

# Summer Peaks in Uptake of Human Papillomavirus and Other Adolescent Vaccines in the United States

Jennifer L. Moss<sup>1</sup>, Paul L. Reiter<sup>2</sup>, Barbara K. Rimer<sup>1,3</sup>, Kurt M. Ribisl<sup>1,3</sup>, and Noel T. Brewer<sup>1,3</sup>

## Abstract

**Background:** Seasonality in human papillomavirus (HPV) vaccination could have a large impact on national cancer prevention efforts. We hypothesized that uptake of HPV vaccine and other adolescent vaccines in the United States would be highest in the summer.

**Methods:** Data came from health care provider-verified vaccination records for 70,144 adolescents (ages 13–17 years) from the 2008 to 2012 versions of the National Immunization Survey-Teen. Using the Edwards method for testing annual trends, we examined seasonal patterns in the uptake of HPV and other recommended adolescent vaccines [tetanus, diphtheria, and pertussis (Tdap) booster and meningococcal vaccine]. HPV vaccine initiation (receipt of the first of the three-dose series) data were for female adolescents.

**Results:** Uptake for HPV and other adolescent vaccines peaked in the summer across years and states (all  $P < 0.001$ ). Uptake was

five times as frequent at the peak as at the trough for HPV vaccine, and HPV vaccine initiation was highest in June, July, and August (percent of doses delivered in these months: 38.7%). The same pattern existed for Tdap booster and meningococcal vaccine. Concomitant (same-day) vaccination of HPV vaccine with other adolescent vaccines also demonstrated summer peaks each year nationally (all  $P < 0.001$ ).

**Conclusion:** Uptake of adolescent vaccines increased dramatically in summer months. These summer peaks are an important opportunity for interventions focused on concomitant vaccination.

**Impact:** The potential cancer prevention impact of HPV vaccination programs could be increased, for example, by delivering messages about concomitant vaccination during the summer, when adolescents and their parents might be most open to them. *Cancer Epidemiol Biomarkers Prev*; 25(2); 274–81. ©2015 AACR.

## Introduction

Human papillomavirus (HPV) vaccination is a potent tool for preventing several cancers, including cervical, anal, vulvar, vaginal, and likely oropharyngeal cancers (1), but vaccination coverage is suboptimal (2). In the United States, the Healthy People 2020 goal is for 80% of 13- to 15-year-old adolescents to have received the three-dose HPV vaccine, as well as two other adolescent vaccines: tetanus, diphtheria, and pertussis (Tdap) booster and meningococcal vaccine (3). Coverage for Tdap booster has surpassed that goal, and meningococcal vaccine is quickly approaching it (2, 4). However, only 28% of females and 7% of males in this age group had received the entire three-dose HPV vaccine series as of 2012 (4). Improving these low rates of HPV vaccination could have a tremendous impact on population health. Achieving 80% coverage with HPV vaccination could

prevent an additional 53,000 cases of cervical cancer over the lifetime of females who are now age 12 years or younger (5). For this reason, national organizations including the Centers for Disease Control and Prevention (CDC), the National Cancer Institute, and the President's Cancer Panel have prioritized increasing HPV vaccination (e.g., refs. 3, 5, 6).

A highly promising way to increase HPV vaccination coverage is through concomitant administration of HPV vaccines with Tdap boosters or meningococcal vaccines, also called "same day" or "bundled" vaccination (1, 7). Concomitant vaccination is an effective and safe practice (7–10) that CDC endorses (1). A recent study by Stokley and colleagues (11) demonstrated that, if all adolescent girls born in 2000 who received another vaccine had concomitantly received HPV vaccines, coverage for the latter vaccines among this group would have increased from 47% to 91%. However, very few studies have investigated concomitant vaccination.

Cancer prevention efforts focused on improving coverage with HPV vaccine and national efforts focused on improving coverage with the entire adolescent vaccine platform (Tdap booster, meningococcal, and HPV vaccines) have not considered seasonal peaks in administration. These peaks may be especially pertinent in the United States, which has an opportunistic vaccination program and school entry requirements in some states (12). Seasonal peaks may arise due to parents seeking to comply with vaccination school entry requirements (13) before the school year begins, among other factors. Indeed, adolescent vaccination rates in New York City and several states show preliminary evidence of summer peaks

<sup>1</sup>Gillings School of Global Public Health, University of North Carolina, Chapel Hill, North Carolina. <sup>2</sup>College of Medicine, The Ohio State University, Columbus, Ohio. <sup>3</sup>Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, North Carolina.

**Note:** Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (<http://cebp.aacrjournals.org/>).

**Corresponding Author:** Noel T. Brewer, Department of Health Behavior, Gillings School of Global Public Health, University of North Carolina, 325 Rosenau Hall, CB 7440, Chapel Hill, NC 27599. Phone: 919-966-3282; Fax: 919-966-2921; E-mail: ntb@unc.edu

doi: 10.1158/1055-9965.EPI-15-0574

©2015 American Association for Cancer Research.

(14, 15), but no studies that we are aware of have examined seasonality on a national level or for concomitant vaccination. In the same way that retailers focus promotional efforts for some products around holidays to maximize impact, identifying summer peaks in adolescent vaccination could highlight times when quality improvement or promotional programs may have higher impact on coverage, an especially important consideration for HPV vaccination (16, 17). We sought to establish whether summer peaks exist in adolescent vaccination in the United States to support efforts to address low HPV vaccination coverage. These peaks could affect clinical practice, timing of public health programs, and timing of promotional efforts in regards to improving HPV vaccination and cancer prevention.

## Materials and Methods

### Data source

Data came from the 2008 to 2012 versions of the National Immunization Survey (NIS) – Teen conducted by the CDC (18). NIS-Teen is a two-part survey consisting of telephone interviews administered to a national probability sample of caregivers of 13- to 17-year-old adolescents (hereafter referred to as "parents") and questionnaires mailed to adolescents' health care providers. In 2008 to 2010, NIS-Teen staff contacted parents through landline numbers, and in 2011 to 2012, staff also contacted parents through cell phone numbers.

