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Evidence-based commentaries on women's reproductive health

ABSTRACT & COMMENTARY

Barriers to Abortion Care and Self-Managed Abortion

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SYNOPSIS: In this prospective national study among people searching for abortion care online, 28% of respondents reported attempting self-managed abortion. Respondents living farther from an abortion facility and facing barriers to care were more likely to attempt self-managed abortion.

SOURCE: Upadhyay UD, Cartwright AF, Grossman D. Barriers to abortion care and incidence of attempted self-managed abortion among individuals searching Google for abortion care: A national prospective study. *Contraception* 2021; Sep 21:S0010-7824(21)00385-1. doi: 10.1016/j.contraception.2021.09.009. [Online ahead of print].

As barriers to abortion access increase in the United States, a person experiencing an unwanted pregnancy may consider a self-managed abortion (SMA) — attempting to end the pregnancy without clinical supervision. Previously described methods of SMA include ordering medications online (including mifepristone and misoprostol, the medications used in medically supervised medication abortion) and ingesting herbs, supplements, or vitamins. Technically, obtaining abortion pills online without medical supervision is illegal in the United States. Prior estimates of SMA, ranging from 2% to 7%, have come from patients seeking care in abortion clinics.[1,2] Because these estimates exclude patients who do not reach the abortion clinic, they likely are underestimates. By recruiting from among people who searched for abortion services online, this study may reach those who will never make it to an abortion clinic. In addition, given the associated stigma of SMA, online surveys may allow for more comfort and privacy around discussing SMA, which could reduce both recall and social desirability bias.

This analysis comes from the Google Ads Abortion Access Study, a prospective cohort study among women in the United States searching online for an abortion from 2017 to 2018.[3] Using advertisements in Google search results, the study recruited individuals who used search terms, such as "abortion clinic near me." Ads were targeted by state to generate a sample that included all 50 states. Individuals who clicked the ad then completed an eligibility screener. To be included, respondents had to be pregnant currently and considering an abortion. Eligible respondents then completed demographic and pregnancy characteristic

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information. They were contacted four weeks later with a follow-up survey about pregnancy outcomes, barriers to accessing care, and SMA.

This study focuses on SMA attempts. Specifically, participants were asked about using abortion pills obtained online, trying to end the pregnancy without medical help, using emergency contraception (EC) after already pregnant, inflicting self-harm, or taking other medications or herbs to end the pregnancy. Of note, these data were collected before medically supervised telemedicine abortion services were available. The study team measured state-level policy environments based on the number of laws restricting abortion in the participant's state as well as distance to the nearest abortion facility. The team also asked about logistical and financial barriers to obtaining an abortion.

Of all respondents who met eligibility criteria and provided complete SMA data, 28% (95% confidence interval [CI], 25% to 31%) attempted at least one method of SMA and 7% reported more than one. The most commonly reported SMA methods were taking herbs, supplements, or vitamins. Commonly reported substances were vitamin C, blue or black cohosh, unspecified herbs or teas, cinnamon, parsley, and fruits, such as pineapple, papaya, pomegranate, and dong quai. About 19% of respondents attempting SMA reported taking EC after confirming pregnancy; 18% took mifepristone and/or misoprostol on their own (although not through online services); 18% inflicted harm on themselves; 10% used smoking, alcohol, or other substances; and 7% took other prescription or over-the-counter medications. While the survey did not ask specifically about subsequent morbidity or mortality related to SMA, participants were able to write in methods of SMA not captured in the survey. Per the authors, the most extreme method reported was "attempting to penetrate the cervix with a hook."

Although most respondents reported at least one barrier to abortion care, a higher proportion of those who attempted SMA reported at least one barrier to care, as compared to those who did not attempt SMA (98% vs. 94%, $P = 0.03$). Respondents with difficulty meeting basic needs, with no or undetermined health insurance, and those living farther from an abortion facility were more likely to attempt SMA. Those who attempted SMA were more likely to be pregnant and seeking abortion at follow-up than those who did not (39% vs. 30%, $P < 0.001$). However, those who ordered abortion pills online all reported successfully ending the pregnancy. Barriers to care and distance to the nearest abortion facility also were significantly associated with SMA attempts. Specifically, respondents who had to keep their abortion secret, who feared for their well-being, and who needed to gather money to travel or for the abortion had higher odds of attempting SMA (adjusted odds ratio [aOR], 2.00; 95% CI, 1.36-2.94). Respondents living 50 to 100 miles (aOR, 1.77; 95% CI, 1.01-3.10) and 100 or more miles (aOR, 2.31; 95% CI, 1.18-4.50) from the nearest abortion facility had significantly higher odds of SMA than those living less than five miles from a facility, a much shorter distance.

