

Ensuring Optimal Glycemic Control for Hospitalized Patients: *The Role of the Hospitalist*

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Speaker:
David Baldwin, Jr, MD

Dr Baldwin reports receiving research support from Boehringer Ingelheim and Novo Nordisk.

Learning Objectives

After participating this activity, the participant will demonstrate the ability to:

- **DESCRIBE** the use of various insulins for glycemic control in hospitalized patients.
- **EVALUATE** strategies to safely maintain glycemic control during transitions of care in hospitalized patients.
- **DEVELOP** individualized glucose management plans for patients in the hospital setting.

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Overview

- Preoperative planning for patients with diabetes
- Day-of-surgery management of diabetes
- Postoperative management of hyperglycemia: why bother?
- Post-op management of hyperglycemia
 - Using IV infusion in the ICU
 - Using SQ insulin on the general surgical unit
- What are risks for hypoglycemia and how do we mitigate them?
- Discharge planning: how to use the HbA_{1c}

Preoperative Planning for Patients with Diabetes Mellitus

- Record an accurate description of antidiabetes medications, especially combination oral agents (eg, metformin and pioglitazone, sitagliptin/metformin, etc) and insulins. Remember Novolin or Humulin are not types of insulin; they are brand families of insulins.
- The best way to assess the presence of and the control of chronic hyperglycemia is HbA_{1c}. A value >6.5% is diagnostic of diabetes and well-controlled patients have an HbA_{1c} of 6%–8%.

Preoperative Planning for Patients with Diabetes Mellitus

- **HbA_{1c} is recommended to be done for all inpatients with diabetes or new hyperglycemia if not done within the past 2 months.* A current value should be a part of your pre-op evaluation for all patients with a history of diabetes or for patients with newly discovered hyperglycemia. If not checked pre-op, you are just going to have to do on POD-1; so you might as well do it pre-op where it will be valuable in pre-op planning.**

Rush University Protocol for the Preoperative Management of Antidiabetic Therapies Other Than Insulin

- **Sulfonylureas**
 - Glyburide, glipizide, glimepiride, repaglinide, nateglinide
- **Metformin**
- **Pioglitazone**
- **Exenatide, liraglutide, dulaglutide**
- **Sitagliptin, linagliptin, saxagliptin, alogliptin**
- **Alpha-glucosidase inhibitors**
- **SGLT-2 inhibitors (eg, canaglifozin)**

**May take all with food the night prior to surgery;
Take none on the morning of surgery.**

Rush University Protocol for the Preoperative Management of Insulin Therapy

Medications at Home	Day Before and Morning of Surgery
Long lasting insulin glargine (Lantus) detemir (Levemir) degludec (Tresiba)	<ul style="list-style-type: none">• Take your full normal dose on the evening before; or• the full dose on the morning of surgery if prescribed daily either AM or PM• If prescribed twice a day, take the full dose during both the AM and PM
Intermediate lasting insulin NPH (Novolin or Humulin)	Take the full dose the night before surgery and take 50% of the AM dose on the morning of surgery.
Rapid-acting insulins: aspart (Novolog) lispro (Humalog) glulisine (Apidra) regular (Novolin or Humulin)	Take the day before surgery if eating a normal diet. Do not take on the morning of surgery.

Rush University Protocol for the Preoperative Management of Insulin Therapy

- **What about premixed insulins?**
 - **Humulin or Novolin 70/30 (NPH/regular)**
 - **Humalog 75/25 (NPH/lispro)**
 - **Humalog 50/50 (NPH/lispro)**
 - **Novolog 70/30 (NPH/aspart)**
- **Take the full dose with dinner the night before surgery**
- **Take none on the morning of surgery**

Rush University Protocol for the Preoperative Management of Insulin Therapy

Insulin Pump Patients

- **Except for minor brief procedures, it is undesirable to have an SQ insulin infusion running during and after surgery**
- **OR staff and post-op recovery staff have no familiarity with insulin pumps**
- **These patients are obviously not in full command of their faculties**
- **There is no reason to take a high-risk drug and create an even higher-risk situation**

Rush University Protocol for the Preoperative Management of Insulin Therapy

Insulin Pump Patients

- **Patients should get specific instructions from their endocrinologist. The ideal approach is to convert to insulin glargine the night before surgery. The glargine dose should equal the total 24-hour basal insulin dose delivered by the pump. After the glargine is given, disconnect the pump 2 hours later and leave it at home. Otherwise the patient will have to be converted in the pre-op holding area by the endocrine service.**

