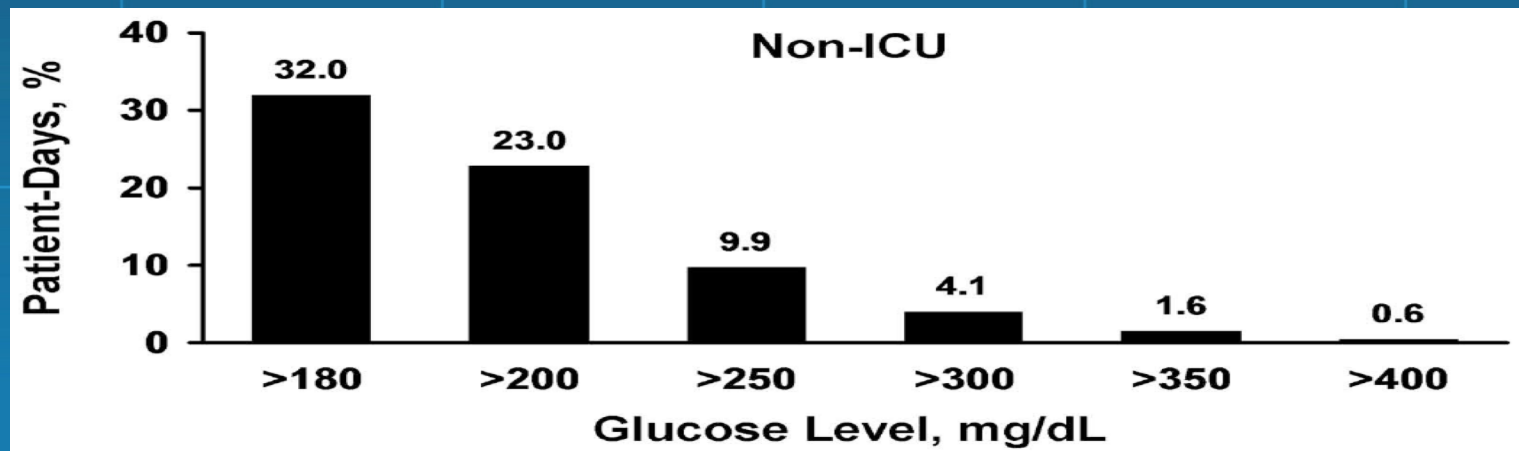
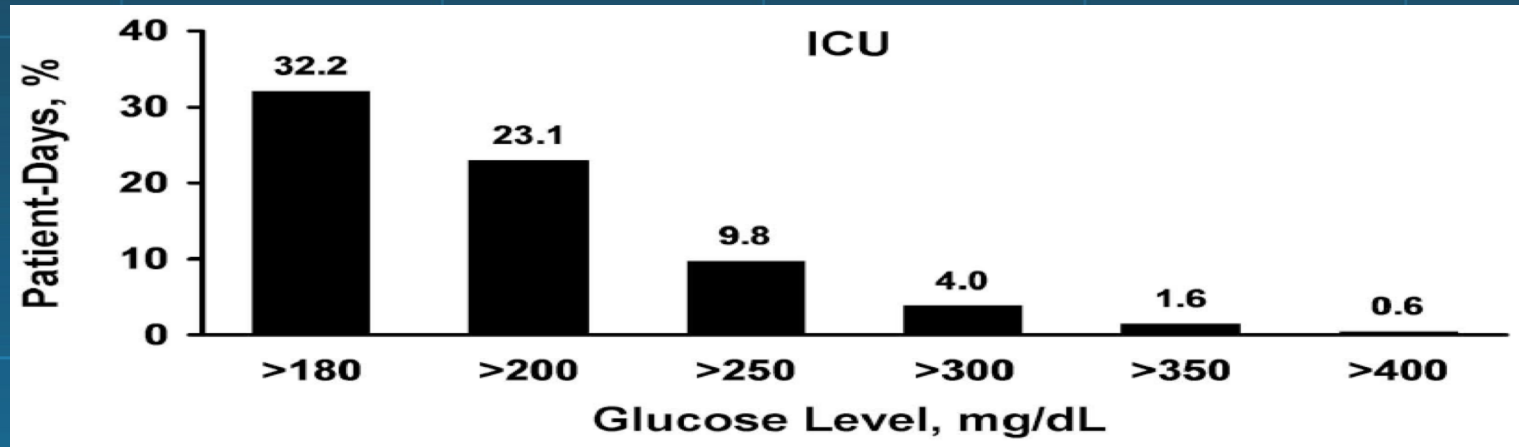


Management of Hyperglycemia in the Critical Care Setting



Distribution of Patient-Day-Weighted Mean POC-BG Values for ICU

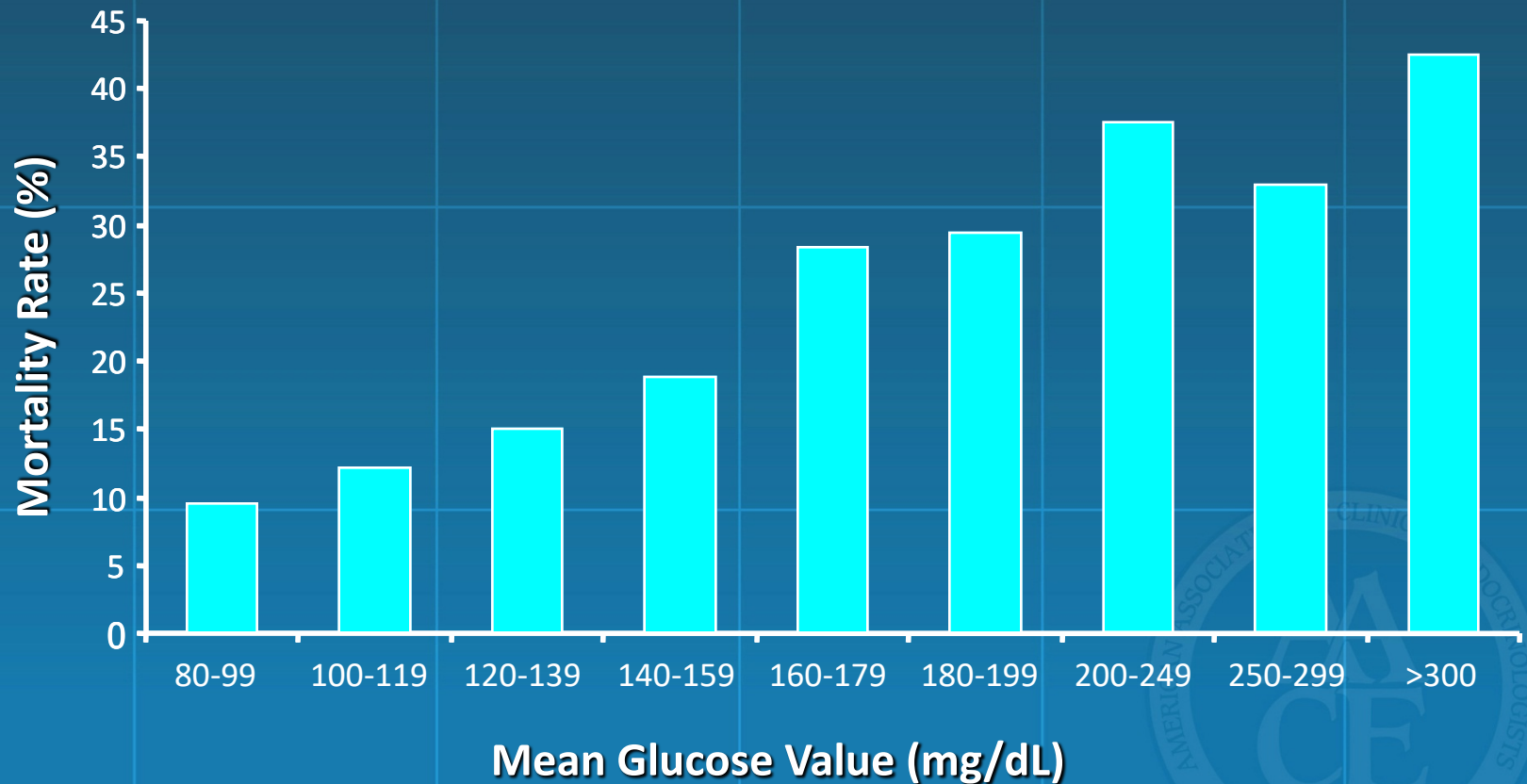


~12 million BG readings from 653,359 ICU patients; mean POC-BG: 167 mg/dL.

