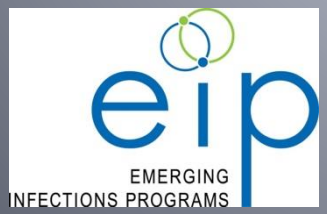
Connecticut HPV-IMPACT: Summary of findings

2008 – 2014



Yale SCHOOL OF PUBLIC HEALTH

HPV-IMPACT overview

- Population-based approach to monitoring human papillomavirus (HPV) vaccine impact on cervical cancer precursors and associated HPV types
- Basic surveillance includes reporting from pathology labs of cervical intraepithelial neoplasia grades 2 and 3 and adenocarcinoma in situ
- Enhanced surveillance includes collection of vaccine histories and residual specimen for HPV typing among women ages 18-39 years
- 5 sites in US (CT, NY, TN, CA, OR) funded by CDC through Emerging Infections Program network

HPV-IMPACT in Connecticut

CONNECTICUT DEPARTMENT OF PUBLIC HEALTH
Keeping Connecticut Healthy

Connecticut Epidemiologist

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Changes to the lists of Reportable Diseases and Laboratory Reportable Significant Findings

Human Papillomavirus (HPV) related cervical neoplasia- added

HPV infection with a high-risk HPV type underlies all cases of cervical cancer, ~90% of anal cancer, ~40% of vulvar, vaginal and penile cancers, and ~12% of oropharyngeal cancers. An HPV vaccine was licensed in June 2006. This vaccine is highly efficacious in preventing cervical intraepithelial neoplasia grades 2 and 3 (CIN 2/3) and adenocarcinoma-in-situ (AIS) in females vaccinated before having type-specific HPV infection (~100% efficacious against HPV types 16 and 18; 70-80% efficacious against all HPV types).

Surgical pathology laboratories are required to report all newly diagnosed cases of CIN2/3, and AIS or their equivalent. At the DPH's request and if adequate tissue is available, laboratories are required to send fixed tissue from the specimen used to diagnose CIN2/3 or cervical AIS for HPV typing per instructions from the DPH. Footnote (10) was added to the OL-15C. The purpose of this HPV surveillance is to monitor the statewide impact of the vaccine on the incidence and epidemiology of biopsy-proven early outcomes of HPV infection that lead to cervical cancer. It will also monitor the impact of the vaccine on the types of HPV causing biopsy-proven disease.

Mandatory statewide in CT reporting since 2008.

The challenges of catch-up vaccination among women ages 19 – 27 years

Table 1. Correlates of No Vaccination History

	Vaccination History	No Vaccination History	Unadjusted Odds Ratio (95% CI)	Adjusted* Odds Ratio (95% CI)
Total (n=269)	116 (43.1)	153 (56.9)	NA	NA
Age (y) (n=269)				
18–22	61 (50.4)	60 (49.6)	1.00	1.00
23–27	55 (37.2)	93 (62.8)	1.72 (1.05–2.80)*	1.81 (1.05–3.12)†
Race (n=249)				
White	91 (47.6)	100 (52.4)	1.00	1.00
African American	11 (30.6)	25 (69.4)	2.07 (0.96–4.44)	1.31 (0.56–3.04)
Other	6 (27.3)	16 (72.7)	2.43 (0.91–6.47)	2.09 (0.65–6.76)
Ethnicity (n=266)				
Non-Hispanic	99 (44.8)	122 (55.2)	1.00	1.00
Hispanic	16 (35.6)	29 (64.4)	1.47 (0.76–2.86)	0.96 (0.36–2.62)
Insurance type (n=253)				
Private	89 (52.3)	81 (47.7)	1.00	1.00
Public	16 (22.9)	54 (77.1)	3.66 (1.94–6.90)‡	2.74 (1.32–5.69)§
None	2 (15.4)	11 (84.6)	5.97 (1.28–27.73)†	5.02 (1.06–23.81)†

