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INSIDE

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Effect of Dabigatran on Referrals to and Switching from Warfarin

ABSTRACT & COMMENTARY

By Harold L. Karpman, MD, FACC, FACP

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

Synopsis: *The frequency of initial prescriptions of dabigatran for stroke prevention in atrial fibrillation and the frequency of transition from warfarin to dabigatran both proved to be less than anticipated.*

Source: Atay JK, et al. Effect of dabigatran on referrals to and switching from warfarin in two academic anticoagulation management services. *Am J Cardiol* 2013;112:387-389.

DABIGATRAN HAS BEEN DEMONSTRATED TO DECREASE THE RATE OF STROKE and systemic embolism in patients with nonvalvular atrial fibrillation (AF) by one-third, while also decreasing the rate of intracranial bleeding by two-thirds compared with warfarin.[1] It is prescribed in a fixed dose (75-150 mg twice daily), is the first of several newer oral anticoagulants that may be administered without requiring laboratory coagulation monitoring, and has minimal drug-food and drug-drug interactions.[2] On the basis of the ease of administration, equal or superior efficacy, and improved safety with respect to intracranial hemorrhage, it was anticipated that this new drug would replace warfarin for many patients.[3]

Atay and colleagues followed patients referred to two anticoagulation management services for stroke prevention in nonvalvular AF to determine how the rate of referral for warfarin management would be affected and how many existing patients would be switched from warfarin to dabigatran.[4] The anticoagulation management service at Brigham and Women's Hospital in Boston, Massachusetts (service 1) followed 1225 patients and a similar facility at the University of Michigan in Ann Arbor, Michigan (service 2) followed 1137 patients with nonvalvular AF. Only 81 patients (6.6%) from service 1 and 44 patients

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(3.9%) from service 2 switched from warfarin to dabigatran. The frequency of initial prescription of dabigatran for stroke prevention in AF as well as the frequency of transition from warfarin to dabigatran proved to be less than was expected.

■ COMMENTARY

The results of the data assembled by Atay et al should be carefully considered, but the limitations of the study are significant. It must be recognized that the patients did not come from office-based or community-based practices, but instead were referred from within university or teaching hospital environments, the period of observation was quite short, and the volume of patients was relatively small. The study focused only on dabigatran and did not include any of the other new anticoagulants such as rivaroxaban. Finally, the many reasons for slow adoption and cautious prescription of novel anticoagulants must be recognized. For example, the observed comparitive benefits of the newer anticoagulant agents would diminish when warfarin was well-managed.[5] Also, there are concerns regarding the lack of specific reversal agents for the newer anticoagulants. Concerns also initially existed regarding an increase in cerebral bleeding episodes when taking the newer agents compared with what would be expected with warfarin, although the FDA recently indicated that bleeding rates associated with dabigatran did not appear to be higher than the bleeding rates associated with warfarin use.[5] Furthermore, since medication adherence rates for patients with chronic disease states are extremely low,[7] in the range of 43-78%, and without the regular prothrombin time management needed for patients on warfarin therapy, physicians have no way of assessing whether the patients are really taking the newer anticoagulants as prescribed. Finally, it should be recognized that dabigatran has a much shorter half-life than warfarin and, therefore, a missed dose of the newer agents will leave the patient unprotected from stroke risk.

Obviously, it's much more convenient for AF patients to use one of the newer anticoagulant agents. However, for the many reasons outlined above, patients should be carefully selected and fully informed on how important it is for them to take their medications regularly as prescribed. As more data become available from the use of these novel agents in office-based patients from the several large observational studies that are now in progress, it is very likely that warfarin use will decrease, despite the limitations of the newer anticoagulant agents outlined above and the increased cost of these newer agents which, incidentally, will probably diminish as more of them become available. ■

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Omega 3s and the Prostate: Good or Bad?

ABSTRACT & COMMENTARY

By Luke Fortney, MD

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Dr. Fortney reports no financial relationships relevant to this field of study. This article originally appeared in the August 2013 issue of Integrative Medicine Alert.

Synopsis: *Among men diagnosed with prostate cancer, those with the highest levels of plasma omega-3 fatty acids demonstrated an increased risk for developing prostate cancer, bringing into question various recommendations for increased omega-3 intake.*

Source: Brasky TM, et al. Plasma phospholipid fatty acids and prostate cancer risk in the SELECT trial. *J Natl Cancer Inst* 2013;105:1132-1141.

