

# Inpatient Management of Diabetes Mellitus



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# Studies that brought attention to inpatient glucose control

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- ❑ In critically ill patients in a SICU, maintenance of near-normal blood glucose resulted in a 43% reduction in ICU mortality and a 34% reduction in overall hospital mortality (“Leuven surgical trial”)
- ❑ Strict glycemic control was associated with fewer infections, less renal failure, fewer blood transfusions, better recovery from stroke, and less need for mechanical ventilation.
- ❑ 3-year mortality after AMI was reduced from 44% to 33% with strict glycemic control.

Van den Berghe G, Wouters P, Weekers F, *et al.* Intensive insulin therapy in critically ill patients. *N Engl J Med.* 2001;345:1359-1367.

Malmberg K *et al.* Diabetes and Insulin-Glucose Infusion in Acute Myocardial Infarction (DIGAMI) study. *Circulation.*1999;99:2626-2632.

Finney SJ *et al.* Glucose control and mortality in critically ill patients. *JAMA.*2003;290:2041-2047.

# The controversy

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- ❑ Previously, based on the van den Berghe study with SICU patients in 2001, the goal for ICU patients was to keep blood glucose as close to normal as possible (80-110).
- ❑ But even van den Berghe's study in the MICU ("Leuven medical trial") in 2006 failed to show benefit with these strict goals.

# Newer studies

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- **European Glucontrol Trial** (Feb 2007 *Crit Care Med*):
  - A. 500 ICU pts with goal glucose 80-110
  - B. 500 ICU pts with goal glucose 140-180No difference in mortality between these 2 groups.  
Increased incidence of hypoglycemia in group A.
  
- **VISEP Trial** (*NEJM* Jan 2008): 500 ICU pts with sepsis
  - Intense goal of 110 (mean AM BG 112): hypoglycemia 17%, serious adverse events 11%
  - Conventional goal of 180-200 (mean AM BG 151): hypoglycemia 4%, serious adverse events 5%At 28 days, no difference in mortality or organ failure. Study was stopped early due to serious adverse events related to hypoglycemia. Hypoglycemia (BG <40) identified as independent risk factor for mortality.

# Recent meta-analysis of RCTs

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- ❑ One meta-analysis of 8000 patients showed no difference in mortality between intense (BG 80-110) and conventional (BG <180-200) group.
- ❑ Another of 13,000 patients showed a favorable effect of intensive therapy on mortality in surgical ICU patients only.

Wiener RS, Wiener DC, Larson RJ. Benefits and risks of tight glucose control in critically ill adults: a meta-analysis. *JAMA*. 2008;300:933-944.

Griesdale DE, de Souza RJ, van Dam RM, et al. Intensive insulin therapy and mortality among critically ill patients: a meta-analysis including NICE-SUGAR study data. *CMAJ*. doi:10.1503/cmaj.090206.

# The latest study

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- NICE-SUGAR (*NEJM* Mar 2009): Largest study (6000 patients) thus far. Multi-center RCT. All MICU, whether DM or not.

Intense group: goal BG 81-108, 27.5% mortality, 6.8% incidence of hypoglycemia

Conventional group: goal BG 144-180, 24.9% mortality, 0.5% incidence of hypoglycemia.

Significant increase in mortality at 90 days in Intense group (27.5% vs. 24.9%, P value 0.02)

No significant difference in LOS, days on ventilator, or need for dialysis.

# The tightrope

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## Hyperglycemia

- ❑ Increased length of ICU and hospital stay
- ❑ Increased incidence of nosocomial infection
- ❑ Worse neurologic outcomes
- ❑ Increase duration of mechanical ventilation
- ❑ Increased mortality

