





## Cervical Cancer: Latest Update on Screening and Prevention

**Satellite Conference and Live Webcast**  
**Wednesday, June 26, 2019**  
**1:00 – 3:00 p.m. Central Time**

Produced by the Alabama Department of Public Health  
 Video Communications and Distance Learning Division

## Faculty

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### Outline

- ▶ Cervical cancer in Alabama
- ▶ Screening for Cervical cancer
- ▶ How can you provide more services to underserved women?
- ▶ Prevention of Cervical cancer through vaccination

CANCER PREVENTION & CONTROL PROGRAM

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## Cervical Cancer

- ▶ 13,240 new cases in 2018
- ▶ 4,170 deaths related to cervical cancer
- ▶ Risk factors:
  - HPV high risk positivity
  - HIV or other immunosuppression
  - Smoking
  - Poor access to care, no recent screening

Jemal et al Cancer Statistics 2014

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## Cervical Cancer in Alabama 2017

**Alabama ranks 5<sup>th</sup> in cervical cancer incidence (new cases) and 1<sup>st</sup> in cervical cancer mortality (deaths) in the United States.**

	Alabama		United States	
	Incidence	Mortality	Incidence	Mortality
ALL Women	<b>8.6</b>	<b>3.2</b>	7.6	2.3
White	8.2	2.7	7.2	1.9
African American	<b>10.6</b>	<b>5.2</b>	10.2	4.6

Note: Rates are per 100,000 and age-adjusted to the 2000 US Standard Population. Data years include 2002-2006. Rank is determined by lowest number being the worst and highest number being the best. Ranks only include state registries meeting NAACCR high quality data criteria. Data Source: Data as of June 2009 reported by NAACCR as meeting high quality standards for 2002-2006 and include data from state and provincial cancer registries participating in SEER, NPCR, or both, in the U.S. and the Canadian Cancer Registry in Canada and underlying United States mortality data provided by NCHS ([www.cdc.gov/nchs](http://www.cdc.gov/nchs)). ACS 2009 Supplemental Data.

Hurley DM, Ehlers ME, Balick-Aldrich SW, et al. Cervical Cancer in South Carolina: Epidemiologic Profile. South Carolina Central Cancer Registry, Columbia, SC: South Carolina Department of Health and Environmental Control, Office of Public Health Statistics and Information Services, Central Cancer Registry, September 2009.

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### Case #1

- ▶ 32 yo F G2P2 presents with a new pap of squamous cell carcinoma
  - Last pap was 4 years ago – ASC–H
  - No symptoms
  - Normal periods
- ▶ Could this have been prevented 4 years ago?
  - What was her HPV status?
  - Did she even come in for follow-up?
  - What else could have been done after treatment?

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Screening detects CIN3 (“pre-cancer”)

↓

Treating CIN3 prevents cancer

↓

Goal of screening is to detect CIN3 and *prevent* cervical cancer

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### Current Guidelines

Saslow, JLGTD 2012.

Screening Population	ACS/ASCCP/ASCP/ACOG Recommendations (2012)
Age <21 years	No screening
Age 21–29 years	Pap test alone (no HPV test) every 3 years
Age 30–65 years	Pap + HPV co-test every 5 years recommended Pap test alone every 3 years acceptable
Age >65 years	No screening if: • Adequate prior screening • No history of CIN2+ in the past 20 years • No history of in utero DES exposure or immunocompromise
Post-hysterectomy	No screening if: • Cervix removed • No history of CIN2+ in the past 20 years • NOTE: Evidence of adequate prior screening NOT required

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### Long-term persistent HPV is especially high risk

- 8,656 women age 20–29
- Co-testing years 1 & 3
- Followed 12 years for CIN3+
- Risk of CIN3+
  - Persistent HPV16±: 47%
  - Persistent HPV±: 19%
  - HPV–: 2%
- **HPV history is an important risk modifier**

Kjaer, J Natl Cancer Inst 2010.

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### All women with persistent High risk HPV develop CIN 2 or greater

Elfgrén, AOG 2017.

