UPDATE

Update in Women's Health

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INTRODUCTION: The aim of this clinical update is to summarize articles and guidelines published in the last year with the potential to change current clinical practice as it relates to women's health.

METHODS: We used two independent search strategies to identify articles relevant to women's health published between March 1, 2007 and February 29, 2008. First, we reviewed the Cochrane Database of Systematic Reviews and journal indices from the ACP Journal Club, Annals of Internal Medicine, Archives of Internal Medicine, British Medical Journal, Circulation, Diabetes, JAMA, JGIM, Journal of Women's Health, Lancet, NEJM, Obstetrics and Gynecology, and Women's Health Journal Watch. Second, we performed a MEDLINE search using the medical subject heading term "sex factors." The authors, who all have clinical and/or research experience in the area of women's health, reviewed all article titles, abstracts, and, when indicated, full publications. We excluded articles related to obstetrical aspects of women's health focusing on those relevant to general internists. We had two acceptance criteria, scientific rigor and potential to impact women's health. We also identified new and/or updated women's health guidelines released during the same time period.

RESULTS: We identified over 250 publications with potential relevance to women's health. Forty-six articles were selected for presentation as part of the Clinical Update, and nine were selected for a more detailed discussion in this paper. Evidence-based women's health guidelines are listed in Table 1.

KEY WORDS: women's health; osteoporosis; preconception counseling; HPV vaccine; obesity; cardiovascular disease

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CARDIOVASCULAR DISEASE

GUSTO V update: women experience more bleeding complications and have a higher mortality after thrombolytic treatment for myocardial infarction.

Reynolds HR, Farkouh ME, Lincoff AM, Hsu A, Swahn E, Sadowski ZP, White JA, Popol EJ, Hochman JS. Impact of female

sex on death and bleeding after fibrinolytic treatment of myocardial infarction in GUSTO V. Arch Intern Med 2007; 167: 2054–2060.

What do we know? Several studies suggest that the under-use of reperfusion therapy in women may account for higher mortality rates after myocardial infarction (MI), compared with men^{1,2}. While the GUSTO V clinical trial was not designed specifically to examine this issue, the fact that ALL participants received some type of reperfusion therapy allows for a post-hoc analysis to examine whether differences in reperfusion rates contribute to the disparity in gender-specific mortality.

What does this study add? Retrospective sex analysis was reported from GUSTO V, a clinical trial that compared two fibrinolytic regimens for acute ST-elevation myocardial infarction (MI) in over 16,000 patients at 800 hospitals in 20 countries from 1999 to 2001. The primary endpoint, all-cause mortality at 30 days, was twice as high for women compared with men (9.8 vs. 4.4%; $p < 0.001$), persisted after adjustment for differences in baseline characteristics (OR 2.00, 95% CI 1.59–2.53), and was still present at 1 year (HR 1.14, 95% CI 1.01–1.29). Women were more likely to have post-MI cardiovascular complications, including recurrent ischemia and myocardial rupture, as well as bleeding complications (25.2 vs. 14.4%; $p < 0.01$), including intracranial hemorrhage (1.2 vs. 0.4%; $p < 0.01$). Consistent with prior studies, women were referred less frequently for coronary angiography and had lower rates of percutaneous coronary intervention. This result is disturbing given the higher rates of recurrent ischemia, which should have resulted in increased utilization of percutaneous interventions.

Since all participants received thrombolytics, outcome differences may be related to differences in care provided to women and men. Prospective clinical trials powered to examine gender-specific differences in the harms and benefits of all interventions for acute myocardial ischemia are needed.

How should I change my clinical practice? Women not only present with different symptoms of MI; they have higher mortality rates, receive less frequent angiography and experience higher bleeding rates after thrombolytics than men. This study highlights the importance of examining gender differences in the harms and benefits of therapeutic interventions, but does not answer the question of what intervention is most effective for women with acute MI. Until additional gender-specific information is available, clinicians should be aware that women receiving thrombolytics are at a higher risk of bleeding than men and strive to ensure that women with acute MI have equivalent access to percutaneous interventions.

