

An Update on Cervical Cancer Screening and Prevention in Alabama

**Satellite Conference and Live Webcast
Thursday, January 28, 2016
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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Disclosure

- **I have received reimbursement from Cepheid for travel to an Investigator's Meeting**

Objectives

- **Describe the recommended cervical cancer screening guidelines**
 - **USPSTF**
 - **ACS / ASCCP / ASCP**
 - **ACOG**

Objectives

- **Understand the performance of available screening tests**
 - **Pap alone**
 - **Pap + human papillomavirus (HPV) testing [co-testing]**

Current Screening Guidelines

CLINICAL GUIDELINE |

Annals of Internal Medicine

Screening for Cervical Cancer: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyci, MD, MPH, on behalf of the U.S. Preventive Services Task Force*

GA CANCER | CLIN 2012;00000000

American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology Screening Guidelines for the Prevention and Early Detection of Cervical Cancer



The American College of
Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

Debbie Saslow, PhD¹; Diane Solomon, MD²; Herschel W. Lawson, MD³; Maureen Kilackey, MD⁴; Shafiq I. Kulsingam, PhD⁵; Joanna Cain, MD⁶; Francisco A. R. Garcia, MD, MPH⁷; Ann T. Moriarty, MD⁸; Alan G. Waxman, MD, MPH⁹; David C. Wilbur, MD¹⁰; Nicolas Wentzensen, MD, PhD, MS¹¹; Levi S. Downs, Jr, MD¹²; Mark Spitzer, MD¹³; Anna-Barbara Moscicki, MD¹⁴; Eduardo L. Franco, DrPH¹⁵; Mark H. Stoler, MD¹⁶; Mark Schiffman, MD¹⁷; Philip F. Castle, PhD, MPH^{18*}; Fuan R. Myers, MD, MPH^{19*}

PRACTICE BULLETIN

CLINICAL MANAGEMENT GUIDELINES FOR OBSTETRICIAN-GYNECOLOGISTS

NUMBER 157, JANUARY 2016

(Replaces Practice Bulletin Number 131, November 2012)

Cervical Cancer Screening and Prevention

Annals of Internal Medicine

U.S. Preventive Services Task Force
www.USPreventiveServicesTaskForce.org

SCREENING FOR CERVICAL CANCER
CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population	Women Aged 21 to 65 Years	Women Aged 30 to 65 Years	Women Younger Than Age 21 Years	Women Older Than Age 65 Years Who Have Had Adequate Prior Screening and Are Not High Risk	Women After Hysterectomy With Removal of the Cervix With No History of High-Grade Precancer or Cervical Cancer	Women Younger Than Age 30 Years
Recommendation	Screen with cytology (Pap smear) every 3 years. Grade: A	Screen with cytology every 2 years or co-testing (cytology/ human papillomavirus testing [HPV]) every 5 years. Grade: A	Do not screen. Grade: D	Do not screen. Grade: D	Do not screen. Grade: D	Do not screen with HPV testing (alone or with cytology). Grade: D
Risk Assessment	HPV infection is associated with nearly all cases of cervical cancer. Other factors that increase a woman's risk for cervical cancer include HIV infection, a compromised immune system, in utero exposure to diethylstilbestrol, and previous treatment of a high-grade precancerous lesion or cervical cancer.					
Screening Tests and Interval	Screening women aged 21 to 65 years every 3 years with cytology provides a reasonable balance between benefits and harms. Screening with cytology more often than every 3 years confers little additional benefit, with large increases in harms. HPV testing combined with cytology (co-testing) every 5 years in women aged 30 to 65 years offers a comparable balance of benefits and harms, and is therefore a reasonable alternative for women in this age group who would prefer to extend the screening interval.					
Timing of Screening	Screening women younger than age 21 years, regardless of sexual history, leads to more harms than benefits. Clinicians and patients should base the decision to not screen on whether the patient meets the criteria for adequate prior testing and appropriate follow-up, per established guidelines.					
Interventions	Screening aims to identify high-grade precancerous cervical lesions to prevent development of cervical cancer and early-stage asymptomatic, invasive cervical cancer. High-grade lesions may be treated with ablative and excisional therapies, including cryotherapy, laser ablation, loop excision, and cold-knife conization. Early-stage cervical cancer may be treated with surgery (hysterectomy) or chemotherapy.					
Balance of Benefits and Harms	The benefits of screening with cytology every 3 years substantially outweigh the harms.	The benefits of screening with co-testing (cytology/HPV testing) every 5 years outweigh the harms.	The harms of screening earlier than age 21 years outweigh the benefits.	The benefits of screening after age 65 years do not outweigh the potential harms.	The harms of screening after hysterectomy outweigh the benefits.	The potential harms of screening with HPV testing (alone or with cytology) outweigh the potential benefits.
USPSTF Relevant USPSTF Recommendations	The USPSTF has made recommendations on screening for breast cancer and ovarian cancer, as well as genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility. These recommendations are available at: www.uspreventiveservicestaskforce.org.					

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to www.uspreventiveservicestaskforce.org.

TABLE 1. Summary of Recommendations

POPULATION	PAGE NUMBER	RECOMMENDED SCREENING METHOD ¹	MANAGEMENT OF SCREEN RESULTS	COMMENTS
Aged <21 y	7	No screening		HPV testing should not be used for screening or management of ASC-IR in this age group.
Aged 21-29 y	8-9	Cytology alone every 3 y	HPV-positive ASC-US ² or cytology of LSIL or more severe: Refer to ASCCP guidelines ² Cytology negative or HPV-negative ASC-US ² : Rescreen with cytology in 3 y	HPV testing should not be used for screening in this age group.
Aged 30-65 y	9-16	HPV and cytology "cotesting" every 5 y (preferred)	HPV-positive ASC-US or cytology of LSIL or more severe: Refer to ASCCP guidelines ² HPV positive, cytology negative: Option 1: 12-mo follow-up with cotesting Option 2: Test for HPV16 or HPV16/18 genotypes • If HPV16 or HPV16/18 positive: refer to colposcopy • If HPV16 or HPV16/18 negative: 12-mo follow-up with cotesting Cotest negative or HPV-negative ASC-US: Rescreen with cotesting in 5 y	Screening by HPV testing alone is not recommended for most clinical settings.
		Cytology alone every 3 y (acceptable)	HPV-positive ASC-IR ³ or cytology of LSIL or more severe: Refer to ASCCP guidelines ² Cytology negative or HPV-negative ASC-US ² : Rescreen with cytology in 3 y	
Aged >65 y	16-17	No screening following adequate negative prior screening		Women with a history of CIN2 or a more severe diagnosis should continue routine screening for at least 20 y.
After hysterectomy	17-18	No screening		Apply to women without a cervix and without a history of CIN2 or a more severe diagnosis in the past 20 y or cervical cancer ever.
HPV vaccinated	18-19		Follow age-specific recommendations (same as unvaccinated women)	

