Clinical Pearls to Improve Safety and Patient Care in the Hospital Setting:
Addressing Challenges of Insulin Therapy

A supplement based on a symposium conducted at the 47th American Society of Health-System Pharmacists’ Midyear Clinical Meeting and Exhibition

This enduring activity is supported by an educational grant from Novo Nordisk Inc.

Jointly sponsored by: AACME and MedEdGroup
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Target Audience
This educational activity has been designed to meet the educational needs of health care-system pharmacists involved in the management of hospitalized patients with diabetes and/or hyperglycemia. Other health care professionals may also participate.

Activity Overview
This supplement focuses on the importance of addressing hyperglycemia in the inpatient setting, whether in patients with known diabetes or those without diabetes. In reviewing the most recent recommendations from major medical societies on the management of inpatient hyperglycemia, the important topic of avoiding the risks of hypoglycemia and the safe use of insulin is discussed. Central to ensuring the safe and effective balancing act of achieving normoglycemia is the need for involvement of multiple stakeholders and a multidisciplinary team, of which the pharmacist is a key player.

Learning Objectives
After completing this educational activity, the learner should be better able to:
- State recent recommendations for glycemic targets for the inpatient setting and the value of glycemic control on outcomes during hospitalization
- Explain to other members of the diabetes management team why sliding scale insulin should not be the treatment of choice for insulin administration in the hospital setting
- Select appropriate types of insulin agents to meet patients’ physiologic insulin needs
- Formulate a plan to improve the safe and effective use of insulin in their hospital setting

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Level A (randomized controlled trial/meta-analysis): High-quality, randomized controlled trial (RCT) that considers all important outcomes. High-quality meta-analysis (quantitative systematic review) using comprehensive search strategies.

Level B (other evidence): A well-designed, nonrandomized clinical trial. A nonquantitative systematic review with appropriate search strategies and well-substantiated conclusions. Includes lower-quality RCTs, clinical cohort studies, and case-controlled studies with nonbiased selection of study participants and consistent findings. Other evidence, such as high-quality, historical, uncontrolled studies, or well-designed epidemiologic studies with compelling findings, is also included.

Level C (consensus/expert opinion): Consensus viewpoint or expert opinion.
Introduction
The number of hospital discharges with diabetes as “any-listed” diagnosis increased from 2.8 million to nearly 5.5 million from 1988 to 2009.\(^1\) Hospitalizations account for the largest portion of the direct cost of diabetes care, or approximately 50% of the $27 billion per year (Figure 1).\(^1\) Reducing the risk of hospitalization by improving outpatient diabetes care is one way that pharmacists can improve these staggering numbers. A second way is to reduce the cost of the hospitalizations that do occur, through improving outcomes and reducing lengths of stay. Hospitalization also is an opportunity to identify the one-third of patients who have diabetes in the United States but may be unaware of their disease status,\(^2\) and to make improvements in the large numbers of patients who experience poor glycemic control on their current glycemic control regimens.\(^3\)

Hyperglycemia is common in hospitalized patients (Figure 2).\(^4\) It may be present in up to 40% of patients, and 30% of those with hyperglycemia may have no prior history of diabetes.\(^5\) Whether this represents undiagnosed diabetes or stress hyperglycemia resulting from acute illness, it is something that should be ascertained before the patient is discharged. Patients who have documented hyperglycemia while hospitalized should have a glycated hemoglobin (A1C) test performed before discharge if one has not been performed in the previous 2 to 3 months; this can identify patients with diabetes (A1C >6.5%), although it is not as sensitive as the use of fasting plasma glucose levels.\(^6\)

Consequence of Inpatient Hyperglycemia
Historically, hyperglycemia in hospitalized patients was not treated until glucose levels became very high because it was thought to be a protective mechanism. However, in the last several decades we have learned that hyperglycemia is an independent risk factor for poor outcomes in hospital-
It is associated with increased morbidity and mortality,8-14 longer length of stay, increased costs,15 and higher risk of rehospitalization.16 Table 1 summarizes a few examples of poor outcomes observed with hyperglycemia in different patient groups. One of the better-defined morbidities is the increased risk of infection in patients with hyperglycemia;17 this has been well documented with deep sternal wound infections (an infection that is very expensive) in patients undergoing coronary artery bypass graft surgery.18-21 The risks associated with hyperglycemia in the hospital appear to be greater in patients with no known history of diabetes compared with those with established diabetes (Figure 3),22,23 perhaps because these patients are not acclimated to high levels of glucose. This suggests that we should pay even closer attention to patients with new hyperglycemia or new diagnoses of diabetes in the hospital, and in educating such patients before discharge. Persistent hyperglycemia may be a better marker for poor outcomes than admission blood glucose levels.24

Inpatient Glycemic Goals
Although outpatient glucose targets have been established for decades, it was not until 2004 that a professional society first established any inpatient treatment goals for hyperglycemia.25 This was in large part prompted by a randomized controlled clinical trial conducted in Belgium that showed a dramatic reduction in morbidity and mortality with the use of intravenous (IV) insulin infusions to treat hyperglycemia in critically ill patients.26 This study, along with other retrospective or observational data,27-29 led to the first recommendations for very strict blood glucose targets in critically ill patients (80-110 mg/dL). However, the ability to achieve these goals was limited by a relatively high frequency of hypoglycemia.26,30-33 There is indeed a J-curve for glucose—both hyperglycemia and hypoglycemia are associated with adverse outcomes.24 It became clear that there was a risk for hypoglycemia without a protocol using glucometrics to safely achieve goals, a topic we will

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**Table 1: Examples of Poor Outcomes Associated with Inpatient Hyperglycemia**

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient Population</th>
<th>Significant Hyperglycemia-Related Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pasquel et al, 2010</td>
<td>Total parenteral nutrition</td>
<td>1Mortality, pneumonia risk, acute renal failure</td>
</tr>
<tr>
<td>Frisch et al, 2010</td>
<td>Noncardiac surgery</td>
<td>1Mortality, surgery-specific risk</td>
</tr>
<tr>
<td>Schlenk et al, 2009</td>
<td>Aneurysmal subarachnoid hemorrhage</td>
<td>1Mortality impaired prognosis</td>
</tr>
<tr>
<td>Bochicchio et al, 2007</td>
<td>Critically injured trauma patients</td>
<td>1LOS, mortality, ventilator time, infection</td>
</tr>
<tr>
<td>Baker et al, 2006</td>
<td>Chronic obstructive pulmonary disease</td>
<td>1LOS, mortality, adverse outcomes</td>
</tr>
<tr>
<td>McAllister et al, 2005</td>
<td>Community-acquired pneumonia</td>
<td>1LOS, mortality, complications</td>
</tr>
</tbody>
</table>

LOS = length of stay.

