HPV Genotype Trumps Race or Ethnicity As a Risk Factor for Cervical Cancer

Mark H. Stoler, MD
Professor Emeritus of Pathology and Clinical Gynecology
University of Virginia Health System
Department of Pathology
Charlottesville, VA, USA

Disclosures

- Dr. Stoler is a consultant to BD Diagnostics

The BD Onclarity™ HPV Assay is CE-marked in the EU; however, this product is not approved for clinical diagnostic use in the United States and several other global markets.

Objectives

- Cervical cancer rates vary across the world and within countries
- Reasons for this variability:
  - access to screening,
  - quality of screening,
  - potential differences in susceptibility to HPV by race and ethnicity
  - relative virulence of HPV genotypes.

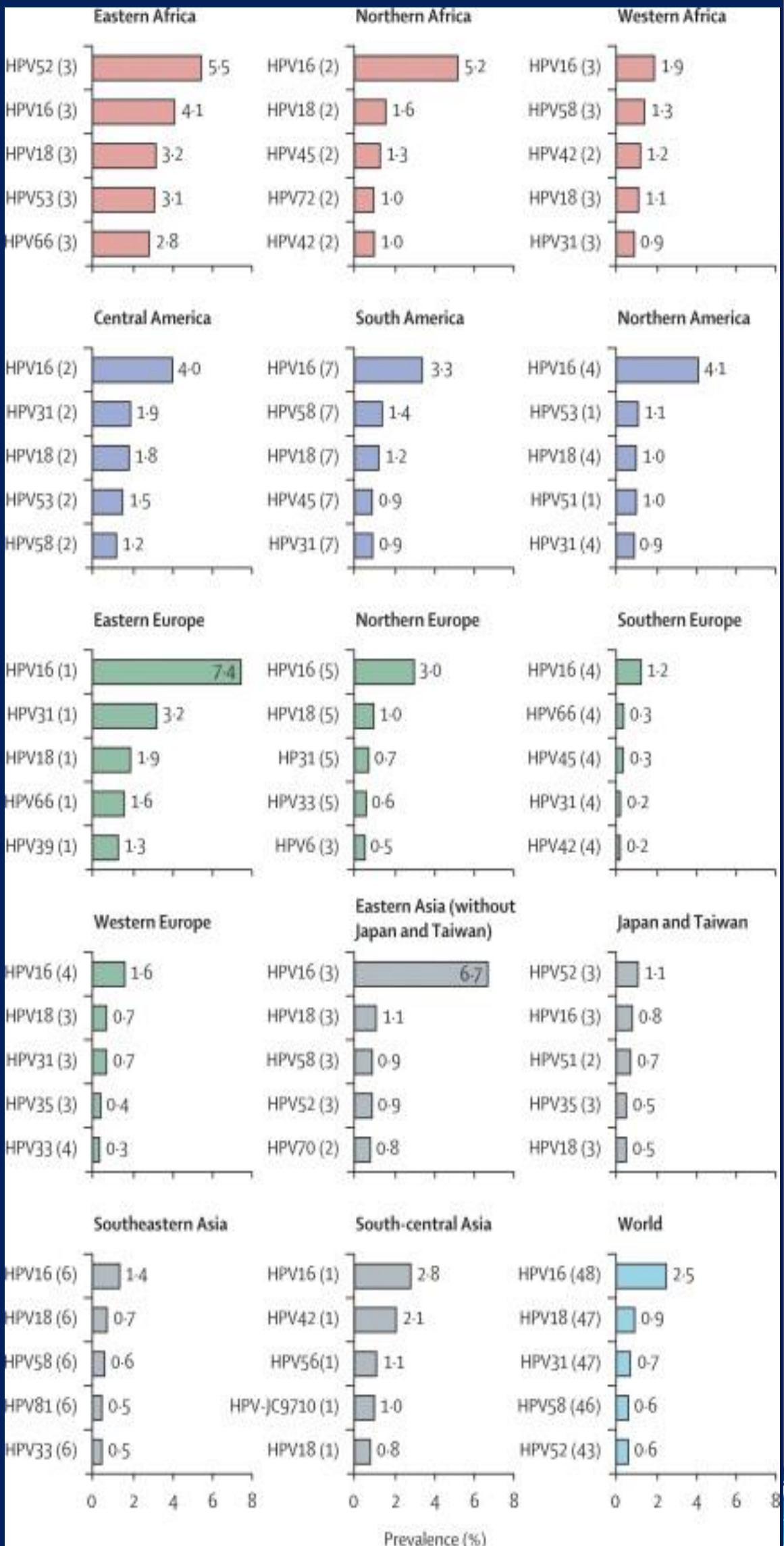
FROM ALTS Regarding Race

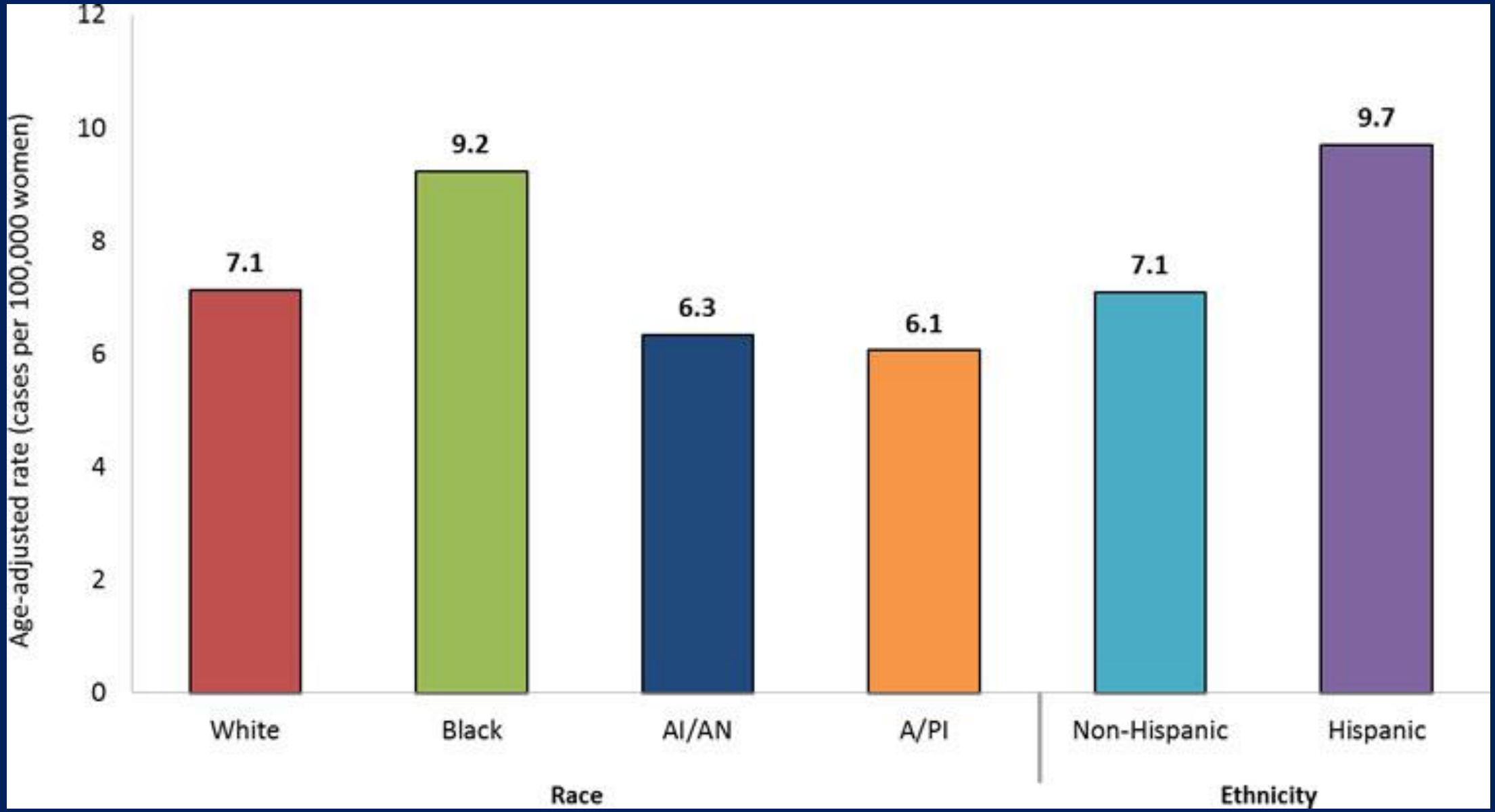
The two most common classifications of race and ethnicity in the study population were White, non-Hispanic (59%) and African-American (32%). Comparing these two groups, African-American women had a higher risk of persistence of HPV infections (OR1.16; 95% CI: 1.01–1.32).