■ COMMENTARY

SMA is an understudied aspect of abortion care. By recruiting participants online from outside abortion clinics, this study provides a higher estimate of SMA than those reported previously in the literature (28% compared to 2% to 7%).[1,2,4] This study also expands our understanding of how patients attempt SMA, since it allowed patients to list SMA methods in a private and non-stigmatizing way. Although most of the reported SMA methods are unlikely to cause harm, they are either ineffective for inducing abortion or are much less effective than taking mifepristone and misoprostol. SMA has been reported to delay accessing abortion care since patients may not realize that SMA methods were unsuccessful, which itself could lead to worse clinical outcomes.[5] Although rare, this study documents harmful SMA techniques, including inflicting physical harm on oneself. The documentation of such methods is concerning and requires attention, given the potential for maternal morbidity or mortality.

Although this study occurred before telemedicine medication abortion services under medical supervision were available, it documents an interest in these services, since many respondents ordered abortion medications online. It joins mounting evidence that telemedicine abortion is not only safe but patient-centered.[3] Yet, instead of expanding these services, currently 19 states have effectively banned telemedicine abortion, as has the U.S. Food and Drug Administration by prohibiting medication dispensing without in-clinic visits.[6] Although state policy environment was not associated directly with SMA attempts, the need to obtain money to pay for the abortion or associated costs and the need to travel long distances were. Time and again, we find that patients seeking abortion are resilient and can overcome specific restrictions intended to dissuade them from seeking this

care. But restrictions that worsen structural barriers to care, that increase costs (such as a lack of health insurance or Medicaid coverage for abortion), and that increase travel distances to the nearest clinic (such as targeted restrictions on abortion providers that lead to clinic closures) are much harder to overcome. These barriers particularly affect people of color, people with low incomes, and other historically marginalized groups who are disproportionally affected by abortion restrictions.

Better understanding the associations between structural barriers and SMA becomes particularly relevant as patients face mounting abortion restrictions throughout the United States.[7] Senate Bill 8, a near total ban on abortion enacted in the state of Texas in September 2021, has led to a 14-fold increase in driving distance to get an abortion among women of reproductive age within Texas counties.[8] With one in 10 women in the United States living in Texas, Senate Bill 8 and others like it are creating a public health crisis that studies, such as this one, only begin to describe. ■

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ABSTRACT & COMMENTARY

Is Prenatal Screening for GBS Cost-Effective in the United States?

By Ahizechukwu C. Eke, MD, PhD MPH

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SYNOPSIS: In this cost-effectiveness study, screening for group B streptococcus (GBS) at 36 0/7 to 37 6/7 weeks, with rescreening (if GBS results are negative after five weeks of initial screening), is the most cost-effective strategy.

SOURCE: Williams M, Zantow E, Turrentine M. Cost effectiveness of latest recommendations for group B streptococci screening in the United States. *Obstet Gynecol* 2020;135:789-798.

Group B streptococcus (*Streptococcus agalactiae*, or GBS) is an anaerobic gram-positive bacterium that is a normal commensal in the lower genital tract of 5% to 30% of pregnant women.[1,2] The prevalence of early-onset GBS disease in the United States varies by state, from 0.1-0.8/1,000 deliveries.[3] GBS colonization in the female genital tract at the time of delivery is the most common route of fetal/neonatal infection, but risk factors for GBS during pregnancy include GBS bacteriuria in a current pregnancy, previous neonate with early-onset GBS, maternal pyrexia (> 38°C), prolonged rupture of membranes (> 18 hours), and preterm labor.[4,5]

GBS is the most common cause of early-onset neonatal sepsis, neonatal morbidity, and mortality in the United States, with case fatality rates as high as 15%.[1,6] Because the predictive values of GBS swabs collected at < 36 weeks of gestation do not provide an adequate culture-to-delivery window that can allow for deliveries that occur at 41 0/7 weeks of gestation, the current recommendation is to collect genital swabs for GBS between 36 and 37 weeks of gestation.[7] In 2020, the American College of Obstetricians & Gynecologists (ACOG) changed its GBS prenatal screening guidelines, encouraging screening for GBS at 36 to 37 weeks (as opposed to previous guidelines recommending screening at 35 to 37 weeks of gestation).[8] To determine if this new gestational age screening window is cost-effective, Williams and colleagues conducted this cost-effectiveness analysis.[7]