Use Amiodarone Cautiously in Women with Atrial Fibrillation.

Essebag V, Reynolds MR, Hadjis T, et al. Sex differences in the relationship between amiodarone use and the need for

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Table 1. Important Women's Health Guidelines in 2007–2008: New or Updated

Topic	Issuing organization	Updated recommendations and comments
Mammography screening in women 40–49 ¹⁷	ACP	Individualized risk assessment and informed decision making should be used to guide decisions about mammography screening in this age group. To aid in the risk assessment, a discussion of the risk factors, which if present in a woman in her 40s increases her risk to above that of an average 50-year-old woman, is provided in the guidelines. In addition, available risk prediction models, such as the NIH Web site calculator (http://www.cancer.gov/bcrisktool/) can also be used to estimate quantitative breast cancer risk. This model was updated in 2008 with race-specific data for calculating risk in African-American women. ¹⁸ The harms and benefits of mammography should be discussed and incorporated along with a woman's preferences and breast cancer risk profile into the decision on when to begin screening. If a woman decides to forgo mammography, the decision should be readdressed every 1 to 2 years.
STD screening guidelines ¹⁹	USPSTF and CDC	Routine screening for this infection is now recommended for ALL sexually active women age 24 and under, based on the recent high prevalence estimates for chlamydia. It is not recommended for women (pregnant or nonpregnant) age 25 and older, unless they are at increased risk for infection.
STD treatment guidelines ²⁰	CDC	Fluoroquinolones are NO longer recommended for treatment of N. gonorrhea, due to increasing resistance (as high as 15% of isolates in 2006). For uncomplicated infections, treatment of gonorrhea should be initiated with ceftriaxone 125 mg IM or cefixime 400 mg PO and co-treatment for chlamydia infection (unless ruled out with testing). Recent estimates demonstrate that almost 50% of persons with gonorrhea have concomitant chlamydia infection ²¹ .

STD = sexually transmitted disease, NIH = National Institutes of Health, ACP = American College of Physicians, USPSTF = United States Prevention Services Task Force, CDC = Centers for Disease Control

permanent pacing in patients with atrial fibrillation. Arch Intern Med. 2007;167:1648–1653.

What do we know? Patients with atrial fibrillation who have been converted to sinus rhythm require maintenance therapy, most effectively achieved with amiodarone^{3,4}. Prior studies suggest that women may experience a greater risk of side effects from this and other antiarrhythmic drugs, including bradyarrhythmias requiring pacemaker insertion⁵.

What does this study add? The authors evaluated the outcomes of 1,005 patients with newly diagnosed atrial fibrillation or atrial flutter enrolled in a standardized registry as part of a prospective cohort study involving 17 centers in the US and Canada. Treatment for atrial arrhythmia was determined by the local practitioner. Thirty-two patients were excluded because a pacing device was implanted prior to the study. Of the 973 participants remaining in the analysis, 40% were female, the average age was 66 years, and the mean follow-up was 2 years. The primary outcome was insertion of a new permanent pacemaker for a bradyarrhythmia. Multivariable Cox regression models that included time-dependent covariates accounting for medication exposure and adjusted for age, sex, atrial flutter, coronary artery disease, heart failure, and hypertension were developed.

Amiodarone use was associated with a two-fold risk of pacemaker insertion (HR, 2.01; 95% CI, 1.08–3.76), which was significantly higher in women than in men (HR, 4.69; 95% CI, 1.99–11.05 versus HR, 1.05; 95% CI, 0.42–2.58, P value for interaction, 0.02) and persisted after adjusting for amiodarone dose, weight, BMI, and use of other antiarrhythmic or rate control drugs. Despite prior studies demonstrating that the bradycardic effect of amiodarone is dose related, women were at increased risk for pacemaker insertion whether taking daily doses above or below 200 mg. Of the 85 patients requiring pacemaker insertion, the most common reason was bradyarrhythmia (n=60), including sick sinus syndrome and AV block. Older age and atrial flutter were found to be independent risk

factors for increased use of pacemaker insertion. There was no association between the use of sotalol or class 1 anti-arrhythmic agents and pacemaker insertion.

