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Factors influencing Human papillomavirus (HPV) vaccination series completion in Mississippi Medicaid

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ABSTRACT

Purpose: To identify factors associated with Human Papillomavirus (HPV) vaccine series completion among vaccine initiators in Mississippi Medicaid.
Methods: 2013–2018 Mississippi Medicaid administrative claims data were analyzed. Female and male beneficiaries aged 9 to 26 years who initiated HPV vaccination in the identification period were assessed for completion of age-appropriate number of recommended doses within a period of 12 months. Sex-stratified multivariable logistic regression was used to examine factors associated with HPV vaccine series completion in the study sample.
Results: A total of 18,110 female and 18,186 male beneficiaries initiated HPV vaccine between January 1, 2014 and June 30, 2017. Most of the initiators belonged to ages 11 to 12 years, African American race, managed care plans and Central Mississippi public health region. The vaccine series completion rate was 34% for females and 30% for males. Younger age at initiation was a significant predictor of vaccine series completion in both sexes. Specifically, initiators in age groups 9 to 10 and 11 to 12 years, respectively, had greater odds of completion, while initiators aged 15 to 26 years had lower odds of completion compared to initiators aged 13 to 14 years. Female and male beneficiaries in managed care plans (vs. fee-for-service) and of African American race (vs. Caucasians) had lower odds of completing the vaccine series. Female and male beneficiaries who initiated HPV vaccine series with a pediatrician had the highest completion rates.
Conclusion: HPV vaccination series completion rate in Mississippi Medicaid was suboptimal despite the high HPV-related cancer incidence in the state. HPV vaccine series completion is influenced by various sociodemographic factors. There is a need for robust education and public health programs to encourage completion of recommended doses.

1. Introduction

Human Papillomaviruses (HPVs) are a group of more than 150 viruses, which commonly affect teens and adults. Most HPV infections resolve on their own. However, some sexually transmitted HPVs cause genital warts and others cause several types of cancers such as cancer of the cervix, vagina, vulva, penis, anus and oropharynx [1]. An HPV-associated cancer is a specific cellular type of cancer that is diagnosed in a part of the body where HPV is often found [2]. It is estimated that 79% of HPV-associated cancers can be attributed to the virus [2]. According to data from cancer registries, the incidence of HPV-associated cancers in Mississippi (MS) is estimated to be 14.3 per 100,000 persons, compared to the national average of 11.7 per 100,000 persons [3].

Three vaccines, Gardasil® (4vHPV), Cervarix® (2vHPV) and Gardasil®9 (9vHPV) were licensed by the Food and Drug Administration (FDA) for immunization against HPV. The Advisory Committee on Immunization Practices (ACIP) recommends initiation of the HPV vaccination series at ages 11 to 12 years, however, vaccine initiation can occur as early as 9 years of age [4]. Prior to October 2016, a 3-dose immunization schedule within a period of 12 months was recommended, irrespective of age at initiation [5,6]. However, results from a 9vHPV vaccine clinical trial showed

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noninferior immunogenicity with 2 doses administered in male and female participants of ages 9 to 14 years compared to 3 doses administered in older female participants [7]. Similar findings were shown for 2vHPV and 4vHPV vaccines, respectively [8]. Consequently in October 2016, ACIP voted to reduce the recommended number of doses for completion for children who initiate before the age of 15 years to two doses [9]. Three doses continued to be the recommended number for completion if initiated at 15 years of age or later [9]. As of 2017, Gardasil®9 is the only vaccine available in the United States [10] and a policy update in 2018 expanded the maximum age limit for HPV vaccine receipt to 45 years [11].