SCREENING FOR CERVICAL CANCER CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION						
Population	Women Aged 21 to 65 Years	Women Aged 30 to 65 Years	Women Younger Than Age 21 Years	Women Older Than Age 65 Years Who Have Had Adequate Prior Screening and Are Not High Risk	Women After Hysterectomy With Removal of the Cervix With No History of High-Grade Precancer or Cervical Cancer	Women Younger Than Age 30 Years
Recommendation	Screen with cytology (Pap smear) every 3 years Grade: A	Screen with cytology every 3 years or co-testing (cytology/human papillomavirus testing [HPV]) every 5 years Grade: A	Do not screen Grade: D	Do not screen Grade: D	Do not screen Grade: D	Do not screen with HPV testing (alone or with cytology) Grade: D
Risk Assessment	HPV infection is associated with nearly all cases of cervical cancer. Other factors that increase a woman's risk for cervical cancer include HIV infection, a compromised immune system, in utero exposure to diethylstilbestrol, and previous treatment of a high-grade precancerous lesion or cervical cancer.					
Screening Tests and Interval	Screening women aged 21 to 65 years every 3 years with cytology provides a reasonable balance between benefits and harms. Screening with cytology more often than every 3 years confers little additional benefit, with large increases in harms. HPV testing combined with cytology (co-testing) every 5 years in women aged 30 to 65 years offers a comparable balance of benefits and harms, and is therefore a reasonable alternative for women in this age group who would prefer to extend the screening interval.					
Timing of Screening	Screening women younger than age 21 years, regardless of sexual history, leads to more harms than benefits.					
Interventions	Screening aims to identify high-grade precancerous cervical lesions to prevent development of cervical cancer and early-stage squamous intraepithelial lesions (cervical cancer). High-grade lesions may be treated with ablative and excisional therapies, including cryotherapy, laser ablation, loop resection, and cold-knife conization. Early-stage cervical cancer may be treated with surgery (hysterectomy) or chemotherapy.					
Balance of Benefits and Harms	The benefits of screening with cytology every 3 years substantially outweigh the harms.	The benefits of screening with co-testing (cytology/HPV testing) every 5 years outweigh the harms.	The harms of screening earlier than age 21 years outweigh the benefits.	The benefits of screening after age 65 years do not outweigh the potential harms.	The harms of screening after hysterectomy outweigh the benefits.	The potential harms of screening with HPV testing (alone or with cytology) outweigh the potential benefits.
Other Relevant USPSTF Recommendations	The USPSTF has made recommendations on screening for breast cancer and ovarian cancer, as well as genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility. These recommendations are available at www.uspreventiveservicestaskforce.org .					

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to www.uspreventiveservicestaskforce.org.

NO Cervical Cancer Screening in Age < 21. Why??

- HPV is VERY common in this age group
- Rate of cervical cancer in this population extremely low
 - 0.1/100,000 cases in adolescents 15-19 years
 - 1.3/100,000 cases in young women 20-24 years

NO Cervical Cancer Screening in Age < 21. Why??

- By comparison, rate of cervical cancer in women who should be screened:
 - 7.7/100,000 in all women
 - 15.8/100,000 in women 40-44 years

High HPV Prevalence in Teens and Young Adults

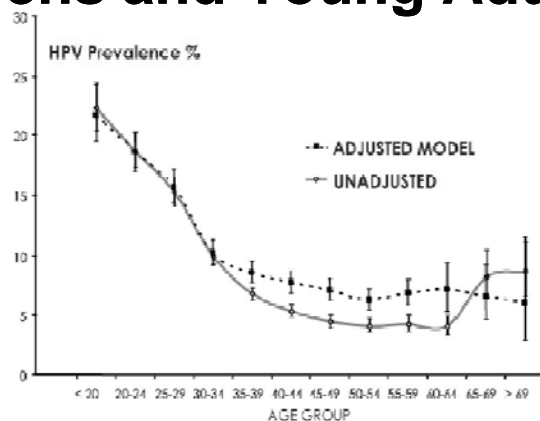
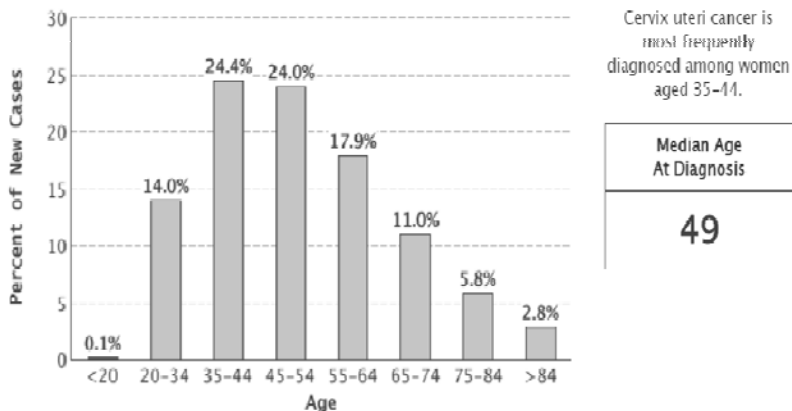


Fig. 1. Age-specific HPV prevalence among women with normal cytology. Crude and adjusted estimates are presented based on the meta-analysis of 78 studies. Age-specific prevalence estimates were calculated by means of logistic models based on a discriminatory analysis that included geographical area, study type, study design, youngest and oldest age values of each study, publication year, sampling collection device, cell storage medium, HPV assay, primer used and HPV type-specific assay. Adapted from [46].

Burchell *et al. Vaccine* 2006;24S3: 52-61.

Why CC Screening is NOT Recommended for Age < 21

Percent of New Cases by Age Group: Cervix Uteri Cancer

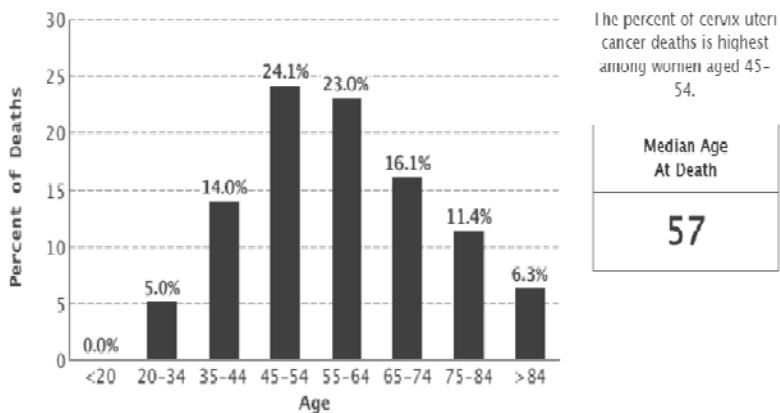


SEER 18 2008-2012, All Races, Females

Accessed at: <http://seer.cancer.gov/statfacts/html/cervix.html>

Why CC Screening is NOT Recommended for Age < 21

Percent of Deaths by Age Group: Cervix Uteri Cancer



U.S. 2008-2012, All Races, Females

Accessed at: <http://seer.cancer.gov/statfacts/html/cervix.html>

TABLE 1. Summary of Recommendations

POPULATION	PAGE NUMBER	RECOMMENDED SCREENING METHOD ^a	MANAGEMENT OF SCREEN RESULTS	COMMENTS
Aged < 21 y	7	No screening		HPV testing should not be used for screening or management of ASC-US in this age group
Aged 21-29 y	8-9	Cytology alone every 3 y	HPV-positive ASC-US ^b or cytology of LSIL or more severe: Refer to ASCCP guidelines ² Cytology negative or HPV-negative ASC-US ^b : Rescreen with cytology in 3 y	HPV testing should not be used for screening in this age group
Aged 30-65 y	9-16	HPV and cytology "cotesting" every 5 y (preferred)	HPV-positive ASC-US or cytology of LSIL or more severe: Refer to ASCCP guidelines ² HPV positive, cytology reactive: Option 1: 12-mo follow-up with cotesting Option 2: Test for HPV16 or HPV16/18 genotypes • If HPV16 or HPV16/18 positive: refer to colposcopy • If HPV16 or HPV16/18 negative: 12-mo follow-up with cotesting Cotest negative or HPV-negative ASC-US: Rescreen with cotesting in 5 y	Screening by HPV testing alone is not recommended for most clinical settings
		Cytology alone every 3 y (acceptable)	HPV-positive ASC-US ^b or cytology of LSIL or more severe: Refer to ASCCP guidelines ² Cytology negative or HPV-negative ASC-US ^b : Rescreen with cytology in 3 y	
Aged > 65 y	10-17	No screening following adequate negative prior screening		Women with a history of CIN2 or a more severe diagnosis should continue routine screening for at least 20 y
After hysterectomy	17-18	No screening		Applies to women without a cervix and without a history of CIN2 or a more severe diagnosis in the past 30 y or cervical cancer ever
HPV vaccinated	18-19	Follow age-specific recommendations (same as unvaccinated women)		

