Glycemic Control in the Intensive Care Unit:
Practices, Promises, & Pitfalls

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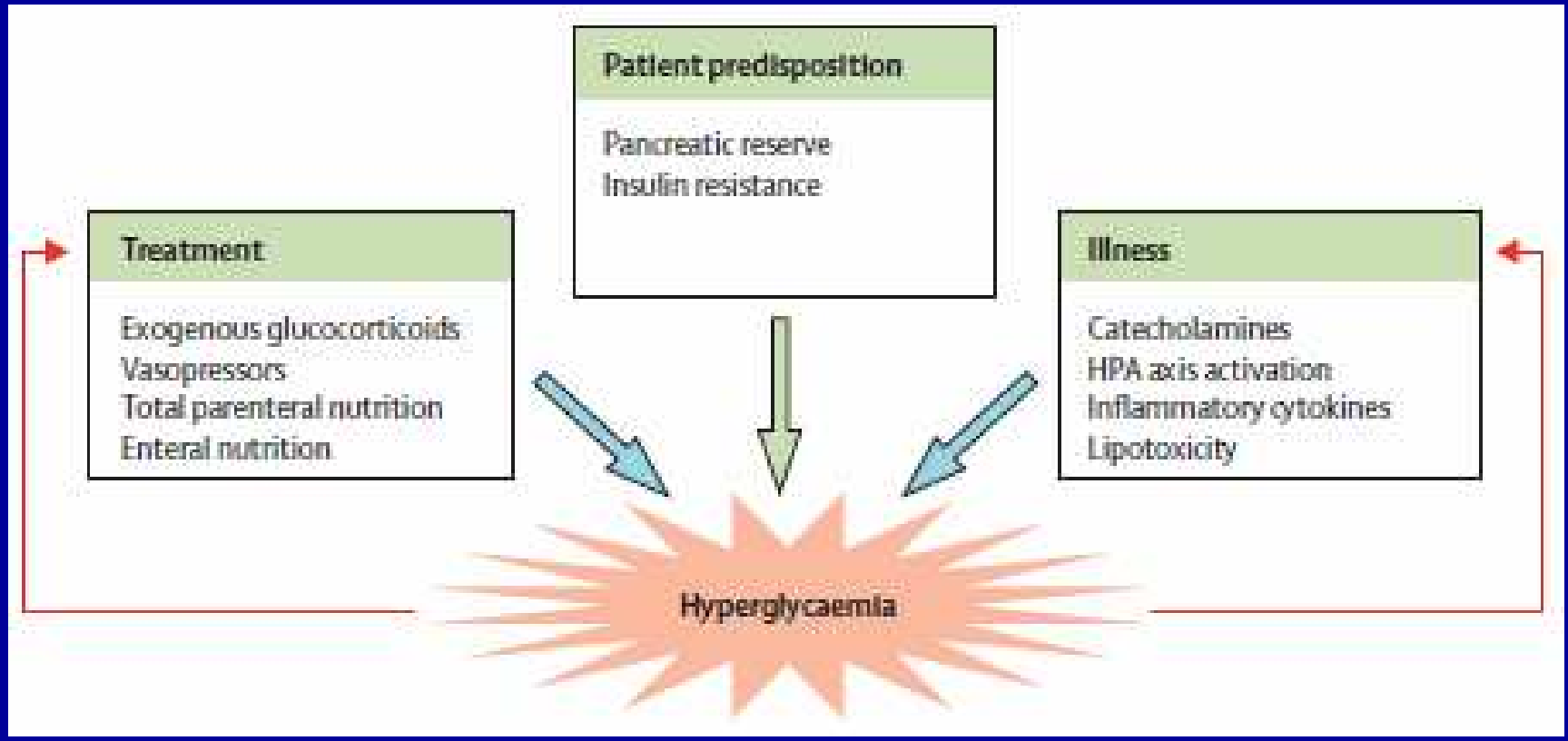
Lecture Outline

- Etiologies for hyperglycemia in the critically ill patient
- Is hyperglycemia bad?
- Intensive insulin therapy
- Hypoglycemia
- Practical aspects of managing hyperglycemia



Dungan KM et al. Lancet. 2009;373:1798-1807.

Is Hyperglycemia Bad?

Retrospective study of 1,826 consecutive Med-Surg ICU patients.
Mean plasma glucose conc during ICU stay.

Mean* (mg/dL)	Mortality rate (%)	No. of patients
80-99	9.6	264
100-119	12.2	491
120-139	15.1	338
140-159	18.8	202
160-179	28.4	141
180-199	29.4	102
200-249	37.5	144
250-299	32.9	70
>300	42.5	40

*Glucose values expressed as a range of mean values. The χ^2 test was used for trend ($P<.001$).

Krinsley. Mayo Clin Proc.2003;78:1471-8.

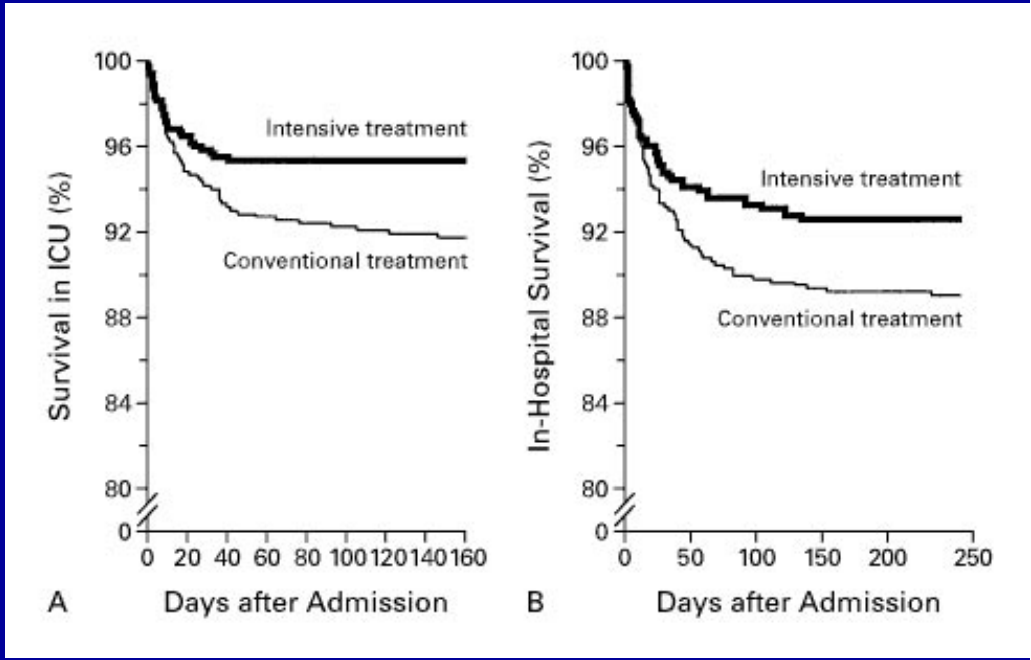
Does Intensive Insulin Therapy Improve Clinical Outcome?

- Leuven I (2001)
- Leuven II (2006)
- VISEP (2008)
- Glucontrol (2009)
- NICE-Sugar (2009)

Leuven I

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

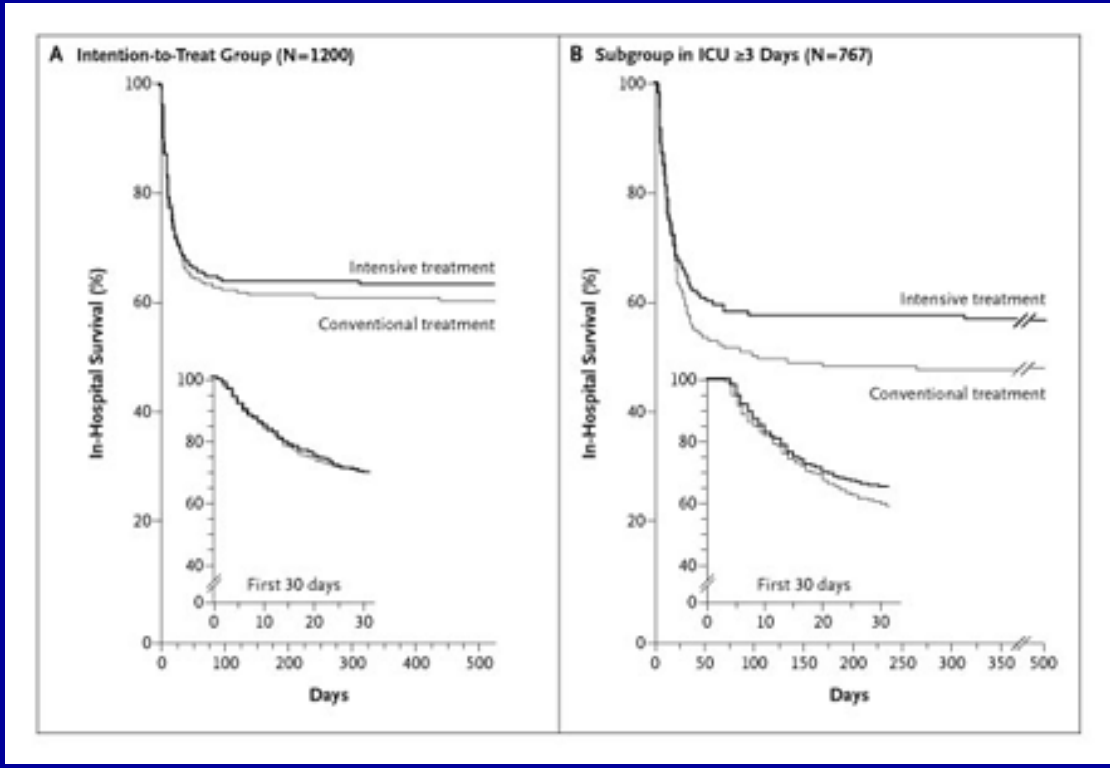
- 1548 SICU patients randomized to IIT vs Con Tx
- ITT: 80 to 110 mg/dL
- Con Tx: RHI infusion if BG > 215 with BG @ 180 to 200 mg/dL
- BG checked q 1– 4 h
- Mortality improved: 8.0% to 4.6% overall
- 20.2% to 10.6% if in ICU > 5 d



Leuven II

Van den Berghe G et al. NEJM. 2006;354:449-61.

- 1200 MICU patients
- Mortality in the intent to treat (overall population) was 24.2% versus 26.8% for the ITT and Con Tx groups, respectively (p = NS).
- Mortality was improved for those patients who were in the ICU ≥ 3 days (31.3 versus 38.1%, respectively, p < 0.05)



VISEP study

Efficacy of Volume Substitution and Insulin Therapy in Severe Sepsis

Brunkhorst FM et al. NEJM.2008;358:125-39.

- 537 ICU patients with severe sepsis randomized to IIT or Con Tx AND received either 10% Pentastarch or Ringer's Lactate for fluid resuscitation
- Con Tx: BG maintained at 180 to 200 mg/dL with RHI infusion
- ITT: BG maintained at 80 to 110 mg/dL with RHI infusion using the Leuven (II) algorithm.
- ARF – 2 X baseline sCr or need for CRRT

VISEP study

Efficacy of Volume Substitution and Insulin Therapy in Severe Sepsis

Brunkhorst FM et al. NEJM.2008;358:125-39.

