



# Data Brief:

## HPV-Associated Cancers in Massachusetts

Massachusetts Department of Public Health

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### PURPOSE

The purpose of this report is to present the epidemiology of human papillomavirus (HPV) associated cancers in Massachusetts from 2004 to 2014. HPV-associated cancers include anal, cervical, oropharyngeal, penile, rectal, vaginal, and vulvar cancers. Oropharyngeal cancers include cancers that occur on the base of the tongue, tonsils, soft palate, and other oropharynx. This report describes the incidence, mortality, trends over time, percentage of cancers attributable to HPV infection, and compares the findings from Massachusetts to national data. Data are from the Massachusetts Cancer Registry (MCR) and the Massachusetts Registry of Viral Records and Statistics (MRVRS). Rates of HPV vaccination are examined in Massachusetts.

### KEY POINTS

- In Massachusetts from 2004-2014, oropharyngeal cancer was the most common HPV-associated cancer among males and cervical cancer was the most common HPV-associated cancer among females.
- Oropharyngeal cancer was the most common cause of death from an HPV-associated cancer for males and cervical cancer was the most common cause of death from an HPV-associated cancer for females from 2008-2014 in Massachusetts.
- The incidence rate of HPV-associated cancers in Massachusetts have been increasing by 1.3% each year from 2004-2014 with statistical significance. The incidence rates of oropharyngeal cancer among males, anal cancer among females, and vulvar cancer among females have been increasing with statistical significance. The incidence rate of cervical cancer among females in Massachusetts has been decreasing with statistical significance.

### HPV-ASSOCIATED CANCERS IN MASSACHUSETTS

**Table 1. Total cases and age-adjusted incidence rates<sup>^</sup> of HPV-associated cancers, Massachusetts, 2004-2014**

Cancer Site	Male		Cancer Site	Female	
	Cases	Incidence Rate <sup>^</sup>		Cases	Incidence Rate <sup>^</sup>
All HPV-associated	3,912	9.99	All HPV-associated	5,130	11.84
Oropharynx	3,127	7.85	Cervix	2,193	5.46
Anus	422	1.09	Vulva	1,046	2.24
Penis	328	0.95	Oropharynx	869	1.91
Rectum	35	0.10	Anus	765	1.69
			Vagina	180	0.38
			Rectum	77	0.17

<sup>^</sup>per 100,000 and age-standardized to the 2000 U.S. population; 1 person did not identify as male or female; data source: Massachusetts Cancer Registry

**Table 2. Total deaths and age-adjusted mortality rates<sup>^</sup> of HPV-associated cancers, Massachusetts, 2008-2014**

Male			Female		
Cancer Site	Deaths	Mortality Rate <sup>^</sup>	Cancer Site	Deaths	Mortality Rate <sup>^</sup>
All HPV-associated	682	2.77	All HPV-associated	956	3.08
Oropharynx	586	2.35	Cervix	374	1.29
Penis	49	0.23	Oropharynx	234	0.73
Anus	47	0.19	Vulva	221	0.67
			Anus	74	0.23
			Vagina	53	0.15

<sup>^</sup>per 100,000 and age-standardized to the 2000 U.S. population; 1 person did not identify as male or female; data source: Massachusetts Registry of Vital Records and Statistics

**New Cases**

- From 2004-2014, 3,912 males and 5,130 females were diagnosed with a HPV-associated cancer in Massachusetts.
- In Massachusetts, oropharyngeal cancer was the most common HPV-associated cancer diagnosed in males. Cervical cancer was the most common HPV-associated cancer diagnosed in females.

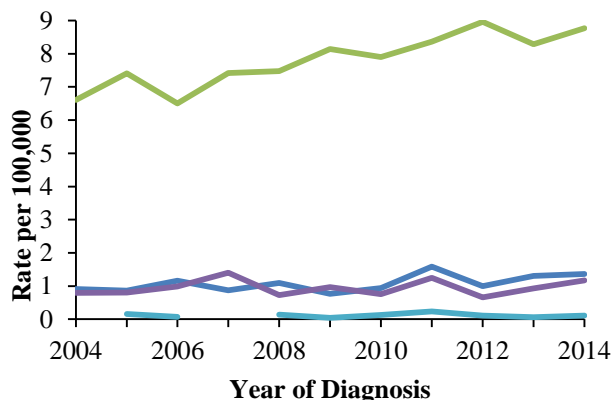
**Deaths**

- From 2008-2014, 682 males and 956 females died from a HPV-associated cancer in Massachusetts.
- In Massachusetts, oropharyngeal cancer was the leading cause of death from an HPV-associated cancer in males. Cervical cancer was the leading cause of death from an HPV-associated cancer in females.