While initiation is the necessary first step, completing the series is required to ensure effective immunization. Studies report HPV vaccine completion rates ranging from 23 to 60% and vaccine recipient's characteristics such as younger age, Caucasian race, higher education level, higher household income and health insurance coverage are factors associated with greater likelihood of vaccine series completion [12–18]. However, these studies primarily utilized data from national or regional surveys and managed care organizations. Little is known about factors that influence vaccine series completion in the Medicaid population. As of July 2017, an estimated 60% of MS population under 19 years of age was enrolled to receive health benefits through Medicaid fee-for-service (FFS), Children's Health Insurance Program (CHIP) or Medicaid's managed care programs [19,20]. Given the high HPV-related cancer rates [21] and the substantial Medicaid-served population in the state, the current study examined HPV vaccine series completion rate and factors associated with completion in MS Medicaid beneficiaries aged 9 to 26 years.

2. Methods

2.1. Study design and sample

An observational retrospective cohort study was conducted using MS Medicaid administrative claims data from January 1, 2013 to June 30, 2018. The period from January 1, 2014 to June 30, 2017 was used as the sample identification period (see Fig. 1). MS Medicaid beneficiaries aged 9 to 26 years who had at least one medical claim for an HPV vaccine identified using Current Procedural Terminology (CPT) codes for a quadrivalent, a bivalent or a 9-valent vaccine (90649, 90,650 or 90651, respectively) during the identification period were included in this study. The first identified claim for each beneficiary was recorded as the index event and the corresponding date as the index vaccination date. 12-months prior to the index vaccination date were used as a wash-out period to exclude beneficiaries with previous HPV vaccine claims. The 12-month period following the index vaccination date was used to follow beneficiaries. Beneficiaries who were pregnant at any time from the start of identification period (i.e. January 1, 2014) to the end of follow-up period (i.e. June 30, 2018) were excluded. This analytic sample of beneficiaries were identified as "initiators". Initiators were required to be continuously enrolled in MS Medicaid during the wash-out and the follow-up periods, respectively. Initiators were followed for 12 months post-index vaccination date to assess receipt of the remaining of the recommended doses of the vaccine. The study received approval from the University of Mississippi's Institutional Review Board.

2.2. Study variables

The main outcome of interest was HPV vaccine series completion in the follow-up period. The operationalization of vaccine series completion was guided by the most recent vaccine efficacy data [8] and the subsequent ACIP recommendation for HPV vaccine series completion [9]. Therefore, initiators who were younger than 15 years of age were considered as having "completed" the series if they had at least 2 HPV vaccine claims during the follow-up period. Initiators who were 15 years of age or older were considered as having "completed" if they received at least 3 doses in the follow-up period. We did not use an operational definition of completion for beneficiaries based on guidelines as of the time of their initiation because the primary focus of the current study is adequate vaccination rather than adherence to guidelines. Further, HPV vaccine claims within a 7-day window were considered as part of the