Outcome	IIT (n=247)	Con Tx (n =290)	P <
Death at 28 d	24.7%	26.0%	NS
Death at 90 d	39.7%	35.4%	NS
ICU stay (d)	16 (8 – 30)	14 (7 -25)	0.06
ARF	31.1%	26.6%	NS
BG ≤ 40 mg/dL	17.0%	4.1%	0.001

Glucontrol Study

Preiser JC et al. Inten Care Med.2009:In press.

- 21 ICUs across Europe
- Upon admission to the medical-surgical ICU adult patients were randomized to IIT or Con Tx (intended sample size was 1,750 patients/group)
- IIT: BG 80 to 110 mg/dL by continuous RHI infusion
- Conv Tx: 140 to 180 mg/dL by continuous RHI infusion
- BG monitored q 1 – 4 hrs

Glucontrol Study

Preiser JC et al. Intensive Care Med.2009:35:1738-48.

Outcome	IIT (n=536)	Con Tx (n=542)	P <
ICU Mortality	13.4%	11.0%	NS
Mortality	23.3%	19.4%	NS
Hosp LOS (d)	16 (11-29)	16 (11-29)	NS
RHI duration(d)	5 (2-9)	2 (0-5)	0.0001
Rate (units/hr)	1.3 (0.7-2.3)	0.3 (0-1.3)	0.0001
N with BG $\leq$ 40	8.7%	2.7%	0.0001

Glucontrol Study

Preiser JC et al. Intensive Care Med.2009:35:1738-48.

- **"The trial was stopped early due to the high rate of unintended protocol violations."** ***[RND: …likely leading to severe hypoglycemia.]***

NICE-SUGAR study

(Normoglycemia in Intensive Care Evaluation – Survival Using Glucose Algorithm Regulation)

New Engl J Med.2009;360:1283-1297

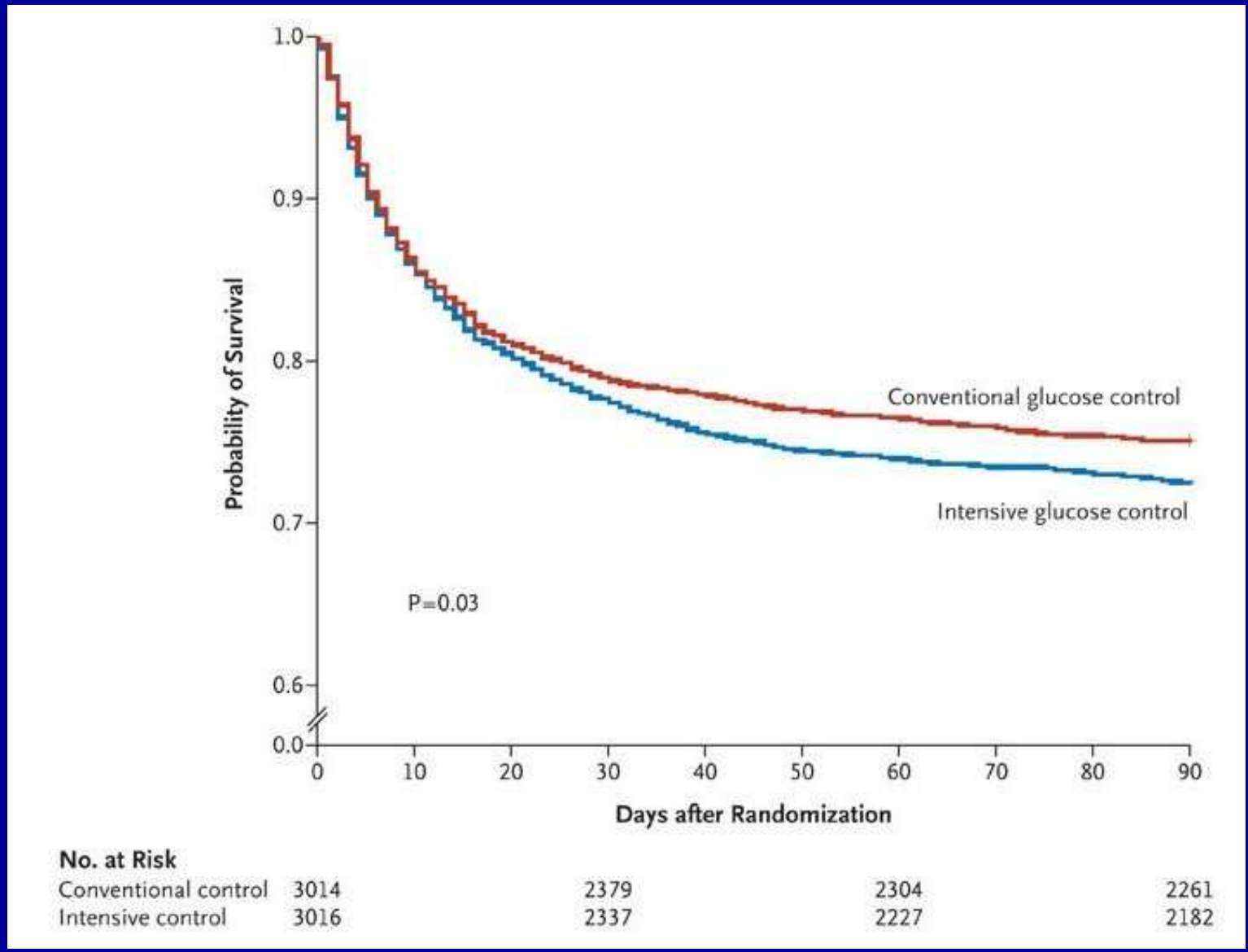
- Australia, New Zealand, Canada
- Within 24 hrs of admit to ICU (mixed population), 6,104 patients randomized to ITT (81 to 108 mg/dL) or Con Tx (≤ 180 mg/dL; insulin therapy d/c if BG < 144 mg/dL)
- ITT was guided by a treatment algorithm
- BG obtained 1 – 4 hours
- Followed while in ICU or 90 days

NICE-SUGAR study

(Normoglycemia in Intensive Care Evaluation – Survival Using Glucose Algorithm Regulation)

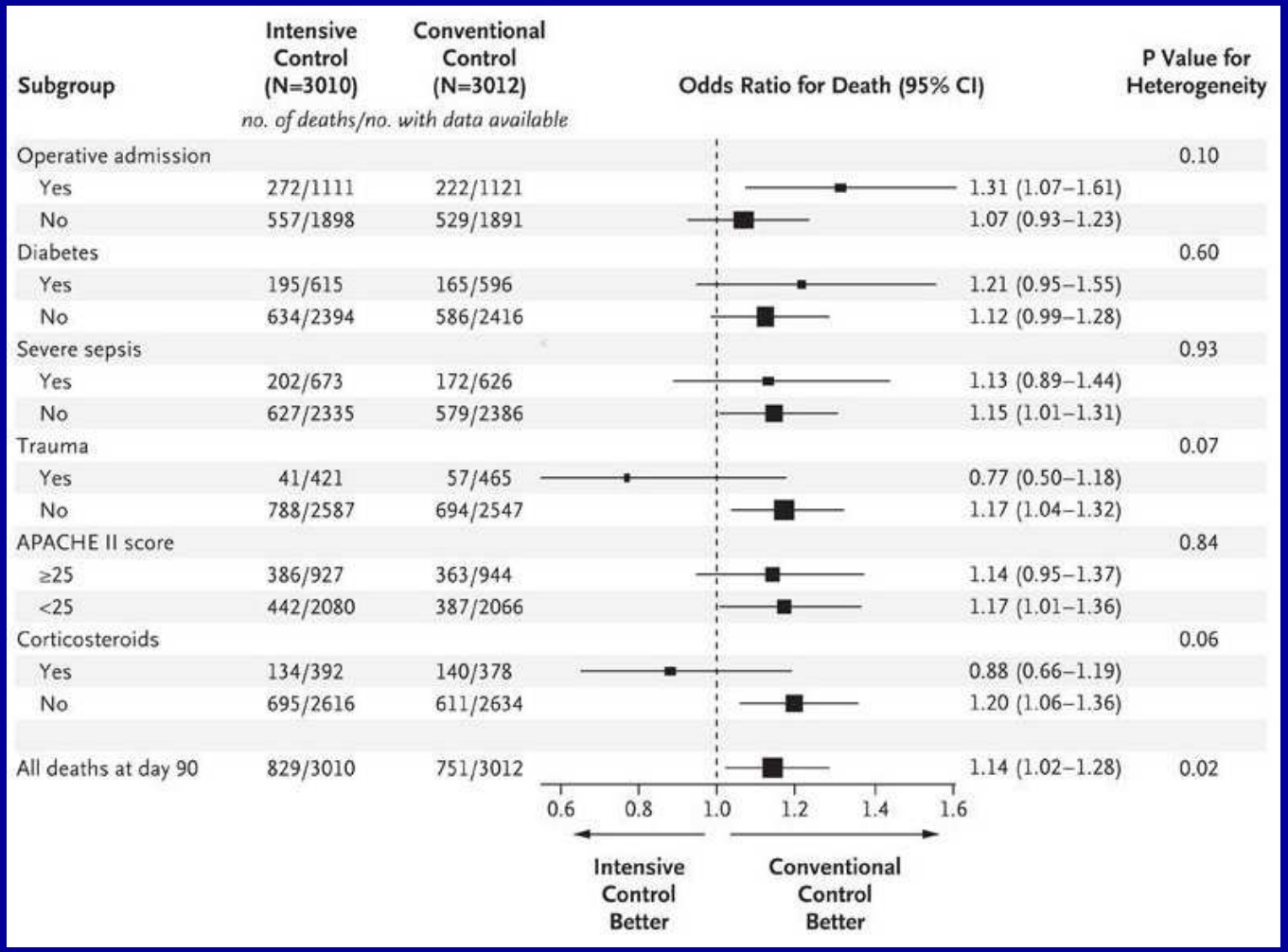
Finfer S et al. New Engl J Med.2009;360:1283-1297

Outcome	IIT	Con Tx	P <
Death- day 90	27.5%	24.9%	0.02
Death- day 28	22.3%	20.8%	N.S.
ICU days	6 (2-11)	6 (2 -11)	N.S.
Mech vent days	6.6 ± 6.6	6.6 ± 6.5	N.S.
Hospital days	17 (8-35)	17 (8-35)	N.S.
BG ≤ 40 mg/dL	6.8%	0.5%	0.001



Finfer S et al. New Engl J Med.2009;360:1283-1297

Who benefits from IIT?
Should the target BG range be changed?