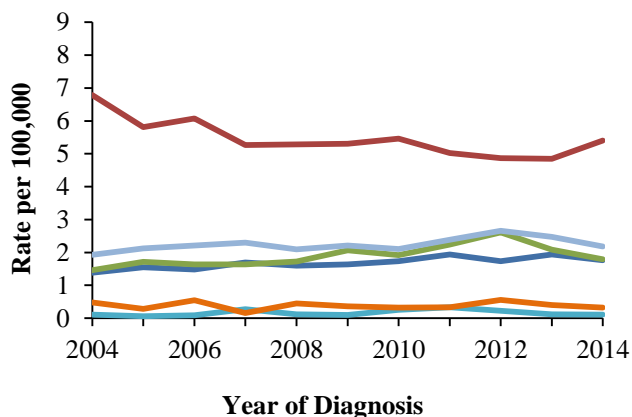
**HPV-ASSOCIATED CANCER TRENDS**

**Figure 1. Trends in the incidence rates<sup>^</sup> of HPV-associated cancers, Massachusetts, 2004-2014**

**By Cancer Site among Males**



**By Cancer Site among Females**



— Anal (APC 2004-2014 = 4.23)  
— Oropharyngeal (APC 2004-2014 = 2.82\*)  
— Penile (APC 2004-2014 = 1.16)  
— Rectal (APC 2005-2014 = -1.71)

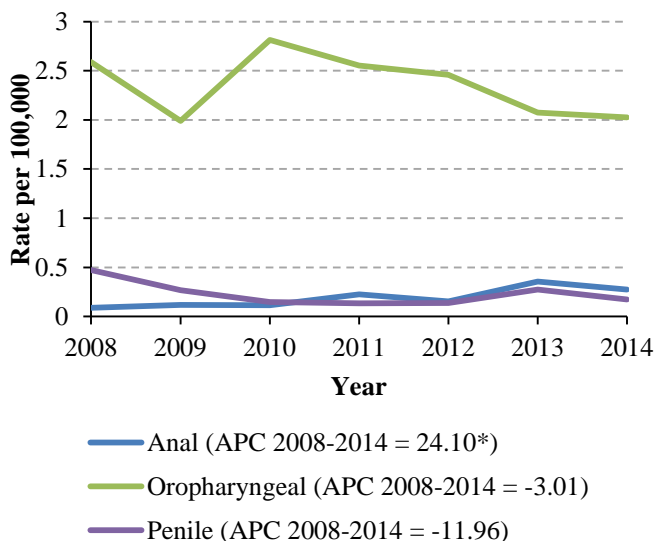
— Anal (APC 2004-2014 = 2.64\*)  
— Cervical (APC 2004-2014 = -2.41\*)  
— Oropharyngeal (APC 2004-2012 = 6.62\*, APC 2012-2014 = -13.73)  
— Rectal (APC 2004-2014 = 4.76)  
— Vaginal (APC 2004-2014 = -0.82)  
— Vulvar (APC 2004-2014 = 1.70\*)

	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Overall incidence, male	8.31	9.24	8.73	9.68	9.43	9.92	9.72	11.43	10.72	10.58	11.41
Overall incidence, female	12.15	11.55	12.04	11.32	11.27	11.68	11.81	12.25	12.66	11.86	11.57

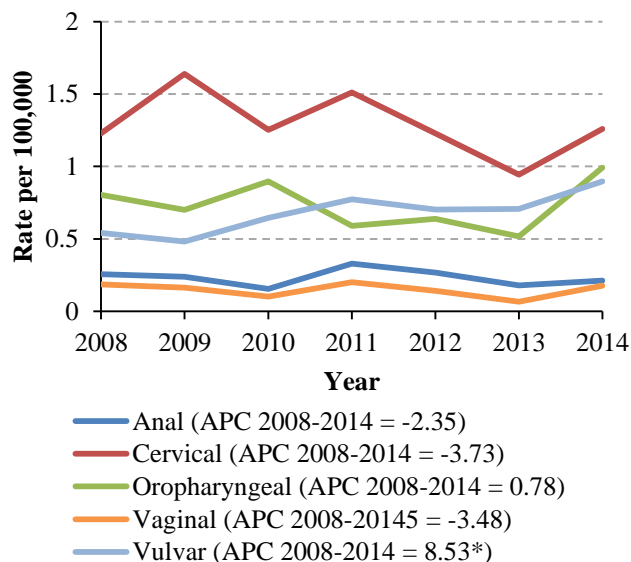
<sup>^</sup>per 100,000 and age-standardized to the 2000 U.S. population; \*indicates a statistically significant trend (p<0.05); APC = Annual Percent Change; Data source: Massachusetts Cancer Registry

