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KONTROLA GLYKÉMIE

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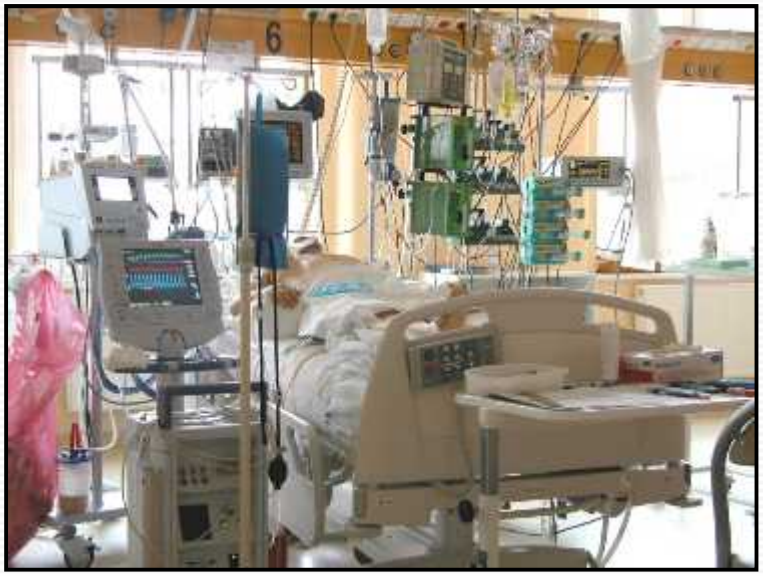

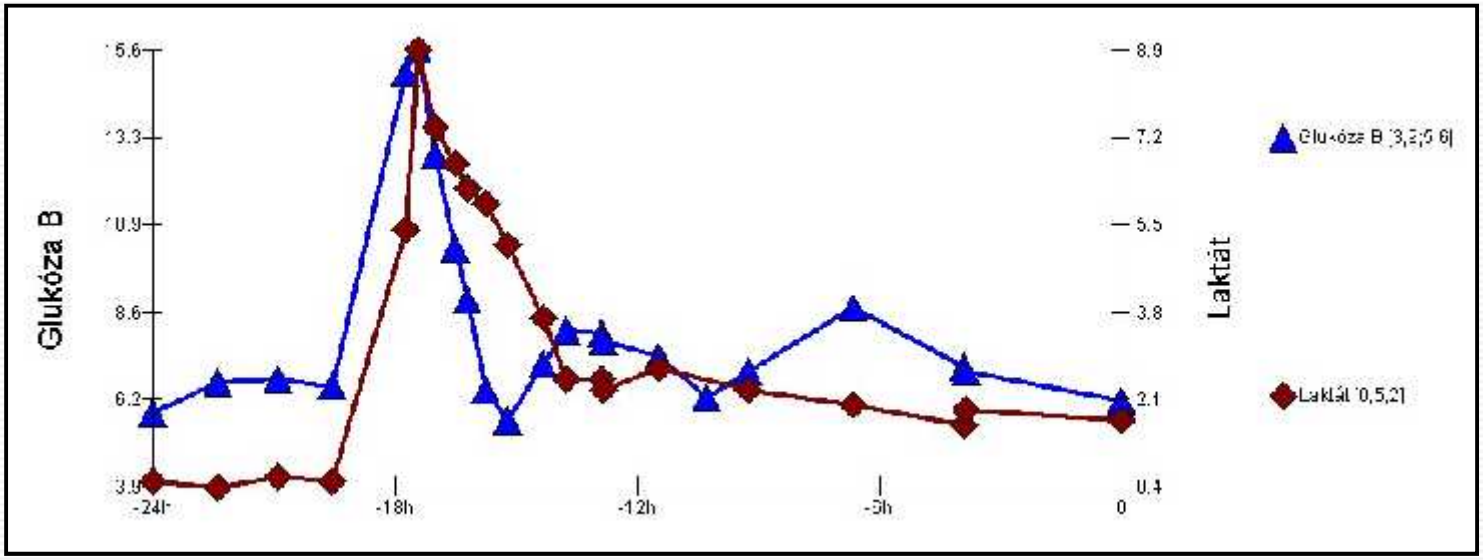
Glukóza B
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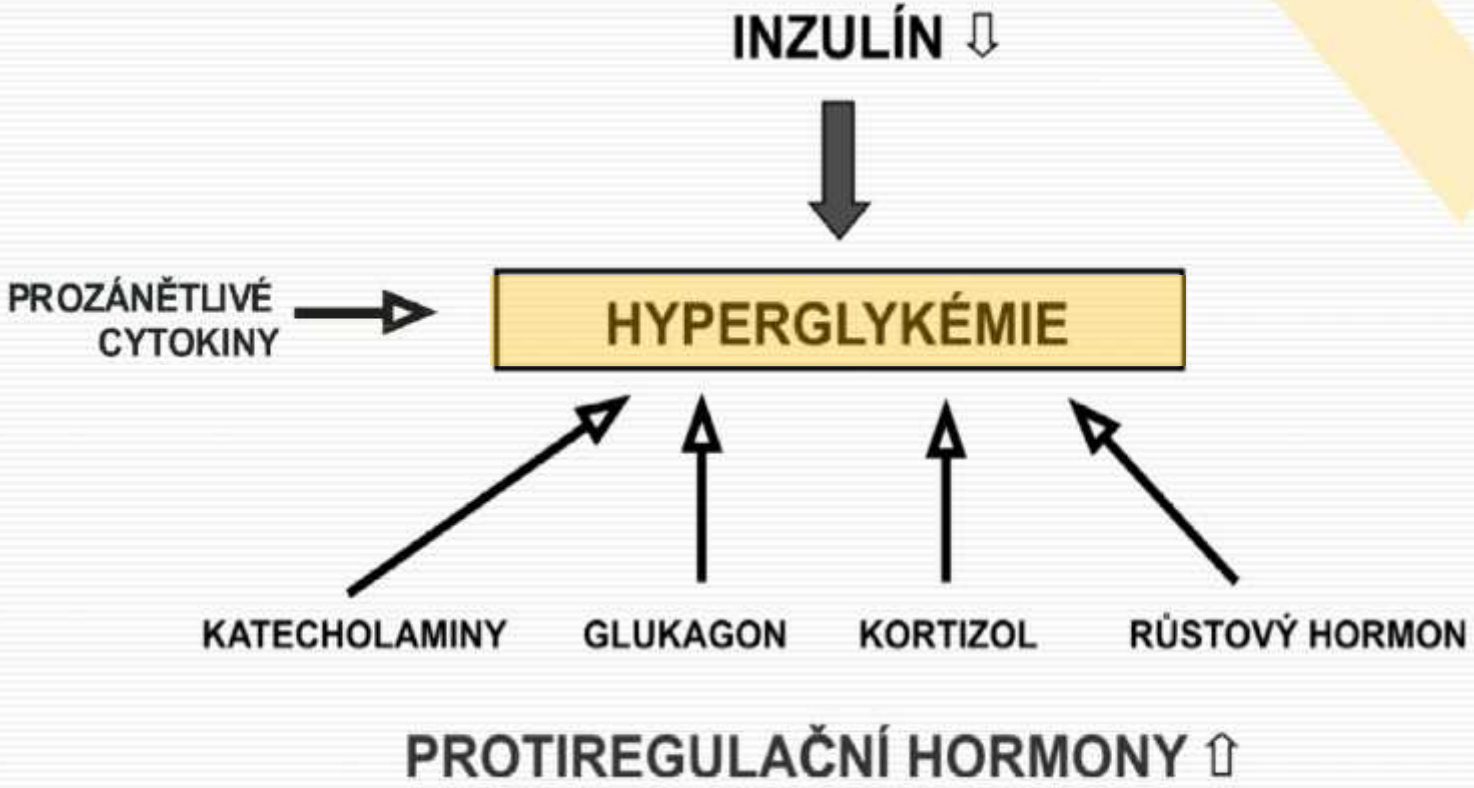
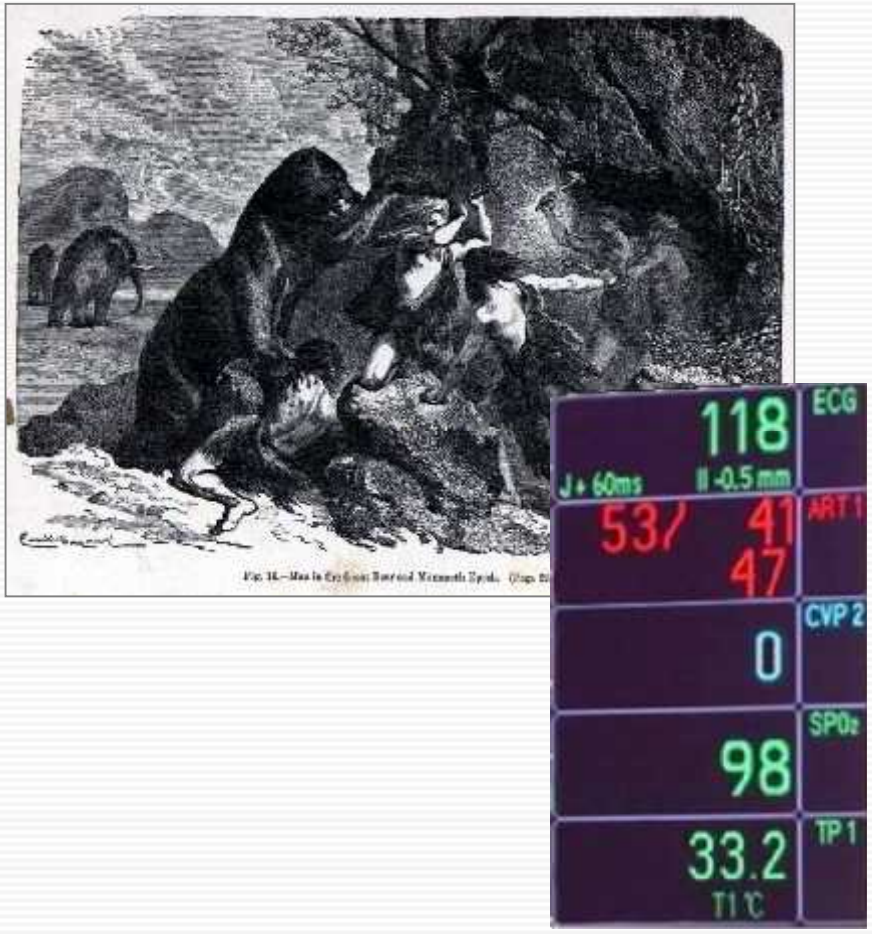
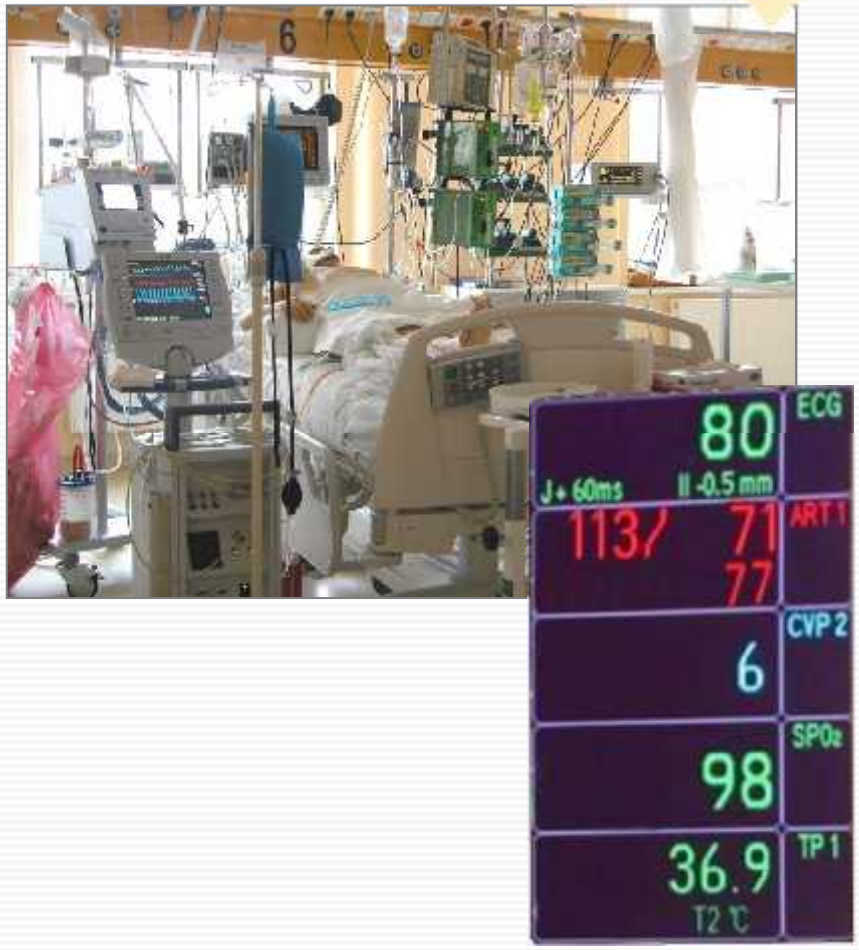
STRESOVÁ HYPERGLYKÉMIE




118
ECG
J+ 60ms
II -0.5 mm
53/ 41
47
ART 1
0
CVP 2
98
SPO2
33.2
T1 ℃
TP 1


80
ECG
J+ 60ms
II -0.5 mm
113/ 71
77
ART 1
6
CVP 2
98
SPO2
36.9
T2 ℃
TP 1

NEGATIVNÍ EFEKT HYPERGLYKÉMIE

- redukuje koronární kolaterální průtok a zvětšuje rozsah myokardiální nekrózy
- destabilizuje atheromové pláty, vede k akutnímu koronárnímu syndromu
- zhoršuje ischemicko-reperfúzní postižení
- zhoršuje ischemický preconditioning
  (Marfella, Diabetes Care 2000; Marfella, Diabetologia 2000; Kersten, Am J Physiol 1998; Kersten, Am J Physiol Heart Circ Physiol 2001; Verma, J Thorac Cardiovasc Surg 2002)
- zvyšuje riziko trombózy
  (Sakamotol, Thromb Haemost 2000; Knobler, Thromb Res 1998; Gresele, J Am Coll Cardiol 2003)
- způsobuje endoteliální dysfunkci a aktivuje rozvoj systémového zánětu
  (Beckman, Circulation 2001; Williams, Circulation 1998; Title, J Am Coll Cardiol 2000)
- snižuje cerebrální krevní průtok, zhoršuje ischemické poškození
  (Lin B, Acta Neuropathologica 1998; Gisselsson, J Cereb Blood Flow Metab 1999; Hoxworth, Brain Res 1999; Li, Stroke 2000; Capes, Stroke 2001)
- ovlivňuje rozsah renálního postižení u pacientů po kardiochirurgickém
  (Meldrum, J Surg Res 1999; Van den Berghel, N Engl J Med 2001)
- zvyšuje počet infekčních pooperačních komplikací
  (Butler, Pharmacotherapy 2005; Van den Berghe, N Engl J Med 2006; Van den Berghel, N Engl J Med 2001; Gale, Am Surg 2007)

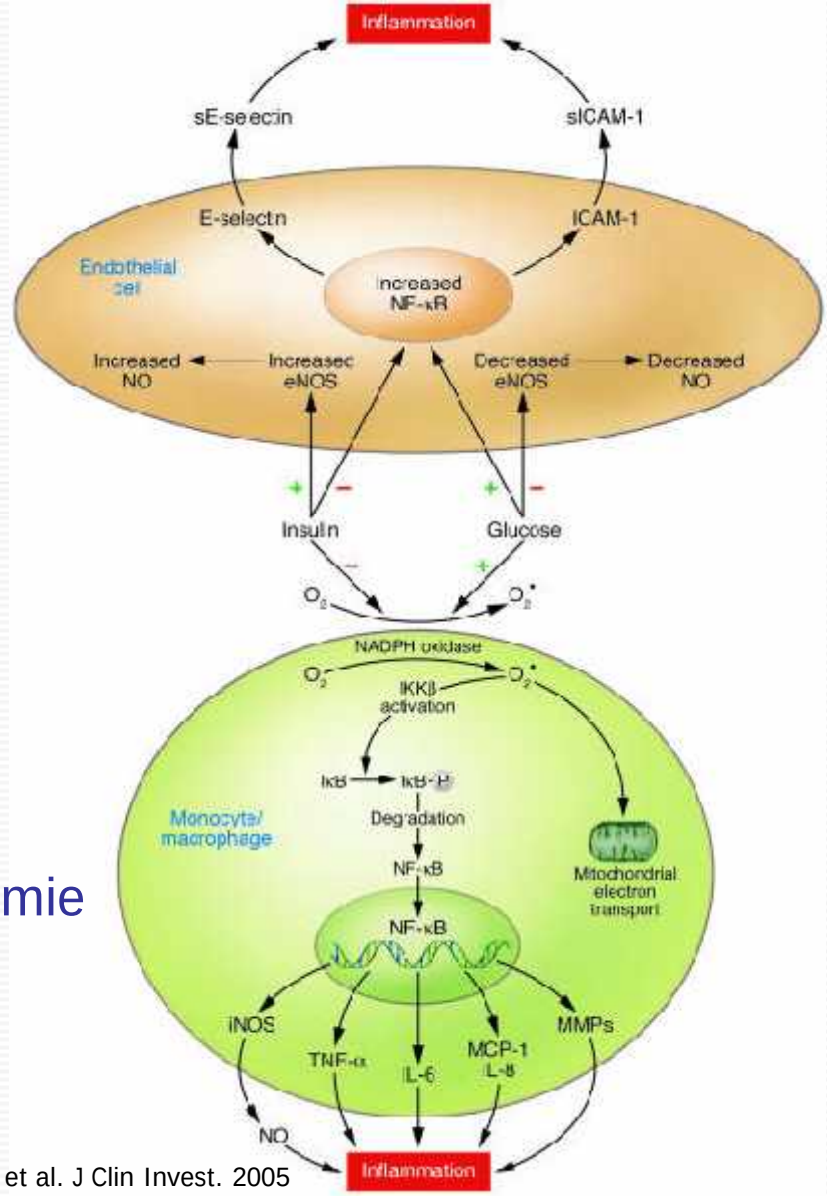
EFEKT HYPERGLYKÉMIE

- přímý toxický vliv glukózy
- cestou zvýšení intracelulárního oxidativního stresu při vyšší produkci mitochodriálních peroxidů

(Quijano, Am J Physiol Heart Circ Physiol 2007; Vanhorebeek, Lancet 2005; Beal, JAMA 1994; Corstjens, Crit Care 2006; Henderson, CJEM 2006; Turina, Crit Care Med 2006)

- Větší poškození než vlastní hypoglykémie způsobí reperfůze glukózou !

