

Update on Inpatient Diabetes Management ICU Care

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Disclosures

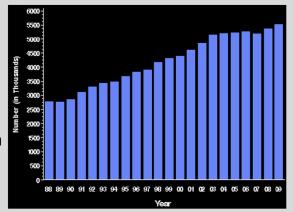
- Research support: Novo Nordisk, Sanofi, Abbott, Viacyte
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- Honoraria: UpToDate, Elsevier, CMHC, ACHL

Outline

- Background
- DKA
- IV Insulin
- Glucose Monitoring

Prevalence of Diabetes in the Hospital

- •23% of all discharges
 - -Higher LOS
 - -Greater costs
 - -More comorbidities
 - -~20% (1.7-1.9 million) are early readmissions with annual cost: \$25 billion



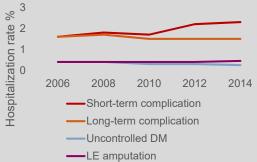
CDC's Division of Diabetes Translation. Available at: www.cdc.gov/dlabetes/shome/index.htm|
https://www.cdc.gov/dlabetes/shome/index.html
Fraze et al. HCUP Statistical Brief #93, 2008, www.hcup-us.ahrq.gov
American Diabetes Association. *Diabetes Care*. Mar 6 2013.
Healthcare Cost and Utilization Project (HCUP). Agency for Healthcare Research and Quality (AHRQ). 2014
Available at: http://hcupnet.ahrq.gov/HCUPnet.jsp.

Diabetes Hospitalizations

- In 2016, there were 7.8 million hospitalizations among patients with Dx code for DM1
- · DM or hyperglycemia associated with greater²
 - Costs
 - o LOS
 - Mortality
 - Complications
 - Readmissions

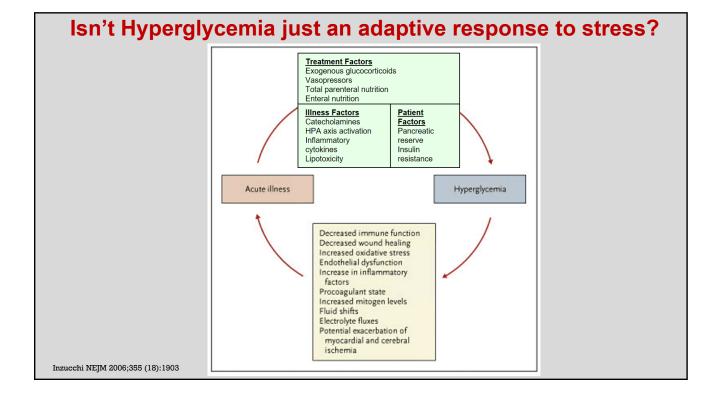
preventable hospitalizations

Age-adjusted diabetes-related



Data extrapolated from National Inpatient Sample

- 1. National diabetes statistics report 2020. https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf
- Dhatariya et al. www.endotext.org
- Rubens et al. Diabetes Care 2018;41:372-373



What should be the Target Glucose Range?

80-110 mg/dl

- Too much hypoglycemia
- · May increase mortality

110-140 mg/dl

High risk populations? (CT surgery) May be appropriate at some institutions

140-180 mg/dl

- Multi-center study data
 Acceptable range until further data
- >180 mg/dl
- Fluid and electrolyte shifts
 - Impaired immune function

AACE/ADA CONSENSUS STATEMENT ON INPATIENT GLYCEMIC CONTROL; Endocr Pract 2009;15(4) ADA Standards of Care;Diabetes Care 2021 Endocrine Society Guidelines 2013

Risk Factors for Hypoglycemia--ICU

	OR	95% CI
DM	2.6	1.5-4.7
Sepsis	2.2	1.2-4.1
CVVHD	3.7	1.6-8.6
↑CHO	6.6	1.9-23
Insulin prior to admit	17	2.3-127
Insulin use	5.4	2.8-10
Shock	1.8	1.1-2.9
Prior Hypoglycemia	2.3	1.1-4.7

Reduce insulin, increase monitoring if

- Any form of carbohydrate is interrupted
- Declining renal or hepatic function

Vriesendorp et al. Crit Care Med 2006;34:96

Consensus Definition of Ketoacidosis

- Consensus: ADA, AACE, AADE, Endocrine Society,
 JDRF, Pediatric Endocrine Society, T1D Exchange
 - -Urine/serum ketones >ULN
 - −Bicarb <15 mmol/l or pH <7.3
 - -AG not included
 - Does not account for acidosis from other causes