Swanson CM, et al. *Endocr Pract.* 2011;17:853-861.

AACE Inpatient Glycemic Control Resource Center

Hyperglycemia and Mortality in the Medical Intensive Care Unit

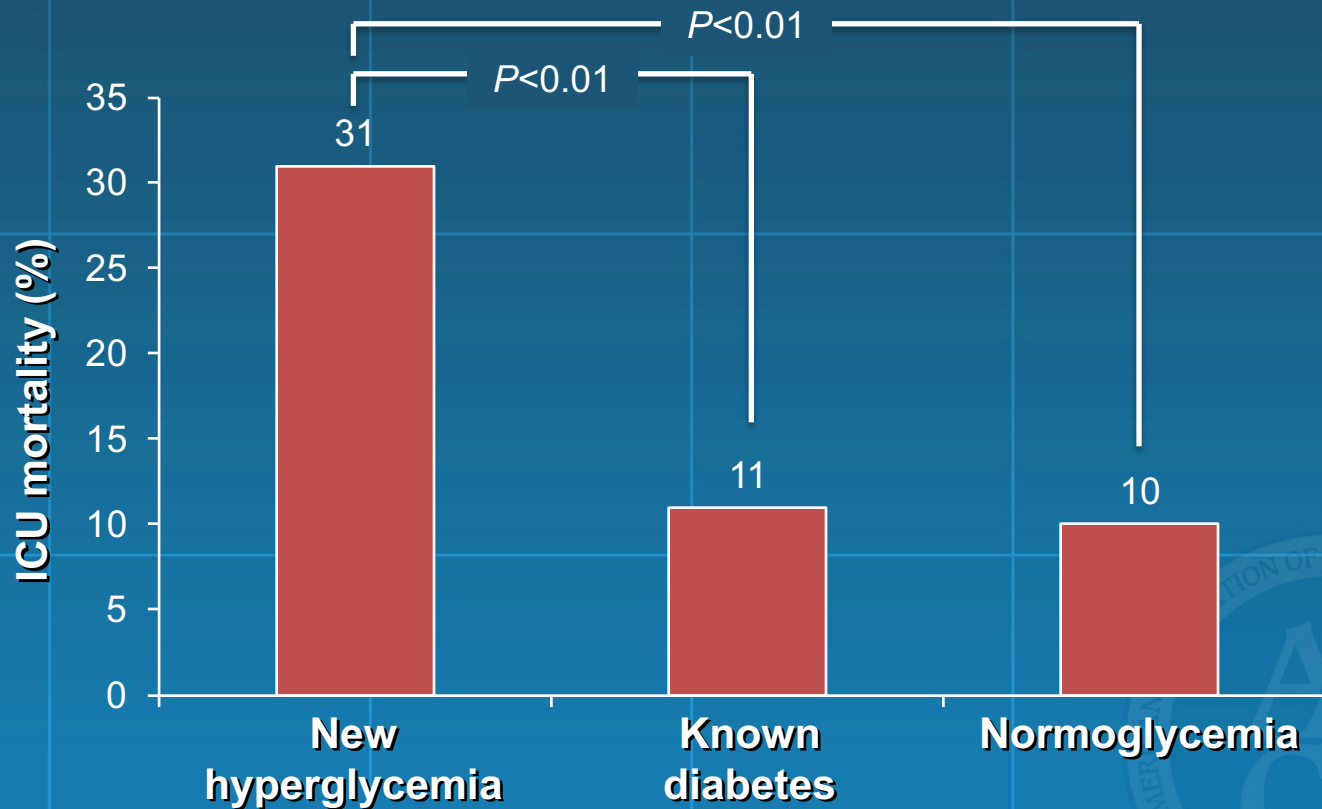


N=1826 ICU patients.

Krinsley JS. *Mayo Clin Proc.* 2003;78:1471-1478.

AACE Inpatient Glycemic Control Resource Center

Hyperglycemia: An Independent Marker of ICU Mortality



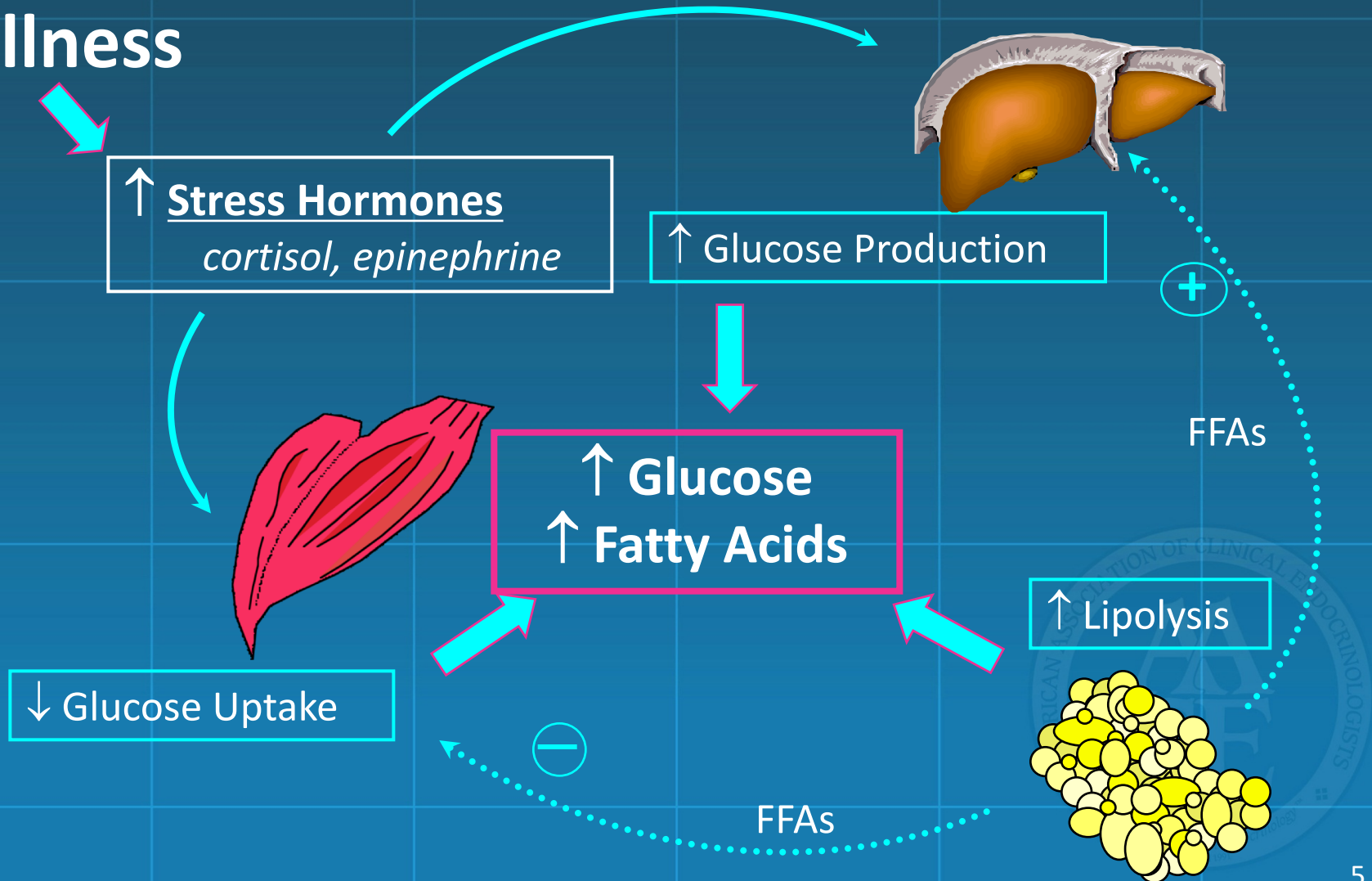
ICU, intensive care unit.