Predictors of human papillomavirus persistence among women with equivocal or mildly abnormal cytology Int. J. Cancer: 126, 684–691 (2010)

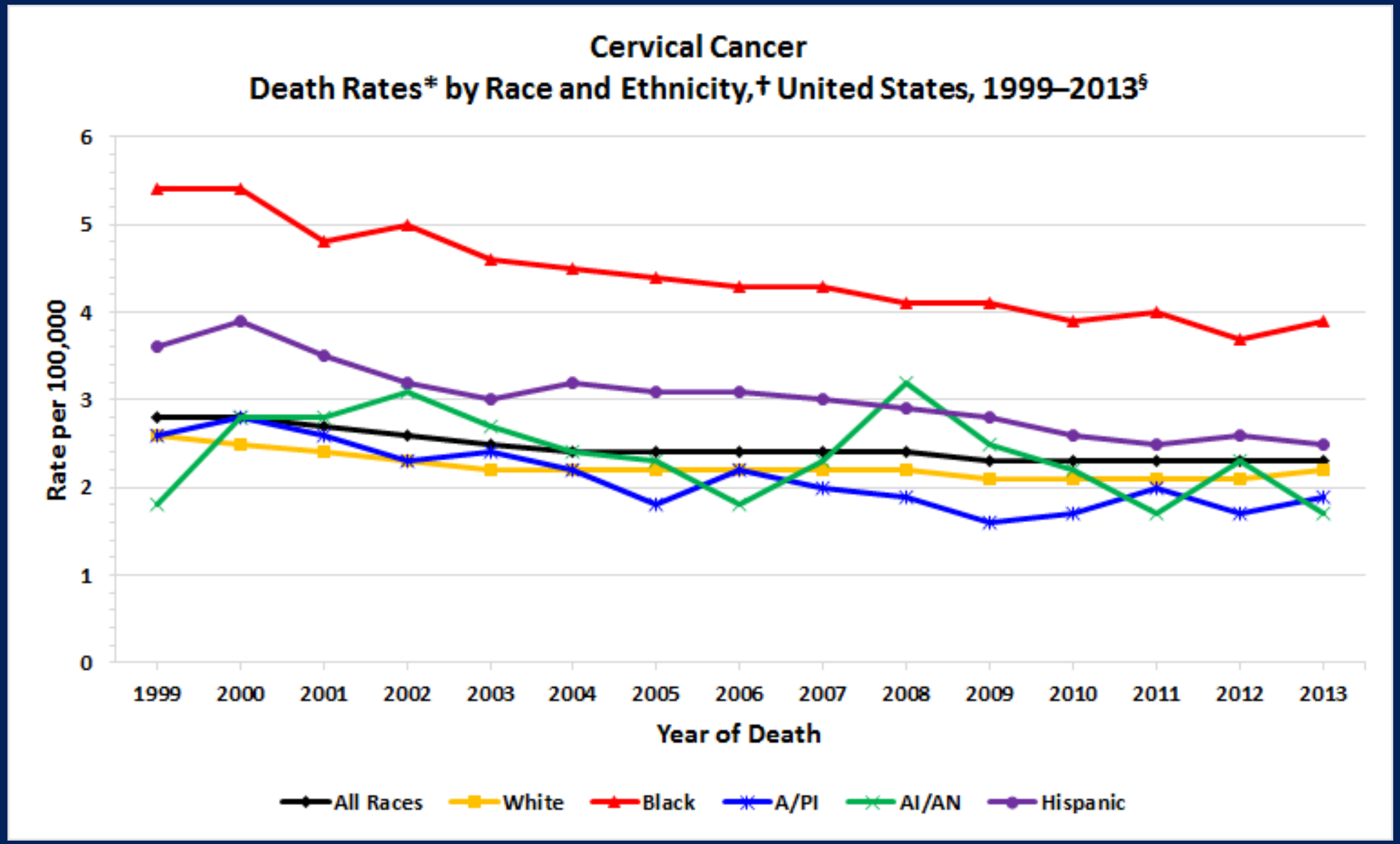
HPV in NILM

de Sanjose etal Lancet Infect Dis 2007; 7:453–59




Age-adjusted rate (cases per 100,000 women)
12
10
8
6
4
2
0
7.1
9.2
6.3
6.1
7.1
9.7
White
Black
AI/AN
A/PI
Non-Hispanic
Hispanic
Race
Ethnicity