The authors hypothesize that the adverse effects of amiodarone are related to its long half life and to sex-specific differences in pharmacokinetics and pharmacodynamics. The main limitations are the lack of randomization and the absence of tissue and serum concentrations of amiodarone.

How should I change my clinical practice? Rate control has become the standard of care in atrial fibrillation, decreasing the need for amiodarone in current therapy. Among patients who require rhythm control (e.g., those who are cardioverted), physicians should use amiodarone cautiously in women and in elderly patients, weighing the risk of pacemaker insertion with the benefit of maintenance therapy (even at low doses).

OBESEITY

Atkins, even more than other diets, is effective with weight loss and improved BP control among pre-menopausal women followed for 1 year.

Gardner CD, Kiazand A, Alhassan S, Kim S, Stafford RS, Balise RR, Kraemer HC, King AC. Comparison of the Atkins, Zone, Ornish, and LEARN diets for change in weight and related factors among overweight premenopausal women. The A TO Z Weight Loss Study: a randomized trial. JAMA 2007; 297: 969–977.

What do we know? Limited evidence exists about the efficacy of different dietary programs.

What does this study add? Three popular diets were compared with a diet developed based on national guidelines in a randomized clinical trial to determine their effectiveness on weight loss and metabolic parameters (e.g., lipid profile, glucose levels). The Atkins diet (very low carbohydrate, high protein, high fat), the Zone (low in carbohydrates), and Ornish

(very high in carbohydrates) were compared with the LEARN diet (lifestyle, exercise, attitudes, relationships and nutrition: low in fat, high in carbohydrates). Subjects included 311 pre-menopausal women aged 25 to 50 years old with a body mass index of 27 to 40 (overweight to obese), whose weight and medications had been stable for the previous 2 to 3 months. Exclusion criteria included women with diabetes or medication use for cardiovascular risk factors. Participants were randomized, received a book and 8 weekly 1-h educational classes about the program they were enrolled in, along with \$25 to \$75 financial incentives for participation. Serial assessments were performed at baseline, 2, 6, and 12 months and included a 3-day dietary recall, measurements of height, weight, resting blood pressure, and metabolic laboratory tests. The primary outcome was weight loss at 12 months.

Class participation, defined as at least 75% class attendance, was 85–89%. Overall, retention rates were 76–88% with no significant differences between treatment programs. Total dietary intake decreased in all the diet treatment programs. Participants lost 2–5 kg of body weight over 12 months. Those who used Atkins lost more weight at 2, 6, and 12 months than Ornish, LEARN, or Zone participants (Fig. 1). The Atkins diet also more effectively elevated HDL and lowered blood pressure and triglycerides.

How should I change my clinical practice? Impressive data were released this year demonstrating the benefits of bariatric surgery on sustained weight loss and mortality⁶. This dietary study demonstrates that non-invasive options can also achieve significant weight loss and other positive metabolic effects. The challenge remains for patients to commit to the process of change.

Figure 1. Weight change relative to baseline. Legend: Baseline values were carried forward for any missing values. The overall diet group $\times$ time interaction was significant ($P < 0.001$). The analysis of variance test for differences among diet groups in weight change from baseline was significant at 2 and 6 months ($P < 0.001$) and at 12 months ($P = 0.01$). Analyses of all pairwise differences by the Tukey standardized range test (< 0.05) indicate that the Atkins diet group was significantly different than all other diet groups at 2 and 6 months and that the Atkins diet group was significantly different than the Zone diet group at 12 months. There were no significant differences among the Zone, LEARN, or Ornish diet groups at any time point. Error bars indicate standard error of the mean. Source: Gardner CD, Kiazand A, Alhassan S. Comparison of Atkins, Zone, Ornish, and LEARN Diets for Change in Weight and Related Risk Factors Among Overweight Premenopausal Women. *JAMA*. 2007; 297: 969–77. Permission for reproduction granted.