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**Figure 3: In-hospital Mortality in Patients with Normoglycemia, Known Diabetes, and Newly Discovered Hyperglycemia**

- **Total In-patient Mortality**
  - Normoglycemia: 1.7%
  - Known Diabetes: 3.0%
  - New Hyperglycemia: 16%*

- **NON ICU Mortality**
  - Normoglycemia: 0.8%
  - Known Diabetes: 1.7%
  - New Hyperglycemia: 10%*

- **ICU Mortality**
  - Normoglycemia: 10%
  - Known Diabetes: 11%
  - New Hyperglycemia: 31%*

*P < 0.01

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Inpatient Hyperglycemia Guidelines

Figure 4: Treatment Considerations for Management of Inpatient Hyperglycemia

<table>
<thead>
<tr>
<th>Hospitalized patients with hyperglycemia (BG &gt;180 mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critically ill patients</td>
</tr>
<tr>
<td>Scheduled subcutaneous insulin injections (basal, prandial, correction) adjusted to maintain premeal BG &lt;140 mg/dL and random BG &lt;180 mg/dL</td>
</tr>
<tr>
<td>Noncritically ill patients</td>
</tr>
</tbody>
</table>

Non-insulin antihyperglycemic agents have a limited role in acute care settings and practitioners should consider discontinuing them in favor of insulin during acute illness.

BG = blood glucose; IV = intravenous.

The results of the Normoglycemia in Intensive Care Evaluation and Survival Using Glucose Algorithm Regulation study and 2 meta-analyses confirmed the risk of hypoglycemia with aggressive glucose goals in critically ill patients and led to the reevaluation of inpatient hyperglycemia goals. These were readjusted by the American Association of Clinical Endocrinologists (AACE) and the American Diabetes Association (ADA) in 2009 (Figure 4). Figure 4 also provides the treatment goals and treatment considerations for non-critically ill patients as put forth by the AACE/ADA, and those by the Endocrine Society in 2012.

Insulin in Critically Ill Patients

The AACE/ADA treatment recommendations provide guidance on the role of IV insulin in critically ill patients, as do recommendations from the Society for Hospital Medicine. Insulin, specifically an IV insulin infusion, is the preferred method of treating hyperglycemia in critically ill patients because it is potent, rapidly acting, easily titrated, not limited by contraindications, and without dose limits to its efficacy. It is, however, an agent with a narrow therapeu tic index and a “high alert” medication, meaning that it has a very high risk of causing injury when misused and it requires strategies to ensure that the correct drug is given in the proper dosage to the appropriate patient at the correct time, and through the proper route of administration. It is recommended that institutions use a single insulin concentration in these infusions to avoid any confusion about dose or potential errors related to having more than 1 concentration. IV insulin infusion concentrations should be standardized throughout the hospital with the use of regular insulin in concentrations of 1 unit/mL or 0.5 unit/mL.

There are more than 25 published insulin infusion protocols, the majority of which use manual blood glucose calculations and a handful of which use computerized algorithms. When evaluating protocols, features to consider are patient characteristics, target glucose levels, time to achieve target glucose levels, incidence of hypoglycemia, rationale for adjusting the rates of insulin infusion, and methods of blood-glucose measurements. IV insulin is ideally administered by means of a validated protocol that allows for predefined adjustments in the insulin infusion rate based on insulin dose and glycemic fluctuations as measured by glucometrics. Glucometrics is the systemic analysis of blood glucose data that are flexible in blood glucose timing and advise insulin dosing in a graduated manner can be simple, safe, and effective methods for maintaining glycemic control. These algorithms utilize a multiplication factor that takes into account the rate of insulin and rate of change in blood glucose over time. What can be problematic are “fixed” protocols that do not take into account the rate of change of blood glucose levels. For example, a patient whose blood glucose level has dropped by 70 mg/dL in an hour but is still in a “safe” range (eg, dropped from 190 mg/dL to 120 mg/dL) might stay at the same rate of insulin by a fixed protocol, but if that rate of change were to continue, in the next hour, their blood glucose level could drop to 50 mg/dL, clearly putting them in danger. In critically ill patients, accurate bedside blood glucose monitoring should be done frequently—ranging from every 30 minutes to every 2 hours. Automation and standardization of the glucose measurement process have the potential to greatly improve glycemic control, clinical outcomes, and safety while reducing cost. The resources required to monitor glycemia in hospitalized patients have thus far limited the implementation of intensive glucose management in critically ill patients. One can foresee a role for continuous glucose monitoring in the hospital setting much as we have continuous blood pressure monitoring now.

Potassium should be monitored and given if necessary (consider delaying insulin infusion until potassium is >3.0-3.5 mEq/L). Insulin is known to drive potassium intracellularly and may exacerbate hypokalemia and lead to arrhythmias. When a patient is stable and transferred out of a critical care unit, IV insulin is generally discontinued and the use of scheduled subcutaneous insulin is implemented.

How does one convert a patient...
Case Study: Transition from IV Infusion to Scheduled Subcutaneous Insulin Injections

GH is a 68-year-old man who has had type 2 diabetes for 10 years. He was admitted to the cardiac intensive care unit for stent placement. In the past few hours, his IV insulin infusion requirements were 3 units/hour. He is now moving to a general medical floor. He is awake, alert, and eating. His 24-hour insulin requirements are determined by multiplying his calculated total daily dose of IV insulin (3 units × 24 hours = 72 units) by 0.6 (60%), which equates to roughly 40 units; half of this will meet his basal or background insulin needs and half will meet his mealtime or prandial insulin needs. This is a conservative estimate of his insulin needs and may need to be titrated. Thus, he should receive 20 units of a long-acting basal insulin analogue at bedtime and 7 units of a rapid-acting insulin analogue 3 times a day, with the first bite of each meal. In addition, he should have correctional insulin ordered to cover unanticipated premeal hyperglycemia.

from an IV insulin infusion to scheduled subcutaneous insulin? The total daily dose of subcutaneous insulin is extrapolated from the average IV insulin rate per hour over a period of time when the patient has been stable. This is multiplied by 24 to obtain 24-hour insulin requirements. Insulin may also adsorb to plastic tubing, which may decrease the concentration of an insulin solution delivered from an IV infusion set. Additionally, the patient may be eating all of their meals immediately or receiving all their caloric intake provided by enteral or parenteral methods. Thus, the 24-hour total daily dose is often then multiplied by a fraction (0.6 to 0.8) for a starting total daily subcutaneous dose. This is then divided into basal and prandial components. Basal or background insulin comprises about 50% of insulin needs; the other 50% is split over 3 meals.

Because of the rapid onset of action (and offset of action) of IV insulin, it is necessary to start subcutaneous insulin before IV insulin is discontinued. Generally speaking, basal insulin should be administered 2 hours before discontinuing IV insulin.50

Insulin in Non-Critically Ill Patients

In non-critically ill patients, regularly scheduled subcutaneous insulin is the preferred method of managing hyperglycemia. This consists of basal insulin to cover background insulin needs, prandial insulin to cover mealtime or nutritional needs (Figure 5), and the occasional use of supplemental or correctional insulin (in the form of rapid-acting insulin) in addition to the basal and prandial insulin (insulin terminology is shown in Table 2). This is different from sliding scale insulin, which is the use of short- or rapid-acting insulin in the absence of basal insulin. Of course, the need for prandial or nutritional insulin will depend on the patient’s status (Table 3).50 Subcutaneous insulin can be augmented with premeal supplemental-dose insulin to correct premeal hyperglycemia.50

Sliding scale insulin is not recommended by the major medical societies.7 Sliding scale insulin usually consists of regular insulin given alone. This technique has been shown to be ineffective for several reasons. It is a reactive approach that can lead to rapid swings in blood glucose, resulting in hyperglycemia and hypoglycemia. It can increase the risk for “stacking” of insulin, which can precipitate hypoglycemia. It is often an admission regimen that is likely to be used throughout hospitalization without appropriate modification for changes in the patient’s health status. Clinical trials have shown that it is less effective than scheduled basal bolus insulin (Figure 6).51

How does one establish a scheduled subcutaneous insulin regimen if the patient was not receiving IV insulin? This is usually a weight-based calculation, again starting with calculating a total daily dose, then dividing it into basal and prandial components. One can start higher or lower. A conservative start is between 0.5 and 0.6 units of insulin per kg of body weight per day.