CDC


Cervical Cancer
Death Rates* by Race and Ethnicity,† United States, 1999–2013§
Rate per 100,000
0
1
2
3
4
5
6
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
Year of Death
All Races
White
Black
A/PI
AI/AN
Hispanic

CDC

METHODS

≥ 25 study population (29,489)

27,365 subjects were grouped by age, race (African American (AA) vs White (W)) or Ethnicity (Hispanic (H) vs Not Hispanic (NH))

5,392 have per protocol colposcopic assessment. NILM & HPV double negative subjects (21,973) are assumed to have ≤CIN2.

Assay performance and prevalence of CIN2+ and CIN 3+ for each group were determined

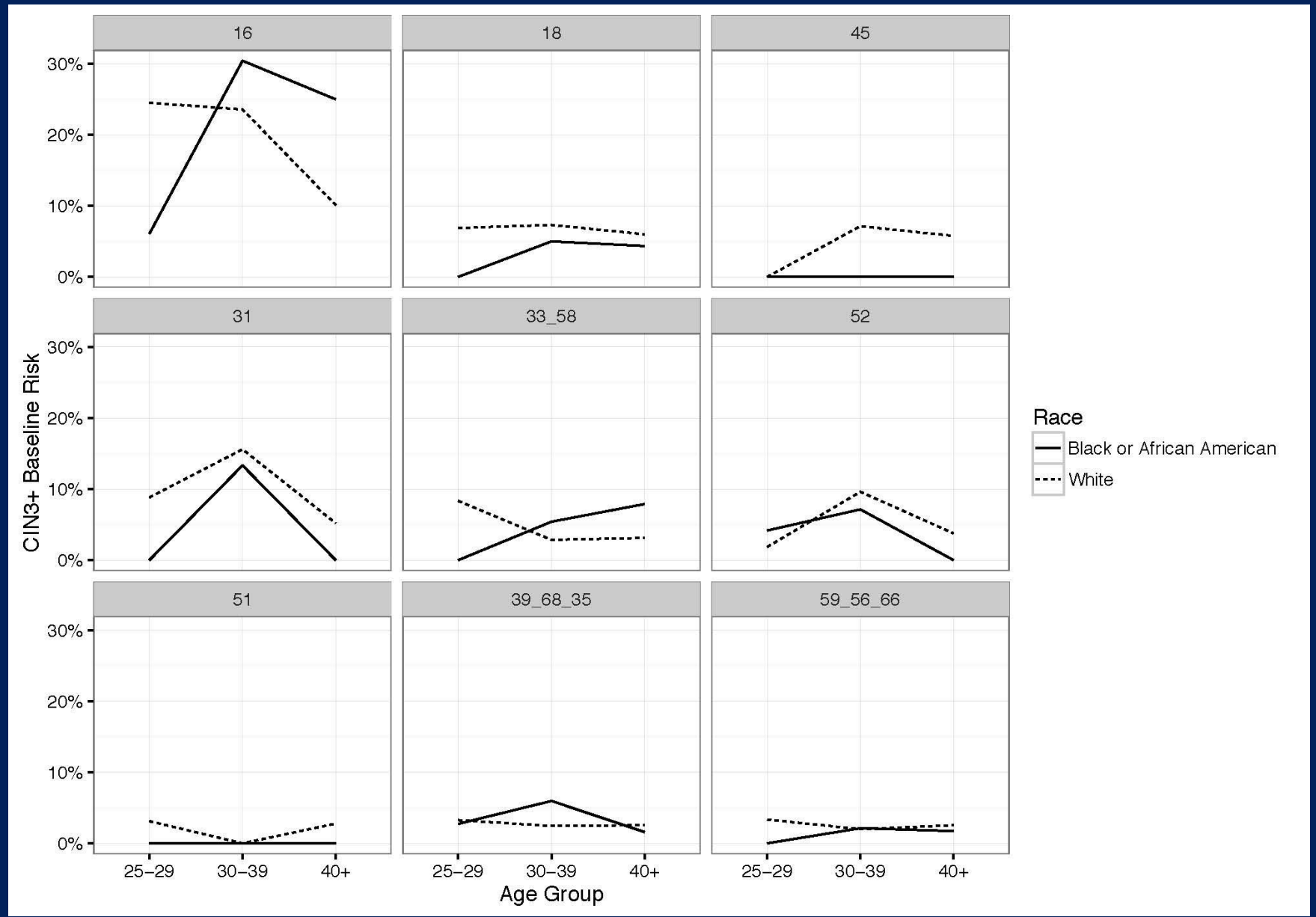
Subject Demographics

Age	N	Race			Ethnicity	
		African American	White	Other	Hispanic	Not Hispanic
25-29	5427	1201/5427 (22.1%)	4047/5427 (74.6%)	179/5427 (3.3%)	980/5427 (18.1%)	4447/5427 (81.9%)
30-39	9467	1743/9467 (18.4%)	7364/9467 (77.8%)	360/9467 (3.8%)	2056/9467 (21.7%)	7411/9467 (78.3%)
40+	14595	2356/14595 (16.1%)	11890/14595 (81.5%)	349/14595 (2.4%)	2827/14595 (19.4%)	11768/14595 (80.6%)
All	29489	5300/29489 (18.0%)	23301/29489 (79.0%)	888/29489 (3.0%)	5863/29489 (19.9%)	23626/29489 (80.1%)

RESULTS

The population was 18%AA, 79%W, 19.9%H and 80.1%NH.
HPV prevalence decreases with age but varied by group;
AA(14.2%) > H(11.3%) >W(9.5%).
The assay sensitivity did not vary among groups
Of the 2845 HPV+ subjects:

- HPV16 is 38% more common(MC) in W vs. AA,