OSTEOPOROSIS

Low BMD and Vertebral Fractures Predict New Vertebral Fractures Within 15 Years.

Cauley JA, Hochberg MC, Lui L. Long-term Risk of Incident Vertebral Fractures. *JAMA* 2007;298:2761–2767.

What do we know? Approximately 30–50% of women develop vertebral fractures⁷, which are associated with a decrease in survival and predict future osteoporotic fractures^{8–10}. Whether this future fracture risk is independent of BMD and whether the risk persists over 5 years is unclear.

What does this study add? This study examined the absolute risk of subsequent vertebral fracture as predicted by BMD and prevalent vertebral fracture. Investigators used a sub-group from the Study of Osteoporotic Fractures (SOF), a longitudinal cohort study, involving 9,704 women, aged > 65 years. Baseline BMD and vertebral X-ray films were performed on 2,680 white women who completed a 15-year follow-up visit. Incident vertebral fractures were defined as a decrease of 20% or more and at least 4 mm in length in any of the vertebral height measurements.

Eighteen percent of women (487/2,680) had an incident vertebral fracture. Rates of incident vertebral fractures were 41.4% and 14.2% among women with and without a prevalent vertebral fracture at baseline, respectively (OR, 4.21, 95% CI 3.33–5.34). This increase was independent of BMD and other risk factors. Low BMD at every site was also independently associated with increased risk. Together, low BMD and prevalent vertebral fracture were associated with a high risk for incident vertebral fracture. The absolute risk of vertebral fracture ranged from 56% among women who had both a total hip BMD T score of -2.5 or less and a prevalent vertebral fracture, to 9% for women with normal BMD and no prevalent fracture.

This study is limited by: (1) it only included white women, and (2) women who returned for a follow-up visit at 15 years were much healthier at baseline than those who did not, leading to a potential underestimation of the risk for vertebral fracture.

How should I change my clinical practice? Vertebral fractures are strong predictors of future fracture risk, independent of BMD, and should be incorporated into risk models.

Any fracture in older women should raise suspicion for osteoporosis.

Mackey DC, Lui L, Cawthon PM, et al. High-trauma fractures and low bone mineral density in older women and men. *JAMA* 2007;298:2381–2388.

What do we know? Low trauma fractures and falls from standing height or less are categorized as osteoporotic because they are related to low bone mineral density (BMD) and future fracture risk¹¹. High trauma fractures (e.g., those resulting from motor vehicle crashes and falls from greater than standing height) may have a similar correlation to BMD and future fracture risk^{12,13} and deserve further study.

What does this study add? This study used data from two cohorts, 8,022 women (Study of Osteoporotic Fractures, SOF, 1988–2006) followed for an average of 9.1 years and 5,995 men (Osteoporotic Fractures in Men Study Group, MrOS, 2000–2007) followed for an average of 5.1 years. The participants were community-dwelling adults throughout the US aged 65 years or older. Hip and spine BMD were assessed by dual-energy X-ray absorptiometry. Participants were contacted

every 4 months to determine if (and how) they had sustained a fracture. Fractures were assessed as low or high trauma, without knowledge of BMD. Multivariate Cox hazards regression models were adjusted for age, height, weight, one or more medical conditions, smoking history, fractures since age 50, fall in the past year, use of hormone replacement therapy, and functional status.

