


**Harnessing What We Know  
About HPV to Eliminate  
Cervical Cancer:  
Putting the Pieces Together for  
Prevention and Treatment**

**Jennifer Young Pierce, MD, MPH**  
**Professor of Gyn Oncology**  
**Division Director, Cancer Control and  
Prevention**



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**Disclosures**

- No disclosures



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**Objectives**

- What are the latest data on HPV and HPV-related cancers?
- What is the latest info on cervical cancer screening?
- What tools are available to increase HPV vaccination?
- What role can you play in eliminating HPV-related disease?



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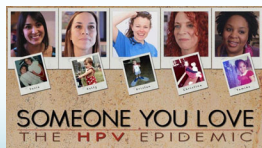
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## Someone you love: The HPV Epidemic

- 80 million adults currently infected with HPV
- 80% chance of infection in your lifetime
- More common than the common cold



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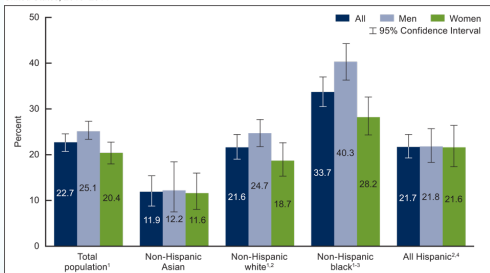
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Figure 4. Prevalence of high-risk genital HPV among adults aged 18–59, by race and Hispanic origin and sex: United States, 2013–2014



<sup>1</sup>Percentage for men is significantly higher than women.  
<sup>2</sup>Percentage is significantly different from non-Hispanic Asian, all, men, and women.  
<sup>3</sup>Percentage is significantly different from non-Hispanic white, all, men, and women.  
<sup>4</sup>Percentage is significantly different from non-Hispanic black, all, men, and women.  
 NOTES: HPV is human papillomavirus. High-risk genital HPV means tested positive to one or more of the 14 high-risk HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, or 68) from a genital swab sample. Percent samples were available only for 2013–2014, so all results presented were limited to that cycle. Access data table for Figure 4 at: [https://www.cdc.gov/nchs/data/tables/nchs2014\\_table.pdf#4](https://www.cdc.gov/nchs/data/tables/nchs2014_table.pdf#4).  
 SOURCE: NCHS, National Health and Nutrition Examination Survey, 2013–2014.



