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ABSTRACT & COMMENTARY

News From the WHI: Soft Drink Consumption and Bone Health

By Jeffrey T. Jensen, MD, MPH, Editor

SYNOPSIS: Participants from the Women's Health Initiative (WHI) study who reported consumption of more than two soft drinks per day showed a higher incidence of hip fracture compared to those consuming no soft drinks.

SOURCE: Kremer PA, Laughlin GA, Shadyab AH, et al. Association between soft drink consumption and osteoporotic fractures among postmenopausal women: The Women's Health Initiative. *Menopause* 2019;26:1234-1241.

Epidemiologic studies have demonstrated an association between the consumption of carbonated soft drinks and low bone density and fracture in children and young adults, but the relationship is less clear for postmenopausal women.

In this secondary analysis of data from the Women's Health Initiative (WHI) study, researchers evaluated the association between soft drink consumption and osteoporotic fractures in postmenopausal women. The authors noted that more than 8.9 million osteoporotic fractures occur annually worldwide, and the incidence of hip fracture is expected to reach 2.6 million by 2025, nearly doubling to 4.5 million by 2050. Given the high morbidity (40% of people with hip fractures are unable to walk independently one year after the fracture) and mortality (21.2% at one year) of hip fracture in elderly populations, modifiable factors that affect this risk deserve study. In this study, the term soft drink refers to carbonated, nonalcoholic beverages.

The authors used data collected from women enrolled in the observational study of the WHI. They sent annual questionnaires to a group of 72,342 eligible women, who provided information on soda intake (total, caffeinated, and caffeine-free) during the sixth follow-up year. These questionnaires included questions about various health behaviors and outcomes, including hospitalizations and clinical fractures. Bone mineral density (BMD) measurements were available only for a subgroup of these women.

When possible, the investigators used hospital records to validate the self-report of hip fracture, a primary outcome. To evaluate the main exposure of

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total soft drink intake, a validated dietary questionnaire specifically asked about consumption of common carbonated, nonalcoholic beverages by their brand names, with caffeinated and caffeine-free soft drinks categorized separately. For the analysis, the investigators categorized intake of soft drinks as none; up to 2; 2.1-5; 5.1-14; and more than 14 servings per week.

The investigators used a variety of statistical models to adjust minimally and fully for baseline characteristics, including age, race/ethnicity, body mass index (BMI), hormone therapy, smoking status, alcohol use, oral contraceptive use, self-rated general health status, diabetes mellitus, osteoporosis therapy, thiazides, glucocorticoids, thyroid hormone, calcium and vitamin D supplements, coffee intake, total energy expenditure, income, and maternal hip fracture. They then constructed hazard ratios (HRs) and 95% confidence intervals (CI).

A total of 72,342 women contributed 700,388 woman/years of follow-up, with a median duration of 11.9 years. Hip fracture was reported by 2,578 women (3.5% of the sample). Both the minimally and fully adjusted survival models showed a 26% increased risk of hip fracture among women who drank on average 14 or more soft drink servings per week compared with no servings (HR, 1.26; 95% CI, 1.01-1.56). Of interest, the HRs associated with consumption of 14 or more servings per week of non-caffeinated soft drinks remained significantly elevated in most of the models, while those for caffeinated beverages did not. However, the strength of the association for both types of beverages increased in a subgroup analysis that only considered fully adjudicated hip fractures (overall: HR, 1.45; 95% CI, 1.07-1.95; caffeine-free: HR, 1.43; 95% CI, 0.97-2.11; and caffeinated: HR, 1.48; 95% CI, 1.00-2.26).

The authors concluded that high soda consumption has a modest impact on increasing the risk of fracture in postmenopausal women.

■ COMMENTARY

We know that low BMD and hip fractures are predictable consequences of menopause, and that hormone therapy prevents postmenopausal bone loss, maintains or improves BMD, and prevents fractures.[1,2] So why focus on this study of soft drink exposure?

