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Original Article

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**IMPACT OF A HYPOGLYCEMIA REDUCTION BUNDLE AND A SYSTEMS APPROACH TO
INPATIENT GLYCEMIC MANAGEMENT**

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Abstract

Objective:

Uncontrolled hyperglycemia and iatrogenic hypoglycemia represent common and frequently preventable quality and safety issues. We sought to demonstrate the effectiveness of a hypoglycemia reduction bundle, proactive surveillance of glycemic outliers, and an interdisciplinary data-driven approach to glycemic management.

Methods:

Population- all hospitalized adult non-critical care (non-ICU) patients with hyperglycemia and / or a diagnosis of diabetes admitted to our 550 bed academic center across five calendar-years (CY).

Interventions – hypoglycemia reduction bundle targeting most common remediable contributors to iatrogenic hypoglycemia; Clinical decision support in standardized order sets and glucose management pages; Measure-vention (Daily *measurement* of glycemic outliers with concurrent *intervention* by the inpatient diabetes team); Educational programs.

Measures and analysis - Pearson chi-square value with relative risks (RRs) and 95% confidence intervals (CI) were calculated to compare glycemic control, hypoglycemia, and hypoglycemia management parameters across the baseline time period (TP1, CY 2009-2010), transitional (TP2, CY 2011-2012), and mature post-intervention phase (TP3, CY 2013). Hypoglycemia defined < 70 mg/dL, severe hypoglycemia < 40 mg/dL, severe hyperglycemia > 299 mg/dL.

Results:

22,990 non-ICU patients, representing 94,900 patient-days of observation were included over five year study. The RR TP3:TP1 for glycemic excursions was reduced significantly: hypoglycemic stay, 0.71 (0.65,0.79); severe hypoglycemic stay, 0.44(0.34, 0.58) ; recurrent hypoglycemic day during stay, 0.78 (0.64,0.94); severe hypoglycemic day, 0.48 (0.37,0.62); severe hyperglycemic day (>299 mg/dL), 0.76 (0.73,0.80).

Conclusion:

Hyperglycemia and hypoglycemia event rates were both improved, with the most marked effect on severe hypoglycemic events. Most of these interventions should be portable to other hospitals.

Key Words: Diabetes, hospital, glycemic control, hypoglycemia, insulin, quality improvement

Abbreviations:

BC-ADM = Board Certified, Advanced Diabetes Management; **BSN** = Bachelor of Science, Nursing; **CDE** = Certified Diabetes Educator; **FNP-BC** = Family Nurse Practitioner- Board Certified; **MD** = Medical Doctor; **MHSM** = Master of Arts Health Services Management; **MPH** = Masters Public Health; **MS** = Master of Sciences; **PHN** = Public Health Nurse; **SFHM** = Senior Fellow Hospital Medicine.

Introduction

Uncontrolled hyperglycemia and iatrogenic hypoglycemia represent common inpatient quality and safety issues associated with a broad range of adverse outcomes [1-4], and insulin is one of the most common sources of inpatient adverse drug events [2,5,6]. Professional societies, standards organizations and “Partnerships for Patients” efforts have highlighted the importance of optimizing inpatient glycemic control and reducing hypoglycemia. [2-4,7-11]

Despite significant gains in inpatient glycemic control and dissemination of our glycemic management strategies in past years at our institution [8,9, 12-15], we noted multiple continuing opportunities for improvement. These included knowledge deficits in our providers, improper insulin prescribing practices, and lapses in coordination of care. We were particularly motivated to address hypoglycemia after we examined the quality of hypoglycemia management and the most common inciting factors for iatrogenic hypoglycemia in our medical center in 2008, [16] and again in 2011. Our studies found that over half of hypoglycemia cases were potentially preventable. The most common remedial causes of iatrogenic hypoglycemia were:

1. Prescribing insulin regimens that do not conform to best-practice standards.
2. Failure to appropriately identify and mitigate the source of an initial hypoglycemic event, leading to recurrent hypoglycemic events.
3. Failure to anticipate and appropriately respond to unexpected interruptions of nutrition in a patient receiving nutritional insulin, leading to nutrition / insulin mismatch.

We found that nursing staff did not follow the hypoglycemia management protocol reliably. We observed long glucose re-testing delays after hypoglycemic events, poor documentation, and long intervals until hypoglycemia resolution. Others have reported similar findings.[17-19]

We hypothesized that we could significantly reduce iatrogenic hypoglycemia in our non-ICU population by introducing a hypoglycemia reduction bundle addressing these causes, while simultaneously continuing to reduce uncontrolled hyperglycemia. We further hypothesized that identifying and addressing quality outliers in real time (as opposed to relying solely on month-to-month glucometrics) would further reduce undesirable glycemic excursions. We have termed this form of active surveillance measure-vention, coupling real-time *measurement* and identification of uncontrolled patients to spur concurrent *interventions*. The measure-vention technique was first demonstrated to be successful in optimizing thromboprophylaxis, and has since been utilized for a number of improvement efforts in our institution and others. [20-22] We report the impact of our improvement methods and implementation of a hypoglycemia reduction bundle on inpatient hypoglycemia, hyperglycemia, hypoglycemia management below, in an effort to describe and disseminate successful strategies for improvement to inpatient glycemic control teams.

Methods

Study design, population, and data sources

We used a proven performance improvement framework [8,9] and conducted institutional review board (IRB) approved prospective observational research in parallel with performance improvement efforts, with a waiver of individual informed consent.

The population of interest was defined as hospitalized adult non-critical care (non-ICU) patients with hyperglycemia and / or a diagnosis of Diabetes (ICD-9 codes 250.xx), admitted to our 550 bed academic center over calendar years (CY) 2009-2013. The CY 2009-2010 are referred to as the baseline or pre-

interventional time period (TP 1). Blood glucose meter data analysis was initiated to review quarterly performance, but all interventions were limited to routine nursing care, as no active surveillance was in place, and the hypoglycemia reduction bundle and other interventions were not yet formulated. A multidisciplinary improvement team introduced a series of interventions during a two year transitional period (CY 2011-2012, TP2) and continued to observe the impact across a more mature post-intervention phase (CY 2013, TP3).

We used only point-of-care blood glucose (BG) values obtained during the hospital stay. Glucose values from the first hospital day were included, but values from the Emergency Department and other pre-admission sources were not. Laboratory BG values were not included, nor were glucose values captured in arterial or venous blood gasses. Hyperglycemia was defined as any BG ≥ 180 mg/dL, or two days with presumed fasting values > 140 mg/dL obtained between 5 am and 9 am. Patients needed at minimum four point-of-care blood glucose (BG) readings across two calendar days to be included in the analysis. Patients without a Diabetes diagnosis who did not meet criteria for hyperglycemia were excluded from the analysis. Obstetrics wards / pregnant patients, and pediatric age groups under the age of sixteen were also excluded. Glucometrics (described below) were reported to the improvement team and other groups on a regular basis throughout the intervention period.

