

# OB/GYN Clinical [ALERT]

Evidence-based commentaries  
on women's reproductive health

## SPECIAL FEATURE

# 2016 USPSTF Update: Recommendations for and Effectiveness of Screening Mammography

By Jeffrey T. Jensen, MD, MPH

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**SYNOPSIS:** The U.S. Preventive Services Task Force recently released updates to the 2009 recommendations on breast cancer screening. Additional studies published since the last review strengthen the conclusion that mammography screening results in a reduction in the risk of death from breast cancer. The available evidence supports that benefits of screening mammography exceed harm when screening begins at age 50 and is conducted every two years through age 74.

In November 2009, the U.S. Preventive Services Task Force (USPSTF) released revised recommendations on breast cancer screening that made front-page news. These recommendations, based on a systematic review of the literature, sought to balance the potential benefits of screening mammography with risk and harm. The report left women's health professional groups and breast cancer patient advocacy groups stunned. The USPSTF recommended that women start mammogram screening at age 50, and continue with biannual screening until age 75. These contrasted sharply with the recommendations from the American College of Obstetricians and Gynecologists (ACOG), the American College of Surgeons, and the American College of Radiologists, all of whom

recommended annual mammograms beginning at 40 with no fixed upper age limit. While some professional groups (American Academy of Family Physicians, American College of Physicians) adopted the USPSTF guidelines, the recommendations became deeply politicized. Some saw the report as a government plot to save on health care dollars at the expense of women's health.

The issue threatened to derail the Affordable Care Act, as a key provision was the mandate that private insurers cover procedures for which the USPSTF issued a grade of "A" (high certainty that the net benefit is substantial) or "B" (high certainty that the net benefit is moderate or moderate certainty that the net benefit is moderate to

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substantial) recommendation, but not lower  
grades. Fierce lobbying led to passage of a  
convoluted law that created an exemption for  
mammography to ensure coverage for annual  
screening tests, and for exams for women aged  
40 to 49 years (a grade “C” — benefit not  
clear — recommendation in 2009). However,  
a “Cinderella” clause in the law required this  
exemption to expire once the USPSTF issued  
new recommendations.

Last spring, the USPSTF released the draft  
of their updated recommendations to  
public comment. In making the revised  
recommendations, the USPSTF took into  
account new information that strengthened  
the conclusions from 2009. The outcry  
from advocates was immediate and forceful.  
Like me, you may have received an email  
from Hologic, a leading manufacturer of  
mammography equipment, urging you to  
contact your congressman in support of  
legislation to ensure access to mammography  
and supplemental screens. This lobbying must  
have worked; a rider extending the exception  
for the grade “C” recommendation for private  
insurance coverage of screening mammography  
was inserted into the Consolidated  
Appropriations Act omnibus spending bill that  
passed Congress last December<sup>1</sup> (impressive,  
given the inaction of Congress on so many  
other pressing issues). This congressional  
action maintaining coverage apparently  
cleared the way for publication of the revised  
recommendations.

On Jan. 12, 2016, the *Annals of Internal  
Medicine* and USPSTF website simultaneously  
released electronic publication of the new  
clinical guidance<sup>2</sup> along with four original  
research papers,<sup>4,6-8</sup> three reviews,<sup>3,9,10</sup>  
four editorials,<sup>1,11-13</sup> and one patient  
summary.<sup>5</sup> In this issue, I want to take on the  
recommendations for screening. Next month,  
I will discuss the potential harms of screening,  
and the risks and benefits of supplemental  
screening for women with dense breasts.

## WHAT ARE THE NEW USPSTF RECOMMENDATIONS?

The USPSTF recommends biennial screening  
mammography for all women aged 50 to  
74 years (B recommendation).<sup>2</sup> For women  
< 50 years of age, the recommendation for  
screening mammography received a “C” grade  
(moderate certainty that the net benefit of  
screening, while positive, is small). The current  
evidence was deemed insufficient to assess the  
balance of benefits and harms of screening  
mammography in women aged 75 years or

older (I statement, grade of “I” = insufficient).

