Overcoming Vaccine Hesitancy and Preventing Cancer Through Adaptive Learning Artificial Intelligence and Refinement of Reminder Interventions and Campaigns

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Abstract

Background: Despite HPV vaccination preventing six cancers and being recommended for over a decade, uptake remains low in the U.S. and Utah, even as oropharyngeal cancer incidence (59,000 in 2025) surpasses cervical cancer, rising most rapidly among men, especially non-Hispanic white men.

Methods: Evaluated sociodemographic factors and trends of HPV missed vaccination opportunities (HPV-MVOs) among children/adolescents (C/A) 9-18 years old in the Utah Immunization Information System (USIIS) over 5.5 years. Examined the impact of rurality on HPV-MVOs among n=685,614 C/A and explored ethnicity as a moderator. Conducted logistic regression, mediation analyses, and EMM (Effect Measure Modification) using R.

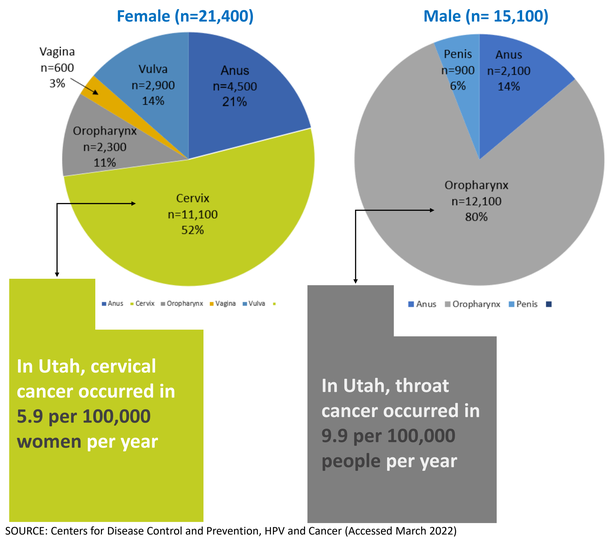
Results: During 2017-2023, 70% of Utah adolescents had at least one HPV-MVO, averaging 2.14(SD=1.56) per individual. Those who were Latino/a (aOR=1.26 [95%CI: 1.13-1.42]), those with stable insurance (aOR=1.15 [95% CI: 1.14-1.16]), and those in rural areas (aOR=1.04 [95% CI: 1.02-1.06]) had higher odds of an HPV-MVO. Insurance stability mediated 17.7% of the effect of rurality on HPV-MVO, with the indirect effect moderated by race and ethnicity (p<.0001).

Conclusion: Rurality, race, and ethnicity are significant and relevant factors of HPV-MVO. Insurance mediates the effect of rurality on HPV-MVO and interacts differently across racial and ethnic groups, highlighting the need for tailored interventions.

Introduction

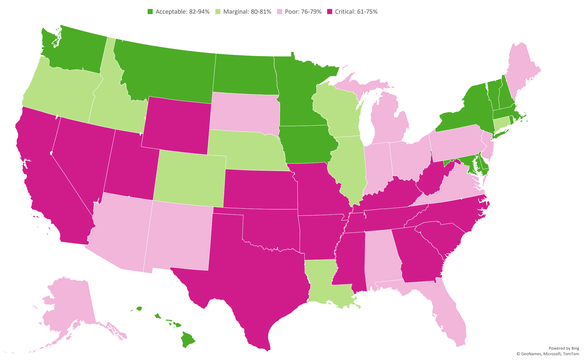
As shown in **Fig. 1**, in the U.S. and Utah, oropharyngeal cancer incidence (59,000 new cases predicted for 2025) has outpaced cervical cancer (13,000 new cases predicted for 2025) and is increasing more among men (2.7% versus 1% overall annual increase), particularly among non-Hispanic white men (3% annual increase). Both cancer types are caused by the human papillomavirus (HPV) and are preventable. Despite preventing six types of cancers and being widely available for over a decade, HPV vaccination remains low in the U.S. and in Utah (**Fig. 2**).