	Ever Heard of HPV Vaccine (n=151 Unvaccinated Women)			Provider Has Talked With Patient About Vaccine (n=261)		
	Yes	No	*P**	Yes	No	*P**
Insurance type						
Private insurance	75 (93.7)	5 (6.3)		138 (81.7)	31 (18.3)	
Public insurance	39 (73.6)	14 (26.4)	.001	41 (59.4)	28 (40.6)	<.001
None	7 (63.6)	4 (36.4)	.011†	8 (61.5)	5 (38.5)	.138†

57% of women eligible for catch-up vaccination *not* vaccinated

Significantly *higher* rates of non-vaccination among publicly insured (77%) and uninsured (85%)

Lack of provider discussions about vaccine *higher* among publicly insured (41%) and uninsured (39%) compared to privately insured (18%)

Mehta NR et al. *Obstetrics and Gynecology* 2012;119:575-581.

Disparities in high-grade cervical lesions by area poverty

TABLE 1—Census Tract Distributions of Poverty, Race, Ethnicity, City Status, Age, and Cervical Intraepithelial Neoplasia Grade 2 or Higher and Adenocarcinoma In Situ Rates and Rate Ratios Among Women Aged 20–39 years: Connecticut, 2008–2009

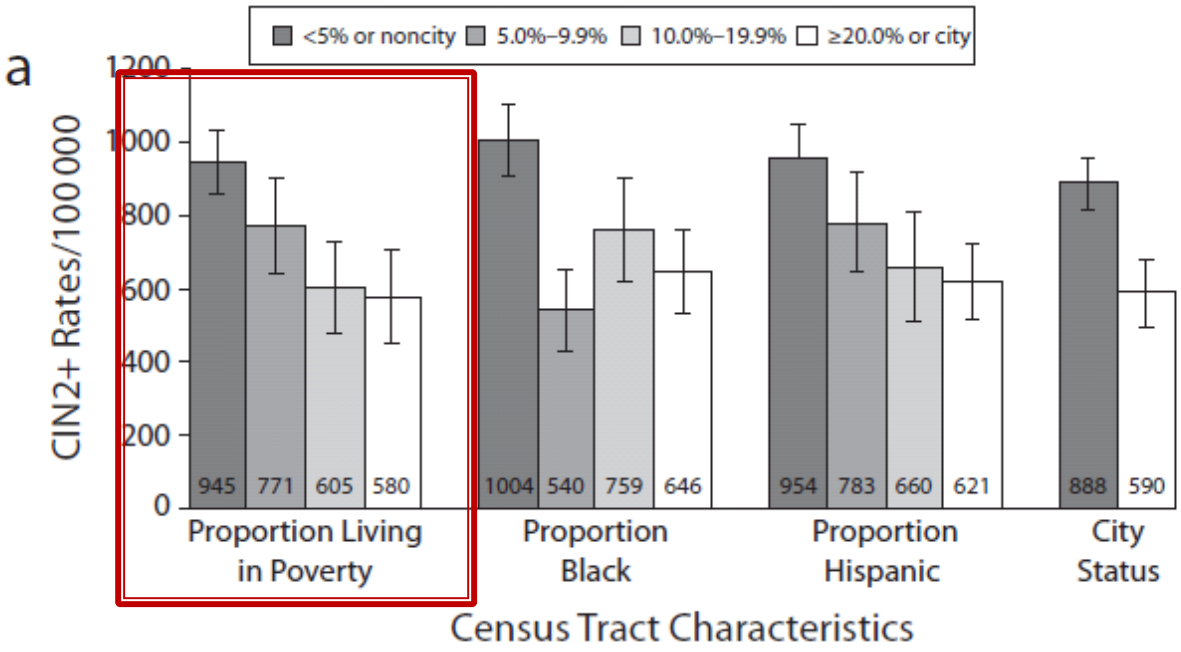
	Census Tracts, No. (%)	Women Aged 20–39 Years, No. (%)	Average Annual Cases, No.	Annual Rate per 100 000 Female Population, No.	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
Total	811	471 390	1968.5	417.6		
Proportion of the population living below federal poverty level						
< 5.0	528 (65.1)	291 278 (61.8)	1136.0	390.0	1.0** (Ref)	1.0** (Ref)
5.0–9.9	118 (14.5)	82 526 (17.5)	364.0	441.1	1.13*** (1.04, 1.23)	1.09 (0.98, 1.21)
10.0–19.9	79 (9.7)	53 023 (11.2)	240.0	452.6	1.16*** (1.05, 1.28)	1.15 (1.00, 1.32)
≥ 20.0	86 (10.6)	44 563 (9.5)	228.5	512.8	1.32† (1.19, 1.45)	1.35† (1.14, 1.59)

Women living in highest poverty areas are *35% more likely* to have high-grade cervical lesions compared to lowest poverty areas.