SCREENING FOR CERVICAL CANCER
CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population	Women Aged 21 to 65 Years	Women Aged 30 to 65 Years	Women Younger Than Age 21 Years	Women Older Than Age 65 Years Who Have Had Adequate Prior Screening and Are Not High Risk	Women Older Than Age 65 Years Who Have Had Inadequate Prior Screening and Are Not High Risk	Women Older Than Age 65 Years Who Have a History of High-Grade Precancer or Cervical Cancer
Recommendation	Screen with cytology (Pap smear) every 3 years Grade: A	Screen with cytology every 3 years or cotesting (cytology/ human papillomavirus testing [HPV]) every 5 years Grade: A	Do not screen Grade: D	Do not screen Grade: D	Do not screen Grade: D	Do not screen with HPV testing (alone or with cytology) Grade: D
HPV Infection	HPV infection is associated with nearly all cases of cervical cancer. Other factors that increase a woman's risk for cervical cancer include HIV infection, a compromised immune system, in utero exposure to diethylstilbestrol, and previous treatment of a high-grade precancerous lesion or cervical cancer.					
Screening Tests and Interval	Screening women aged 21 to 65 years every 3 years with cytology provides a reasonable balance between benefits and harms. Screening with cytology more often than every 3 years carries little additional benefit, with large increases in harms. HPV testing, combined with cytology (co-testing) every 5 years in women aged 30 to 65 years offers a comparable balance of benefits and harms, and is therefore a reasonable alternative for women in this age group who would prefer to extend the screening interval.					
Timing of Screening	Screening women younger than age 21 years, regardless of sexual history, leads to more harms than benefits. Clinicians and patients should base the decision to end screening on whether the patient meets the criteria for adequate prior testing and appropriate follow-up, per established guidelines.					
Interventions	Screening aims to identify high-grade precancerous cervical lesions to prevent development of cervical cancer and early-stage asymptomatic invasive cervical cancer. High-grade lesions may be treated with ablation and/or conization (excisional therapy, including cryotherapy, laser ablation,LEEP, and cold-knife conization). Early-stage cervical cancer may be treated with surgery (hysterectomy) or chemotherapy.					
Balance of Benefits and Harms	The benefits of screening with cytology every 3 years substantially outweigh the harms.	The benefits of screening with cotesting (cytology/HPV testing) every 5 years outweigh the harms.	The harms of screening earlier than age 21 years outweigh the benefits.	The benefits of screening after age 65 years do not outweigh the potential harms.	The harms of screening after hysterectomy outweigh the benefits.	The potential harms of screening with HPV testing alone or with cytology outweigh the potential benefits.
Other Relevant USPSTF Recommendations	The USPSTF has made recommendations on screening for breast cancer and ovarian cancer, as well as genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility. These recommendations are available at www.uspreventiveservicestaskforce.org .					

This summary of the evidence supports the current screening recommendations. For more information, visit www.uspreventiveservicestaskforce.org.

High HPV Prevalence in Teens and Young Adults

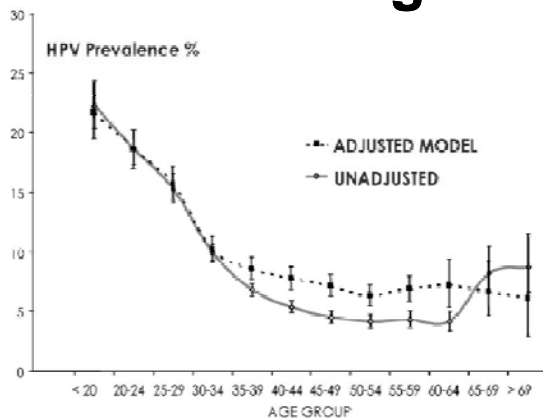


Fig. 1. Age-specific HPV prevalence among women with normal cytology. Crude and adjusted estimates are presented based on the meta-analysis of 78 studies. Age-specific prevalence estimates were calculated by means of logistic models based on a discriminatory analysis that included geographical area, study type, study design, youngest and oldest age values of each study, publication year, sampling collection device, cell storage medium, HPV assay, primer used and HPV type-specific assay. Adapted from [46].

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TABLE 1. Summary of Recommendations

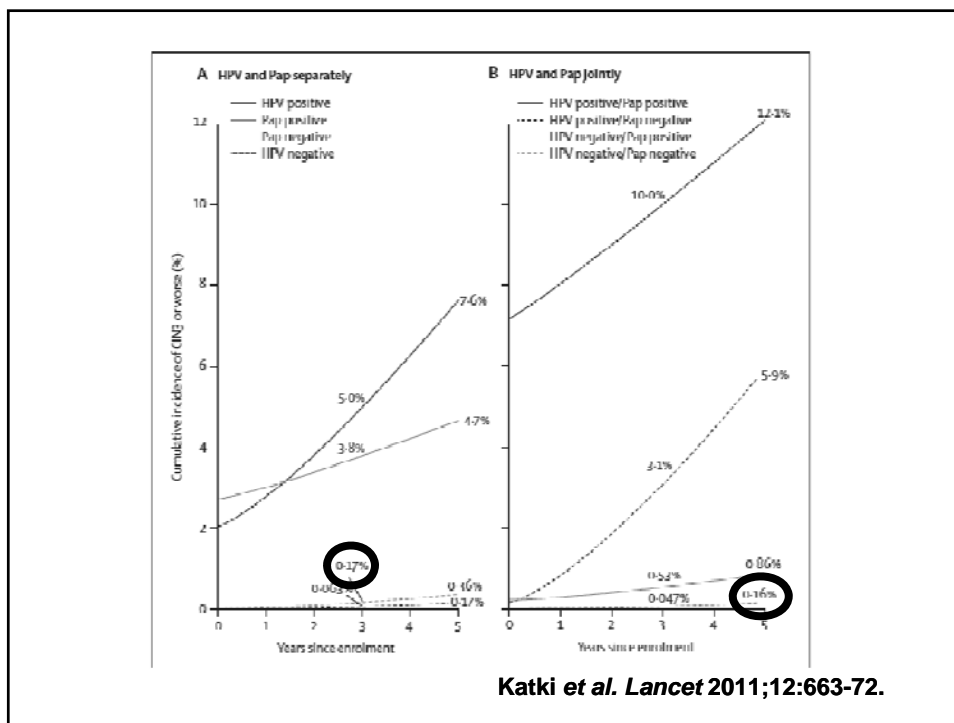
POPULATION	PAGE NUMBER	RECOMMENDED SCREENING METHOD ^a	MANAGEMENT OF SCREEN RESULTS	COMMENTS
Aged < 21 y	7	No screening		HPV testing should not be used for screening or management of ASC-US in this age group
Aged 21-29 y	8-9	Cytology alone every 3 y	HPV positive ASC-US ^b or cytology of LSIL or more severe: Refer to ASCCP guidelines ² Cytology negative or HPV-negative ASC-US ^b : Rescreen with cytology in 3 y	HPV testing should not be used for screening in this age group
Aged 30-65 y	9-16	HPV and cytology "cotesting" every 5 y (preferred) Cytology alone every 3 y (acceptable)	HPV-positive ASC-US or cytology of LSIL or more severe: Refer to ASCCP guidelines ² HPV positive, cytology negative: Option 1: 12-mo follow-up with cotesting Option 2: Test for HPV16 or HPV16/18 genotypes • If HPV16 or HPV16/18 positive: refer to colposcopy • If HPV16 or HPV16/18 negative: 12-mo follow-up with cotesting Cotest negative or HPV-negative ASC-US: Rescreen with cotesting in 5 y HPV positive ASC-US ^b or cytology of LSIL or more severe: Refer to ASCCP guidelines ² Cytology negative or HPV-negative ASC-US ^b : Rescreen with cytology in 3 y	Screening by HPV testing alone is not recommended for most clinical settings
Aged > 65 y	16-17	No screening following adequate negative prior screening		Women with a history of CIN2 or a more severe diagnosis should continue routine screening for at least 20 y
After hysterectomy	17-18	No screening		Applies to women without a cervix and without a history of CIN2 or a more severe diagnosis in the past 20 y or cervical cancer cure
HPV vaccinees	18-19		Follow age-specific recommendations (same as unvaccinated women)	

