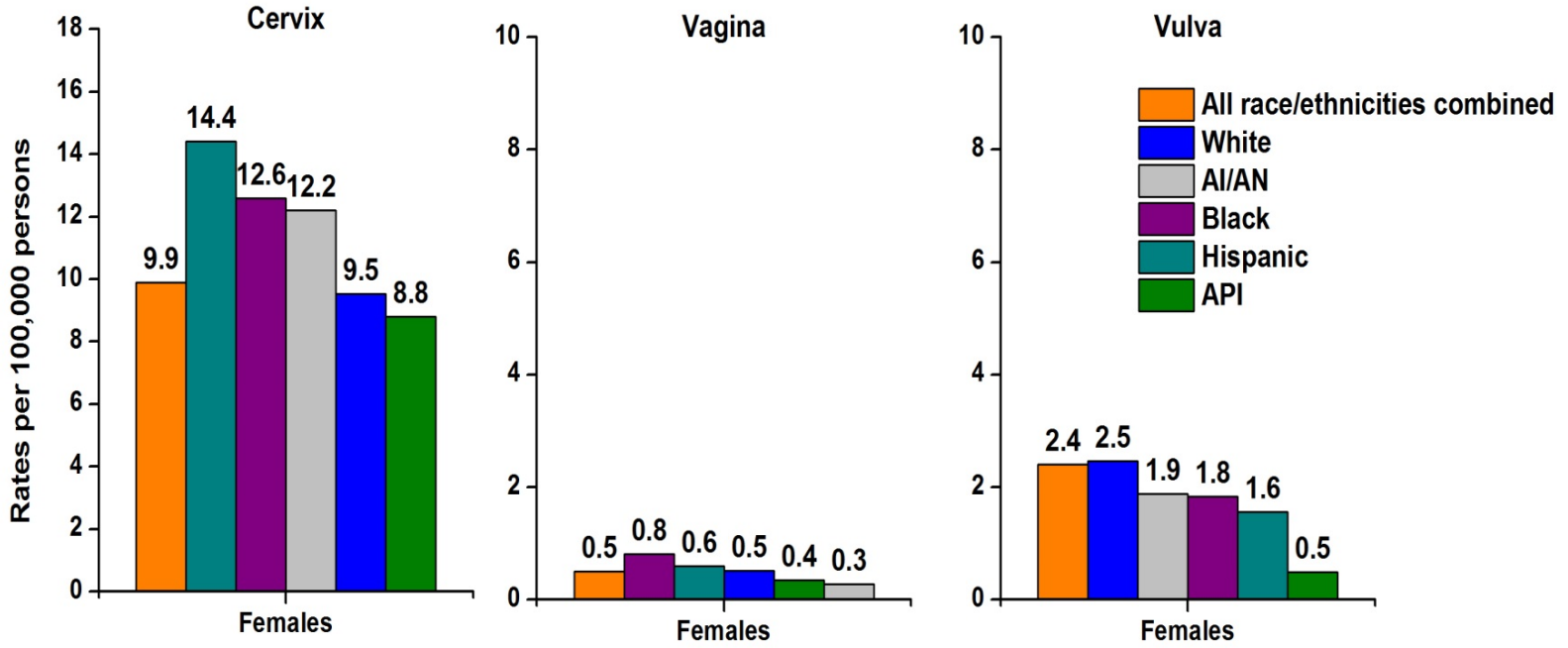
Population-Based HPV Genotype Attribution in HPV-Associated Cancers, United States

Mona Saraiya MD, MPH
NCCDPHP/CDC

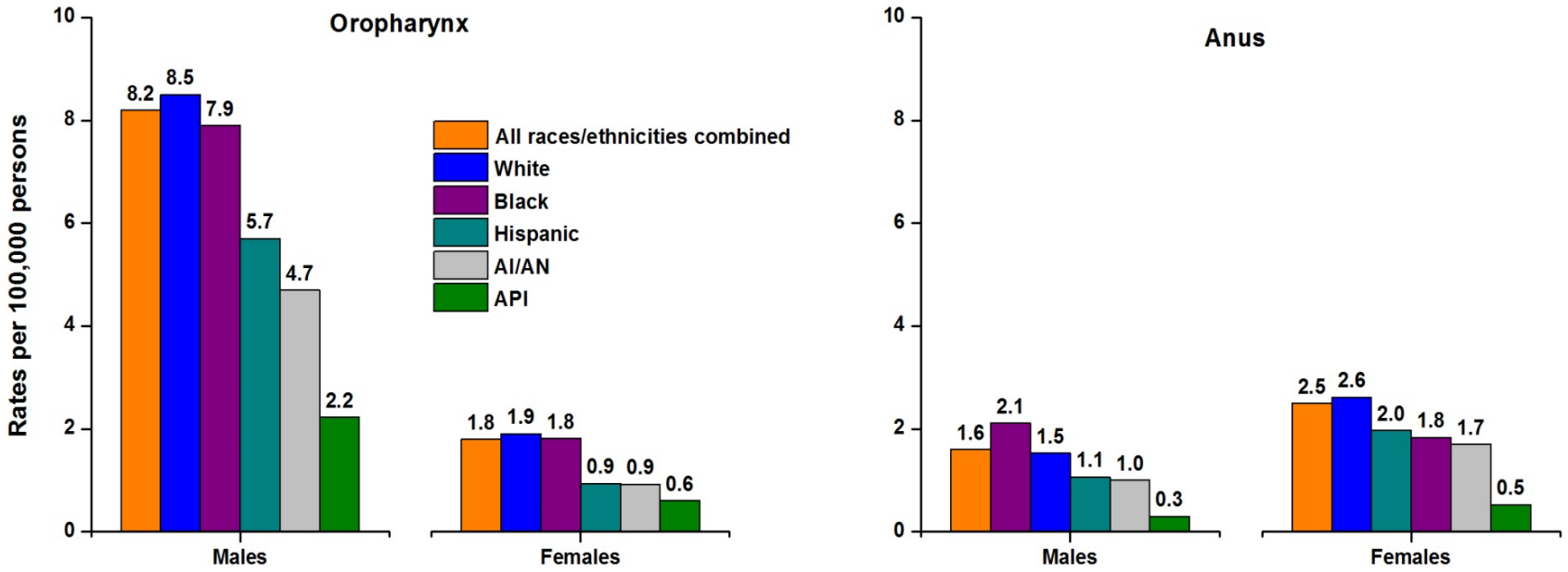
Advisory Committee on Immunization Practices
February 27, 2014
Atlanta, GA

