Resolve to Prevent Cancer: HPV and Adolescent Vaccine Schedules

Michelle I. Silver, Ph.D., ScM

Assistant Professor Department of Surgery Division of Public Health Sciences

Washington University in St. Louis School of Medicine

Cervical* Cancer Is Preventable

- Cause is known (HPV), multiple effective screening and treatment options exist, and prevention is available (vaccine)
- Yet, ~ 660,000 new cases of cervical cancer and 350,000 deaths each year worldwide
 - > 85% occur in low- and middle-income countries (LMICs)
 - ~ 12,000 new cases and 4,000 deaths a year in the US

*I am using cervical cancer as the example here as that is where my research has focused, but much of what I will present applies to other HPV-related cancers as well (oral, anal, vaginal, penile, vulvar)

Cervical Cancer Incidence and Mortality

- Screening primarily accounts for the dramatic reductions in the US and other places with 'organized' screening
- Large disparities in cervical cancer incidence and mortality exist globally, nationally, and locally

National Disparities in Cervical Cancer

- Incidence rate: 7.5 per 100,000 women
- Mortality rate: 2.2 per 100,000 women

	Incidence*	Difference^ (%)	Mortality*	Difference^ (%)
White	7.3	-2.7	2.1	-4.5
Black	8.2	+9.3	3.3	+50.0
Hispanic	9.7	+29.3	2.4	+13.6
American Indian/ Alaska Native	5.8	-22.7	1.6	-27.3
Asian/ Pacific Islander	5.7	-24.0	1.5	-31.8

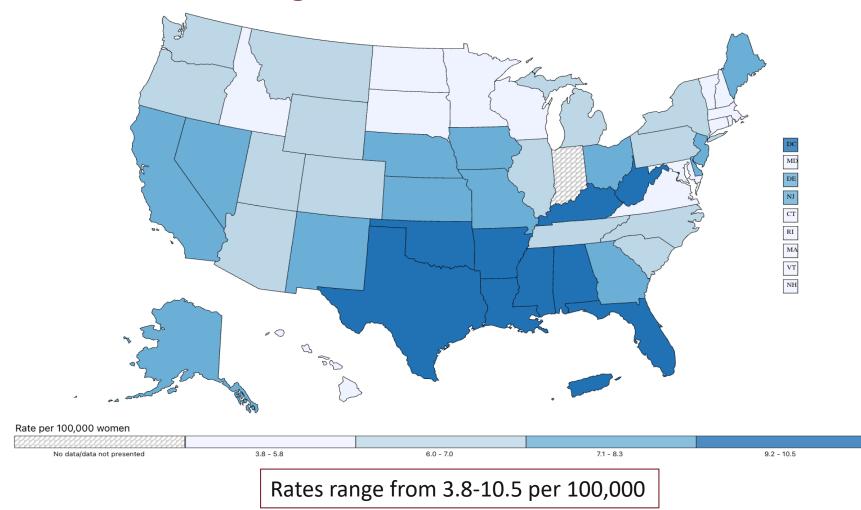
* Per 100,000 women

^ Relative to the national average

U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool, based on 2021 submission data (1999-2019): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; www.cdc.gov/cancer/dataviz, released in June 2022.

🕃 Washington University in St.Louis • School of Medicine

Rate of New Cancers in the United States, 2021 Cervix, All Ages, All Races and Ethnicities



Source - U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; <u>https://www.cdc.gov/cancer/dataviz</u>, released in June 2024.

Cervical Cancer in Missouri

	Incidence*	Mortality*
Missouri	8.9	2.4
White	8.6	2.1
Black	10.3	5.1

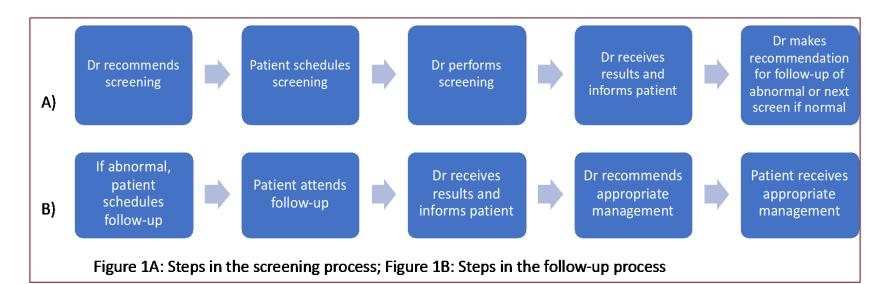
* Per 100,000 women

- Black women in Missouri have <u>20% higher incidence</u> of cervical and <u>243% higher mortality</u> from cervical cancer than white women in the state
 - The disparity is much more extreme here than national rates show
- We know there are still further disparities within the state (i.e.: rural/urban)

Washington University in St.Louis • School of Medicine

What is contributing to these disparities?

