

Population Based Surveillance for High-grade Pre-invasive Cervical Cancer in Three Central Cancer Registries, United States 2009

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BACKGROUND AND RATIONALE

Timeline of Genital HPV-related Endpoints

t_0 =HPV infection
(Days)

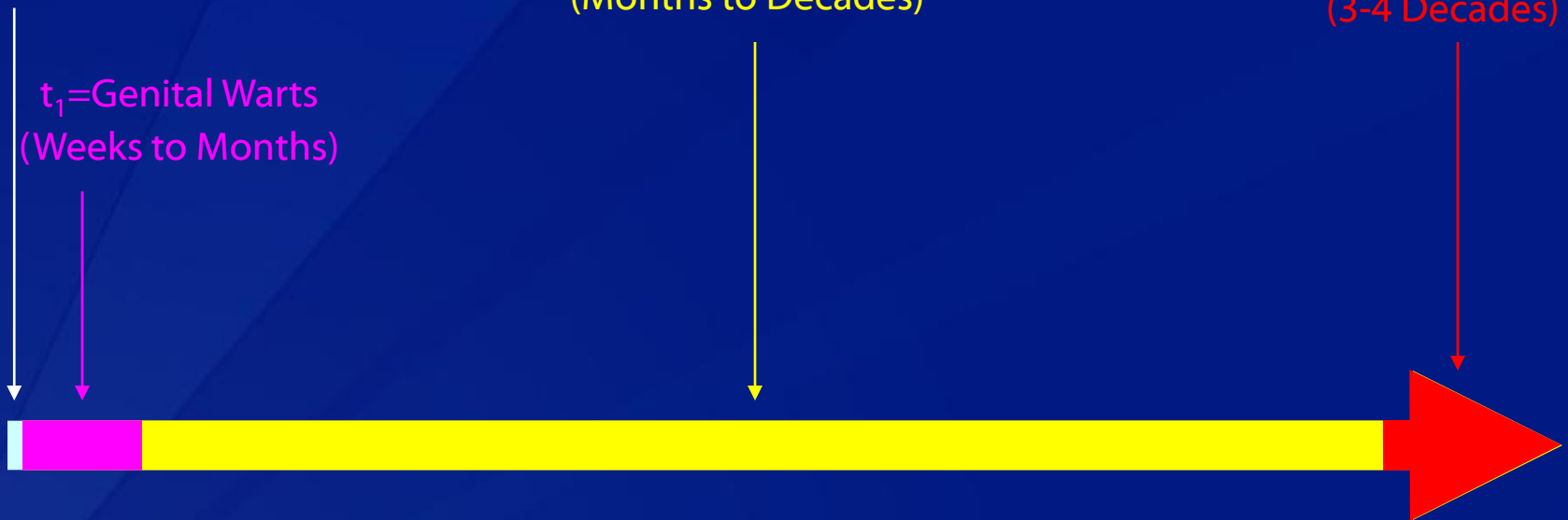
t_1 =Genital Warts
(Weeks to Months)

t_2 =Cervical Cancer Precursors
CIN 1, 2, 3 & AIS
(Months to Decades)

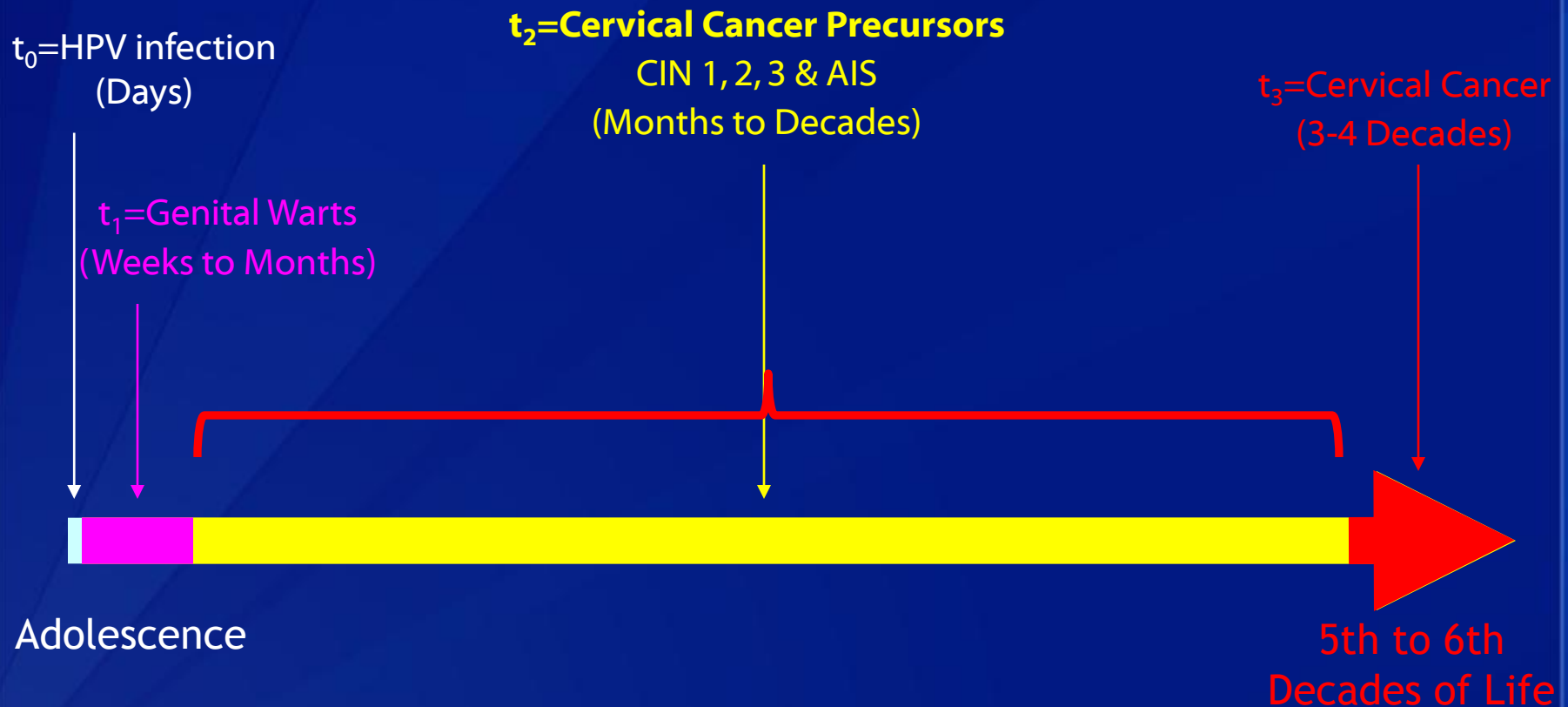
t_3 =Cervical Cancer
(3-4 Decades)