Umpierrez GE, et al. *J Clin Endocrinol Metab.* 2002;87:978-982.

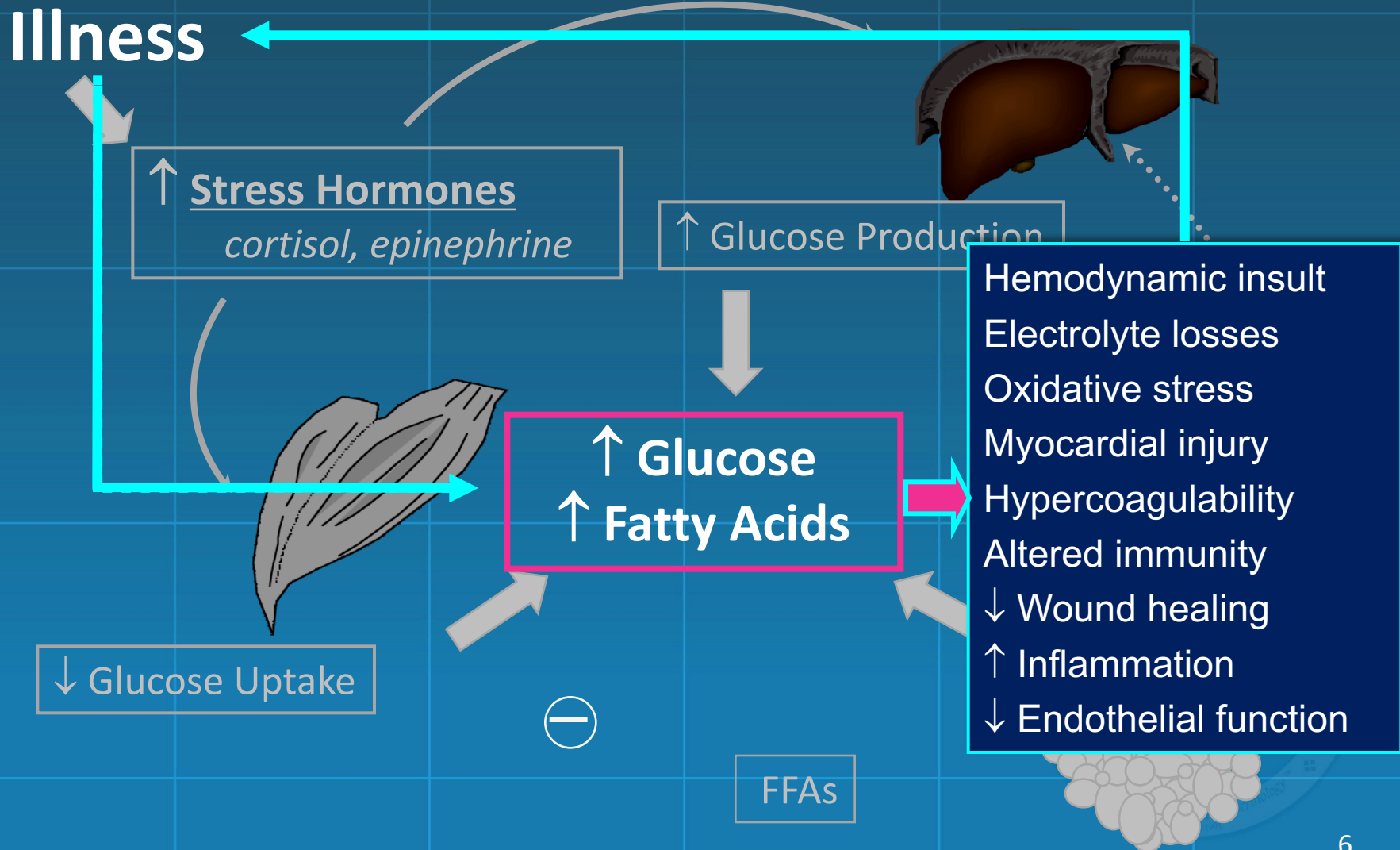
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Illness Leads to Stress Hyperglycemia

Illness



Stress Hyperglycemia Exacerbates Illness



Guidelines From Professional Organizations on the Management of Glucose Levels in the ICU

Year	Organization	Patient Population	Treatment Threshold	Target Glucose Level	Definition of Hypoglycemia	Updated Since NICE_SUGAR Trial, 2009
2009	American Association of Clinical Endocrinologists and American Diabetes Association	ICU patients	180	140-180	<70	Yes
2009	Surviving Sepsis Campaign	ICU patients	180	150	Not stated	Yes
2009	Institute for Healthcare Improvement	ICU patients	180	<180	<40	Yes
2008	American Heart Association	ICU patients with acute coronary syndromes	180	90-140	Not stated	No
2007	European Society of Cardiology and European Association for the Study of Diabetes	ICU patients with cardiac disorders	Not stated	"Strict"	Not stated	No

AACE/ADA Recommendations: All Patients in Critical Care

- Blood glucose target: 140-180 mg/dL
- Intravenous insulin infusion preferred
- Hypoglycemia
 - Reassess the regimen if blood glucose level is <100 mg/dL
 - Modify the regimen if blood glucose level is <70 mg/dL

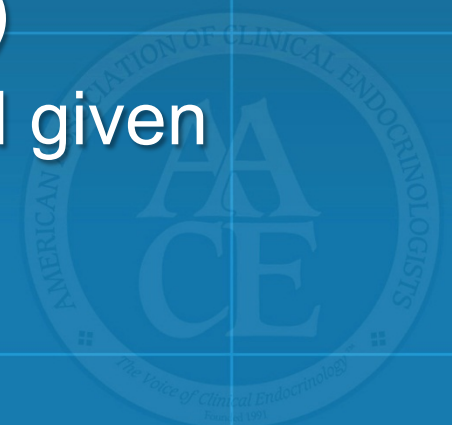


Indications for IV Insulin Therapy

- Diabetic ketoacidosis
- Nonketotic hyperosmolar state
- Critical care illness (surgical, medical)
- Postcardiac surgery
- Myocardial infarction or cardiogenic shock
- NPO status in type 1 diabetes
- Labor and delivery
- Glucose exacerbated by high-dose glucocorticoid therapy
- Perioperative period
- After organ transplant
- Total parenteral nutrition therapy

