Improving Glycemic Control in the Critical Care Setting
Outline

• Review current guidelines
• Review current glycemic targets
• DKA Treatment
• Building a “perfect” glycemic control protocol
• Transition from IV to SQ insulin
• Special Situations
Antihyperglycemic Therapy
Any patient with a blood glucose >180
Check every patient at least once

Insulin
Recommended

Oral Hypoglycemics
Not appropriate

Intravenous Insulin
Critically ill patients
Goal 140-180

Subcutaneous Insulin
Non-critically ill patients

Daily Dose

Scheduled
Basal

Nutritional

Correctional

ADA/SCC Target Glucose Levels in Critical Care/ICU Patients

- **American Diabetes Association**
  - Starting threshold >180 mg/dL
  - Once IV insulin is started, glucose level should be maintained between 140 and 180 mg/dL
  - Lower glucose targets (110-140 mg/dL) may be appropriate in selected patients
  - Targets <110 mg/dL or >180 mg/dL are not recommended

- **Society of Critical Care Medicine**
  - Starting threshold of >150 mg/dL and absolutely at 180 mg/dL
  - Use protocol to achieve low rate of hypoglycemia <70 mg/dL
  - Minimal excursions of <100 mg/dL

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1. Diabetes Care 2016; 39 (Suppl. 1):S99-S104
Insulin Infusions: Indications

• DKA/HHS; aggressive and intended to lower blood glucose rapidly

• Critical Illness with hyperglycemia; initiate infusion when BG:
  • ADA/AACE: BG >180 mg/dL
  • SCCM: BG >150 mg/dL

1. Diabetes Care 2016; 39 (Suppl. 1):S99-S104
DKA: Treatment

• Hydration
• Electrolytes
• Insulin
• Co-morbid conditions and/or precipitating factors

Kitabchi Diabetes Care 2006
Fluids

- Normal saline initially, 1-2L in the first hour
- If (corrected) sodium is normal or elevated, use \( \frac{1}{2} \) NS thereafter ( +/- dextrose, +/- potassium)
  - Dextrose if BG <200
  - Potassium if K is 3.3-5.2
- Monitor
  - Electrolytes, q2h to start
  - Blood pressure
  - Urine output
  - Osmolality if renal or cardiac disease
Electrolytes

• Potassium
  – <3.3; replace by IV before insulin
  – 3.3-5.2; add 20-30mEq to IVF

• Bicarbonate, only for pH <6.9
  – 3 amps in 1L d5W until pH>7

• Phosphate
  – Treat if <1.0mg/dL or if severe cardiac-pulmonary compromise
Insulin Infusion

• Bolus of 0.1 Unit/kg
• Infusion at 0.1 unit/kg/hr
• (Alternatively, infuse at 0.15 units/kg, no bolus)
• Goal is to decrease BG 50-75/hr
• Evaluate hourly and adjust accordingly
• What about the diet?
Diagnostic Work Up

- Urinalysis
- Complete Blood Count
- Electrolytes with calculated anion gap
  - Na – (Cl + CO2)
  - Corrected Sodium
- Osmolality
  - Osmolar gap = Osm – (2xNa + BG/18)
- EKG
- Rule out infection
- Blood Gas (optional)
Insulin Infusions: Highs and Lows

Top Causes of Hyperglycemia in the ICU
- Insulin infusion protocol ineffective
- Poor utilization of protocol

Top Causes of Hypoglycemia in the ICU
- Insulin infusion protocol ineffective
- Not following insulin infusion protocol
- Carbohydrate mismatch

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 Ingredients for Insulin Infusion
Order Sets and Protocols

Table 2. Components of a Safe and Effective Insulin Infusion Protocol

- Includes appropriate glycemic targets
- Identifies threshold for implementation
- Is nurse-managed and easy to implement
- Provides clear, specific directions for blood glucose monitoring and titration
- Includes titration based on both current blood glucose level and rate of change*
- Is safe: carries a low risk for hypoglycemia and includes an embedded protocol for treatment of hypoglycemia should it occur
- Is effective: gets patients to target quickly and maintains blood glucose within the target range with minimal titration
- Includes a plan for transition to subcutaneous insulin

*Rate of change is calculated based on the slope of the blood glucose trend line and is frequently incorporated into column-based protocols by movement to a more aggressive algorithm if blood glucose is not declining by ~ 40–75 mg/dl or to a less aggressive algorithm if blood glucose is declining too rapidly.