Incidence of HPV-associated Cancers by Race in the United States



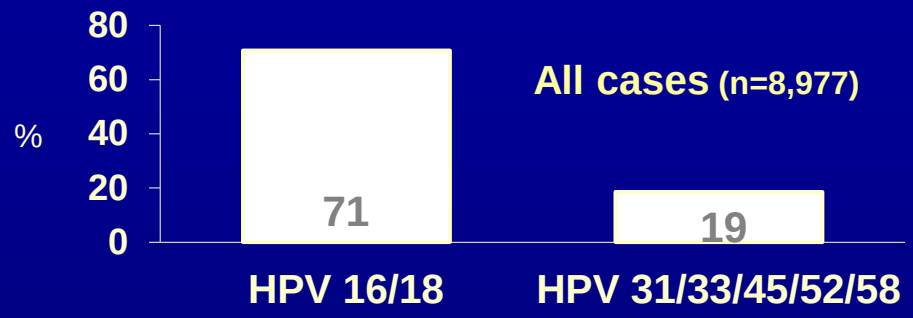
Jemal et al, J Natl Cancer Inst 2013
API: Asian/Pacific Islander
AI/AN: American Indian Alaska Native

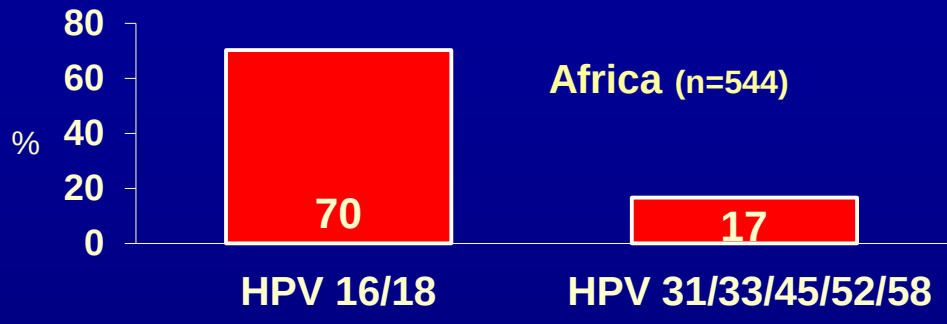
Incidence of HPV-associated Cancers by Race and Gender in the United States

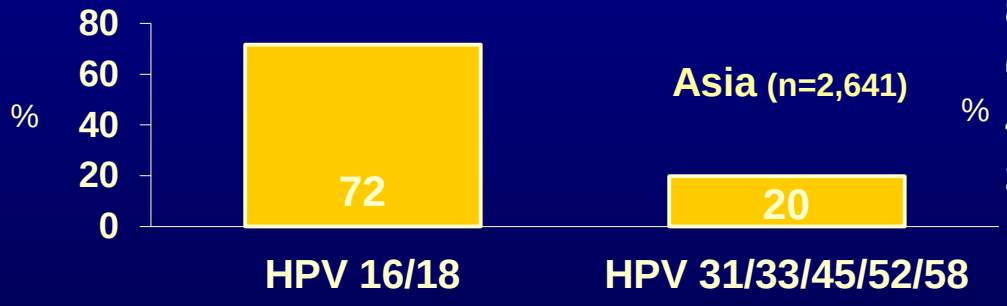


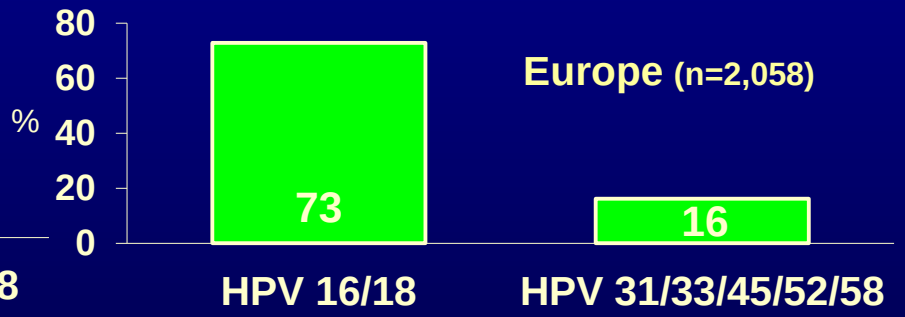
Jemal et al, J Natl Cancer Inst 2013
API: Asian/Pacific Islander
AI/AN: American Indian Alaska Native