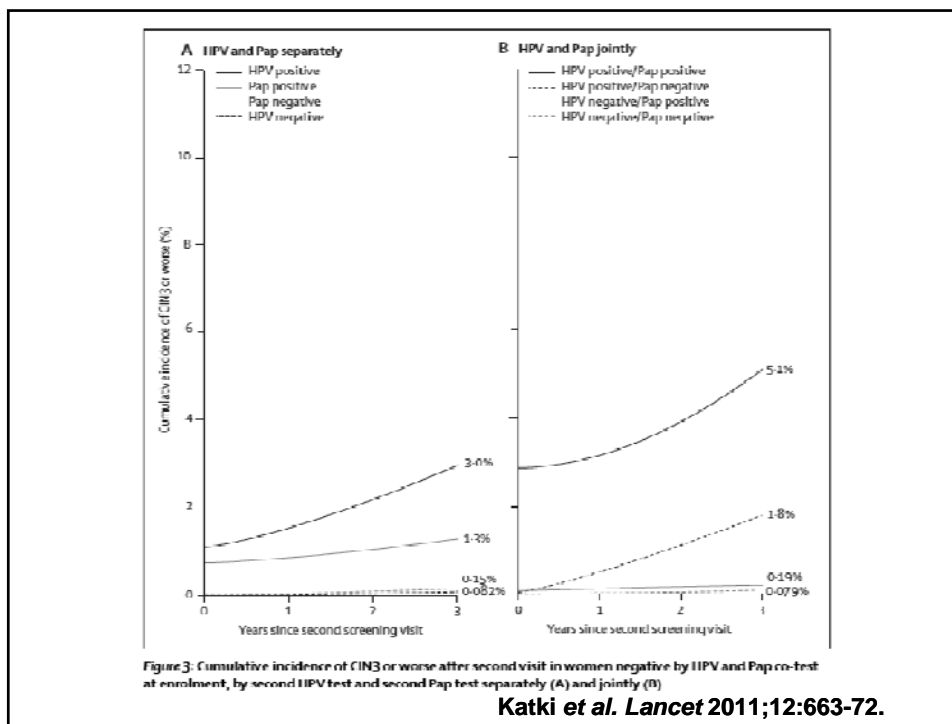
SCREENING FOR CERVICAL CANCER

CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population	Women Aged 21 to 65 Years	Women Aged 30 to 65 Years	Women Younger Than Age 21 Years	Women Older Than Age 65 Years Who Have Had Adequate Prior Screening and Are Not High Risk	Women After Hysterectomy With Removal of the Cervix With No History of High-Grade Precancer or Cervical Cancer	Women Younger Than Age 30 Years
Recommendation	Screen with cytology (Pap smear) every 3 years Grade: A	Screen with cytology every 2 years or co-testing (cytology/HPV testing) every 5 years Grade: A	Do not screen Grade: D	Do not screen Grade: D	Do not screen Grade: D	Do not screen with HPV testing (alone or with cytology) Grade: U
Risk Assessment	HPV infection is associated with nearly all cases of cervical cancer. Other factors that increase a woman's risk for cervical cancer include HIV infection, a compromised immune system, smoking, exposure to diethylstilbestrol, and previous treatment of a high-grade precancerous lesion or cervical cancer.					
Screening Tools and Interval	Screening women aged 21 to 65 years every 3 years with cytology provides a reasonable balance between benefits and harms. Screening with cytology or co-testing every 5 years (when both additional benefit, with less harm, to women in favor.					
Timing of Screening	Screening women younger than age 21 years, regardless of sexual history, leads to more harms than benefits. Clinicians and patients should favor the harm to avoid screening or delaying the patient until the criteria for adequate prior testing and appropriate follow-up, per established guidelines.					
Interventions	Screening aims to identify high-grade precancerous cervical lesions to prevent development of cervical cancer and early-stage asymptomatic invasive cervical cancer. High-grade lesions may be treated with ablative and excisional therapies, including cryotherapy, laser ablation, loop excision, and cold-knife conization. Early-stage cervical cancer may be treated with surgery (hysterectomy) or chemotherapy.					
Balance of Benefits and Harms	The benefits of screening with cytology every 3 years substantially outweigh the harms.	The benefits of screening with co-testing (cytology/HPV testing) every 5 years outweigh the harms.	The harms of screening younger than age 21 years outweigh the benefits.	The benefits of screening older than age 65 years do not outweigh the potential harms.	The harms of screening after hysterectomy outweigh the benefits.	The potential harms of screening with HPV testing (alone or with cytology) outweigh the potential benefits.
Other Relevant USPSTF Recommendations	The USPSTF has made recommendations on screening for breast cancer and ovarian cancer, as well as genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility. These recommendations are available at www.uspreventiveservicestaskforce.org .					

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to www.uspreventiveservicestaskforce.org.





Rationale for Screening Guidelines Based on KPNC Data

- Every 3 year cytology screening interval

was equivalent in risk to

- Every 5 year cytology + hrHPV (“co-testing”) interval

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			Cytology negative or HPV-negative ASC-US ^b : Rescreen with cytology in 3 y	
Aged 30-65 y	9-16	HPV and cytology "cotesting" every 5 y (preferred)	HPV-positive ASC-US or cytology of LSIL or more severe: Refer to ASCCP guidelines ²	Screening by HPV testing alone is not recommended for most clinical settings
			HPV positive, cytology negative: Option 1: 12-mo follow-up with cotesting Option 2: Test for HPV16 or HPV16/18 genotypes • If HPV16 or HPV16/18 positive: refer to colposcopy • If HPV16 or HPV16/18 negative: 12 mo follow up with cotesting	
			Cotest negative or HPV-negative ASC-US: Rescreen with cotesting in 5 y	
			Cytology alone every 3 y (acceptable)	
Aged >65 y	16-17	No screening following atypical negative prior screening		Women with a history of CIN2 or a more severe diagnosis should continue routine screening for at least 20 y
	17-18	No screening		Applies to women without a cervix and without a history of CIN2 or a more severe diagnosis in the past 20 y or cervical cancer
HPV vaccinated	18-19		Follow age-specific recommendations (same as unvaccinated women)	

SCREENING FOR CERVICAL CANCER
Clinical Summary of U.S. Preventive Services Task Force Recommendation

