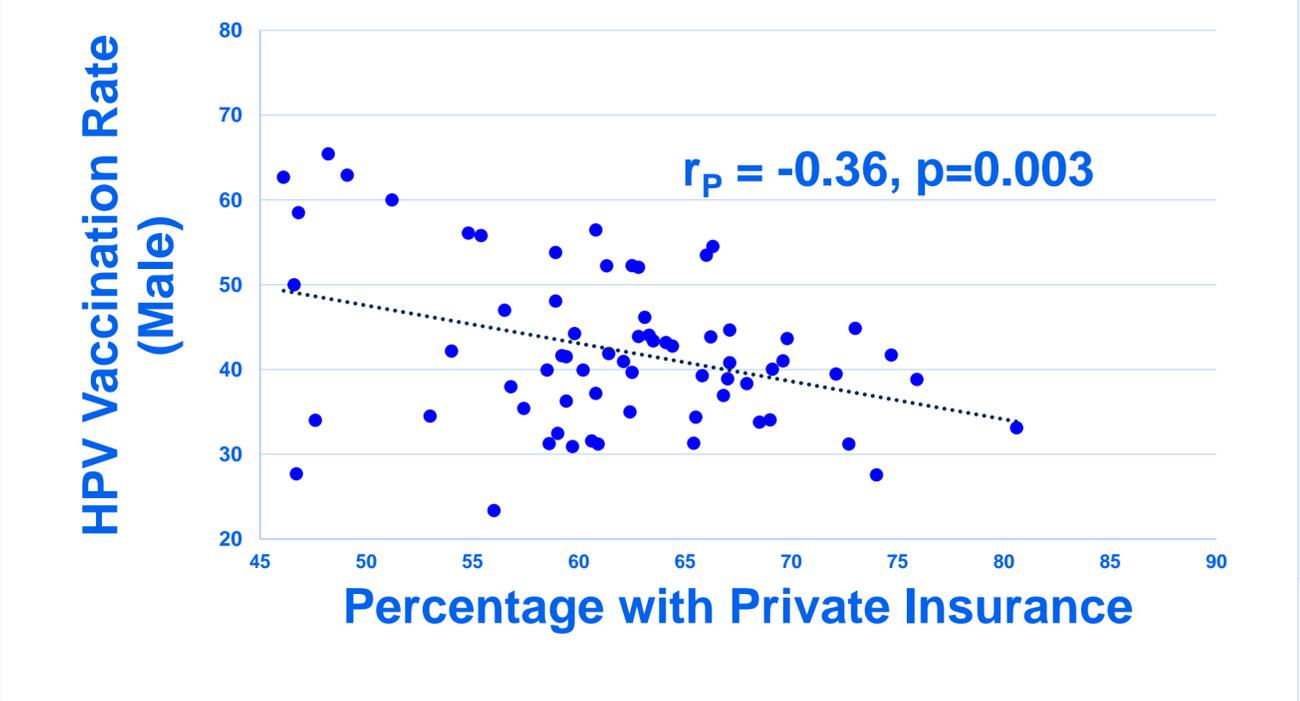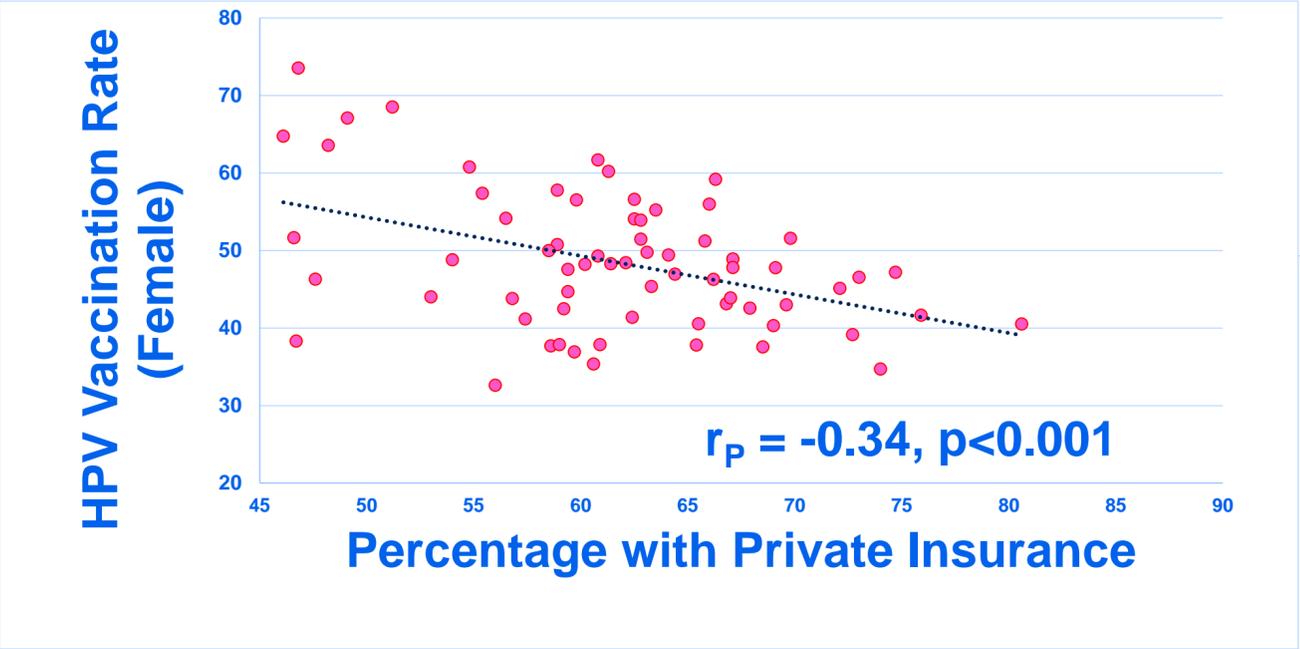
# HPV vaccine uptake by county variables

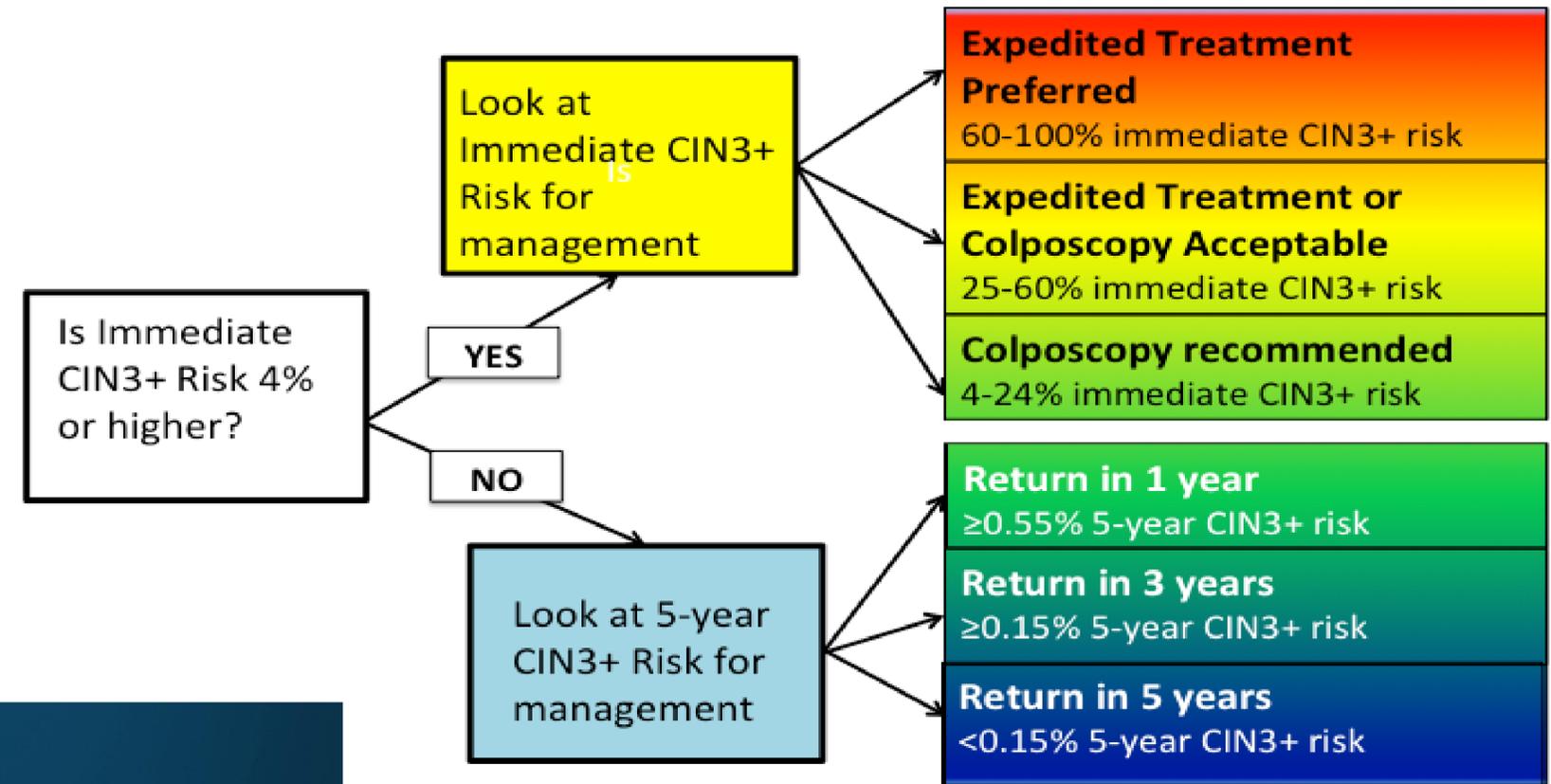| Variable | Correlation to HPV vax Uptake: Males | Correlation to HPV vax Uptake: Females | Correlation to HPV vax Uptake: Total | P value |
|---|---|---|---|---|
| **Rurality (RUCC code)** | **-0.23** | **-0.31** | **-0.27** | **0.025** |
| **Median HH income** | **-0.36** | **-0.43** | **-0.40** | **0.0007** |
| **% below poverty** | **0.35** | **0.41** | **0.39** | **0.0011** |
| **PCP ratio** | **0.052** | **0.060** | **0.058** | **0.66** |
| **Number of Pediatricians** | **0.054** | **-0.012** | **0.024** | **0.85** |