Subgroup	Intensive Control (N=3010)	Conventional Control (N=3012)	Odds Ratio for Death (95% CI)	P Value for Heterogeneity
	no. of deaths/no. with data available			
Operative admission				0.10
Yes	272/1111	222/1121	1.31 (1.07–1.61)	
No	557/1898	529/1891	1.07 (0.93–1.23)	
Diabetes				0.60
Yes	195/615	165/596	1.21 (0.95–1.55)	
No	634/2394	586/2416	1.12 (0.99–1.28)	
Severe sepsis				0.93
Yes	202/673	172/626	1.13 (0.89–1.44)	
No	627/2335	579/2386	1.15 (1.01–1.31)	
Trauma				0.07
Yes	41/421	57/465	0.77 (0.50–1.18)	
No	788/2587	694/2547	1.17 (1.04–1.32)	
APACHE II score				0.84
≥25	386/927	363/944	1.14 (0.95–1.37)	
<25	442/2080	387/2066	1.17 (1.01–1.36)	
Corticosteroids				0.06
Yes	134/392	140/378	0.88 (0.66–1.19)	
No	695/2616	611/2634	1.20 (1.06–1.36)	
All deaths at day 90	829/3010	751/3012	1.14 (1.02–1.28)	0.02

Finfer S et al. New Engl J Med.2009;360:1283-1297

Hyperglycemic Control in Trauma Patients

Study	N	BG Target (mg/dL)	Outcome
Bochicchio GV, J Trauma 2007	896	< 140	↓Mortality, ↓LOS, ↓Infections, ↓Vent (d)
Scalea TM, Ann Surg 2007	2,129	100 - 150	↓Mortality, ↓LOS, ↓Infections, ↓Vent (d)
Collier B, JPEN 2005	818	< 150	↓Mortality, ↓LOS, ↓Vent (d)
NICE-SUGAR	IIT was favorable in trauma patients		

Hyperglycemic Control in Cardiothoracic Patients

Study	N	BG Target (mg/dL)	Outcome
Lazar HL, Circulation 2004	141	126 - 200	↓LOS, ↓Infections, ↓Vent (d)
Furnary AP, J Thorac Cardio Surg 2003	3554	100 - 150	↓Mortality, ↓Sternal wound infections
Leuven I NEJM 2001	~60% CT surgery patients		

Intensive Insulin Therapy or Not?

Consensus Statement on Inpatient Glycemic Control
June, 2009

For critically ill patients:

- **BG levels should be maintained between 140 mg and 180 mg/dL. Greater benefit may be realized at the lower end of this range.**
- **Somewhat lower glucose targets may be appropriate in selected patients.**
- **Targets < 110 mg/dL are not recommended.**
- **Use of RHI protocols with demonstrated safety and efficacy *[avoiding hypoglycemia]* is highly recommended.**

Am Assoc Clin Endo/ADA. Diabetes Care. 2009;32:1119-1131.

Intensive Insulin Therapy or Not?

Consensus Statement on Inpatient Glycemic Control June, 2009

For non-critically ill patients:

- **Pre-meal glucose targets should be < 140 mg/dL with random BG values < 180 mg/dL, as long as these targets can be safely achieved.**
- **Consideration should be given to reassessing the insulin regimen if BG levels decline below 100 mg/dL.**
- **Modification of the regimen is necessary when the BG values are < 70 mg/dL.**

Am Assoc Clin Endo/ADA. Diabetes Care. 2009;32:1119-1131.

Intensive Insulin Therapy or Not?

Dickerson's Recommendation

- **Critically ill trauma patients, CT surgery patients : Insulin protocols that safely and effectively keep BG levels > 70 mg/dL and < 150 mg/dL.**
- **Other critically ill patients: Insulin protocols that safely and effectively keep BG > 70 mg/dL and < 180 mg/dL would be acceptable.**
- **For non-critically ill patients, all random BG < 180 mg/dL.**

Hypoglycemia
From Intensive Insulin Therapy

The Major and Serious Pitfall!

Incidence of Severe Hypoglycemia (≤ 40 mg/dL)

Study	IIT	Con Tx	P <
Leuven I	5.1%	0.8%	-
Leuven II	18.7%	3.1%	-
NICE-SUGAR	6.8%	0.5%	0.001
VISEP	17.0%	4.1%	0.001
Glucontrol	8.7%	2.7%	0.0001

Risk Factors for Severe Hypoglycemia

Vriesendorp et al. Crit Care Med.2006;34:96-101.

Predisposing Factor	Odds Ratio
• CRRT	• 14
• Decrease in nutrition without an adjustment in RHI infusion	• 6.6
• Simultaneous use of octreotide and RHI	• 6.0
• Insulin use	• 5.3
• Diabetes mellitus	• 2.6
• Sepsis	• 2.2
• Inotropic/vasopressor support	• 1.8

Potential Limitations of the Major Trials

- Too tight of a target BG range
- Complexity of the protocol itself
- BG monitoring duration too long (e.g., up to 4 hours)
- Development of Acute Kidney Injury or presence of chronic kidney disease without altering the insulin infusion protocol

Why the higher incidence of severe hypoglycemia in Leuven II?

- **Leuven I: ITT: 80 to 110 mg/dL (infusion team)**
- **Leuven II: ITT: 80 to 110 mg/dL (adjustments made by RNs in the ICU from titration guidelines adapted from the first study)**

Leuven II Algorithm (used by VISEP)

TEST	RESULT	ACTION
Measure glucose on entry to ICU	BG>11.1 mmol/l ?	Start insulin 2-4 IU/h
	BG 11.1 – 6.1 mmol/l ?	Start insulin 1-2 IU/h
	BG<6.1 mmol/l ?	Don't start insulin but continue BG monitoring every 4 h
Measure glucose every 1-2 h until normal range	BG>7.8 mmol/l?	Increase insulin dose by 1-2 IU/h
	BG 5.1 – 7.8 mmol/l ?	Increase insulin dose by 0.5-1 IU/h
	BG approaching normal range ?	Adjust insulin dose by 0.1-0.5 IU/h
Measure glucose every 4 h	BG approaching normal range ?	Adjust insulin dose by 0.1-0.5 IU/h
	BG normal ?	Insulin dose unchanged
	BG falling steeply ?	Reduce insulin dose by half and check more frequently
	BG 3.3-4.4 mmol/l ?	Reduce insulin dose and check BG within 1 h
	BG 2.2-3.3 mmol/l ?	Stop insulin infusion, assure adequate baseline glucose intake and check BG within 1 h
	BG <2.2 mmol/l ?	Stop insulin infusion, assure adequate baseline glucose intake, administer glucose per 10 g IV boluses and check BG within 1 h

Glucontrol Study

Preiser JC et al. Inten Care Med.2009:In press.

Intensive Insulin Therapy Protocol

5. STARTING PERFUSION

Blood glucose level	Insulin infusion rate
< 6·1 mmol/L	On hold
6·1 mmol/L-7·8 mmol/L	1 UI / H
7·8 mmol/L-10·0 mmol/L	2 UI / H
> 10·0 mmol/L	4 UI / H

IV Bolus of 1-2 UI Insulin are allowed if target value is not fast enough reached.

6. MAINTENANCE PERFUSION

Blood glucose level	Incremental Insulin infusion rate
> 16·7 mmol/L	+3 UI/H
10·0-16·7 mmol/L	+2 UI/H
7·8-10·0 mmol/L	+1 UI/H
6·1-7·8 mmol/L	+0·5 UI/H
4·4-6·1 mmol/L	+ 0 UI/H (target range)
2·2-4·4 mmol/L	Stop insulin, Hourly control of glycaemia until > 4·4 mmol/L
< 2·2 mmol/L	Stop insulin, 12gr glucose IVD, Call immediately physician, Hourly control of blood glucose level until > 4·4 mmol/L

81 - 108	> 108	decrease of less than 36	between - 1 and -35		10	Current dose (Units/hour) x (current BSL ÷ previous BSL)		1 hour
81 - 108	> 108	decrease of more than 35	< -35		57	Current dose (Units/hour) x (current BSL ÷ previous BSL)	ASK DOCTOR TO REVIEW	30 and 60 minutes
109 - 143	≤ 144	decrease	<0		41	Current insulin dose (Units/hour)	Plus optional 1 unit stat dose	1 hour
109 - 144	≤ 144	same or increase	>=0		42	Current insulin dose (Units/hour) + 1 unit/hour	Plus optional 1 unit stat dose	1 hour
109 - 144	> 144	decrease of less than 36	between - 1 and -35		41	Current insulin dose (Units/hour)	Plus optional 1 unit stat dose	1 hour
109 - 144	> 144	decrease of 36 to 71	between - 36 and -71		33	Current dose (Units/hour) x (current BSL ÷ previous BSL)	Or maintain current dose	1 hour
109 - 144	> 144	decrease of more than 71	< -71		57	Current dose (Units/hour) x (current BSL ÷ previous BSL)	ASK DOCTOR TO REVIEW	30 and 60 minutes
145 - 180	< 145				43	Current insulin dose (Units/hour) + 2 units/hour	Plus 1 to 2 unit stat dose	1 hour
145 - 180	145 - 180				44	Current insulin dose (Units/hour) + 1 unit/hour	Plus 1 to 2 unit stat dose	1 hour
145 - 180	≥ 181	decrease of 1 to 18	between -1 and -18		44	Current insulin dose (Units/hour) + 1 unit/hour	Plus 1 to 2 unit stat dose	1 hour
145 - 180	≥ 181	decrease of 19 to 36	between - 19 and -36		42	Current insulin dose (Units/hour) + 1 unit/hour	Plus optional 1 unit stat dose	1 hour
145 - 180	> 181	decrease of more than 36	< -36		33	Current dose (Units/hour) x (current BSL ÷ previous BSL)	Or maintain current dose	1 hour
> 180	≤ 144				45	Current insulin dose (Units/hour) + 2(current BSL ÷ previous BSL) Units/hour	Plus 1 to 2 unit stat dose	1 hour
> 180	147 - 180				43	Current insulin dose (Units/hour) + 2 units/hour	Plus 1 to 2 unit stat dose	1 hour
> 180	> 180	increase	>0		45	Current insulin dose (Units/hour) + 2(current BSL ÷ previous BSL) Units/hour	Plus 1 to 2 unit stat dose	1 hour

Table 1A: INSULIN BOLUS ORDERED		
Blood Glucose (mg/dL)	Regular Insulin Intravenous Push (units)	Insulin Infusion Rate (units/hour)
Under 110	0	0.5
110-179	2	1
180-240	4	2
241-300	6	3

Table 1B: NO INSULIN BOLUS		
Blood Glucose (mg/dL)	Regular Insulin Intravenous Push (units)	Insulin Infusion Rate (units/hour)
Under 110	0	0.5
110-179	0	1
180-240	0	2
241-300	0	3

Table 2: ADJUSTMENT FACTOR (MULTIPLICATION) FACTORS

CURRENT Blood Glucose	CHANGE IN Blood Glucose since the prior reading				
	DEcreased more than 30	DEcreased 11-30	No change +/- 10	INcreased 11-30	INcreased more than 30
60-90	X 0.25*	X 0.50*	Continue Current Rate		X 1.5
91-120	X 0.50*	X 0.75*	Continue Current Rate	X 1.5	
121-150	X 0.75*	Continue Current Rate	X 1.5		X 2.0
151-180	Continue Current Rate	X 1.5		X 2.0	
Above 180		X 1.5	X 2.0		

Cyrus RM et al. Ann Pharmacother.2009;43:1413-1418.

Evaluation of Compliance with a Paper-based Insulin Infusion Protocol

- Retrospective Chart Review
- 72 patients receiving IV RHI infusion
- Infusion rate correctly adjusted - 68%
- Infusion rate decreased inappropriately - 13%
- Infusion rate increased inappropriately - 6%
- Infusion rate unchanged inappropriately - 13%
- BG msmts > 20 min past specified time - 26%

Cyrus RM et al. Ann Pharmacother.2009;43:1413-1418.

