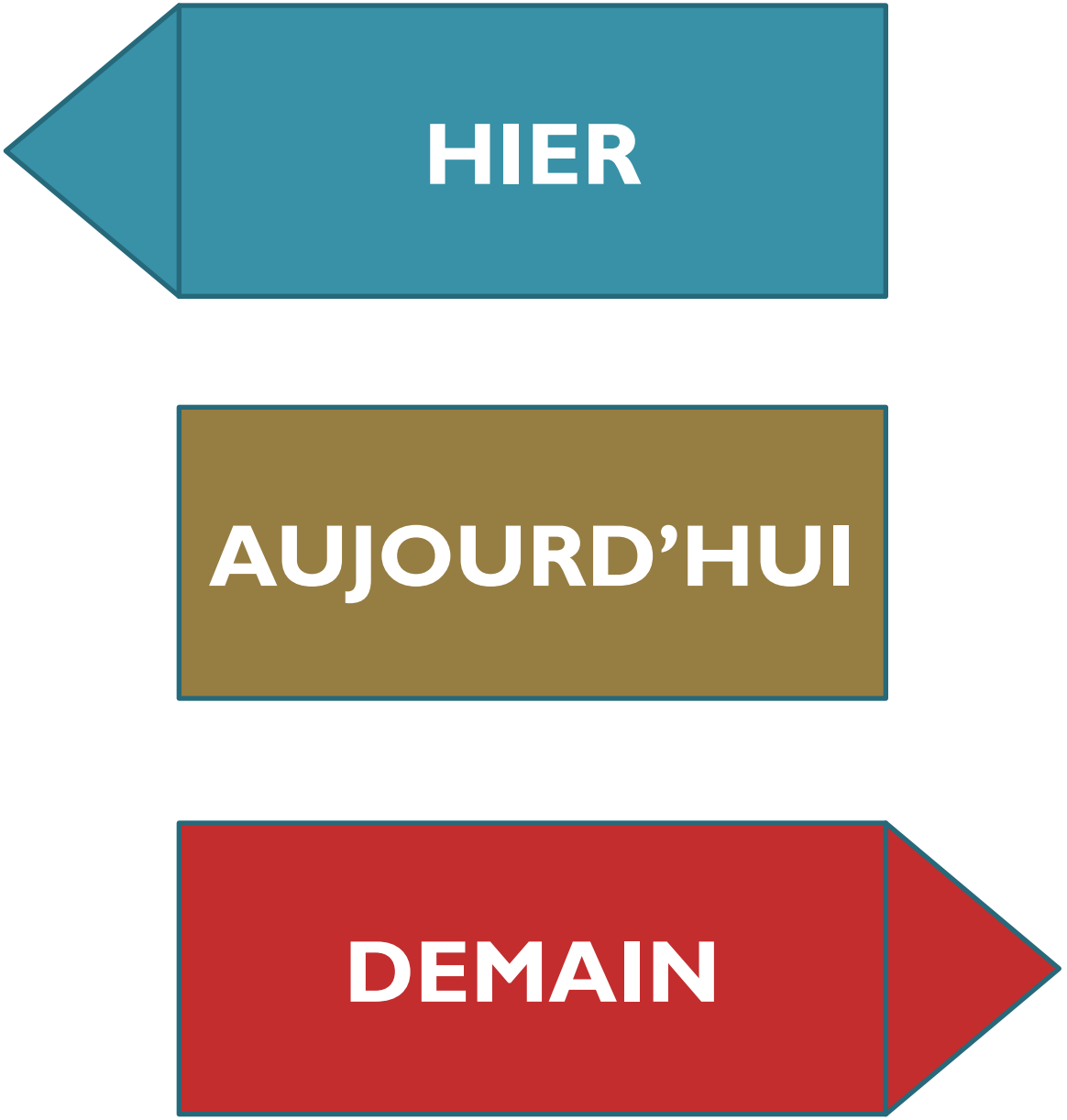
Gestion de la glycémie aux soins intensifs

Jean-Charles Preiser,
Dept Intensive care
Erasme University Hospital, Brussels

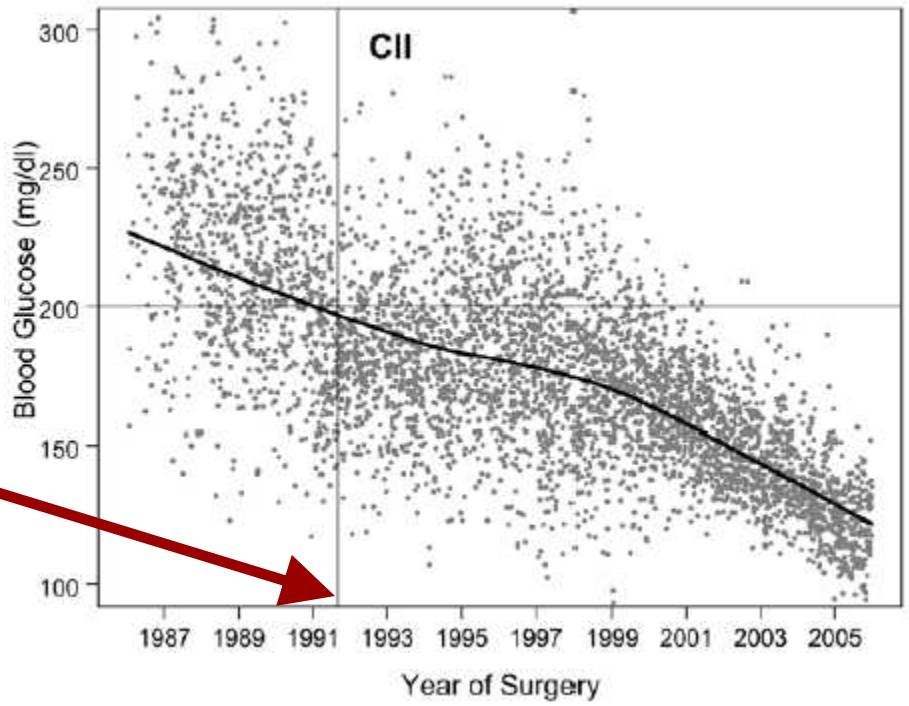
SIZ nursing
Mons
5 avril 2019


HIER
AUJOURD'HUI
DEMAIN

>1970-2009

Progressive Decline In Blood Glucose with Portland Protocol

Furnary Semin Thorac Cardiovasc Surg. 2006;18:302



Introduce Portland Protocol

RESEARCH ARTICLE

A systematic scoping review on the consequences of stress-related hyperglycaemia

Elena Olariu[1], Nicholas Pooley[1], Aurélie Danel[2], Montserrat Miret[2], Jean-Charles Preiser[3]*

1 PHMR Ltd, London, United Kingdom, **2** Nestlé Health Science, Vevey, Switzerland, **3** Department of Intensive Care, Erasme University Hospital, Université Libre de Bruxelles, Brussels, Belgium

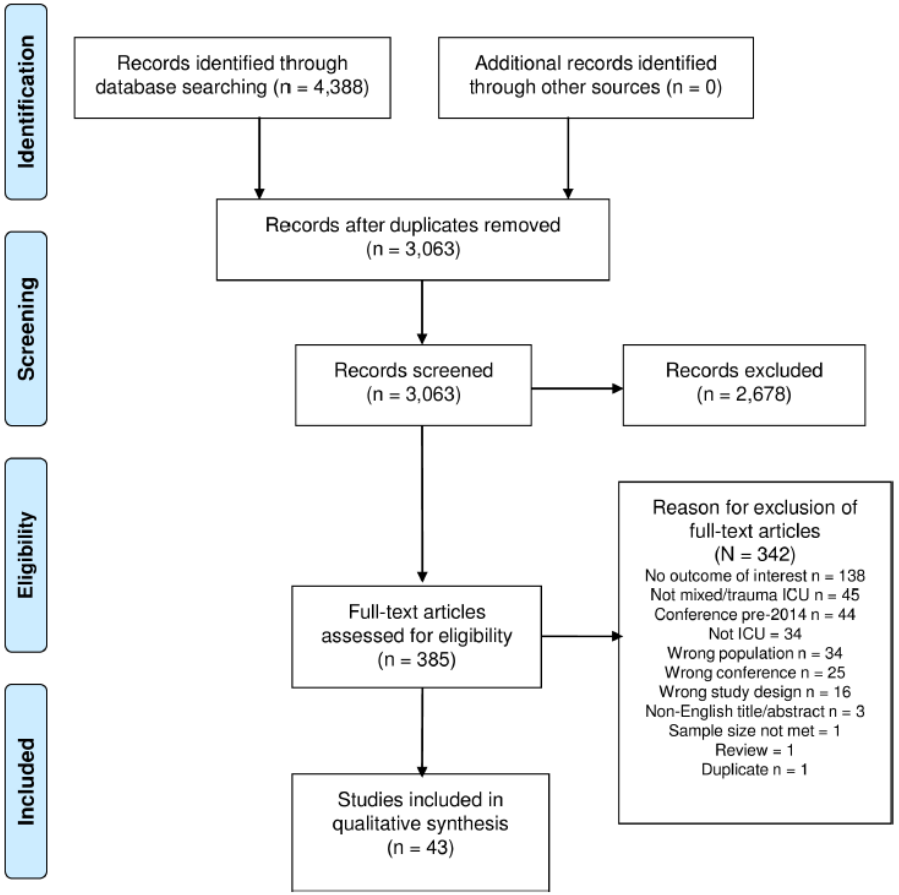


Fig 1. Flow of studies in the systematic scoping review and reasons for exclusion.

