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- *STI Quarterly*: New study points to long-term effectiveness of 9-valent HPV vaccine; *Mycoplasma genitalium*: Science focuses on sexually transmitted infection


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# Task Force Issues Cervical Cancer Screening Guidance: What Changes Can Clinicians Expect?

*Ages 30-65: Cervical cytology every three years or HPV testing every five years*

The U.S. Preventive Services Task Force (USPSTF) has just released draft guidance on cervical cancer screening, with a major proposed change stating that for average-risk women ages 30-65, testing may be done with either cervical cytology alone every three years or with high-risk human papillomavirus (hrHPV) testing every five years. Co-testing no longer is required.[1]

"WOMEN AGES 30 TO 65, THEREFORE, HAVE A CHOICE BETWEEN THE PAP TEST EVERY THREE YEARS OR HRHPV TEST EVERY FIVE YEARS."
— MAUREEN PHIPPS, MD, MPH, WARREN ALPERT MEDICAL SCHOOL, BROWN UNIVERSITY, PROVIDENCE, RI

Guidance highlights are as follows:

- The USPSTF recommends screening for cervical cancer in women 21-29 years of age every three years with cervical cytology alone. For women 30-65 years of age, the task force recommends either screening with cervical cytology alone every three years or screening with hrHPV testing alone every five years.
- The task force recommends against screening for cervical cancer in women older than 65 years of age who have had adequate prior screening and are not otherwise at high risk for cervical cancer.
- The task force recommends against screening for cervical cancer in women younger than 21 years of age. This recommendation does not apply to women living with HIV or who




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otherwise have a compromised immune system.

- The USPSTF recommends against screening for cervical cancer in women who have had a hysterectomy with removal of the cervix and who do not have a history of a high-grade precancerous lesion (cervical intraepithelial neoplasia grade 2 or 3) or cervical cancer.

The guidance does not apply to women who are already at high risk for the disease, such as those who have been diagnosed with a high-grade precancerous cervical lesion or those who have a weakened immune system.

"The task force looked at the evidence on the effectiveness of different screening tests and intervals based on age, and found that after age 30, the Pap test and hrHPV tests are both effective for cervical cancer screening," stated task force member **Maureen Phipps**, MD, MPH, department chair and Chace-Joukowsky professor of obstetrics and gynecology and assistant dean for teaching and research on women's health at the Warren Alpert Medical School of Brown University in Providence, RI, in a release accompanying the proposed guidance. "Women ages 30 to 65, therefore, have a choice between the Pap test every three years or hrHPV test every five years."

## Understand Screening Options

Reproductive health clinicians are familiar with the traditional Pap test, used to identify abnormal cervical cells such as ASC-US (atypical squamous cells of undetermined significance) and LSIL (low-grade squamous intraepithelial lesion) immediately after collection. Clinicians now can choose from five different hrHPV tests, approved by the Food and Drug Administration (FDA): the Hybrid Capture 2 and the Cobas hrHPV, Aptima hrHPV Assay, and the Cervista hrHPV 16/18 and Cervista high-risk hrHPV. These hrHPV tests have been approved for screening patients with abnormal cytology results to determine the need for colposcopy referral and for use in women 30 years of age and older in conjunction with cytology to determine possible high-risk hrHPV type. In 2014, the FDA approved the Cobas hrHPV test as a primary cervical cancer screening test for women 25 years of age or older.

Regular screening for women 21-65 years of age greatly reduces the rate of cervical cancer and the number of deaths resulting from cervical cancer.[2] The most effective screening test depends on a woman's age, according to the USPSTF evidence search. For women ages 21-29, many HPV infections will resolve on their own, so the Pap test is most effective.[3] For women from age 30 to 65, HPV infections are more likely to lead to cancer, so either Pap tests or hrHPV tests are effective for screening, the evidence review noted.[1]

"Cervical cancer screening can lead to follow-up testing and treatment procedures that can cause harms such as vaginal bleeding, pain, infection, and complications during future pregnancies," reads the draft guidance. "However, because screening for cervical cancer saves lives and identifies cervical cancer early, when it is treatable, the Task Force concludes that the benefits of screening outweigh any possible harms

## EXECUTIVE SUMMARY

The U.S. Preventive Services Task Force has released draft guidance on cervical cancer screening, with a major proposed change stating that for average-risk women ages 30-65 years, testing may be done with either cervical cytology alone every three years or with high-risk human papillomavirus testing alone every five years. Co-testing no longer is required.

- Women who are older than 65 years of age who have had adequate prior screening and are not otherwise at high risk for cervical cancer do not require screening.
- Women younger than 21 years of age should not be screened for cervical cancer, the guidance states. This recommendation does not apply to women living with HIV or who otherwise have a compromised immune system.

for women ages 21 to 65," the document says.

## Organizations Weigh In

**Haywood Brown**, MD, president of the American College of Obstetricians and Gynecologists (ACOG), and **Anna-Barbara Moscicki**, MD, president of The American Society for Colposcopy and Cervical Pathology (ASCCP), issued a joint statement on the proposed guidance.

"At this time, ACOG continues to affirm the clinical guidance included in Practice Bulletin No. 168, 'Cervical Cancer Screening and Prevention,' which recommends that for women aged 30-65 years, co-testing with cytology and high-risk HPV testing every five years is preferred, and screening with cytology alone every three years is acceptable," the statement reads.

The task force's draft recommendations for routine cervical cancer screening in women younger than 21 years of age, for women ages 21-29, and for women older than 65 years of age who have been adequately screened previously have not changed and remain the same as ACOG's current guidance, the joint statement notes.