THE ROLE OF OMEGA-3 FATTY ACIDS IN PROSTATE CANCER risk has been inconsistent and it has been difficult to draw practical and clinically useful conclusions from the research. Previous studies have shown an association with lower prostate-specific antigen (PSA) values and increased intake of omega-3s, to increased prostate cancer incidence in others. The case-cohort study by Brasky et al — a subanalysis of the larger SELECT trial (Selenium and Vitamin E Cancer Prevention Trial) — supports those previous reports that suggest a concern about increased prostate cancer risk and omega-3 fatty acids. In this recent study, researchers evaluated data from 834 men who eventually were diagnosed with prostate cancer, 156 of whom were found to have high-grade cancers. Compared to 1393 age- and race-matched controls, men with the highest levels of plasma omega-3 fatty acids demonstrated an increased risk in developing both low- and high-grade prostate cancers. Using proportional hazards models, the researchers estimated that omega-3s were associated with a 43% increased risk for prostate cancer overall and a 71% increase in aggressive prostate cancer (hazard ratio, 1.43 and 1.71, respectively). However, overall relative risk is small. Given the consistency of these results, the authors concluded that omega-3 fatty acids, in contrast to conventional wisdom, may be associated with prostate tumorigenesis.

■ COMMENTARY

This study has significant limitations. First, these data do not demonstrate a cause and effect relationship between fish oil intake and prostate cancer incidence or severity. Second, because the data were extracted retroactively from a larger, retrospective, case-control study that was not designed to determine if fish oil intake is implicated as either a benefit or risk in prostate cancer risk, controls for other potential factors that may influence risk are lacking. For example, the researchers did not assess any of the participants' dietary intake of omega-3s over time. Other important prostate cancer risk variables — such as smoking status, alcohol use, family history of prostate cancer, and obesity — were not adequately controlled in this study. Additionally, these results are based on only one measure of plasma omega-3 levels taken at one particular moment in time, which can be variable depending on a person's recent dietary habits and other behaviors. A better indicator of long-term omega-3 intake and tissue status is the "omega-3 index," which measures red blood cell levels of eicosapentaenoic acid (EPA) and docosapentaenoic acid (DHA). Although the data presented in this study hint at DHA possibly playing more of a role in prostate cancer risk compared to EPA, this distinction is not clear or definitive.

The story of prostate cancer is a messy one at best. While prostate cancer is the leading diagnosed cancer in men and second leading cause of cancer-related death among men in the United States, only 2.8% of men ultimately die from complications directly related to prostate cancer itself. The lifetime risk for being diagnosed with prostate cancer is 15.9%, while 70% of deaths due to prostate cancer occur after 75 years of age. Even though the majority of men will eventually harbor prostate cancer cells if they live long enough, detection typically will either be elusive with screening or result in morbidity from invasive testing and treatment. This being said, it is still challenging to determine exactly which prostate cancers will go on to be aggressive and life-threatening and which are slow-growing and benign.[1]

Detection is further complicated by the fact that PSA screening is incomplete at best. In its most recent update, the United States Preventative Services Task Force simply recommends against PSA-based screening for prostate cancer (D recommendation). This evaluation is based largely on the fact that approximately 80% of positive PSA tests are actually false-positives. A third of men who eventually undergo prostate biopsy testing report major problems later. Five out of 1000 men will go on to die within 1 month of prostate cancer surgery, while up to three of 10 will experience significant morbidity such as urinary incontinence, bowel dysfunction, persistent pain, and erectile dysfunction. As such, there is convincing evidence that PSA screening leads to significant overdiagnosis and resulting treatment complications.[1]

With this being said, many men and their physicians look toward prevention to avoid this dilemma altogether. Pros-

tate cancer risk is affected variably by age, race, dietary factors, weight, and chronic diseases such as diabetes, obesity, and cardiovascular disease. In general, prostate cancer mortality is significantly lower among Japanese men, but this cultural protection is lost among Japanese men who migrate to the United States and adapt Western habits, including a standard American diet (SAD). For comparison, this effect is also seen in Polish immigrants.[2]