Patient Receiving TPN or Continuous Tube Feeds

Matching Insulin and Intake

- Basal Insulin requirements
- Nutritional Insulin Requirements
- Infusion
- Blood Glucose (mg/dL)

Blood Glucose (mg/dL) vs. Insulin Infusion (Units/hr)

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An interruption in nutrition requires a response!

Mismatched Insulin and Intake

Blood Glucose (mg/dL)

Insulin Infusion (Units/hr)

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Option 1: You can adjust the insulin

Adjust the Insulin

- Basal Insulin requirements
- Nutritional Insulin Requirements
- Infusion
- Blood Glucose (mg/dL)
Option 2: Start alternative dextrose source

Matching Insulin and Intake

- Basal Insulin requirements
- Nutritional Insulin Requirements
- Infusion
- Blood Glucose (mg/dL)
Have a plan
Example of EMR Alert:
TF on hold + Insulin Adjustment

• Will appear for pt’s with “0” charted for TF rate + “on insulin”

• Potential Problems
  – RNs don’t consistently chart TF interruptions in I/O
  – Charting not always timely if at all
Laminated pink caution sign has “Nutrition on Hold Unexpectedly Algorithm” On the back for quick reference
Special Case:
Eating while receiving insulin infusion

- Plasma insulin
- Basal Insulin (infusion)
- Nutritional Insulin (SubQ analog)

Breakfast, Lunch, Dinner

Time: 8:00, 12:00, 16:00, 20:00, 24:00, 4:00
Insulin Concentration

- Prepare all insulin infusions in pharmacy

- Use one standard insulin concentration throughout the hospital if possible or confined to special patient populations e.g. PEDS, L&D

- Most common concentration recommended is 1 unit/mL

Jacobi Crit Care Med 2012, ASHP, ISMP
## Some Approaches

<table>
<thead>
<tr>
<th>Order Set(s)</th>
<th>UCSD</th>
<th>VMMC</th>
<th>NYPH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Order Set(s)</td>
<td>Computer (EPIC)</td>
<td>Computer (Cerner)</td>
<td>Computer (Sunrise)</td>
</tr>
<tr>
<td>Protocol(s)</td>
<td>Computerized-web-based</td>
<td>Paper (3 sets)</td>
<td>Paper (2 sets)</td>
</tr>
<tr>
<td>BG Target</td>
<td>90-150 (ICU) 90-180 (Step-down) 120-200 (OR)</td>
<td>100-180</td>
<td>100-140 (eg SICU) And/or 140-180 (eg Neuro ICU)</td>
</tr>
<tr>
<td>Formula</td>
<td>BG value and rate of change</td>
<td>BG value and rate of change</td>
<td>BG value and rate of change</td>
</tr>
</tbody>
</table>
**VMMC (Cerner EMR): 3 Insulin Infusion Order Sets**

<table>
<thead>
<tr>
<th>Component</th>
<th>Order Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV FLUIDS</td>
<td></td>
</tr>
<tr>
<td>Step 1: Rehydration</td>
<td>Most patient with hyperglycemic crisis have moderate to severe dehydration.</td>
</tr>
<tr>
<td></td>
<td>Begin rehydration with isotonic saline at 1 L/hr up to four hours.</td>
</tr>
<tr>
<td>IV Fluid - Bolus HOSP</td>
<td></td>
</tr>
<tr>
<td>Step 2: Maintenance while blood glucose is &gt; 200 mg/dL</td>
<td>Supplement potassium in IV fluids if potassium is normal or low, but &gt; 3.3, or &lt; 3.3, then replace potassium by IV prior to starting insulin therapy.</td>
</tr>
<tr>
<td>Sodium Chloride 0.9% 1000 mL + potassium chloride-additive 30 mEq</td>
<td>Rate: 150 mL/hr, Infuse 1 sachet over 6.7 hr, Volume 1,000 mL, IV, Routine, Start: 02/08/2016 13:18</td>
</tr>
<tr>
<td>Potassium supplementation not required if potassium &gt; 3.3</td>
<td>rate: 150 mL/hr, Volume 1,000 mL, IV, Routine</td>
</tr>
<tr>
<td>Sodium Chloride 0.9%</td>
<td>Rate: 150 mL/hr, Volume 1,000 mL, IV, Routine, Note: Begin when blood glucose ≤ 200 mg/dL for patients with low serum sodium</td>
</tr>
<tr>
<td>Dextrose 5% with 0.5% NaCl</td>
<td>Rate: 150 mL/hr, Volume 1,000 mL, IV, Routine, Note: Begin when blood glucose ≤ 200 mg/dL for patients with high or normal serum sodium</td>
</tr>
<tr>
<td>Dextrose 5% with 0.45% NaCl</td>
<td>Rate: 150 mL/hr, Volume 1,000 mL, IV, Routine, Note: Begin when blood glucose ≤ 200 mg/dL for patients with high or normal serum sodium</td>
</tr>
</tbody>
</table>