Presented By:    Jennifer Young Pierce, MD, MPH

# Cervical cancer management in US

- **Primary Prevention** ➡️ **Vaccination**

- **Secondary Prevention** ➡️ **Screening and Treatment**

- **Early Diagnosis** ➡️ **Surgery**

- **Advanced Disease** ➡️ **Chemoradiation**

- **Metastatic Disease** ➡️ **Combination chemotherapy**

Presented By: **Jennifer Young Pierce, MD, MPH**

# 2020 ASCCP Cervical cancer screening guidelines

- **Evolving guidelines to include multiple modalities:**
  - **HPV as primary screening**
  - **HPV cotesting**
  - **Pap testing**
- **Takes into account patient's previous history**
- **Requires an app**

Is Immediate CIN3+ Risk 4% or higher?

**YES** → Look at Immediate CIN3+ Risk for management

- **Expedited Treatment Preferred** — 60-100% immediate CIN3+ risk
- **Expedited Treatment or Colposcopy Acceptable** — 25-60% immediate CIN3+ risk
- **Colposcopy recommended** — 4-24% immediate CIN3+ risk

**NO** → Look at 5-year CIN3+ Risk for management

- **Return in 1 year** — ≥0.55% 5-year CIN3+ risk
- **Return in 3 years** — ≥0.15% 5-year CIN3+ risk
- **Return in 5 years** — <0.15% 5-year CIN3+ risk

ASCCP Mobile App
www.asccp.org/APP

Algorithms © American Society Colposcopy and Cervical Cancer

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# Differences in screening account for mortality but not for disparities
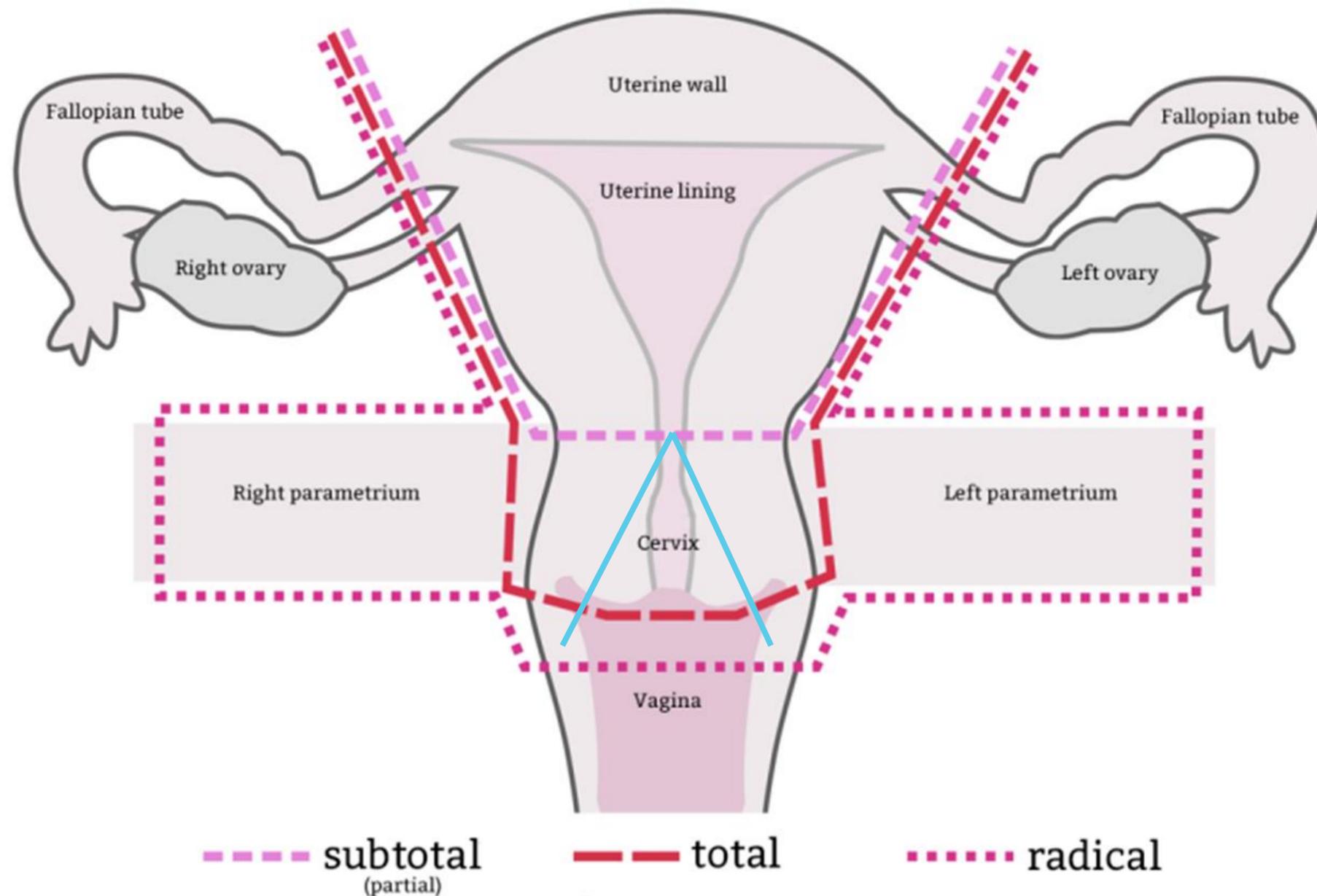
- **No differences by race in recent pap,** Sabatino et al 2013

- **No differences by race or rurality in adherence to screening,** Eggleston 2007  DOI: 10.1097/01.AOG.0000266396.25244.68

- **Possibly some differences in adherence to follow-up,** Bernard 2005 DOI: 10.1097/01.AOG.0000159549.56601.75

# Cervical cancer management in US

- **Primary Prevention** ➡ **Vaccination**

- **Secondary Prevention** ➡ **Screening and Treatment**

- **Early Diagnosis** ➡ **Surgery**

- **Advanced Disease** ➡ **Chemoradiation**

- **Metastatic Disease** ➡ **Combination chemotherapy**

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# Resection of cervical cancer: Choosing wisely



