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# Clinical Briefs in **Primary Care**™

The essential monthly primary care update

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## Zinc and vitamin C for pressure ulcers?

**Source:** Jamshed N, Schneider JI. Is the use of supplemental vitamin C and zinc for the prevention and treatment of pressure ulcers evidence-based? *Annals of Long-Term Care: Clinical Care and Aging* 2010;18:28-32.

ELDERLY PATIENTS, PARTICULARLY THOSE residing in nursing homes, are at risk for pressure ulcers (PrU) with recent reviews indicating a nursing home prevalence approximating 10%. Prevention and treatment of PrU commonly includes zinc and vitamin C (Z&C), based upon observations (animal studies) that both are necessary for optimum wound healing. Additional support for this concept comes from recognition of the sometimes marginal nutritional status of senior citizens. Some studies have shown malnutrition to result in an increase risk for PrU by as much as two-fold, but other studies disagree.

For vitamin C, a study performed in the 1970s reported increased wound healing, but the study only contained 20 patients, and subsequent trials have not been able to consistently show similar improvements.

For zinc, one study of senior citizens (n = 672) showed a small but statistically significant difference favoring supplementation, but study design and confounding issues preclude a final word on the subject. Overall, studies have been infrequent, small, and unable to provide a definitive conclusion.

Although generally considered safe, zinc and vitamin C do have associated adverse effect profiles, including increased risk of oxalic acid stones (vitamin C) and

copper deficiency (high-dose zinc).

Based upon their literature review, the authors conclude that supplementation of Z&C above recommended dietary intake is not supported, and could have important adverse effects.

## Dutasteride reduces prostate cancer risk

**Source:** Andriole GL, et al. Effect of dutasteride on the risk of prostate cancer. *N Engl J Med* 2010;362:1192-1202.

THE PROSTATE CANCER PREVENTION TRIAL did not ignite advocacy among clinicians for chemoprevention of prostate cancer (PCA). Although this large trial showed an overall reduction in total cancers (about 23%), high-grade tumors were actually statistically significantly increased. Several reasonable explanations for this phenomenon were offered; however, the disquieting consideration that 5-alpha-reductase inhibitors might be efficacious for reduction of low-grade tumors — but not effective for the more important high Gleason score tumors — remained.

Dutasteride and finasteride are very similar in their effects on the prostate, although there are both pharmacokinetic and pharmacodynamic differences. For instance, dutasteride has a much longer half-life (5 weeks), and dutasteride blocks both arms of the 5-alpha-reductase pathway (types 1 and 2), whereas finasteride only blocks type 2. Because both agents are highly efficacious in reducing intraprostatic levels of dihydrotestosterone, the putative culprit in generating BPH and possibly related to development of PCA, many experts consider them clinically comparable.

The REDUCE Trial (Reduction by Dutasteride of Prostate Cancer Events) enrolled men age 50-75 with a PSA of 2.5-10 ng/mL with negative prostate biopsy at baseline. Subjects were randomized to dutasteride 0.5 mg/day or placebo and followed for 4 years, receiving biopsies at year 2 and year 4.

At the completion of the trial, dutasteride was associated with an overall PCA relative risk reduction of 23%; encouragingly, this trial did not show a statistically significantly increased risk of high Gleason score tumors. Because dutasteride also provides favorable symptom benefits for BPH, clinicians may want to re-examine the balance of risks and benefits of 5-alpha-reductase inhibitors.

## New short-course topical treatment for actinic keratoses

**Source:** Swanson N, et al. Imiquimod 2.5% and 3.75% for the treatment of actinic keratoses: Results of two placebo-controlled studies of daily application to the face and balding scalp for two 2-week cycles. *J Am Acad Dermatol* 2010;62:582-590.

ACTINIC KERATOSES (AKs) RECENTLY HAVE been recognized as both a cosmetic and a dermatopathologic problem, since they are precursors to squamous cell carcinoma. Indeed, current literature suggests that AKs be considered squamous cell carcinoma in situ. AKs treatment includes cryotherapy, excision, chemical destruction (e.g., 5-fluorouracil, diclofenac), immune activation (imiquimod [IMQ]), and others. Because topical treatment courses

are sometimes protracted, and induce unpleasant cutaneous inflammatory changes, clinicians desire simpler, gentler methods.

Swanson et al randomized patients with AKs on the face and scalp to IMQ or placebo (n = 479). IMQ was applied as pulse therapy: qd for 2 weeks, then no treatment for 2 weeks, then repeat (total = 14 days of treatment). Outcomes were measured at 8 weeks.