Each year, NIS-Teen collected provider-verified vaccination data for about 20,000 adolescents living in the 50 states and Washington D.C. (hereafter referred to collectively as "states"), for a cumulative total of 99,921 adolescents (18). Because we were interested in dates of adolescent vaccination, which is conditional on receiving at least one vaccine, we excluded participants whose providers reported that they had not received any adolescent vaccine ( $n = 21,574$ ). In addition, we excluded participants who had received at least one vaccine, but their providers reported that administration fell outside of the study period (2007 to 2012;  $n = 8,203$ ), for a final analytic sample of 70,144 adolescents. NIS-Teen staff calculated sampling weights for each participant with provider-verified data to account for nonequal probability of selection.

Data collection for NIS-Teen was approved by the National Center for Health Statistics (NCHS) Research Ethics Review Board. Analysis of de-identified data from the survey is exempt from the federal regulations for the protection of human research participants. Analysis of restricted data through the NCHS Research Data Center is also approved by the NCHS Ethics Review Board. The University of North Carolina Institutional Review Board exempted our study from review.

### Measures

Health care providers reported whether adolescents received HPV vaccine, Tdap booster, and meningococcal vaccine, and, if so, the month, date, and year of administration. Although data collection took place beginning in 2008, we included instances of vaccination that occurred on or after January 1, 2007 in this analysis, because providers could report vaccinations that took place up to the date of the parent telephone interviews. We analyzed HPV vaccine initiation (receipt of the first of the three-dose series) only among female adolescents, because the CDC did not introduce a recommendation for routine adminis-

tration to male adolescents until 2011 (19). We coded participants as receiving vaccines concomitantly if providers reported administration of two or more vaccines on the same day (7). Thus, we captured whether adolescents concomitantly received four possible combinations of vaccines: (i) HPV vaccine and Tdap booster; (ii) HPV and meningococcal vaccines; (iii) Tdap booster and meningococcal vaccine; and (iv) HPV vaccine, Tdap booster, and meningococcal vaccine ("all three"). State of residence and demographic characteristics came from parental report in the telephone interview.

### Data analysis

**Data preparation.** We combined data from the 2008 to 2012 versions of NIS-Teen using NCHS's recommended procedures that include creating new weighting variables (18). Then, we categorized participants according to the month and year in which they received vaccines and generated weighted estimates of the total number of vaccines administered in each month of the study period. We standardized the length of each month by dividing the monthly vaccination totals by the number of days in the month and multiplying by 30. This approach may be unnecessary when analyzing large samples (20), but some researchers have noted the value of standardization to remove the influence of month length from studies of seasonality (21, 22). For analyses that aggregated vaccination data from multiple years, we weighted each year's observations so that years contributed equally.

To create figures depicting vaccination peaks, we put the number of people receiving vaccines each month on a common metric, following recommendations by Rau and others (20, 21, 23). We calculated the number of people who received particular vaccines each month and scaled the data so that the yearly total was 1,200. Any month with a scaled vaccination total exceeding 100 contained greater vaccination than would be expected if vaccination were randomly distributed over time, and any month with a scaled vaccination total of less than 100 contained less vaccination than expected. This approach facilitates descriptive comparison of peaks between geographic units with different population sizes. As a supplementary analysis, we created figures depicting Tdap booster and meningococcal vaccination peaks stratified by adolescent sex to examine comparability with the HPV vaccination peaks for female adolescents only. Note that the inferential procedures used the month- and year-standardized data (described above), not these scaled observations.

**Inferential analysis.** We examined seasonal peaks in the United States overall and within each state for all study years combined, and then for the United States within each study year. These three approaches allowed us to check for consistency of cyclical patterns across geography and time. We performed these calculations separately for HPV vaccine, Tdap booster, and meningococcal vaccine, and for each of the concomitant vaccination outcomes. Small sample sizes precluded generating estimates for each study year separately within states; for concomitant vaccination within states; and for 2012, the final study year, separately from the preceding years.

To test the statistical significance of seasonal peaks, we used the Edwards method (20, 21), the most commonly used analytic approach in seasonality research (21). Briefly, the Edwards method involves fitting a harmonic sine curve with one peak and one

Moss et al.

trough to the observed monthly data. (Before implementing these methods, we verified with visual inspection that the data did not follow a qualitatively different form, e.g., bimodal, which would require different analytic tools.) Edwards *T* statistic, which measures how far the fitted curve differs from nonseasonality (a flat line), follows a  $\chi^2$  distribution with two degrees of freedom. The ratio of highest to lowest (RHL) incidence examines the amplitude of the fitted curve to describe the relative increase in the outcome at the cycle's maximum (its peak) compared with its minimum (its trough; refs. 20, 21). Previous public health studies have used the Edwards method to assess cyclical patterns in outcomes such as cardiovascular disease, suicide, and malaria (24–26). For each vaccination outcome in the current study, we fitted a sine curve to the observed data and calculated the resulting

*T* statistic. In addition, we calculated the RHL to summarize the magnitude of the peaks.

All analyses were conducted in the SAS version 9.2. Statistical tests used a two-tailed *P* value of 0.05. Analyses incorporated survey weights to account for nonequal probability of selection.

## Results

The 70,144 vaccinated adolescents were nearly evenly distributed by sex and age (Table 1). Most adolescents were non-Hispanic white (57.2%), had private health insurance (60.7%), and had a preventive health care visit in the last year (87.5%). The majority of adolescents lived in metropolitan areas (85.7%) and in households above the poverty level (74.3%).