(Suh SW. J. Clin. Invest 2007. 117(4):910-918)

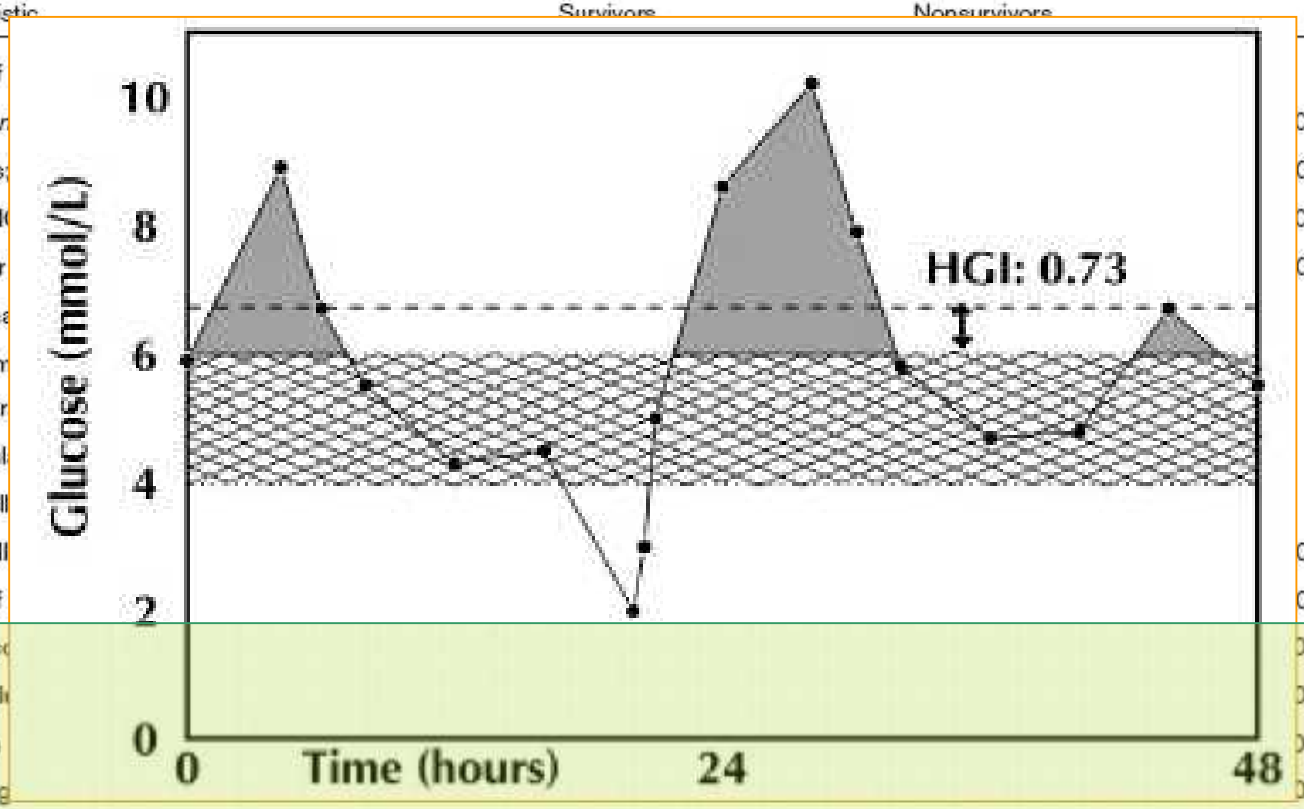


Dandona et al. J Clin Invest. 2005

EFEKT HYPERGLYKÉMIE

Characteristics for surviving and non-surviving patients and results of univariate analysis of glucose indices

Characteristic	Survivors	Nonsurvivors	*P*
Number of			
Male sex (*n*			0.18
Age (years;			0.001
Length of I			0.12
Reason for			0.001
Trauma			
Abdom			
Liver tr			
Vascul			
Miscell			
APACHE II			0.001
Number of			0.001
Mean gluc			0.001
Morning gl			0.001
Admission			0.07
Maximum g			0.001
HGI (mmol/l)	0.9 (0.3–2.1)	1.8 (0.7–3.4)	<0.001



Values are expressed as median (interquartile range) unless otherwise stated. APACHE, Acute Physiology and Chronic Health Evaluation; HGI, hyperglycaemic index; ICU, intensive care unit; SD, standard deviation.

The New England
Journal of Medicine

VOLUME 345 NOVEMBER 8, 2001 NUMBER 19

INTENSIVE INSULIN THERAPY IN CRITICALLY ILL PATIENTS

GREET VAN DEN BERGHE, M.D., PH.D., PIETER WOUTERS, M.SC., FRANK WEEKERS, M.D., CHARLES VERWAEST, M.D., FRANS BRUYNINCKX, M.D., MIET SCHETZ, M.D., PH.D., DIRK VLASSELAERS, M.D., PATRICK FERDINANDE, M.D., PH.D., PETER LAUWERS, M.D., AND ROGER BOUILLON, M.D., PH.D.

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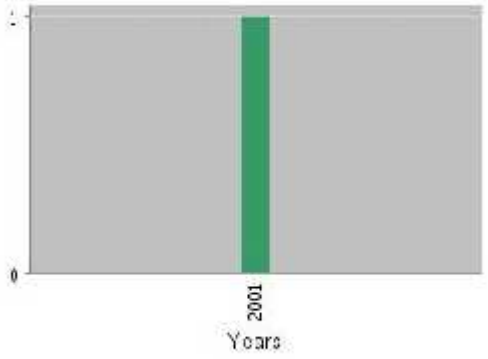

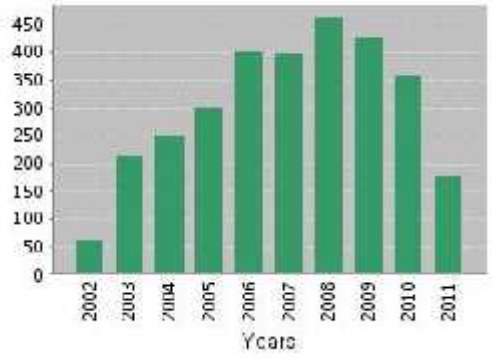

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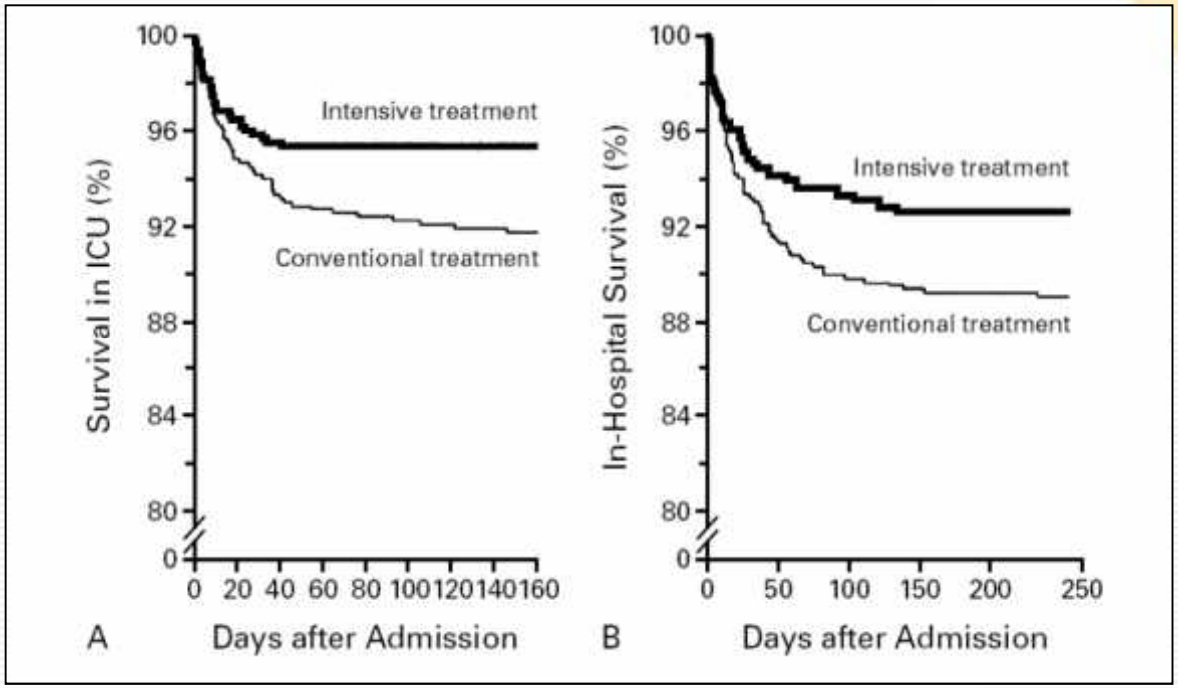
	400	463	427	380	178	3,064	306.40
☐ 1. Title: Intensive insulin therapy in critically ill patients Author(s): Van den Berghe G, Wouters P, Weekers F, et al Source: NEW ENGLAND JOURNAL OF MEDICINE Volume: 345 Issue: 19 Pages: 1359-1367 Published: NOV 8 2001	400	463	427	380	178	3,064	306.40



Van den Berghe et al. N Engl J Med 2001;345:1359-67

HYPERGLYKÉMIE U KRITICKY NEMOCNÝCH

- Van den Berghe et al. - (kardio)chirurgičtí pacienti
  N Engl J Med 2001;345:1359-67

- Finney et al. - chirurgičtí pacienti
  JAMA 2003;290:2041-47

- Furnary et al. - kardiochirurgičtí pacienti
  J Thorac Cardiovasc Surg 2003;125:1007-21

- Krinsley - chirurgičtí / interní pacienti
  Mayo Clin Proc 2004;79:992-1000

- Van den Berghe et al. - interní pacienti
  N Engl J Med 2006;354:449-61

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HYPERGLYKÉMIE U KRITICKY NEMOCNÝCH

- VISEP (2003)
- GLUCONTROL (2007)
- Gandhi (2007)
- Treggiari (2008)
- Arabi (2008)
- NICE-SUGAR (2009)

HYPERGLYKÉMIE U KRITICKY NEMOCNÝCH

	Intensive Insulin Therapy (n = 142)	Conventional Insulin Therapy (n = 123)	*p*
Cause of death			
Multi-organ failure, n (%)	13 (9.2)	14 (11.4)	0.60
Brain death, n (%)	1 (0.7)	4 (3.3)	0.19
Other causes, n (%)	3 (2.1)	6 (4.9)	0.31
Hospital mortality, n (%)	38 (26.8)	46 (37.4)	0.06
ICU LOS, mean ± SD, days	9.8 ± 9.0	9.7 ± 7.8	0.90
Hospital LOS, mean ± SD, days	48.7 ± 62.8	50.4 ± 65.6	0.83
ICU acquired sepsis			
All sepsis episodes, n (%)	53 (37.3)	45 (36.6)	0.90
Severe sepsis/septic shock, n (%)	25 (17.6)	29 (23.6)	0.23
Mechanical ventilation duration, mean ± SD, days	8.3 ± 8.3	9.2 ± 7.9	0.38
PRBC transfusion, mean ± SD, units	1.6 ± 4.4	1.8 ± 3.4	0.76
New renal replacement therapy, n (%)	14 (9.9)	15 (12.2)	0.54

ICU, intensive care unit; LOS, length of stay; PRBC, packed red blood cell.

Arabi et al. Crit Care Med 2008; 36:3190–3197)

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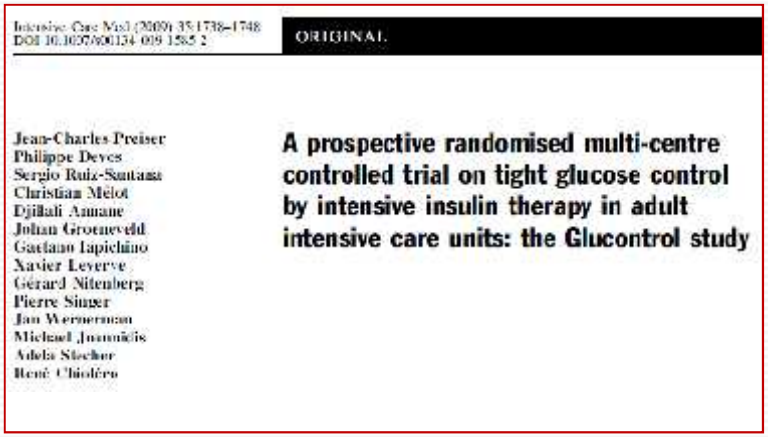

Intensive Care Med (2009) 35:1738–1748
DOI 10.1007/s00134-009-1585-2

ORIGINAL

Jean-Charles Preiser
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Gérard Nitenberg
Pierre Singer
Jan Wernerman
Michael Joannidis
Adela Stecher
René Chioléro

A prospective randomised multi-centre controlled trial on tight glucose control by intensive insulin therapy in adult intensive care units: the Glucontrol study

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Intensive Insulin Therapy and Pentastarch Resuscitation in Severe Sepsis

Frank M. Brunkhorst, M.D., Christoph Engel, M.D., Frank Bloos, M.D., Ph.D., Andreas Meier-Hellmann, M.D., Max Ragaller, M.D., Norbert Weiler, M.D., Onnen Moerer, M.D., Matthias Gruendling, M.D., Michael Oppert, M.D., Stefan Grond, M.D., Derk Olthoff, M.D., Ulrich Jaschinski, M.D., Stefan John, M.D., Rolf Rossaint, M.D., Tobias Welte, M.D., Martin Schaefer, M.D., Peter Kern, M.D., Evelyn Kuhnt, M.Sc., Michael Kiehntopf, M.D., Christiane Hartog, M.D., Charles Natanson, M.D., Markus Loeffler, M.D., Ph.D., and Konrad Reinhart, M.D., for the German Competence Network Sepsis (SepNet)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Intensive Insulin Therapy and Pentastarch Resuscitation in Severe Sepsis

Nutrition and Blood Glucose Control

Data regarding nutritional intake and blood glucose levels are shown in Figure 1 and in Table 4 of the Supplementary Appendix. In the intensive-therapy group, 243 of 247 patients (98.4%) received insulin on at least one study day for glucose values above the target range (>110 mg per deciliter), whereas only 215 of 290 patients (74.1%) in the conventional-therapy group needed insulin because glucose values were outside the target range (≥200 mg per deciliter) (P<0.001). During the study period, mean morning blood glucose levels were lower in the intensive-therapy group (m
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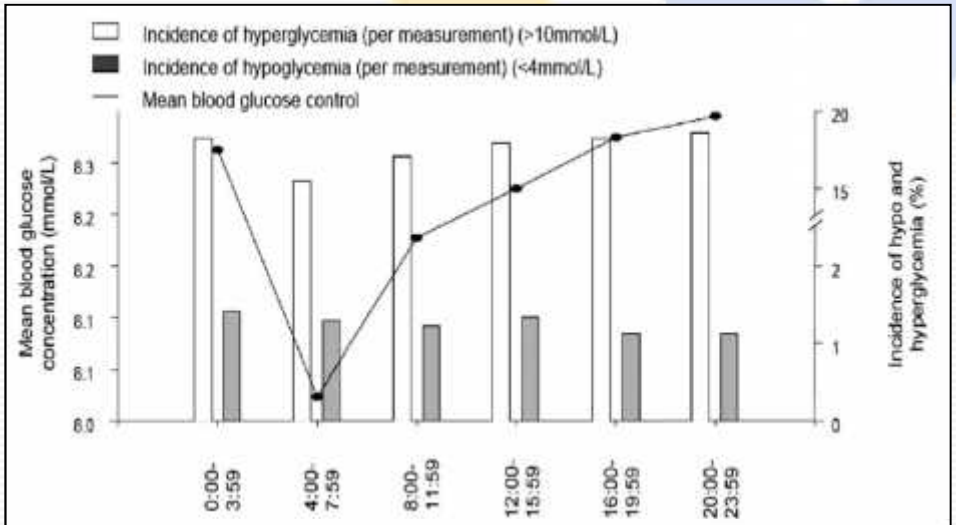

Figure 5. Circadian rhythm of blood glucose control and incidence of hypo- and hyperglycemia in the total cohort of all four hospitals. Mean blood glucose control and the incidence of hypo- and hyperglycemia show significant variation (*p* values: mean blood glucose control, $p < .0001$; hyperglycemia [>10 mmol/L], $p < .0001$; and hypoglycemia [<4 mmol/L], $p = .0034$).

Egi M et al. Crit Care Med 2007; 35:416-21

Table 2. (Continued.)

Variable	Insulin Therapy				Fluid Resuscitation		
	All Patients (N=537)	Conventional (N=290)	Intensive (N=247)	P Value†	Ringer's Lactate (N=275)	HES (N=262)	P Value‡
Hypoglycemia (≤40 mg/dl)				<0.001			0.85
No. of patients/total no.	54/537	12/290	42/247		27/275	27/262	
Percent (95% CI)	10.1 (7.5–12.6)	4.1 (1.9–6.4)	17.0 (12.3–21.7)		9.8 (6.3–13.3)	10.3 (6.6–14.0)	

Intensive Care Med (2009) 35:1738–1748
DOI 10.1007/s00134-009-1585-2

ORIGINAL

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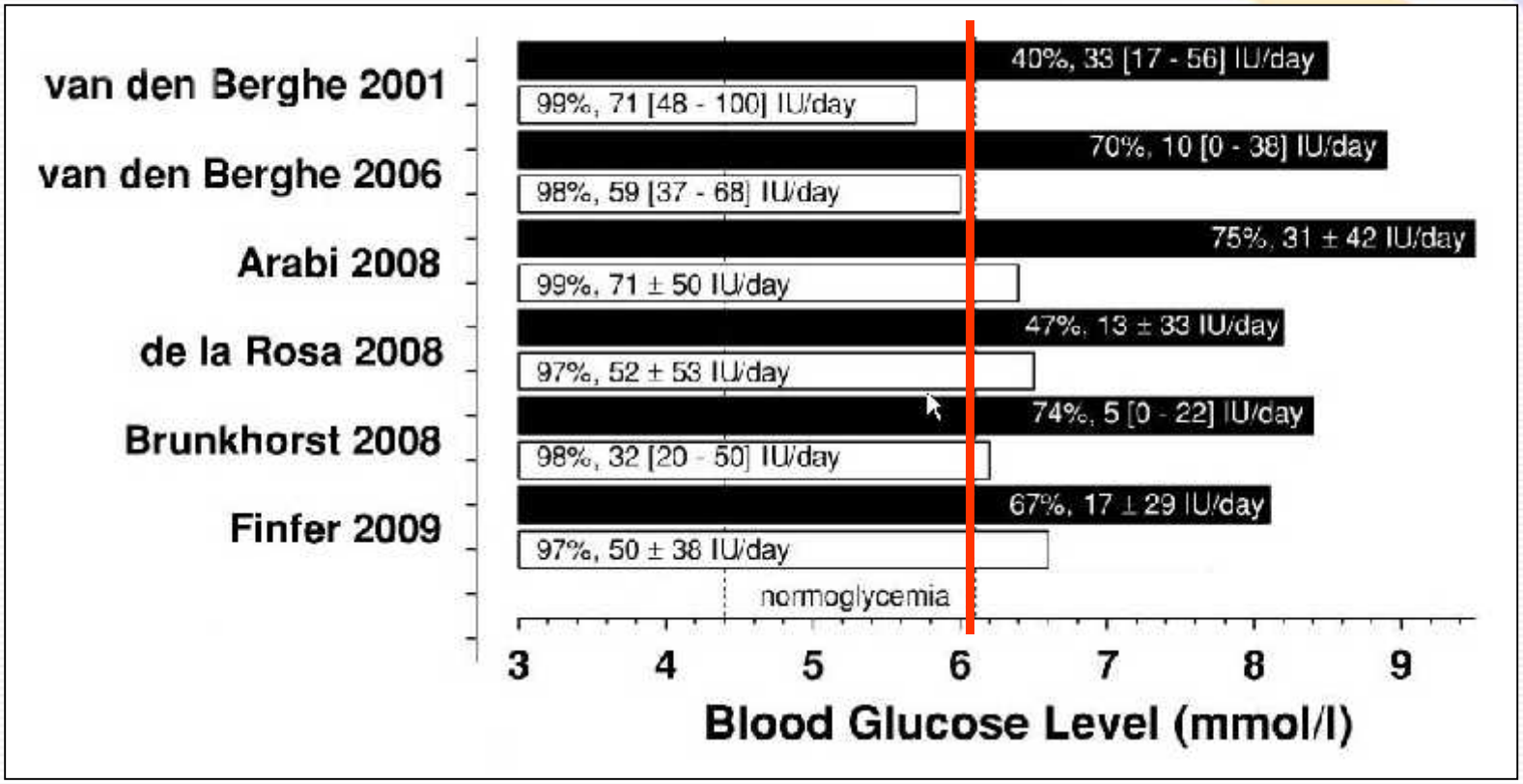
A prospective randomised multi-centre controlled trial on tight glucose control by intensive insulin therapy in adult intensive care units: the Glucontrol study

Table 3 Outcome data, treatment-related variables, nutritional management and therapeutic variables glucose control

	Group 1 BG target 7.8–10.0 mmol/L $N = 542$	Group 2 BG target 4.4–6.1 mmol/L $N = 536$	p Value
Glucose control and insulin therapy			
Blood glucose concentrations calculated from all readings (mmol/L) [median (IQR)]	8.0 (7.1–9.0)	6.5 (6.0–7.2)	<0.0001
Blood glucose concentrations calculated from morning readings (mmol/L) [median (IQR)]	7.7 (6.7–8.8)	6.1 (5.5–6.8)	<0.0001
Rate of hypoglycaemia calculated from BG % (n)	2.7 (13)	8.7 (44)	<0.0001
Estimated duration of hypoglycaemia (min) in patients presenting hypoglycaemic episode [median (IQR)]	59 (37–76)	52 (13–135)	0.887
Proportion of time in range			
(% of all BG readings)	34.7 (164)	42.8 (196)	0.0118
(% of morning BG)	39.5 (187)	45.1 (207)	0.0856
p value (difference between all readings and morning BG)	NS	NS	
Median of the proportion of time in range (%) (IQR)	34.3 (18.5–50.1)	39.3 (26.2–53.6)	
Proportion of time below the range			
(% of all BG readings)	50.3 (238)	5.9 (27)	<0.0001
(% of morning BG)	51.2 (242)	5.2 (24)	
p value (difference between all readings and morning BG)	NS	NS	<0.0001
Median of the proportion of time below range (%) (IQR)	44.7 (24.3–75.8)	5.1 (1.1–9.2)	
Proportion of time above the range			
(% of all BG readings)	14.9 (71)	51.3 (236)	<0.0001
(% of morning BG)	9.3 (44)	49.7 (228)	
p value (difference between all readings and morning BG)	0.0072	NS	<0.0001
Median of the proportion of time above range (%) (IQR)	7.6 (0.0–25.3)	52.6 (39.2–67.4)	
AUChigh (hour mmol L^{-1}) [median(IQR)]	4.1 (0–40.2)	79.3 (25.9–181.1)	<0.0001
AUClow (hour mmol L^{-1}) [median(IQR)]	42.3 (12.8–125.9)	2.1 (0.2–6.1)	<0.0001
Hyperglycaemic index (mmol L^{-1}) [median(IQR)]	0.06 (0.00–0.33)	0.78 (0.39–1.39)	<0.0001
Hypoglycaemic index (mmol L^{-1}) [median (IQR)]	0.44 (0.22–0.94)	0.33 (0.03–0.85)	<0.0001