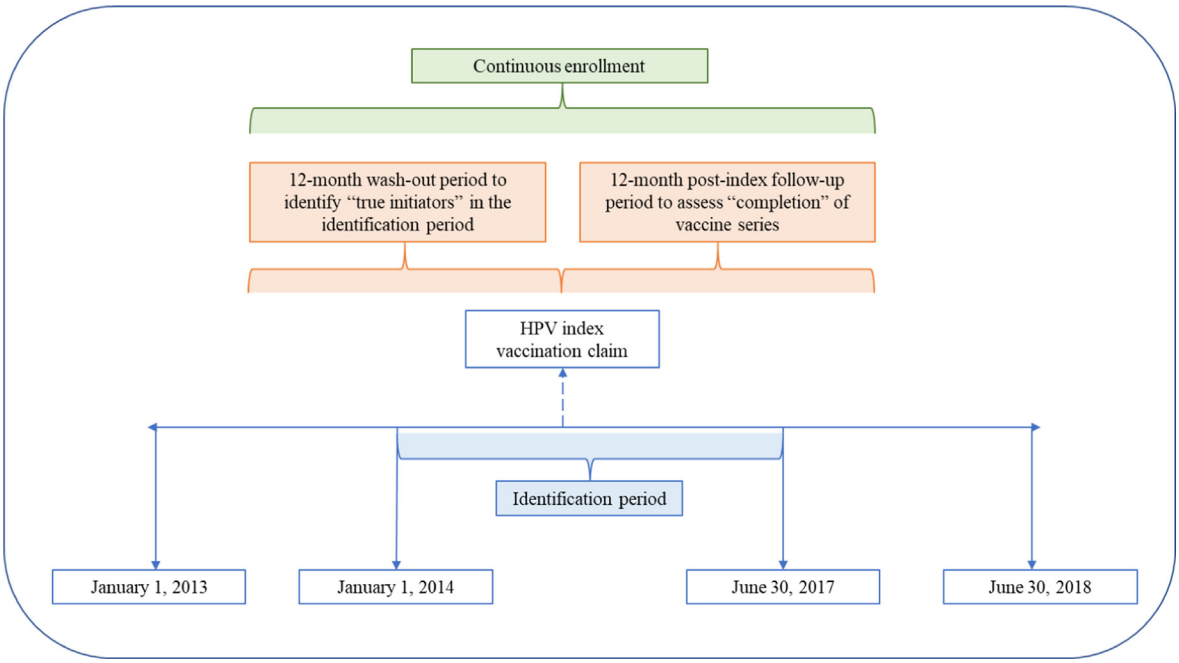

Fig. 1. Diagrammatic description of the study design.

same vaccination event as a conservative approach to avoid double-counting of vaccination doses. This approach was based on recent findings from Layton et al.'s study evaluating variation in vaccination coding in Medicaid data [22].

Sociodemographic characteristics including age at initiation, sex, race, health plan at initiation and MS public health region were obtained for all beneficiaries from the enrollment file. Based on their age at initiation, beneficiaries were categorized into four age groups: 9 to 10, 11 to 12, 13 to 14, 15 to 26 years of age. These four categories were identified to account for updated ACIP guidelines for series completion mentioned above as well as differential coverage policies for vaccines in Mississippi Medicaid based on age. The cost of HPV vaccine for children below 19 years of age is covered through Vaccines for Children (VFC), a federally funded program available through the Centers for Disease Control and Prevention (CDC) [23], and for adults 19 years and older by Mississippi Division of Medicaid [24]. The race variable included four categories: Caucasian, African American, Hispanic and others (included Asian/Pacific Islander, Native American/Alaskan and all others). A beneficiary's county of residence at the time of enrollment was used to classify the sample in to three public health regions in MS (Northern, Southern and Central). This variable was used to examine geographic variation in vaccination completion rates. Health plan at initiation and type of provider who initiated the series were also included in the model. The plan variable consisted of two categories: FFS and managed care plans. Provider type who administered the initial dose was categorized as follows: pediatricians, family physicians, other physician specialties, nurse practitioners and other providers.

2.3. Statistical analysis

Given certain key gender-based differences in recommendations, perspectives and rates of vaccination that have been observed over time [25], stratified analysis was conducted for males and females. Sample characteristics were reported as proportions for categorical variables. Completion rate within each sex was calculated as the percentage of "completers" across characteristics including age group, race/ethnicity, geographic location in terms of MS public health region, plan at initiation and provider who initiated the HPV vaccine series. Multivariable logistic regression, controlling for aforementioned characteristics, was used to evaluate association between various factors and completion of the vaccine series. A significance level of $\alpha = 0.05$ was used for all analyses. All analyses were conducted in SAS 9.4 (SAS Institute, Cary, NC).

3. Results

3.1. Sample characteristics

A total of 36,296 beneficiaries were identified as "initiators", of which 18,110 (49.9%) were female and 18,186 (50%) were male (see Fig. 2). The overall vaccine series completion, as defined in the current study, was 34% for females and 30% for males. The total analytic sample consisted of a higher proportion of children of age 11 to 14 years (73% of females, 71% of males), African Americans (71% of females and males, respectively) and beneficiaries enrolled in managed care at the time of initiation (65% of females, 64% of males) as presented in table 1. More than half of all initial doses were administered by pediatricians (35% of females, 39% of males), other providers (30% of females, 26% of males) and nurse practitioners (24% of females and males, respectively) combined. A major proportion of beneficiaries resided in Central MS (41% of females, 40% of males) at the time of enrollment.