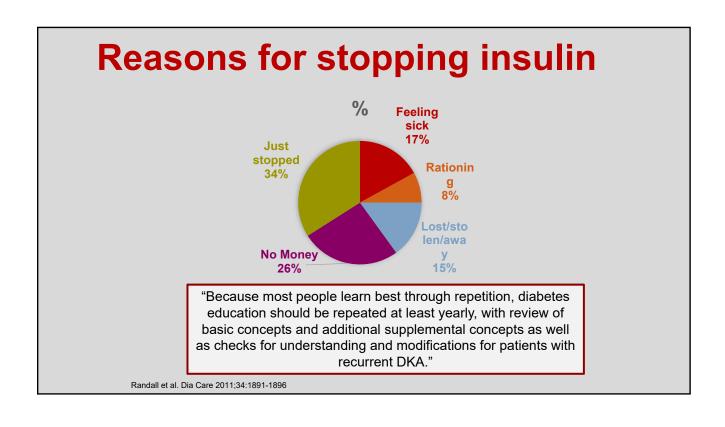
Agiostratidou et al. Diab Care 2017;40(12):1622-1630

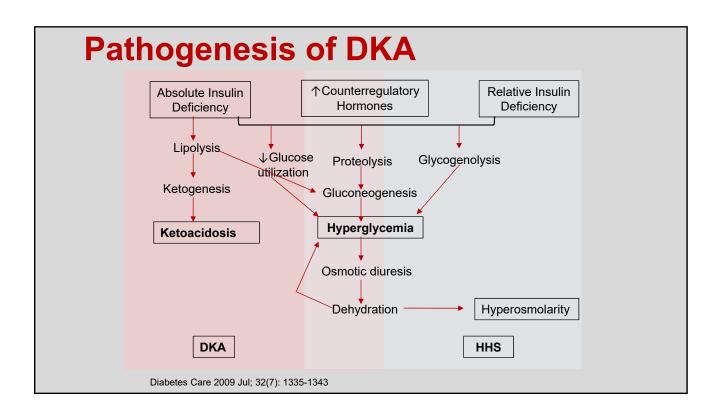
Risk Factors for DKA

Retrospective cohort

	First DKA N=73	Recurrent DKA N=91	P-value
Age	41	41	0.71
BMI	29	26	0.05
DM duration	9.5	14.3	< 0.0001
Homeless	6.9%	23%	0.005
Insured	26%	48%	0.01
Follows in DM clinic	27%	67%	< 0.001
Prior DM Education	56%	84%	< 0.0001
H/o depression	28%	42%	0.03
Alcohol	25%	40%	0.047
Illicit substance	23%	52%	< 0.001
A1c	12.4%	12.1%	0.21

Randall et al. Dia Care 2011;34:1891-1896





DKA with SGLT2 inhibitors in patients with T2D

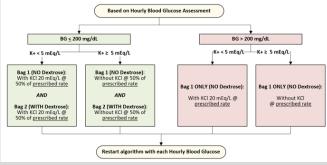
- Risk of DKA increased with SGLT2i ~2.2-2.5-fold¹
- Mechanism:
 - Reduced ketone clearance
 - Glycosuria → euglycemic DKA
 - Natriuresis
 - 一个glucagon->lipolysis

Criteria for holding dose:2

- Symptoms consistent with DKA
- Fasting/inability to eat
- Dehydration
- Unusual physical activity
- Excess EtOH use
- · Hospitalization/procedures (hold 3 days prior)
 - . Fralick et al. N Engl J Med 2017;376(23):2300-02
 - 2. Danne et al. Diabetes Care. 2019 Jun;42(6):1147-1154

DKA 2-bag Method

- Maintains constant fluid, electrolyte and insulin infusion while titrating 1 bag with dextrose and 1 without in response to changing BG
- Associated with
 - Earlier resolution of DKA^{1,2}
 - Less waste of partially used fluids¹
 - Possibly less hypoglycemia²

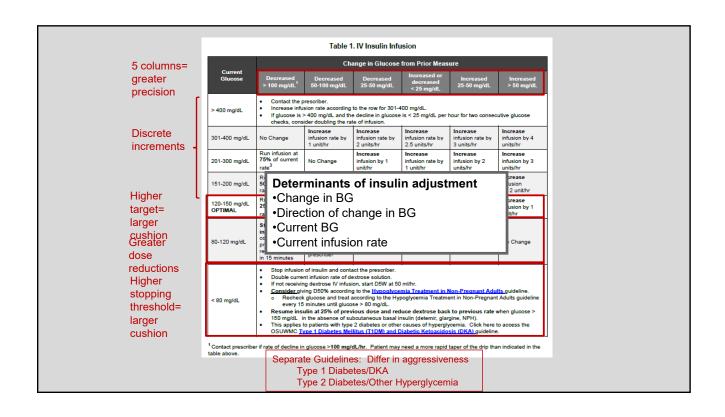


- 1. Haas et al. J Emerg Med. 2018;54(5):593-599
- 2. Munir et al. DI.BMJ Open Diabetes Res Care. 2017 Aug 11;5(1):e000395