## “Leuven surgical trial” 2001



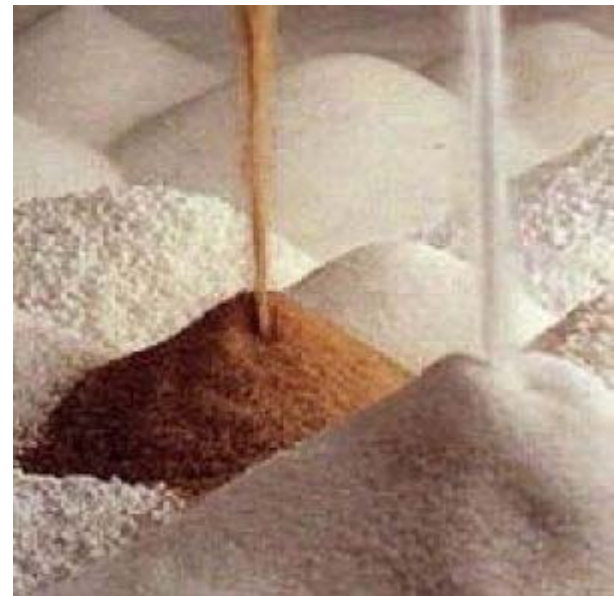
# The tightrope (continued)

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## Hypoglycemia

- ❑ Arrhythmias
- ❑ Cardiac ischemia
- ❑ Mental status changes
- ❑ Seizures
- ❑ Death

**“NICE-SUGAR” 2009**



# The differences and the flaws

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## **Leuven**

- ❑ SICU patients only
- ❑ “Conventional” glucose range high (BG 180-200)
- ❑ Patients given 200 gm IV glucose on first day in ICU
- ❑ High mortality rates (8% vs. typical 2%)
- ❑ Belgium

## **NICE-SUGAR**

- ❑ Mixed ICU
- ❑ “Conventional” glucose range lower (BG 140-180)
- ❑ Unknown mechanism of harm
- ❑ Enteral rather than parenteral nutrition
- ❑ Multiple centers, using a computerized treatment algorithm
- ❑ Australia, Canada

# AAACE/ADA Consensus Statement

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- Expert opinion based on the aforementioned studies.
- Critically ill: insulin infusion with starting threshold BG of 180, goal 140-180. No target <110.
- Noncritically ill:  
Preprandial 90-140 mg/dL  
Postprandial <180 mg/dL  
Reassess regimen if BG <100, and modify if any BG <70.

# More on inpatient goals

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- ❑ Keep in mind that hypoglycemia can be fatal and must be avoided.
- ❑ A single episode of severe hypoglycemia (BG<40) is associated with an increased risk in mortality(56 vs. 40%).
- ❑ Hyperglycemia (BG>200 mg/dl) is associated with infection, post-operative complications, increase LOS, dehydration, glycosuria, DKA, and death.
- ❑ Achieving these goals takes vigilance.