Adolescence

5th to 6th
Decades of Life



Timeline of Genital HPV-related Endpoints



HPV Vaccine

- ❑ **Quadrivalent vaccine licensed in females June 2006, Bivalent licensed in Oct 2009**
 - Routine recommendation for girls aged 11-12 yrs, catch up to age 26 yrs
 - Quadrivalent vaccine also licensed and recommended (permissive) for males aged 9-26 yrs
- ❑ **Anticipated reductions in cervical cancers, other anogenital cancers**
- ❑ **National Immunization Survey –Teen 2009**
 - 44% of girls aged 13-17 received at least 1 dose
 - 27% received all 3 doses

Need for Surveillance to Monitor Vaccine Impact on HPV Outcomes

□ Monitoring impact of vaccines important

- Assess progress of immunization programs
- Demonstrating population impact of vaccine
- Evaluating policy needs

□ Novel approaches required for HPV

- Multiple clinical outcomes
- Time intervals between infection and outcomes
- Existence of secondary prevention program for cervical cancer
- Vaccination <-> screening programs <-> outcomes

□ What is the return on public health investment?

Cancer Registries and Pre-invasive Cervical Cancer Surveillance

- ❑ Previous experience collecting cervical carcinoma *in situ* (CIS/CIN 3) in NPCR and SEER
- ❑ Decision to discontinue collection of CIS data in 1996 based on concerns over new nomenclature and potential misclassification of cases
 - Michigan Central Cancer Registry has continued to collect CIS data
- ❑ More time has passed since nomenclature introduced
- ❑ Due to introduction of HPV vaccine, more need to collect these data

NPCR CIN 3/AIS SURVEILLANCE PILOT PROJECT

NPCR CIN 3/AIS Surveillance Pilot Project

❑ Funded four central cancer registries

- **Michigan Central Cancer Registry** (NPCR and SEER, geographically distinct sites)
- **Louisiana Tumor Registry** (NPCR and SEER)
- **Kentucky Central Cancer Registry** (NPCR and SEER)
- **Los Angeles County Cancer Surveillance Program** (NPCR and SEER)

❑ Common protocol

- Endpoints
- Issues around nomenclature and misclassification
- Most efficient methods - rapid case ascertainment
- Data limited to 24 variables (almost all NAACCR v. 11)

Eligible Cases – Pilot Project

□ Pathology report information

- All resident cases diagnosed as CIN 3, CIS, or AIS
- Severe dysplasia
- Histology codes:

Squamous carcinoma in situ:

- 8010/2 Carcinoma in situ
- 8050/2 Papillary carcinoma in situ
- 8052/2 Papillary squamous cell carcinoma, non-invasive
- 8070/2 Squamous cell carcinoma in situ, NOS
- 8071/2 Squamous cell carcinoma, keratinizing, NOS, in situ
- 8072/2 Squamous cell carcinoma, large cell, non-keratinizing, in situ
- 8076/2 Squamous cell carcinoma in situ w/quest. stromal invasion
- 8077/2 Squamous intraepithelial neoplasia grade III

Adenocarcinoma in situ

- 8140/2 Adenocarcinoma in situ
- 8560/2 Adenosquamous carcinoma

Case Finding – Pilot Project

- ❑ **Pathology laboratories**
 - Private, reference, or hospital labs
- ❑ **Manual review or electronic search of pathology reports**
 - E-path reporting – modification of AIM software selection criteria
- ❑ **Cases submitted using established registry procedures**
 - Electronic reporting by hospital tumor registrars
 - Electronic reporting by pathology laboratories
 - Central registry field staff case finding
 - Hospital medical record department submissions
- ❑ **Follow-back to reporting source or physician office for:**
 - Diagnosis, lesion behavior, histology, date of diagnosis
 - City/County/State of diagnosis, date of birth, race, ethnicity

Quality Review and Timeline – Pilot Project

□ **Quality control activities**

- Edit checks and visual editing
- Checking for duplicate reports
- Case finding audits

□ **Pilot project timeline**

- Non research determination by CDC
- Pre-pilot period (Sept-Dec 2008)
- Data collection Jan 2009-Dec 2009
- Continued collection through 2010
- Pilot project ended March 2011

**RESULTS FROM 3 REGISTRIES, 2009
PILOT PROJECT**

CIN 3/AIS Female Population and Case Counts, Three States 2009

	Total		Kentucky		Louisiana		Michigan	
	N	%	N	%	N	%	N	%
Female 2009								
Population	10,026,024	100	2,196,707	21.91	2,762,444	27.55	5,066,873	50.54
Cases	5565	100	1636	29.40	1255	22.55	2674	48.05
Squamous carcinoma in situ	5348	96.10	1583	96.76	1232	98.17	2533	94.73
Adenocarcinoma in situ	218	3.92	53	3.24	24	1.91	141	5.27