**Table 2: Insulin Terminology**

<table>
<thead>
<tr>
<th>Type of Insulin</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal insulin</td>
<td>-Controls fasting and premeal glucose -Neutral protamine Hagedorn or long-acting basal insulin analogues</td>
</tr>
<tr>
<td>Nutritional insulin</td>
<td>-Controls glucose from nutritional sources such as discrete meals, tube feeds, or total parenteral nutrition -Short-acting (regular) insulin or rapid-acting insulin analogues</td>
</tr>
<tr>
<td>Supplemental/correctional insulin</td>
<td>-Used to cover unexpected hyperglycemia that was not controlled by scheduled basal and nutritional insulin -Short-acting (regular) insulin or rapid-acting insulin analogues</td>
</tr>
<tr>
<td>Sliding scale insulin</td>
<td>-Usually consists of regular insulin given in the absence of regularly scheduled insulin or any basal insulin</td>
</tr>
</tbody>
</table>

**Figure 5: Basal, Bolus, and Correctional Insulin to Meet Physiological Insulin Needs**

- **Basal insulin**
  - Controls fasting and premeal glucose
- **Nutritional or Mealtime insulin (bolus)**
  - Controls fasting and premeal glucose
- **Correction or Supplemental insulin**
  - Supplements regular insulin as needed

**Normal Secretory Pattern of Insulin**

- **Breakfast**
- **Lunch**
- **Dinner**
- **Bedtime**

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(units/kg/day) for patients with type 2 diabetes.\textsuperscript{52} If there are concerns about hypoglycemia, then a lower total daily dose may be used to start, for example, 0.3 to 0.4 units/kg/day.\textsuperscript{52} Factors such as increased age or impaired renal function may be considered risk factors for hypoglycemia.\textsuperscript{53} Best practice suggests to administer basal insulin once (glargine/detemir) or twice (neutral protamine Hagedorn) daily, at the same time each day. Rapid-acting (prandial) insulin should be given in 3 equally divided doses before each meal. Prandial insulin should not be given if a patient is not able to eat or misses a meal due to a procedure. Insulin doses should be adjusted according to the results of bedside blood glucose measurements.

Correctional insulin or supplemental insulin should be included as a component of a scheduled insulin regimen for treatment of blood glucose values above the desired target; if high glucose levels persist, then doses should be adjusted the following day. The total daily dose should be adjusted up or down based on past response to insulin, presence of hyperglycemia-inducing agents (eg, corticosteroids), stress, and other factors. There are many types of insulin products available. Table 4 summarizes the pharmacokinetic features of these agents.\textsuperscript{54} Long-acting basal insulin analogues provide background insulin needs that closely mimic the body’s slow steady release of insulin, more so than intermediate-acting insulin. Rapid-acting insulin analogues (aspart, glulisine, lispro) mimic the release of insulin after carbohydrate injection much more than rapid-acting insulin and do not require administration 30 minutes prior to food intake to “line up” with glucose excursions.\textsuperscript{55} As such, they are associated with less hypoglycemia, and thus may be preferred in the inpatient setting.
particularly when it may be difficult to know if the patient will be eating or not. For more information on insulin in the inpatient setting, see the article by Morales in this supplement.

**Oral Agents and Non-Insulin Antihyperglycemic Agents**

There is no extensive published experience with non-insulin agents in the hospital. Each of the major classes of oral agents has features that limit its use in the hospital setting. Sulfonylureas may lead to hypoglycemia if nutrition is interrupted, and some of them are contraindicated in patients with renal impairment. Metformin is contraindicated in the setting of decreased renal blood flow, surgery, and with use of iodinated contrast dyes. Thiazolidinediones are not rapidly effective; they also are associated with edema and heart failure. The incretin-based therapies (glucagon-like peptide-1 [GLP-1] receptor agonists, dipeptidyl peptidase-4 inhibitors) have a greater effect on postprandial glucose and would be effective primarily in patients who are able to eat. GLP-1 receptor agonists are associated with nausea.

**Hypoglycemia**

Hypoglycemia is a legitimate safety concern with insulin therapy. It is important to have a clear definition of hypoglycemia. In the hospital setting, this definition should be used as a signal to adjust or discontinue insulin therapy. Therefore, the threshold for altering therapy should not be set too low. The ADA defines hypoglycemia as a blood glucose level less than 70 mg/dL; both the AACE and ADA agree that insulin therapy should be adjusted if this occurs and that insulin regimens be reevaluated at levels of 100 mg/dL. There should be hypoglycemia protocols in place that allow nurses to treat without delay (ie, without waiting for doctor orders). Insulin infusions should be discontinued (or reduced, if the patient is a type 1 diabetic), and glucose administered. The route, dose, and form of glucose administration will depend on the patient’s level of cognition (Figure 7). Repetition of blood glucose monitoring and of glucose administration is required until the patient is stabilized. Assessing causality and adjusting treatment is then necessary. Look for the cause of hypoglycemia and determine if other treatment changes are needed.

**Conclusion**

Achieving glycemic control in the hospital setting remains challenging. Pharmacists are integral members of the multidisciplinary team required to implement cultural change to achieve systemwide improvements. Pharmacists seeking to implement the findings of published evidence into their practice face many potential barriers. For more on the role of pharmacists, see the article by Triplitt et al in this supplement. There are no standardized “how to” guidelines, there are no
perfect protocols, and change can be slow and tedious. Glycemic control in the hospital may be improved by assessing current treatment approaches, making incremental changes, and looking for obvious ways to improve the safe and effective delivery of insulin therapy. Although the data continue to evolve, it is generally accepted that extremes of inpatient hyperglycemia and hypoglycemia should be avoided. Recent data show that across the nation, hospitals are tracking their efforts and that the prevalence of severe hypoglycemia is low (Figure 8). Pharmacists should be aware of current treatment guidelines and insulin regimens that are physiologically based with a focus on preventing hyperglycemia and hypoglycemia.

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**Introduction**

Insulin is the cornerstone for the management of inpatient hyperglycemia control for many reasons. Unlike insulin, there is little published evidence supporting the use of non-insulin therapies in the hospital setting. Oral therapies are not easily titrated to the changing needs of the acutely ill hospitalized patient and many patients may have contraindications to non-insulin agents as a result of their conditions (e.g., renal impairment, congestive heart failure) or medications, or they may temporarily lack the ability to take oral medications. Furthermore, insulin has distinct advantages for managing hyperglycemia in the hospital setting: it corrects hyperglycemia rapidly and effectively, its efficacy is not dose-limited, it is easily titrated, and in its modern formulations, it has no contraindications to its use.

Insulin does, however, have some disadvantages, including a low therapeutic index and hypoglycemia as a dose-limiting toxicity. Additionally, it is a “high-alert” medication, meaning that inappropriate or unsafe use is highly likely to cause the patient severe harm. Therefore, strategies that maximize its safe and effective use are essential to ensuring appropriate patient outcomes.