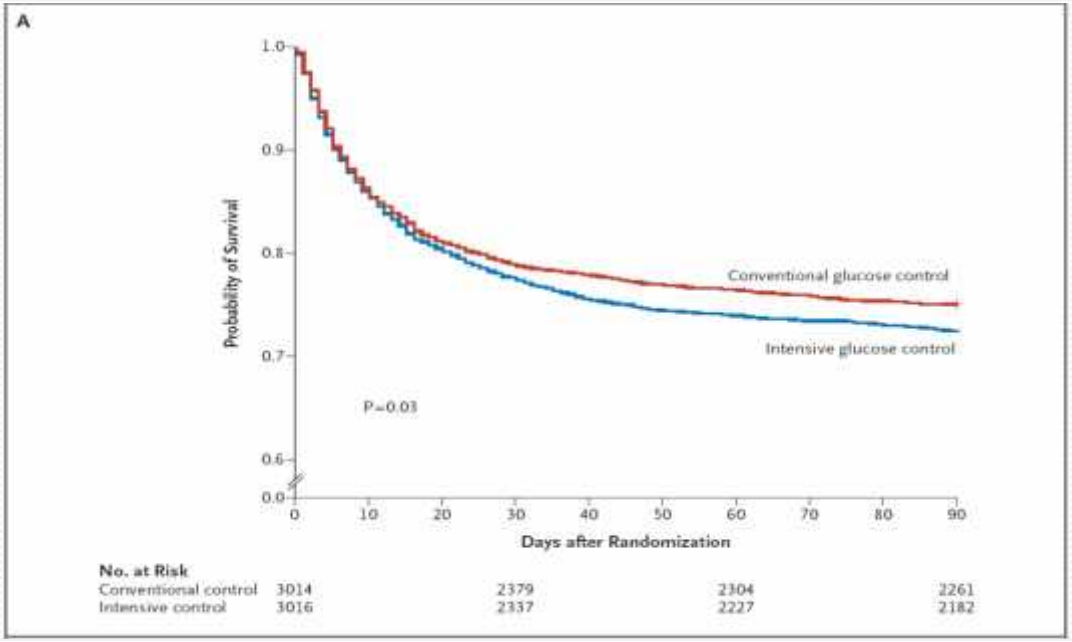
Schultz MJ et al. Intensive Care Med. 2010; 36(1): 173-4.

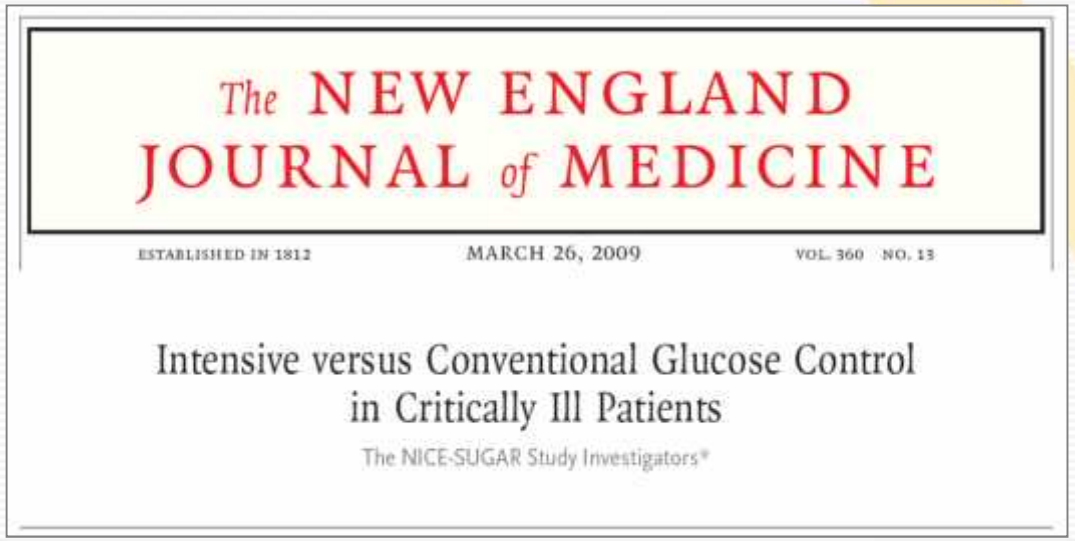
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 26, 2009 VOL. 360 NO. 13

Intensive versus Conventional Glucose Control in Critically Ill Patients

The NICE-SUGAR Study Investigators*





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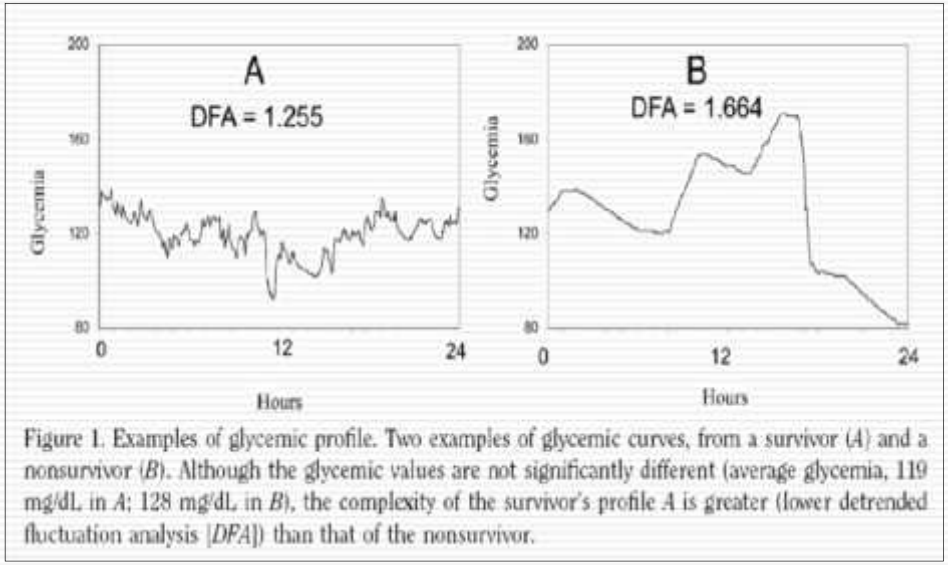
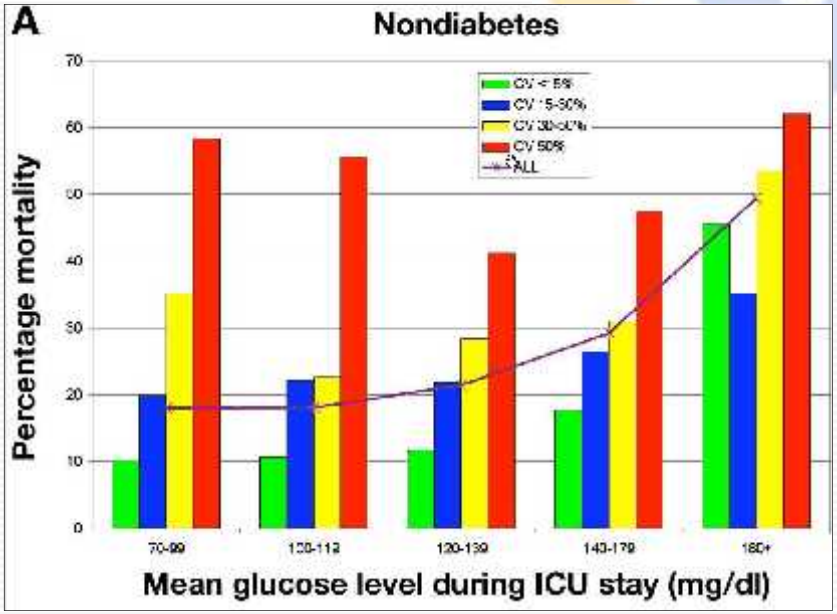


Figure 1. Examples of glycemic profile. Two examples of glycemic curves, from a survivor (*A*) and a nonsurvivor (*B*). Although the glycemic values are not significantly different (average glycemia, 119 mg/dL in *A*; 128 mg/dL in *B*), the complexity of the survivor's profile *A* is greater (lower detrended fluctuation analysis [*DFA*]) than that of the nonsurvivor.

Lundelin et al. Crit Care Med 2010; 38:849-54



Krinsley JS. J Diabetes Sci Technol. 2009 Nov 1;3(6):1292-301

Summary of crude clinical outcomes stratified by hypoglycemia and blood glucose variability

Clinical outcome	Total (n = 66,184)	Hypoglycemic episode only (n = 7209)	Blood glucose variability (n = 1913)	Neither (n = 57,969)	*P* value
ICU length of stay (days) [median (IQR)]	1.9 (1.0 to 4.4)	2.0 (1.0 to 4.6)	2.7 (1.3 to 5.5)	1.9 (1.0 to 4.3)	0.001
Hospital length of stay (days) [median (IQR)]	10.7 (5.9 to 21.0)	10.0 (4.4 to 21.5)	11.4 (4.9 to 24.1)	10.7 (6.0 to 20.9)	0.001
ICU mortality (%)	11.1	17.3	22.6	9.8	<0.001
Hospital mortality (%)	16.9	24.3	30.7	15.5	<0.001

ICU = intensive care unit; IQR = intra-quartile range.

Bagshaw SM et al. Crit Care. 2009;13(3):R91

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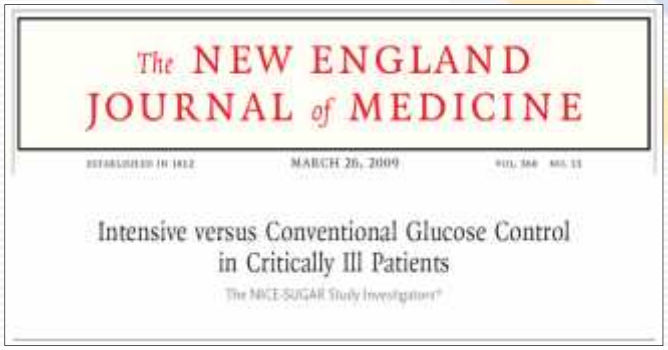
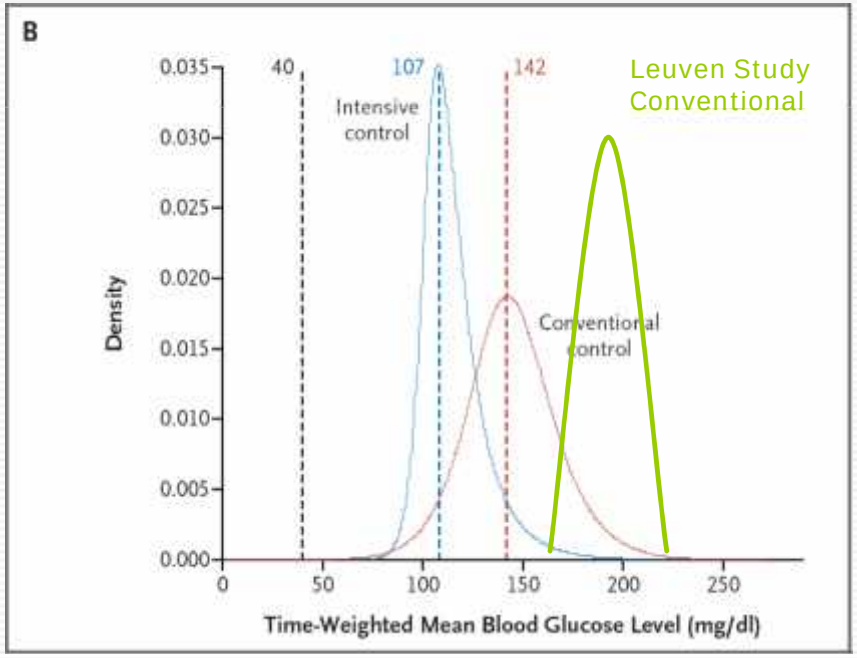


Table 1
Key differences between the Leuven studies[8,10] and NICE-SUGAR[16].

	Leuven adult studies	NICE-SUGAR
Number of patients	2748	6104
Setting	2 × 1 centre	42 centres
Patient sample (% of admissions)	60% (medical), 95% (surgical)	15%
Methodological aspects		
Comparator group target	10–12 mmol/L (180–215 mg/dL)	7.8–10 mmol/L (140–180 mg/dL)
Intervention target	<6.1 mmol/L (<110 mg/dL)	<6.0 mmol/L (<108 mg/dL)
Blood sampling site	Predominantly arterial line	Arterial/venous/capillary
Glucose measurement tool	ABL Radiometer bloodgas analyzer (surgical)	Not standardized
	HemoCue (medical)	All types glucometers allowed
Insulin infusion	Continuous only via central line	Continuous + bolus via all routes
	Syringe pump	All types of pumps allowed
Nurse instructions	Guideline + Intuitive decision making	A strict "if-then" algorithm
Feeding route first week	Parenteral + Enteral	Enteral only
Average kcal received during ICUstay	1100 kcal/day	880 kcal/day
Therapy compliance		
Blood glucose target reached	70%	<50%
Overlap in blood glucose between two groups	<10%	>50%
Outcome		
Hypoglycaemia	× 6	× 13
Morbidity	Reduced organ failure and infections	Neutral
Mortality	Lowered by absolute 3%	Increased by absolute 3%
Therapy withdrawal policy	Late	Early



D. Mesotten, G. Van den Berghe / Best Practice & Research Clinical Anaesthesiology 23 (2009

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Comparator group target	10–12 mmol/L (180–215 mg/dL)	7.8–10 mmol/L (140–180 mg/dL)
Intervention target	<6.1 mmol/L (<110 mg/dL)	<6.0 mmol/L (<108 mg/dL)
Blood sampling site	Predominantly arterial line	Arterial/venous/capillary
Glucose measurement tool	ABL Radiometer bloodgas analyzer (surgical)	Not standardized
	HemoCue (medical)	All types glucometers allowed
Insulin infusion	Continuous only via central line	Continuous + bolus via all routes
	Syringe pump	All types of pumps allowed
Nurse instructions	Guideline + Intuitive decision making	A strict "if-then" algorithm
Feeding route first week	Parenteral + Enteral	Enteral only
Average kcal received during ICUstay	1100 kcal/day	880 kcal/day
Therapy compliance		
Blood glucose target reached	70%	<50%
Overlap in blood glucose between two groups	<10%	>50%
Outcome		
Hypoglycaemia	× 6	× 13
Morbidity	Reduced organ failure and infections	Neutral
Mortality	Lowered by absolute 3%	Increased by absolute 3%
Therapy withdrawal policy	Late	Early

D. Mesotten, G. Van den Berghe / Best Practice & Research Clinical Anaesthesiology 23 (2009) 421-9

ORIGINAL ARTICLE

Hypoglycemia and Risk of Death in Critically Ill Patients

The NICE-SUGAR Study Investigators*

BACKGROUND

Whether hypoglycemia leads to death in critically ill patients is unclear.

N ENGL J MED 367;12 NEJM.ORG SEPTEMBER 20, 2012

Figure 2. Hazard Ratio for Death According to Treatment Assignment and Status with Respect to Diabetes and Postoperative Status at Baseline.

The relationship between moderate or severe hypoglycemia and death did not differ significantly between patients assigned to intensive glucose control and those assigned to conventional glucose control (Panel A). The relationship was similar among patients with and those without a diagnosis of diabetes (Panel B), but it was stronger among postoperative patients (those admitted to the ICU directly from the operating room or recovery room) than among nonpostoperative patients (Panel C). The size of the squares is proportional to the number of deaths.

N Engl J Med 2012; 367:1108-1118

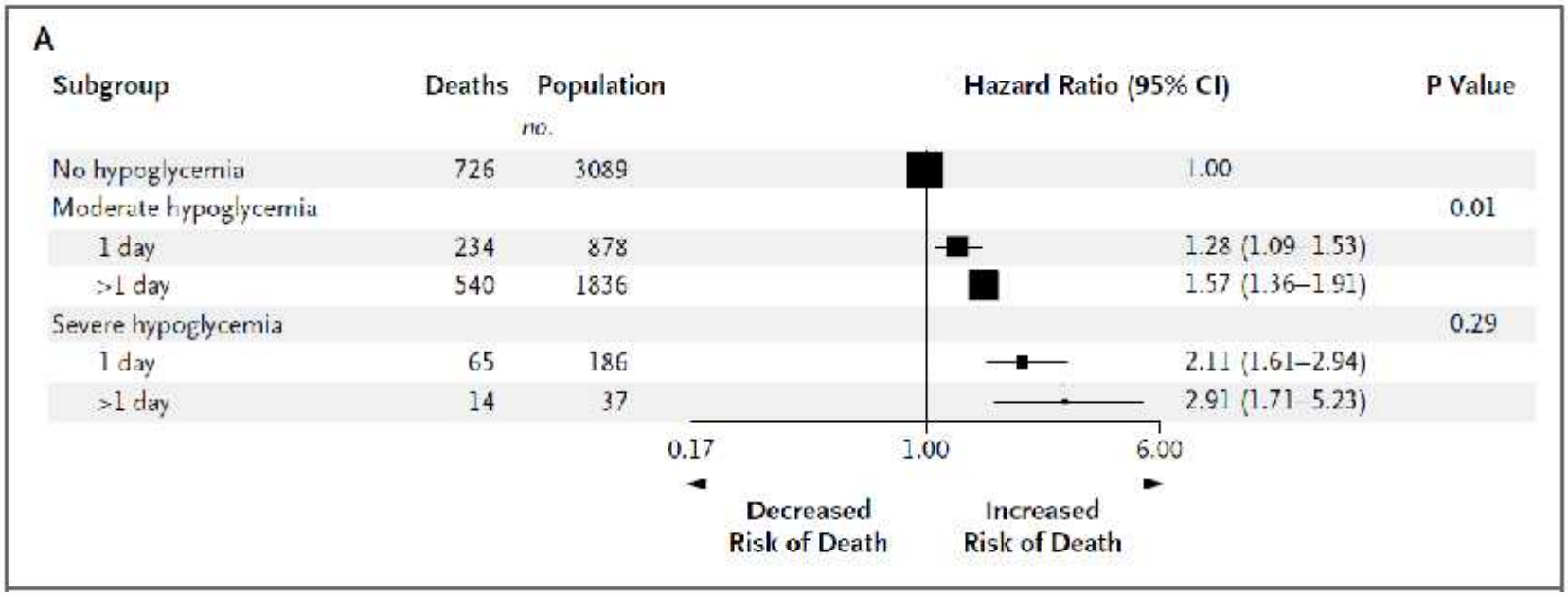

Figure 3. Hazard Ratio for Death According to the Occurrence of Hypoglycemia on 1 Day or More Than 1 Day and Receipt or Nonreceipt of Insulin Therapy at the Time of the First Hypoglycemic Episode.

The risk of death was increased among patients who had moderate hypoglycemia on more than 1 day, as compared with just 1 day (Panel A), and among patients who were not receiving insulin when hypoglycemia first occurred, as compared with those who were receiving insulin (Panel B). The interval from the first episode of hypoglycemia to death was shorter among patients who were not being treated with insulin when hypoglycemia first occurred ($P=0.004$ and $P<0.001$ for moderate and severe hypoglycemia, respectively). The size of the squares is proportional to the number of deaths.