Insulin Drip Protocol

When to initiate: 3 consecutive BG >200 mg/dL Target: 120 -150 mg/dl

- Serum or capillary glucose q1hour.
- Dextrose at 10 ml/hour during infusion
- Initiate infusion at 2 units/hour.
- Rate of decline of glucose should be <100mg/dl/hour
- If patient is eating, administer SQ rapid acting insulin.
- Hypoglycemia alone does not justify prolonged cessation



Computerized algorithms

- May be integrated within EMR
- Learns patient insulin sensitivity
- Built-in meal boluses
- Fewer fingerstick BG, more timely
- Less nursing judgement, time, more satisfaction
- Meta-analysis (13 studies) vs. paper algorithm
 - ↓mean glucose -23.74, (95% CI: -24.45 -23.02), p <0.00001</p>
 - $-\uparrow$ % of time in target.
 - ↓ hyperglycemia (1.3 ± 1.2% vs 6.5 ± 2%, p<0.05).

Higgs M, Fernandez R. JBI Database System Rev Implement Rep. 2015;13(5):205-43.

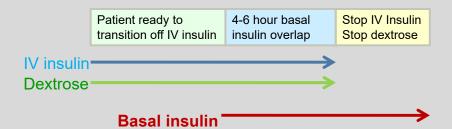
Physiologic Insulin Regimen

3 Components

		Examples
	Basal	Long-acting insulin analogue
		NPH
		Continuous SQ rapid acting insulin analogue (pump)
		IV insulin drip
	Prandial	Rapid-acting insulin analogue
BOLUS		Regular insulin (tube feeds)
БОПОЗ	Correction	See prandial insulin
	(supplemental)	IV insulin drip

Rapid acting insulin analogues: Aspart (Novolog), Lispro (Humalog), Glulisine (Apidra); Long acting insulin analogues: glargine (Lantus), detemir (levemir)

Conversion to SQ Insulin



Basal insulin dose = Average infusion rate X 15 2 unit/hr x 15 = 30 units

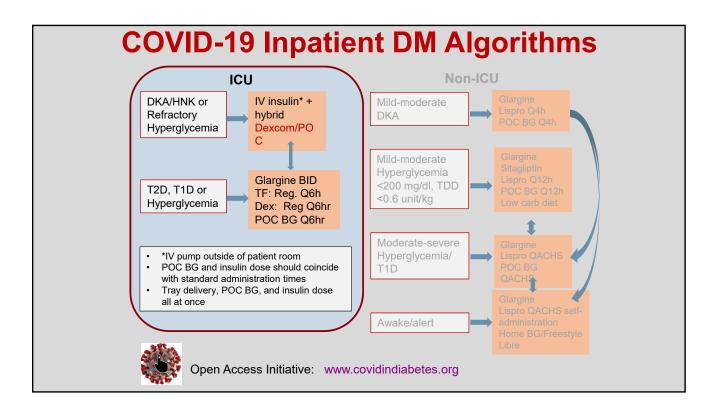
- •Assumes that the drip is not being used for meal coverage
- •Compare to home dose of insulin and weight-based needs

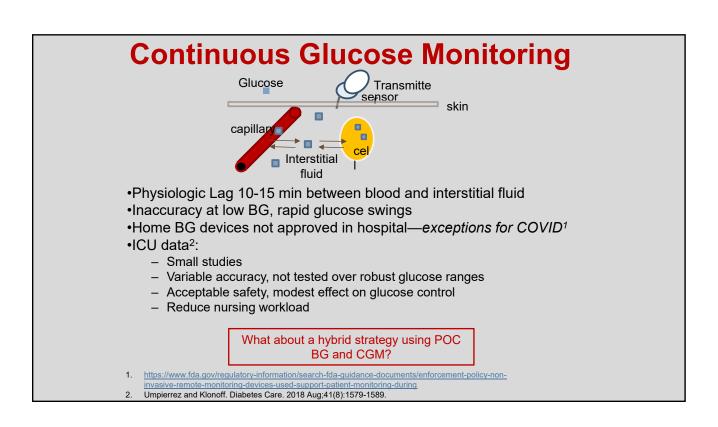
Tube Feeds Possible Approaches:

	Continuous TF	Overnight TF		
Basal Insulin	<50% of TDD (basal insulin not always necessary)			
Regular	50-100% of TDD divided evenly Q6hr	30 min. prior to start of TF and midway		
NPH (optional)		30 min prior to start of TF		
Correction dose regular insulin	prn Q6hr	prn Q6hr		

Anticipatory orders are crucial:

- Hold if TF stop or anticipated to stop within 6 hours of dose
- Hold if BG <100
- If unanticipated TF cessation: check BG Q1hr x 6hr and start D5 at same rate TF were running until TF restart or 6 hours after last dose of regular insulin





Can a Hyb	orid BG	and CGM Model be used safely in the ICU?	
	Stage	POC Glucose Testing Procedures	
		Proceed to Q6 hour POC testing when 2 consecutive hourly POC readings meet criteria: 1. CGM within 20% of POC (POC > 100 mg/dl) 2. CGM within 20 mg/dl of POC (POC < 100 mg/dl)	
		 Revert from Q6 hour to Q1 hour POC if any CGM value does not meet the validation criteria Obtain 1 time POC glucose if: No CGM value No trend arrow Urgent low soon or low threshold alert Signs and symptoms do not match glucose readings Change in clinical status, such as intubation, hemodynamic compromise, or change in nutrition New sensor 	
	Not FDA ap	Mitigation of Risk: Sensor validation Alert threshold 100 mg/dl Predictive alert Continuous data Clinical context Diabetes consult	

High level results 19 patients, Vent: 89%, Vasopressor: 37%, Dialysis: 42% Median time to validation: 137 min (IQR 114, 206) MARD: 13.9—no apparent effect of O2 sat, MAP, vasopressor, renal replacement, anticoagulation, vent support TIR (70-180 mg/dl) - Day 1: 64±23% - Day 2-7: 72±16% • TBR (70 mg/dl) - Day 1: 1.5 +/-4.1% Day 2-7: 0.16 +/- 0.35% 30 # POC BG 20 # CGM values 10 recorded in EMR # CGM values for titration Day 1 Day 2 Day 3 Day 4 Day 5

Initial treatment of diabetic ketoacidosis in the emergency department

Minimizing blood loss in patients getting hourly blood glucose tests



Inpatient Diabetes Management in the Non-ICU Setting

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Outline

- Background
- Target Glucoses
- Inpatient Therapy
- Hospital Discharge Planning

Prevalence of Diabetes in the Hospital

- Diabetes
 - -34.2 million people have diabetes (10.5% of the US population)
- Prediabetes
 - -88 million people aged 18 years or older have prediabetes (34.5% of the adult US population)
- 23% of all hospital discharges
 - Higher length of stay

Available at: http://hcupnet.ahrq.gov/HCUPnet.jsp

- ~20% (1.7-1.9 million) are early readmissions with annual cost: \$25 billion

CDC's Division of Diabetes Translation. Available at: www.cdc.gov/diabetes/shmer/index.htm. https://www.cdc.gov/diabetes/homer/index.html Fraze et al. HCUP Statistical Brief #93, 2008, www.hcup-us.ahrq.gov American Diabetes Association. Diabetes Care. Mar 6 2013. Healthcare Cost and Utilization Project (HCUP). Agency for Healthcare Research and Quality (AHRQ). 2014.

What should be the Target Glucose Range?

80-110 mg/dl

- Significant hypoglycemia
- Possible risk of increased mortality

110-140 mg/dl Consider for High risk populations (CT surgery)

140-180 mg/dl Acceptable range until further data available

>180 mg/dl

- Associated with fluid and electrolyte shifts
- · Impaired immune function

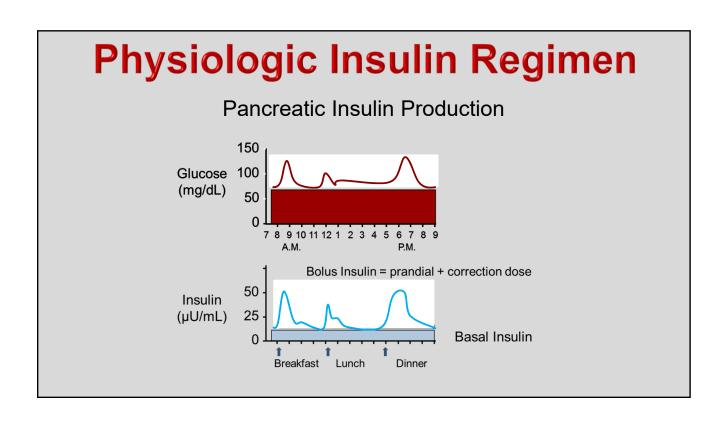
AACE/ADA CONSENSUS STATEMENT ON INPATIENT GLYCEMIC CONTROL; Endocr Pract 2009;15(4) ADA Standards of Care;Diabetes Care 2019 Endocrine Society Guidelines 2013

