

## Special Women's Health Edition



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## Cervical Cancer Screening: Recommendations, Strategies and Co-testing

Edward Evantash, M.D., F.A.C.O.G.

Medical Director and Vice President, Medical Affairs, Hologic, Inc.

Cervical cancer screening is one of the most successful stories in the history of screening programs in the United States. Largely due to the introduction and widespread use of screening with the Pap test, the incidence of and mortality from cervical cancer have been steadily declining over the last 40 years.<sup>1</sup> With continued advances in the understanding of the etiologic relationship between human papillomavirus (HPV) and cervical cancer, guidelines for cervical cancer screening have evolved rapidly. This has proven difficult for clinicians to stay current on the latest recommendations.<sup>2</sup> It is not uncommon for healthcare providers to spend significant time searching the most recently published algorithms to understand which pathways are most applicable for their patients. Ultimately,

*Continued on pg 6*

1. American Cancer Society. (2014). *What Are the Key Statistics about Cervical Cancer?* (Data File) Retrieved from <http://www.cancer.org/cancer/cervicalcancer/detailedguide/cervical-cancer-key-statistics>.
2. Verilli, L., Winer, R.L., & Mao, C. (2014). Adherence to Cervical Cancer Screening Guidelines by Gynecologists in the Pacific Northwest. *Journal of Lower Genital Tract Disease*, 18(3), 228-234.



To schedule an appointment with Mike, please contact him at [michael.s.coats@questdiagnostics.com](mailto:michael.s.coats@questdiagnostics.com)

## Mike Coats Named as DLO Women's Health Specialist

Michael (Mike) Coats has been named DLO's Women's Health Senior Account Executive. In this role Mike's sole focus will be to provide Women's Health leadership to the DLO sales team and to our clients. Mike has served as a Physician Account Executive for DLO since 2010 in southwest Oklahoma. Prior to DLO, Mike sold for a pharmaceutical company as a cardiovascular specialist. Mike has been a consistent producer for DLO and in 2013 he was ranked in the top 10% of the Quest Diagnostics sales force nationally. more innovative testing in the area of women's health," said DLO Executive Sales Director Jeff McCown. "We have a very unique offering in the state with exclusive TEM-PCR™ technology for women's health panels and a partnership to offer leading edge NIPT products. Mike's new focus will help get our clients properly trained and equipped to better serve their patients."

Mike earned his bachelor's degree from the University of Oklahoma in Norman where he also played for and served as captain of the OU football team. He resides in Oklahoma City with his wife and five children.

"We're very excited to have Mike in this important role as we continue to offer

## Heart Health

# Treatment for Women with Coronary Heart Disease; Are We Measuring Up?

Sandra L. Vogel, RN

Clinical Liaison, Medical Affairs, Quest Diagnostics

On May 15<sup>th</sup> Diagnostic Laboratory of Oklahoma (DLO) helped sponsor Oklahoma City's local American Heart Association's (AHA) "Go Red for Women" luncheon. The Go Red for Women campaign is the world's largest network standing together to end heart disease in women.

Oklahoma women have some of the highest risk factors in the nation, as the following facts clearly show.<sup>1</sup>

- CHD and Stroke account for >31% of all female deaths
- Approximately 15 women die from CHD and stroke each day
- Stroke is the 4th cause of death for women
- Close to 62% of women are overweight or obese
- More than 25% of women smoke cigarettes

Nationwide, diabetes also contributes to this increase risk in women. A systematic review and meta-analysis published May of this year found on PubMed, revealed that women have >40% greater risk of incident CHD compared to men with diabetes. Future studies are warranted to more clearly understand the reasons and mechanisms responsible for the substantial gender differences in diabetes related - CHD risk.<sup>2</sup>

**Women and CHD:** We have talked about it, studied it, reviewed it. So what have we learned? The AHA conducted a national survey in 2012, looking at "Fifteen Year Trends (1997-2012) in Awareness of Heart Disease in Women".<sup>3</sup> During the decade after the launch of AHA's Go Red campaign, the awareness of heart disease as the

leading killer in women nearly doubled.<sup>3</sup> During the same time period the death rate from CHD among men and women declined approximately 50%.<sup>3</sup> However, the rate of awareness among women overall has not significantly changed in the past six years. We know that among white, black and Hispanic women awareness has improved over the past 15 years, but remains suboptimal.<sup>3</sup> Continued effort is needed to reach at risk populations. Public health campaigns like the AHA's "Go Red", and the National Heart, Lung, and Blood Institute's "Heart Truth" campaigns help bring focus on evidence-based strategies to prevent CHD and, to send messages that resonate and empower women to take action.

