Linking IIS and Clinical Databases to Assess HPV Vaccine Effectiveness

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Outline

- Background of HPV-related disease
- Study Aim and Methods
- Study Results
- Conclusions

Background

HPV Infection in the US

- HPV is the most common sexually transmitted infection
  - Prevalence: 79 million cases
  - Incidence: 14 million cases/year
    - 50% are 15-24 years
- Most infections are short-lived, and resolve within 1–2 years
- HPV-related disease results from persistent infection

Source: CDC Fact Sheet. http://www.cdc.gov/std/hpv/stdfact-hpv.htm . February 2013.

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Incidence of HPV-related Disease in the US

- Genital warts
  - Incidence in 2013: 404,000 cases[1]
- Cervical cancer
  - Estimated annual incidence: 12,990[2]
- Other HPV-related cancers
  - Includes vaginal, vulvar, penile, anal, and oropharyngeal cancers
  - Estimated annual incidence: 12,000 in men; 9,000 in women[3]

Sources:
1. 2014 Sexually Transmitted Diseases Surveillance. Centers for Disease Control and Prevention. http://www.cdc.gov/std/stats14/tables/45.htm
2. SEER Cancer Statistics Factsheets: Cervix Uteri Cancer. National Cancer Institute. Bethesda,MD http://seer.cancer.gov/statfacts/html/cervix.html
3. HPV and Cancer. Centers for Disease Control and Prevention. http://www.cdc.gov/cancer/hpv/statistics/cases.htm.

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9-valent HPV Vaccine Recommendations

L1 VLP types*	6, 11, 16, 18, 32, 33, 45, 52, 58
Recommended Age Group	Females and males 11–12 years Catch-up through 26 years for females, MSM, immunocompromised Catch-up through 21 years for males
Schedule	2 or 3 dose series

*L1: Major Capsid Protein; VLP: Virus-like particle

Source: https://www.cdc.gov/mmwr/volumes/65/wr/mm6549a5.htm

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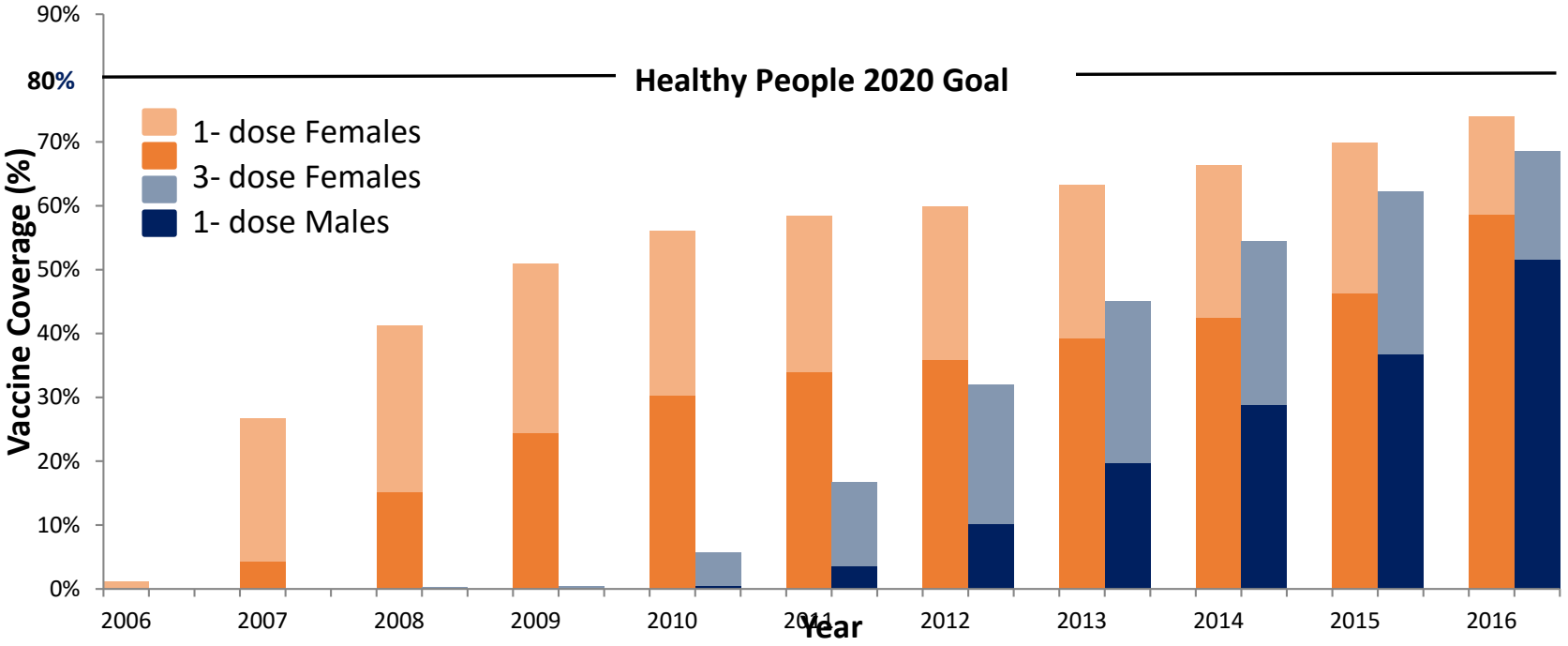
HPV Vaccine Coverage Among Females and Males 13–17 Years, NYC



Source: NYC DOHMH Citywide Immunization Registry (numerators) and NYC DOHMH Epiquery and 2010 US Census (population estimates).