RHI infusion (NSS-UT/The MED)

1.	100 units regular human insulin in 100 mL NS	
2.	Begin infusion at _____ units/hr.	
3.	Check accuchecks every _____ hour(s).	
4.	If enteral feeding or parenteral nutrition is turned off for any reason, continue regular insulin infusion and infuse ☐ D5W or ☐ D5NS intravenously at the same rate as the nutrition formulation.	
5.	Use scale as follows:	
	Less than 60	stop insulin infusion, give ½ amp D50W, and restart insulin infusion when blood glucose >100 mg/dL at ½ the last rate
	61-100	decrease drip by 50% (round to the nearest whole unit/mL)
	101-125	no change
	126-175	increase infusion by 1 unit/hr
	176-200	increase infusion by 2 units/hr
	201-225	increase infusion by 3 units/hr
	226-250	increase infusion by 4 units/hr
	251-275	increase infusion by 5 units/hr
	276-300	increase infusion by 6 units/hr
	>300	increase infusion by 6 units/hr and call MD

Evaluation of Nursing Adherence to a Paper-based Insulin Infusion Algorithm

- 40 patients receiving IV RHI infusion
- 4,150 BG measurements
- 88% compliance with protocol
- Most common protocol violations: no change in RHI infusion rate when a rate change was warranted (66% of violations)
- Violations accounted for a single episode BG < 60 mg/dL in 4 pts and 65 episodes BG > 150 mg/dL in 18 pts

Johnson JL et al. Abstract submitted for consideration of presentation and publication. 2010.

Severe Hypoglycemia and Renal Failure during the Major Trials

Reported incidence of severe hypoglycemia and renal failure from the major trials

Trial	Prevalence	
	Renal failure	Severe hypoglycemia (BG <40 mg/dL or 2.2 mmol/L)
Leuven 1 [3]	4 patients with dialysis before ICU admission	5.1%
Leuven 2 [31]	6.2% before ICU admission 20% with AKI	18.7%
NICE-SUGAR [2]	35% with "renal dysfunction" 15.4% received CRRT	6.8%
VISEP [29]	31.1% with AKI	17.0%
Glucontrol [30]	523 days of CRRT	8.7%

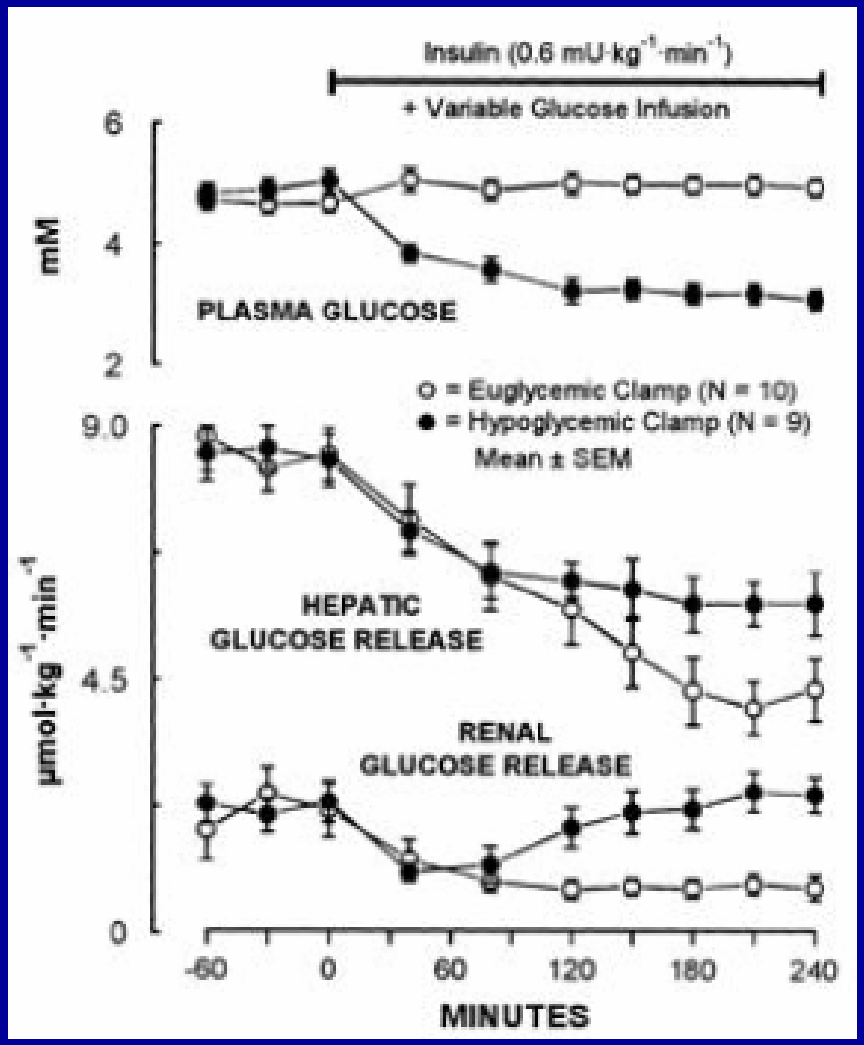
AKI, acute kidney injury; BG, blood glucose; CRRT, continuous renal replacement therapy; ICU, intensive care unit

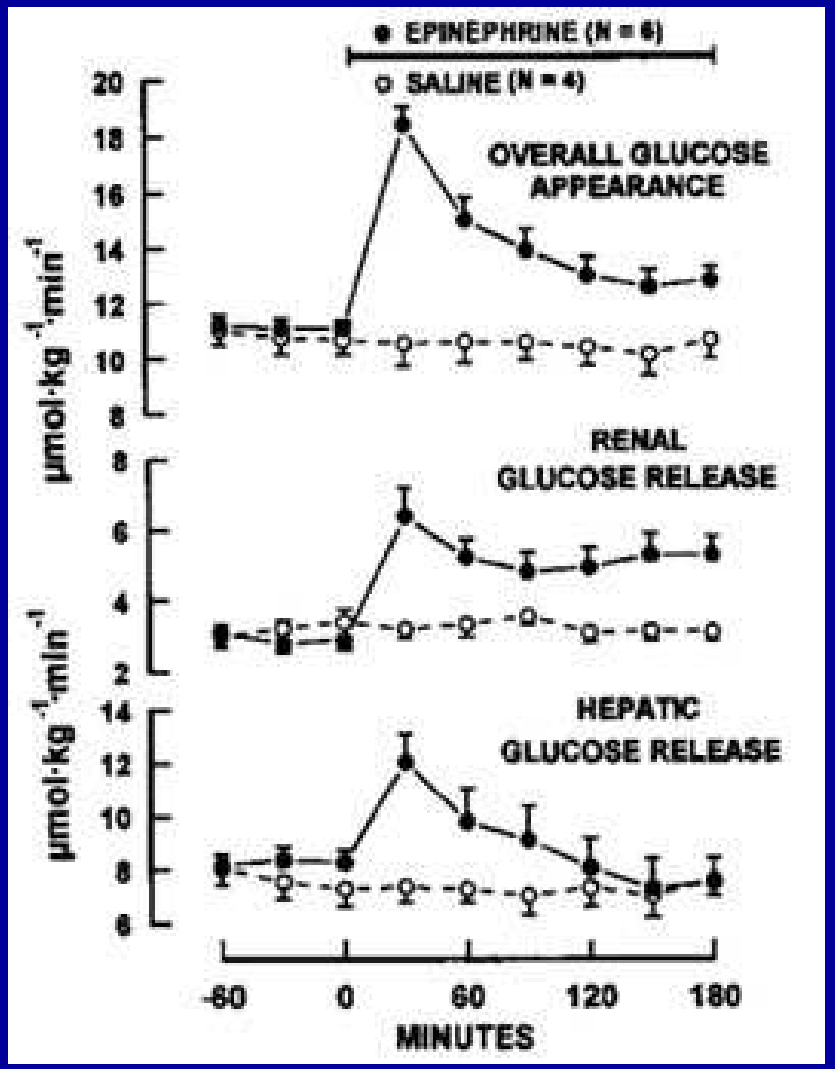
Dickerson RN et al. Nutrition.2011; In press.

Insulin Metabolism in Renal Failure

Author/Year	Group	N	Findings
Silvers A, 1969	Normal DM HD	6 8 4	$t_{1/2}$ = 15.2 ± 1.4 min $t_{1/2}$ = 11.6 ± 0.3 min $t_{1/2}$ = 39.2 ± 6.2 min
Rabkin R, 1970	GFR 61±11 GFR 36 ± 7	6 7	Renal insulin extraction ↓ from 106 ± 21 to 60 ± 12 ml/min
Fuss M, 1974	Normal CRI	7 5	Cl_B = 611 ± 48 ml/min Cl_B = 326 ± 34 ml/min
Biesenback G, 2003	DM Type-1 DM Type-2	20 20	38% to 51% ↓ in insulin req when CrCl ↓ from 80 to 10 ml/min

Role of the Kidney in Glucose Regulation





Meyer C et al. Diabetes. 1999;48:943-948.

Stumvoll M et al. J Clin Invest. 1995;96:2528-33.

Conventional RHI algorithm		"Old" Modified RHI algorithm	
BG	Intervention	BG	Intervention
≤ 70*	Stop RHI, give ½ amp D50W	≤ 70*	Stop RHI, give ½ amp D50W
71 - 100	Decrease RHI by 50%	71 - 100	Decrease RHI by 50%
101 - 125	No Change	101 - 125	No Change
126 - 175	Increase RHI by 1 unit/hr	126 - 175	Increase RHI by 1 unit/hr
176 - 200	Increase RHI by 2 units/hr	176 - 225	Increase RHI by 2 units/hr
201 - 225	Increase RHI by 3 units/hr	226 - 275	Increase RHI by 3 units/hr
226 - 250	Increase RHI by 4 units/hr	276 - 325	Increase RHI by 4 units/hr
251 - 275	Increase RHI by 5 units/hr	> 325	Increase RHI by 4 units/hr and call MD
276 - 300	Increase RHI by 6 units/hr	DO NOT USE THIS ALGORITHM!	
> 300	Increase RHI by 6 units/hr and call MD		

Applied nutritional investigation

Increased hypoglycemia associated with renal failure during continuous intravenous insulin infusion and specialized nutritional support

Roland N. Dickerson Pharm.D[a,*], Leslie A.
George O. Maish III M.D[b], Martin A. Croce

Variable	Without RF ($n = 40$)	With RF ($n = 21$)	P
Men/women	33/7	19/2	NS
Race			
Caucasian	29	9	0.04
African-American	10	12	
Hispanic	1	0	
Diagnosis			
MVA	27	7	NS
Fall	6	5	
GSW	3	5	
Other	4	4	
History of DM	16 (40%)	11 (52%)	NS
Age (y)	57 ± 16	60 ± 16	NS
Weight (kg)	99 ± 33	100 ± 30	NS
BMI (kg/m^2)	32 ± 10	33 ± 9	NS
Albumin			NS
g/dL	1.9 ± 0.5	2.1 ± 0.8	
g/L	19 ± 5	21 ± 8	
Prealbumin			NS
mg/dL	9.7 ± 4.4	9.8 ± 4.0	
mg/L	97 ± 44	98 ± 40	
WBC count (cells/mm^3)	12.9 ± 6.7	13.9 ± 4.6	NS
Serum creatinine			0.001
mg/dL	1.2 ± 0.5	3.2 ± 1.8	
µmol/L	106 ± 44	283 ± 159	
Predicted CrCl (mL/min)	73 ± 34	36 ± 20	0.001
PN/EN	16/24	5/16	NS
PN/EN duration (d)	39 ± 53	31 ± 22	NS
Sepsis	14 (35%)	12 (57%)	NS
ISS	33 ± 10	31 ± 13	NS
ICU length of stay (d)	36 ± 37	27 ± 14	NS
Hospital length of stay (d)	45 ± 38	38 ± 26	NS
Survival (lived/died)	22/18	17/4	NS

Dickerson RN et al. Nutrition.2011; In press.