Conversion of Insulin Pump Basal Infusion to Once-Daily Insulin Glargine



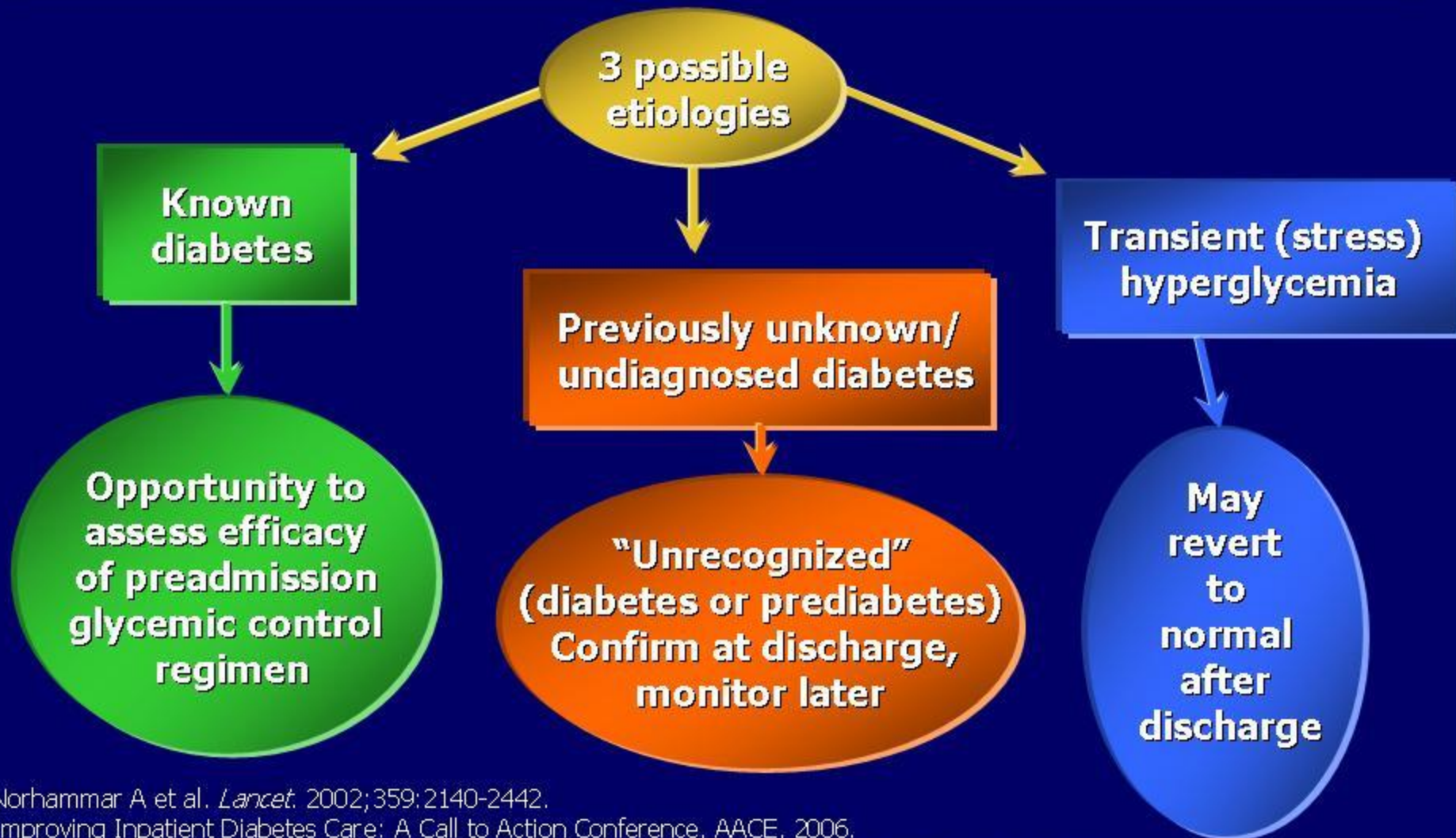
Potential Consequences of Hyperglycemia in the Hospital

- Impaired leukocyte function
 - Chemotaxis
 - Phagocytosis
 - Bacteriocidal activity
 - Risk of bacteremia especially high in patients on TPN with poorly controlled glucose
- Poor wound healing and surgical site infection
- Volume depletion
- Signal to your patient that glucose control is unimportant

Barriers to Glucose Control in the Hospital

- Elevated levels of glucose counter-regulatory hormones
- Nausea, vomiting, anorexia, NPO status
- Erratic meal timing, tests, etc
- IV glucose
- Enteral high-calorie tube feeds
- Glucocorticoid therapy
- Reduced signs and symptoms of hypoglycemia
- Physician indifference and lack of attention to required adjustments in therapy

Hyperglycemia in Hospitalized Patients



Norhammar A et al. *Lancet*. 2002;359:2140-2442.

Improving Inpatient Diabetes Care: A Call to Action Conference, AACE, 2006.

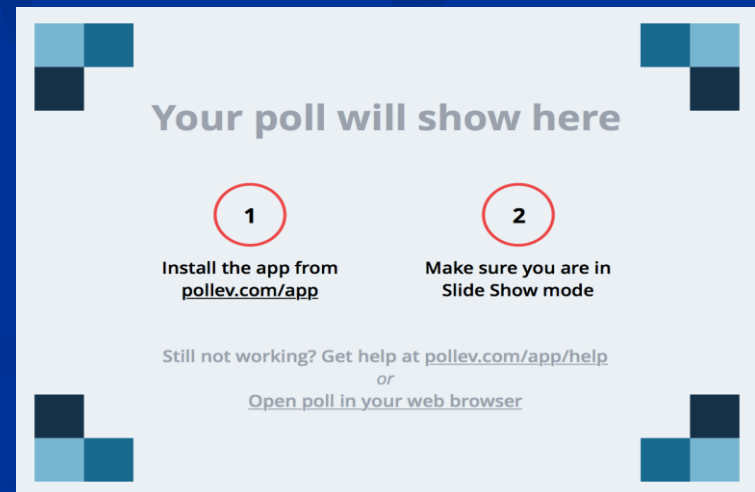
Available at: <http://www.aace.com/meetings/consensus/IIDC/IDGC0207.pdf>. Accessed June 5, 2006.

Significant Postoperative Infections After Elective Abdominal Surgery: Risks with Elevated Postoperative Blood Glucose

- 100 consecutive patients with diabetes
- Patients who had blood glucose (BG) >220 mg/dL on POD-1 had a risk of any infection that was 2.7x higher than patients with all BGs <220 mg/dL
- The risk of serious infections was 5.7x higher in patients with POD-1 BG >220 mg/dL
- Glucose control in the first 24- to 48-hour post-op window of time was pivotal to the risk of developing post-op infections

Postoperative Management of Hyperglycemia

- 61-year-old man is admitted to the floor after undergoing elective hemicolectomy. BG was 224 mg/dL in pre-op holding. He was given intra-op dexamethasone and BG at 2:30 PM was 387 mg/dL. What to do?
 - Transfer emergently to the ICU for IV insulin infusion
 - Order 10 units of rapid-acting insulin and follow BG every 4 hours
 - Begin weight-based SQ insulin glargine or NPH (0.4 units/kg/day) as well as weight-based correction with rapid-acting insulin (0.2 units/kg) every 2–4 hours