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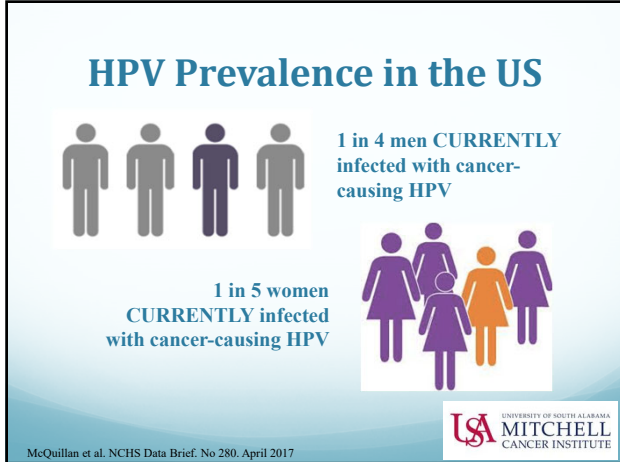
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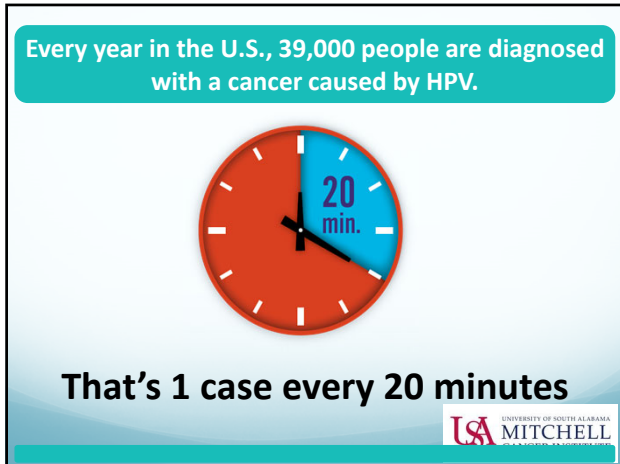
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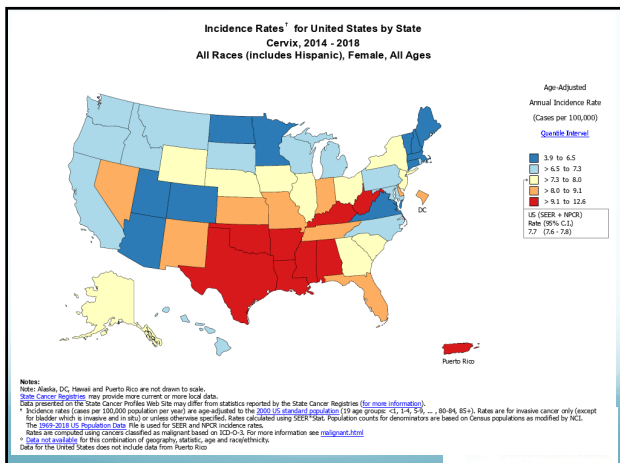
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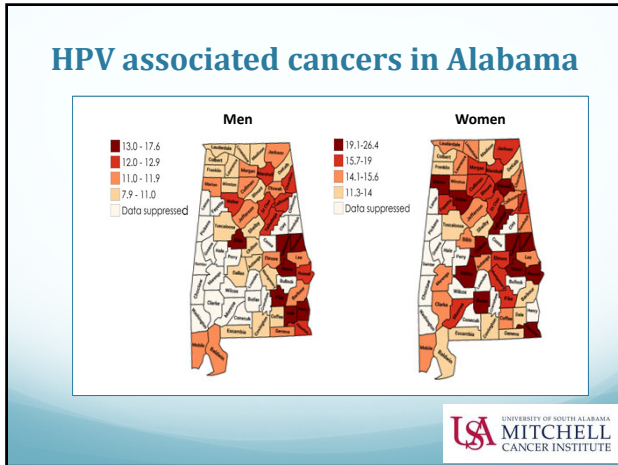
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### HPV cancers in Alabama

HPV-associated Cancer Incidence Rates and Counts for Alabama				
Primary Site Group	by Primary Site Group, by Sex, 2012-2015			
	Female		Male	
	Rate	Count	Rate	Count
Cervix	9.2	942	N/A	N/A
Vagina	0.6	73	N/A	N/A
Vulva	2.0	243	N/A	N/A
HPV-associated Oropharynx*	2.1	254	9.2	1,038
Anus	1.7	216	1.1	115
Rectum and Rectosigmoid Junction	0.4	52	0.2	24
Penis	N/A	N/A	0.9	89

Rates are per 100,000 and age-adjusted to the 2000 U.S. (19 age groups) standard.  
 Rates and counts are for malignant tumors only.  
 \* Includes the following ICD-O-3 site codes: C019, C024, C028, C051, C052, C090, C091, C098, C099, C100, C101, C102, C104, C108, C109, C140, C142, and C148.  
 All cancer sites other than cervix were limited to squamous cell carcinomas only meaning ICD-O-3 histology codes 8050 to 8084 and 8120 to 8131.  
 Source: Alabama Statewide Cancer Registry, 2018.

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### Cervical pre-cancer in U.S. females

- 1.4 million new cases of low grade cervical dysplasia
- 330,000 new cases of high grade cervical dysplasia

Koshlitz Sex Transm Dis. 2004.  
Schiffman Arch Pathol Lab Med. 2003.