Population	Women Aged 21 to 65 Years	Women Aged 30 to 65 Years	Women Younger Than Age 21 Years	Women Older Than Age 65 Years Who Have Had Adequate Prior Screening and Are Not High Risk	Women After Hysterectomy With Removal of the Cervix With No History of High-Grade Precancer or Cervical Cancer	Women Younger Than Age 20 Years
Recommendation	Screen with cytology (Pap smear) every 3 years Grade: A	Screen with cytology every 3 years or co-testing (cytology/HPV testing) every 5 years Grade: A	Do not screen Grade: D	Do not screen Grade: D	Do not screen Grade: D	Do not screen with HPV testing (alone or with cytology) Grade: D
Risk Assessment	HPV infection is associated with nearly all cases of cervical cancer. Other factors that increase a woman's risk for cervical cancer include HPV infection, a history of human papillomavirus (HPV) infection, and a history of high-grade precancerous lesions or cervical cancer.					
Screening Test and Interval	Screening women aged 21 to 65 years every 3 years with cytology provides a reasonable balance between benefits and harms. Screening with cytology or co-testing every 3 years reduces the risk of advanced disease, with large increases in harms. HPV testing combined with cytology (co-testing) every 3 years in women aged 20 to 65 years offers a comparable balance of benefits and harms, and is therefore a reasonable alternative for women in this age group who would prefer to extend the screening interval.					
Timing of Screening	Screening women younger than age 21 years, regardless of sexual history, leads to more harms than benefits. Clinicians and patients should base the decision on whether the patient needs the criteria for adequate prior testing and appropriate follow-up, per established guidelines.					
Interventions	Screening aims to identify high-grade precancerous cervical lesions to prevent development of cervical cancer and neoplasia, and to detect and treat early-stage cervical cancer. High-grade lesions may be treated with ablation and excisional therapies, including cryotherapy, loop excision, large excision, and cold knife conization. Early-stage cervical cancer may be treated with surgery (hysterectomy) or chemotherapy.					
Balance of Benefits and Harms	The benefits of screening with cytology every 3 years substantially outweigh the harms.	The benefits of screening with co-testing (cytology/HPV testing) every 3 years outweigh the harms.	The harms of screening earlier than age 21 years outweigh the benefits.	The benefits of screening after age 65 years do not outweigh the potential harms.	The harms of screening after hysterectomy outweigh the benefits.	The potential harms of screening with HPV testing (alone or with cytology) outweigh the potential benefits.
Other Relevant USPSTF Recommendations	The USPSTF has made recommendations on screening for breast cancer and ovarian cancer, as well as gonorrhea, risk assessment, and BRCA testing. For more information, please go to www.preventiveservices.taskforce.org .					

1. For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to www.preventiveservices.taskforce.org.

Exiting From Screening: What Defines “Adequate Negative Prior Screening”?

- In the last 10 years, the patient must have had
 - 3 consecutive negative cytology results, OR
 - 2 consecutive negative co-tests
- With the most recent test in the last 5 years

The Harms Outweigh the Benefits of Screening at > 65 Years Old

TABLE 6. Evidence for Stopping Screening

OUTCOME*	MAIN RESULT	NO. OF STUDIES	QUALITY OF EVIDENCE	COMMENTS
CIN3+	N/A			
Cancer incidence	Continued screening to age 90 y prevents only 1.6 cancer cases and 0.5 cancer deaths per 1000 women	1 ⁶³	Moderate to low	Modeling study; consistent with other modeling studies
Colposcopies	Continued screening to age 90 y results in an additional 127 colposcopies per 1000 women	1 ⁶²	Moderate to low	Modeling study

CIN3+ indicates cervical intraepithelial neoplasia of grade 3 or more severe diagnosis; N/A, not applicable.

*Patients/population was comprised of women aged older than 65 years. The intervention was no further screening, and the comparator was screening with cytology every 3 or 5 years.

Saslow *et al. Ca Cancer J Clin* 2012;62:147-72.

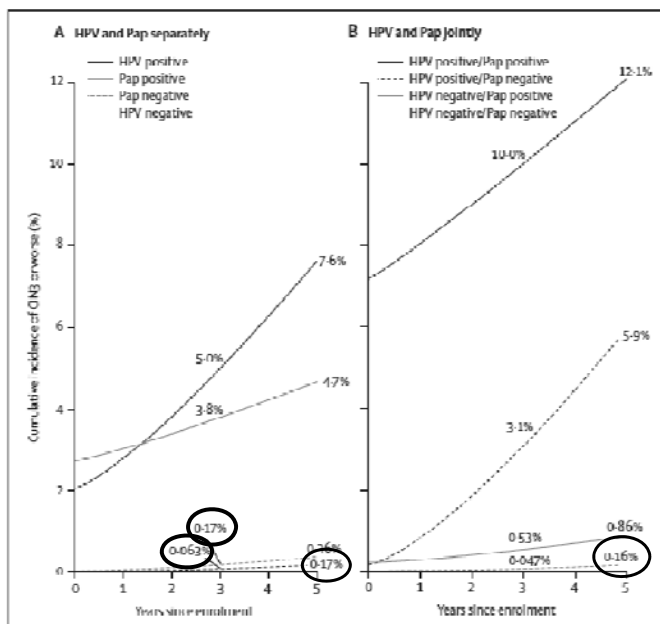
HPV as a Primary Screening Test

Guidelines

Use of Primary High-Risk Human Papillomavirus Testing for Cervical Cancer Screening

Interim Clinical Guidance

Warner K. Huh, MD, Kevin A. Ault, MD, David Chelmow, MD, Diane D. Davey, MD, Robert A. Goulart, MD, Francisco A. R. Garcia, MD, MPH, Walter K. Kinney, MD, L. Stewart Massad, MD, Edward J. Mayeaux, MD, Debbie Saslow, PhD, Mark Schiffman, MD, MPH, Nicolas Wentzensen, MD, PhD, Herschel W. Lawson, MD, and Mark H. Finstein, MD, MS



Katki et al. Lancet 2011;12:663-72.

HPV as a Primary Screening Test

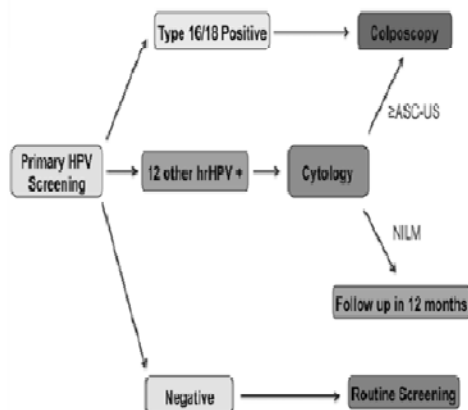


Fig. 1. Recommended primary HPV screening algorithm. HPV, human papillomavirus; hrHPV, high-risk human papillomavirus; ASC-US, atypical squamous cells of undetermined significance; NILM, negative for intraepithelial lesion or malignancy.

14th. Primary hrHPV Screening Interim Guidance. Obstet Gynecol 2015.

TABLE 1. Summary of Recommendations

POPULATION	PAGE NUMBER	RECOMMENDED SCREENING METHOD ^a	MANAGEMENT OF SCREEN RESULTS	COMMENTS
Aged <21 y	7	No screening		HPV testing should not be used for screening or management of ASC-US in this age group
Aged 21-29 y	8-9	Cytology alone every 3 y	HPV-positive ASC-US ^b or cytology of LSIL or more severe: Refer to ASCCP guidelines. ⁷ Cytology negative or HPV-negative ASC-US ^b : Rescreen with cytology in 3 y	HPV testing should not be used for screening in this age group
Aged 30-65 y	9-16	HPV and cytology "co-testing" every 5 y (preferred) Cytology alone every 3 y (acceptable)	HPV-positive ASC-US or cytology of LSIL or more severe: Refer to ASCCP guidelines. HPV positive, cytology negative: Option 1: 12 mo follow-up with co-testing Option 2: Test for HPV16 or HPV16/18 genotypes • If HPV16 or HPV16/18 positive, refer to colposcopy • If HPV16 or HPV16/18 negative: 12-mo follow-up with co-testing Cytology negative or HPV-negative ASC-US: Rescreen with co-testing in 5 y HPV-positive ASC-US ^b or cytology of LSIL or more severe: Refer to ASCCP guidelines. ⁴ Cytology negative or HPV-negative ASC-US ^b : Rescreen with cytology in 3 y	Screening by HPV testing alone is not recommended for most clinical settings
Aged >65 y	16-17	No screening following adequate negative prior screening		Women with a history of CIN2 or a more severe diagnosis should continue routine screening for at least 20 y
After hysterectomy	17-18	No screening		Applies to women without a cervix and without a history of CIN2 or a more severe diagnosis in the past 20 y or cervical cancer ever
HPV vaccinated	18-19		Follow age-specific recommendations (same as unvaccinated women)	