It is easy to see why so much emphasis has been directed toward environmental factors in prostate cancer risk. As such, it has long been supposed that the fatty acid content of varying diets plays a significant role in prostate tumorigenesis. For example, the omega-6 to omega-3 fatty acid ratio of the SAD is 15:1, as opposed to 4:1 in a traditional Japanese diet. It has been proposed that omega-3s slow down tumorigenesis, induce apoptosis, decline proliferation, diminish PSA doubling time, and inhibit androgen-sensitive proliferation of prostate cancer cells as possible mechanisms. Recent studies have even demonstrated that omega-3s were able to prevent progression of laboratory human prostate cancer cell lines, while omega-6s accelerated their growth.[3] Another study went further in showing that a diet rich in omega-3s in mice slowed down prostate tumorigenesis.[4] In a well-done, randomized, controlled study published in 2013 by Safarinejad et al, the case for omega-3s' role in decreasing prostate cancer risk went even further in showing that supplementation with omega-3s actually decreased PSA levels among healthy men. In addition, PSA levels increased significantly over 12 weeks among participants who were given omega-6 fatty acid supplements.[5]

Because lifestyle changes, especially dietary factors, appear to significantly affect the risk for developing prostate cancer, clinicians and patients are in need of guidelines and evidence-based recommendations that may favorably improve their chances. The omega-3 narrative in prostate cancer prevention appeared to be gaining momentum until Brasky et al released their findings showing that omega-3s may actually accelerate prostate cancer among men who have already been diagnosed. If we accept the authors' conclusions, the omega-3 fatty acid and prostate cancer story appears to share similarities with the vitamins and lifestyle (VITAL) study from 2008, which reported higher incidence of lung cancer among smokers who supplemented with vitamin E.[6] In both instances, the trail of evidence appeared to be going in one direction, when the narrative took an abrupt turn among a certain demographic. It has been proposed that high-dose omega-3 supplementation — similar to vitamin E supplementation in smokers — may actually increase oxidative stress, resulting in further DNA damage and thereby increasing the risk for prostate cancer. This mechanism also may be at work in people who have several cardiovascular risk factors, as seen in a recent study in the *New England Journal of Medicine* that showed no improvement in morbidity or mortality when supplemented with 1 g of omega-3 fatty acids daily.[7]

In general, while the evidence overall supports the health and safety claims of omega-3s — particularly through eating a healthful diet[8] — patients diagnosed with prostate cancer or those at high risk for prostate cancer would be well-advised to use some caution with supplementation of high doses of omega-3s in the context of obesity, smoking, or eating a SAD. Nonetheless, the mystery of what lifestyle factors, in what patients, and how various dietary components contribute to prostate cancer continues. For example, one study showed that Yup'ik Eskimos in Alaska, who eat a traditional diet that includes consumption of up to 20 times more omega-3 fatty acids compared to people living in the lower 48 states, have lower rates of diabetes and obesity.[9] In another study of Inuit communities in Canada, where smoking rates are higher than other Canadian region, no increase of prostate cancer incidence was reported.[10] Finally, a similarly designed cohort study found that in a setting of very high fish consumption, no association was found with early or midlife prostate cancer risk, while salted or smoked fish may increase the risk of advanced prostate cancer.[11]

Bottom Lines

1) In this study, among men who are eventually diagnosed with prostate cancer, those with the highest short-term and isolated plasma omega-3 fatty acids levels also appeared to have increased risk of developing both low- and high-grade prostate cancers.

2) There are many significant methodological concerns limiting the clinical relevance of the study results.

3) Although there is continuing discrepancy in the medical literature, overall recommendations for patients will largely remain unchanged. For prostate cancer mortality prevention, clinicians are advised to continue encouraging patients adhere to a healthy lifestyle, which means eating a variety of healthy whole foods (including foods high in omega-3 fatty acids such as salmon up to twice a week),[12] getting regular exercise, keeping body mass index < 30, and avoiding tobacco.[13] ■

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Azithromycin — The Heart of the Matter Redux: Pre-existing Risks Tell the Tale

ABSTRACT & COMMENTARY

By Stan Deresinski, MD, FACP, FIDSA

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Dr. Deresinski does research for the National Institutes of Health and is an advisory board member and consultant for Merck. This article originally appeared in the July 2013 issue of Infectious Disease Alert.

Source: Svanström H, et al. Use of azithromycin and death from cardiovascular causes. *N Engl J Med* 2013;368:1704-1712.