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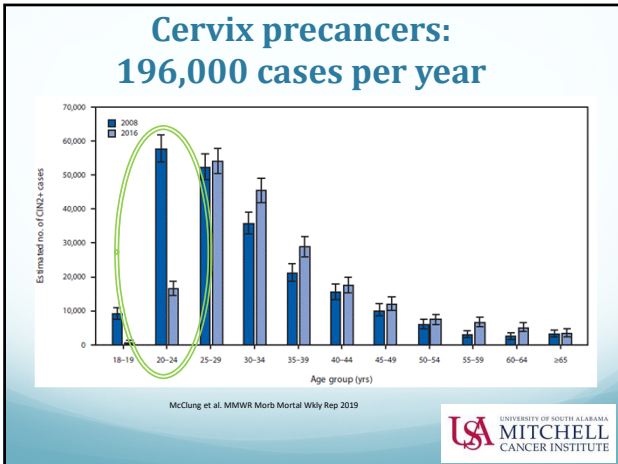
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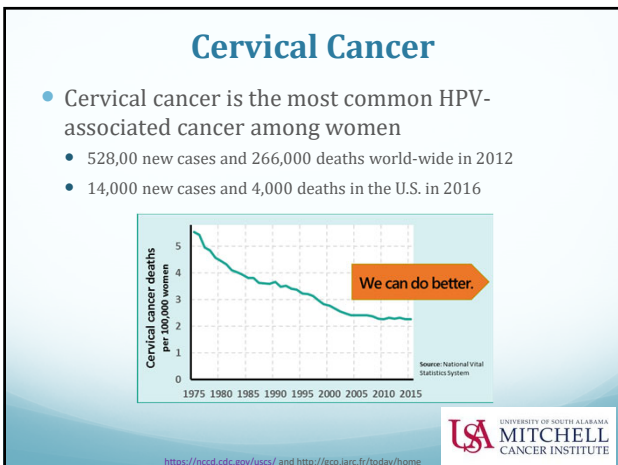
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## Objectives

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## Patient Case

- 36 yo F G3P3 presents for annual gyn. No complaints.
  - Previous paps in 2017 & 2020: negative cytology, HPV+
  - Pap performed at visit
- Pap results: Negative, HPV +
- What do you do now? What is something you should be concerned about?



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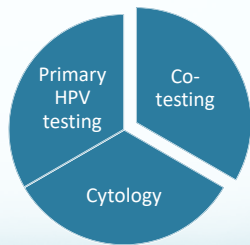
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## We need management strategies that match our screening options

- 3 screening options available
- Management options needed to be versatile enough to apply to any of the three options



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### Negative cytology: the great pretender

- HPV and cytology predict risk on date of screening
- Only HPV predicted 5-year risk of CIN3 and cancer

Katki et al, *J Low Genit Tract Dis*, 2013

Dillner J et al. *BMJ* 2008; 377:a1754.

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### HPV 16/18 Testing

RISK STRATIFICATION USING HPV Types 16 and 18: Portland Study Findings.<sup>1,2</sup>

- CIN3+ identified in 21% of cytology-negative, HPV 16-positive women at 10-yr. follow-up
- CIN3+ identified in 18% of cytology-negative, HPV 18-positive women at 10-yr. follow-up
- CIN3+ identified in only 1.5% of all other cytology-negative, high-risk HPV positive women at 10-yr. follow-up

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### Cervical Adenocarcinoma

HPV detected in 93%<sup>1</sup>

63% of adenocarcinoma followed an initial HPV positive, cytology – negative result.<sup>2</sup>

1. Castellsaque X, et al. 2006
2. Katki HA, et al. 2011

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## New ASCCP app: Guiding principles



- HPV based testing is the basis for risk estimation (primary hpv testing or cotesting)
- Personalized risk based management is possible with knowledge of current results and past history
- Guidelines allow updates to incorporate new test methods as they are validated and to adjust for decreasing cin3+risks as more patients who received hpv vaccination reach screening age
- Colposcopy practice must follow guidance detailed in the ASCCP colposcopy standards

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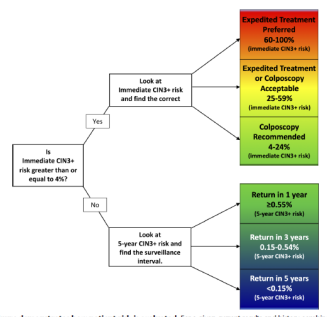
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## Clinical action thresholds & Corresponding Risk Strata



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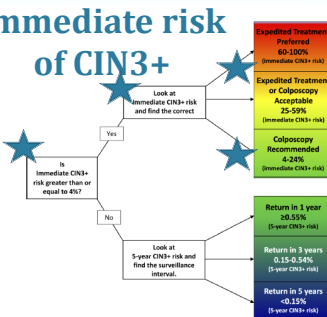
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## Immediate risk of CIN3+



