Diabetes Update-2019

Inpatient Glucose Management

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Overview

- Types of Diabetes
- Hyperglycemia and outcomes in hospitalized patients
- Potential mechanisms for poor outcomes in hyperglycemic patients
- Review interventional studies related to glucose management
- Hypoglycemia- Inevitable or ‘managed risk’
- Strategies for improving inpatient control

Types of Diabetes:

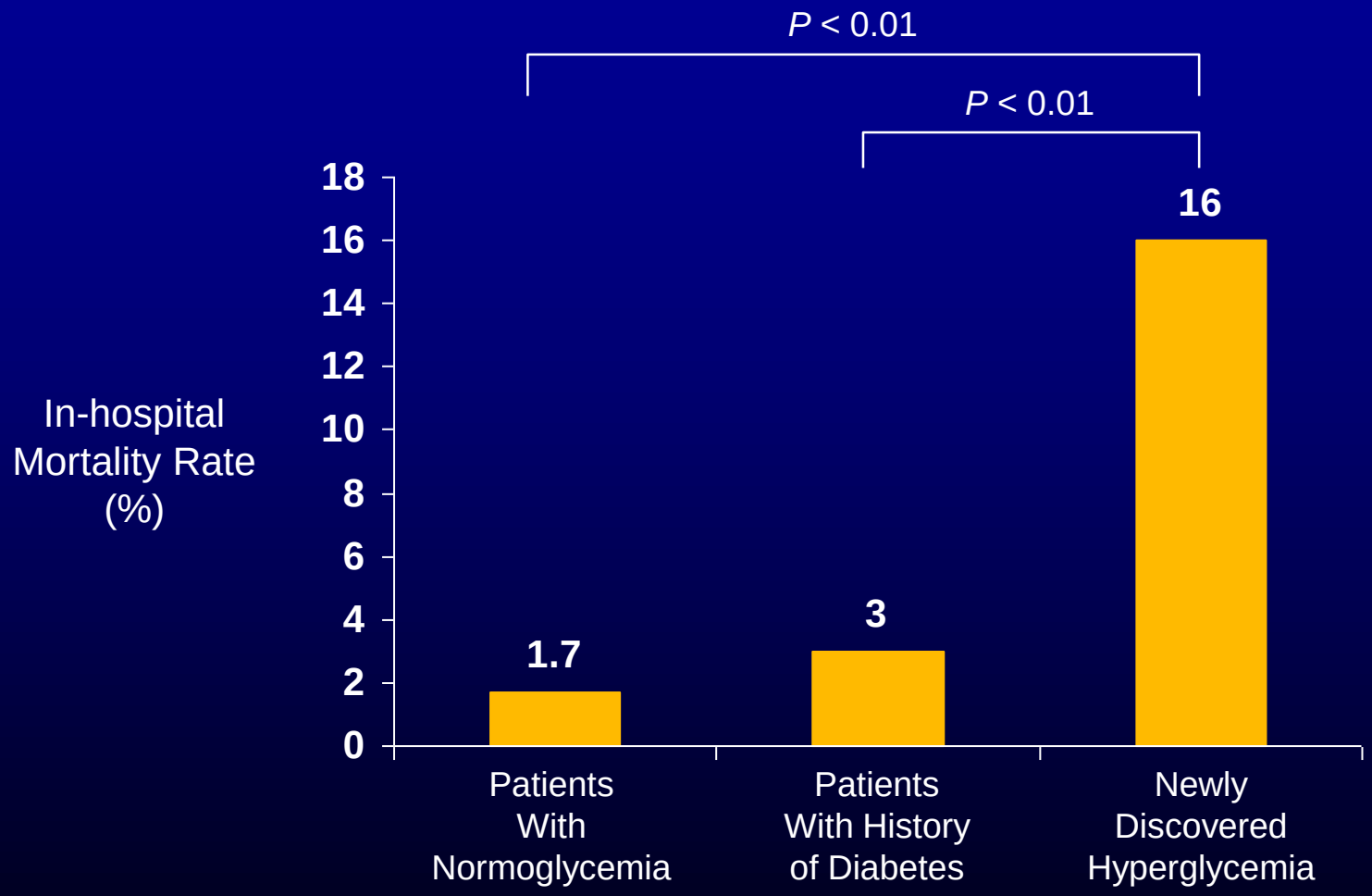
- Type 1 Diabetes Mellitus [IDDM or Juvenile Diabetes]
- Type 2 Diabetes Mellitus [NIDDM or Adult Onset Diabetes]
- Type 1.5 Diabetes Mellitus [LADA Diabetes]
- Gestational Diabetes [GDM]
- MODY [Monogenic Diabetes- 6 types- at least 8 mutations]
- Secondary Diabetes: Steroid induced, CFRDM

2018 Swedish/Finnish study

Precision Medicine

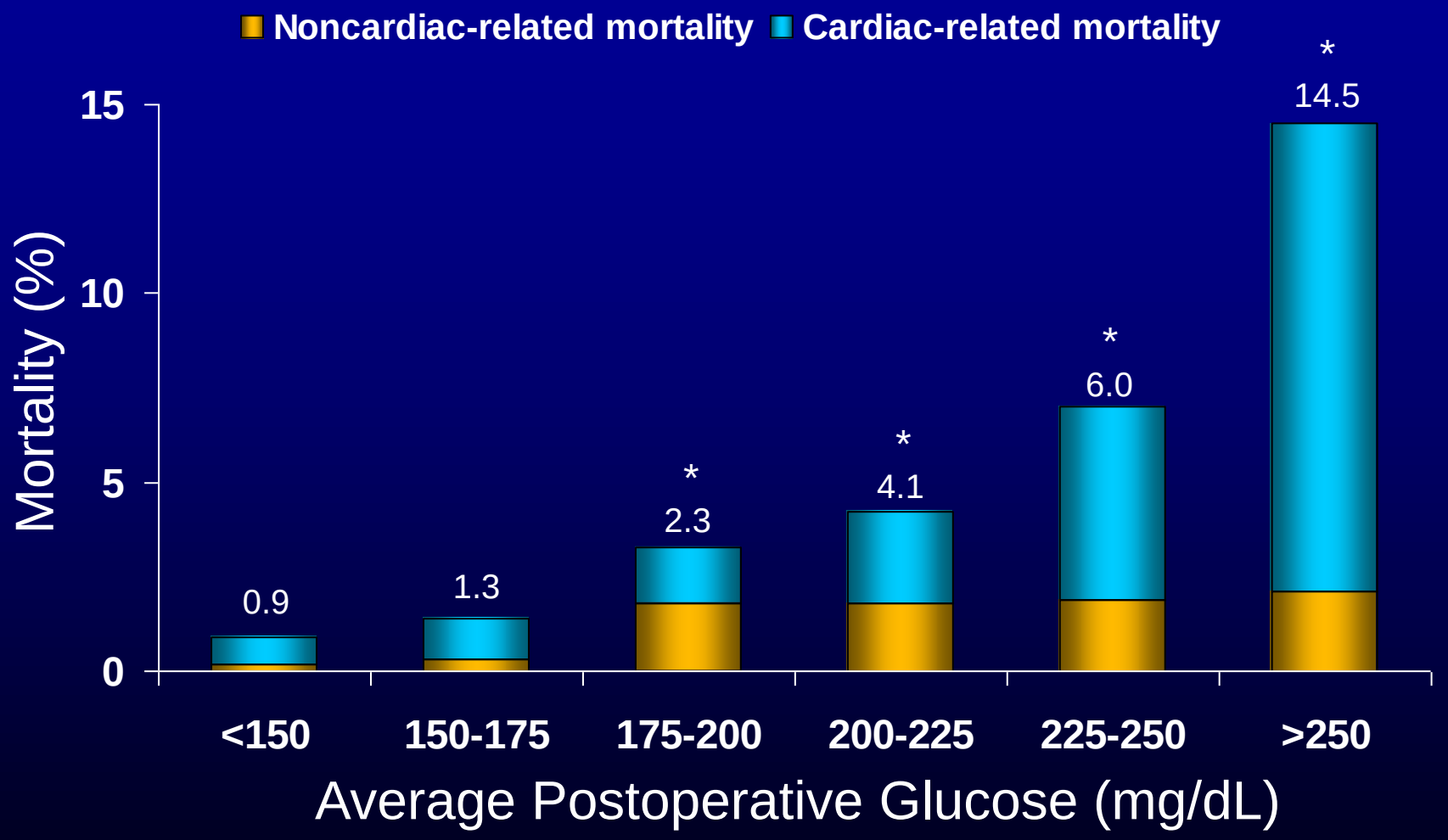
- **Five clusters of DM based on**
  - **BMI**
  - **Age at DM diagnosis**
  - **HbA1c**
  - **Beta cell function/reserve**
  - **Insulin resistance**
  - **Diabetes related Antibodies**

Hyperglycemia Is an Independent Marker of Inpatient Mortality in Patients With Undiagnosed Diabetes



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

Postoperative Glycemic Control Correlates With Cardiac-Related Mortality



* (*P*<.001).