In the past, 15 years we have made progress, yet more needs to be done.

Where does the continued focus need to be targeted? First, efforts must continue to build on these gains in awareness, and encourage women to speak up and take action to improve their overall risk of CHD. Second, providers need to talk to their patients and discuss what their risk profiles look like. Third, providers need to educate patients about what options are available for evaluating risk, and recommend actionable steps to reduce the risks, including heart healthy lifestyles.

**Moving Forward:** Let's take a look at evolving technology that will better screen for early CHD in women.

Advanced lipid testing has been available commercially for nearly decades. Continued evolution in methodology has resulted in more accurate and clinically useful information.<sup>4</sup> The National Cholesterol Education Guidelines simply are not enough. A focus on LDL-cholesterol has been shown to fail to identify 75% of patients under 55 who had their first MI, and was insufficient to determine risk and to manage CHD patients.<sup>5</sup> Cholesterol concentration is an important marker of risk, but it is more important to consider size and number of these atherogenic particles, and the inflammation that is occurring with the infiltration into the arterial wall.<sup>6</sup> An elevated total LDL particle number

1. American Heart Association. (2014). *FACTS sheet: Cardiovascular Disease: Women's No. 1 Health Threat*. Washington, D.C. Retrieved from [http://www.heart.org/idc/groups/heart-public/@wcm/@adv/documents/downloadable/ucm\\_462778.pdf](http://www.heart.org/idc/groups/heart-public/@wcm/@adv/documents/downloadable/ucm_462778.pdf).

2. Peters, S. A. E., et al., (2014). Diabetes as risk factor for incident coronary heart disease in women compared with men. *Diabetologia*, 57(8), 1542-1551.

3. Mosca, L., et al., (2013). Fifteen-Year Trends in Awareness of Heart Disease in Women: Results of a 2012 American Heart Association National Survey. *Circulation*, 127, 1254-1263. doi: 10.1161/CIR.0b013e318287cf2f

4. American Heart Association. (2008). Lipid Management to reduce CV risk: A new strategy required. *Circulation*, 117, 560-568.

5. Akosah, K.O., et al., (2003). Preventing myocardial infarction in the young adult in the first place: how do the national cholesterol education panel iii guidelines perform? *Journal of the American College of Cardiology*, 41(9), 1475-1479.

6. Masunuru, K., et al., (2009). Ion Mobility Analysis of Lipoprotein Subfractions Identifies Three Independent Axes of Cardiovascular Risk. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 29, 1975-1980.



DLO employees attend Go Red for Women

is associated with a 1.4X increased risk; and small to medium LDL particles are associated with a 1.3 – 1.4X increased risk.<sup>6</sup> This increased risk is often not apparent on standard blood lipid testing.

Direct quantitative measurement of lipoproteins allows changes in the amount of each subclass to be monitored in response to therapy. This new tool coupled with measuring arterial inflammation markers, provides physicians with increased insight to better manage treatment decisions for their patients.

Ongoing provider support is included with Cardio IQ testing. Clinical Liaisons are available to help providers with test interpretation and possible treatment options. Clinical Educators are ready to support patients with a plan to follow their provider's goals for them. As providers and educators of women's health, we need to continue blazing the CHD prevention trail forward.

We appreciate the Oklahoma AHA Women's Go Red campaign, for keeping the conversation alive!

7. Stampfer, M.J., et al., (2000). Primary Prevention of Coronary Heart Disease in Women through Diet and Lifestyle. *New England Journal of Medicine*, 343, 16-22. doi: 10.1056/NEJM200007063430103

NIPT offerings. Offering access to this test strongly aligns with our strategy to deliver guideline-backed testing services based on the most advanced technologies in order to improve healthcare for patients."