Forty percent of women in the SOF ($n=3,211$) sustained low trauma fractures and 3% ($n=264$) high trauma fractures. Each 1-standard deviation reduction in total hip BMD correlated with increased risk of both low (RH, 1.49; 95% CI, 1.42–1.57) and high trauma fracture (RH, 1.45; 95% CI, 1.42–1.57). This relationship held for men as well. Women with high-trauma fracture had lower body weight, lower body mass index, and were more likely to report a fracture since age 50 years and a fall in the previous year, compared to those without fractures. The subsequent fracture risk was similar between high and low trauma fracture (high: 34% 95% CI, 7%–67% vs. low: 31%, 95% CI, 20–43%) in women.

The main limitations of this study are that fractures were self-reported, vertebral fractures were not included, and there was no information about bisphosphonate use. In addition, subjects were older, predominantly Caucasian and healthy volunteers, limiting the applicability of these findings to a younger and more general population.

How should I change my clinical practice? A thorough evaluation for underlying osteoporosis and efforts to reduce future fractures should be offered to all older patients regardless of gender and type of non-spine fracture.

CANCER RISK AND PREVENTION

Limit CT scan use in younger patients and women to reduce future cancer risks.

Einstein AJ, Henzlova MJ, Rajagopalan S. Estimating risk of cancer associated with radiation exposure from 64-slice computed tomography coronary angiography. *JAMA* 2007;298(3): 317–23.

What do we know? Very little is known about the risk of cancer from computed tomography (CT), despite higher doses of radiation from CT scans and increased use. The largest increases in CT use are seen in pediatric populations and adult screening¹⁴.

What does this study add? This study estimated the organ-specific and whole body lifetime attributable risks (LAR) of cancer associated with radiation exposure from a computed tomography coronary angiography (CTCA) study. The influence of age, sex, and scan protocol on cancer risk was also assessed. The investigators used current data available on the health risks from radiation, obtained from the National Academies' Biological Effects of Ionizing Radiation (BEIR) VII Phase 2 report. This report, presented to Congress in 2005, contains risk estimates for cancer from low level exposure to ionizing radiation and is based on data from epidemiological models, atomic bomb survivor studies, and medical and occupational radiation studies.

This study demonstrated that LARs of cancer were increased and associated with: female gender, younger age, and scan/tube protocol. The risk of cancer was higher among women in all age groups (Fig. 2), particularly for women exposed in their 20s (LAR: 1 in 143 for women versus 1 in 686 for men). This risk declined with age (1 in 1,338 for an 80-year-old woman). The major differences between women and men were (1) increased radiosensitivity among women and (2) the cancer risk attributable to exposure of the breast in the field of irradiation. Combined protocols with extended fields (e.g., through the aortic arch), such as the common "triple rule-out" scan, which evaluates for CAD, aortic dissection, and pulmonary embolism, were associated with increased risk of cancer. Tube current reduction lowered risk.

How should I change my clinical practice? Until empirical data become available, use CT scans cautiously, especially in young women. Consider alternative diagnostic modalities, such as MRI and ultrasound.

Use HPV vaccine early and continue to screen regularly with conventional pap smears.

The Future II Study Group. Effect of prophylactic human papillomavirus L1 virus like particle vaccine on risk of cervical intraepithelial neoplasia grade, grade 3, and adenocarcinoma in situ: a combined analysis of four randomized clinical trials. *Lancet* 2007;369:1861–8.

What do we know? Cervical cancer is common¹⁵ and potentially preventable since the etiology of 100% of cervical cancer and its obligate precursors appears to be due to infection with the HPV virus. Vaccines directed against two of the most common oncogenic strains (HPV 16 and HPV 18

Figure 2. Organ contributions to lifetime attributable risk of cancer incidence from a single standard computed tomography coronary angiography (CTCA) scan. Source for Figure 2: Einstein AJ, Henzlova MJ, Rajagopalan S. Estimating Risk of Cancer Associated with Radiation Exposure From 64-Slice Computed Tomography Coronary Angiography. *JAMA*. 2007; 298: 317–23. Permission for reproduction granted.

serotypes) have been developed, but there are limited data as to their efficacy in preventing cervical cancer.