For the purposes of the development of the decision analytic model, the pregnant cohort was divided into two universal GBS screening strategies: strategy A, GBS screening at 35 0/7 to 37 6/7 weeks of gestation, with those screening positive treated in the intrapartum period; and strategy B, GBS screening at 36 0/7 to 37 6/7 weeks of gestation, and

rescreening for GBS if five weeks had elapsed from the initial screening (and the woman still was pregnant), with those screening positive treated in the intrapartum period.[7] Both screening strategies (A and B) were compared to a reference scenario that treated cases of neonatal GBS disease in the absence of maternal GBS screening during pregnancy (no screening).

To parameterize their Markov model, the authors made a number of assumptions. First, there was no delay in the availability of prenatal GBS results at the time when pregnant women presented during labor; second, GBS culture was 100% sensitive in isolating women whose genital tracts were colonized with GBS; third, antibiotic prophylaxis was universally available at the time of delivery and would be administered for at least four hours during labor; fourth, all women who screened positive to GBS received intravenous antibiotics; and fifth, all women who reported a high risk for anaphylaxis to penicillin would have culture sensitivities performed and those who were penicillin allergic would receive appropriate antibiotic therapy.[7] Women with clinical indications for antibiotic prophylaxis at the time of delivery (GBS bacteriuria in a current pregnancy, previous neonate with early-onset GBS, maternal pyrexia [> 38°C], prolonged rupture of membranes [> 18 hours], and preterm labor) were excluded from the analysis.[7]

In the analysis, the primary measure of effectiveness was neonatal quality-adjusted life years (QALYs). Health-related quality of life scores were calculated as the number of life-years for term neonates with early-onset GBS and long-term sequelae divided by normal life-expectancy.[7] Direct medical costs and indirect lifetime costs were obtained from the literature, while the GBS screening culture and antibiotic costs were obtained from the Medicare Clinical Lab Fee Schedule of 2017.[7] A one-way sensitivity analysis was performed, varying all base-rate parameters at one time using the lower and upper bounds of reported measures to estimate the minimum and maximum range of estimated costs. Mean incremental cost-effectiveness ratios (ICERs) were used to express cost-effectiveness under a willingness to pay threshold of $100,000/QALY gained. Costs were expressed in 2019 U.S. dollars, and health utilities were expressed in QALYs and discounted at 3% per year. Costs were examined from a healthcare and societal perspective and were derived using the consumer price index for healthcare.[7]

The authors demonstrated that strategy B (i.e., GBS screening at 36 0/7 to 37 6/7 weeks of gestation, and rescreening for GBS if five weeks had elapsed from the initial screening [and the woman was undelivered]) resulted in 3,723,641 pregnant women being tested (a 3% increase over women screened with strategy A), a 6% increase in neonatal QALYs gained (2,162 vs. 2,037), 12% fewer cases of neonatal deaths (30 vs. 34), and a 10% estimated reduction in total societal healthcare expenditures as the result of early-onset GBS disease ($639 million vs. $707 million) when compared to strategy A.[7] These benefits in strategy B required a greater number of pregnant women treated with antibiotics to prevent one case of early-onset neonatal GBS compared to strategy A (261 vs. 245). Earlier onset GBS cases were prevented with strategies A and B compared to no GBS screening. An estimated $1.26 billion (range $682 million to $1.83 billion) in direct and indirect healthcare costs were saved with strategy B when compared to no intervention, while an estimated $73 million (range $39 million to $106 million) in direct and indirect healthcare costs were saved with strategy B when compared to strategy A. Strategy B was most cost-effective for neonatal costs and QALYs gained, with an ICER of $43,205/QALY gained. One-way sensitivity analysis results remained robust and showed mean ICER for costs and probabilities that were lower than a willingness to pay threshold of $100,000/QALYs gained.

