Forego post-meal glucose testing in the hospital

We enthusiastically agree with most of the recommendations in "It's time to abandon the sliding scale" (*J Fam Pract*. 2011;60:266-270), but we see an inconsistency.

Guthrie et al support the use of the postprandial fingerstick as a measure of glycemic control, and note its endorsement in the product inserts for 2 well-known rapid-acting analog insulins. However, neither the RABBIT-2 study cited by the authors nor the 2010 American Diabetes Association (ADA) standards of care take this position. In RABBIT-2, preprandial fingersticks were used exclusively,[1] and the ADA standards recommend correction doses, or supplemental insulin, to correct pre-meal hyperglycemia.[2] The 2004 ADA position statement on inpatient glycemic control[3] cited by the authors does not differentiate between preprandial and postprandial fingersticks.

We believe that postprandial testing, while often useful in the outpatient setting, is rarely helpful in the hospital, where such testing can lead to too-frequent dosing of rapid-acting insulin. And, because the serum glucose is not known until after the meal, an appropriate pre-meal insulin dose cannot be prescribed until the following day. Since the relatively recent relaxation of standards in inpatient glycemic control,[2] postprandial monitoring rarely leads to meaningful improvement in glycemic control.

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1. Umpierrez GE, et al. Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes (RABBIT 2 trial). *Diabetes Care*. 2007;30:2181-2186.
2. Executive summary: standards of medical care in diabetes—2011. *Diabetes Care*. 2011;34(suppl 1):S4-S10.
3. Clement S, et al. Management of diabetes and hyperglycemia in hospitals. *Diabetes Care*. 2004;27:553-591.

The authors respond:

The issue raised by Drs. Moore and Williams is vital to management with modern insulins. To address it fully, however, an understanding of the pharmacodynamics of rapid-acting insulins is required.

In brief, the pharmacokinetic value of insulin is the time at which amounts of insulin in the bloodstream are measurable. The pharmacodynamic value—the time at which there is enough insulin in the bloodstream to control glucose levels—is much shorter. For rapid-acting insulin at the usual doses, this value is about 3 to 4 hours.

The problem is that pre-meal glucose levels are measured 4 to 6 hours after the rapid-acting insulin is administered; thus, a blood glucose level measured at 6:00 PM reveals nothing about the rapid-acting insulin given at noon. Pre-meal measurements more accurately reflect the basal insulin than the bolus insulin. Corrections made at that time can cause problems at the peak time of the insulin, 1 to 3 hours later.

We correct this problem in the outpatient setting by changing the insulin dose by the amount of food to be eaten, not by the blood glucose level at the time, then looking at the pattern of values over several days and making corrections as needed. This is harder to do in the hospital because the patient is there for a shorter time. So we make rounds in the late afternoon, when the blood glucose values for the day (except for the evening) are available in a tabular form, and use them, along with values from the previous day(s), to look for a pattern.

Using a patterned approach with both pre- and post-meal blood glucose values will improve control of diabetes; if IV insulin is used, values are obtained hourly and the insulin drip titrated within a certain range to meet the needs of the individual patient.

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Making a case for rosiglitazone

In "Is your patient still using rosiglitazone?" (*J Fam Pract*. 2011;60:282-284), Drs. Gov-Ari

and Stevermer question the continued use of rosiglitazone for type 2 diabetes in view of a reported increase in the risk of acute myocardial infarction (MI) associated with it. As a physician who continues to prescribe rosiglitazone, I would like to explain my rationale.

The meta-analysis upon which the various FDA advisories are based, like all meta-analyses, is "exploratory" or "hypothesis generating." It is not gold-standard evidence from randomized controlled trials (RCTs), on which evidence-based medicine must be based. Neither of the 2 RCTs that have been done showed an increase in acute MI associated with the use of this drug.[1,2]

No patient in my practice who is taking rosiglitazone has sustained an acute MI. I have shown that the prediction of the population at risk of atherothrombotic disease, which includes acute MI, is independent of blood sugar levels.[3]

Hence, after appropriate counseling, I continue to prescribe rosiglitazone for patients who are willing to take it. After all, pioglitazone costs about $100/month more than rosiglitazone, and for many of my patients the increased cost would be devastating.

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1. Home PD, et al. Rosiglitazone evaluated for cardiovascular outcomes in oral agent combination therapy for type 2 diabetes (RECORD): *Lancet.* 2009;373:2125-2135.
2. The BARI 2D Study Group. A randomized trial of therapies for type 2 diabetes and coronary artery disease. *N Engl J Med.* 2009;360:2503-2515.
3. Feeman WE Jr. Diabetes mellitus is not a coronary heart disease equivalent. *Am J Cardiol.* 2010;105:754-755.

The authors respond:

We appreciate Dr. Feeman's response to our PURL, which was based on a recent meta-analysis of RCTs of rosiglitazone.[1] We are happy that none of his patients has been harmed by rosiglitazone, but note that the increase in MIs would be an uncommon event in most primary care practices. Over a 5-year period of rosiglitazone use, only one in 37 to 52 people would have suffered an MI. In a single practice, this rate of events would be difficult to detect, given the already elevated baseline risk in a diabetic population.

While we also agree that a well-done RCT may be superior to a meta-analysis, we disagree with the statement that evidence-based medicine should not be based on systematic reviews or meta-analyses. The problem is that the appropriate RCTs are often not done, in many cases because of logistic and financial issues. Almost none of the RCTs of rosiglitazone had the power to detect the increase in MIs. Few, if any, of the 56 trials included in the meta-analysis found a statistically significant difference in MI rate; however, the overall meta-analysis found an important increase (OR=1.28; 95% CI, 1.02-1.63). One of the advantages of meta-analyses is their ability to detect uncommon events distributed over a series of different studies.[2] Safety evaluations are a particularly important use of meta-analyses, since drugs are often approved without any single RCT large enough to detect an important increase in serious adverse events.

The FDA has added restrictions to the use of rosiglitazone in the form of a Risk Evaluation and Mitigation Strategy (REMS), a program used to manage serious risks of marketed drugs.[3] Only patients already successfully treated with rosiglitazone can enroll in the program, unless their physician does not wish to use pioglitazone when other antidiabetic agents have failed to provide adequate control. Prescribers and patients must enroll in the REMS program to be able to prescribe and receive the medication, which will be available only through specially certified pharmacies and dispensed only by mail. This additional step reflects the FDA's significant concerns about MIs associated with rosiglitazone. We also note that at a popular Internet pharmacy (www.drugstore.com), the difference in cost between rosiglitazone and pioglitazone is less than $90 for a 90-day supply.

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1. Nissen SE, Wolski K. Rosiglitazone revisited: an updated meta-analysis of risk for myocardial infarction and cardiovascular mortality. *Arch Intern Med.* 2010;170:1191-1201.
2. Mulrow CD. Rationale for systematic reviews. *BMJ.* 1994; 309:597-599.
3. US FDA Drug Safety Communication: Updated Risk Evaluation and Mitigation Strategy (REMS) to restrict access to rosiglitazone-containing medicines including Avandia, Avandamet, and Avandaryl. Last updated May 18, 2011. Available at: http://www.fda.gov/Drugs/DrugSafety/ucm255005.htm. Accessed June 13, 2011.

No patient in my practice who is taking rosiglitazone has sustained an acute MI.