Svanström and colleagues in Copenhagen examined the risk of cardiovascular deaths in association with azithromycin use in a nationwide historical cohort study of Danish adults aged 18-64 years. They compared 1,102,050 episodes of azithromycin use with the same number of episodes of no use of antibiotic agents with 1:1 matching using propensity scoring. The risk of cardiovascular mortality with current use of the azalide (but not with past or future use) was increased (rate ratio, 2.85; 95% CI, 1.13-7.24). There was, however, no excess cardiovascular mortality with current azithromycin use when compared to current use of penicillin V with crude rates of 1.1 and 1.5 per 1000 person years, respectively, and when adjusted, a rate ratio of 0.93 (95% CI, 0.56-1.55). Thus, the investigators concluded that "Azithromycin use was not associated with an increased risk of death from cardiovascular causes in a general population of young and middle-aged adults."

■ COMMENTARY

The FDA recently updated the azithromycin prescribing information to state: "Health care professionals should consider the risk of fatal heart rhythms with azithromycin when considering treatment options for patients who are already at risk for cardiovascular events. FDA notes that the potential risk of QT prolongation with azithromycin should be placed in appropriate context when choosing an antibacterial drug: Alternative drugs in the macrolide class, or non-macrolides such as the fluoroquinolones, also have the potential for QT prolongation or other significant side effects that should be considered when choosing an antibacterial drug."[1]

This statement was based, in part, on extensive analysis of data by Ray and colleagues,[2] which has been previously discussed in *Infectious Disease Alert*.[3] Those investigators retrospectively examined the risk of cardiovascular death among patients 30-74 years of age enrolled in the Tennessee Medicaid program and who had been prescribed azithromycin between 1992 and 2006. Compared to "no antibiotic" controls, the hazard ratio for cardiovascular death during 5 days of prescribed azithromycin therapy was 2.88 (95% confidence interval [CI], 1.79-4.63; $P < 0.001$) and that of death from any cause was 1.85 (95% CI, 1.25-2.75; $P = 0.002$). In contrast to the findings of the Danish investigators in a comparison with penicillin V use, Ray et al found that azithromycin therapy was also associated with an increased hazard ratio for both cardiovascular and total deaths when compared to amoxicillin therapy, which itself had no increased hazard relative to "no antibiotic" controls. Relative to amoxicillin, azithromycin was associated with an estimated 47 added cardio-

vascular deaths per 1 million prescriptions. The degree of hazard was, however, strongly associated with the presence of pre-existing cardiac risk factors.

It is likely to be the prevalence of such pre-existing conditions that distinguishes the patient populations in the two studies, with the Danes apparently being the healthier group. This is consistent with the observation that the cardiovascular mortality in azithromycin recipients was 85.2 deaths per million courses in Tennessee and only 15.4 per million courses in Denmark, suggesting significant differences in baseline risk.

Another potential confounding factor could be differences in the genetic makeup of the populations studied. Analysis of DNA from 44 victims of sudden cardiac death in Denmark from 2000-2006 who were < 35 years of age found that only 11% had one of the three major long-QT syndrome mutations associated with increased risk of sudden cardiac death.[4] This contrasts with reports of rates of approximately 20% found in New Zealand and at the Mayo Clinic in Minnesota. The population of Denmark is much more homogenous than that of the United States and the prevalence of genetic polymorphisms that put individuals at risk of death due to cardiac arrhythmias may differ.

There may, however, be additional poorly understood factors that could confound our understanding of this problem. As pointed out by Molsholder and colleagues in a commentary accompanying the article by Svanström et al, a recent Canadian study found lower 30-day mortality in outpatients with community-acquired pneumonia (CAP) who were treated with azithromycin than in those treated with a fluoroquinolone.[5] Also pointed out is a recent meta-analysis of inpatients with CAP in which those receiving a macrolide had significantly lower mortality than in those receiving non-macrolides. Azithromycin is now widely used in trachoma control and eradication programs, which could be disrupted by unequivocal evidence of associated increased risk of cardiovascular deaths. A recent report, however, found no difference in mortality between individuals aged at least 30 years or those 10-29 years of age who received azithromycin and those who did not in an eradication program in Ethiopia.[6] In fact, those who received azithromycin had a lower risk of mortality than did members of the same household who never received the drug.

Approximately one-eighth of the U.S. population — 40.3 million people — received an outpatient prescription for azithromycin in 2011. Thus, resolving the issue of the potential increase in cardiovascular deaths with azithromycin use is no trivial matter. The most reasonable analysis of the data available to date is that azithromycin may be associated with increased risk of cardiovascular death in individuals with pre-existing risk factors, such as cardiac disease or coadministration of drugs that prolong cardiac repolarization. ■

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Pharmacology Update

Brimonidine Tartrate Topical Gel (Mirvaso®)

By William T. Elliott, MD, FACP, and James Chan, PharmD, PhD

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Drs. Elliott and Chan report no financial relationships relevant to this field of study.