A December 2012 medical opinion from the American Congress of Obstetricians and Gynecologists (ACOG) and the Society of Maternal Fetal Medicine (SMFM) supports the use of cell-free fetal DNA testing as an option for primary screening for women at increased risk of aneuploidy (abnormal chromosomal number), including those 35 years of age or older or who have a history of ultrasound abnormalities in pregnancy.

"We are pleased to establish a nationwide partnership with Quest, the world's leading provider of diagnostic information services," said William Welch, Chief Executive Officer of Sequenom, Inc. "Quest is a superb partner to further extend access to our MaterniT21 PLUS test to physicians and their patients seeking to make the most well informed decisions possible."

Sequenom Laboratories was the first to market a noninvasive prenatal laboratory-developed test for fetal chromosomal aneuploidies. The MaterniT21 PLUS test analyzes the relative amount of 21, 18, 13, as well as select other chromosomal material and micro deletions and duplications in cell-free DNA. The MaterniT21 PLUS test may be used for pregnant women at increased risk for fetal chromosomal abnormalities.

Once available, physicians will be able to order the test through Quest Diagnostics, which will forward specimens for testing to Sequenom Laboratories. Estimates suggest about 750,000 pregnancies may be at high risk for fetal chromosomal abnormalities each year in the United States.

In 2013, Quest Diagnostics introduced Cardio IQ testing using the Ion Mobility laboratory method. This method allows separation of lipoprotein particles to be characterized without any modification of the particles that could impact their size. Particles are electrophoretically separated in a gas phase, distinguishing particles on the basis of size. Size separated particles are detected and counted by light scattering.

## Prenatal Screening

The following is a news release from Sequenom, Inc.

## Sequenom Laboratories and Quest Diagnostics collaborate to expand patient access to the MaterniT21™ PLUS noninvasive prenatal test

MADISON, N.J. and SAN DIEGO, June 16, 2014 /PRNewswire/- Sequenom, Inc., a life sciences company providing innovative genetic analysis solutions, and Quest Diagnostics announced an agreement under which Quest will offer national access to Sequenom Laboratories' MaterniT21™ PLUS laboratory-developed test (LDT). Using a maternal blood sample, the noninvasive prenatal test (NIPT) analyzes chromosomal material in cell-free fetal DNA of pregnant women at increased risk for fetal chromosomal abnormalities. Quest expects to begin offering access to the test in the third quarter.

In addition, Quest has formed a license agreement with Sequenom for certain NIPT patents and patent applications. The license agreement is the first formed by Sequenom with a commercial lab in the United States. Quest intends to use the intellectual property for the purposes of developing and validating its own proprietary lab-developed NIPT test. Quest expects to introduce this new offering in 2015. Additional terms of the agreement were not disclosed.

"Noninvasive prenatal testing is one of the most promising new areas of medicine because it delivers highly actionable insights for empowering critical health decisions," said Charles (Buck) Strom, M.D., Ph.D., Senior Medical Director, Genetics, Quest Diagnostics. "The MaterniT21 PLUS test stands out for its technological sophistication and clinical usefulness, and is the most well validated to date of the

# Comprehensive Screening for Sexually Transmitted Disease Pathogens Improves Patient and Financial Outcomes

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 Kettering Health Network, Dayton Ohio  
 IDWeek Fall 2013- Abstract 4170

## Background:

The silent epidemic of sexually transmitted diseases (STD) and related complications represent a significant health issue world-wide and impacts patients, infants and community. The US has the highest rate of STD with about 19 million new infections occurring each year. STD organisms are all part of an ecological pool which simply share one thing in common: sex which predisposes patients to coinfection. The STD pool is not exclusive to Gonorrhea (GC) and Chlamydia (CTA), but inclusive for GC, CTA, Herpes (HSV) and Trichomonas (TVA). Asymptomatic shedding accounts for significant transmission. Routine comprehensive screening for all important agents will reduce infection by identifying those who need treatment with molecular technology being the technology of choice.