**Table 1.** Descriptive statistics of participating parents and their adolescent children (source: National Immunization Survey-Teen, administered 2008 to 2012)

	Total sample <i>n</i> (%)	Female <i>n</i> (%)	Male <i>n</i> (%)
Total	70,144	35,774 (52.1%)	34,370 (47.9%)
Survey year			
2008	7,519 (12.5%)	4,365 (13.8%)	3,154 (11.0%)
2009	12,118 (17.4%)	6,516 (18.2%)	5,602 (16.4%)
2010	14,111 (20.7%)	7,209 (20.5%)	6,902 (20.8%)
2011	19,481 (23.9%)	9,584 (23.1%)	9,897 (24.9%)
2012	16,915 (25.5%)	8,100 (24.3%)	8,815 (26.9%)
<b>Adolescent characteristics</b>			
Age (years)			
13	15,302 (21.1%)	7,519 (20.4%)	7,783 (21.9%)
14	15,323 (21.0%)	7,593 (20.4%)	7,730 (21.6%)
15	14,633 (22.0%)	7,481 (22.0%)	7,152 (22.0%)
16	13,566 (19.6%)	7,092 (19.9%)	6,474 (19.2%)
17	11,320 (16.4%)	6,089 (17.3%)	5,231 (15.3%)
Race/ethnicity			
Hispanic	9,502 (20.5%)	4,875 (20.6%)	4,627 (20.3%)
Non-Hispanic white	47,691 (57.2%)	24,239 (56.9%)	23,452 (57.6%)
Non-Hispanic black	7,079 (14.4%)	3,604 (14.4%)	3,475 (14.3%)
Other	5,872 (8.0%)	3,056 (8.1%)	2,816 (7.8%)
Private health insurance			
Yes	47,846 (60.7%)	24,474 (61.0%)	23,372 (60.3%)
No	21,925 (39.3%)	11,114 (39.0%)	10,811 (39.7%)
Preventive visit in the last year			
Yes	61,988 (87.5%)	31,692 (88.0%)	30,926 (87.0%)
No	8,156 (12.5%)	4,082 (12.0%)	4,074 (13.0%)
<b>Parent characteristics</b>			
Relationship of respondent to adolescent			
Mother/female guardian	55,852 (77.1%)	28,739 (78.5%)	27,113 (75.5%)
Father/male guardian	11,223 (17.0%)	5,469 (15.7%)	5,754 (18.4%)
Other	3,069 (5.9%)	1,566 (5.8%)	1,503 (6.1%)
Mother's education level			
Less than high school	6,486 (13.8%)	3,355 (13.9%)	3,131 (13.7%)
High school	13,239 (25.2%)	6,665 (24.7%)	6,574 (25.7%)
Some post-high school	19,466 (25.6%)	10,029 (26.2%)	9,437 (24.9%)
College graduate	30,953 (35.4%)	15,725 (35.2%)	15,228 (35.6%)
<b>Household characteristics</b>			
Poverty status			
Below poverty level	9,902 (20.7%)	5,101 (21.0%)	4,801 (20.3%)
Above poverty level	57,584 (74.3%)	29,347 (74.0%)	28,237 (74.6%)
Unknown	2,658 (5.1%)	1,326 (5.0%)	1,332 (5.1%)
Urbanicity			
Nonmetropolitan	13,076 (14.3%)	6,807 (14.5%)	6,269 (14.0%)
Metropolitan	50,373 (85.7%)	25,727 (85.5%)	24,646 (86.0%)
Census region			
Northeast	15,356 (19.6%)	7,836 (19.7%)	7,520 (19.5%)
Midwest	15,524 (21.5%)	8,001 (21.4%)	7,523 (21.6%)
South	23,845 (34.5%)	12,107 (34.3%)	11,738 (34.7%)
West	15,419 (24.4%)	7,830 (24.6%)	7,589 (24.1%)

NOTE: Frequencies are unweighted; proportions are weighted.

**Table 2.** Adolescent vaccination coverage and vaccine doses administered per month in the United States, 2007–2012 (source: National Immunization Survey–Teen, administered 2008 to 2012;  $n = 70,144$  adolescents)

	Single vaccination			Concomitant vaccination			
	HPV <sup>a</sup>	Tdap	Meng	HPV <sup>a</sup> and Tdap	HPV <sup>a</sup> and Meng	Tdap and Meng	All three
Overall coverage	47.9%	65.5%	58.9%	15.5%	21.6%	30.3%	7.9%
Month							
January	8.0%	6.7%	6.2%	10.2%	7.1%	6.3%	8.9%
February	7.6%	6.3%	7.2%	5.3%	7.2%	6.0%	5.7%
March	7.2%	7.8%	7.6%	6.9%	7.8%	8.2%	6.9%
April	8.0%	8.1%	7.8%	8.2%	8.9%	8.4%	9.3%
May	6.8%	8.6%	7.4%	7.8%	7.2%	8.2%	8.5%
June	10.2%	9.2%	10.0%	8.5%	8.5%	9.1%	8.0%
July	12.6%	12.0%	13.1%	13.0%	12.8%	12.9%	13.3%
August	15.9%	19.0%	18.0%	20.0%	17.6%	18.9%	20.3%
September	7.4%	8.2%	7.9%	7.7%	9.0%	7.8%	6.2%
October	7.2%	6.5%	6.4%	6.1%	6.1%	6.8%	6.5%
November	5.6%	4.4%	5.2%	3.9%	5.1%	4.4%	4.2%
December	3.5%	3.2%	3.4%	2.4%	2.7%	2.9%	2.2%

NOTE: Proportions are weighted. Statistics for HPV, HPV and Tdap, HPV and Meng, and all three vaccines are for female adolescents only.

Abbreviation: Meng, meningococcal vaccine.

<sup>a</sup>Uptake of first dose among female adolescents only.

About 48% of female adolescents initiated HPV vaccination between 2008 and 2012 (Table 2). Among female and male adolescents, coverage was 66% for Tdap booster and 59% for meningococcal vaccination. Concomitant HPV vaccination was far less frequent: among females, 16% received HPV vaccine concomitantly with Tdap booster, 22% concomitantly with meningococcal vaccine, and 8% received all three vaccines concomitantly. Among female and male adolescents, 30% received Tdap and meningococcal vaccines concomitantly.

#### Uptake of HPV vaccines

HPV vaccination among female adolescents increased in late spring, peaked in August, and decreased rapidly thereafter (black line in Fig. 1A). Uptake was highest in June, July, and August, when health care providers delivered 38.7% of all vaccine doses (Table 2). This pattern reflects a substantial summer peak in HPV vaccination ( $P < 0.001$ ; Table 3). The RHL for this curve was 4.7, indicating that vaccination was about five times as frequent at the cycle's peak as at its trough.