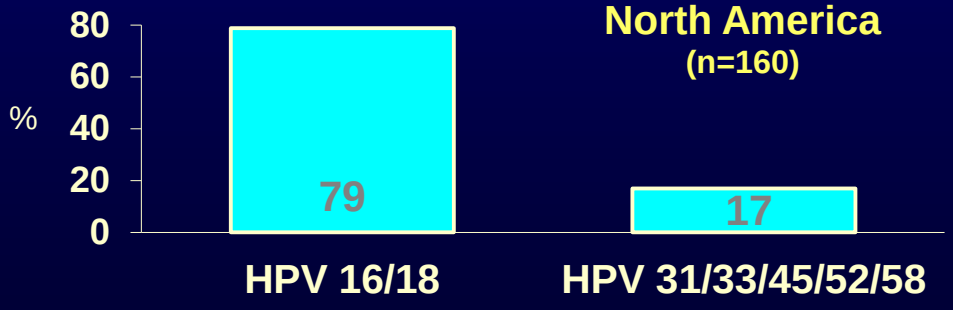
Relative Contribution of HPV16/18 and HPV 31/33/45/52/58 in Invasive Cervical Cancer by Region

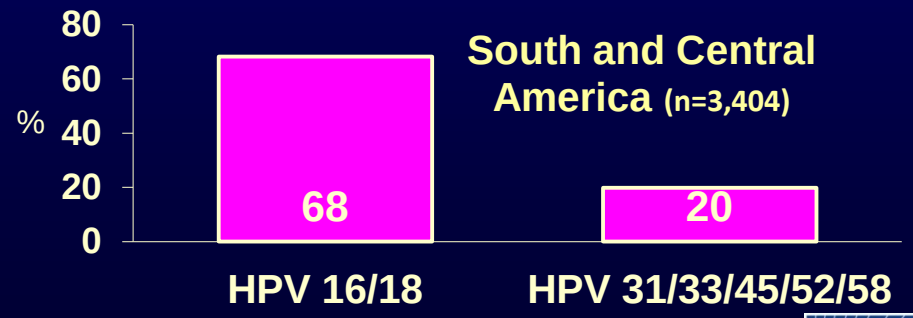












*Denominator is among all HPV positives, Serrano et al, Infectious Agents and Cancer, 2012

CDC
Centers for Disease Control and Prevention

Previous Estimated Percentages of HPV Attribution in the U.S.

Cancer	HPV Attributable % (95% CI)	HPV 16/18 Attributable % (95% CI)
Cervical	96 (95-97)	76 (NA)
Vaginal	64 (43-82)	56 (35-76)
Vulvar	51 (37-65)	44 (30-58)
Anal	93 (86-97)	87 (82-91)
Penile	36 (26-47)*	31 (22-42)
Oropharyngeal	63 (50-75)	60 (47-72)

Gillison, Cancer 2008
% Any HPV is percentage HPV detected in all cancers
*% HPV for penile cancer is % where any oncogenic HPV type detected
% HPV 16/18 is percentage HPV 16/18 detected among all cancers