Uterine wall

Fallopian tube

Uterine lining

Fallopian tube

Right ovary

Left ovary

Right parametrium

Left parametrium

Cervix

Vagina

subtotal (partial) — total — radical

## Stage IA1 to Stage IB2

- **Conization vs trachelectomy**

- **Less push for parametrectomy**

- **Lymphadenectomy vs sentinel LND**

- **Open vs laparoscopic or robotic**

Presented By: Jennifer Young Pierce, MD, MPH

# Cervical cancer management in US

- **Primary Prevention** ➡ **Vaccination**

- **Secondary Prevention** ➡ **Screening and Treatment**

- **Early Diagnosis** ➡ **Surgery**

- **Advanced Disease** ➡ **Chemoradiation**

- **Metastatic Disease** ➡ **Combination chemotherapy**

Presented By: **Jennifer Young Pierce, MD, MPH**

# Black and White women receive different treatments

Presented By:

**Jennifer Young Pierce, MD, MPH**
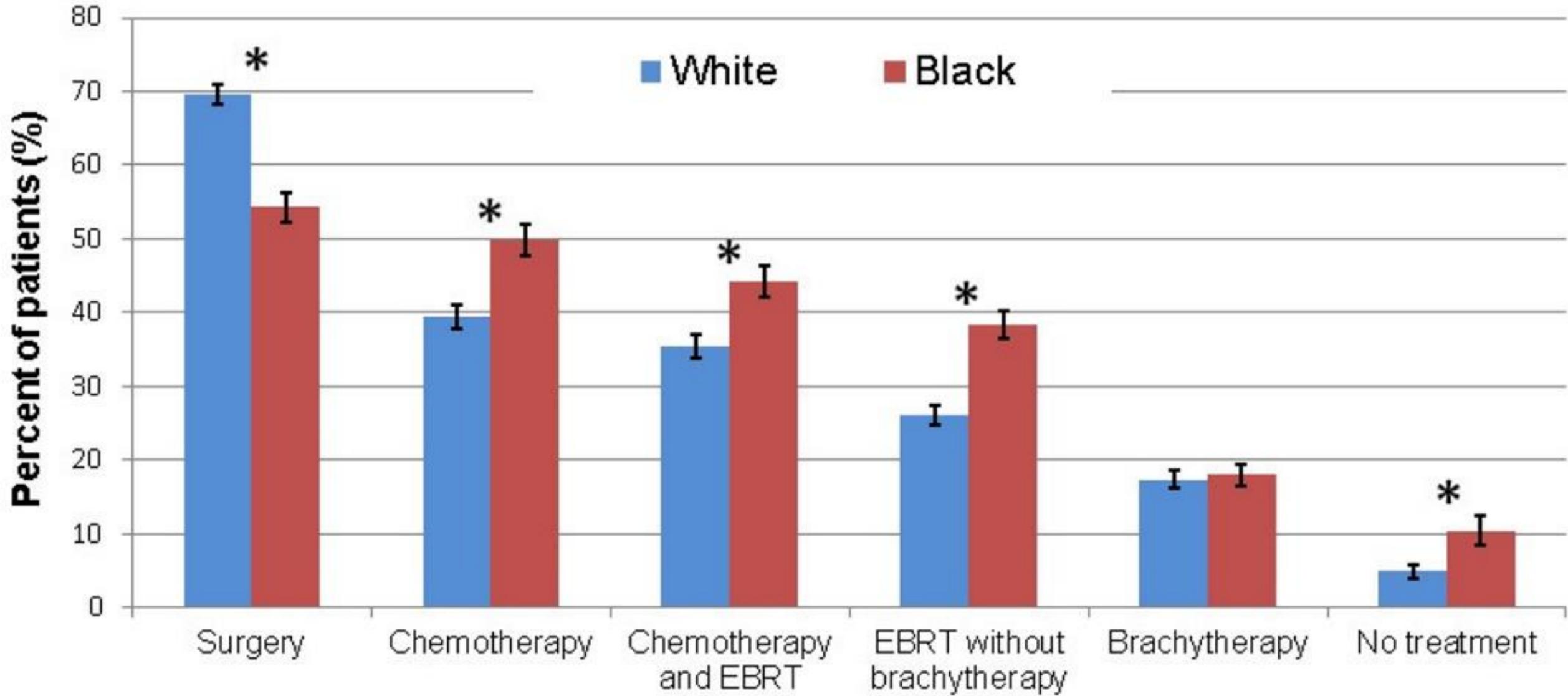
# Access vs aggressive cancer?

## Howell et al 1999 SEER database study

- Mortality 36% African American (AA) vs 24% Caucasian American (CA)
- Adjusted HR 1.30 (95% CI 1.14, 1.48) controlling for stage and other factors
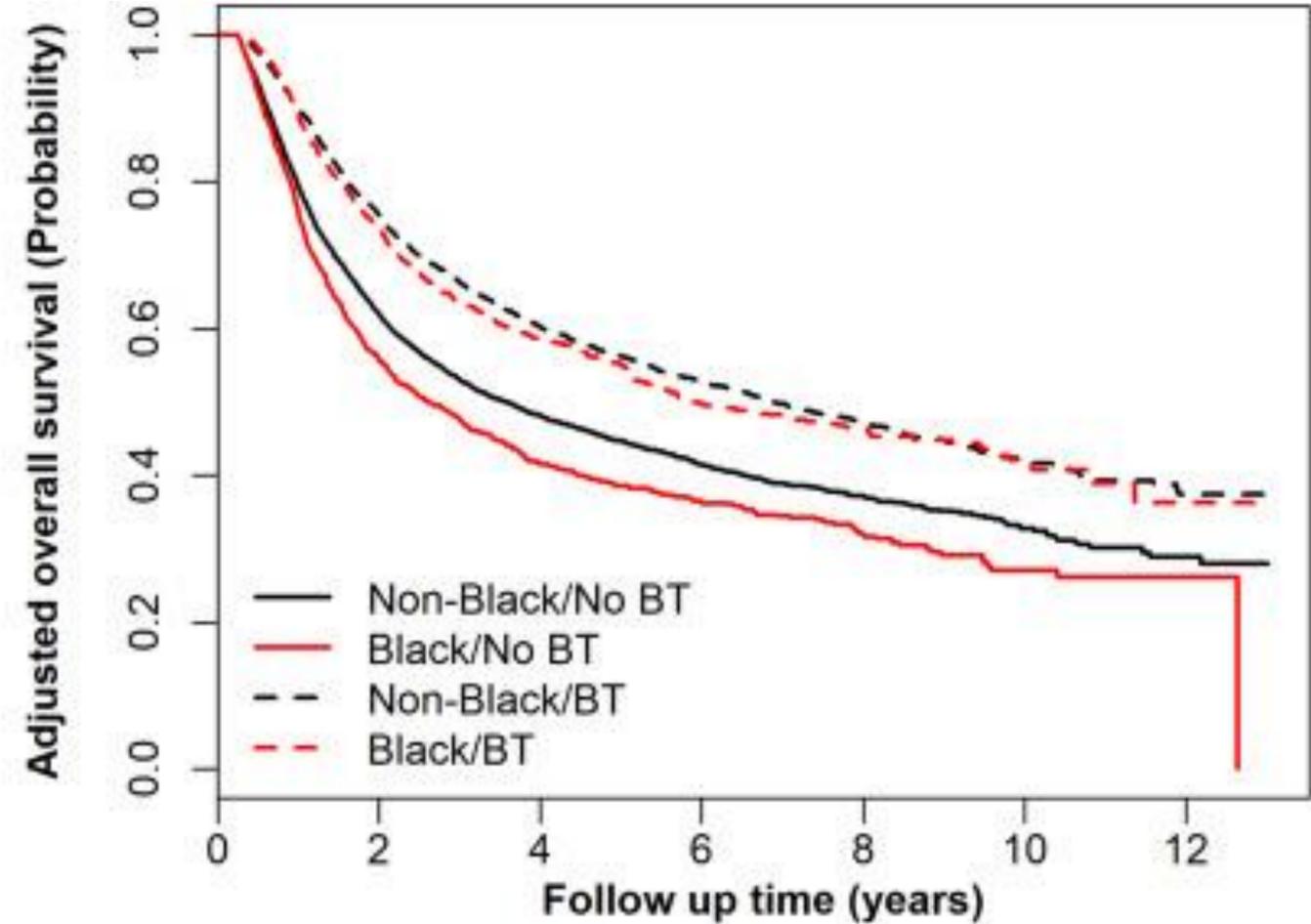
## Farley et al 2000

