



HPV Update

Melanie Nichols, MSN FNP-BC

South Carolina Department of Health and Environmental Control
Healthy People. Healthy Communities.

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Disclosures

- None

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Objectives

- Understand the different available vaccines and the importance of the HPV vaccine
- Review the current PAP Guidelines as they relate to HPV
- Discuss options for follow-up on clients with HPV

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How common is HPV in the US?

- 79 million currently infected
- 14 million new infections every year
- Nearly everyone who is sexually active will have HPV at some point in their lives
- 1 in 100 sexually active adults have genital warts
- 12,000 women diagnosed with cervical cancer every year and more than 4,000 die from cervical cancer

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Vaccine Availability



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Year	Age and Sex Recommendations	Vaccines Recommended ¹⁾	Number of Doses
2006	Female: Routine vaccination at age 11 or 12 years, earlier can be started at age 9 years. Vaccination recommended through age 26 years if not vaccinated previously.	aHPV	3 6, 11, 16 & 18
2009	Female: Recommendation as in 2006. Male: May be vaccinated at age 9-26 years.	aHPV, 2aHPV 16 & 18 4aHPV Cerv. efficient ²⁾	3
2011	Female: Recommendation as in 2006. Male: Routine vaccination at age 11 or 12 years, earlier can be started at age 9 years. Vaccination recommended through age 27 years if not vaccinated previously. Vaccination recommended through age 26 years for men who have sex with men ³⁾ .	aHPV, 2aHPV	3
2015	Female: Recommendation as in 2006. Male: Recommendation as in 2011.	aHPV, 2aHPV 9aHPV, 11, 13, 45, 52 & 58	3
2016	Female: Recommendation as in 2006. Male: Recommendation as in 2011.	aHPV, 2aHPV 9aHPV	3 ⁴⁾ or 6-12 months after initial administration ⁵⁾
	Male: Recommendation as in 2011.	aHPV, 9aHPV	3 2 for persons starting series at older ages and for persons with immunocompromising conditions

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HPV4 versus HPV2

TABLE 1. Selected characteristics of quadrivalent human papillomavirus vaccine (HPV4) and bivalent human papillomavirus vaccine (HPV2).

Characteristic	HPV4	HPV2
Manufacturer	Merck Company	Merck Company
Human composition (1)	20 µg HPV 4	10 µg HPV 2
HPV types	HPV 6, 11, 16, and 18	HPV 16 and 18
Adjuvant	AS02	AS02
Protein	200 µg amorphous aluminum hydroxyphosphate sulfate	200 µg aluminum hydroxide
Protein	None	50 µg 2-O-deoxy-4'-methylthiothymine (spike)
Other content	Sodium chloride, L-histidine, polysorbate 80, sodium borate, and water for injection	Sodium chloride and sodium dihydrogen phosphate dehydrate, and water for injection
Temperature storage	Store refrigerated at 30°–40°F (2°–8°C). Do not freeze.	Store refrigerated at 30°–40°F (2°–8°C). Do not freeze.
Volume per dose	0.5 mL	0.5 mL
Administration	Intramuscular	Intramuscular
Schedule/Intervals	Second and third doses 1 to 3 months and 6 months after first	Second and third doses 1 to 3 months and 6 months after first

1. Both vaccines are composed of similar protein particles (L2) prepared from recombinant L1 gene constructs of human papillomavirus (HPV). The vaccine are not live vaccines.

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Efficacy of HPV2 and HPV4

TABLE 2. Efficacy of bivalent human papillomavirus vaccine (HPV2) and quadrivalent human papillomavirus vaccine (HPV4) in females.

Vaccine/Outcome (HPV type)	Vaccine		Control		Vaccine efficacy % (95% CI)
	No.	Cases	No.	Cases	
Bivalent vaccine (HPV2)					
Control or ADP*					100% (CI)
HPV 16 and/or 18	7,344	4	7,322	95	97.9 (76.9–98.3)
HPV 16	6,303	2	6,435	46	96.7 (82.3–99.4)
HPV 18	6,796	0	6,148	15	98.7 (85.1–99.5)
Quadrivalent vaccine (HPV4)					
Control or ADP**					100% (CI)
HPV 6, 11, 16, and/or 18	7,864	2	7,882	112	98.2 (93.2–99.0)
HPV 16	6,647	2	6,435	41	97.9 (81.1–98.7)
HPV 18	7,382	0	7,316	29	100.0 (96.8–100.0)
HPV2 vs HPV4***					
HPV 6, 11, 16, and/or 18	7,800	0	7,802	23	100.0 (93.8–100.0)
HPV 16	6,854	0	6,437	17	100.0 (76.5–100.0)
HPV 18	7,424	0	7,249	2	100.0 (100–100.0)
Genital warts***					
HPV 6 and/or 11	6,932	2	6,898	189	99.0 (76.2–99.5)