Components of IV Insulin Therapy

- Concentrations should be standardized throughout the hospital
 - Regular insulin in concentrations of 1 U/mL or 0.5 U/mL
 - Infusion controller adjustable in 0.1-U doses
- Accurate bedside blood glucose monitoring done hourly (every 2 hours if stable)
- Potassium should be monitored and given if necessary

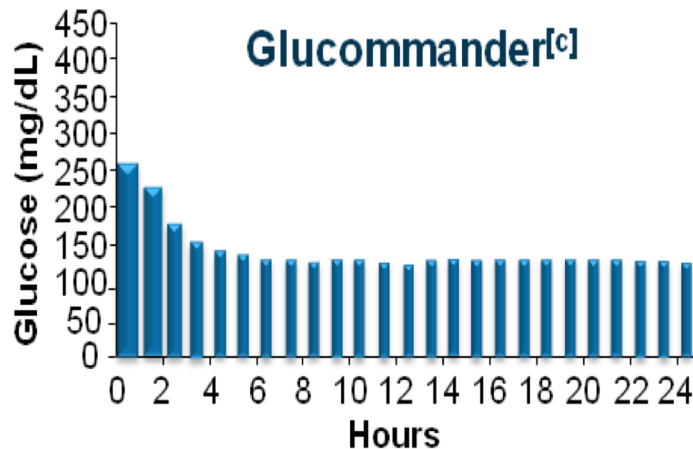
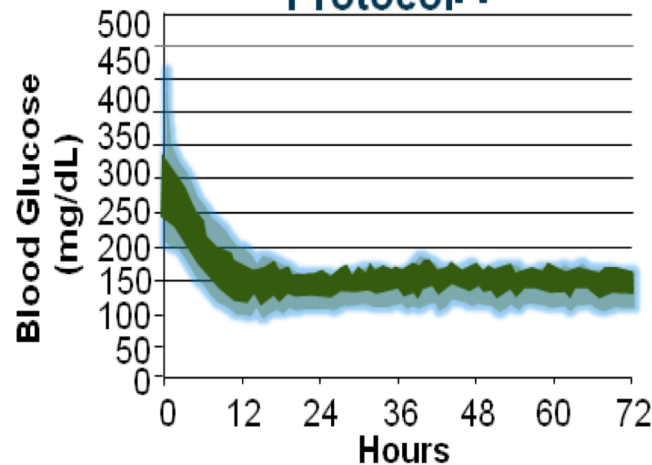


Achieving Glycemic Targets in the ICU

Leuven SICU Study^[a]

- IIT group had lower average blood sugars (103 ± 19 vs 153 ± 33 mg/dL) than CIT group

Yale MICU Insulin Infusion Protocol^[b]



NICE-SUGAR^[d]

- Mean blood glucose level significantly lower in the IIT group than in the CIT group (115 ± 18 vs 144 ± 23 mg/dL; $P < .001$)

a. Van den Berghe G, et al. *N Engl J Med*. 2001;345:1359-1367. b. Goldberg PA, et al. *Diabetes Care*. 2004;27:461-467. c. Davidson PC, et al. *Diabetes Care*. 2005;28:2418-2423; d. Finfer S, et al. *N Engl J Med*. 2009;360:1283-1297.

Example: Updated Yale Insulin Infusion Protocol

Insulin infusion: Mix 1 U regular human insulin per 1 mL 0.9% NaCl
Administer via infusion pump in increments of 0.5 U/h

Blood glucose target range:

120-160 mg/dL

Use glucose meter to monitor blood glucose hourly

Bolus and initial infusion rate:

Divide initial BG by 100, round to nearest 0.5 U
for bolus and initial infusion rates

Example: Initial BG = 325 mg/dL: $325/100 = 3.25$, round up to 3.5:
IV bolus = 3.5 U + start infusion at 3.5 U/h

Subsequent rate adjustments:

Changes in infusion rate are determined by the current infusion rate and the hourly rate of change from the prior BG level



Yale-New Haven Hospital ICU Insulin Infusion Protocol (IIP) for Adults



The following IIP is intended for use in hyperglycemic adult patients in the ICU, adapted from our earlier protocols, in keeping with the latest glucose guidelines from national organizations. It should NOT be used in diabetic ketoacidosis (DKA) or hyperosmolar hyperglycemic state (HHS), as these patients may require higher initial insulin doses, IV dextrose at some point, and important adjunctive therapies for their fluid/acid-base/electrolyte/divalent status. (See 'DKA Guidelines' in YNH Clinical Practice Manual (CPM) for further instructions.) In any patient with BG >500 mg/dL, the initial orders should also be carefully reviewed with the MD, since a higher initial insulin dose and additional monitoring/therapy may be required. If the patient's response to the insulin infusion is at any time unusual or unexpected, or if any situation arises that is not adequately addressed by this protocol, the MD must be contacted for assessment and further orders.

Getting Started

- 1.) **PATIENT SELECTION:** Begin IIP in any ICU patient with more than 2 BGs >180 mg/dl who is not expected to rapidly normalize their glycemic status. Patients who are eating (see #9 below); transferring out of ICU imminently (<24 hrs); or pre-terminal or being considered for CMO status are generally not appropriate candidates for this IIP.
- 2.) **TARGET BLOOD GLUCOSE (BG) RANGE:** **120-160 mg/dL**
- 3.) **ORDERS:** MD order required for use in the ICU.
- 4.) **INSULIN INFUSION SOLUTION:** Obtain from pharmacy (1 unit Regular Human Insulin / 1 cc 0.9 % NaCl).
- 5.) **PRIMING:** Before connecting, flush 20 cc infusion through all tubing.
- 6.) **ADMINISTRATION:** Via infusion pump in 0.5 units/hr increments.
- 7.) **BOLUS & INITIAL INFUSION RATE:** Divide initial BG level by 100, then round to nearest 0.5 units for bolus AND initial infusion rate.
Examples: 1.) Initial BG = 325 mg/dL: $325 \div 100 = 3.25$, round \uparrow to 3.5: IV bolus 3.5 units + start infusion @ 3.5 units/hr.
 2.) Initial BG = 274 mg/dL: $274 \div 100 = 2.74$, round \downarrow to 2.5: IV bolus 2.5 units + start infusion @ 2.5 units/hr.
- 8.) **CAUTION:** If enteral/parenteral (TPN, PPN, Tube feeds) nutrition abruptly stopped, reduce infusion rate by 50%.
- 9.) Patients requiring IV insulin are usually NPO. In the rare patient who is eating, consider giving SQ Aspart PC to 'cover' the meal (administer 1 unit /15 grams carbohydrates consumed (usual dose 3-6 units.) In this circumstance don't increase infusion rate during the first 3 hrs PC.
- 10.) Patients with T1DM, insulin-requiring T2DM, and those requiring >1 unit/hr should be transitioned to SQ insulin prior to discharge from ICU.

BG Monitoring

While on infusion, use glucose meter to check BG hourly. Once stable (3 consecutive values in target range), may reduce checks to **q 2 hr**. If stable for 12-24 hrs, may space checks to **q 4 hr**. *Resume hourly checks until stable again if:* any BG out of range; any change in insulin infusion rate; any significant change in clinical condition; initiation/discontinuation of steroids, pressors, TPN/PPN/tube feeds, dialysis, CVVH, or CAVH. In patients who are vasoconstricted/hypotensive, capillary BG (i.e., fingersticks) may be inaccurate; venous or arterial blood is preferred in this setting.