- Review of 1553 women in US Military HC System
- No difference in age, grade, stage, histology, or treatment
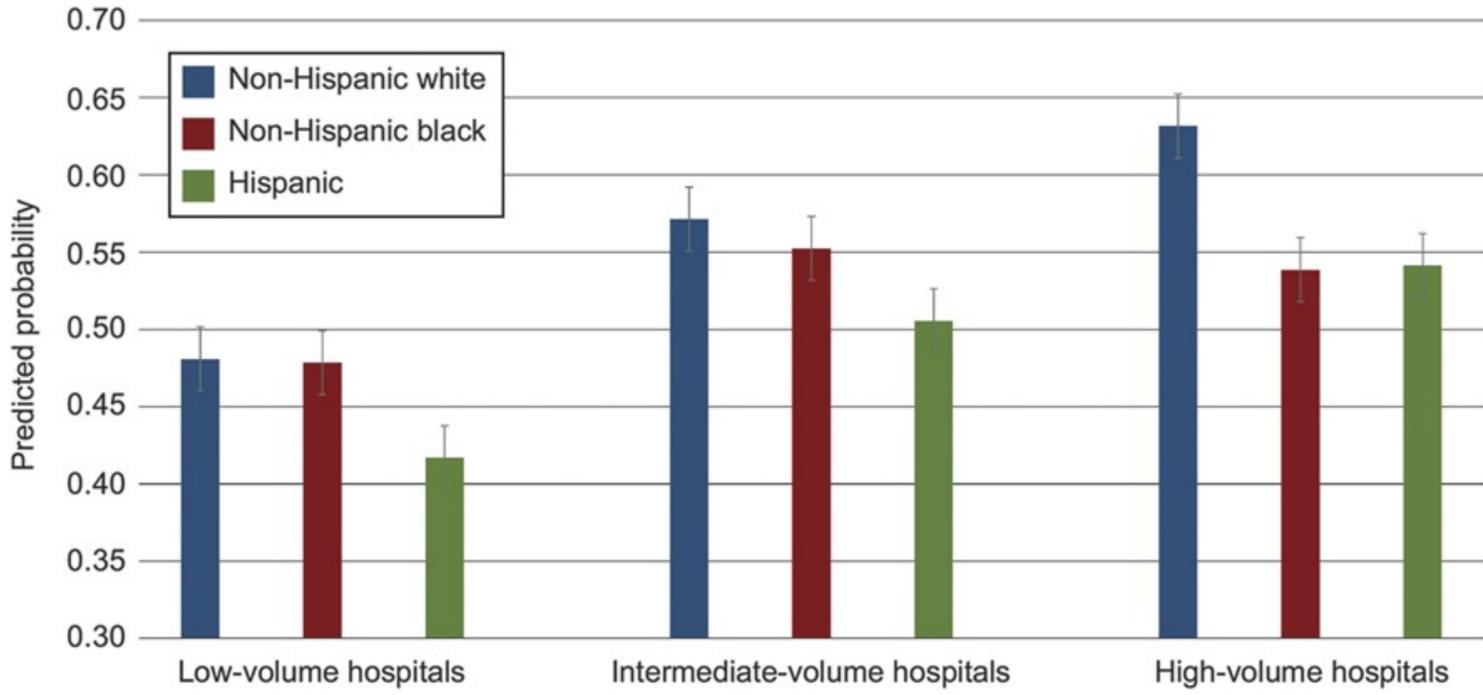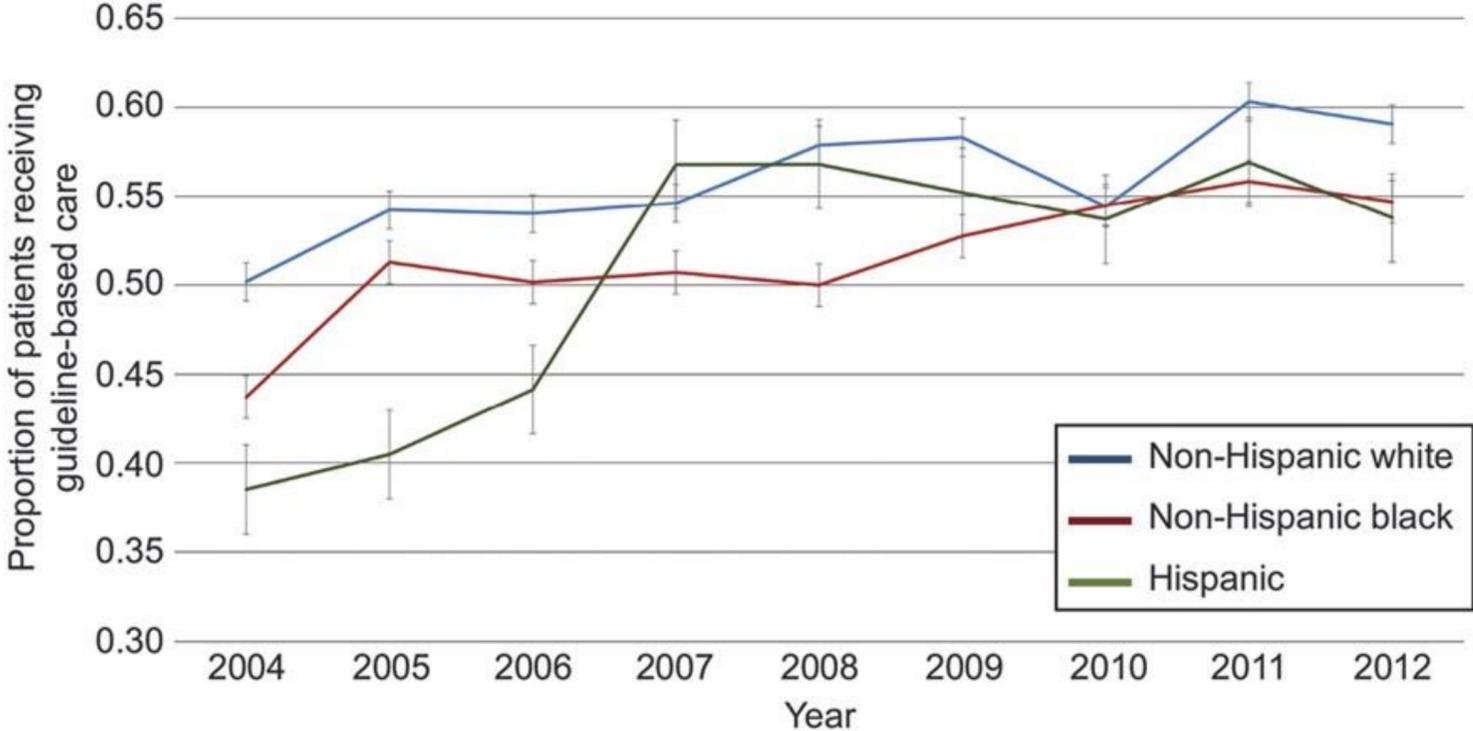- No difference in survival 76% AA vs 75% CA

## Sapp et al 2008

- AA Race associated with lower survival
- Deep stromal invasion significantly associated with lower survival
- Interaction between the two p=0.005
- Combined effect HR for death 7.04 (95% CI 2.48-19.94)