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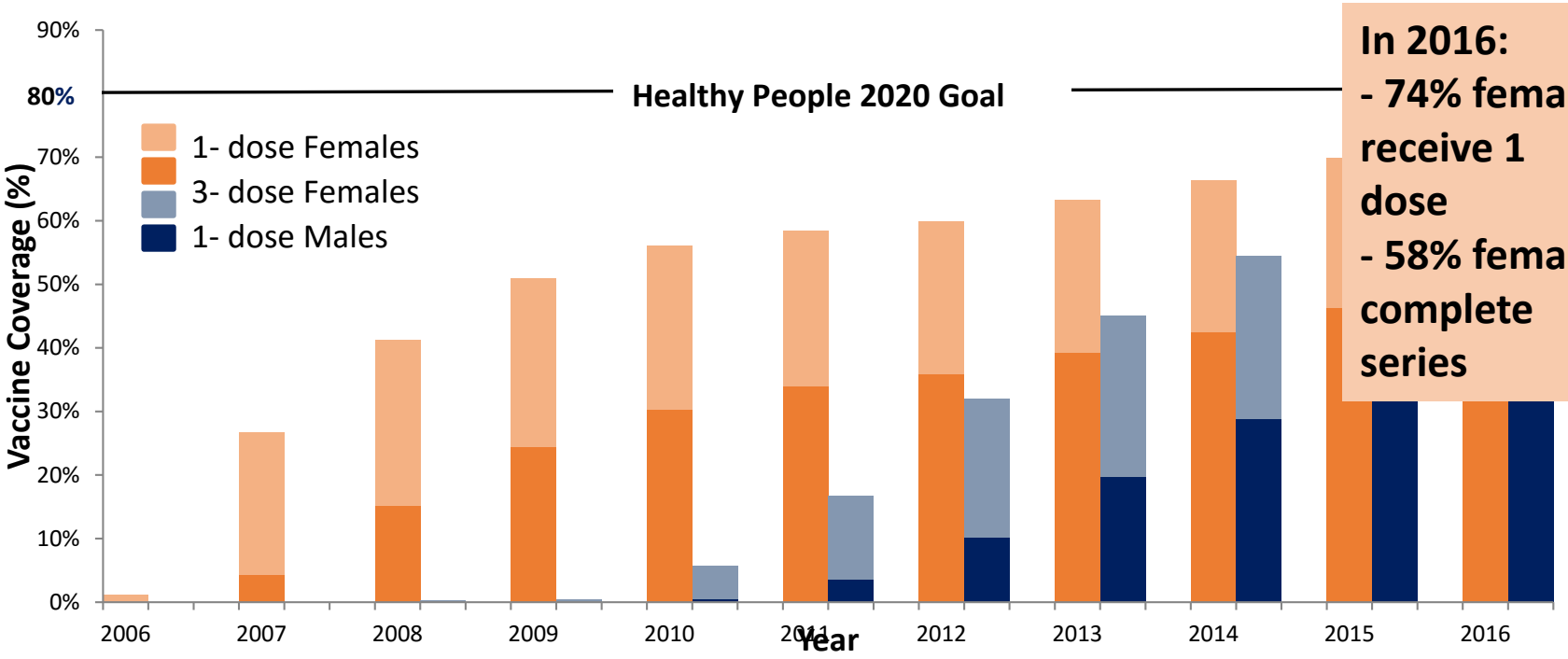

In 2016:
- 74% females receive 1 dose
- 58% females complete series

Source: NYC DOHMH Citywide Immunization Registry (numerators) and NYC DOHMH Epiquery and 2010 US Census (population estimates).

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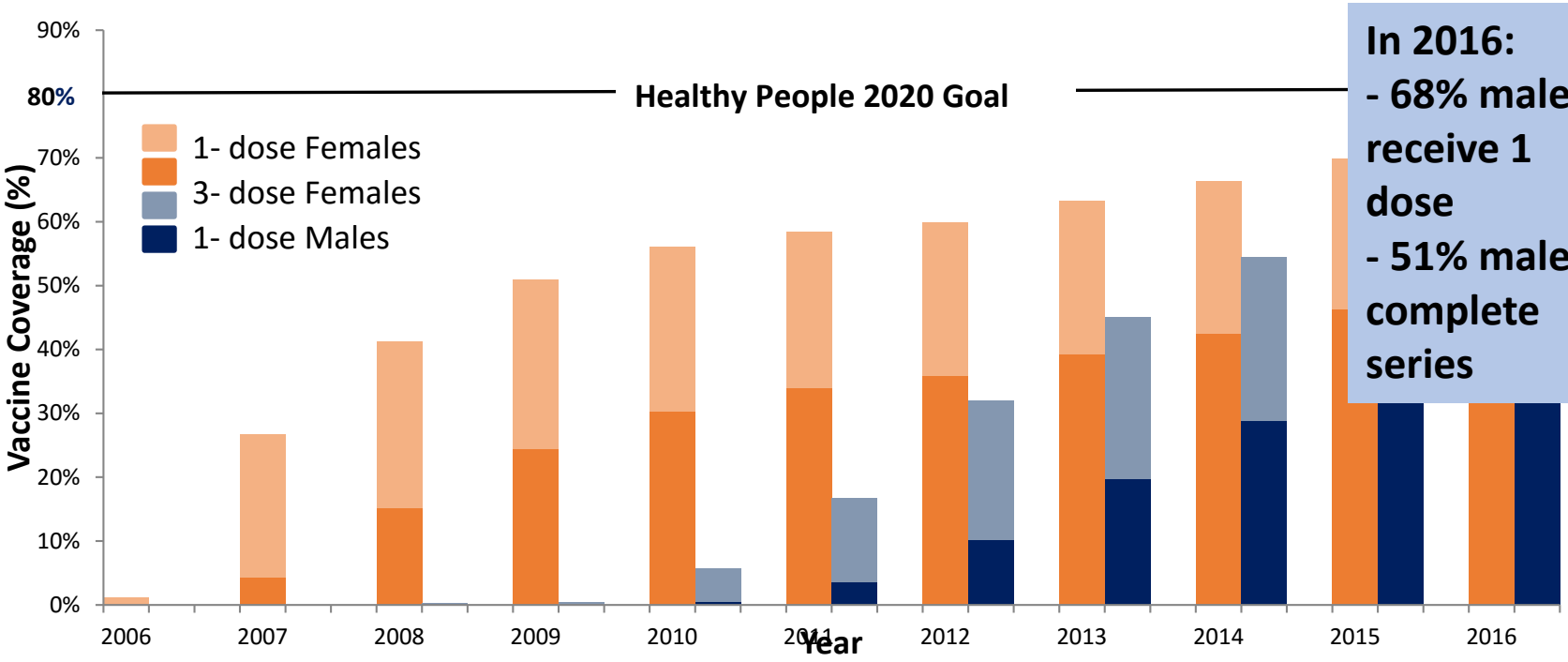
HPV Vaccine Coverage Among Females and Males 13–17 Years, NYC



In 2016:
- 68% males receive 1 dose
- 51% males complete series

Source: NYC DOHMH Citywide Immunization Registry (numerators) and NYC DOHMH Epiquery and 2010 US Census (population estimates).