HPV vaccination in individual states (gray lines in Fig. 1A) largely demonstrated the same summer peaks as in the United States overall, with summer peaks evident in each state (all  $P < 0.001$ ; Supplementary Table S1). The RHLs of states' cycles varied from 2.5 in New Mexico to 98.2 in Nevada. This pattern of summer peaks in vaccination was evident in all study years (all  $P < 0.001$ ; Fig. 2; Table 3). The RHLs of the peaks for HPV vaccine varied little from year to year, with no clear pattern, ranging from 4.5 in 2008 to 5.7 in 2010.

#### Uptake of other adolescent vaccines

Tdap booster and meningococcal vaccination (among female and male adolescents in the United States) largely reflected the same patterns as HPV vaccination, increasing in late spring, peaking in August, and decreasing rapidly thereafter (black lines in Fig. 1B and C). Health care providers administered about 40% of all Tdap booster and meningococcal vaccine doses during June, July, and August (40.2% and 41.1%, respectively; Table 2). Each vaccination outcome demonstrated summer peaks across and within study years (Fig. 2; Table 3) and within individual states (gray lines in Fig. 1B and C; Supplementary Table S1; all  $P < 0.001$ ). The average RHL was 5.1 for Tdap booster and 10.1 for

meningococcal vaccine (Table 3). Tdap booster and meningococcal vaccination cycles were similar for female and male adolescents (Supplementary Fig. S1).

#### Concomitant uptake of HPV vaccines with other adolescent vaccines

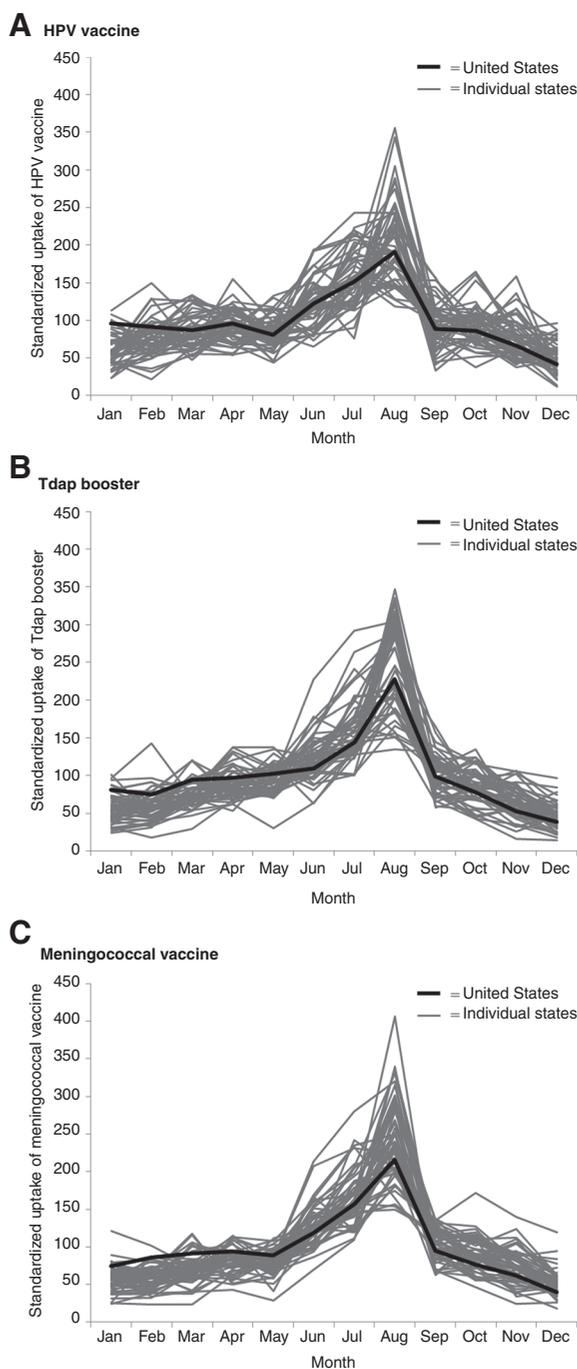
Concomitant vaccination largely reflected the same patterns as HPV and other adolescent vaccination individually, increasing in late spring, peaking in August, and decreasing rapidly thereafter (Supplementary Fig. S2). Health care providers delivered about 40% of all concomitant vaccinations during June, July, and August (HPV vaccine and Tdap booster: 41.5%; HPV and meningococcal vaccines: 38.9%; Tdap booster and meningococcal vaccines: 40.9%; all three vaccines: 41.6%; Table 2). Each concomitant vaccination outcome demonstrated summer peaks for the United States, both across and within study years (all  $P < 0.001$ ; Supplementary Fig. S2; Table 4). The average RHL was 4.6 for HPV vaccines and Tdap booster, 4.2 for HPV and meningococcal vaccines, 5.6 for Tdap booster and meningococcal vaccines, and 3.3 for all three vaccines.

## Discussion

Cancer prevention efforts focused on HPV vaccination generally have not considered the possibility of seasonal variation in uptake. We found evidence of large summer peaks in uptake of HPV vaccines and its concomitant delivery with other adolescent vaccines. From 2007 to 2012, health care providers administered around 40% of these vaccines during June, July, and August. HPV vaccination was about five times as high at the peak of the yearly cycle as compared with vaccination at the trough. This pattern of summer peaks for HPV vaccination (and uptake of other adolescent vaccines) occurred across years and within each state. Concomitant vaccination demonstrated similar summer peaks, although the overall prevalence was much lower, reflecting considerable missed opportunities. Leveraging these results could improve adolescent primary care and population health, particularly in increasing vaccination coverage and reducing the burden of HPV-associated cancers.

We found evidence of substantial missed opportunities for cancer prevention through HPV vaccination, especially alongside

Moss et al.