## Method:

The initial clinical validation of 20 symptomatic emergency department (ED) patients were tested for GC, CTA, HSV and TVA using TEM-PCR™ (Target Enriched Multiplex PCR) STD5 Diatherix proprietary assay. The STD5 panel is a comprehensive, rapid, sensitive and specific test for the detection of five common pathogens associated with STD in both symptomatic and asymptomatic patients.

Following the initial clinical validation, TEM-PCR STD5 was implemented for all routine testing of specimens (swabs and urine) submitted for STD evaluation. A retrospective analysis of the performance of this test was conducted (n=1855) on samples received March through August 2013 from ED, women’s centers and urgent care.

## Results:

### Initial Clinical Validation Symptomatic Emergency Department Patients:

Of the 20 ED patients, 19/20 had GC/CTA ordered; 1/20 was a GC screen only which was positive for CTA. 6/20 patients were positive for HSV2, one for HSV1 with coexisting oral lesions. 7/19 patients were positive for CTA and 3/19 for GC. One patient had both GC and HSV2. 5/20 were positive for TVA.

Chlamydia	HSV 1	HSV 2	GC	TRIC	Culture Results
Pos	Neg	Neg	Neg	neg	Neg
Neg	Pos	Neg	Neg	neg	HSV 1
Pos	Neg	Neg	Neg	Neg	Neg
Neg	Neg	Pos	Neg	Neg	Neg
Pos	Neg	Neg	Neg	Neg	Neg (Clue cells)
Neg	Neg	Neg	Neg	Pos	Tric (Group B strep)
Neg	Neg	Pos	Neg	Neg	Neg
Pos	Neg	Neg	Neg	Neg	Neg (Heavy Gardnerella, Group B strep)
Pos	Neg	Neg	Neg	Neg	Neg
Neg	Neg	Pos	Neg	Neg	Neg
Neg	Neg	Neg	Pos	Neg	Neg
Pos	Neg	Neg	Neg	Pos	Neg
Pos	Neg	Neg	Neg	Neg	Neg (Heavy Gardnerella, Group B strep)
Neg	Neg	Pos	Neg	Pos	Neg (Heavy Gardnerella, Group B strep, Candida albicans)
Neg	Neg	Neg	Pos	Neg	Neg (Candida albicans)
Neg	Neg	Pos	Pos	Neg	Neg (Clue cells, Gardnerella, Candida albicans)
Neg	Neg	Neg	Neg	Pos	Tric (Heavy Gardnerella)
Pos	Neg	Neg	Neg	Neg	GC SCREEN ONLY-NO GROWTH
Neg	Neg	Neg	Neg	Pos	Neg
Neg	Neg	Pos	Neg	Neg	Neg ( Heavy Gardnerella, Group B strep)

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## Comprehensive Screening for STD Pathogens Improves Patient Outcomes:

335 of 1855 were positive for at least one STD pathogen resulting in 18% detection rate. 130 of 1855 were positive for GC and/or CTA resulting in a 7% positive rate. Utilization of comprehensive screening panel improved detection rate by 11% and resulted in the detection of an additional 27 coinfections.

In addition, the utilization of TEM-PCR STD5 improved TVA detection rate by 53%. These data suggest that 53/100 patients will experience improved outcomes when tested for TVA by TEM-PCR when compared to microscopy.

## Conclusions:

The data suggest multiple cases of HSV and TVA are missed when patients are tested for GC/CTA only. The burden of TVA and the substantial evidence linking it to adverse health outcomes, including pelvic inflammatory disease, preterm delivery, cervical cancer, and increased susceptibility to HIV, speaks to the appropriateness of its inclusion in routine screening. Many patients with HSV had no visible lesions and were often misdiagnosed as urinary tract infection due to dysuria and pyuria. Primary infection with HSV was detected in two such patients both of which were pregnant. Microscopic evidence of BV as well as culture for organisms such as Gardnerella can be misleading

and when present may mask STD pathogens leading to inappropriate therapy and prolonged illness which often increases in severity. Four emergency department patients had multiple prior visits with repeated pelvic and gall bladder ultrasounds, and abdominal CAT scans. Significant downstream testing results in patients who test negative for GC and CTA when the etiology of HSV1 and 2 and TVA is unsuspected. These data suggest the comprehensive testing using technology such as TEM-PCR improves the outcome of patients with STD and impacts cost.