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Early Impact of HPV Vaccine on Proximal Outcomes

- In the US
  - NHANES study
  - 64% reduction in vaccine-type HPV among females 14-19 years
  - 34% decrease among females 20-24 years[1]
- In Australia
  - National school-wide vaccination program
  - 77% reduction in vaccine-type HPV prevalence among females 18-24 years
  - 93% reduction in genital warts among the females <21 years[2]
- In Connecticut
  - Statewide high grade cervical lesion surveillance registry
  - 17% decrease in high grade cervical lesions among women 21-24 years from 2008-2011[3]

Sources:
1. Markowitz et al. *Pediatrics.* 2016 Feb 23;137(2):e20151968.;
2. Ali et al. *BMJ.* 2013 Apr 18;346.
3. Niccolai, et al. *Cancer Epidemiol Biomarkers Prev*. 2013. Aug; 22(8); 1446-50.

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Cervical Cancer Screening Recommendations, USPSTF 2012

- Pap smear every 3 years for women ages 21–65 years
- Option of pap smear and HPV-DNA testing (co-testing) every 5 years for women ages 30–65 years

Source: United States Preventive Services Task Force
https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/cervical-cancer-screening

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Methods

Study Aim

Utilize two DOHMH data systems to examine the relationship between HPV vaccine status and proximal HPV-related outcomes in women who attended Sexual Health Clinics in NYC from 2011-2015

Data Sources

Citywide Immunization Registry (CIR)

- Available since 1997
- Mandated reporting of all immunizations given to people under 19 years since 2005
- Written or verbal consent for reporting immunizations in people 19 years and over

STD-Electronic Medical Record (STD-EMR)

- Available since 2005
- Utilized by 8 Sexual Health Clinics run by DOHMH

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Study Design

Retrospective cohort

Inclusion Criteria

- Women who had a Pap smear performed at Sexual Health Clinics from 2011–2015
- Women ≤ 24 years at the time of the Pap smear
- Women whose Pap smear yielded a conclusive result

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Data Linkage Process

BOTH	• Discussion on methodology
BOI	• IRB exception application submission and approval
STD	• Identification of women who had a Pap smear from 2011–2015 in STD-EMR • First Pap smear data used in analysis
BOI	• BSTDC data match to immunization records in CIR using last name, first name, middle name, DOB, gender, mother's maiden name, phone number, address
BOI	• CIR data extraction of all immunizations given
STD	• STD- EMR data extraction (e.g., Pap smear results, genital warts, race/ ethnicity) followed by de-identification of records to create analytic dataset
BOI	• Final dataset refined to include only those who had immunizations after 9 years of age and women who were 24 years and younger at time of Pap

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Variables Considered in Analysis

- HPV vaccination (number of doses)
- Age at HPV vaccine initiation
- Age at time of clinic visit
- Result of 1st Pap smear at clinic
- History of STIs up to date of visit
- History of genital warts up to date of visit
- Race/Ethnicity
- Poverty (Neighborhood level)

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Data Linkage Results

9,912

- Initial data pulled from STD-EMR
- Number of unique women with 1+ Pap smear 2011-2015

4,197

- 42% matched to CIR

2,975

- 71% found to have immunizations after 9 years of age

2,132 (Final analytic dataset)

- 72% were 24 years and younger

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Results

Patient Characteristics (1)

Age range	**14- 24 years (Mean = 22 years)**
Race/ethnicity	
NH-Black, % (n)	**55.5% (1,183)**
Hispanic, % (n)	**33.5% (715)**
NH-Other, % (n)	**5.0% (107)**
NH-White, % (n)	**3.0% (65)**
Asian, % (n)	**2.9% (62)**
Census Tract Poverty Level *	
30 – 100% (very high poverty levels)	**39.6% (811)**
20 – < 30%	**24.3% (498)**
10 – < 20%	**22.8% (467)**
0 – < 10% (low poverty levels)	**13.2% (270)**

*Based on a geocoded dataset with 2046 observations (96% of final analytic set)

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Patient Characteristics (2)

Total number of observations	2,132
At least 1 dose HPV vaccine received, % (n)	53.4% (1,139)
At least 2 doses HPV vaccine received, % (n)	32.6% (694)
At least 3 dose HPV vaccine received, % (n)	20.9% (445)
Patients with STI history, % (n)*	58.9% (1,256)
Patients with genital warts history, % (n) Ł	4.7% (101)

*STI history includes clinic-diagnosed and self-reported diagnoses of Gonorrhea, Chlamydia, Syphilis, and HIV

Ł Genital warts history includes clinic-diagnosed and self-reported diagnoses of genital warts