If you have followed my commentaries, you know my concern for studies that show statistically significant but clinically unimportant relationships. At first glance, this paper illustrates this type of study. Given the large number of participants, this secondary analysis yielded statistically significant CIs for some outcomes. But the magnitude of the risk estimates (less than 2.0) reflects a weak association that in most cases should not influence practice patterns. Well-designed double-blind, randomized studies do provide greater evidence for validity of a weak association. The randomized estrogen-only and combined estrogen/progestin study arms of the WHI provided this degree of resolution. In contrast, the observational arm of the WHI did not involve randomization. Women enrolled in this study comprised a cohort based on providing answers to a questionnaire on soft drink exposure during year six of the observation period.

Since patterns of soft drink consumption were evaluated as an exposure, and not an experimental condition, the opportunity for confounding exists. To account for this, the investigators used several models of statistical adjustment for the analysis and considered several baseline characteristics, such as BMI, race, and smoking as potential confounders. In general, the result of an increase in the risk of fracture associated with consumption of two or more soft drinks per day was durable across the several models of adjustment. As expected, increasing the number of adjustments widened the CIs, with many comparisons losing statistical significance (e.g., CI includes 1.0).

Although the potential for unmeasured confounding variables always remains, let's assume that the point estimates supporting the main conclusion that soft drink consumption increases the risk of fracture by 26% (HR, 1.26; 95% CI, 1.01-1.56) reflects truth. In the main WHI randomized studies, women assigned to conjugated equine estrogens (CEE) plus medroxyprogesterone acetate (MPA) had increased HRs of 1.24 (95% CI, 1.01-1.53) for breast cancer and 1.18 (95% CI, 0.95-1.45) for coronary heart disease,

and a decrease fracture risk of 33% (HR, 0.67; 95% CI, 0.47-0.95) compared to placebo. Considering the importance attributed to risk estimates of this magnitude in the main WHI findings, the magnitude of the impact of soda consumption (a modifiable risk) on fracture risk (26%) seems more compelling.

A contrarian would argue that none of these relationships necessarily has clinical importance. One woman's modifiable risk is another's elixir of life. For example, premenopausal exposure to alcohol does not influence bone density or fracture risk,[3] but it does increase breast cancer risk.[4] Also, good news for caffeine in this study (no increase in risk).

I believe this paper provides additional useful information when counseling women on the risks and benefits of menopausal hormone therapy. The clinician should guide the discussion to consider lifestyle choices important to individual women. Putting risk into perspective requires a translation into real numbers of events.[5] Among other outcomes from the WHI main findings, the attributable risk associated with CEE/MPA was nine additional cases of breast cancer and six additional cases of coronary heart disease in 10,000 exposed women. At the same time, CEE/MPA prevented six cases of fracture and six cases of colorectal cancer per 10,000 women.[6] So, raise your glass of wine, mug of beer, or can of soda. Life is full of risks and benefits. Lucky are those who get to choose. ■

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ABSTRACT & COMMENTARY

Influenza and Pertussis Vaccines for Pregnant Women: Are We Doing Enough to Encourage Vaccination?

By Rebecca H. Allen, MD, MPH

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Dr. Allen reports she receives grant/research support from Bayer and is a consultant for Merck.

SYNOPSIS: In this cross-sectional analysis, pregnant women disproportionately accounted for 24-34% of influenza-associated hospitalizations among women aged 15 to 44 years, and infants younger than 2 months of age comprised the highest proportion of pertussis deaths. The reasons why pregnant women did not elect recommended immunizations included not believing they were effective, not knowing they should receive Tdap every pregnancy, and being concerned that the vaccines would harm the fetus.

SOURCE: Lindley MC, Kahn KE, Bardenheier BH, et al. Vital signs: Burden and prevention of influenza and pertussis among pregnant women and infants — United States. *MMWR Morb Mortal Wkly Rep* 2019;68:885–892.