What does this study add? This is an analysis of initial data from the first four large randomized controlled trials examining the effect of a prophylactic quadrivalent HPV 6/11/16/18 vaccine on the incidence of HPV-related cervical lesions. The four trials included over 20,000 women aged 16–26, from the Americas, Europe and Asia-Pacific. Vaccine or placebo was administered at day 1 and at months 2 and 6, and the mean follow-up was 3 years after the first dose. At enrollment, women underwent serum sampling for antibodies to HPV 6/11/16/18, and a pelvic exam was performed with cervicovaginal specimens collected for Pap testing and HPV DNA testing. The trials did not exclude women with serological evidence of prior or ongoing HPV infection. Periodic Pap tests and HPV testing were performed at 6–12-month intervals throughout the study. The primary endpoint was the combined incidence of HPV 16/18 related cervical intraepithelial neoplasia (CIN) 2/3, adenocarcinoma in situ, or cervical cancer.

These studies demonstrated that HPV vaccination is effective (99%, 95% CI 93–100) at decreasing HPV 16/18-related high-grade CIN and carcinoma in situ among HPV naïve individuals. Importantly, the vaccine was less effective (44%) among those already exposed to the HPV strains, suggesting that vaccination should be given to women younger than 16. In addition, the vaccine had little effectiveness (18%, 95% CI 7–29) in decreasing the rate of cervical disease resulting from any HPV type. These results suggest that a significant burden of pre-malignant disease may be caused by other HPV strains and highlights the importance of continued screening with Pap smears in vaccinated women.

Limitations include the fact that cervical dysplasia, rather than cervical cancer, was used as an efficacy endpoint and the lack of data on the duration of vaccine effectiveness.

How should I change my clinical practice? Vaccination should optimally be administered before HPV exposure from sexual activity, and providers should continue regular cervical cancer screening for vaccinated patients. However, longer term data are needed before widespread vaccination programs are recommended.

PRECONCEPTION COUNSELING

SSRI use in pregnancy safe overall, with the exception of a few individual SSRIs that confer increased risk for some rare defects.

Louik C, Lin AE, Werler MM, Hernandez-Diaz S, Mitchell AA. First-Trimester Use of Selective Serotonin-Reuptake Inhibitors and the Risk of Birth Defects. *NEJM*. 2007;356:2675–83.

What do we know? Up to 10% of women experience depression during pregnancy¹⁶. Selective serotonin-reuptake inhibitors (SSRIs) have been increasingly used in pregnant women. Recently, some SSRIs have been implicated in the development of birth defects.

What does this study add? This study assessed the association between a woman's first-trimester use of SSRIs and the risk of birth defects. The authors used retrospective data from the Sloan Epidemiology Center Birth Defects Study, which identifies infants with a wide range of malformations in five study centers. Mothers of these infants who agreed to participate comprised the study group. A control group was

obtained from mothers of non-malformed infants from study centers and within a random population sample from Massachusetts. Approximately 60% of women in both groups participated, and surveys were administered within 6 months of delivery to assess self report of specific SSRI use. Exposure was defined as the use of any SSRI from 28 days before the last menstrual period through 112 days after the last menstrual period.

A total of 9,849 infants with malformations and 5,860 control infants were included. There was no significant increase in the risk of craniosynostosis or omphalocele associated with SSRIs as a group or individually. There was no significant increase in the overall risk of congenital heart defects with SSRIs, but there were associations between specific heart defects and specific SSRIs. Sertraline increased the risk of septal defects (OR 2.0; 95% CI 1.2–4.0), and paroxetine increased the risk of right ventricular outflow tract obstruction (OR 3.3; 95% CI 1.3–8.8). In exploratory analyses, several other significant associations between specific SSRI use and birth defects were identified: sertraline with anal atresia and limb-reduction defects, and paroxetine with neural-tube defects and clubfoot.