**MEDICATIONS**

Pharmacy to Dose medication. Pharmacy will select initial bolus and infusion rate. RN to manage infusion titration per protocol. Contact Pharmacy at D2873 to communicate additional information that may alter standard dosing.

**Pharmacy to Dose Med**

<table>
<thead>
<tr>
<th>Weight</th>
<th>Bolus Dose</th>
<th>Start Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;122.4 kg</td>
<td>12.5 units</td>
<td>12.5 units/hr</td>
</tr>
<tr>
<td>117.3-122.4 kg</td>
<td>12 units</td>
<td>12 units/hr</td>
</tr>
<tr>
<td>112.5-117.4 kg</td>
<td>11.5 units</td>
<td>11.5 units/hr</td>
</tr>
</tbody>
</table>

**Details for Pharmacy to Dose Med**

- **Pharmacist to Dose Med**
  - Infusion - DKA/HHS Protocol
  - Insulin Infusion - DKA/HHS Protocol
  - Insulin Infusion - Medical Protocol
  - Insulin Infusion - Surgical Protocol

- **Indication**
  - per DKA/HHS insulin protocol

- **Route of Administration**
  - IV
  - Priority: Routine
  - Duration Unit: Routine

- **For Insulin Infusion Only**
  - Initiation

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**Review Schedule**

Remaining Administrations: 0 Stop (Unknown)

- **Requested Start Date/Time**
  - 02/08/2016 13:18

**Stop Date/Time**

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**SHM**

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UCSD (Epic EMR): Insulin Infusion Order set

**Order Sets**

- **IP/ED GEN Intravenous Insulin Infusion Therapy**
- **Patient Care**
  - Patient Care Orders
  - Glucose (POC)
    - Routine, EVERY HOUR First occurrence Today at 1400 Until Specified
    - Check fingerstick glucose hourly per computer protocol. May check glucose every 2 hours if 3 consecutive blood sugars are within the protocol target range.
  - Nursing Misc Orders: Please page pharmacist with insulin computer protocol questions.
    - Routine, ONGOING starting Today at 1345 Until Specified
    - Specify: Please page pharmacist with insulin computer protocol questions.

**Medications**

- **Insulin Infusion**
  - Insulin Infusion
    - insulin regular (HUMULIN, NOVOLIN) 100 Units in sodium chloride 0.9% 100 mL infusion
      - Intravenous, Continuous starting Today at 1400 Until Discontinued
      - Infuse per insulin computer protocol
    - And
      - insulin regular (HUMULIN, NOVOLIN) IV bolus from bag 1-15 Units
        - 1-15 Units, Intravenous, Once PRN, 1 dose starting Today at 1331 Until Discontinued. Per insulin computer protocol
        - Bolus dose per insulin computer protocol. Do NOT administer a bolus dose upon initiation of the insulin infusion if a separately ordered bolus dose of insulin was administered within the last two hours.