3.2. Factors associated with HPV vaccine series completion

There was a wide variation in vaccine series completion rates by age group, race, initiating provider type, health plan at initiation and MS public health region among female and male beneficiaries (Table 1). The highest completion rates were observed in the age group of 9 to 10 years for females (56%) and males (47%), respectively. A decline in completion rate was observed in the older age group of 15 to 26 years, with rates falling drastically to 9% in females and 7% in males, respectively. The current study found that 19% of beneficiaries 15 years or older had only received 2 of the required 3 doses and therefore were classified as "non-completers". Among different racial groups, Hispanics had the highest completion rate of 46% in females and 42% in males. The lowest completion rate was observed for African Americans in females (31%) and for "Other" in males (27%) respectively. Beneficiaries enrolled in managed care had a lower completion rate than those enrolled in FFS. Beneficiaries with pediatricians as the initiating provider had the highest completion rate (40% in females, 36% in males) followed by other physician specialties (34% in females and 31% in males), excluding family practitioners. Beneficiaries residing in Northern MS public health region at enrollment had the highest completion rates of 37% in females and 34% in males, followed by the Southern and the Central regions, each with completion rates of 33% in females and 28% in males.

Table 2 presents results from multivariable logistic regression model with all factors in the model stratified by sex. Beneficiaries who initiated at ages 9 to 10 (females: aOR = 2.22, 95% CI = (1.88, 2.63); males: aOR = 1.75, 95% CI = (1.45, 2.11)) and 11 to 12 (females: aOR = 1.71, 95% CI = (1.59, 1.84); males: aOR = 1.72, 95% CI = (1.60, 1.86)) had greater odds of completion, while those who initiated at 15 to 26 (females: aOR = 0.20, 95% CI = (0.18, 0.23); males: aOR = 0.16, 95% CI = (0.15, 0.19)) had lower odds of completion than beneficiaries who initiated at 13 to 14 years. Among females and males, African Americans had lower odds of completing the vaccine series than Caucasians (females: aOR = 0.68, 95% CI = (0.63, 0.73); males: aOR = 0.71, 95% CI = (0.66, 0.77)). Beneficiaries enrolled in managed care at initiation had lower odds of completion than those in FFS (females: aOR = 0.92, 95% CI = (0.85, 0.98); males: aOR = 0.81, 95% CI = (0.76, 0.87)). Compared to any provider type, female and male beneficiaries who received their first dose from a pediatrician had greater odds of completing the series. Geographically, the odds of completion was higher for male beneficiaries residing in Northern (aOR = 1.12, 95% CI = (1.03, 1.21)) and lower for those in Southern MS public health regions (aOR = 0.88, 95% CI = (0.81, 0.96)) compared to the Central region. The odds of completion for female beneficiaries in Southern MS public health region was significantly lower than those in the Central region (aOR = 0.91, 95% CI = (0.84 – 0.99)).

4. Discussion

Our study is one of the first to assess factors associated with HPV vaccine series completion in a state's Medicaid program following changes in vaccine availability and ACIP guidelines [9,10]. Cook et al. assessed HPV vaccine completion in Florida's Medicaid program using data from 2006 to 2008, the years immediately following vaccine introduction [26]. They found a completion rate of 26.9% among initiators and found that older beneficiaries and African Americans were less likely to complete the vaccine series [26]. In our study, the overall HPV vaccine series completion rate within 12 months among eligible female and male Mississippi Medicaid beneficiaries who had initiated HPV vaccine between January 1,