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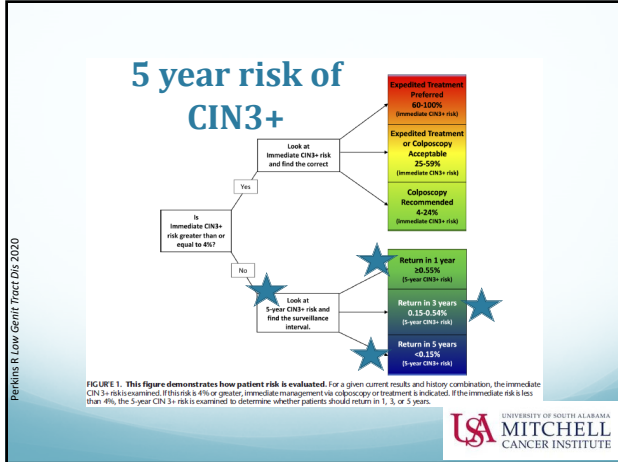
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### Women <25 years old *a whole different ball of wax*

- 2006 HPV vaccination became available
- Likelihood of a non16/18 HPV infection when abnormalities noted
  - More likely to regress
  - Less likely to make cancer or move quickly
- Risk estimates are challenging here
- Cervical cancer rare; HPV prevalent
- High grade lesions are prevalent & likely to regress

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### Improve follow-up!

- Counsel patients on abnormal results
- Postpartum discharge paperwork → reminder to follow-up.
  - Schedule appointment before discharge
- GYN or surgical coordinators:
  - Can keep a list of abnormal paps for colpo clinic.
  - Ensure patients have appointment set up
  - Navigate no shows
- Recommend HPV vaccination after treatment

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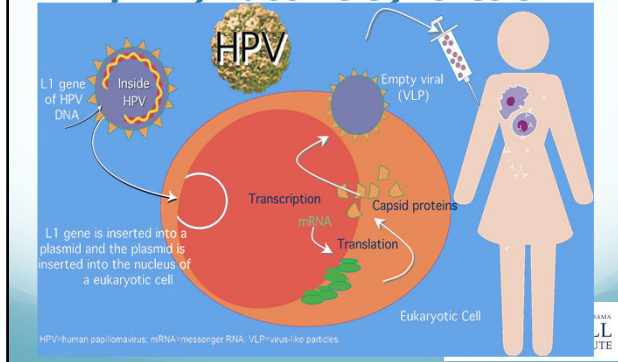
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## HPV L1 Virus-Like Particle (VLP) Vaccine Synthesis



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## HPV Vaccines

Gardasil (HPV4)	Gardasil-9 (HPV9)	Cervarix (HPV2)
Merck & Co.	Merck & Co.	GlaxoSmithKline
Quadrivalent 6,11,16,18	Nanovalent 6,11,16,18,31,33,45,52,58	Bivalent 16,18
70% of HPV related cancers 90% Genital warts	90% HPV related cancers 90% Genital warts	70% HPV related cancers
Females, aged 11-12; can get as early as 9 and up to age 26		
Males, aged 11-12; can get as early as 9 and up to age 26		(Not licensed by FDA for males)

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## HPV Vaccination is Recommended at Age 11 or 12 Years

**Girls & Boys can start HPV vaccination at age 9**

**Preteens should finish the HPV vaccine series before their 13<sup>th</sup> birthday**




Plus girls 13-45 years old who haven't started or finished HPV vaccine series



Plus boys 13-45 years old who haven't started or finished HPV vaccine series

Meites et al. MMWR. 2016.



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## HPV Vaccination is Safe

- HPV vaccine safety studies have been very reassuring
  - 106 studies on 2.5 million people in 6 countries
  - As safe as every other vaccine
- To date, we have not observed any signal that shows that HPV vaccination causes...
- Clinicians can reassure parents who may have concerns, that HPV vaccination is safe.