**Hypoglycemia and Hypoglycemia Definitions and Implications**

Table 1 provides the reader with the American Association of Clinical Endocrinologists and American Diabetes Association’s recommendations for glucose levels that warrant attention and action, along with physiologic implications of hyperglycemia. Hypoglycemia is associated with increased morbidity, mortality, and length of stay in multiple populations of hospitalized patients (critically ill and noncritically ill patients). Importantly, hyperglycemia in the hospital setting is associated with poor outcomes in both patients with known diabetes and those without diabetes. In fact, the prognosis is worse in patients with no known diabetes, so hyperglycemia in the hospital setting should not be ignored.

Interventional studies have shown that improving hyperglycemia improves patient outcomes, but this has to be balanced by avoiding hypoglycemia, which is also associated with increased mortality in the hospital setting and after discharge (Figure 1). Hypoglycemia is also associated with increased length of stay and increased hospital costs (Table 2 and Table 3). Efforts to implement intensive glycemic control in critically ill patients have been associated with an increased risk of hypoglycemia and death and have caused the reevaluation of glycemic targets in the hospital. The Normoglycemia in Intensive Care Evaluation–Survival Using Glucose Algorithm Regulation study was a multicenter trial involving 6104 patients wherein the intensive-control group achieved a mean blood glucose level of 115 mg/dL compared with the conventional treatment group, who achieved a mean blood glucose level of 144 mg/dL. The intensively treated group had an increase of 2.6 percentage points in the absolute risk of death at 90 days. Not surprisingly,

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**Table 1: AACE/ADA Target Inpatient Hyperglycemia and Hypoglycemia Definitions and Implications**

<table>
<thead>
<tr>
<th>BG Value</th>
<th>Definition</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;140 mg/dL</td>
<td>Hyperglycemia</td>
<td>Pre-meal levels persistently above this level may necessitate treatment</td>
</tr>
<tr>
<td>&gt;180 mg/dL</td>
<td>Hyperglycemia</td>
<td>No random blood glucose levels should be, in general, above this goal</td>
</tr>
<tr>
<td>&lt;70 mg/dL</td>
<td>Hypoglycemia</td>
<td>Standard definition in outpatients, correlates with the initial threshold for release of counter-regulatory hormones</td>
</tr>
<tr>
<td>&lt;40 mg/dL</td>
<td>Severe hypoglycemia</td>
<td>Increased mortality, cognitive impairment begins at 50 mg/dL in normal individuals</td>
</tr>
</tbody>
</table>

*Some patients may be maintained at a glucose range below and/or above these cut-off points.
Reassess insulin regimen if BG levels fall below 100 mg/dL.
AACE = American Association of Clinical Endocrinologists; ADA = American Diabetes Association; BG = blood glucose.
severe hypoglycemia occurred more frequently in the group of patients randomly assigned to intensive therapy. Attempts to understand the reasons for this led to a detailed assessment of data by the investigators on hypoglycemia and the risk of death from their previously published study. More frequent hypoglycemia and severe hypoglycemia in the absence of insulin therapy were associated with a higher risk of death, raising the question if hypoglycemia is a marker for more severe underlying disease or an inappropriate counter-regulatory mechanism.

A Brief Look at the Pathophysiology Associated with Hyperglycemia and Hypoglycemia

Before discussing approaches to improving the safety and effectiveness of inpatient insulin therapy, it is helpful to review some of the mechanisms that we currently understand about the pathophysiology of hyperglycemia and hypoglycemia in hospitalized patients.

The presumed links between high blood glucose levels and poor outcomes have centered on the immune system, vascular responses, mediators of inflammation, and brain cell responses, although they are by no means fully understood. Hyperglycemia causes immune suppression, although the overall magnitude and mechanism by which it does so are somewhat unclear. Acute hyperglycemia has a number of effects on the cardiovascular system. It impairs protective mechanisms against ischemic insult and may induce cardiac myocyte death by ischemia-reperfusion cellular injury or through an increased rate of apoptosis. Other effects include blood pressure changes, catecholamine abnormalities, and electrophysiolog-

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**Figure 1**: Inpatient Hypoglycemia Was Strongly Correlated with Inpatient and Post-Discharge Death and Increased LOS in Non-ICU Settings. 4368 Admissions of 2582 Patients with Diabetes; Hypoglycemia: BG ≤ 50mg/dL

**Table 2**: Retrospective Analysis of the Length of Stay and Inpatient Mortality in Patients with Diabetes Who Had an Episode of Hypoglycemia in a Noncritical Care Setting (N = 6374 admissions)

<table>
<thead>
<tr>
<th>Lowest Recorded Blood Glucose Level</th>
<th>Number of Admissions</th>
<th>Length of Stay (Relative Risk)</th>
<th>Inpatient Mortality (Relative Risk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;70 mg/dL</td>
<td>5726</td>
<td>1.0 (reference value)</td>
<td>1.0 (reference value)</td>
</tr>
<tr>
<td>&gt;40-70 mg/dL</td>
<td>500</td>
<td>1.51</td>
<td>1.62</td>
</tr>
<tr>
<td>≤40 mg/dL</td>
<td>148</td>
<td>2.33</td>
<td>2.05</td>
</tr>
</tbody>
</table>
Safety of Insulin in Inpatient Glycemic Management

Table 3: Hypoglycemia Is Associated with Increased Health Care Costs\(^2^3\)

<table>
<thead>
<tr>
<th>Hospital Outcomes, Mean</th>
<th>Patients with Hypoglycemia (Blood Glucose &lt;70 mg/dL)</th>
<th>Patients Without Hypoglycemia</th>
<th>Between-Group Difference or Odds Ratio (Unadjusted)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean Value</td>
<td>n</td>
<td>Mean Value</td>
</tr>
<tr>
<td>Length of hospital stay, days</td>
<td>8234</td>
<td>11.7</td>
<td>95,579</td>
<td>5.1</td>
</tr>
<tr>
<td>Hospital mortality, %</td>
<td>7994</td>
<td>4.8</td>
<td>93,012</td>
<td>2.3</td>
</tr>
<tr>
<td>Discharged to skilled nursing facility, %</td>
<td>7787</td>
<td>26.5</td>
<td>93,134</td>
<td>14.5</td>
</tr>
<tr>
<td>Total hospital charges, 2006 $</td>
<td>6020</td>
<td>85,905</td>
<td>72,681</td>
<td>54,038</td>
</tr>
</tbody>
</table>

Figure 2: Maintaining Physiologic Insulin Delivery in the Hospital: Scheduled Basal Bolus Subcutaneous Insulin plus Correctional Insulin

Insulin Therapy in the Hospital

In critically ill patients, intravenous insulin therapy is the treatment of choice to control hyperglycemia. This is generally accomplished through the use of standardized infusions of regular human insulin.\(^2^3\) There are few, if any, advantages to the use of insulin analogues in the critical care setting. Intravenous administration is not an approved indication for insulin analogues because of its expense and lack of favorable pharmacokinetic and pharmacodynamic profiles when infused continuously. A validated insulin infusion protocol that is well tolerated, and is most appropriate and practical for the respective institution (based on available resources and support), is recommended, along with a hypoglycemia protocol that includes frequent blood glucose monitoring.\(^3^2\)