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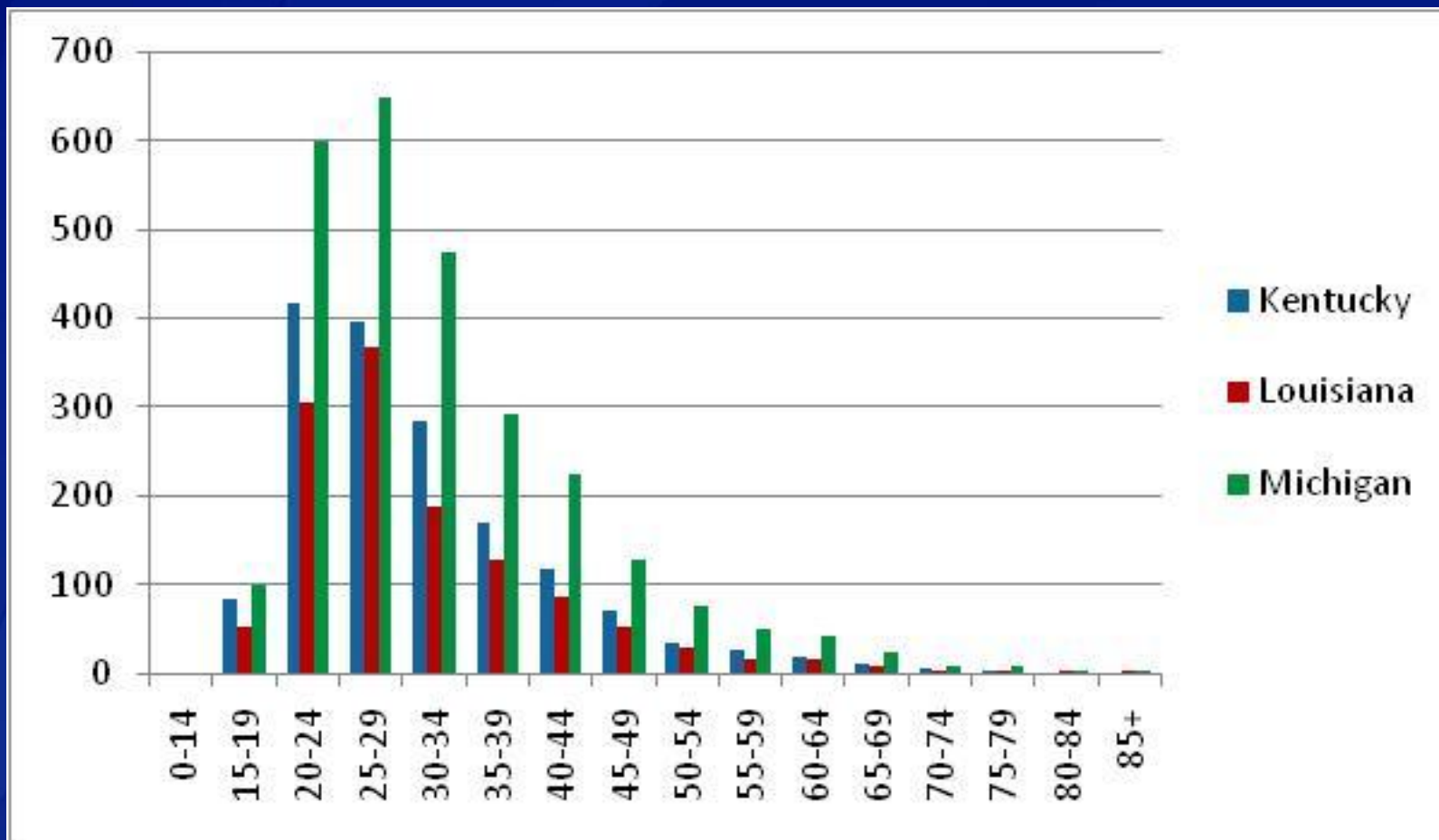
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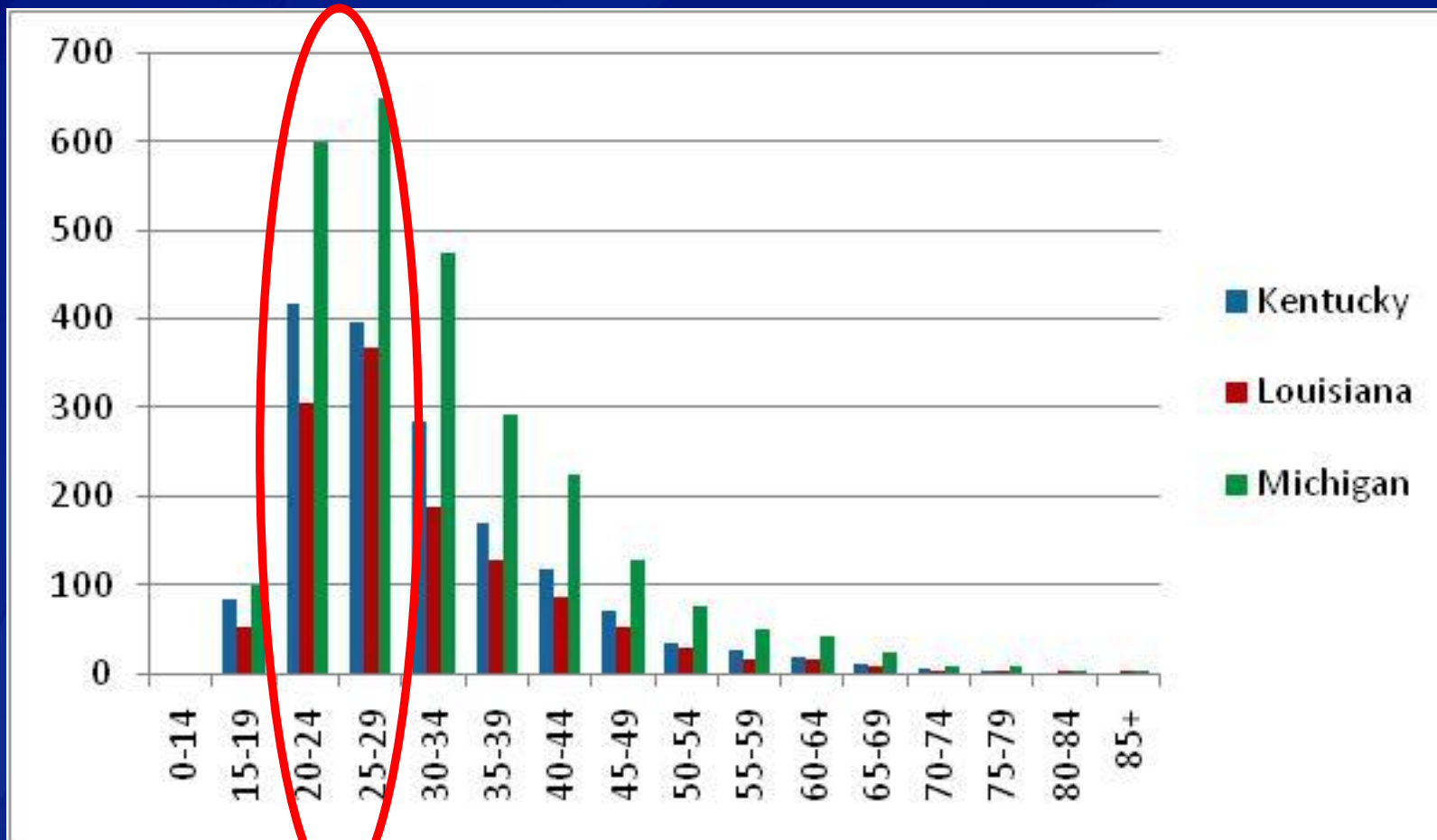
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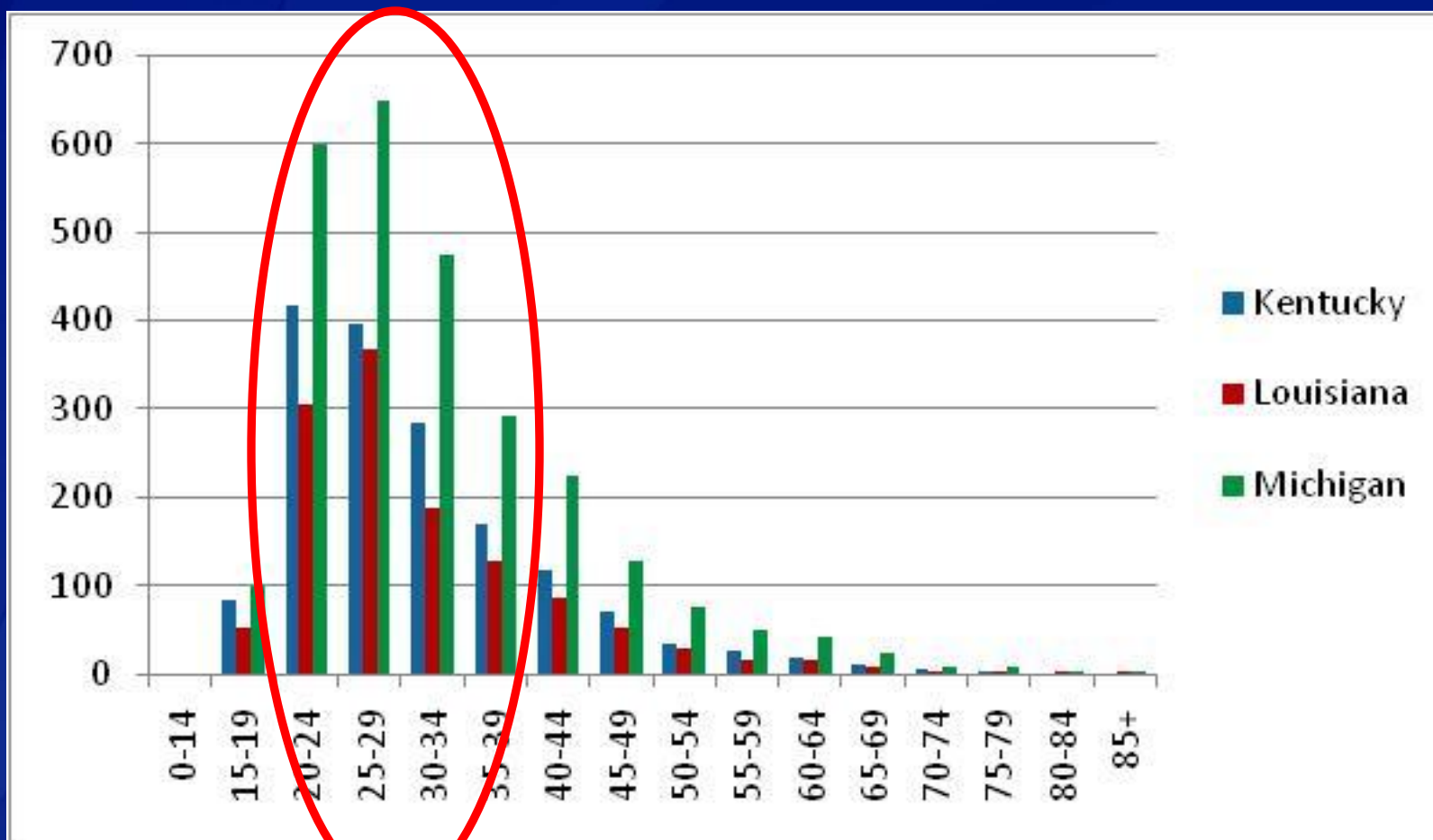
CIN 3/AIS Case Counts by Age Category, Three States 2009