- Decades of data show screening test efficacy, particularly when repeated over a lifetime
- If it's not the screening test itself, then there must be other systemic or structural factors influencing this
 - Cost, access, etc.

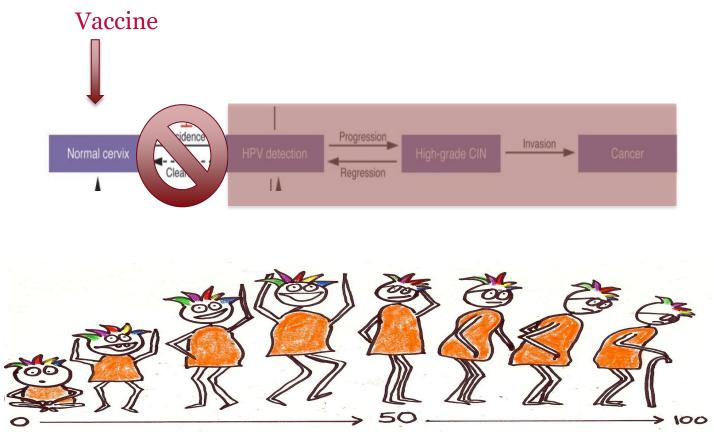


School of Medicine Washington University in St.Louis • School of Medicine

Cervical Cancer Elimination Goals

- WHO has a goal to reduce the incidence of cervical cancer to < 4 cases per 100,000 women in every country by 2030
- To achieve this, they set the 90–70–90 target to:
 - Vaccinate 90% of girls by age 15
 - Screen 70% of women with a high-performance test at least twice by age 45
 - Treat 90% of women identified with cervical precancer or cancer

Cervical Cancer Prevention: Vaccination



Gravitt PE. J Clin Invest. 2012:121(12):4593-99.

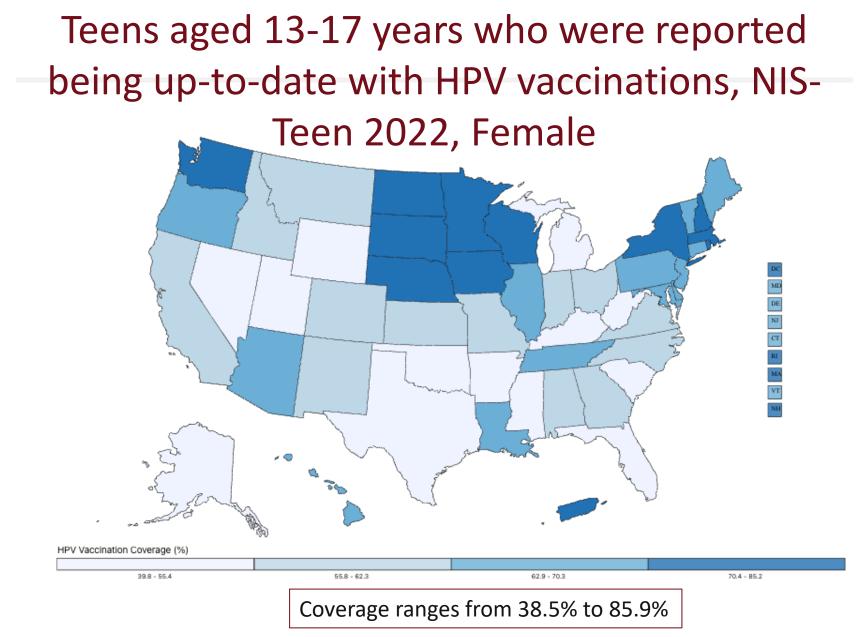
Washington University in St.Louis • School of Medicine

HPV Vaccine

- 2 vaccines licensed in 2006 containing HPV 16 and 18, which cause ~70% of cervical cancers
 - Gardasil4 also contains HPV 6 and 11, which are low-risk (non-carcinogenic) types that cause genital warts
- Newest vaccine (Gardasil9) includes additional 5 high-risk HPV types, potentially eliminating the cause of 90% of cervical cancers
 - Doesn't target many common lower-risk types that can still cause mild Pap abnormalities, but carry virtually no risk of invasive disease