SCREENING FOR CERVICAL CANCER
CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population	Women Aged 21 to 24 Years	Women Aged 25 to 29 Years	Women Aged 30 to 39 Years	Women (Older Than Age 40) Who Have Had Adequate Prior Screening and Are Not High Risk	Women After Hysterectomy With Removal of the Cervix With No History of High-Grade Precancer or	Women Younger Than Age 21 Years
Recommendation	Screen with cytology (Pap smear) every 3 years Grade: A	Screen with cytology every 3 years or co-testing (cytology/human papillomavirus testing [HPV]) every 5 years Grade: A	Do not screen Grade: D	Do not screen Grade: D	Do not screen Grade: D	Do not screen with HPV testing (alone or with cytology) Grade: D
Risk Assessment	HPV infection is associated with nearly all cases of cervical cancer. Other factors that increase a woman's risk for cervical cancer include HIV infection, a compromised immune system, in utero exposure to diethylstilbestrol, and previous treatment of a high-grade precancerous lesion or cervical cancer.					
Screening Tests and Interval	Screening women aged 21 to 65 years every 3 years with cytology provides a reasonable balance between benefits and harms. Screening with cytology more often than every 3 years confers little additional benefit, with large increases in harms. HPV testing (combined with cytology [co-testing]) every 5 years in women aged 30 to 65 years offers a comparable balance of benefits and harms, and is therefore a reasonable alternative for women in this age group who would prefer to extend the screening interval.					
Timing of Screening	Screening women younger than age 21 years, regardless of sexual history, leads to more harms than benefits. Clinicians and patients should base the decision to start screening on whether the patient meets the criteria for adequate prior testing and appropriate follow-up, per established guidelines.					
Interventions	Screening aims to identify high-grade precancerous cervical lesions to prevent development of cervical cancer and early-stage asymptomatic invasive cervical cancer. High-grade lesions may be treated with ablation and resectional therapies, including cryotherapy, laser ablation, loop excision, and cold-knife conization. Early-stage cervical cancer may be treated with surgery (hysterectomy) or chemoradiation.					
Balance of Benefits and Harms	The benefits of screening with cytology every 3 years substantially outweigh the harms.	The benefits of screening with co-testing (cytology/HPV testing) every 5 years outweigh the harms.	The harms of screening women from age 21 years outweigh the benefits.	The benefits of screening women from age 65 years do not outweigh the potential harms.	The harms of screening after hysterectomy outweigh the benefits.	The potential harms of screening with HPV testing (alone or with cytology) outweigh the potential benefits.
Other Relevant USST Recommendations	The USST has made recommendations on screening for breast cancer and ovarian cancer, as well as genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility. These recommendations are available at www.uspreventiveservicestaskforce.org .					

As a courtesy of the publisher, you may be invited to make this recommendation, the full assessment letter, editorial, and supporting documents, please go to www.uspreventiveservicestaskforce.org.

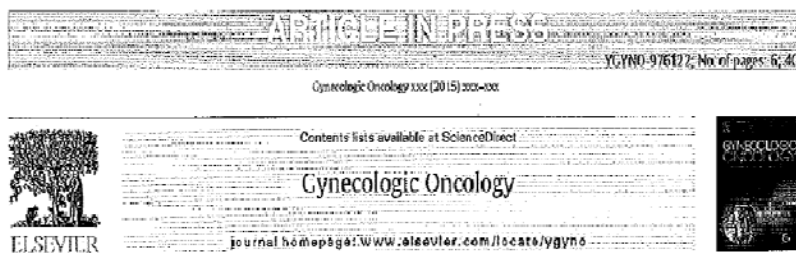
Why Don't We Screen After Hysterectomy?

- **Vaginal cancer is much less common than cervical cancer**
 - **500 HPV-associated vaginal cancers per year from 2004-2008 (cervix approx 12,000)**
 - **0.4 – 0.6 per 100,000 women (cervix 7.7 per 100,000)**

CDC *MMWR* 2012;61:258-61. Cramer DW *Am J Obstet Gynecol* 1974;118:443-460.

Why Don't We Screen After Hysterectomy?

- **Abnormal vaginal smears are common, but cancer is rare**
 - **Pearce et al. NEJM 1996**
 - **9,610 vaginal cytology samples after hysterectomy**
 - **1.1% abnormal, no ValN3 or vaginal cancers found**



A common clinical dilemma: Management of abnormal vaginal cytology and human papillomavirus test results

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An Update on HPV Vaccination

Disclosure

- **I have received reimbursement from Cepheid for travel to an Investigator's Meeting**

Objectives

- **Describe the current recommendations for HPV vaccination**
- **Describe the benefits of HPV vaccination**
- **Describe the available HPV vaccines**
- **Describe the uptake of HPV vaccination in Alabama and in the United States**

HPV - Associated Conditions

- **Genital warts**
- **Cervical dysplasia**
- **Cervical cancer**
- **Vaginal cancer**
- **Vulvar cancer**
- **Anal cancer**
- **Penile cancer**

HPV - Associated Conditions

- Head and neck cancer
- Recurrent respiratory papillomatosis

High HPV Prevalence in Teens and Young Adults

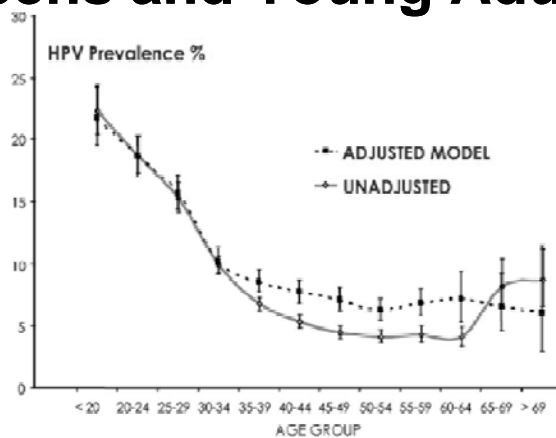
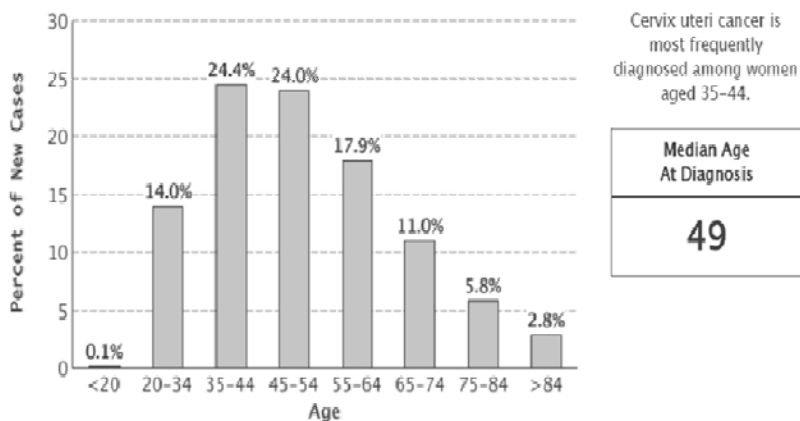


Fig. 1. Age-specific HPV prevalence among women with normal cytology. Crude and adjusted estimates are presented based on the meta-analysis of 78 studies. Age-specific prevalence estimates were calculated by means of logistic models based on a discriminatory analysis that included geographical area, study type, study design, youngest and oldest age values of each study, publication year, sampling collection device, cell storage medium, HPV assay, primer used and HPV type-specific assay. Adapted from [46].

Burchell *et al. Vaccine* 2006;24S3: 52-61.