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### Comparison of Three Screening Strategies

ATHENA trial  
 ≥ 25yo, 42,209 women  
 3-year cumulative incidence rate of CIN3+

	Risk of CIN3+ if negative (%)	Sensitivity (%)	Specificity (%)
Cytology alone	0.8 (0.5-1.1)	47.8 (41.6-54.1)	97.1 (96.9-97.2)
Cytology + HPV cotest	0.3 (0.1-0.6)	61.7 (56.0-67.5)	94.6 (94.4-94.8)
Primary HPV	0.3 (0.1-0.7)	76.1 (70.3-81.8)	93.5 (93.3-93.8)

**Conclusions:**  
 -Greater number of CIN3+ cases detected with primary HPV screening or cotesting  
 -Greater reassurance of low CIN3 risk with a negative hrHPV test vs negative pap test  
 -Able to predict future risk of CIN with HPV testing

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Wright TC et al Gyn Onc 2014

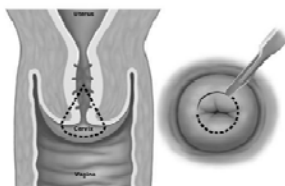
### Observational Studies

- ▶ Meta-analysis
  - 4 RCTs cotesting vs. cytology+ 1 RCT hrHPV vs. cytology
  - Including hrHPV → 40% decrease incidence of ICC
- ▶ 4 cohort studies
  - Similar findings to RCT
  - hrHPV- → very low rates of CIN3+ regardless of cytology results
  - Minimal risk of missing ICC with negative hrHPV or cotest

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

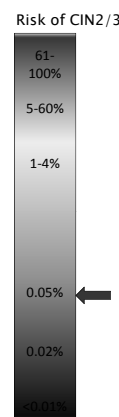
- ▶ 1.4 million new cases of low grade cervical dysplasia
- ▶ 330,000 new cases of high grade cervical dysplasia
  - 30% will progress
  - LEEP vs Cone
  - Follow-up



Kostian et al. *Preventive Medicine* 2004.  
 Schiffman *Arch Pathol Lab Med*, 2003.

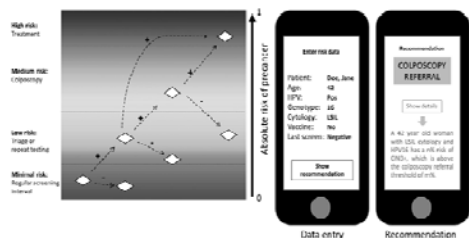
### New ASCCP risk-based guidelines

- ▶ Patient's current test results and past history
- ▶ Risk matrix is used to calculate her risk of CIN2/3
- ▶ Computer program generates risk score
- ▶ Recommends next step in management



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### New ASCCP risk-based guidelines

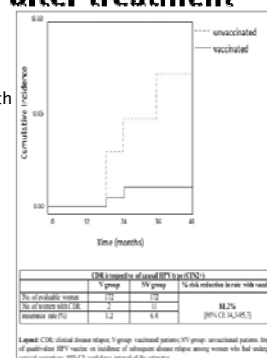


Schiffman, *J Lower Genit Tract Dis* 2017

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### HPV vaccination after treatment

- ▶ Gheraldi et al Dec 2018
  - Prospective cohort study 20-45
  - Received 1st 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

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## Placing Screening Strategies in Context

- ▶ Different strategies may be needed to further decrease cervical cancer incidence and mortality in these areas/populations
- ▶ Self-sampling with primary hrHPV testing
  - Particularly in under-screened populations with low interaction with the healthcare system

CERVICAL CANCER	NEW CASES	DEATHS
WORLDWIDE (2018)	569,847	111,394
AMERICAN CANCER SOCIETY (2015)	13,249	4,170



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## Current cervical cancer screening best practice

- ▶ HPV testing plus Pap over 30
  - NOT reflex – need to know the HPV status of nl pap
- ▶ HR HPV + – look hard for disease
- ▶ Consider “look and LEEP” strategy for HSIL paps
- ▶ Consider vaccination after treatment
- ▶ Await upcoming screening guidelines

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- ▶ Alabama received a grade of “F” as an overall grade in women’s health and ranked 50<sup>th</sup>