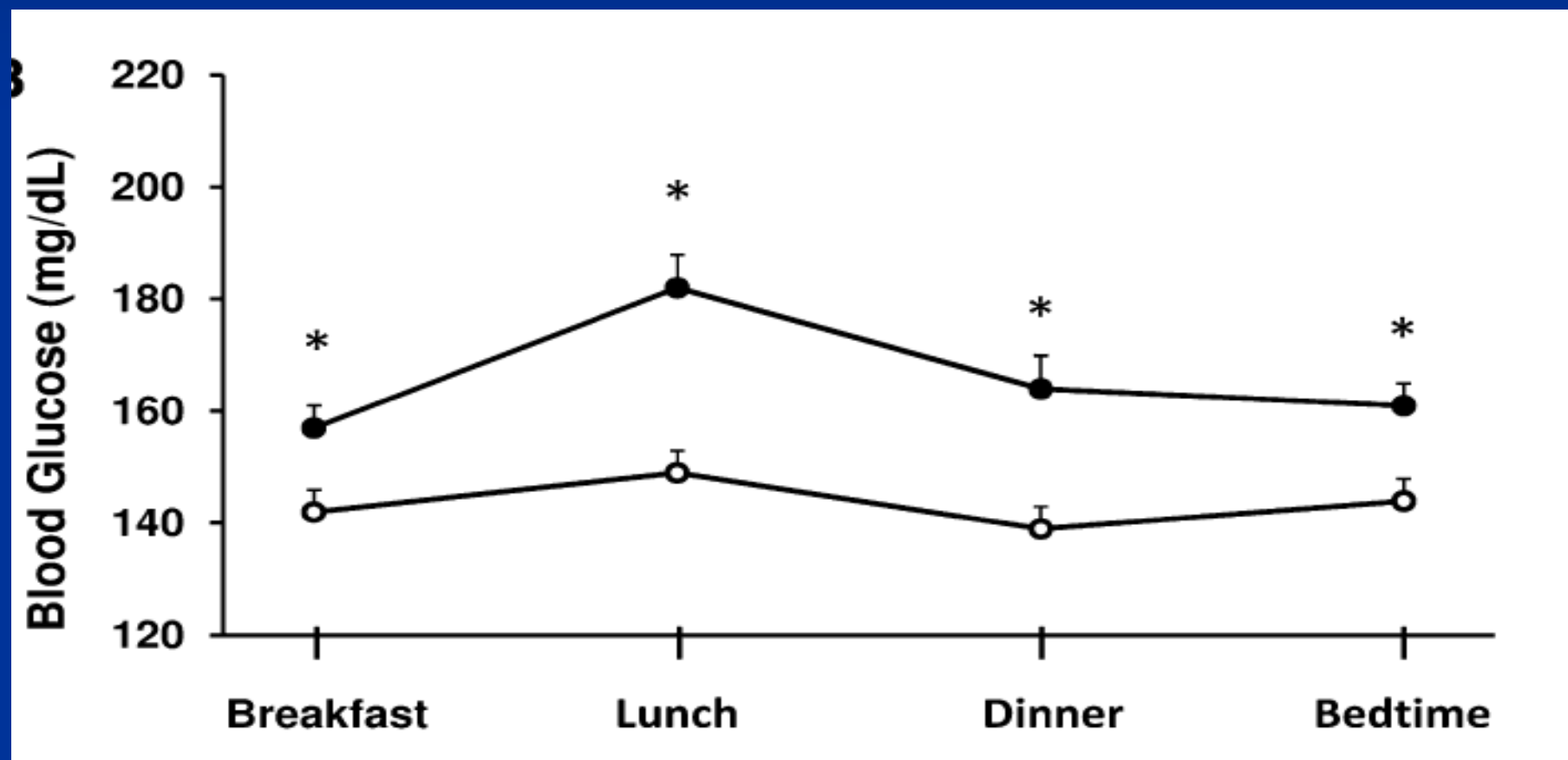
Postoperative Management of Hyperglycemia

- Transferring emergently to the ICU for IV insulin infusion is a very impractical approach, will take a lot of time, will significantly raise costs, and is not necessary
- 10 units of SQ rapid-acting insulin is unlikely to move the BG unless the patient weighs 50 kg given the dexamethasone. Giving rapid-acting insulin in the absence of adequate basal insulin will not control post-op hyperglycemia
- Begin weight-based SQ insulin glargine or NPH (0.4 units/kg/day) as well as weight-based correction with rapid-acting insulin (0.2 units/kg) every 2–4 hours

Randomized Study of Basal-Bolus Insulin Therapy in the Inpatient Management of Patients with Type 2 Diabetes Undergoing General Surgery (RABBIT 2 Surgery)

- **104 patients randomized to sliding-scale regular insulin every 6 hours**
- **107 patients randomized to glargine 0.25 units/kg plus glulisine 0.08 units/kg with meals when eating**

Randomized Study of Basal-Bolus Insulin Therapy in the Inpatient Management of Patients With Type 2 Diabetes Undergoing General Surgery



RABBIT 2 Surgery—Outcomes

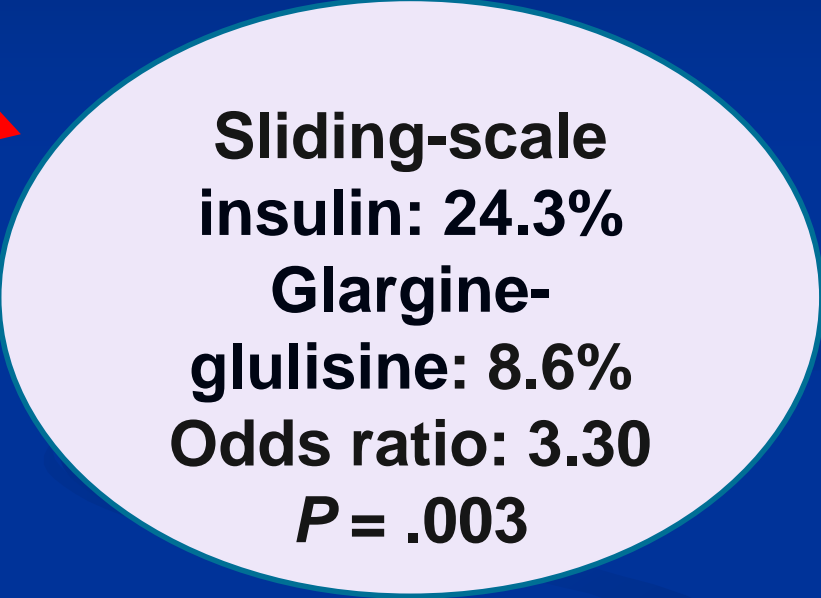
- Composite outcome incidence of:

- Wound infection

- Pneumonia

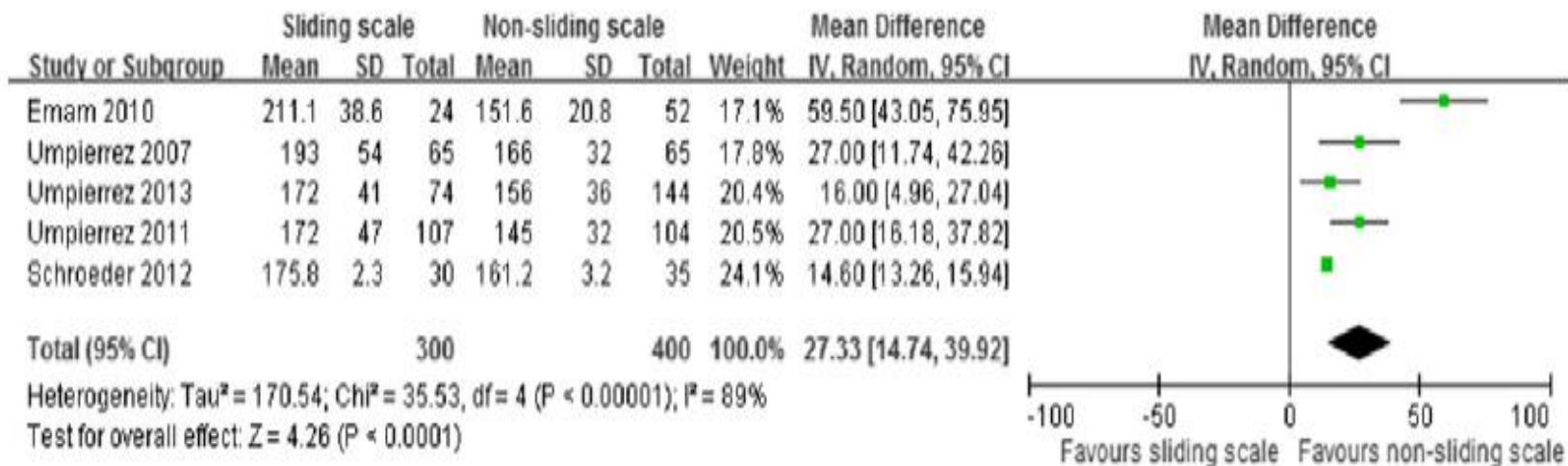
- Acute renal failure

- Bacteremia



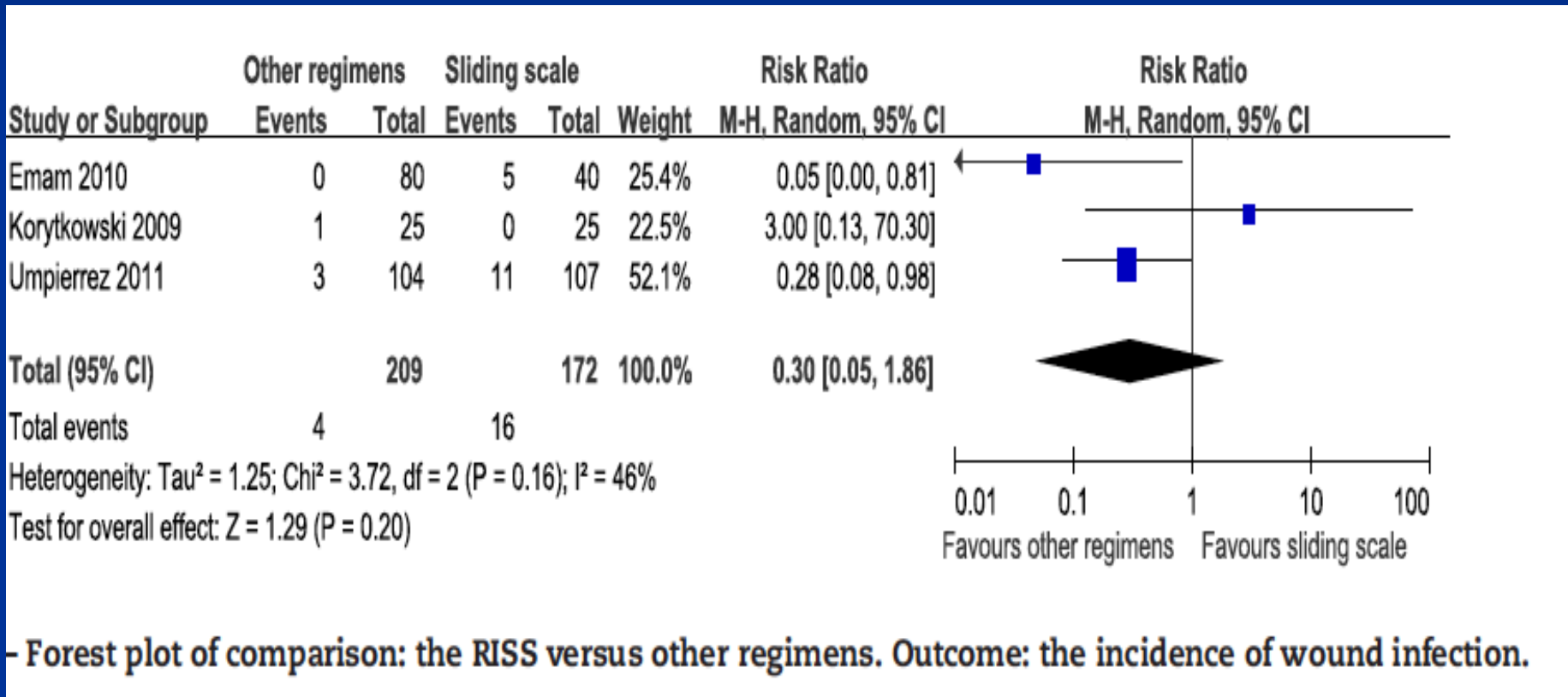
Sliding-scale
insulin: 24.3%
Glargine-
glulisine: 8.6%
Odds ratio: 3.30
 $P = .003$

The Inferiority of Sliding-Scale Insulin: Where's the Basal?



- Forest plot of comparison: the RISS versus non insulin sliding-scale. Outcome: the mean blood glucose level, mg/dL.

The Inferiority of Sliding-Scale Insulin: Where's the Basal?



