Clinical Briefs in Primary Care™

The essential monthly primary care update

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## Dietary added sugar and lipids

**Source:** Welsh JA, et al. *JAMA* 2010;303:1490-1497.

Processed foods often contain added sucrose or high-fructose corn syrup to enhance palatability. Such added sugars (aSUG) may comprise as much as 16% of Americans' caloric intake. The Institute of Medicine suggests a 25% maximum of daily calories from aSUG and the American Heart Association suggests a 5% maximum. The incidence of obesity, diabetes, and dental caries is associated with increased aSUG, but the relationship between aSUG and lipids is less well-defined.

Welsh et al studied the relationship between aSUG and lipids in NHANES participants (n = 6113). Overall, approximately 16% of calories daily were supplied by aSUG in this population of adults. Excluded from analysis were persons with dietary reports that appeared unreliable (e.g., < 600 calories/d), marked triglyceride elevation, BMI > 65 kg/m$^2$, and those taking cholesterol-lowering medications.

There was a statistically significant association between progressively higher levels of aSUG and lower HDL. Similarly, LDL and triglyceride levels were linearly related to aSUG, although the LDL results were not statistically significant in men.

The mechanism(s) by which aSUG consumption is related to lipid levels is incompletely understood, although it is recognized that fructose may stimulate hepatic lipid production and reduce peripheral lipid clearance. Although not demonstrated in a clinical trial, conceptually, reductions in aSUG on a population-wide basis could have important public health benefits. ■

## Underrecognition of adverse effects

**Source:** Zimmerman M, et al. *J Clin Psychiatry* 2010;71:484-490.

The design of clinical trials sometimes allows for failed detection of adverse effects related to medication. Perhaps the most widely recognized disconnect is in relation to ACE inhibitors: Prescribing information suggests a very low incidence of cough (typically < 10%), yet clinical experience suggests twice that frequency. The primary reason for this incongruence is that most side effects are passively reported; for a variety of reasons, patients may fail to spontaneously report adversities that could be related to medication.

Zimmerman et al addressed this issue among depressed outpatients treated with a variety of antidepressants and anxiolytics. Subjects were seen by board-certified psychiatrists, and after their office visits, filled out questionnaires addressing adverse effects possibly related to medication.

Over a 6-week interval, more than 25% of the 2233 reported side effects occurred at least daily, but fortunately, the majority were rated low on the severity scale. Only about 20% of individuals rated adverse effects as 4-5 on a 5-point scale.

Overall, 20 times more adverse effects were identified by questionnaire than in psychiatrists' records. Comparison limited to either highly frequent or bothersome adverse effects still found that questionnaires identified 2-3 times as many adversities as clinicians had recorded.

A number of explanations can clarify some of this discrepancy: Psychiatrists may not record all adverse effects they see, patients may not report all issues that bother them (or minimize the bother), and some adverse effects may be so anticipated that their presence does not merit specific notice. In any case, it appears that patients shoulder a much higher level of adverse effect burden when treated for depression than would be readily apparent from review of their clinical records. ■

## Female sexual dysfunction in diabetes

**Source:** Esposito K, et al. *Int J Impot Research* 2010;22:179-184.

Male sexual dysfunction is well recognized as a consequence of diabetes. Currently, there are no approved medications for treatment of female sexual dysfunction (FSD), though epidemiologic surveys suggest that the population prevalence of FSD rivals that of male sexual dysfunction. FSD is typically categorized as either disorders of desire, arousal, orgasm, or pain. Of course, FSD subcategories are commonly comorbid.

This study recruited adult type 2 diabetic women (mean age, 58 years) attending a clinic in Italy for routine care of diabetes to complete the Female Sexual Function Index, a validated instrument for assessing FSD.

Overall, the prevalence of FSD in the entire population was 53%. This is similar to, but even greater than, the prevalence reported in two large population surveys (both with broader age range, and not limited to diabetics), which indicated an FSD

prevalence of 43%. FSD was 30% more frequent in postmenopausal women than premenopausal women and was associated with depression. The only recognized protective factor was physical activity.