# What about oral DM medications?

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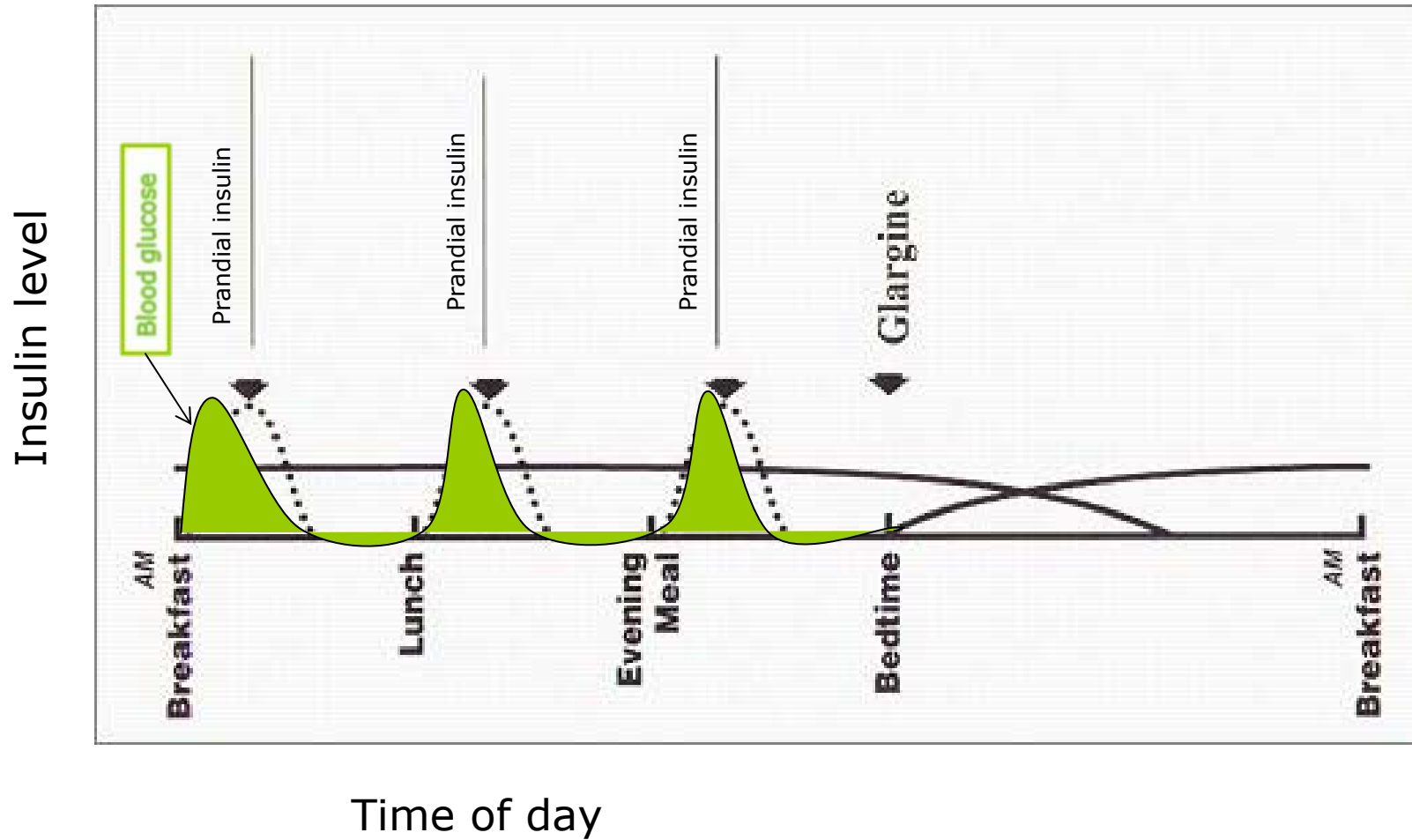
- ❑ Metformin: contraindicated in renal failure, dehydration, sepsis, liver disease, radiocontrast studies
- ❑ Thiazolidinediones (Actos): contraindicated in CHF
- ❑ Sulfonylureas (glipizide, glyburide): risk of hypoglycemia. Generally should be stopped on admission. Can be continued in stable patient eating reliably. Must be stopped with AMI.
- ❑ DPP-IV inhibitor (Januvia): affects post-prandial glucose. No role in NPO pt.
- ❑ GLP-1 agonist (Byetta): affects post-prandial glucose. Causes nausea.



# Pharmacokinetics of Type of Insulin

	Type	Onset	Peak	Duration
Rapid	Lispro	5-15 min	30-90 min	4-6 hours
	Aspart			
	Glulisine			
Short	Regular	30-60 min	2-4 hours	5-8 hours
	NPH	1-3 hours	4-10 hours	12-20 hours
Intermediate	Lente	1-4 hours	6-12 hours	12-24 hours
	Ultralente	4-6 hours	8-14 hours	18-36 hours
Long	Glargine	2-4 hours	No peak	18-24 hours
	Detemir	2-4 hours	No peak	6-24 hours