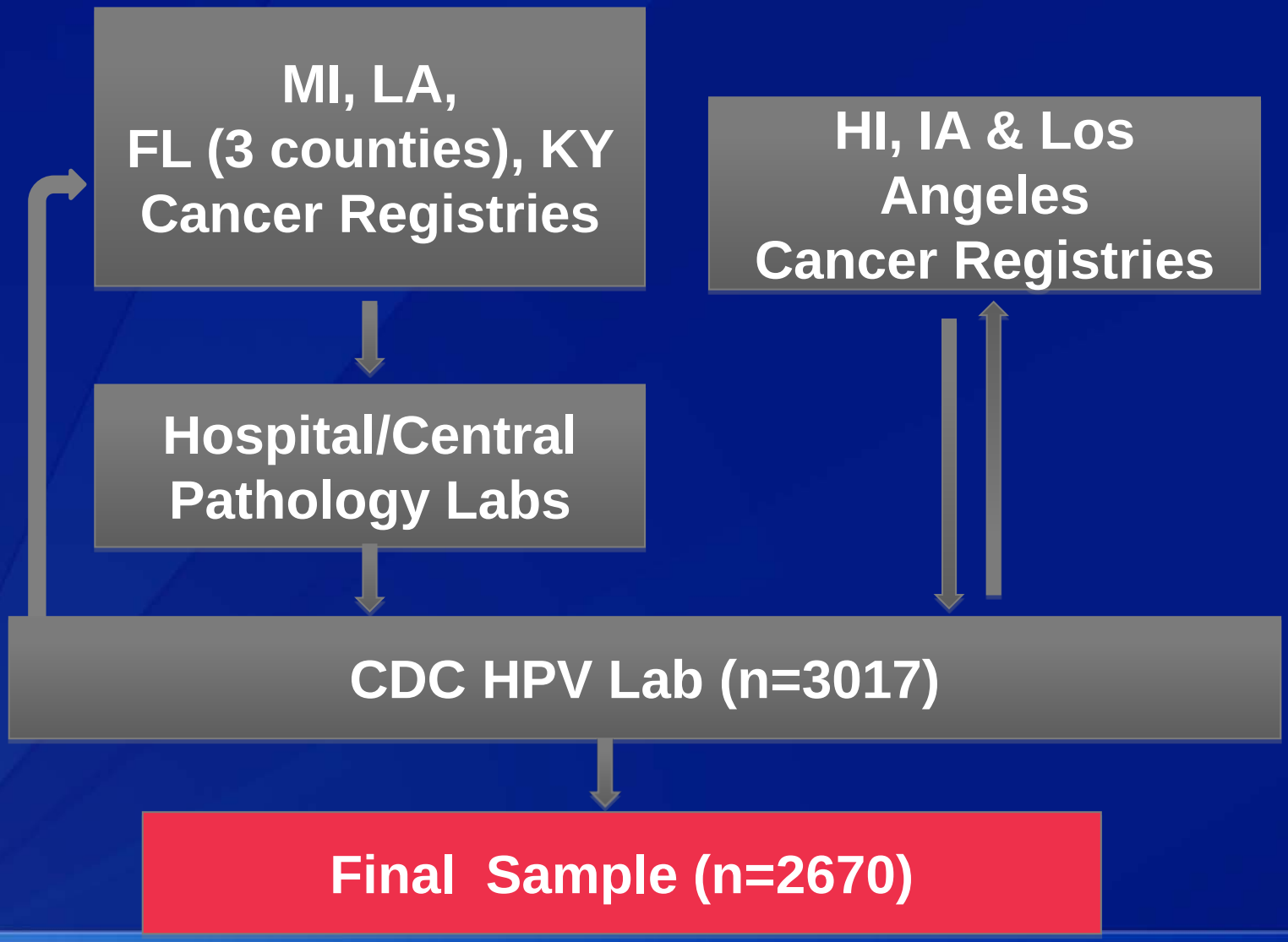
Objectives

- To establish systematic population-based approach to monitoring of HPV types in cervical cancer and other HPV-associated cancers in the United States
- To determine attribution of HPV 16/18 and additional types in candidate 9-valent vaccines
- To determine HPV type attribution by race/ethnicity

Study Design-HPV Typing of Cancers in U.S.

- Majority cases diagnosed from 2004-2005
- 4 cancer registries (KY, MI, LA, and FL) recruited pathology labs
- 3 (HI, IA, and Los Angeles) cancer registries used repositories
- Invasive cancers and *in situ* cervical cancer (CIN3)
- Systematic sampling of cancers with large burden and entire sampling for rare cancers
- HPV genotyping by CDC Lab
- Attribution method same (previous presentation)
  - HPV 16/18
  - HPV 31/33/45/52/58
  - Other HPV types
  - HPV negative
- Denominator includes all cancers