SUBJECT AREA RANKINGS AND GRADES: WOMEN'S HEALTH OUTCOMES

STATE	Health Outcomes		STATE	Health Outcomes	
	Rank	Grade		Rank	Grade
Alabama	50	F	Montana	15	B
Alaska	79	C	Nevada	31	C
Arizona	20	B	New Hampshire	20	C
Arkansas	45	F	New Jersey	9	A-
California	14	D	New Mexico	28	C
Colorado	8	A	New York	17	B
Connecticut	3	A	North Carolina	29	C
Delaware	27	C	North Dakota	7	A
Florida	73	C+	Ohio	40	D+
Georgia	36	D	Oklahoma	46	D-
Hawaii	4	A	Oregon	25	C+
Idaho	32	D+	Pennsylvania	37	D
Illinois	21	C+	Rhode Island	19	B-
Indiana	58	D	South Carolina	49	D-
Iowa	12	D+	South Dakota	7	A-
Kansas	31	D+	Tennessee	44	F
Kentucky	42	F	Texas	35	D
Louisiana	43	F	Utah	13	B+
Maine	31	D	Vermont	11	B+
Maryland	22	C+	Virginia	18	B
Massachusetts	5	A	Washington	21	C
Michigan	42	F	West Virginia	42	F
Minnesota	1	A+	Wisconsin	12	B
Mississippi	47	F	Wyoming	23	D+
Missouri	29	D-			

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## High incidence and mortality rates of cervical cancer despite high participation in screening.

- Disconnect between screening and mortality
- ▶ New Tools:
  - HPV vaccination (lower than ideal)
  - HPV testing
- ▶ Opportunities available to partner with APDH and others for coverage, follow-up

Scarinci IC, Garcia FAR, Kobetz E, Partridge EE, Brandt HM, et al. Cervical cancer prevention: New tools and old barriers. Cancer 2010 Jun 1;116(11):2531–42.

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## Alabama Breast and Cervical Early Detection Program

- ▶ State and Federal dollars to improve access to screening and diagnostic services for women by defraying the cost of these services from the patient.
- ▶ ADPH provides: patient recruitment, targeted outreach, population health and systems change implementation services, professional development and provider outreach and support services
- ▶ Selecting patients for ABCEDP
  - Women have to qualify financially and be approved
  - Must occur prior to screening appointment
  - Can include uninsured and underinsured
  - Have to be reapproved every year
  - Reimbursement is at Medicare rate

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## ABC Coverage

- ▶ Clinical breast examinations
- ▶ Screening tests:
  - Pap
  - Pelvic examinations
  - HPV testing
  - Mammogram
- ▶ Follow-up testing:
  - Cervical: colposcopy, biopsies, LEEP, conization
    - \*if precancer or cancer is found, pt qualifies for emergency Medicaid to cover cost of treatment
  - Breast cancer: repeat imaging, ultrasound, biopsy
    - \*if precancer or cancer is found, pt qualifies for emergency Medicaid to cover cost of treatment

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## Also covered

- ▶ Counseling visit for all high grade abnormal pap tests and colposcopy results
- ▶ LSIL pap results / CIN 1 biopsy results not covered for separate counseling visit
  - Follow-up plan for LSIL/CIN 1 is repeat HPV test in 1 year
- ▶ LEEP or conization procedure, as indicated
- ▶ Referral to treatment and patient navigation services

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## Women who qualify for BCN also qualify for the Wise women Program.

- ▶ Services covered include:
  - Heart disease, stroke, and diabetes risk factor screening
    - BP
    - Weight/BMI/waist & hip circumference
    - Lipid panel, HbA1c, glucose
    - Health behavior assessment
  - Referral and follow-up
  - Counseling and links to community programs for nutrition, physical activity, and tobacco cessation resources

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## What's at Stake

- ▶ Higher Mortality rates for breast and cervical cancers in Alabama
- ▶ Higher Incidence rates
- ▶ Increased late stage diagnosis of cancers
- ▶ Ability to treat some preventable cancers
- ▶ All people having the ability to have better health outcomes

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## What needs to happen?

- ▶ Increased number of women enrolled in ABC prior to screening
- ▶ Increased number of Wise Woman participants
- ▶ Increased treatment of preinvasive disease
- ▶ Increased follow-up of abnormal paps (due to patient coverage and navigation)
- ▶ Increased number of colposcopy providers in Alabama

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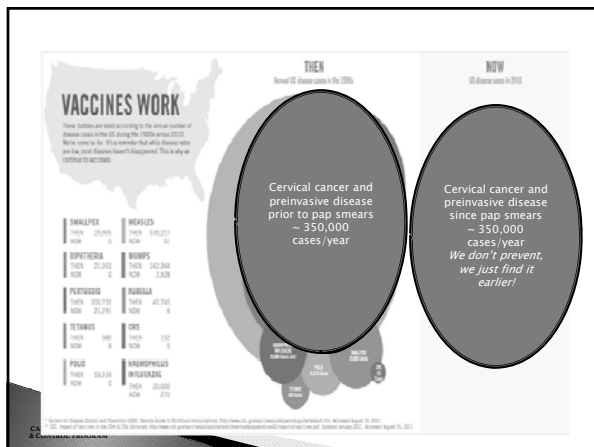
### Case #2