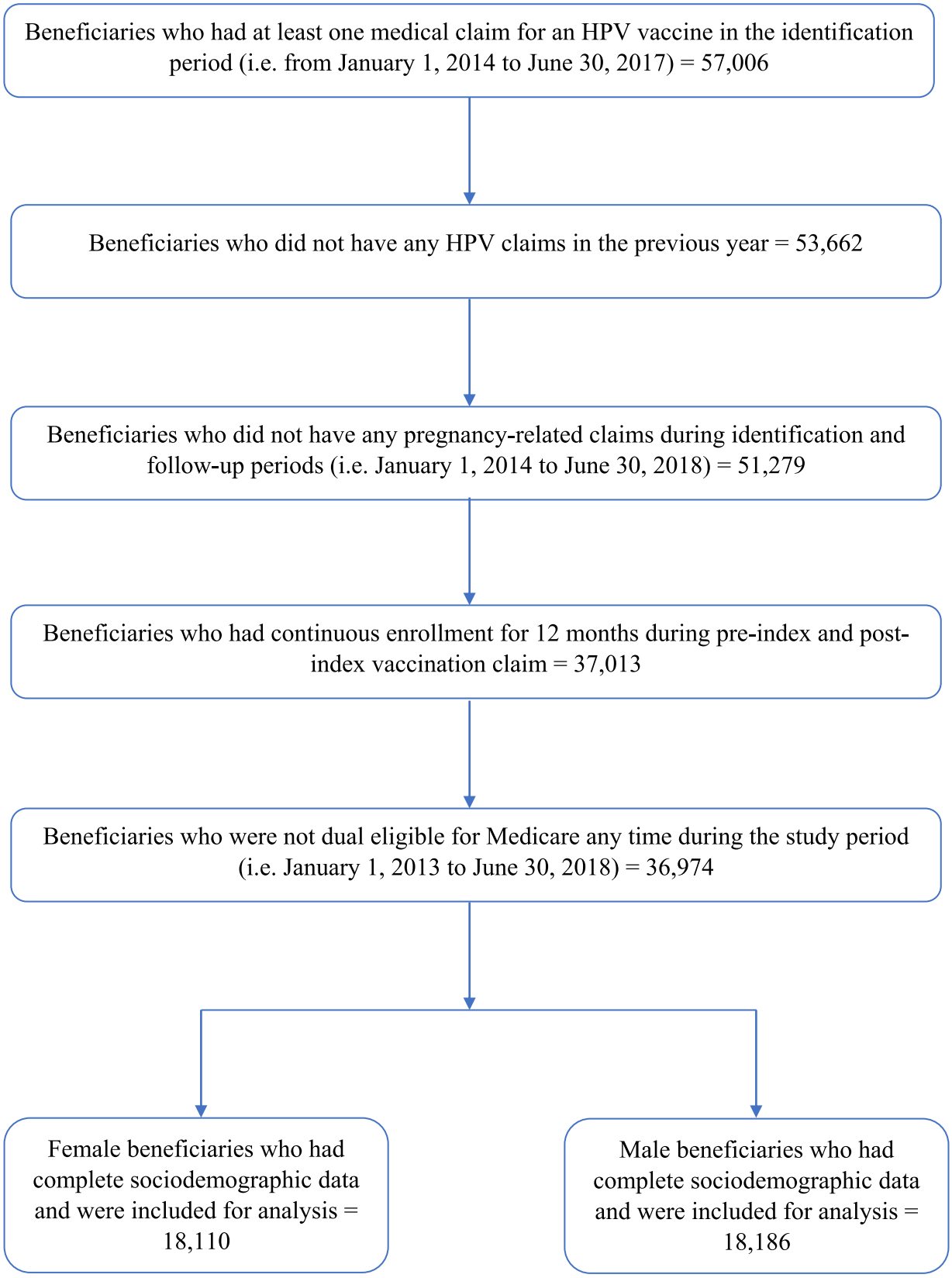

Fig. 2. Attrition table for beneficiaries included based on study eligibility criteria.