The USPSTF also evaluated supplemental  
imaging modalities. It concluded that the  
evidence for benefits and harms of digital  
breast tomosynthesis (DBT) as a primary  
screening method for breast cancer was  
insufficient (I statement). The task force also  
found the current evidence insufficient to assess  
the benefits and harms of adjunctive screening  
modalities (breast ultrasonography, magnetic  
resonance imaging [MRI], DBT, or other  
methods) in women identified to have dense  
breasts on an otherwise negative screening  
mammogram (I statement).

## TO WHOM DO THE RECOMMENDATIONS APPLY?

The target population for the USPSTF  
recommendation includes women ≥ 40 years  
of age without clinical breast abnormalities or  
symptoms that would trigger the order of a  
diagnostic test. The recommendations do not  
apply to women at high risk of breast cancer  
(i.e., preexisting breast cancer or high-risk  
breast lesions, hereditary genetic syndromes  
associated with breast cancer, or previous large  
doses of chest radiation before age 30 years).  
The recommendations do apply to women  
with standard risk factors such as positive  
family history (without hereditary genetic  
syndrome).<sup>3</sup>

## HOW EFFECTIVE IS BREAST CANCER SCREENING?

The USPSTF found adequate evidence that  
mammography screening reduces breast  
cancer mortality in women aged 40 to 74  
years.<sup>3</sup> The number of breast cancer deaths  
averted increases with age; women aged 40  
to 49 years benefit the least and women aged  
60 to 69 years benefit the most. At age 70,  
the benefit declines and after age 75 there is  
insufficient evidence of benefit. This increased  
benefit associated with age reflects the fact  
that age is the most important risk factor for  
breast cancer. In other words, the increased  
benefit observed with age is due to the increase  
in absolute risk. Overall, a meta-analysis of  
mammography trials indicated a protective  
effect. The relative risk (RRs) reduction  
for breast cancer mortality was small and  
nonsignificant for women aged 39 to 49 years  
(RR, 0.92; 95% confidence interval [CI], 0.75-  
1.02), but strengthened and became significant  
for women 50 to 59 years (RR, 0.86; 95%  
CI, 0.68-0.97) and for those 60 to 69 years  
(RR, 0.67; 95% CI, 0.54-0.83). Although the  
point estimate for those aged 70 to 74 years  
was protective (RR, 0.8; 95% CI, 0.51-1.28),

the CI broadly overlaps 1.0. Looking at this another way, screening mammography would be expected to avert three deaths in 10,000 women aged 39-49 screened over 10 years, 8 deaths among 10,000 women 50-59, 21 deaths per 10,000 aged 60-69, and 13 deaths among women 70-74.

A major limitation of the conclusions is the use of outdated imaging technologies and treatments in the majority of studies that supplied evidence for the meta-analysis. However, it remains controversial whether improved imaging contributes to a meaningful reductions in mortality or simply a greater risk of overdiagnosis (more on this next month).

The take home message from the USPSTF review can be summarized as follows: Although breast cancer mortality is generally reduced with mammography screening, estimates are not statistically significant at all ages (in particular for women < 50 years and > 70 years), and the magnitudes of effect are small, ranging from a low of 8% in women ages 40-49 to a high of 33% in women ages 60-69. Overall, mammography screening will prevent < 1 death per 1000 women screened over 10 years for all age groups except women aged 60-69.