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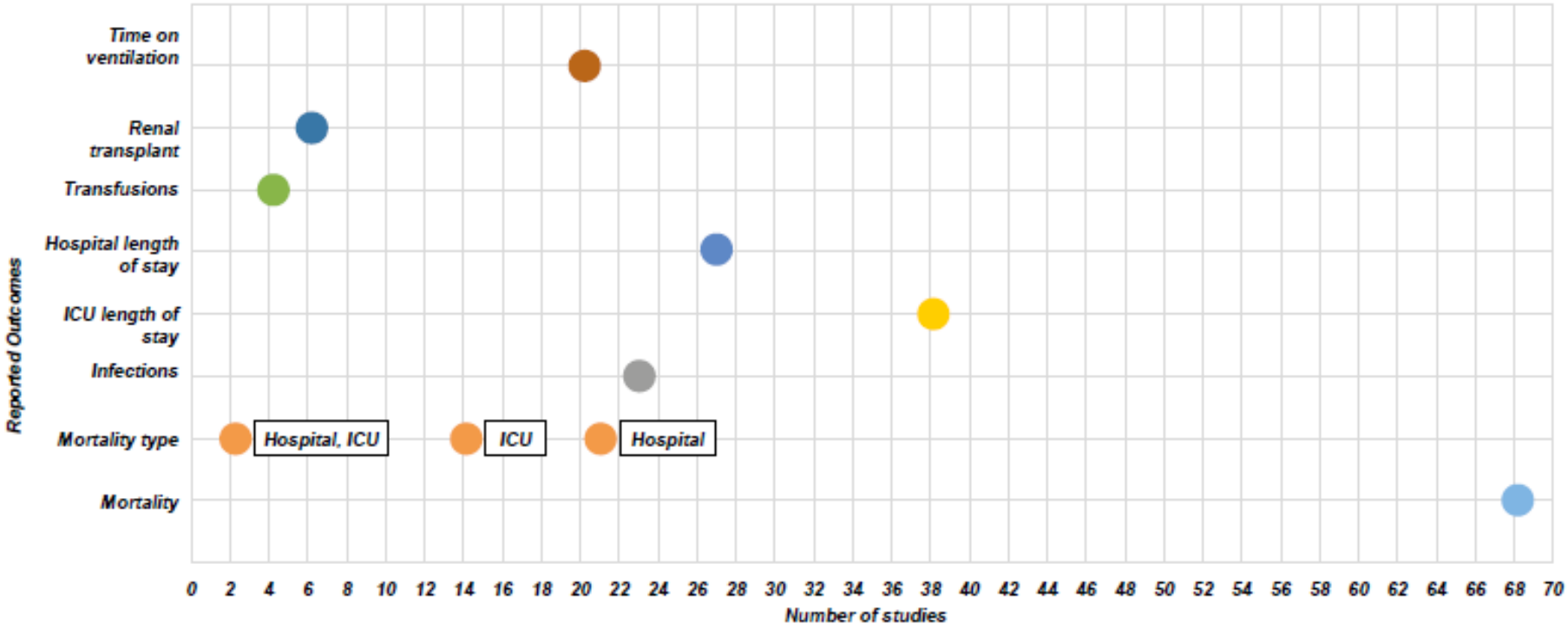

Figure 2 – Distribution of reported outcomes in observational studies on the clinical burden of hyperglycaemia in intensive care units (ICU)

RESEARCH ARTICLE

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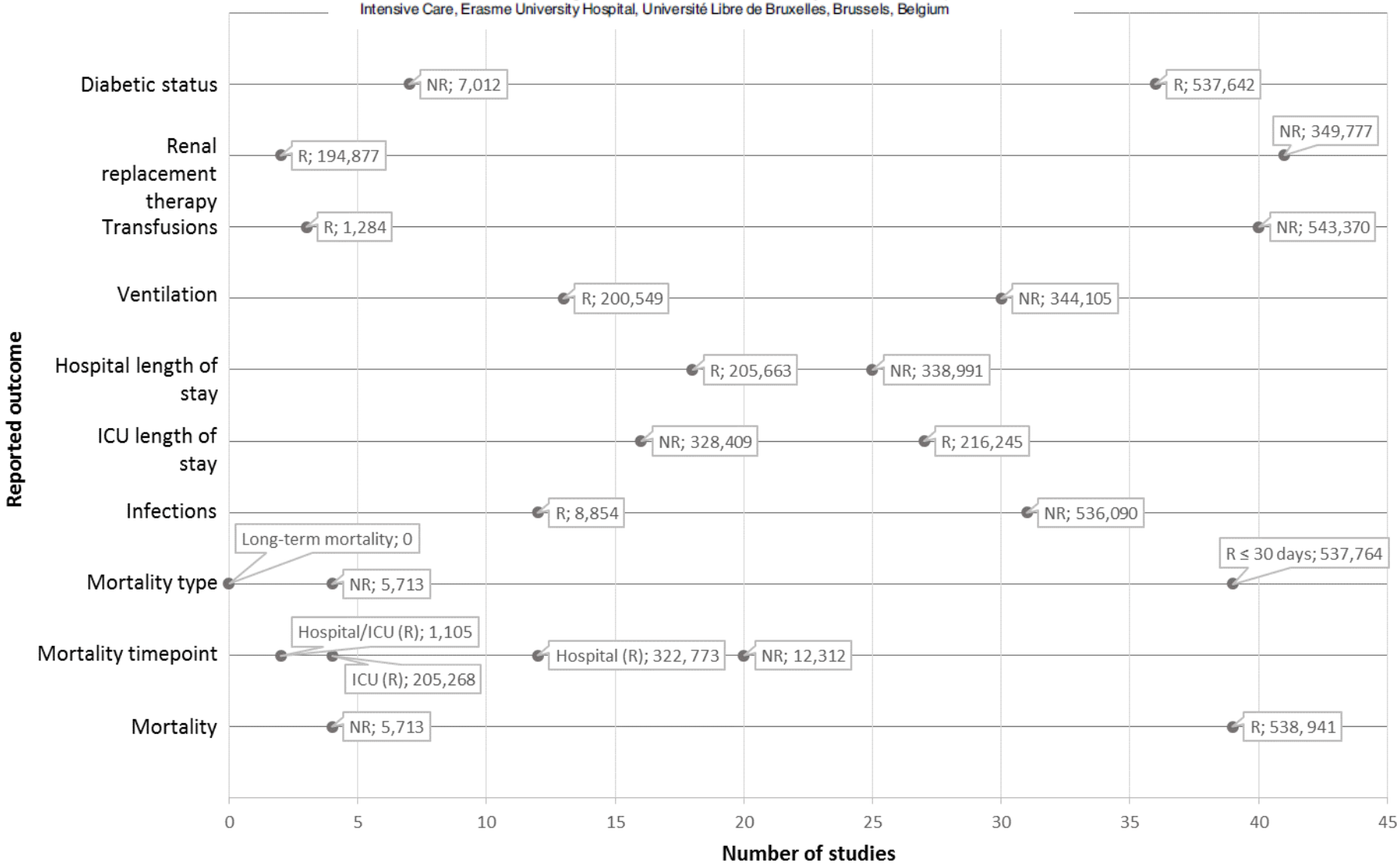

RESEARCH ARTICLE

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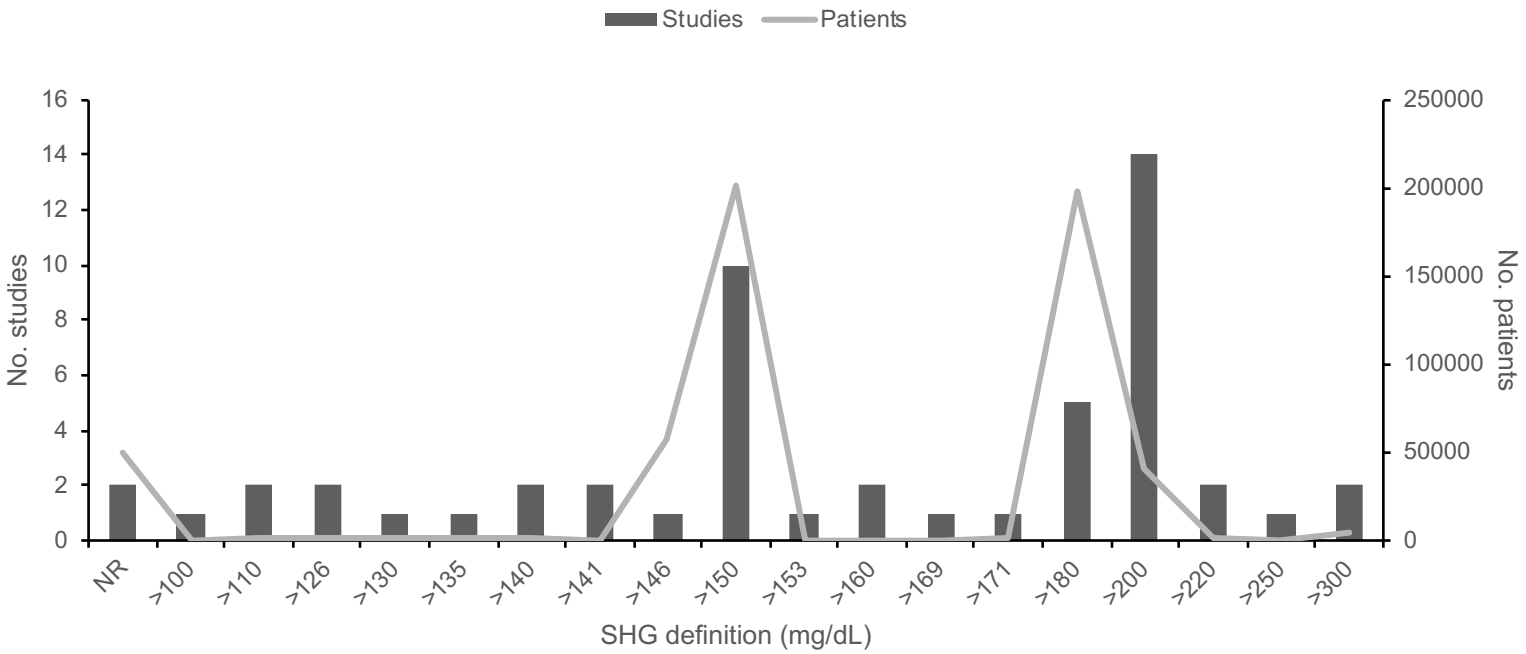



Walt Disney
Pictures Presents
CINDERELLA II
Dreams Come True
DVD

Intensive insulin therapy : Mortality

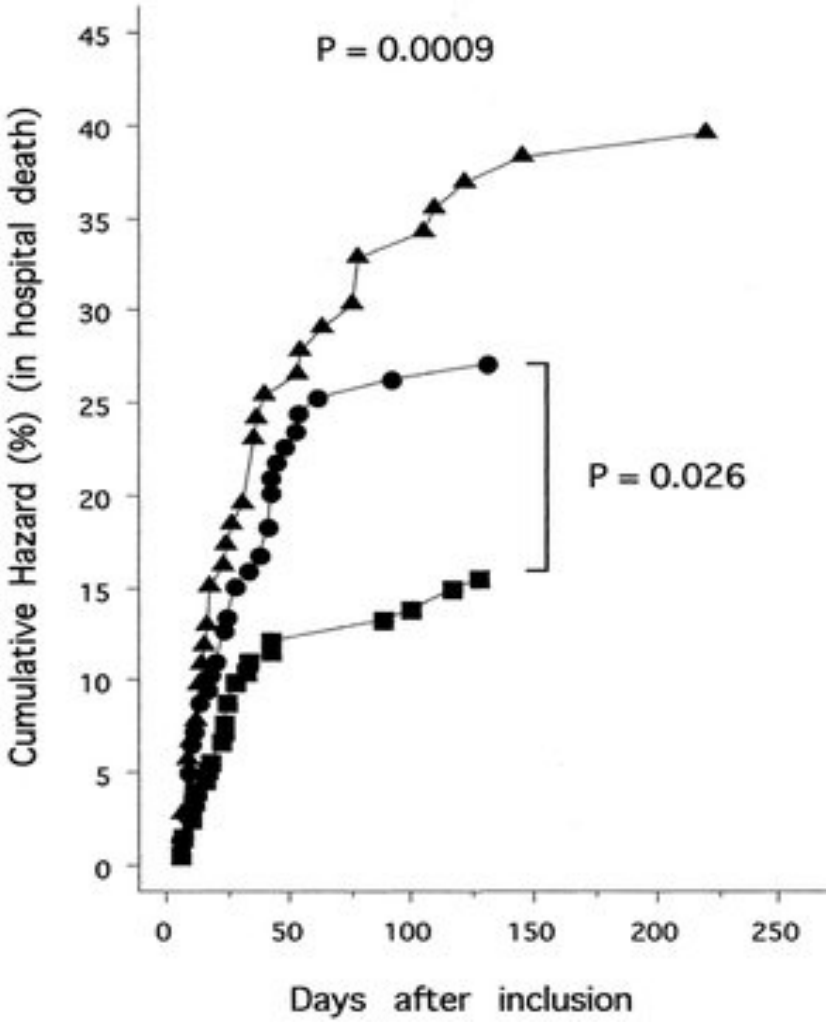
Intensive treatment → 4.4 – 6.1 mmol/L *versus*
Conventional treatment → 10.0 – 11.1 mmol/L