**Figure 1.** Summer peaks in adolescent vaccine uptake in the United States and individual states. Uptake standardized at 100 per month for 2007 to 2012. Source: National Immunization Survey-Teen, administered 2008 to 2012.

other adolescent vaccines. Overall, a minority of adolescents received HPV vaccine concomitantly with another adolescent vaccine, and many adolescents received Tdap booster or meningococcal vaccination without concomitant HPV vaccination. Increasing concomitant HPV vaccination could greatly improve national cancer prevention efforts. An opportunity for delivering

catch-up doses of HPV vaccine that we did not study is concomitant delivery with booster doses of meningococcal vaccine in adolescents beginning at age 16 years (1). In addition, given the temporal sequence of the HPV vaccine series, more research is needed on seasonal patterns in administration of all three HPV vaccine doses. Specifically, if adolescents who initiated HPV vaccination adhered to the recommended administration schedule for doses 2 and 3 [1–2 months and 6 months after the first dose, respectively (1)], HPV vaccine completion may, for example, have a secondary peak in February (6 months after the peak in initiation). A related point is that adolescents may have received doses 2 or 3 of HPV vaccine concomitantly with Tdap booster or meningococcal vaccine, and our current analysis of concomitant HPV vaccination would not have detected those incidences. Interventions that exploit trends in HPV vaccination (especially when delivered concomitantly) could improve coverage levels and offer greater cancer prevention to young people throughout their lifetimes.

Additional research is needed to understand how these vaccination cycles emerge. Vaccination requirements for school entry may encourage parents and adolescents to seek vaccination in the summer, especially in August, which coincides with the beginning of the school year in most areas of the United States. (14). These policies could also explain some of the difference in magnitude of summer peaks for Tdap booster versus meningococcal vaccine: generally, states with requirements for the latter vaccine adopted them more recently. Their more recent implementation may exaggerate the observed summer peaks as parents newly rush to comply. Although national guidelines began recommending routine administration of Tdap booster and meningococcal vaccine in 2005, and HPV vaccines in female adolescents in 2006 (1), subsequent adoption of school entry requirements has been quite varied across states: As of 2012, 42 states had Tdap booster requirements, 14 had meningococcal vaccination requirements, and only 2 had HPV vaccination requirements (13). Despite the low prevalence of HPV vaccination requirements, we still observed summer peaks for that behavior across the United States. This cyclical pattern could come about through carry-over effects of policies for Tdap or meningococcal vaccination (which are much more common), specifically through concomitant administration of a vaccine targeted by a school entry requirement along with HPV vaccine. Alternative explanations for the summer peaks include adolescents receiving vaccinations during physical exams required for summer camps and the relative ease of seeking adolescent vaccination when students are out of school.

Our national results extend the findings of two smaller descriptive studies. Sull and colleagues (14) used the New York City immunization information system (IIS) to measure monthly administration of adolescent vaccines among 11-year-old adolescents from 2005 to 2013. Starting in 2007, they found small increases in uptake of HPV vaccine, and large increases in uptake of Tdap booster and meningococcal vaccine, in the summer compared with the rest of the year. Cullen and colleagues (15) used IIS data at eight sentinel sites in the United States to analyze the weekly number of HPV vaccine doses administered among male and female adolescents ages 11 to 18 years. The authors reported relative increases in HPV vaccination during the summers of 2010 to 2012. Using nationally representative data, we more precisely quantified the magnitude of summer peaks across

**Table 3.** Magnitude of summer peaks in adolescent vaccination in the United States (source: National Immunization Survey-Teen, administered 2008 to 2012;  $n = 70,144$  adolescents)

	HPV <sup>a</sup>		Tdap		Mening	
	<i>T</i>	Magnitude [RHL (var)]	<i>T</i>	Magnitude [RHL (var)]	<i>T</i>	Magnitude [RHL (var)]
Combined years	5,037,752 <sup>b</sup>	4.7 (0.01)	12,173,702 <sup>b</sup>	5.1 (0.01)	19,067,776 <sup>b</sup>	10.1 (0.01)
Year						
2007	2,145,027 <sup>b</sup>	5.7 (0.01)	3,552,048 <sup>b</sup>	4.6 (0.01)	4,793,365 <sup>b</sup>	7.5 (0.01)
2008	1,349,452 <sup>b</sup>	4.5 (0.01)	3,099,100 <sup>b</sup>	4.5 (0.01)	5,333,919 <sup>b</sup>	8.3 (0.01)
2009	876,756 <sup>b</sup>	5.3 (0.01)	2,458,182 <sup>b</sup>	5.0 (0.01)	3,873,037 <sup>b</sup>	9.1 (0.01)
2010	563,744 <sup>b</sup>	5.7 (0.01)	1,654,178 <sup>b</sup>	5.7 (0.01)	2,366,461 <sup>b</sup>	10.5 (0.01)
2011	341,771 <sup>b</sup>	4.8 (0.01)	868,275 <sup>b</sup>	6.6 (0.01)	1,354,808 <sup>b</sup>	21.2 (0.01)

Abbreviation: Mening, meningococcal vaccine; *T*, Edwards *T* statistic; RHL, ratio of highest to lowest vaccination; var, variance.

<sup>a</sup>Uptake of first dose among female adolescents only.

<sup>b</sup> $P < 0.001$ .

time and for each state, tested their statistical significance, which has not been done previously, and examined cycles in concomitant vaccination.

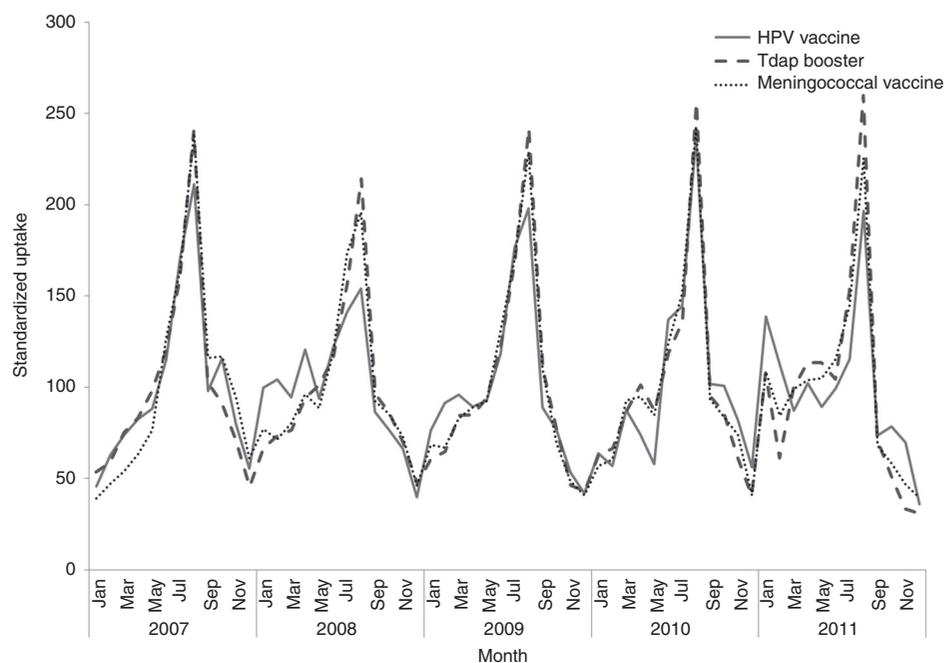
Summer peaks in adolescent vaccination influence clinical practice for pediatric and family medicine physicians in at least three important ways. First, immunization quality improvement efforts are best suited to the spring months, because the relative decrease in vaccination during those times affords more organizational capacity to make structural changes in preparation for summer increases in vaccination (27, 28). Second, summer peaks in uptake of Tdap booster and meningococcal vaccine translate into increased opportunities for providers to recommend and administer HPV vaccine concomitantly. Given that a provider's recommendation is the strongest and most consistent correlate of adolescent vaccination (29, 30), recommending concomitant vaccination during immunization visits in the summer could bring about large increases in HPV vaccination coverage. Third, clinics require greater supplies of adolescent vaccines during the summer. Some clinicians have reported that HPV vaccine is expensive or burdensome to stock (31, 32), but the results of the current study emphasize the

