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Options might begin to emerge with new data out on LARC

Time to embrace evidence-based practice as choice options may expand

Progress is being made on the long-acting reversible contraception (LARC) front to promote top-tier effective methods to women.

According to the New York City-based Guttmacher Institute, in 2009, 8.5% of women using contraceptives relied on such LARC methods as the implant (Nexplanon, Merck & Co., Whitehouse Station, NJ) and the intrauterine device (IUD), reflecting a rise from 5.5% in 2007 and 2.4% in 2002.[1] Currently U.S.-approved IUDs include ParaGard, Teva Women's Health, North Wales, PA, and Mirena, Bayer HealthCare Pharmaceuticals, Wayne, NJ. Most of the women who use long-acting reversible methods choose IUDs; nearly 8% of women using contraception use the IUD, and less than 1% use the implant.[1]

With a 2012 American College of Obstetricians and Gynecologists committee opinion stating that long-acting reversible contraceptives such as the IUD and the contraceptive implant are safe, effective, and appropriate options for adolescents.[2] *(To read more about the opinion, see the* Contraceptive Technology Update *article, "Long-acting methods*

EXECUTIVE SUMMARY

The American College of Obstetricians and Gynecologists says that long-acting reversible contraception (LARC) methods are safe, effective, and appropriate options for teens, but some might perceive high discontinuation rates among younger women and therefore steer patients away from them.

- Data from the St. Louis Contraceptive CHOICE Project indicates that discontinuation rates of LARC methods at six months is low (less than 10%) and is not increased in teens and young women.
- A new international study looking at the 13.5 mg levonorgestrel IUD plus a 19.5 mg levonorgestrel device in advanced clinical trials suggest both are safe and effective. In the 13.5 mg and 19.5 mg groups, 21.9% and 19.1% discontinued the study over three years, respectively, including 1.0% and 1.2% who stopped due to serious adverse events and 4.7% and 4.9% who left due to menstrual bleeding disturbances.

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safe for teens: include options in your counseling," December 2012, p. 133.) However, some providers might perceive high discontinuation rates among younger women and therefore steer patients away from LARC methods.[3]

New analysis of data from the St. Louis Contraceptive CHOICE Project should eliminate such a perception. The analysis indicates that rates of discontinuation of LARC methods at six months is low (less than 10%) and not increased in adolescents and young women.[2]

Discontinuation rates measured

Researchers at the Washington University School of Medicine in St. Louis designed the analysis to measure discontinuation within six months among users of the levonorgestrel intrauterine system, copper IUD, and the etonogestrel implant, and to identify baseline characteristics associated with early discontinuation. They drew data from the project, a cohort study of 9,256 participants provided with no-cost contraception and followed with telephone interviews at three and six months

The analysts used logistic regression to investigate characteristics associated with early discontinuation of the two IUDs and implant and determined reasons for discontinuation. A total of 6,167 participants were eligible for the analysis; follow-up data were available for 5,928 participants. More than 90% (5,495) were using their method at six months and 433 (7%) had discontinued. Discontinuation rates were 7.3%, 8.0%, and 6.9% for the levonorgestrel intrauterine system, copper IUD, and implant, respectively.

After adjusting for age, race, marital status, low socioeconomic status, and history of sexually transmitted infection, analysts found that unmarried women were slightly more likely to discontinue compared with married women (adjusted odds ratio [OR] 1.26, 95% confidence interval [CI] 1.01-1.59 and adjusted OR 1.62, 95% CI 1.11-2.37, respectively). No other baseline characteristics, including younger age (ages 14-19), were associated with early discontinuation. The most common reason given for discontinuation was cramping among IUD users and irregular or frequent bleeding among implant users.[3]

"Rates of discontinuation of long-acting reversible contraception at six months is low and not increased in adolescents and young women," state the researchers. "Intrauterine devices and the implant should be considered as first-line contraceptive options among all women to reduce unintended pregnancy."

(Interested in getting a LARC program going at your facility? Visit the "LARC First" resource web site, www.larcfirst.com, put together by the Contraceptive CHOICE Project. Get troubleshooting tips on LARC insertions and removals,

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Editorial Questions

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staff cross-training information, contraceptive counseling scripts, and more.)

New options in research

More patients and providers might be interested in intrauterine contraception with the 2013 advent of Skyla, a new intrauterine system from Bayer HealthCare Pharmaceuticals of Wayne, NJ. The small, flexible plastic T-shaped device contains 13.5 mg levonorgestrel; its body measures 28 mm x 30 mm. The drug is released at an average in vivo rate of approximately 6 mcg/day over three years. It is approved for up to three years of contraceptive use. *(To read more above the device, see the* CTU *article, "FDA approves smaller levonorgestrel intrauterine system — a 'mini-Mirena,'" March 2013, p. 25.)*

Andrew Kaunitz, MD, professor and associate chair in the Obstetrics and Gynecology Department at the University of Florida College of Medicine — Jacksonville, said, "I find the smaller LNG IUD a welcome option in my practice, particularly for nulliparous women and others who may have a tighter or less flexible cervix."

A just-published international study looks at both the U.S.-approved 13.5 mg levonorgestrel IUD, as well as a 19.5 mg levonorgestrel device that is now in advanced clinical trials in the United States. Both devices were found to be safe and effective in preventing pregnancies, data suggests.[4]

To perform the study, researchers enrolled nulliparous and parous women ages 18-35 with regular menstrual cycles who were requesting contraception. Participants were randomized to three years of treatment with one of the two studied levonorgestrel intrauterine contraceptive systems. The primary outcome was the pregnancy rate, calculated as the Pearl Index.