■ COMMENTARY

The United States first embarked on a universal prenatal screening strategy for GBS in 2002, following a publication by the Centers for Disease Control and Prevention (CDC) that demonstrated screening for GBS was cost-effective.[9] While universal screening for GBS currently is recommended in the United States at 36 0/7 to 37 6/7 weeks (irrespective of the anticipated route of delivery, vaginal or cesarean), some centers still practice risk-based screening, with the rationale that one-quarter of women who screen positive to GBS prior to 36 to 37 weeks of gestation will screen negative at the time of delivery, and many women who screen GBS positive do not transmit GBS to their fetuses (even when they go untreated).[10] Hence, there currently is a debate whether screening for GBS at 36 0/7 to 37 6/7 weeks of gestation is cost-effective.

Williams and colleagues demonstrated that universal screening for GBS at 36 0/7 to 37 6/7 weeks of gestation is cost-effective.[7] In addition, screening for GBS meets the Wilson and Jungner's criteria, which includes that GBS remains an important health problem; GBS infection has a well-described latent stage and natural history; there are suitable testing algorithms for GBS diagnosis and treatment; case finding for GBS involves a continuous process; and the total cost of finding a case of GBS during pregnancy is economically plausible when compared to the alternative of no screening, resulting in early-onset neonatal GBS infection.[11]

The ACOG practice bulletin recommends intrapartum antibiotic prophylaxis for pregnant women who screen positive for GBS in a current pregnancy.[8] Antibiotic prophylaxis also is recommended for pregnant women who are GBS unknown presenting in labor with risk factors for GBS (GBS bacteriuria earlier in pregnancy, preterm labor, history of a previous neonate with early-onset GBS, maternal pyrexia [> 38°C], and prolonged rupture of membranes [> 18 hours]). The recommended treatment regimen is with intravenous benzylpenicillin (penicillin G), 5 million units as a loading dose, followed by 3 million units every four hours until delivery. To optimize the efficacy of intrapartum therapy, the first dose of benzylpenicillin should be at least four hours prior to delivery. Pregnant women with mild penicillin allergy (e.g., rash) are treated with

intravenous cefuroxime 1.5-g loading dose, followed by 750 mg every eight hours until delivery, while those with severe penicillin allergy (e.g., hives, anaphylaxis) are best treated with intravenous vancomycin 1 g every 12 hours until delivery. Clindamycin is used in GBS-positive women with low risk for anaphylaxis and confirmation that the GBS is susceptible.[8]

In conclusion, universal screening for GBS at 36 0/7 to 37 6/7 weeks of gestation, with rescreening (if GBS results are negative after five weeks of initial screening), as recommended by ACOG, is cost-effective, and therefore should be practiced.[8] ■

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ABSTRACT & COMMENTARY

Zuranolone Trial Shows Early Promise as an Oral Neuroactive Steroid for the Treatment of Postpartum Depression

By Nicole Cirino, MD, CST, IF

Reproductive Psychiatrist, Professor of Psychiatry and OB/GYN, Oregon Health & Science University, Portland

SYNOPSIS: Zuranolone was approved by the Food and Drug Administration for the treatment of postpartum depression (PPD) in March 2019. One potential factor identified in PPD etiology is the dramatic perinatal changes in circulating levels of allopregnanolone, a neuroactive steroid with gamma-aminobutyric acid type A ($GABA_A$) receptor positive allosteric modulator properties. In brain regions associated with emotion and self-perception, neural network connectivity supported by GABAergic signaling is positively correlated with plasma allopregnanolone concentrations in individuals with PPD vs. healthy postpartum female individuals.

SOURCE: Deligiannidis KM, Meltzer-Brody S, Gunduz-Bruce H, et al. Effect of zuranolone vs placebo in postpartum depression: A randomized clinical trial. *JAMA Psychiatry* 2021;78:951-959.

This trial by Deligiannidis et al was a Phase III, double-blind, randomized, placebo-controlled clinical trial for postpartum depression (PPD) conducted between January 2017 and December 2018 in 27 enrolling U.S. sites. Participants were women 18 to 45 years of age, who delivered within six months, with PPD without psychosis. The major depressive episode (MDE) with perinatal onset being studied must have begun either in the third trimester or four or fewer weeks post-delivery with a baseline 17-item Hamilton Rating Scale for Depression (HAMD-17) score of 26 or higher (severe depression).

Patients were randomized 1:1 to receive zuranolone 30 mg or matching placebo capsules daily, taken at night for two weeks. Time points were evaluated day 3 through day 45, four weeks after treatment was discontinued. Patients were not permitted to breastfeed for the 14 days of treatment and the seven-day period following treatment.