## Self-collection on Horizon?

Not all women have easy access to cervical cancer screening because of geography or socioeconomic status. Recent research indicates that self-collected swabs are effective, and may lead to increased access to testing.[4-5]

The FDA will hold a public workshop, "Self-Collection Devices for Pap Test," in January 2018 to obtain feedback about the feasibility, benefits, risks, impact on current standard of care, and validation approaches for self-collection devices for cervical cancer screening by Pap testing.

The task force notes that hrHPV testing samples offer the potential to be collected by the patient and mailed to health programs for analysis. While self-collection may be one strategy for increasing screening rates among at-risk populations, comparative studies are needed to verify their use and to identify effective strategies for implementation.

Many patients and clinicians traditionally have used the cervical cancer screening visit as an opportunity to discuss other health problems and preventive measures.

"The potential for self-screening for hrHPV is exciting, but also is the source of much concern for providers who use this screening as a reason for interacting with their patients periodically," notes **Anita Nelson**, MD, professor and chair of the obstetrics and gynecology department at Western University of Health Sciences in Pomona, CA. ■

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# U.S. MEC Updates Contraceptive Information for Women With HIV

Women now account for 19% of the 39,513 new HIV diagnoses in the United States in 2015. Heterosexual sex accounted for 86% of these diagnoses, according to the most recent statistics.[1]

In an update to its U.S. Medical Eligibility Criteria for Contraceptive Use, 2016, the Centers for Disease Control and Prevention (CDC) is revising its recommendation on the use of the progestin-only contraception injection depot medroxyprogesterone acetate (DMPA) by women at high risk for HIV from Category 1 (no restriction) to Category 2 (benefits outweigh theoretical or proven risks).[2]

The guidance indicates that women at high risk for HIV should continue to have access to the contraceptive shot, but should be counseled about a possible, but uncertain, increased risk of contracting HIV and how to reduce their risk.

The CDC has been closely monitoring evidence on whether use of hormonal contraceptives is associated with an increased risk of HIV acquisition among non-infected women, says **Naomi Tepper**, MD, MPH, a CDC medical officer.

"Studies report inconsistent results on whether use of progestin-only injectables, including DMPA, is associated with an increased risk of HIV acquisition," says Tepper. "More recent studies and a new meta-analysis suggest a possible increased risk of HIV acquisition among women using progestin-only injectables, although results varied across individual studies, and most of these studies had methodologic weaknesses."

In light of the published meta-analysis,[3] the World Health Organization (WHO) updated its guidance, changing its classification of long-acting injectable contraceptives like DMPA from "use without restriction" to "benefits outweigh theoretical or proven risks."[4]

"In order to keep its guidance for providers up to date, CDC considered the entire body of evidence, recently updated WHO guidance on this issue, other factors such as potential biological mechanisms and the context of family planning in the U.S., and individual input from external experts in HIV or family planning," says Tepper. "The agency determined that the updated WHO recommendations were applicable to the United States and decided to adopt the WHO recommendations."

An accompanying clarification to the U.S. guidance notes that there is evidence of a possible increased risk of acquiring HIV among progestin-only injectable users. It goes on to state that it is not clear whether the effect is due to methodological issues with the evidence or a real biological effect. All women at risk for HIV infection, regardless of contraceptive choice, should be counseled about how to reduce their risk, the guidance states.[2]

Scientists now are involved with the ECHO Study (Evidence for Contraceptive Options and HIV Outcomes), launched in December 2015. It is the first randomized clinical trial designed to assess the risk of HIV acquisition by women using one of three contraceptives: DMPA, the levonorgestrel implant Jadelle, and the copper IUD. The study, spread across 12 research sites in Kenya, South Africa, Swaziland, and Zambia, also is designed to evaluate the performance of these methods in relation to pregnancy rates, side effects, and women's patterns of use. More than half of the intended 7,800 voluntary participants have been enrolled. Initial results are expected in early 2019.

Women who are at high risk of unintended pregnancy and HIV have multiple concerns — HIV infection

## EXECUTIVE SUMMARY

The Centers for Disease Control and Prevention is revising its recommendation on the use of the progestin-only contraception injection depot medroxyprogesterone acetate (DMPA) by women at high risk for HIV from Category 1 (no restriction) to Category 2 (benefits outweigh theoretical or proven risks).

- The guidance indicates that women at high risk for HIV should continue to have access to the contraceptive shot, but also should be counseled about a possible, but uncertain, increased risk of contracting HIV and how to reduce their risk.
- The change follows the World Health Organization's update of its recommendations on DMPA use in women at risk for HIV. Such action comes after the 2016 publication of a meta-analysis suggesting a possible increased risk of HIV acquisition among women using progestin-only injectables.

is associated with adverse pregnancy outcomes for both the mother and child, including increased morbidity during pregnancy and perinatal HIV transmission.[5]

The most recent statistics on U.S. contraceptive trends indicate that while overall use of DMPA in the United States is low (4.5%), among current contraceptive users during 2011-2013, use was higher among black women (10%), women ages 15-24 (8.5%), those who had income of less than 150% of the federal poverty level (7.3%), and women who had less than a high school education (10.1%).[6] While the rate of unintended pregnancy is declining, the latest data indicate that 45% of pregnancies in the United States were unintended in 2011, with higher percentages among women ages 15-19 (75%) and black women (64%).[7]

Women at high risk for HIV have many options available when it comes to contraception. Recommendations for other hormonal contraceptive methods, including combined hormonal methods, implants, and progestin-only pills, have no restriction on their use (U.S. MEC category 1). No change was made in their use in this update. For both the copper-T and the levonorgestrel intrauterine devices, the U.S. MEC classifies use as Category 2 — the benefits outweigh theoretical or proven risks.[8] ■

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# Vending Machines Expand Options for College Health Emergency Contraception

While age restrictions on levonorgestrel emergency contraceptive pills (ECPs) were removed in 2013, access to pills is often tricky, even for college-age students. Now, Stanford University and University of California locations in Santa Barbara and Davis are among the latest campuses that have installed vending machines stocked with ECPs.