Variable	Without RF ($n = 40$)	With RF ($n = 21$)	P
Hospital day infusion initiated (d)	7.6 ± 7.8	8.5 ± 7.0	NS
After initiation of PN/EN (d)	4.4 ± 5.5	5.0 ± 7.2	NS
Duration of insulin infusion (d)	11.9 ± 12.1	9.2 ± 4.9	NS
Average amount of insulin received (U/d)	93 ± 43	105 ± 40	NS
Average carbohydrate intake (g/d)	163 ± 81	161 ± 97	NS
Hours to achieve BG 70–149 mg/dL (3.9–8.3 mmol/L)	5.0 ± 3.0	6.1 ± 3.3	NS
BG during insulin infusion (mg/dL)	122 ± 15	133 ± 14	0.01
BG 70–149 mg/dL (3.9–8.3 mmol/L) (h/d)	19.6 ± 4.7	16.1 ± 3.3	0.001
BG >149 mg/dL (>8.3 mmol/L) (h/d)	3.4 ± 3.0	6.9 ± 3.2	0.001
BG <70 mg/dL (<3.9 mmol/L) (h/d)	0.7 ± 0.8	1.4 ± 1.1	0.01
BG <60 mg/dL (<3.3 mmol/L)	14 (35%)	16 (76%)	0.005
BG <40 mg/dL (<2.2 mmol/L)	0 (0%)	6 (29%)	0.001

Dickerson RN et al. Nutrition.2011; In press.

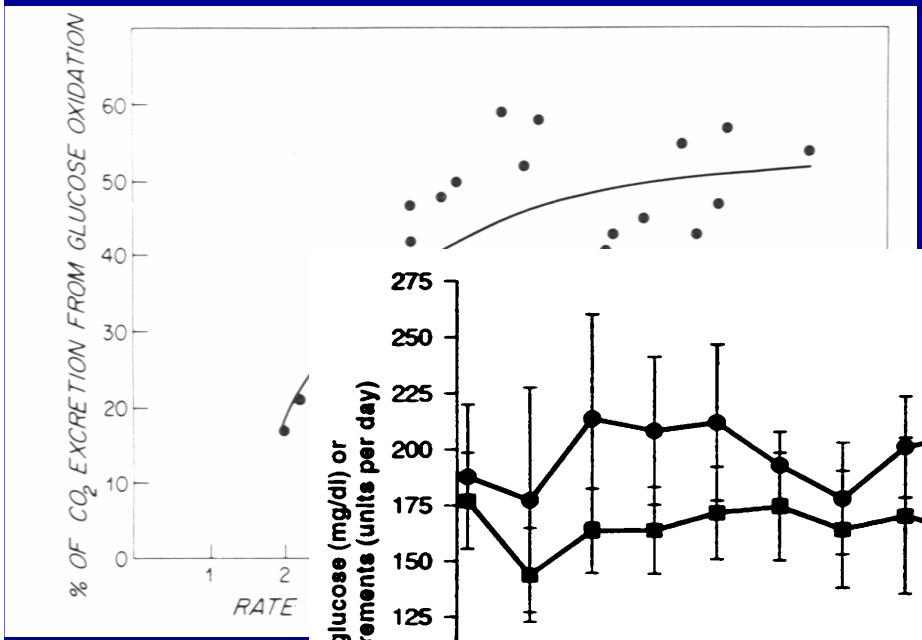
"Old" Modified RHI algorithm		"New" Modified RHI algorithm	
BG	Intervention	BG	Intervention
≤ 70*	Stop RHI, give ½ amp D50W, restart RHI at ½ last rate when BG > 100. Call MD.	≤ 40	Stop RHI, give 1 amp D50W, check BG every 30 min until BG > 70. Call MD.
71 - 100	Decrease RHI by 50%	≤ 70	Stop RHI, give ½ amp D50W, restart RHI at ½ last rate when BG > 100
101 - 125	No Change	71 - 125	Decrease RHI by 50%
126 - 175	Increase RHI by 1 unit/hr	126 - 150	No Change
176 - 225	Increase RHI by 2 units/hr	151 - 200	Increase RHI by 1 unit/hr
226- 275	Increase RHI by 3 units/hr	201 - 250	Increase RHI by 2 units/hr
275- 325	Increase RHI by 4 units/hr	251 - 300	Increase RHI by 3 units/hr
> 325	Increase RHI by 4 units/hr and call MD	> 300	Increase RHI by 4 units/hr and call MD

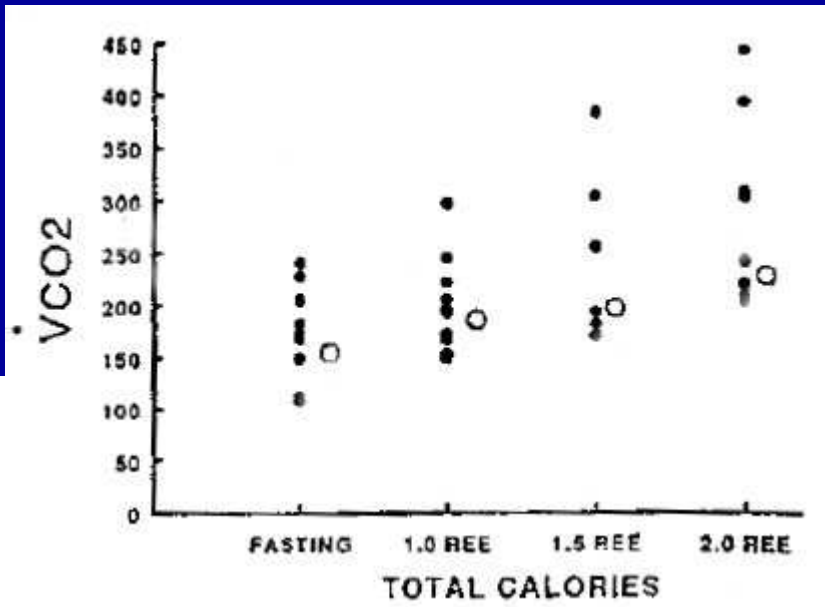
Practical Aspects of Glycemic Control in the ICU

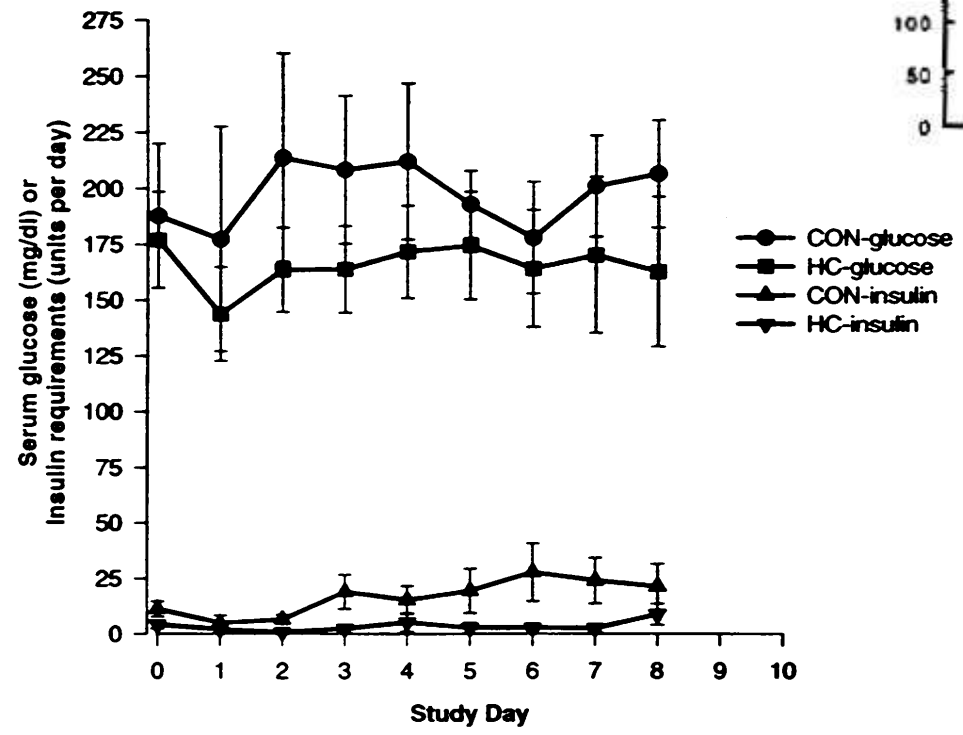
- Considerations in Developing an Appropriate Nutrition Regimen
- Insulin Therapy

Considerations in Developing an Appropriate Nutrient Regimen

- **Do not overfeed!**







Considerations in Developing an Appropriate Nutrient Regimen

- **Do not overfeed!**
- **Stop other exogenous sources of dextrose/glucose /carbohydrates!**

D5W

D5 LR

D5 NS

2NS

Considerations in Developing an Appropriate Nutrient Regimen

- **Do not overfeed!**
- **Stop other exogenous sources of dextrose/glucose /carbohydrates!**
- **Use a reduced CHO/higher fat based regimen**

Disease-Specific EN in Hyperglycemic Critically ill Patients

Mesejo A et al. Clin Nutr.2003;22:295-305.

Outcome	DM EN (n=26)	STD EN (n=24)	P <
Mean BG	163 ± 46	216 ± 57	0.001
RHI rec'd- IU/d	9 (2 – 28)	30 (22 – 57)	0.001
CHOrec'd- g/d	160 ± 22	201 ± 25	0.001
RHI/g CHO	.07 (.02-.22)	.18 (.22-.35)	0.02
Kcals rec'd /d	1599 ± 226	1664 ± 203	NS
EN duration- d	11 ± 7	11 ± 7	NS

Insulin Therapy

- Sliding scale insulin coverage
- Continuous intravenous RHI infusion
- Continuous intravenous RHI infusion for patients with AKI
- Use of intermediate or long acting insulin for enterally fed patients

SSI coverage (NSS – UT/The MED)

1) Discontinue previous insulin order

2) Check accuchecks every _____ hours

3) Give regular human insulin

4) Choose the scale:

SLIDING SCALES	BLOOD GLUCOSE (mg/dL)									
	0-60	61-125	126-150	151-175	176-200	201-225	226-250	251-275	276-300	>300
☐ ☐ IV ☐ SUBQ	One half ampule D50W or 8 ounces of orange juice, call MD	0 units	2 units	4 units	6 units	8 units	10 units	12 units	14 units	16 units, draw BMP, call MD
☐ ☐ IV ☐ SUBQ	One half ampule D50W or 8 ounces of orange juice, call MD	0 units	3 units	6 units	9 units	12 units	15 units	18 units	21 units	24 units, draw stat BMP, call MD