Overall, 1,432 and 1,452 women in the 13.5 mg intrauterine contraceptive system and 19.5 mg intrauterine contraceptive system groups, respectively, had a placement attempted and were included in the full analysis set to evaluate efficacy and safety. Mean (standard deviation) age was 27.1 (4.8) years; 39.2% were nulliparous. Over the three-year period, 0.33 pregnancies per 100 women-years (95% CI 0.16-0.60) were observed with the 13.5 mg intrauterine contraceptive system compared with 0.31 per 100 women-years (95% CI 0.15-0.57) with the 19.5 mg intrauterine contraceptive system. Kaplan-Meier estimates for that period were 0.009 and 0.010, respectively. Partial expulsions occurred in 4.56% and 3.58% of treatment groups, respectively. Ten of the 20 pregnancies were ectopic. Serious adverse events included six cases of pelvic inflammatory disease and one partial uterine perforation.[4]

Scientists note that in the 13.5 mg system and 19.5 mg system groups, 21.9% and 19.1% of women discontinued for any adverse event over three years, including 1.0% and 1.2% who discontinued for serious adverse events and 4.7% and 4.9% who discontinued for disturbances in menstrual bleeding, including amenorrhea, respectively. In total, 57% and 60% of women completed three years of treatment with the 13.5 mg system and 19.5 mg system, respectively.[4]

"By demonstrating the safety and efficacy of low-dose intrauterine contraceptive devices, this study will help expand the contraceptive options available to women who have not had children before," says **Anita Nelson**, MD, professor in the Obstetrics and Gynecology Department at the David Geffen School of Medicine at the University of California in Los Angeles and corresponding author of the study. "Additionally, a lower dose system may be preferable to women who are seeking to reduce their exposure to synthetic hormones."

Don't forget IUD for EC

As more women become aware of the IUD as a LARC option, don't forget to educate on its use as an extremely effective form of emergency contraception (EC).

Planned Parenthood League of Massachusetts (PPLM) in Boston launched its EC4U campaign in November 2013 to educate its patients about EC and raise awareness among women in Massachusetts of the variety of EC options available to them.

All seven PPLM locations across Massachusetts carry the full range of EC options: the copper IUD (ParaGard); levonorgestrel emergency contraceptives pills Plan B One-Step (Teva) and Next Choice (Actavis, Parsippany, NJ); and the ulipristal acetate pill, ella (Actavis).

Staff members at the seven sites educate patients on the benefits of each of these methods. Information about the copper IUD denotes that it is most effective method; it can be used up to five days after unprotected sex and also can be left in place as a highly effective method of contracep-

tion for up to 12 years after insertion.

In an announcement of the new program, **Marty Walz**, president and chief executive officer of the Massachusetts organization, said, "As the state's leading women's healthcare provider and advocate, PPLM is proud to launch EC4U as part of our work to increase access to emergency contraception, reduce unintended pregnancies, and keep women healthy."

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Interpregnancy interval — You can help women

There is work to do

Reducing the proportion of pregnancies conceived within 18 months of a previous birth is one of the objectives of the U.S. Department of Health and Human Services' Healthy People 2020, the national 10-year plan for health promotion and disease prevention.[1] There is work to do.

A 2013 published study indicates that more than one-third (35%) of all repeat pregnancies in the United States are conceived within 18 months of the previous birth.[2] Such short interpregnancy intervals are associated with adverse maternal and child health outcomes, such as increased risk of preterm birth and infants with low birth weight.[3]

New research released online indicates that provision of effective contraception at the time of postpartum follow-up is a key strategy for achieving optimal interpregnancy intervals.[4] Results of the study suggest that compared to women using barrier methods, the use of long-acting reversible contraception (LARC) in the postpartum period increases the odds of achieving an optimal interpregnancy interval nearly four times greater than those relying on barrier methods.[4]

Members of the University of California, San Francisco (UCSF) Family PACT (Planning, Access, Care, and Treatment) evaluation team designed the study with an objective to determine the use of contraceptive methods, defined by effectiveness, length of coverage, and their association with short interpregnancy intervals, controlling for provider type and client demographics. Family PACT is California's Medicaid family planning expansion program; the evaluation team has worked extensively on access to and quality of family planning care for low-income women, men, and adolescents, explains **Heike Thiel de Bocanegra**, PhD, MPH, evaluation team director in the UCSF Bixby Center for Global Reproductive Health and assistant professor in UCSF's Department of Obstetrics, Gynecology, and Reproductive Sciences.

It is difficult to have objective quality indicators for contraceptive use because birth records and claims data do not capture pregnancy intention or client contraceptive preference, says Thiel de Bocanegra. The Healthy People 2020 objective to avoid pregnancies for 18 months after a birth is one of the few objective recommendations in the field of family planning, she notes.

Researchers identified a cohort of 117,644 women from the 2008 California Birth Statistical Master file with second or higher order birth and at least one Medicaid (Family PACT or Medi-Cal) claim within 18 months after index birth. They looked at the effect of contraceptive method provision on the odds of having an optimal interpregnancy interval, controlling for covariates.

EXECUTIVE SUMMARY

New research indicates that provision of effective contraception at the time of postpartum follow-up is a key strategy for achieving optimal interpregnancy intervals.

- Results of the study suggest that, compared to women using barrier methods, the use of long-acting reversible contraception in the postpartum period increases the odds of achieving an optimal interpregnancy interval nearly four times greater than those relying on barrier methods.
- Short interpregnancy intervals are associated with adverse maternal and child health outcomes, such as increased risk of preterm birth and infants with low birth weight.