Adjusting Infusion Rate

If BG < 50 mg/dL:

D/C INSULIN INFUSION & administer 1 amp (25 g) D50 IV; recheck BG q 15 minutes until ≥ 90 mg/dl.

➔ Then, recheck BG q 1 hr; when ≥ 140 mg/dL, wait 30 min, restart insulin infusion at 50% of most recent rate

If BG 50-74 mg/dL:

D/C INSULIN INFUSION & administer 1/2 Amp (12.5 g) D50 IV; recheck BG q 15 minutes until ≥ 90 mg/dl.

➔ Then, recheck BG q 1 hr; when ≥ 140 mg/dL, wait 30 min, then restart infusion at 50% of most recent rate.

If BG 75-99 mg/dL:

D/C INSULIN INFUSION. Recheck BG q 15 minutes until BG reaches or remains ≥ 90 mg/dl.

➔ Then, recheck BG q 1 hr; when ≥ 140 mg/dL, wait 30 min, then restart infusion at 75% of most recent rate.



If BG \geq 100 mg/dL

YNHH ICU Insulin Infusion Protocol



Target BG: 120-160

Begin IV insulin:

BG \div 100 = ____ U/hr

STEP 1: Determine the CURRENT BG LEVEL - identifies a COLUMN in the table:

BG 100-119 mg/dL	BG 120-159 mg/dL	BG 160-199 mg/dL	BG \geq 200 mg/dL
------------------	------------------	------------------	---------------------

STEP 2: Determine the RATE OF CHANGE from the prior BG level - identifies a CELL in the table - Then move right for **INSTRUCTIONS**:
[Note: If the last BG was measured 2 or more hrs before the current BG, calculate the hourly rate of change. Example: If the BG at 2PM was 150 mg/dL and the BG at 4PM is 120 mg/dL, the total change over 2 hours is -30 mg/dL; however, the hourly change is -30 mg/dL \div 2 hours = -15 mg/dL/hr.]

BG 100-119 mg/dL	BG 120-159 mg/dL	BG 160-199 mg/dL	BG \geq 200 mg/dL	INSTRUCTIONS*
		BG \uparrow by > 60 mg/dL/hr	BG \uparrow	\uparrow INFUSION by "2 Δ "
	BG \uparrow by > 40 mg/dL/hr	BG \uparrow by 1-60 mg/dL/hr OR BG UNCHANGED	BG UNCHANGED OR BG \downarrow by 1-20 mg/dL/hr	\uparrow INFUSION by " Δ "
BG \uparrow	BG \uparrow by 1-40 mg/dL/hr, BG UNCHANGED, OR BG \downarrow by 1-20 mg/dL/hr	BG \downarrow by 1-40 mg/dL/hr	BG \downarrow by 21-60 mg/dL/hr	NO INFUSION CHANGE
BG UNCHANGED OR BG \downarrow by 1-20 mg/dL/hr	BG \downarrow by 21-40 mg/dL/hr	BG \downarrow by 41-60 mg/dL/hr	BG \downarrow by 61-80 mg/dL/hr	\downarrow INFUSION by " Δ "
BG \downarrow by > 20 mg/dL/hr <i>see below</i> [†]	BG \downarrow by > 40 mg/dL/hr	BG \downarrow by > 60 mg/dL/hr	BG \downarrow by > 80 mg/dL/hr	HOLD x 30 min, then \downarrow INFUSION by "2 Δ "

[†] D/C INSULIN INFUSION;
 \sqrt BG in 15 min to be sure
 ≥ 90 mg/dL. Then recheck BG
 q 1 hr; when ≥ 140 mg/dL,
 restart infusion @75% of
 most recent rate.

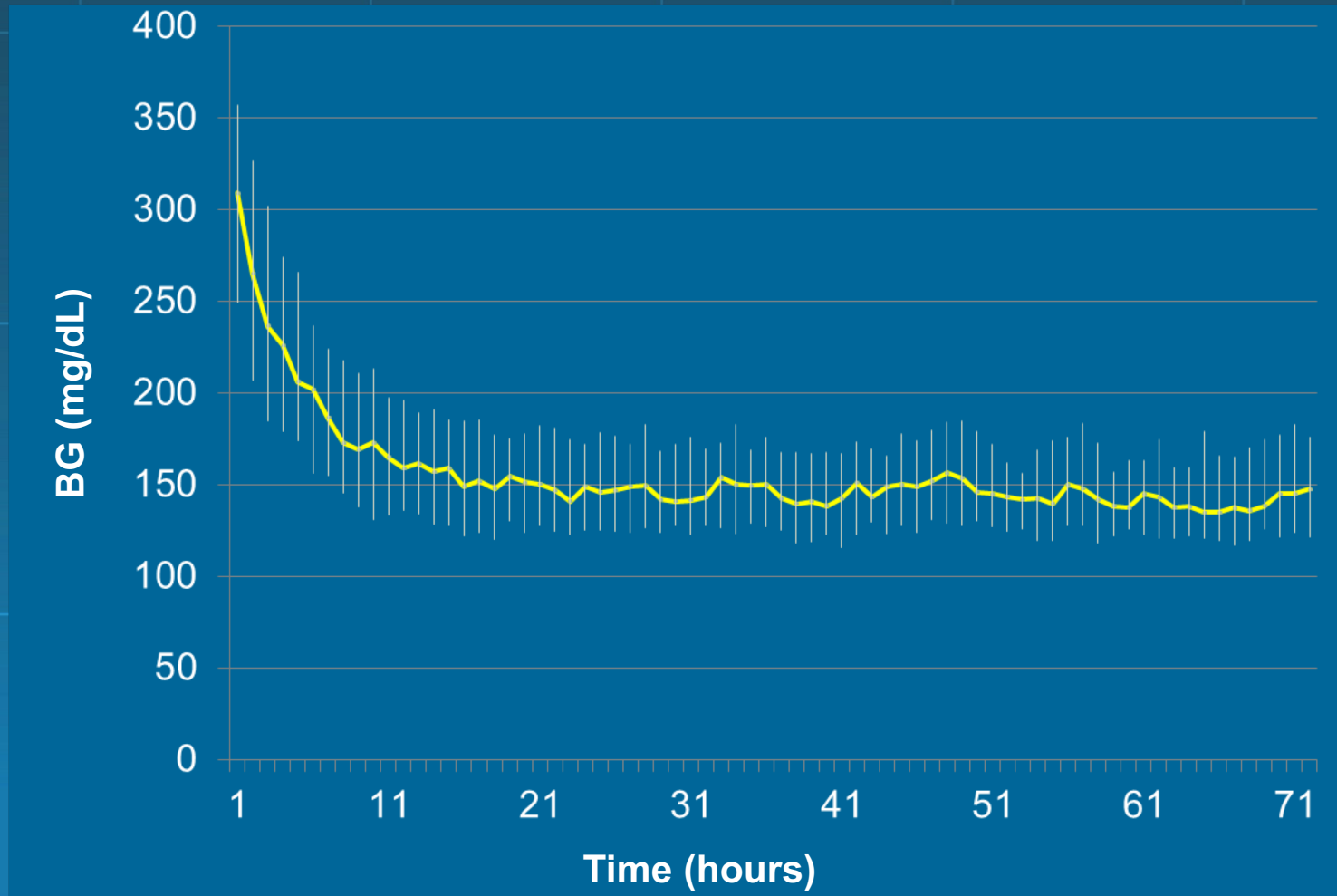
STEP 3: CHANGES IN INFUSION RATE* (" Δ ")
 are determined by the current rate:

Current Rate (Units/hr)	Δ = Rate Change (Units/hr)	2 Δ = 2X Rate Change (Units/hr)
< 3.0	0.5	1
3.0 – 6.0	1	2
6.5 – 9.5	1.5	3
10.0 – 14.5	2	4
15 – 19.5	3*	6*
$\geq 20^*$	4*	8*

* Depending on the clinical circumstances, infusion rates typically range between 2-10 units/hr. Doses in excess of 20 units/hr are unusual, and, if required, the responsible MD should be notified to explore other potential contributing factors (including technical problems, such as dilution errors, etc.)