<https://www.cdc.gov/vaccines/imz/iac/vaccines/hpv/hpv-safety.html>



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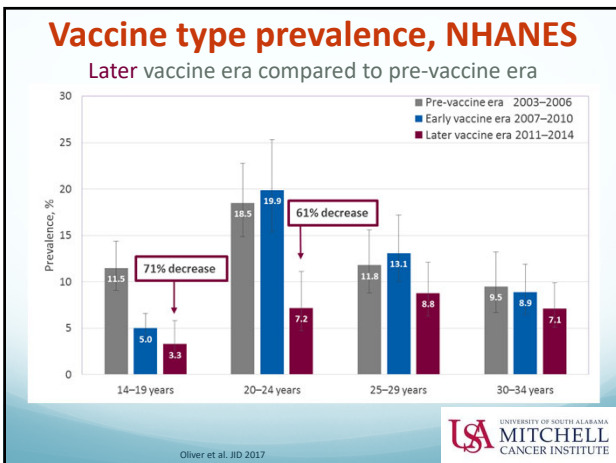
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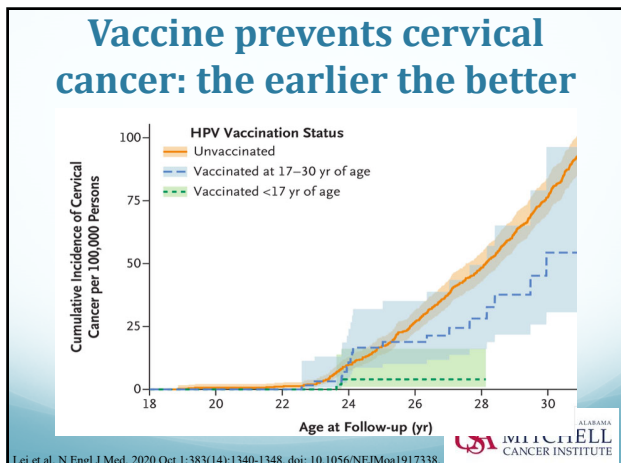
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### Population based study in Finland

End-point	HPV-vaccinated women (33 792 person years)		Non-HPV-vaccinated women (174 340 person years)	
	n	Rate (95% CI)	n	Rate (95% CI)
<b>Cervical cancer</b>				
HPV16	0	–	9	5.2 (2.7 to 9.9)
HPV18	0	–	2	1.1 (0.3 to 4.6)
HPV16/18	0	–	11	6.3 (3.5 to 11.4)
HPV33	0	–	2	1.1 (0.3 to 4.6)
HPV45	0	–	1	0.6 (0.1 to 4.1)
HPV52†	0	–	1†	0.6 (0.1 to 4.1)
Any HPV	0	–	14	8.0 (4.8 to 13.6)
<b>Vaginal cancer</b>				
HPV16	0	–	1	0.6 (0.1 to 4.1)
<b>Vulvar cancer</b>				
HPV52†	0	–	1	0.6 (0.1 to 4.1)
<b>Tongue cancer</b>				
HPV213	0	–	1	0.6 (0.1 to 4.1)

Lehtinen et al. BMJ Open. 2021 Dec 30;11(12):e050669. ALABAMA CANCER INSTITUTE

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### Vaccination protects against Cancer!

Malignancy	HPV Vaccinated Women		Non-HPV vaccinated Women	
	Person years	n	Person years	n
Cervical cancer	65,656	0	124,245	8
Vulvar cancer	65,656	0	124,245	1
Oropharyngeal cancer	65,656	0	124,245	1
Other HPV cancers	65,656	0	124,245	0
<b>All HPV cancers</b>	<b>65,656</b>	<b>0</b>	<b>124,245</b>	<b>10</b>
Breast cancer	65,656	2	124,245	10
Thyroid cancer	65,656	1	124,245	9
Melanoma	65,656	3	124,245	13
Non-melanoma skin cancers	65,656	2	124,245	3
<b>Total</b>	<b>65,656</b>	<b>8</b>	<b>124,245</b>	<b>45</b>

Luostarinen et al. Int J cancer. 00,00-00 (2018). ALABAMA CANCER INSTITUTE

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## What about...

- Efficacy in HPV + women<sup>1</sup>
  - 100% effective in preventing CIN 2/3 from vaccine viral types for neg women
  - 94% effective in preventing vulvar/vaginal disease
  - Colposcopy or post appt – 40-45% reduction in recurrence in vaccinated population, Huh et al 2010
- Women aged 24-45<sup>2</sup>
  - Study of 3819 women
  - 67% naïve to 6,11,16,18
  - Only 0.7% of women + for >1 vaccine viral types

1. FUTURE II Study Group. *J Infect Dis* 2007; 196: 1438.  
 2. Makhija S, FUTURE III Investigators. *Gyn Oncology* 2008, abstract.