Analysis indicates the average length of contraceptive coverage was 3.81 months, with most women receiving user-dependent hormonal contraceptives as their most effective method (55%, n=65,103) and one-third (33%; n=39,090) with no contraceptive claim. A much smaller percentage used barrier methods (7%, n=8,320), followed by LARC (LARC, n=5,131, 4%).

According to the research, women who used LARC methods had 3.89 times the odds and women who used user-dependent hormonal methods had 1.89 times the odds of achieving an optimal birth interval compared to women who used barrier methods only. Women with no method had 0.66 times the odds. When considering user-dependent methods, for each additional month of contraceptive coverage, the odds of having an optimal birth interval increased by 8% (odds ratio 1.08, confidence interval: 1.08-1.09). Women who were seen by Family PACT or by both Family PACT and Medi-Cal providers had significantly higher odds of optimal birth intervals compared to women served by Medi-Cal only, researchers report.[4]

Time for a change

"Access to and utilization of family planning services are critical to achieving a longer birth interval," state the UCSF researchers. "The positive association of optimal birth intervals corresponding to the method tier demonstrates the advantage of using methods with longer duration and lower rates of contraceptive failure."

It is time to make structural changes to allow more women to get access to effective, reversible methods as easily as they receive irreversible sterilization during their delivery and hospitalization, says **Anita Nelson**, MD, professor in the Obstetrics and Gynecology Department at the David Geffen School of Medicine at the University of California in Los Angeles.

"We also need to change the timing of the routine postpartum visit from six to three weeks after delivery, before it's too late," says Nelson. "Unless we show women how important we think contraception is to their children, we will continue to have unintended and short-interval pregnancy."

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Check treatment options for dysmenorrhea

Primary dysmenorrhea, or painful menstruation, is the most common cause of pelvic pain in women; as many as 90% of adolescent girls and more than 50% of menstruating women worldwide report symptoms, with 10-20% of them describing their pain as severe and distressing.[1-5]

Early research indicates that women with moderate to severe menstrual cramps might find relief in vaginal administration of sildenafil citrate (Viagra, Pfizer., New York City), a drug commonly used for erectile dysfunction.[6]

Why look at what is commonly called "the little blue pill" for possible pain relief of severe menstrual cramps? Sildenafil citrate, which is a nitric oxide donor drug, might help with pelvic pain because it might augment relaxant effects of the drug on myometrial cells, reverse the vasocon-

EXECUTIVE SUMMARY

Early research indicates that women with moderate to severe menstrual cramps might find relief in vaginal administration of sildenafil citrate (Viagra, Pfizer), a drug commonly used for erectile dysfunction.

- Primary dysmenorrhea, or painful menstruation, is the most common cause of pelvic pain in women; as many as 90% of adolescent girls and more than 50% of menstruating women worldwide report symptoms, with 10-20% of them describing their pain as severe and distressing.
- Nonsteroidal anti-inflammatory drugs (NSAIDs), which likely act by reducing uterine hypercontractility, offer effective treatment of primary dysmenorrhea. Combined oral contraceptives also are effective at easing menstrual cramping.

striction caused by prostaglandins, and improve uterine blood flow.[7,8] Although nitric oxide donor drugs cause vasodilatation and successfully alleviate pain, the incidence of side effects, such as headaches, might be too high for routine clinical use with oral route, researchers note.

Rapid absorption and quick pain relief are of utmost importance in treating dysmenorrhea, says **Richard Legro**, MD, professor of obstetrics and gynecology and public health sciences at Penn State University's College of Medicine in Hershey, PA. Vaginal administration accomplishes both and avoids the first pass effect of drug administration, he notes.

Vaginal administration has been effective in other treatments, observes Legro. One example is bromocriptine given for the treatment of hyperprolactinemia; oral administration has been associated with nausea and orthostatic hypertension. Data indicates that when the drug has been given vaginally, it has ameliorated those side effects,[9] he notes.

Check the details

To conduct the study, researchers developed a double-blind, randomized, controlled trial comparing vaginal preparation of sildenafil citrate (100 mg single dose) to a placebo in 62 patients with primary dysmenorrhea.

The primary outcome was total pain relief over four consecutive hours comparing sildenafil citrate to placebo. Secondary outcomes were pain relief as measured by the visual analog scale and uterine artery pulsatility index. Subjects included women ages 18 to 35 with moderate to severe symptoms. Of the 29 women screened for the study, 25 were randomized to receive sildenafil or the placebo drug.

Data indicates the sildenafil citrate group had better pain relief compared with the placebo group [mean standard deviation (SD): 11.9 (3.2) versus 6.4

(2.1), respectively; difference in means = 5.3; 95% confidence interval (CI): (2.9,7.6); P < 0.001)]. On the visual analog scale, sildenafil citrate provided better pain relief than placebo at each time point. At the two-hour point, the pulsatility index was significantly lower in the sildenafil citrate group compared with the placebo group [mean SD: 1.6 (0.6) versus 2.3 (0.5), respectively; difference in means = -0.7; 95% CI: (-1.2, -0.1);P = 0.01)].[6]

The research group has applied for research project grant (R01) funding from the National Institutes of Health to pursue further testing of the drug for primary dysmenorrhea treatment, says Legro.

"If future studies confirm these findings, sildenafil may become a treatment option for patients with primary dysmenorrhea," said Legro. "Since primary dysmenorrhea is a condition that most women suffer from and seek treatment for at some points in their lives, the quest for new medication is justified."

What's available now?

What causes menstrual cramping? Prostaglandin is produced in the uterus at the time of menstruation and can cause uterine contractions that are associated with menstrual cramping. Women who produce high levels of prostaglandin have more intense contractions and more severe cramping.