As the authors note, these findings should be interpreted with caution. Multiple comparisons were performed, increasing the likelihood of chance associations, and, despite the large size of the study, congenital malformations are so rare it is hard to distinguish true risk from random variation.

How should I change clinical practice? This study suggests that many SSRIs are safe to use in the first trimester of pregnancy, but that specific SSRIs may increase the risk of specific birth defects and should be avoided. However, it must be kept in mind that the occurrence of these defects is so rare that the absolute increase in risk is small.

Women of childbearing age frequently fill prescriptions for potentially teratogenic medications without documentation of contraceptive counseling.

Schwarz DB, Postlethwaite DA, Hung Y, Armstrong MA. Documentation of Contraception and Pregnancy When Prescribing Potentially Teratogenic Medications for Reproductive-Age Women. *Ann Int Med*. 2007; 147: 370–376.

What do we know? Very little is known about how often contraception or contraception counseling is provided to women of reproductive age when prescribed potentially teratogenic medication.

What does this study add? This study was designed to assess pregnancy rates and the frequency of contraceptive counseling documented for women of reproductive age who filled prescriptions for class D or X drugs. The authors conducted a retrospective cohort study of 488,175 women between the ages of 15–44 years of age who had continuous pharmacy and member benefits from Kaiser Permanente Northern California during 2001. They abstracted data from the Pharmacy Information Data Management System related to Class A, B, D, X, and contraceptive medications filled. Information on insertion of IUDs, placement of a contraceptive implant, diaphragm, or cervical cap fitting, and sterilization were abstracted from the Outpatient Services Clinical Record System. In addition to documentation of use of any of these methods of contraception, women were considered to have received contraceptive counseling if there was documentation of contraceptive counseling, oral contraceptive management, or family planning counseling. Data on pregnancy tests

performed within 3 months of a woman filling a prescription for the classes of drugs studied were also abstracted from the Kaiser database.

A class D or X medication was prescribed for 1 in 6 women of reproductive age, 48% by internists and family practitioners. Almost half had no contraceptive method dispensed, had not been sterilized, and had no documentation of contraceptive counseling in the 2 years before filling one of these prescriptions. This rate was not higher than among women prescribed class A or B prescriptions. Statin prescriptions were the least likely to have documentation of contraceptive use, sterilization, or counseling. Women who filled class D or X prescriptions were only slightly less likely than women who filled a class A or B prescription to have a positive pregnancy test (1.0% vs. 1.4% of prescriptions).

How should I change clinical practice? Physicians should be aware of the teratogenic risk class of drugs they prescribe and provide contraception or counseling on pregnancy prevention to reproductive-age women taking these medications.

Conflict of Interest: None disclosed.