A HIGHLY SELECTIVE ALPHA-2 ADRENERGIC RECEPTOR AGONIST has been approved by the FDA for the treatment of persistent facial erythema of rosacea in adults. Brimonidine has been used as an ophthalmic agent to treat glaucoma for years. It is marketed as a topical gel by Galderma Laboratories as Mirvaso.

Indications

Brimonidine gel is indicated for the topical treatment of persistent (nontransient) facial erythema of rosacea in adults.[1]

Dosage

The recommended dose is to apply a small amount (pea size) once daily to five areas of the face (forehead,

chin, nose, and each cheek).[1] Brimonidine gel is available as a 0.33% gel in 30 g and 45 g tubes. Each gram contains 3.3 mg of brimonidine.

Potential Advantages

Brimonidine provides a topical agent with a different mechanism of action for the treatment of erythema of rosacea.

Potential Disadvantages

Brimonidine affects the symptom but not the basic pathophysiology of the condition (i.e., inflammation, altered innate immune response). Patients with depression, CAD, Raynaud's, or other conditions that may be exacerbated by an alpha-2 adrenergic agonist should use the drug with caution. Some subjects in the clinical trial reported that when the drug wore off the return of erythema was worse than at baseline.[1]

Comments

Brimonidine is an alpha-2 adrenergic agonist that reduces erythema by direct vasoconstriction. This results in reduced erythema, a common symptom of rosacea. Efficacy in moderate-to-severe persistent rosacea was evaluated in two randomized, double-blind, vehicle-controlled trials.[1] Subjects were randomized to brimonidine topical gel (0.33%) or vehicle, applied once daily for 4 weeks. Baseline disease severity was based on a 5-point Clinical Erythema Assessement (CEA) scale and a self-administered Patient Self Assessment (PSA) scale. The scale for CEA is as follows: 4 — severe erythema, fiery redness; 3 — moderate erythema, marked redness; 2 — mild erythema, definite redness; 1 — almost clear, slight redness; and 0 — clear skin with no sign of erythema.[2] For PSA: 4 — completely unacceptable redness; 3 — more redness than I prefer; 2 — somewhat more redness than I prefer; 1 — nearly clear of unwanted redness; 0 — clear of unwanted redness.[2] The primary efficacy endpoint was a 2-grade improvement in both CEA and PSA measured on hours 3, 6, 9, and at day 29. Response ranged from 23-31% in study 1 and 18-25% in study 2 for brimonidine compared to 9-11% for the vehicle. Topical brimonidine appears to be well tolerated. The most common adverse events were flushing and erythema that ranged from 3-4%.

Clinical Implications

Rosacea is a common inflammatory skin condition affecting more than 10 million Americans.[3] Symptoms include erythema and flushing (dilated blood vessels) as well as papules and pustules. There is no cure for rosacea but treatment may control symptoms. Current topical medications include metronidazole, azelaic acid, and oral antibiotics (e.g., doxycycline).[4] The primary objective of these treatments is to reduce the number of papules and/or pustules, although some reduction in erythema has been observed. Brimonidine on the other hand is used primarily to reduce erythema. This suggests combination therapy may be indicated in some patients. The wholesale cost for brimonidine gel is $247.20 for a 30 g tube. As a comparison, azelaic acid gel (15%) is $193.48 for 50 g and metronidazole cream (0.75%) is $448 for 45 g. ■

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CME Objectives

Upon completion of this educational activity, participants should be able to:

- describe new findings in the differential diagnosis and treatment of various diseases;
- describe the advantages, disadvantages and controversies surrounding the latest advances in the diagnosis and treatment of disease;
- identify cost-effective treatment regimens;
- explain the advantages and disadvantages of new disease screening procedures.

CME Questions

1. **In this university/teaching hospital study, the frequency of initial prescription of dabigatran for stroke prevention in atrial fibrillation and the frequency of transition from warfarin to dabigatran:**
   a. were both less than expected.
   b. were both more than expected.
   c. was related to both the sex and the age of the patients.
   d. None of the above

2. **The results of a recent research trial show that 1 g of fish oil supplementation:**
   a. reduces recurrence of nonfatal myocardial infarction.
   b. does not affect cardiovascular morbidity nor mortality in high cardiovascular risk people.
   c. significantly affects secondary cardiovascular disease prevention.
   d. slightly increases the risk of fatal stroke.