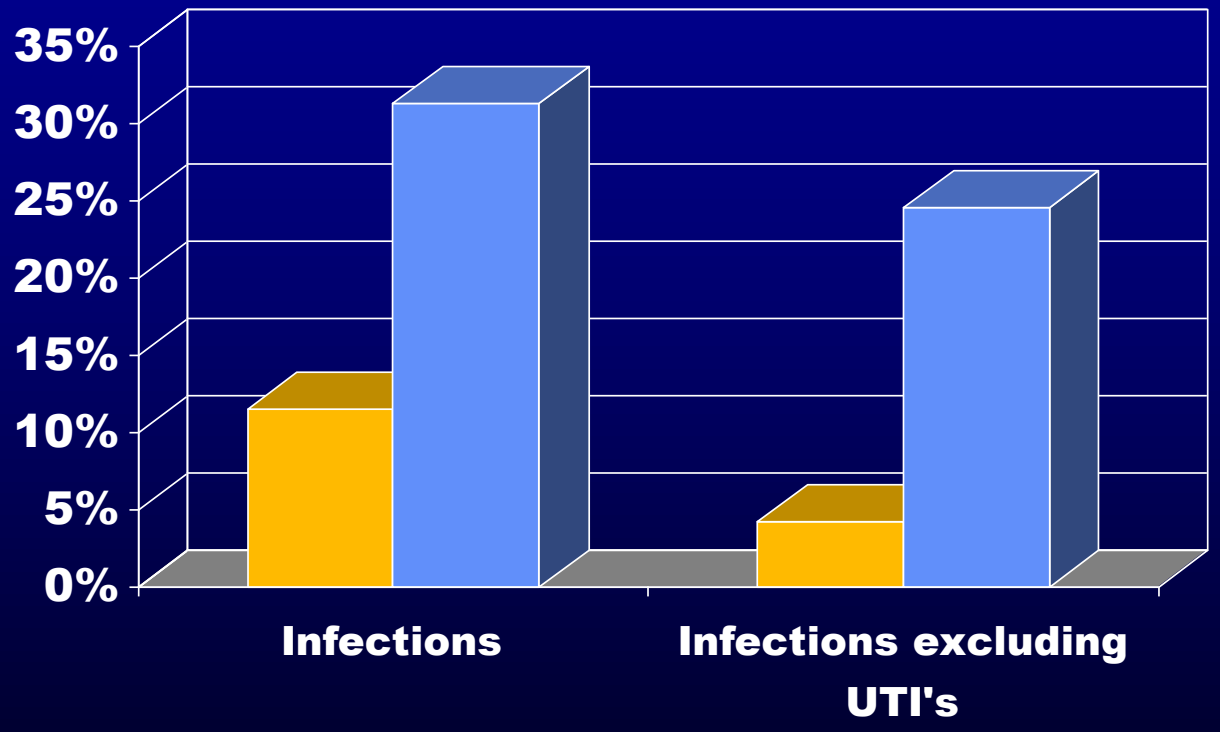
Furnary AP et al. *J Thorac Cardiovasc Surg*. 2003;125:1007-1021.

Poor Outcomes Correlate With Hyperglycemia After Acute Ischemic Stroke

Outcome	Blood Glucose at Admission		
	BG <130 mg/dL (n=385)	BG ≥130 mg/dL (n=258)	*P* value
Length of stay	6 ± 0.3	7.2 ± 0.4	.015
Discharged to home	79%	73%	.07
In-hospital mortality	5%	7%	.15
30-Day mortality	5%	10%	.018
1-Year mortality	11%	18%	.009

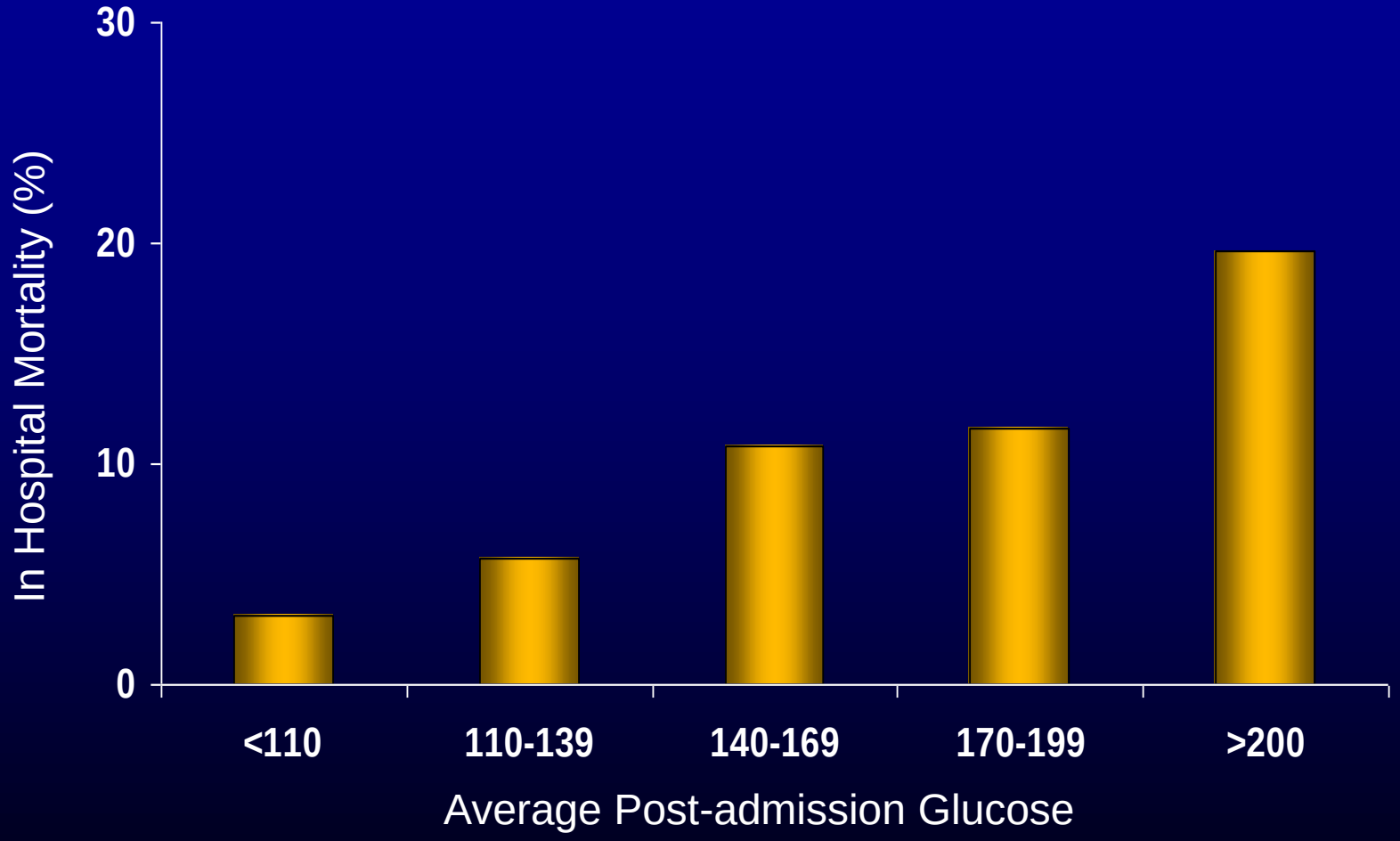
Williams LS et al. *Neurology*. 2002;59:67-71.

Rates of Nosocomial Infection in 100 Uninfected Diabetics Undergoing Elective Surgery



Pomposelli et al. *JPEN* 1998; 22:2, 77-81

Hyperglycemia and Poor Outcomes Following Myocardial Infarction



Arch Intern Med. 2009;169(5):438-446

Pathophysiology of Hyperglycemia

- Hyperglycemia is associated with increased neuron damage following brain ischemia
- Hyperglycemia leads to increased platelet aggregation and thrombosis
- Insulin decreases arterial levels of free fatty acids
- Hyperglycemia leads to increased cytokine levels and inflammation
- Neutrophil
  - Adherence, chemotaxis, phagocytosis and extravasation are all inhibited by increased glucose concentrations

Diabetes Care. 2004;27:553-591, Diabetes 1989;38:1031-5, Diabetes Care 2001;24:1634-9