US HPV Vaccine Recommendations

- Current Recommendation in the US: 2 doses if <15 years; 3 doses if 15+
 - Push toward earlier vaccination (9-11 vs 12-13)
- Advisory Committee on Immunization Practices (ACIP) has recommended HPV vaccine initiation at ages 11-12, but American Academy of Pediatrics (AAP) shifted their recommendation earlier—to ages 9-11



Source - U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; <u>https://www.cdc.gov/cancer/dataviz</u>, released in June 2024.

HPV Vaccine Uptake

- In 2022, 60.6% of teens aged 13-17 years who were <u>up-to-date</u> with HPV vaccinations in the United States
 - Decreased from 61.4% in 2020
 - Missouri: 55.9%
- Large disparity in MO between metropolitan statistical areas (MSAs) and non-MSAs (rural areas) for 1+ doses (80% vs. 72%) and being up to date (64% vs. 53%), respectively

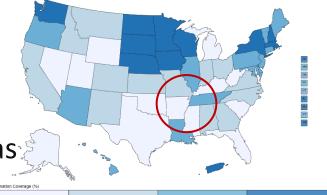
Vaccine Hesitancy Survey

- Goal: To understand the factors driving HPV vaccine hesitancy in areas with particularly low uptake in adolescents
 - Identify characteristics of vaccine hesitant parents
 - Are there factors that make parents more or less likely to vaccinate their children for HPV?
 - In addition to sociodemographics, are there additional factors such as beliefs about vaccines, sources of health information and trust in those sources that influence vaccine decisions?

Survey Methodology

- Survey administered to parents of 9-17 years olds in MO, TN, AR, MS, and Southern IL
- To ensure a diverse sample, we implemented (and exceeded) quotas for accrual:

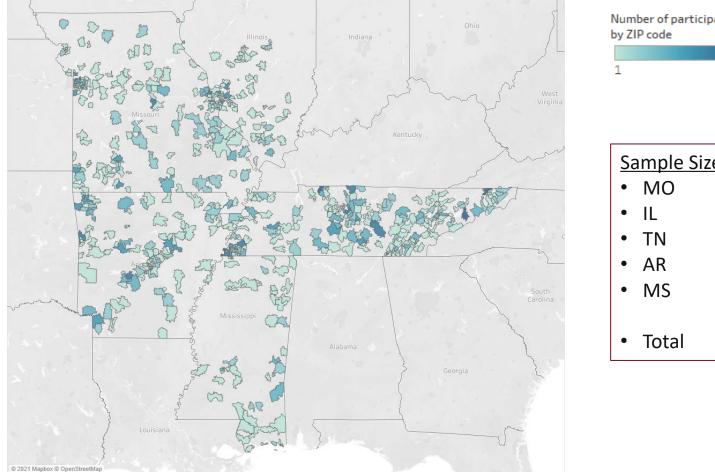
	Goal	Ac	crual
Race			
Non-White	20% (min)	258	25.4%
White	80% (max)	758	74.6%
Geographic Area	3		
Non-urban	30% (min)	324	31.9%
Urban	70% (max)	692	68.1%



Washington University in St.Louis • School of Medicine

Geographic Distribution of Sample

Distribution of Responses



Number of participants

<u>Sa</u>	ample S	ize by State
•	MO	N= 316
•	IL	N=78
•	ΤN	N=363
•	AR	N=193
•	MS	N=66
•	Total	N=1016
<u> </u>		

Washington University in St.Louis • School of Medicine

Participant Characteristics

Parents

- Race: 77% white, 15% black, 9% other race
 - Varied by state from 69-83% white; 9-21% black, 3-13% other race
- Gender: 75% of respondents were female

Children

- Age: Mean= 13, SD= 2.6
- Gender: 51% male, 48% female

Children's Childhood Vaccination Status

	Total	AR	IL	мо	MS	TN
	%	%	%	%	%	%
MMR						
Vaccinated	94.3	96.1	90.6	94.0	92.8	94.7
Tdap						
Vaccinated	93.1	93.7	92.9	92.6	91.7	93.7
Meningococcal						
Vaccinated	86.0	91.2	79.8	85.6	82.1	85.7
Annual flu (20-21)						
Vaccinated	48.3	58.7	42.9	45.7	49.5	46.1
HPV						
Vaccinated	32.1	32.1	35.6	30.9	39.3	31.1