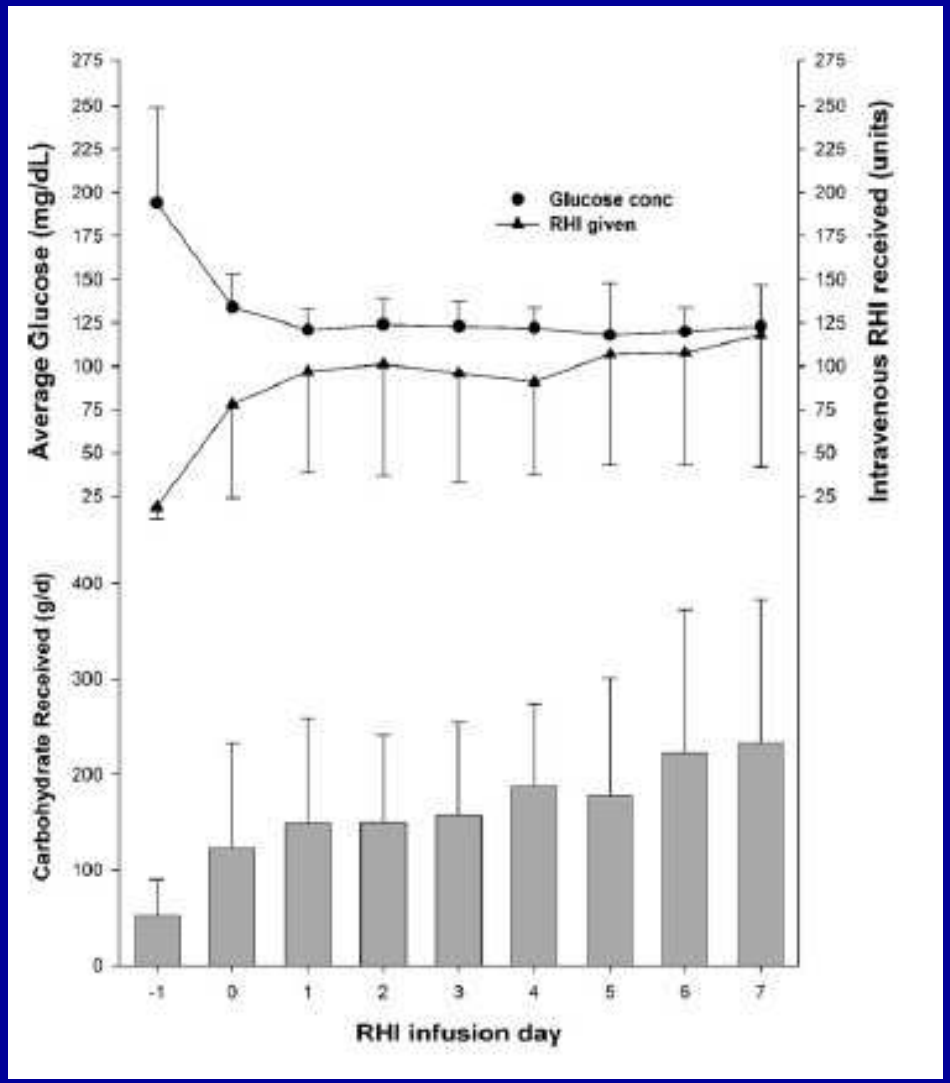
Indications for a Continuous Intravenous RHI Infusion

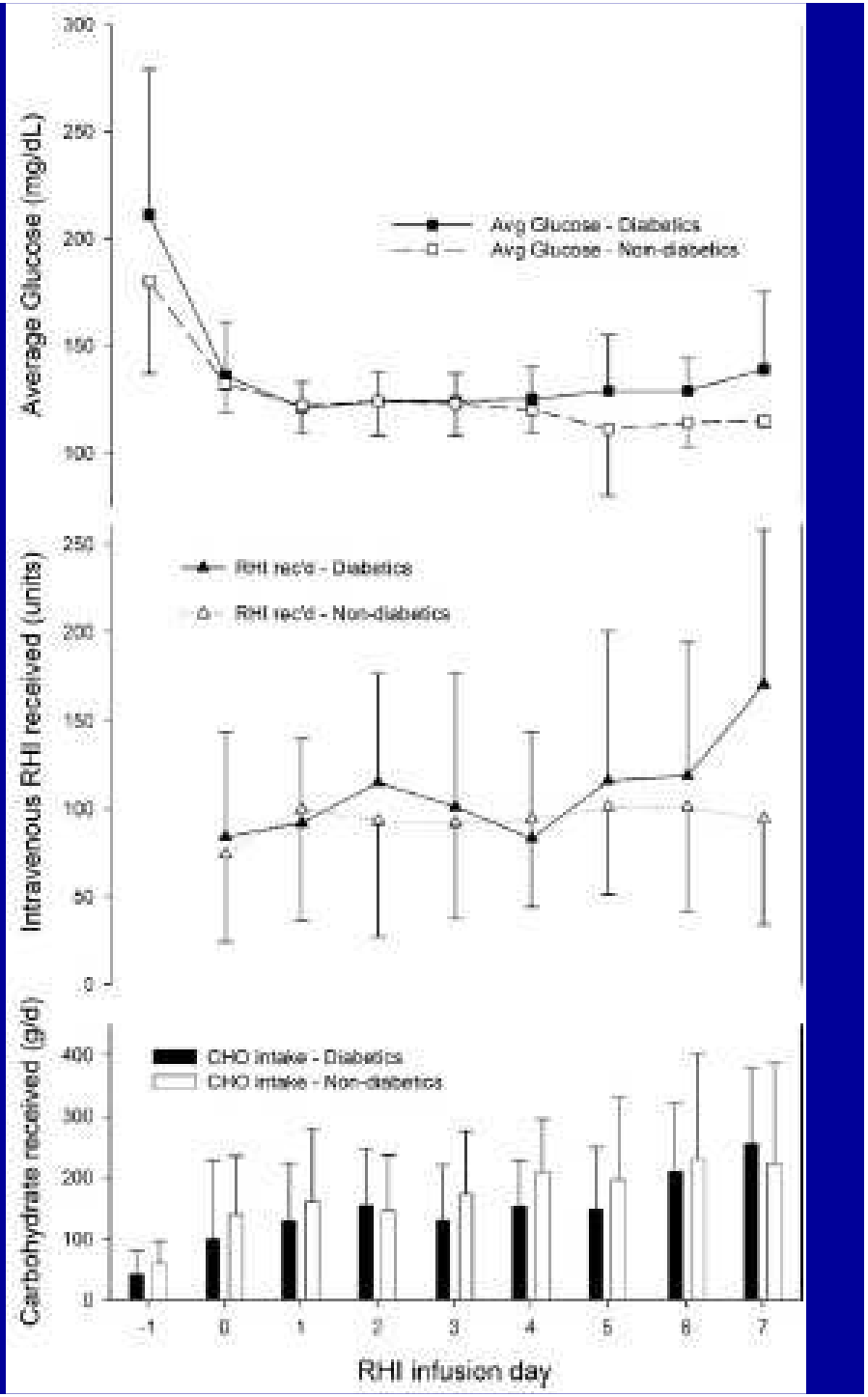
- Blood glucose ≥ 180 mg/dL before the initiation of specialized nutrition support
- Blood glucose > 150 mg/dL before the initiation of specialized nutrition support and a history of diabetes mellitus
- Persistent hyperglycemia (blood glucose > 150 mg/dL; especially in high risk populations) during specialized nutrition support despite efforts to control the hyperglycemia.

Dickerson RN et al. Nutrition.2008;24:536-545.

RHI infusion (NSS-UT/The MED)

1.	100 units regular human insulin in 100 mL NS	
2.	Begin infusion at _____ units/hr.	
3.	Check accuchecks every _____ hour(s).	
4.	If enteral feeding or parenteral nutrition is turned off for any reason, continue regular insulin infusion and infuse ☐ D5W or ☐ D5NS intravenously at the same rate as the nutrition formulation.	
5.	Use scale as follows:	
	Less than 60	stop insulin infusion, give ½ amp D50W, and restart insulin infusion when blood glucose >100 mg/dL at ½ the last rate
	61-100	decrease drip by 50% (round to the nearest whole unit/mL)
	101-125	no change
	126-175	increase infusion by 1 unit/hr
	176-200	increase infusion by 2 units/hr
	201-225	increase infusion by 3 units/hr
	226-250	increase infusion by 4 units/hr
	251-275	increase infusion by 5 units/hr
	276-300	increase infusion by 6 units/hr
	>300	increase infusion by 6 units/hr and call MD





Dickerson RN et al. Nutrition.2008;24:536-545.

Transitioning to an Intermediate or Long-Acting Insulin from a RHI infusion

NPH

- Intermediate acting insulin
- Onset: 1 - 2 hours
- Peak: 4 - 8 hours
- Duration: 10 to 24 hours (may be shorter for critically ill patients)

Insulin Glargine

- Long acting insulin
- Onset: 1 hour
- Peak: ?
- Duration: 24 hours (may be shorter for critically ill patients)

Transitioning to an Intermediate or Long-Acting Insulin from a RHI infusion

- The patient must be stable on a constant RHI infusion dose and ideally < 3 – 4 units/hr
- Only for patients receiving enteral nutrition
- Use with extreme caution in patients with renal failure, and patients ≥ 60 years of age
- Start with ~ ½ to ⅔ of the amount given as sliding scale coverage or RHI infusion the day before
- If enteral feeding off, hold NPH and hang D5W at same rate as enteral eeding

Hypoglycemia from NPH Insulin During Continuous EN is More Prevalent for Critically Ill Older Patients

Variable	Total Population	Age > 60 yrs	Age ≤ 60 yrs	P <
N	66	34	32	-
Male/Female	49/17	24/10	30/2	NS
Lived/Died	61/5	31/3	30/2	NS
Age (yrs)	58 ± 15	71 ± 8	45 ± 8	0.001
Weight (kg)	92 ± 23	90 ± 23	95 ± 23	NS
Diabetes (n)	37 (56%)	20 (54%)	14 (48%)	NS
Creatinine (mg/dL)	0.9 ± 0.3	0.9 ± 0.3	0.9 ± 0.3	NS
Albumin (g/dL)	2.1 ± 0.6	1.9 ± 0.5	2.2 ± 0.6	NS
Hospital LOS (d)	40 ± 27	38 + 25	42 ± 28	NS

Quallich V et al. Submitted for consideration of presentation and publication.