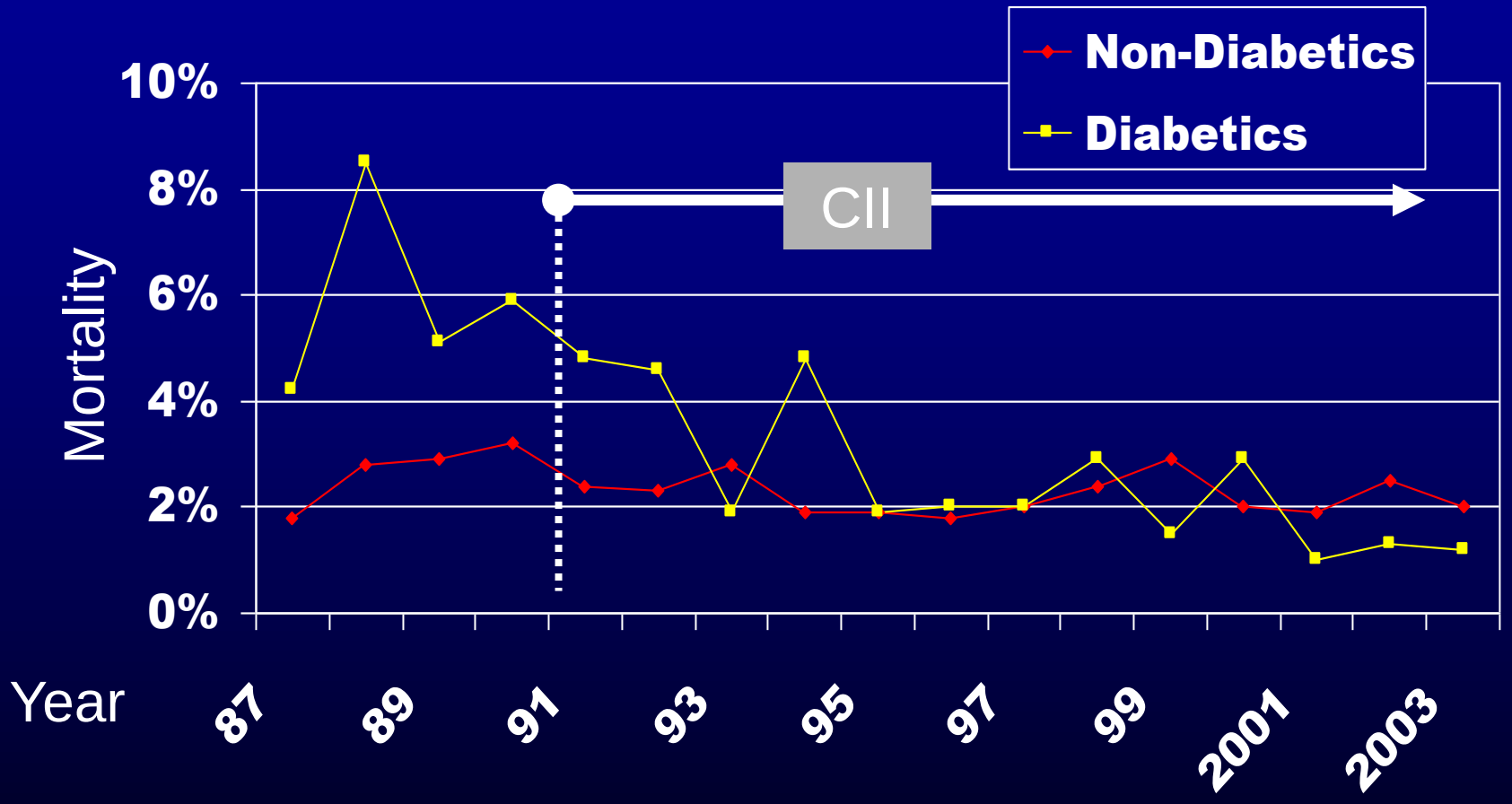
Intervention Studies

Insulin and Sternal Wound Infections

- Furnary et al studied 2467 patients undergoing open heart operations
- The first 968 patients were treated with a sliding scale to keep glucose near 200
- The next 1499 patients received an insulin infusion to keep glucose 150-200

Ann Thorac Surg 1999;67:352-62

Insulin and Mortality in CABG patients



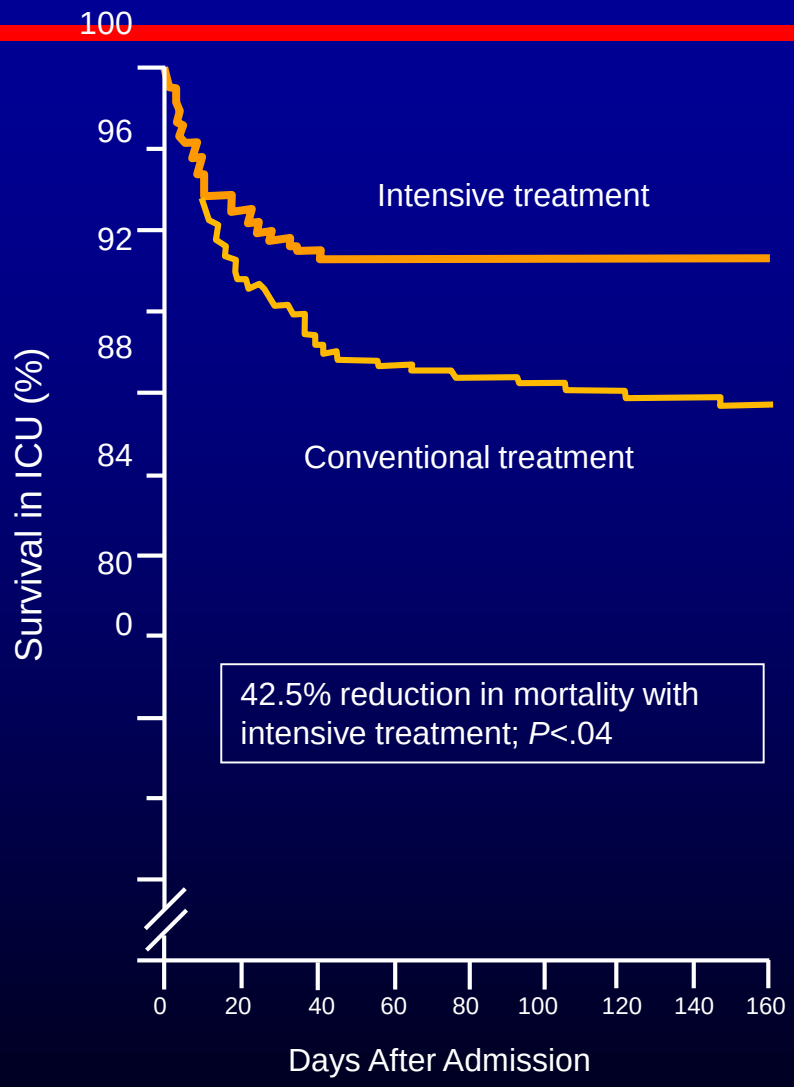
Furnary AP *Endocr Pract*. 2004;10(suppl 2):21-33.

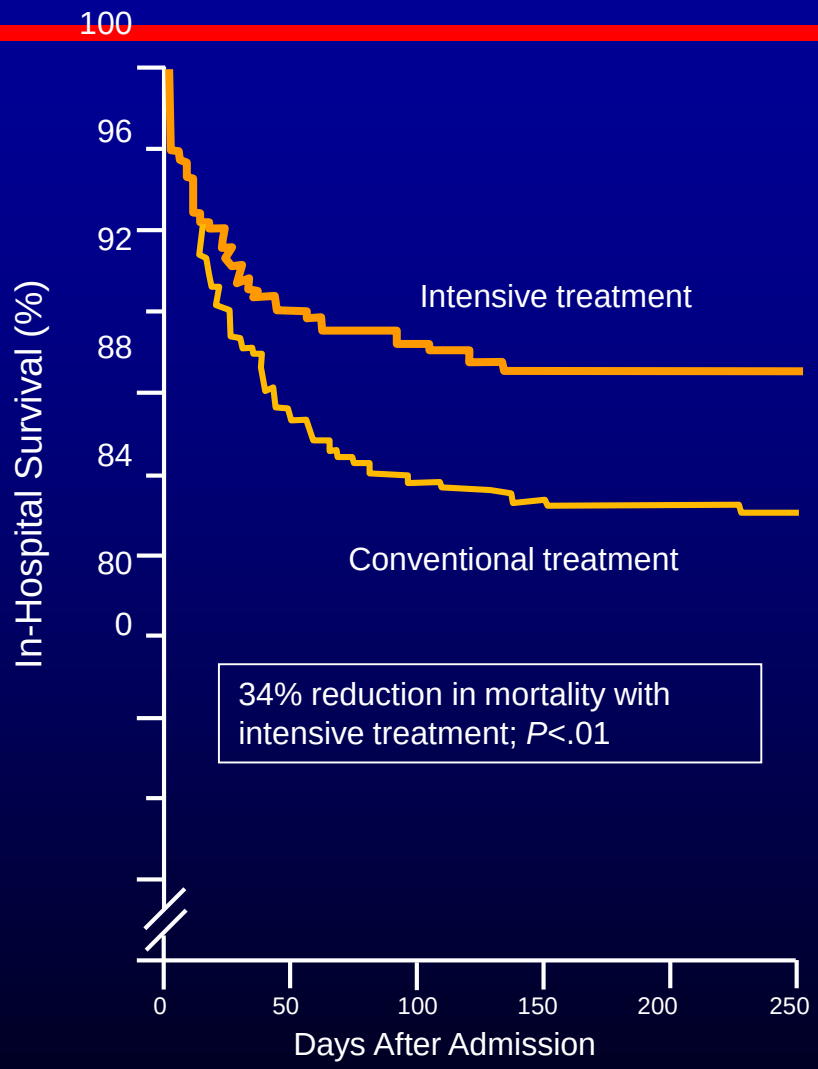
Intensive Insulin in the Critically Ill- (Leuven I)