- **Fingerstick Glucose Orders for Hypoglycemia Protocol**
  - Glucose (POC)
    - Routine, PRN starting Today at 1331 Until Specified
    - Test blood glucose within 15 to 30 minutes of the initial glucose test showing blood glucose < 70 mg/dl with or without symptoms OR glucose < 80 mg/dl with symptoms (eg, shakiness, diaphoresis, confusion, irritability). If blood glucose is still below 80 mg/dL after treatment, RE-TREAT and check blood glucose again in 15 to 30 minutes. Continue to check blood glucose every 15 to 30 minutes until the glucose is greater than or equal to 80 mg/dL for TWO consecutive values.
UCSD: Insulin Infusion Calculator (web-based, lives outside of EPIC)

- RNs utilize the **Insulin Computer Calculator** per UCSD protocol
  - **Log-in** to the secure web-based insulin computer protocol site
  - **Select** the patient’s unit and patient
  - **Enter** the blood glucose levels as directed
  - **Add comments** (as needed) where indicated
Computer program provides recommendation for bolus and rate on initiation and then recommendations for hourly adjustment of infusion rate per hourly BG checks thereafter.

UCSD: Insulin Infusion Calculator (web-based, lives outside of EPIC)

- Bolus with 5.4 units
- Adjust Insulin Infusion Rate to 3.6 units/hr
- Blood Glucose to Achieve (90 - 150 mg/dL)

Current Glucose: 241

PID: 798110
Unit: *ICU
First Name: Patrick
Last Name: Oshea
NYPH Critical Care Drips

Requested By: Me

Date: __-__-__

Time: ________

Source:

Session

Type: Standard

Reason:

Manual Entry

Searching for...

-insulin drip-

<table>
<thead>
<tr>
<th>Order</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin DRIP 100 Unit/100ml</td>
<td>$12.02/vial</td>
</tr>
<tr>
<td>Insulin Drip Adult ICU Goal BG 100-140 (NOT DKA/HHS)</td>
<td></td>
</tr>
<tr>
<td>Insulin Drip Adult ICU Goal BG 140-180 (NOT DKA/HHS)</td>
<td></td>
</tr>
</tbody>
</table>

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## Criteria for Transition to SubQ Insulin

<table>
<thead>
<tr>
<th>DKA</th>
<th>HHS</th>
<th>Hyperglycemia in CC</th>
</tr>
</thead>
<tbody>
<tr>
<td>BG &lt;200</td>
<td>BG &lt;300</td>
<td>Resolution critical illness</td>
</tr>
<tr>
<td>Two of the following: Gap &lt;12</td>
<td>Normal osmolality</td>
<td>Off vasopressors</td>
</tr>
<tr>
<td>Bicarbonate &gt;15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pH &gt;7.3</td>
<td>Normal mentation</td>
<td>Stable infusion rate for ~6hrs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Transition to SubQ

- Overlap IV and SubQ by two hours
- Know the home regimen and whether or not it was adequate.
- Formula
  - Average rate method
  - Weight based dosing
  - Individualize…
Transition to SubQ Insulin

• Step 1

• Is patient ready for transition from IV to SubQ insulin?
  – Critical illness resolved? Off pressors?
  – DKA/HHS resolved?
  – Rate stable for ~ 6hrs?
Transition to SubQ Insulin (Cont.)

• Step 2

  – Does patient have history of DM? A1C?

  • No DM and A1C <6.0% --> correction scale only
  • Yes DM or A1C >6.0% --> basal bolus regimen
Transition to SubQ Insulin (Cont.)

• Step 3
  – Use 80% of the lowest of the following to determine TDD:
    • the dose administered over the last 12 hours multiplied by 2
    • the dose administered over the last 24 hours
    • Use average hourly rate over the last 6 hrs (if stable) and multiply by 20 (80%)
    • Weight
Transition to SubQ Insulin (Cont.)

• Step 4
  – Determine if TDD = basal or basal + nutritional
    • If basal dose only, then dose can be doubled and divided accordingly when nutrition added
    • If basal + nutritional, then give 50% as basal and 50% as bolus
  • Give basal insulin dose and turn off insulin drip 2 hrs later
**Transition from IV to SQ Insulin Protocol**

(This protocol applies only to patients on an insulin drip for >24 hours. Physician to make a clinical judgment on all others.)