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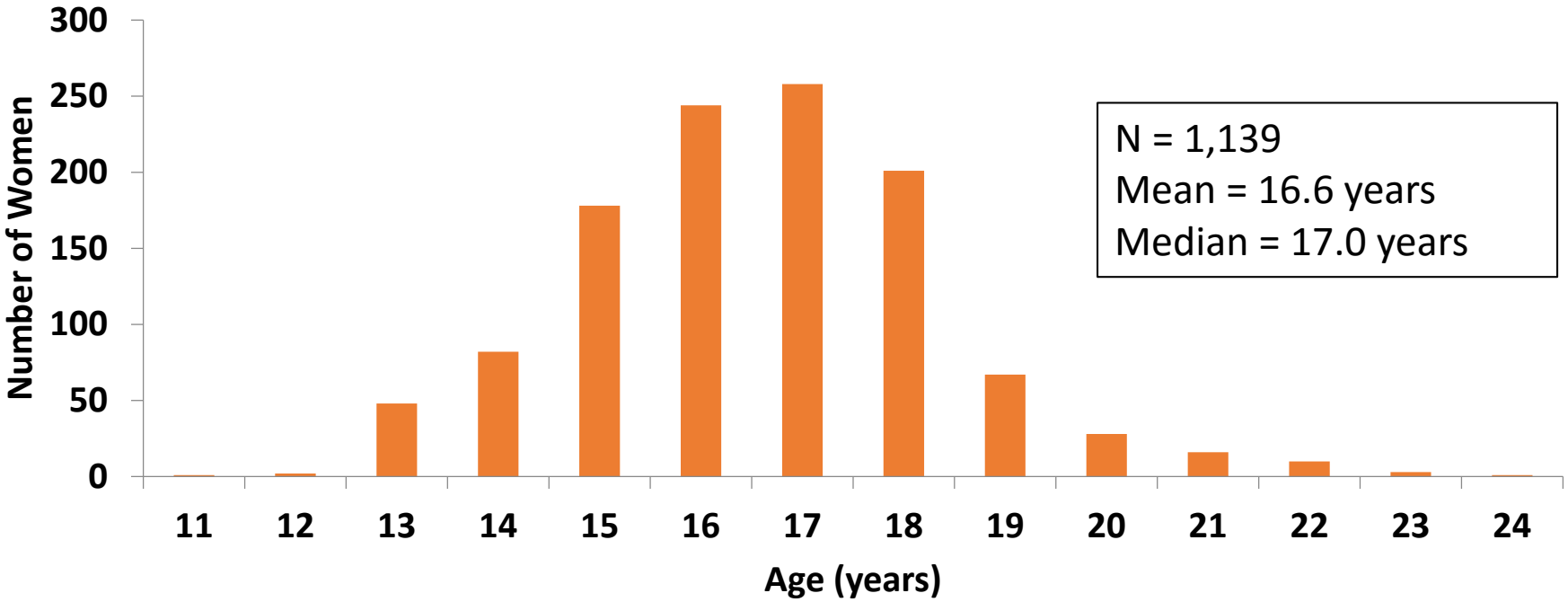
Age Distribution at First HPV Vaccine Dose



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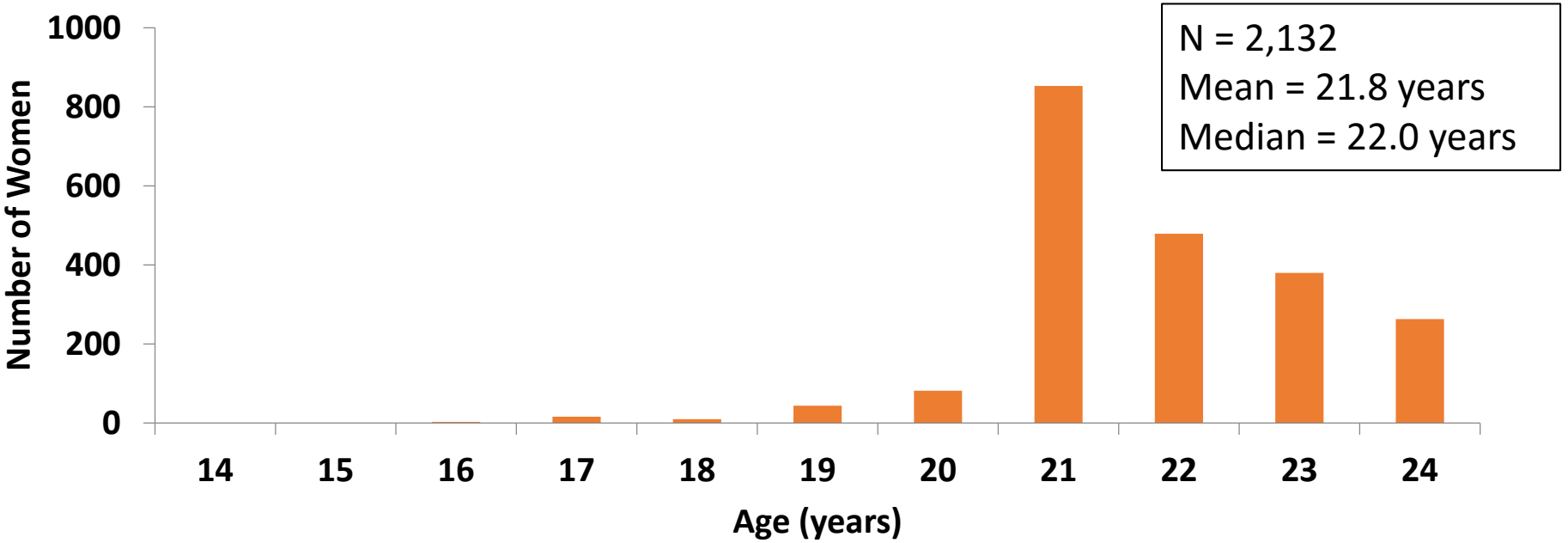
Age Distribution at First Pap Smear Performed at Clinic, 2011–2015