A systematic review of evidence indicates that nonsteroidal anti-inflammatory drugs (NSAIDs), which likely act by reducing uterine hypercontractility, offer effective treatment of primary dysmenorrhea. Unfortunately, not all women can use NSAIDs; gastrointestinal effects are not uncommon.[10] Even in those women who are able to use NSAIDs, such drugs are not completely effective.[11]

For women who want an alternative to NSAIDs, birth control pills represent an effective option for treatment of painful menstrual cramps. Oral contraceptives prevent ovulation, which in turn reduces the amount of prostaglandin produced in the uterus. By doing so, birth control pills relieve menstrual cramping. According to Contraceptive Technology, the levonorgestrel intrauterine device (Mirena, Bayer HealthCare Pharmaceuticals, Wayne, NJ) also is an excellent choice for women with dysmenorrhea because menstrual blood loss and duration of bleeding are reduced.[12]

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Options being eyed for transdermal contraception

Transdermal contraception provides a family planning option that is not dependent on daily dosing. While potential options are in development, the only transdermal contraceptive approved in the United States is the Ortho Evra patch, marketed by Ortho Women's Health & Urology, Raritan, NJ.

Evra received Food and Drug Administration (FDA) approval in 2001. Since that time, its labeling has been edited to address issues relating to the risk of venous thromboembolism and exposure to contraceptive hormones seen with Ortho Evra as compared to certain combined oral contraceptives. *(See the* Contraceptive Technology Update *article, "Set to change: Patch, drospirenone OC labels," February 2012, p. 13.)*

Many women prefer using a weekly patch to having to remember daily oral contraceptive tablets, says **Andrew Kaunitz**, MD, professor and associate chair in the Obstetrics and Gynecology Department at the University of Florida College of Medicine — Jacksonville. The currently marketed ethinyl estradiol/ norelgestromin patch results in blood levels similar to those associated with use of high-dose 50 mcg ethinyl estradiol oral contraceptives, says Kaunitz.

An investigational combination hormonal contraceptive patch has been designed to deliver a low dose of ethinyl estradiol and levonorgestrel comparable to low-dose combination oral contraceptives. Developed by Agile Therapeutics of Princeton, NJ, as AG200-15, the drug is under review by the FDA. The company has registered the trademarked name Twirla for the investigational drug. It is designed to deliver 120 mg/day levonorgestrel with 25 mg/day ethinyl estradiol. *(To read more about the drug, see the* CTU *articles "Check methods with combined hormones," April 2013, p. 40, and "Data out on potential contraceptive patch," August 2012, p. 88.)*

In a phase III pivotal trial of AG200-15, results suggest the study drug had significantly greater compliance (defined as no missed days of contraception in the cycle) than an oral contraceptive.[1]

Of 1,328 women (mean age, 26.4 years; 60% new hormonal contraceptives users; 46% non-Caucasian; 33% obese), 998 received the patch and 330 received an oral contraceptive for the first six study cycles. Women in the study were treated for one year (13 cycles) with the patch or for six cycles with the Pill, followed by seven cycles of patch use. Subjects recorded patch application and pill-taking on diary cards. Cycles with perfect compliance were defined as cycles with 21 days of patch wear without missed days or any patch worn for more than seven days or cycles with 21 days of pill-taking without days of missed pills.

Over the first six cycles, the percentage of cycles with perfect compliance was significantly higher in the patch versus the pill group (90.5% vs. 78.8%,

EXECUTIVE SUMMARY

Transdermal contraception provides a family planning option that is not dependent on daily dosing. The only transdermal contraceptive approved in the United States is the Ortho Evra patch.

- An investigational combination hormonal contraceptive patch has been designed to deliver a low dose of ethinyl estradiol and levonorgestrel comparable to low-dose combination oral contraceptives. Developed by Agile Therapeutics as AG200-15, the drug is under U.S. regulatory review.
- Bayer HealthCare has submitted an application for marketing authorization in the European Union for a transparent low-dose contraceptive patch containing ethinyl estradiol/ gestodene. Gestodene, while used in as a contraceptive agent in Europe for many years, is not available in any U.S.-approved contraceptive.

P less than .001). Compliance with the patch improved over the six treatment cycles, while compliance with the Pill worsened over the six cycles.[1]

Additional research indicates the investigational low-estrogen patch is as effective as conventional oral contraceptives; an additional finding of the trial is that the efficacy of the investigational patch did not decline in obese women.[2]

"Should this lower-estrogen patch receive FDA-approval, our patients would have access to a lower dose transdermal contraceptive system," says Kaunitz, who served as lead clinical investigator in the AG200-15 trials.

Potential option eyed

Berlin, Germany-based Bayer HealthCare submitted an application for marketing authorization in the European Union for a new transparent low dose contraceptive patch containing ethinyl estradiol/ gestodene in September 2012, confirms company spokesperson **Marcy Funk**. Named FC-Patch Low, the patch is transparent and contains 0.55 mg ethinyl estradiol and 2.1 mg gestodene. While gestodene has been in use as a contraceptive agent in European countries for more than 20 years, no U.S.-approved birth control method contains it.

In a 2013 study, a combined oral contraceptive containing 0.03 mg of ethinyl estradiol and 0.15 mg levonorgestrel and the Bayer patch showed comparable influence on hemostatic endpoints.[3] Both treatments were well-tolerated by subjects.[3]

Earlier research indicates that the good skin absorption properties of gestodene, and the low absolute dose required for contraceptive efficacy, suggest it can be offered in a small patch size.[4,5]

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Clinicians missing mark on sex talk with teens

As a family planning clinician, you should be prepared to discuss sexuality with your adolescent patients. Know, however, that you might be the first provider to do so. In a study looking at discussions held between pediatricians and family medicine physicians and teen-age patients, results show less than two-thirds of such interactions included talk about sex, sexuality, or dating during annual visits.[1]

Previous studies on discussions of sex during doctors' visits have been based on information teens or physicians have reported after visits.[2,3] To capture naturally occurring conversations, scientists in the current study used audio recordings of annual visits, including camp and sports physicals, for 253 adolescents. The patients, ages 12 to 17, visited pediatricians and family medicine physicians at 11 North Carolina clinics.