The idea to make ECPs available from vending machines on college campuses is not new. In 2010, Shippensburg University in Pennsylvania began making EC available though a vending machine inside the student health center. University officials installed the machine after a student survey indicated 85% of respondents supported such accessibility. Since the machine is inside the health center, it is accessible only to students and employees.

What legal issues, if any, may arise from the availability of ECPs on college campuses via vending machines? According to **Michelle Mello**, PhD, JD, professor of law at Stanford Law School and professor of health research and policy at Stanford School of Medicine, liability risk is "vanishingly small," and is outweighed by the benefits of having ready access to emergency contraception.

"Anytime a consumer buys a drug over the counter, rather than with a doctor's prescription, there's a risk that because she's not getting counseling about the drug, she won't have as good an understanding of the dosing instructions or side effects," said Mello in a statement. "But vendors aren't likely to be held responsible for that."

## The Need Is Real

According to **Rachel Mack**, interim director of marketing and

communications at the American College Health Association (ACHA), 17.8% (male: 14.8%; female: 19.1%) of sexually active undergraduate college students reported use or partner use of emergency contraception ("morning after pill") within the past 12 months in the organization's most recent survey. Students who responded "not sexually active" were excluded from the analysis.

According to results from ACHA's most recent survey, performed in 2014, the contraceptive methods that were most commonly listed as being prescribed at health centers were oral contraceptives (97.2%), the ring (95.8%), the shot (94.2%), the patch (86.7%), and emergency contraception (82.2%).[1] About 72% (96 schools) of the 133 schools that answered the question, "Does your health center prescribe, dispense, administer or refer for any of the following contraceptive methods?" reported dispensing emergency contraception, while 82.2% (111 schools of 135) said they prescribed EC, said Mack.

## Why Vending Machines?

Colleges and universities have received requests for vending machine ECPs because some student health centers are closed on the weekend and nearby pharmacies may not offer 24/7 access. Dartmouth College in Hanover, NH, offers ECPs and a small selection of non-prescription drugs and health supplies, such as cold medicines, condoms, thermometers, and lip balm, at its student health center, while Pomona College in Claremont, CA, stocks a machine with condoms, ECPs, and a large selection of general health products at its student health services' wellness room.

Despite policy changes that started in 2013 and were intended to improve access to EC, there still are persistent barriers to access. Restrictions on generic forms of EC were removed in 2014. However, packaging still had to include a "use recommendation" that mentioned the intended users were limited to women 17 years of age or older. The use recommendation, while not enforceable, was related to Frazer, PA-based Teva Women's Health's patent on Plan B One-Step, the initial levonorgestrel EC pill. This recommendation was removed in 2016 when the market exclusivity for Plan B One-Step expired.

Data from a 2016 published analysis of an online questionnaire gathered via an EC-focused listserv for reproductive health professionals indicate that changes in the regulatory status of emergency contraception have resulted in widespread confusion about how it may be sold.[2]

Respondents indicated that a majority (65%) stocked emergency contraception on over-the-counter shelves, although only 22% of these displayed it without a locked security enclosure. Chain pharmacies were more likely to to stock EC on shelves than were independent pharmacies (77% vs. 5%; $P = 0.000$), but there was variation among stores in the same chain. Among stores that were checked, 40% incorrectly reported an age restriction for non-prescription purchase of emergency contraception, while 95% correctly stated that men can buy ECPs. The average price for brand LNG EC was $49.64 and for generic LNG EC was $40.05.[2]

In a more recent study, which used female mystery callers to contact pharmacies in Nashville, Philadelphia, Cleveland, Austin, and Portland, correct information about over-the-counter access was provided only 51.6% of the time. Accuracy did not differ according to the pharmacy's neighborhood income (47.9% vs. 55.3%, adjusted OR 0.89; 95% confidence interval [CI], 0.71–1.11) and was not significantly different from 2012 ($P = 0.37$).[3]

A new website and app, Nurx (www.Nurx.com), is looking to change the game in delivery of not just emergency contraception, but other forms of hormonal contraception as well. Women in Texas, California, New York, Washington, Pennsylvania, Illinois, Virginia, Florida, Indiana, Massachusetts, New Jersey, Michigan, Missouri, Minnesota, and the District of Columbia now can communicate with a healthcare provider online


## EXECUTIVE SUMMARY

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- Colleges and universities have received requests for vending machine ECPs because some student health centers are closed on the weekend and nearby pharmacies may not offer 24/7 access.
- According to the American College Health Association's most recent data, 17.8% (male: 14.8%; female: 19.1%) of sexually active undergraduate college students reported use or partner use of ECPs within the past 12 months.

and have prescriptions ordered and delivered to their homes. The company is partnering with licensed medical providers and pharmacies in hopes of expanding the program to other states. ■

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# Clinician Alert: STIs Hit High-water Mark

More than 2 million cases of chlamydia, gonorrhea, and syphilis were reported in the United States in 2016, the highest number ever, according to the latest surveillance from the Centers for Disease Control and Prevention (CDC).[1]

Most of the new diagnoses of sexually transmitted infections (STIs) were attributed to chlamydia (about 1.6 million), with 470,000 cases of gonorrhea and almost 28,000 cases of primary and secondary syphilis.