The primary endpoint was a change from baseline in HAMD-17 score for zuranolone vs. placebo at day 15. Secondary endpoints included changes from baseline in HAMD-17 total score at other time points, HAMD-17 response (≥ 50% score reduction), and remission (score ≤ 7) rates. The study population had a mean age of 29.3 years (standard deviation [SD] 5.4 years) in the zuranolone group and 27.4 years (SD 5.3 years) in the placebo group (range, 18 to 44 years). Most patients identified as white (placebo group, 54% vs. zuranolone group, 58%) or Black/African American (placebo group, 42% vs. zuranolone group, 41%). Twenty-four percent of the placebo group vs. 21% of the zuranolone group identified as Hispanic or Latina.

At baseline, 21% vs. 18% of patients in the zuranolone and placebo groups, respectively, were taking stable doses of antidepressant medications.

Safety and tolerability were evaluated by adverse events (AEs), vital signs, clinical laboratory evaluations, electrocardiogram parameters, and the Columbia-Suicide Severity Rating Scale. Results showed that by day 3, women receiving zuranolone experienced a greater reduction in HAMD-17 scores than women receiving placebo (mean reduction, 12.5 vs. 9.8; *P* = 0.03). At day 3, a higher percentage of patients in the zuranolone group achieved HAMD-17 remission vs. the placebo group (19% vs. 5%, respectively; odds ratio [OR], 3.9; 95% confidence interval [CI], 1.2-12.2; *P* = 0.02). Remission, defined as a HAMD-17 score of 7 or less, also was more common in the zuranolone group at day 8 (32% vs. 19%; *P* = 0.020) and day 15 (45% vs. 23%; *P* = 0.011). At day 15, the primary endpoint and final day of treatment, there was a significantly greater reduction from baseline in HAMD-17 total score with zuranolone compared with placebo (-17.8 points vs. -13.6 points; 95% CI; *P* = 0.003; effect size, 0.53.)

Greater reductions from baseline in HAMD-17 score favoring zuranolone compared with placebo were observed at all measured time points from day 3 through day 45. At day 45, four weeks after study drug cessation, HAMD-17 response was 75% in the zuranolone group vs. 57% in the placebo group (OR, 2.3; 95% CI, 1.1-4.6; *P* = 0.02) and HAMD-17 remission was 53% in the zuranolone group vs. 30% in the placebo group (OR, 2.5; 95% CI, 1.3-5.0; *P* = 0.009). Improvements in anxiety, a common PPD symptom/comorbidity, and in clinician-measured global functioning (CGI-I) also were sustained through day 45.

Generally, zuranolone was well tolerated. The most common treatment-emergent AEs in the zuranolone group vs. placebo group were somnolence (15% vs. 11%), headache (9% vs. 12%), dizziness (8% vs. 6%), and sedation (5% vs. 0%), respectively. Three patients in the zuranolone group experienced severe treatment-emergent AEs (sedation, n = 1; confusional state, n = 1; migraine, n = 1), and three patients in the placebo group experienced severe treatment-emergent AEs (back pain/muscle spasms, n = 1; headache/oropharyngeal pain, n = 1; menorrhagia, n = 1). The patient in the zuranolone group experienced a confusional state on day 3, involving the inability to remember the exact sequence of the day's events, along with sedation, which resolved within seven hours. There was no indication of an increase in suicidal ideation or suicidal behavior over baseline, as measured with the Columbia Suicide Severity Rating Scale (C-SSRS) in either group.

■ COMMENTARY

Currently, none of the monoaminergic antidepressants (e.g., selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, or atypical antidepressants) have specific indications for PPD, despite being used widely, largely because of the lack of specific data in the PPD population.

I have written previously about brexanolone, which was the first drug to be approved by the U.S. Food and Drug Administration (FDA) specifically for the treatment of postpartum depression in adults. Brexanolone, a 60-hour infusion, demonstrated reductions in depressive symptoms in three double-blind, randomized, placebo-controlled trials.[1] The same company, Sage Therapeutics, Inc., funded this trial, and zuranolone has been nicknamed the "little sister" of brexanolone.

This is not the first randomized controlled trial looking at the effectiveness of zuranolone. In 2019, zuranolone failed to meet its primary endpoint in a double-blind, placebo-controlled, pivotal Phase III study for adults with major depressive disorder (MDD). In that study, 581 patients were randomized to receive zuranolone or placebo once nightly for two weeks. The primary endpoint of the study was the same as the earlier study — change from baseline in the HAMD-17 total score at day 15.[2]

The use of brexanolone has been limited because of the need for a 60-hour infusion in a monitored setting requiring relatively high cost. In addition, brexanolone had some potentially serious side effects, including excessive sedation and sudden loss of consciousness. Thus, the FDA required a Risk Evaluation and Mitigation Strategy (REMS) for healthcare facilities seeking to administer it. It seems unlikely that zuranolone will require a REMS.