Result	Control	Intensive	%.	p
1. ICU mortality (%)	8.0	4.6	- 47%	< 0.004
• First 5 d. of ICU stay (%)	1.8	1.7		NS
• ICU stay > 5d (%)	20.2	10.6	- 48%	0.005
• Diabetic pat. > 5d (%)	20.6	10.7	- 48%	0.005
2. Hospital mortality (%)	10.9	7.2	- 34%	0.01

N Engl J Med 2001; 345 1359

CUMULATIVE RISK OF DEATH IN ICU PATIENTS

Squares : glycemia < 110 mg/dl
Circles: glycemia 110-150 mg/dl
Triangles: glycemia > 150 mg/dl



Van den Berghe Crit Care Med 2003;31:359

AUJOURD'HUI

2009-2019

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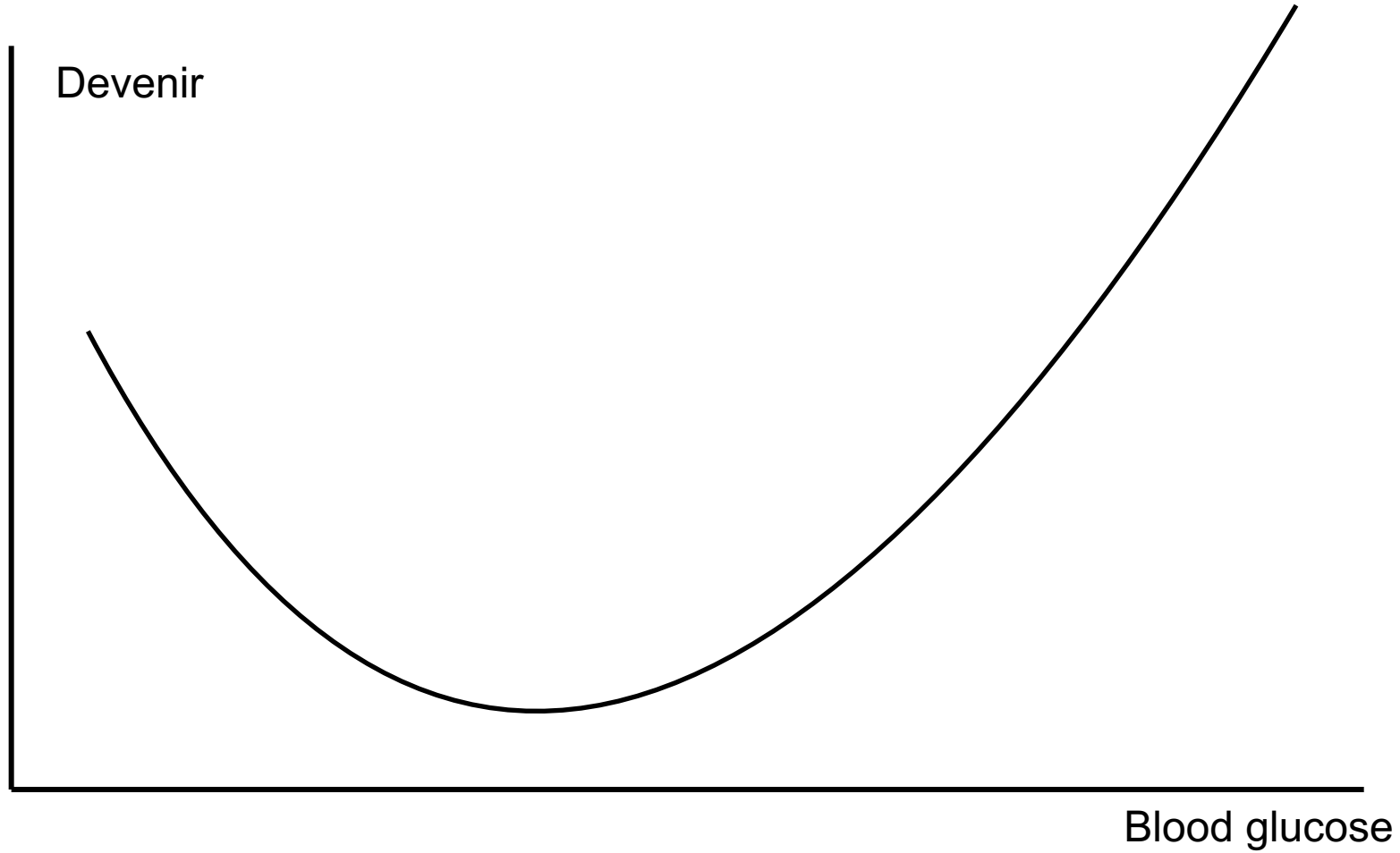
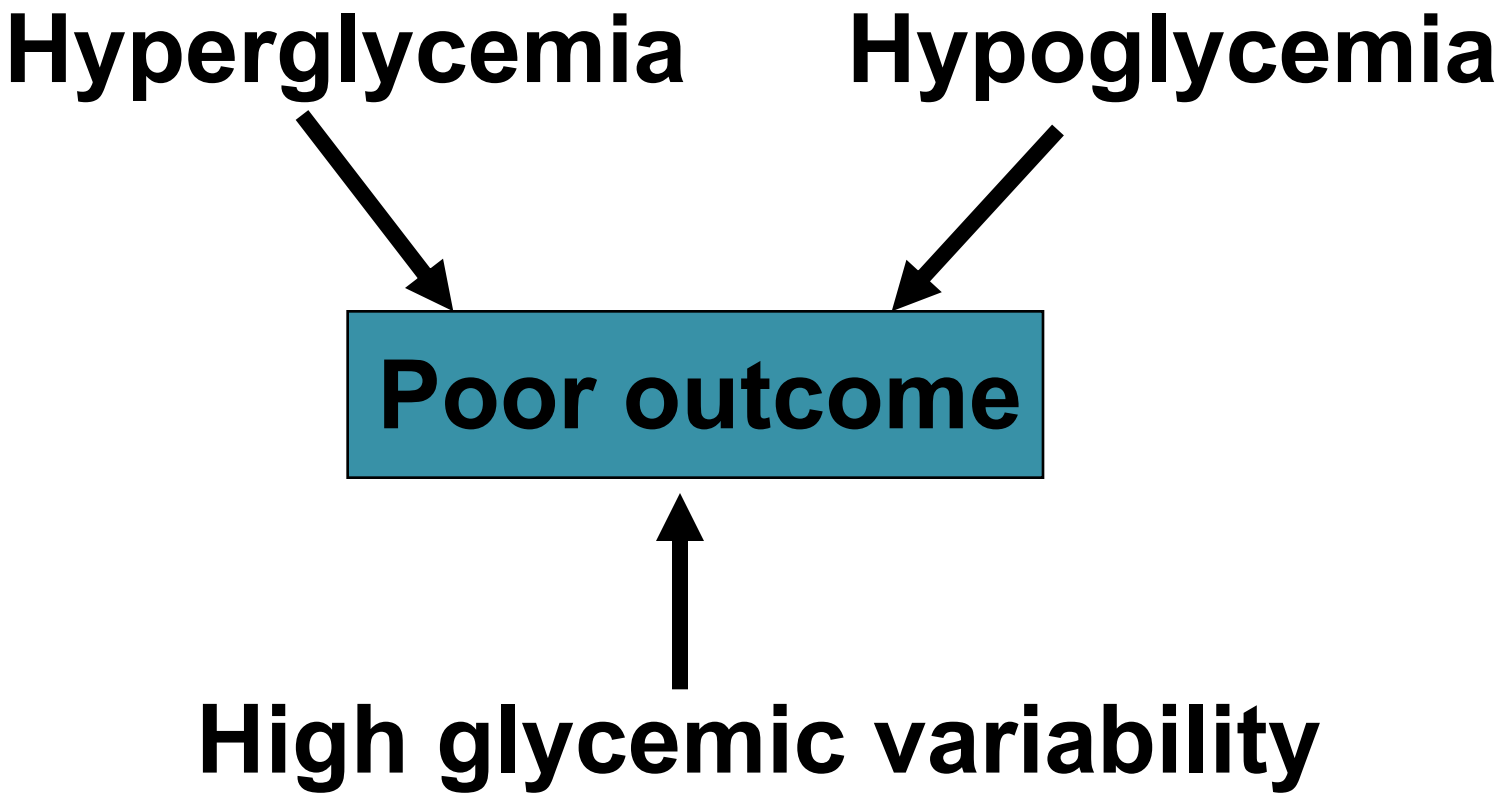


In critically ill patients…



Association between intensive care unit-acquired dysglycemia and in-hospital mortality*.