CIN 3/AIS Case Counts by Age Category, Three States 2009



CIN 3/AIS Case Counts by Age Category, Three States 2009



CIN 3/AIS Incidence per 100,000 by Age Category, Three States 2009

	Kentucky	Louisiana	Michigan
Age at Diagnosis			
0-14	0.00	0.00	0.00
15-19	59.75	33.21	27.91
20-24	287.43	178.70	175.69
25-29	265.25	215.90	211.74
30-34	207.29	130.58	165.19
35-39	117.48	91.89	89.74
40-44	78.98	59.00	64.61
45-49	43.29	30.33	33.24
50-54	21.74	17.60	19.26
55-59	18.06	10.33	14.38
60-64	14.69	12.55	14.62
65-69	11.68	9.81	11.20
70-74	8.09	5.51	4.21
75-79	4.90	3.30	4.96
80-84	0.00	2.03	1.67
85+	0.00	4.11	2.36

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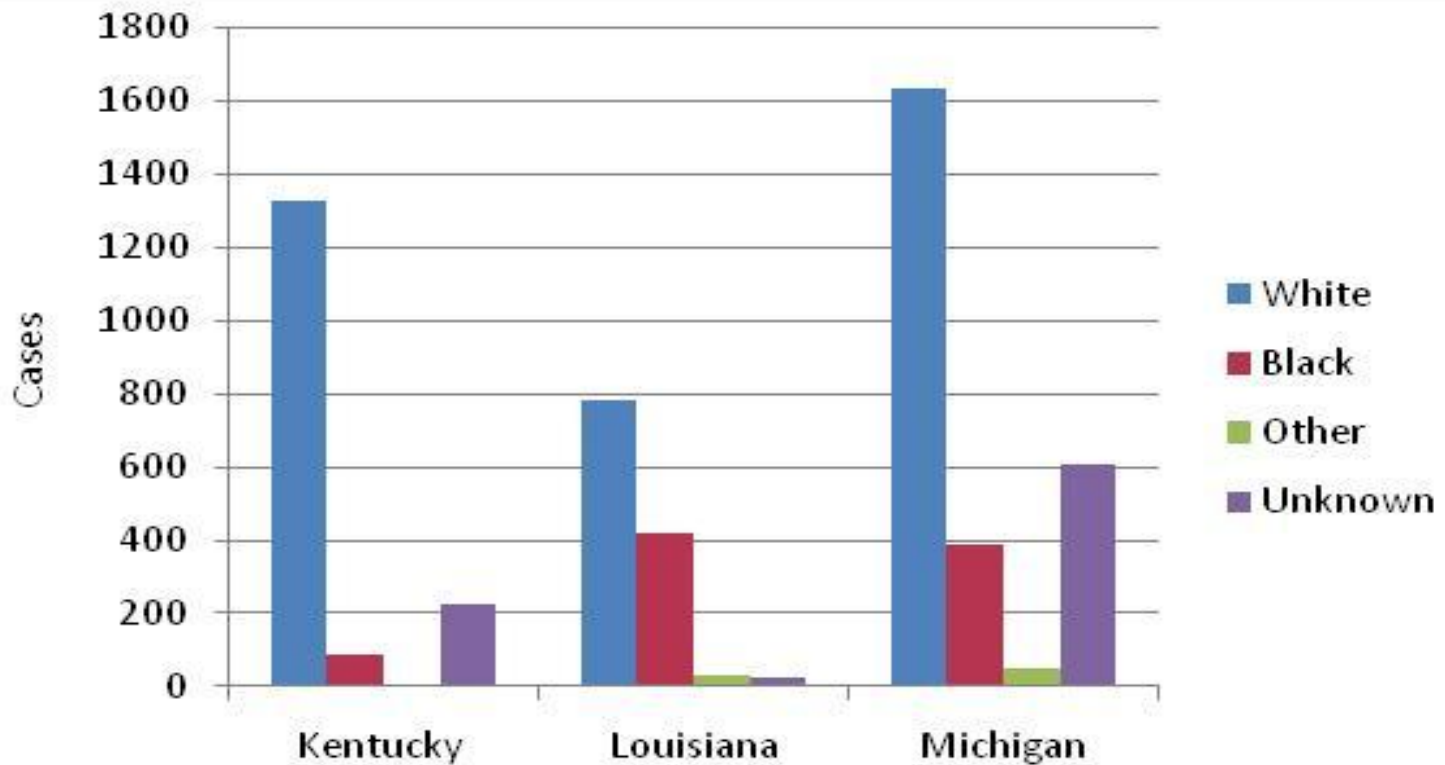
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CIN 3/AIS Age-Adjusted Incidence per 100,000, Three States 2009