**Step 1:** Is the patient ready for transition?
- Patient meets following criteria:
  - Pt is not critically ill or requiring vasopressors
  - Blood glucose in target range all of last 6 hours

  **Yes**

  **No** Continue Insulin Drip

**Step 2:** Does patient need scheduled subcutaneous insulin?
- NO:
  - Patients with no history of diabetes AND HbA1C < 6.0%
- YES:
  - All patients with DM 1
  - Patients with DM 2 and insulin drip rate > 1.0 unit/hour
  - Patients with HbA1C > 6.0%

  **Yes**

  **No** Transition to Correction Scale Only

**Step 3:** Calculate Total Daily Dose Insulin Requirement (call Pharmacy to use insulin calculator transition and/or use equation below)
- Average the rate of insulin infusion over the previous 6 hours and multiply this number by 20. (24 is not used for safety reasons.)
- (avg drip rate) ______ units/hr x 20 = ______ (calculated insulin)

**Step 4:** Evaluate patient nutrition while on drip to determine insulin distribution
- **Full nutrition:** Pt is currently eating >50% of their meals, on goal tube feeds, goal TPN or receiving Dextrose IVF > 50mL/hr
- **Minimal nutrition:** Pt is currently NPO, taking <50% of their meals, is on a zero carbohydrate clear liquid diet, or 6 hours used in Step 3 calculation is period of fasting (i.e. overnight).

**Full Nutrition:** calculated insulin = TDD
1. Give 50% of the TDD as basal insulin ordered as Lantus (glargine) once daily to be administered 2 hours before stopping the insulin infusion.
2. Give 50% of the TDD as nutritional insulin divided TD if tolerating meals (Lispro) or C46 hours if on continuous tube feeds (Regular) using CPOE orderset.
3. Order appropriate correction scale once drip is discontinued using CPOE orderset.

**Minimal Nutrition:** calculated insulin = BASAL insulin
1. Give 100% of calculated insulin as basal insulin ordered as Lantus (glargine) once daily to be administered 2 hours before stopping the insulin infusion.
2. Add nutritional insulin when clinically indicated.
3. Order appropriate correction scale once drip is discontinued using CPOE orderset.

Address all questions to ICU Pharmacist or Endocrine/Diabetes pager HC 290-4920, LJ 290-5272.
Example of hardwired transition algorithm at VMMC
Common Pitfalls

• No overlap between infusion & subcutaneous insulin

• Premature transition, difficult to determine a stable rate

• Mismatch between insulin infusion & nutritional status on infusion and at transition
  – Interruptions of tube feeds/TPN
  – Unclear whether or not infusion used to meet nutritional needs

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Key Points

• Insulin infusion protocols (IIPs) indicated for:
  – DKA/HHS
  – Critically ill patients BG >180 mg/dL

• DKA Treatment: Focus on hydration, electrolytes, insulin, and precipitating factors

• Safe & effective IIPs: clear, concise, BG direction & rate of change and hypoglycemia management & prevention

• Transition from IIP to subcutaneous regimen is complex and involves a delicate balance of art & science
Special Situations

• Continuous Nutrition
  – Tube feeds
  – TPN
• Steroids
• Perioperative BG Control
Patient receiving continuous TF or TPN

Continuous nutrition coverage options:
- Analog q4hr
- Regular q6hr
- Intermediate q12hr
- Long acting q12-24hr
Tube Feedings and TPN

• “Super Nutrition”

• Often requires higher ratio of nutritional insulin compared to basal given continuous delivery of high levels of carbohydrates

• Can be as much as 40:60, 30:70 or even 20:80 ratio of basal:nutrition
Tube Feeding and TPN: Insulin Strategies

• Several options to cover *nutritional* component
  • Rapid acting q4hr
  • Regular q6hr
  • Intermediate (NPH) q12hr
  • Long acting q12-24hr
  • For TPN- regular insulin can be added to TPN

• Choice should be uniform across institution

• Indication and holding parameters should be included in every nutritional insulin order so RN knows when to give and when to hold

• Increase basal insulin carefully in case nutrition is interrupted
Interruption in Nutrition

- Unexpected
  - Pt on continuous TF pulls out NG tube
    - Middle of the night?
    - 1 hour after nutritional insulin given?
    - 5 hours after nutritional insulin given?
- Expected
  - Pt on continuous TF going to Radiology
    - 1 hr for CT?
    - 6 hrs for procedure?