importance of maintaining adequate supplies of adolescent vaccines during the summer to meet the demand for adolescent vaccination.

In addition, these summer peaks in adolescent vaccination have implications for public health practice, research, and policy. Adolescent vaccination programs may serve as cues to action (33), but these effects typically decay (34); therefore, they may be especially fruitful if they occur in the summer or late spring to capitalize on the existing peaks (similar to the phenomenon of increasing advertising for consumer shopping during the winter holiday season; ref. 35). National efforts to change the vaccination infrastructure [e.g., by introducing improved vaccine formulations (36) or improving functionality of reminder-recall systems (37)] could focus on winter or spring months when demand is lower and disruptions to clinical operations would have the least impact on coverage. In addition, public health researchers should account for these cyclical patterns when conducting evaluations to avoid misattributing secular increases in coverage in the summer to promotion or intervention programs. This issue of potential confounding is of greatest concern for uncontrolled research study designs.

**Figure 2.**

Summer peaks in adolescent vaccine uptake in the United States, by year. Uptake standardized at 100 per month for 2007 to 2012. Source: National Immunization Survey-Teen, administered 2008 to 2012.



Moss et al.

**Table 4.** Magnitude of summer peaks in concomitant adolescent vaccination in the United States (source: National Immunization Survey-Teen, administered 2008 to 2012;  $n = 70,144$  adolescents)

	HPV <sup>a</sup> and Tdap		HPV <sup>a</sup> and Meng		Tdap and Meng		All three	
	<i>T</i>	Magnitude [RHL (var)]	<i>T</i>	Magnitude [RHL (var)]	<i>T</i>	Magnitude [RHL (var)]	<i>T</i>	Magnitude [RHL (var)]
Combined years	1,504,766 <sup>b</sup>	4.6 (0.01)	1,915,599 <sup>b</sup>	4.2 (0.01)	6,848,772 <sup>b</sup>	5.6 (0.01)	744,320 <sup>b</sup>	3.3 (0.01)
Year								
2007	640,471 <sup>b</sup>	6.2 (0.01)	761,522 <sup>b</sup>	4.8 (0.01)	1,641,649 <sup>b</sup>	5.1 (0.01)	288,103 <sup>b</sup>	4.5 (0.01)
2008	373,947 <sup>b</sup>	4.0 (0.01)	619,119 <sup>b</sup>	4.3 (0.01)	1,756,694 <sup>b</sup>	4.7 (0.01)	195,484 <sup>b</sup>	3.1 (0.01)
2009	395,753 <sup>b</sup>	7.2 (0.01)	487,682 <sup>b</sup>	6.4 (0.01)	1,420,718 <sup>b</sup>	4.8 (0.01)	213,425 <sup>b</sup>	4.2 (0.01)
2010	280,421 <sup>b</sup>	10.4 (0.01)	243,709 <sup>b</sup>	5.8 (0.01)	1,152,333 <sup>b</sup>	7.5 (0.01)	160,424 <sup>b</sup>	5.6 (0.01)
2011	135,135 <sup>b</sup>	8.3 (0.01)	128,367 <sup>b</sup>	5.2 (0.01)	482,161 <sup>b</sup>	6.9 (0.01)	38,752 <sup>b</sup>	3.3 (0.01)

HPV, human papillomavirus vaccine; Tdap, tetanus, diphtheria, and pertussis booster; Meng, meningococcal vaccine; *T*, Edwards *T* statistic; RHL, ratio of highest to lowest vaccination; var, variance.

<sup>a</sup>Uptake of first dose among female adolescents only.

<sup>b</sup> $P < 0.001$ .

Study strengths include health care provider-verified vaccination data drawn from several years of a large, nationally representative survey (18). Analyses employed an inferential statistical technique that supports inferences beyond descriptive approaches used previously (14, 15). There are several study limitations: we could not distinguish between adolescents' current states of residence (the unit of analysis in this study) and the states in which they received their vaccines. For adolescents who relocated during the time between vaccination and participation in NIS-Teen, the states in which they received vaccines may have been misattributed. However, given the similarity of the vaccination cycles evident across states and across years, the effect of this misattribution was likely minimal. In addition, in survey years 2008 to 2010, NIS-Teen staff contacted participants through landline phones only, and in survey years 2011 to 2012, they contacted participants through landline and cell phones, which could introduce some systematic difference in samples across years (18). Because of small cell sizes, we were unable to evaluate summer peaks in 2012, and sparseness of data may have introduced noise into the estimates for the more recent years (especially for concomitant vaccination). As more data are accumulated, these patterns may become more robust and allow analysis of summer peaks for more recent years. Another potential limitation is that we examined cycles in HPV vaccination only among female adolescents, due to when recommendations for males became part of practice (19). However, our analyses of Tdap booster and meningococcal vaccination stratified by sex demonstrated very similar results, a finding that suggests that summer peaks in HPV vaccination could emerge among male adolescents, as well. Finally, in our analyses, we could not explore potential explanations for the relatively low levels of concomitant vaccination (especially for HPV vaccine alongside Tdap boosters or meningococcal vaccines). Thus, we could not discern whether, for example, health care providers did not make recommendations or whether they made recommendations and parents declined concomitant vaccination. These two explanations would suggest different interventions to promote concomitant vaccination (i.e., provider-focused, parent-focused, or both), an important topic for future studies.