N Engl J Med 2012; 367:1108-1118

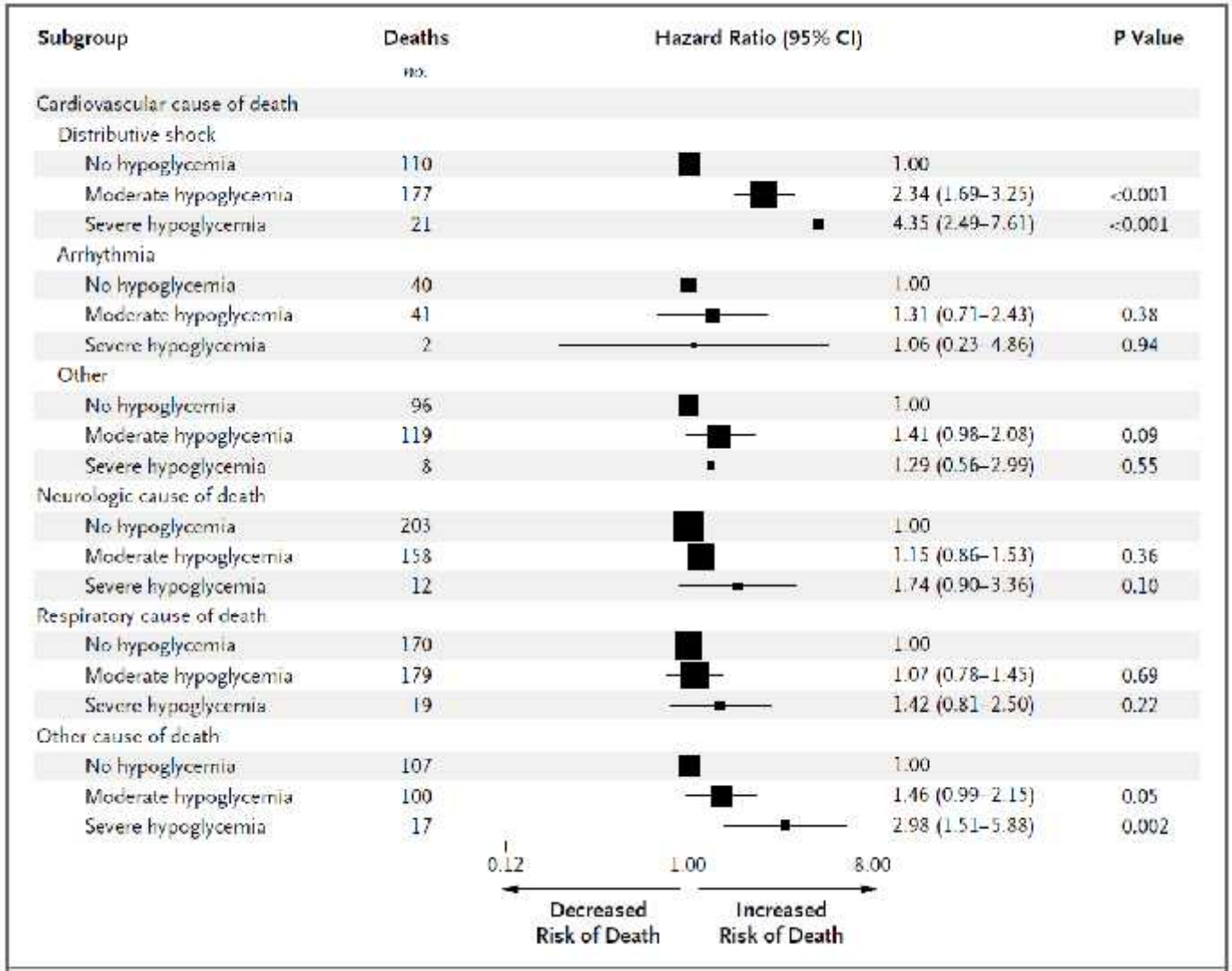

Figure 4. Hazard Ratio for Death from Specific Causes According to the Occurrence of Moderate or Severe Hypoglycemia.

The hazard ratio for death from distributive (vasodilated) shock was significantly higher for patients with moderate or severe hypoglycemia than for those who did not have hypoglycemia. Patients with severe hypoglycemia also had an increased hazard ratio for death from miscellaneous causes. The size of the squares is proportional to the number of deaths.

N Engl J Med 2012; 367:1108-1118

ORIGINAL ARTICLE

Hypoglycemia and Risk of Death in Critically Ill Patients

The NICE-SUGAR Study Investigators*

CONCLUSIONS

In critically ill patients, intensive glucose control leads to moderate and severe hypoglycemia, both of which are associated with an increased risk of death. The association exhibits a dose–response relationship and is strongest for death from distributive shock. However, these data cannot prove a causal relationship. (Funded by the Australian National Health and Medical Research Council and others; NICE-SUGAR ClinicalTrials.gov number, NCT00220987.)


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... all the best in pulmonary & critical care
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2012
Intensive glucose control probably kills, says NICE-SUGAR post-hoc (NEJM)
Critical Care, GI and Nutrition, Randomized Controlled Trials
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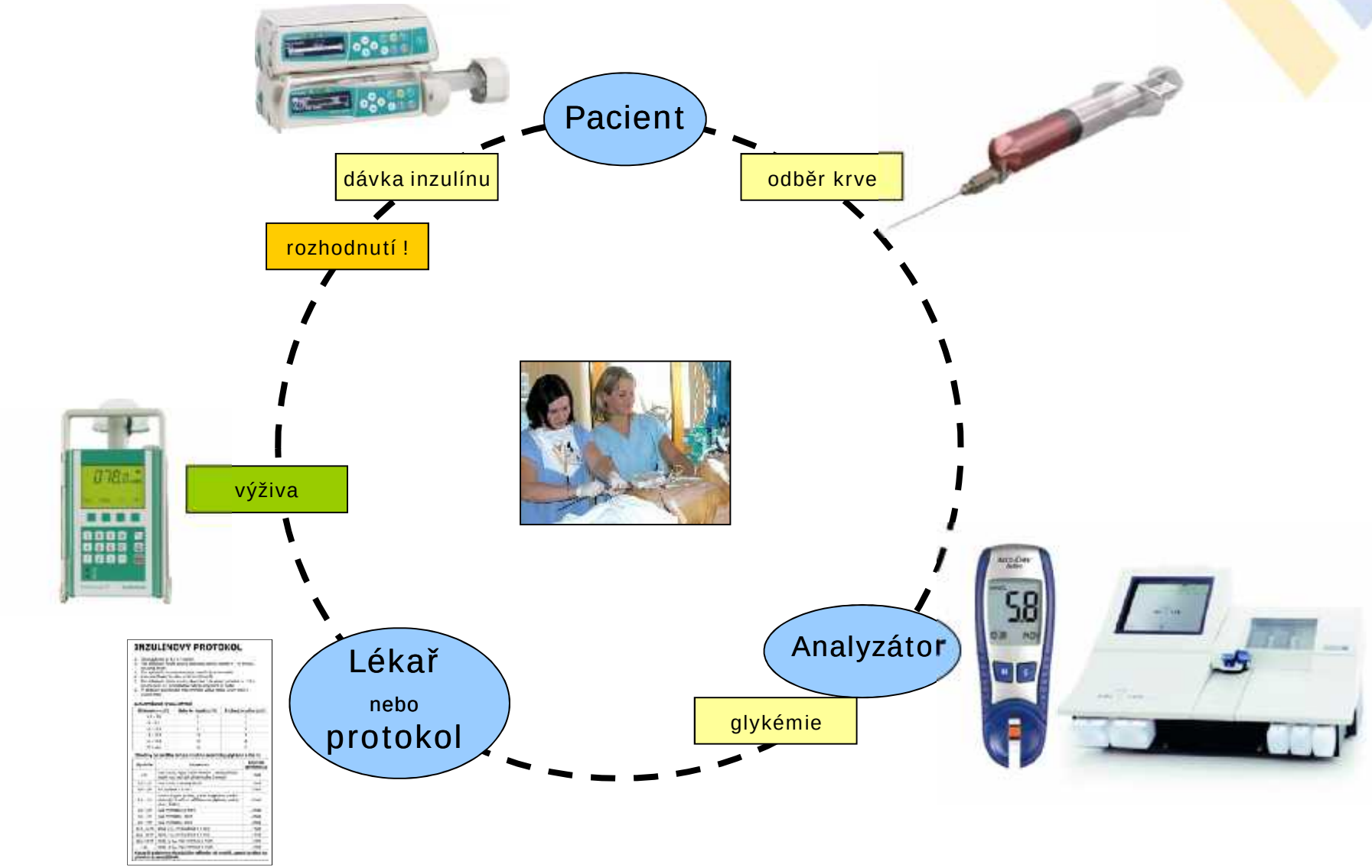
Pacient
dávka inzulínu
odběr krve
rozhodnutí !
výživa
Lékař
nebo
protokol
Analyzátor
glykémie
INZULÍNOVÝ PROTOKOL


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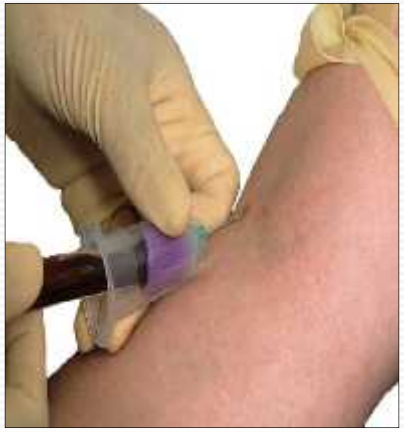
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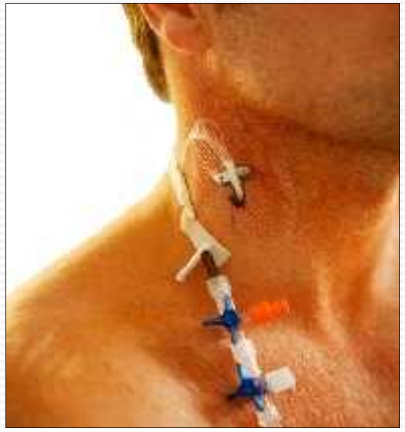
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Fekih Hassen M. Diabetes Res Clin Pract. 2010 Jan;87(1):87-91
Critchell CD et al. Intensive Care Med. 2007 Dec;33(12):2079-84
Hassen FM. Diabetes Res Clin Pract. 2010 Jan;87(1):87-91

Analysis and Value, mmol/L	Vasopressor-Dependent n	Vasopressor-Dependent % Agreement	Edematous n	Edematous % Agreement	Postsurgical n	Postsurgical % Agreement	All n	All % Agreement
Glucose meter, capillary blood (fingersticks)								
<4.5	8	25.0 (0–55.0)	21	23.8 (5.6–42.0)	9	33.3 (2.5–64.1)	38	26.3[a,b,c] (12.3–40.3)
≥4.5	28	71.4 (54.7–88.2)	22	86.4 (72.0–100.0)	30	60.0 (42.5–77.5)	80	71.3[e] (61.3–81.2)
Total	36	61.1 (45.2–77.0)	43	55.8 (40.9–70.7)	39	53.8[d] (38.2–69.5)	118	56.8[e,f] (47.8–65.7)
Glucose meter, arterial blood								
<4.5	8	50.0 (15.4–84.6)	20	55.0 (33.2–76.8)	8	62.5 (28.9–96.0)	36	55.6[a,g] (39.3–71.8)
≥4.5	26	73.1 (56.0–90.1)	22	86.4 (72.0–100.0)	29	72.4 (56.1–88.7)	77	76.6[g] (67.2–86.1)
Total	34	67.6 (51.9–83.4)	42	71.4 (57.8–85.1)	37	70.3 (55.5–85.0)	113	69.9[e] (61.5–78.3)
Blood gas/ chemistry, arterial blood								
<4.5	8	62.5 (53.5–100.0)	20	60.0 (38.5–81.5)	9	77.8 (50.6–100)	37	64.9[h] (49.5–78.4)
≥4.5	28	75.0 (59.0–91.0)	21	85.7 (70.7–100.0)	29	86.2 (73.7–98.8)	78	82.1 (73.5–90.6)
Total	36	72.2 (57.5–86.9)	41	73.2 (59.6–86.7)	38	84.2[d] (72.6–95.8)	115	76.5[f] (68.8–84.3)

[a] $p = .0126$; [b] $p = .0003$; [c] $p < .001$; [d] $p = .0045$; [e] $p = .0196$; [f] $p = .0022$; [g] $p = .0391$. The tested methods of glucose measurement were said to agree with the reference standard measurement (laboratory) when they both resulted in the same clinical intervention according to institutional protocol (Table 1). If the tested method and reference standard would result in different clinical interventions, they were said to disagree. The "n" values reflect the number of paired observations analyzed.

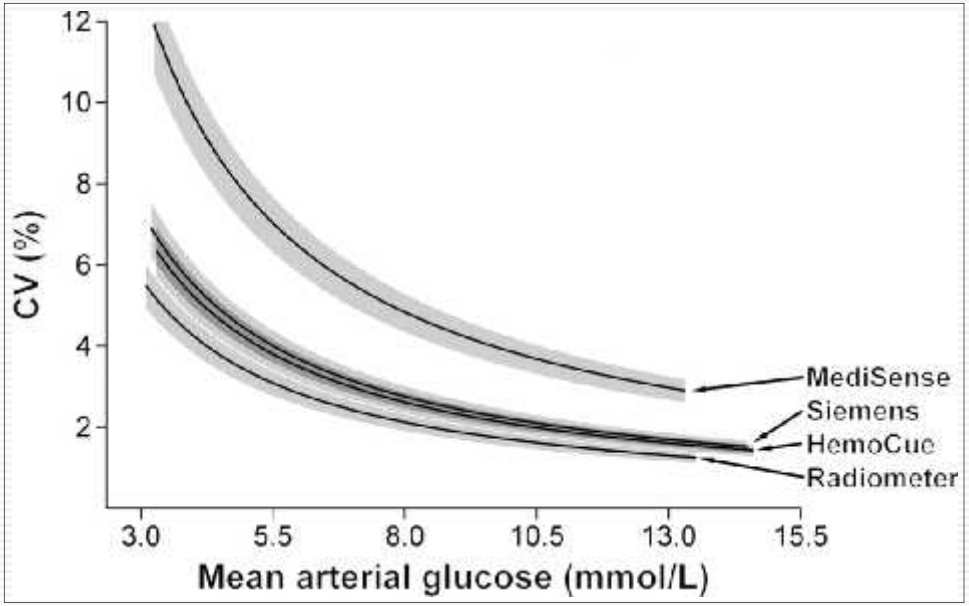
Kanji et al. Crit Care Med 2005; 33:2778–2785

Table 1.
Correlation Coefficients (r^2)

	Accu-Chek	Hemocue
ABL all ranges	0.97	0.94
ABL TGC ranges	0.66	0.56
ABL low ranges	0.73	0.78
ABL high ranges	0.96	0.92

ABL, blood gas analyzer; TGC range, tight glycemic control range (80–110 mg/dl); low range, BG <80 mg/dl; high range, BG >110 mg/dl.

Vlasselaers D. et al. J Diabetes Sci Technol 2008;2(6):932-938



Watkinson PJ et al. Ann Clin Biochem. 2012 Mar;49(Pt 2):144-51

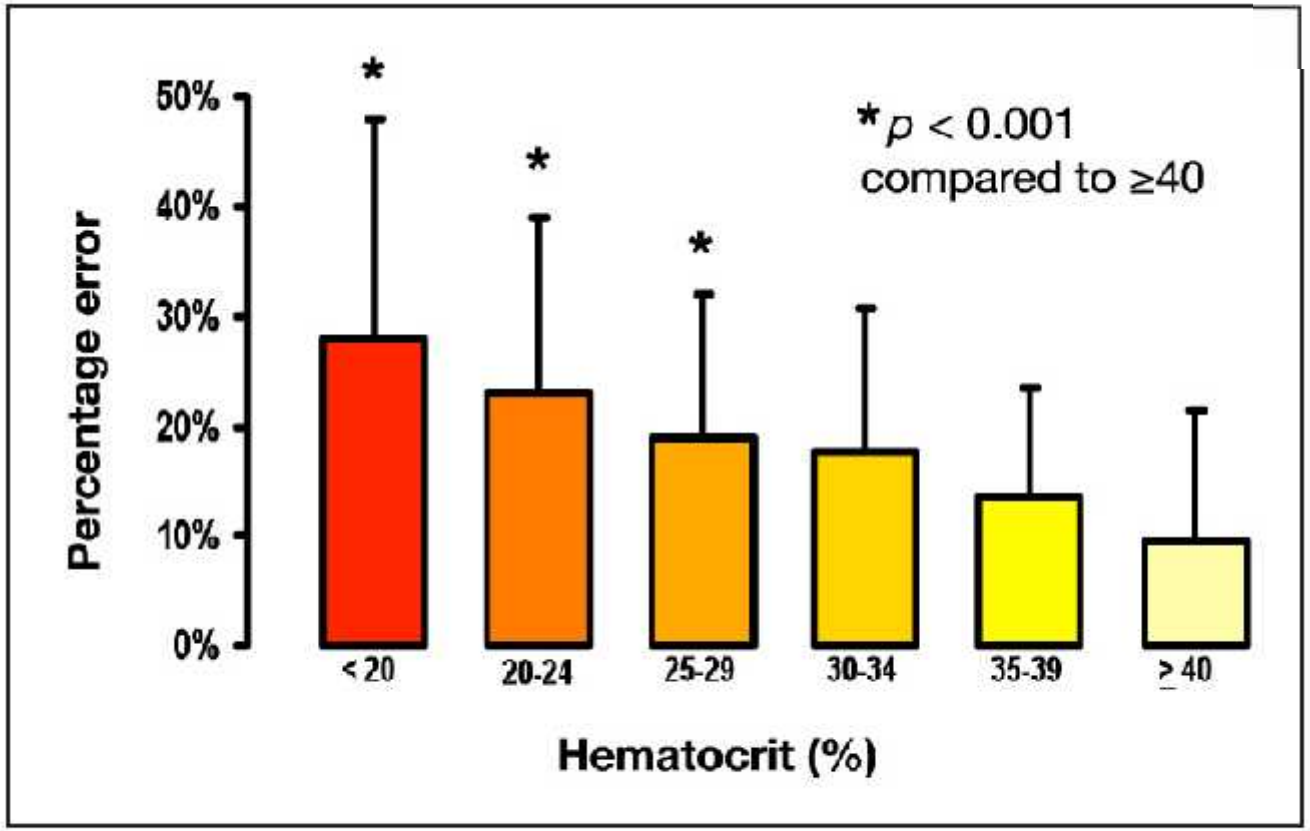
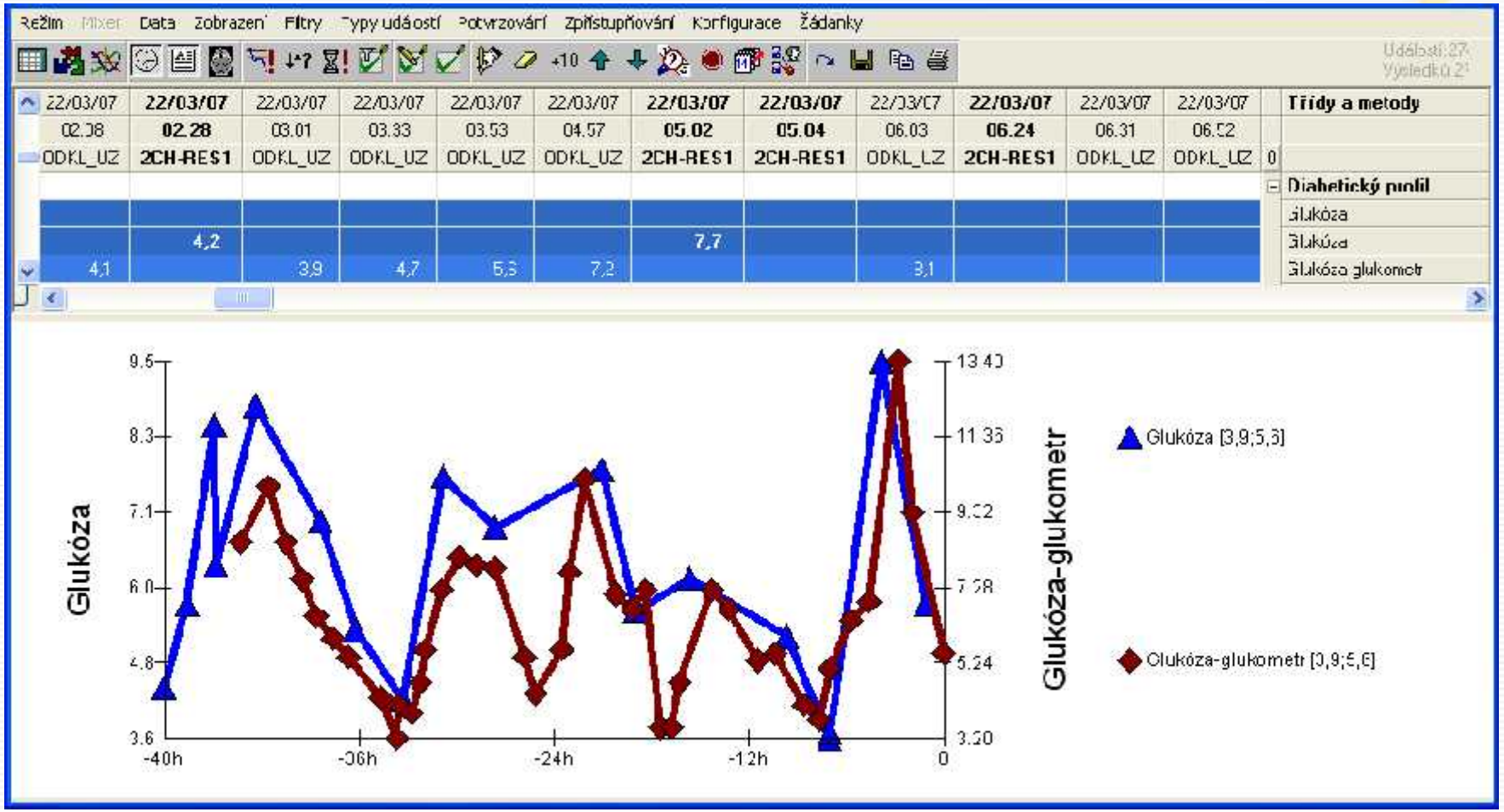


Figure 3. Glucometer error increases in a linearly as HCT decreases.