During 2011-2013, the rate of reported chlamydial infection decreased to 443.5 cases per 100,000 population, followed by an increase in the rate of reported cases over each of the next three years, the new surveillance notes. During 2015-2016, the rate increased 4.7%, from 475.0 to 497.3 cases per 100,000 population.[1]

While chlamydia, gonorrhea, and syphilis may be treated with antibiotics, such serious health consequences as infertility, ectopic pregnancy, stillbirth in infants, and increased risk for HIV transmission can arise if cases are not addressed.

Of particular concern to public health officials is the rise in congenital syphilis. The growth in cases of syphilis among newborns between 2014 and 2016 has accelerated: In 2014, there were 461 reported cases of congenital syphilis, while in 2016, there were 628 reported cases. Untreated maternal infection can lead to fetal death, preterm birth, and congenital infection in a proportion of surviving infants, leading to physical and mental developmental disabilities.[2] Most cases of congenital syphilis can be prevented if women are screened for syphilis and treated early during their prenatal care visits.

"Every baby born with syphilis represents a tragic systems failure," said **Gail Bolan**, MD, director of the CDC's Division of STD Prevention in a statement. "All it takes is a simple STD test and antibiotic treatment to prevent this enormous heartache and help assure a healthy start for the next generation of Americans."

## EXECUTIVE SUMMARY


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- Most of the new diagnoses of sexually transmitted infections were attributed to chlamydia (about 1.6 million), with 470,000 cases of gonorrhea and almost 28,000 cases of primary and secondary syphilis.
- While all three infections may be treated with antibiotics, such serious health consequences as infertility, ectopic pregnancy, stillbirth in infants, and increased risk for HIV transmission can arise if cases are not addressed.


## Men Also at Risk

Another highlight from the recent report is the growth of gonorrhea in men. While the STI increased among men and women in 2016, the largest increases were seen among men. Men who have sex with men (MSM) may be most affected, research indicates.[3]

Finding new options for treatment of gonorrhea has become a high priority for public health officials. A cluster of gonorrhea infections that shows both decreased susceptibility to ceftriaxone and very high-level resistance to azithromycin has been identified.[4] (Contraceptive Technology Update *reported on the incident; see the January 2017 article, "STDs at Unprecedented High in United States," available at* http://bit.ly/2hrYtkh.) Ceftriaxone plus azithromycin is the only recommended treatment for gonorrhea.[5]

"Because we have seen indications in recent years that drug resistance could soon jeopardize the last recommended treatment for gonorrhea, it is vitally important to strengthen the timeliness of our surveillance efforts to preserve our ability to treat gonorrhea," says **Elizabeth Torrone**, PhD,

an epidemiologist in the CDC's Division of STD Prevention. "CDC recently launched a new program 'SURRG' — Strengthening the U.S. Response to Resistant Gonorrhea — a system designed to enhance domestic gonorrhea surveillance and infrastructure by working with local and state health departments to detect emerging resistance in the laboratory and stopping transmission through field investigation."

## Be Sure to Screen

What can you do as a provider to stem the tide? The CDC suggests that all clinicians should make STD screening and timely treatment a standard part of medical care, especially for pregnant women and MSM. Look to seamlessly integrating STD screening and treatment into prenatal care and HIV prevention and care services, the CDC recommends.

What are testing recommendations for your patients? The CDC suggests the following:

- All adults and adolescents from ages 13-64 should be tested at least once for HIV.
- **Annual chlamydia screening is recommended for all sexually active women younger than 25 years of age, as well as for older women with such risk factors as new or multiple sex partners, or a sex partner who has a sexually transmitted infection.**
- Annual gonorrhea screening is recommended for all sexually active women younger than 25 years of age, as well as for older women with risk factors (new or multiple sex partners, or a sex partner who has a sexually transmitted infection).
- Syphilis, HIV, and hepatitis B screening is recommended for all pregnant women. Chlamydia and gonorrhea screening for at-risk pregnant women should start early in pregnancy, with repeat testing as needed, to protect the health of mothers and infants.
- Screening should be performed at least once a year for syphilis, chlamydia, and gonorrhea for all sexually active gay, bisexual, and other men who have sex with men. Those MSM who have multiple or anonymous partners should be screened more frequently for STDs, such as at three- to six-month intervals.

Sexually active gay and bisexual men also may benefit from more frequent HIV testing.

- Patients who have unsafe sex or share injection drug equipment should get tested for HIV at least once a year.[6] ■

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# Low Rates of Adherence to PID Guidance Found in Emergency Departments

Research analyzing trends in the nation's emergency departments indicates low rates of HIV and syphilis screening among teens diagnosed with pelvic inflammatory disease (PID), despite the high risk for such infections. Data also suggest low rates of adherence to national PID treatment guidelines as well.[1]

A complication of undiagnosed or undertreated sexually transmitted infection (STI), PID can signal patients at heightened risk for syphilis or HIV, state the research paper authors. PID occurs when microorganisms ascend from the vagina or cervix to the fallopian tubes and other upper genital tract structures; it can lead to infertility, ectopic pregnancy, and chronic pelvic pain.[2] Timely treatment with antibiotics can prevent severe damage to the reproductive organs; clinicians should refer to recommended treatment regimens in the Centers for Disease Control and Prevention (CDC) 2015 STD Treatment

Guidelines.[3] (*Check the guidance online at http://bit.ly/2k86xqp.*)

"As a clinician who practices exclusively in the emergency department (ED), I saw an opportunity to make real and lasting improvements to the health of teens and adolescents who receive care in the ED setting," says **Monika Goyal**, MD, MSCE, assistant professor of pediatrics and emergency medicine, director of research, division of emergency medicine, and attending physician at Children's National Health System at George Washington University. "As a first step, the field needed a stronger evidence base to characterize the unmet need in order to begin to consider potential interventions tailored to teens and youths."