This cross-sectional study was conducted by the Centers for Disease Control and Prevention (CDC) to estimate influenza and Tdap vaccination rates among pregnant women. This researchers also evaluated influenza hospitalization among pregnant women and infant hospitalization and death associated with influenza and pertussis. To ascertain vaccination rates, an internet survey was conducted March 27-April 8, 2019, among U.S. adult women ages 18-49 years who reported being pregnant any time since Aug. 1, 2018. A total of 2,626 women completed the survey, and the data were weighted to reflect age, race/ethnicity, and geographic distribution of the U.S. population of pregnant women. Participants' pregnancy and vaccination status was self-reported and not verified via medical record review. To assess

hospitalization rates, data from national surveillance systems (Influenza Hospitalization Surveillance Network and the Influenza-Associated Pediatric Mortality Surveillance System) for the 2010-2011 through 2017-2018 influenza seasons were queried to quantify the proportion of influenza-associated hospitalizations among pregnant women ages 15-44 years and the number of influenza-associated hospitalizations and deaths among infants younger than 6 months of age. From 2010-2017, pertussis case counts, hospitalizations, and mortality in infants younger than 2 months of age also were obtained from the National Notifiable Diseases Surveillance System.

During the 2010-2011 through 2017-2018 influenza seasons, 2,341 influenza-associated hospitalizations among pregnant women were reported. Pregnant women accounted for 24-34% of the hospitalizations among women ages 15 to 44 years. During the same period, among infants younger than 6 months of age, there were 100 laboratory-confirmed influenza-associated deaths, with an average rate of influenza-associated hospitalizations of 133 per 100,000. From 2010-2017, there were 3,928 pertussis hospitalizations among infants younger than 2 months of age, with 77 deaths, accounting for 69% of pertussis deaths among infants younger than 12 months of age.

In the internet survey conducted as part of this study, 53.7% of eligible respondents reported influenza vaccination before or during pregnancy, and 54.9% reported Tdap vaccination during pregnancy. Only 35% of participants reported receiving both vaccines. Compared to the referent group, vaccination coverage for both influenza and Tdap was lower among non-Hispanic black women, and women who had less than a college education, were unmarried, lived below the poverty line, lived in the South, were publicly insured, and did not report a vaccination offer or referral from a healthcare provider. Healthcare provider offer or referral for vaccination was reported by 73.3% of respondents for influenza vaccine and 76.0% of respondents for Tdap. Among those who received an offer or referral, 65.7% received the influenza vaccine and 70.5% received the Tdap. Participants most commonly reported opting not to receive the influenza vaccine because they believed it was ineffective (17.6%). For Tdap, the most commonly reported reason for not getting vaccinated was not realizing that it was needed during each pregnancy (37.9%). For both vaccines, the second most common reason for electing not to receive the vaccine was concern about safety risks to their infant (influenza = 15.9%; Tdap = 17.1%).

■ COMMENTARY

This timely report by the CDC emphasizes that we all can do more to encourage pregnant women to receive influenza and pertussis vaccines. While pregnant women make up only 9% of the population of women ages 15 to 44 years, they accounted for 24-34% of influenza hospitalizations during the eight years of surveillance. Infants younger than 2 months of age cannot receive the Tdap vaccine themselves and infants younger than 6 months of age cannot receive the influenza vaccine. Therefore, their protection against these diseases relies on antibodies passed through the placenta during pregnancy from their mother's immunization.[1,2] It is estimated that influenza vaccination during pregnancy lowers the risk of influenza hospitalization in pregnant women by an average of 40% and by 72% in infants younger than 6 months of age.[3] Similarly, Tdap vaccination during pregnancy lowers the risk of whooping cough in infants younger than 2 months of age by 78% and hospitalization due to whooping cough by 91%.