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REFERENCES

1. **Barron HV, Bowlby LJ, Breen T, et al.** Use of reperfusion therapy for acute myocardial infarction in the United States: data from the National Registry of Myocardial Infarction 2. *Circulation*. 1998; 97(12): 1150–56.
2. **Maynard C, Litwin PE, Martin JS, Weaver WD.** Gender differences in the treatment and outcome of acute myocardial infarction: results from the Myocardial Infarction Triage and Intervention Registry. *Arch Intern Med*. 1992; 152(5): 972–76.
3. **Letelier LM, Udol K, Ena J, Weaver B, Guyatt GH.** Effectiveness of amiodarone for conversion of atrial fibrillation to sinus rhythm: a meta-analysis. *Arch Intern Med*. 2003; 163(7): 777–85.
4. **Vorperian VR, Havighurst TC, Miller S, January CT.** Adverse effects of low dose amiodarone: a meta-analysis. *J Am Coll Cardiol*. 1997; 30(3): 791–98.
5. **Essebag V, Hadjis T, Platt RW, Pilote L.** Amiodarone and the risk of bradyarrhythmia requiring permanent pacemaker in elderly patients with atrial fibrillation and prior myocardial infarction. *J Am Coll Cardiol*. 2003; 41(2): 249–54.
6. **Sjöström L, Narbro K, Sjöström D, et al.** Effects of bariatric surgery on mortality in Swedish obese subjects. *N Engl J Med*. 2007; 357(7): 741–52.
7. **Melton LJ III, Kan SH, Freye MA, Wahner HW, O'Fallon WM, Riggs BL.** Epidemiology of vertebral fractures in women. *Am J Epidemiol*. 1989; 129(5): 1000–11.
8. **Hasserius R, Karlsson MK, Nilsson BE, et al.** Prevalent vertebral deformities predict increased mortality and increased fracture rate in both men and women: a 10-year population-based study of 598 individuals from the Swedish cohort in the European Vertebral Osteoporosis Study. *Osteoporosis Int*. 2003; 14(1): 61–68.
9. **Kado DM, Duong T, Stone KL, et al.** Incident vertebral fractures and mortality in older women: a prospective study. *Osteoporosis Int*. 2003; 14(7): 589–94.
10. **Lindsay R, Pack S, Li Z.** Longitudinal progression of fracture prevalence through a population of postmenopausal women with osteoporosis. *Osteoporosis Int*. 2005; 16(3): 306–12.
11. **Melton LJ III, Thamer M, Ray NF, et al.** Fractures attributable to osteoporosis: report from the National Osteoporosis foundation. *J Bone Miner Res*. 1997; 12(1): 16–23.
12. **Sanders KM, Pasco JA, Ugoni AM, et al.** The exclusion of high trauma fractures may underestimate the prevalence of bone fragility fractures in the community: the Geelong Osteoporosis Study. *J Bone Miner Res*. 1998; 13(8): 1337–42.
13. **Karlsson MK, Hasserius R, Obrant KJ.** Individuals who sustain nonosteoporotic fractures continue to also sustain fragility fractures. *Calcif Tissue Int*. 1993; 53(4): 229–31.
14. **Brenner DJ, Hall EJ.** Computed tomography—an increasing source of radiation exposure. *New Engl J Med*. 2007; 357(22): 2277–84.
15. **Ferlay J, Bray F, Pisani P, Parkin DM.** GLOBOCAN 2002: cancer incidence, mortality and prevalence worldwide. IARC CancerBase No.5, version 2.0. Lyon, France: IARC Press 2004. <http://www-dep.iarc.fr/>. Accessed January 13, 2009.
16. **Bennett HA, Einarson A, Taddio A, Koren G, Einarson TR.** Prevalence of depression during pregnancy: systematic review. *Obstet Gynecol*. 2004; 103(4): 698–709.
17. **Gaseem A, Snow V, Sherif K, Aronson M, Weiss KB, Owens DK.** Screening mammography for women 40 to 49 years of age: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2007; 146(5): 511–15.
18. **Gail MH, Constantino JP, Pee D, et al.** Projecting individualized absolute invasive breast cancer risk in African American women. *J Natl Cancer Inst*. 2007; 99(2): 1782–92.
19. **U.S. Preventive Services Task Force.** Screening for Chlamydial Infection: US Preventive Services Task Force Recommendation Statement. *Ann Intern Med*. 2007; 147(2): 128–34.
20. **Centers for Disease Control and Prevention.** Update to CDC's Sexually Transmitted Diseases Treatment Guidelines, 2006: Fluoroquinolones No Longer Recommended for Treatment of Gonococcal Infections. *MMWR Morb Mortal Wkly Rep*. 2007; 56(33): 332–36.
21. **Datta SD, Sternberg M, Johnson RE, et al.** Gonorrhea and chlamydia in the United States among persons 14 to 39 years of Age, 1999 to 2002. *Ann Intern Med*. 2007; 147(2): 89–96.