# What is physiologic insulin dosing?



# VCMC Adult Subcutaneous Insulin Orders

		Breakfast	Lunch	Dinner	Bedtime	
		Basal Insulin Orders		Give _____ units of <input type="checkbox"/> Glargine <input type="checkbox"/> NPH <input type="checkbox"/> Other _____		
5. Scheduled Insulin	Prandial Insulin Orders	<input type="checkbox"/> Fixed dosing	Give _____ units of <input type="checkbox"/> Lispro <input type="checkbox"/> Regular <input type="checkbox"/> Other _____	Give _____ units of <input type="checkbox"/> Lispro <input type="checkbox"/> Regular <input type="checkbox"/> Other _____	Give _____ units of <input type="checkbox"/> Lispro <input type="checkbox"/> Regular <input type="checkbox"/> Other _____	
		<input type="checkbox"/> Ratio dosing	Give <input type="checkbox"/> Lispro <input type="checkbox"/> Other _____ at a ratio of _____ units for every _____ grams of carbohydrates	Give <input type="checkbox"/> Lispro <input type="checkbox"/> Other _____ at a ratio of _____ units for every _____ grams of carbohydrates	Give <input type="checkbox"/> Lispro <input type="checkbox"/> Other _____ at a ratio of _____ units for every _____ grams of carbohydrates	
Mixed Insulin (not preferred)		Give _____ units of <input type="checkbox"/> Insulin 70/30 <input type="checkbox"/> Other _____		Give _____ units of <input type="checkbox"/> Insulin 70/30 <input type="checkbox"/> Other _____		

# 3 ways to calculate total daily insulin dose:

## #1. Based on outpatient dosing

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If previously well-controlled, administer home dose of glargine insulin.

If on NPH or 70/30, calculate NPH total per day, then use 80% of this as the glargine dose.

## #2. Transition from insulin drip to subcutaneous insulin

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- Total amount of IV insulin used over the last 24 hours of hospitalization.
  - Use last 8 hours (requirements on admission may be high secondary to acute illness, insulin resistance, etc.)
  - Multiply by 3 to get a 24-hour dose, then give 80% of this as Lantus for coverage of basal insulin needs (consider giving less if pt in renal failure, steroid taper, etc).

# #3. Calculate Total Daily Insulin based on BMI

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3. Calculate an unknown requirement based on BMI.

<b>Insulin resistance</b>	<b>BMI</b>	<b>TDI</b>
Normal	<25	Weight x 0.4 = _____units
Elevated	25-30	Weight x 0.5 = _____units
Severe	>30	Weight x 0.6 = _____units

# Starting basal insulin

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- ❑ Once the TDI is calculated,  $\frac{1}{2}$  should be given as basal (Lantus) insulin, and the other  $\frac{1}{2}$  should be divided by 3 and given as prandial insulin.
- ❑ Quick calculation to remember: start basal insulin 0.2 u/kg/day (even if NPO)
- ❑ AVOID correction dose insulin without concomitant basal insulin.

# Other considerations when calculating insulin based on IV use

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- ❑ Make sure volume resuscitation and pressor support have been discontinued before switching from IV to subcutaneous insulin.
- ❑ Keep patient's PO intake in mind when using the 24-hour IV insulin usage to calculate TDI. If carbohydrate intake has been negligible over this 24-hour period, the total insulin used would translate to a basal (not total) insulin dose.

## 2 ways to calculate prandial insulin dose:

### #1. Ratio dosing

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- ❑ Can start with 1 unit of prandial insulin for every 15 g carbohydrates consumed
- ❑ May need 1:10 or even 1:5 ratio in Type 2 diabetics with insulin resistance
- ❑ At VCMC, on a modified carbohydrate diet, each meal (breakfast, lunch, and dinner) is 60 g carbs. At a 1:15 ratio, patient would get 4 units of rapid-acting insulin with each meal.
- ❑ Calculate the Insulin-to-Carb ratio

# Insulin calculations

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## What is Total Daily Dose (TDD) of insulin?

TDD = 0.4-0.7 x weight in kg \_\_\_\_\_ U/d.

## What is Insulin:Carb ratio?

I:C ratio = 450/TDD → 1 unit covers \_\_\_\_\_ grams of carbohydrates.

## What is Insulin Sensitivity (correction) Factor?

ISF = 1700/TDD → 1 unit reduces blood glucose \_\_\_\_\_ mg/dL.