While there are limitations to self-reported data, this study found that vaccination rates were higher among women who reported being offered or referred for vaccination. However, one-third of women whose providers did offer or refer them for vaccination remained unvaccinated. Unfortunately, the study also showed that immunization rates were lower among women of lower socioeconomic status. We need to do a better job of combating myths that influenza and Tdap vaccines are unsafe or do not work and try to engender trust in the healthcare system. Additionally, OB/GYNs should try to stock recommended vaccines in their offices, since studies show that immunization rates are higher when a healthcare provider can offer and administer a vaccine during the same visit.[4]

The CDC and the American College of Obstetricians and Gynecologists further recommend that healthcare providers:[1-3]

- Discuss the benefits and safety of vaccination with pregnant women early and often.
- Strongly recommend influenza and Tdap vaccines to pregnant women.
- Offer influenza and Tdap vaccines to pregnant women or provide referrals to other vaccination providers.
- Reinforce that maternal vaccination is the best way to protect babies from influenza and whooping cough. ■

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ABSTRACT & COMMENTARY

PARP Inhibitors: An Adjunct to Initial Standard Treatment for Advanced Ovarian Cancer Patients

By Melissa Moffitt, MD

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

SYNOPSIS: The PRIMA study is a randomized, double-blind, multi-institutional, international phase 3 trial testing the PARP inhibitor niraparib against placebo after first-line standard treatment with platinum-based chemotherapy for newly diagnosed ovarian cancer.

SOURCE: González-Martín A, Pothuri B, Vergote I, et al. Niraparib in patients with newly diagnosed advanced ovarian cancer. *N Engl J Med* 2019 Sept. 28. doi: 10.1056/NEJMoa1910962. [Epub ahead of print].

Standard treatment (ST) for newly diagnosed advanced epithelial ovarian cancer generally consists of tumor reductive surgery and platinum-based chemotherapy. This treatment usually is not curative, since 85% of patients experience recurrence.

Poly (ADP-ribose) polymerase (PARP) is a group of enzymes involved in DNA repair. Currently multiple drugs on the market target and inhibit PARP enzymes' ability to repair damaged DNA. If PARP is impaired or inhibited, the cell ultimately dies. PARP inhibition (PARPi) has emerged as one of the new targeted treatments used in cancer care. Until this point, it also has been considered "personalized medicine," as PARPi has been used as maintenance treatment after initial ST primarily in two sets of women: those with a germline breast cancer gene (BRCA) mutation; and those without a germline BRCA mutation, but with ovarian cancer that has developed a somatic BRCA mutation or BRCA-related mutation.

BRCA genes rely on other genes to function. When there are somatic mutations in tumor BRCA or the genes that BRCA requires to function, the BRCA gene cannot act as a tumor suppressor. When ovarian cancer tumors express somatic BRCA mutations or mutations in the genes BRCA relies on, this is referred to as homologous-recombination deficiency (HRD). Currently, for a patient to be a candidate for PARPi at initial diagnosis after ST, she must have proven HRD. Thus, nearly all advanced-stage epithelial ovarian cancer patients undergo germline BRCA mutation testing and tumor molecular analysis. In women with HRD, PARPi after initial ST lengthens progression-free survival 36 months compared to placebo, with a hazard ratio (HR) for disease progression or death of 0.30 (95% confidence interval [CI], 0.23-0.41).[1] In the same study, PARPi after initial ST not only lengthened the initial remission, but after recurrence, the progression-free survival after second-line treatment also was longer than in those who received placebo, showing that PARPi has a sustained effect. PARPi gives some ovarian cancer patients a very realistic hope for longer life.