Niccolai LM et al. *American Journal of Public Health* 2013;103:156-163.

Disparities in high-grade cervical lesions by area poverty among younger women

FIGURE 1—Rates of CIN2+/AIS by poverty, race, ethnicity, and city status in women aged (a) 20–24 years, (b) 25–29 years, (c) 30–34 years, and (d) 35–39 years.



Women living in highest poverty areas are *21% less likely* to have high-grade cervical lesions compared to lowest poverty areas.

Niccolai LM et al. *American Journal of Public Health* 2013;103:156-163.

Trends in HGCL over time

Table 1. Annual rate of high-grade cervical lesions per 100,000 female population ages 21 to 39 years by age and area-level characteristics in Connecticut, 2008–2011

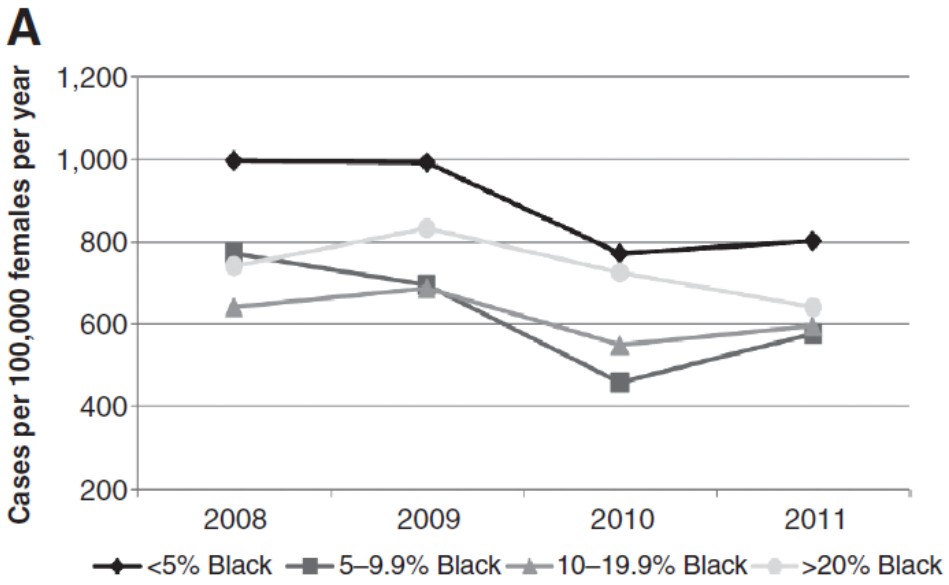
			Rates (cases per 100,000 female population per year)					
	Number of women	Number of cases	2008	2009	2010	2011	Difference 2008 to 2011 (95% CI)	P_{trend}
TOTAL	411,624	8,146	512	517	475	476	−36 (−66 to −5)	0.002
Age								
21-24	87,507	2,657	834	849	665	688	−146 (−228 to −65)	<0.001
25-29	106,159	2,648	631	639	625	600	−31 (−98–35)	0.320
39-34	104,194	1,777	415	424	423	443	+29 (−27–85)	0.344
35-39	113,764	1,064	241	232	236	227	−14 (−54–26)	0.546

Significant declines in HGCL occurred during 2008–2011 overall and among women ages 21–24 years.

Niccolai LM et al. *Cancer Epidemiology, Biomarkers and Prevention* 2013;22:1446-50.

Trends in HGCL over time by area race

Figure 1. Trends in annual rates of high-grade cervical lesions per 100,000 female population ages 21 to 24 years in Connecticut, 2008 to 2011 by census tract level area-based measures of (A) race, (B) ethnicity, (C) poverty, and (D) county type (urban vs. nonurban).