Badawi, Omar; PharmD, MPH; Waite, Michael; Fuhrman, Steven; Zuckerman, Ilene; PharmD, PhD

Critical Care Medicine. 40(12):3180-3188, December 2012.
DOI: 10.1097/CCM.0b013e3182656ae5

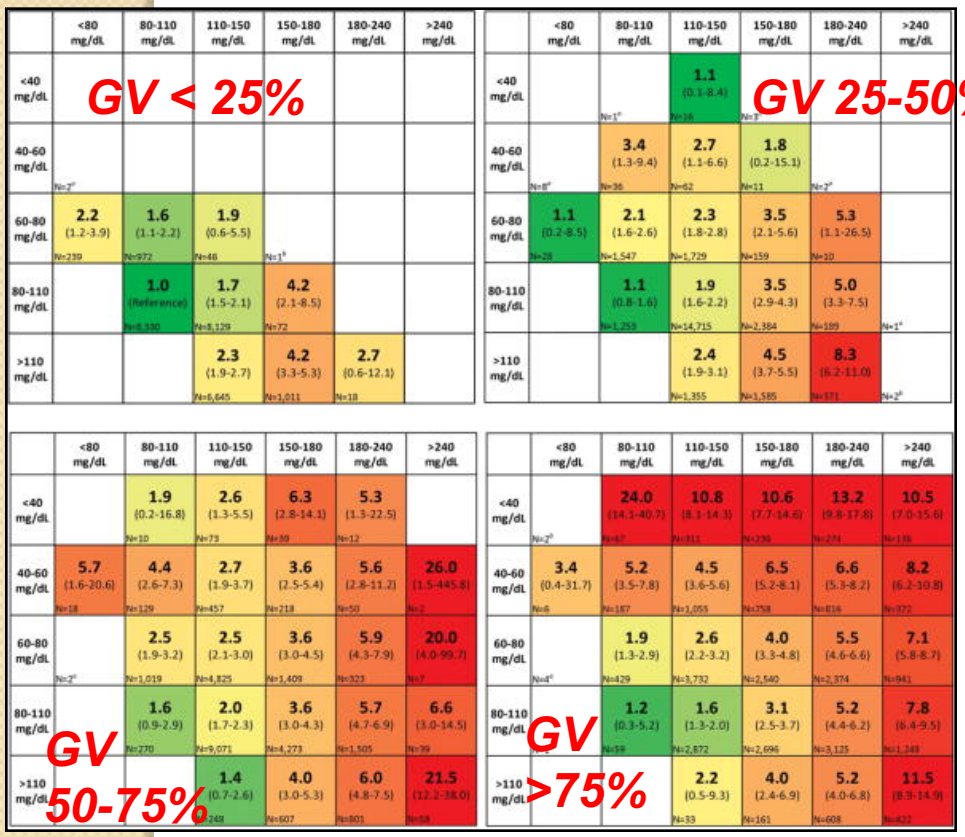
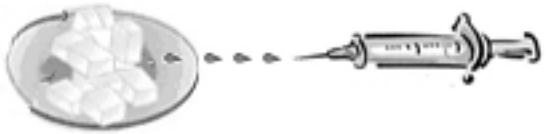


Figure 2 . Adjusted odds ratios (ORs) for hospital mortality by categories of intensive care unit (ICU)-acquired hyperglycemia, hypoglycemia, and variability. A total of 101,862 patients at risk for ICU-acquired dysglycemia are stratified by their combination of lowest single glucose value (y-axis), highest average daily glucose (x-axis), and by quartile of variability (lowest 25th percentile in top left and highest 25th percentile in bottom right).


Walt Disney
Pictures Presents
Cinderella II
Dreams Come True
DVD


By far the most terrifying film
you will ever see.
aninconvenienttruth
A GLOBAL WARNING



GLUCONTROL

A Multi-Centre Study Comparing the Effects of Two Glucose Control Regimens by Insulin in Intensive Care Unit Patients

Intensive Care Med 2009;35:1738

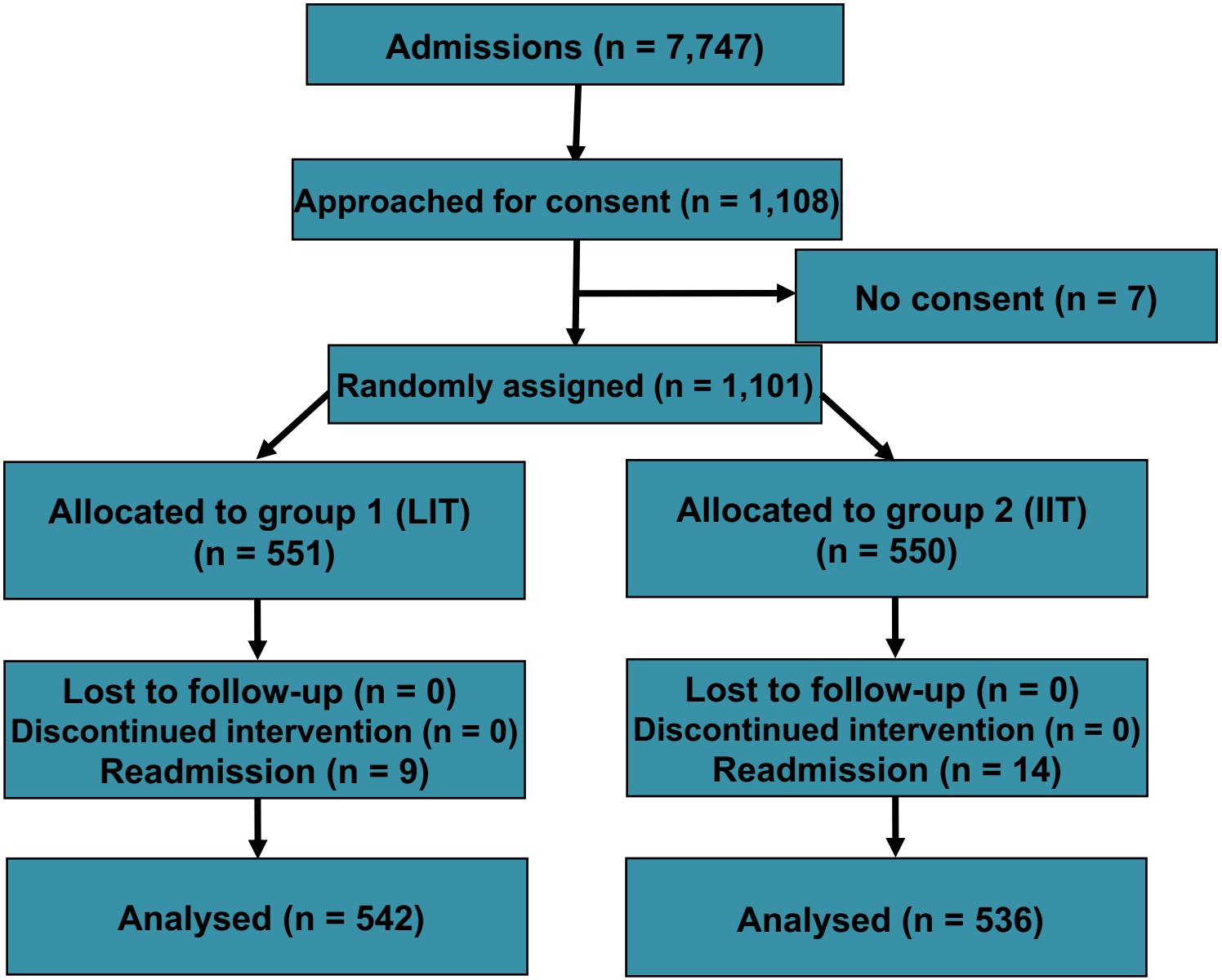
EUROPEAN CRITICAL CARE RESEARCH NETWORK

ECCRN

Endorsed by the ECCRN of the European Society of Intensive Care Medicine

EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

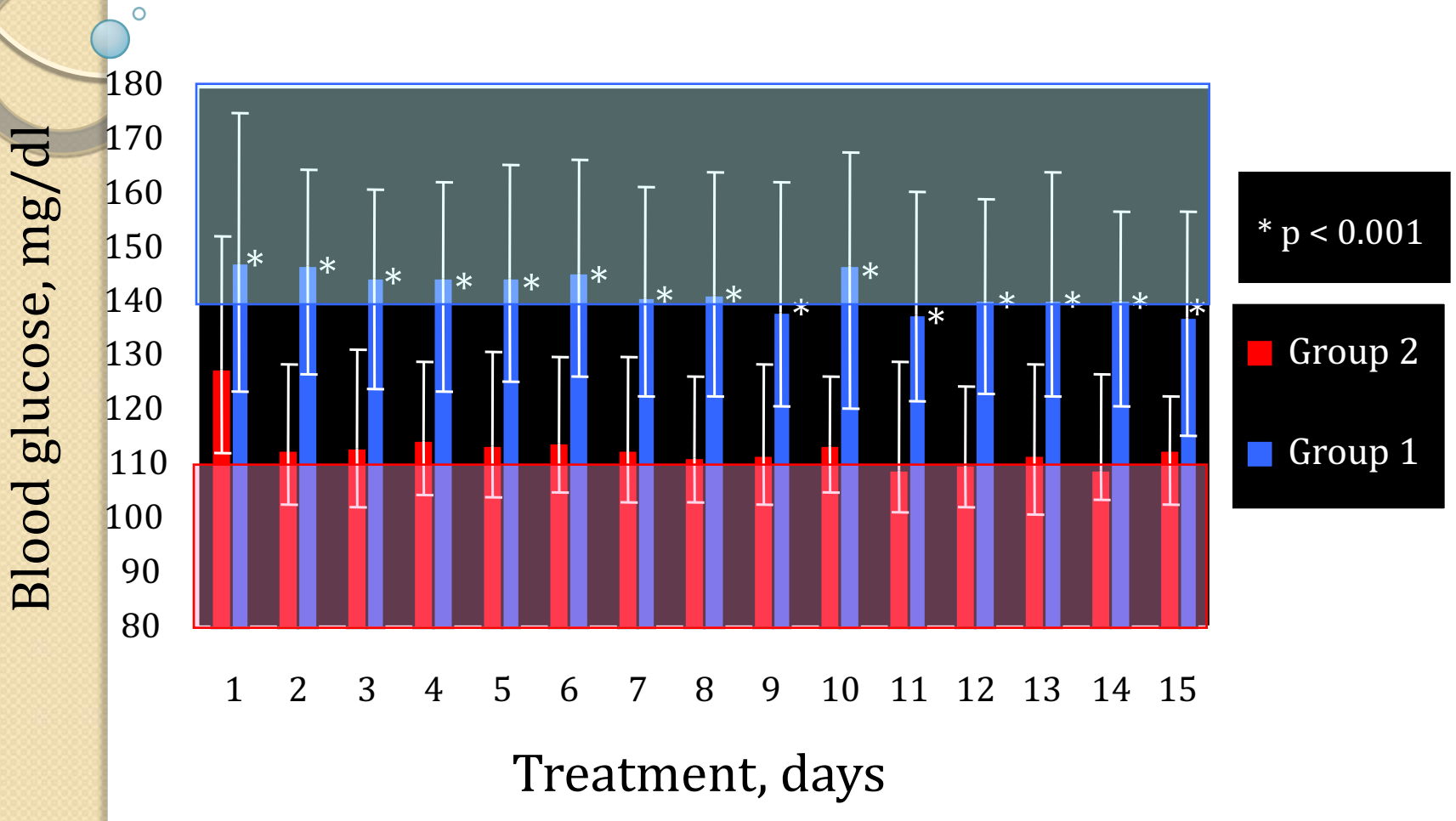
Glucontrol study flow chart



Insulin therapy

Time from admission to start of insulin drip, hours (median(IQR))	0 (0-10)	0(0-12)	0.312
Patients treated with IV insulin, % (n)	66.2 (313)	96.3 (442)	<.0001
Rate of insulin infusion (IU/h) (median(IQR))	0.32 (0-1.27)	1.30 (0.65-2.3)	<.0001
Duration of insulin treatment in hours median (IQR)	10 (0-43)	36 (13-96)	<.0001
Days on insulin (median (IQR))	2(0-5)	5(2-9)	<.0001
Insulin-free days (median (IQR))	2(0-5)	0(0-1)	<.0001