Some studies have suggested that PARPi after ovarian cancer recurrence and second-line treatment benefits a wider spectrum of ovarian cancer patients than just those with BRCA mutations or HRD. In the PRIMA study, González-Martín and colleagues evaluated PARPi in patients with and without HRD but at the time of initial diagnosis, after ST. The authors enrolled 733 women with an initial diagnosis of advanced-stage, high-grade serous and endometrioid ovarian cancers after those patients had achieved a complete or partial response to ST. Many of the patients enrolled were at high risk for early recurrence (suboptimal tumor reductive surgery, inoperable cancer, stage IV disease, etc.), so shorter than usual progression-free survivals were expected.

All the enrolled patients were randomized 2:1 to receive PARPi (niraparib) or placebo. All of the patients' tumors were molecularly analyzed; half were found to have HRD. The randomization was double-blinded and stratified according to HRD status and whether patients received neoadjuvant chemotherapy. The patients took their oral treatments daily, starting within three months of finishing initial standard ovarian cancer treatment and continuing until cancer progression or 36 months. The patients were assessed every three months with imaging until the oral medication was discontinued. The primary endpoints were progression-free survival in patients with HRD and progression-free survival in all enrolled patients. As expected, the women with HRD had great benefit from PARPi: The median progression-free survival in patients with HRD who received niraparib was 22 months vs. 10 months in those who received placebo, with HR, 0.43 (95% CI, 0.31-0.59) for disease

progression or death. Importantly, those without HRD also benefited from PARPi, with a median progression-free survival of 8.1 months compared to five months for those who received placebo, with HR, 0.68 (95% CI, 0.49-0.94). Thus, median progression-free survival for all the women in the study (those with and without HRD) was improved with PARPi: 14 months vs. eight months for those who received placebo, with HR, 0.62 (95% CI, 0.50-0.76). However, even those patients with the worst prognoses were found to benefit from PARPi: Patients with only a partial response to chemotherapy who received PARPi had eight months of progression-free survival, compared to five months for those who received placebo. Similarly, in those patients whose initial treatment included neoadjuvant chemotherapy, those who received PARPi had 14 months of progression-free survival, whereas those who received placebo had only eight months of progression-free survival.

[Median progression-free survival for all the women in the study was improved with poly (ADP-ribose) polymerase inhibition.]

Side effects of niraparib include bone marrow suppression, low-grade nausea, and fatigue.

■ COMMENTARY

PARP inhibitors are revolutionizing ovarian cancer treatment. For some oncologists, these medications are familiar, since they are used upfront for the treatment of BRCA and HRD patients. PRIMA changes this scenario significantly, as it shows that all patients with advanced-stage, high-grade serous or endometrioid ovarian cancer may benefit from using a PARP inhibitor after finishing initial treatment with surgery and platinum-based chemotherapy, independent of BRCA or HRD. While BRCA germline testing remains important for cascade testing of family members, we no longer need to obtain BRCA germline testing right away during treatment, as PARPi now has been shown to be effective in all patients independent of BRCA status. In addition, we have been sending each patient's ovarian cancer for molecular analysis, hoping they will have HRD, and thus qualify for initial treatment with PARPi. This molecular analysis is costly. The PRIMA study suggests that we can forgo molecular analysis and perhaps perform it later, when necessary, on fewer patients when seeking a new, targeted treatment option for subsequent recurrences. This likely will result in a substantial savings for our healthcare system.

In addition, the ovarian cancer patients whose initial remission lasts longer than six months are considered platinum-sensitive. We have been able to use PARPi in platinum-sensitive patients after their second-line treatment as long as they have had a response to second-line platinum therapy. These patients were already known to have the best prognosis of ovarian cancer patients, and it has been wonderful having this new tool to extend their second and subsequent remissions. However, it is the patients who are at highest risk of recurrence — those who are suboptimally tumor reduced or those who never had a complete response after initial treatment — for whom we are desperate for new treatments. PRIMA gives us a new tool to use for our most unfortunate patients, allowing even them to have a glimmer of hope for longer life. ■

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ABSTRACT & COMMENTARY

The Affordable Care Act: Progress in Reducing the Rate of Unintended Pregnancy

By Jeffrey T. Jensen, MD, MPH, Editor

SYNOPSIS: Data from the latest release of the National Survey of Family Growth supports that the contraception coverage mandate of the Affordable Care Act has resulted in a decrease in the incidence of unintended pregnancy, particularly among women with government coverage.