## Correction Dose calculation:

CD = (Actual glucose – Target glucose) / ISF

## #2. Fixed dosing

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- Usually start with 4-5 units of Lispro with each meal, adjusting the dose by 1-2 units daily, to a goal peak glucose <180.
- Alternatively, use 50% of the total daily insulin, divide by 3, and give with each meal.
- To calculate a fixed dose of prandial insulin, use 0.05-0.1 U/kg/meal. Adjust by 1-2 units daily if response is inadequate.

# Why you should not use the term “sliding scale insulin”

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- ❑ Hyperglycemia is treated only after it occurs, causing a roller coaster pattern of glucose values.
- ❑ No basal insulin is provided and no insulin is given for normal blood glucose values.
- ❑ Correction Dose therapy is different: doses are proportionate to daily insulin requirements and are given as a supplement to, not a replacement for, the basic insulin regimen.
- ❑ SSI does not take variables into account: degree of insulin resistance, renal function, age, severity of illness, nutrition status, steroid use, etc.

6. **Supplemental (premeal) correction dose insulin:** to be administered in addition to scheduled insulin dose to correct premeal hyperglycemia. Use selected algorithm below.

**6. Supplemental (Premeal) Correction Dose Insulin**

Lispro

Regular

Other \_\_\_\_\_

**Low-dose Algorithm**

For pts requiring  $\leq 40$  units of insulin/day.

Premeal BG (mg/dL)	Additional insulin (units)
150-199	1
200-249	2
250-299	3
300-349	4
> 349	5

Reduce HS correction dose by half.

**High-dose Algorithm**

For pts requiring  $> 80$  units of insulin/day

Premeal BG (mg/dL)	Additional insulin (units)
150-199	2
200-249	4
250-299	7
300-349	10
> 349	12

Reduce HS correction dose by half.

**Medium-dose Algorithm**

For pts requiring 40-80 units of insulin/day.

Premeal BG (mg/dL)	Additional insulin (units)
150-199	1
200-249	3
250-299	5
300-349	7
> 349	8

Reduce HS correction dose by half.

**Individualized Algorithm**

Premeal BG (mg/dL)	Additional insulin (units)
150-199	
200-249	
250-299	
300-349	
> 349	

Reduce HS correction dose by half.

# Supplemental Correction Dose Insulin

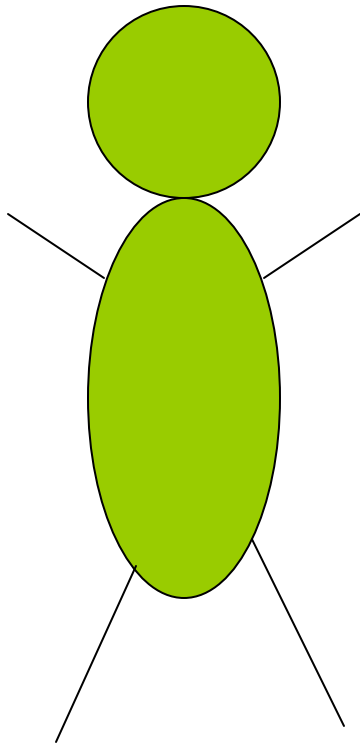
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- Choose based on previous known insulin requirement
  - In patients not previously on insulin, consider selection based on BMI:
    - For pts with Normal BMI  $<25$ , consider low-dose algorithm
    - For pts with Overweight/Obese BMI  $\geq 25$ , consider high-dose algorithm
- Calculate Insulin Sensitivity Factor (ISF)