- Van Den Berghe et al enrolled 1548 ventilated patients mostly post cardiac surgery
- 13% of these patients had diabetes
  - Patients were randomized to:
    - intensive treatment- infusion to maintain glucose between 80-110mg/dl
    - conventional treatment- targeting a glucose of 180-200mg/dl
- Mean glucose in the intensive treatment group was 103 and conventional group was 153
- Hypoglycemic events (glucose<40) occurred in 5.1% of patients in the intensive treatment group vs. 0.76% of patients in the conventional group

Van den Berghe G et al. *NEJM* 2001;345: 1359-67

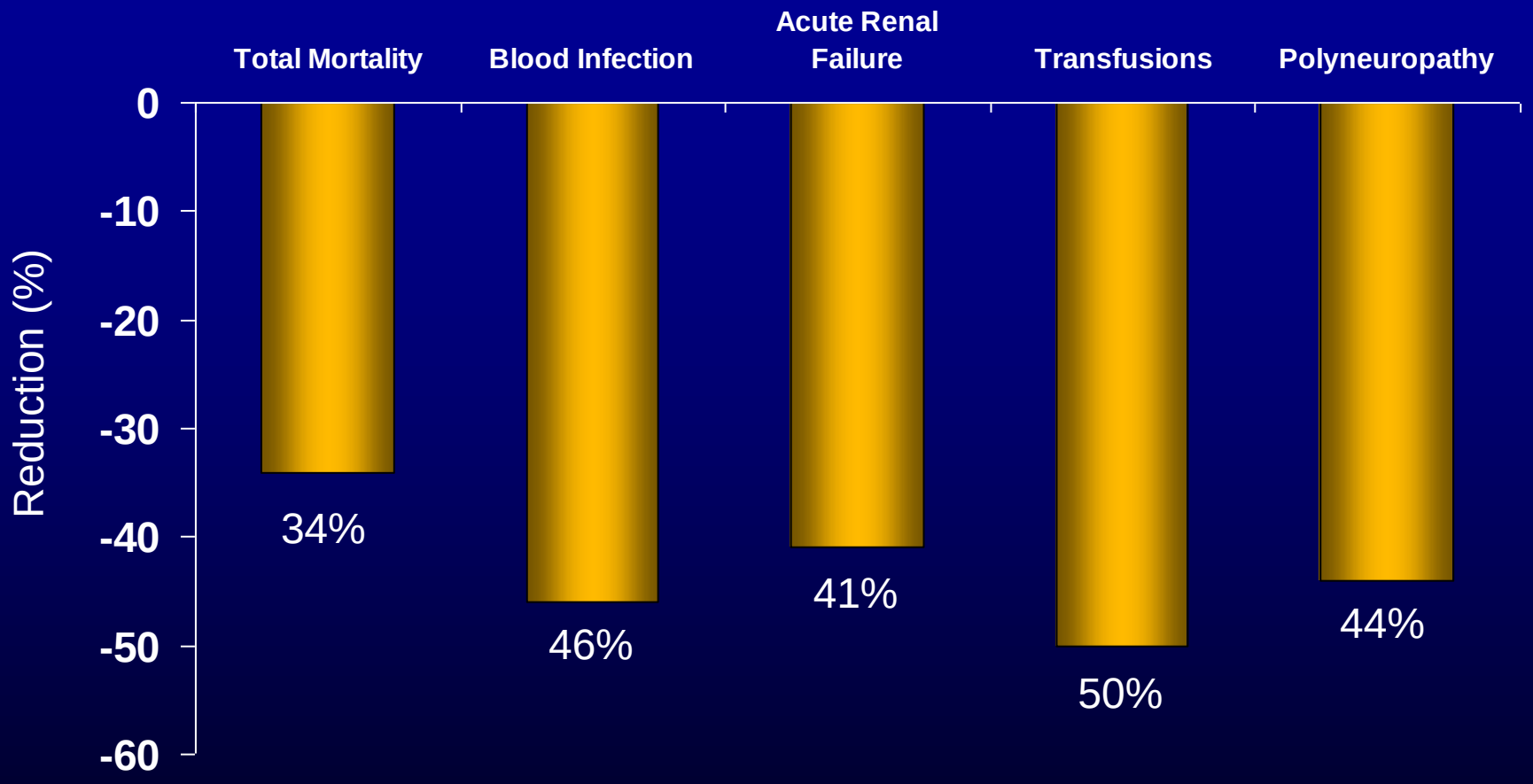
Intensive Insulin in the Critically Ill





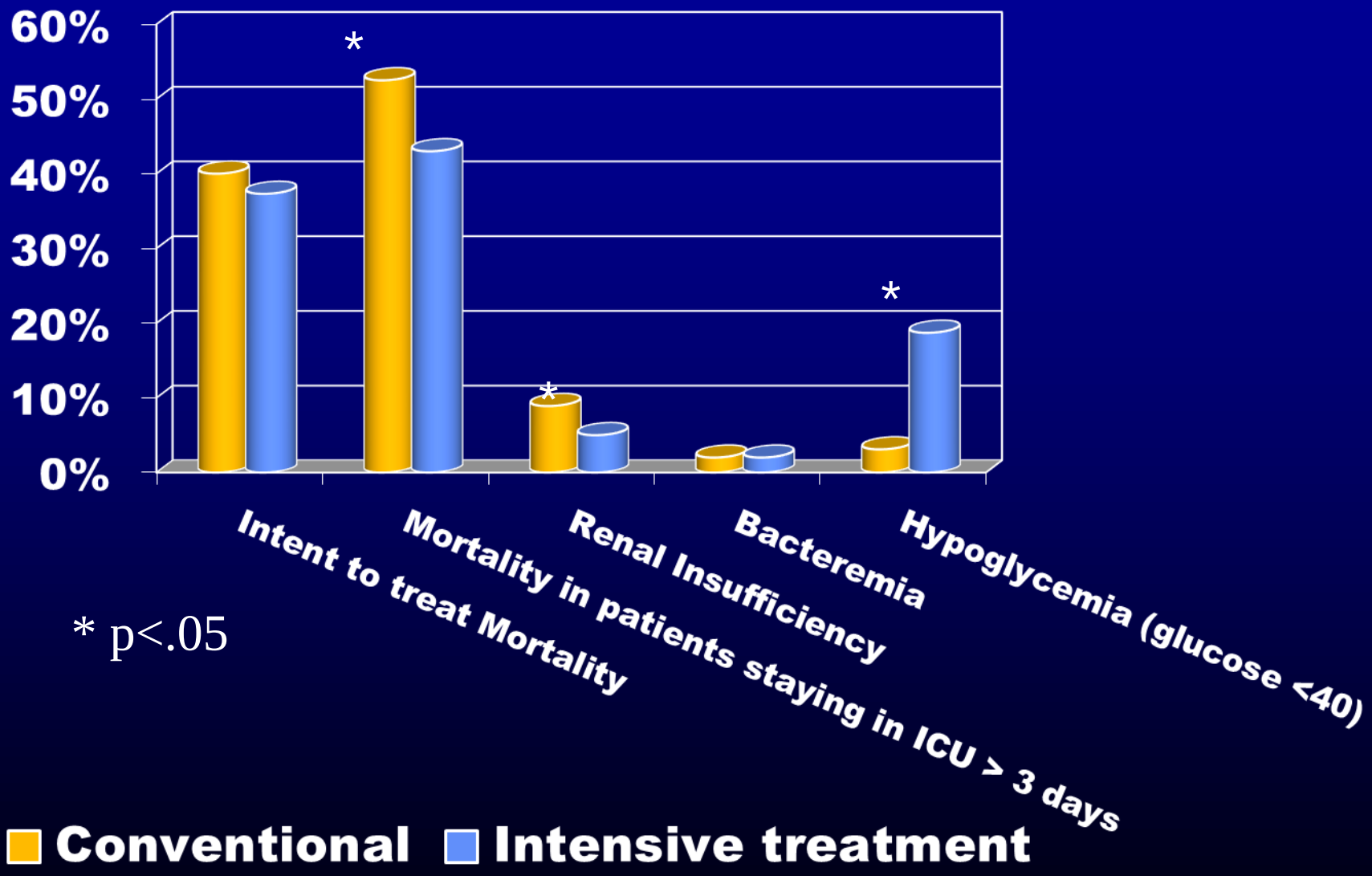
Van den Berghe G et al. *N Engl J Med.* 2001;345:1359-1367.

Benefits of IV Insulin Treatment in Critically Ill Hospitalized Patients



Van den Berghe G et al. *N Engl J Med.* 2001;345:1359-1367.