FIG. 1. Six Known HPV Cancers by Sex, Avg. Num. of New Cases, US, 2014-2018



SOURCE: Centers for Disease Control and Prevention, HPV and Cancer (Accessed March 2022)

Fig. 2. HPV Vaccination (>=1 Dose) Coverage Rates Among Male and Female Adolescents Aged 13–17 Years,
United States, 2022 (CDC NISTEEN)



Objectives

This study seeks to evaluate sociodemographic factors and characterize spatial and temporal trends of HPV missed vaccination opportunities (HPV-MVO) to support the development of a machine learning (ML) algorithm for HPV-MVO predictive models for an HPV vaccination reminder and recall chatbot application.

This study was able to:

- Examine the impact of rurality on HPV-MVOs among children/adolescents (C/A)
- Examine insurance stability and ethnicity as mediators
- Develop initial models of these characteristics to inform the HPV-MVO predictive models

Methods & Material

- Using the Utah State Immunization Registry Information System (USIIS), we analyzed vaccination records of individuals aged 9-18 years old, over 5.5 years (01/01/2017-05/19/2023). This data consisted of the following:
  - 4,861,1447 total vaccination records
  - 1,093,533 individual records
- We examined vaccination records from 685,614 C/A for the impact of rurality on HPV missed vaccination opportunities (HPV-MVOs) among children/adolescents (C/A).
- We explored ethnicity as a moderator of the indirect relationship between rurality and HPV-MVO (**Fig. 3**).
- Logistic regression and mediation analyses were conducted, and EMM (Effect Measure Modification) was assessed using R.

Study Definitions

- **HPV missed vaccination opportunities (HPV-MVOs)** – an event in which an individual received an immunization, other than the HPV vaccine for which they were due or overdue, within three weeks of the event.
- **Insurance stability -** utilizing private insurance only at each visit throughout the study period.

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Results

During 2017-2023, of Utah adolescents ages 9-17:

- 47.1% did not receive any HPV doses
- 70% had at least one HPV-MVO
- Averaged 2.14 HPV-MVO per individual (SD=1.56)

Utahn adolescents with higher odds of HPV-MVO compared with their counterparts included:

- Latino/a (aOR=1.26 [95%CI: 1.13-1.42])
- with stable insurance (aOR=1.15 [95% CI: 1.14-1.16])
- lived in rural areas (aOR=1.04 [95% CI: 1.02-1.06])

Mediation analyses revealed:

- 17.7% of the effect was mediated by insurance stability (p<.0001)
- The total indirect effect (β=-.0250, p<.0001) through insurance was larger than the direct effect (β=-.0181, p<.0001)
- The indirect effect was moderated by race and ethnicity (p<.05)

Table 1. Demographics and characteristics of adolescents (9-18 years) by any missed HPV vaccination opportunities within USIIS (2017-2023)

	Any Missed HPV Vaccination Opportunities		
	No	Yes	
Characteristic	N = 198,041[1]	N = 487,573[1]	p-value
HPV Age at Initiation	12.57 ± 1.97	13.35 ± 2.36	**<0.001**
Missing	0	341,201	
Sex Assigned (Binary)			**<0.001**
Female	98,388 (50%)	237,781 (49%)	
Male	99,247 (50%)	247,179 (51%)	
Missing	406	2,613	
Race and Ethnicity			**<0.001**
American Indian / Alaska Native	3,408 (1.8%)	6,591 (1.4%)	
Asian, Asian American	4,564 (2.4%)	12,472 (2.7%)	
Biracial, multiracial, of mixed race	37,232 (20%)	64,690 (14%)	
Black and African American	4,328 (2.3%)	8,936 (1.9%)	
Hawaiian or Pacific Islander	3,731 (2.0%)	6,690 (1.5%)	
Latino/a, Latinx, Latine	398 (0.2%)	1,270 (0.3%)	
Other	1,779 (0.9%)	4,860 (1.1%)	
White Alone	135,094 (71%)	353,154 (77%)	
Missing	7,507	28,910	
Insurance Stability			**<0.001**
Instability	93,930 (47%)	202,711 (42%)	
Stable	104,111 (53%)	284,862 (58%)	
Rurality (RUCC >=4)			**<0.001**
Rural	16,008 (8.1%)	41,033 (8.6%)	
Urban	180,591 (92%)	436,633 (91%)	
Missing	1,442	9,907	
Number of Missed Opportunities	--	2.14 ± 1.56	**<0.001**