The researchers listened to the recordings for any mention of sexual activity, sexuality, or dating. Their analysis shows physicians brought up sex in 65% of visits, with conversations lasting an average of 36 seconds. The other 35% of visits included no mention of sex.

"As researchers, we knew no study has existed

EXECUTIVE SUMMARY

In a study looking at discussions held between pediatricians and family medicine physicians and teen-age patients, results show less than two-thirds of such interactions included talk about sex, sexuality, or dating during annual visits.

- Physicians brought up sex in 65% of visits, with conversations lasting an average of 36 seconds. The other 35% of visits included no mention of sex.
- Engage adolescents in discussions about sex. In the current study, none of the adolescents initiated discussions on sex, which reinforces the need for clinicians to start the conversation.

that has examined how these conversations sounded, and we wanted a better idea of where current practice stands regarding these discussions," explains **Stewart Alexander**, PhD, associate professor of medicine in the Department of Medicine at Duke

University Medical Center, Durham, NC. "Initially, we were planning to examine the quality of counseling teens about sex but found that the conversations were quite different — even when they occurred."

As researchers listened to the provider-patient interactions, they realized that specific training might be able to help providers improve these discussions, says Alexander, who served as lead author of the current paper. The research team is developing training to address these issues, Alexander states.

Check your approach

It is important for providers to engage adolescents in discussions about sex. In the current study, none of the adolescents initiated discussions on sex, which reinforces the need for clinicians to start the conversation. As research progresses in identifying successful strategies providers can use to engage teens in discussions to help promote healthy sexual development and decision making, what can you do to facilitate such interactions with your adolescent patients?

For starters, clinicians wishing to address issues of sexuality with adolescents should remember that confidentiality discussions are best when they occur before the topics of sex are introduced, says **Dennis Fortenberry**, MD, MS, professor of pediatrics and medicine at the Indiana University School of Medicine in Indianapolis. Younger adolescents might have limited understanding of the legal and ethical nuances of confidentiality, but almost all have definite understandings of privacy, explains Fortenberry, a co-author of the current study.

One way to introduce sexuality with young patients is to ask first about relationships, says Fortenberry. For young people in a relationship, follow-up questions can address specific behaviors with their relationship partner, their feelings about those behaviors (including whether the behavior was consensual), and expectations for future behaviors, he states.

"These types of questions allow exploration as well of the adolescent's boundaries about sexual activity, which are quite clearly formed for many," says Fortenberry, who has guided an Indiana University research program focused on adolescents during the past 17 years. "I often ask specifically about kissing because it is a very common experience, is associated with far less social disapproval than other forms of sexual interaction, and is easy to acknowledge."

For young people who don't identify a current relationship, clinicians can follow up with a question about past relationships and behaviors, or with a question about sexual contact with someone who wasn't considered a relationship partner, says Fortenberry.

When responding to reports of specific sexual behaviors, including abstinence, Fortenberry suggests a question such as "what was good (or bad) about your decision to have sex?" or "what was good (or bad) about your decision to abstain?"

What is "sex talk?"

Some clinicians use questions about pubertal development as an entrée to asking about sex, says Fortenberry. However, asking young men about pubic hair development or young women about their menstrual periods does not constitute "sex talk." *[Looking for more information on conducting initial reproductive health visits in teens? Check the HEEADSSS (Home environment, Education and employment, Eating, peer-related Activities, Drugs, Sexuality, Suicide/depression, and Safety from injury and violence) method of interviewing covered in the* Contraceptive Technology Update *article, "How to get into heads of teens in initial visit," January 2014, p. 8.]*

Clinicians also should remember that many young people are still developing a sexual identity so that unwarranted assumptions about heterosexuality often are revealed through the use of specific words that presume the gender of a partner, observes Fortenberry. Gender-neutral questions can allow discussions with sexual minority youth who often feel invisible in sexuality discussions, he states.

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Contraceptive coverage heads to Supreme Court

By **Adam Sonfield**
Senior Public Policy Associate
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Washington, DC

With Congress in a seemingly perpetual state of deadlock, one of the most anticipated actions on federal reproductive health policy will instead be taken by the U.S. Supreme Court this spring. On March 25, 2014, the Supreme Court is slated to hear oral arguments on two challenges to the Affordable Care Act's (ACA) contraceptive coverage guarantee: Sebelius v. Hobby Lobby Stores, in which the 10th Circuit Court of Appeals sided with an Oklahoma-based craft supply chain store, and Conestoga Wood Specialties v. Sebelius, in which the Third Circuit ruled against a Pennsylvania-based furniture manufacturer. A final ruling on the cases is likely to be announced in June.

The federal contraceptive coverage guarantee — part of a broader requirement for private health plans to cover dozens of key preventive care services without out-of-pocket costs for patients — has been met with controversy since the outset. Social conservatives inside and outside of Congress repeatedly have demanded that the requirement be repealed or that it exempt any employer asserting a religious or moral objection to coverage of some or all forms of contraception, regardless of the beliefs and needs of employees and dependents.