Leuven II- Intensive Insulin in MICU:
Patients with expected LOS >3 days



* p<.05

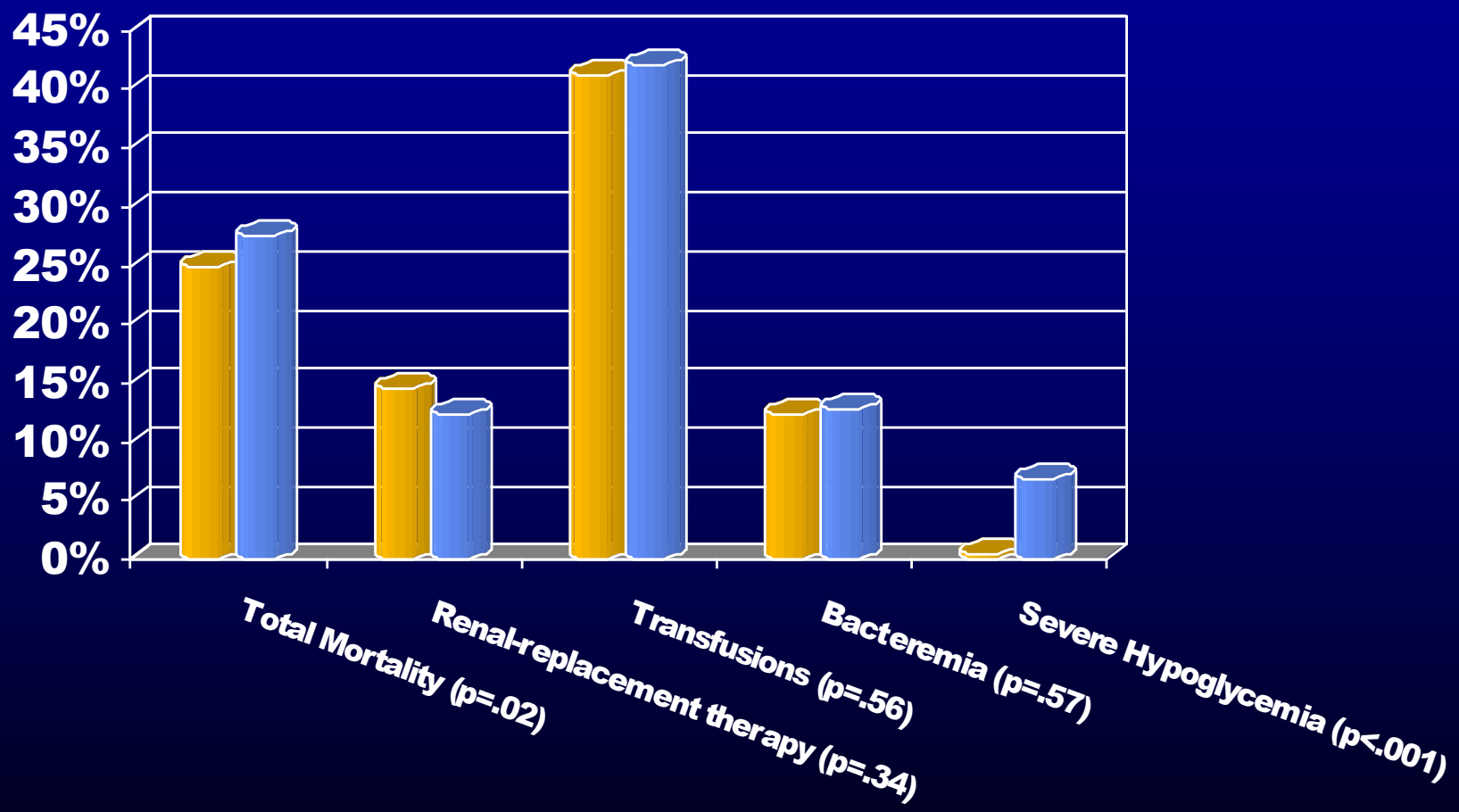
Van den Berghe G et al. *N Engl J Med.* 2006;354;5:449-61.

NICE-SUGAR

- Randomized trial of 6104 patients
  - 42 hospitals in Australia, New Zealand, and Canada
  - Enrolled patients with an expected LOS of 3 days and had an arterial line
  - Intervention discontinued when patient was eating or discharged from ICU
- Reason for ICU admission:
  - 37% Operative
  - 63% Non-Operative
- Patients were randomized to:
    - intensive treatment- infusion to maintain glucose between 81-108 mg/dl
    - conventional treatment- targeting a glucose of <180mg/dl
- Mean glucose in the intensive treatment group was 115mg/dl and conventional group was 144mg/dl

NEJM 2009;360:1283-97

NICE-SUGAR Results



Critical Care Med 2008;36:12 1-8

Inpatient Hypoglycemia: Mortality

Hospital Location	No hypos	Hypos
ICU (<81 mg/dL)[1]	19.7%	36.6%
ICU (<81 mg/dL)[2]	15.5%	25.6%
ICU (≤40 mg/dL)[3]	23%	52%
AMI (<60 mg/dl)[4]	9.6%	12.7%
Wards (≤50 mg/dL)[5]	0.82%	2.96%

1. Egi M et al, Hypoglycemia and outcomes in critically ill patients. Mayo Clin Proc 2010;85(3):217-24. 2. Bagshaw SM et al, the impact of early hypoglycemia and blood glucose variability on outcomes in critical illness. Crit Care Med 2009;13(3):R91 3. Van den Berge et al, Intensive insulin therapy in mixed medical/surgical intensive care units. Diabetes 2006;55(11):3151-9. 4. Kosiborod M et al, Relationship between spontaneous and iatrogenic hypoglycemia and mortality in patients hospitalized with acute myocardial infarction. JAMA 2009;301(15):1556-64. 5. Turchin A et al, Hypoglycemia and clinical outcomes in patients with diabetes hospitalized in the general ward. Diabetes Care 2009;32(7):1153-7.

How do we use this data to care for our patients?

Glycemic Targets in Noncritical Care Setting

- Maintain fasting and preprandial BG <140 mg/dL
- Modify therapy when BG <100 mg/dL to avoid risk of hypoglycemia
- Maintain random BG <180 mg/dL
- More stringent targets may be appropriate in stable patients with previous tight glycemic control
- Less stringent targets may be appropriate in terminally ill patients or in patients with severe comorbidities

Moghissi ES, et al. *Endocrine Pract.* 2009;15:353-369.
Umpierrez GE, et al. *J Clin Endocrinol Metab*. 2012;97:16-38.

Barriers to Inpatient Glucose Control

- Infection, fever, stress, glucocorticoids, surgery all exacerbate hyperglycemia
- Patients may eat less or have meals held
- Timing of insulin administration and meals are often disrupted
- Oral medications are often held

Limitations of Oral Agents for Managing In-Hospital Hyperglycemia

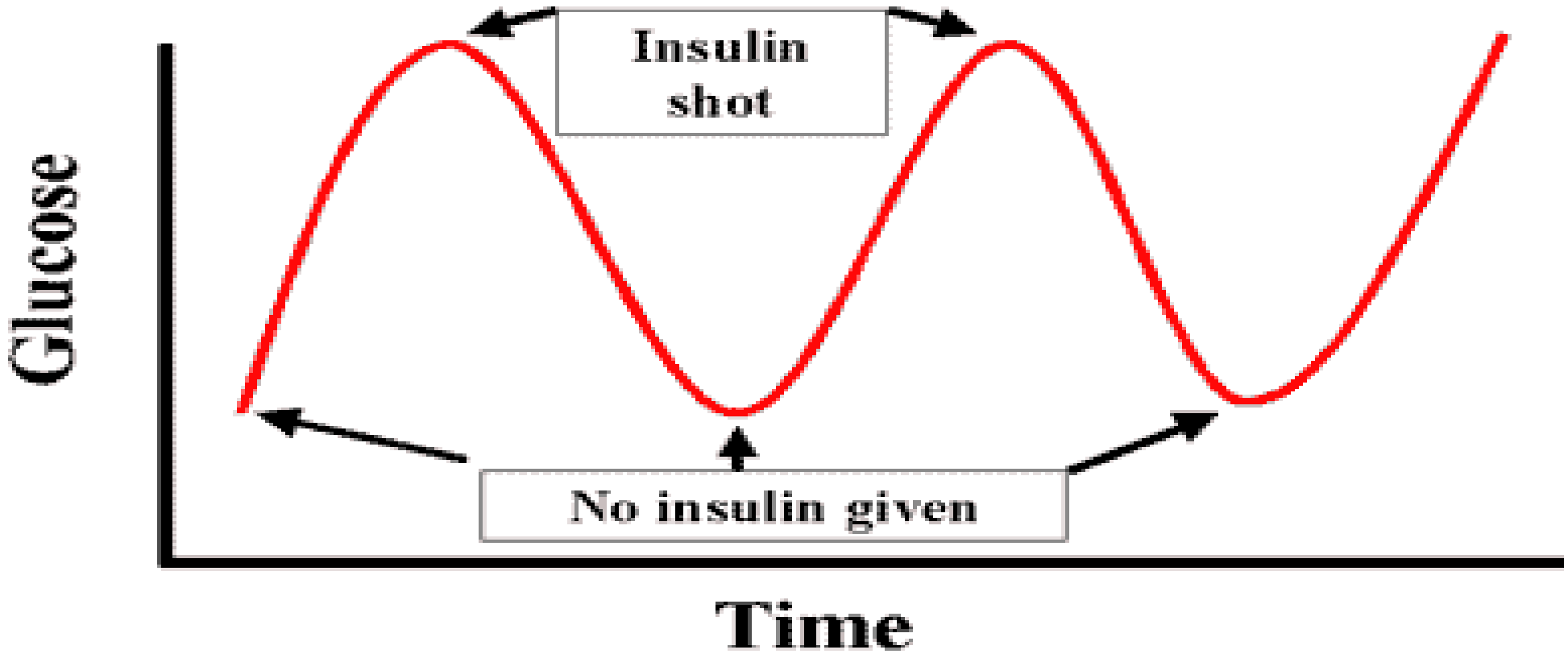
- Sulfonylureas
  - No rapid dose adjustment
  - Risk of hypoglycemia in patients not eating normally
- Metformin
  - No rapid dose adjustment
  - Mostly contraindicated due to increased risk of lactic acidosis in hospitalized patients (ie, intravenous contrast, renal failure, congestive heart failure)
- Thiazolidinediones
  - No rapid dose adjustment
  - Mostly contraindicated in heart failure, hepatic dysfunction

Clement S et al. *Diabetes Care*. 2004;27:553-591.