To that end, during the past 10 years, Goyal has developed a research program dedicated to improving the timely diagnosis and appropriate treatment of STIs among adolescents seen in the emergency department.

## Check the Numbers

To determine the frequency of HIV and syphilis screening among adolescents diagnosed with PID, Goyal and fellow researchers performed a cross-sectional study, using the Pediatric Health Information System database of 48 children's hospitals from 2010 through 2015, looking at all ED visits by females 21 years of age or younger with an ICD 9 or ICD 10 code diagnosis of PID to calculate the frequency of HIV, syphilis, gonorrhea, and chlamydia testing. The researchers used separate multivariable logistic regression analyses to identify patient-level factors such as age, race/ethnicity, insurance status, and disposition, as well as hospital-level factors such as geographic region and bed number, associated with HIV and syphilis testing. Researchers also calculated the rates of prescribed antibiotics that adhered to published CDC PID treatment guidelines for the concurrent year.

The analysis detected 10,698 PID diagnoses. The girls' mean age was recorded as 16.7; nearly 54% were non-Latino black, and 37.8% ultimately were hospitalized. While data indicate that testing for other sexually transmitted infections, such as gonorrhea and chlamydia, occurred in more than 80% of patients diagnosed with PID, just 27.7% underwent syphilis screening, and just 22% were screened for HIV.[1] The CDC recommends that all women diagnosed with PID be screened for HIV, and also calls for syphilis screening for people at high risk for infection.[3]

The CDC recommends that presumptive treatment for PID should be started in sexually active young women and other women at risk for STIs if they are experiencing pelvic or lower abdominal pain, if no cause for the illness other than PID can be identified, and if one or more of the following minimum clinical criteria are present on pelvic examination:

- cervical motion tenderness; or
- uterine tenderness; or
- adnexal tenderness.[4]

## Time to Make a Difference

Young people 15-24 years of age account for half of the nearly 20 million new STIs that occur each year in the United States.[5] Many of them view the emergency department as the primary place to receive healthcare, says Goyal. If clinicians could increase STI screening rates in the ED setting, there could be a "tremendous impact" on the STI epidemic, notes Goyal.

Goyal and her research team have developed an audio-computer–assisted self-interview sexual health survey that can help ED clinicians increase testing rates among high-risk adolescents. Their research, presented at the 2016 American Academy of Pediatrics National Conference and Exhibition in San Francisco, indicates that providing sexual health survey-derived decision support to emergency department clinicians led to increased testing rates for STI in adolescents at high risk for infection, particularly in those presenting asymptomatic for infection.[6]

Because chlamydia and gonorrhea often have no symptoms, many women may not know they are infected and could be at risk for PID,

## EXECUTIVE SUMMARY

Research analyzing trends in the nation's emergency departments indicates low rates of HIV and syphilis screening among teens diagnosed with pelvic inflammatory disease, despite the high risk for such infections. Data also suggest low rates of adherence to national treatment guidelines.

- A complication of undiagnosed or undertreated sexually transmitted infection, pelvic inflammatory disease can signal patients at heightened risk for syphilis or HIV.
- Pelvic inflammatory disease occurs when microorganisms ascend from the vagina or cervix to the fallopian tubes and other upper genital tract structures; it can lead to infertility, ectopic pregnancy, and chronic pelvic pain.

notes **Kristen Kreisel**, PhD, a CDC epidemiologist.

"If not treated, PID may lead to infertility, ectopic pregnancy, and chronic pelvic pain," states Kreisel. "Annual chlamydia and gonorrhea screening of sexually active women 25 years and younger is critical to reduce the burden of these STIs and their potential long-term consequences." ■

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TEEN TOPICS

# HIV Pre-exposure Prophylaxis for Adolescents: A Health Equity and Reproductive Justice Issue


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In the United States, adolescents and young adults (AYA) ages 13-24 years accounted for 22% of all new HIV infections in 2014, with rates of acquisition highest (80%) among young men who have sex with men (MSM).[1] People of color have a much greater lifetime risk of HIV compared to non-Hispanic whites, and data suggest that unless prevention efforts improve, 40% of black young MSM will acquire HIV by age 40.[2] Stark disparities in HIV infection also exist by geographic location, where rates of HIV diagnoses among young adults in 2015 were disproportionately high in the South.[3]

The 2020 U.S. National HIV/AIDS Strategy (NHAS) lays out its vision: "The United States will become a place where new HIV infections are rare and when they do occur, every person regardless of age, gender, race/ethnicity, sexual orientation, gender identity or socio-economic circumstance, will have unfettered access to high quality, life-extending care, free from stigma and discrimination."[4]

Primary goals of the National Strategy include: reducing HIV-related disparities and health inequities and providing full access to comprehensive pre-exposure prophylaxis (PrEP) services with support for medication adherence for those using PrEP.[4]

## PrEP Is Proven to Work

Daily use of the anti-HIV medication known as PrEP by people who are HIV-negative has demonstrated a reduction in HIV transmission rates by up to 75% in heterosexual partners and up to 99% among MSM and transgender women.[5,6] Unfortunately, due to limited data among adolescents, PrEP was FDA-approved in 2012 as Truvada only for adults ages 18 years and older.