#### WHAT ARE THE KEY CAVEATS OF THE RECOMMENDATIONS?

In making recommendations for screening tests, the USPSTF considered both benefits and harms. The published recommendations reflect the best available evidence. Although only screening every 2 years for women at average risk aged 50-74 years received a “B” grade, the task force did not recommend *against* screening women < 50 years or > 75 years of age. Instead, they suggested that women and their health care providers thoughtfully consider the potential benefits and harms of screening. To quote the recommendations “For women in their 40s, the number who benefit from starting regular screening mammography is smaller and the number experiencing harm is larger compared with older women. For women in their 40s, the benefit still outweighs the harms, but to a smaller degree; this balance may therefore be more subject to individual values and preferences than it is in older women. Women in their 40s must weigh a very important but infrequent benefit (reduction in breast cancer deaths) against a group of meaningful and more common harms (overdiagnosis and overtreatment, unnecessary and sometimes invasive follow-up testing, and psychological harms associated with false-positive test results, and false reassurance from false-negative test results). Women who value the possible benefit of screening mammography more than they value avoiding its harms can make an informed decision to begin screening.” A variety of common risk factors may influence the equation. For example, women aged 40 to 49 years who have a known first-degree relative (parent, child, or sibling) with breast cancer should consider initiating screening earlier than age 50 years.

#### SUMMARY

ACOG continues to recommend annual mammograms starting at age 40, and insurers will continue to cover this. This might be the right decision for some women, but not all women. If routine annual mammograms starting at 40 is your standard recommendation, I would encourage you to read the full details of the USPSTF recommendations and associated reports. Unfortunately, this is not a simple discussion anymore. But in my experience, each woman knows what is right for herself. ■

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# Fluconazole Use During Pregnancy

By *Rebecca H. Allen, MD, MPH*

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Dr. Allen reports she is a Nexplanon trainer for Merck, a Liletta trainer for Actavis, and on the advisory board for Bayer, Actavis, and Vermillion.

**SYNOPSIS:** In this large cohort study from Denmark, use of oral fluconazole during pregnancy was associated with a slightly increased risk of spontaneous abortion and no increased risk of stillbirth.

**SOURCE:** Molgaard-Nielsen D, et al. Association between use of oral fluconazole during pregnancy and risk of spontaneous abortion and stillbirth. *JAMA* 2016;315:58-67.

This is a retrospective cohort study from Denmark that compared the risk of spontaneous abortion (7 through 22 gestational weeks) and stillbirth ( $\geq 23$  weeks) among oral fluconazole-exposed pregnancies to matched controls. The investigators used the country's Medical Birth Register and the National Patient Register to identify all pregnancies ending with a singleton live birth, stillbirth, spontaneous abortion, or other abortion (ectopic, induced, molar) between Jan. 1, 1997, and Dec. 31, 2013. They were able to link this information by unique personal identifiers to the National Prescription Register and other national databases to obtain data on prescription drug use and other variables, such as age, education, parity, and medical history. Ascertainment of exposure started at gestational week 7 in order to avoid bias from unrecognized early pregnancy losses. Each fluconazole-exposed pregnancy was matched to up to 4 unexposed control pregnancies based on age, calendar year, gestational age, and a propensity score, which determined the probability of fluconazole treatment given all maternal baseline characteristics.

The study included a total of 1,405,663 pregnancies. Among oral fluconazole-exposed pregnancies, 147/3315 (4.43%) spontaneous abortions (SABs) occurred compared to 563/13,246 (4.25%) in the unexposed matched control pregnancies (hazard ratio [HR], 1.48; 95% confidence interval [CI], 1.23-1.75). A total of 21/5382 (0.39%) stillbirths occurred in pregnancies exposed to oral fluconazole compared to 77/21,506 (0.36%) unexposed matched pregnancies (HR, 1.32; 95% CI, 0.82-2.14). For the dosage analysis, in the 150-300 mg fluconazole group, there were 132/2986 (4.42%) SABs (HR, 1.4; 95% CI, 1.22-1.77), and in the 350-560 mg group, there were 15/345 (4.3%) SABs (HR, 1.55; 95% CI, 0.94-2.58). Further preplanned sensitivity analyses revealed that timing of fluconazole exposure in pregnancy did not change the results. To control for confounding by indication, a comparison between women prescribed oral fluconazole and topical azoles was conducted. Oral fluconazole-exposed pregnancies experienced 130/2823 (4.6%) SABs compared to 118/2823 (4.2%) topical azole-exposed pregnancies (HR, 1.62; 95% CI, 1.26-2.07). The HRs for SAB were

attenuated and not statistically significant when the same mother was compared using a pregnancy exposed to fluconazole and one unexposed.