Mann AE et al. J Diabetes Sci Technol 2009;3(6):1319-1329


Režim
Data
Zobrazení
Filtry
Typy událostí
Potvrzování
Zpřístupňování
Konfigurace
Žádanky
Třídy a metody
Diabetický profil
Glukóza
Glukóza
Glukóza glukometr
4,2
7,7
4,1
3,9
4,7
5,3
7,2
3,1
Glukóza
Glukóza-glukometr
Glukóza [3,9;5,3]
Glukóza-glukometr [3,9;5,6]
-40h
-36h
-24h
-12h
0

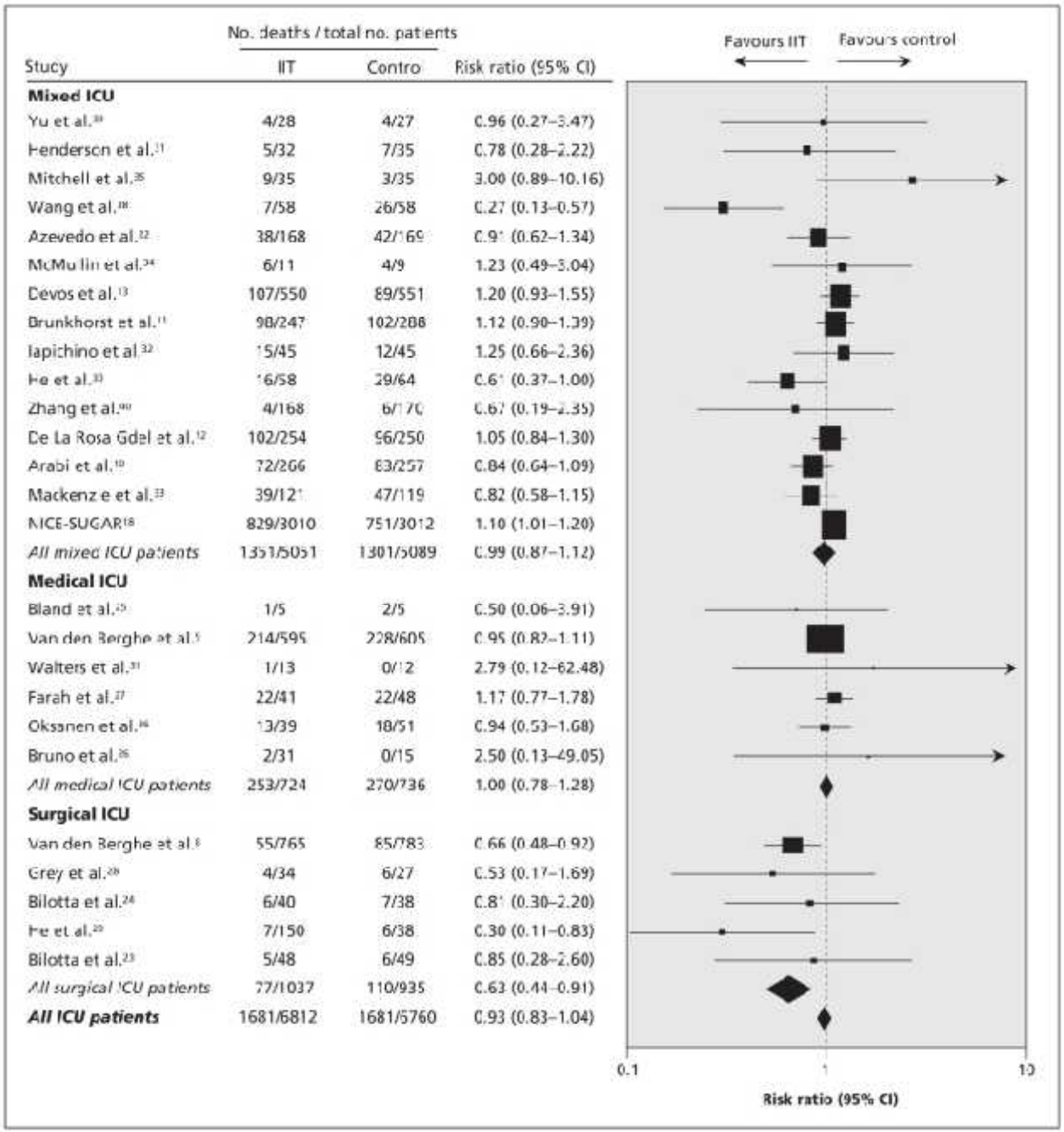
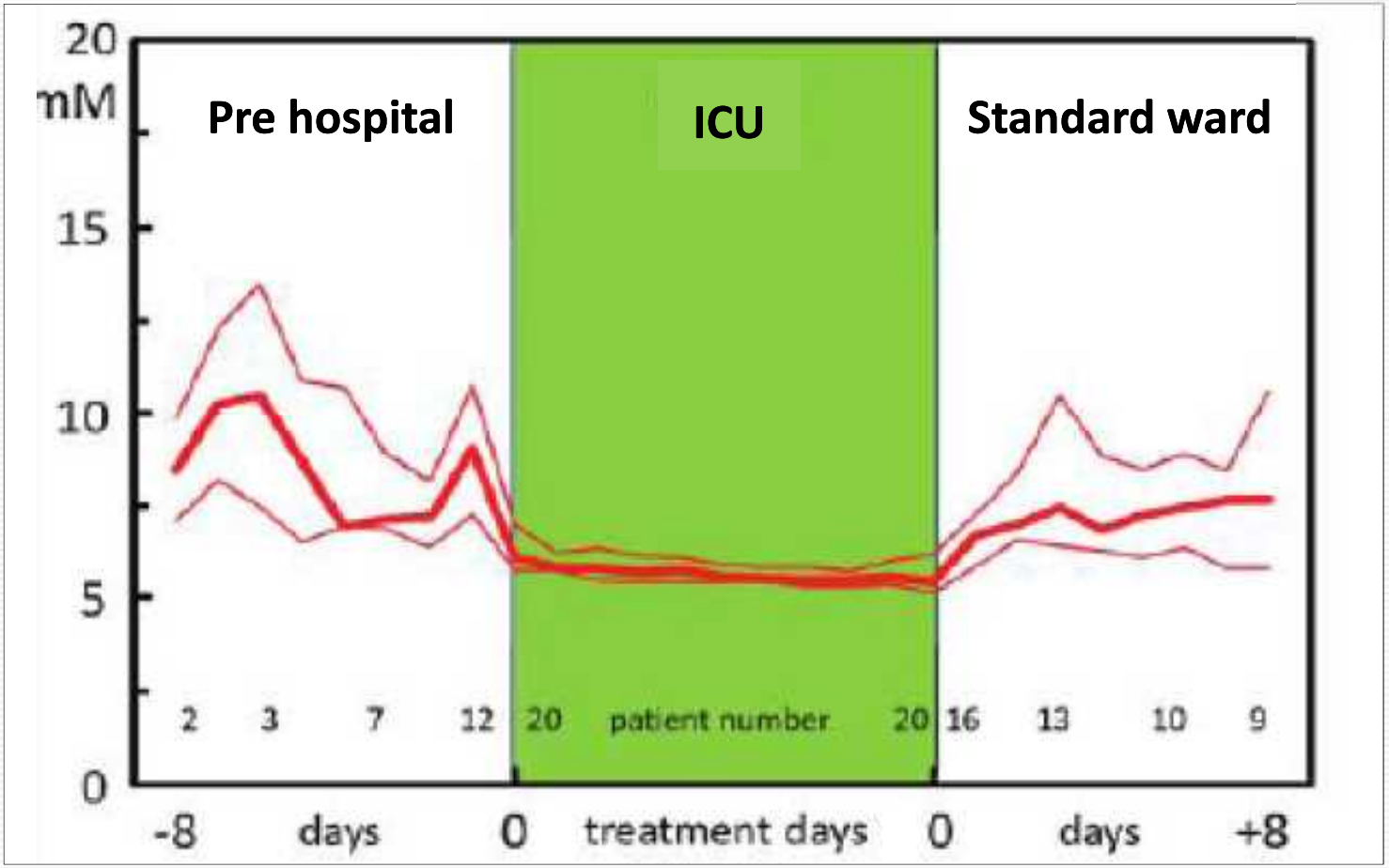


Figure 2: Risk ratios of mortality in clinical trials comparing intensive insulin therapy (IIT) to conventional glycemic control stratified by type of ICU. Tests for heterogeneity: mixed ICU: Q statistic = 29.54 ($p < 0.01$), I^2 = 52.6%; medical ICU: Q statistic = 2.05 ($p = 0.84$), I^2 = 0.0%; surgical ICU: Q statistic = 2.78 ($p = 0.60$), I^2 statistic 0.0%; all ICU patients: Q statistic = 46.67 ($p < 0.01$), I^2 = 46.4%. Note: CI = confidence interval.

Griesdale et al. CMAJ. 2009 April 14; 180(8): 821–827.


20
mM
15
10
5
0
Pre hospital
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Standard ward
2
3
7
12
20
patient number
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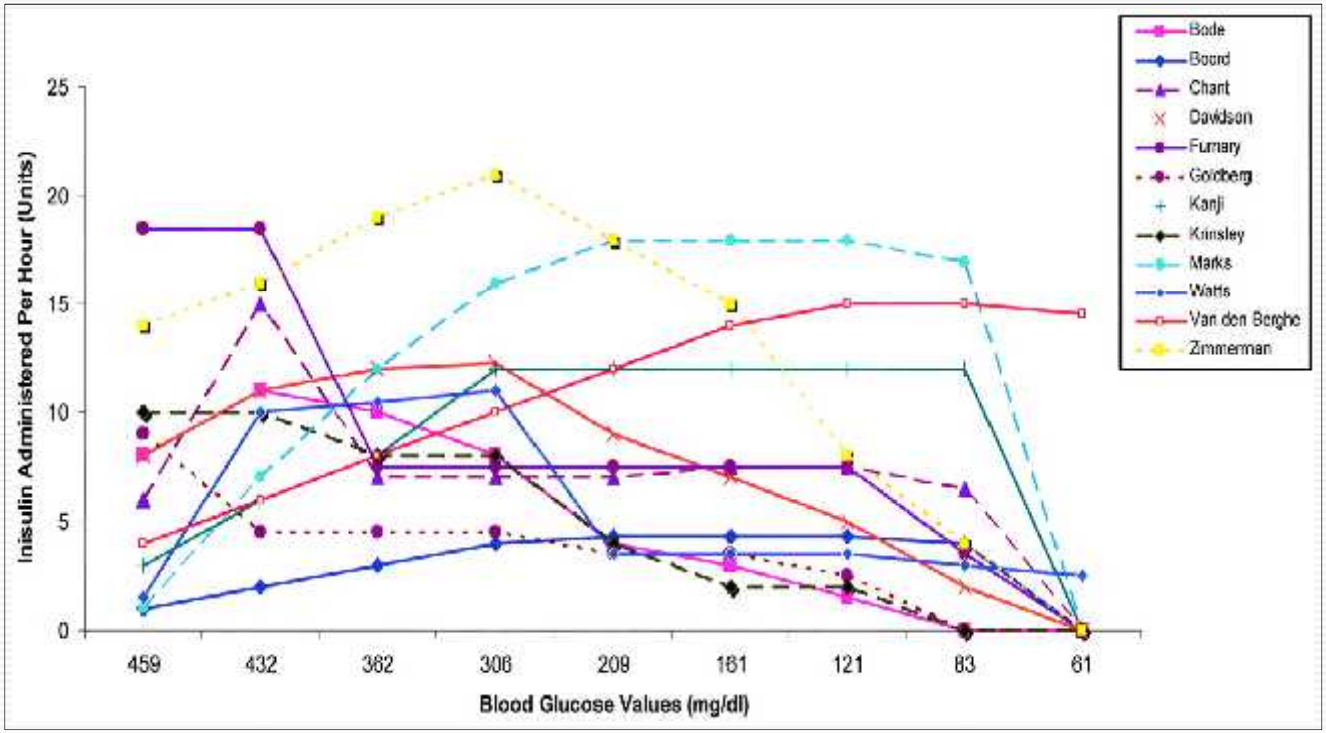
16
13
10
9
-8
days
0
treatment days
0
days
+8



Author	Target glucose (mg/dl)
Bode	100–150
Boord	120–180
Chant	90–144
Davidson	<180
Furnary	100–150
Goldberg	100–139
Kanji	80–110
Krinsley	<140
Marks	120–180
Van den Berghe	80–110
Watts	120–180
Zimmerman	101–150

Wilson et al. Diabetes Care 2007 Apr;30(4):1005-11

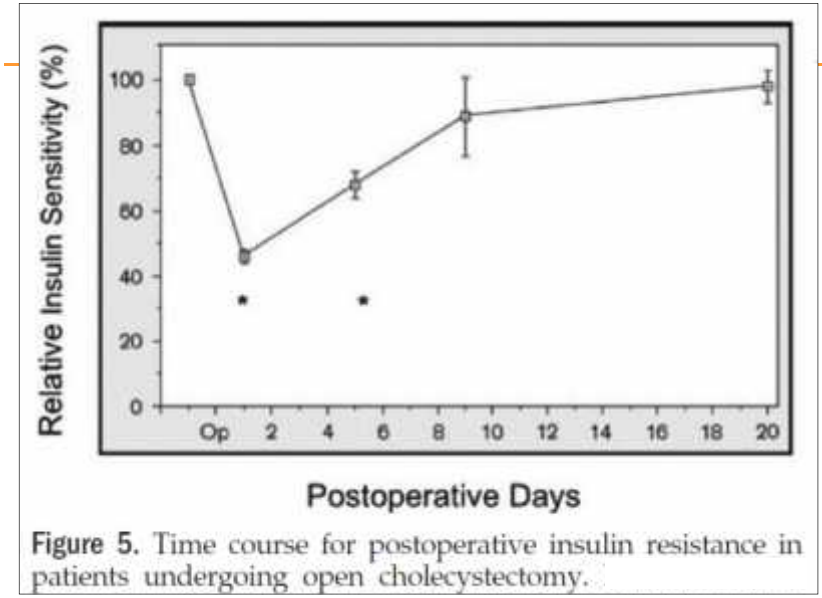
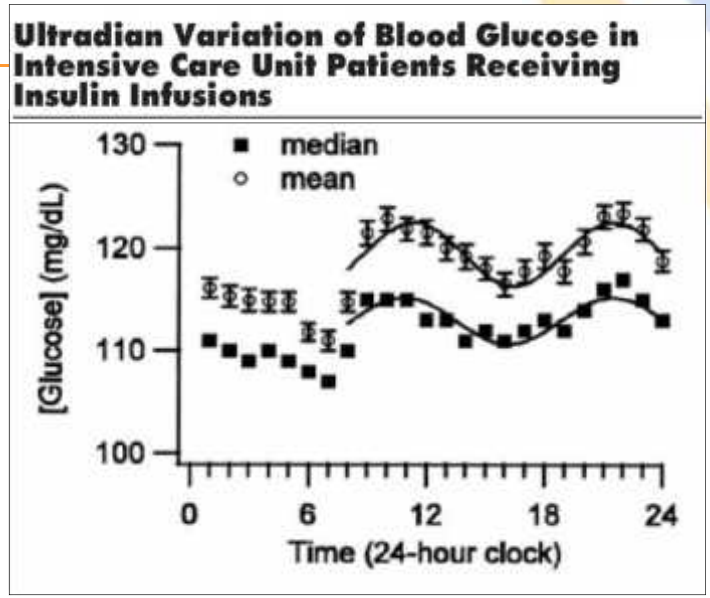


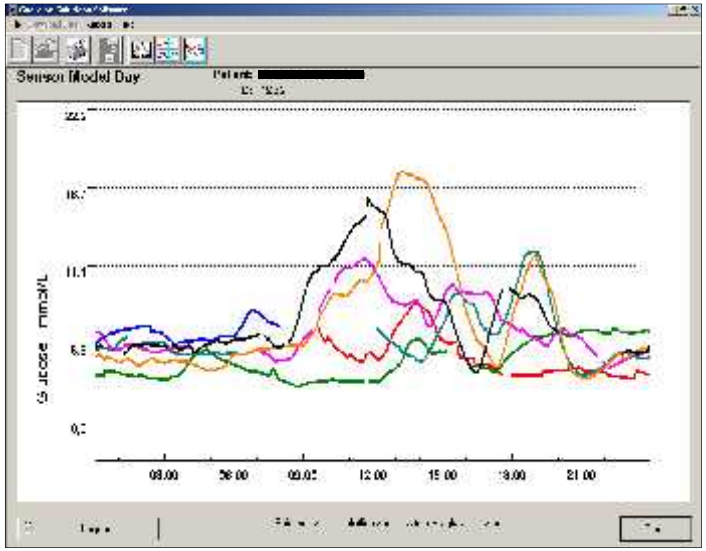
Figure 5. Time course for postoperative insulin resistance in patients undergoing open cholecystectomy.