IMQ produced a 72%-82% reduction in AKs lesions; higher doses produced complete clearing in 59% (vs 6% with placebo). A companion article in the same journal showed similar clearance rates for a longer regimen (3-week treatment courses). This simpler regimen was well tolerated, and provides a quick and effective route for topical treatment of AKs.

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## After bariatric surgery: The role of exercise

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**Source:** Evans RK. Maintaining weight loss momentum after bariatric surgery. *Am J Lifestyle Med* 2010;4:124-127.

**B**ARIATRIC SURGERY IS INCREASINGLY RECOGNIZED as a rational therapeutic option for morbid obesity and obese patients with comorbidities such as diabetes. On average, bariatric surgery produces a 35% reduction in body weight, but patients regain varying amounts of weight over time. Studies of the role of diet after bariatric surgery have helped to direct long-term

postoperative dietary management, but less information is available to guide exercise advice.

In the period after postoperative weight-loss stabilization, the weekly amount of exercise does correlate with sustained weight loss. Unfortunately, 37%-51% of postoperative subjects have been found to be noncompliant with exercise recommendations. Curiously, adherence to exercise in some trial data was greater before surgery than afterward, as if subjects felt they no longer needed exercise to the same degree now that surgery had been performed.

Bariatric surgery does not completely and permanently resolve weight-management issues in obese subjects. The high frequency with which post-surgical patients are noncompliant with exercise recommendations, with anticipated weight gain consequences, should spur clinicians to bolster patient education.

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## What aspect of HTN produces toxicity?

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**Source:** Rothwell PM, et al. Prognostic significance of visit-to-visit variability, maximum systolic blood pressure, and episodic hypertension. *Lancet* 2010;375:895-905.

**A** WELL-ESTABLISHED BODY OF EPIDEMIOLOGIC literature supports a continuous graded risk between systolic blood pressure (SBP) and CV risk. This relationship has held constant whether one considers office BP, home BP, or ambulatory blood pressure monitoring (ABPM). Because BP is variable over time, it is unclear whether the toxicity of BP to the vasculature is more strongly associated with mean BP, maximum BP, pulse pressure (SBP - DBP), or BP variability. Circadian rhythm of BP has also been recognized to be particularly associated with adverse outcomes: ABPM subjects whose BP does not decline overnight (called non-dippers) have greatly increased CV risk, well beyond what would be expected simply by having a greater total number of hours of exposure to elevated BP.

Rothwell et al used a data set comprised of persons who had sustained a TIA in large clinical trials (n = 2006), including the UK TIA Trial and ASCOT. Visit-to-visit BP variability and maximum SBP

were better predictors of adverse outcome than mean SBP. Similarly, persons with episodic HTN (normal BP on some occasions, elevated on others) were also at increased stroke risk, surpassing risk for stable BP.

It remains to be elucidated why these subgroups of individuals with BP variability have a greater risk burden. Although the associations between maximum SBP, BP variability, and episodic BP elevations were consistent, this does not establish causation. Perhaps the strongest cautionary message from this trial is that clinicians should not fall prey to false reassurance when they see a mixed BP response pattern including some BP measurements at goal and others elevated; such episodic elevations are consequential.

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## Depression and sleep disturbance

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**Source:** Van Mill JG, et al. Insomnia and sleep duration in a large cohort of patients with major depressive disorder and anxiety disorders. *J Clin Psychiatry* 2010;71:239-246.

**B**OTH ANXIETY AND DEPRESSION DISORDERS have a strong association with sleep disturbance. The association between sleep and depression is bidirectional: Depression is often manifest by or leads to sleep disturbance, and persistent insomnia increases risk of depression.

Van Mill et al sought to elucidate further the relationship between sleep disorders and depression by analyzing subjects in the Netherlands Study of Depression and Anxiety cohort (n = 2619).

In this population of subjects (approximately three-fourths suffered from depression and/or anxiety), almost half scored at least 9 on the Insomnia Rating Scale (IRS; the same metric that was employed in the Women's Health Initiative), fulfilling criteria for clinically significant insomnia. Insomnia scores were related to both anxiety and depression, but worse for depression, and highest for comorbid depression and anxiety. Interestingly, even persons with depression or anxiety in remission had elevated scores on the IRS. The authors suggest that, based upon their data, inquiry into sleep status is valuable not only during both depression and anxiety, but even during periods of remission.

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