P<.001 for <5% black
P=.009 for 5-9.9% black
NS for 10-19.9% black
NS for >20% black

Declines in HGCL were greatest in areas with lowest proportions of black residents among women ages 21–24 years.

Niccolai LM et al. *Cancer Epidemiology, Biomarkers and Prevention* 2013;22:1446-50.

Disparities in HPV types by area poverty

TABLE 3. Correlates of HPV 16/18 Prevalence in CIN2/3/AIS Lesions: Adjusted Associations Between Individual- and Area-Level Characteristics (n = 671)

Characteristic	Adjusted Prevalence Ratio (95% CI)[a]	*P*
Individual-level characteristics		
Race/ethnicity		
Black	0.54 (0.34, 0.88)	.010
Hispanic	0.59 (0.40, 0.88)	.010
White	1.0	
Age, y		
18-29	1.73 (1.23, 2.44)	.001
30-39	1.0	
Diagnosis		
CIN2	0.34 (0.25, 0.48)	<.001
CIN 2/3, 3, or AIS	1.0	
Area-level characteristics		
Proportion in poverty		
≥20%	0.59 (0.40, 0.87)	.007
<20%	1.0	

Black women *46% less likely* HPV 16/18
Hispanic women *41% less likely* HPV 16/18

Women in higher poverty areas *41% less likely* HPV 16/18

Niccolai LM et al. *Cancer* 2013;119:3052-8.

New cervical cancer screening guidelines: who will be missed?

Table 3
CIN 2+/AIS cases and annual rates per 100,000 female population age 13-20 by county-Connecticut, 2008-2010

County	CIN 2+/AIS	Annual rate per 100,000 female population age 13-20	CIN 3	Annual rate per 100,000 female population age 13-20
Fairfield	147	101.42	15	11.03
Hartford	189	133.76	38	26.89
Litchfield	43	156.94	9	32.85
Middlesex	33	138.27	0	0
New Haven	163	112.83	32	22.15
New London	60	141.30	13	30.62
Tolland	25	74.48	1	2.98
Windham	13	63.11	2	9.71
Cases missing county data	8	...	...	...
Total:	681	117.70	110	19.01

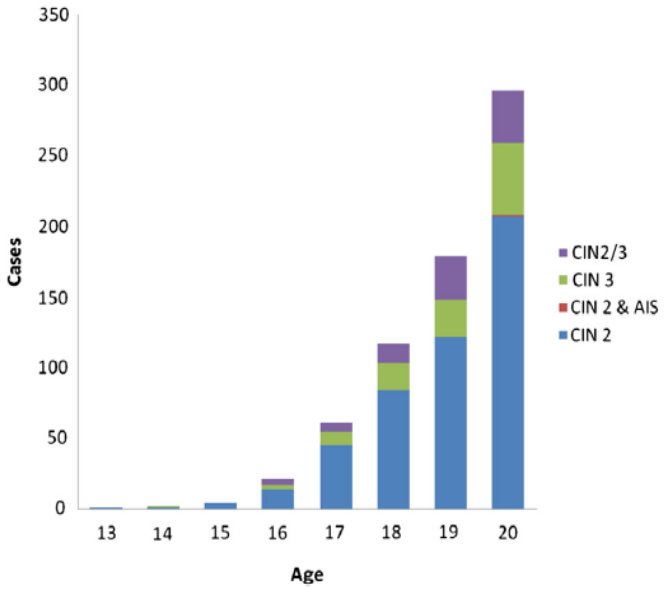


Fig. 1. Number of cases of CIN 2/AIS in adolescent females by age-Connecticut, 2008-2010.

Most cases are CIN2 and likely to regress
CIN3, though relatively rare, may be missed in a small number of young women

DeCew AE et al. *Journal of Pediatric and Adolescent Gynecology* 2013;26:346-349.