Akhtar S et al. Anesthesia & Analgesia 2010; 110(2):478-97

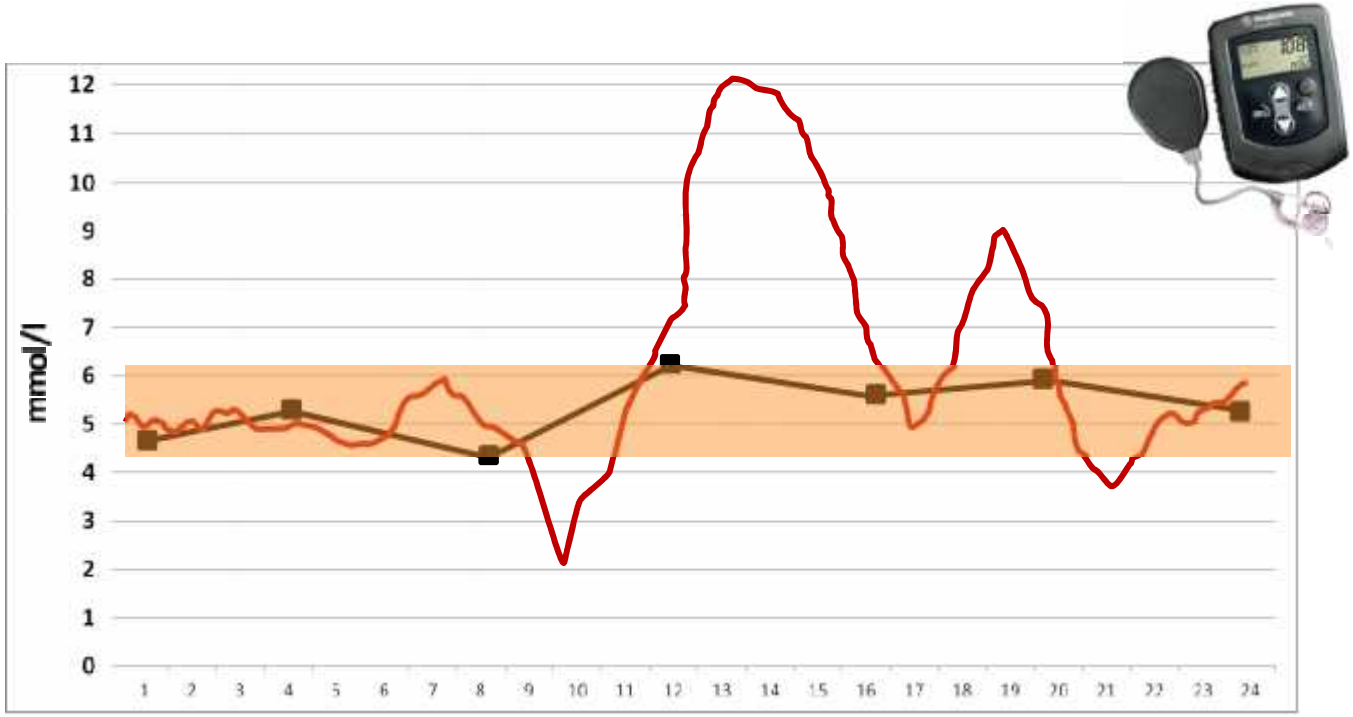


Smith et al. Diabetes Care 2007; 30(10):2503-5

- změny inzulínové rezistence
- cirkadiální rytmus glykémie



Blaha et al. 2008


mmol/l
12
11
10
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4
3
2
1
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24

PREDISPONUJÍCÍ FAKTORY HYPOGLYKÉMIE NA ICU:

- CVVH (bikarbonátový substituční roztok)
- snížení nutriční podpory bez snížení rychlosti infuze inzulínu
- inzulín
- DM
- sepse
- inotropní podpora

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

INZULÍNOVÝ PROTOKOL: “PAPÍROVÝ“

- nejčastější varianta
- nejjednodušší na implementaci
- nejsnadněji auditovatelná
- dobře přenositelná
- nejlevnější

INZULÍNOVÝ PROTOKOL:

"PAPÍROVÝ" "SLIDING SCALE"

Guidelines for the application of insulin at MUG:

1. Application of insulin
   a. Insulin infusion for all insulin dependent diabetic patients and TX-patients
   b Insulin bolus for all other patients
2. Preparation of insulin infusion
   a. Standard concentration is 100IU insulin in 50ml Voluven
   b. Solution is stable for at the most 24h
3. Determination of glucose concentration
   a. Measurement using laboratory analyser or Reflo-Check
   b Measurement in undiluted arterial blood or capillary blood
   c. Frequency of measurement:
      i. First measurement at admission
      ii. At least six measurements per day or 1-2 hourly if requested from treating physician
      iii. 60 minutes after each intervention (change of infusion rate or bolus)
      iv. 60 minutes after stop of glucose infusion or nutrition
4. Glucose target value
   a. ICU: 80-110mg/dl (below 120 mg/dl)
   b. General ward: <200 mg/dl
5. Insulin Dosing Scheme
   a. Insulin Infusion
      i. BG >220 8IE/h
      ii. 150 < BG < 220 6IE/h
      iii. 120 < BG < 150 4IE/h
      iv. 60 < BG < 80 Insulin Stop
      v. BG < 60 Insulin Stop + 10g Glucose (20%) intravenous
   b Insulin Bolus
      i. BG > 220 8IE
      ii. 150 < BG < 220 6IE
      iii. 120 < BG < 150 4IE

(2) Intravenous insulin infusion sliding scale

Medication: 100 U human regular insulin in 100 mL of 0.9% saline. Use infusion pump to control rate.

Blood or plasma glucose (mg/dL)	Insulin infusion rate (U/h)	Specific physician order, insulin infusion rate (U/h)*
>400†	8	
351-400†	6	
301-350†	4	
250-300†	3	
200-249†	2.5	
150-199	2	2
120-149	1.5	1.5
100-119	1	1
70-99	0	0
<70	0	0

*Hypoglycemic risk increases when insulin infusion rate is increased for glucose concentrations of <200 mg/dL. A new physician order must be completed for each increase in infusion rate.

†If glucose level does not decrease to goal range within 4 hours, the insulin infusion rate should be increased progressively by 50% increments for each glucose range of ≥200 mg/dL.

Nurse-driven protocol

1. Monitor glucose at bedside hourly until levels have been stabilized in a range (100-200 mg/dL) for 4 hours (confirm with a laboratory glucose test if bedside glucose is >400 mg/dL)
2. Decrease frequency of glucose measurements to every 2 hours after glucose level has been stabilized for 4 hours
3. Notify physician if:
   a. Glucose decreases by more than 80 mg/dL per hour
   b. Glucose remains >250 mg/dL for 2 hourly measurements
   c. Glucose is <70 mg/dL

Rady et al. Mayo Clin Proc 2005; 80(2):1558-1567

INZULÍNOVÝ PROTOKOL:

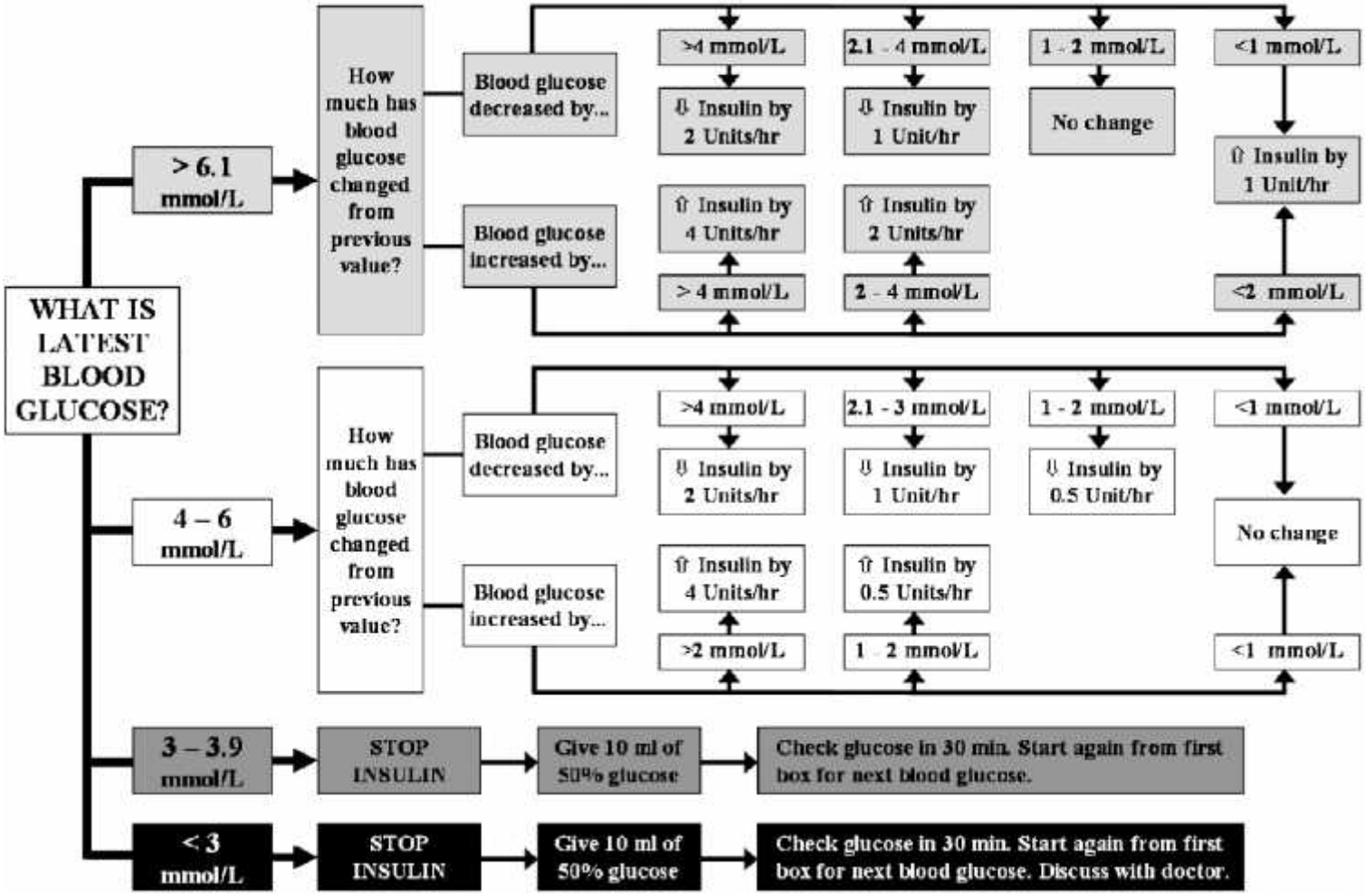
"PARÍROVÝ" LEUVEN PROTOCOL ("DYNAMIC SCALE")

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

INZULÍNOVÝ PROTOKOL:

"PARÍROVÝ" BATH ALGORITHM (ADAPTED) ("DYNAMIC SCALE")

Starting rate for insulin infusion:	
BG (mmo/l)	Starting insulin infusion rate (ml/h)
3 – 6.1	0
6.2 – 9.9	1
10 – 12	2
>12	4

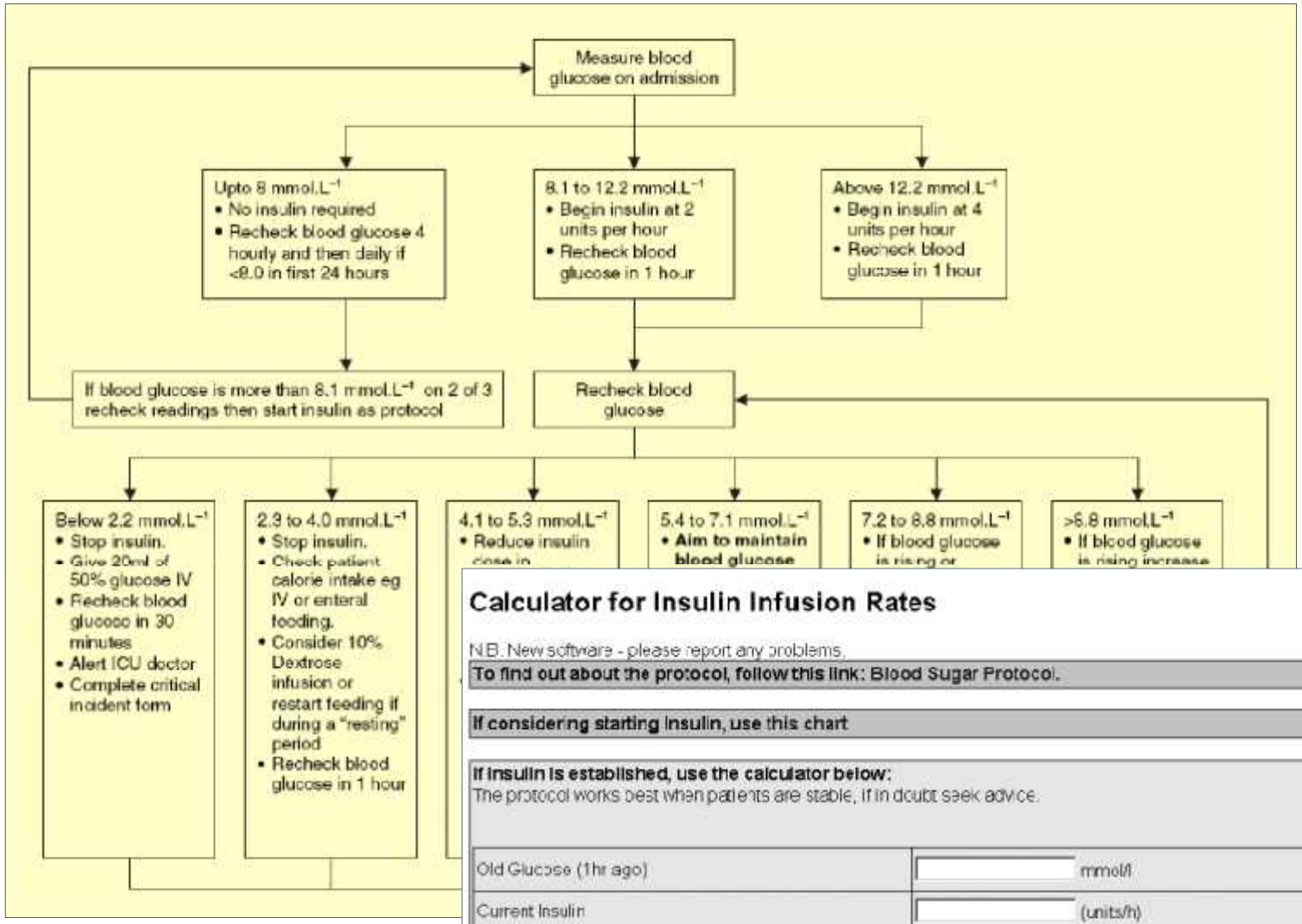


Laver et al: Anaesth Intensive Care 2004; 32:311-316

INZULÍNOVÝ PROTOKOL: ELEKTRONICKÁ VERZE PAPÍROVÉHO

- zjednodušuje užití komplikovanějších protokolů
- zrychluje získání doporučení rychlosti inzulinu
- poskytuje přehledné informace
- snižuje riziko chybné interpretace protokolu
- upozorňuje na rizika !

- nutné technické vybavení
- riziko chybného zadání údajů



Thomas et al: Anaesthesia 2005, 60:1093-1

Calculator for Insulin Infusion Rates

N.B. New software - please report any problems.

To find out about the protocol, follow this link: Blood Sugar Protocol.

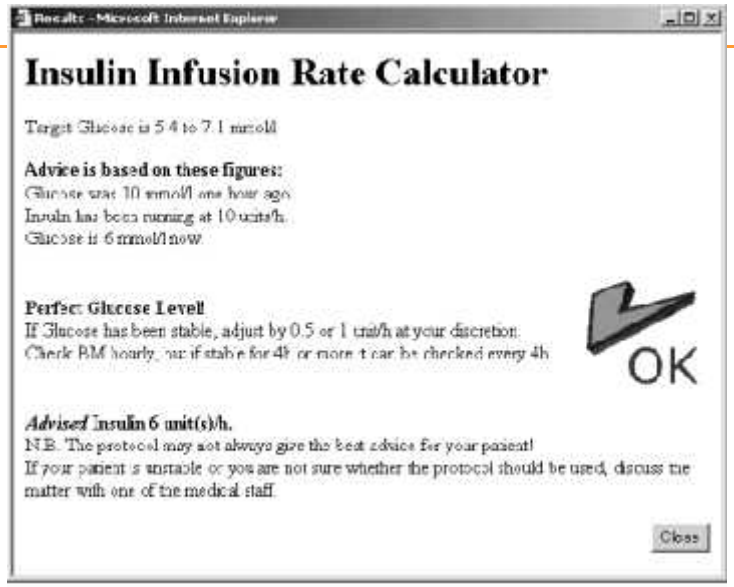
If considering starting insulin, use this chart

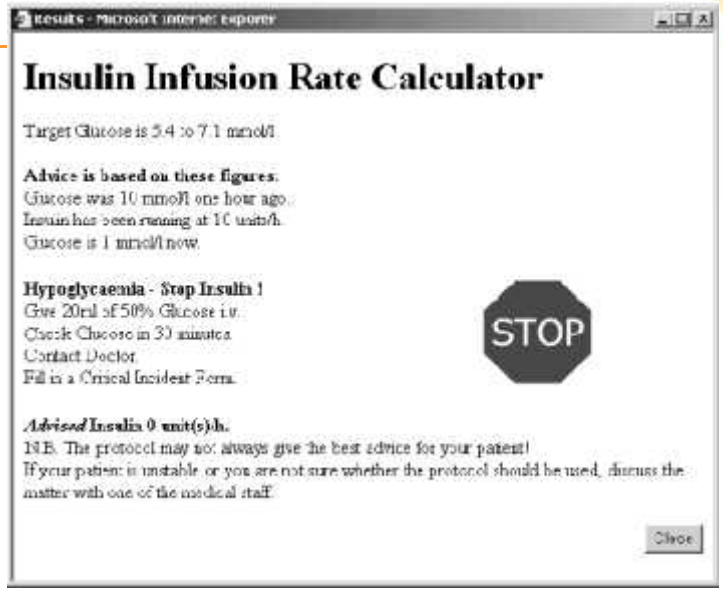
If insulin is established, use the calculator below:

The protocol works best when patients are stable, if in doubt seek advice.

Old Glucose (1hr ago)		mmol/l
Current Insulin		(units/h)
Current Glucose		mmol/l

Go





	Before protocol August 2002 – March 2003	Initial protocol May 2003 – July 2004	Revised protocol July 2004 – November 2004
Glucose levels for results linked to daily summaries; mmol.l^{-1}	7.3 (1.8)	6.6 (1.6)	6.2 (1.3)
Proportion of glucose levels < 6.1 mmol.l^{-1}; %	30.2 (32.7)	42.6 (34.1)	48.8 (32.7)
Proportion of glucose levels < 8 mmol.l^{-1}; %	69.3 (32.5)	81.3 (27.0)	88.8 (19.5)
Glucose levels for all results from 06.00 to 12.00 h; mmol.l^{-1}	7.2 (2.3)	6.6 (1.9)	6.4 (1.6)

Thomas et al: Anaesthesia 2005, 60:1093-1100

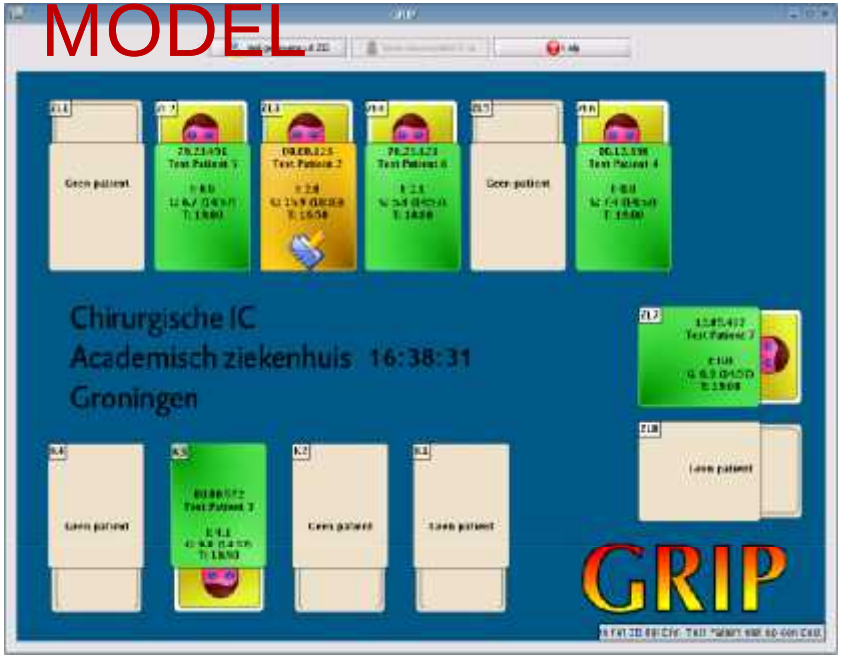
INZULÍNOVÝ PROTOKOL: MATEMATICKÝ MODEL

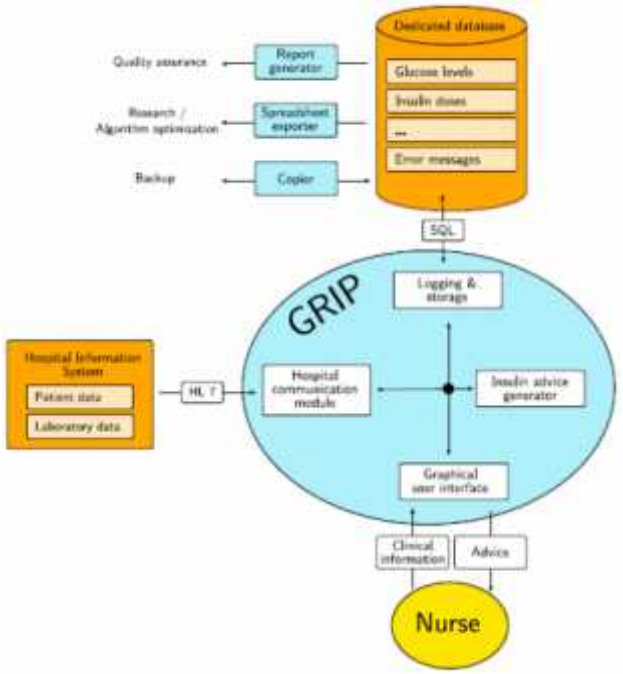
-
- možnost propojení více vstupů (výživa...)
- možnost rozhodovacích prvků

- snižuje riziko chybné interpretace protokolu

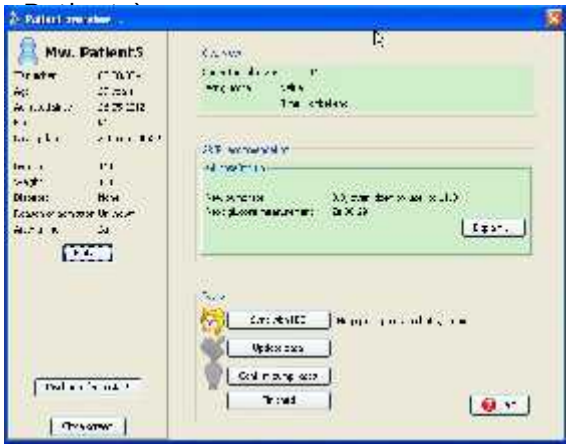
- nutné technické vybavení
- riziko chybného zadání údajů

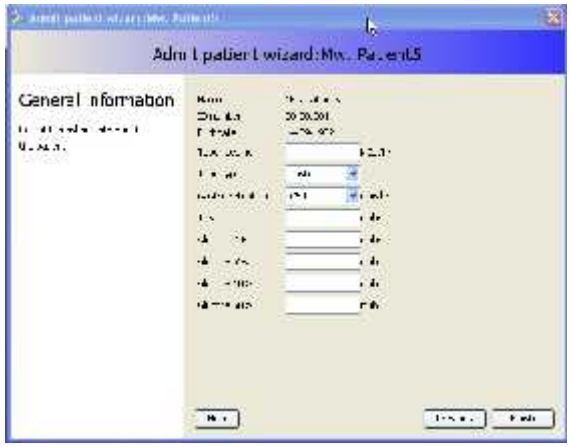
INZULÍNOVÝ PROTOKOL: MATEMATICKÝ MODEL





GRIP (Glucose Regulation for Intensive care





Vogelzang et al: BMC Medical Informatics and Decision Making 2005, 5:38 http://grip-glucose.sourceforge.net

POČÍTAČOVÝ INZULÍNOVÝ PROTOKOL

Review

Health technology assessment review: Computerized glucose regulation in the intensive care unit - how to create artificial control

Miriam Hoekstra[1], Mathijs Vogelzang[2,3], Evgeny Verbitskiy[4,5] and Maarten WN Nijsten[6]

Conclusion

Computer-assisted glycemic control has proven to be more safe and effective than paper protocols in ICU patients. A successful system is nurse-centered, fully integrated into the routine workflow, transparent, and uses patient-specific information with intermittent glucose measurements and variant sampling intervals.