The Obama administration has tried to defuse these objections, by crafting an exemption for health plans offered by houses of worship and other religious employers, narrowly defined, and by providing an "accommodation" for religiously affiliated nonprofit organizations, such as some universities, hospitals, and social relief agencies. Employees of those latter organizations still must receive coverage of the full range of contraceptive methods and services without out-of-pocket costs, but that coverage must be provided by the organization's insurance company. The employer, however, does not have to "contract, arrange, pay, or refer" for any contraceptive coverage to which they object on religious grounds.[1]

Wave of lawsuits emerges

This compromise has satisfied some but not all of the administration's critics, and one result has been a wave of lawsuits; nearly 80 of them are pending as of January 2014.[2] More than 30 of those lawsuits have been brought by nonprofit organizations that object to the scope and structure of the accommodation, with some plaintiffs arguing that the requirement to sign a form asserting their objection to contraceptive coverage in order to take advantage of the accommodation is itself a violation of their religious rights.

However, most of the pending lawsuits, including the two before the Supreme Court, have been brought by for-profit companies, which are eligible for neither the exemption nor the accommodation. These cases involve challenges under the First Amendment's protection for religious exercise and under a 1993 federal law called the Religious Freedom Restoration Act. One central question is whether a company can cite these protections: Does it qualify as a "person" that can have religious beliefs and put them into practice?

In the two Supreme Court cases, the businesses are for-profit corporations owned privately by members of a single family, and both the owners and the corporations themselves are plaintiffs. In both cases, the plaintiffs object to coverage of specific contraceptive methods and services: emergency contraceptive pills (including Plan B and ella); copper and hormonal intrauterine devices; and counseling and education about these methods, which they assert can cause an abortion. In part because of these specifics, it is unclear whether any of the other lawsuits might remain relevant even after the Supreme Court issues a ruling. It does not appear that the contraceptive coverage guarantee itself is in danger of being struck down, but a ruling could have a significant effect on how many women will be able to obtain coverage and how expansive that coverage might be.

What is to come?

That question is a meaningful one to the millions of Americans who have already benefited from the coverage protections and from the millions more who will gain these protections going forward. According to a Guttmacher Institute study released in December, the proportion of

privately insured U.S. women who paid $0 out of pocket for oral contraceptive pills increased sharply, from 15% in fall 2012 (before the contraceptive coverage guarantee took effect for most women) to 40% in spring 2013 (after the requirement came into force for millions).[3]

A similar increase, from 23% to 52%, was seen among vaginal ring users with private insurance, although media reports and evidence from insurance companies' own publicly available documents indicate that the federal rules are being interpreted inconsistently for some methods and services.[4]

The impact of the guarantee can be expected to grow further as it is phased in to additional plans: the number of covered workers enrolled in "grandfathered" plans — existing plans given a temporary reprieve from many of the ACA's new rules — has been declining rapidly, as Congress intended, from 48% in 2012 to 36% in 2013.[5]

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COMING IN FUTURE MONTHS

- ■ Science investigates intrauterine ball contraceptive
- ■ Using social media to promote adolescent health
- ■ Potential herpes simplex virus therapy in focus
- ■ Nitrous oxide checked for pain management with IUD insertion

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CNE/CME QUESTIONS

1. What is the approved indication for use of Skyla, the levonorgestrel intrauterine system?
   A. Three years
   B. Five years
   C. 10 years
   D. 12 years

2. The U.S. Department of Health and Human Services' Healthy People 2020 seeks to reduce the proportion of pregnancies conceived within what timespan from a previous birth?
   A. 12 months
   B. 18 months
   C. 24 months
   D. 30 months

3. A systematic review of evidence indicates which is the most effective treatment of primary dysmenorrhea?
   A. Topical heat therapy
   B. Fennel
   C. Nonsteroidal anti-inflammatory drugs
   D. Vitamin B6

4. What are the hormones contained in the AG200-15 contraceptive patch under development by Agile Therapeutics?
   A. Ethinyl estradiol and gestodene
   B. Ethinyl estradiol and norethindrone acetate
   C. Ethinyl estradiol and desogestrel
   D. Ethinyl estradiol and levonorgestrel

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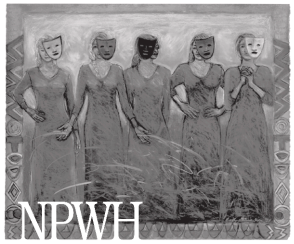

S · T · I
QUARTERLY

New data emerges on use of pre-exposure prophylaxis (PrEP)

No link seen between regimen use and increased sexual risk behavior

Pre-exposure prophylaxis (PrEP) with tenofovir disoproxil fumarate and emtricitabine (Truvada, Gilead Sciences, Foster City, CA) has proven effective in HIV prevention in high-risk groups, with the Food and Drug Administration approving such indication for emtricitabine's use in 2012.

While the Centers for Disease Control and Prevention (CDC) has provided interim guidance for PrEP use, a national survey of infectious disease physicians shows only 9% have prescribed it.[1] Those numbers might change; just-published data indicates that there is no link between use of the PrEP regimen and increased sexual risk behavior.[2]

The findings build upon data from the 2010 Global Pre-exposure Prophylaxis Initiative (iPrEx) clinical study, which reported that emtricitabine, originally approved to treat HIV-positive patients, also was effective in preventing new infections in people likely to come in contact with the virus.[3] A 2012 follow-up study bolstered such findings, with data suggesting that taking emtricitabine regularly reduced risk of HIV infection by more than 90%.[4] *(To read* Contraceptive Technology Update's *latest coverage of PrEP research and protocols, see "Check interim guidance for PrEP in men, women," October 2012, p. 113.)*

Biological markers eyed

Questions have been raised whether taking the drug regimen could lead to a behavioral effect called risk compensation, whereby individuals adjust their behavior in response to a change in their perceived level of risk. While participants in the iPrEX trial self-reported decreases in sexual risk behavior over the course of the study, scientists involved in the current analysis decided to examine those findings more closely by studying biological markers of risk behavior.