Interventions and Improvement Techniques

Organizational structure

Three advanced practice nurses / clinical diabetes educators were recruited in January –May 2012, supervised originally by a single Endocrinology faculty member, augmented in October 2013 with the addition of another part time Endocrinologist. Rather than taking over the care of patients' diabetes, this inpatient diabetes team act as consultants, change agents, and educators. Consults and targeted provider education were triggered by proactive surveillance of glycemic outliers, as well as more

traditional methods such as calls from the primary team or nursing. An interdisciplinary glycemic control committee met monthly, with representation from Endocrinology, Hospital Medicine, Surgery, Nursing, Informatics, Pharmacy, Dietary, Nutrition services, Laboratory, and other disciplines on an ad hoc basis. Monthly reports of progress and barriers were made to medical staff committees, and glycemic control goals were incorporated into executive and medical staff incentive plans. Examples of incentive goals would be a reduction in patient-days with hypoglycemic events (BG < 70 mg/dL) or patient-stays with a day-weighted mean BG \geq 180 mg/dL. Nurses were recruited from each unit to form a diabetes initiative group (DIG). Members of DIG served as unit champions for diabetes care and disseminated important information regarding diabetes nursing care.

Subcutaneous insulin order sets, protocols, and an insulin management algorithm

Extensive clinical decision support (CDS) to guide appropriate subcutaneous insulin ordering and glycemic monitoring was integrated into our electronic health record (EHR) order sets. The CDS offered guidance on dosing, and matched pre-formatted insulin regimens with a variety of nutritional intake patterns (**Figure 1**), allowing incorporation of standardized administration instructions, indications, and holding parameters to help improve reliable and appropriate insulin administration. Insulin could now only easily be ordered via the order set. While our electronic health record makes it feasible to order insulin by alternative methods, it is inconvenient, essentially establishing a forcing function to increase exposure to the embedded protocol-driven CDS. A glucose management page displayed several variables that impact glycemic control together in an organized manner (**Figure 2**), enabling providers to quickly assess the patient's glycemic trend and contributing factors.

Active surveillance of outliers and measure-vention

Glycemic outlier reports capturing all patients in the hospital with a BG <80mg/dL or >180mg/dL during the preceding three days were integrated into our EHR, allowing the inpatient diabetes team to perform active surveillance for potential lapses in care. The roster of glycemic outliers linked to the graphic glucose management page served as the basis for our measure-vention process. The diabetes team was empowered by select services (Transplant services, Cardiology) to initiate pre-authorized consultation for inpatients with triggers such as poor glycemic control or new insulin initiations, and in some cases, write orders to expedite care or avoid transcription errors in more complicated circumstances. For all other services without these agreements, the inpatient diabetes team contacted the primary team to offer advice or consultation, and the primary team executed all orders.

Hypoglycemia reduction bundle

We implemented a bundle of interventions to address the top causes of remediable iatrogenic hypoglycemia from our previous studies. **Table 1** summarizes the Hypoglycemia Reduction Bundle strategies. To improve prescribing practices, we implemented pre-formatted insulin regimens in our updated insulin order sets in the early transition period (TP2) as described above. These order sets were designed to guide providers in ordering insulin in a safe, standardized manner, while retaining ease of use and flexibility. CDS was added to encourage more liberal glycemic targets and lower insulin dosing for patients with hypoglycemia risk factors, comfort care situations, and the like.

During the revision of the hypoglycemia management protocol in early TP2, we included a step highlighting the assessment of the initial hypoglycemia episode in order to determine the cause and appropriate steps to prevent further episodes. Education on this step and how to assess the cause of initial hypoglycemia was rolled out through our DIG group, discussed at monthly nursing unit meetings,

and reinforced by the measure-vention process. Timely management of hypoglycemia and standardized documentation were also emphasized in educational efforts and audited with feedback to nursing staff.

In TP2 the “Nutrition on Hold Unexpectedly” algorithm (**Figure 3**) was introduced to address nutritional insulin mismatch, the most prominent source of iatrogenic hypoglycemia in our institution. Common scenarios included sudden interruption of enteral tube feeds or TPN, unscheduled NPO status, and nausea or poor appetite in patients on full doses of nutritional insulin. Complimenting this protocol, comments allowing nurses to hold the nutritional insulin dose until after the meal in the setting of nausea or poor appetite, and guidance to adjust the dose of nutritional insulin based on the percent of tray consumed were added to nutritional insulin orders and the medication administration record.

“Give within 15 minutes of meal: may give just after meal if patient nauseated or has poor appetite. If lispro insulin is deferred until after the meal, administer as follows: give 0 units if patient ate less than 50% of meal, give half of the scheduled dose if patient ate 50% of meal, and give the full dose if patient ate more than 50% of meal. Do NOT administer nutritional lispro insulin if nutrition is interrupted.”

This guidance provided nurses with the flexibility to match the dose of nutritional insulin to the amount of food consumed and reduced calls to the ordering providers.

Coordination of tray delivery, testing, and insulin administration

Problems with the coordination of tray delivery, BG testing, and insulin administration were problematic in our medical center even though we don’t have “room service” delivery of meals. An internal study on tray timing and content demonstrated variability of tray arrival, and carbohydrate portions that were often oversized and not standardized. The Nutrition Services department improved standardization of the carbohydrate content of trays, timing of tray delivery and availability of low and zero carbohydrate snacks. The kitchen staff was educated on diabetes, the impact of carbohydrate servings on blood

glucose, and the rationale for inpatient glycemic control. A schedule was made with a 15 minute window for meal cart delivery, and phone calls were initiated to each unit to announce imminent arrival or delay of the meal carts. Nursing staff and assistants were trained to treat nutrition delivery, BG testing, and insulin administration as a unified process, and audit and feedback were used to reinforce this.

Education and competency training – physicians, nurses, patients

Ordering providers were the target audience for a computerized learning module entitled “Inpatient Diabetes Management for Physicians/Providers” which focused on ten main concepts of inpatient glycemic control in a case based, pre-test/post-test format. Education slides with voice over learning were incorporated into the pre-test component and an 80% pass rate was required to document competency and earn CME credit for the post-test component. The educational module was adopted by the Hospital Medicine division then rolled out to pharmacists, dietitians, Family Medicine faculty, and Internal Medicine residents. Noon conferences reinforcing basic concepts and appropriate order set use with a case based, interactive format were held for the same groups.

Nursing education included competency training and ongoing refreshers. Safe insulin management was incorporated into the Nursing Annual Update online module, Nursing Grand Rounds and other nursing education formats, along with short, focused education at nursing unit meetings. For example, when the topic of the month is basal insulin, 2-3 minute “pearls” on basal insulin are presented followed by a few short cases applying these pearls to routine clinical practice.