## ■ COMMENTARY

Pregnancy is a risk factor for vulvovaginal candidiasis.<sup>1</sup> The Centers for Disease Control and Prevention recommends treating pregnant women with vulvovaginal candidiasis with a 7-day course of topical azoles.<sup>2</sup> A longer duration of therapy (7 days vs 1 or 3 days) is typically prescribed in pregnancy. The CDC specifically does not endorse the use of oral fluconazole in pregnancy for vulvovaginal candidiasis due to a lack of safety data (rated FDA pregnancy risk factor category C for single-dose vaginal candidiasis and D for all other indications). Despite this, many practitioners and patients prefer oral dosing to topical vaginal creams during pregnancy. Previous studies have not shown an association between exposure to low-dose oral fluconazole (150 mg) used to treat vulvovaginal candidiasis and birth defects nor with spontaneous abortion or stillbirth.<sup>3,4,5</sup> Nevertheless, prior studies of SAB and stillbirth were small, so the investigators conducted the largest study to date on the relationship between oral fluconazole use and pregnancy loss. In the primary analysis, the authors found an almost 50% increased risk of SAB but no increased risk of stillbirth.

The investigators were able to take advantage of Denmark's national health registries to link data on office visits, hospitalizations, and prescription use in a large group of pregnant women. This makes the study powerful in detecting rare outcomes. I commend the investigators for thinking about possible confounding factors in their study design. Comparing women who took oral fluconazole to topical azoles was very important because these women share the diagnosis of vulvovaginal candidiasis and presumably similar risk factors. However, one could argue that women who received oral fluconazole had more severe infections than those who received topical azoles. The authors also controlled for confounders by comparing fluconazole-exposed pregnancies to women who were using other antibiotics, were hospitalized with infection, or were using antihypertensives; this did not change the results. Nevertheless, the comparisons of women who

were treated with fluconazole in one pregnancy and not in another pregnancy resulted in lower HRs and nonsignificant results. The authors acknowledged that this could indicate residual confounding from either a hereditary predisposition to miscarriage or lifestyle factors (smoking and alcohol consumption, for example). Yet, they discounted that because this analysis was based on smaller numbers of exposed individuals than the main analysis (69 subjects vs 147 subjects).

What could be the possible mechanism of action at work here? Fluconazole has not been shown to be teratogenic; therefore, fatal congenital anomalies are not a likely explanation.<sup>3</sup> Abortions have been caused in animals using fluconazole, but in much higher doses than those recommended for humans. The authors only speculated that since fluconazole inhibits the fungal CYP51 enzyme, it may also interfere with human CYP450 enzymes that might be important during in utero development. Could the *Candida* infection itself cause miscarriage and stillbirth? Ascending *Candida* infection into the uterus causing chorioamnionitis, miscarriage, and preterm delivery is extremely rare but has been described.<sup>1</sup> Therefore, it is unclear what the causal pathway would be.

What should be the proper interpretation of this epidemiologic study? The HR of < 2 is not a strong association and indicates susceptibility to bias. Importantly,

the within-mother analysis did not show any increased risk of SAB; that would seem to be the best study design because the woman is compared to herself with and without oral fluconazole in pregnancy. My take-home from this article is that there might be a slightly increased risk of miscarriage but it is not certain. It is hard to imagine that a 150 mg dose of oral fluconazole would be powerful enough to cause miscarriage. Nevertheless, I would not prescribe oral fluconazole as first-line therapy for symptomatic vulvovaginal candidiasis in pregnancy anyway. Since topical therapy is an effective alternative to oral dosing, it makes sense to prescribe vaginal treatments first to reduce any unnecessary systemic drug exposure in pregnancy. ■

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## ABSTRACT & COMMENTARY

# Use of CNMs and Hospitalists

By John C. Hobbins, MD

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Dr. Hobbins reports no financial relationships relevant to this field of study.