Hypoglycemia from NPH Insulin During Continuous EN is More Prevalent for Critically Ill Older Patients

Variable	Total Population	Age > 60 y	Age ≤ 60 y	P <
N	66	34	32	-
NPH dose (units/d)	33 ± 17	32 ± 15	35 ± 18	NS
Supplemental RHI (units/d)	32 ± 23	29 ± 17	35 ± 29	NS
CHO intake (g/d)	146 ± 51	142 ± 48	150 ± 55	NS
BG 60 –150 mg/dL (hr/d)	18 ± 4	17 ± 4	18 ± 4	NS
BG >150 mg/dL (hr/d)	6 ± 4	5 ± 4	6 ± 5	NS
BG < 60 mg/dL (hr/d)	0 ± 1	1 ± 1	0 ± 1	0.001
BG < 60 mg/dL (n)	31 (47%)	21 (68%)	10 (31%)	0.03
BG < 40 mg/dL (n)	6 (9%)	5 (16%)	1 (3%)	NS

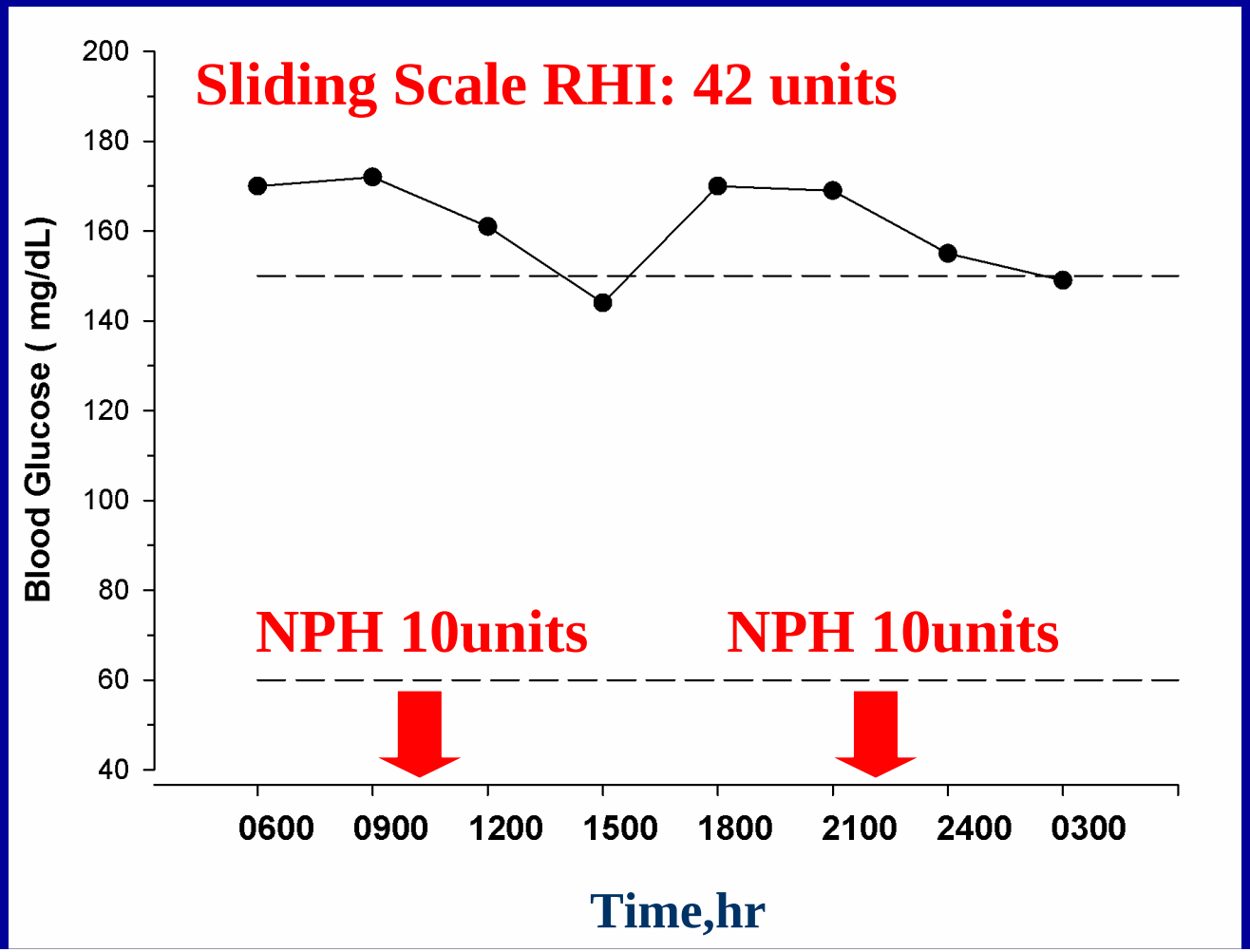
Quallich V et al. Submitted for consideration of presentation and publication.

Intermediate-Acting Insulin for Patients Receiving Specialized Enteral Nutrition Support: A Case Study

- 44 year old 100 kg man admitted to the TICU following a MVA with multiple fractures and TBI
- History of diabetes mellitus
- Given continuous feeding with a diabetic formula
- Given sliding scale insulin RHI coverage: 3's Q4hr
- He was started on NPH SC every 12 hrs due to persistent hyperglycemia

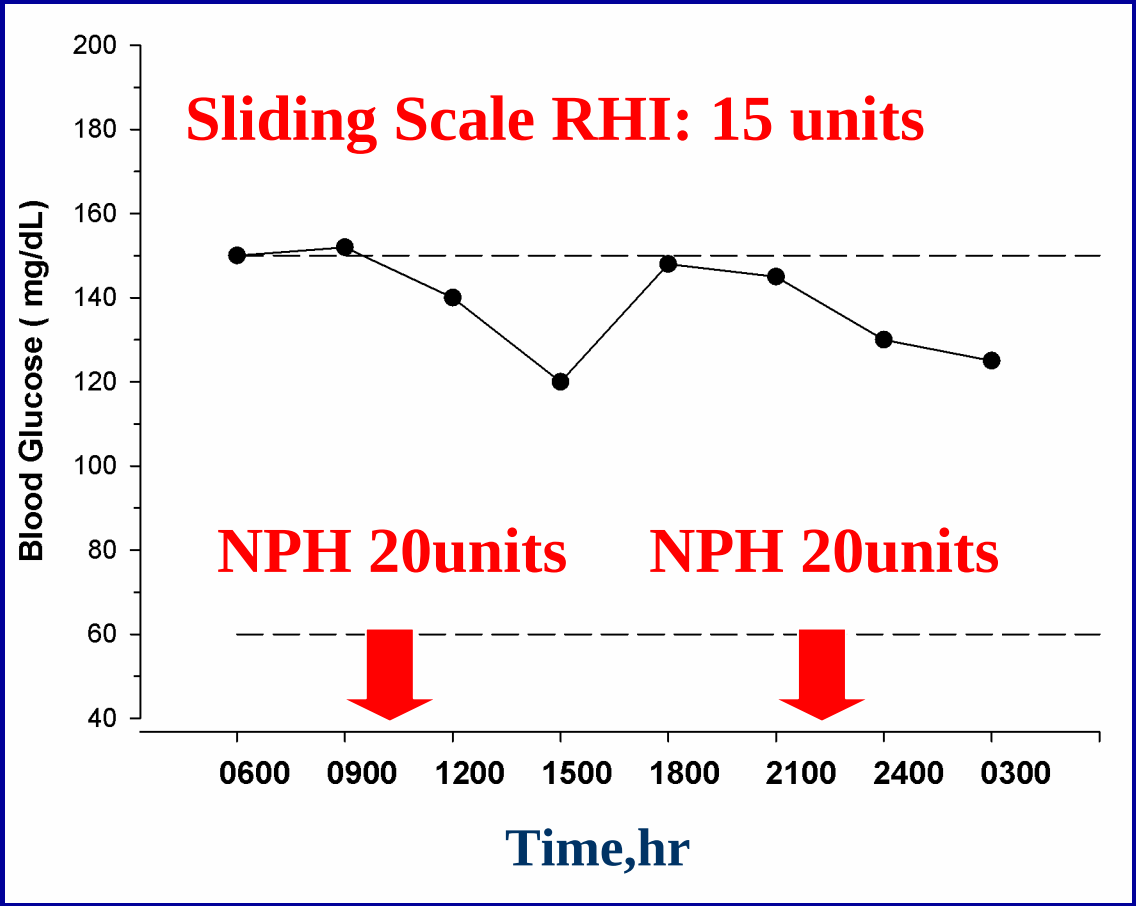
Intermediate-Acting Insulin for Patients Receiving Specialized Nutrition Support

Scenario 1: Increased BG for most accucheks



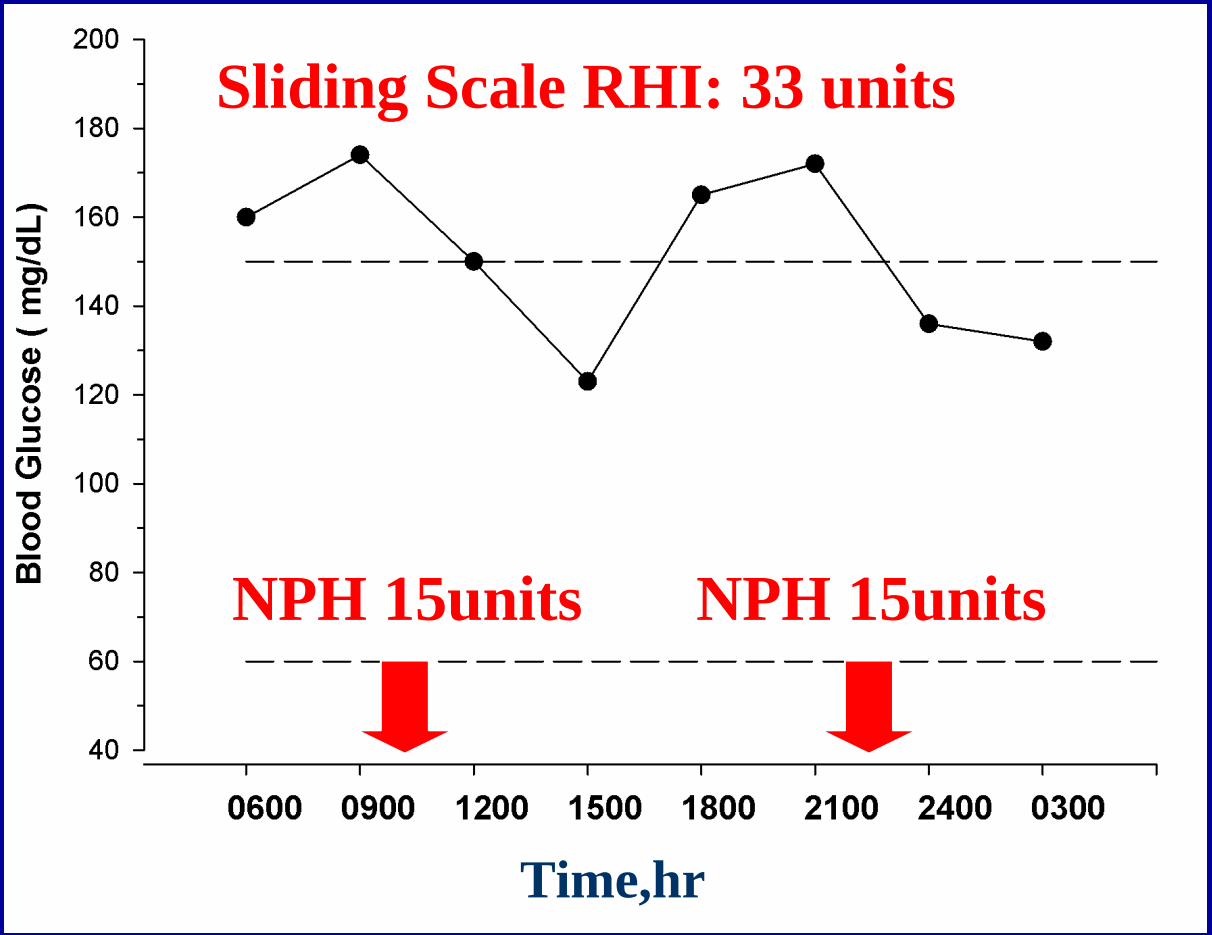
Intermediate-Acting Insulin for Patients Receiving Specialized Nutrition Support