By Louis Kuritzky, MD, Clinical Assistant Professor, University of Florida, Gainesville

Dr. Kuritzky is an advisor for Endo, Kowa, Pricara, and Takeda.

Osteoporosis: Are Two Drugs Better Than One?

Source: Tsai JN, et al. *Lancet* 2013;382:50-56.

Most women today who are receiving pharmacotherapy for treatment of osteoporosis receive oral bisphosphonates (e.g., alendronate, risedronate). Other effective treatments, like teriparatide (TERI) and denosumab (DENO) are usually reserved for more severe cases, in some part because they require parenteral administration.

Even though osteoporosis treatments have shown risk reduction for fracture and improved bone mineral density (BMD), restoration of full bone integrity remains a challenge. As one of the few anabolic tools (as opposed to anticatabolic tools like bisphosphonates), some investigators have tried to augment the favorable activity of TERI by combination with bisphosphonates, but the results have been disappointing. Whether the addition of DENO to TERI might be beneficial was the subject of investigation by Tsai et al. Postmenopausal women with osteoporosis (n = 100) were randomized to DENO, TERI, or both for 6 months. The primary outcome of the study was improvement in BMD.

Combination TERI+DENO appeared to be synergistic, with improvements in BMD greater than either agent alone and arithmetically greater than the anticipated benefit of combined monotherapies. For example, BMD increases at the hip were 4.2% for TERI+DENO, 0.8% for TERI, and 2.1% for DENO. These data support the consideration of TERI+DENO in highest-risk patients, those unable to take other treatments, or patients who fail to respond to other regimens. ■

Long-Term Impact of Weight Management on Blood Pressure

Source: Tyson CC, et al. *J Clin Hypertens* 2013;15:458-464.

The weight loss maintenance (WLM) trial randomized adults (n = 741) with hypertension (HTN) and/or dyslipidemia — but without evidence of cardiovascular disease — to one of several weight loss management programs. Although the initial outcome reports from WLM addressed the relative efficacies of different weight loss strategies over time, this report stratified study participants into those who lost, maintained, or gained weight over the 5-year study period. Tyson et al compared blood pressure effects between the three categories of weight impact, irrespective of which particular method of weight loss had been applied.

At study end, the weight-stable group had gained 0.6 kg, as compared with a 9.1 kg increase in the weight-gain group, and a 7.1 kg decrease in the weight-loss group. The weight-stable and the weight-gain groups were noted to have similar increases in systolic blood pressure (SBP) over 5 years (SBP increase mean 4.2 mmHg), whereas the weight-loss group SBP was not statistically significantly changed.

In contrast to some other trials that report a "legacy effect" (prolonged beneficial impact of early intervention, even after the intervention has ceased), initial weight loss in WLM was not associated with favorable SBP effects if weight was regained. On the other hand, sustained modest weight reduction (< 10% of baseline BMI) had a sustained effect to maintain SBP. Although simply maintaining weight over the long term might appear to be a laudable goal, it is apparently insufficient to favorably affect SBP. ■

The WEAVE Study: Does Special Training in Domestic Violence Improve Outcomes?

Source: Hegarty K, et al. *Lancet* 2013;382:249-258.

Intimate partner violence (IPV) is a public health problem that knows no boundaries of age, country of residence or origin, economic status, or education. Primary care clinicians, particularly family physicians, are often the first point of clinical contact for victims of IPV, but may lack confidence in their ability to identify and/or address IPV. Hegarty et al report on a trial from Australia in which women who screened positive for concerns about fear of their partner (n = 272) received care from family physicians who were randomized to receive special training in IPV or no intervention. The intervention group physicians participated in the Healthy Relationships Training program, which is intended to provide the ability to respond effectively to women who have experienced IPV and give brief counseling. The primary outcomes of the trial were changes in quality of life (as per the WHO QOL-BREF), safety planning and behavior, and mental health (as per the SF-12) at 1 year.

At 1 year, there was no difference in the primary endpoint between the intervention group and controls. A favorable impact on depression (a secondary endpoint) was seen. However, since the primary endpoint was not achieved, the potential for benefits on depression must remain considered as hypothesis generating. ■

In Future Issues: Antibiotic Prescribing for Adults in Ambulatory Care