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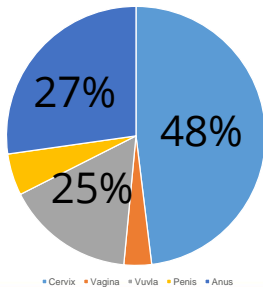
Why 9 HPV Types?

Broader disease coverage due to more HPV types

Worldwide estimated type contribution for certain HPV-related cancer and disease cases	4 HPV types cause: (6, 11, 16, and 18)	5 HPV types cause an additional: (31, 33, 45, 52, and 58)	9 HPV types cause a total of: (6, 11, 16, 18, 31, 33, 45, 52, and 58)
Cervical cancer ²	70% ²	20% ²	90% ²
Vulvar cancer ^{3,a}	75% ³	15% ³	90% ³
Vaginal cancer ^{4,a}	65% ⁴	20% ⁴	85% ⁴
Anal cancer ^{5,a}	85% ⁵	5%–10% ⁵	90%–95% ⁵
High-grade cervical precancers ^{6,a,b}	50% ⁶	30% ⁶	80% ⁶
Low-grade cervical lesions ^{6,a}	25% ⁶	25% ⁶	50% ⁶
Genital warts ⁷	90% ⁷	No contribution ⁷	90% ⁷

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Average Number of HPV Related Cancers Per Year



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Outcome	Population	Comparison Years	Main Findings
HPV prevalence	Female participants National Health and Nutrition Examination Surveys	2007-2010 with 2003-2006	56% decrease in prevalence of 4HPV types in cervical-vaginal samples among 14- to 19-year-olds (11.5%-5.1%)
		2009-2012 with 2003-2006	64% decrease in prevalence of 4HPV types in cervical-vaginal samples among 14- to 19-year-olds (11.5%-4.3%) and 34% decrease among 20- to 24-year-olds (8.5%-12.1%)
	Female enrollees screened for cervical cancer in integrated health care plans, northwestern United States	2011-2014 with 2003-2006	71% decrease in prevalence of 4HPV types in cervical-vaginal samples among 14- to 19-year-olds (11.5%-3.3%) and 61% decrease among 20- to 24-year-olds (8.5%-7.2%)
		2012-2013 with 2007	42% decrease in prevalence of 4HPV types among 20- to 29-year-olds (10.6%-6.2%)
	Female patients attending primary care and sexually transmitted disease clinics, Cincinnati, Ohio	2009-2010 with 2006-2007	58% decrease in prevalence of 4HPV types among 13- to 26-year-olds (31.7%-13.4%)
	2013-2014 with 2006-2007	75% decrease in prevalence of 4HPV types in cervical-vaginal samples among 13- to 26-year-olds (34.8%-8.7%)	
Genital warts	Female and male enrollees; claims data from privately insured patients, nationwide database	2007-2010 with prevaccine era	Decrease in anogenital wart prevalence among female enrollees aged 15-19 years, from 2.9/100,000 person-years in 2006 to 1.8/100,000 person-years in 2010
	Female and male enrollees; claims data from primary care clinics, Boston, Massachusetts area	2013 with 2004	Decrease in rate of genital warts in 16- to 26-year-olds, from 3.5% to 1.5% among female and from 3.6% to 2.9% among male enrollees
Cervical cancer precursors	Population-based surveillance in 5 sites across the United States	2013-2014 with 2008-2010	CIN2+ decrease in estimated screened women, from 690 to 207/100,000 among 18- to 20-year-olds and from 1107 to 732/100,000 among 21- to 24-year-olds
	Statewide surveillance, New Mexico	2014 with 2007	CIN2 decrease in estimated screened women, from 896 to 415/100,000 among 15- to 19-year-olds and from 1028 to 627/100,000 among 20- to 24-year-olds
	Claims data from privately insured women, nationwide database	2014 with 2007	CIN2+ decrease in screened women, from 14.8 to 4.9/1000 person-years among 15- to 19-year-olds and from 20.5 to 11.3/1000 person-years among 20- to 24-year-olds