In the first open-label study to examine the safety, adherence, tolerability, and changes in sexual risk behavior among young MSM, Project PrEP enrolled a diverse sample of 78 eligible, consenting participants (ages 15-17) at high risk for acquiring HIV and provided them with daily tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) as PrEP for 48 weeks. All study participants tested HIV-negative at the start of the study, and received individualized counseling about HIV risk. During

the 48 weeks of PrEP use, adherence decreased at each follow-up period, 23 sexually transmitted infections were diagnosed in 12 participants, and three young males became infected with HIV, although blood samples insinuate they were taking less than two PrEP doses each week.[7]

The results of this groundbreaking behavioral invention provide evidence that PrEP is both safe and tolerable for adolescents younger than 18 years of age, with few adverse effects, and no increase in sexually risky behaviors during the study period. An editorial accompanying this study argues that the findings also reveal youth may need more support from a multiteam, interdisciplinary, community-oriented approach to address the social and structural barriers that affect their access to PrEP, adherence levels, and interpretation of HIV risk.[8]

## How to Overcome Barriers?

Barriers to HIV PrEP access and prevention include: stigma around HIV and sexual identity, homophobia/transphobia, minority stress, as well as provider discomfort and lack of knowledge about PrEP. Additionally, the previous U.S. history of medical abuse and forced sterilization among people of color contributes to a justified distrust of healthcare and social service systems.[9] Access to PrEP is not just a public health issue, but equally important, an equity and justice issue.

Reproductive justice, a term coined by women of color, includes AYA's equitable access to HIV prevention and care, free from discrimination and violence, to live healthy, productive lives with dignity.[10] The Society for Adolescent Health and Medicine position paper on the use of medication by AYA further emphasizes that medication regimens should center on the experiences of youth and be "built around the life context of the AYA." The society recommends a nonjudgmental and empowering approach to increase adherence of medications, and underscores the importance of access to medications easily, confidentially, at low or no cost, and free from stigma.[11]

Youth-serving health professionals can work toward ensuring equitable access to HIV PrEP for all adolescents. Use the following resources to expand training and education:

- Primary Care Development Corporation (PCDC) High Impact Prevention (HIP): www.pcdc.org/hip;
- University of California San Francisco Clinician Consultation Center, National Rapid Response for HIV Management and Bloodborne Pathogen Exposures: http://nccc.ucsf.edu.

By reducing HIV-related disparities, and increasing individual choice around sex, sexuality, and HIV prevention, clinicians can work toward ensuring reproductive justice.[12] ■

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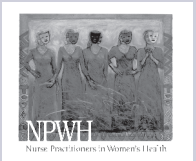



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## CME/CE INSTRUCTIONS

To earn credit for this activity, please follow these instructions:

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## CME/CE QUESTIONS

1. **What is the latest proposed guidance from the United States Preventive Services Task Force regarding cervical cancer screening?**

   a. For average-risk women ages 30-65, screening with high-risk HPV testing alone is recommended as an alternative to cervical cytology alone, and co-testing no longer is recommended.
   b. For average-risk women ages 30-65, screening with high-risk HPV testing alone is recommended as an alternative to cervical cytology alone; co-testing still is recommended.
   c. For average-risk women ages 21 and younger, screening with high-risk HPV testing alone is recommended as an alternative to cervical cytology alone, and co-testing no longer is recommended.
   d. For average-risk women ages 30-45, screening with high-risk HPV testing alone is recommended as an alternative to cervical cytology alone, and co-testing no longer is recommended.

2. **The most recent update to the U.S. Medical Eligibility Criteria for Contraceptive Use, 2016 places use of DMPA (depot medroxyprogesterone acetate) by women at high risk for HIV in what category?**

   a. Category 1 (no restriction)
   b. Category 2 (benefits outweigh theoretical or proven risks)
   c. Category 3 (use usually is not recommended unless other more appropriate methods are not available or acceptable)
   d. Category 4 (should not be used)

3. **According to the latest guidance from the Centers for Disease Control and Prevention, what is the recommended treatment for uncomplicated gonorrhea?**

   a. Ceftriaxone
   b. Azithromycin
   c. Cefixime
   d. Ceftriaxone plus azithromycin

4. **Which one of the following minimum clinical criteria does *not* need to be present on pelvic examination to begin presumptive treatment for pelvic inflammatory disease?**

   a. Cervical motion tenderness
   b. Uterine tenderness
   c. Adnexal tenderness
   d. Vaginal discharge

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A SUPPLEMENT TO CONTRACEPTIVE TECHNOLOGY UPDATE

# New Study Points to Long-term Effectiveness of 9-Valent HPV Vaccine

*Vaccine could prevent 90% of cervical cancer cases worldwide*

Results of a new study add confirmatory evidence that vaccination with Gardasil 9 (Merck and Co., Whitehouse Station, NJ) can reduce 90% of cervical cancers worldwide.[1] The vaccine is designed to target four types of human papillomavirus (HPV) — 16, 18, 6, and 11 — as well as an additional five HPV types that are the next most commonly associated with cervical cancer (HPV 31, 33, 45, 52, and 58). Researchers from the international study conclude that the 9-valent vaccine potentially could provide broader coverage and prevent 90% of cervical cancer cases worldwide.[1]

"We're on the verge of a dramatic change that will positively affect all individuals, particularly women, in the United States," said lead author **Warner Huh**, MD, professor and director of the University of Alabama at Birmingham (UAB) Division of Gynecologic Oncology and a senior scientist at the UAB Comprehensive Cancer Center, in a statement accompanying the study. "The challenge is to get the new vaccine into widespread use among young women."