Limitations of Oral Agents for Managing In-Hospital Hyperglycemia

- Same can be said of the newer oral Agents
  - DPP-4 Inhibitors
  - SGLT2 Inhibitors

Roller Coaster Effect of Insulin Sliding Scale

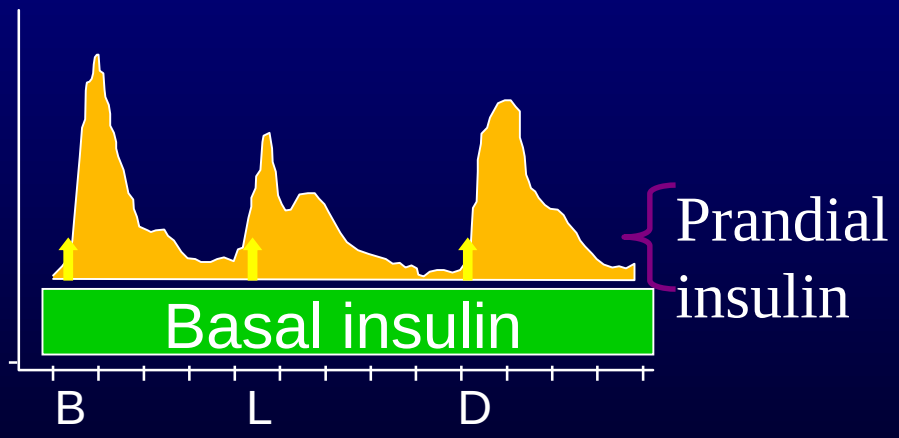


Using Insulin in the Hospital

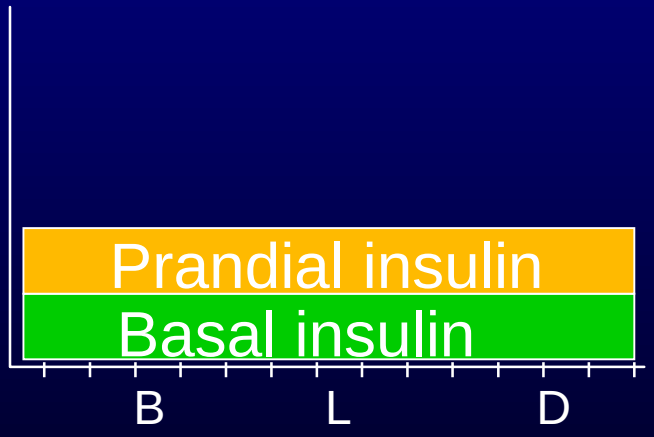
- First, Determine Source/Route of Nutrition
- Second, Estimate a Starting Dose of Scheduled Insulin
- Third, Know the Kinetics of the insulin you are using and make a plan

Source of Nutrition- Effects on Insulin Secretion

The Eating Patient



Pt. Receiving Continuous Feeds

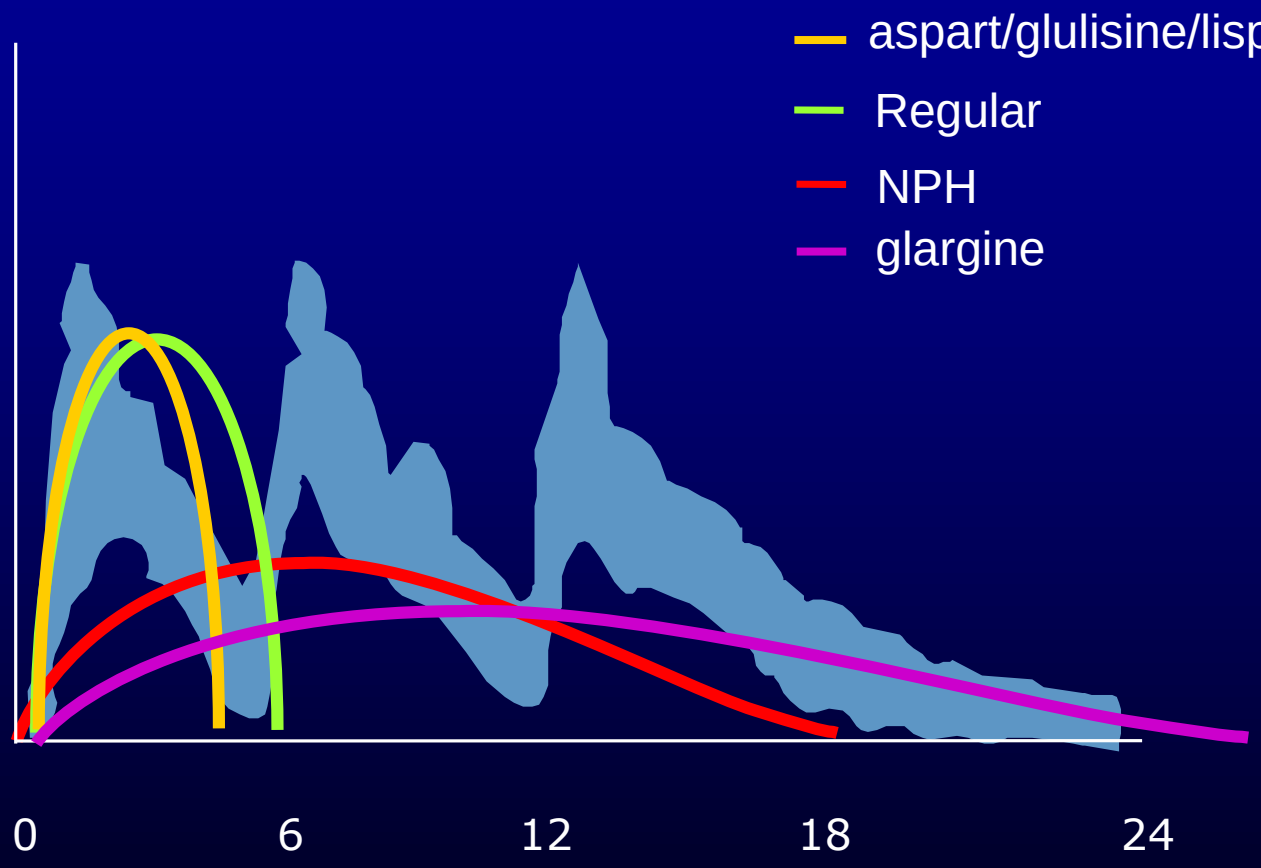


Estimating a Starting Dose

- Use patient's home regimen
  - Adjust as clinically indicated
- Make a weight based estimate*
  - Start 0.4units/kg for glucose 140-200
  - Start 0.5 units/kg for glucose 201-400
  - Consider lower starting dose with significant renal or hepatic impairment
- Estimate basal insulin and carb count
  - Difficult to achieve in the hospital
  - If attempting, estimate basal insulin (.2-.25 units/kg/day)
    - Type 1: Give 1 unit per 15g carbohydrates
    - Type 2: Give 1 unit per 10g carbohydrates