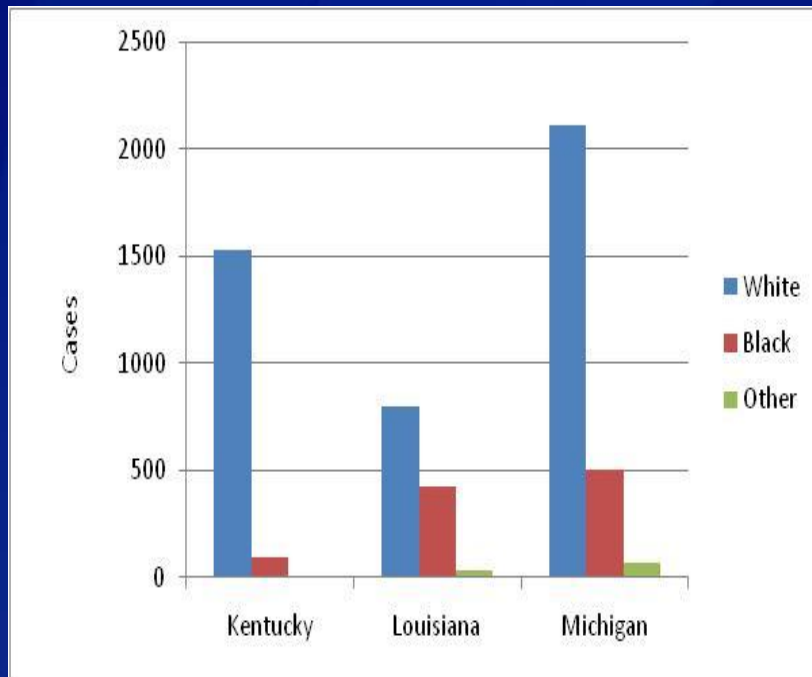
	Kentucky		Louisiana		Michigan	
	Incidence	(95% CL)	Incidence	(95% CL)	Incidence	(95% CL)
CIN3/AIS	77.9	(77.6, 78.3)	54.7	(54.4, 55.0)	57.2	(56.9, 57.5)
Invasive Cervical Cancer	9.0	(7.8, 10.4)	8.8	(7.6, 10.1)	8.0	(7.2, 8.8)

- Population (denominator): US Census vintage 2009 bridged-race estimates for year 2009, National Center for Health Statistics.
- Age-adjustment based on year 2000 US Standard Population.
- 95% confidence limits estimated using methodology of Tiwari RC, Clegg LX, Zou Z 2006. Stat Methods Med Res15: 547-569.

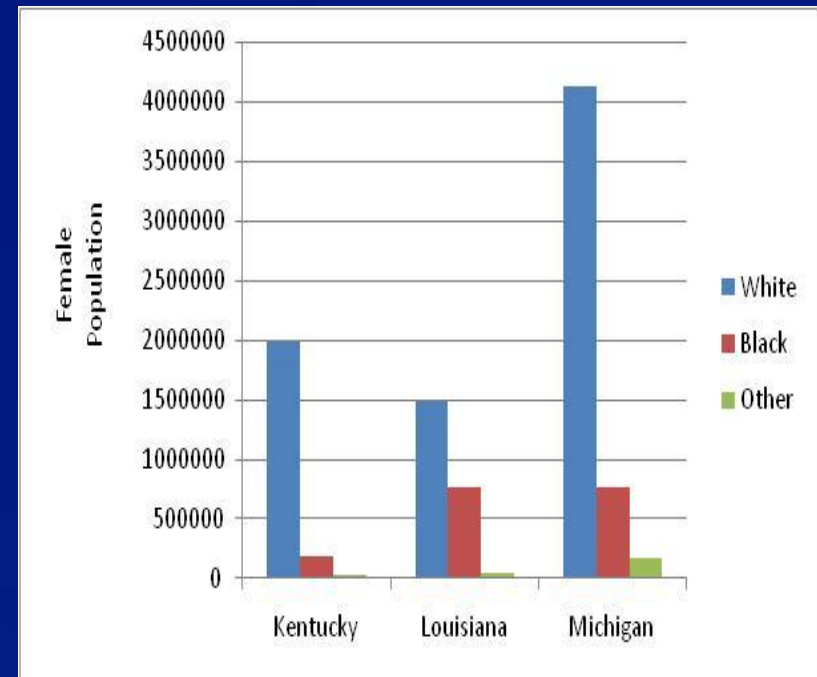
CIN 3/AIS Case Counts by Race, Three States 2009



CIN 3/AIS Case Counts and Female Population by Race, Three States 2009



Cases by Race



Female Population by Race

Assumption: distribution of race (black, white, other) among cases for which race is unknown reflects distribution of race when restricted to cases for which race is known.