Postoperative Blood Glucose Management

Target populations

- Preexisting diabetes
- Major surgery (eg, cardiothoracic, transplantation)
- Enteral tube feeding
- TPN
- Glucocorticoid therapy
- New hyperglycemia—BG >160 mg/dL

Initial approach

- Begin point-of-care BG testing every 6 hours
 - Discontinue oral antidiabetic medications
 - Initiate SQ basal-bolus insulin regimen
- OR
- Begin an IV insulin infusion

Guidelines for the Use of IV Insulin – Society of Critical Care Medicine 2012

- Initiate IV insulin infusion when BG >150 mg/dL and absolutely before >180 mg/dL
- Utilize a protocol that maintains glucose level ~150 mg/dL while avoiding any readings <70 mg/dL
- Adequate training of RN users is mandatory.
- Test BG hourly, preferably utilizing arterial or central venous blood
- Utilize a specific protocol to transition patients from IV insulin to an SQ insulin regimen consisting of both basal insulin and mealtime insulin

Summary: IV Insulin

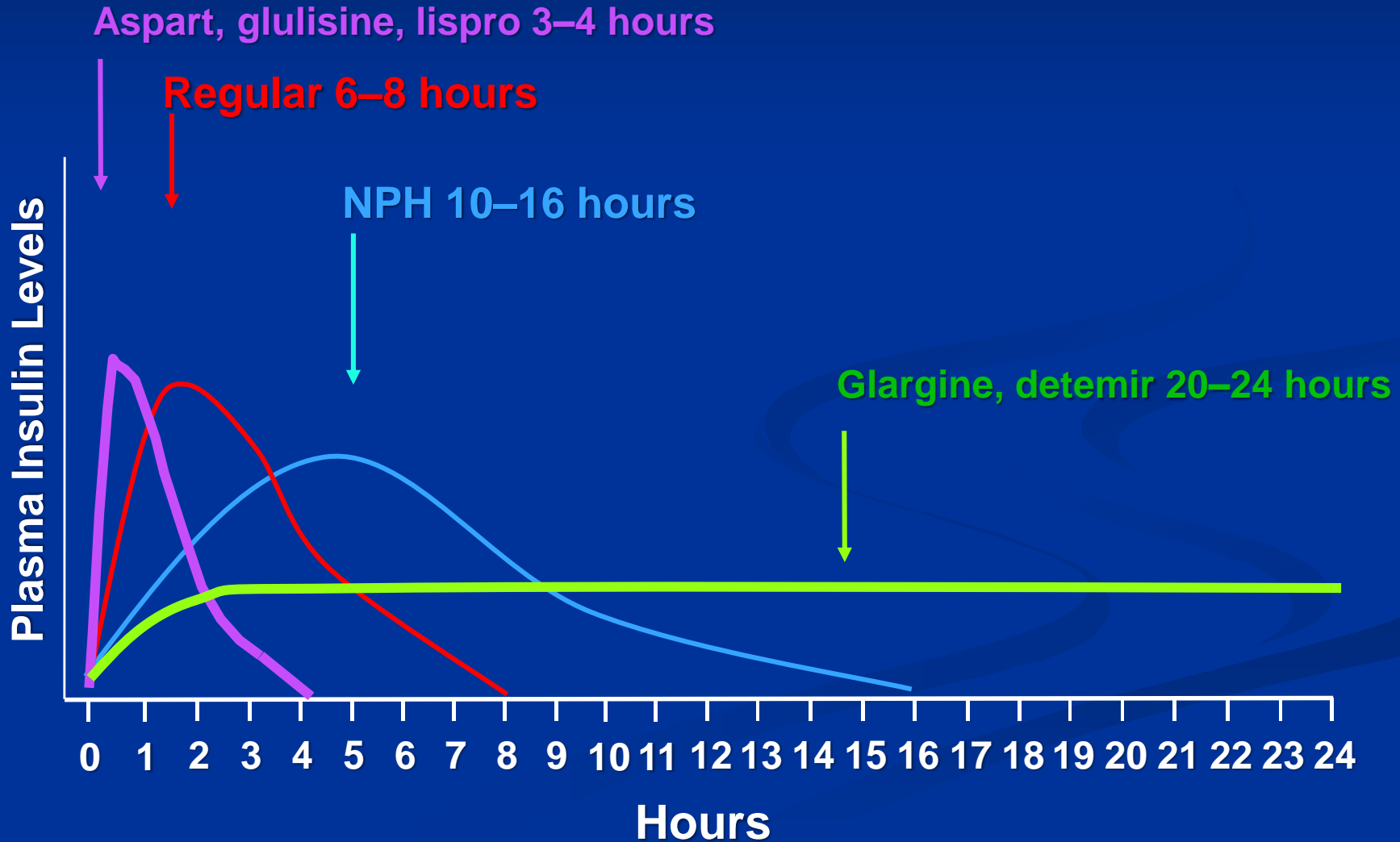
- Begin IV insulin in the ICU when BG is >150–180 mg/dL
- Use a specific single protocol and a well-trained nursing team
- Use a computer-controlled protocol if possible
- Use a glucose target of ~130–170 mg/dL
- Pick your glucose target based on the success of your unit/protocol to keep:
 - BG <70 mg/dL at no more than 1:100–200 readings
 - BG <40 mg/dL at no more than 1:3000 readings

Glucose Control After IV Insulin Infusion

When ready to transition to SQ insulin, assess current rate of IV insulin infusion:

- Give glargine insulin SQ at dose of 20x the current stable IV insulin rate, and stop IV insulin infusion 2–3 hours later
- Adjust glargine insulin daily to maintain fasting morning glucose 100–130 mg/dL
- When eating, add rapid-acting insulin analog with each meal beginning with 1/6th of the dose of glargine
- Adjust rapid-acting insulin to maintain preprandial glucoses 130–160 mg/dL