- HAVE A PLAN & AN Order!!

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Patient receiving continuous TF or TPN

Continuous nutrition coverage options:
- Rapid acting q4hr
- Regular q6hr
- Intermediate q12hr
- Long acting q12-24hr
1 Hour After Nutritional Insulin Given
5 Hours After Nutritional Insulin Given
Steroids

- Steroids commonly prescribed in hospital
  - COPD & asthma exacerbations
  - Transplant patients
  - Anti-emetic for chemotherapy
  - Post-operatively, e.g. orthopedics

- Steroids cause general insulin resistance w/ much less effect on gluconeogenesis

- Glucose elevation predominantly postprandial hyperglycemia, relative lack of fasting hyperglycemia
8am Once Daily Steroid Dosing

Steroid Effect

6a 8a 10a 12p 2p 4p 6p 8p 10p 12a 2a 4a
Relative Potencies of Systemic Glucocorticoids

<table>
<thead>
<tr>
<th>CORTICOSTEROID</th>
<th>ACTIVITY</th>
<th>RELATIVE POTENCY</th>
<th>EQUIVALENT DOSE (MG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone</td>
<td>Long-acting</td>
<td>25</td>
<td>0.75</td>
</tr>
<tr>
<td>Prednisone</td>
<td>Intermediate-acting</td>
<td>4</td>
<td>5.0</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>Intermediate-acting</td>
<td>5</td>
<td>4.0</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>Short-acting</td>
<td>1.0</td>
<td>20.0</td>
</tr>
</tbody>
</table>

Equivalent Physiologic Replacement Doses:
- Dexamethasone: 0.8-1.2 mg
- Prednisone: 5-7.5 mg
- Hydrocortisone: 20-30 mg
Treatment of Steroid Induced Hyperglycemia

• Insulin dosing depends on frequency/timing of steroid administration (eg once daily, BID, TID, QID)

• Treatment may consists of:
  – Large doses of rapid-acting pre meal +/- basal insulin
  OR
  – NPH alone or in addition to usual basal + bolus regimen

• Avoid significant increases in basal insulin with once daily steroid dosing, as overnight hypoglycemia may occur

• Insulin doses should be adjusted in concert with steroid dose changes
Basal heavy regimen to cover BID-QID steroids when steroid tapered to *once daily* → significantly increases risk of hypos...

Titrate insulin simultaneously with steroids!!
Tapering Steroids

- Decrease nutritional insulin dose and/or NPH dose as you taper steroids

- Be sure to adjust basal insulin dose if dose was increased to cover BID-QID dosed steroids
Perioperative Glycemic Control

• Perioperative hyperglycemia associated with worse outcomes
  – Malglycemia causes oxidative stress
  – Increased risk of inflammation & infection
  – Increased risk of thrombosis
• Association between hyperglycemia in postop period & adverse outcomes, e.g. infections, arrhythmias and renal impairment
• Published studies show interventions to improve glycemic control reduces risk of complications

Akhtar Anesth Analg 2010, Diabetes Care 2009
Whitcomb et al. (2005), Freire et al. (2005), Zerr KJ, et al. (1997)
Standards of Care

• A1c value should be obtained preoperatively for those with diabetes or diabetes risk factors, with appropriate adjustment in the outpatient regimen prior to surgery.

• Use intravenous insulin infusions in patients with type 1 or type 2 diabetes treated with insulin and undergoing major surgical procedures, with target glucose between 120 and 180 mg/dL.

• Administer subcutaneous correction dose insulin or an intravenous insulin infusion during minor or short surgical procedures, with target glucose between 140 and 180 mg/dL, and monitoring every 1 – 2 hours, depending on insulin used and type of surgery.
Standards of Care (Cont.)

• Anesthesiologist and OR team should make sure that:
  – Glucose levels are monitored at least every hour for patients on infusion.
  – If using insulin during surgery, potassium levels are measured every 4 to 6 hours during surgery.
  – Glucose is measured in the recovery room immediately after surgery.

Thank you!

• Questions…?