A patient education series was also created to help standardize diabetes education for patients. The education series incorporated short online education videos coupled with standardized teach back

questions, handouts, and live demonstrations to provide patients with basic information in several learning formats while improving nursing efficiency.

Unit specific reports were created to provide regular feedback to nursing units on several core measures of inpatient glycemic control including hyperglycemia, hypoglycemia and hypoglycemia management (**Figure 4**). These reports show unit-specific six month trends and a one month snap shot of how each unit compares to other similar units. The performance of all units was made transparent, engendering friendly competition.

Measures and Data Collection

Glucose meter data captured each BG value, along with a patient identifier, ward, date, and time of collection. BG values < 10 mg/dL were set to 10 mg/dL and readings > 600 mg/dL were re-set to 601 mg/dL; Glucometrics summarizing rates of hyperglycemia, hypoglycemia, recurrent hypoglycemia, and the timeliness of hypoglycemia management and resolution were devised.

Glucometrics were expressed using the patient-day for most parameters, a common practice with the advantage of providing a uniform unit of time, adjusting to some degree for repeated testing around glycemic excursions and other local variations in testing patterns.[14,23,24] The degree of glycemic control was summarized as a day-weighted mean for the population (i.e., the mean of all readings for one patient-day, then averaged across all patient-days in that group), the percent of patient-days with a mean (day-weighted) ≥ 180 mg/dL, and the percent of patient-days with any BG > 299 mg/dL. In a similar fashion, hypoglycemia is summarized as the percent of patient days with at least one BG < 70, and severe hypoglycemia as the percent of patient-days with any glucose < 40 mg/dL. Selected metrics were also expressed with the patient-stay as the unit of analysis (e.g. the percent of patients with at

least one hypoglycemic event during their stay, the percent of hypoglycemic patients with recurrent hypoglycemic-days during their stay, and the percent of patients with a day-weighted mean ≥ 180 mg/dL over the course of their stay). A patient-stay included all patient-days with point-of-care BG readings from non-ICU units. ICU days in the middle of a non-ICU stay were excluded, but patient-days on both sides of the ICU stay were linked by administrative patient identifiers.

Hypoglycemia management was assessed by timeliness of response and by markers of recurrent hypoglycemia. The mean / median times to repeat glucose testing and to resolution after a hypoglycemic event were calculated from time interval data. Time intervals were capped at 240 minutes to prevent undue influence from outlier values, and values obtained within 10 minutes of the index hypoglycemic value were excluded to eliminate reflexive repeat testing and focus on assessments after therapy. Recurrent hypoglycemia was defined by the percent of patients with hypoglycemia who suffered one or more recurrent hypoglycemic days.

Analysis

Pearson chi square value with relative risks (RRs) and 95% confidence intervals (CI) were calculated to compare glycemic control, hypoglycemia, and hypoglycemia management parameters across the three time periods:

- Baseline pre-intervention period (TP1): CY 2009-2010 (24 months)
- Transitional period (TP2): CY 2011-2012 (24 months)
- Mature, post-intervention phase (TP3): CY 2013 (12 months)

A p value of less than 0.05 was determined as significant and data were analyzed using STATA, ver. 10, College Station, TX.

For dichotomous variables, we assigned the RR of hypoglycemic and hyperglycemic parameters during the baseline TP1 a value of 1.0, and calculated the RR and CIs for the same parameters during TP2 and TP3.

For continuous data (glucose value means and minutes to hypoglycemia resolution), one-way analysis of variance was used, with post-hoc Bonferroni corrections for multiple group comparisons across the 3 time periods.

Results

During the five year observation period 22,990 non-ICU patients, representing 94,900 patient-days had a diagnosis of diabetes and / or met criteria for hyperglycemia (**Table 2**). The number of patients meeting diabetes or hyperglycemia criteria increased over the years in the study, reflecting expansion of our medical center. Average length of stay, age, gender distribution, the proportion of patients with a diagnosis of diabetes, and case mix index scores did not significantly change over the three time periods. Another marker of severity of illness, the percent of patients with any intensive care unit exposure during their stay increased from TP1 to TP2 and TP3 (19.7% vs 27.0% in TP2 and TP3, $p < 0.05$, Pearson chi square). The first BG values obtained during the hospitalization were analyzed. The percent of patients with the first BG ≥ 180 mg/dL was 45% in TP1, 43.1% in TP2, and 42.4% in TP3. The percent of patients with a first BG > 299 mg/dL was 9.3%, 10.1%, and 10.1%.

Hypoglycemia Rates

Analysis by patient-stay

In TP1, 13.7% (917 of 6,681) of the patients with diabetes / hyperglycemia suffered from at least one hypoglycemic event (BG < 70 mg/dL), and 2.9% (195) of the patients suffered from at least one severe hypoglycemic event (BG < 40 mg/dL) during the course of their non-ICU stay (**Table 3**). The percent of

patients with a hypoglycemic patient-stay dropped significantly in TP2 to 11.8% (RR 0.86 [CI 0.79, 0.93]), and again in TP3 to 9.8% (RR 0.71 [CI 0.65, 0.79]). The percent of patient-stays with severe hypoglycemia fell over the three time periods (2.9% vs 1.8% vs 1.3%), representing a RR for a severe hypoglycemic stay in TP3:TP1 of 0.44 (CI 0.34, 0.58). Of the 917 patients experiencing a hypoglycemic event in TP1, 260 (28.3%) experienced at least one additional day with another hypoglycemic event. The risk of a patient with hypoglycemia suffering from recurrence fell to 22% in TP3, representing a RR for recurrence in TP3:TP1 of 0.78 (CI 0.64, 0.94).

Analysis by patient-day

The percent of patient-days with hypoglycemia fell over the study period (4.4% vs 4.3% vs 3.2%), reaching a statistically significant reduction in TP3 (RR of TP3:TP1 0.73 [CI 0.66, 0.79]). The percent of patient-days with severe hypoglycemia fell by more than 50% across the three time periods (0.73% vs 0.45% vs 0.35%), with a RR TP3:TP1 of 0.48 (CI 0.37, 0.62). This month to month monitoring of this parameter is captured as a statistical process control (SPC) chart in **Figure 5**.

Hypoglycemia Management

The mean intervals for rechecking BG after a hypoglycemic event improved from 53.0 minutes to 41.7 minutes, while the mean time interval for documented resolution of a hypoglycemic event improved from 64.1 minutes to 49.0 minutes (**Table 4**).

The improvement in recurrent hypoglycemia rate described above is also interpreted as a marker of hypoglycemia management and secondary hypoglycemia prevention, via assessment and appropriate interventions taken for the index hypoglycemic event.