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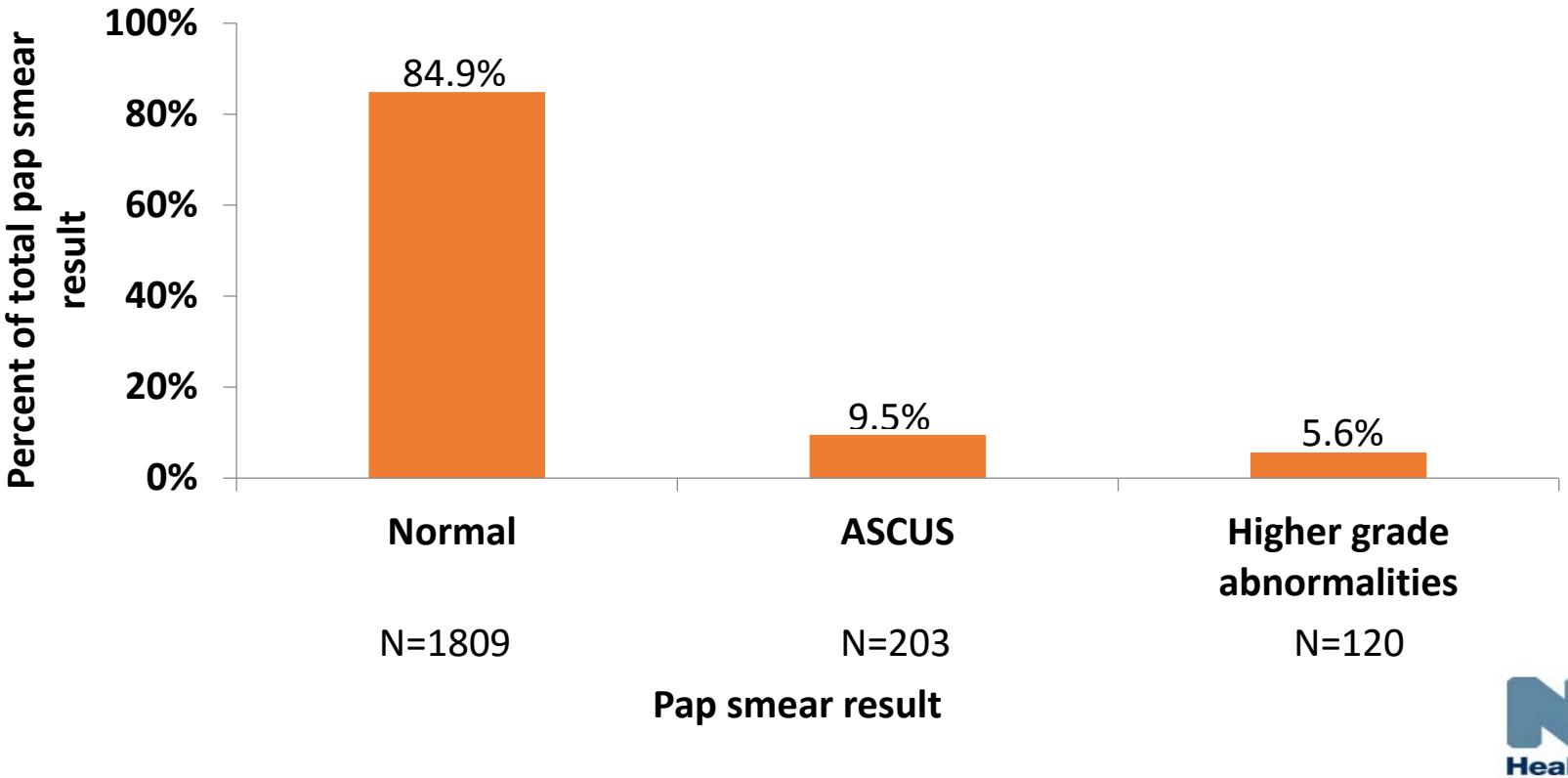
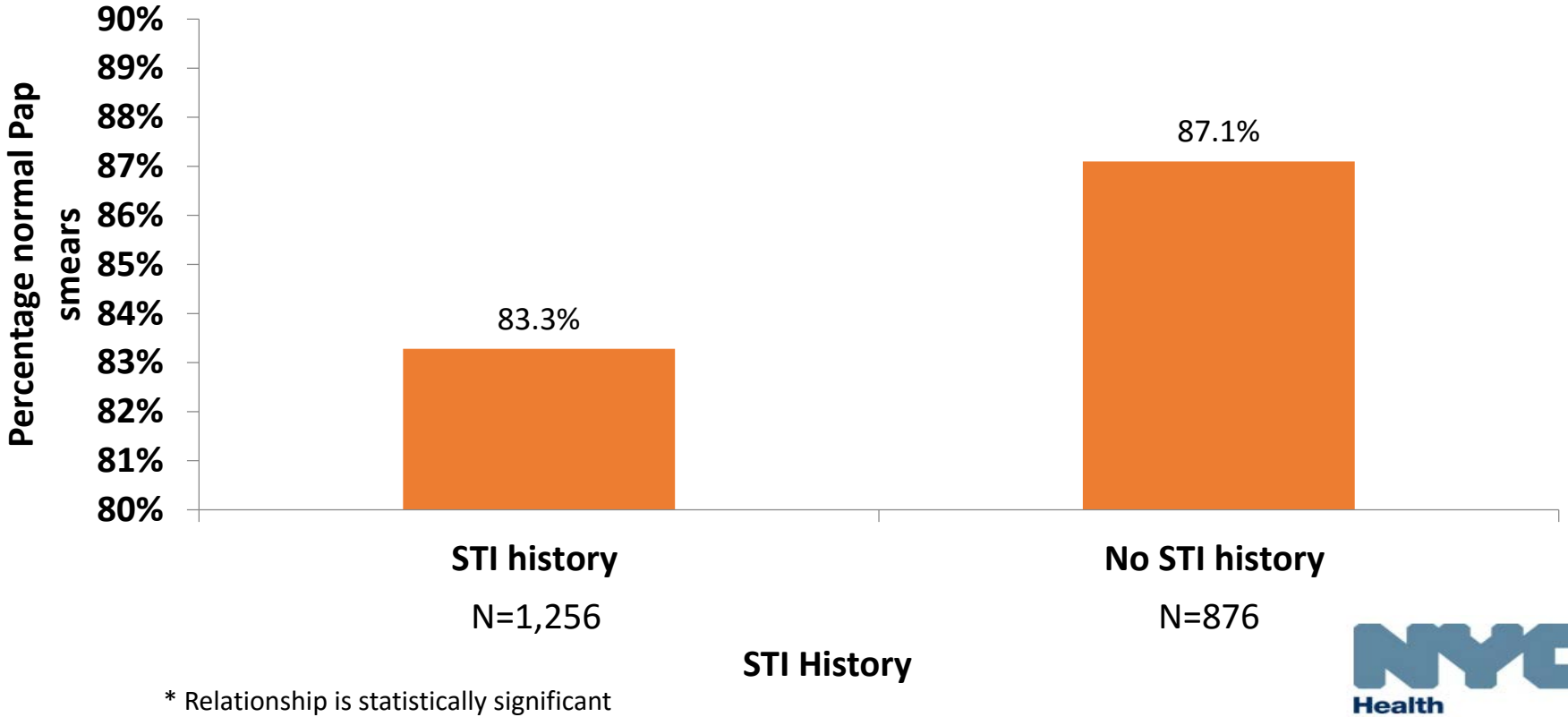
Frequency of Pap Smear Results, 2011–2015