CIN 3/AIS Crude Incidence by Race, Three States 2009

	Kentucky		Louisiana		Michigan	
	Incidence	(95% CL)	Incidence	(95% CL)	Incidence	(95% CL)
White	77.3	(73.5, 81.2)	53.8	(50.2, 57.6)	51.1	(49.0, 53.3)
Black	54.3	(44.4, 66.1)	55.2	(50.1, 60.6)	64.9	(59.4, 70.8)
Other	14.4	(5.5, 34.1)	60.3	(42.2, 84.7)	38.2	(29.8, 48.6)

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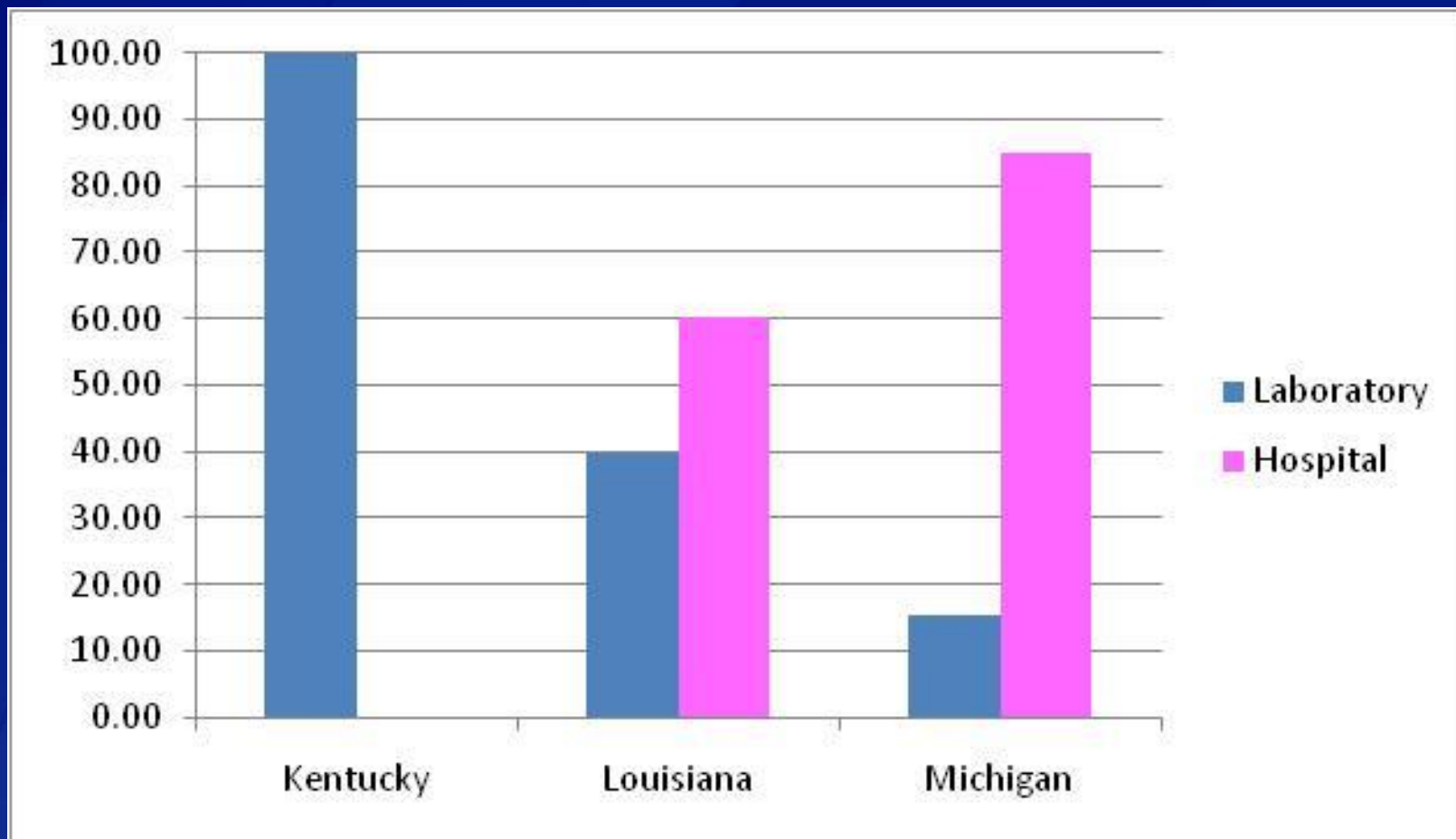
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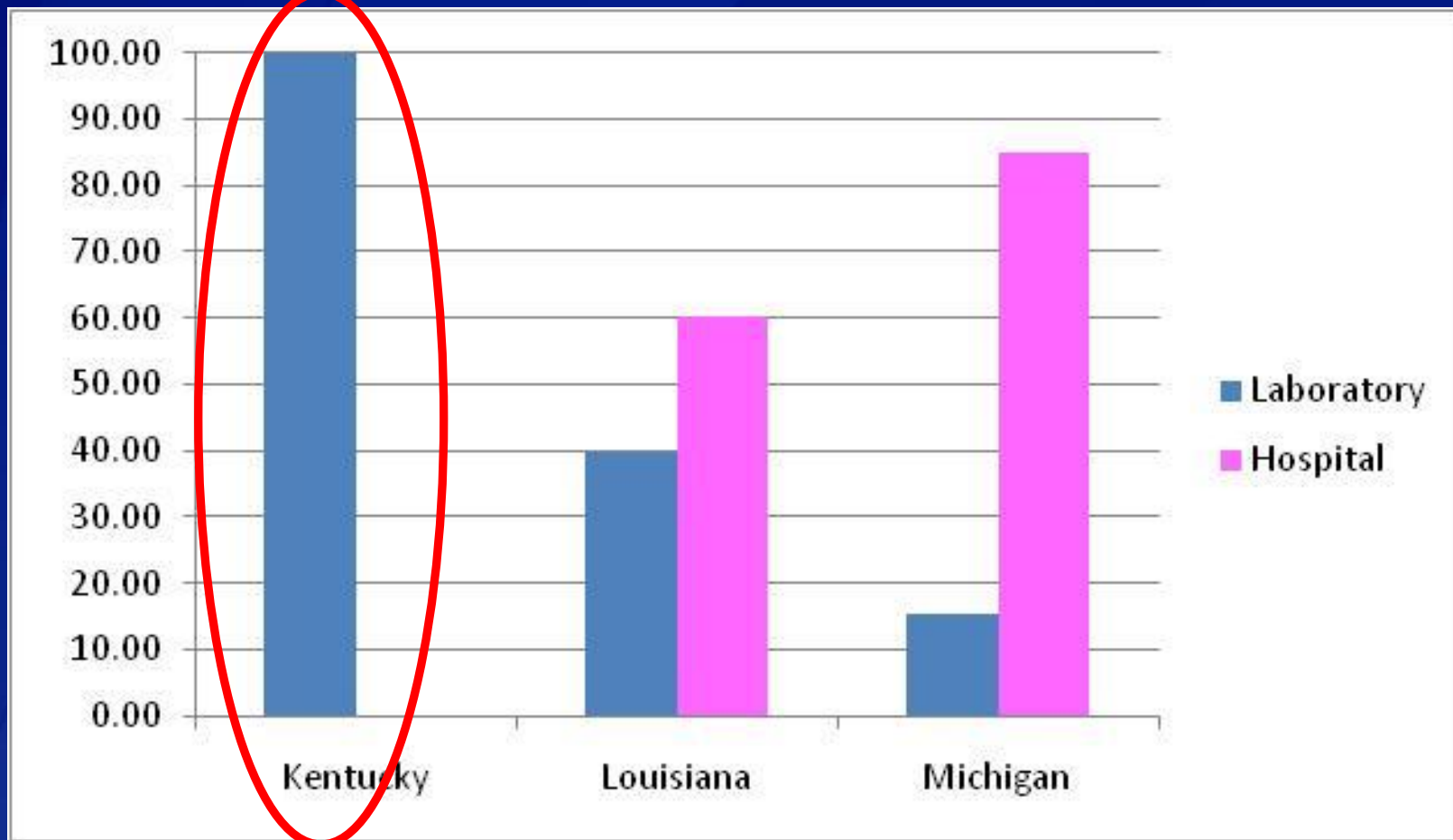
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Reporting Sources for CIN 3/AIS Cases, Three States 2009