Diabetes Care 30:2181-2186, 2007

Kinetics of Insulins



Bolus- Rapid
Bolus- Rapid

Intermediate

Basal- long duration

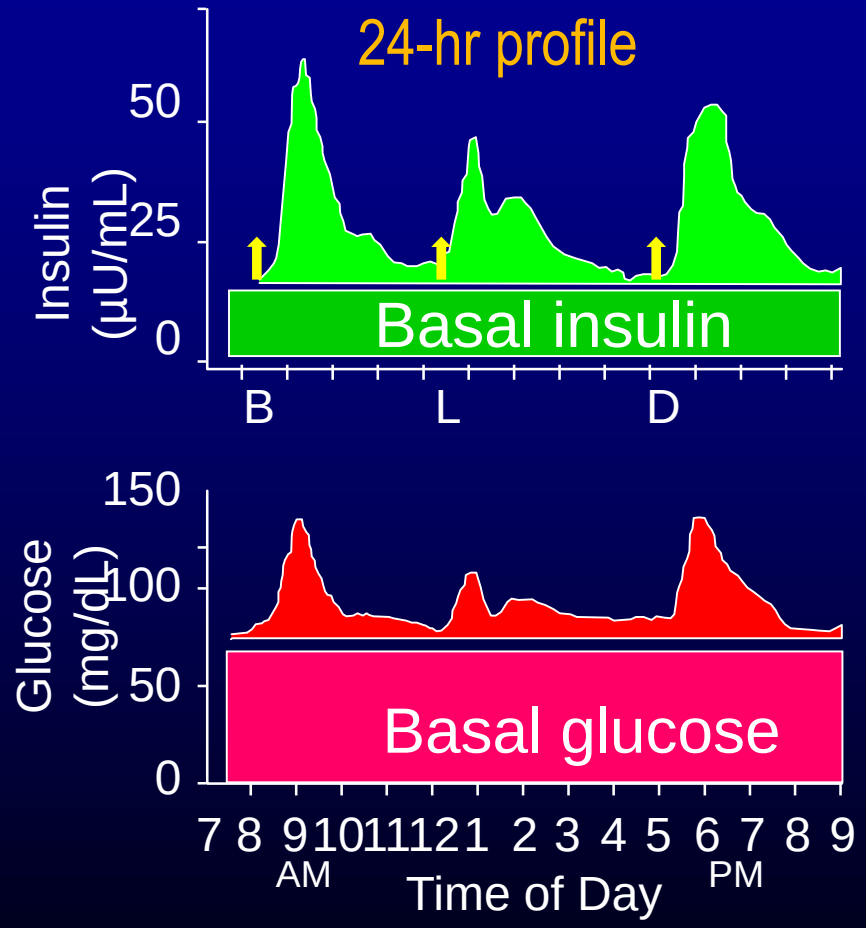
Pharmacokinetics of the most commonly used insulin preparations

Insulin type	Approximate onset of action	Peak effect	Approximate duration of action*
Lispro, aspart, faster aspart, glulisine	3 to 15 minutes	45 to 75 minutes	2 to 4 hours
Regular	30 minutes	2 to 4 hours	5 to 8 hours
NPH	2 hours	4 to 12 hours	8 to 18 hours, with usual duration of action around 12 hours
Insulin glargine	2 hours	No peak	20 to >24 hours
Insulin detemir	2 hours	3 to 9 hours	6 to 24 hours¶
NPL	2 hours	6 hours	15 hours
Insulin degludec	2 hours	No peak	>40 hours

NPH: neutral protamine hagedorn; NPL: neutral protamine lispro.
* Glucose-lowering action may vary considerably in different individuals or within the same individual.
¶ Duration of action is dose dependent. At higher doses (≥0.8 units/kg), mean duration of action is longer and less variable (22 to 23 hours).

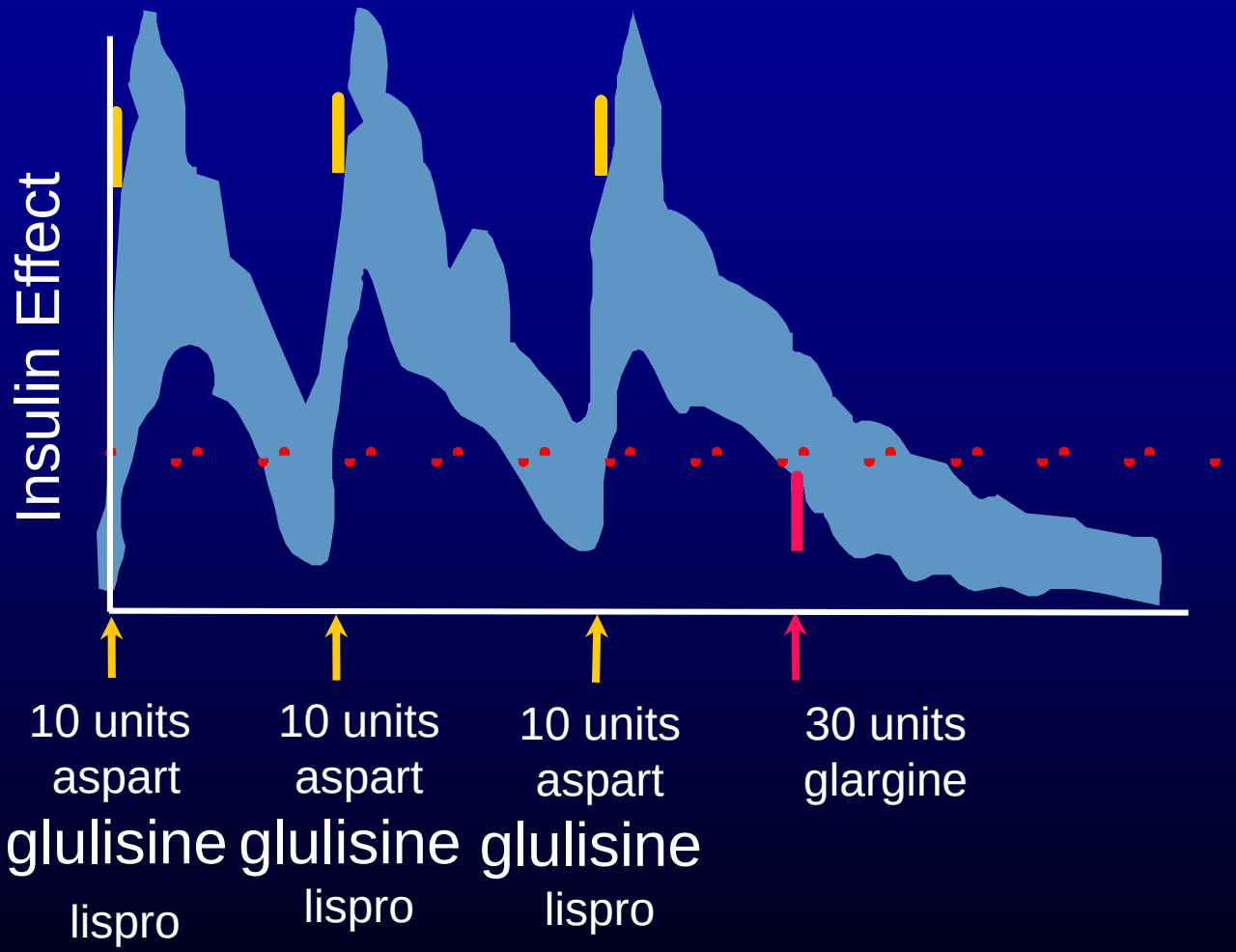
Mimicking Nature With Insulin Basal/Bolus Concept

Physiologic Insulin Secretion



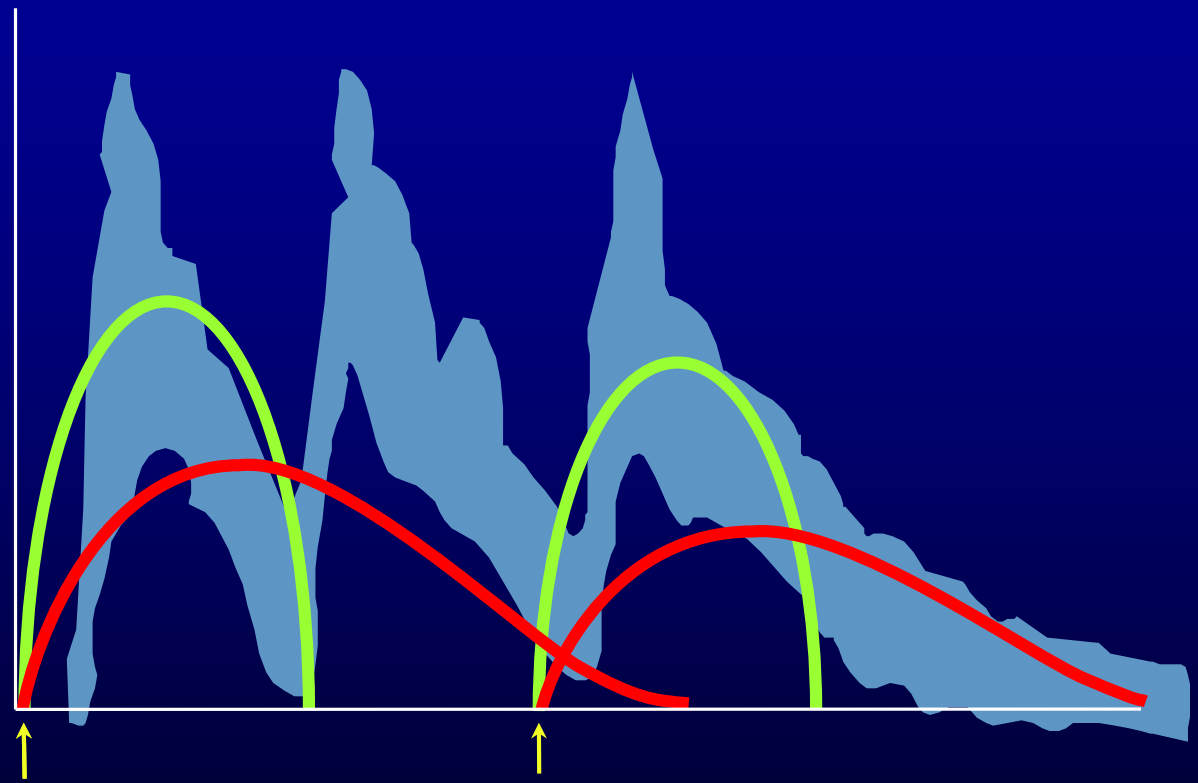
Adapted from Bergenstal RM et al. In: DeGroot LJ, Jameson JL, eds. *Endocrinology.* 4th ed. Philadelphia, Pa: WB Saunders Co.; 2001:821