Glycemic Control and Severe Hyperglycemia

Glycemic control as measured by the patient-day weighted mean improved significantly from 175.2 mg/dL (TP1) to 171.3 mg/dL in TP2, $p < 0.001$, and 170.6 mg/dL in TP3, $p < 0.001$, shown in **Table 5**. The Bonferroni correction for multiple comparisons to TP1 to TP2 and TP3 is $p < 0.01$. The percent of patient-days with a mean BG ≥ 180 mg/dL fell from 37.1% in TP1 to 35.2% in TP 2 and 35.3% in TP3, representing small but statistically significant improvements compared to TP1 (TP2:TP1 RR 0.96 [CI 0.94, 0.98]; TP3:TP1 RR 0.97 (0.94, 0.99)). The percent of patient-stays with a mean BG ≥ 180 mg/dL also trended down in TP2 and TP3 compared to TP1, but this trend in improvement failed to reach statistical significance.

The percent of patient-days with severe hyperglycemia (>299 mg/dL) was reduced in a step-wise fashion over the three time periods (14.7% vs 12.0% vs 10.8%, RR TP3:TP1 0.76 [CI 0.73,0.80]).

Discussion

Our study convincingly demonstrates that a significant reduction in inpatient hypoglycemic events is possible by interventions focused on common causes of remediable hypoglycemic events, such as inappropriate insulin prescribing, failure to address unexpected nutritional interruption, and failure to respond appropriately to the first hypoglycemic event. Importantly, these reductions in hypoglycemic events are not gained at the expense of increased hyperglycemia, as we reduced unwanted hyperglycemic excursions during the same time frame.

Strengths and Limitations

Our study has several strengths. This study is large, incorporating nearly 23,000 patients and 95,000 inpatient-days of observation over a five year time period, including all patients with inclusion criteria for hyperglycemia and / or diabetes. The observation period is long enough that observation bias is not a factor. We used high quality glucometrics largely congruent with both Society of Hospital Medicine

(SHM) Glycemic Control Task Force recommendations [14,23-25] and Yale Glucometrics, and examined data by both patient-stay and patient-day.

The improvements seen are fairly dramatic for an institution in absolute terms, because inpatient hyperglycemia and hypoglycemia are relatively common. For example, on an annualized basis for our 550 bed hospital, our efforts resulted in 236 fewer hypoglycemic stays and 296 fewer hypoglycemic days. Both ends of the extreme glycemic spectrum saw improvement, creating a win/win situation for glycemic control efforts. On an annualized basis, for example, 98 fewer patients suffer from severe (<40 mg/dL) hypoglycemia, while also averting 939 patient-days with severe hyperglycemia (> 299 mg/dL).

Other institutions should be able to replicate many of our interventions, including protocol driven order sets with embedded CDS, flow sheets, educational programs, and much of the hypoglycemia reduction bundle. Measure-vention techniques may be more dependent on the environment for success. Daily reports identifying outliers in glycemic control should be fairly easy to replicate, but medical centers need an effective means to further triage these patients, and intervene if a true deficit in care is present. We successfully modeled triggered consultation in our institution, allowing for glycemic management consultations based on measure-vention, and this was very well accepted in our institution, but this acceptance could vary.

The main limitation of this study lies in the observational study design. There were multiple interventions and improvement strategies deployed in concert, and it is difficult to specify which interventions had the largest impact. Since we did not perform a randomized trial, one might reasonably question if demographic shifts or secular changes were responsible for the improvement, rather than our interventions. However, several factors make this unlikely. First, the study population is well-

defined, having diabetes or documented hyperglycemia inclusion criteria in all three time periods. Second, the demographics and severity of illness remained constant, or actually worked against improvement trends (for example, significantly fewer patients were sick enough to be in the ICU during their stay in the baseline time period, and the percent of patients with initial BG values ≥ 180 mg/dL at presentation went up across the three time periods). Third, the magnitude of improvement is not feasibly explained by demographic or secular changes.

Our glucometrics include only point-of-care BG values, which have some inherent limitations in accuracy. By excluding glucose values captured in laboratory tests and blood gasses, we miss some glycemic excursions of potential importance. We made this choice because point-of-care BG tests are the most common source of data used to guide care in the hospital setting and to avoid duplicate or “mirror” BG readings. Furthermore, prior studies have established that the addition of laboratory BG readings has minimal impact on hyperglycemia or hypoglycemia rates. [23]

Another limitation is that we have not attempted to link the improvements in hypoglycemia and glycemic control to outcomes such as mortality, infection rates, or costs. In the absence of a randomized trial design, controlling for confounders and attributing improvements to glycemic control parameters would be questionable, considering the wide range of ongoing improvement efforts in our medical center in this same time frame.

Conclusion

We used a multidisciplinary approach with multiple mutually reinforcing interventions to cut severe inpatient hypoglycemia by more than half, while simultaneously improving glycemic control. Active

surveillance (measure-vention) and a hypoglycemia reduction bundle, coupled with ongoing education and robust standardized order sets and documentation were the keys to success.

It is hard to overstate the importance of good glucometric reports to inform the improvement effort, both month to month reports, and real time measurements enabling active surveillance. During the course of this work, we exported our measurement techniques to the SHM website, allowing other sites access to high quality metrics at low or no cost. As described in two of the references [25, 26], these metrics have also made it possible to compare hospitals to each other, establish benchmarks for performance, and place our performance in perspective. In the last round of published benchmarking [26], our center placed in the top quartile on both hypoglycemia and glycemic control parameters. This feat was accomplished by only 8 of 76 hospitals, and our center was the only academic center establishing this benchmark. As we prepare to update the extensive SHM glycemic control online resources, we will post examples of how to leverage the EHR to reinforce the insulin management protocols and promote safe use of insulin, along with sharing an array of improvement tools. We believe that well over half of iatrogenic hypoglycemia is preventable. The benchmarking studies reveal extreme variability in glycemic control and hypoglycemia rates, with some sites having hypoglycemia rates 5-6 times our rates. Marked reductions in hypoglycemia are possible if we can disseminate our lessons learned, and the attendant tools, to a broader audience of hospital improvement teams.

Conflict of Interest and Acknowledgments

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FIGURE LEGENDS

Figure 1. Screen shot of subcutaneous insulin orders in the electronic health record. The ordering provider selects the nutritional intake, which opens up the most appropriate insulin regimen.

Figure 2. Screen shot of the glucose management page in the electronic health record. This pulls together pertinent information to assist in insulin adjustment for the individual provider, and allows for rapid triage in measure-vention.

Figure 3. Algorithm to guide assessment and interventions when nutrition is unexpectedly on hold for a patient.

Figure 4. Unit specific report depicting the percent of hypoglycemic events with the next documented glucose documented within 30 minutes. A variety of these reports were shared with all units each month.

Figure 5. Statistical process control (SPC) chart, or p-chart, depicting the percent of patient-days with severe hypoglycemia over time.