Hoekstra M, Vogelzang M et al. Critical Care 2009, 13:223

Table 1

Summary of published computer-assisted glucose regulation protocols, designed for critically ill patients

Reference	N	Patient type	APACHE II	Target range (mmol/L)	Performance	Hypoglycaemia[a]	Measurements per patient per day
Boord *et al.* [21]	204	Surgical ICU	?	4.4 to 6.1	49% of time in range	0.2% <2.2 mmol/L	~16 (12 to 24)[b]
Cordingley *et al.* [22]	16	Mixed ICU	16.6	4.4 to 6.1	63% of time in range	0 <2.2 mmol/L	10.9
Davidson *et al.* [23]	5,808	General medical and surgical floors	?	Variable	'Stable glucose'	0.5% <2.6 mmol/L	~16 (12 to 24)[b]
Dortch *et al.* [24]	243	Trauma ICU	ISS 27.5	4.4 to 6.1	42% of measurements in range	0.2% <2.2 mmol/L	10.7
Hermayer *et al.* [25]	66	CABG	?	4.4 to 6.7	Mean BG 6.4 mmol/L	0.10% <2.2 mmol/L	16.2[c]
Horvorka *et al.* [26]	30	Cardiac surgery	?	4.4 to 6.1	60% of time in range	0 <2.9 mmol/L	15
Juneja *et al.* [27]	2,898	Mixed ICU	?	4.4 to 6.1	61% of measurements in range	0.4% <2.6 mmol/L	~16 (12 to 24)[b]
Lehr *et al.* [28]	661	Mixed ICU	15	4.5 to 7.2	95% of measurements in the range 3.7 to 12.1 mmol/L	1.7% of patients with a single episode <2.2 mmol/L	~12 (6 to 24)[d]
Meyfroidt *et al.* [29]	179	Mixed ICU	13	4.5 to 7.5	53% of time in range	0.05% <2.2 mmol/L	3.4
Morris *et al.* [30]	776	Mixed ICU	21.8	4.4 to 6.1	42% of measurements in range	0.33% <2.2 mmol/L	~12 (6 to 24)[d]
NICE-SUGAR [13]: intensive control	3,054	Mixed ICU	21.1	4.5 to 6.0	Mean time-weighted BG 6.4 mmol/L	6.8% <2.2 mmol/L	~12 (6 to 24)[d]
NICE-SUGAR [13]: conventional control	3,050	Mixed ICU	21.1	8.0 to 10.0	Mean time-weighted BG 8.0 mmol/L	0.8% <2.2 mmol/L	~12 (6 to 24)[d]
Pachler *et al.* [31]	25	Medical ICU	26.6	4.4 to 6.1	HGI = 0.4 mmol/L	1 episode <2.2 mmol/L	12.3
Plank *et al.* [32]	30	Cardiac surgery	11.4	4.4 to 6.1	53% of time in range	0 <2.2 mmol/L	24
Rood *et al.* [33]	66	Mixed ICU	19.5	4.0 to 7.0	54% of time in range	0.09% of time <2.5 mmol/L	9.9[c]
Saager *et al.* [34]	20	Cardiac surgery	?	5.0 to 8.3	94% of time in range	5 episodes <3.3 mmol/L	24
Shulman *et al.* [35]	50	Mixed ICU	23	4.4 to 6.1	23% of time in range	0.04% of time <2.2 mmol/L	12.7
Thomas *et al.* [36]	603	Mixed ICU	14.4	5.4 to 7.1	85% of measurements <8 mmol/L	19 episodes	~12 (6 to 24)[d]
Toschlog *et al.* [37]	128	Trauma	ISS 24.5	4.4 to 7.2	Mean BG 6.4 mmol/L	32% of patients with a single episode <2.8 mmol/L	?
Vogelzang *et al.* [38]	2,800	Mixed ICU	14	4.0 to 7.5	87% of time in range	0.04% <2.2 mmol/L	5.9

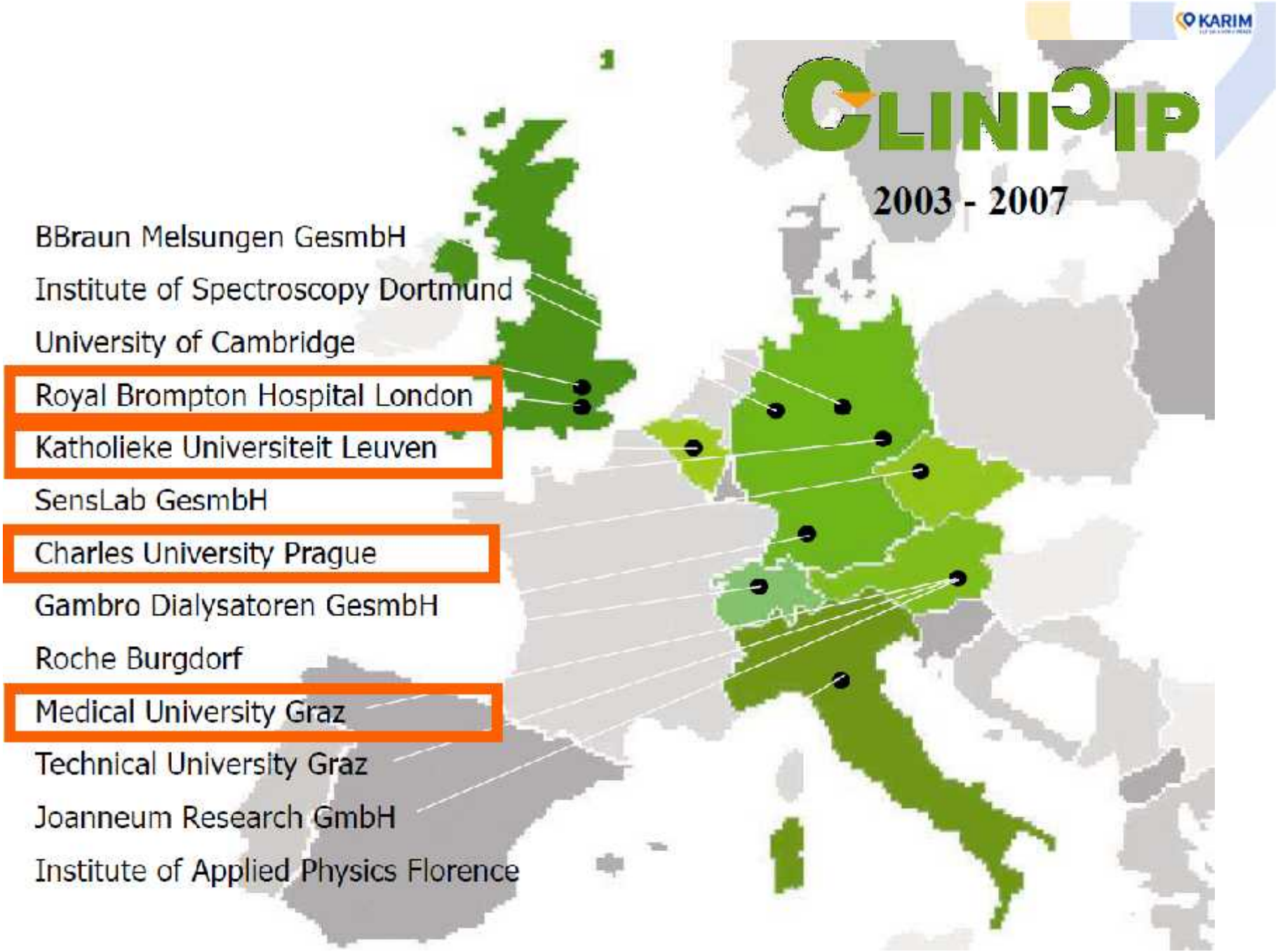
[a]Hypoglycaemia is represented as the proportion of all measurements, unless otherwise specified. [b]No exact data, but protocol has 'hourly to two-hourly measurements'. [c]Calculated from number of measurements and length of stay. [d]No exact data, but protocol has 'hourly to four-hourly measurements'. APACHE, Acute Physiology and Chronic Health Evaluation II; BG, blood glucose; CABG, coronary artery bypass grafting; HGI, hyperglycaemic index; ISS, Injury Severity Score; NICE SUGAR, The Normoglycaemia in Intensive Care Evaluation - Survival Using Algorithm Regulation.

- 5 % všech hodnot glykémie zadaných do protokolu se neshoduje s naměřenými hodnotami
- nastavená rychlost inzulínu se od doporučení protokolu liší o 2 %

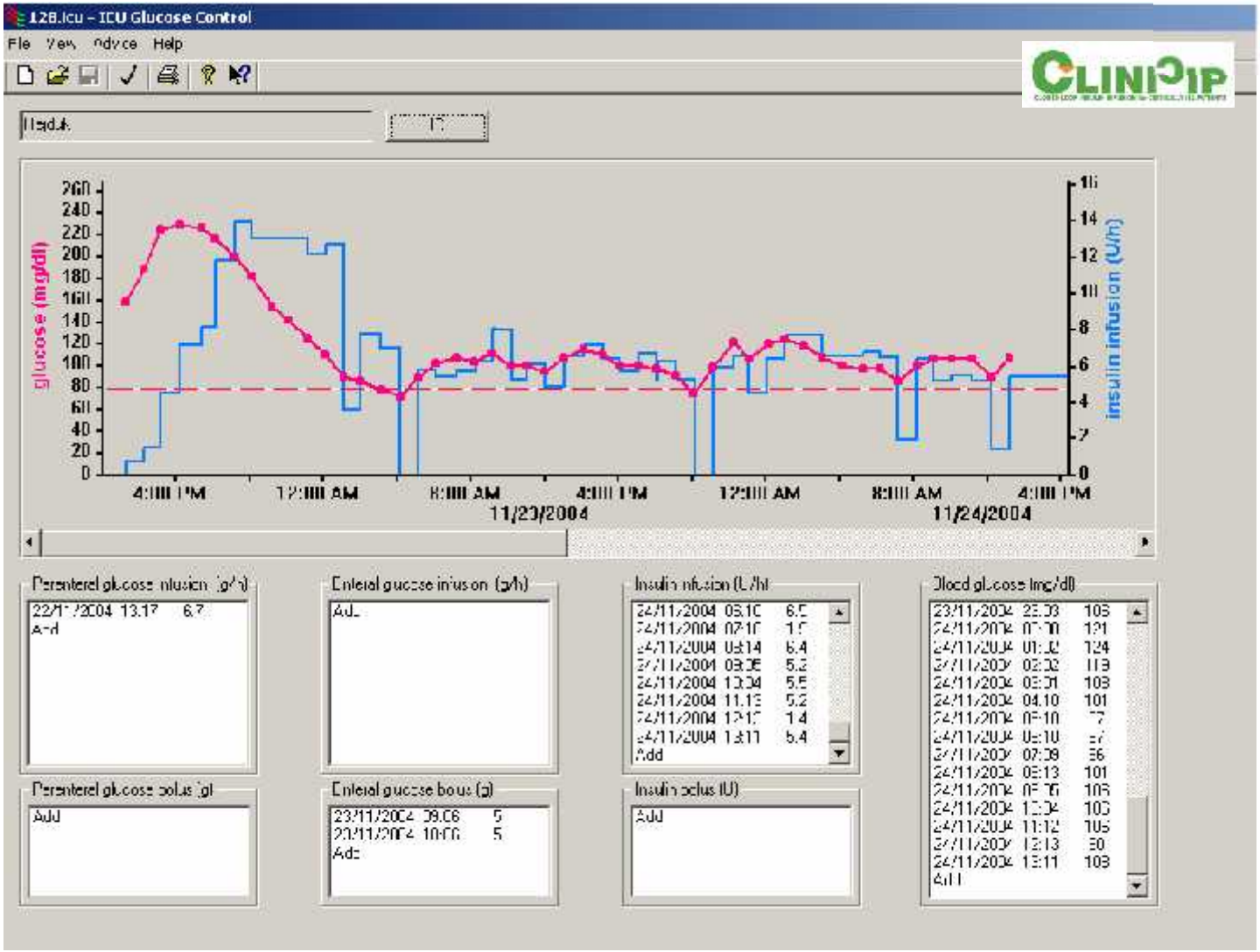
  - 23 %

- 83 % ignorovaných doporučení bylo pro „obavy z hypoglykémie“
- riziko „nenastavení infusních pump“ (např. při souběžné akutní situaci)

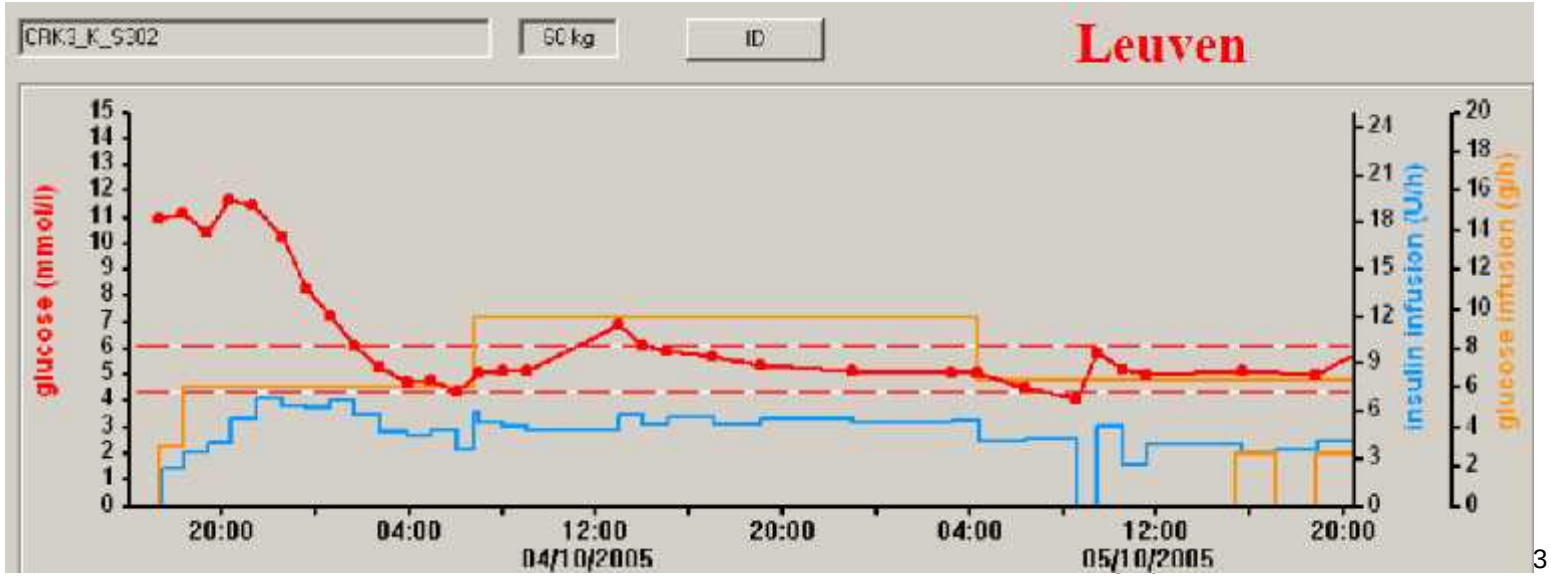
Campion TR et al. International Journal Of Medical Informatics 80 (2011) 863–871
Campion TR et al. J. Am. Med. Inform. Assoc. 18 (May (3)) (2011) 251–258.
Anger KE et al. Pharmacotherapy 26 (February (2)) (2006) 214–228.