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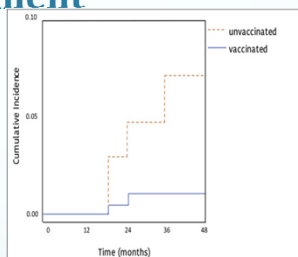
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## HPV vaccination after treatment

- Gheraldi et al Dec 2018
  - Prospective cohort study 20-45
  - Received 1<sup>st</sup> dose 1 month post LEEP, 2 subsequent doses
  - Patients self-selected cohort
  - 248 vaccinated – 2 recurred
  - 276 followup only – 11 recurred
- 81.2 % reduction in recurrence with vaccination

Gheraldi et al. *Gyn Onc* Dec 2018



CIR (respective of causal HPV type (CN2-))			
	V-group	NV-group	% risk reduction in rate with vaccine
No. of evaluable women	137	139	
No. of women with CIR	7	11	81.2%
recurrence rate (%)	1.2	6.4	[95% CI: 34.3-95.7]

Legend: CIR, clinical disease relapse; V-group, vaccinated patients; NV-group, unvaccinated patients. Impact of quadrivalent HPV vaccine on incidence of subsequent disease relapse among women who had undergone cervical conization. 95%CI confidence interval of the estimate.

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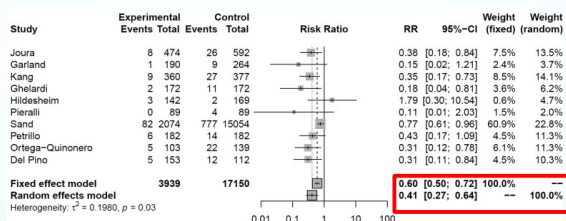
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## HPV vaccination after treatment

\*off label use\*



- 2020 meta-analysis
  - All studies looking at prophylactic HPV vaccination just before or just after conization
  - Overall RR reduction 59% in favor of vaccination



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## Global elimination

- In May 2018, the WHO Director-General announced a global call for action to eliminate cervical cancer, underscoring renewed political will to make elimination a reality and calling for all stakeholders to unite behind this common goal.
  - For the first time ever, the world has committed to eliminate a cancer
- In August 2020 the World Health Assembly adopted the [Global Strategy for cervical cancer elimination](#).
  - Vaccinate 90% of girls with HPV vaccine by age 15
  - Screen 70% of women using high performance test by age 35 and 45
  - Treat 90% of women with pre-cancer and 90% with invasive cancer
  - Reach and maintain an incidence rate of below 4 per 100,000 women
  - Lowers cervical cancer incidence by 97% by 2120
    - 62 million deaths averted

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### Life Course Approach to Cervical Cancer Prevention and Control

Primary Prevention	Secondary Prevention	Tertiary Prevention
<b>Girls 9-14 years</b> • HPV vaccination <b>Girls and boys, as appropriate</b> • Health information and warnings about tobacco use • Sexuality education tailored to age & culture • Condom promotion/provision for those engaged in sexual activity • Male circumcision	<b>Women &gt; 30 years of age</b> • "Screen and treat" – single visit approach • Point-of-care rapid HPV testing for high risk HPV types • Followed by immediate treatment • On site treatment	<b>All women as needed</b> Treatment of invasive cancer at any age and palliative care • Ablative surgery • Radiotherapy • Chemotherapy • Palliative Care

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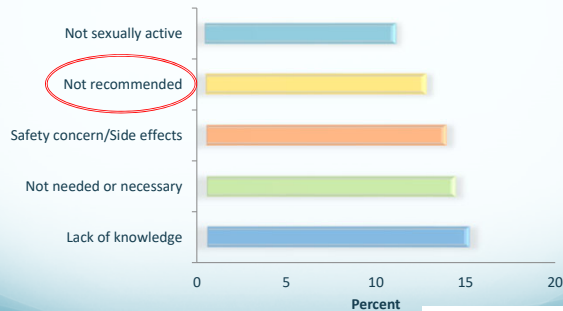
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## Reasons parents won't initiate HPV vaccination for children



Stokley et al. MMWR. 2014.