2014 and June 30, 2017 was 34% and 30%, respectively. The completion rate for females observed in this study falls within the 28 to 50% range observed in other studies among 9 to 26-year-old females [12,13,27,28]. This wide variation in completion rates across studies may be attributed to the different sampling frames and time periods used. An observed completion rate

Table 1
HPV vaccine series completion[a] rates among initiators in Mississippi Medicaid, January 1, 2014 – June 30, 2017.

Characteristics	Female beneficiaries (N = 18,110)			Male beneficiaries (N = 18,186)		
	Initiators N (%)	Completers[b] N (%)	Completion rate[c] (%)	Initiators N (%)	Completers[b] N (%)	Completion rate[c] (%)
Age group at initiation						
9 to 10	634 (3.5)	353 (5.8)	55.7	511 (2.8)	239 (4.4)	46.8
11 to 12	7560 (41.8)	3527 (57.6)	46.7	6984 (38.4)	3063 (56.5)	43.9
13 to 14	5596 (31.0)	1851 (30.2)	33.1	5867 (32.3)	1785 (32.9)	30.4
15 to 26	4320 (23.9)	395 (6.5)	9.1	4824 (26.5)	334 (6.2)	6.9
Race						
Caucasian	4364 (24.1)	1741 (28.4)	39.9	4245 (23.3)	1504 (27.7)	35.4
African American	12,861 (71.0)	4007 (65.4)	31.2	12,959 (71.3)	3545 (65.4)	27.4
Hispanic	675 (3.7)	311 (5.1)	46.1	716 (3.9)	301 (5.6)	42.0
Other[d]	210 (1.2)	67 (1.1)	31.9	266 (1.5)	71 (1.3)	26.7
Plan at initiation						
FFS	6400 (35.3)	2206 (36.0)	34.5	6590 (36.2)	2069 (38.2)	31.4
Managed Care	11,710 (64.7)	3920 (64.0)	33.5	11,596 (63.8)	3352 (61.8)	28.9
Type of provider who initiated the initiating dose						
Pediatrician	6400 (35.3)	2580 (42.1)	40.3	7009 (38.5)	2488 (45.9)	35.5
Family Practice	1309 (7.2)	385 (6.3)	29.4	1407 (7.7)	356 (6.6)	25.3
Other physician specialties	600 (3.3)	202 (3.3)	33.7	691 (3.8)	215 (4.0)	31.1
Nurse practitioner	4416 (24.4)	1390 (22.7)	31.5	4270 (23.5)	1136 (21.0)	26.6
Other provider types	5385 (29.7)	1569 (25.6)	29.1	4809 (26.4)	1226 (22.6)	25.5
MS public health region[c]						
Northern	5250 (29.0)	1918 (31.3)	36.5	5322 (29.3)	1783 (32.9)	33.5
Southern	5373 (29.7)	1768 (28.9)	32.9	5520 (30.4)	1556 (28.7)	28.2
Central	7487 (41.3)	2440 (39.8)	32.6	7344 (40.4)	2082 (38.4)	28.4

HPV = Human papillomavirus; MS = Mississippi.
[a] Advisory Committee on Immunization Practices 2016 guideline was used as a basis to define vaccine series completion. Completion was defined as receipt of 2 doses if initiated before the age of 15 years and 3 doses if initiated at 15 years of age or later.
[b] Includes beneficiaries who received 4 doses, which was less than 0.1% of the study sample.
[c] Overall completion rate for females was 33.8% (6,126 of 18,110) and for males was 29.8% (5,421 of 18,186).
[d] 'Other' race includes Asian/Pacific Islander, Native American/Alaskan, Mixed race and others.

Table 2
Sex-stratified multivariable logistic regression results for factors associated with HPV vaccine series completion[a] among initiators in Mississippi Medicaid, January 1, 2014 – June 30, 2017.

