Revisions to Guideline 6:

- 6.1: Use of an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin receptor blocker (ARB) for the primary prevention of diabetic kidney disease in normotensive normoalbuminuric patients with diabetes is not recommended (1A)
- 6.2: Use of an ACE inhibitor or an ARB in normotensive patients with diabetes and albuminuria levels ≥30 mg/g who are at high risk of diabetic kidney disease or its progression is not recommended (2C)

Clinical evidence has failed to provide evidence that ACE inhibitors or ARBs can prevent the development of microalbuminuria in normotensive normoalbuminuric patients, but there are some signs that renin-angiotensin system (RAS) blockade may be effective in preventing the development of microalbuminuria in patients with type 2 diabetes. Prof. Bilous cautioned that the majority of the patients in all of the studies were hypertensive. In addition, there were varying levels of blood pressure control among the studies, with the studies achieving the best control being neutral in terms of any preventive effect. What the studies do tell us, Prof. Bilous said, is that "we need to manage blood pressure effectively in patients with type 2 diabetes, and while RAS blockade may be an important part of that blood pressure control, it may not be the RAS blockers *per se* that reduce albuminuria."

Managing Hyperglycemia in Hospitalized Patients

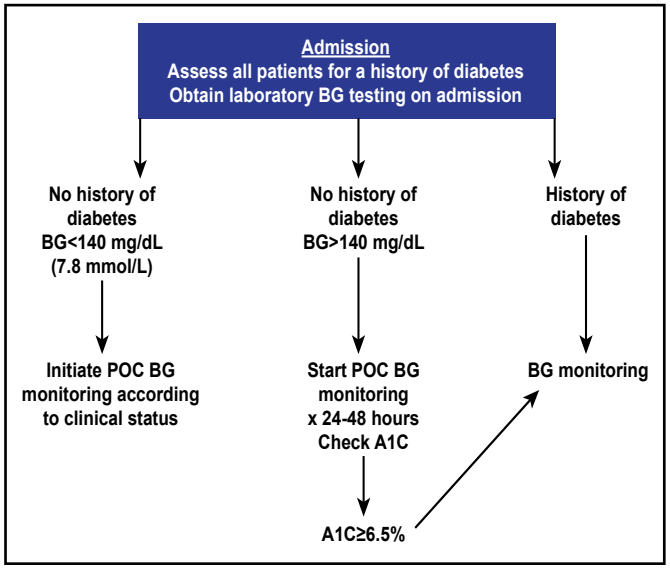
Written by Phil Vinall

Hyperglycemia occurs frequently in hospitalized patients and affects outcomes, including mortality, inpatient complications, length of stay, and overall hospital costs [Schmeltz LR, Ferrise C. *Hosp Pract (Minneap.)* 2012]. Observational and randomized controlled studies indicate that improving glycemic control results in lower rates of hospital complications in general medicine and surgery patients [Umpierrez GE et al. *J Clin Endocrinol Metab* 2012]. Guillermo E. Umpierrez, MD, Emory University School of Medicine, Atlanta, Georgia, USA, reviewed the latest Endocrine Society Clinical Practice Guidelines for the management of hyperglycemia in hospitalized patients in noncritical care settings [Umpierrez GE et al. *J Clin Endocrinol Metab* 2012].

The guideline objectives include: identifying best practices for recognizing and diagnosing hyperglycemia and diabetes in the hospital setting; identifying appropriate glycemic targets and the rationale for modifying them; understanding how to best reach glycemic targets safely; and recognizing and addressing specific aspects of management (eg, transitions of care and medical nutrition therapy [MNT]).

Dr. Umpierrez's presentation covered the diagnosis and recognition of hyperglycemia and diabetes in the hospital setting (Figure 1). He described the benefits and risks of using HbA1C for diagnosis (ie, values can be altered with several conditions, and analysis should be performed using a method that is certified by the National Glycohemoglobin Standardization program) [Suadek CD et al. *JAMA* 2006].

Figure 1. Diagnosis and Recognition of Hyperglycemia and Diabetes in the Hospital Setting.



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He discussed monitoring of glycemia and glycemic targets (Table 1) in the noncritical care setting (ie, a premeal glucose target of <140 mg/dL [7.8 mmol/L] and a random blood glucose of <180 mg/dL [10.0 mmol/L]) for the majority of patients with noncritical illness [Umpierrez GE et al**.** *J Clin Endocrinol Metab* 2012]. He also covered MNT, transition from home to hospital, and pharmacological therapy (eg, scheduled subcutaneous insulin therapy consisting of basal or intermediate-acting insulin given once or twice a day in combination with rapid- or short-acting insulin administered before meals in patients who are eating; Table 2).

Table 1. Glycemic Targets in the Noncritical Care Setting.