- ▶ 27 yo F G4P4 with a pap of HSIL and biopsy proven squamous cell carcinoma
  - On visualization of the cervix she has a 8 cm lesion on anterior lip of cervix
  - Pelvic exam, consistent with parametrial extension
  - Imaging confirms Stage IV diagnosis
- ▶ How could this have been prevented?
  - Age at first pregnancy was 16
  - Gardasil recommended at age 11-12 up to age 26

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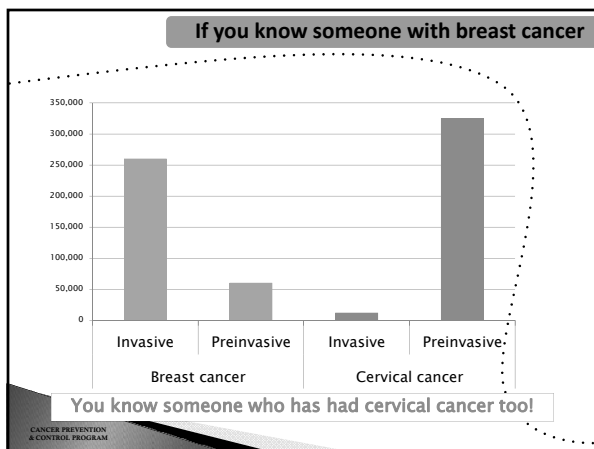
### HPV vaccine myth #1

Cervical cancer is just not as big a deal as other vaccine preventable diseases



### HPV vaccine myth #2

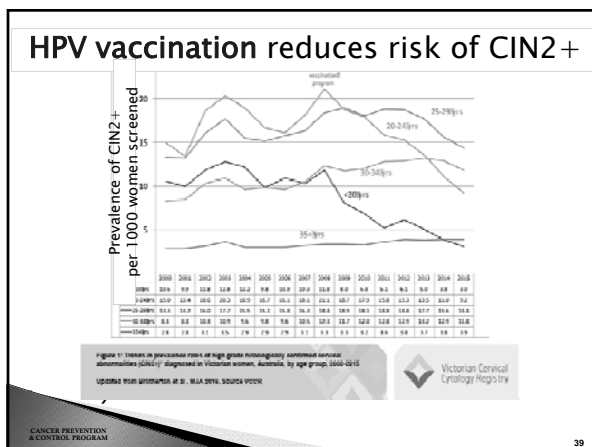
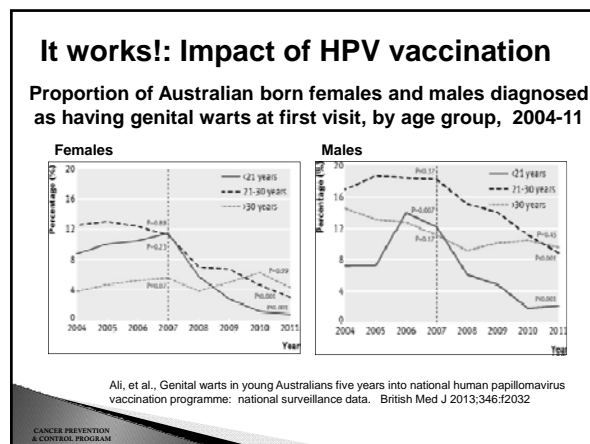
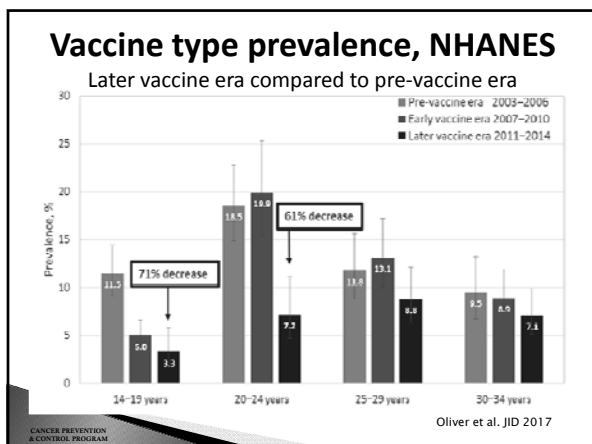
I don't know anyone with cervical cancer. It's pretty rare.