The etiology of FSD in diabetes is unclear, and may include vascular, neurologic, and endocrinologic factors. The high prevalence of FSD in diabetic women should motivate clinicians to be more proactive in its identification. ■

## Vitamin D from the sun or supplements?

**Source:** Terushkin V, et al. *J Am Acad Dermatol* 2010;62:929.e1-9.

While I cannot speak for you, my recent experience is that under every rock I overturn is a vitamin D-deficient patient. At least that's what checking 25-OH vitamin D levels (the currently recommended test for vitamin D status) suggests. Should we recommend sun exposure, supplements, or both to address hypovitaminosis D?

Terushkin et al compared the amount of sun exposure necessary to provide the same plasma vitamin D levels as a 400 IU/d vitamin D supplement. They chose to study individuals in Miami, FL, and Boston, MA. Of course, sun exposure varies depending upon geography and season, as well as skin type. In July, the amount of sun time to provide as much systemic vitamin D as 400 IU orally was the same in both cities (3 min at 12 noon). A darker-skinned individual would require 5 min.

During winter months, there were marked differences in required exposure time. In Miami, 6 min of sun vs 23 min of sun in Boston would be required. Since most individuals do not expose 25% of the body surface (the face is only 3.5%) to sun during the winter in cities like Boston, a correspondingly greater time exposure would be required … an unlikely scenario.

Because of the concern about sun exposure and its relationship to photoaging and skin cancer, as well as the neglect of optimum sunscreen utilization, the authors of this article favor vitamin D supplementation over sun exposure as the safest way to maintain vitamin D adequacy. ■

## Exenatide + rosiglitazone added to metformin

**Source:** DeFronzo RA, et al. *Diabetes Care* 2010;33:951-957.

It is widely recognized that approximately half of beta-cell function (BCF) has been lost by the time type 2 diabetes (DM2) is diagnosed. Additionally, it appears that despite vigorous treatment, loss of BCF continues inexorably.

The most recently published treatment algorithm for DM2 management by the ADA suggests that initial therapy should be lifestyle with metformin, unless a specific contraindication to metformin exists. Over time, however, most patients will require augmentation of treatment.

Exenatide (EXE) and rosiglitazone (ROS) are effective therapies for glucose control and work by complementary mechanisms of action. Additionally, sometimes thiazolidinedione therapy is compromised by weight gain, but since exenatide consistently provides weight loss, their combination is clinically sensible.

DM2 subjects already on treatment with lifestyle plus metformin (n = 101) were randomly assigned to add-on therapy with EXE alone, ROS alone, or EXE + ROS, and followed for 20 weeks. BCF was measured by the glucose disposition index.

In addition to the anticipated reduction in A1c by polypharmacy, EXE + ROS provided significant improvements in insulin secretion and overall BCF. Long-term studies are necessary to discern whether these favorable effects can be sustained and translated into risk reduction for macro- and/or microvascular outcomes. ■

## Intensive BP control in diabetes

**Source:** Accord Study Group. *N Engl J Med* 2010;362:1575-1585.

Because it is recognized that type 2 diabetics (DM2) incur greater risk of CV outcomes than the general population, consensus groups have advocated BP < 130/80 mmHg as a preferred goal, in contrast to 140/90 mmHg for the general hypertensive population. Despite enthusiasm for this posture, and essentially global advocacy for the concept that lower is better in diabetes, no prospective, randomized trial has been done that confirms such benefits. The ACCORD trial was designed to compare CV outcomes achieved with tight BP control (SBP < 120 mmHg) vs standard therapy (SBP < 140 mmHg). The ACCORD trial had several limbs, including a glucose control and a lipid control arm, which were not addressed in this publication.

Almost 5000 diabetics were randomly assigned to intensive BP vs standard BP treatment and followed for the primary endpoint of (composite) nonfatal MI and stroke, or CV death over a mean 4.7-year follow-up.

The tight control arm managed to achieve an SBP of 119.3 mmHg, compared to the standard treatment group SBP of 133.5 mmHg; of course, the number of medications required to attain control was substantially greater in the tight control group (3.4 drugs vs 2.3 drugs). Intensive BP lowering did not reduce the primary endpoint. Intensive BP control was associated with more adverse events.

No hypertension guidelines have been issued since the publication and promulgation of the ACCORD BP trial. Expert opinions vary in interpretation of this outcome. I have suggested that, in the absence of proven benefit by greater BP lowering, achievement of < 140/90 mmHg now represents a reasonable goal until further literature suggests otherwise. ■

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