The range of insulin agents needed in general medical and surgical units is greater than in the intensive care unit. In noncritically ill hyperglycemic patients, the use of regularly scheduled basal bolus insulin (along with correctional insulin) is recommended, rather than sliding scale insulin regimens, for the most physiologic approach to correcting hyperglycemia (Figure 2).\(^1^5\) This requires the use of at least 2 types of insulin: a long-acting insulin to cover basal or background insulin needs between meals, and a short- or rapid-acting insulin to address prandial or mealtime-related glucose excursions. In noncritically ill patients, there are advantages to insulin analogues over regular human insulin and neutral protamine Hagedorn (NPH) insulin. As demonstrated in Figure 3, regular

ic changes. Hyperglycemia may also result in effects that favor thrombosis through increased levels of plasminogen activator inhibitor-1 and endothelial dysfunction. Moderate elevations of glucose may result in the release of inflammatory cytokines such as interleukins and tumor-necrosis factors, among others. Acute hyperglycemia is associated with cerebral ischemic damage and many of the factors that link hyperglycemia to cardiovascular dysfunction may also contribute to cerebrovascular dysfunction.\(^2\) Similarly, hypoglycemia is also associated with cardiac arrhythmias through calcium and potassium channel flux, troponin and troponymosin binding, inflammation, and central nervous system dysfunction. Like hyperglycemia, hypoglycemia appears to be a pro-inflammatory and arrhythmogenic state.\(^2^9\) For example, hypoglycemia can cause an acquired long QT syndrome through sympathoadrenal stimulation, which includes catecholamine-mediated hypokalemia.\(^3^0\)

All available evidence suggests that both hyperglycemia and hypoglycemia should be avoided in inpatients.\(^3^1\)
human insulin, because it has to be absorbed through the subcutis, has a longer onset of action than rapid-acting insulin analogues (aspart, glulisine, lispro), which were designed to be more rapidly absorbed. In general, regular human insulin must be injected at least 20 to 30 minutes prior to meals, which may be difficult to coordinate (whether by nursing schedule, dietary delivery, or patient activity) with food intake. In contrast, the rapid-acting analogues can be injected with the first bite of food and still be effective. The rapid-acting analogues also have a shorter duration of action, which reduces the risks of intra-meal hypoglycemia.

### Basal Insulin Analogaues

Looking more closely at basal insulin analogues, which have been a major therapeutic advance in the management of diabetes, and have been pharmaceutically more difficult to develop, there are many interesting aspects to consider. Some of the properties of an ideal basal insulin analogue are summarized in Table 4. For a long time, NPH insulin was the only longer-acting insulin available. It is an intermediate-acting agent, however, with a pronounced peak, with a duration of action far less than 24 hours—typically 6 to 8 hours. This means that it may still have activity at the time a mealtime dose of insulin is administered, with the potential for insulin “stacking” and an increased risk of hypoglycemia. Additionally, NPH is associated with substantial intra- and inter-patient variability. It may have a role in the hospital setting for patients receiving tube feedings or for patients receiving high-dose corticosteroids, which can result in greater postprandial glycemic excursions. Insulin glargine, the first long-acting basal insulin analogue, and insulin detemir, can both provide once-daily basal insulin coverage, and both are relatively, but not entirely, peakless; their pharmacokinetic profiles change slightly with dose, and duration of action is dose-dependent. In some patients, particularly those with low insulin requirements or type 1 diabetes, there may be a need to give a long-acting insulin analogue twice a day; insulin detemir is indicated for once- or twice-daily use.

The important benefit of long-acting basal insulin analogues over NPH insulin is a decreased risk of hypoglycemia, particularly nocturnal hypoglycemia. This safety advantage has been observed in trends of hypoglycemia rates in the major landmark trials in diabetes—the United Kingdom Prospective Diabetes Study, the Diabetes Control and Complications Trial (where only NPH insulin was available), the Treating To Target in Type 2 diabetes study (4-T), where insulin detemir was the basal insulin analogue used, and Outcome Reduction with an Initial Glargine Intervention trial (where the insulin glargine was evaluated). Sleep markedly weakens the neuroendocrine defense mechanism against hypoglycemia by shifting the glycemic threshold for counter-regulatory activation to lower
levels, making nocturnal hypoglycemia particularly worrisome.44

Emerging Basal Insulin Analogues

The quest continues to improve the therapeutic index of insulin therapy, particularly basal insulin replacement therapy. As stated before, hypoglycemia is the limiting factor in the search for optimal glycemic control with insulin therapy. Efforts to reduce pharmacokinetic and pharmacodynamic variability, provide true 24-hour coverage, and reduce the risks of hypoglycemia are ongoing. Emerging “ultra long-acting” basal insulin analogues may more closely match the desired parameters of an ideal basal insulin analogue. The investigational agent LY2605541 is a pegylated form of insulin lispro, designed to have a long-acting, once-daily profile. Currently in phase 2 development, the available data show that it has less intra-day variability to insulin glargine and may be associated with some weight loss (or at least no weight gain, which is typical of insulin therapy) in patients with type 2 diabetes (Table 5).45 More importantly, in patients with type 1 diabetes, LY2605541 is associated with an approximately 25% lower risk of nocturnal hypoglycemia compared with insulin glargine (Table 6).46 Rates of overall hypoglycemia were a bit greater (this may have to do with pushing of the dose in these dose-finding studies, since the glycated hemoglobin reductions were also greater, which may or may not be seen when this insulin is used clinically).46 Patients receiving pegylated lispro lost weight (−0.6 kg), whereas those treated with insulin glargine gained weight (0.3 kg; treatment difference, −0.8 kg; \( P = .001 \)). Alanine aminotransferase and aspartate aminotransferase remained within normal range but were significantly higher with pegylated lispro.46

In November 2012, an advisory panel to the FDA recommended approval of insulin degludec. In January 2013, the European Commission granted marketing authorization for long-acting insulin degludec. In a Complete Response Letter issued in February, the FDA requested data from a dedicated cardiovascular outcomes trial before the review of the New Drug Application can be completed. This basal insulin, with improved pharmacokinetic properties, is produced by acylation of fatty acids that enable soluble, high-molecular weight complexes to form postinjection. These highly self-associated hexamers then slowly disassemble

![Figure 3: Time-Action Profiles of Insulin Products](33)

NPH = neutral protamine Hagedorn.
Reprinted with permission from reference 33.

![Figure 4: Formation of Insulin Degludec](47)

Insulin degludec is injected subcutaneously as a zinc phenol formulation containing insulin degludec dihexamer. Rapid loss of phenol changes the degludec hexamers and multi-hexamer chains form. With slow diffusion of zinc, these chains break down into dimers, which quickly dissociate into readily absorbed monomers.
Reprinted with permission from reference 47.
Figure 5: Insulin Degludec® Versus Insulin Glargine (Both plus Rapid-Acting Insulin) in Patients with T2DM: Confirmed Nocturnal Hypoglycemia

- Insulin degludec + Insulin aspart (n=753)
- Insulin glargine + Insulin aspart (n=251)

25% risk reduction
RR: 0.75
[0.58; 0.99] significant

**Conclusion**

The treatment of inpatient hyperglycemia has been a journey, which started with very little guidance and data, to a place where guidelines have been developed and updated as evidence and experience have emerged to better guide clinicians. The systematic review of available data and progression of practical recommendations and guidance on appropriate treatment goals, insulin regimens, and pharmaceutical advancements are improving the ability to achieve safe and effective management of hyperglycemia in the hospital setting. Practical attention to details such as the development and implementation of protocols for treating hyperglycemia, hypoglycemia, and the use of more physiologic insulin agents and regimens supports the safe use of insulin in the hospital setting.