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### HPV vaccine myth #3

There's not enough time to be sure it works.



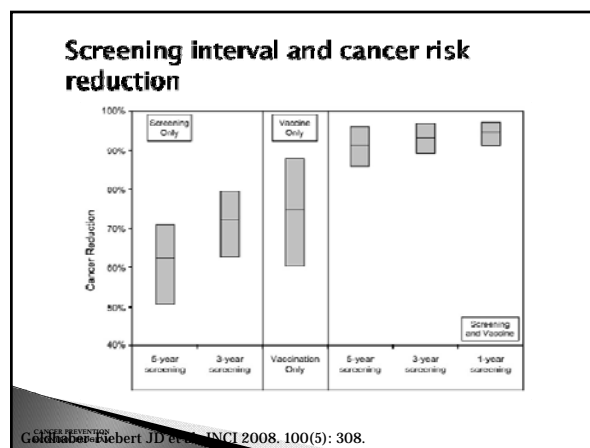
### Vaccination protects against Cancer!

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)

### HPV vaccine myth #4

Paps are just as good at preventing cervical cancer so we don't need to vaccinate.



## HPV vaccine myth #5

I have concerns about HPV vaccine safety.

## 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/vaccinesafety/vaccines/hpv/hpv-safety-faqs.html>

### HPV Vaccines Objectives

- ▶ HPV vaccination is **safe**.
- ▶ HPV vaccination **works**.
- ▶ HPV vaccination **lasts**.

### HPV Vaccination in United States

2017 NIS-TEEN Data – ages 13-17 yo

HPV Vaccination	United States	
	Females 2017	Males 2017
≥1 dose	68.6%	62.6%
HPV UTD	53.1%	44.3%

<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6429a3.htm>

### HPV Vaccination is Recommended

**Girls & Boys Age 11-12 can start HPV vaccination at age 9**

Preteens should finish HPV vaccine series before 13

Plus girls 13-26 years old who haven't started or finished HPV vaccine series

Plus boys 13-26 years old who haven't started or finished HPV vaccine series

Meites et al. MMWR: 2016.

### Reasons parents won't vaccinate for HPV

Not sexually active	12%
Not recommended	14%
Safety concern/Side...	15%
Not needed or...	15%
Lack of knowledge	16%

Percent

Stokley et al. MMWR. 2014.



## Provider recommendation in vaccination

- ▶ Overall uptake of HPV vaccine 66.5% US (46.9–92.1%)
- ▶ If provider recommended vaccination
  - 74.4% (58.9–92.8%)
- ▶ No provider recommendation
  - 39.9% (16.0 – 88.6%)
- ▶ Any provider counts!
  - Obgyn of mom
  - Pharmacist
  - Dentist

Lu et al. Feb 2019. J of Pediatrics

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## NCI Consensus Statement 1/27/16

NCI-designated Cancer  
Centers/Networks Updated HPV  
Vaccination Recommendations

"As national clinical data call for increased childhood vaccination rates, we encourage all health care providers to be advocates for cancer prevention by making strong recommendations for childhood HPV vaccination. We ask providers to join forces to educate parents, guardians and colleagues about the importance and benefits of HPV vaccination.

• We have two age 11-12 wome vaccine a three-dose vaccine themselves against HPV. We encourage all health care providers to be advocates for cancer prevention by making strong recommendations for childhood HPV vaccination. We ask providers to join forces to educate parents, guardians and colleagues about the importance and benefits of HPV vaccination.



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## Championing the HPV Vaccine

- ▶ Obvious
  - Giving presentations to groups of doctors, patients, parents
  - Sharing medically factual information on social media
  - Recommending HPV vaccine to patients and families
  - Connect HPV cancer survivors to advocacy opportunities
- ▶ Maybe not so obvious
  - Policy change to encourage vaccination
    - Vaccination in pharmacies
    - School-based vaccination programs
    - Quality metrics connected to payment
  - Coalition building through cancer center networks and others



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## Conclusions

- ▶ The burden of HPV-related disease continues to increase in Alabama and US
- ▶ Screening with pap testing only not enough
  - HPV testing
  - HPV vaccination
- ▶ We can do more to improve vaccination rates
  - Start in your own practice
  - Use social media
  - Build partnerships
  - Be a resource to your family/friends/relatives

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