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## Paging Goldilocks: How Much Glycemic Control Is Just Right?

There is no doubt that hyperglycemia among hospitalized patients correlates with worse prognosis. Further, there are well-documented mechanisms by which poor glycemic control may directly impact outcomes. For example, hyperglycemia and insulin deficiency can impair neutrophil function, exacerbate inflammation, and impair endothelium-mediated dilatation,<sup>1,2</sup> whereas hypoglycemia increases sympathetic tone. And both severe hyperglycemia and hypoglycemia, of course, can precipitate altered mental status. But certainly not all of the morbid outcomes *associated* with poor glycemic control in the hospital—including infection, cardiac events and death—are *caused* by poor glycemic control in the hospital. Elevated glucose levels in the hospital are often seen in sicker patients with raging stress hormones and in brittle diabetics with a present-on-admission condition that has been ravaging their vasculature for years. This means that virtually all observational studies demonstrating worse outcomes in the setting of poor glucose control in the hospital will be severely confounded by comorbid illness, and much confounding will remain even after multivariate adjustment.<sup>3</sup>

Nonetheless, high-quality randomized controlled trials that have focused on critically ill patients,<sup>4,5</sup> rather than general medical patients, have generated intense interest and fostered the belief that controlling the glucose level of all hospitalized patients is probably a good idea. (Although, more recently, even the data supporting glycemic control in the critically ill have been challenged.)<sup>6</sup> Enthusiasm for implementing aggressive glycemic control protocols outside of the intensive care unit (ICU) appears widespread, as is evident in this issue of *JHM*.<sup>7-11</sup> In this issue, two articles detail the challenges of implementing glycemia control protocols.<sup>7,8</sup> The research teams employed different protocols and used different metrics, but there are common themes: (1) The process was iterative. Interventions were piloted, then rolled out, and substantial effort was needed to foster continued attention to the interventions. (2) The process was multidisciplinary. Buy-in and input were needed not only from physicians, but also from nurses, pharmacists, dieticians, clinical data system experts, and probably patients. (3) Impacting process measures was easier than impacting surrogate outcome measures. Specifically, despite dramatic changes in the use of carefully vetted order sets and protocols, the impact on glycemia was modest and sometimes inconsistent.

These studies illustrate that implementing protocols to control glycemia is neither easy, nor consistently associated with improved glycemic control—let alone improved major clinical outcomes. Three complementary observational studies<sup>9-11</sup> further illustrate how hard it is to optimize glycemic control in the hospital setting. Together, the observational and interventional

studies demonstrate how difficult it is to measure success. Should we focus on the mean glucose value achieved or the frequency of extreme glucose values (which are, by definition, more dangerous)? Should we look at glycemic control in every patient who is placed on a protocol, even those who barely need any insulin at all, or should we focus our interventions and analyses on those patients with more severe dysglycemia at baseline? This latter issue is fundamentally important, since the rollout of any systemwide glycemia protocol that results in higher catchment rates will appear more effective than it really is by enriching the postintervention data with healthier patients.

Before embarking on time-intensive efforts to improve care, maybe we should be sure that the evidence supports our efforts.<sup>12</sup> Recent recommendations from the American Diabetes Association state that for “non-critically ill patients: there is no clear evidence for specific blood glucose goals.”<sup>13</sup> (This recommendation, based on “expert consensus or clinical experience,” further states that “because cohort data suggest that outcomes are better in hospitalized patients with fasting glucose <126 mg/dL and all random glucose values <180 to 200 mg/dL, these goals are reasonable if they can be safely achieved.”) But given the challenges associated with implementing glycemia protocols, one might argue that hospitalists should invest their quality improvement efforts elsewhere.

So where does this leave us? What target glucose is not too high, not too low, but “just right”? Given the ever-increasing number of quality improvement measures and interventions that are expected in the hospital, what amount of time, effort, and money devoted to improving inpatient glycemic control is “just right”? And what do our patients think? Should we be feeding our patients low glycemic load diets, or letting them indulge in one of the few creature comforts remaining in a semiprivate room?

What is clear from the results of the research published in this issue of *JHM* (regardless of whether we think that an inpatient pre-meal glucose of 160 mg/dL is good, bad, or neither), is that we need to continue to develop systems, strategies, and teams to rapidly disseminate quality improvement interventions locally. We need multidisciplinary input—from physicians, nurses, dietitians, pharmacists, and patients—to do it right. So, even if the pendulum swings away from tight glycemic control in the hospital, the lessons we learned from these authors’ valiant efforts to tame inpatient glycemia may provide us

with the tools and knowledge required to successfully tackle other clinical issues such as delirium prevention, pain control, medication reconciliation, and handoffs. The striking obstacles (both in implementation and analysis) faced and overcome by the authors of the articles in this issue of *JHM* will hopefully embolden them to take on other quality improvement interventions that are perhaps more likely to help hospitalized patients.

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