What distinguishes zuranolone from brexanolone is that it has much better oral bioavailability and, thus, does not have to be administered intravenously. It can be taken as an oral medication, just like conventional antidepressants. However, the onset of action of oral zuranolone does not compare to the rapid onset of the brexanolone infusion. In the integrated brexanolone data, the rapid response rate was significant compared to placebo at hours 24, 48, 60, and 72 and at days 7 and 30.[1] Studies now are underway to look at the safety of home infusion of brexanolone, but it has not yet been established as a viable modality of treatment.[3]

In summary, this trial expands our current research and continues to focus on the new approach to the treatment of PPD using neuroactive steroid agents. Some potential advantages over traditional antidepressants are the shorter duration of treatment (two weeks, compared to antidepressants, which can require months of treatment), minimal adverse effects shown thus far, and the targeted treatment specifically for PPD vs. general adult MDD. Thus far, the disadvantages of neuroactive steroids over antidepressants include a lack of data in lactation (in this trial, breastfeeding was halted for three weeks as a safety measure), unclear efficacy for anxiety as compared to traditional antidepressants, cost, and accessibility. We still have a way to go to establish whether either brexanolone infusion or oral zuranolone will be as accessible or as effective as traditional antidepressants for the treatment of PPD, but having a neuroactive steroid agent as an alternative or adjunct to treatment of PPD is promising. ■

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ABSTRACT & COMMENTARY

Are Female Surgeons at Higher Risk for Infertility and Pregnancy Complications?

By Rebecca H. Allen, MD, MPH, Editor

SYNOPSIS: In this cross-sectional national survey of 850 surgeons, compared to the partners of male surgeons, female surgeons were more likely to have fewer children (1.8 vs. 2.3) and to delay having children because of surgical training (65% vs. 44%). Female surgeons also were more likely to use assisted reproductive technology (25% vs. 17%).

SOURCE: Rangel EL, Castillo-Angeles M, Easter SR, et al. Incidence of infertility and pregnancy complications in US female surgeons. *JAMA Surg* 2021;156:905-915.

Female surgeons undergo long training periods and often delay childbearing.[1] This study was conducted to determine whether working as a surgeon influenced rates of infertility and pregnancy complications. This was a cross-sectional electronic survey that was created after conducting focus groups of male and female faculty and resident surgeons in two academic teaching hospitals regarding infertility, barriers to childbearing, and pregnancy complications. After testing, the final survey collected data on demographic characteristics, practice information, work hours, family goals, use of assisted reproductive technology, and multiple gestations. Antepartum, intrapartum, postpartum, and neonatal complications also were queried. The survey was distributed via emails and newsletters to multiple surgical societies between November 2020 and February 2021, as well as through targeted social media platforms. The target participants were male and female surgeons and surgical trainees in the United States, with nonchildbearing surgeons being asked to answer questions about their partner's pregnancies. Surgeons who had never attempted a pregnancy, male surgeons whose partners also were surgeons, and female surgeons in same-sex relationships in which the gestational carrier could not be confirmed were excluded.

After applying exclusion criteria, 850 respondents were included in the analysis, with 692 (81.4%) being female. The control group (n = 158) ended up including only the childbearing partners of male surgeons. Because of the manner in which the survey was distributed, a response rate could not be calculated. Compared with male surgeons' partners, female surgeons had fewer children (1.8 vs. 2.3, $P < 0.001$), were more likely to delay having children because of surgical training (65% vs. 44%, $P < 0.001$), and were more likely to use assisted reproductive technology (25% vs. 17%, $P < 0.04$). Female surgeons also were more likely to be older at first birth (median age 33 years vs. 31 years, $P < 0.001$) and were more likely to work more than 60 hours per week during pregnancy (57% vs. 10%, $P < 0.001$). Among female surgeons, 290 (42%) experienced a pregnancy loss, with 85% having a loss at < 10 weeks' gestation, 32% between 10 weeks' and 20 weeks' gestation, and 3.8% at 20 or more weeks' gestation. Major pregnancy complications (preeclampsia, placental abruption, malplacentation, intrauterine growth restriction, preterm labor/preterm premature rupture of the membranes, and placental insufficiency/oligohydramnios) were more common for female surgeons after controlling for age, hours worked per week, race and ethnicity, in vitro fertilization usage, and multiple gestations (odds ratio, 1.72; 95% confidence interval, 1.11-2.66). Preterm delivery rates and neonatal complications were similar between the two groups.