GLUCONTROL



Median with IQR

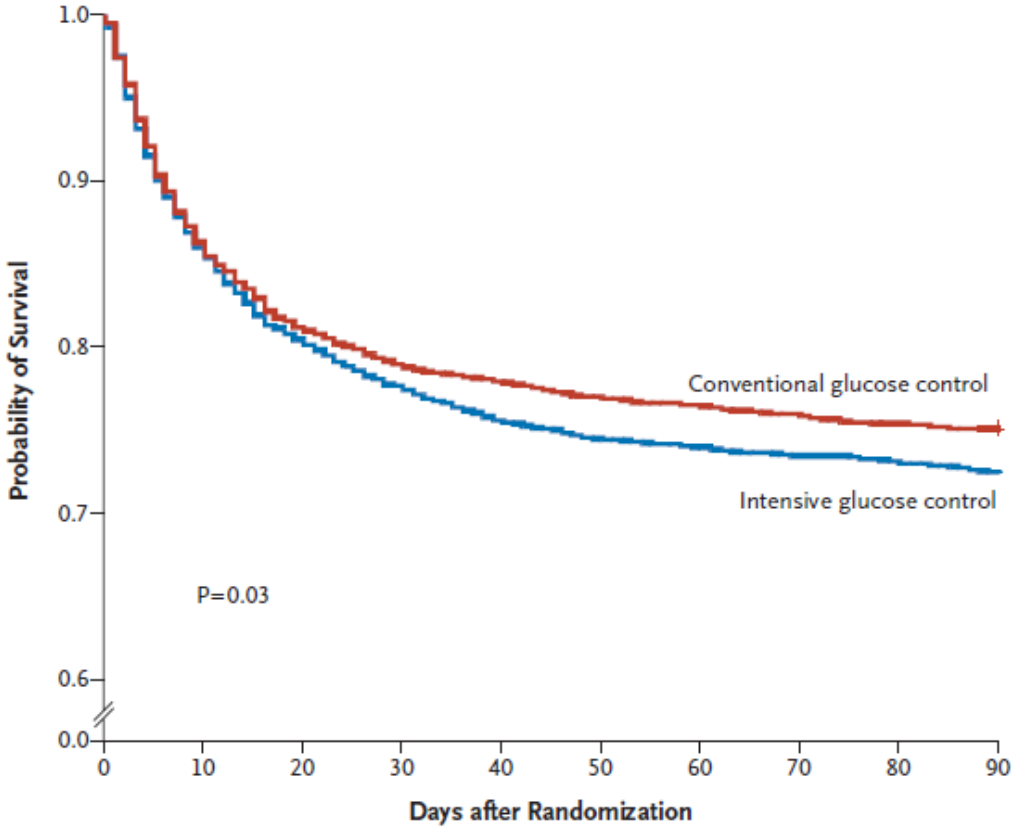
	Group 1 BG target 7.8-10.0 mmol/L N=542	Group 2 BG target 4.4-6.1 mmol/L N=536	p value
Outcome data			
ICU mortality (%)	83 (15.3)	92 (17.2)	0.410
- Short-stayers (LOS ≤ 3 days) n = 281	17/154 (11.0)	17/127 (13.4)	0.5483
- Long-stayers (LOS > 3 days) n = 787	66/388 (17.0)	75/399 (18.8)	0.5135
28-day mortality (%) **Patients still in ICU at D28 (n):**	83 (15.3) 33	100 (18.7) 34	0.1438
Hospital mortality (%)	105 (19.4)	125 (23.3)	0.1136
ICU LOS (days) (median (IQR))	6 (3-13)	6 (3-13)	0.238
Total ICU stay (LOS)	5433	5090	
Hospital LOS (days) (median (IQR))	16 (11-29)	16 (11-29)	0.708

GLUCONTROL

RISK OF DEATH

Univariable analysis			
	Crude OR	95 % CI	p
Group 2	1.28	0.88 - 1.88	0.198
Multivariable analysis			
	Adjusted OR	95 % CI	p
Group 2	1.31	0.88 – 1.95	0.178
Gender (male)	1.78	1.15 - 2.75	0.0093
Age, yr	1.02	1.01 – 1.04	0.0011
Apache II	1.04	1.02 – 1.07	0.0003
SOFA	1.08	1.01 – 1.16	0.0291

NICE-SUGAR trial



No. at Risk				
Conventional control	3014	2379	2304	2261
Intensive control	3016	2337	2227	2182

ORIGINAL ARTICLE

Tight Glycemic Control in Critically Ill Children

M.S.D. Agus, D. Wypij, E.L. Hirshberg, V. Srinivasan, E.V. Faustino, P.M. Luckett, J.L. Alexander, L.A. Asaro, M.A.Q. Curley, G.M. Steil, and V.M. Nadkarni, for the HALF-PINT Study Investigators and the PALISI Network*

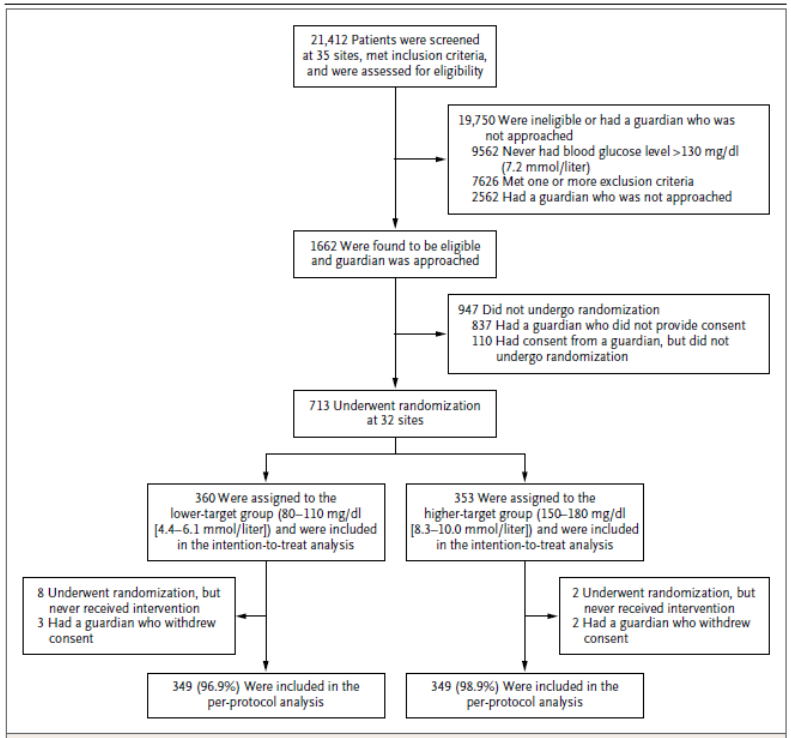


Figure 1. Assessment, Randomization, and Follow-up of the Study Patients.

The informed-consent rate was 50% (825 of 1662 patients). Only patients with a measured blood glucose level greater than 130 mg per deciliter were assessed for exclusion criteria. Two additional patients underwent randomization and were in the study when it was stopped early; these patients are not included in the analyses according to the stipulation of the data and safety monitoring board. Additional details are provided in Tables S1 and S2 in the Supplementary Appendix.

Tight Glycer

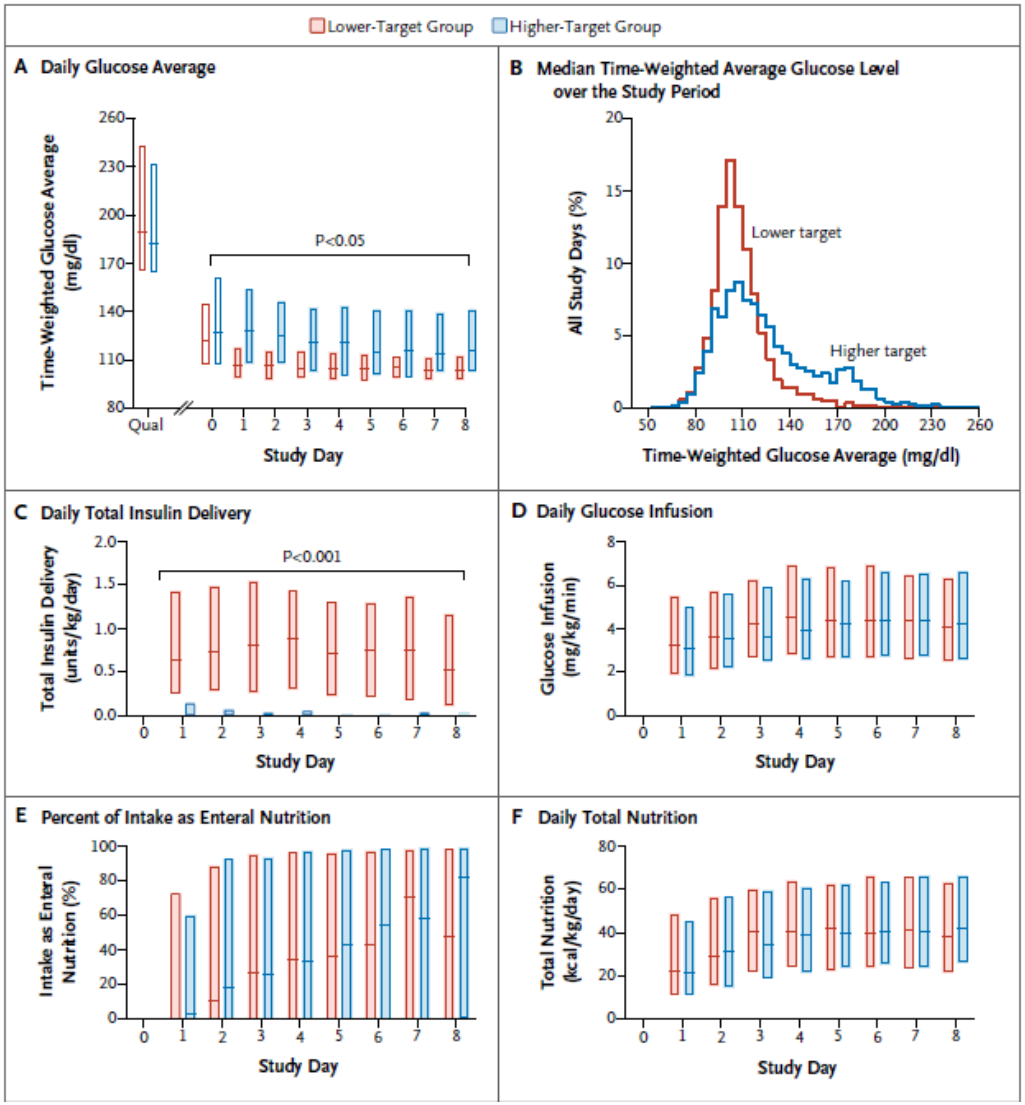
M.S.D. Agus, D. Wypij, E.L.
J.L. Alexander, L.A. Asar
for the HALF-PINT