SOURCE: MacCallum-Bridges CL, Margerison CE. The Affordable Care Act contraception mandate & unintended pregnancy in women of reproductive age: An analysis of the National Survey of Family Growth, 2008-2010 v. 2013-2015. *Contraception* 2019 Oct. 23; doi: 10.1016/j.contraception.2019.09.003. [Online ahead of print].

Although unintended pregnancy has declined in recent years, about 50% of all pregnancies are mistimed or unwanted at conception. Although controversy exists regarding the best strategies to ensure all pregnancies are both wanted and planned, considerable evidence supports the importance of access to family planning services. In this study, MacCallum-Bridges and Margerison compared data from before and after implementation of the contraception coverage mandate of the Affordable Care Act (ACA), arguably the most significant step to improve access in U.S. history. The ACA mandate required that insurance plans provide Food and Drug Administration (FDA)-approved female contraception and contraceptive services without co-pays, starting Aug. 1, 2012.

The authors used cross-sectional data from the 2006-2010 and 2013-2015 cycles of the National Survey of Family Growth (NSFG), a nationally representative survey of noninstitutionalized men and women in the United States ages 15-44 years. They included interview responses from sexually active women of reproductive age (18-44 years) at risk for pregnancy. The sample intervals allowed them to compare pre- and post-mandate periods, and to control for seasonality in unintended pregnancies (24 months in both the pre-mandate [July 2008-June 2010] and post-mandate [September 2013-August 2015] periods). They calculated odds ratios for unintended pregnancy, and adjusted these for potential confounders (insurance type, race/ethnicity, age group, income level, educational level, and relationship status) in a variety of models. They also evaluated the effect of contraceptive use, and specifically long-acting reversible contraception (LARC) use, in other models.

The basic demographic characteristics of the survey respondents did not change between the pre-mandate and post-mandate periods. However, insurance coverage increased, highest and lowest income levels increased, education level increased, and current LARC use increased (from 8.9% to 13.4%, $P < 0.01$). The proportion of women reporting an unintended pregnancy in the prior year decreased from 5.5% in the pre-mandate period to 4.9% in the post-mandate period ($P = 0.45$). The percentage of pregnancies that were unintended decreased from 44.7% in the pre-mandate period to 37.9% in the post-mandate period ($P = 0.21$).

Although the odds ratios comparing unintended pregnancy in the pre- and post-mandate periods did not differ significantly for most comparisons, the point estimates favored the post-mandate period. The odds of experiencing an unintended pregnancy in the prior year decreased 15% overall (odds ratio [OR], 0.85; 95% confidence interval [CI], 0.62). Notably, the authors observed the greatest reduction in the group of women with government-sponsored insurance (OR, 0.63; 95% CI, 0.41-0.97).

■ COMMENTARY

Another election is right around the corner, and healthcare remains a primary focus of the policy debate (at least for those who still care about policy). The only outcome that appears certain is that the ACA will change.

Republicans seem to have lost steam for repeal-and-replace legislation for the ACA, but we can expect more attempts if they remain in power after 2020. But more people, even in red states, seem to have recognized the benefits of the ACA, as evidenced in victories by Democrats in the gubernatorial elections in Kentucky and Louisiana. Expanded eligibility for Medicaid to individuals with incomes up to 138% of the federal poverty level has been of particular benefit to single women. Individuals with incomes between 100% and 400% of the federal poverty level receive refundable tax credits to lower the cost of their monthly premiums.[1] Between 2013 and 2015, the proportion of women 15-44 years of age who were uninsured fell by 36%. The ACA mandated that marketplace plans cover core sexual and reproductive health services, including contraception care, at no cost.