Washington University in St.Louis • School of Medicine

Children's HPV Vaccine Status

	Total	AR	IL	МО	MS	TN
	%	%	%	%	%	%
Yes	32.1	32.1	35.6	30.9	39.3	31.1
Not yet, but planning to	21.7	19.7	21.7	21.9	25.0	21.8
Not yet, I haven't decided	12.2	14.6	8.5	14.7	8.9	10.0
Νο	27.5	26.7	26.4	28.1	25.0	28.3
Don't know	6.5	6.9	7.8	4.5	1.8	8.8

Washington University in St.Louis • School of Medicine

Parental Reasons for Choosing HPV Vaccination

Why did you choose to vaccinate?* (N=531)	N	%
Physician recommendation	413	78
The vaccine is safe and effective	143	27
To prevent genital warts or other disease	81	15
A family member or friend recommendation	56	11
My child is sexually active	17	3
Some other reason	31	6

*select all that apply

Washington University in St.Louis • School of Medicine

Parental Reasons for Not Vaccinating Yet (though they are planning to)

What are some reasons that you have not vaccinated yet?* (N=358)	N	%
My child is not old enough	160	45
I have not scheduled an appointment	119	33
Influences of the COVID-19 pandemic	71	20
My clinic isn't scheduling vaccinations right now	18	5
I haven't had time	18	5
Difficulty due to transportation	12	3
Cost	4	1
Some other reason	24	7

*select all that apply

Washington University in St.Louis • School of Medicine

Parental Reasons for Not Vaccinating Yet (they have not made a decision yet)

What information do you need to make a decision? (N=202)	Ν	%
Information on safety of the vaccine	112	55
A physician's recommendation	98	49
Information on how well the vaccine works	94	47
If it is safe right now during the COVID-19 pandemic	46	23
I want to know what other parents are doing	19	9
My child's school to require it	13	6
Some other reason	24	12
*aplast all that apply		

*select all that apply

Washington University in St.Louis • School of Medicine

Parental Reasons for Choosing Not to Vaccinate for HPV

Why did you choose not to vaccinate?* (N=455)	N	%
My child is not sexually active	155	34
Concerns about safety	140	31
My child doesn't need it	109	24
I didn't know it was recommended for my child	71	16
I don't know what it is	41	9
I am concerned it would lead to my child being sexually active or promiscuous	12	3
We can't afford it	5	1
Some other reason	44	10

*select all that apply

Parent's Knowledge and Beliefs

	Total	AR	IL	MO	MS	TN
	%	%	%	%	%	%
Can HPV vaccine prevent some cancers?						
Yes	57.8	57.5	61.5	59.5	56.1	55.9
No	9.2	5.7	12.8	9.2	7.6	10.5
Don't know/ Not sure	33.1	36.8	25.6	31.3	36.4	33.6
Ideal age for HPV Vaccine?						
Don't know	19.5	21.8	20.5	16.5	21.2	20.4
9	3.9	2.1	6.4	3.5	7.6	4.1
10	4.7	6.2	3.9	5.4	1.5	4.1
11	7.0	6.7	5.1	6.7	6.1	8.0
12	23.9	28.5	28.2	23.7	22.7	21.0
13	12.9	9.3	14.1	14.2	18.3	12.4
14	5.4	5.2	5.1	6.7	3.0	5.0
15	6.9	6.7	5.1	6.3	7.6	7.7
16	4.3	2.6	3.9	4.1	9.1	4.7
17	1.2	1.0	0	2.5	0	0.6
18	6.0	7.3	5.1	5.7	3.0	6.3

Washington University in St.Louis • School of Medicine

Results

- Only 16% of parents thought the ideal age for vaccination was 9-11 years
- <u>19% of children ages 9-12</u> had received at least one dose of HPV vaccine, while <u>52% of 13–17-year-olds</u> had received at least one dose
- 13–17-year-olds were <u>6 times as likely to be vaccinated</u> as 9-12 year olds (OR: 6.01, 95% CI: 3.98-9.08)