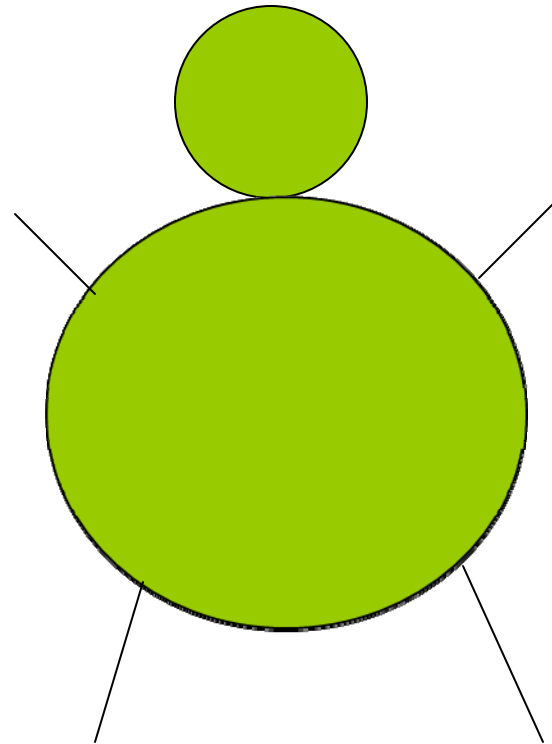
# Insulin sensitivity

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**Wt 70 kg → ISF 25**



**Wt 140 kg → ISF 12**



# Adjusting insulin

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- Adjust basal insulin dose by 10-20% daily until target glucose is reached
- Adjust prandial insulin by 1-2 U/dose daily if response is inadequate

# Pre-operative patients who are NPO

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- ❑ HOLD all prandial short-acting insulin.
- ❑ Continue to give supplemental correction dose insulin according to algorithm.
- ❑ Give 80-100% of glargine insulin at bedtime.
- ❑ Reduce nighttime NPH dose by 20%
- ❑ Reduce next morning NPH or Glargine dose by 50%.
- ❑ Consider D<sub>5</sub> IV in pts undergoing prolonged surgery or surgery late in the day (5 g/hour or ~100 ml/hour).

## VCMC Adult Insulin Infusion Orders (not for DKA)

- Discontinue all previous insulin orders.
- Initiate insulin infusion of **Regular** insulin 100 units/100 mL 0.9% normal saline via an infusion device.
- Add glycohemoglobin (HbA1c) to next blood draw if not done in the last 30 days.

**Goal BG Range:**

- 100-150 mg/dL (most ICU patients)
- 110-180 mg/dL (most DOU patients)
- Other \_\_\_\_\_ - \_\_\_\_\_

**Initiating the infusion:**

**Algorithm 1:** Start here for most patients.

**Algorithm 2:** Start here if s/p CABG, solid organ transplant, receiving glucocorticoids, or patient receiving >80 units/day of insulin as an outpatient.

**Algorithm 3:** NO PATIENTS START HERE.

**Algorithm 4:** NO PATIENTS START HERE.

- Start insulin infusion with **Algorithm 1**
- Start insulin infusion with **Algorithm 2**

**Moving Algorithms:** Move up or down only one algorithm per BG check.

● **MOVING UP:** Algorithm failure is defined as BG out of goal range (see above) and BG that has not decreased by at least 40 mg/dL in one hour.

● **MOVING DOWN:** When BG < 100 mg/dL or if BG decreases > 40 mg/dL in an hour. Restart insulin drip when BG is greater than 100 mg/dL and move down an algorithm.

Algorithm 1		Algorithm 2		Algorithm 3		Algorithm 4	
BG	Units/hr	BG	Units/hr	BG	Units/hr	BG	Units/hr
<70 = Hypoglycemia (see below for treatment)							
<100	Off	<100	Off	<100	Off	<100	Off
100-119	0.2	100-119	0.5	100-119	1	100-119	1.5
120-139	0.5	120-139	1	120-139	2	120-139	3
140-159	1	140-159	1.5	140-159	3	140-159	5
160-179	1.5	160-179	2	160-179	4	160-179	7
180-209	2	180-209	3	180-209	5	180-209	9
210-239	2	210-239	4	210-239	6	210-239	12
240-269	3	240-269	5	240-269	8	240-269	16
270-299	3	270-299	6	270-299	10	270-299	20
300-329	4	300-329	7	300-329	12	300-329	24
330-359	4	330-359	8	330-359	14	>330	28
>360	6	>360	12	>360	16		

**Patients who are eating:**

- Administer subcutaneous prandial (mealtime) lispro (Humalog) insulin immediately post-meal, IN ADDITION TO intravenous insulin infusion, based on the Insulin-to-Carbohydrate ratio below.