**References**


42. Holman RR, Farmer AJ, Davies MJ, et


A Snapshot of the Various Roles of Pharmacists’ Participation in Influencing Inpatient Glycemic Control

Curtis Triplitt, PharmD, CDE; Paul M. Szumita, PharmD, BCPS; Susan Ann Cornell, BS, PharmD, CDE

Introduction

The attitude and management approaches toward hyperglycemia in the hospital setting have evolved substantially over the past decade. Prior to that, there was a general lack of recognition of the need to identify and treat hyperglycemia among hospitalized patients. To safely achieve recommended targets, the multidisciplinary involvement of pharmacists, nurses, and physicians, as well as other health care professionals, is needed. Pharmacists are critical to the safe and effective use of insulin in the inpatient setting and the education of patients as they are transitioned to outpatient care. The role of pharmacists varies greatly in part because hospitals vary greatly in how they have adopted recommendations for managing hyperglycemia in the inpatient setting, their use of protocols, the resources available to them, the culture within which they must work, and the nature of their patient populations. There are many opportunities for pharmacists to increase their involvement in improving glycemic control, just as there are many competing priorities for their time and resources. This article provides an overview of some of the different possibilities that exist and reflects the authors’ experiences.

Roles can be broadly categorized into those of systemic implementation or more specific glycemic control teams or patient-specific roles (Table).

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Department of Pharmacy Services
Brigham and Women’s Hospital
Pharmacy Administration; L-2
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Pharmacists have many roles in the management of glucose in the inpatient setting. I am an integral member of the multidisciplinary “steering committee/task force team” and manage glucose levels on an individual patient basis. At my institution, the steering committee is the “Diabetes Subcommittee” of the larger Pharmacy and Therapeutics Committee with oversight of all things

<table>
<thead>
<tr>
<th>Table: Potential Roles for Pharmacists in Implementing Improvements in Inpatient Glycemic Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systematic implementation</td>
</tr>
<tr>
<td>On or lead glycemic management steering committee/task forces</td>
</tr>
<tr>
<td>Develop/implement guidelines and order sets</td>
</tr>
<tr>
<td>Assessment of practice—pre and post change (PDSA [plan, do, study, act])</td>
</tr>
<tr>
<td>Edit the guidelines and order sets per feedback and metrics</td>
</tr>
<tr>
<td>Point person for any glucose-related issue in the institution</td>
</tr>
<tr>
<td>Implementation of order sets and guidelines on a patient-specific basis</td>
</tr>
<tr>
<td>Prioritizing glucose management in each of the sub-specialized areas of the hospital</td>
</tr>
<tr>
<td>Advocate or champion for glucose on non-glucose management teams (intensive care unit, internal medicine, surgical patient, transplant, oncology)</td>
</tr>
</tbody>
</table>

- Practices in an urban, 800-bed hospital
- Protocols for critically ill patient are fully implemented, with thresholds for intravenous (IV) insulin set at >150 mg/dL
- Hypoglycemia protocols also fully implemented (threshold set at 70 mg/dL)
- Protocols for perioperative hyperglycemia also fully implemented, as are those for noncritically ill patients
- Institution uses computerized order entry for insulin therapy
- Integral member of diabetes management team
- Barriers are numerous—daily/weekly/monthly/yearly continuous journey
- The key is to have a multidisciplinary team of champions to help lead change and sustain gains
related to glucose management. My fellow Brigham and Women’s Hospital pharmacists and I also manage glucose on a patient-specific basis as clinical pharmacists in the intensive care unit, general wards, and other areas of the hospital, applying the strategies recommended by the steering committee.

“Physical champions” refers to small group of individuals willing to accept the responsibility to encourage positive changes in clinical practice. Our multidisciplinary team consists of a group of physical champions responsible for oversight, development, implementation, education, and quality assessment of policies, order sets, protocols, and guidelines. In preparation for discharge, we also coordinate efforts for patients and staff to have access to critical glycemic management medications and materials, including glucose monitors and test strips for patient self-testing. This steering committee/task force is crucial to ensure policies, order sets, protocols, and guidelines are continually critiqued, monitored, and improved. We have researched compliance with IV insulin protocols, acceptance of insulin delivery devices, glucometrics, and outcomes with both IV and subcutaneous insulin regimens.

To improve management one needs an indicator that correlates with blood glucose levels during the short interval of an inpatient stay, usually a few days; therefore, glucometrics are good measurements for quality in the inpatient setting. Glycated hemoglobin responds too slowly to measure glucose fluctuations over days. Instead, studies of inpatient glycemia have correlated outcomes with glucose measurements: both single glucose values (admission, random, fasting, and maximal glucose) and mean glucose values (admission, first 24 hours of hospitalization, fasting, post-operative, and overall mean).

We continue to find challenges to overcome within our institution. There are seemingly countless barriers to glycemic management in the inpatient setting that we are continually analyzing. One of our recent challenges has been developing guidelines for the management of glucose in the pre-, peri-, and post-procedure/operative settings. These guidelines are particularly challenging given the diverse practice settings and lack of consensus guidelines in the literature in this setting.

Our pharmacists on various team/care areas (intensive care unit, emergency department, oncology, orthopedics, general surgery, general/internal medicine, cardiology, vascular and transplant, and others) help implement the hospital guidelines in all areas of the hospital that pharmacists cover. A part of every inpatient clinical pharmacist’s duties includes oversight of glucose management. Unless the patient’s admitting diagnosis is directly related to complications of diabetes, glucose management may not be an area of focus of the primary team; therefore a great opportunity for clinical pharmacists on that team is to assist with proper management pathways. The Figure shows a stepwise approach that can be taken to begin to address glucose control in the hospital setting.²

Curtis Triplitt, PharmD, CDE
Assistant Professor, Department of Medicine
Division of Diabetes
University of Texas Health Science Center at San Antonio
Texas Diabetes Institute
San Antonio, Texas

• Practices in an urban, 500-bed hospital system
• Protocols for critically ill patients are fully implemented, with thresholds for IV insulin set at >180 mg/dL
• Hypoglycemia protocols also fully implemented (threshold set at 70 mg/dL)
• Protocols for perioperative hyperglycemia and noncritically ill patients partially implemented
• Institution uses computerized order entry for insulin therapy
• Acts as consultant for select cases from staff, as no glycemic control team exists

As mostly an outpatient diabetes specialist pharmacist, my role is as a consultant to inpatient pharmacists. I am asked specific questions about all aspects of inpatient glycemic control. Questions have ranged from those about glycemic control in the transplant setting, to hypoglycemia treatment in inpatients, to advising on how basal insulin in general medicine wards should be administered. In addition, I also serve on the Pharmacy and Therapeutics Diabetes/Endocrine subcommittee. Through this, inpatient and outpatient issues on glycemic control agents are discussed. We are currently involved in addressing the use of oral diabetes agents in the inpatient setting. Our general policy has been to discontinue their use in favor of insulin therapy, which is more suited to the changing needs of acutely ill patients, and who may also have transient contraindications to oral agents. However, some clinicians may feel strongly about continuing oral agents, especially in stable patients ready to be discharged in the next 1 to 2 days. Through a non-formulary request, this is usually granted approval for use, but must be closely monitored. As I have traveled and spoken at many hospitals, I find our hospital is actually in the minority by not allowing oral agents to continue. Clearly, if the obvious issues of contraindications are aggressively addressed, then oral agents could be continued. Proper use, proper monitoring, and timely discontinuation in the event of serious adverse events are important roles for the pharmacist in developing policies and procedures.