■ COMMENTARY

This study sought to describe the experiences of female surgeons in the United States and how training affected their pregnancy outcomes. The study used the partners of male surgeons as the control group, given that the socioeconomic circumstances of both groups likely would be similar. The study did not include obstetrician-gynecologist surgeons but only general surgeons and subspecialties. According to the article, women now make up 38% of surgical residents and 21% of practicing surgeons in the United States. Yet, surgical training, lasting between five and seven years after medical school, is demanding in terms of work hours and physical exertion. Most residencies offer little support for pregnancy and lactation; therefore, many individuals choose to delay childbearing until the completion of training, which was confirmed in this study.[1] Delaying childbearing can place the patient in an age bracket (35 years of age and older, advanced maternal age) where complications, such as infertility, pregnancy loss, and preeclampsia, are higher.

This survey report received a lot of attention in the lay press because of its dramatic findings.[1] The results demonstrated

struggles with infertility, which likely are age-related, and pregnancy loss rates higher than average, which the authors theorized were related to work hours and physical exertion. There are some data suggesting that adverse pregnancy outcomes may be related to working more than 40 hours per week, prolonged standing, and shift and night work.[2] Looking at the data, the difference between the two groups in major pregnancy complications was driven by a difference in preeclampsia rates only. There was no difference in placental disorders or preterm labor or delivery, interestingly. The methodology of this analysis had several limitations, however. Since there was no way to determine a response rate, there could be sampling bias, since those surgeons who were more interested in the topic because of personal pregnancy complications chose to answer the survey compared to those who did not have that history. Furthermore, there could be recall bias and inaccuracies in the recollection of certain pregnancy complication details. Finally, the control group was much smaller and, again, there could be sampling bias in terms of which male surgeons responded to the survey. Certainly, the approach was not a random representative sample of surgeons in the United States.

Nevertheless, the authors made several recommendations for surgical training programs and surgical departments to better facilitate pregnancy earlier in a surgeon's career if desired. These included having policies that support schedule flexibility for pregnant surgeons, at least six weeks (and ideally 12 weeks) of paid parental leave exclusive of vacation time, even if this required an extension of residency or fellowship training, and lactation support. An interesting idea was to have the service coverage during leave performed by moonlighting physicians or advance practice clinicians to avoid resentment from colleagues. There is documented stigma associated with childbearing during surgical training.[1] An accompanying editorial called out the American Board of Surgery policies that only allow trainees two weeks of parental leave.[3] Certainly, the field of medicine, and the country as a whole, can do better with parental leave policies, since the United States is one of the few countries without a federally supported paid parental leave program. We need to do a better job supporting physicians at all stages in their career, from medical school to residency to faculty, with family building. ■

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CME/CE QUESTIONS

1. **In the study by Upadhyay et al, which of the following was associated with increased odds of attempting self-managed abortion?**
   a. Living less than 50 miles from the nearest abortion facility
   b. Higher numbers of abortion restrictions at the state-level
   c. Having to keep the abortion a secret
   d. Lower levels of education
2. **Which of the following is *not* a risk factor for group B streptococcus (GBS) infection in a current pregnancy?**
   a. GBS bacteriuria
   b. History of a previous neonate with late-onset GBS
   c. Maternal pyrexia (> 38°C)
   d. Prolonged rupture of membranes (> 18 hours)
3. **Which of the following statements about zuranolone is true according to the randomized controlled trial by Deligiannidis et al?**
   a. Zuranolone compared to selective serotonin reuptake inhibitors shows superior response rates for women with postpartum depression (PPD).
   b. Zuranolone currently is the second Food and Drug Administration-approved medication for PPD.
   c. Thus far, zuranolone has been studied as a daily oral dose for 14 days of treatment.
   d. Zuranolone can be given orally or via infusion.
4. **In the study by Rangel et al, female surgeons had a higher risk of all of the following *except*:**
   a. delaying childbearing.
   b. use of assisted reproductive technologies.
   c. fewer children.
   d. preterm delivery.