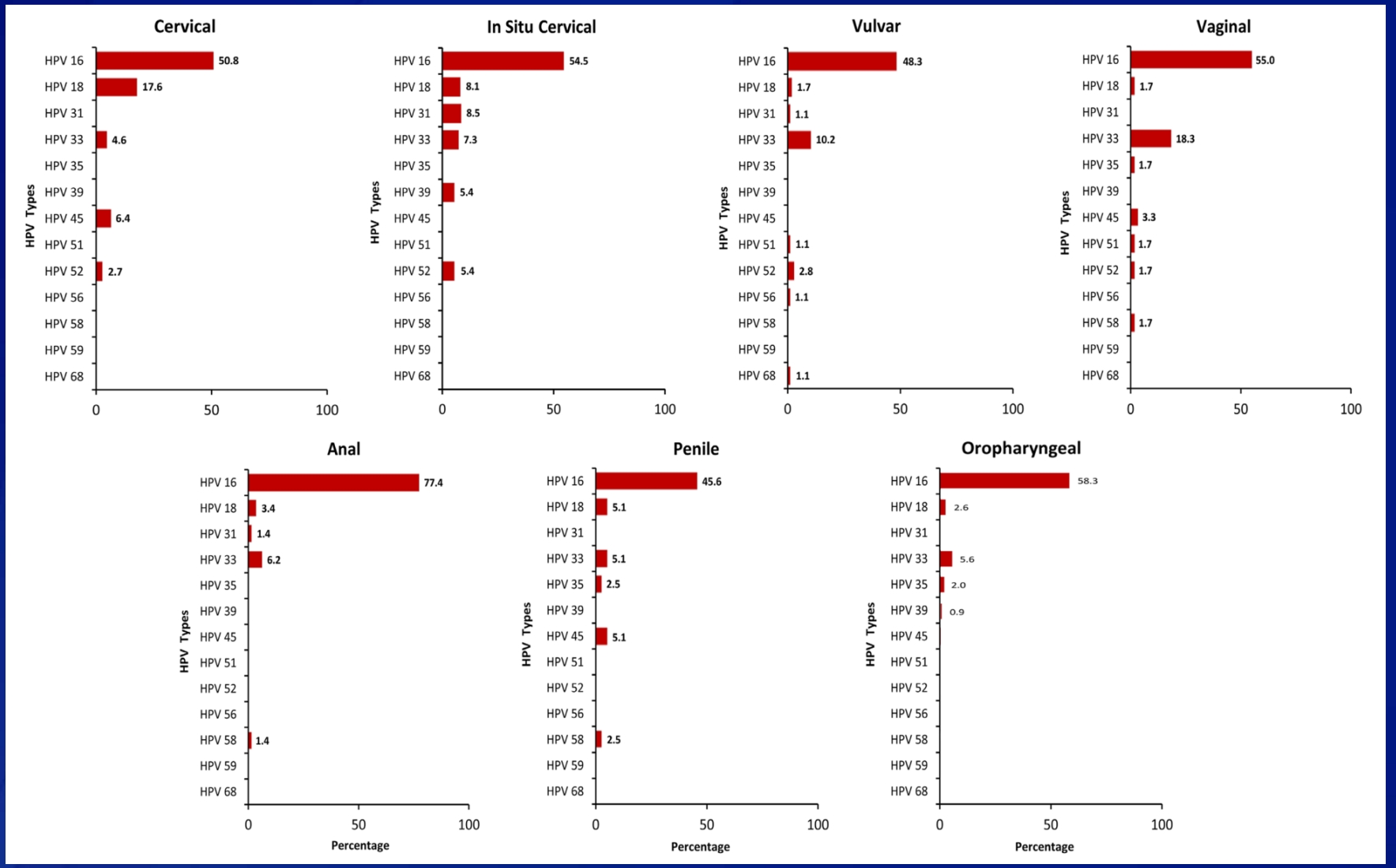
Tissue Submission Process



HPV Detection by Cancer Site

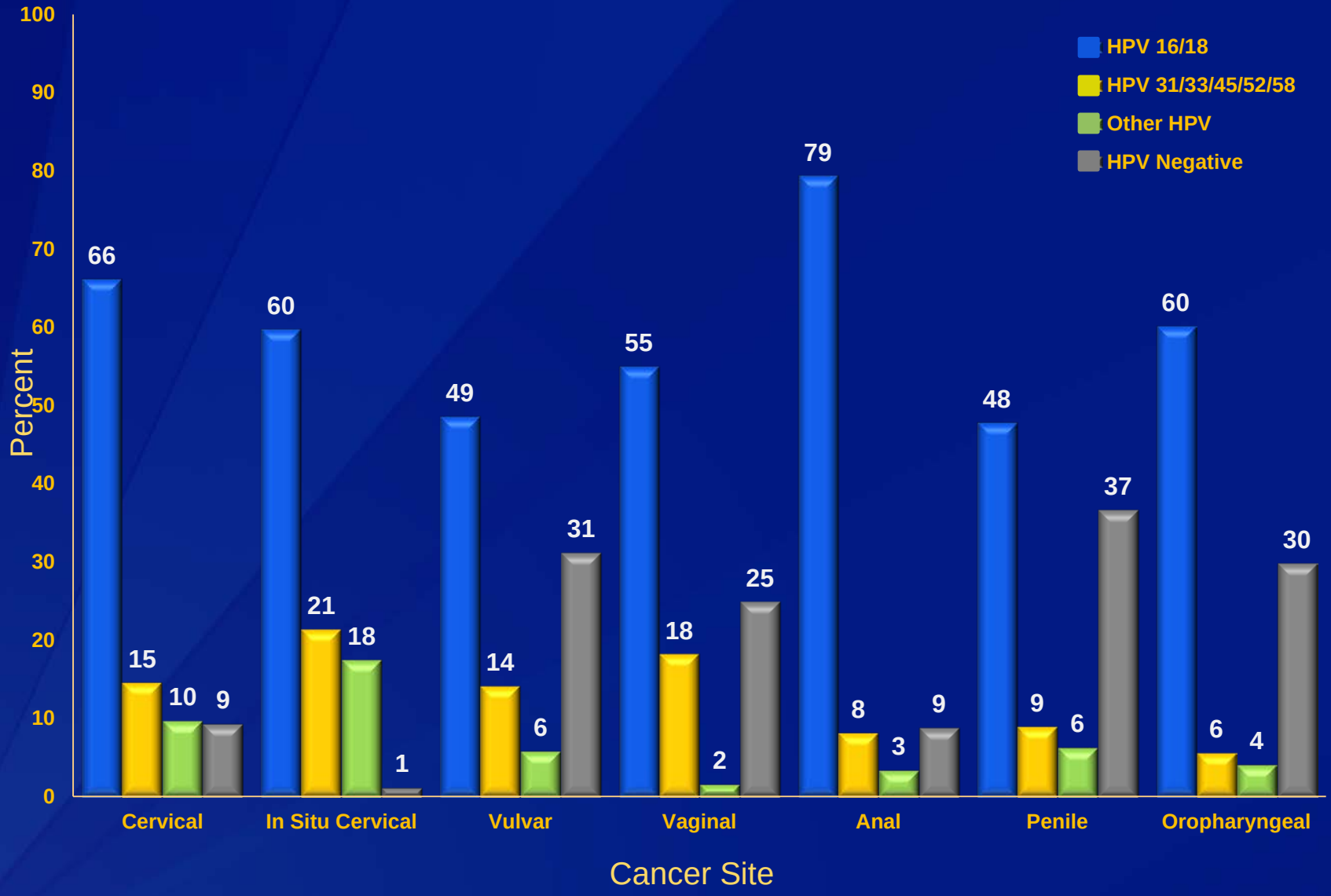
Saraiya et al, presented at International Papillomavirus Conference 2012, Puerto Rico