[1] Frequency (%)

FIG. 3. Mediation Model with Race and Ethnicity Moderating the Indirect Effect of Rurality on HPV-MVO

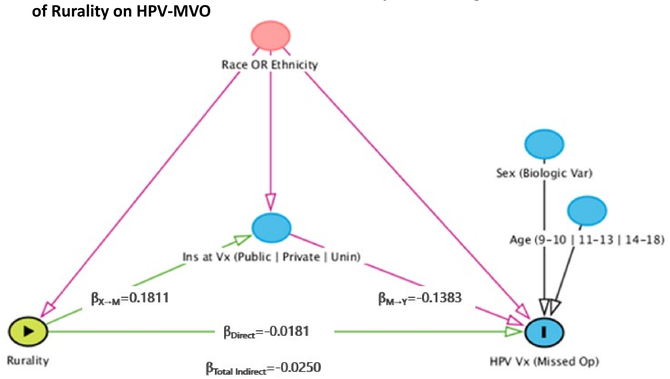

Table 2. Adjusted odds of an HPV-MVO among adolescents (9-18 years), Utah (2017-2023)

	OR[1,2]	95% CI[2]	p-value
Rurality (RUCC)			
Rural	1.04	1.02, 1.06	<0.01
Urban	*ref*	*ref*	
Race and Ethnicity			
American Indian / Alaska Native	0.76	0.73, 0.80	<0.01
Asian, Asian American	1.06	1.03, 1.10	<0.01
Biracial, multiracial, of mixed race	0.70	0.69, 0.71	<0.01
Black and African American	0.81	0.78, 0.84	<0.01
Hawaiian or Pacific Islander	0.70	0.67, 0.73	<0.01
Latino/a, Latinx, Latine	1.26	1.13, 1.42	<0.01
Other	1.04	0.99, 1.10	0.12
White Alone	*ref*	*ref*	
Insurance Stability			
Instability (Any Public Health Ins)	*ref*	*ref*	
Stable	1.15	1.14, 1.16	<0.01

[1] Adjusted Odds (minimally sufficient, as indicated in the DAG) of missing an HPV vaccination opportunity, by rurality (Urban as ref)
[2] OR = Odds Ratio, CI = Confidence Interval

Conclusion

Rurality, race, and ethnicity are significant and relevant factors of HPV-MVO. Using publicly funded health insurance partially mediates the effect of rurality on HPV-MVO and interacts differentially across racial and ethnic groups, highlighting the need for tailored interventions.

Future Direction & Recommendations

To maximize the effectiveness and impact of HPV vaccination efforts among C/As, the unique interplay of rurality, insurance stability, and race and ethnicity should be considered during the intervention and campaign design phases.

With the 1U4U's generous grant, we were able to utilize state IIS records to understand the relationship between rurality and HPV-MVOs and revise our initially proposed model.

Next Steps:

- Update models (**Fig. 4**) Develop spatiotemporal models of HPV-MVO
- Utilize machine learning to develop, review, select, and tune the best-performing HPV-MVO predictive algorithm
- Integrate algorithm(s) into an HPV vaccination chatbot (software simulating conversation)
  - Study Name: ***PROMISE: Predicting HPV Missed Vaccination Opportunities to Improve Cervical Cancer Equity***
    - Aimed at developing *"PIPA" (Personalized Immunization Partner and Assistant)*
    - Breast and Gynecologic Cancers Center Funding
    - Partnership with Biomedical Informatics

FIG. 4. Serial Mediation of Indirect Effect of Race and Ethnicity on HPV-MVO