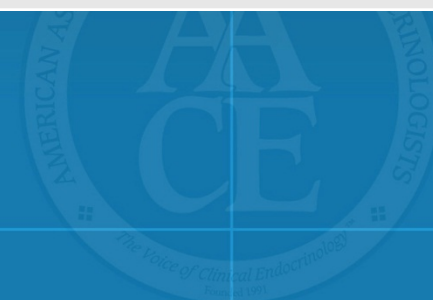
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 Yale-New Haven Hospital
 (July 2009, revised 8/30/10, 11/18/10, 1/3/11)

Insulin Infusion Protocol Performance



Results

Variable	Median Value (interquartile range)
Preinfusion BG, mg/dL	309 (251-359)
BG once target (<160 mg/dL) reached, mg/dL	150 (127-180)
Nadir BG during infusion, mg/dL	89 (80-101)
Time to target (BG <160 mg/dL), h	7 (5-12)
Hours on infusion	59 (25-127)
Infusion dose, units/h	3.5 (2.5-4.5)

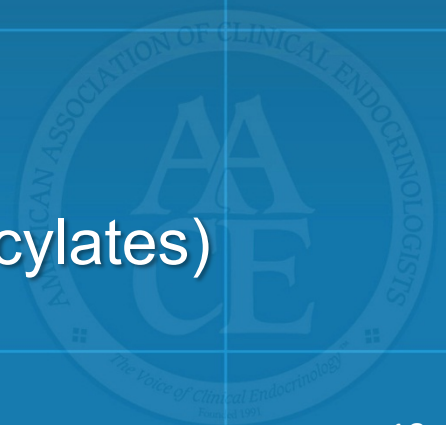


An Optimal IV Insulin Protocol

- Validated
- Reaches and maintains blood glucose successfully within a prespecified target range
- Includes a clear algorithm for making temporary corrective changes in the IV insulin rate, as patient requirements change
- Incorporates rate of change in BG, not just the absolute values
- Incorporates the current IV insulin rate
- Minimizes hypoglycemia—provides specific directions for its treatment when it occurs
- Provides specific guidelines for timing and selection of doses for the transition to subcutaneous insulin

Bedside Glucose Monitoring

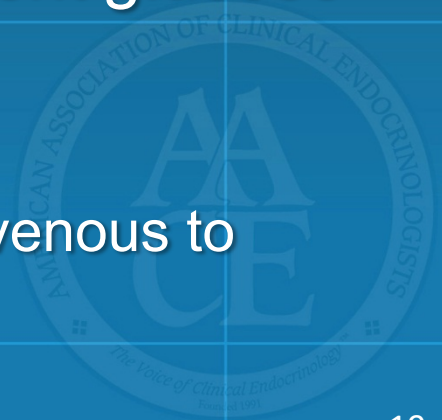
- Point-of-care measurement
 - Most practical and actionable for guiding treatment
 - But need to consider limitations in accuracy
- Strong quality-control program essential
- Specific situations rendering capillary tests inaccurate
 - Shock, hypoxia, dehydration
 - Extremes in hematocrit
 - Elevated bilirubin, triglycerides
 - Drugs (acetaminophen, dopamine, salicylates)



IV Insulin Protocols

Key Points

- Several published protocols for intravenous insulin infusions
 - Each may be suitable for different patient populations
- Ideal protocol: one that will work in a given institution
 - All protocol implementation will require multidisciplinary interaction and education
- Other protocols needed to make inpatient glucose management a success include
 - Protocols to manage hypoglycemia
 - Protocols to guide the transition from intravenous to subcutaneous therapy



TRANSITION FROM IV TO SC INSULIN



Considerations for Transition From IV to SC Insulin

- Which patients on IV insulin will need a transition to scheduled SC insulin?
 - Type 1 DM
 - Type 2 DM on insulin prior to admission
 - Type 2 DM (or new hyperglycemia) requiring ≥ 2 units/hour of insulin



Transition From IV Insulin to SC Insulin

- IV insulin should be transitioned to SC basal bolus insulin therapy
 - When patient begins to eat and BG levels are stable
- Because of short half-life of IV insulin, SC basal insulin should be administered at least 1-2 hours prior to discontinuing the drip



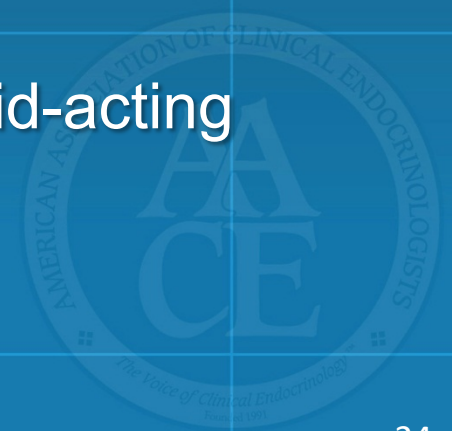
Additional Questions to Consider When Converting to SC Insulin

- Is the patient eating? If so, what and when?
- What are the concomitant therapies?
 - Glucocorticoids?
 - Inotropes?
 - Vasoconstrictors?
- Will resolution of the illness(es) or change in concomitant therapies reduce insulin needs?

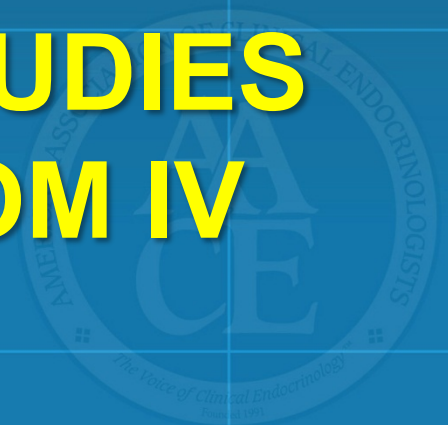


Calculating the SC Insulin Dose

- Establish the 24-hour insulin requirement by extrapolating from the average intravenous insulin dose required over the previous 6-8 hours (if stable)
- Take 60%-80% of the total daily dose (TDD)
 - Give one-half as an intermediate-acting or long-acting insulin for basal coverage
 - Give other half as a short-acting or rapid-acting insulin in divided doses before meal



OTHER PUBLISHED STUDIES FOR CONVERSION FROM IV TO SC



Bode: Transition From IV Insulin Infusion to SC Insulin Therapy

Example: Patient has received an average of 2 U/h IV during previous 6 h. Recommended doses are as follows:

SC TDD is 80% of 24-h insulin requirement:

$$80\% \text{ of } (2 \text{ U/h} \times 24) = 38 \text{ U}$$

Basal dose is 50% of SC TDD:

$$50\% \text{ of } 38 \text{ U} = 19 \text{ U of long-lasting analogue}$$

Bolus total dose is 50% of SC TDD:

$$50\% \text{ of } 38 \text{ U} = 19 \text{ U of total prandial rapid-acting analogue or } \sim 6 \text{ U with each meal}$$

Correction dose is actual BG minus target BG divided by the CF, and CF is equal to 1700 divided by TDD:

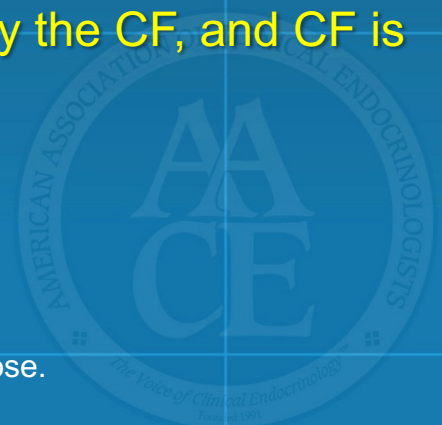
$$\text{CF} = 1700 \div 38 = \sim 40 \text{ mg/dL}$$

$$\text{Correction dose} = (\text{BG} - 100) \div 40$$

BG, blood glucose; CF, correction factor; IV, intravenous; SC, subcutaneous; TDD, total daily dose.