REFERENCES

1. Centers for Disease Control and Prevention. Hospitalizations for Diabetes and Any-Listed Diagnosis. Available at <http://www.cdc.gov/diabetes/statistics/dmany/index.htm>. Accessed December 2012.
2. **Moghissi ES, Korytkowski MT, DiNardo M. et al.** American Association of Clinical Endocrinologists and American Diabetes Association Consensus Statement on Inpatient Glycemic Control. *Diabetes Care-2009*. 32:1119-1131.
3. National Quality Forum (NQF). Safe Practices for Better Healthcare—2010 Update: A Consensus Report. Safe Practice 32: Glycemic Control. 361-369. Washington, DC: NQF; 2010.

4. **Umpierrez GE, Hellman R, Korytkowski MT, et al.** Management of Hyperglycemia in Hospitalized Patients in the Non-critical Care Setting: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metabol.* 97:16-38.
5. **Hellman R.** A systems approach to reducing errors in insulin therapy in the inpatient setting. *Endocr Pract.* 2006;12:49-55.
6. **Braithwaite SS, Buie MM, Thompson CL, et al.** Hospital hypoglycemia: not only treatment but also prevention. *Endocr Pract.* 2004;10:89-99.
7. The Joint Commission. Advanced Certification in Inpatient Diabetes. Accessed Dec 12,2012.
http://www.jointcommission.org/certification/inpatient_diabetes.aspx.
8. Society of Hospital Medicine Glycemic Control Resource Room. Last accessed electronically on July 4, 2010 at: <http://www.hospitalmedicine.org/ResourceRoomRedesign/GlycemicControl.cfm>
9. Improving Care of the Hospitalized Patient with Hyperglycemia and Diabetes. From the SHM Glycemic Control Task Force *J Hosp Med.* 3(S5):S1-83.
10. **Brendle TA.** Surgical Care Improvement Project and the perioperative nurse's role. *AORN J.* 2007;86:94-101.
11. Centers from Medicare & Medicaid Services, Center for Medicare and Medicaid Innovation. Partnership for Patients. Accessed December 10, 2012.
<http://www.innovations.cms.gov/initiatives/Partnership-for-Patients/index.html>.
12. **Maynard G, Lee J, Phillips GW, et al.** Improved Inpatient Use of Basal Insulin, Reduced Hypoglycemia, and Improved Glycemic Control: Effect of Structured Subcutaneous Insulin Orders and an Insulin Management Algorithm. *J Hosp Med* Jan 2009, Vol 4:3-15.
13. **Lee J, Clay B, Ziband Z, et al.** Indication Based Ordering: A New Paradigm for Glycemic Control in Hospitalized Inpatients *J Diabetes Science Tech* May 2008, Vol 2:349 – 356.

14. **Schnipper JL, Magee MF, Inzucchi SE, et al.** SHM Glycemic Control Task Force Summary: Practical Recommendations for Assessing the Impact of Glycemic Control Efforts. *J Hosp Med.* 3: 66 – 75, 2008
15. **Rogers K, Childers D, Messler J, et al.** Glycemic Control Mentored Implementation: Creating a National Network of Shared Information. *Joint Commission J Qual and Patient Safety* 2014;40:111-118.
16. **Maynard GA, Huynh MP, Renvall M.** Iatrogenic Inpatient Hypoglycemia: Risk Factors, Treatment, and Prevention: Analysis of Current Practice at an Academic Medical Center with Implications for Improvement Efforts. *Diabetes Spectr.* 21: 241-247, 2008
17. **Varghese P, Gleason V, Sorokin R, et al.** Hypoglycemia in hospitalized patients treated with antihyperglycemic agents. *J Hosp Med.* 2: 234-240, 2007
18. **Garg R, Bhutani H, Jarry A, et al.** Provider response to insulin-induced hypoglycemic in hospitalized patient. *J Hosp Med.* 2: 258-260, 2007
19. **Cobaugh DJ, Maynard G, Cooper L, et al.** Enhancing insulin-use safety in hospitals: Practical recommendations from an ASHP Foundation expert consensus panel. *Am J Health Syst Pharm.* 70:1404-1413,2013
20. **Maynard G, Stein J.** Designing and Implementing Effective VTE Prevention Protocols: Lessons from Collaboratives. *J Thromb Thrombolysis* 2010 Feb;29:159-166.
21. **Maynard G, Morris T, Jenkins I, et al.** Optimizing prevention of hospital acquired venous thromboembolism: prospective validation of a VTE risk assessment model. *J Hosp Med* 2010 Jan;5:10-18.
22. **Maynard G, Stein J.** Preventing Hospital-Acquired Venous Thromboembolism: A Guide for Effective Quality Improvement. Prepared by the Society of Hospital Medicine. AHRQ Publication No. 08-0075.

Rockville, MD: Agency for Healthcare Research and Quality. September 2008, last accessed September 15, 2008 at <http://www.ahrq.gov/qual/vegguide/>.

23. **Goldberg PA, Bozzo JE, Thomas PG, Mesmer MM, Sakharova OV, Radford MJ, Inzucchi SE.** "Glucometrics" – Assessing the Quality of Inpatient Glucose Management. *Diabetes Technology & Therapeutics*. 8:560-569, 2006
24. **Thomas P, Inzucchi SE.** An Internet Service Supporting Quality Assessment of Inpatient Glycemic Control. *J Diabetes Sci Technol*. 2: 402-408, 2008
25. **Maynard G, Schnipper JL, Messler J, et al.** Design and Implementation of a Web-Based Reporting and Benchmarking Center for Inpatient Glucometrics. *J Diabetes Sci Technol*. published online 2014 May 12;
26. **Maynard G, Ramos P, Kulasa K, Rogers KM, Messler J, Schnipper JL.** How Sweet is It? The Use of Benchmarking to Optimize Inpatient Glycemic Control. *Diabetes Spectrum* 2014;27:212-217.