The increased risk of HGCL for black and Hispanic women compared to white women is higher in areas of high proportion black females

Individual measures	Area measures			
	≥20% Black		<20% Black	
	RR	95% CI	RR	95% CI
White (Reference)	1.00		1.00	
Black	2.38**	(1.82, 3.04)	1.46*	(1.07, 1.99)
Hispanic	2.19**	(1.65, 2.90)	1.65**	(1.28, 2.11)

Higher proportion of black residents:
138% and 119% increased risk for black and Hispanic women compared to white women, respectively

Lower proportion of black residents:
46% and 65% increased risk for black and Hispanic women compared to white women, respectively

P<.05 for interaction

Waggaman C et al. *Cancer Epidemiology* 2014;38:248-252.

Challenges of assessing HPV vaccine history among young women

Table 1
Vaccination history in medical records and patients interviews ($n = 1720$).

Vaccination history	Biopsy or vaccine provider record *n* (% of total)	Patient interview *n* (% of total)
Yes, at least 1 dose	330 (19%)	266 (15%)
No	795 (46%)	703 (41%)
Missing/unknown	581 (34%)	22 (1%)
Data collection not done: record not available or patient not reachable	14 (1%)	729 (43%)
TOTAL	1720	1720

Medical records are often missing (34%)
Patients often cannot be interviewed (43%)

Table 2
Vaccination history[a] concordance between medical records and patient interviews ($n = 991$ of 1720 women for whom data collection was completed by both sources).

Patient interview	Biopsy or vaccine provider record review			
	Yes	No	Unknown	Total
Yes	219	14	33	266
No	7	601	95	703
Missing/do not know	1	5	16	22
TOTAL	227	620	144	991

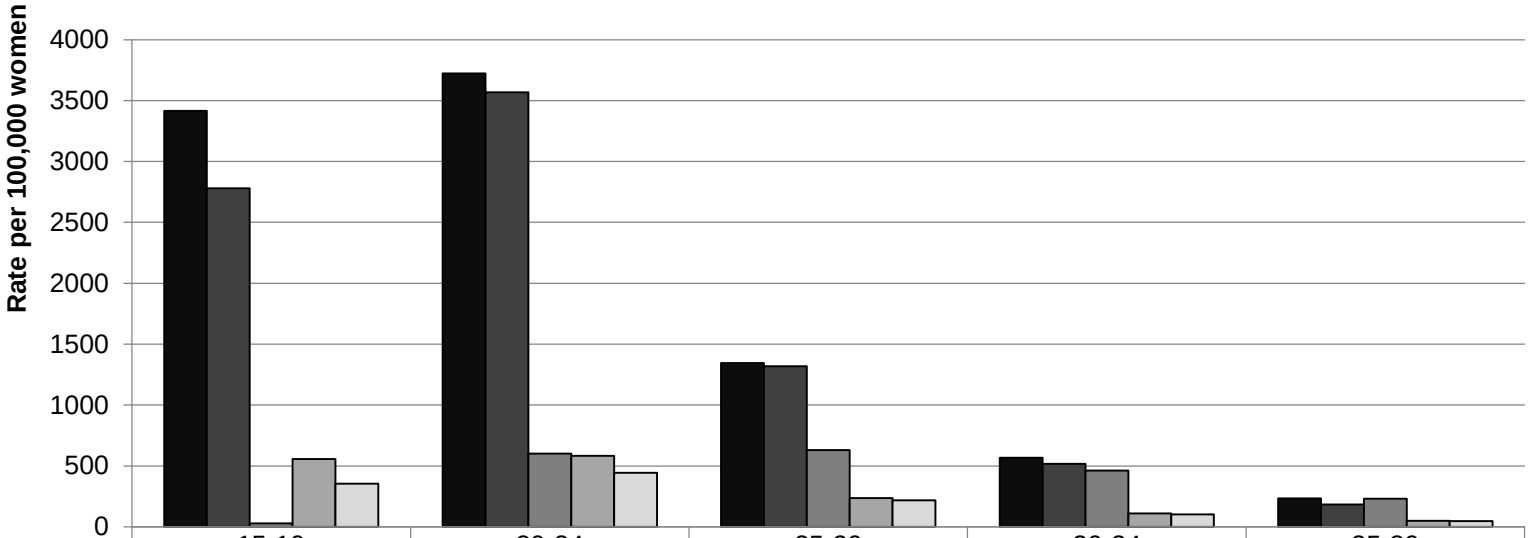
[a] At least one dose.