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### Single Organism Detected: N=298

Organism	GC	Chlamydia	Tric	HSV II	HSV I
Number	33	87	147	25	6

### Codetection With One or More Targets: N=37

Organism	GC/CTA	GC/TVA	CTA/TVA	HSV1/TVA	HSV 2/TVA	GC/CTA/TVA
Number	10	5	12	1	6	3

N=1855 Patients

N Positive Patients=335

TVA +/Wet Prep-	81
TVA +/Wet Prep+	73
TVA-/Wet Prep -	86
TVA-/Wet Prep +	1
<b>n=241</b>	

## CDC's STI Screening Recommendations

*Excerpted from "CDC FACT SHEET: Incidence, Prevalence, and Cost of Sexually Transmitted Infections in the United States," February 2013, Center for Disease Control. See more at [www.cdc.gov/std](http://www.cdc.gov/std).*

### CDC Recommended STI Screening Requirements

- All adults and adolescents should be tested at least once for HIV.
- Annual chlamydia screening for all sexually active women age 25 and under, as well as older women with risk factors such as new or multiple sex partners.
- Yearly gonorrhea screening for at-risk sexually active women (e.g., those with new or multiple sex partners, and women who live in communities with a high burden of disease).
- Syphilis, HIV, chlamydia, and hepatitis B screening for all pregnant women, and gonorrhea screening for at-risk pregnant women at the first prenatal visit, to protect the health of mothers and their infants.
- Trichomoniasis screening should be conducted at least annually for all HIV-infected women.
- Screening at least once a year for syphilis, chlamydia, gonorrhea, and HIV for all sexually active gay men, bisexual men, and other men who have sex with men

(MSM). MSM who have multiple or anonymous partners should be screened more frequently for STIs (e.g., at 3 to 6 month intervals). In addition, MSM who have sex in conjunction with illicit drug use (particularly methamphetamine use) or whose sex partners participate in these activities should be screened more frequently.

### STI Facts for Oklahoma

*Excerpted from the CDC's 2010 (most recent) "Oklahoma HIV/STD Epidemiology Profile Update."*

- Oklahoma had a Chlamydia incidence rate of 381.2 per 100,000 in 2010
- Chlamydia accounted for 76% of all reported STDs in Oklahoma for 2010
- In 2010, females made up 72% of Chlamydia cases in Oklahoma
- Oklahoma had a Gonorrhea incidence rate of 166.5 per 100,000 in 2010
- 57% of the reported Gonorrhea cases in 2010 in Oklahoma were females
- In 2010 Blacks had the highest rate of Chlamydia and Gonorrhea of all racial groups in Oklahoma

the most important question still remains for all of us who treat patients: what is the best way to screen for cervical cancer or precursors likely to progress to invasive cancer without causing undue burden. This article will summarize the most recent guidelines and the evidence supporting those recommendations.

In 2012, an update to the American Cancer Society guidelines for cervical cancer screening was published reflecting the best evidence-based practices reviewed in the peer-reviewed literature.<sup>3</sup> These recommendations are illustrated in Table 1 set forth on page 7.<sup>3</sup> In summary, women less than 21 years of age should not be screened regardless of the time of sexual initiation or other risk factors; women 21-29 years of age should be screened with cytology every 3 years; women 30-65 years old should preferably be screened by cytology and HPV testing (“co-testing”) every 5 years although cytology alone every 3 years is acceptable; women over the age of 65 years of age may discontinue screening unless there is a history of CIN2+ within the last 20 years.