Normal Pap Smear Result by STI History, 2011–2015*



* Relationship is statistically significant

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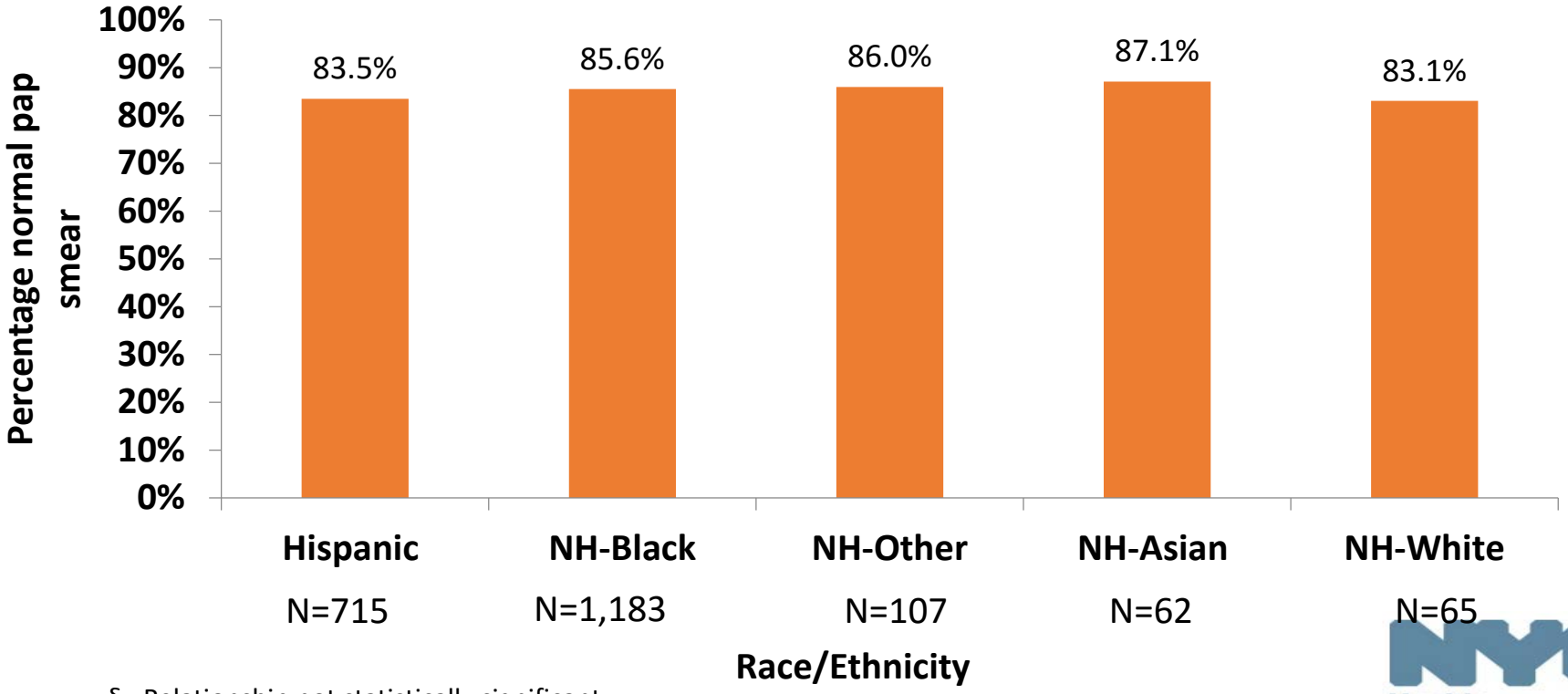
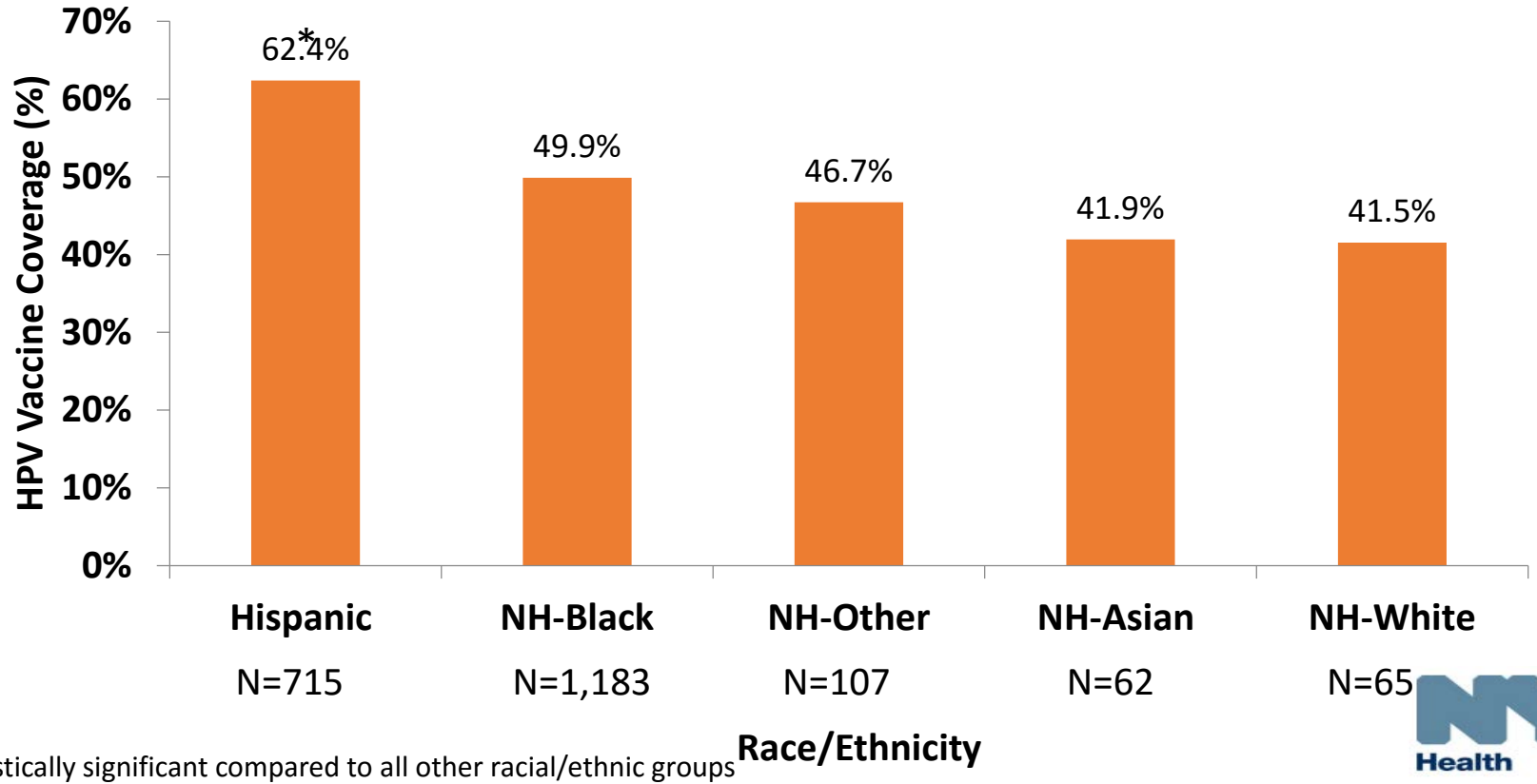
Normal Pap Smear Result by Race/ Ethnicity, 2011–2015δ