Top 5 Oncogenic Types in Select Cancers



Saraiya et al, presented at AACR Health Disparities in Cancer, 2013

Type Attribution by Cancer Site

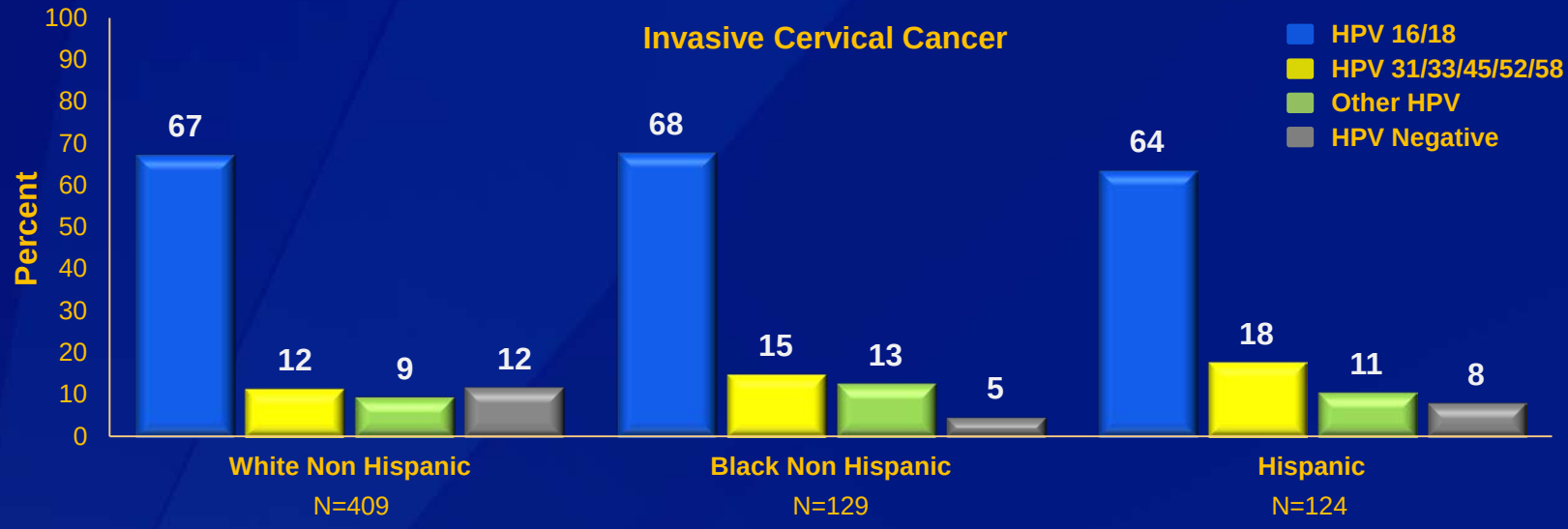


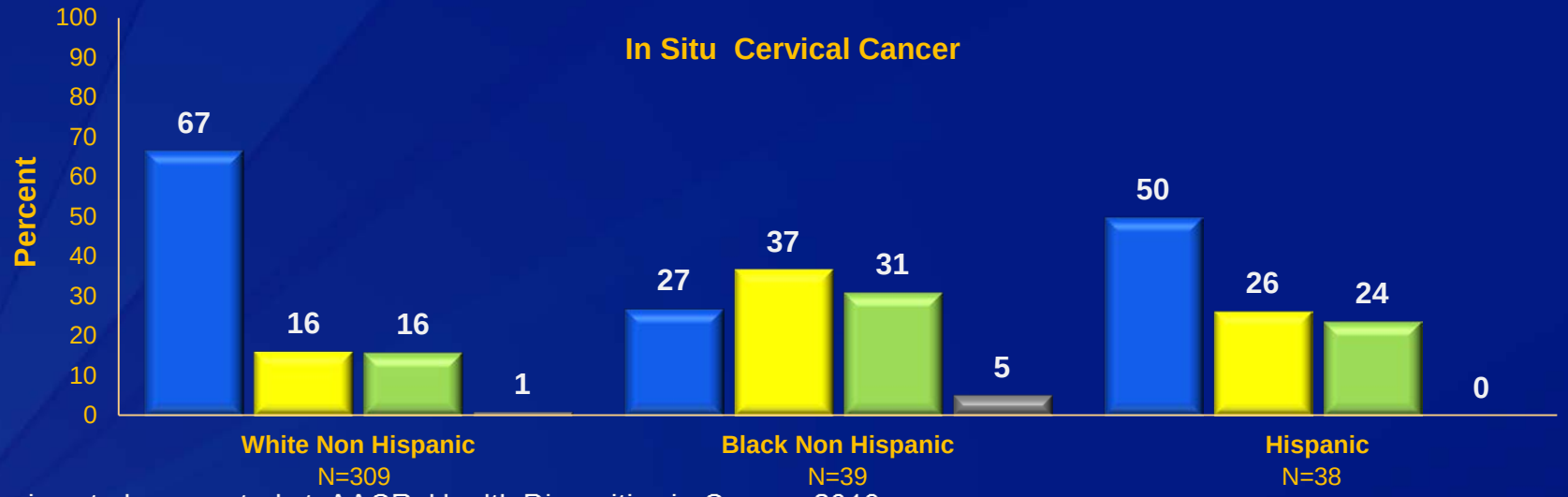
Saraiya et al, presented at AACR Health Disparities in Cancer, 2013

HPV Type Attribution: General Findings

- By age
  - Higher proportion of cancers in younger age groups attributable to HPV 16/18 (data not shown)
- By race/ethnicity
  - No differences for cancers except
    - *In situ* cervical cancer
    - Oropharyngeal cancers
- By gender
  - No differences for cancers except oropharyngeal cancers