Presented By: Jennifer Young Pierce, MD, MPH

# Racial disparities in treatment with brachytherapy

Presented By: **Jennifer Young Pierce, MD, MPH**

# Can uniformity of treatment and guideline-based care eliminate disparities?

Presented By: **Jennifer Young Pierce, MD, MPH**

# Genetic alterations related to race may contribute to disparities

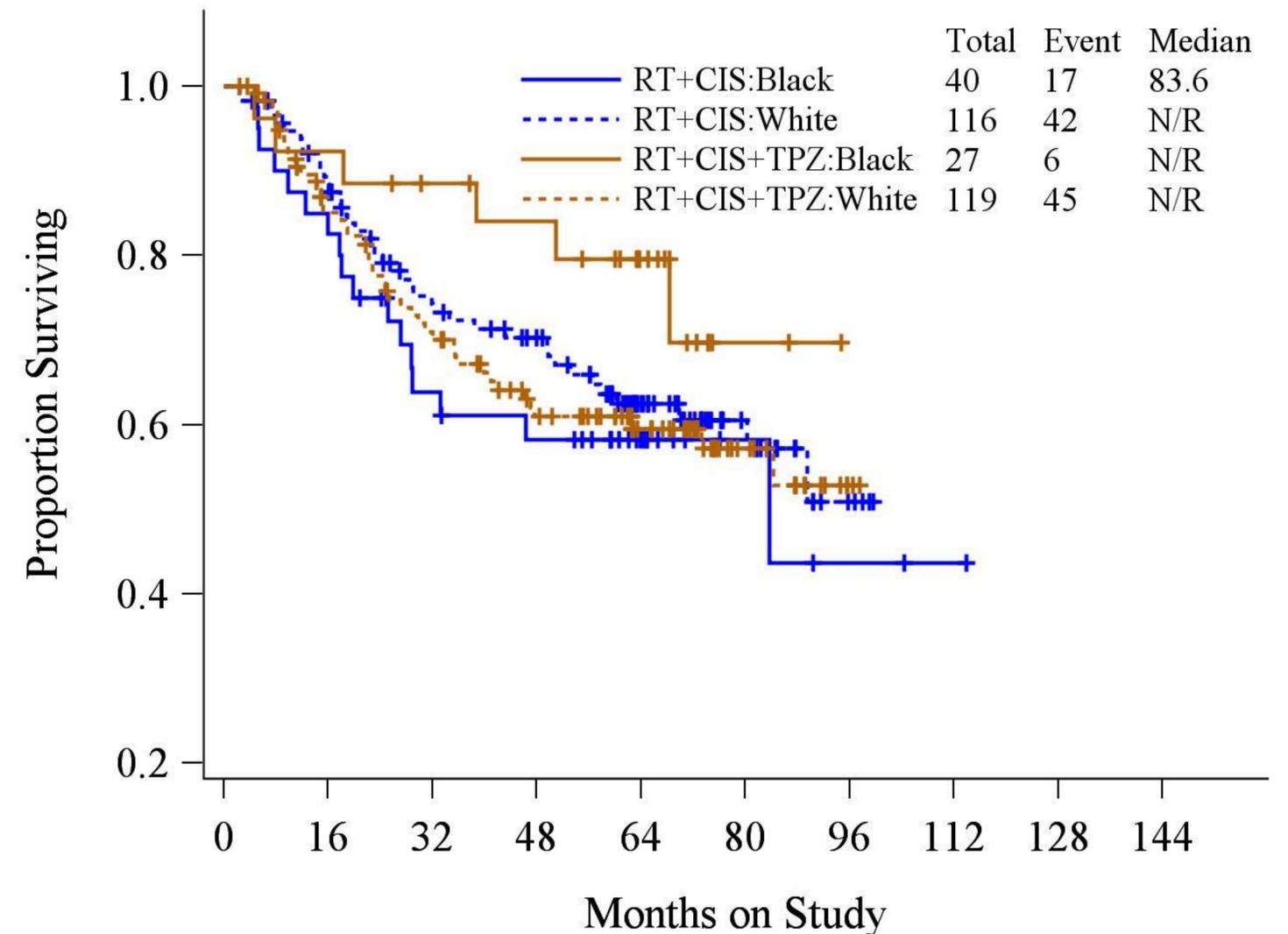**Increasing data supports molecular differences at the tumor level by race in other cancers**



Biological factors contributing to ovarian cancer disparity

| Mutations | Polymorphism | Alteration in gene expression | Differential methylation |
|-----------|--------------|-------------------------------|--------------------------|
| BRCA-1 BRCA-2 | Vitamin D receptor Androgen receptor TGFbetaR1 p53 | PSPHL BCAT1 | TUSC3 SPARC |
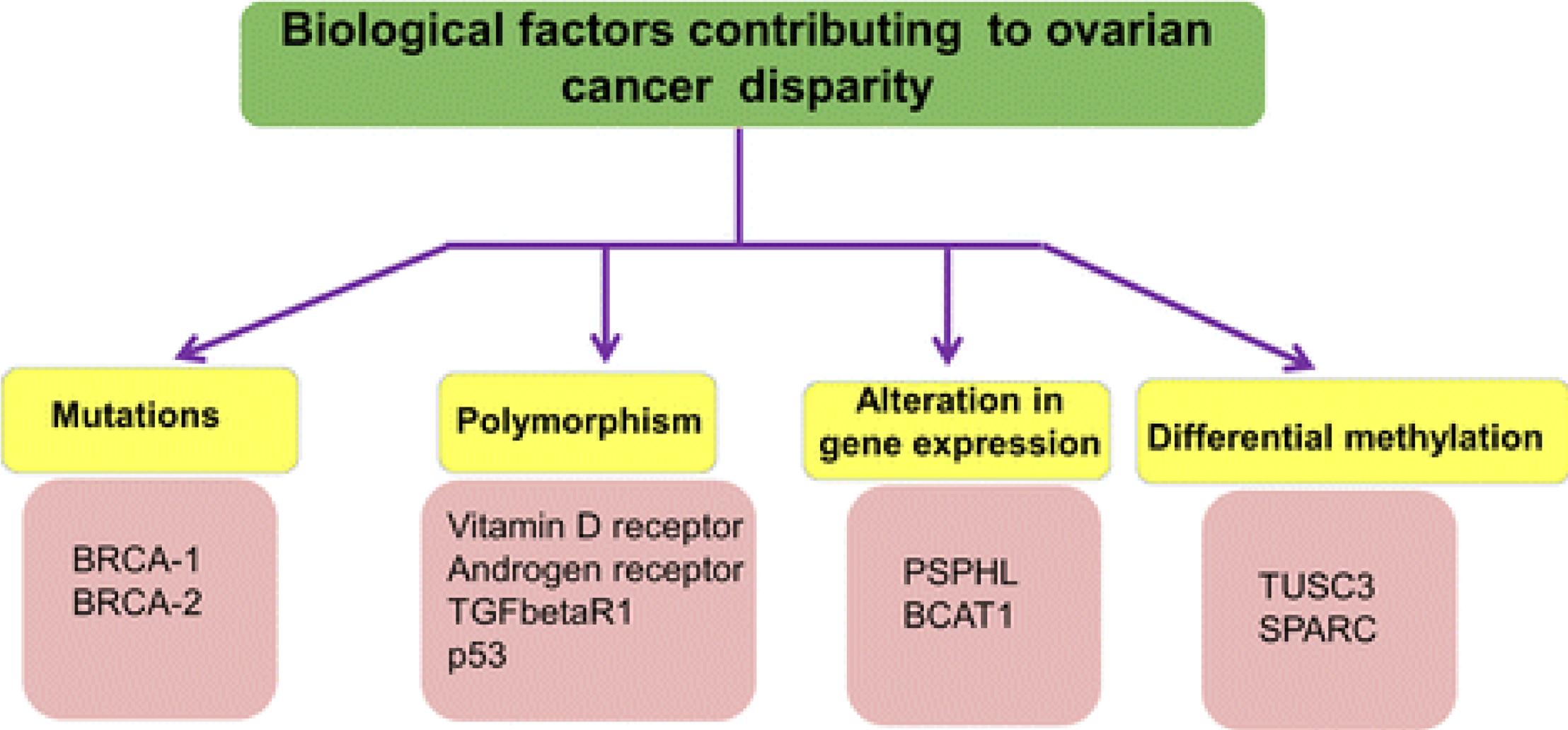
*Guttery et al. Oncotarget 2018.*

Presented By:   Jennifer Young Pierce, MD, MPH

# Differences in response to therapy by race on trials

**Analysis of GOG clinical trials for racial disparity**

**Locally advanced cervical cancer treated on Phase III GOG trials:**

191: Phase III trial of maintaining Hb > 12 with erythropoietin during chemoradiation