EXECUTIVE SUMMARY

Pre-exposure prophylaxis (PrEP) with tenofovir disoproxil fumarate and emtricitabine (Truvada, Gilead Sciences) has proven effective in HIV prevention in high-risk groups, with the Food and Drug Administration approving such indication for emtricitabine's use in 2012.

- While the Centers for Disease Control and Prevention has provided interim guidance for PrEP use, a national survey of infectious disease physicians shows only 9% have prescribed it.
- More providers might consider PrEP use now that just-published data indicates that there is no link between use of the PrEP regimen and increased sexual risk behavior.

Statement of Financial Disclosure: Consulting Editor **Robert A. Hatcher**, MD, MPH, Author **Rebecca Bowers**, and Executive Editor **Joy Dickinson** report no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study. **Melanie Deal,** nurse reviewer, discloses that she is on the speakers bureau for Actavis and Merck & Co. and the advisory board for Actavis, Teva, and Hologic.

To perform the study, investigators assessed sexual practices at baseline and quarterly thereafter; perceived treatment assignment and PrEP efficacy beliefs were assessed at 12 weeks. Among participants with one or more follow-up behavioral assessment, sexual behavior, syphilis, and HIV infection were compared by perceived treatment assignment, actual treatment assignment, and perceived PrEP efficacy.

Overall, acute HIV infection and syphilis decreased during follow-up. Compared with participants believing they were receiving placebo, participants believing they were receiving emtricitabine/tenofovir disoproxil fumarate reported more receptive anal intercourse partners prior to initiating drug (12.8 vs. 7.7, P=0.04). Belief in receiving the study drug protocol was not associated with an increase in receptive anal intercourse with no condom from baseline through follow-up (risk ratio [RR] 0.9, 95% confidence interval [CI]: 0.6-1.4; P=0.75), nor with a decrease after stopping study drug (RR 0.8, 95% CI: 0.5-1.3; P=0.46). In the placebo arm, there were trends toward lower HIV incidence among participants believing they were receiving the study drug protocol (incidence rate ratio [IRR] 0.8, 95% CI: 0.4-1.8; P=0.26) and also believing it was highly effective (IRR 0.5, 95% CI: 0.1-1.7; P=0.12).[2]

"Our results suggest that HIV prevention strategies such as Truvada don't result in risk compensation because they provide an opportunity for participants to actively engage in and reduce their risk of HIV infection," says **Robert Grant**, MD, MPH, professor at the University of California, San Francisco and an investigator in the university-affiliated Gladstone Institutes. "Engagement, which also includes counseling, provision of condoms, and management of other sexually transmitted infections leads to motivation, which comes at a time when motivation for preventing new HIV infections is vital to curbing the spread of this worldwide epidemic."

Who's using protocol?

The CDC offers support on PrEP use at its site, http://1.usa.gov/1fzbtkI. *(See other resource information at end of this story.)* The interim guidance includes information for injecting drug users, heterosexually active adults, and men who have sex with men. However, clinicians are slow to embrace PrEP, results of a national survey show.[1]

Maile Karris, MD, assistant professor of medicine in the Division of Infectious Diseases, Department of Medicine, at University of California San Diego, and lead author of the current paper, says, "I personally have been a proponent of PrEP, but upon talking to colleagues, I found a great deal of differences in opinions and practices just within our San Diego HIV community. This led me to wonder how PrEP opinions and practices truly differed among infectious diseases physicians across the country and what clinical practice factors contributed to those views."

Karris and the research team surveyed adult infectious disease physicians from a national network about their opinions and current practices of PrEP. While most clinicians supported PrEP, only 9% had provided it. Despite CDC guidance, PrEP practices were variable and clinicians reported many barriers to its real-world provision, survey findings indicate.

An analysis of the actual use of tenofovir/emtricitabine was presented at the 2013 Interscience Conference on Antimicrobial Agents and Chemotherapy. It drew data from a nationally representative patient database, as well as information from more than 50% of the dispensing pharmacies in the United States, and applied an algorithm to exclude the use of tenofovir/emtricitabine for any other reason but as PrEP.[5]

A total of 1,774 individuals were prescribed PrEP between January 2011 and March 2013, the data shows. Half of the users of tenofovir/emtricitabine for PrEP were women; 32% of users were in the South, with 24% in the Northeast and West, and 18% in the Midwest. PrEP prescribers were mainly primary care providers, including emergency department clinicians; infectious diseases specialists accounted for just 12% of prescriptions.[5]

A coalition of more than 50 women from leading AIDS and women's health organizations is looking to U.S. government agencies to coordinate a national agenda for more information on how PrEP can best be made available as to more women at risk of HIV infection. The U.S. Women and PrEP Working Group issued the call to government officials following release of data at the 2013 Conference on Retroviruses and Opportunistic Infections showing that none of three interventions tested in a large scale trial among African women, known as VOICE (Vaginal and Oral Interventions to Control the Epidemic) – daily oral tenofovir, daily oral tenofovir/emtricitabine, and daily 1% vaginal tenofovir gel – provided additional protec-

tion against HIV.[6]

Male and female condoms are "wonderful" HIV prevention options that work for many women and their partners, observed **Erika Aaron**, RN, CRNP, MSN, assistant professor in the Division of Infectious Diseases and HIV Medicine at Drexel University School of Medicine in Philadelphia, in a statement released by the U.S. Women and PrEP Working Group. However, some women feel that they can't insist their partners use condoms, and many young women and their HIV-positive partners want to have children, Aaron said.