What Algorithm is the patient receiving at the time of the meal?	Algorithm 1	Algorithm 2	Algorithm 3	Algorithm 4
Insulin-to-Carbohydrate ratio	1 unit of insulin for 15 grams of carbohydrates	1 unit of insulin for 10 grams of carbohydrates	1 unit of insulin for 7 grams of carbohydrates	1 unit of insulin for 5 grams of carbohydrates

- See reverse for additional guidelines.

Physician Signature \_\_\_\_\_ Date \_\_\_\_\_ Time \_\_\_\_\_



VENTURA COUNTY MEDICAL CENTER  
SANTA PAULA HOSPITAL  
**ADULT INSULIN INFUSION ORDERS**

# Discharge planning

## Effective Discharge Planning



- A1C obtained prior to discharge
- Timely referral to inpatient diabetes educator if applicable
- Post hospital plan of care discussed with patients during hospital stay – Nursing to reinforce
- Reconciliation of medications - If new to insulin / regime discussed with patient and patient practices giving insulin prior to discharge. Insulin instruction sheet given to patient to take home
- DME supplies – meter, syringes, lancet, needles, etc.
- Referral for outpatient diabetes self-management, if appropriate
- Follow-up care with PCP within 15-30 days, or if new to insulin within 7-14 days

# Discharge planning

## Recommended Treatment Strategies for Transition to Discharge



- Patients with known diabetes and an elevated A1C
  - If A1C 7-8%: Increase dose of home oral agents, add a third agent or add basal insulin at bedtime
  - A1C >8%: If already on two oral agents, add once daily basal insulin at bedtime
  - If A1C 9-10%: Consider discharging home on basal and bolus insulin regime. Use the amount of basal insulin required in the hospital
  - Continue multiple daily dose as started in the hospital

# Discharging the diabetic patient

Patient Name/Addressograph

## Diabetes Discharge Prescription

Allergies:						QTY	REF
<b>Insulin:</b>							
"Basal Insulin" (specify insulin type)-----sig-----							
"Mealtime Insulin"(specify insulin type)-----						1 Vial	
----- sig: Inject sub Q three times daily before each meal							
-----units PLUS Correction Scale selected below.							
<b>Physician to designate insulin Correction Dose :</b>							
<b>Correction Scale: Specify insulin type</b>							
	MILD Insulin Sensitive Lean/Elderly/Renal	MODERATE Average weight	AGGRESSIVE Insulin Resistant Infectors/ Obese/ Steroids	CUSTOM	BG mg/dL	----- Vial	
151-200	1 Units	2 Units	4 Units	Units	151-200		
201-250	2 Units	3 Units	5 Units	Units	201-250		
251-300	3 Units	5 Units	7 Units	Units	251-300		
301-350	4 Units	6 Units	8 Units	Units	301-350		
351-400	5 Units	7 Units	10 Units	Units	351-400		
>400	Call MD	Call MD	Call MD	Call MD	>400		
Basal Insulin (Specify type)----- sig:						-----vial	
Short acting/ Rapid acting Insulin (Specify type)-----sig:						-----vial	
<b>Oral Diabetes Medication:</b>							
-----mg sig:-----							
-----mg sig:-----							
-----mg sig:-----							
-----mg sig:-----							
-----mg sig:-----							
-----mg sig:-----							
<b>OTHER:</b>							
Insulin Syringes: (specify type)-----						Box of -----	
Alcohol Wipes						Box of -----	
Glucose Tablets						----- size	
Glucose get 15						-----tube	
----- Test Strips or generic(Testing----- times daily)							
Lancets (Testing ----- times daily)							
<b>**This prescription NOT VALID for Controlled Substances**</b>							
Physician Printed Name Signature						Date	
Address						Telephone	
						License	
						DEA Number	

# The Diabetes Checklist

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## All diabetics

- ❑ Glucometer
- ❑ Lancing device (comes with glucometer)
- ❑ Lancets
- ❑ Alcohol wipes
- ❑ Test strips



## Diabetics on insulin

- ❑ Insulin syringes (with needles)