14. Diabetes Care in the Hospital: Standards of Medical Care in Diabetes—2018

American Diabetes Association

Diabetes Care 2018;41(Suppl. 1):S144-S151 | https://doi.org/10.2337/dc18-S014

- The preferred treatment for non-critically ill patients is a basal plus bolus correction regimen.
- For those with good nutritional intake carbohydrate coverage should be added as well



Determining Insulin Dosing

Total Daily Insulin Dose = (0.3-0.5 units/kg)(Total body weight in kg)

Typically half of the total daily dose is given as a basal insulin (0.15-0.25 units/kg)

Typically the remaining half is given as mealtime/bolus coverage if the patient is felt to be a candidate for bolus coverage

Basal Insulin Initiation in Patients not Receiving IV Insulin Therapy

	Insulin naïve	Not insulin naïve
Age >70 years +/- GFR < 60 ml/min	0.1-0.15 unit/kg	Evaluate based upon home medication
BG between 140- 200 mg/dL		adherence, home BG trends, A1c on
BG > 200 mg/dL	0.25 units/kg	admission, current oral intake, additional factors (such as renal function)

Endocrine Society Guidelines 2012

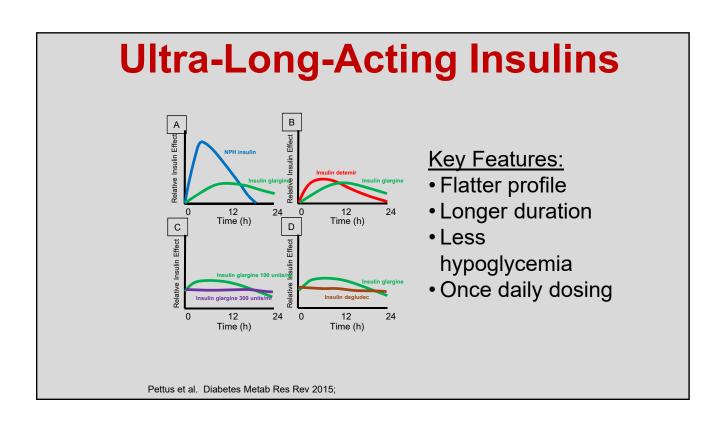
Basal insulins

The Ohio State University Wexner Medical Center and The James Comprehensive Cancer Center

INSULIN INTERCHANGE GUIDELINES

- Therapeutic interchange:
 - Glargine U100→U300: 1:1
 - Glargine U300→U100: decrease dose 20%
 - Degludec → other: 1:1, consider dose reduction

					Disposable Pens and Pen with Cartridges			
	Onset	Peak	Duratio n	Vial	Dosing Range per injection (Unit)	Dosing Increment per Injection (Unit)	Dispensing Amount	
Basal Insulin								
NPH Daily or BID	1-2 hr	4-8 hr	10-20 hr	10 mL, 1000 unit	Kwikpen: 1-60	1	Pen: 3 ml, 300 unit	
Detemir Levemir	3-4 hr	Nearl y flat	Up to 24 hr	10 mL, 1000 unit	Flextouch: 1-80	1	Pen: 3 ml, 300 unit	
Glargine (U100) Lantus/Basaglar	3-4 hr	Nearl y flat	Approx 24 hr	10 mL, 1000 unit	Solostar: 1-80	1	Pen: 3 ml, 300 unit	
Glargine (U300) <i>Touje</i> o	6 hr	Flat	24-30 hr	N/A	Solostar: 1-80	1	Pen: 1.5 ml, 450 unit	
Degludec (U100) Tresiba	1 hr	Flat	24-30 hr	N/A	Flextouch: 1-80	1	Pen: 3 ml, 300 unit	
Degludec (U200) Tresiba	1 hr	Flat	24-30 hr	N/A	Flextouch: 2- 160	2	Pen: 3 ml, 600 unit	