In summary, we found marked summer peaks in uptake of adolescent vaccines from 2007 to 2012. For the United States and for individual states, vaccination increased substantially during the summer months. Health care providers administered about 40% of all adolescent vaccines during June, July, and August. These cycles have implications for both clinical practice (e.g.,

recommending concomitant vaccination during the summer) and public health (e.g., timing of vaccine promotion programs). Future studies should evaluate how cyclical patterns emerge and how promotion programs can harness these patterns to improve population-level coverage with adolescent vaccines and offer greater protection from HPV-attributable cancers.

#### Disclosure of Potential Conflicts of Interest

P.L. Reiter reports receiving a commercial research grant from Cervical Cancer-Free America via an unrestricted educational grant from GlaxoSmith-Kline. N.T. Brewer reports receiving a commercial research grant from Merck and GlaxoSmithKline; has received speakers bureau honoraria from Merck; and is a consultant/advisory board member for Merck. No potential conflicts of interest were disclosed by the other authors.

#### Disclaimer

The research in this article was conducted while J.L. Moss was a Special Sworn Status researcher of the U.S. Census Bureau at the Center for Economic Studies. Research results and conclusions expressed are those of the authors and do not necessarily reflect the views of the Census Bureau. All results have been reviewed to ensure that no confidential information is disclosed.

#### Authors' Contributions

**Conception and design:** J.L. Moss, P.L. Reiter, B.K. Rimer, K.M. Ribisl, N.T. Brewer

**Development of methodology:** J.L. Moss, N.T. Brewer

**Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis):** J.L. Moss, P.L. Reiter, B.K. Rimer, K.M. Ribisl, N.T. Brewer

**Writing, review, and/or revision of the manuscript:** J.L. Moss, P.L. Reiter, B.K. Rimer, K.M. Ribisl, N.T. Brewer

**Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases):** J.L. Moss

**Study supervision:** N.T. Brewer

#### Acknowledgments

The authors thank William Grider, PhD, (U.S. Census Bureau) and Robert Krasowski, MA, MS, (National Center for Health Statistics) for their technical assistance on this project (their work on this project was uncompensated).

#### Grant Support

This study was supported by an NIH grant (F31 CA189411; Principal investigator: J.L. Moss).

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Received June 3, 2015; revised November 12, 2015; accepted December 6, 2015; published OnlineFirst December 16, 2015.