HPV Attribution by Race/Ethnicity
Invasive vs. In Situ Cervical Cancer



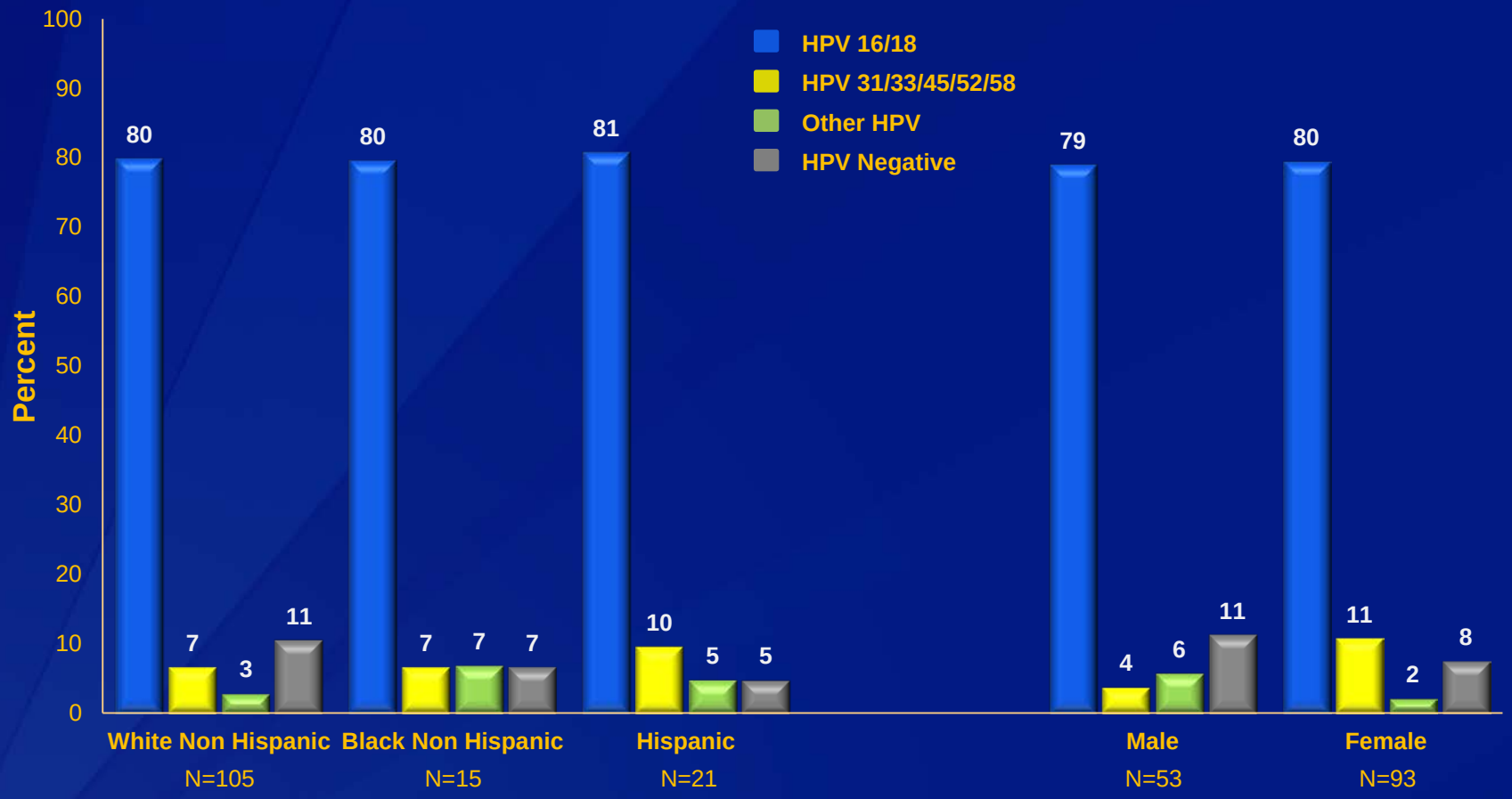


Saraiya et al, presented at AACR Health Disparities in Cancer, 2013

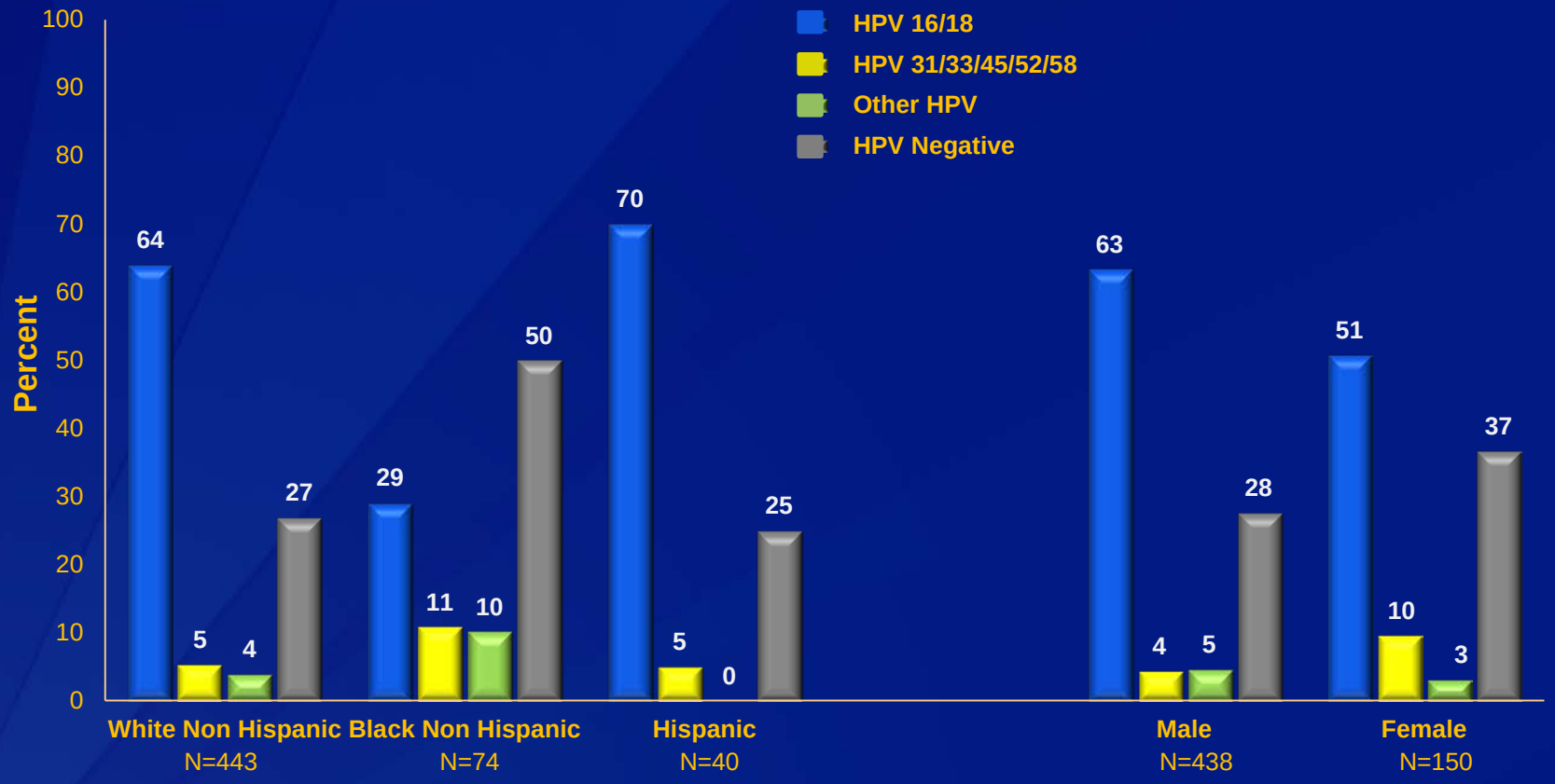
Why Would Cervical Cancers be HPV Negative?

- A previous study found 99.7% positive: based on multiple HPV assays and cancers that met select criteria
- Misclassification of the anatomic site (lower segment uterine cancers not distinguished from upper segment cervical cancers)
- False negative
  - HPV is there but could not be detected with current assay
  - The specimen/tissue is not well preserved
- True HPV negative
  - Rare histologies

HPV Attribution by Race and Gender, Anal Cancer



HPV Attribution by Race/Ethnicity and Gender, Oropharyngeal Cancer



Revised Estimated Percentages of Cancers Attributed to HPV in the U.S.

Cancer	HPV attributable % (95% CI)	HPV 16/18 attributable % (95% CI)	HPV 31/33/45/52/58 attributable % (95% CI)
Cervical	91 (88-92)	66 (63-69)	15 (12-17)
Vaginal	75 (63-84)	55 (43-67)	18 (11-30)
Vulvar	69 (62-75)	49 (41-56)	14 (10-20)
Anal			
Male	89 (77-95)	79 (66-88)	4 (1-13)
Female	92 (85-96)	80 (70-87)	11 (6-19)
Penile	63 (52-73)	48 (37-59)	9 (4-17)
Oropharyngeal			
Male	72 (68-76)	63 (59-68)	4 (3-7)
Female	63 (55-71)	51 (43-59)	9 (6-15)

Summary

- 62% (95% CI 60-65) of invasive cancers* attributable to HPV 16/18
  - Range, 48% penile -79% anal
  - 62% for females; 63% for males
