



Pre-invasive Cervical Cancer HPV Genotyping Study in Kentucky: Preliminary Results

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Topics to be covered

- Describe the pre-invasive cervical cancer surveillance project in Kentucky
- Describe the pre-invasive cervical cancer HPV genotyping study in Kentucky and Preliminary Results

Purpose of the Pre-Invasive Cervical Cancer (CIN-3 and AIS) Surveillance Project in Kentucky

- To develop a system for monitoring changes in the incidence of pre-invasive cervical cancer (CIN-3 and AIS) in the population as vaccination against HPV increases.

Specific Aims of the Pre-Invasive Cervical Cancer (CIN-3 and AIS) Surveillance Project in Kentucky

- To develop a system that will ensure complete and uniform population-based reporting of pre-invasive cervical cancer cases in Kentucky.
- To capture all pre-invasive cervical cancer cases within two months of diagnosis.
- To design the system so that it does not adversely affect the work of hospital registrars.

Process of developing the Kentucky Pre-Invasive Cervical Cancer Surveillance System

- 48 hospital and freestanding pathology labs were identified as sources of pre-invasive cervical cancer cases.
- Each case submitted by any lab is reviewed by a CTR to determine if it meets the criteria for inclusion.
- Each case that meets the criteria for this study is entered into the pre-invasive cervical cancer data system.
- Follow back to the physician's office or to the hospital cancer registrar is done to obtain any missing information (i.e. race, county of residence at diagnosis, etc.)
- QA edits are run periodically to identify potential errors.

Number of New Pre-Invasive Cervical Cancer (CIN-3 & AIS) Occurring monthly in Kentucky

Month	2009	2010	2011	2012
January	152	104	128	109
February	155	107	111	112
March	138	152	126	146
April	146	108	106	144
May	113	114	102	135
June	151	136	100	117
July	132	107	106	129
August	143	138	104	139
September	131	108	134	89
October	157	96	120	109
November	115	105	123	109
December	107	94	128	79
Total per year	1640	1369	1388	1417

Pre-Invasive Cervical Cancer HPV Genotyping Study: Collaborators

University of Kentucky (UK)

- Thomas Tucker (PI)
- Eric Durbin
- Brent Shelton
- Andrew Shearer
- Mary Jane Byrne

Centers for Disease Prevention and Control (CDC)

- Meg Watson
- Mona Saraiya
- Beth Unger
- Trevor Thompson
- Elaine Flagg

Pre-Invasive Cervical Cancer HPV Genotyping Study: Research Questions

- Are the HPV genotypes different for **non-Appalachian white women** diagnosed with pre-invasive cervical cancer (CIN-3) compared to **Appalachian white women**?
- Are the HPV genotypes different for **non-Appalachian white women** diagnosed with pre-invasive cervical cancer (CIN-3) compared to **non-Appalachian black women**?
- Are the HPV genotypes different for **white women diagnosed with CIN-3** compared to **white women diagnosed with AIS**?

Study Procedures

- The Kentucky Cancer Registry (KCR) served as the “Honest Broker” for this study.
- KCR solicited the required tissue blocks from each of 48 the labs where the tissue was stored.
- Tissue blocks were sent directly to KCR, the blocks were anonymized and given a unique code.
- The coded blocks were cut by the Markey Cancer Center, Biospecimens and Tissue Procurement Research Lab and the tissue specimens sent to CDC for genotyping.
- The original blocks were returned to the contributing lab by KCR.
- All of the HPV genotyping was done at CDC.
- The HPV genotype or types for each specimen and the associated unique code were then returned to KCR and linked with other data in the pre-invasive cervical cancer surveillance database to create a research data set.

Study Population

- All Kentucky women age 18 or older diagnosed with CIN-3 or AIS between January 1, 2009 and December 31, 2012 were available for this study.
- The cases were divided into four strata (non-Appalachian white women, non-Appalachian black women, Appalachian white women and AIS cases).
- A total of 4903 pre-invasive cervical cancer cases fell into one of these strata.
- 3099 were non-Appalachian white women diagnosed with CIN-3.
- 290 were non-Appalachian black women diagnosed with CIN-3.
- 1360 were Appalachian white women diagnosed with CIN-3.
- 154 were white women diagnosed with AIS.
- The recruitment goal was to obtain tissue specimens from a random sample of 150 cases in each strata (for a total of 600 cases). A random sample of 200 cases was drawn from each strata except AIS to allow replacement for cases for which tissue could not be obtained.