Bode BW, et al. *Endocr Pract.* 2004;10(suppl 2):71-80.

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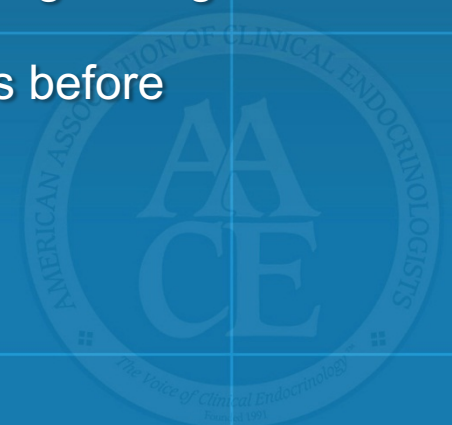


DeSantis: Transition From IV Insulin Infusion to SC Insulin Therapy

Model From a Tertiary Care Center

Example 1: Conversion from intravenous insulin therapy

1. Intravenous insulin drip rate averaged 1.8 U/h with final glucose level 98 mg/dL
2. Calculate average insulin infusion rate for last 6 h = 2.1 U/h and multiply x 24 to get total daily insulin requirement ($2.1 \times 24 = 50 \text{ U/24 h}$)
3. Multiply this 24-h dose (50 U) x 80% to obtain glargine dose = 40 U, which is given and the infusion is stopped
4. Multiply the glargine dose by 10% to give as a rapid-acting insulin (eg, aspart, lispro, or glulisine) at the time the glargine is given and the infusion is stopped
5. Give 10% of the glargine dose as prandial doses before each meal

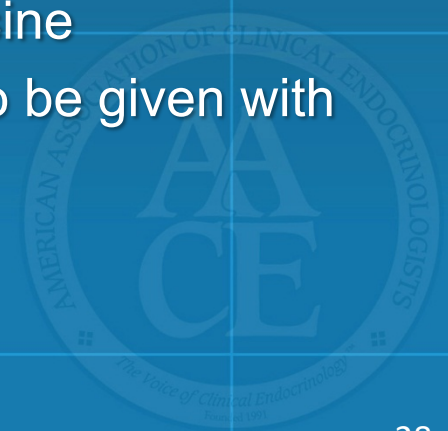


DeSantis: Transition From IV Insulin Infusion to SC Insulin Therapy

Model From a Tertiary Care Center

Example 2: Estimating insulin doses when no IV insulin therapy has been given

1. Calculate estimated total daily dose of insulin as follows:
 - Type 2 diabetes (known): 0.5 to 0.7 U/kg
 - Type 1 diabetes (known): 0.3 to 0.5 U/kg
 - Unknown 0.3 to 0.5 U/kg
2. Divide total daily dose of insulin into 50% basal as glargine and 50% prandial as aspart, lispro, or glulisine
3. Divide prandial insulin into 3 equal doses to be given with meals



Furnary: Transition From IV Insulin Infusion to SC Insulin Therapy

Conversion Protocol

- Initiate prandial doses of rapid-acting analogue with the first dietary trays, even if patient is receiving IV insulin infusion
- Find a 6- to 8-h interval during IV insulin infusion when the following conditions are met:
 - Out of the ICU
 - No oral intake (eg, nighttime)
 - No IV dextrose administration
- Use the average insulin infusion rate during this interval to project an average 24-h based insulin requirement (6-h total dose x 4; 8-h total dose x 3, and so forth)
- Calculate the initial insulin glargine dose at 80% of the 24-h basal insulin requirement during the previous time interval
- Stop IV infusion of insulin 2 h after first insulin glargine dose
- Monitor blood glucose preprandially, at bedtime, and at 3:00 a.m.
- Order a correction dose algorithm for use of a rapid-acting analogue to treat hyperglycemia to start after IV insulin infusion is terminated
- Revise total 24-h dose of insulin daily
- Revise the distribution of basal and prandial insulin daily to approach 50% basal and 50% prandial

Proposed Predictors for Successful Transition From IV Insulin Infusion to SC Insulin Therapy

More likely to successfully transition without a loss of glycemic control

- Underwent uncomplicated CABG and/or valve surgery and discharged from ICU extubated
- Taking liquids/regular meals
- Following house/ADA diet
- Stable renal function
- Observed for 6-8 h before breakfast to determine basal insulin requirement
- With type 2 diabetes or hospitalization-related hyperglycemia
- Receiving ≤ 2 U/h insulin infusion with concomitant BG < 130 mg/dL
- Basal insulin dose ≤ 48 U/d while receiving insulin drip

More likely to experience increasing blood glucose or increased complications on early transition to SC insulin

- Underwent complex heart surgeries
- At high risk for mediastinitis in ICU
- Receiving pressors
- Require intra-aortic balloon pump
- Receiving corticosteroids
- BG > 130 mg/dL while receiving insulin infusion
- With type 1 diabetes
- Basal insulin dose projected to be > 48 U/d while receiving insulin drip
- Basal insulin infusion rate > 2 U/h to maintain BG < 130 mg/dL

Successful Strategies for Implementation

- Champion(s)
- Administrative support
- Multidisciplinary steering committee to drive the development of initiatives
 - Medical staff, nursing and case management, pharmacy, nutrition services, dietary, laboratory, quality improvement, information systems, administration
- Assessment of current processes, quality of care, and barriers to practice change

Development and Implementation

- Standardized order sets
 - BG measurement
 - Treatment of hyperglycemia AND hypoglycemia
- Protocols, algorithms
- Policies
- Educational programs (physicians and nurses)
- Glycemic Management Clinical Team
- Metrics for evaluation



Metrics for Evaluation

- A system to track hospital glucose data on an ongoing basis can be used to:
 - Assess the quality of care delivered
 - Allow for continuous improvement of processes and protocols
 - Provide momentum



Requirements for Protocol Implementation

- Multidisciplinary team
- Administration support
- Pharmacy & Therapeutics Committee approval
- Forms (orders, flow sheet, med Kardex)
- Education: nursing, pharmacy, physicians, and NP/PA
- Monitoring/quality assurance



Education Is Key to Success

- Education
- Education
- Education
- Needs to be provided on a regular basis and can be given through a variety of approaches