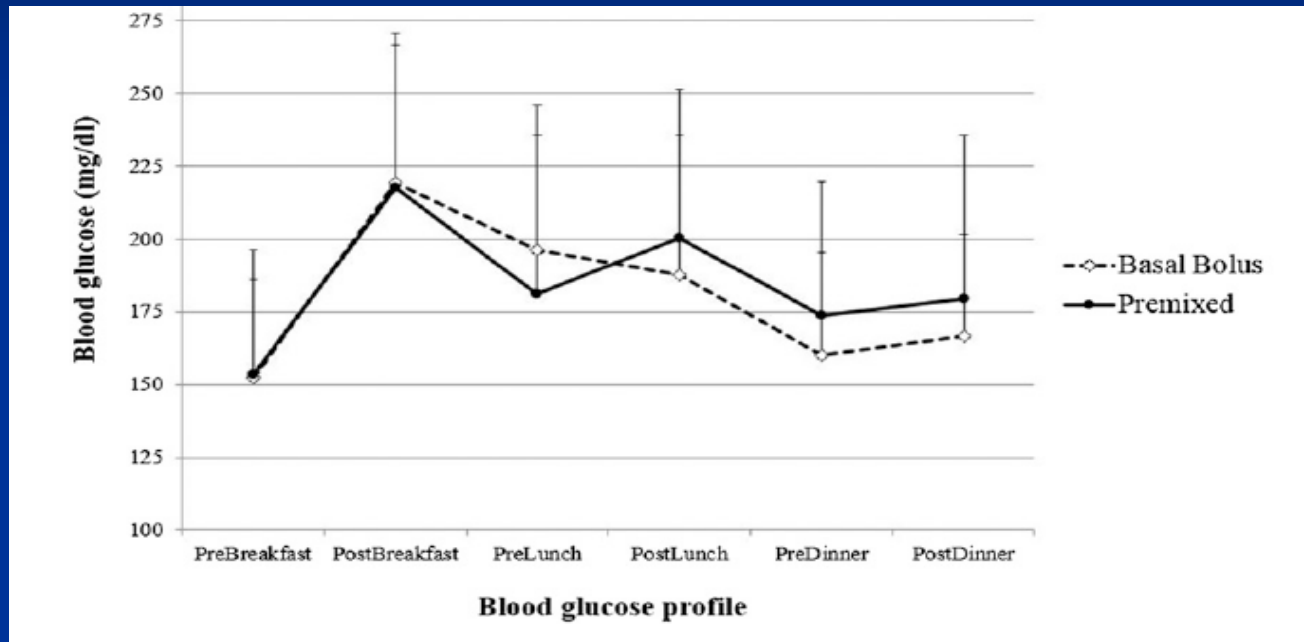
Action Profiles (SQ) of Insulin Analogues



Glucose Control in Non-ICU Postoperative Patients

- On the PM POD-0 if glucose >160 mg/dL begin SQ daily glargine insulin at 0.2–0.4 units/kg
- Adjust glargine insulin every day to maintain a fasting morning glucose 100–130 mg/dL
- When beginning to eat, add rapid-acting insulin analog with meals beginning with 1/6th of the dose of glargine
- Increase rapid-acting insulin analog as needed usually to 1/3rd of the daily dose of glargine
- Remember the golden rule of insulin dosing: all 3 mealtime insulin doses should add up to the daily basal insulin dose in patients consuming 100% of a PO diet
- Adjust rapid-acting insulin doses every day to maintain preprandial glucose 130–160 mg/dL

Comparison of Basal-Bolus and Premixed Insulin Regimens in Hospitalized Patients with Type 2 Diabetes



	Glargine and Glulisine	70/30 Premixed Insulin
Mean blood glucose	175 ± 32 mg/dL	179 ± 43 mg/dL
Percent of patients with blood glucose <70 mg/dL	24.2%	64.1%

Poor Glucose Control and Treatment Intensification in Hospitalized Patients with Diabetes

- Hyperglycemia (>180 mg/dL) was documented at least once for 82.5% of patient admissions
- Antihyperglycemic treatment was intensified for 22.0% of inpatient days with hyperglycemia
- Low frequency of treatment intensification (scheduled or sliding-scale insulin) was associated with poor reduction in BG
- Hypoglycemia (<50 mg/dL) was documented in only 2.2% of inpatient days after antihyperglycemic treatment intensification

Inpatient Postoperative Glucose Control Special Situations

■ Enteral tube feeding

- Begin NPH insulin at 0.1 units/kg every 12 hours if glucose >160 – 180 mg/dL

Or

- Begin insulin glargine at 0.2–0.3 units/kg every 24 hours
- Adjust SQ insulin daily to maintain glucose 140–160 mg/mL
- Remember to order dextrose 10% IV at the same rate as the tube feeding to be started immediately if the tube feeding ever stops to prevent hypoglycemia

Inpatient Postoperative Glucose Control Special Situations

■ TPN

- Begin by adding regular insulin to the TPN bag at 0.1 units per gram of dextrose if BG is >140–160 mg/dL
- Adjust insulin in TPN bag daily to maintain BG 120–150 mg/dL
- Can cover with a dose of NPH in the AM if BG >160 mg/dL (10% of current TPN insulin dose)

Inpatient Postoperative Glucose Control Special Situations

■ Glucocorticoid therapy

- All patients with steroid-caused or steroid-worsened hyperglycemia will need insulin.
- Daily glargine or BID NPH coupled with rapid-acting insulin is appropriate for patients receiving dexamethasone or twice-daily methylprednisolone/prednisone.
- NPH and rapid-acting insulin QAM is appropriate for patients receiving prednisone QAM.
- Significant up-titrations are usually needed twice daily to bring BG levels back under 180–200 mg/dL.

Inpatient Postoperative Glucose Control Special Situations

■ Glucocorticoid therapy

- Since glucocorticoid dosing in hospitalized patients frequently changes from day to day, pay close attention to daily insulin dose titration and to enteral or parenteral carbohydrate intake.
- Premixed insulins such as 70/30 or 75/25 are not useful because of their inherent inflexibility for dosing.
- The sole use of rapid-acting insulin without concomitant basal insulin is doomed to failure.