Table 1. Hypoglycemia Reduction Bundle

Failure Mode	Hypoglycemia Reduction Bundle Strategies and Solutions
<i>Inappropriate prescribing</i>	<ul style="list-style-type: none"> • Standardized order sets for subcutaneous insulin, IV insulin, transitions, and monitoring. • Pre-formatted insulin regimens to match nutritional intake patterns. • Forcing functions (mandating use of protocol-driven orders) • Intelligent clinical decision support (CDS) in order sets. • Elimination of free text insulin orders • CDS discouraging correction / sliding scale insulin as primary strategy to control hyperglycemia. • Educational tools for physicians, nursing, pharmacists, and patients.
<i>Glycemic target too low</i>	<ul style="list-style-type: none"> • CDS to tailor glycemic targets for those at risk of hypoglycemia.
<i>Matching nutritional intake to insulin dosing</i>	<ul style="list-style-type: none"> • Policies, protocols, and order set CDS for managing unexpected interruption of nutrition. • Coordination of nutrition delivery, glucose testing, and insulin administration • Patient and family educational tools.
<i>Failure to</i>	<ul style="list-style-type: none"> • Hypoglycemia management protocol that features a structured

<i>manage hypoglycemia and adjust regimen appropriately</i>	<p>assessment of the etiology, and suggests mitigation strategies.</p> <ul style="list-style-type: none"> • Regular feedback on glucometrics, tracking timeliness of hypoglycemia management, and the percentage of patients with one hypoglycemic event that suffer another hypoglycemic day
<i>Monitoring deficiencies and failure to proactively recognize and manage glycemic excursions</i>	<ul style="list-style-type: none"> • Tracking, trending, and feedback of glycemic control, hypoglycemia, and hypoglycemia management parameters on a monthly basis. • EHR daily reports of glycemic outliers serve as a stimulus for concurrent intervention, aka measure-vention. • Glycemic control flow sheets that graphically display glycemic trends and insulin dosing, and pull together other pertinent parameters to assist with management (eg serum creatinine, A1c) assist in measure-vention and also raise awareness of glycemic control issues for the primary inpatient team.
<i>Storing and dispensing</i>	<ul style="list-style-type: none"> • Insulin concentrations limited to U-100. • Insulin and syringes are clearly labeled and segregated from other medications.
<i>Administering</i>	<ul style="list-style-type: none"> • IV bolus and infusion insulin prepared only in pharmacy.

¹ IV = intravenous; CDS = Clinical Decision Support; EHR – Electronic Health Record

Table 2: Population Characteristics – Patients with a Diagnosis of Diabetes Mellitus and / or Documented Hyperglycemia

		Baseline	Transition	Mature
Time Period (TP)		(TP1)	(TP2)	(TP3)
Calendar Year		2009 - 2010	2011 - 2012	2013
Patients meeting criteria of Diabetes Mellitus diagnosis or Hyperglycemia N = 22,990 patients	Patient-days (94,900)	29,517	41,136	24,247
	Patient-stays (22,990)	6,681	10,272	6,037
	% males	53.0%	55.6%	55.7%
	Average Age \pm SD	59.7 \pm 14.7	60.5 \pm 14.9	60.5 \pm 15.2
	Mean Length of Stay	6.0 \pm 5.1	6.0 \pm 5.3	6.2 \pm 5.5
	% with ICU days	19.7%*	27.0%	27.0%
	Case mix index score [#]			
	Mean \pm SD	2.1 \pm 1.9	2.3 \pm 2.2	2.1 \pm 2.2
	Median score	2.0	2.0	2.0
	Diabetes diagnosis	46.8%	47.0%	50.7%
	% 1 st BG \geq 180 mg/dL	9.3%	10.1%	10.1%
	% 1 st BG \geq 299 mg/dL	45.0%	43.1%	42.4%

TP = time period; SD = Standard Deviation; ICU = Intensive Care Unit / Critical Care
BG = blood glucose (point of care)

[#] APR DRG Case Mix adjustment

*statistically significant $p < .05$, Pearson chi square

Table 3. Hypoglycemia Rates for Patients with a Diagnosis of Diabetes Mellitus or Hyperglycemia

¹	Baseline	Transition	Mature	
Time Period (TP)	(TP1)	(TP2)	(TP3)	RR
Calendar Year	2009 – 2010	2011 – 2012	2013	TP3: TP2
Analysis by patient-stay				
Monitored patient-stays	6681	10272	6037	
Hypoglycemic stays (%)	917 (13.7%)	1205 (11.8%)	591 (9.8%)	
RR Hypoglycemic Stay	1.0	0.86*	0.71*	0.84*
95% confidence interval		0.79, 0.93	0.65, 0.79	0.76, 0.92
Severe Hypo Stays (%)	195 (2.9%)	178 (1.8%)	77 (1.3%)	
RR Severe Hypo Stay	1.0	0.59*	0.44*	0.74\$
95% confidence interval		0.48, 0.73	0.34, 0.58	0.56, 0.97
Stays w/ > 1 Hypo Day	260 (28.4%)	364 (30.2%)	130 (22.0%)	
RR stays w/ > 1 Hypo Day		1.07	0.78*	0.73*
95% confidence interval	1.0	0.93, 1.22	0.64, 0.94	0.61, 0.87
Analysis by patient-day				
Monitored patient-days	29,517	41,136	24,247	
Hypoglycemic days (%)	1293 (4.4%)	1749 (4.3%)	771 (3.2%)	
RR Hypoglycemic Day	1.0	0.97	0.73*	0.75*
95% confidence interval		0.90, 1.04	0.66, 0.79	0.69, 0.81
Severe Hypo Days (%)	214 (0.73)	186 (0.45)	84 (0.35)	

RR Severe Hypo Day	1.0	0.62*	0.48*	0.77\$
95% confidence interval		0.51, 0.76	0.37, 0.62	0.59, 0.99

* p value is < 0.001

\$ p value < 0.05

¹ TP = Time Period; RR = Relative Risk; mg/dl = milligrams per deciliter; Hypo = Hypoglycemia: Hypoglycemia is defined as a glucose < 70 mg/dl, Severe hypoglycemia is defined as a glucose < 40 mg/dl; w/ = with. Stays with > 1 Hypo Day = Recurrent patient-day with hypoglycemia in patient who already suffered at least one day with a hypoglycemic event.

Table 4. Timeliness of hypoglycemia management

¹	Baseline	Transition	Mature	
Time Period (TP)	(TP1)	(TP2)	(TP3)	
Calendar Year	2009 - 2010	2011 – 2012	2013	p value
Hypoglycemic events (N=4,758)	1,655	2,191	912	
*Mean interval to next BG \pm SEM	53.0 \pm 1.2	42.1 \pm 0.8	41.7 \pm 1.4	0.001
Median interval to next BG	33.0	30.0	29.0	
Resolution events (N=4,655)	1,603	2,149	903	
*Mean interval to documented resolution \pm SD	64.1 \pm 1.3	50.5 \pm 0.9	49.0 \pm 1.5	0.001
Median interval to documented resolution	44.0	36.0	35.0	
*Bonferonni correction for multiple group comparisons across 3 time periods. p < 0.01				

¹ TP = Time Period; BG = Blood Glucose; N = total number of events across all time periods; SD = standard deviation; SEM = Standard Error of Mean

Table 5. Glycemic Control Summary for 22,990 patients with a diagnosis of Diabetes Mellitus or documented Hyperglycemia