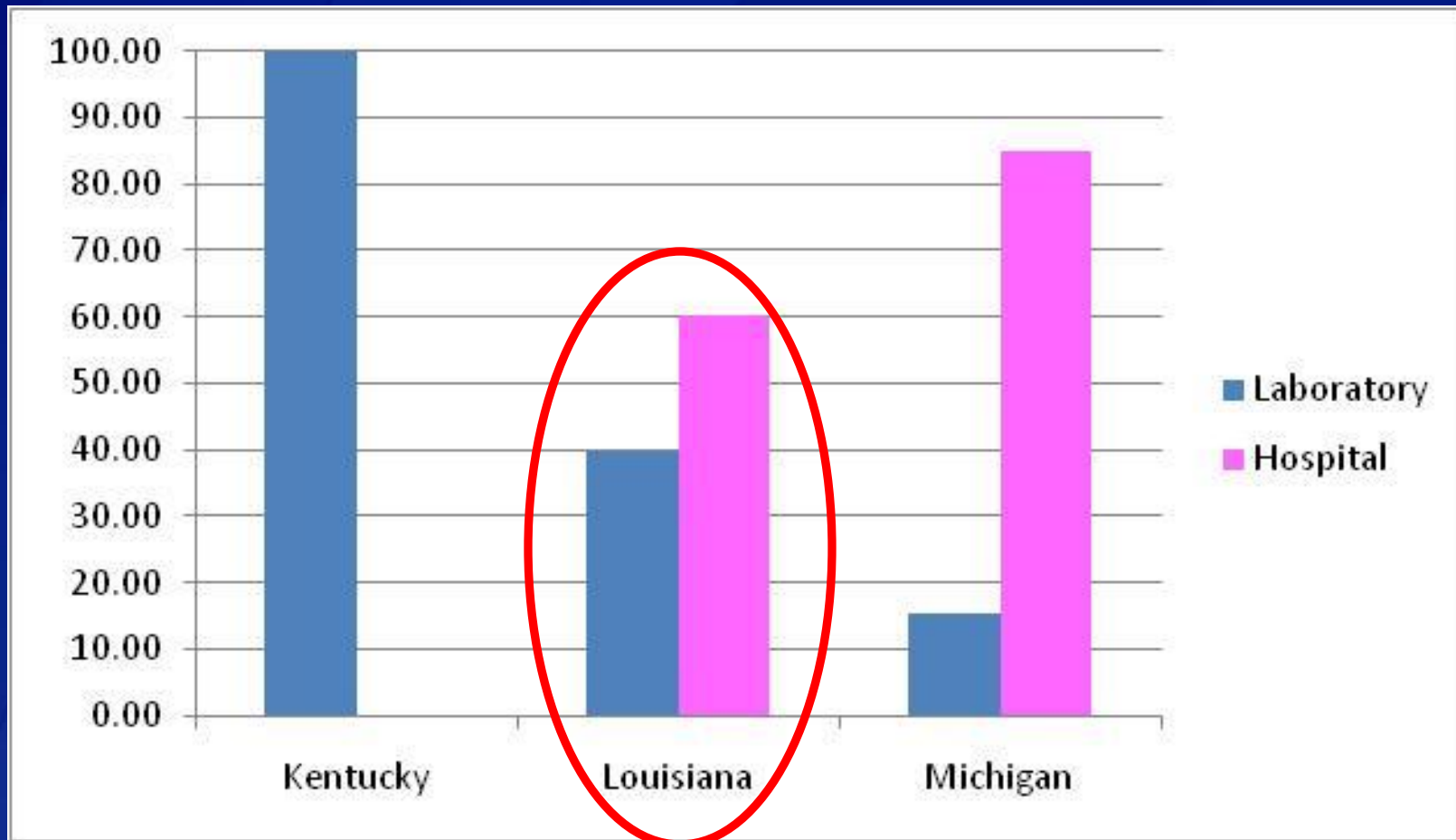
Contribution (Percentage) of Reporting Sources within Each Registry