**SYNOPSIS:** A study assessing the effects of instituting a model of certified nurse midwife with MD laborist backup on a private patient population showed a decrease in cesarean section rate and an increase in vaginal birth after cesarean delivery rate without any change in combined neonatal outcome.

**SOURCE:** Rosenstein MG, et al. The association of expanded access to a collaborative midwifery and laborist model with Cesarean delivery rates. *Obstet Gynecol* 2015;126:716-723.

For many reasons, there has been a recent trend for labor management to be overseen in shift fashion by hospitalists (“laborists”), but little attention has been directed to the patient-related benefits and/or liabilities of these programs. To address these needs, Rosenstein et al launched a study to assess various clinical outcome measures before and after adopting a combined laborist/certified nurse midwife (CNM) program.

Marin County Hospital delivers care to a mixed pregnant population of public and private patients. Prior to 2011, the public patients insured under California’s Medi-Cal program, comprising about half of the patients, were cared for predominantly by CNMs, with backup by in-house “laborist” MDs employed by the hospital. The private patients were delivered by private practitioners,

often taking calls from their offices or homes. In 2011, it became economically unfeasible to support the laborist/CNM type of coverage for the public patients only, so this type of coverage was expanded to include private patients wishing to use this practice model. Ten private physicians from community practices were hired part time to provide in-house shift coverage for the public and private patients in the new program. They functioned as backups to on-duty CNMs. Those not choosing this program were followed by the original private practice model. The apparent win/win aspect of the new program was more convenient for the physicians and, interestingly, became progressively more appealing to the private patient population as demonstrated by the CNM/laborist private deliveries increasing from 21% initially to 42% three years later.

The authors focused on three dependent variables: cesarean section rate (CSR), rate of vaginal birth after cesarean (VBAC), and combined neonatal outcomes, and comparisons were made between public and private patients before and after the program launched.

Between April 2005 and March 2014, there were 13,194 births, and of those meeting study criteria, 3413 were delivered before 2011 and 1474 were delivered after this time. Half of the patients had private insurance (49%). In publicly funded patients, 80-90% of deliveries were by CNMs before and after the program began.

In the private nulliparous group, the CSR decreased from 31.7% to 25% with the new program (odds ratio, 0.56; 95% confidence interval, 0.39-0.81). In contrast, the public patient CSR remained essentially the same at 15.5-16.1% throughout the study period. Interestingly, in the private group, the CSR rose steadily at a rate of 0.6% prior to the program's start but had an immediate drop of 6.9% over the first year, while continuing to drop at 2% per year thereafter. VBAC rates in privates increased from 13.3% to 22.4% ( $P < 0.002$ ). VBACs in the publicly insured patients stayed about the same, but the slope showed a gradual downward trend before and through the program's initiation (following a nationwide pattern). There were no significant differences in combined neonatal morbidity between groups before or after the program began.

#### ■ COMMENTARY

This study indicated that moving from a typical private practice labor model of having physicians from individual practices exclusively managing and delivering the patients in their practices to a combined CNM/laborist model resulted in lower CSRs and higher VBAC rates. The predominantly CNM-delivered public patients had consistently lower CSRs and higher VBAC rates than the private model, but there was little difference before and after the program began. The

authors also noted that the new model was less expensive to maintain.

So the new system seemed to attain the goals set forth by the American College of Obstetricians and Gynecologists to reduce the CSR without adversely affecting neonatal outcomes, while costing less.

The "good old days" credo of following one's patients in labor from start to finish, resorting to a handoff only when the doctor was too tired to function properly, is becoming a relic. Actually, this concept has been undergoing a fade out for many years, giving way to a model based on part-time employment, physician convenience, and, potentially, better patient safety. The CNMs provide the adjunctive components of competency and compassion.