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Recurrent Respiratory Papillomatosis (RPR)

- RPR - a condition of condylomatous lesions of the airway secondary to HPV infection
 - Affects children or young adults
 - Primarily by HPV 6 and 11
 - >5% of cases caused by HPV 16 or other types

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Juvenile Onset (JORRP)

- RPR occurring before age 14
- Transmission from an HPV-infected mother to her neonate
 - Most cases between the ages of 1 and 4 years
- Offspring of women with genital warts are estimated to have over 200 times the risk of JORRP (7 of 1,000)



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Prevalence

- 3 per 1 million person-years in children
- 3 to 7 per 100,000 for both pediatric and adult disease



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Impact of HPV vaccination on anogenital warts and respiratory papillomatosis

- Anogenital Warts
 - 2 cases in 6,718 vaccinated women
 - 186 cases that occurred in 6,647 controls
 - Vaccine efficacy of 98.9%
- RPR
 - Decrease expected based on declines of genital warts

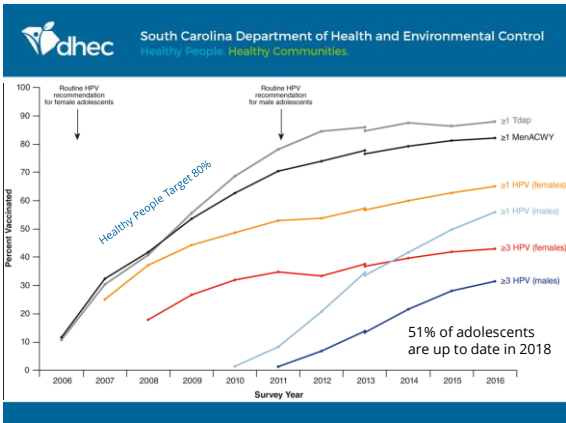


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Safety

- Prelicensure trial >15,000 participants
 - Favorable findings with expected fever and injection site reactions
- Vaccine Adverse Event Reporting System (VAERS), Vaccine Safety Datalink (VSD), Clinical Immunization Safety Assessment Network, and FDA – consider vaccine safe
- Autoimmune and neurological conditions examined by VSD and in other studies are reassuring with no other confirmed safety signals identified

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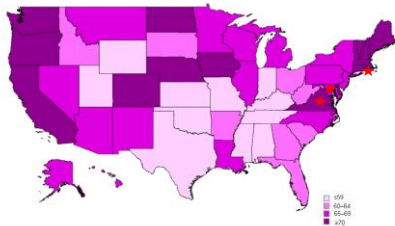
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Barriers to Uptake

- Marketing
 - Sexually active vs anticancer
- Social Media
- School Requirements
 - Rhode Island, Virginia, and District of Columbia
 - Other states trying, but unsuccessful

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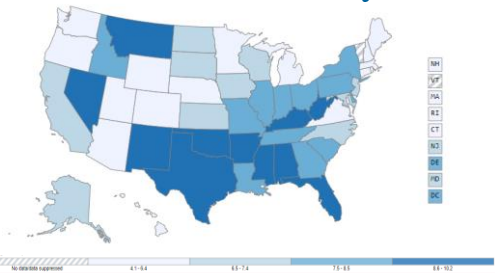
SUPPLEMENTARY FIGURE 2. Estimated coverage with ≥ 1 doses of HPV vaccine* among adolescents aged 13–17 years† — National Immunization Survey-Teen, United States, 2017



Abbreviation: HPV = human papillomavirus.
*Nine-valent quadrivalent or bivalent. Percentages reported among females and males are combined.
†Includes adolescents born January 1999 through February 2009.

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2016 Cervical Cancer Rates by CDC



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Australia

HPV Vaccination Recommendations:
2006 Females | 2011 Males

- 2007 – National HPV Vaccination Program in schools and community for women
- 2013 – Added males
- HPV rates dropping with just the quadrivalent
- Genital warts – decreasing significantly with herd immunity effects

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Adolescents Rates in AU for HPV Vaccine in 2016

- 15 year-old Females
 - Dose 1 87%
 - Dose 2 84%
 - Dose 3 79%
- 15 year-old males
 - Dose 1 81%
 - Dose 2 79%
 - Dose 3 73%



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Estimates of genital HPV prevalence among sexually active women aged 18-24 years, by HPV type, Australia, 2005-2012 (n = 1,260)