¹	Baseline	Transition	Mature	
Time Period (TP)	(TP1)	(TP2)	(TP3)	RR
Calendar Year	2009 - 2010	2011 – 2012	2013	TP3: TP2
Monitored Patient-Days	29,517	41,136	24,247	
Glucose DWM BG ± SD	175.2 ± 57.7	171.3 ± 57.0 [#]	170.6 ± 55.6 [#]	
Median patient-day glucose	162.4	159.2	160.0	
Days w/ mean BG ≥ 180 mg/dL	10,944	14,474	8,606	
% Days w/ mean ≥ 180 mg/dL	37.1%	35.2%	35.5%	
RR Day w/ mean ≥ 180 mg/dL	1.0	0.96*	0.97*	1.0
95% confidence interval		0.94, 0.98	0.94, 0.99	0.93, 1.02
Days with any BG > 299 mg/dL	4,338	4,948	2,625	
% Days with BG > 299 mg/dL	14.7%	12.0%	10.8%	
RR Day w/ BG > 299 mg/dL	1.0	0.84*	0.76*	0.91*
95% confidence interval		0.81, 0.87	0.73, 0.80	0.87, 0.95
Patient – Stays	6,681	10,272	6,037	
Stays w/ mean BG ≥ 180 mg/dL	2,460	3,684	2,146	
% Stays with mean ≥ 180 mg/dL	36.8%	36.0%	35.5%	
RR Stay with mean ≥ 180 mg/dL	1.0	0.98	0.97	0.99
95% confidence interval		0.94, 1.02	0.93, 1.02	0.95, 1.03

Patient Stay averages are day-weighted

* p value of < .01; [#] p value < 0.001, Bonferroni adjusted p value < 0.01

¹ TP = Time Period; SD = Standard Deviation; mg/dl = milligrams per deciliter; RR = Relative Risk; BG = Blood Glucose; DWM = day-weighted mean; w/ = with;

▼ Medications — **Required**

[Link to UCSD Inpatient Diabetic Management Algorithm](#)

▼ Insulin Regimen - Select Your Patient's Nutritional Intake Pattern — **Required**

Any previous inpatient insulin orders (except an insulin infusion, when transitioning from IV to SQ insulin) should be discontinued when writing new insulin orders using this order set.

NOTE: Correctional insulin only options **are not appropriate** for type 1 diabetics or for patients with fasting glucose values above 150 mg/dL.

For those patients transitioning from an insulin infusion: the Total Daily Dose (TDD) of insulin may be estimated using one of the following methods:

1. If the patient is receiving TPN or tube feeds, or is eating well, take the average insulin rate for the previous 6 hours and multiply by 20 to get the TDD.
 2. If the patient is not currently receiving adequate nutrition, double the total number of units obtained by method #1 to get the TDD.
 3. The **first** dose of glargine should be given **two hours** prior to discontinuing the insulin infusion.
-

- ☐ Insulin Regimen - Patient Eating or Receiving Bolus Tube Feeds (Equivalent Lispro Dosing for Each Meal)
- ☐ Insulin Regimen - Patient Eating or Receiving Bolus Tube Feeds (Individualized Lispro Dosing for Each Meal)
- ☐ Insulin Regimen - Patient Eating or Receiving Bolus Tube Feeds (Patient Requesting Lispro Dosing Based on Carb Counting)
- ☐ Insulin Regimen - Patient on 24-Hour Continuous Tube Feeds or TPN
- ☐ Insulin Regimen - Patient on Night-Only Continuous Tube Feeds or TPN
- ☐ Insulin Regimen - Patient NPO or on Clear Liquids
- ☐ Insulin Regimen - Correctional Insulin Only in Patient Eating Meals
- ☐ Insulin Regimen - Correctional Insulin Only in Patient NPO or on Clear Liquids

Hover over any graph point to see the associated value.

Glucose Management [05/19/12 1600 - 05/25/12 2359] in 8hr interval

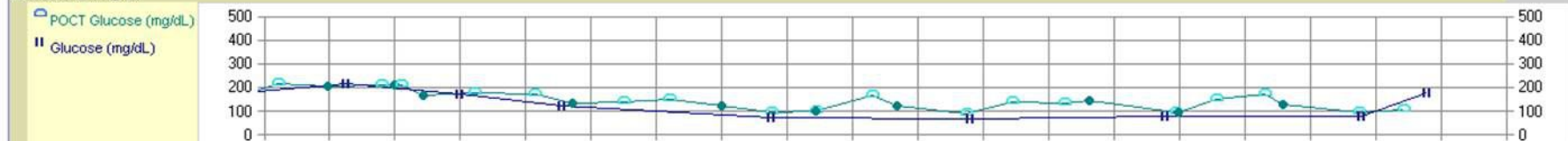
Today Saturday 1600 - Today 2359

24 Hrs 8 Hrs 4 Hrs 1 Hr All

Date: 05/19 05/20 05/21 05/22 05/23 05/24 05/25

8 Hrs: 16-00 00-08 08-16 16-00 00-08 08-16 16-00 00-08 08-16 16-00 00-08 08-16 16-00 00-08 08-16 16-00 00-08 08-16 16-00

Glucose (mg/dl)



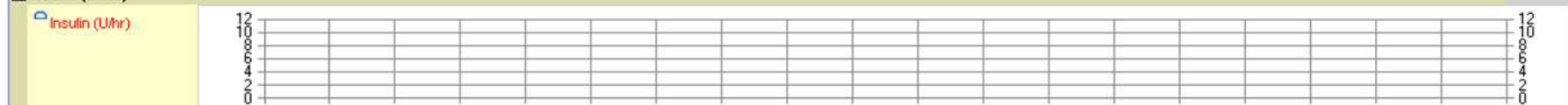
Glucose

POCT Glucose	206!	209	164!	179	131!	141	124	94	101	120	90	140	145	96	151	127!	95	104
Glucose		214	173		120			73			70			79		76	179	

A1C and Serum Cr

Glyco Hgb (A1C)																		
Creatinine		0.88	0.94		1.13			0.96			0.79			0.88		0.71	0.84	

Insulin (units)



Antidiabetic

insulin glargine Soln(Units)			10			10			10									
insulin lispro Soln(Units)													3	3				
insulin regular Soln(Units)	6	3	1	2	1		1			1								

Steroids

methylPREDNISolone sodium succi...			160			120			80		40				20		20	
predniSONE Tabs(mg)																		

Diet

Diet Status	PO	PO			PO	PO			PO	PO			PO			NPO	NPO	
Number of Items Taken			5	5		1	2		2.5			1.5			3		1.75	
Number of Items on Tray			4	5		5	5		5			4			5		4	

Patient is unexpectedly made NPO and/or nutrition is on hold or interrupted.

Patient on insulin drip

Consider starting D10 at tube feed/TPN infusion rate*
(caution patients with cerebral edema or hyponatremia)

Resume q 1 hour glucose monitoring until glucose in range for 3 consecutive readings, per protocol

If BG < 70 mg/dL or 70-79 mg/dL and symptomatic,
Follow hospital hypoglycemia protocol.
Recheck BG within 15-30 minutes per protocol

If > 2 consecutive BG < 80 mg/dL, notify MD. Pharmacy may be contacted for further consultation.