The patients one might suspect to be the least satisfied are those possibly expecting to be managed throughout their pregnancies and delivered by the physician whom they had personally chosen to undertake their care. However, this has become an unrealistic expectation, since for years the obstetrician often has been juggling many balls in the air, only one of which involves labor management. And the warm and fuzzy aspects of labor management that are touted on websites and call-waiting advertisements are often provided at least as well by CNMs. So, although some of us old timers might lament the probable demise of the old model, it seems that patients don't expect this type of continuity of care anyway. Nevertheless, it is hoped that while we are adapting to the various new pressures of practicing medicine in an era of complicated electronic medical records, imposed documentation, relentless regulations, malpractice worries, and the current "punch in and punch out" mentality, the compassion and warmth with which we have always tried to deliver care can be retained. ■

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## ABSTRACT & COMMENTARY

# By Using In Vitro Fertilization, Pregnancy Rates Can Approach Those in Fertile Women

By Robert W. Rebar, MD

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Dr. Rebar reports no financial relationships relevant to this field of study.

SYNOPSIS: Cumulative live-birth rates were more than 65% after the sixth cycle of in vitro fertilization.

SOURCE: Smith AD, et al. Live-birth rates associated with repeat in vitro fertilization treatment cycles. *JAMA* 2015;314:2654-2662.

In vitro fertilization (IVF) has permitted previously infertile women without hope of pregnancy to build families. It has been more successful than anyone ever imagined. Now, investigators have used data involving ovarian stimulation cycles initiated between January 2003 and Dec. 31, 2010,

with live-birth outcome data collected up to June 2012 to determine the extent to which repeat IVF cycles continue to increase the likelihood of a live birth (defined as an infant born alive after 24 weeks' gestation and surviving longer than 1 month) for women undergoing IVF in the United

Kingdom. A cycle was defined as the initiation of treatment with ovarian stimulation and all resulting separate fresh or frozen embryo transfers.

The cohort consisted of 156,947 women of median age 35 years at start of treatment with a median duration of infertility of 4 years undergoing 257,398 IVF ovarian stimulation cycles. The live-birth rate for the first cycle was 29.5%. The overall cumulative live-birth rate after the sixth cycle was 65.3% (95% confidence interval [CI], 64.8-65.8%) and continued to increase up to the ninth cycle. As expected, live-birth rates decreased with age, with women < 40 years of age achieving a cumulative prognosis-adjusted live-birth rate of 68.4% after six cycles and those aged 40-42 years achieving a cumulative live-birth rate of 31.5% with six cycles. For women > 42 years of age, live-birth rates within each cycle were < 4%. The authors suggested that the data support extending the number of IVF cycles undertaken beyond three or four.

#### ■ COMMENTARY

I chose to review this article as an introduction to a discussion about the current status of IVF. I was actually surprised that this study was accepted for publication in a major journal. It is true that data collected by the CDC on a per-cycle rather than a per-patient basis do not permit easy calculation of cumulative data in the United States, but we would anticipate that such calculations would result in at least similar cumulative pregnancy rates for IVF in the United States. However, I believe that the technological advances that have occurred in this field will lead to this study being of historical interest only.

I say that because the physical, emotional, and financial demands of IVF make most women unwilling to endure more than a couple of cycles of IVF. However, it soon should be possible to achieve the kinds of cumulative pregnancies detailed in this study without enduring so many IVF cycles. What advances should make this possible?

First and foremost has been the improvement in live-birth rates in any given IVF cycle itself. There have been significant improvements in both ovarian stimulation and culture techniques. The use of ultrasound-guided embryo transfer has no doubt had an effect as well. Live-birth rates have increased slowly but significantly since the birth of the first IVF baby in 1978.