  - Overall - 25,500 cases annually

- 11% (95% CI 10-13) of invasive cancers attributable to additional 5 types in candidate 9-valent vaccine
  - Range, 6% oropharyngeal-18% vaginal
  - 14% for females; 5% for males
  - Overall - 4000 cases annually

* Limited to cervical, vulvar, vaginal, anal, penile, and oropharyngeal cancers

Summary (cont'd)

- Racial ethnic differences
  - HPV 16/18 attribution did not differ for invasive cancers except oropharyngeal cancers
  - Lower percentage of oropharyngeal cancers attributable to HPV (or HPV 16/18) among blacks
- These data will be useful in estimating the impact of the candidate 9-valent vaccine on cancers and for cost-effective analyses

Acknowledgements-Study

CDC Cancer

Trevor Thompson, Meg Watson, Zahava Berkowitz

CDC HPV Lab

Elizabeth Unger, Martin Steinau, Daisy Lee, Mariella Zamaroon, Julia Gargano

Battelle

Christopher Lyu,Dale Rhoda, April Greek

Florida

Youjie Huang,Jill Mackinnon, Carlos Alvarez

Florida Central Lab

Ed Wilkinson, Martha Campbell, Amy Wright

Louisiana

Ed Peters, Lauren Cole

Michigan

Glenn Copeland, Lara Ashley, Won Silva

Iowa

Charles Lynch, Freda Selk

Los Angeles

Maria Sibug-Saber , Wendy Cozen

Hawaii

Brenda Hernandez, Marc Goodman,

Kentucky

Claudia Hopenhayn, Amy Christian, Tom Tucker

HPV Typing of Cancers Workgroup

Multiple Pathology Labs in 7 Cancer Registries

Acknowledgements

- Lauri Markowitz
- Elizabeth Unger
- Susan Hariri
- Eileen Dunne
- Harrell Chesson