Characteristics	Odds ratio (95% CI)[b]	
	Females (N = 18,110)	Males (N = 18,186)
Age group		
9 to 10	**2.22 (1.88 – 2.63)**	**1.75 (1.45 – 2.11)**
11 to 12	**1.71 (1.59 – 1.84)**	**1.72 (1.60 – 1.86)**
13 to 14	1.00	1.00
15 to 18	**0.20 (0.18 – 0.23)**	**0.16 (0.15 – 0.19)**
Race		
Caucasian	1.00	1.00
African American	**0.68 (0.63 – 0.73)**	**0.71 (0.66 – 0.77)**
Hispanic	1.00 (0.84 – 1.19)	1.14 (0.96 – 1.36)
Other[c]	0.83 (0.60 – 1.14)	0.80 (0.59 – 1.08)
Plan at initiation		
Managed Care	**0.92 (0.85 – 0.98)**	**0.81 (0.76 – 0.87)**
FFS	1.00	1.00
Type of provider who initiated the 1st dose		
Pediatrician	1.00	1.00
Family Practice	**0.76 (0.66 – 0.87)**	**0.76 (0.66 – 0.87)**
Other physician specialties	**0.81 (0.67 – 0.97)**	**0.79 (0.66 – 0.95)**
Nurse practitioner	**0.74 (0.68–0.81)**	**0.70 (0.64 – 0.76)**
Other provider types	**0.70 (0.64–0.76)**	**0.62 (0.57 – 0.68)**
MS public health region		
Northern	1.09 (1.00–1.18)	**1.12 (1.03 – 1.21)**
Southern	**0.91 (0.84 – 0.99)**	**0.88 (0.81 – 0.96)**
Central	1.00	1.00

HPV = Human papillomavirus; CI = Confidence interval; MS = Mississippi
[a] Advisory Committee on Immunization Practices 2016 guideline was used as a basis to define vaccine series completion. Completion was defined as receipt of 2 doses if initiated before the age of 15 years and 3 doses if initiated at 15 years of age or later.
[b] Model was adjusted for variables presented in the table. c-statistic for the model with female and male beneficiaries was 0.7, respectively.
[c] 'Other' race includes Asian/Pacific Islander, Native American/Alaskan, Mixed race and others.

of about 30% among males in our study is higher than the 24.3% reported by Ackerson et al. in a sample of 9 to 17-year-old males enrolled in a managed care organization (MCO) [15], but lower than the rates (33 to 36%) reported by Spencer et al. in a sample of privately insured 9 to 26-year-old males [28]. It is worth noticing that most of these studies were published at a time when 3 doses were required for series completion [5,6]. Sensitivity analysis with a 3-dose requirement for vaccine series completion regardless of age at initiation produced a completion rate of 13% for females and 10% for males in our sample. Less than 0.1% of the analytic sample received 4 doses, reasons for which cannot be verified given the nature of the data used.

There were disparities in HPV vaccine completion based on age, gender and race/ethnicity in our study. Younger age has consistently been reported as a significant predictor of series completion across most previous studies [13,15,16,27,29–31]. CDC-funded VFC program pays for vaccinations for children below 19 years of age that qualify for Medicaid, are uninsured, or are American Indian/Alaskan Native [23]. Based on CDC guidelines, the HPV vaccine was covered by MS Division of Medicaid for adults 19 years and older [24]. Therefore, vaccine cost would not be considered a barrier for MS Medicaid beneficiaries of any age group. However, not only did pre-teens have better completion rates in the bivariate analysis, but they also had greater odds of successful vaccine series completion than the older age groups after controlling for various other factors. The literature suggests that parental concerns regarding early or increased sexual activity might contribute to vaccine hesitancy or delay [32,33]. However, evidence from recent studies shows that early HPV vaccination does not result in increased sexual activity or risky sexual behaviors among children [34–36]. Therefore, the responsibility falls on healthcare providers and health promotion agencies to educate parents and caregivers in order to help them make an informed decision in a timely manner.