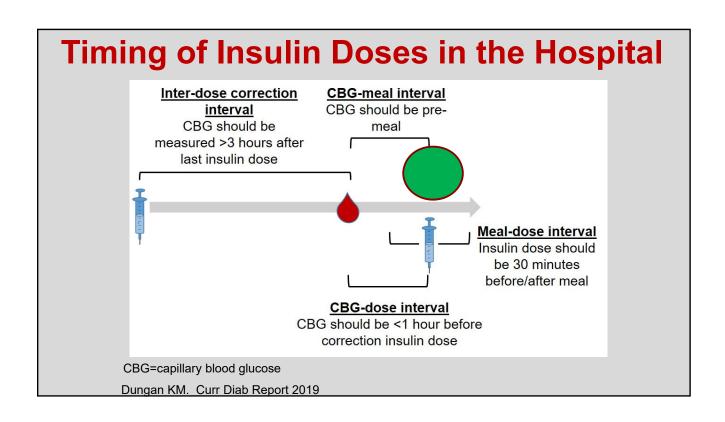


	Bolus Insulins						
					Dispo	sable Pens and F	en with Cartridges
Preparation	Action Onset	Peak	Action Duration	Vial	Dosing Range per injection (Unit)	Dosing Increment per Injection (Unit)	Dispensing Amount
Bolus Insulin							
Regular	30 min	2-4 hr	6 hr	10 mL, 1000 unit	Kwikpen: 1-60 NovoPen3 PenMate: 1-60	1	Pen: 3 ml, 300 unit Cartridge: 3 ml, 300 unit
Aspart Novolog	15 min	1-2 hr	4 hr	10 mL, 1000 unit	Echo: 0.5-30	0.5	Cartridge: 3 ml, 300 unit
Novolog				N/A	Flextouch: 1-60	1	Pen: 3 ml, 300 unit
Glulisine Admelog	15 min	1-2 hr	4 hr	10 mL, 1000 unit	Solostar pen: 1-80	1	Pen: 3 ml, 300 unit
Lianza (11100)				10 mL, 1000	Luxura: 0.5-30	0.5	Cartridge: 3 ml, 300 unit
Lispro (U100) Humalog	15 min	1-2 hr		unit	Kwikpen/Solostar: 1-60	1	Pen: 3 ml, 300 unit
Admelog				N/A	Kwikpen: 0.5-30	0.5	Pen 3 ml, 300 unit
Lispro (U200) Humalog	15 min	1-2 hr	4 hr	N/A	Kwikpen: 1-60	1	Pen: 3 ml, 300 unit
Fiasp.	10 min	1 hr	3.5 hr	10 mL, 1000 unit	Flextouch: 1-60 Cartridge: 0.5-30		
-Less hypoglycemia with insulin analogs compared to regular human insulin							

OSU Rapid Acting Insulin Order Panels

	Approximate total daily dose	I:CHO	Supplemental
Low	<20 unit	1 unit/20 gm	1 unit/100 mg/dl
Standard	20-60	1 unit/10 gm	1 unit/50 mg/dl
High	60-100	1 unit/5 gm	1 unit/25 mg/dl

Insulin:Carb ratio = 500/total daily dose of insulin Supplemental (correction) factor: 1 unit per (1500/total daily dose) mg/dl



Should Non-Insulin Agents be Discontinued Inpatient?

Factors to influence decision: short hospital stays, previous good control, no contra-indications

- DPP-IV inhibitors well tolerated but have limited efficacy.
- · Continue home weekly GLP-1

Caution	MTF	SFU	TZD	DPP-4i	SGLT2i	GLP-1 RA	Insulin
Kidney disease	Risk of lactic acidosis	Prolonged hypoglycemia	Fluid overload	Adjust dose	Fluid shift	GI side effects→ fluid status	Reduced clearance
Hypoglycemia	N	Υ	N	N	N	N	Υ
Other	GI side effects Lactic acidosis (IV contrast)		Heart failure	?Pancreatitis	GU infection DKA	GI side effects ?Pancreatitis	
Examples	Metformin	Glimepiride Glipizide Glyburide	Pioglitazone	Sitagliptin Linagliptin Saxagliptin Allogliptin	Empagliflozin Canagliflozin Dapagliflozin Ertugliflozin	Exenatide Exenatide QW Liraglutide Dulaglutide Semaglutide	See other

MTF=metformin, SFU=Sulfonylureas, TZD=thiazolidinediones, GLP-1RA= Glucagon-like Peptide-1 Receptor agonist, SGLT2i=Sodium-Glucose Cotransporter-2 inhibitor.

What to do for a Procedure

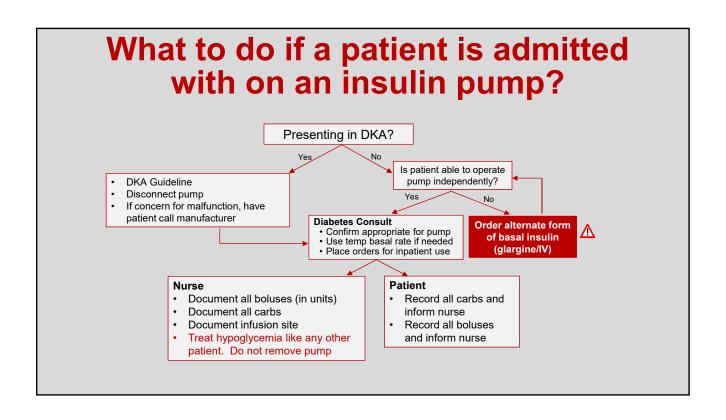
- As a general rule DO NOT HOLD basal insulin
 - Consider reducing by 20-50%, especially if there is suspicion that it is being used for prandial coverage (basal insulin >50% of total daily insulin dose)
- Do hold meal time insulin

*Under no circumstances should you withhold basal insulin from a patient with Type 1 Diabetes!