**Figure 2. Trends in the mortality rates<sup>^</sup> of HPV-associated cancers, Massachusetts, 2008-2014**

**By Cancer Site among Males**



**By Cancer Site among Females**



	2008	2009	2010	2011	2012	2013	2014
Overall mortality, male	3.15	2.37	3.08	2.91	2.75	2.71	2.48
Overall mortality, female	3.02	3.22	3.05	3.41	2.98	2.41	3.54

<sup>^</sup>per 100,000 and age-standardized to the 2000 U.S. population; \*indicates a statistically significant trend (p<0.05); APC = Annual Percent Change; Data source: Massachusetts Registry of Vital Records and Statistics

**Incidence**

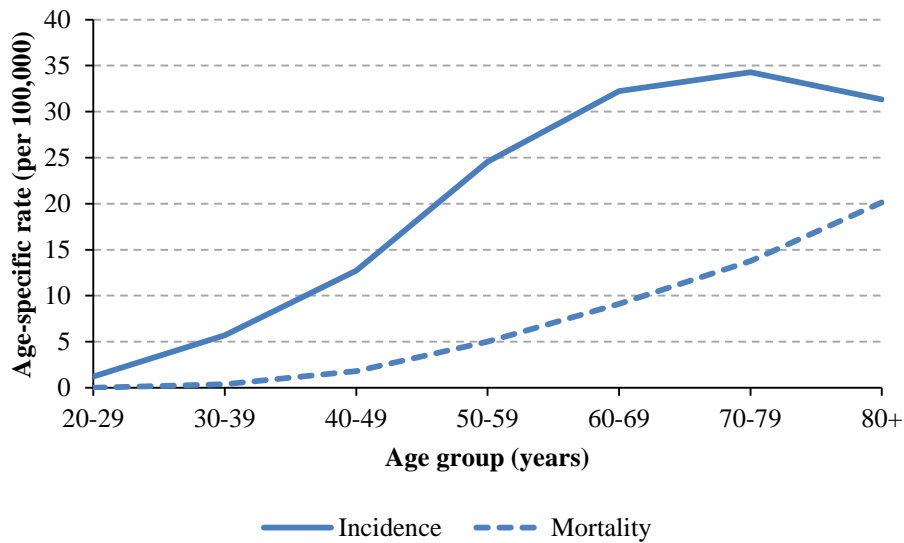
- The age-adjusted incidence rate of all HPV-associated cancers was 11.0 cases per 100,000. The incidence rate increased by 1.3% annually from 2004-2014 with statistical significance.
- The age-adjusted incidence rate of HPV-associated cancers was 1.2 times higher among Massachusetts females than among males (11.8 and 10.0 per 100,000 respectively during 2004-2014).
- The incidence rate among males increased by 2.8% annually from 2004-2014 with statistical significance. The incidence rate among females increased by 0.2% annually from 2004-2014 without statistical significance.
- Among males, the incidence rate of oropharyngeal cancer increased by 2.8% annually from 2004-2014 with statistical significance.
- Among females, the incidence rate of cervical cancer decreased by 2.4% annually and the incidence rate of anal and vulvar cancer increased by 2.6% and 1.7% annually, respectively, all with statistical significance.

**Mortality**

- The age-adjusted mortality rate of all HPV-associated cancers was 3.0 deaths per 100,000. The mortality rate decreased without statistical significance by 0.7% annually from 2008-2014.
- The age-adjusted mortality rate of HPV-associated cancers was 1.1 times higher among Massachusetts females than among males (3.1 and 2.8 per 100,000 respectively during 2008-2014).
- The mortality rate among males decreased by 2.3% annually from 2008-2014 without statistical significance. The mortality rate among females increased by 0.1% annually from 2008-2014 without statistical significance.
- Among males, the mortality rate of anal cancer increased by 24.1% annually from 2008-2014 with statistical significance.
- Among females, the mortality rate of vulvar cancer increased by 8.5% annually from 2008-2014 with statistical significance.