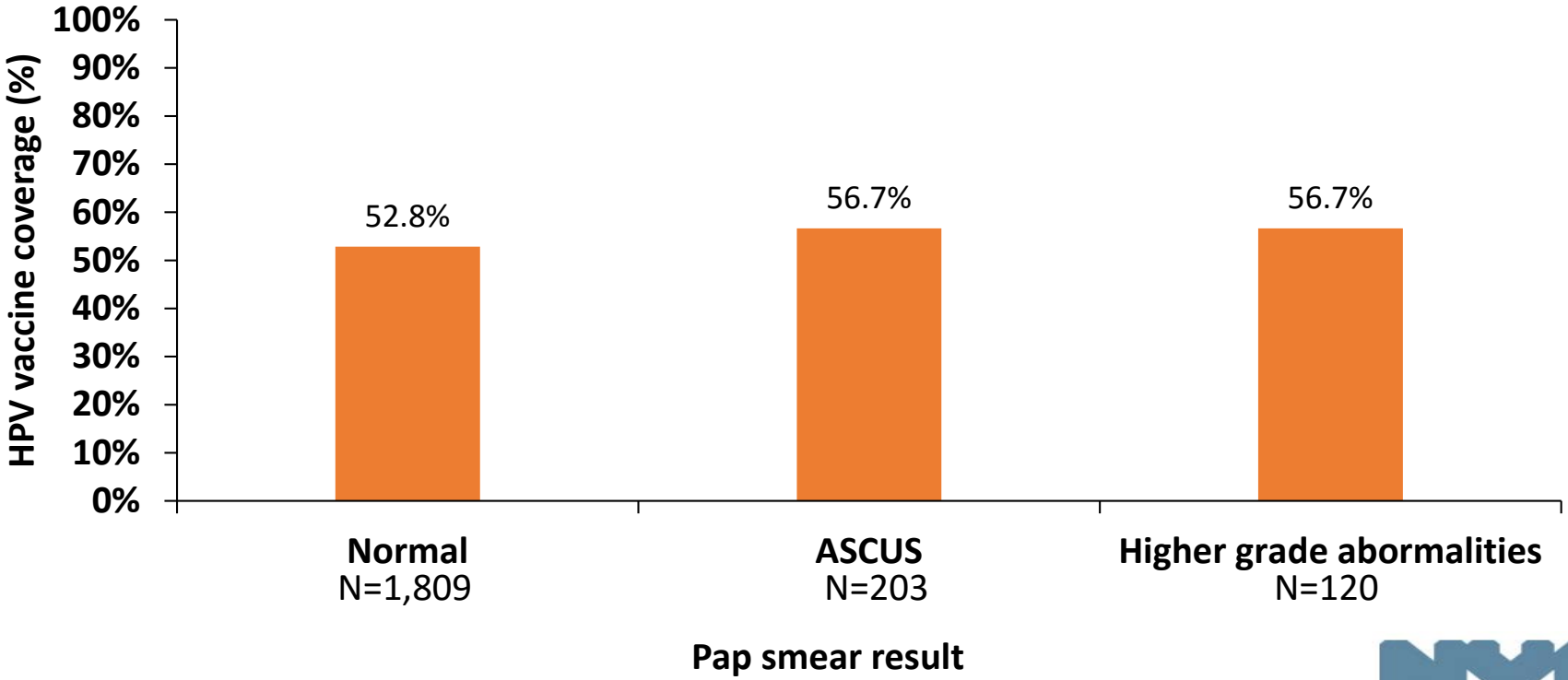
δ : Relationship not statistically significant