Table 1. Characteristics of the Study Patients at Baseline, According to Study Group.*

Characteristic	Lower Target (N=349)	Higher Target (N=349)
Age at ICU admission		
Median (IQR) — yr	5.5 (1.4–12.5)	6.7 (1.7–12.8)
Age group — no. (%)		
<2 yr	100 (28.7)	101 (28.9)
2 to <7 yr	94 (26.9)	82 (23.5)
7 to <18 yr	155 (44.4)	166 (47.6)
Female sex — no. (%)	164 (47.0)	169 (48.4)
Black race — no./total no. (%)†	86/336 (25.6)	85/335 (25.4)
Hispanic ethnic group — no./total no. (%)†	79/348 (22.7)	82/347 (23.6)
Pediatric Cerebral Performance Category of 1 — no. (%)‡	242 (69.3)	237 (67.9)
Pediatric Overall Performance Category of 1 — no. (%)‡	226 (64.8)	217 (62.2)
Any known genetic syndrome — no. (%)	59 (16.9)	69 (19.8)
Primary reason for ICU admission — no. (%)		
Respiratory, including infection	182 (52.1)	183 (52.4)
Cardiovascular, including shock	58 (16.6)	51 (14.6)
Neurologic	30 (8.6)	34 (9.7)
Traumatic	35 (10.0)	24 (6.9)
Postoperative care	18 (5.2)	31 (8.9)
Gastrointestinal or hepatic	16 (4.6)	15 (4.3)
Other§	10 (2.9)	11 (3.2)
Insulin at randomization — no. (%)	44 (12.6)	57 (16.3)
Glucocorticoid therapy at randomization — no. (%)	184 (52.7)	178 (51.0)
Inotropic support for hypotension at randomization — no. (%)	182 (52.1)	168 (48.1)
Invasive mechanical ventilation at randomization — no. (%)		
Endotracheal tube	336 (96.3)	331 (94.8)
Tracheostomy	8 (2.3)	13 (3.7)
None	5 (1.4)	5 (1.4)
ECMO at randomization — no. (%)	13 (3.7)	20 (5.7)
PRISM III-12 score¶		
Median	12	12
IQR	7–19	7–18
Risk of death in the ICU, according to PRISM III-12 score — %		
Median	11.7	9.5
IQR	2.7–39.1	2.9–30.9

ORIGINAL ARTICLE

Tight Glycemic Control in Critically Ill



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M.S.D. Agus, D. Wypij, E.L. Hirshberg, V. Srinivasan, E.V. Faustino, P.M. Luckett, J.L. Alexander, L.A. Asaro, M.A.Q. Curley, G.M. Steil, and V.M. Nadkarni, for the HALF-PINT Study Investigators and the PALISI Network*

Table 3. Study Outcomes and Adverse Events, According to Study Group, in the Per-Protocol Population.

Variable	Lower Target (N=349)	Higher Target (N=349)	P Value*
No. of ICU-free days through day 28			0.86
Median	20.0	19.4	
IQR	1.0–24.2	7.1–23.9	
Assigned zero ICU-free days — no. (%)	87 (24.9)	70 (20.1)	0.14
Died by day 28	47 (13.5)	32 (9.2)	
Did not meet ICU discharge criteria by day 28	33 (9.5)	37 (10.6)	
Transferred to an ICU in a nonparticipating institution by day 28	7 (2.0)	1 (0.3)	
No. of ventilator-free days through day 28			0.84
Median	21.8	20.9	
IQR	8.4–25.0	11.9–24.4	
No. of hospital-free days through day 28			0.60
Median	8	6	
IQR	0–17	0–16	
Hospital mortality — no. (%)			
At day 28	47 (13.5)	32 (9.2)	0.09
At day 90	52 (14.9)	40 (11.5)	0.22
Maximum PELOD score†			0.38
Median	13	13	
IQR	11–23	11–22	

CHEST

Original Research

CRITICAL CARE MEDICINE

Toward Understanding Tight Glycemic Control in the ICU

A Systematic Review and Metaanalysis

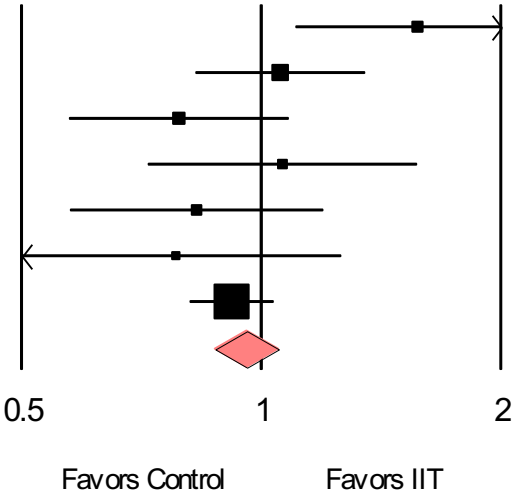
Paul E. Marik, MD, FCCP; and Jean-Charles Preiser, MD

CHEST 2010; 137(3):544–551

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Van den Berghe-2001	1.572	1.102	2.242	2.498	0.012
Van den Berghe-2006	1.057	0.826	1.353	0.441	0.659
Glucotrol-2006	0.788	0.573	1.085	-1.460	0.144
VISEP-2008	1.064	0.720	1.572	0.310	0.757
De La Rosa-2008	0.830	0.574	1.199	-0.994	0.320
Arabi-2008	0.781	0.484	1.262	-1.009	0.313
NICE-SUGAR 2009	0.918	0.812	1.038	-1.361	0.173
	0.954	0.871	1.046	-0.995	0.320

Statistics for each study

Odds ratio and 95% CI



Meta Analysis

CHEST

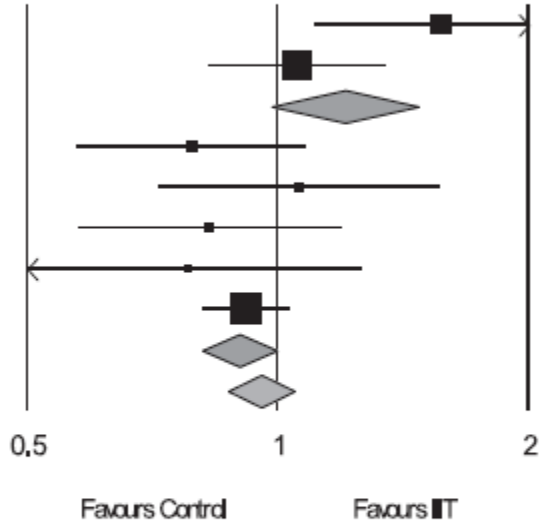
Original Research

CRITICAL CARE MEDICINE

Toward Understanding Tight Glycemic Control in the ICU

A Systematic Review and Metaanalysis

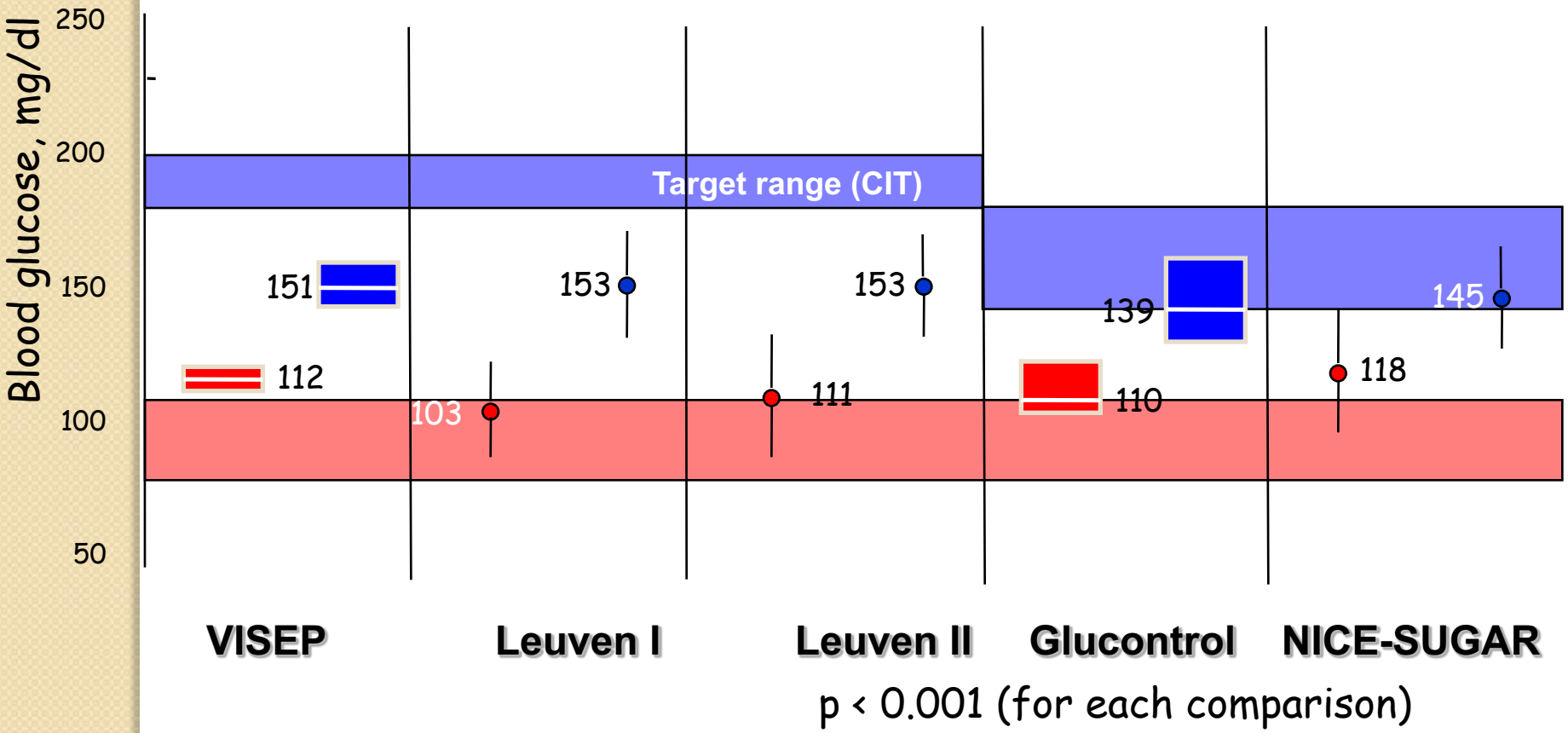
Group by Nutrition	Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
a-TPN	Van den Berghe-2001	1.572	1.102	2.242	2.498	0.012
a-TPN	Van den Berghe-2006	1.057	0.826	1.353	0.441	0.659
a-TPN		1.203	0.982	1.474	1.789	0.074
b-ENT	Glucotrol-2006	0.788	0.573	1.085	-1.460	0.144
b-ENT	VISEP-2008	1.064	0.720	1.572	0.310	0.757
b-ENT	De La Rosa-2008	0.830	0.574	1.199	-0.994	0.320
b-ENT	Arabi-2008	0.781	0.484	1.262	-1.009	0.313
b-ENT	NICE-SUGAR 2009	0.918	0.812	1.038	-1.361	0.173
b-ENT		0.899	0.811	0.997	-2.025	0.043
Overall		0.954	0.871	1.046	-0.995	0.320



Meta Analysis

FIGURE 2. Effect of intensive insulin therapy (IIT) on 28-day mortality. a-TPN = parenteral nutrition; b-ENT = enteral nutrition.