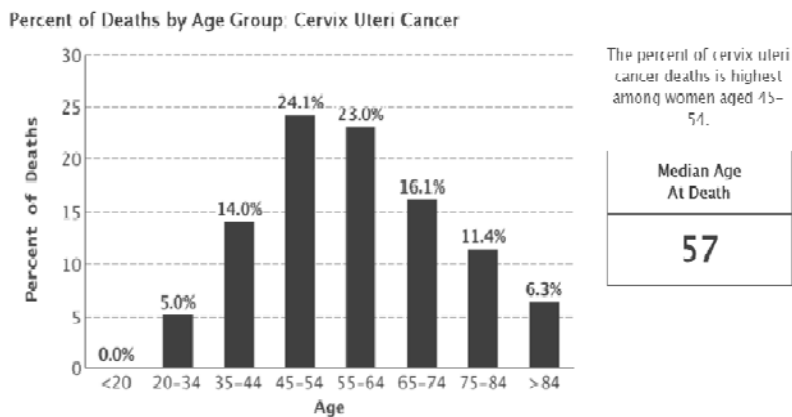
Percent of New Cases by Age Group: Cervix Uteri Cancer



SEER 18 2008-2012. All Races, Females

Accessed at: <http://seer.cancer.gov/statfacts/html/cervix.html>

Percent of Deaths by Age Group: Cervix Uteri Cancer



U.S. 2008-2012, All Races, Females

Accessed at: <http://seer.cancer.gov/statfacts/html/cervix.html>

CDC Recommendations for HPV Vaccination

Centers for Disease Control and Prevention

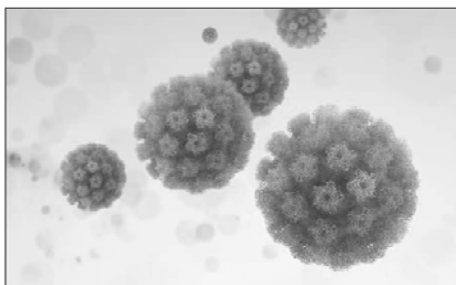
MMWR

Morbidity and Mortality Weekly Report

Recommendations and Reports / Vol. 63 / No. 5

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Human Papillomavirus Vaccination Recommendations of the Advisory Committee on Immunization Practices (ACIP)



What is the HPV Vaccine Made Of?

- **Non-infectious virus like particles (VLPs) produced by L1 protein – the major capsid (external) protein of HPV**
– Type-specific
- **These VLPs elicit a humoral immune response (neutralizing antibodies)**
- **Aluminum adjuvant**

HPV4 (Quadrivalent Vaccine)

- **“Gardasil”**
- **Approved for females and males by the FDA in 2006**
- **Contains type-specific VLPs prepared by the L1 proteins of HPV6, 11, 16 and 18**

HPV4 (Quadrivalent Vaccine)

- **3 doses recommended**
 - **0 months**
 - **1-2 months**
 - **6 months**

HPV2 (Bivalent Vaccine)

- **“Cervarix”**
- **Approved for females by the FDA in 2009**
- **Contains type-specific VLPs prepared by the L1 proteins of HPV16 and 18**

HPV2 (Bivalent Vaccine)

- **3 doses recommended**
 - **0 months**
 - **1-2 months**
 - **6 months**

2014 CDC ACIP Recommendations

TABLE 1. Human papillomavirus vaccines licensed in the United States and ACIP recommendations for vaccination, 2006–2014

Characteristic	Quadrivalent HPV vaccine (HPV4)	Bivalent HPV vaccine (HPV2)
Manufacturer	Merck and Co, Inc.	CloverSmithKline
HPV types	HPV 6, 11, 16, 18	HPV 16, 18
Year of licensure (age range)	Females: 2006 (9–26 years) Males: 2009 (9–26 years)	Females: 2009 (10–25 years) Not licensed for use in males
ACIP recommendations, 2006 ¹	Females: routine vaccination with 3-dose series at age 11 or 12 years ^{1,2} and through age 26 years if not vaccinated previously	
ACIP recommendations, 2009 ³	Females: either vaccine for routine vaccination with 3-dose series at age 11 or 12 years ^{1,4} and through age 26 years if not vaccinated previously Males aged 9–26 years may be vaccinated, but vaccination not routinely recommended for males	
ACIP recommendations, 2011 ^{5,6}	Females: either vaccine for routine vaccination with 3-dose series at age 11 or 12 years ^{1,5,6} and through age 26 years if not vaccinated previously Males: routine vaccination with 3-dose series at age 11 or 12 years ^{1,3} and through age 21 years if not vaccinated previously ^{7,8} Vaccination recommended through age 26 years for men who have sex with men and men who are immunocompromised (including those with HIV infection)	

Abbreviations: ACIP = Advisory Committee on Immunization Practices; HIV = human immunodeficiency virus; HPV = human papillomavirus.

¹ Source: CDC. Quadrivalent human papillomavirus vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2007;56(No. RR-2).

² A 3-dose series at intervals of 0, 1–2, and 6 months.

³ Vaccination series can be started at age 9 years.

⁴ Sources: CDC. FDA licensure of bivalent human papillomavirus vaccine (HPV2, Cervarix) for use in females and updated HPV vaccination recommendations from the Advisory Committee on Immunization Practices (ACIP). MMWR 2010;59:626–9. CDC. FDA licensure of quadrivalent human papillomavirus vaccine (HPV4, Gardasil) for use in males and guidance from the Advisory Committee on Immunization Practices (ACIP). MMWR 2010;59:630–2.

⁵ Source: CDC. Recommendations on the use of a quadrivalent human papillomavirus vaccine in males—Advisory Committee on Immunization Practices (ACIP), 2011. MMWR 2011;60(1):10–8.

⁶ Males aged 17–26 years may be vaccinated.

Use of 9-Valent Human Papillomavirus (HPV) Vaccine: Updated HPV Vaccination Recommendations of the Advisory Committee on Immunization Practices

Emiko Petrosky, MD^{1,2}, Joseph A. Bocchini Jr, MD³, Susan Hariri, PhD⁴, Harrell Chesson, PhD⁵, C. Robinette Curtis, MD⁶, Mona Saraiya, MD⁶, Elizabeth R. Unger, PhD, MD⁶, Lauri E. Markowitz, MD² (Author affiliations at end of text)

- **“Gardasil-9”**
- **Approved for females & males by the FDA on 12/10/14**
- **Contains type-specific VLPs prepared by the L1 proteins of HPV6, 11, 16 and 18, 31, 33, 45, 52, 58**