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## Give an Effective Recommendation to Receive HPV Vaccine

- *An effective recommendation from you is the main reason parents decide to vaccinate*
- Many moms in focus groups stated that they trust their child's doctor and would get the vaccine for their child as long as they received a recommendation from the doctor
- Moms also reported information from their own physician would have helped them to decide

Smith et al. Vaccine. 2016. Unpublished CDC data, 2013.



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## Increasing HPV vaccine rates in your practice

- Educate entire staff on the importance
  - Make sure that everyone is on board and all concerns are addressed
- Know the billing codes and stock the vaccine
- Advertise – have posters up and flyers ready



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## Identify Patients: Take a good history

- Make sure HPV vaccination status is on your intake/history form as well as for each annual exam – up to age 40
- Find a place to document this in the chart/standard H&P or annual note
- Make sure to ask about series completion not just initiation
  - HPV vaccine series can be completed AT ANY TIME from last dose, you don't need to start over
  - HPV vaccine series can be completed WITH ANY VACCINE, you don't need to do HPV-9 x 3
  - Completion is always recommended for maximum protection
  - Vaccinate regardless of HPV status



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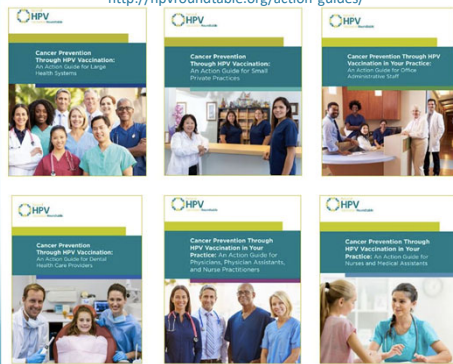
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## National HPV Roundtable Action Guides

<http://hpvroundtable.org/action-guides/>



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## Championing the HPV Vaccine

- Obvious
  - Giving presentations to groups of doctors, patients, parents
  - Sharing medically factual information on social media
- Maybe not so obvious
  - Policy change to encourage vaccination
    - Start with advocating for pharmacists to be able to give HPV to all without a script
  - Coalition building through cancer center networks and others



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## Linda Hayes – survivor turned Cervivor


- Survivors sharing their stories
  - Pair with or educate community health workers
- Meeting communities where they are
  - Reimbursing CHW for their time and/or travel
  - Making sure FQHC and other community health centers look like places you would want to receive care
  - Address inequitable care and local CHC and FQHC work on relationships with their communities

Linda's Story – A Cervical Cancer Advocate Educates Her Community



August 15, 2023

Meet Linda Hayes, an advocate channeling her experience to educate and inspire her community in Chambers County, Alabama.



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## Work in Alabama

- Alabama Adolescent Immunization Task Force
  - Provider education
    - Webinar/video conf/AFIX visits to all AAP AAFP
    - In office education and QI with Vax2stopcancer
    - Dental education just beginning
- Public awareness
  - Wipeout Cervical cancer Initiative
  - Billboards
  - Social media
  - GO Teal and White Campaign
- Policy change
  - Insurance coverage for older adults
  - HEDIS measures for adolescent vaccination
  - Requiring immunization registry input by VFC providers



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**Partners in Non-Physician Settings**

- Schools
  - School nurses
  - School physicals
- Pharmacies
- Dentists
- Outreach opportunities
  - Alabama HOPE project
  - Mobile Health Units
- Public health partners
  - ADPH Cancer control Division
  - ADPH Immunization Division



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**Conclusions**

- The burden of HPV-related disease is starting to decline globally but there is more to do!
- Decreasing mortality from cervical cancer
  - Increase HPV testing
  - Improve follow-up by utilizing Breast and cervical program
  - Vaccinate after treatment
- Championing the HPV vaccine
  - Start in your own practice
  - Use social media, traditional media, and small media to increase awareness and knowledge
  - Build partnerships in your community – dentists, pharmacies, peds
  - Be a resource to your patients on HPV related disease and risk
  - Evaluate and advocate for policy change at all levels that will increase HPV vaccination



62

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**Questions?**

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