**PATTERNS IN HPV-ASSOCIATED CANCER INCIDENCE AND MORTALITY BY AGE**

**Figure 3. Age-specific incidence (2004-2014) and mortality (2008-2014) rates<sup>^</sup> of HPV-associated cancers, Massachusetts**



	Age Group (Years)						
	20-29	30-39	40-49	50-59	60-69	70-79	80+
Incidence	1.21	5.71	12.73	24.53	32.22	34.28	31.32
Mortality	-	0.37	1.81	5.00	9.09	13.77	20.13

<sup>^</sup>per 100,000; cells with fewer than 10 people not shown; Data source: Massachusetts Cancer Registry and Massachusetts Registry of Vital Records and Statistics

**Incidence by age group**

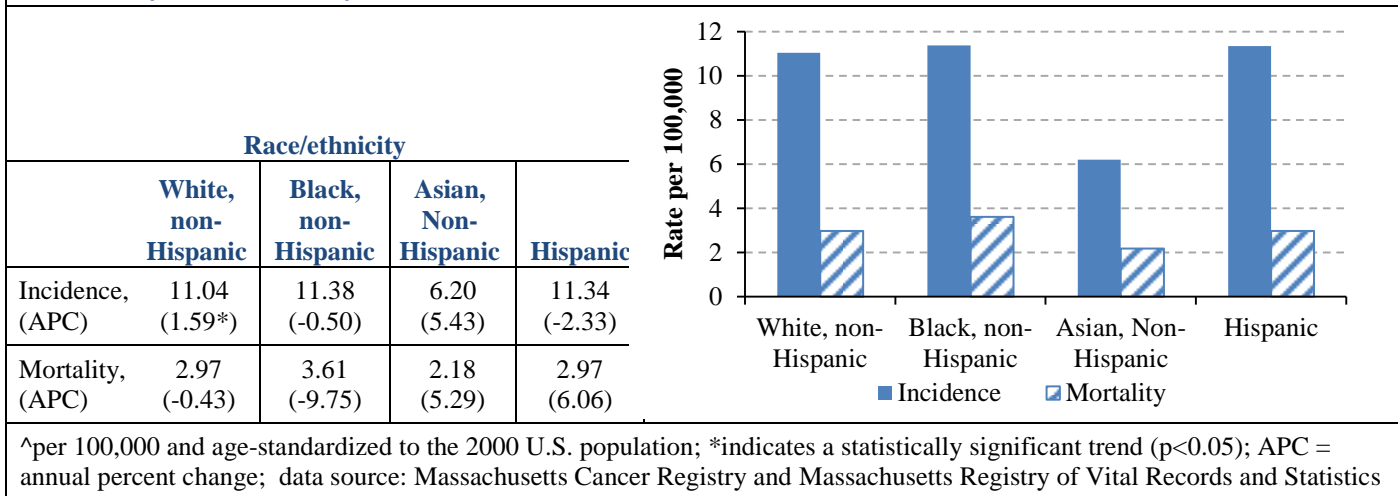
- The highest age-specific incidence rate of HPV-associated cancers was seen among people in their 70s from 2004-2014.
- Among the most common HPV-associated cancer in males, oropharyngeal cancer, the highest age-specific incidence rates from 2004-2014 were among males diagnosed in their 60s (30.2 cases per 100,000 males) and 70s (24.7 cases per 100,000 males).
- Among the most common HPV-associated cancer in females, cervical cancer, the highest age-specific incidence rates from 2004-2014 were among females diagnosed in their 40s (9.8 cases per 100,000 females) and 60s (9.3 cases per 100,000 females).

**Mortality by age group**

- The highest age-specific mortality rate of HPV-associated cancers was seen among people in their 80s from 2004-2014.
- Among the HPV-associated cancer with the highest mortality in males, oropharyngeal cancer, the highest age-specific mortality rates from 2008-2014 were among males in their 80s and older (12.0 deaths per 100,000 males) and 70s (11.8 deaths per 100,000 males).
- Among the HPV-associated cancer with the highest mortality in females, cervical cancer, the highest age-specific mortality rates from 2008-2014 were among females in their 80s and older (3.8 deaths per 100,000 females) and 60s (3.6 deaths per 100,000 females).