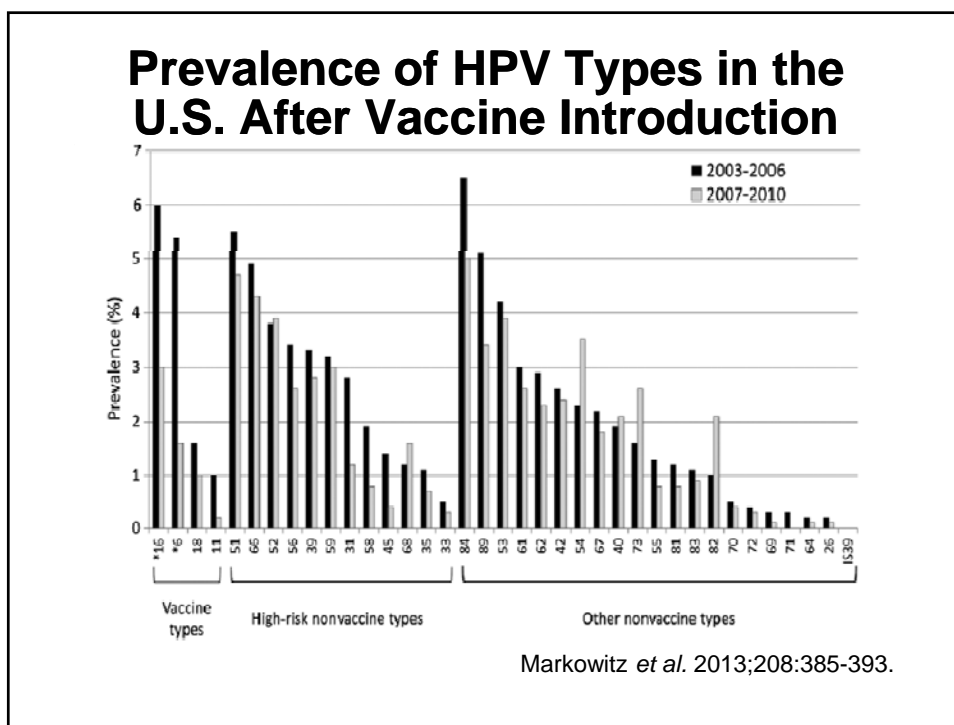
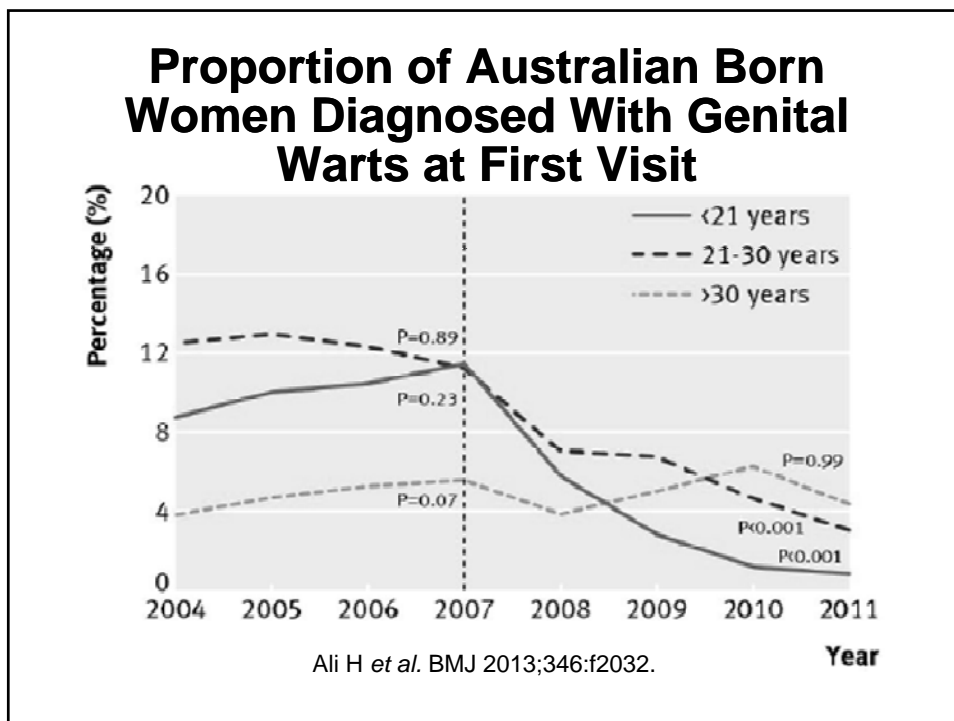
**Use of 9-Valent Human Papillomavirus (HPV) Vaccine: Updated HPV
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- **3 doses recommended**
 - 0 months
 - 1-2 months
 - 6 months

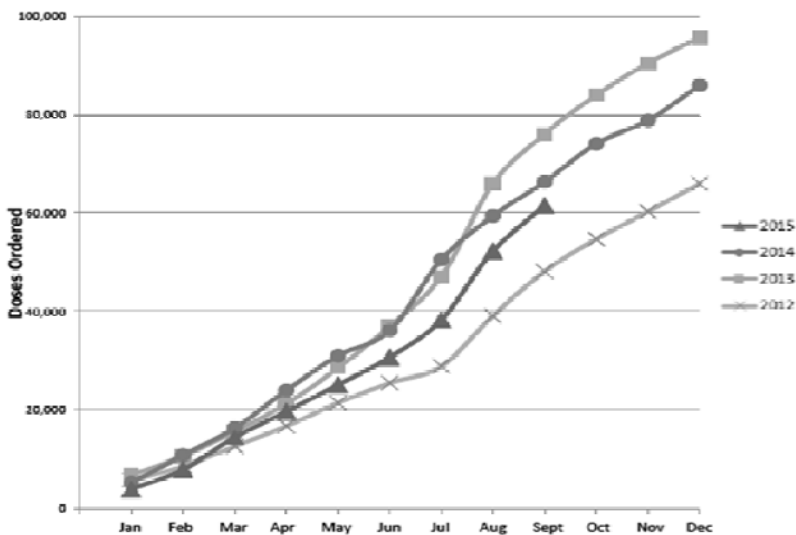
Current CDC ACIP Recommendations

- **Routine vaccination for girls and boys
age 11-12 years old**
- **Catch-up vaccination for girls
age 13-26 and boys age 13-21**
- **Vaccination up to age 26 for men who
have sex with men,
immunocompromised males, or HIV
positive males**



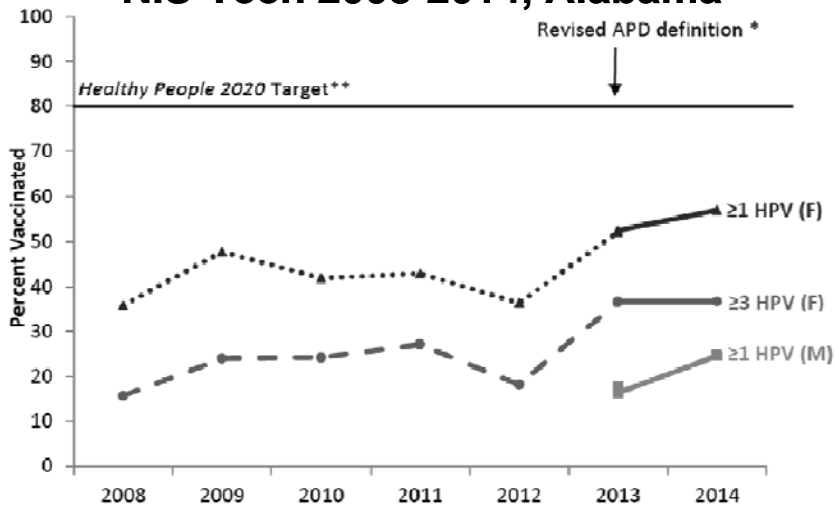
HPV Vaccine Ordering Trends in AL

Cumulative Year-to-date Total of Publicly* Ordered HPV Vaccination Doses in AL (2012-2015)



CDC Vaccine Tracking System: tracks orders for publicly funded vaccine.

Estimated HPV Vaccination Coverage Among Adolescents Aged 13-15 Years, NIS-Teen 2008-2014, Alabama



References

- High HPV Prevalence in Teens and Young Adults - Burchell *et al. Vaccine* 2006;24S3: 52-61
- Why CC Screening is NOT recommended for age < 21 <http://seer.cancer.gov/statfacts/html/cervix.html>
- HPV and Pap separately & HPV and Pap jointly slides - Katki *et al. Lancet* 2011;12:663-72.
- The harms outweigh the benefits of screening at > 65 years old - Saslow *et al. Ca Cancer J Clin* 2012;62: 147-72.
- Why don't we screen after hysterectomy? - CDC *MMWR* 2012;61:258-61. Cramer DW *Am J Obstet Gynecol* 1974;118:443-460.

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- High HPV Prevalence in Teens and Young Adults - Burchell *et al. Vaccine* 2006;24S3: 52-61
- Proportion of Australian Born Women Diagnosed with Genital Warts at First Visit - Ali H *et al. BMJ* 2013;346:f2032
- Prevalence of HPV Types in the U.S. After Vaccine Introduction - Markowitz *et al.* 2013;208:385-393.