More than 70% of our sample was composed of African Americans. Similar to other studies, they had lower odds of completion compared to Caucasians [12,14,15,26,27,37–39]. Since health insurance coverage is not the issue in the current study, there is a need to examine other underlying social or cultural phenomena that may be contributing to racial/ethnic disparities in this sample. It was interesting to see that Hispanics had greater completion rates than Caucasians, however this effect was found to be non-significant in the adjusted model. A previous study by Henry et al. observed higher vaccine initiation rates among Hispanic girls from predominantly Hispanic or mixed race communities [40]. They hypothesized various reasons that could potentially explain this phenomenon such as targeted promotional efforts focusing on poor, racial/ethnic communities where cervical cancer rates might be the highest, stronger social support networks and availability of more health-promoting resources. Future research should examine facilitators and barriers of HPV vaccination series initiation and completion in Hispanic communities in Mississippi.

In our study, beneficiaries enrolled in managed care plans had lower odds of completion than beneficiaries enrolled in FFS, which could be due to the lack of a validated quality measure tying a provider's performance to HPV vaccine series completion. Beneficiaries who received their first HPV dose from a pediatrician had higher completion rates, a finding that is consistent with previously published studies [13,15,16,27,37]. While pediatricians, family practitioners and other physician specialties administered most of the initiating and completing doses, nurse practitioners accounted for over 20% of the completers. The "other providers" category included all other provider types and health agencies. Due to the secondary nature of our data, we only had access to the place of service for the latter and could not verify the specialty of the service rendering provider at the health agencies. We did not find any pharmacy claims for HPV vaccine in the identification period. This could be linked to two policy issues: (1) lack of pharmacists who are enrolled as VFC providers and are therefore, ineligible for reimbursement under the program, and (2) HPV vaccines administered at a pharmacy venue are not eligible for reimbursement under MS Medicaid's administrative code for immunizations [24]. Several studies have shown that pharmacists as immunizers have a significant impact on improving immunization rates for other vaccines [41,42]. However, their potential in serving the Medicaid population remains to be seen. Our study also identified geographic variation in completion rates, which can be ascribed to the Northern MS public health region's proximity to university-affiliated medical centers and a network of premier health care institutions in the Memphis metropolitan statistical area.

4.1. Limitations

There are certain limitations to the current study that should be mentioned. First, our study sample is not representative of the US population and hence our findings cannot be generalized to samples beyond MS Medicaid beneficiaries. Second, we used a secondary data source which draws conclusions from encounters that resulted in an administrative claim. Any encounters outside of Medicaid or those that did not result in a claim (encounters paid for in cash or through other health benefit programs, for example) cannot be evaluated. Third, beneficiaries who did not have continuous enrollment for 12 months after the initial vaccine dose were excluded because of the assumption that enrollment would be a pre-requisite for getting additional vaccine doses. Lastly, we might have missed beneficiaries who received the recommended number of doses over a period longer than 12 months. However, since there are no guidelines regarding vaccine series completion beyond 12 months, we utilized a 12-month follow-up period based on noninferiority, immunogenicity trial data for 9vHPV vaccine [7].

4.2. Conclusion

In conclusion, HPV vaccine completion remains suboptimal in Mississippi Medicaid. There is a need for educational activities that emphasize on HPV vaccination as cancer prevention and stimulate conversation about the benefits of early vaccination with patients, parents and caregivers. Population-based strategies that increased vaccine availability and interventions that targeted both providers and patients have shown to greatly impact vaccine uptake [43] and should be considered while planning new approaches.

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CRediT authorship contribution statement

Sushmitha Inguva: Conceptualization, Methodology, Formal analysis, Writing - original draft, Visualization, Project administration. **Marie Barnard:** Conceptualization, Methodology, Writing - original draft, Project administration. **Lori M. Ward:** Conceptualization, Writing - review & editing. **Yi Yang:** Writing - review & editing. **Eric Pittman:** Writing - review & editing. **Benjamin F. Banahan:** Visualization, Writing - review & editing. **Terri R. Kirby:** Writing - review & editing. **Sara L. Noble:** Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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