## PATTERNS IN HPV-ASSOCIATED CANCER INCIDENCE AND MORTALITY BY RACE/ETHNICITY

**Figure 4. Age-adjusted incidence (2004-2014) and mortality (2008-2014) rates<sup>^</sup> of HPV-associated cancers by race/ethnicity, Massachusetts**



### Incidence by race/ethnicity

- The age-adjusted incidence rate of HPV-associated cancers was highest among non-Hispanic blacks (11.4 per 100,000), followed by Hispanics (11.3), non-Hispanic whites (11.0), and Asians (6.2).
- Non-Hispanic whites had the only statistically significant increase in the incidence rate of HPV-associated cancers (1.6%) from 2004-2014.

### Mortality by race/ethnicity

- The age-adjusted mortality rate of HPV-associated cancers was highest among non-Hispanic blacks (3.6 deaths per 100,000), followed by Hispanics (3.0), non-Hispanic whites (3.0), and Asians (2.2).
- There were no statistically significant changes in the annual mortality rates of HPV-associated cancers for any race/ethnicity from 2008-2014.

## HPV-ASSOCIATED CANCER INCIDENCE ATTRIBUTABLE TO HPV

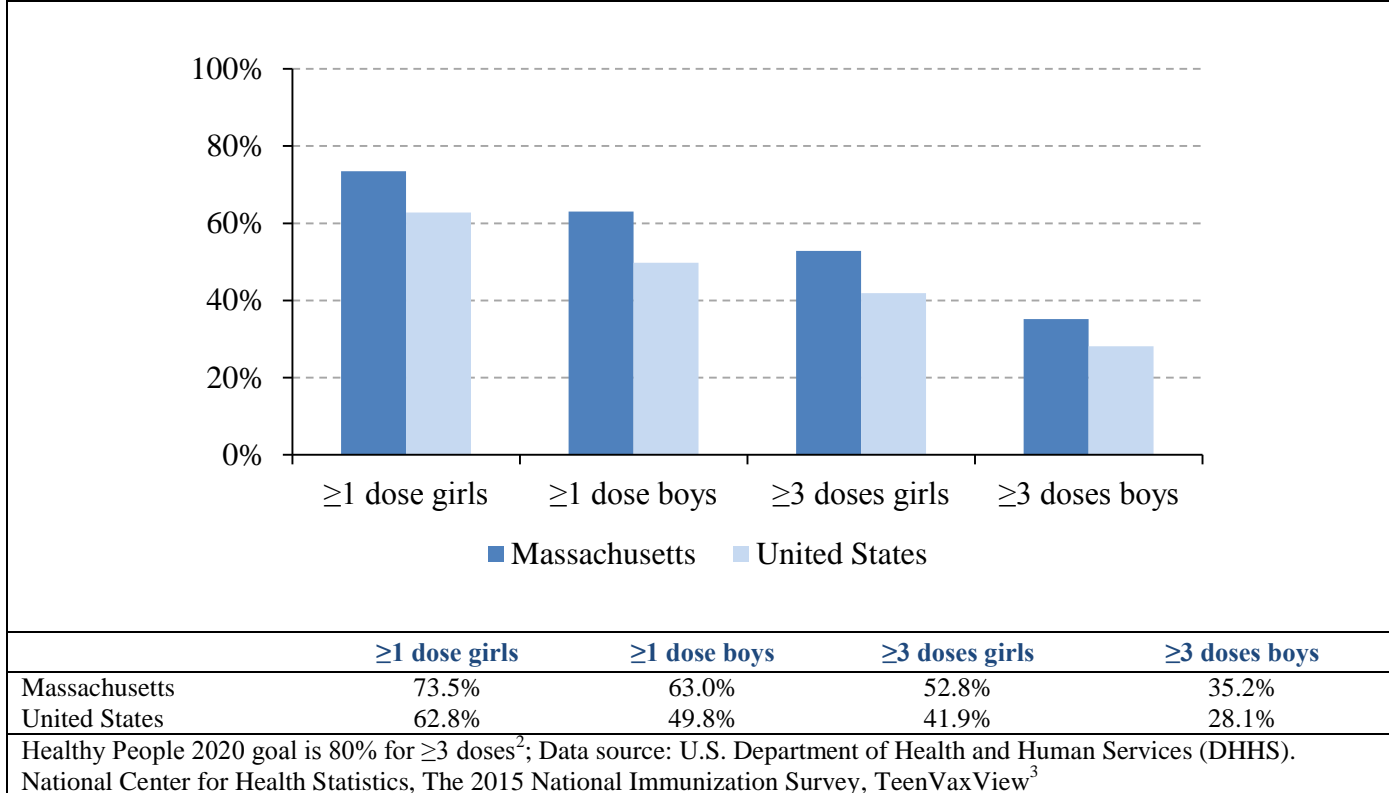
**Table 3. Estimated annual average number of HPV-associated cancer cases attributable to HPV, Massachusetts, 2004-2014**