> "WE'RE ON THE VERGE OF A DRAMATIC CHANGE THAT WILL POSITIVELY AFFECT ALL INDIVIDUALS, PARTICULARLY WOMEN, IN THE UNITED STATES."

The Food and Drug Administration (FDA) approved the vaccine in 2014. In October 2016, the FDA approved a two-dose schedule for HPV vaccine for adolescents ages 9-14. (Contraceptive Technology Update *reported on the change; see the January 2017 article, "Just Two HPV Shots Recommended for Younger Teens" available at* http://bit.ly/2li1dma.) In individuals ages 15-26, Gardasil 9 is administered with a three-dose schedule at 0, two months, and six months.

## More Than 100 Sites in Study

More than 100 sites in Austria, Brazil, Canada, Chile, Colombia, Denmark, Germany, Hong Kong, Japan, Mexico, New Zealand, Norway, Peru, South Korea, Sweden, Taiwan, Thailand, and the United States participated in the randomized, double-blind efficacy, immunogenicity, and safety study. Half of the 14,215 women, ages 16-26, received the quadrivalent vaccine, with the other half vaccinated with the 9-valent shot. All participants received gynecological exams for six years to look for evidence of infections or disease, and with blood tests performed to check antibody levels against HPV.

Data indicate the 9-valent shot showed 97.4% efficacy to prevent infections and disease caused by the five additional HPV genotypes not included in the quadrivalent vaccine. The 9-valent shot also produced similar antibody protection against the four HPV genotypes found in the quadrivalent vaccine. Both vaccines had similar safety profiles.[1]

The 9-valent vaccine now is licensed in more than 40 countries for the prevention of HPV-related anogenital cancers and pre-cancer, and genital warts, says **Anna Giuliano**, PhD, Director of the Center for Infection

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Research in Cancer at the Moffitt Cancer Center in Tampa. Guiliano served as one of the investigators in the trial.

"The results of this study support comprehensive vaccination programs and inform public health decision related to implementation," said Giuliano in a press statement accompanying the study.

## Is 'Herd Immunity' Taking Effect?

Results from another recently published study indicate that the decline in HPV infections among unvaccinated 18- to 26-year-old women suggests that young women in the United States are beginning to benefit from herd immunity resulting from the introduction of the HPV vaccine.[2]

To review the changes in vaginal HPV prevalence between 2009-2010 and 2013-2014 among U.S. women who were vaccinated and unvaccinated, the researchers used cross-sectional survey data from three different cycles of the National Health and Nutrition Examination Survey to assess HPV prevalence among women ages 18-59. The information was separated into four age groups (18-26, 27-34, 35-44, and 45-49) to look at the changes over time among the women of different age groups after the vaccine became available. The researchers used multivariable analyses, which controlled for descriptive variables, to assess the prevalence of quadrivalent vaccine-type HPV according to the women's vaccination status.

The analysis indicated a "significant decrease" in the prevalence of vaccine-type HPV among women ages 18-59 from 2009-2010 to 2013-2014. The decline was only significant in those ages 18-26 when the sample was stratified into the four age groups, researchers note. Among women ages 18-26 who were vaccinated, the HPV prevalence stayed low from 2009-2010 (3.9%) to 2013-2014 (2.0%; prevalence ratio 0.51, 95% confidence interval [CI], 0.18-1.46). Women ages 18-26 who were unvaccinated also showed a decrease over the time period, from 19.5% in 2009-2010 to 9.7% in 2013-2014 (prevalence ratio 0.44, 95% CI, 0.22-0.91). Among the women 26 years of age or older who were unvaccinated, the prevalence did not change greatly.[2]

## EXECUTIVE SUMMARY

Results of a new study add confirmatory evidence that vaccination with Gardasil 9 can reduce 90% of cervical cancers worldwide.

- The vaccine is designed to target four types of human papillomavirus (HPV) — 16, 18, 6, and 11 — as well as an additional five HPV types that are the next most commonly associated with cervical cancer (HPV 31, 33, 45, 52, and 58).
- Researchers from the international study conclude that the 9-valent vaccine potentially could provide broader coverage and prevent 90% of cervical cancer cases worldwide.

## Data Adding Up

Clinical evidence has been published recently to support recommendations by the Centers for Disease Control and Prevention (CDC) for a two-dose HPV vaccine to prevent genital warts, showing that the two-dose vaccine provides the same level of protection as three doses.[3] (*See the August 2017 article, "Researchers Affirm Effectiveness Of Two-Dose HPV Vaccine," at* http://bit.ly/2txoDbW.)

Conducted by researchers from the Boston Medical Center, Boston University School of Medicine; the Veterans Affairs Boston Healthcare System; and the Lombardi Comprehensive Cancer Center at the Georgetown University Medical Center in Washington, DC, the study looked at nearly 400,000 U.S. females ages 9-18 to determine the rate of genital warts based on the number of doses of vaccine that were received. The analysis indicates that receipt of two or three doses of the vaccine was effective. Both regimens provided significantly more protection against genital warts than a single dose or no doses of the vaccine.[3]

What can you do to increase vaccination rates? According to the CDC, receiving a recommendation for vaccination from a provider is the main reason parents choose to vaccinate their children. Clinicians make use of available opportunities by recommending the HPV vaccine strongly to parents of children 11 to 12 years of age at the same time and in the same way that they do for Tdap and meningococcal vaccines.

Recent data indicate that six of 10 U.S. parents now are choosing to have their teens vaccinated against HPV.[4] However, while most teens are receiving their first dose of the vaccine, many are not completing the full vaccination schedule, data indicate. (*Get more information; see the November 2017 article, "More Parents Choosing The HPV Shot For Teens," at* http://bit.ly/2fVqL7m.)