Conclusions

- Overall adolescent HPV vaccination rates for survey participants across this 5-state region was 42.3%, which is very low compared to the national average
- Despite recommendations to initiate HPV vaccine at earlier ages of 9-11 years, most parents still believed that 12-15 years (or older) is the ideal age to vaccinate their children
 - Uptake is less than half for 9–12-year-olds compared to 13–17-yearolds
- Efforts are needed to educate both parents and providers on the benefit of earlier age of HPV vaccine initiation





Influences of sociodemographic characteristics and parental HPV vaccination hesitancy on HPV vaccination coverage in five US states

<u>T. Shato ^{a b} A ⊠</u>, <u>S. Humble ^b</u>, <u>A. Anandarajah ^{b c}</u>, <u>A. Barnette ^d</u>, <u>H.M. Brandt ^e</u>, <u>J. Garbutt ^f</u>,

L. Klesges ^b, V.S Thompson ^{c f}, M.I. Silver ^g

The association of caregiver attitudes, information sources, and trust with HPV vaccine initiation among adolescents

Akila Anandarajah 🕿 💿, Thembekile Shato 💿, Sarah Humble 💿, Alan R. Barnette, Heather M. Brandt 💿, Lisa M. Klesges 💿, Vetta L. Sanders Thompson 💿 & Michelle I. Silver 💿 ...show less Article: 2300879 | Received 04 Sep 2023, Accepted 28 Dec 2023, Published online: 04 Jan 2024

Associations of geographic-based socioeconomic factors and HPV vaccination among male and female children in five US states

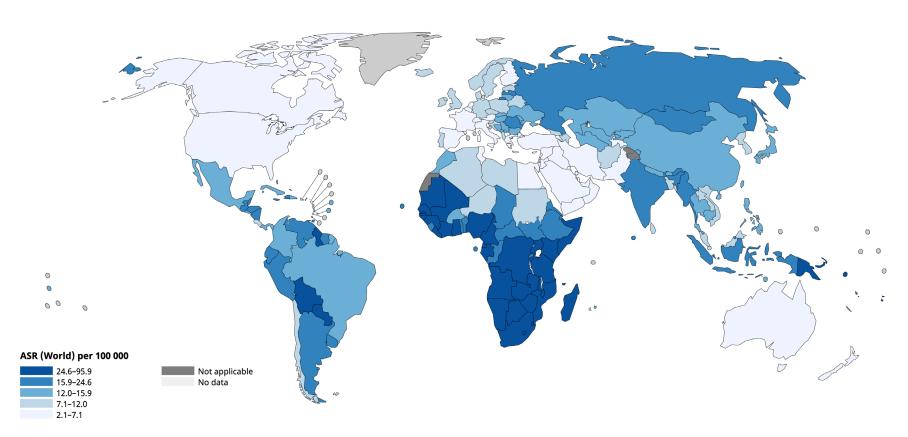
Serena Xiong [⊠], Sarah Humble, Alan Barnette, <u>Heather Brandt</u>, <u>Vetta Thompson</u>, <u>Lisa M. Klesges</u> & <u>Michelle I. Silver</u>

BMC Public Health 24, Article number: 702 (2024) Cite this article

Washington University in St.Louis • School of Medicine

Cervical Cancer Worldwide

Age-Standardized Rate (World) per 100 000, Incidence, Females, in 2022 Cervix uteri



Remember: US range: 3.8-10.5

All rights reserved. The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization / International Agency for Research on Cancer concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate borderlines for which there may not yet be full agreement. Cancer TODAY | IARC https://gco.iarc.who.int/today Data version: Globocan 2022 (version 1.1) - 08.02.2024 © All Rights Reserved 2024 International Agency for Research on Cancer

World Health Organization

Washington University in St. Louis • School of Medicine

Cervical Cancer Worldwide

- > 85% occur in LMICs
- Many factors contribute to this burden including: lack of access to screening and treatment, lack of vaccination, HIV
 - In southern Africa, 64% of women with cervical cancer also have HIV, and survival rates are at least 25% lower with HIV
- WHO 2030 target of 90% of girls vaccinated fully by age 15 worldwide. LMICs, are well below this target.
 - By 2019, only 31% of girls in SSA had received one dose; even fewer had two doses (20%), though coverage varies greatly by country