Pulsed Steroid Dosing

- Difficult to control
- Treatment
 - -Insulin drip
 - -NPH 0.5 units per 1 mg of prednisone is an option
 - -Increase prandial insulin (e.g. $1:10 \rightarrow 1:5$)
 - If NPO use regular insulin for correction every 6 hours
- Preemptively reduce insulin in anticipation of reduction in steroid dosing

Clore et al. Endocr Pract. 2009;15:469-474



Glucose Testing

- Glucometers typically have approval for hospital use for venous and arterial specimens
- Capillary use MAY not be intended for those that are critically ill
 - Capillary whole blood specimens (e.g. obtained by finger stick) should not be used in patients receiving intensive medical intervention/therapy ...
 - Examples include...severe hypotension, shock, hyperosmolar-hyperglycemia (with or without ketosis), and severe dehydration.

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Hypoglycemia



Hypoglycemia Treatment in Non-Pregnant Adults

Goal

This guideline is designed to treat events of hypoglycemia, either spontaneous or insulin-induced, and to decrease glycemic variability associated with treatment of hypoglycemia.

- A hypoglycemia management protocol should be adopted and implemented by each hospital
- Each patient should have an established plan for treating hypoglycemia
- Hypoglycemia should be tracked and documented in the medical record

Diabetes Care 2018;41(Suppl. 1):S144-S151 | https://doi.org/10.2337/dc18-S014

OSU Hypoglycemia Treatment Guideline

Treat based upon BG level Recheck Q15 min until BG >80 mg/dl

Blood Glucose (BG) Level		Follow Up		
60-69 mg/dl or 70-79 with symptoms	Next meal less than 1 hr (15 g oral carbohydrate, choose one) 4 0z juice or regular soda 1 tibsp jelly or sugar 3 glucose tablets 1 tube dextrose gel	Next meal 1-2 hrs (choose one) 3 graham crackers 6 saltine crackers 8 oz skim milk	Next meal more than 2 hrs (choose one) • ½ sandwich • 3 graham crackers with one thosp peanut butter	Recheck BG q15 min and treat accordingly until ≥ 80 mg/d Once BG ≥80
45-59 mg/dl	Next meal less than 1 hr (20 g oral carbohydrate, choose one) • 6 oz juice or regular pop • 1 ½ tbsp of jelly or sugar • 4 glucose tablets • 1 ½ tubes dextrose gel	Next meal 1-2 hrs (choose one) 3 graham crackers 6 saltine crackers 8 oz skim milk	Next meal more than 2 hrs_(choose one) • ½ sandwich (15 g) • 3 graham crackers with one tbsp peanut butter	mg/dl, recheck BG q1h x 2, then resume point-of-care glucose as previously ordered
	Call House Officer to report E	3G and action taken		
<45 mg/dl	Next meal less than 1 hour (30 g oral carbohydrate, choose one) 8 oz juice or regular soda 2 thsp jelly or sugar 6 glucose tablets 2 tubes dextrose gel	Next meal 1-2 hours (choose one) • 3 graham crackers • 6 saltine crackers • 8 oz skim milk	Next meal more than 2 hours (choose one) • 1 sandwich (30 g) • 3 graham crackers with one tisp peanut butter	Recheck BG q15 min and treat accordingly until ≥80 mg/dl. Once BG >80 mg/dl, recheck BG q1h x 4, then resume point-of-care
	Call House Officer to report E	3G and action ten	•	glucose as previously ordered

"Choose one item from one column based on next meal time. If the next meal is 1-2 hours away, include complex carbohydrate as suggested by the examples. If the next meal is >2 hours away include protein as suggested by the examples.

If patient is uncooperative or does not have available enteral access, see Table 2, next page

Van Berkel et al. Intensive Crit Care Nurs. 2017 Aug 4. pii: S0964-3397(17)30063-0

Risk Factors for Inpatient Hypoglycemia

)
	OR	95% CI
DM	2.6	1.5-4.7
Sepsis	2.2	1.2-4.1
↓CHO Intake	6.6	1.9-23
Inpatient Insulin use	5.4	2.8-10
Shock	1.8	1.1-2.9
Prior History of Hypoglycemia	2.3	1.1-4.7

Reduce insulin, increase monitoring if

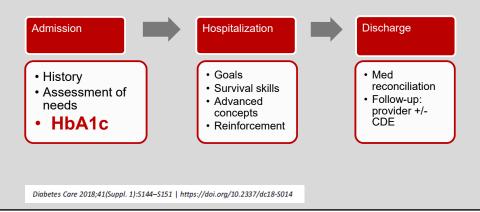
- •Any form of carbohydrate is interrupted
- •In setting of declining renal or hepatic function