Cervical cancer in women less than 21 years old is rare and screening has not changed the incidence of cervical cancer in this age group. Additionally, many young women may have transient infections or dysplastic lesions that are years removed from malignant transformation, though a diagnosis of infection with HPV may have a stigmatizing effect and even lead to unnecessary treatment. This is similar to the concerns in well-screened women 65 years of age and older who also have a low risk of cervical cancer and CIN2+ even with a new HPV infection. The screening strategies are intended to balance the benefits of screening with the potential harms.<sup>3</sup>

The majority of women screened for cervical cancer are between the ages of 30 and 65 years old. Co-testing, the preferred screening method<sup>3</sup>, increases the sensitivity for CIN3+ compared with cytology alone.<sup>4</sup> Additionally, co-testing confers a lower subsequent risk of CIN3+ thereby permitting a lengthening of the screening interval.<sup>4</sup>

This presents a clinical dilemma when faced with managing the patient who tests negative on cytology but is positive

for high-risk HPV. The counseling of patients who test positive for high-risk HPV can be challenging especially in the absence of identifiable cellular abnormalities. As clinicians, we want to be able to direct our patients to appropriate follow-up and treatment without causing unnecessary anxiety or discomfort – primo non nocere.

It is for this reason that the specificity of the HPV assay is most relevant to clinical care. HPV DNA assays only detect the presence of the HPV virus, but most HPV infections are transient and few are associated with CIN3 or progression to cancer.<sup>5</sup> As opposed to testing for other viruses such as HIV, the goal is not to detect all HPV but only those types that are clinically significant – those associated with severe dysplasia at colposcopy.

**“...the goal is not to detect all HPV but only those types that are clinically significant... An effective approach for detection of cervical disease is to target those oncogenic elements of HPV that foster persistent viral infection and cellular transformation.”<sup>6</sup>**

The presence of HPV does not mean that cervical dysplasia or cervical cancer is present. An effective approach for detection of cervical disease is to target those oncogenic elements of HPV that foster persistent viral infection and cellular transformation.<sup>6</sup> Certain HPV proteins, E6 and E7, are responsible for viral replication and transformation of the host cell.<sup>7</sup> Their overexpression, which can be measured as E6/E7 messenger RNA (mRNA) transcripts, indicates HPV oncogenic activity and may be used as a clinically predictive marker to identify women at risk of developing high-grade cervical dysplastic lesions.<sup>6</sup> The Aptima® HPV Assay is an E6/E7 oncogene mRNA-based assay that has been shown to have equivalent sensitivity and improved specificity for the detection of clinically significant disease compared to DNA- based HPV assays.<sup>8</sup>

3. Saslow, Debbie, et al., (2012). 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. *American Journal of Clinical Pathology*, 137(4), 516-42.

4. Dillner, J., et al., (2008). Long term predictive values of cytology and human papillomavirus testing in cervical cancer screening: joint European cohort study. *BMJ*, 337, a1754.

5. Moscicki, A.B., Schiffman, M., Kjaer, S., & Villa, L.L. (2006). Chapter 5: Updating the natural history of HPV and anogenital cancer. *Vaccine*, 24(suppl 3), S42-51.

6. Monsonogo, Joseph, et al., (2011). Evaluation of oncogenic human papillomavirus RNA and DNA tests with liquid-based cytology in primary cervical cancer screening: the FASE study. *International Journal of Cancer*, 129(3), 691-701.

7. Huh, W. (2009). Human papillomavirus infection; a concise review of natural history. *Obstetrics & Gynecology*, 114(1), 139-143.

8. Arbyn, M., et al., (2013). The APTIMA HPV assay versus the Hybrid Capture 2 test in triage of women with ASC-US or LSIL cervical cytology: a meta-analysis of the diagnostic accuracy. *International Journal of Cancer*, 132(1), 101-8.

If the results of co-testing are discordant with a negative cytology but positive for high-risk HPV, the clinician has the option of either repeating the Pap test and HPV assay in 12 months or reflexing for HPV 16/18 genotypes.<sup>3</sup> Since not all high-risk HPV types have the same oncogenic potential, the least risky HPV types can be managed conservatively with one-year follow-up. The more oncogenic types, HPV 16/18, account for over 70% of cervical cancers.<sup>9</sup> The Aptima® HPV 16 18/45 Genotype Assay identifies HPV types 16, 18/45, which together are associated with 75% of squamous cell carcinoma and 93% of adenocarcinomas.<sup>10,11</sup>

Despite the impact of Pap-based screening strategies to reduce the incidence of squamous cell carcinoma, cervical adenocarcinoma has been increasing over the

last few decades.<sup>1</sup> The addition of the HPV assay and HPV genotyping may improve the identification of women with adenocarcinoma and its precursors. If HPV 16, 18/45 genotyping is positive, the patient should be referred for immediate colposcopy.