219: Phase III trial randomized weekly cisplatin and irradiation +/-tirapazamine

233: Utility of Preop PET/CT prior to primary chemoradiation



| | Total | Event | Median |
|---|---|---|---|
| RT+CIS:Black | 40 | 17 | 83.6 |
| RT+CIS:White | 116 | 42 | N/R |
| RT+CIS+TPZ:Black | 27 | 6 | N/R |
| RT+CIS+TPZ:White | 119 | 45 | N/R |

**5 yr OS AA w/ TPZ vs AA w/o**
**79% vs 61 % (p=0.123)**

*Young Pierce et al NRG 2016*

Presented By:  Jennifer Young Pierce, MD, MPH

# Cervical cancer management in US

- **Primary Prevention** ➡ **Vaccination**

- **Secondary Prevention** ➡ **Screening and Treatment**

- **Early Diagnosis** ➡ **Radical hysterectomy**

- **Advanced Disease** ➡ **Chemoradiation**

- **Metastatic Disease** ➡ **Combination chemotherapy**

Presented By: Jennifer Young Pierce, MD, MPH

# NCI Alert: GOG 240 shows Bevacizumab added to chemotherapy for metastatic disease improves survival

**Improved overall survival at 12 mo from ~30% to 60%**
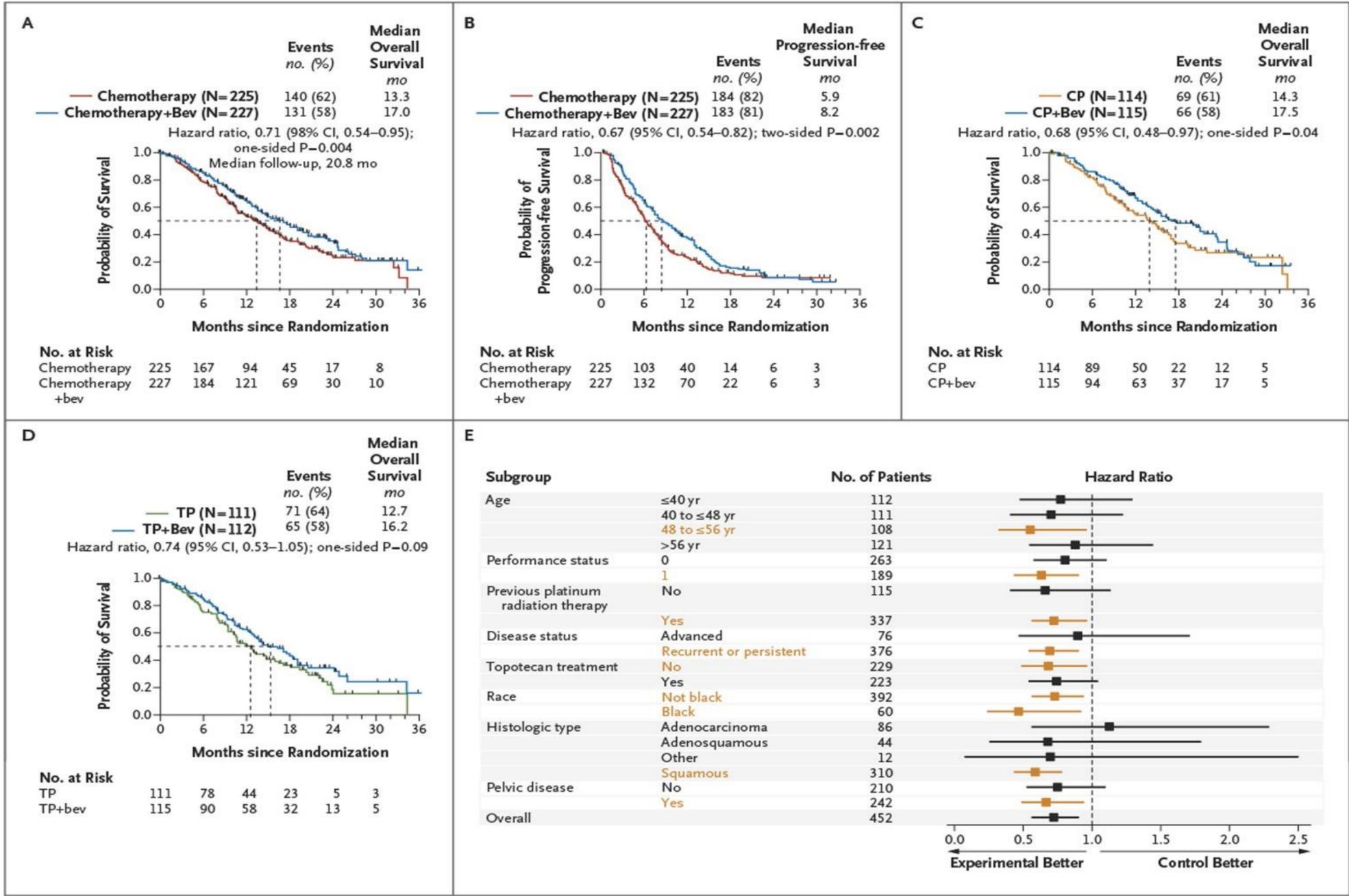
# Immunotherapy for cervical cancer

| / | KEYNOTE-158 [8] | CheckMate 358 [20] |
|---|---|---|
| Treatment | pembrolizumab | nivolumab |
| n | 98 | 19 |
| ORR (95% CI) | 12.2% (6.5 to 20.4) | 26.3% (9.1 to 51.2) |
| DCR (95% CI) | 30.6% (21.7 to 40.7) | 68.4% (43.4 to 87.4) |
| Best overall response | | |
| CR | 3 (3.1%) | 3 (15.8%) |
| PR | 9 (9.2%) | 2 (10.5%) |
| SD | 18 (18.4%) | 8 (42.1%) |
| PD | 55 (56.1%) | 6 (31.6%) |
| Not able to be evaluated* | 5 (5.1%) | 0 (0%) |
| Not able to be assessed# | 8 (8.2%) | 0 (0%) |

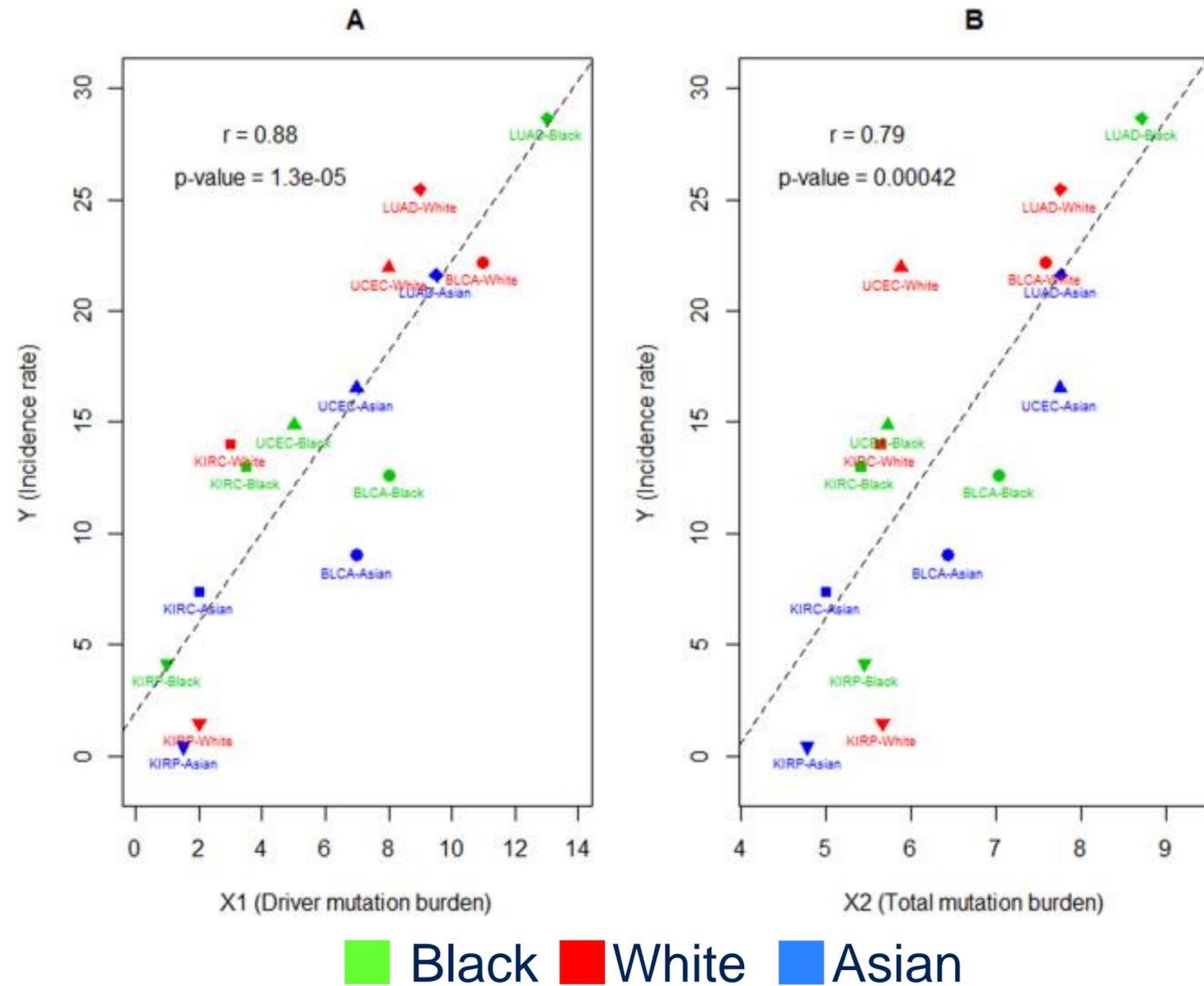- **Pembroluzimab 200mg IV q3 FDA approved for pd-1 + r/m cervical cancer**
  - Q6 wk dosing approved 4/20
- **Ongoing study in:**
  - **Combination therapy**
  - **Use of checkpoint inhibition in combination with chemoradiation**