Scenario 1: Increase the dose of NPH



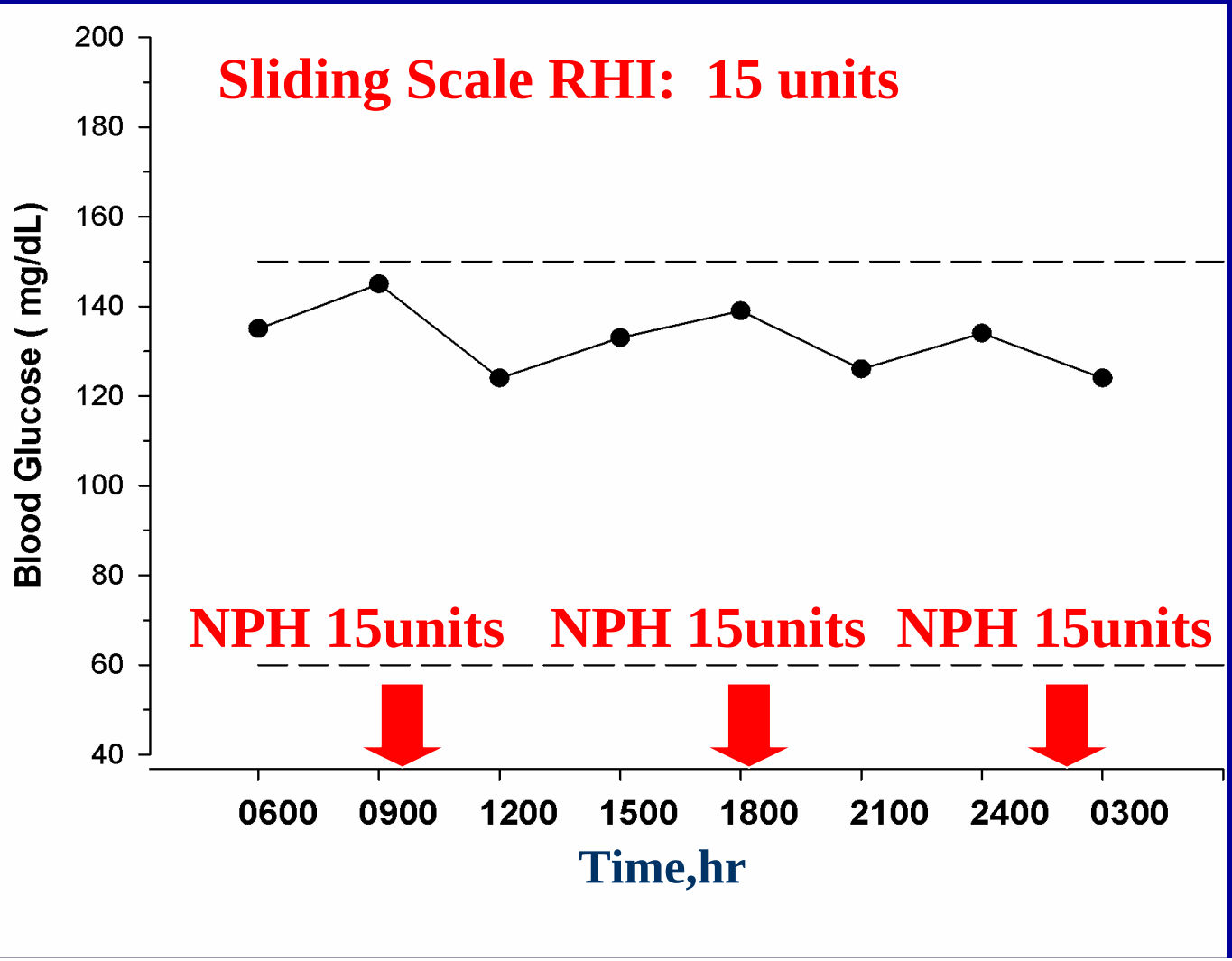
Intermediate-Acting Insulin for Patients Receiving Specialized Nutrition Support

Scenario 2: Increased BG near next dose of NPH



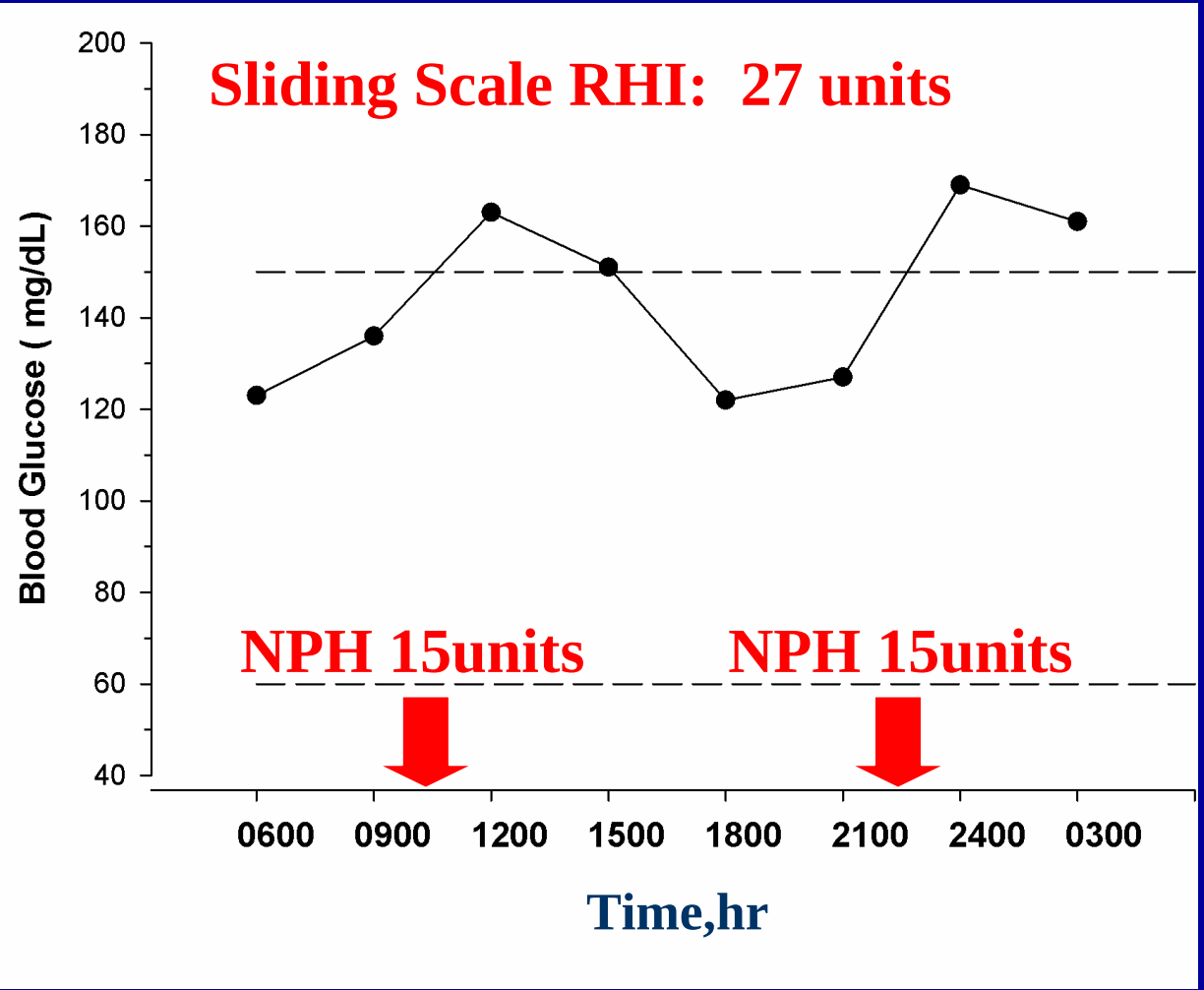
Intermediate-Acting Insulin for Patients Receiving Specialized Nutrition Support

Scenario 2: Decrease the interval of NPH



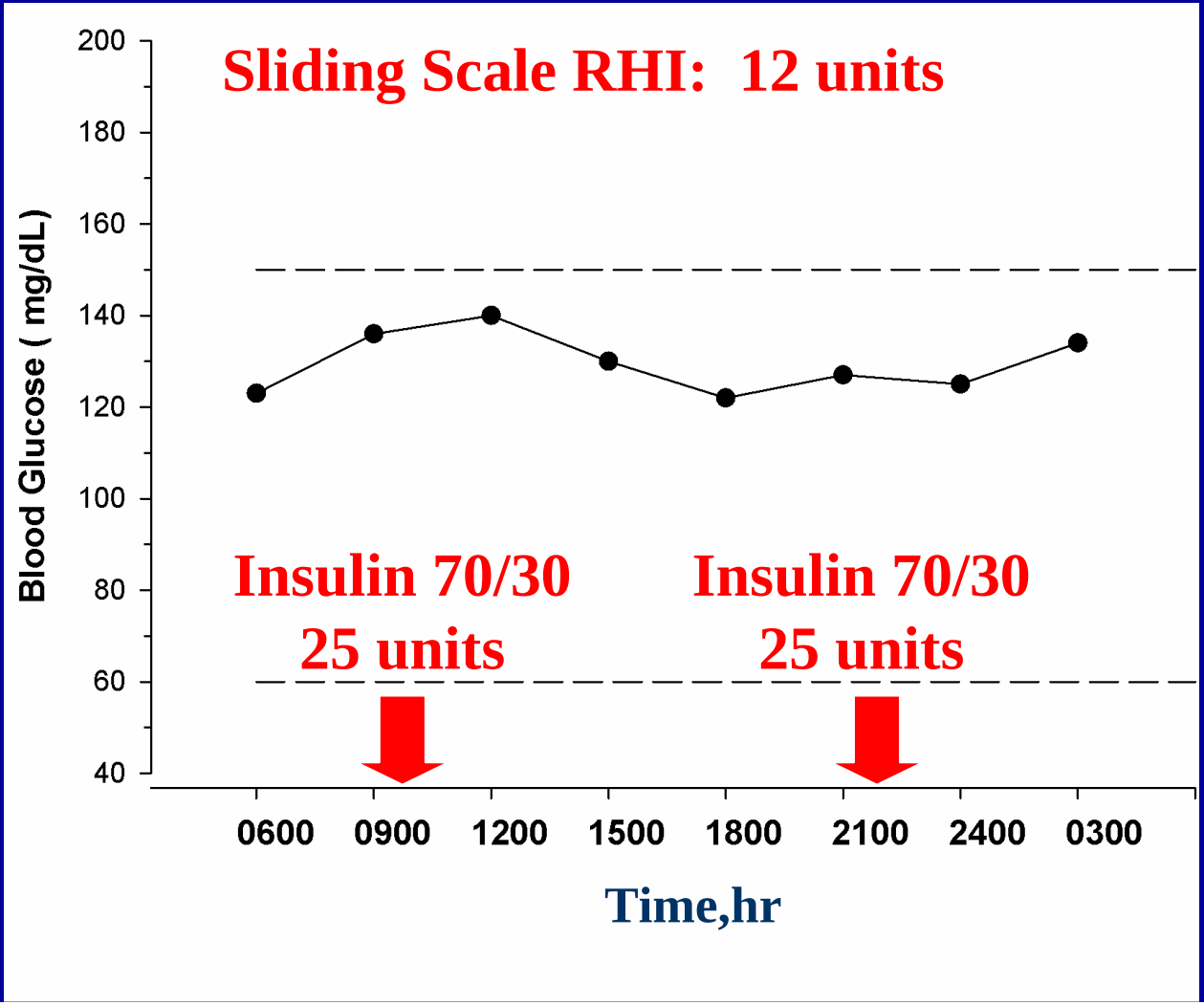
Intermediate-Acting Insulin for Patients Receiving Specialized Nutrition Support

Scenario 3: Delayed Onset of NPH



Intermediate-Acting Insulin for Patients Receiving Specialized Nutrition Support

Scenario 3: Use Humulin 70/30 and increase dose



Questions?