HPV type	Pre-vaccination era (2005-07) (n = 262)	Post-vaccination era (2010-12) (n = 1,098)		
	Overall population prevalence	Overall population prevalence	Prevalence in vaccinated	Prevalence in unvaccinated
HPV 6	5.0%	0.0%	0.2%	2.7%
HPV 11	1.2%	0.4%	0%	1.3%
HPV 16	21.3%	4.2%	1.0%	12.1%
HPV 18	8.4%	1.9%	0.0%	7.4%
HPV 31	5.0%	4.0%	2.7%	8.1%
HPV 33	4.0%	1.5%	1.4%	2.0%
HPV 45	1.0%	2.6%	1.7%	6.0%
HPV 52	7.4%	8.2%	6.9%	9.4%
HPV 58	5.0%	3.4%	3.9%	2.7%
HPV 611	6.9%	1.3%	0.2%	4.0%
HPV 16/18	26.2%	5.4%	2.1%	16.1%
HPV 31/33/45	9.4%	7.8%	5.0%	14.8%
4-HPV types ^a	28.7%	6.5%	2.3%	18.8%
High-risk HPV types ^b	47.0%	34.9%	34.4%	44.3%
All HPV types	59.9%	48.8%	40.4%	55.7%

4-HPV: 2006 Females | 2011 Males
9-HPV: 2015 Females | 2015 Males



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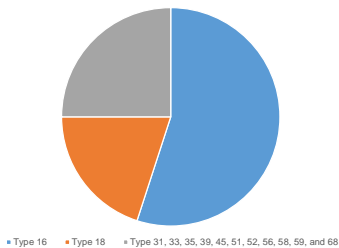
HPV Leads to Cervical Cancer

- Nearly all cases of cervical cancer can be attributed to HPV
- Over 99% of precancerous lesions and cervical carcinomas are caused by high-risk HPV infections



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HPV Causing Squamous Cell Carcinomas



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5 Ways to Boost Your HPV Vaccination Rates

- Bundle your recommendation
- Ensure a consistent message
- Use every opportunity to vaccinate
- Provide personal examples
- Effectively answer questions

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Bundle Your Recommendation

- 3 Vaccines
 - Meningitis
 - HPV cancers
 - Whooping Cough
- Do you have any questions about these vaccines?

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Use Every Opportunity to Vaccinate

- Establish a policy to check patients' immunization status at every visit
- Call to remind families about getting vaccines
- Develop a process where all clinicians in your practice compare HPV vaccination rates

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Provide Personal Examples

- Share how you recommended the vaccine to your own children, grandchildren, nieces, nephews, etc.
- Even future plans to recommend to your younger kids

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Effectively Answer Questions

- Most common questions about HPV vaccine
- Be prepared to answer
 - Succinctly
 - Accurately
 - Empathetically
 - Using terms that they understand

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Two common questions:

- **Why do they need HPV vaccine at such a young age?**
 - Vaccines protect your child before they are exposed to a disease. That's why we give the HPV vaccine earlier rather than later, to protect them long before they are ever exposed.
 - Also, if your child gets the shot now, they will only need two doses. If you wait until your child is older, he/she may end up needing three shots.
- **I'm worried my child will think that getting this vaccine makes it OK to have sex.**
 - Studies tell us that getting HPV vaccine doesn't make kids more likely to start having sex. I made sure my child (or grandchild, etc.) got HPV vaccine, and I recommend we give your child her first HPV shot today.

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PAP Guidelines



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When to PAP:

ACOG guidelines reflect these age-based recommendations for cervical cancer screening*

Age	Pap [†]	High-risk HPV	HPV genotyping
Under 21	Not recommended	Not recommended	Not recommended
21 - 29	Recommended every 3 years	Recommended to be used as a "reflex test" only when Pap result is ASC-US	Not recommended
30 - 65	Recommended co-testing (using Pap and HPV concurrently) every 5 years (preferred), or cytology alone every 3 years		Option to use as "reflex test" in co-tested patients whose Pap is negative and HPV result is positive
Over 65	Screening should be discontinued if patient has had adequate negative prior screening results [‡] and no history of CIN [‡] Recommend continuing age-based screening for 100 years in those patients with a history of CIN2, CIN3, or adenocarcinoma in situ		