	Average Annual Number	Attributable to any HPV type Number (%)	Attributable to HPV 16/18 Number (%)	Attributable to HPV 16/18/31/33/45/52/58 Number (%)
Cervical	199	180 (90.6)	130 (66.2)	160 (80.9)
Vulvar	95	70 (68.8)	50 (48.6)	60 (62.8)
Vaginal	16	10 (75.0)	10 (55.1)	10 (73.4)
Penile	30	20 (63.3)	10 (47.9)	20 (56.9)
Anal	108	100 (91.1)	90 (79.4)	90 (87.6)
Male	38	30 (88.7)	30 (79.1)	30 (82.9)
Female	70	60 (92.5)	60 (79.5)	60 (90.3)
Rectal	10	10 (91.1)	10 (79.4)	10 (87.6)
Male	3	- (88.7)	- (79.1)	- (82.9)
Female	7	10 (92.5)	10 (79.5)	10 (90.3)
Oropharyngeal	363	250 (70.1)	220 (60.2)	240 (65.9)
Male	284	210 (72.4)	180 (63.4)	190 (67.8)
Female	79	50 (63.3)	40 (50.8)	50 (60.3)
<b>Total</b>	<b>822</b>	<b>640 (-)</b>	<b>520 (-)</b>	<b>590 (-)</b>

Number attributable to HPV is rounded to the nearest 10; Data source: Massachusetts Cancer Registry and percentages from Saraiya et al, *JNCI*, 2015<sup>1</sup>; no direct evidence of HPV strains was collected in MCR

## HPV VACCINATION IN MASSACHUSETTS COMPARED TO THE UNITED STATES

**Figure 5. Percent of teens, ages 13-17, receiving the HPV vaccine in Massachusetts and the United States, 2015**



### Cancers attributable to HPV

- In Massachusetts, 640 cases of HPV-associated cancers were estimated to be attributable to infection with any strain of HPV each year.
- Of those 640 cases attributable to any strain of HPV, 520 (81%) cases each year were attributable to HPV 16 and 18. All available HPV vaccines protect against HPV 16 and 18.
- Of those 640 cases attributable to any strain of HPV, 590 (92%) were attributable to HPV 16, 18, 31, 33, 45, 52, and 58. The 9 valent vaccine protects against those seven HPV strains.

### HPV vaccination

- In Massachusetts, 70.6% of females age 18-26 reported having ever received a HPV vaccine in the 2015 BRFSS. Of those who ever received a HPV vaccine, 78.2% reported they completed the vaccine series.
- Among younger Massachusetts teens ages 13-17 years old, 73.5% of females and 62.8% of males reported ever having at least one dose of the HPV vaccine. Teens in Massachusetts have a higher prevalence of the HPV vaccine compared to the United States.<sup>3</sup>

## HPV-ASSOCIATED CANCER IN MASSACHUSETTS COMPARED TO THE UNITED STATES

**Table 4. Age-adjusted incidence rate<sup>^</sup> of HPV-associated cancers by site in Massachusetts compared to the United States, 2008-2012**

	Massachusetts	United States
Cervical	5.2	7.4
Vulvar	0.4	0.4
Vaginal	2.3	2.0
Penile	0.9	0.8
Rectal	0.2	0.2
Male	0.1	0.2
Female	0.2	0.3
Anal	1.4	1.5
Male	1.1	1.1
Female	1.7	1.8
Oropharyngeal	5.0	4.5
Male	8.2	7.6
Female	2.1	1.7

<sup>^</sup>Age-standardized to the 2000 U.S. population, Data source: Massachusetts Cancer Registry and US data from source 4