HPV, HIV, and Cervical Cancer in Zambia

 Table 1: Cervical Cancer, HIV, and HPV Vaccine Statistics in Zambia, Sub-Saharan

 Africa, and the United States ^{1-5,8,29,}

Zambia	SSA	USA
65.5	34.8	6.2
43.4	22.5	2.1
Women: 6% Men: 2.8%	Women: 1.7% Men: 0.7%	Women: <0.1% Men: <0.1%
	31%	75.1%
	20%	58.6%
	65.5 43.4 Women: 6%	65.5 34.8 43.4 22.5 Women: 6% Women: 1.7% Men: 2.8% Men: 0.7% 31%

WHO HPV Vaccine recommendations

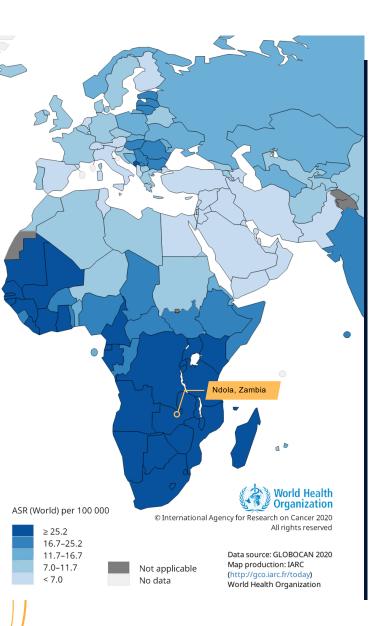
- A one or two-dose schedule for girls 9-14 years old
- A one or two-dose schedule for girls 15-20 years old
- Two doses with a 6-month interval for women older than 21 years
- Immunocompromised individuals should receive at a minimum two doses and where possible three doses
 - Emphasizes importance of prioritizing vaccine for immunocompromised people, including those living with HIV

Reaching for Equity in Adolescent Care through HPV Vaccination



Part of NCI's U01 Consortium on Implementation Science for Cancer Control in People Living with HIV in Low- and Middle-Income Countries

🐷 Washington University in St.Louis • School of Medicine



Study Justification

Cervical cancer is largely vaccine-preventable, but is the leading cause of cancer deaths in Zambia

Cervical cancer burden is unequally borne by women living with HIV

WHO recommends 2-3 dose vaccination schedule for people living with HIV

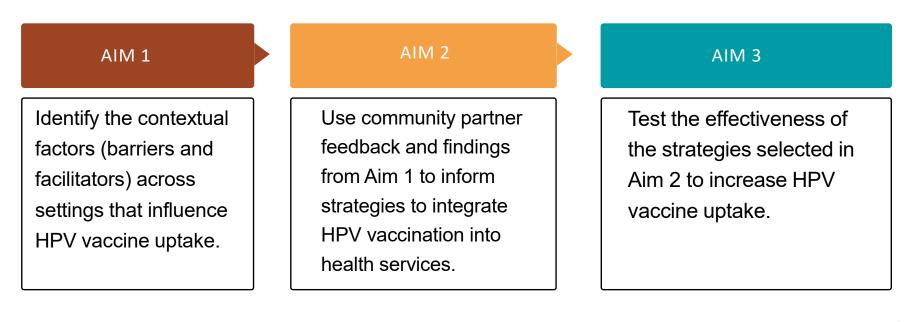
Challenges of introducing extra doses in current school-based and community campaigns



Washington University in St. Louis • School of Medicine

Study Aims

Our study aims to integrate HPV vaccination into adolescent HIV clinics so girls living with HIV can get all needed doses





Project Launch: November 2022

PLOS ONE

Leveraging health infrastructure to optimize HPV vaccination for adolescents in Zambia: Protocol for an implementation study

Sam Miti, Thembekile Shato, Comfort Asante, Ana Baumann, Gershom Chongwe, Patricia M. Bobo, Michelle I. Silver 🐖, Jean M. Hunleth 🕷 🖬

Published: May 9, 2023 • https://doi.org/10.1371/journal.pone.0285031





- Publication of protocol paper
- Two stakeholder kickoff meetings:
 - Participants from 14 organizations at local, district, and provincial levels who work in health, education, HIV care, and other adolescent services
 - Provided project feedback and recommendations for additional stakeholders
 REACH



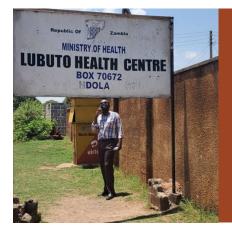
Study Locations

REACH is partnering with three distinct settings in and around Ndola, a city on the Copperbelt:



Urban Pediatric Hospital

Arthur Davison Children's Hospital– Large, Urban tertiary referral hospital with 2nd largest pediatric and adolescent care center in Zambia