HPV Vaccine Coverage by Race/ Ethnicity, 2011-2015



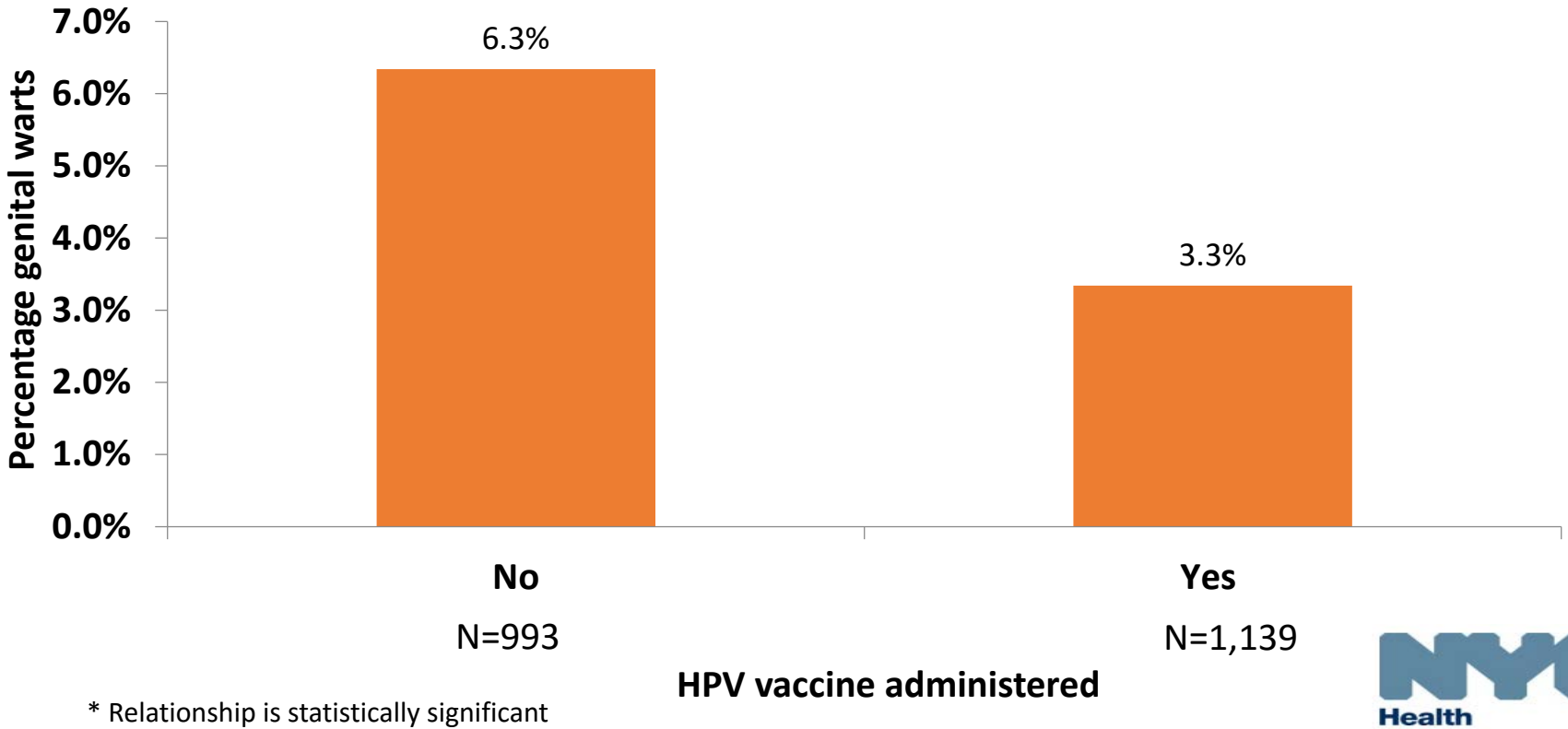
* Statistically significant compared to all other racial/ethnic groups

HPV Vaccine Coverage by Pap Smear Result, 2011–2015δ



δ: Relationship not statistically significant

Genital Warts by HPV Vaccination Status, 2011-2015*



* Relationship is statistically significant

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HPV Vaccine Effectiveness on Genital Warts

	+GW	- GW	Total	Relative Risk (RR)
+ HPV vax	38 **a**	1101 **b**	1139	0.03336
- HPV vax	63 **c**	930 **d**	993	0.06344

VE = 1 - Risk Ratio

VE = 1 - 0.5258

VE = 0.4742

VE = 47.4%

95% C.I. (20.6, 65.2)

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Limitations (1)

- Possible underestimation of HPV vaccine coverage due to incomplete CIR capture
  - Adolescent vaccines may not have been consistently captured by CIR in early years following 2005 adolescent vaccine mandated reporting
  - The reporting of adult immunizations to the CIR is not mandated and requires patient consent
  - Women receiving care at Sexual Health Clinics may have received vaccines out of jurisdiction
- Exposure to virus may have preceded HPV vaccine initiation

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Limitations (2)

- Study population may not have had the opportunity to be vaccinated due to:
  - Lag time between vaccine licensure and implementation
  - Vaccine campaign's focus on younger age group
- No follow-up data available for abnormal Pap smears
  - They are currently referred to outside facilities
  - There is no surveillance system for abnormal pap smear results in NYC
- Not generalizable to NYC female population

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Conclusions

Conclusions

- In this pilot study, vaccination was effective in preventing genital warts
- No relationship was found between HPV vaccine and Pap smear results in this pilot
- Linking 2 DOHMH data systems is a useful tool to evaluate vaccine effectiveness
- Recommend repeating analysis at a future date to include cohort of women who had more of an opportunity to be vaccinated

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