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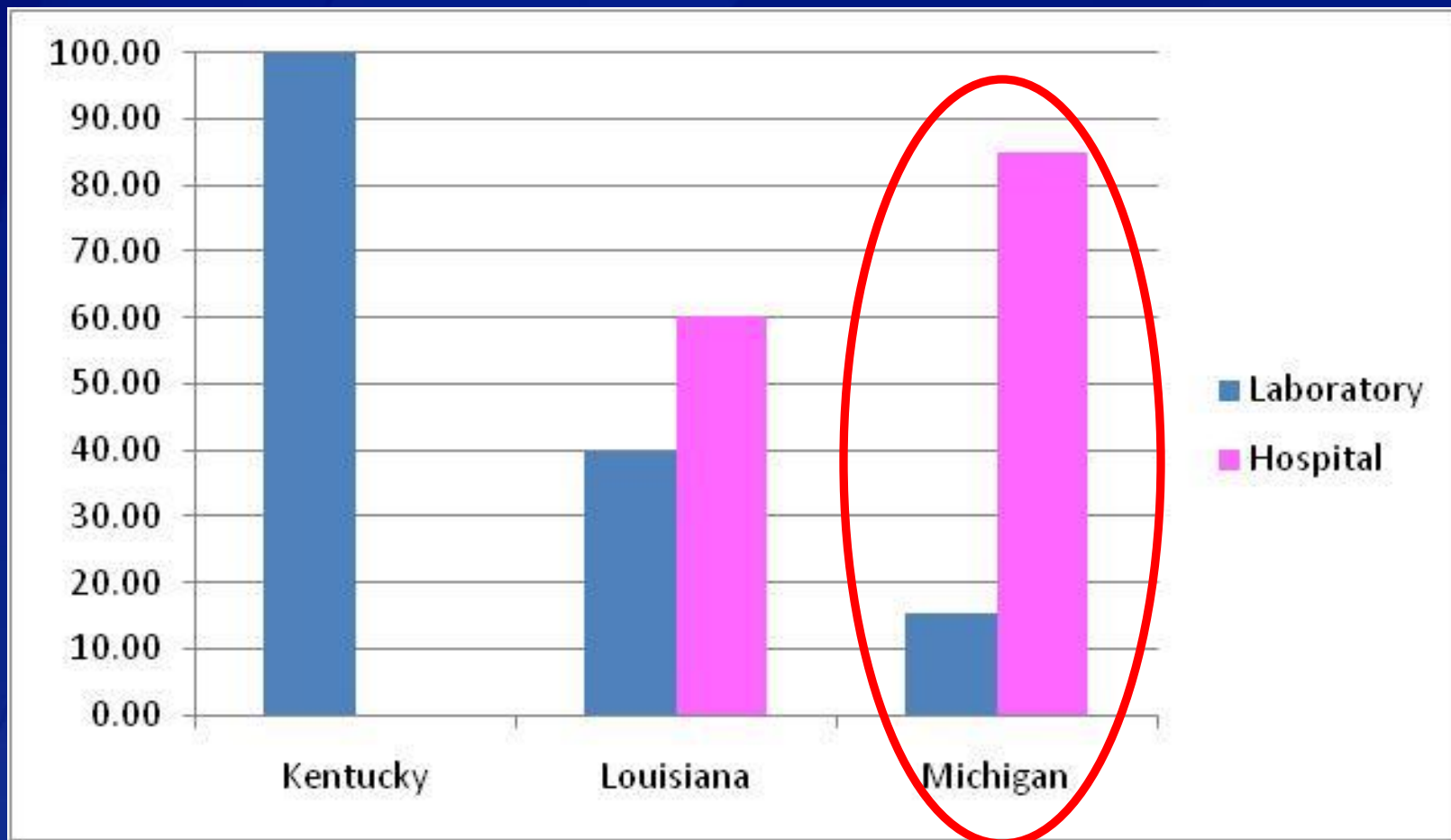
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CONCLUSIONS

Lessons Learned

- ❑ **CIN 3/AIS surveillance is feasible using existing registry infrastructure and procedures**
- ❑ **Electronic laboratory reporting most useful for rapid reporting**
 - E-Path found to be preferred method for electronic reporting
 - Data often incomplete, requiring follow-back
 - Modifications to software to include appropriate CIN 3/AIS search terms requires sufficient time to code and install
 - Existing Health Information Exchanges may also be useful to facilitate rapid reporting
- **Routine contacts with cancer registrars helpful**
 - Transitioning facilities to E-Path will decrease workload and reduce missed cases

Next Steps and Future Directions

- ❑ **Linkage with immunization registry data**
 - Michigan Immunization Registry
- ❑ **Completeness of demographic data**
 - Race, ethnicity
- ❑ **Adequacy of diagnostic terms**
 - CIN 2-3
 - CIN 2/3
 - HSIL (high-grade SIL)
 - CIN 2 and 3
 - CIN 3
 - Severe dysplasia
- ❑ **Additional validation activities**
 - Completeness of data collection
 - Assessment of data quality

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CDC

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Louisiana Tumor Registry

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Kentucky Cancer Registry

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Los Angeles County Cancer Registry

Dennis Deapen
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1600 Clifton Road NE, Atlanta, GA 30333

Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348

E-mail: cdcinfo@cdc.gov Web: <http://www.cdc.gov>

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

CIN 3/AIS Crude Incidence by Race, Three States 2009

	Kentucky		Louisiana		Michigan	
	Incidence	(95% CL)	Incidence	(95% CL)	Incidence	(95% CL)
White	66.7	(63.2, 70.4)	52.8	(49.2, 56.6)	39.5	(37.7, 41.5)
Black	46.9	(37.7, 57.9)	54.2	(49.2, 59.6)	50.2	(45.4, 55.4)
Other	12.4	(4.4, 31.4)	59.2	(41.3, 83.5)	29.6	(22.3, 38.8)

Numerators restricted to cases for which race is known.

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77.9	(60.8, 96.2)	54.7	(41.0, 71.0)	57.2	(43.6, 74.4)

- ❑ Based on year 2000 US Standard Population
- ❑ 95% confidence limits estimated based on Poisson distribution

Expected and Reported CIN 3/AIS Case Counts, Three States 2009

	Total	Kentucky	Louisiana	Michigan
Reported Cases, January-December 2009	5565	1636	1255	2674
Expected Cases Over 12 Months MI 2004-2008 Average Incidence Applied to 2009 State Population	5494	1261	1324	2909
Ratio of Reported to Expected Cases	1.01	1.30	0.95	0.92

Population: US Census vintage 2009 bridged-race estimates for years 2004-2009, National Center for Health Statistics.

Reported and Expected Cases of Pre-Invasive Cervical Lesions, by State

	Total	Kentucky	Louisiana	Michigan
Reported Cases, January-December 2009	5565	1636	1255	2674
Expected Cases Over 12 Months MI 2001-2005 Average Incidence Applied to 2009 State Population	5389	1237	1299	2853
Ratio of Reported to Expected Cases	1.03	1.32	0.97	0.94
Expected Cases Over 12 Months MI 2004-2008 Average Incidence Applied to 2009 State Population	5494	1261	1324	2909
Ratio of Reported to Expected Cases	1.01	1.30	0.95	0.92