Concordance between two sources (83%) and sensitivity of self-report (96%) are high

Niccolai LM et al. *Vaccine* 2014;32:2945-7.

Rates of CIN2+ are as high as gonorrhea among women ages 20–39 years, second most commonly reported disease

Rates of Chlamydia, Gonorrhea, and CIN2/3/AIS by age, 2011



	15-19	20-24	25-29	30-34	35-39
Chlamydia-US	3417	3723	1344	568	234
Chlamydia-CT	2780	3568	1318	518	184
CIN2/3/AIS-CT	29	601	630	461	231
Gonorrhea-US	557	584	237	111	50
Gonorrhea-CT	353	443	217	102	46

Niccolai LM et al. *National STD Prevention Conference,* 2014.

Vaccine effectiveness: early estimates

Table 2. Sample description for women with known vaccine status stratified by HPV type

	Non-vaccine Type n (%)	Vaccine Type n (%)	Total	X^2 probability
Vaccine status				0.0200
Not vaccinated	399 (89.06)	319 (93.82)	718	
Vaccinated	49 (10.94)	21 (6.18)	70	
Total	448	340	788	
Age at vaccination				0.0855
Not Vaccinated	294 (65.63)	247 (72.65)	541	
15-20	48 (10.71)	25 (7.35)	73	
21+	106 (23.66)	68 (20.00)	174	
Diagnosis				<.0001
CIN2	336 (75.00)	187 (55.00)	523	
CIN2/3	43 (9.60)	51 (15.00)	94	
CIN3	69 (15.40)	98 (28.82)	167	
AIS/AIS+CIN	0 (0)	4 (1.18)	4	
Age at diagnosis				
18-20	34 (7.59)	24 (7.06)	58	0.0919
21-24	144 (32.14)	103 (30.29)	247	
25-29	127 (28.35)	126 (37.06)	253	
30-34	87 (19.42)	57 (16.76)	144	
35-39	56 (12.50)	30 (8.82)	86	
Race and ethnicity				
Hispanic	66 (14.73)	48 (14.12)	114	0.0812
White, not Hispanic	186 (41.52)	174 (51.18)	360	
Black, not Hispanic	48 (10.71)	26 (7.65)	74	
Other, not Hispanic	13 (2.90)	7 (2.06)	20	
Race and ethnicity NA	135 (30.13)	85 (25.00)	220	
Insurance type				
Private	309 (68.97)	248 (72.94)	557	0.5537
Public	113 (25.22)	76 (22.35)	189	
Uninsured	7 (1.56)	7 (2.06)	14	
Other Insurance	1 (0.22)	1 (0.29)	2	
Insurance NA	18 (4.02)	8 (2.35)	26	
Year of diagnosis				
2008	167 (37.28)	128 (37.65)	295	0.3880
2009	115 (25.67)	72 (21.18)	187	
2010	89 (19.87)	82 (24.12)	171	
2011	68 (15.18)	54 (15.88)	122	
2012	9 (2.01)	4 (1.18)	13	

Column percentages

Table 3. Unadjusted and adjusted odds ratios for vaccine type

	Unadjusted OR (95% CI)	Full model OR (95% CI)	Reduced model OR (95% CI)
Vaccination status			
Not Vaccinated	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Vaccinated	0.54 (0.32-0.91)**	0.57 (0.30-1.08)*	0.47 (0.27-0.82)***
Age at first vaccine dose			
Not Vaccinated	1.00 (Reference)	1.00 (Reference)	
15-20	0.62 (0.37-1.04)*	0.74 (0.37-1.49)	
21+	0.76 (0.54-1.08)	0.74 (0.48-1.12)	

Women vaccinated >24 months before diagnosis *53% less likely* to be infected with HPV 16/18

Currently, few women vaccinated at younger ages.

Berry J et al. YSPH MPH thesis 2014.