Example: Patient's Total Daily Insulin Estimate=60 Units



Adapted from Leahy J. In: Leahy J, Cefalu W, eds. *Insulin Therapy*. New York, NY: Marcel Dekker Inc.; 2002:87

Example: Patient's Total Daily Insulin Estimate=60 Units



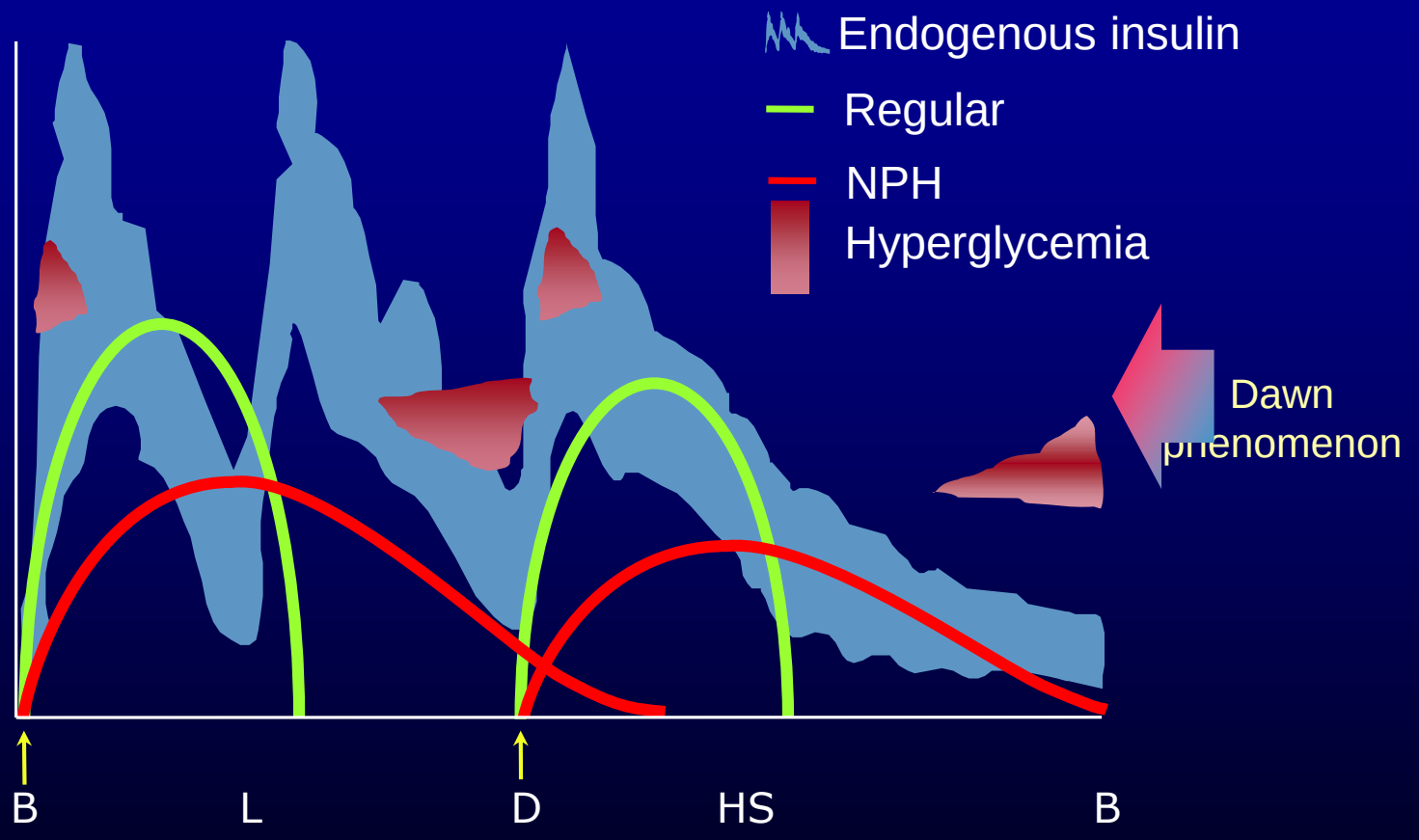
27 units NPH
+13 units regular

40 units of insulin in the a.m.

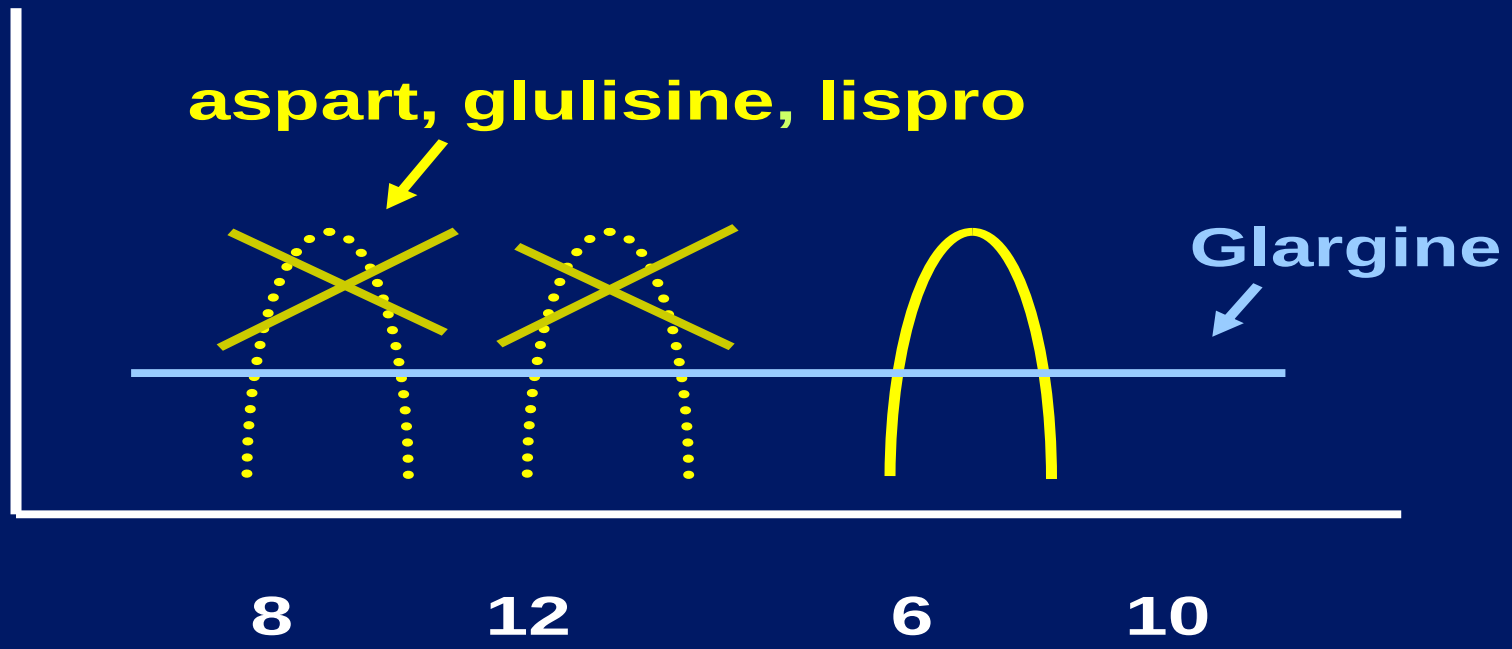
13 units NPH
+7 units regular

20 units of insulin in the p.m.

Twice-Daily Split-Mixed Regimens



Peri-Procedural Management



Case 1

- 23 year poorly compliant T1DM, h/o Meth use, Anxiety/Depression admitted with DKA, which has since resolved and transferred to the floor
- Home insulin regime Lantus 30 units qHS and Humalog 3-8 units Ac
- He does not test his FSG ‘very often’
- Last PCP visit 9 months ago
- Last Endocrinologist visit 4 years

Case 1

	Acs	HS	0200		AcB	pB		AcL	pL		AcS		HS
					Day 1								
FSG	86	277	198		56			351			92		298
Insulin H L	0 30	3	1		0			3+5			0		 15
Food	30%				55%			50%			60%		
					Day 2								
FSG			229		230			145			275		400
Insulin H L			3+2		3+2			3			3+3		5 ?
Food					75%			75%			?		

Take home points:

- Critically evaluate your patients insulin regime, on admission and daily.
- Tailor your program to your patient
- Be aware of insulin “stacking” and appropriate correction insulin doses
- Always re-evaluate a program if the BG is low, and reconsider if <100.
- Take the time to figure out what is happening.
- Look at trends- not just for 24 hrs. but 48-72 hrs.
- Consult the GLUC or NP service if you need help.