BG TARGET IS NOT ALWAYS REACHED !



p < 0.001 (for each comparison)

simplicity versus complexity of implementation of potentially important factors of SGC

easy, simple, distinct and/or clear ← → obscure, indistinct, complex and/or difficult

levels of implementation of SGC

monitoring

Blood Glucose Measurement

what?
arterial blood*
central *or* peripheral
venous blood
capillary

Blood Glucose Measurement

where and how?
at bedside* – blood gas analyzer* *or*
point–of–care device
central laboratory

Blood Glucose Measurement

what?
whole blood*
plasma *or* serum

Blood Glucose Measurement

accurateness?
calibrated* or non –
calibrated devices

insulin delivery

Delivery of Insulin

how?
subcutaneous infusion
peripheral intravenous infusion
central venous infusion*
variations in delivery introduced by co–infusion

Delivery of Insulin

how?
accurate syringe pumps*
volumetric pumps
other

algorithm

SGC algorithm: insulin dosing

from **simple set of rules*** to guidelines of increasing complexity
accepting higher incidence of (mild) hypoglycemia* to fear for (severe) hypoglycemia
accuracy (insulin change should neither be too big nor too small, or changed in the wrong direction)

SGC algorithm: blood glucose measurement timing

from measurements **at strict time points and in between if necessary*** to *a* loose schedule or no schedule at all
punctuality (blood glucose should be measured neither too early nor too late)

Glucose administration

continuous glucose infusion*
balanced enteral feeding/parenteral feeding*

SGC algorithm

"closed loop"
between blood glucose
level and insulin infusion

SGC algorithm

decision support
i.e., with computer
or sliding scales, etc.

SGC algorithm

"expertise"–based*

performance

Training

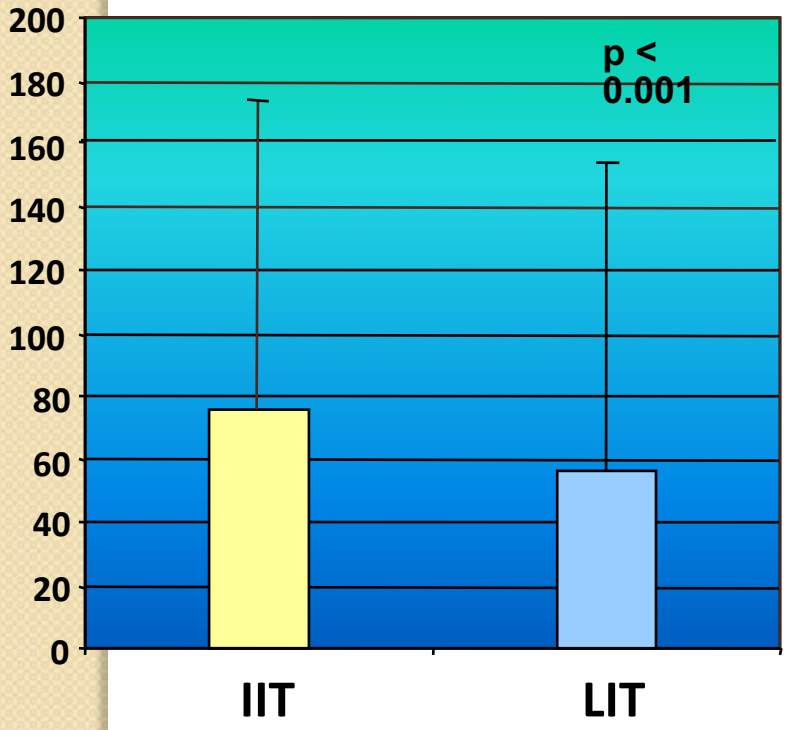
skill*
motivation*

Schultz M. ***Crit Care.*** 2010;14:223

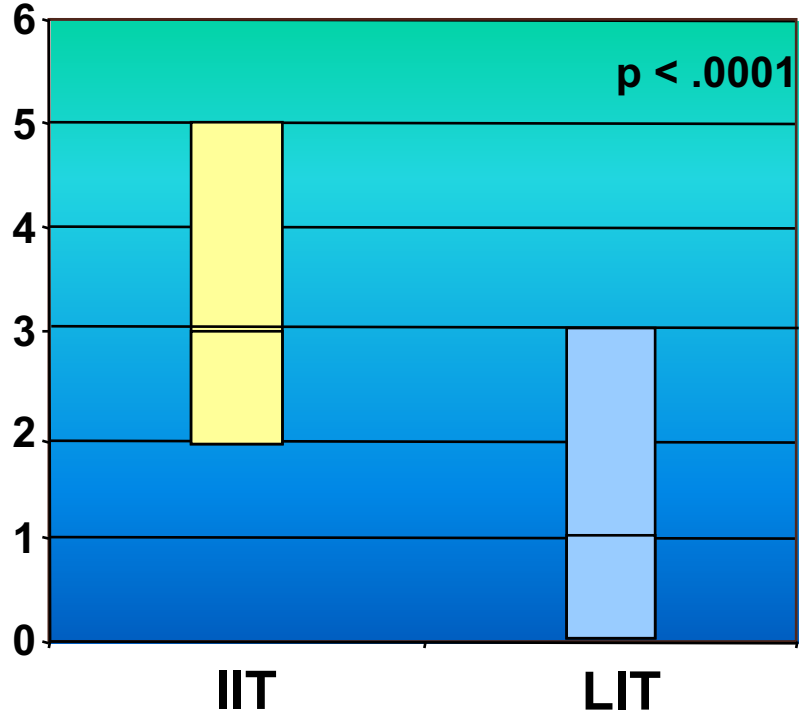
Effects of TGC on nursing workload

Perreaux et al Intensive Care Med 2007 (abstract)

Number of BG checks / stay

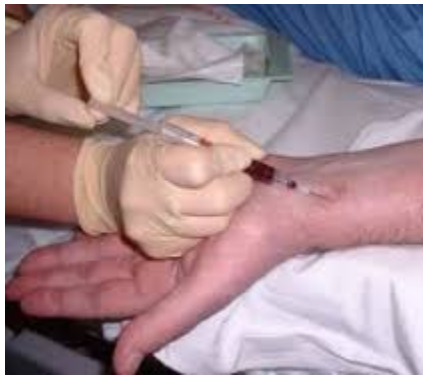


Number of changes in insulin rate/day



In the IIT group, the time devoted to glucose management is increased by 17%, as compared to the LIT group

Comment mesurer ?



Ichai *et al. Critical Care* 2010, **14**:R166
http://ccforum.com/content/14/5/R166

CRITICAL CARE

RESEARCH Open Access

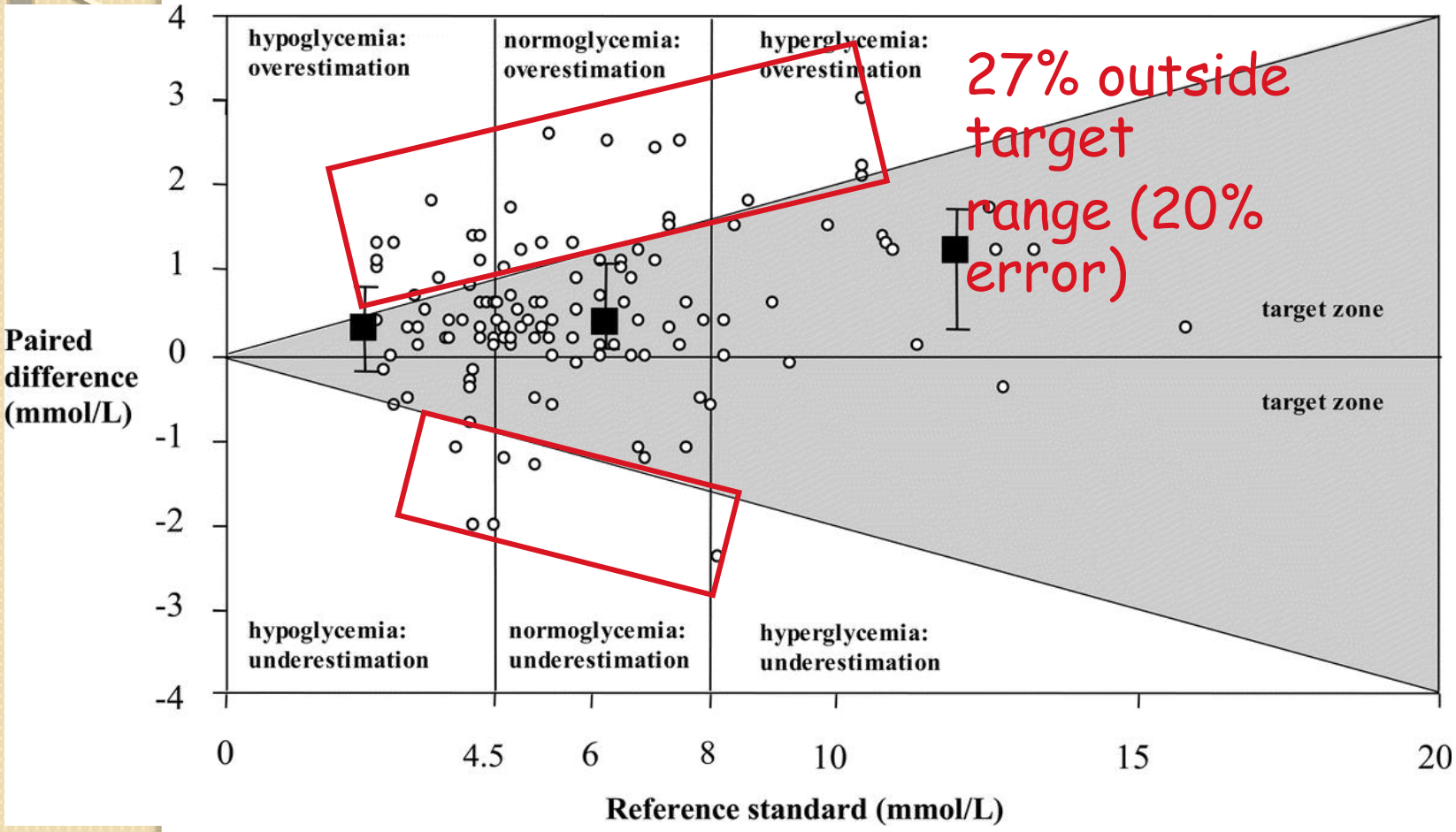
International recommendations for glucose control in adult non diabetic critically ill patients

Carole Ichai[1], Jean-Charles Preiser[2*], for the Société Française d'Anesthésie-Réanimation (SFAR)[3], Société de Réanimation de langue Française (SRLF) and the Experts group[4]

- Il est recommandé de réaliser des mesures de glucose via le laboratoire; cela reste la technique standard actuel.
- Mesurer le glucose dans l'ordre préférentiel suivant : artériel, veineux, capillaire.