Factors Increasing Risk of Hypoglycemia in Hospitalized Patients

- **Factors related to carbohydrate intake**
 - Mistiming of insulin dosage with respect to food
 - Transportation off ward causing meal delay
 - New NPO status
- **Interruption of any of the following:**
 - IV dextrose, TPN, enteral feedings
- **Inadequate glucose monitoring**
- **Medication and medication changes**
- **Liver or renal dysfunction, advanced age**

Inpatient Glargine-Glulisine Dosing in Chronic Renal Failure

- **Multicenter trial**
- **107 patients randomized from general hospital units—70% medical, 30% surgical**
- **Type 2 diabetes duration >1 year**
- **eGFR <45 mL/min, but no patients on dialysis**
- **Initial BG >180 mg/dL**
- **Duration of study >48 hours**
- **No use of any non-insulin diabetic therapies**

Inpatient Glargine-Glulisine Dosing in Chronic Renal Failure

50 subjects

**Glargine 0.25
units/kg daily**

**Glulisine 0.08
units/kg/meal**

57 subjects

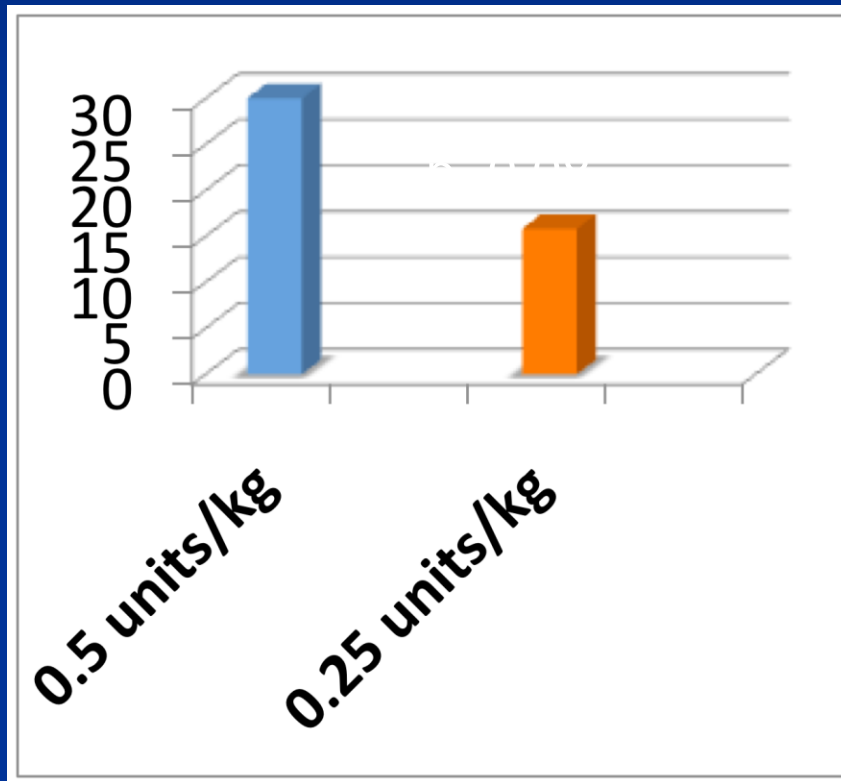
**Glargine 0.125
units/kg daily**

**Glulisine 0.04
units/kg/meal**

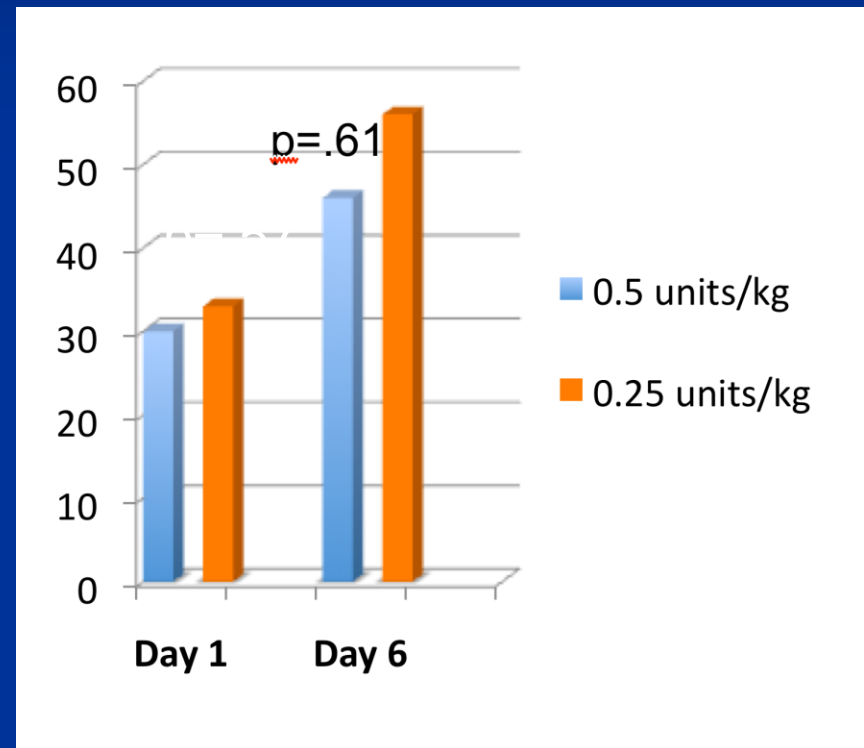
- **BG checked pre-meals and at bedtime.**
- **Insulin doses were adjusted daily aiming to keep all BG readings in the 100–180 mg/dL target range.**

Incidence of Hypoglycemia

Percent of subjects with BG <70 mg/dL



Percent of BGs 100–180 mg/dL



BG <50 mg/dL 0.5 U/kg: 6% of subjects

BG <50 mg/dL 0.25 U/kg: 1.8% of subjects

Inpatient Postoperative Glucose Control Special Situations

- **Insulin therapy in renal failure**
 - Elderly patients may have a substantial decrease in eGFR despite having a mild elevation in serum creatinine. Incorporate eGFR into weight-based initiation of insulin dosing.
 - For patients with eGFR <45 mL/min, reduce the total daily insulin dose by 50% to 0.25 units/kg/day, half basal insulin and half rapid-acting, in order to reduce the frequency of hypoglycemia.
 - This dosing modification of insulin dosing has been shown to reduce the frequency of hypoglycemia in renal failure patients receiving insulin.

Emergent Perioperative Management of Uncontrolled Hyperglycemia

- 51-year-old man presents to the ED with a history of polyuria, abdominal pain, and nausea/vomiting. BP 154/88, HR 112; Temperature = 100.5°; Weight = 102 kg
- BG is 539 mg/dL. DKA is ruled out.
- He is dehydrated with BUN 64, creatinine 2.5.
- He has no PMH but + FH of type 2 diabetes.
- Ultrasound reveals acute cholecystitis.
- He is given 10 units regular insulin SQ in the ED and admitted to the general surgical floor.
- Repeat BG 2 hours later is 398 mg/dL.