Several years ago we had hospitalist champions that forged consensus on implementation of inpatient glycemic control algorithms in surgery and critical care areas. Surprisingly, at least 3 different protocols are currently used throughout the hospital, as recommended by the individual hospitalists/specialists in those areas. Much work is still to be done in our institution, yet on a daily basis, the staff do an incredible job. The greatest barrier to glycemic control in our institution is
Pharmacists’ Role in Inpatient Glycemic Control

often time—time to gather, assess, and analyze glucometrics, find consensus, and implement change in such a rapidly changing environment where wards are full. This is why glycemic champions are important as the driving force for change. What can pharmacists do? Pharmacists must be up-to-date with the current evidence base about inpatient glycemic control. Understanding the underpinnings of currently recommended glycemic control on the inpatient side is paramount. Without this knowledge, becoming an “inpatient glycemic champion” is unlikely. Understanding what your institution currently does is important—are protocols in place? How many protocols are in place? How closely do protocols match those suggested by national consensus statements? What barriers or educational gaps need to be addressed? What processes are in place? Building consensus, implementing change,

<table>
<thead>
<tr>
<th>Figure: Stepwise Approach to Glucose Control Interventions</th>
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<tbody>
<tr>
<td><strong>Stepwise Approach to Glucose Control Interventions</strong></td>
</tr>
<tr>
<td>Identification of the inpatient population facing glucose control problems</td>
</tr>
<tr>
<td>Creation of the “physical champion”</td>
</tr>
<tr>
<td>Formation of multidisciplinary advisory committee/team</td>
</tr>
<tr>
<td>Synthesizing data</td>
</tr>
<tr>
<td>Determining target blood glucose level</td>
</tr>
<tr>
<td>Assessing existing glucose control protocols and institution resources</td>
</tr>
<tr>
<td>Clinician compliance assessment</td>
</tr>
<tr>
<td>Intervention/protocol selection and development</td>
</tr>
<tr>
<td>Continuous education provided to all hospital clinicians and support staff</td>
</tr>
<tr>
<td>Pilot intervention/protocol</td>
</tr>
<tr>
<td>Endorsement from institutional credible bodies</td>
</tr>
<tr>
<td>Implementation of protocol/intervention</td>
</tr>
<tr>
<td>Publication of efficacy, safety, and compliance data</td>
</tr>
<tr>
<td>Available published literature analysis</td>
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<tr>
<td>Existing institutional guidelines</td>
</tr>
<tr>
<td>Efficacy and safety</td>
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<tr>
<td>Compliance assessment</td>
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<tr>
<td>Quality assessment and improvement</td>
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<tr>
<td>End-user satisfaction and feedback</td>
</tr>
<tr>
<td>Benchmarking against other institutions</td>
</tr>
<tr>
<td>Assistance in local and national guideline development</td>
</tr>
</tbody>
</table>

CPOE = computerized physician order entry.

<table>
<thead>
<tr>
<th>Easy ordering</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical reminders</td>
</tr>
<tr>
<td>Incorporation into order entry template (paper or CPOE)</td>
</tr>
<tr>
<td>Coordination of equipment purchasing</td>
</tr>
<tr>
<td>Glucometers, testing strips, Web-based programs, etc</td>
</tr>
</tbody>
</table>

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Pharmacists’ Role in Inpatient Glycemic Control

being reasonable in expectations, and accepting compromise are the ways to build quality improvement over time. Improving inpatient glycemic control is a process and a journey.

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Assistant Professor, Department of Pharmacy Practice
Midwestern University Chicago College of Pharmacy
Downers Grove, Illinois

- Works at a community clinic that transitions patients from 6 different hospitals
- Is a fully integrated member of the team
- Has fully implemented hypoglycemia protocol in institution, with <70 mg/dL set as threshold
- Institution uses computerized order entry for insulin orders

Transitions of care, described as situations when a patient leaves one health care setting and moves to another, are challenging and have been shown to compromise patient care and safety.4 Studies have documented that medication errors frequently occur during transitions of care and that medication reconciliation can reduce such events.5,6 Pharmacists can have a large role in preventing medication errors and improving patient care by providing medication reconciliation at various transition points.

At the DuPage Community Clinic (DCC), a free clinic for residents of DuPage County, Illinois, patients are provided primary care services by a health care team. The DCC collaborates with 6 area hospitals to provide health care services for the patients. My role at the DCC is to develop and oversee the clinical pharmacist–student pharmacist functions. This includes development of the program, recruiting, training, scheduling, pharmacist services implementation, and staffing.

- Triage
  - After the patient is triaged and in the exam room a student-pharmacist will:
    - Perform phase 1 of a medication reconciliation and management service:
      □ Review with the patient their current medications and compare it with DCC medication sheet in the chart.
      □ Assess if the patient is on other medications from another provider, emergency department or critical care visit, or is self-treating. This should include an assessment of any over-the-counter medications a patient may be taking.
      □ List any discrepancies found with a patient’s medications, and report any discrepancies to DCC clinic staff and the pharmacist supervisor.
    - Students also assess the patient’s adherence using the following questions for each medication the patient currently takes:
      - What are you taking this medicine for?
      - How are you currently taking this medicine?
      - What problems have you noticed since taking this medicine?
      - What days of the week do you skip or not take your medication?
      - How often does this happen?
    - Discharge
      - After the patient has been seen by the primary care physician, the student with a pharmacist supervisor will implement phase 2 of the medication reconciliation and management service:
        □ Review and educate the patient on the best way to take each of their medications, including new medications and OTC products.
        □ Explain and discuss discontinued medications.
        □ Assess and review any device technique with the patient for optimal drug delivery (eg, insulin pens, self-monitoring blood glucose meters).
        □ Provide a personalized medication schedule for the patient.
    - After their pharmacist supervisor reviews and signs the schedule form

- Diabetes services
  - Blood sugar monitoring – checkups
    □ Patients are referred to and scheduled with a pharmacist and students for review of their BS record. The pharmacist adjusts and initiates diabetes medication dosing changes, if needed, under protocol.
  - Diabetes education visits
    □ Pharmacists provide diabetes self-management education and training for patients with diabetes and pre-diabetes.

Conclusion
Pharmacists are an integral part of the multidisciplinary team ensuring the safe and effective implementation of inpatient hyperglycemic control and insulin usage and may play different roles depending on where their specific institution is in addressing the important issue of inpatient glycemic control. Important questions for the reader to consider are whether or not blood glucose goals are in place for different patient populations, whether these are consistent with current medical society recommendations;7,9 if protocols are in place for the safe and effective use of insulin,10 and what role the pharmacist can play as a team member either on a system basis or in a patient-specific role.11

References
Pharmacists’ Role in Inpatient Glycemic Control


Clinical Pearls to Improve Safety and Patient Care in the Hospital Setting: Addressing Challenges of Insulin Therapy

1. Which of the following statements is CORRECT about hyperglycemia/diabetes in the hospital setting?
   A. Hyperglycemia may be present in up to 50% of hospitalized patients; 20% of those may have no prior history of diabetes.
   B. Patients with documented hyperglycemia while hospitalized should have an A1C test performed before discharge if one has not been performed in the previous 2 to 3 months.
   C. An A1C test is as sensitive as the use of fasting plasma glucose levels.
   D. Hospitalization accounts for approximately 30% of the direct costs of diabetes.