Second has been the development of successful techniques for embryo cryopreservation. Embryo cryopreservation allows excess embryos to be replaced in cycles removed in time from the initial ovarian stimulation cycle. One recent study noted that transfer of single vitrified and then warmed blastocysts maximizes live-born children while obviously minimizing multiple pregnancies as well as preterm births.<sup>1</sup>

Third has been advances in preimplantation genetic testing (PGT). Comprehensive chromosome screening (CCS) can now utilize any of several genetic platforms, including metaphase comparative genomic hybridization (mCGM),

array comparative genomic hybridization (aCGH), single-nucleotide polymorphism (SNP) microarray, quantitative polymerase chain reaction (qPCR), and most recently next-generation sequencing (NGS), to test the genetic complement of single blastomeres obtained on day 5-6 of embryo development. Typically, the blastocysts are frozen and those that are genetically normal are then thawed and transferred in subsequent cycles. Currently, the major use of this technology is to identify aneuploid embryos. Remember that aneuploidy increases with increasing maternal age and accounts for the increasing rate of miscarriage with maternal age. Thus, the intent of such testing is to identify and transfer only genetically normal embryos. A recent meta-analysis suggested that transferring euploid embryos does in fact increase the rate of live births.<sup>2</sup>

The meta-analysis focused on implantation rate because the three randomized, controlled trials included did not report live-birth rates. Sustained implantation of transferred euploid embryos beyond 20 weeks' gestation was significantly higher after PGT-CCS compared to embryos selected for transfer on the basis of normal morphological characteristics and development (relative risk [RR], 1.39; 95% CI, 1.21-1.60). The authors noted that this suggests that PGT confers a 21% to 60% chance of improved sustained implantation (and presumably live birth). Analysis of data from seven observational studies included in the meta-analysis suggested a similarly increased sustained implantation rate (RR, 1.75; 95% CI, 1.48-2.07). Moreover, the data analyzed suggested that there is no detrimental effect of blastocyst biopsy on subsequent embryo development. While it will take years to determine if tested embryos result in truly normal children, there is no reason to think that this will not be the case.

IVF programs using PGT-CCS must have experience with extended embryo culture and biopsy, a successful program of embryo cryopreservation, and experience with a validated and tested CCS platform. The genetic test used must have a low false detection rate so that normal embryos are not inappropriately excluded from transfer. Another study indicating that selective transfer of euploid embryos after aCGH will result in equal implantation and pregnancy rates in women of all ages up to 42 years also suggests that this technology can increase live-birth rates in older women undergoing IVF.<sup>3</sup> Thus, this technology can be coupled with elective single embryo transfer to result in high live-birth rates and low rates of multiple births.

These advances in IVF technology lead me to conclude that we should see increasing rates of live births and ever decreasing rates of multiple births. I think that I first personally realized the power of IVF when we first used IVF with donor oocytes in women with premature ovarian failure from varied causes. More than 70% of our patients took home babies after no more than two ovarian stimulations of the donors, counting all fresh and frozen-thawed transfers.<sup>4</sup> We really are allowing women without prior hope to deliver babies and build families. ■

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## CME/CE QUESTIONS

1. **The Centers for Disease Control and Prevention recommend oral fluconazole for vulvovaginal candidiasis in pregnancy.**
  - a. True
  - b. False
2. **Which of the following does not fit the findings of the study by Rosenstein et al regarding outcomes after the new laborist/certified nurse midwife model was adopted?**
  - a. The cesarean section rate diminished on the private service.
  - b. The vaginal birth after cesarean rate increased among the publicly funded patients.
  - c. The vaginal birth after cesarean rate increased among the privately funded patients.
  - d. The combined neonatal mortality rate remains the same in both sets of patients.
3. **Cumulative live-birth rates in women undergoing in vitro fertilization utilizing their own oocytes:**
  - a. are greatest in women > 40 years of age.
  - b. increase through at least six cycles of ovarian stimulation.
  - c. increase to about 50% in women undergoing nine cycles of ovarian stimulation.
  - d. do not increase further after two cycles of IVF.
4. **The 2015 requirement for private insurance to cover routine annual mammography in women 40-49 as part of the Affordable Care Act is evidence-based per the USPSTF.**
  - a. True
  - b. False

## [IN FUTURE ISSUES]

Accidental Bowel Leakage

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