Continue q 1-2 hour glucose monitoring per protocol.

Patient on subcutaneous insulin

For patient with glargine insulin order:

Continue glargine insulin. Consider reducing the dose by 20% if tight control or high risk of hypoglycemia

For patient with routine scheduled nutritional insulin (regular or lispro):

If dose of scheduled nutritional insulin given in past 1-6 hours, increase frequency of glucose monitoring q 1-2 hours until insulin action complete

Hold future nutritional insulin until nutrition resumes but continue correction insulin.

If BG < 70 mg/dL or 70-79 mg/dL and symptomatic,
Follow hospital hypoglycemia protocol.
Recheck BG within 15-30 minutes per protocol

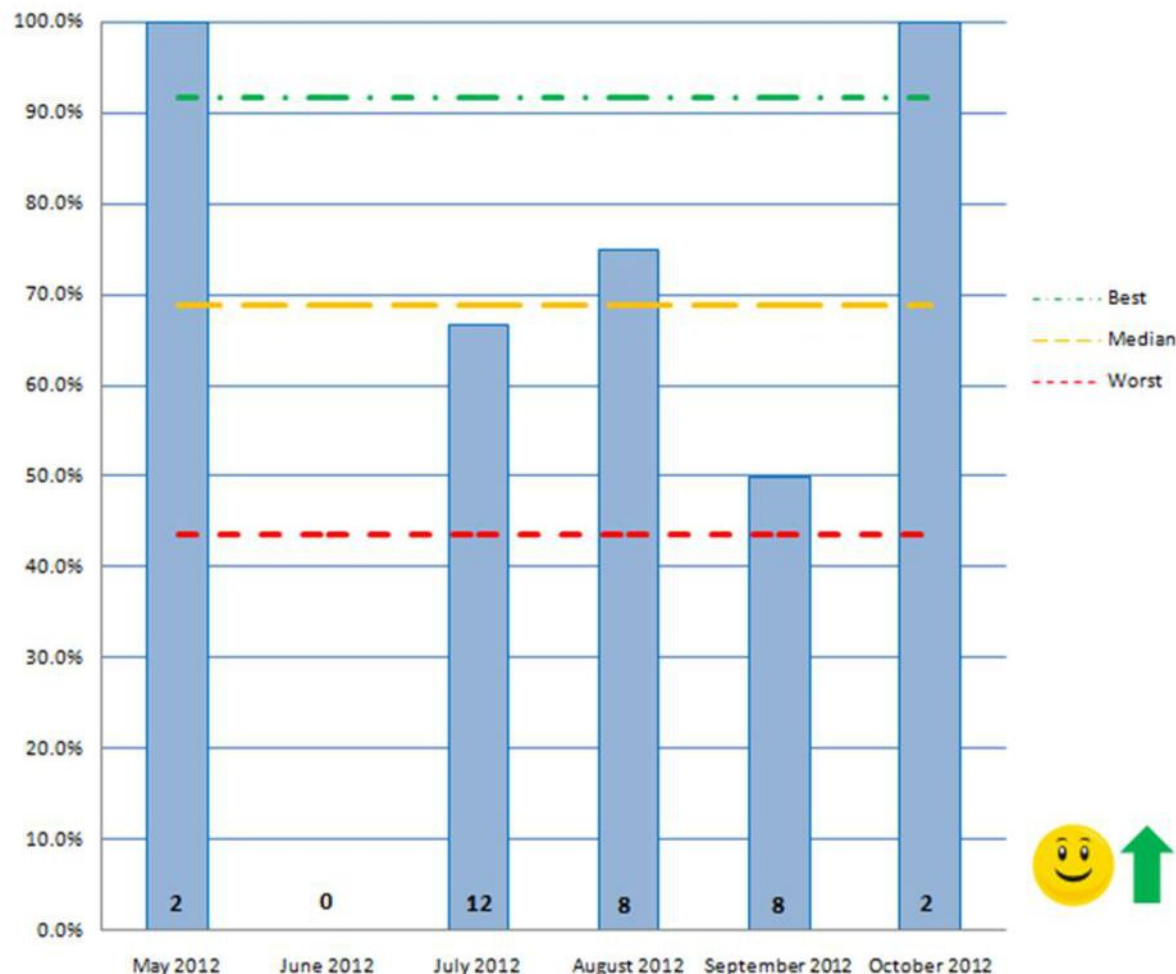
Notify MD. Consider starting D10 at tube feed/TPN infusion rate. Pharmacy may be contacted for further consultation.

Resume q 4-6 hour and prn glucose monitoring.

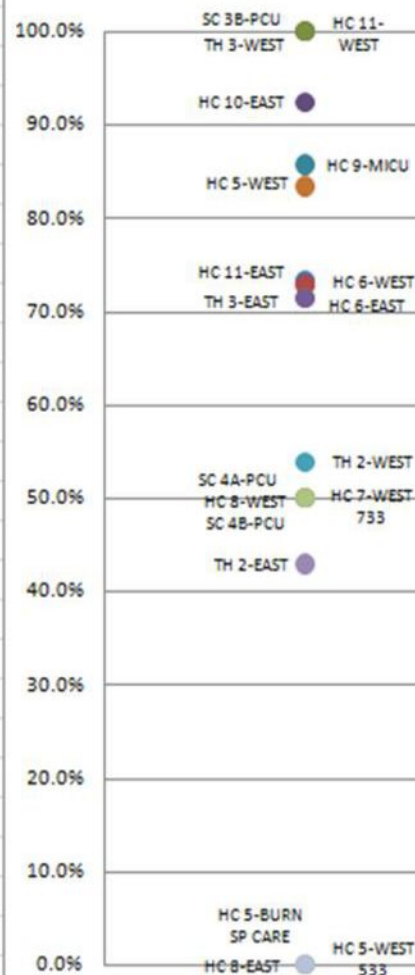
*Alternatives:

1. Decrease Rate of Insulin Drip - Contact pharmacy to decrease insulin drip Insulin Sensitivity Coefficient (ISC):
If drip > 6 units/hr → decrease ISC by 50% and adjust per insulin protocol
If drip < 6 units/hr → decrease ISC to 0.01 and adjust per insulin protocol
2. Stop insulin drip and start subcutaneous insulin correction scale insulin with q2-4h monitoring. Suggest administering lispro q4h or regular insulin q6h. (Patients with Type 1DM need basal insulin at all times, do not use correction scale only for Type 1DM.)
3. Call Pharmacy for assistance

HC 11-WEST



Most Recent Month Ward Rates



* Best, Worst, and Median percentages are based off 5/1/2012 - 10/31/2012 data.

** Numbers at bottom are total events <70

p Chart - Percent Days with Results < 40 (p value .01)