Presented By: **Jennifer Young Pierce, MD, MPH**

# Racial differences in immunotherapy response

## Race differences in tumor mutational burden



Black ■ White ■ Asian

*Zhang et al 2017 doi: 10.1038/s41598-017-13091-y*

## Tumor mutational burden and response rate KEYNOTE 158
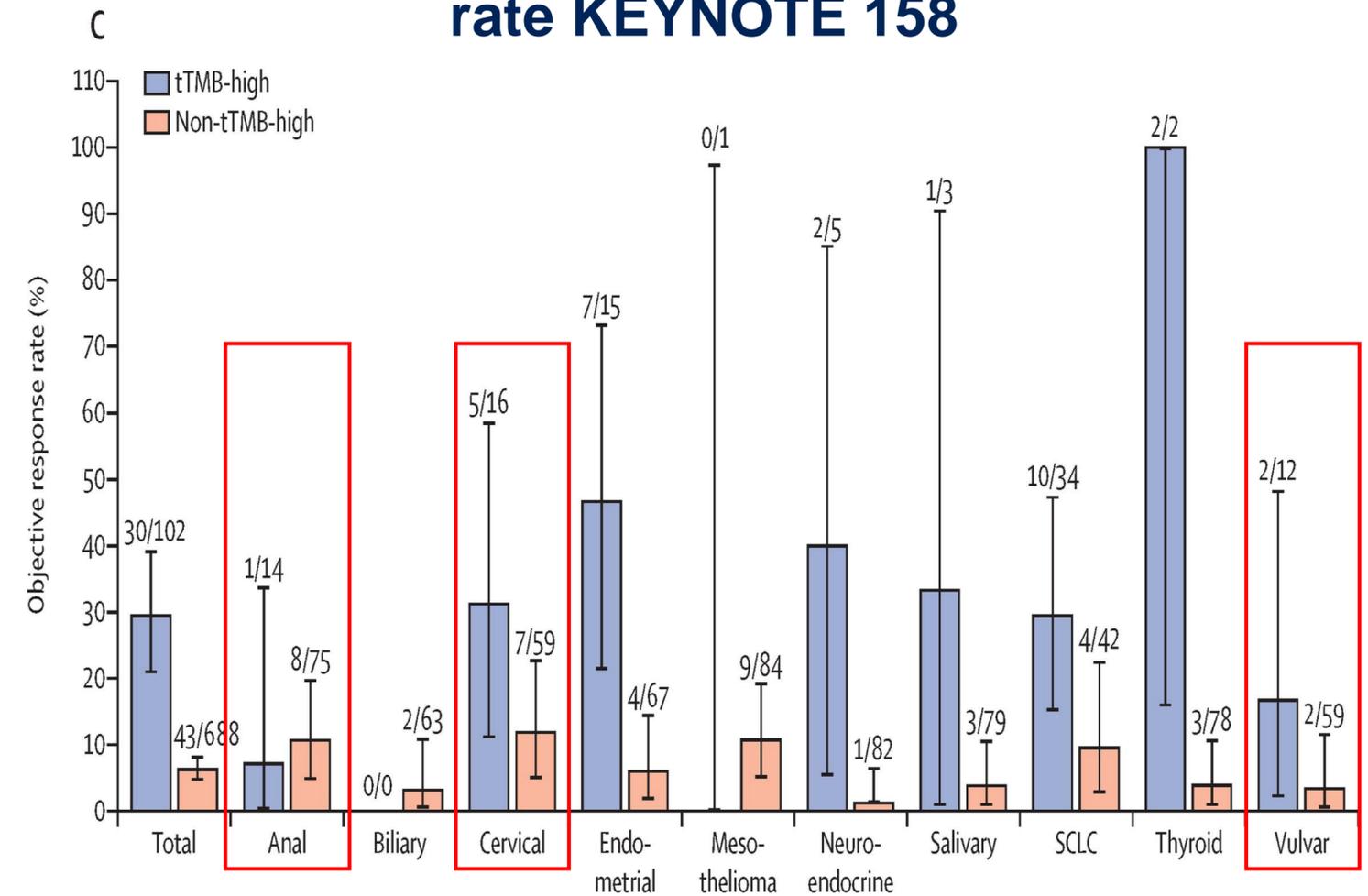


*Marabelle et al 2020. Lancet Oncology DOI: (10.1016/S1470-2045(20)30445-9)*

Presented By: **Jennifer Young Pierce, MD, MPH**

# Emerging immunotherapies

- **Opdivo (nivolumab) with Yervoy (ipilimumab) (anti-CTLA-4)**
  - CheckMate 358 clinical trial presented at the 2019 ESMO
  - 46% of previously untreated and 36% of those receiving prior systemic treatment responded

- **GOG-3028 (C-750-01): RaPiDS Balstilimab (anti-PD1)-Zalifrelimab (anti-CTLA-4) combination**
  - 20% RR including 6% complete response