In women 30 years of age and older, co-testing with Pap test and HPV mRNA, along with genotyping for 16, 18, and 45, provides high sensitivity for the detection of CIN 3 and greater, improved specificity for cervical disease, and may increase the detection of cervical adenocarcinoma and its precursors. This screening strategy balances the benefits of detecting disease while minimizing the potential harms of unnecessary clinical follow-up in healthy women.

**Table 1**  
**Summary of Recommendations**

Population	Page Numbers	Recommended Screening Method*	Management of Screen Results	Comments
Aged <21 y	521-522	No screening		HPV testing should not be used for screening or management of ASC-US in this age group
Aged 21-29 y	522-523	Cytology alone every 3 y	HPV-positive ASC-US <sup>†</sup> or cytology of LSIL or more severe: Refer to ASCCP guidelines <sup>2</sup> Cytology negative or HPV-negative ASC-US <sup>†</sup> : Rescreen with cytology in 3 y	HPV testing should not be used for screening in this age group
Aged 30-65 y	523-529	HPV and cytology "cotesting" every 5 y (preferred)	HPV-positive ASC-US or cytology of LSIL or more severe: Refer to ASCCP guidelines <sup>2</sup> 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 <sup>†</sup>
		Cytology alone every 3 y (acceptable)	HPV-positive ASC-US <sup>†</sup> or cytology of LSIL or more severe: Refer to ASCCP guidelines <sup>2</sup> Cytology negative or HPV-negative ASC-US <sup>†</sup> : Rescreen with cytology in 3 y	
Aged >65 y	529-531	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	531	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	531-533	Follow age-specific recommendations (same as unvaccinated women)		

ASCCP, American Society for Colposcopy and Cervical Pathology; ASC-US, atypical squamous cells of undetermined significance; CIN2, cervical intraepithelial neoplasia grade 2; HPV, human papillomavirus; LSIL, low-grade squamous intraepithelial lesion.  
\* Women should not be screened annually at any age by any method.  
† ASC-US cytology with secondary HPV testing for management decisions.

9. Schiffman, M., Castle, P.E., Jeronimo, J., Rodriquez, A.C., & Wacholder, S. (2007). Human papillomavirus and cervical cancer. *The Lancet*, 370(9590), 890-907.  
10. Guan, P., et al., (2012). Human papilloma types in 115, 789 HPV-positive women: A meta-analysis from cervical infection to cancer. *International Journal of Cancer*, 131(10), 2349-2359.  
11. de Sanjose, S., et al., (2010). Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. *The Lancet Oncology*, 11(11), 1048-56.

## Education Center

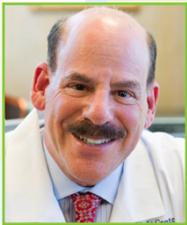
### Online Education Presentations Now Available



#### Review of Clinical Research and the Effective use of Omega -3 & -6 Fatty Acids in Patient Management

Robert Superko, MD and Michael Caulfield, MD, will present the current clinical research on the use of Omega -3 and -6 supplementation and their link to decreased risk of cardiovascular events, including sudden cardiac death. They will also discuss the clinical management of patients including the use of the Omega -3 & -6, fatty acid laboratory test as a marker of cardiovascular risk.

<http://www.education.questdiagnostics.com/presentations>



#### Advanced Insights into Residual Cardiovascular Risk-Another Perspective

Dr. Ian Levenson brings his unique perspective to the discussion of the benefit of going beyond the traditional Lipid Panel. He will review the value of Advanced Cardiovascular Testing and how it can be applied to a large practice that focuses on prevention, general medicine and cardiovascular risk.

<http://education.questdiagnostics.com/presentations>



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