KARIM
CLINICIP
2003 - 2007
BBraun Melsungen GesmbH
Institute of Spectroscopy Dortmund
University of Cambridge
Royal Brompton Hospital London
Katholieke Universiteit Leuven
SensLab GesmbH
Charles University Prague
Gambro Dialysatoren GesmbH
Roche Burgdorf
Medical University Graz
Technical University Graz
Joanneum Research GmbH
Institute of Applied Physics Florence

MPC ALGORITHM (Model Predictive Control)



eMPC algorythm



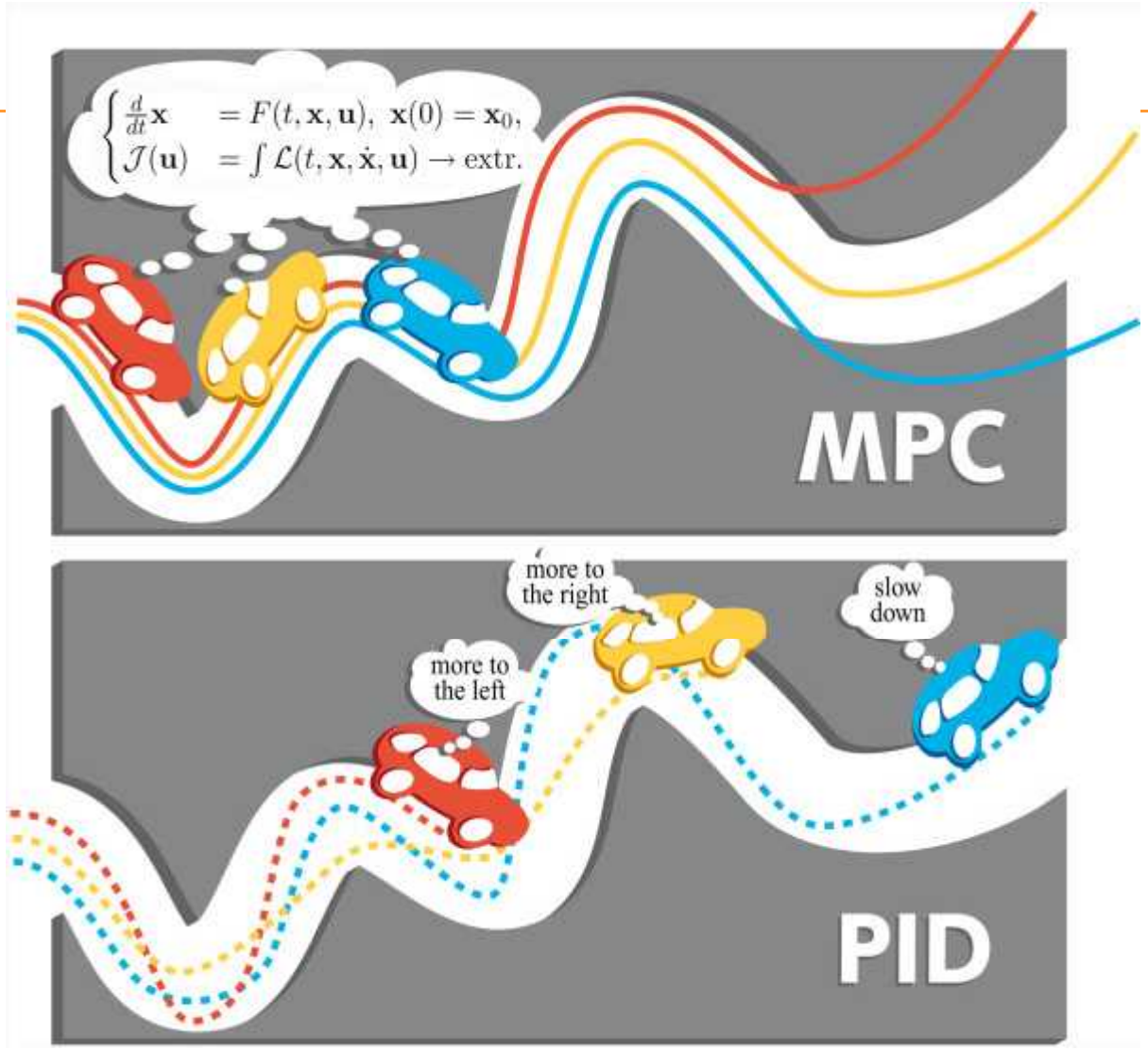


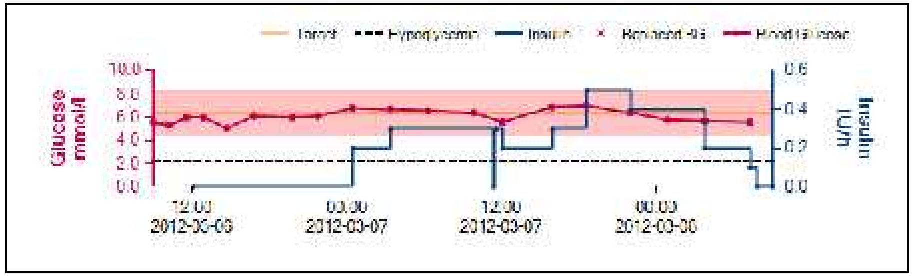
Figure 1
Model Predictive Control (MPC) versus Proportional-Integrate-Derivative (PID) control. When using MPC control, the driver determines ('calculates') his driving strategy before departure after careful investigation of the road. When he uses the correct information (input variables), he stays on the road (yellow car), but small errors in input variables can lead the car in the wrong direction (red and blue cars). The drivers using PID control readjust their driving strategy often by frequently calculating the difference with the 'ideal' track.

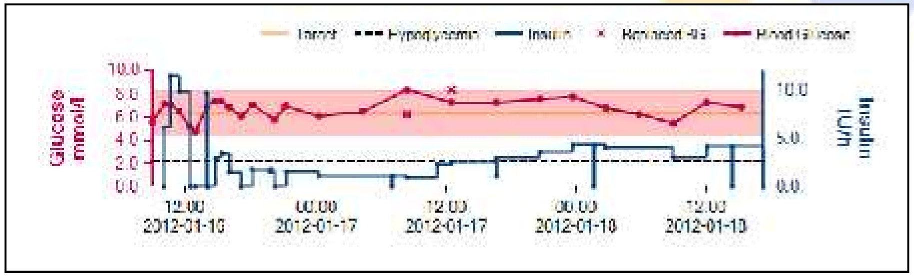
SGC

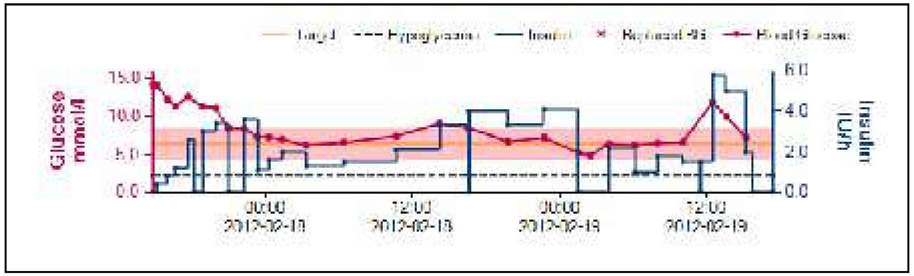
SPACE GLUCOSECONTROL

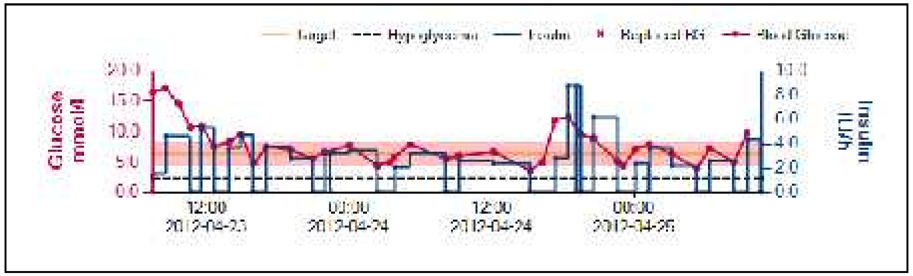
SPACE GLUCOSECONTROL

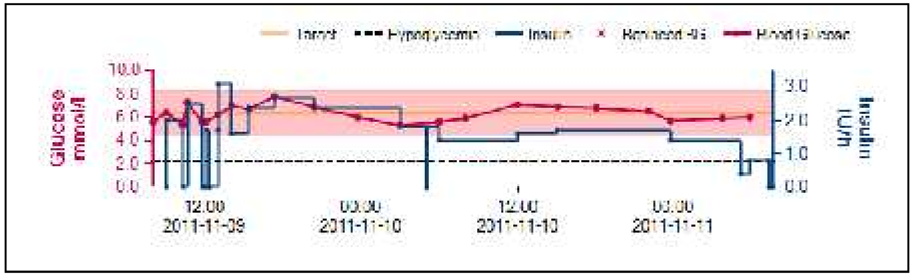
- zvýšená bezpečnost pacienta
- změny výživy jsou vzaty systémem okamžitě v potaz

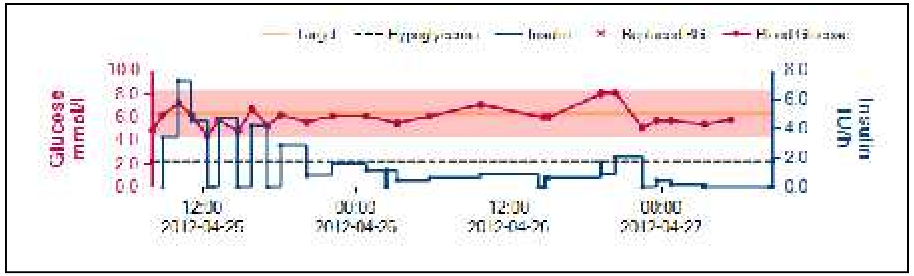

Target
Hypoglycemia
Insulin
Replaced BG
Blood Glucose
Glucose mmol/l
Insulin IU/h

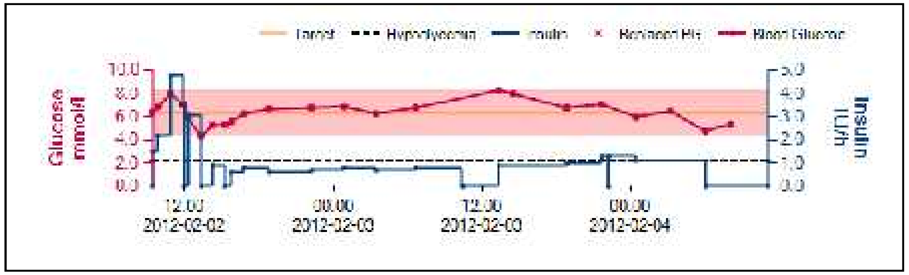

Target
Hypoglycemia
Insulin
Replaced BG
Blood Glucose
Glucose mmol/l
Insulin IU/h

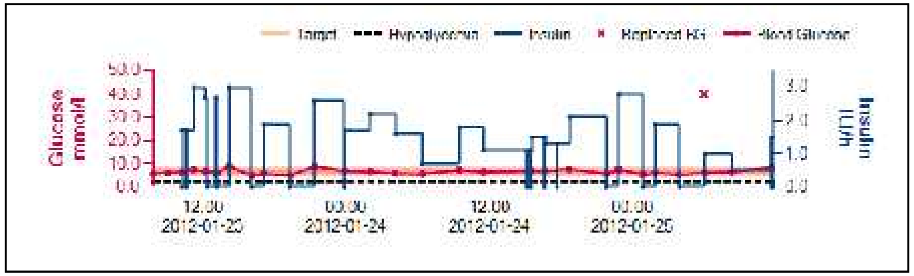

Glucose mmol/l
Insulin IU/h

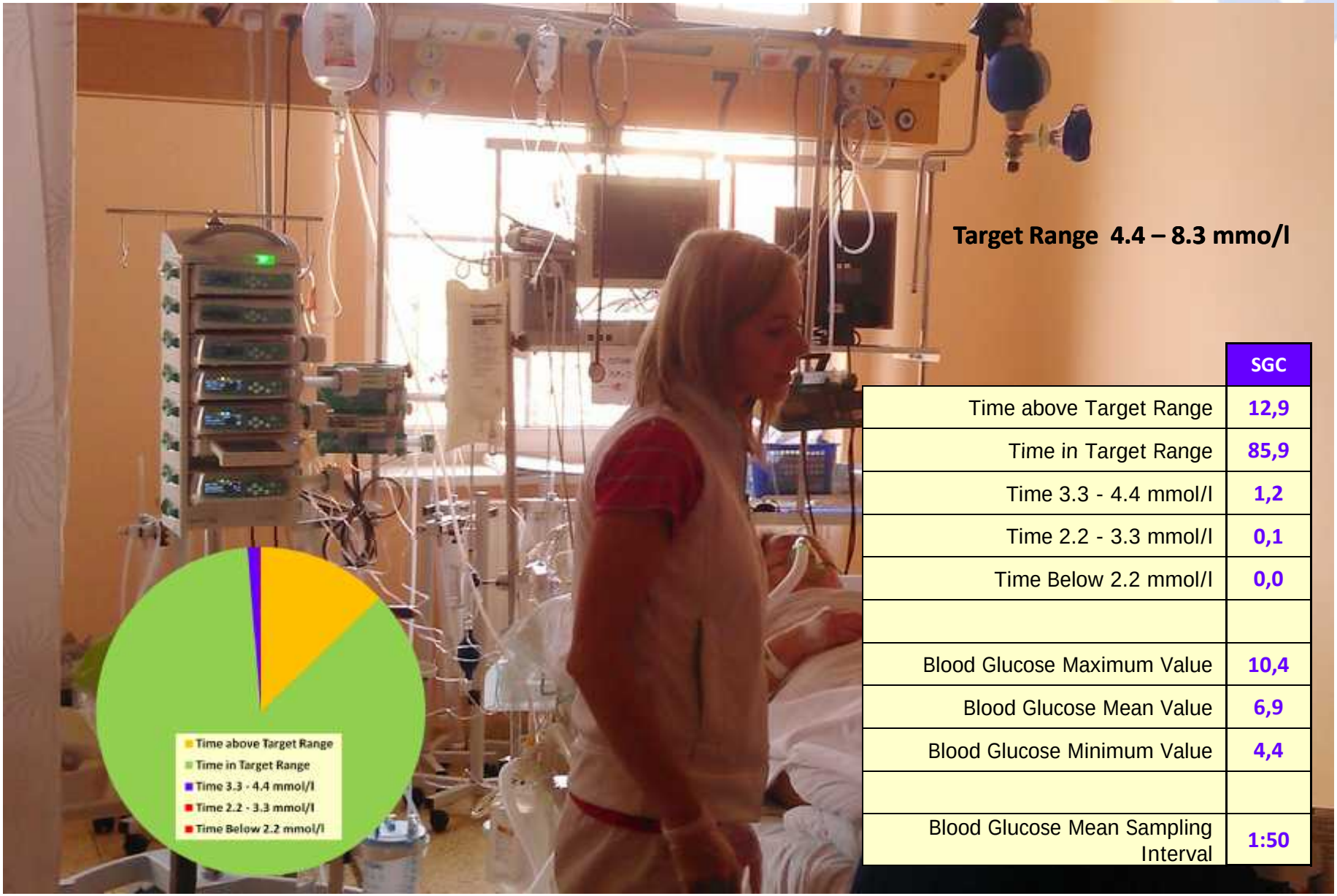

Glucose mmol/l
Insulin IU/h


Target
Hypoglycemia
Insulin
Replaced BG
Blood Glucose
Glucose mmol/l
Insulin IU/h


Glucose mmol/l
Insulin IU/h


Target
Hypoglycemia
Insulin
Replaced BG
Blood Glucose
Glucose mmol/l
Insulin IU/h

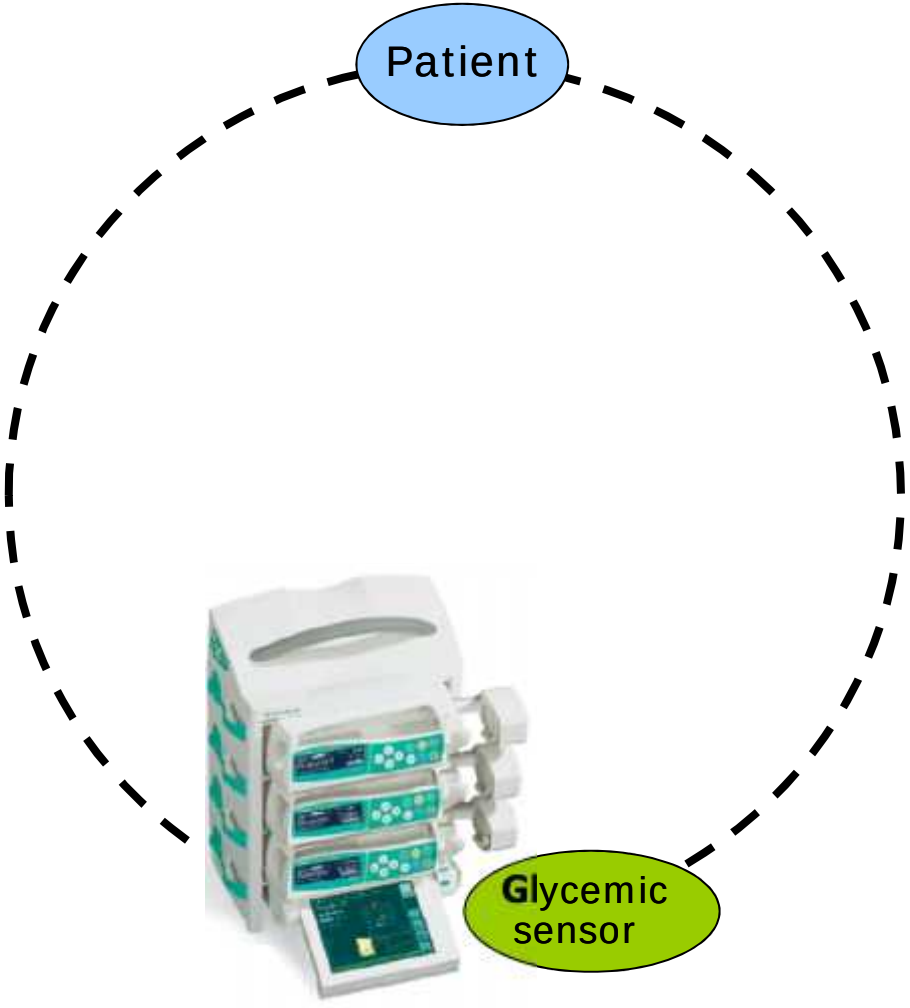

Target
Hypoglycemia
Insulin
Replaced BG
Blood Glucose
Glucose mmol/l
Insulin IU/h

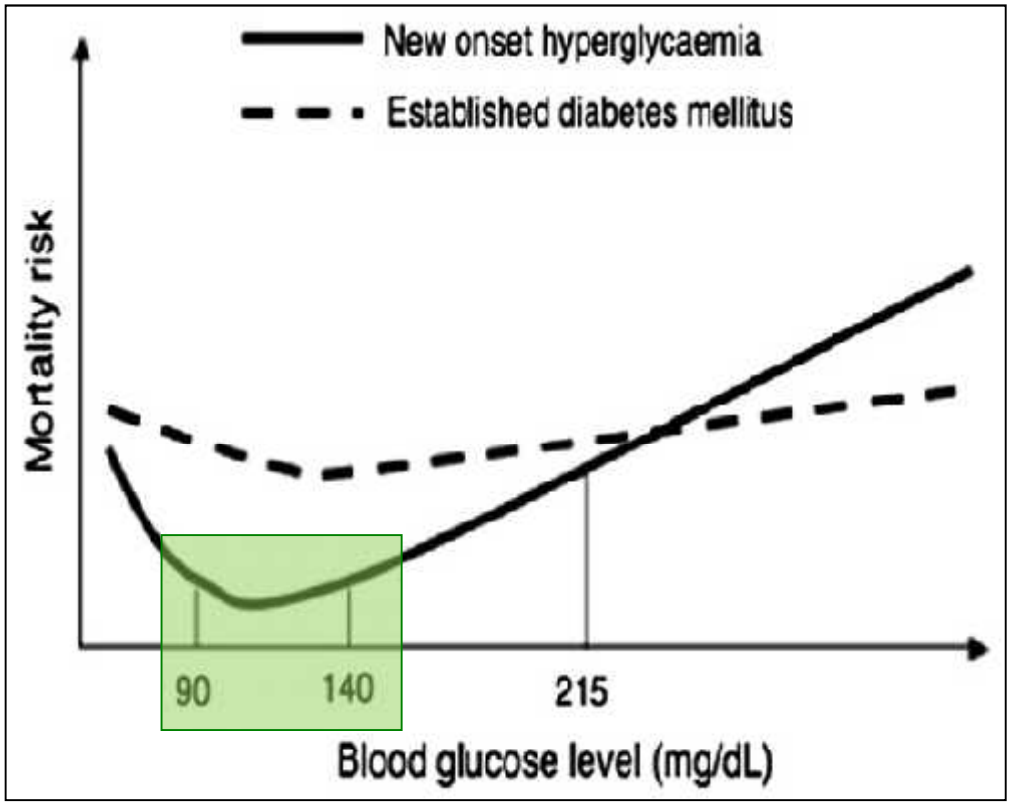


Target Range 4.4 – 8.3 mmo/l

	SGC
Time above Target Range	12,9
Time in Target Range	85,9
Time 3.3 - 4.4 mmol/l	1,2
Time 2.2 - 3.3 mmol/l	0,1
Time Below 2.2 mmol/l	0,0
Blood Glucose Maximum Value	10,4
Blood Glucose Mean Value	6,9
Blood Glucose Minimum Value	4,4
Blood Glucose Mean Sampling Interval	1:50

BUDOUCNOST …?


Patient
Glycemic sensor



D. Mesotten, G. Van den Berghe / Best Practice & Research Clinical Anaesthesiology 2009. 23:421-9

Table 1
Key differences between the Leuven studies[8,10] and NICE-SUGAR[16].

	Leuven adult studies	NICE-SUGAR
Number of patients	2748	6104
Setting	2 × 1 centre	42 centres
Patient sample (% of admission		
Methodological aspects		
Comparator group target		–10 mmol/L (140–180 mg/dL)
Intervention target		.0 mmol/L (<108 mg/dL)
Nurse instructions		trict "if-then" algorithm
Feeding route first week		eral only
Average kcal received during		) kcal/day
Therapy compliance		
Blood glucose target reached		0%
Overlap in blood glucose bet		0%
two groups		
Outcome		
Hypoglycaemia		3
Morbidity		utral
Mortality	Lowered by absolute 3%	Increased by absolute 3%
Therapy withdrawal policy	Late	Early

DĚKUJI ZA POZORNOST !

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