- **Cryopreserved autologous TIL**
  - **Tumor infiltrating lymphocytes**
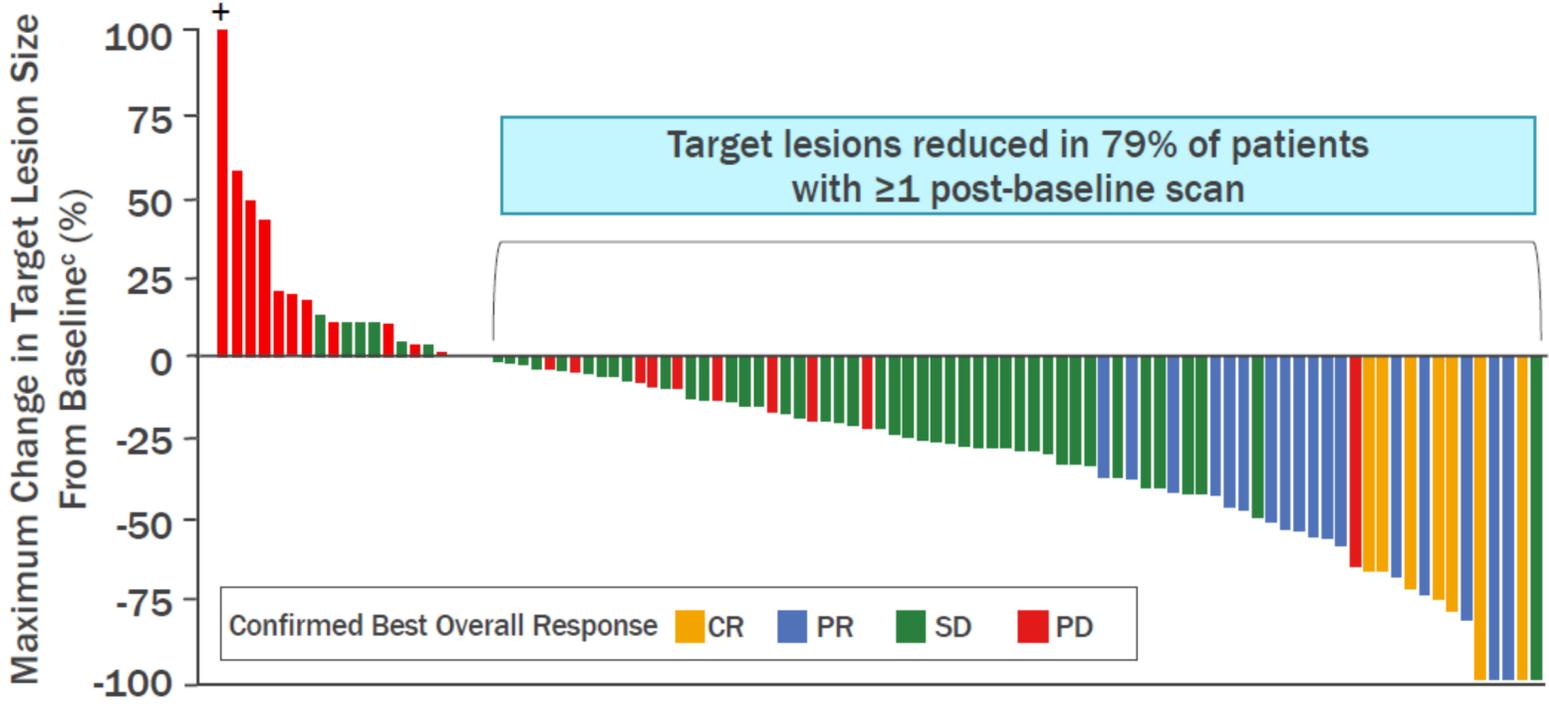  - **Harvested from surgically removed specimen**



**ORR 44%!**

*Naumann W, LBA 62 ESMO 2019. O'Malley DM, LBA34. ESMO 2020*

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# Emerging therapies (continued)

- ## Tissue factor antibody: Tisodamab Vindontin

  - InnovaTV 204/ GOG-3023/ENGOT-cx6
  - Recurrent progressive cervical cancer after platinum-based doublet with bev
  - 2.0 mg/kg IV q 3 weeks
  - Treated 101 women

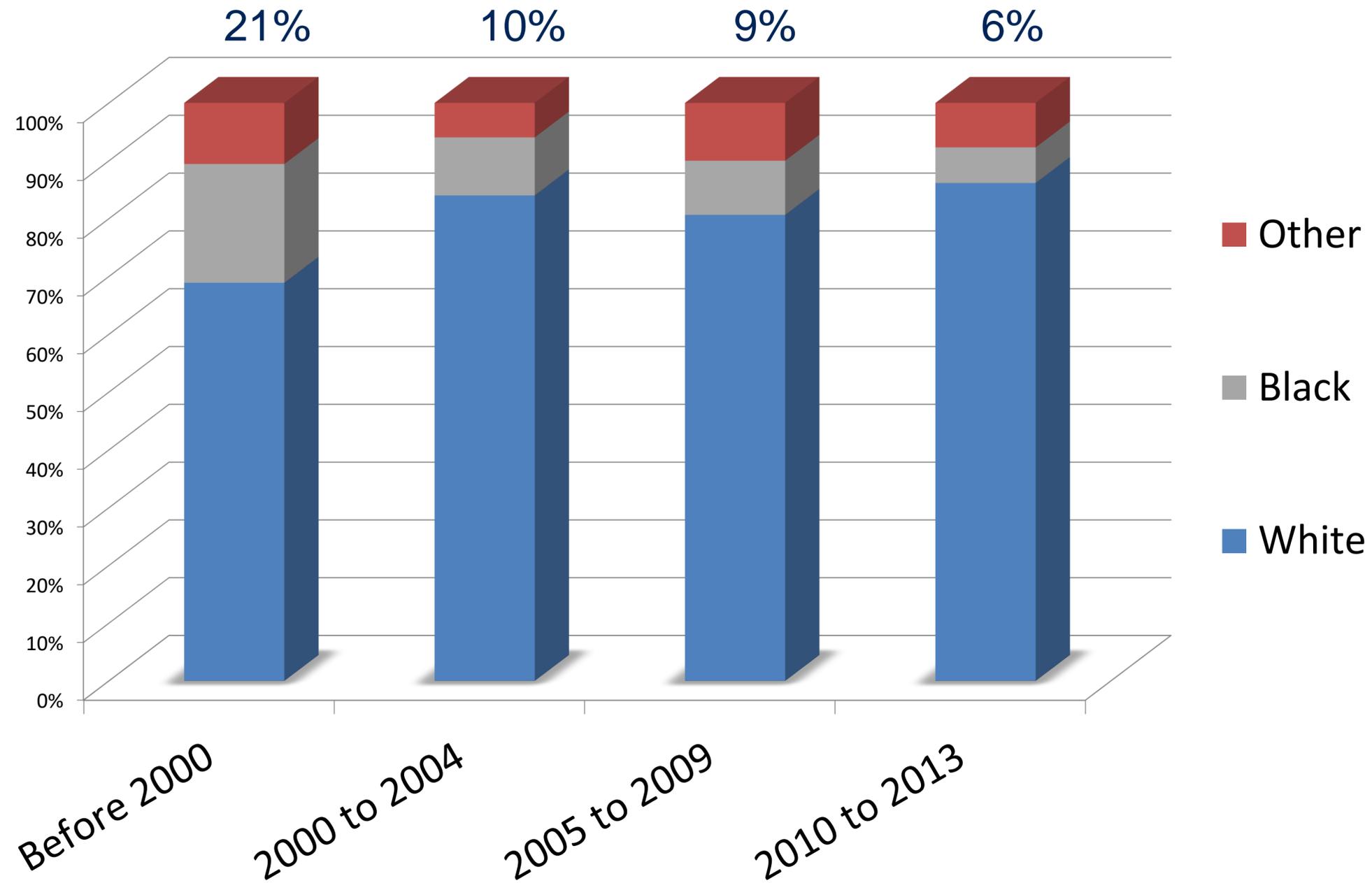| | N=101 |
|---|---|
| Confirmed ORR (95% CI),[a] % | 24 (15.9–33.3) |
| CR, n (%) | 7 (7) |
| PR, n (%) | 17 (17) |
| SD, n (%) | 49 (49) |
| PD, n (%) | 24 (24) |
| Not evaluable, n (%) | 4 (4) |
| Disease control rate (95% CI),[b] % | 72 (62.5–80.7) |
| Median duration of response (95% CI), mo | 8.3 (4.2–NR) |
| Median time to response (range), mo | 1.4 (1.1–5.1) |

Target lesions reduced in 79% of patients with ≥1 post-baseline scan

Maximum Change in Target Lesion Size From Baseline[c] (%)

Confirmed Best Overall Response: CR, PR, SD, PD

*Coleman R, et al. ESMO 2020. LBA32.*

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# Minority participation in GOG studies
## Rocconi et al 2016

# "Too many women are dying from cervical cancer"

- ## Gaffney et al 2018

  - Increasing education and access for HPV vaccination
  - Nontraditional screening methods for unscreened populations
  - Improve adherence to guidelines through healthcare, access, and ethically similar physician population
  - Ensure widespread chemoradiation
  - Identify new targets and mutation-specific trials

- ## Pierce 2021 additions

  - Increase nonwhite enrollees clinical trials
  - Continue to evaluate genetic and post genetic associations with race-ISM

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# THANK YOU!