## References

- Centers for Disease Control and Prevention (CDC). Recommendations and guidelines: Advisory Committee on Immunization Practices; 2015. Available from: <http://www.cdc.gov/vaccines/acip/index.html>.
- Elam-Evans LD, Yankey D, Jeyarajah J, Singleton JA, Curtis RC, MacNeil J, et al. National, regional, state, and selected local area vaccination coverage among adolescents aged 13–17 years - United States, 2013. *MMWR Morb Mortal Wkly Rep* 2014;63:625–33.
- Department of Health and Human Services. Immunization and infectious diseases; 2015. Available from: <http://healthypeople.gov/2020/topics-objectives/2020/objectiveslist.aspx?topicId=23>.
- Centers for Disease Control and Prevention (CDC). National and state vaccination coverage among adolescents aged 13–17 years—United States, 2012. *MMWR Morb Mortal Wkly Rep* 2013;62:685–93.
- President's Cancer Panel. Accelerating HPV vaccine uptake: Urgency for action to prevent cancer. Available from: [http://deainfo.nci.nih.gov/advisory/pcp/annualReports/HPV/PDF/PCP\\_Annual\\_Report\\_2012-2013.pdf](http://deainfo.nci.nih.gov/advisory/pcp/annualReports/HPV/PDF/PCP_Annual_Report_2012-2013.pdf). Updated 2014.
- Centers for Disease Control and Prevention (CDC). HPV vaccine: Safe, effective, and grossly underutilized; 2013. Available from: <http://www.cdc.gov/media/releases/2013/p0725-HPV-vaccine.html>.
- Noronha AS, Markowitz LE, Dunne EF. Systematic review of human papillomavirus vaccine coadministration. *Vaccine* 2014;32:2670–4.
- Arguedas A, Soley C, Loaiza C, Rincon G, Guevara S, Perez A, et al. Safety and immunogenicity of one dose of MenACWY-CRM, an investigational quadrivalent meningococcal glycoconjugate vaccine, when administered to adolescents concomitantly or sequentially with tdap and HPV vaccines. *Vaccine* 2010;28:3171–9.
- Reisinger KS, Block SL, Collins-Ogle M, Marchant C, Catlett M, Radley D, et al. Safety, tolerability, and immunogenicity of Gardasil given concomitantly with Menactra and Adacel. *Pediatrics* 2010;125:1142–51.
- Wheeler CM, Harvey BM, Pichichero ME, Simon MW, Combs SP, Blatter MM, et al. Immunogenicity and safety of human papillomavirus-16/18 AS04-adjuvanted vaccine coadministered with tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine and/or meningococcal conjugate vaccine to healthy girls 11 to 18 years of age: results from a randomized open trial. *Pediatr Infect Dis J* 2011;30:e225–34.
- Stokley S, Jeyarajah J, Yankey D, Cano M, Gee J, Roark J, et al. Human papillomavirus vaccination coverage among adolescents, 2007–2013, and postlicensure vaccine safety monitoring, 2006–2014—United States. *MMWR Morb Mortal Wkly Rep* 2014;63:620–4.
- Laugesen MJ, Mistry R, Carameli KA, Ribisl KM, Needleman J, Bastani R. Early policy responses to the human papillomavirus vaccine in the United States, 2006–2010. *J Adolesc Health* 2014;55:659–64.
- Immunization Action Coalition. State information: State mandates on immunization and vaccine-preventable diseases; 2015. Available from: <http://www.immunize.org/laws>.
- Sull M, Eavey J, Papadouka V, Mandell R, Hansen MA, Zucker JR. Adolescent vaccine co-administration and coverage in New York City: 2007–2013. *Pediatrics* 2014;134:e1576–83.
- Cullen KA, Stokley S, Markowitz LE. Uptake of human papillomavirus vaccine among adolescent males and females: immunization information system sentinel sites, 2009–2012. *Acad Pediatr* 2014;14:497–504.
- Gilkey MB, Dayton AM, Moss JL, Sparks AC, Grimshaw AH, Bowling JM, et al. Increasing provision of adolescent vaccines in primary care: a randomized controlled trial. *Pediatrics* 2014;134:e346–53.
- Moss JL, Reiter PL, Dayton A, Brewer NT. Increasing adolescent immunization by webinar: a brief provider intervention at federally qualified health centers. *Vaccine* 2012;30:4960–3.
- Centers for Disease Control and Prevention (CDC). National Immunization Survey: Datasets for the National Immunization Survey-Teen; 2015. Available from: [http://www.cdc.gov/nchs/nis/data\\_files\\_teen.htm](http://www.cdc.gov/nchs/nis/data_files_teen.htm).
- Centers for Disease Control and Prevention (CDC). Recommendations on the use of quadrivalent human papillomavirus vaccine in males—Advisory Committee on Immunization Practices (ACIP), 2011. *MMWR Morb Mortal Wkly Rep* 2011;60:1705–8.
- Edwards JH. The recognition and estimation of cyclic trends. *Ann Hum Genet* 1961;25:83–7.
- Rau R. Measuring seasonality. In: Rau R, editor. *Seasonality in human mortality: a demographic approach*. Heidelberg, Germany; 2007. p. 39–81.
- Hakko H. Seasonal variation of suicides and homicides in Finland: With special attention to statistical techniques used in seasonality studies [dissertation]. Oulu, Finland: University of Oulu; 2000.
- March L. Some researches concerning the factors of mortality. *J R Stat Soc* 1912;75:505–38.
- Ahlbom A. Seasonal variations in the incidence of acute myocardial infarction in Stockholm. *Scand J Soc Med* 1979;7:127–30.
- Sun J, Guo X, Ma J, Zhang J, Jia C, Xu A. Seasonality of suicide in Shandong China, 1991–2009: associations with gender, age, area and methods of suicide. *J Affect Disord* 2011;135:258–66.
- Yamaguchi S, Dunga A, Broadhead RL, Brabin BJ. Epidemiology of measles in Blantyre, Malawi: analyses of passive surveillance data from 1996 to 1998. *Epidemiol Infect* 2002;129:361–9.
- Alexander JA, Hearld LR. The science of quality improvement implementation: developing capacity to make a difference. *Med Care* 2011;49:S6–20.
- Marshall M, Mountford J. Developing a science of improvement. *J R Soc Med* 2013;106:45–50.
- Small SL, Sampsel CM, Martyn KK, Dempsey AF. Modifiable influences on female HPV vaccine uptake at the clinic encounter level: a literature review. *J Am Assoc Nurse Pract* 2013;26:519–25.
- Dorell C, Yankey D, Kennedy A, Stokley S. Factors that influence parental vaccination decisions for adolescents, 13 to 17 years old: National Immunization Survey-Teen, 2010. *Clin Pediatr* 2013;52:162–70.
- Malo TL, Hassani D, Staras SA, Shenkman EA, Giuliano AR, Vadapampil ST. Do Florida Medicaid providers' barriers to HPV vaccination vary based on VFC program participation? *Matern Child Health J* 2013;17:609–15.
- Keating KM, Brewer NT, Gottlieb SL, Liddon N, Ludema C, Smith JS. Potential barriers to HPV vaccine provision among medical practices in an area with high rates of cervical cancer. *J Adolesc Health* 2008;43:S61–7.
- Skinner JS, Tiro JA, Champion VL. The health belief model. In: Glanz K, Rimer BK, Viswanath K, editors. *Health behavior: theory, research and practice*. 5th ed. San Francisco, CA: Wiley; 2015.
- Wakefield MA, Loken B, Hornik RC. Use of mass media campaigns to change health behaviour. *Lancet* 2010;376:1261–71.
- Warner EJ, Barsky RB. The timing and magnitude of retail store markdowns: evidence from weekends and holidays. *Q J Econ* 1995;110:321–52.
- Petrosky E, Bocchini JA Jr, Hariri S, Chesson H, Curtis CR, Saraiya M, et al. Use of 9-valent human papillomavirus (HPV) vaccine: updated HPV vaccination recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep* 2015;64:300–4.
- Briss PA, Rodewald LE, Hinman AR, Shefer AM, Strikas RA, Bernier RR, et al. Reviews of evidence regarding interventions to improve vaccination coverage in children, adolescents, and adults. The Task Force on Community Preventive Services. *Am J Prev Med* 2000;18:97–140.

# Cancer Epidemiology, Biomarkers & Prevention

## Summer Peaks in Uptake of Human Papillomavirus and Other Adolescent Vaccines in the United States

Jennifer L. Moss, Paul L. Reiter, Barbara K. Rimer, et al.

*Cancer Epidemiol Biomarkers Prev* 2016;25:274-281. Published OnlineFirst December 16, 2015.

**Updated version** Access the most recent version of this article at:  
doi:[10.1158/1055-9965.EPI-15-0574](https://doi.org/10.1158/1055-9965.EPI-15-0574)

**Supplementary Material** Access the most recent supplemental material at:  
<http://cebp.aacrjournals.org/content/suppl/2015/12/16/1055-9965.EPI-15-0574.DC1.html>

**Cited articles** This article cites 28 articles, 6 of which you can access for free at:  
<http://cebp.aacrjournals.org/content/25/2/274.full.html#ref-list-1>

**E-mail alerts** [Sign up to receive free email-alerts](#) related to this article or journal.

**Reprints and Subscriptions** To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at [pubs@aacr.org](mailto:pubs@aacr.org).

**Permissions** To request permission to re-use all or part of this article, contact the AACR Publications Department at [permissions@aacr.org](mailto:permissions@aacr.org).