Peri-urban Clinic

Lubuto Health Centre- Periurban, lower income residential setting clinic with youth friendly services



Rural Hospital

St. Dominic's Mission Hospital- Rural, primarily agricultural area

Washington University in St.Louis • School of Medicine

Aim 1: Understanding Barriers and Facilitators to HPV Vaccination



School of Medicine Washington University in St.Louis • School of Medicine

Findings: HPV Vaccination by Sites, 2023

	ADCH (urban)	Lubuto (peri-urban)	St. Dominic's Mission Hospital (rural)
HPV vaccination available	Not given/No current allocation from MoH	Yes	Yes
Eligibility		Girls 13-16 years	Girls 14-15, not sexually active
Primary time/place vaccination		Child Health Week (2x per year) / schools	Child Health Week (2x per year) / schools
Vaccination available at clinic upon request	No	Yes, MCH, OPD, ART departments	Yes, MCH department
MoH policy change, eligibility 9-14yrs		Awaiting guidance, as soon as stocks available	Awaiting guidance
Informal changes made b/c of REACH	None	Started vaccination in ART department (clinic-initiated in response to REACH kickoff)	None

Washington University in St.Louis • School of Medicine

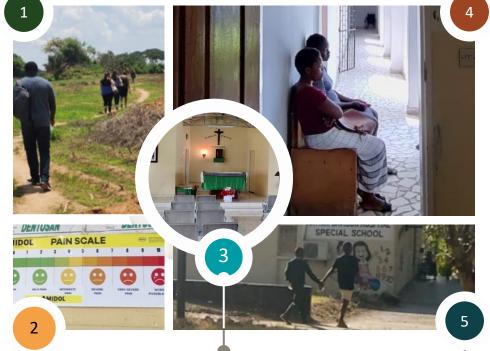
Individual, Household, and Community Level Opportunities and Challenges

Time and distance to clinic

- Responsibilities at home, school, work
- Wait times for services at clinics
- Distance & transportation (esp. rural site)

Information, rumors, and misconceptions

- Limited information on HPV vaccination available to public
- Rumors and misconceptions
 about vaccine
- Outreach and education has shown more willingness to get the vaccine



Trusted community leader influence

- Religious leaders, teachers, and other community leaders influence public opinion
- These leaders are trusted sources and have both encouraged and discouraged vaccination

Parent and family influence

- Parent/guardian consent needed
- Intergenerational discussion on HPV vaccine can be challenging
- Mothers, aunts, elder sisters have shown substantial positive influence

Peer-to-peer influence

- Peers provide information and personal stories to one another
- Peers have swayed decisionmaking to get or avoid the vaccine in schools

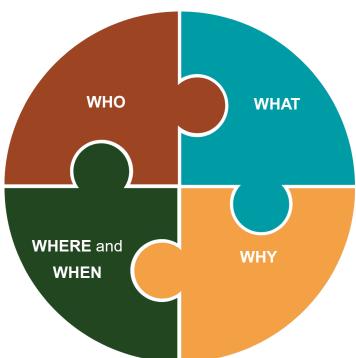


Washington University in St.Louis • School of Medicine

Aim 2: Identify strategies to integrate HPV vaccination into health services

Who are the players, roles, and organizations involved in vaccination and what is coordination between them

Where and when vaccination occurs at study sites and other vaccination locations



What HPV vaccination/ vaccine campaigns entail and what data is collected for monitoring and evaluation

Why isn't everyone getting the vaccines they need? Why are vaccine campaigns succeeding or failing?

THIS WILL LEAD INTO IDENTIFYING HOW TO INCREASE HPV VACCINATION

Washington University in St.Louis • School of Medicine

Acknowledgements

 This research would not be possible without the Vaccine Hesitancy Participants and Study Team and the REACH Participants and Research Team

• Funding:

- <u>Vaccine Hesitancy</u>: NCI supplement to P30 CA091842 and St. Jude Children's Research Hospital including the American Lebanese Syrian Associated Charities
- <u>REACH</u>: NCI U01CA275033 (MPIs: Hunleth, Silver, Miti); Drs. Hunleth and Silver receive further funding for the study from the Foundation for Barnes-Jewish Hospital

Thank You!

Feel free to contact me with questions: <u>michelle.silver@wustl.edu</u>

Washington University in St.Louis • School of Medicine