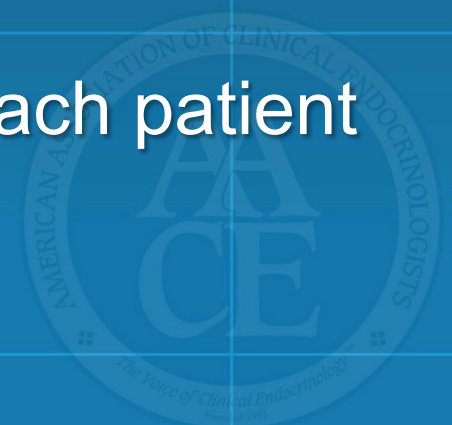
Core Knowledge for Physicians

- Impact of BG on hospital outcomes
- Institutional targets for BG
- Terminology: basal/nutritional/correction
- Insulin product knowledge
- Hypoglycemia prevention and treatment



Core Competencies for Nurses

- Bedside glucose monitoring technique
- Critical and target BG values
- Insulin administration technique
- Optimum timing of subcutaneous insulin shots
- Hypoglycemia prevention and treatment
- BG and insulin dose documentation
- Basic patient education (ability to teach patient “survival skills”)



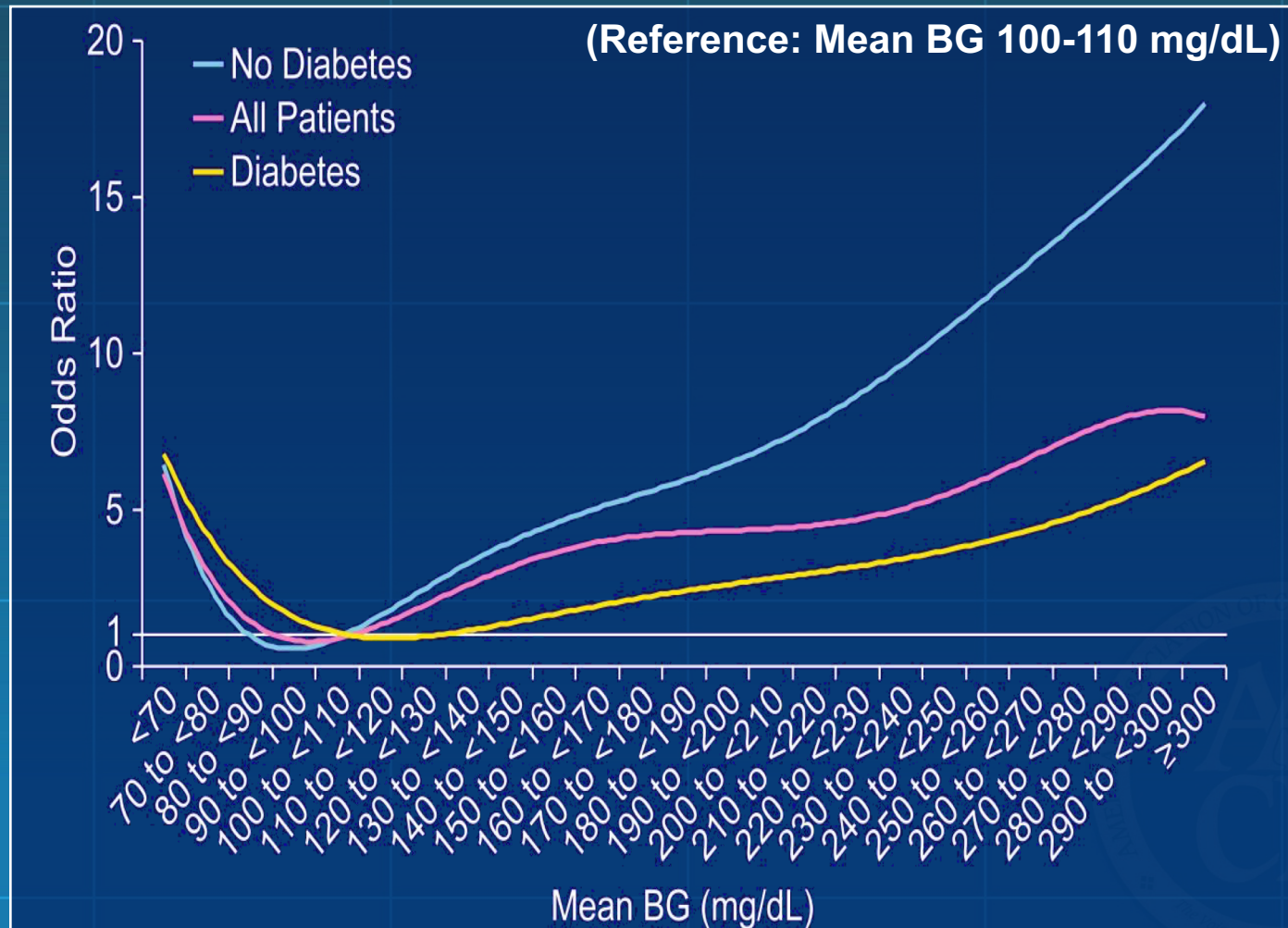
PREVENTION OF HYPOGLYCEMIA



Potential Harm From Insulin Therapy

- The Joint Commission considers insulin to be 1 of the 5 highest-risk medicines in the inpatient setting
 - Consequences of errors with insulin therapy can be catastrophic
- In 2008, insulin accounted for 16.2% of harmful medication errors, more than any other product, in an analysis of the USP MEDMARX reporting program data
- In 2008-2009, 2685 insulin medication error event reports were submitted to the Pennsylvania Patient Safety Authority
 - 78.7% (n=2113) involved a patient (NCC MERP harm index = C to I); 1.8% (n=49) resulted in patient harm (harm index = E to I)
 - Medical surgical units accounted for 22.3% (n=599) of events; pharmacy for 8.7% (n=234), and telemetry for 7.1% (n=191)
 - Drug omission constituted the largest proportion of errors (24.7%, n=662), followed by wrong drug reports (13.9%, n=374), and wrong dose/overdosage (13%, n=348)

Mean Glucose and In-Hospital Mortality in 16,871 Patients With Acute MI



Common Features Increasing Risk of Hypoglycemia in an Inpatient Setting

- Advanced age
- Decreased oral intake
- Chronic renal failure
- Liver disease
- Beta-blockers



Factors Increasing Risk of Hypoglycemia in an Inpatient Setting

- Lack of coordination between dietary and nursing leads to mistiming of insulin dosage with respect to food
- Inadequate glucose monitoring
- Inadequate insulin dose adjustment
- Lack of coordination between transportation and nursing
- Unsafe work environment
- Indecipherable orders



Factors Increasing Risk of Medication Errors With Insulin

- Use of “sliding scale” insulin in the absence of regularly scheduled insulin
- Use of “U” for units being misread as a number
- BG testing reporting and transcription errors
- Similar names of products, manufacturer’s labeling
- Accessibility as floor stock
- Nonstandard compounded IV solutions and infusion rates



Triggering Events for Hypoglycemia

- Transportation off ward causing meal delay
- New NPO status
- Interruption of any of the following:
 - Intravenous dextrose
 - TPN
 - Enteral feedings
 - Continuous renal replacement therapy



Summary

- Hyperglycemia
 - Common in critically patients, both with and without diabetes
 - Predictor of adverse outcomes, including mortality
- Significant improvements in mortality and morbidity with intensive glycemic management have been demonstrated
 - In some randomized controlled trials
 - In “before and after” comparisons
 - Mixed Med-Surg ICU
- Good (140-180 mg/dL), but not stringent (80-110 mg/dL) glucose control most reasonable strategy for critically ill patients
- IV insulin infusion, using a validated protocol to minimize hypoglycemia, is the preferred approach in critical care setting