Pre-Invasive Cervical Cancer HPV Genotyping Study: Tissue Procurement

Pre-Invasive Cervical HPV Genotyping Study Data Collection					
Status	Non-App White	Non-App Black	App White	AIS	Totals
→ Cases collected and sent to CDC	137	130	154	121	542
→ Cases not yet sent to CDC	29	0	0	0	29
Preliminary Results					
→ HPV results available for analysis	113	105	121	82	421
Remaining Cases					
→ Cases pending HPV results	24	25	33	39	121
Total Cases					
→ Total cases obtained for this study	166	130	154	121	571

Pre-Invasive Cervical Cancer HPV Genotyping Study: # and % of Cases Currently Available for Analysis

Groupings	Frequency + (% of 421)
Available for study	421 (100%)
Appalachian white	121 (28.7%)
Non-Appal white	113 (26.8%)
Non-Appal black	105 (24.9%)
AIS white	82(19.5%)

Pre-Invasive Cervical Cancer HPV Genotyping Study: Frequency of HPV Types

HPV Genotyping groups compared	Frequency + (% of 421)
16 (alone or with any other HPV)	246 (58.4%)
16 alone	191 (45.4%)
18 (alone or with any other HPV)	43 (10.2%)
18 alone	32 (7.6%)
31 (alone or with any other HPV)	35 (8.3%)
31 alone	21 (5.0%)
35 (alone or with any other HPV)	21 (5.0%)
35 alone	14 (3.3%)
52 (alone or with any other HPV)	29 (6.9%)
52 alone	16 (3.8%)
18 (with any other HPV except 16)	36 (8.6%)
Any oncogenic HPV except 16 & 18	115 (27.3%)
Any oncogenic HPV	397 (94.3%)
All other	15 (3.6%)
HPV negative	9 (2.1%)
Multiple oncogenic	60 (14.3%)

Total number of HPV Genotypes found per individual	Frequency (% of 421)
0	9(2.1%)
1	330(78.4%)
2	66(15.7%)
3	10(2.4%)
4	5(1.2%)
5	1(0.2%)

For this study, HPV oncogenic types were defined as: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68

Pre-Invasive Cervical Cancer HPV Genotyping Study: Research Question 1

Are HPV genotypes different for Appalachian white vs non-Appalachian white females?

HPV Genotype	Region	% with genotype	p-value
Any oncogenic HPV except 16 & 18	Appalachian	22%	0.0588
	Non-Appalachian	34%	

Pre-Invasive Cervical Cancer HPV Genotyping Study: Research Question 2

Are HPV genotypes different for non-Appalachian white vs non-Appalachian black females?

HPV Genotype	RACE	% with genotype	p-value
→ 16 (alone or with any other HPV)	White	61.1%	0.0208
	Black	44.8%	
→ 16 alone	White	46.9%	0.0120
	Black	29.5%	
→ 35 (alone or with any other HPV)	White	2.7%	0.0043
	Black	13.3%	
→ 35 alone	White	1.8%	0.0158
	Black	9.5%	
→ Any oncogenic HPV except 16 & 18	White	33.6%	0.0539
	Black	46.7%	

Pre-Invasive Cervical Cancer HPV Genotyping Study: Research Question 3

Are HPV genotypes different for white females with CIN-3 vs white females with AIS?

HPV Genotype	CIN-3 Vs. AIS	% with genotype	p-value
18 (alone or with any other HPV)	CIN-3	3.0%	<0.0001
	AIS	39.0%	
18 alone	CIN-3	1.7%	<0.0001
	AIS	32.9%	
31 (alone or with any other HPV)	CIN-3	10.3%	0.001
	AIS	0.0%	
31 alone	CIN-3	7.3%	0.0084
	AIS	0.0%	
52 (alone or with any other HPV)	CIN-3	6.8%	0.0829
	AIS	1.2%	
52 alone	CIN-3	3.4%	0.1177
	AIS	0.0%	
33 (alone or with any other HPV)	CIN-3	0.0%	0.0689
	AIS	4.3%	

Pre-Invasive Cervical Cancer HPV Genotyping Study: Research Question 3 (Continued)

**Are HPV genotypes different for white females with CIN-3
vs white females with AIS?**

HPV Genotype	CIN-3 Vs. AIS	% with genotype	p-value
→ 18 (with any other HPV except 16)	CIN-3	2.1%	<0.0001
	AIS	35.4%	
→ Any oncogenic HPV except 16 & 18	CIN-3	27.8%	<0.0001
	AIS	1.2%	
→ Other HPV <i>types</i>	CIN-3	4.7%	0.0725
	AIS	0.0%	

Preliminary Conclusions

- HPV oncogenic types other than 16 and 18 were more common among non-Appalachian white women diagnosed with CIN-3 compared to Appalachian white women
- HPV 16 alone or with any other HPV type was more common among white women diagnosed with CIN-3 compared to black women.

Thank You!

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Questions?