[The proportion of women reporting an unintended pregnancy in the prior year decreased from 5.5% in the pre-mandate period to 4.9% in the post-mandate period.]

I still hold the old-fashioned belief that data should inform policy. The analysis by MacCallum-Bridges and Margerison provides new information supporting how the ACA affected unintended pregnancy rates. Although the intervention's influence is modest (the ORs all show weak effects and CIs overlap 1.0), the overall trends toward a reduction following the program's implementation are consistent with what we would expect with expanded access. Future analyses should strengthen these associations, as these data reflect the earliest results of the program. I also note that the largest reduction (47% decrease, CI did not overlap 1.0) in unintended pregnancy occurred in women using government insurance. This likely demonstrates the effect of expanded Medicaid on the most vulnerable population of women.

The increase in LARC use likely drove the decrease in unintended pregnancy. The CHOICE study showed the effect of removing cost barriers from contraception

decision-making. Peipert and coauthors compared repeat abortion rates in the St. Louis region, the site of CHOICE, to Kansas City, MO, a community of similar size and ethnic profile and subject to the same state laws.[2] They observed a 20% decline in the number of abortions in the St. Louis area between 2008-2010 compared to no decline in Kansas City or the rest of Missouri, and a significant decrease in the number of repeat abortions.

The Colorado Family Planning Initiative took the concept of the CHOICE project and enacted the changes in real clinics. The state of Colorado received support from a private foundation to increase the availability of LARC methods at Title X–funded clinics through provider training, counseling materials, and no-cost provision of LARC methods in 2009. The program proved wildly successful. LARC use among women 15-24 years old grew from 5% to 19% in this high-risk population. Pregnancy rates decreased by 29% among low-income 15- to 19-year-olds, and 14% for 20- to 24-year-olds, and abortion rates fell 34% and 18%, respectively. The state of Colorado noted a 23% reduction in infant Special Supplemental Nutrition Program for Women, Infants, and Children program enrollment between 2010 and 2013.[3]

As community leaders, clinicians have an obligation to advocate for sound public health policy. The requirement for mandatory contraception coverage provides a lightning rod for some groups to oppose the ACA. As clinicians, we understand how these comprehensive requirements support the reproductive life cycle needs of our patients. Elimination of cost sharing for LARC methods with implementation of the ACA has resulted in an increase in LARC uptake, according to studies using insurance claims databases.[4] We now see early evidence that this is reducing the rate of unintended pregnancy throughout the United States. ■

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CME/CE QUESTIONS

1. Among women in the observational arm of the Women's Health Initiative, a significant increase in the risk of fracture was associated with consumption of:
a. one alcoholic beverage per day.
b. two or more soft drinks per day.
c. 10 to 12 non-caffeinated soft drinks per month.
d. six caffeinated soft drinks per week.

2. In the study by Lindley et al, the most common reason participants gave for not electing to receive Tdap during pregnancy was:
a. They were concerned about harm to the fetus.
b. They were never offered the vaccine.
c. They did not know that the vaccine was needed with each pregnancy.
d. They did not have insurance coverage for the Tdap vaccine.

3. An otherwise healthy 68-year-old woman is diagnosed with Stage IVb high-grade serous ovarian cancer. She has a biopsy-proven 5 cm thoracic lymph node as well as multiple intrahepatic metastatic nodules, and thus is deemed not to be a surgical candidate. Which statement reflects the treatment option that gives her the longest progression-free survival?
a. Platinum-based chemotherapy only
b. Platinum-based chemotherapy followed by PARP inhibition
c. PARP inhibition only
d. Hospice

4. Regarding the most recent trends from the National Survey of Family Growth, which of the following statements is *false*?
a. Unintended pregnancy rates have decreased.
b. Long-acting reversible contraception use has increased.
c. Government-sponsored insurance has increased abortion rates.
d. Insurance coverage has increased.