1.	A premeal glucose target of <140 mg/dL (7.8 mmol/L) and a random blood glucose of <180 mg/dL (10.0 mmol/L) for the majority of hospitalized patients with noncritical illness.
2.	Modification of glycemic targets according to clinical status. For patients who are able to achieve and maintain glycemic control without hypoglycemia, a lower target range may be reasonable. For patients with terminal illness and/or with limited life expectancy or at high risk for hypoglycemia, a higher target range (BG <11.1 mmol/L or 200 mg/dL) may be reasonable.
3.	To avoid hypoglycemia, reassess antidiabetic therapy when BG values fall below 5.6 mmol/L (100 mg/dL). Modification of glucose-lowering treatment is usually necessary when BG values are below 3.9 mmol/L (70 mg/dL).

Source: Umpierrez GE et al. *J Clin Endocrinol Metab* 2012.

Table 2. Example of a Basal Bolus Insulin Regimen for the Management of Noncritically Ill Patients with T2DM.

A. Basal insulin orders

- Discontinue oral diabetes drugs and noninsulin injectable diabetes medications upon hospital admission
- Starting insulin: calculate the total daily dose as follows:
  - 0.2 to 0.3 U/kg of body weight in patients aged ≥70 yr and/or glomerular filtration rate less than 60 ml/min
  - 0.4 U/kg of body weight per day for patients not meeting the criteria above who have BG concentrations of 7.8 to 11.1 mmol/L (140 to 200 mg/dL)
  - 0.5 U/kg of body weight per day for patients not meeting the criteria above when BG concentration is 11.2 to 22.2 mmol/L (201 to 400 mg/dL)
- Total calculated dose as approximately 50% basal insulin and 50% nutritional insulin
- Give basal insulin once (glargine/detemir) or twice (detemir/NPH) daily, at the same time each day
- Give rapid-acting (prandial) insulin in 3 equally divided doses before each meal; hold prandial insulin if patient is not able to eat
- Adjust insulin dose(s) according to the results of bedside BG measurements

B. Supplemental (correction) rapid-acting insulin analog or regular insulin

Supplemental insulin orders

- If a patient is able and expected to eat all or most of his/her meals, give regular or rapid-acting insulin before each meal and at bedtime following the "usual" column (Section C)
- If a patient is not able to eat, give regular insulin every 6 h ours (6–12–6–12) or rapid-acting insulin every 4 to 6 hours following the "sensitive" column (Section C)

Supplemental insulin adjustment

- If fasting glucose and premeal plasma glucose are persistently above 7.8 mmol/L (140 mg/dL) in the absence of hypoglycemia, increase insulin scale of insulin from the insulin-sensitive to the usual or from the usual to the insulin-resistant column
- If a patient develops hypoglycemia [BG <3.8 mmol/L (70 mg/dL)], decrease regular or rapid-acting insulin from the insulin-resistant to the usual column or from the usual to the insulin-sensitive column

C. Supplemental insulin scale

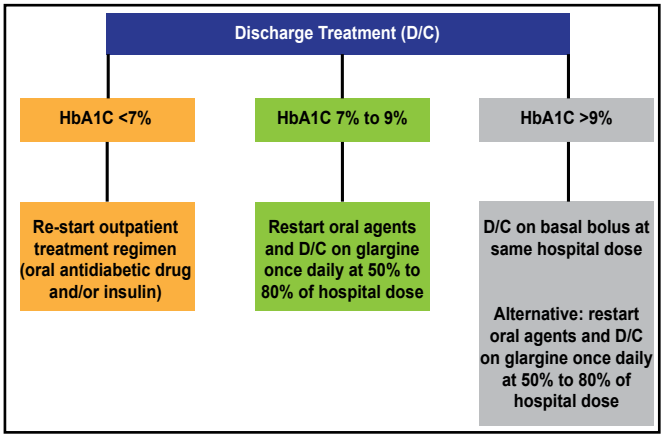
BG (mg/dL)	Insulin-sensitive	Usual	Insulin-resistant
>141–180	2	4	6
181–220	4	6	8
221–260	6	8	10
261–300	8	10	12
301–350	10	12	14
351–400	12	14	16
>400	14	16	18

The numbers in each column of Section C indicate the number of units of regular or rapid-acting insulin analogs per dose. "Supplemental" dose is to be added to the scheduled insulin dose. Give half of supplemental insulin dose at bedtime. If a patient is able and expected to eat all or most of his/her meals, administer supplemental insulin before each meal following the "usual" column dose. Start at insulin-sensitive column in patients who are not eating, elderly patients, and those with impaired renal function. Start at insulin-resistant column in patients receiving corticosteroids and those treated with more than 80 U/d before admission. To convert mg/dL to mmol/L, divide by 18.

Adapted from Clement S et al. *Diabetes Care* 2004; Umpierrez GE et al. *Diabetes Care* 2007; Umpierrez GE et al. *J Clin Endocrinol Metab* 2009.