The implementation of the Affordable Care Act (ACA) may have aided in vaccine uptake. Results of a recent analysis compared vaccination

rates for HPV before and after ACA implementation among females, and examined variation by insurance status and other sociodemographic variables. The proportion of females who reported HPV vaccination increased over time from 16.4% to 27.6%, and those who reported completing the vaccination (receiving three doses) increased from 56.8% to 67.2%.[5]

After implementation of the ACA, respondents were 3.3 times more likely to be vaccinated compared to before ACA implementation (95% CI = 2.0,5.5), adjusting for age, race, and insurance coverage, data analysis indicates. The respondents were more likely to have received two doses (odds ratio [OR] = 2.8, 95% CI = 1.5,5.3) or three doses (OR = 5.8, 95% CI = 2.5,13.6) of the vaccine. The increase in vaccination could be related to the additional coverage of preventive services, including vaccines, that is required by the ACA, researchers note.[5] ■

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# Science Focuses on *Mycoplasma genitalium*

*Mycoplasma genitalium* (MG), a sexually transmitted infection, is a major cause of urethritis in men and is associated with cervicitis, pelvic inflammatory disease, preterm birth, and spontaneous abortion in women. Recent research indicates failure rates following azithromycin treatment have increased due to the emergence of worldwide macrolide antimicrobial resistance of the infection.[1]

Researchers at the University of Bristol's Population Health Sciences recently published a meta-analysis intended to determine rates of MG treatment failure and resistance with different azithromycin treatment regimens.[2] What spurred scientists to look at this subject?


## EXECUTIVE SUMMARY

*Mycoplasma genitalium*, a sexually transmitted infection, is a major cause of urethritis in men and is associated with cervicitis, pelvic inflammatory disease, preterm birth, and spontaneous abortion in women.

- Recent research indicates failure rates following azithromycin treatment have increased due to the emergence of worldwide macrolide antimicrobial resistance against the infection.
- Nucleic acid amplification testing is used, and diagnosis can be made through testing of urine, urethral, vaginal, and cervical swabs and through endometrial biopsies. However, these types of tests are only available in some large medical centers and commercial laboratories.


Publishing this meta-analysis is important now because it quantifies for the first time the risk (12%) of developing macrolide resistance in patients with MG when treated with 1 gram of azithromycin, the first-line global treatment for the infection, says **Paddy Horner**, MD, a consultant senior lecturer at the University of Bristol and lead author of the research paper.

"What's more, given the rapid increase in drug-resistant MG, we don't have the time to wait for the results of randomized controlled trials, which could take up to seven years," says Horner. "In response to this meta-analysis, the online version of the UK NGU [nongonococcal urethritis] guidelines (https://www.bashh.org/guidelines) have been updated, bringing them into line with the 2016 European NGU guidelines."

## Get Up to Speed

First identified in 1980, *Mycoplasma genitalium* is a bacterium that can infect the reproductive tract and is passed through sexual contact. Infection in men can cause urethritis; in women, infection has been linked to cervicitis, pelvic inflammatory disease, and infertility.[3]

According to the Centers for Disease Control and Prevention's (CDC) 2015 guidelines, MG is responsible for approximately 15-20% of nongonococcal urethritis cases, 20-25% of nonchlamydial NGU, and approximately 30% of persistent or recurrent urethritis.[4] In most settings, it is more common than *Neisseria gonorrhoeae* but is less common than *Chlamydia trachomatis*.

*Mycoplasma genitalium* is an organism that grows slowly; its culture can take up to six months, and there are only a few laboratories in the world that are able to recover clinical isolates. Public health officials now look to nucleic acid amplification testing (NAAT) for testing. Diagnosis can be made through NAAT of urine, urethral, vaginal, and cervical swabs, and through endometrial biopsies. These types of tests are only available in some large medical centers and commercial laboratories. At the present time, there is no diagnostic test for *M. genitalium* that is cleared by the Food and Drug Administration. The genetic makeup of the bacteria leads to development of antibiotic resistance; rates of resistance are high, making treatment challenging.

## What Is the Public Health Response?

In 2016, a National Institutes of Allergy and Infectious Diseases-funded Technical Consultation brought together researchers to review current knowledge and concerns about *Mycoplasma genitalium*. A recent supplement of the *Journal of Infectious Diseases* summarizes what is known about its pathogenesis, diagnostic assays, treatment and antimicrobial resistance, and criteria for developing public health control programs.[6]

"We reached a tipping point in our research on *M. genitalium* where there was finally enough data to figure out if we needed a public health response," said **Lisa Manhart**, MPH, PhD, a professor in the Departments of Epidemiology and Global Health at the University of Washington, in a press statement accompanying the publication. "The goal of the consultation was to review the evidence and make some recommendations about whether a national control program in the U.S. was appropriate."

More than 50 researchers from academia, the CDC, and the diagnostics and pharmaceutical industries took part in the technical consultation and development of the consensus recommendations. They determined four main consensus recommendations for future research:

- Clinical trials are needed to determine whether to recommend widespread screening for asymptomatic *M. genitalium* and treatment to improve reproductive health in women.
- More effective antibiotics are needed for infections, given the widespread antibiotic resistance of *M. genitalium*.
- Diagnostic tests designed to include the detection of resistance genes to a spectrum of antibiotic drug classes must be developed and made broadly available.
- More research is necessary to identify new antibiotic targets and potential vaccine targets, and to gain an understanding of the life cycle of *M. genitalium* in reproductive tract tissues.[6] ■

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