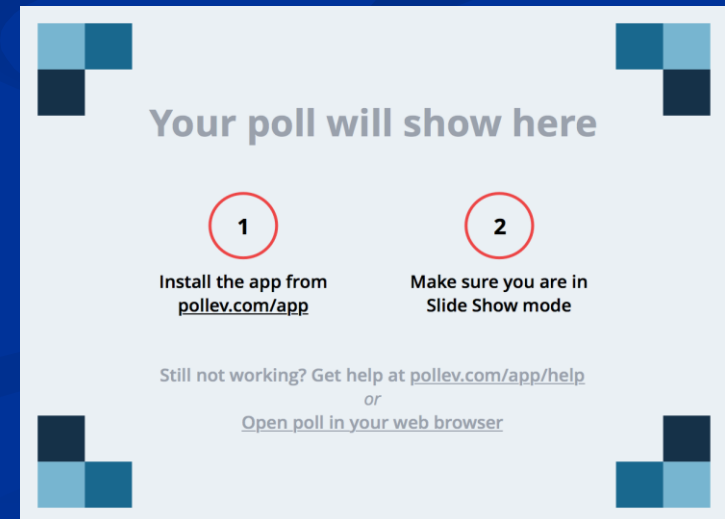
Emergent Perioperative Management of Uncontrolled Hyperglycemia

- Newly diagnosed type 2 diabetes
 - HbA_{1c} is pending.
- Acute cholecystitis, being prepared for surgery
 - IV antibiotics are started.
- Dehydration with acute kidney injury
 - Aggressive volume replacement with IV fluids begun.
- How should you manage this patient's diabetes?

Emergent Perioperative Management of Diabetes

What's the Best Practice?

- Give 0.4 units/kg insulin glargine SQ and 0.2 units/kg rapid-acting insulin SQ
- Give 0.2 units/kg rapid-acting insulin SQ and repeat the BG in 2 hours
- Give 0.2 units/kg insulin glargine SQ and 0.1 units/kg rapid-acting insulin SQ
- Clear the patient for immediate surgery; will implement diabetes management post-op
- Transfer the patient to the ICU for IV insulin



Emergent Perioperative Management of Diabetes: Best Practice

- 0.4 units/kg insulin glargine SQ and 0.2 units/kg rapid-acting insulin SQ is too much insulin to give since eGFR <45 mL/min.
- Give 0.2 units/kg rapid-acting insulin SQ and repeat the BG in 2 hours is only using the sliding-scale approach. This will not be effective!
- Give 0.2 units/kg insulin glargine SQ and 0.1 units/kg rapid-acting insulin SQ. YES!
- Clear the patient for immediate surgery; will implement diabetes management post-op. NO; why deny and delay appropriate management?
- Transfer the patient to the ICU for IV insulin. Not needed if vital signs are stable.

Emergent Perioperative Management of Uncontrolled Hyperglycemia

- Phase 1 (preoperative)
- IV hydration
- Initiation of insulin
- IV insulin infusion—probably not necessary
- Begin basal insulin 0.3 units/kg daily
- Add 0.1 units/kg SQ rapid-acting insulin. Can repeat dose every 2 hours until BG <200
- Check BG every 2 hours until better then every 4–5 hours

Emergent Perioperative Management of Uncontrolled Hyperglycemia

- Phase 2 (immediately postoperative)
- Because of beta-cell glucotoxicity, SQ insulin is the best option for the next 4–8 weeks.
- Adjust the dose of insulin glargine every 24 hours
- Continue correction dosing of rapid-acting insulin every 4–5 hours for glucose >160 mg/dL
- Complete IV hydration
- Add scheduled rapid-acting insulin SQ with meals

Emergent Perioperative Management of Uncontrolled Hyperglycemia

- **Phase 3 (preparing for discharge)**
- **Teach survival skills: diet, insulin, glucose monitoring, hypoglycemia, and provide meter**
- **Can discharge home in 48 hours if you have the necessary resources**
- **Provide rapid access to comprehensive outpatient diabetic education**
- **Provide telephone access for daily or every-other-day insulin dose adjustment**

The Discharge Handoff: Inpatient HbA_{1c}—Avoidance of Clinical Inertia

- **Clinical inertia is defined as the failure to make appropriate intensification in chronic disease management during a patient encounter**
- **HbA_{1c} is ideally suited to universal pre-op/inpatient measurement and therapeutic intensification as needed at the time of hospital discharge**

The Discharge Handoff: Inpatient HbA_{1c}—Avoidance of Clinical Inertia

- 59-year-old man with an 8-year history of type 2 diabetes
- Admitted for peripheral arterial bypass
- For the past year he has been treated with metformin 500 mg BID and glipizide 10 mg BID.
- Initial BG is 249 mg/dL.

The Discharge Handoff: Inpatient HbA_{1c}—Avoidance of Clinical Inertia

- He is taken to the OR and admitted post-op.
- Oral agents are stopped.
- NPH and rapid-acting insulin are begun BID with BG levels stabilizing in the 100–140 mg/dL range.
- After 4 days he is ready for discharge home.

What do you send the patient home on?

The Discharge Handoff: Inpatient HbA_{1c}—Avoidance of Clinical Inertia

What do you send the patient home on?

It all depends on the HbA_{1c}!

The Discharge Handoff: Inpatient HbA_{1c}—Avoidance of Clinical Inertia

Scenario 1
HbA_{1c} = 6.6%

Do nothing
Home on metformin
500 mg BID
and glipizide 10 mg BID

Not Ideal

Increase metformin
to 1000 mg BID
Continue glipizide 10
mg BID

Ideal

The Discharge Handoff: Inpatient HbA_{1c}—Avoidance of Clinical Inertia

Scenario 2
HbA_{1c} = 7.8%

Increase metformin
to 1000 **mg** BID
Continue glipizide
10 **mg** BID

Not Ideal

Increase metformin
to 1000 **mg** BID
Continue glipizide 10
mg BID
and add a **third** agent

Better

The Discharge Handoff: Inpatient HbA_{1c}—Avoidance of Clinical Inertia

Scenario 3
HbA_{1c} = 9.8%

Increase metformin
to 1000 **mg** BID
Continue glipizide 10
mg BID
and add a third agent

Not Ideal

**Continue
insulin!**
(and metformin)

Ideal

Use Your HbA_{1c} to Break the Cycle of Clinical Inertia for Blood Glucose Control in Diabetes

Use This Golden Opportunity