### .DATA SUMMARY

- In Massachusetts from 2004-2014, oropharyngeal cancer was the most common HPV-associated cancer among males and cervical cancer was the most common HPV-associated cancer among females.
- Oropharyngeal cancer was the most common cause of death from an HPV-associated cancer for males and cervical cancer was the most common cause of death from an HPV-associated cancer for females from 2008-2014 in Massachusetts.
- The incidence rate of HPV-associated cancers in Massachusetts has been increasing by 1.3% each year from 2004-2014 with statistical significance. The incidence rates of oropharyngeal cancer among males, anal cancer among females, and vulvar cancer among females have been increasing with statistical significance. The incidence rate of cervical cancer in Massachusetts has been decreasing with statistical significance.
- The mortality rate of HPV-associated cancers in Massachusetts did not experience any statistically significant trends from 2008-2014. The mortality rate of anal cancer among males increased by 24.1% and the mortality rate of vulvar cancer among females increased by 8.5% with statistical significance. However, the absolute number of cancer deaths remains relatively small.
- Massachusetts had a higher incidence rate of oropharyngeal cancer than the United States from 2008-2012
- Massachusetts had a lower incidence rate of cervical cancer than the United States from 2008-2012
- The incidence and mortality rates of HPV-associated cancers were highest among non-Hispanic blacks in Massachusetts, followed by Hispanics and then non-Hispanic whites.
- Each year, the 9 valent HPV vaccine has the potential to prevent an estimated 590 cases of HPV-associated cancer in Massachusetts. Although Massachusetts has higher HPV vaccination rates than the US, it still falls short of the Healthy People 2020 goal.
- The incidence rate of oropharyngeal cancer is higher in Massachusetts than the United States and the incidence rate of cervical cancer is lower in Massachusetts than the United States.



## DISCUSSION AND IMPLICATIONS FOR PREVENTION

The incidence rate of HPV-associated cancers in Massachusetts has been increasing by 1.3% each year from 2004-2014. The mortality rate has not changed significantly. The increase appears to be driven by the increase in oropharyngeal cancer among males.

While cervical and rectal cancers have routine screening tests, there are no routine screening tests for the other HPV-associated cancers. This lack of screening tests makes the HPV vaccine very important for the prevention of HPV-associated cancers. Vaccines for HPV have been approved by the US Food and Drug Administration (FDA) since 2006. Current recommendations from the Advisory Committee on Immunization Practices (ACIP) include:<sup>5</sup>

- Boys and girls are recommended to start the series of vaccines at age 11 or 12.
- People who are not immunocompromised and initiated the HPV vaccine between ages 9 and 14 are recommended to get 2 doses of the HPV vaccine.
- People initiating the HPV vaccine between ages 15 and 26, along with those who are immunocompromised should receive 3 doses of the HPV vaccine.

In summary, the increasing incidence rate of HPV-associated cancer in Massachusetts highlights the need for improved HPV vaccination rates, especially among boys. Improving HPV vaccination coverage has the potential to prevent an estimated 92% of all HPV-associated cancer cases. Individual, community, and statewide interventions to promote healthy lifestyles are needed to reduce the burden of disease.

## DATA SOURCES

### Massachusetts Behavioral Risk Factor Surveillance System (BRFSS):

The Behavioral Risk Factor Surveillance System (BRFSS) is an ongoing random-digit-dial telephone survey of adults age 18 and older in collaboration with the Centers for Disease Control and Prevention (CDC). In Massachusetts, the survey has been conducted since 1986 and collects data on a variety of health risk factors, preventive behaviors, and emerging public health issues. Data are collected on HPV vaccination.<sup>6</sup>

### Massachusetts Cancer Registry (MCR):

Data on the incidence of HPV-associated cancers are provided by the Massachusetts Cancer Registry (MCR), which is part of the Massachusetts Department of Public Health (MDPH). The MCR is a population-based registry that has been collecting reports of newly diagnosed cancer cases since 1982. The North American Association of Central Cancer Registries (NAACCR) has estimated that the MCR case ascertainment is more than 95% complete. The cancer cases in this report are primary invasive cancers diagnosed among Massachusetts residents. The HPV-associated cancer sites include the anus, cervix, oropharynx, penis, rectum, vagina, and vulva. All cancers are restricted to squamous cell carcinomas except for cervical cancer which also includes adenocarcinomas. Incident cases were used from 2004-2014.