"Those women need other options to protect themselves from HIV; PrEP can help them stay HIV-negative," she stated. "We have a moral imperative to find ways to make it available to women who need it and who can use it."

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RESOURCE

• **AVAC**, a New York City-based non-profit organization uses education, policy analysis, advocacy, and a network of global collaborations to accelerate the ethical development and global delivery of AIDS vaccines, male circumcision, microbicides, PrEP, and other emerging HIV prevention options as part of a comprehensive response to the pandemic. It maintains a web site, www.prepwatch.org, which serves as a clearinghouse for information on PrEP for HIV prevention. PrEP Watch includes information on data, additional research, cost, access, and advocacy efforts in the United States and across the globe. ■

What is the role of express STI testing?

Declining resources in the face of increasing demand are causing sexually transmitted infection (STI) clinics to review new strategies to maximize efficiency without compromising quality of care. Just-published research suggests express STI testing, which bypasses lengthy interviews and physical examinations, might be a viable option.[1]

Just-published research centers on a cohort of men attending two Baltimore STI clinics. The paper was published by Susan Tuddenham, MD, MPH, a fellow in the Division of Infectious Diseases at the Johns Hopkins University (JHU) School of Medicine in Baltimore, and **Khalil Ghanem**, MD, PhD, assistant professor of medicine in the Division of Infectious Diseases at the JHU School of Medicine and assistant professor in JHU's Bloomberg School of Public Health. Researchers designed the retrospective study to define the contribution of the physical examination in detecting clinically meaningful diagnoses that might not be identified by current laboratory methods and to identify characteristics that can stratify men into the appropriate risk category.

For determining men's risk of missed diagnosis based on initial screening, patients were retrospectively stratified into three groups based on the self-reported reason for their visit. The first group

EXECUTIVE SUMMARY

Declining resources in the face of increasing demand are causing sexually transmitted infection (STI) clinics to review new strategies to maximize efficiency without compromising quality of care.

•Just-published research suggests express STI testing, which bypasses lengthy interviews and physical examinations, might be a viable option in this direction.

• Express STI testing at the Pima County Health Department in Tucson, AZ, allows patients to complete the screening process in 30 minutes or less. Symptomatic STIs such as chlamydia are more rapidly detected and treated, which helps to decrease the amount of untreated infections within the community, as well as serving as a disease control measure to preventing new infections.

included men who were asymptomatic presenting for general checkups, while the second group included all men who came in complaining of symptoms such as discharge, dysuria, genital lesion, genital itching, rash, and irritation/odor. The third group included asymptomatic men who presented as known contacts of STI-infected partners.

Only men coming in for their first clinic visit were included in this analysis.

After stratifying men on the basis of reason for visit, the researchers compared proportions for diagnoses that would have been missed without physical examination. Logistic regression was used to assess which factors were most predictive of missed diagnoses.

Of 140,052 patient visit records, 58,073 met the entry criterion; the other 81,979 records were excluded because they represented multiple visits. A total of 29,172 men were asymptomatic, 23,971 were symptomatic, and 4,929 were asymptomatic contacts of an infected partner. Analysis suggests 2.7% of asymptomatic patients, 10.4% of symptomatic patients, and 4.5% of contact patients would have had missed diagnoses if no physical examination had been performed. For symptomatic patients, if those reporting rash, lesion, or genital itch were examined, the percent with missed diagnoses would drop to 3.7%.

In a podcast on www.stdpreventiononline.org, a website run by the Centers for Disease Control and Prevention-sponsored Internet & STD Center of Excellence, Ghanem states there are ways to enhance clinic efficiency without compromising patient care, as long as the right subgroup of patients is targeted and as long as clinic leaders know their limitations of their facilities. *(Download the podcast at http://bit.ly/1idRiGB.)*

"I think an expedited approach to a subset of patients can enhance efficiency, as long as clinics have the resources to track those patients who were not treated at the time of their expedited visit and bring them back in a timely manner for treatment," Ghanem says in the podcast.

How does testing work?

Pima County, AZ, is home to more than one million people. Its county health department, based in Tucson, has used express STI testing since 2008, says **Francisco García**, MD, MPH, health department director. The "Express Testing" process began as an alternative effort to offer expedited STI testing for clients who wanted only testing services and were asymptomatic and/or short on time.

How is it determined which patients are best served by express testing?

Patients who present for testing as a part of routine screening, those who are between relationships, or those who are simply concerned they might have had an exposure are ideal for express testing services, says Garcia. Some patients will want only express testing and would rather wait until they receive test results before taking any unnecessary antibiotics, he notes.

Express testing allows patients the ability to complete the screening process in 30 minutes or less, depending on the number of clients present at any given time, says Garcia. Another benefit of express testing is that asymptomatic STIs such as chlamydia are more rapidly detected and treated, thus helping to decrease the amount of untreated infections within the community as well as serving as a disease control measure to preventing new infections, he notes. Gonorrhea, syphilis, and HIV likewise have been successfully detected and appropriate treatment has been offered within a shorter timeframe, he states.

"Increase in routine STI testing, treatment and medical interventions aid in supporting improved health of the community at large," advocates Garcia. *(For more information on express testing, see the* Contraceptive Technology Update *article, "Express STI testing — Can it work in your clinic?" August 2009, p. 90.)* It looks at the experience of Denver Metro Health Clinic, the largest STI clinic and HIV testing facility in the Rocky Mountain region, which uses a triage system to identify low-risk individuals who qualify for an express, testing-only visit to screen for major communicable diseases without a physical examination. A 2008 evaluation of the service indicates the triage system safely and effectively identifies those appropriate for express visits, reduces waiting times for patients, and increases clinic throughput.[2]

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