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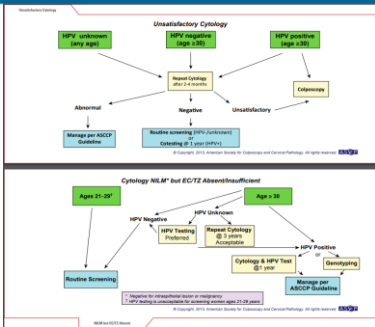


ASCCP Algorithms

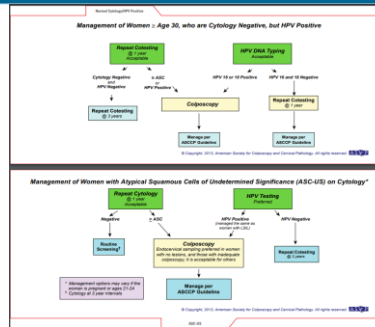
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Cytology versus HPV testing for cervical cancer screening in the general population

- Every 1000 women screened
 - 20 women will have precancerous changes
 - HPV test will correctly identify 18 of these women
 - The Pap test will identify 15 of the women
 - 980 women who will not have precancerous changes
 - HPV test will correctly identify 881 women
 - 99 women will be incorrectly told that they have a lesion
 - Pap test will correctly identify 885 women
 - 95 will be incorrectly told that they have a lesion
 - Women may have their cervix examined or may receive surgery unnecessarily

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On the Horizon???

- Self collect HPV samples
- HPV alone without cytology
- Healthy People 2025 – 80% by age 15
 - Prioritizing HPV vaccination in 2020



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Follow-up on Abnormal PAPs

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Colposcopy

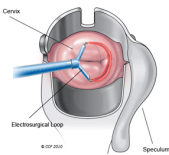
- Excisional Treatments – biopsy – send to lab
 - Loop electrosurgical excision procedure (LEEP)
 - Conization
- Ablative Treatments – destroy
 - Cryotherapy
 - Thermal Coagulation



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LEEP

- Remove abnormal cells from the cervix by using a thin wire loop that acts like a scalpel
- An electric current is passed through the loop, which cuts away a thin layer of the cervix



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Conization

- Excision of a cone-shaped or cylindrical wedge from the cervix uteri
 - includes the transformation zone and all or a portion of the endocervical canal

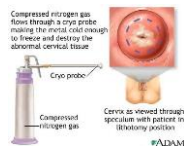


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Cryotherapy

- Extremely cold temperatures to freeze and destroy abnormal tissues
- Used to treat pre-cancerous tumors and/or remove abnormal tissue of the cervix, the lower part of the uterus (womb) that opens into the vagina (birth canal)
- Probe with liquid nitrogen cooled to below -20 degrees Celsius



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Cryotherapy Cont.

- A randomized study in the USA
 - 84% success with LEEP
 - 76% with cryotherapy
- A study from a population-based program in a low-resource setting
 - 70% for CIN 3 lesions treated with cryotherapy at 1-year follow-up
- A recent meta-analysis reported cryotherapy cures 85%–92% of CIN 2 or CIN 3 lesions

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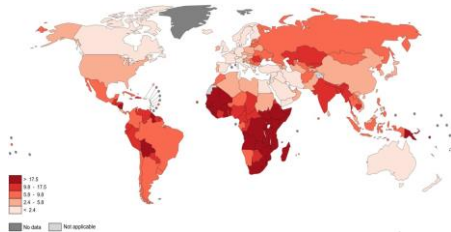
LEEP versus Cryotherapy

- Cryotherapy was found to be 88% effective and LEEP was 94%
- Overall cure rate of symptoms was 82% in cryosurgery and 79% in LEEP
- LEEP seems to have an edge over cryotherapy when used on severe lesions

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Cervical Cancer in Developing Countries

85% of worldwide deaths are in developing countries



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Thermal Coagulation

- Low-cost
- Battery operated
- Autoclave able
- Automatic timer – no watch needed
- No wires or cables required



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Thermal Coagulation Cont.

- 7,088 previously unscreened women attended visual inspection with acetic acid (VIA) clinics between October 2013 and March 2015
 - VIA positivity was 6.1%
 - Almost 90% received same day treatment in the hospital setting
 - 3- to 6-month cure rates of more than 90% are observed

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In Summary

- HPV Vaccine
- Follow Pap Guidelines
- Know your options for follow-up

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CONTACT US

Melanie Nichols, FNP
 SC DHEC Lowcountry Region
 nicholma@dhec.sc.gov

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