### Massachusetts Registry of Vital Records and Statistics (MRVRS):

The oropharyngeal cancer death data are provided by the MDPH's Massachusetts Registry of Vital Records and Statistics (MRVRS). The MRVRS has legal responsibility for collecting reports of death on Massachusetts residents. The MRVRS does not contain information on histology so rectal cancers were excluded from the mortality data due to the rareness of rectal squamous cell cancers. We looked at cancer deaths from 2008-2014 to account for the long survival period of these cancers.

### National Center for Health Statistics (NCHS):

The population estimates used for rate calculations and data on the 2000 US population are provided by the National Center for Health Statistics (NCHS). The NCHS produces population estimates in collaboration with the U.S. Census Bureau's Population Estimation Program.

## TECHNICAL NOTES AND DEFINITIONS

**Age-Adjusted Rates:** Rates were age-adjusted using the direct method of standardization. The weights were the proportions of person-time in the corresponding age groups of the 2000 U.S. Census bureau population per 100,000. Rates were adjusted using eighteen 5-year age groups. Incidence rates were calculated from 2004-2014. Mortality rates were calculated from 2008-2014 to allow for survival time.

**HPV-Associated Cancer Estimates:** Inclusion of selected cancers was based on CDC-defined codes.<sup>4</sup> Since not all HPV-associated cancers are caused by HPV, we used the CDC methodology on HPV-associated cancers to estimate the number of cancers attributable to HPV applying estimated percentages from genotyping studies.<sup>1,4</sup>

**Incidence:** The incident cases of HPV-associated cancer are the number of people who are newly diagnosed with the disease during a specific time period. The incidence data for HPV-associated cancers were collected for cancers with the International Classification of Disease for Oncology (ICD-O) codes: C01.9, C02.4, C02.8, C05.1-5.2, C09.0-10.9, C14.0-14.8, C20.9, C21.0-21.8, C51.0-51.9, C52.9, C53.0-C53.9, and C60.0-60.9.



**Joinpoint Regression Analysis of Cancer Trends:** The annual percent change (APC) is a linear approximation of trends over time. The  $APC = 100 * (e^m - 1)$ , where  $m$  is a slope of the linear regression line, which is an approximation of the function of the natural logarithm of the rates by the year of diagnosis. SEER provides software to calculate the number and location of points where trends change direction (joinpoints).<sup>7</sup>

**Mortality:** The number of deaths was the number of people who died due to an HPV-associated cancer during a specific time period. The mortality data were collected for deaths with International Classification of Diseases tenth edition (ICD-10) codes C01, C02.4-2.9, C05.1-5.2, C09.0-10.9, C14.0-14.8, C20, C21.0-21.8, C51.0-51.9, C52, C53.0-C53.9, and C60.0-60.9.

**Statistically Significant:** Results were considered to be statistically significant when the  $p$  value < 0.05 for all analyses.

## DATA LIMITATIONS

When interpreting the cancer data, it is important to consider certain limitations which include:

- **Under-reporting in areas close to neighboring states:** Although the MCR has reciprocal reporting agreements with 36 states as of April 2015, there may still be some Massachusetts residents who were diagnosed out of state and not reported to the MCR.
- **Interpretation of trends:** Apparent increases or decreases in cancer incidence over time may reflect changes in diagnostic methods or case reporting rather than true changes in cancer occurrence.
- **Small number of cases:** Many of the calculations in this report involved small numbers of cases. As a result, differences in rates may be due to chance, and the data should be interpreted with caution.
- **Estimation of proportion attributable to HPV:** The MCR does not contain information on the HPV DNA present in cancer tissues. Therefore, we consider HPV-associated cancers to be those where HPV DNA is frequently found from other studies. These numbers are the best estimates but may not reflect the true proportion attributable to HPV.
- **Lack of hysterectomy adjustment:** Females who had a hysterectomy should be removed from the population when calculating rates of cervical cancer. The data on hysterectomy status is not available in the MCR dataset so estimates were needed using data from BRFSS to correct the population for the prevalence of hysterectomies. Data collected in the BRFSS were insufficient to calculate the hysterectomy prevalence by age and race/ethnicity or by race/ethnicity alone. Thus, our rate calculations for cervical cancer are likely underestimates of the true incidence rates for cervical cancer in Massachusetts.

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