Other topics included pharmacological treatment of hyperglycemia in the non-intensive care unit setting (eg, avoidance of prolonged use of sliding scale insulin therapy as the sole method for glycemic control in hyperglycemic patients with a history of diabetes during hospitalization) [Umpierrez GE et al. *J Clin Endocrinol Metab* 2012]; insulin therapy in patients with type 2 diabetes [Umpierrez GE et al. *Diabetes Care* 2007]; and transition from hospital to home (Figure 2).

Figure 2. Discharge Insulin Algorithm.



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Special situations include the switch from intravenous continuous insulin infusion to subcutaneous insulin therapy and patients who receive enteral or parenteral nutrition or glucocorticoid therapy. He noted that hyperglycemia during total parenteral nutrition is associated with a greater risk of hospital mortality [Pasquel FJ et al. *Diabetes Care* 2010].

Dr. Umpierrez stressed that MNT is an essential component of the glycemic management program for all hospitalized patients with diabetes and hyperglycemia and that providing meals with a consistent amount of carbohydrates can be useful in coordinating doses of rapid-acting insulin to carbohydrate ingestion. He also reviewed the risks of hypoglycemia in the hospital setting.

According to the guidelines, an in-hospital glycemic control program should include: administrative support for an interdisciplinary steering committee using a systems approach to improve care of inpatients with hyperglycemia and diabetes; a uniform method of collecting and evaluating point-of-care testing and insulin use data as a way of monitoring the safety and efficacy of the glycemic control program; and the provision of accurate devices for glucose measurement at the bedside with ongoing staff competency assessments.

Dr. Umpierrez also specified methods and goals for educating patients and professionals. These include diabetes self-management education that focuses on short-term survival goals; identification of community resources to provide continued support to patients; and ongoing staff education to update diabetes knowledge in general and whenever an adverse event that is related to diabetes management occurs.

CVD Prevention and Treatment in Women With Diabetes

Written by Phil Vinall

Cardiovascular disease (CVD) is the number one killer of women in westernized countries. Its connection to diabetes, a particularly strong risk factor that disproportionately affects women, has been well established. In a session that was devoted to the implications for CVD prevention and the treatment of women with diabetes, L. Kristin Newby, MD, Duke University Medical Center, Durham, North Carolina, USA, discussed differences in current diabetes treatment that are related to gender.

Major randomized controlled trials (RCTs) over the past 1 to 2 decades have changed the practice of CVD prevention in women, with 3 studies having a particular impact on the current guidelines for the prevention of CVD in women. The Women's Health Initiative (WHI) [Rossouw JE et al. *JAMA* 2002] and the Heart and Estrogen/Progestin Replacement Study [Hulley S et al. *JAMA* 1998] were, in large part, responsible for the recommendation that hormone therapy not be used for the primary or secondary prevention of CVD, as it is not effective and may be harmful [Mosca L et al. *Circulation* 2007, 2011]. Aspirin is one of the least expensive and most frequently used preventive therapies for cardiovascular events; however, the Women's Health Study (WHS), which evaluated the use of low-dose aspirin as primary prevention for CVD in women, provided evidence of a sex-based response to aspirin therapy. Among the women in the WHS, aspirin therapy resulted in a significant (p=0.04) overall reduction in stroke (RR, 0.83; 95% CI, 0.69 to 0.99) and a nonsignificant overall 9% reduction in cardiovascular events, a slight increase in the risk of hemorrhagic stroke (RR, 1.24; 95% CI, 0.82 to 1.87; p=NS), and no benefit on myocardial infarction (MI; RR, 1.02; 95% CI, 0.84 to 1.25). To assess for the effect of gender, the authors conducted a gender-specific on aspirin therapy random-effects meta-analysis of data from 6 trials that showed a reduction in risk for MI and no influence on stroke among men but no effect on MI in women and a reduction in the incidence of stroke [Ridker PM et al. *N Engl J Med* 2005].

Aspirin resistance is present in up to 40% of patients with diabetes, and the prevalence of resistance increases with decreasing metabolic control [McGuire D. Braunwald's Heart Disease: A Textbook Of Cardiovascular Medicine 2012. Elsevier]. Large RCTs are currently evaluating if higher doses of aspirin might overcome the effects of resistance, but the 2011 American Heart Association guidelines state that aspirin (75 mg/day to 325 mg/day) should be used in women with coronary heart disease unless contraindicated and that this therapy is reasonable in women with diabetes unless contraindicated. Signals of an increased risk of MI among younger women and risks for bleeding led to the recommendation against routine use of aspirin in healthy women aged <65 years to prevent MI [Mosca L et al. *Circulation* 2011].

Finally, although statin therapy greatly lowers cardiovascular risk, in the WHI study, the incidence of new-onset diabetes mellitus was associated with statin use among postmenopausal women [Culver AL et al. *Arch Intern Med* 2012]. The underpinnings of the recently scrutinized relationship between statin use and new-onset diabetes mellitus are unknown.

Although the data generally support similar treatment responses in women and men and although there is no clear evidence that diabetes alters treatment benefit of