Vriesendorp et al. Crit Care Med 2006;34:96

Discharge Planning

Discharge Planning

- There should be a structured discharge plan tailored to the individual patient with diabetes
- Perform an A1c on all patients with diabetes or hyperglycemia admitted to the hospital (if not done in the prior 3 months)

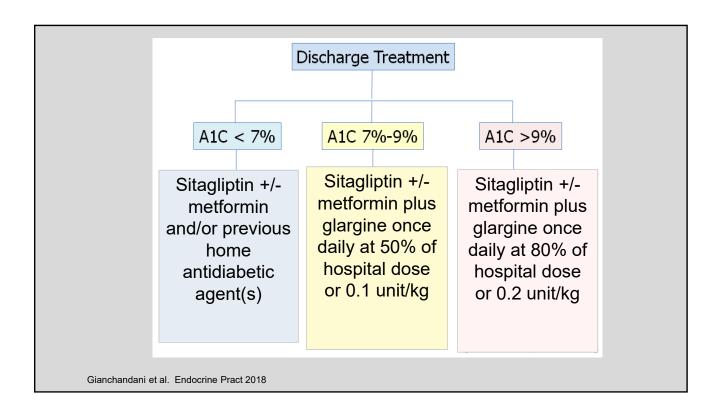


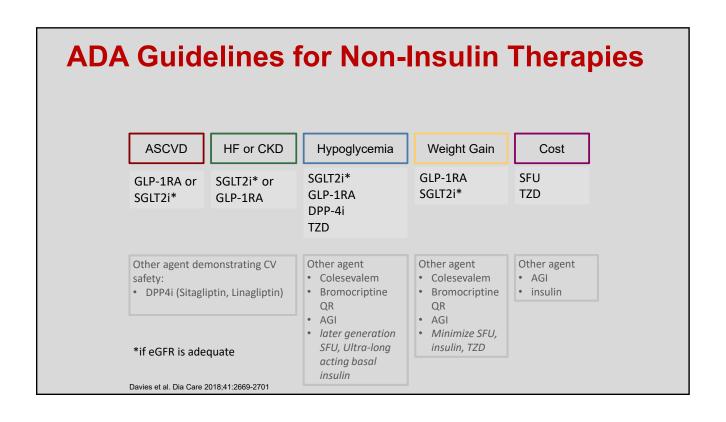
ADA/AACE Recommendations

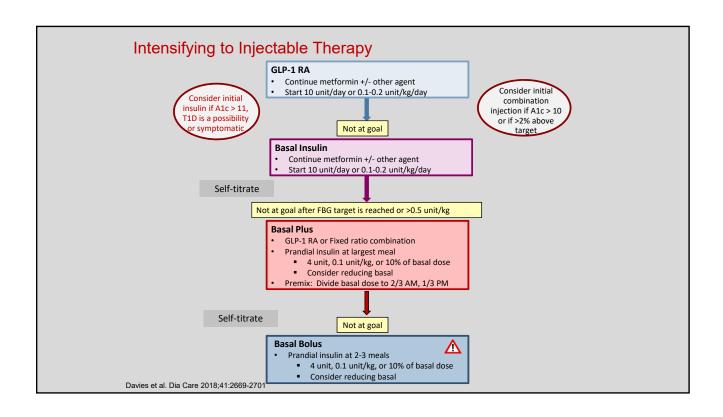
The mean hospital LOS is usually <5 days and the capacity to learn new material may be limited during acute illness. Diabetes-related education is frequently limited to an inventory of basic "survival skills."

- Level of understanding pertaining to diabetes
- Self-monitoring of BG and home BG goals
- Definition, recognition, treatment, and prevention of hyperglycemia and hypoglycemia
- Consistent eating patterns
- When and how to properly take BG-lowering medications, including insulin
- Sick day management
- Proper use and disposal of needles and syringes
- Hospital follow-up plans

Moghissi et al. Diabetes Care. 2009 Jun;32(6):1119-31







Oral therapy in combination with injectable therapies

- Metformin: continue
- DPP4i: stop if using GLP-1RA
- <u>SFU</u>: stop or reduce dose with insulin
- TZD: stop or reduce dose with insulin
- SGLT2i: continue but beware of DKA in insulin requiring patients (provide sick day rules)

Davies et al. Dia Care 2018;41:2669-2701

Conclusions

- 1. Diabetes is a very common diagnosis in the inpatient setting
- 2. Hospitalization provides an opportunity to identify and help improve glycemic control
- 3. Standard protocols help promote consistency and facilitate education
- 4. Transitions of care back to the outpatient setting can create challenges to glycemic control