2. Which of the following statements is NOT correct about hyperglycemia/diabetes in the hospital setting?
   A. Hyperglycemia in acutely ill patients is a protective mechanism.
   B. The risk of hyperglycemia is worse in patients with no prior history of diabetes than in those with diabetes.
   C. Hyperglycemia is associated with increased lengths of stay.
   D. Hyperglycemia is associated with an increased risk of hospitalization.

3. Which of the following is the CURRENT recommended target blood glucose level for critically ill patients?
   A. 80-110 mg/dL
   B. 110-140 mg/dL
   C. 140-180 mg/dL
   D. 180-200 mg/dL

4. Which of the following statements is NOT correct about insulin in the hospital setting?
   A. Fixed insulin protocols are preferred to flexible protocols in the hospital setting.
   B. IV insulin infusion concentrations should be standardized throughout the hospital.
   C. Insulin is a high-alert medication but it is still the preferred method of controlling glucose levels in the hospital setting.
   D. Potassium should be monitored when IV insulin is being administered.

5. JL has been receiving 4 units of IV insulin per hour for the past 4 hours of his ICU stay. He is stable and will be transferred to a general medical floor. What is his 24-hour insulin requirement, using the methodology described in the first article?
   A. 96 units
   B. 75 units
   C. 58 units
   D. 29 units

6. When should JL receive his first dose of basal insulin?
   A. When his IV insulin is discontinued
   B. At least 2 hours before his IV insulin is discontinued
   C. Two hours after his IV insulin is discontinued
   D. In the evening or at bedtime

7. What will be JL’s prandial insulin dose?
   A. 5 units
   B. 10 units
   C. 20 units
   D. 30 units

8. Which of the following is the definition of “sliding scale” insulin?
   A. Controls fasting and premeal glucose
   B. Controls glucose from nutritional sources such as discrete meals, tube feeds, or total parenteral nutrition
   C. Used to cover unexpected hyperglycemia that was not controlled by scheduled basal and nutritional insulin
   D. Usually consists of regular insulin given in the absence of regularly scheduled insulin or any basal insulin

9. Which of the following statements is NOT correct about hypoglycemia in the hospital setting?
   A. Hypoglycemia causes effects that may favor thrombosis.
   B. Acute hypoglycemia has adverse effects on the cardiovascular system.
   C. Hypoglycemia is associated with cardiac arrhythmias.
   D. Hypoglycemia causes immune suppression.

10. Which of the following is the main advantage of long-acting insulin analogues versus NPH insulin?
    A. Greater A1C-lowering ability
    B. Lower cost
    C. Less frequent administration
    D. Lower risk of nocturnal hypoglycemia
Clinical Pearls to Improve Safety and Patient Care in the Hospital Setting: Addressing Challenges of Insulin Therapy

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1. Go online to http://tinyurl.com/PHARMACYBN, click on the blue “Assessment” button, and register or log in (if you previously registered on the site) to complete the activity posttest and evaluation.
   - You must type http:// when entering this URL into the address bar at the top of your Internet browser (do not enter this URL into your browser search box).
2. Complete the paper-based activity posttest and evaluation and fax it to 609-921-6428. Your statement of credit will be issued through CPE Monitor (you must provide your NABP e-Profile ID and Month and Day of Birth) within 6 to 8 weeks following your participation in the activity.

Please print clearly.

Name: _______________________________________________________________________________________
Address: _____________________________________________________________________________________
City: ___________________________ State: ____________________ ZIP: _________________________________
Country: _____________________________________________________________________________________
E-mail address: ________________________________________________________________________________
Reenter e-mail address: __________________________________________________________________________
NABP number: _________________________________________________________________________________
Month and day of birth (MM/DD format) ______________________________________________________________________
Signature ____________________________________________

Professional title:  □ Pharmacist  □ Pharmacy Technician  □ Other _________________________
Practice setting: □ Hospital Pharmacy  □ Other _________________________

POSTTEST FORM
Please refer to the posttest on page 26 for questions. Indicate your answers below, selecting 1 answer choice per question. A score of ≥70% is required to receive credit.

<table>
<thead>
<tr>
<th>Posttest Question Number</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>A</th>
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</table>
EVALUATION FORM

I certify that I have participated in this activity. □

Which of the following best describes your institution?

□ ≤100 beds □ 101-200 beds □ 201-300 beds □ ≥301 beds □ I don’t work in a hospital/health-system.

During a typical week, what percentage of inpatients in your institution have diabetes/hyperglycemia?

□ Less than 20% □ 20-39% □ 40-59% □ 61-79% □ 80% or more □ I do not know.

This activity has or will improve my (check all that apply) □ Competence □ Performance □ Patient outcomes

Please list 1 new concept you learned in this activity.

____________________________________________________
_____________________________________________________________________________________________________________

Please indicate your agreement with the following statements about this activity.

<table>
<thead>
<tr>
<th>Statement</th>
<th>Strongly Agree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>The content covered was useful and relevant to my practice.</td>
<td>5</td>
<td>4</td>
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<tr>
<td>The activity was fair, balanced, and free of commercial bias.</td>
<td>5</td>
<td>4</td>
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<td>The information learned during this activity will help improve my skills or judgment within the next 6 months.</td>
<td>5</td>
<td>4</td>
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<td>I am better able to state recent recommendations for glycemic targets for the inpatient setting and the value of glycemic control on outcomes during hospitalization.</td>
<td>5</td>
<td>4</td>
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<tr>
<td>I am better able to select appropriate types of insulin agents to meet patients’ physiologic insulin needs.</td>
<td>5</td>
<td>4</td>
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<tr>
<td>I am better able to formulate a plan to improve the safe and effective use of insulin in the hospital setting.</td>
<td>5</td>
<td>4</td>
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<tr>
<td>Instructional effectiveness and expertise of authors was excellent.</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>The learning method was excellent.</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Learning assessment questions were appropriate.</td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

If you selected 1 or 2 for any of above, please explain.

Based on the educational content of the activity, what will you do differently in the care of your patients? (check all that apply)

□ Implement new information or skill in my practice
□ Seek additional information
□ Do nothing differently—Current practice reflects activity recommendations
□ Do nothing differently—The content was not convincing
□ Do nothing differently—System barriers prevent me from modifying my practice
□ Not applicable. I have no patient contact.

Please list 1 modification you anticipate making in your practice (if none anticipated, please write “N/A”).

____________________________________________________________________________________________________

What barrier(s) have an impact on your ability to make the practice modification(s) indicated above (check all that apply)?

□ Institutional □ Lack of coordination/communication among care team members
□ Institutional protocols □ Team member resistance
□ Administrative support □ Adverse side effects of treatment
□ Time □ Other (please list) ____________________________

What information would you like to see in future activities that may help you address those barriers?

____________________________________________________________________________________________________________

Suggestions to improve this activity?

_______________________________________________________________________

What patient problems/challenges related to inpatient hyperglycemia in the hospital setting do you feel you are unable to address appropriately or to your satisfaction?

____________________________________________________________________________________________________________

Thank you for participating. As an added bonus, we will inform you of upcoming opportunities for future CPE-certified activities.