- HPV 18 is 50% and HPV 33_58 is 98% MC in AA vs. W.
- HPV 31 is 44% MC in H vs. NH
- HPV 52 is 33% MC in NH vs H. (Table Appended)


16
18
45
31
33_58
52
51
39_68_35
59_56_66
30%
20%
10%
0%
CIN3+ Baseline Risk
25–29
30–39
40+
Age Group
Race
Black or African American
White

CIN3+ risk by genotype, race, and ethnicity

Genotype	Race			Ethnicity			Overall
	African American	White	p-value	Hispanic	Not Hispanic	p-value	
HPV16	15/80 (18.8%)	67/331 (20.2%)	0.886	16/89 (18.0%)	66/322 (20.5%)	0.706	82/411 (20.0%)
HPV31	4/67 (6.0%)	27/254 (10.6%)	0.360	7/92 (7.6%)	24/229 (10.5%)	0.563	31/321 (9.7%)
HPV18	2/60 (3.3%)	8/120 (6.7%)	0.565	1/31 (3.2%)	9/149 (6.0%)	0.848	10/180 (5.6%)
HPV52	4/107 (3.7%)	16/318 (5.0%)	0.778	5/74 (6.8%)	15/351 (4.3%)	0.539	20/425 (4.7%)
HPV33_58	5/121 (4.1%)	8/182 (4.4%)	1.000	2/63 (3.2%)	11/240 (4.6%)	0.887	13/303 (4.3%)
HPV45	0/53 (0.0%)	7/149 (4.7%)	0.242	0/35 (0.0%)	7/167 (4.2%)	0.469	7/202 (3.5%)
HPV39_68_35	7/203 (3.4%)	14/512 (2.7%)	0.792	2/144 (1.4%)	19/571 (3.3%)	0.340	21/715 (2.9%)
HPV59_56_66	2/147 (1.4%)	15/576 (2.6%)	0.560	4/162 (2.5%)	13/561 (2.3%)	1.000	17/723 (2.4%)
HPV51	0/43 (0.0%)	4/191 (2.1%)	0.760	0/53 (0.0%)	4/181 (2.2%)	0.625	4/234 (1.7%)

RESULTS

Genotype predicted risk of CIN2+ and CIN 3+.

For CIN3+ the risk varied ~10 fold (20% to 1.7%) with 16 > 31 > 18 > 52 > 33_58 > 45 > 39_68_35 >59_56 > 66>51.

CONCLUSION

In a US screening population of women ≥25, HPV genotype is the primary driver of CIN2+/CIN3+ risk.