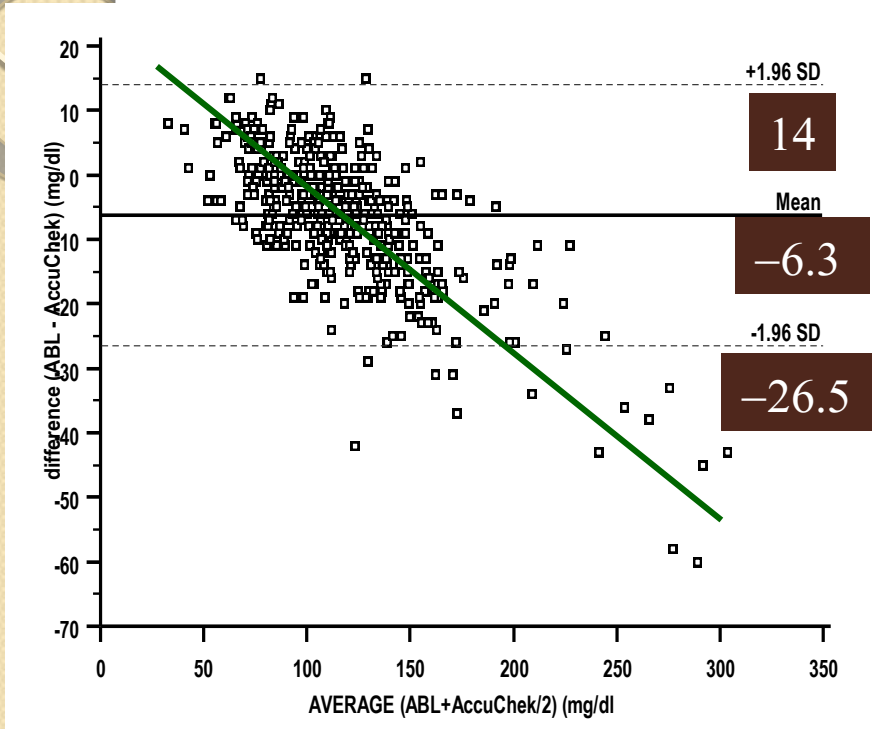
BGM with capillary blood versus central lab

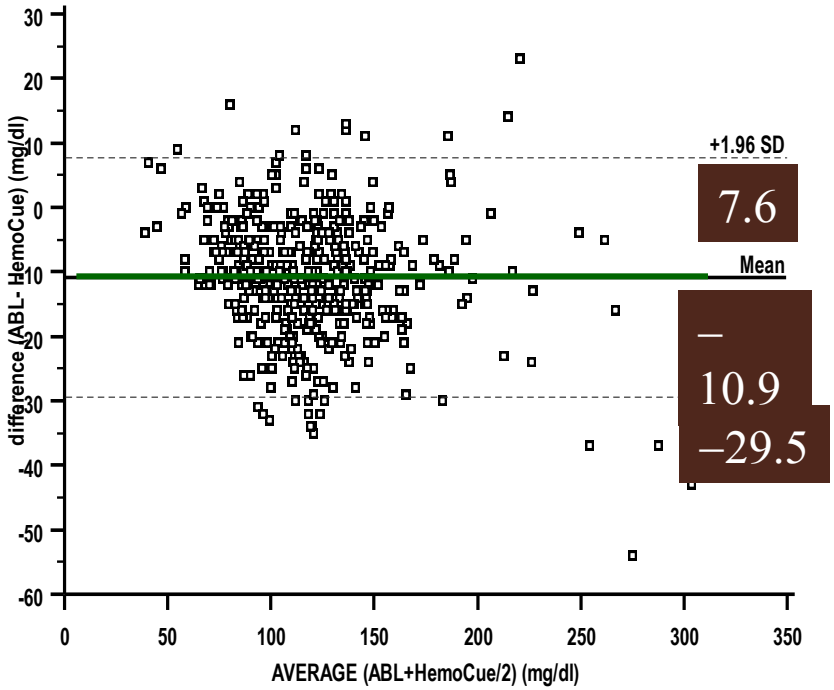
Overestimation of blood glucose levels



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

Bland-Altman (ABL blood gas analyzer)





AccuChek

HemoCue

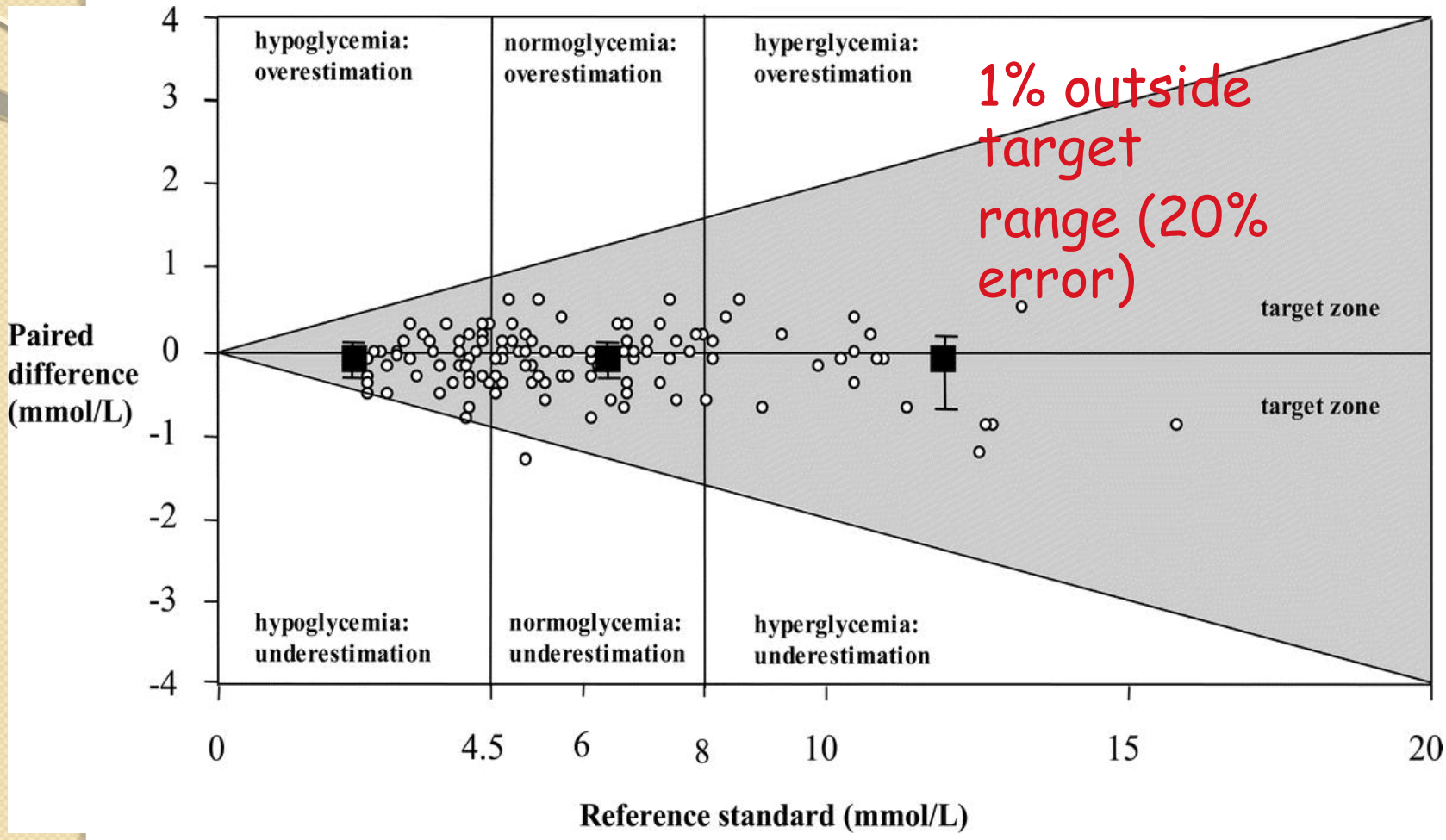
TGC target range = 30 mg/dL

95% CI= 40.5 mg/dL

95% CI= 37.1 mg/dL

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

Blood gas analyzer versus central lab



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

Administration de l'insuline

- IV ou SC ?
- Insuline rapide ou lente ?

Ichai *et al. Critical Care* 2010, **14**:R166
http://ccforum.com/content/14/5/R166

CRITICAL CARE

RESEARCH Open Access

International recommendations for glucose control in adult non diabetic critically ill patients

Carole Ichai[1], Jean-Charles Preiser[2*], for the Société Française d'Anesthésie-Réanimation (SFAR)[3], Société de Réanimation de langue Française (SRLF) and the Experts group[4]

- Recommandation de l'utilisation d'insuline d'action rapide en perfusion continue à la seringue électrique.
- Il est fortement suggéré d'utiliser une voie d'administration fournissant un débit de perfusion d'insuline intraveineux constant.

Ichai *et al. Critical Care* 2010, **14**:R166
http://ccforum.com/content/14/5/R166

CRITICAL CARE

RESEARCH Open Access

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- Il est suggéré d'interrompre la perfusion d'insuline par voie intraveineux lorsque le patient a repris une prise alimentaire et de continuer à surveiller sa glycémie pendant au moins trois contrôle avant le repas.
- Relais d'administration d'insuline en sc SN.

Ichai *et al. Critical Care* 2010, **14**:R166
http://ccforum.com/content/14/5/R166

CRITICAL CARE

RESEARCH Open Access

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- Il est recommandé de ne plus utiliser les Protocol de contrôle de glucose statiques *(= échelle mobile)* qui déterminent le taux de livraison de l'insuline sur base de la dernière mesure de la glycémie.

SLIDING vs DYNAMIC SCALES

- **Échelle mobile/ sliding scales**

↑ Blood glucose

↓ Insulin rate

SLIDING vs DYNAMIC SCALES

- **Échelle mobile/ sliding scales**

↑ Blood glucose

↓

↑ Insulin rate

- **Échelle dynamique/ dynamic scales**

↑ Blood glucose

↓

↑ **change** in insulin rate calculated according to the kinetics of BG and the intakes

Moving beyond tight glucose control to safe effective glucose control

James S Krinsley and Jean-Charles Preiser

Critical Care 2008, **12:** 149

…a glycemic target of 80 to 150 mg/dl is not unreasonable for an ICU to choose initially…

International recommendations for glucose control in adult non diabetic critically ill patients.

Carole Ichai, JC Preiser on behalf of the SFAR/SRLF expert group

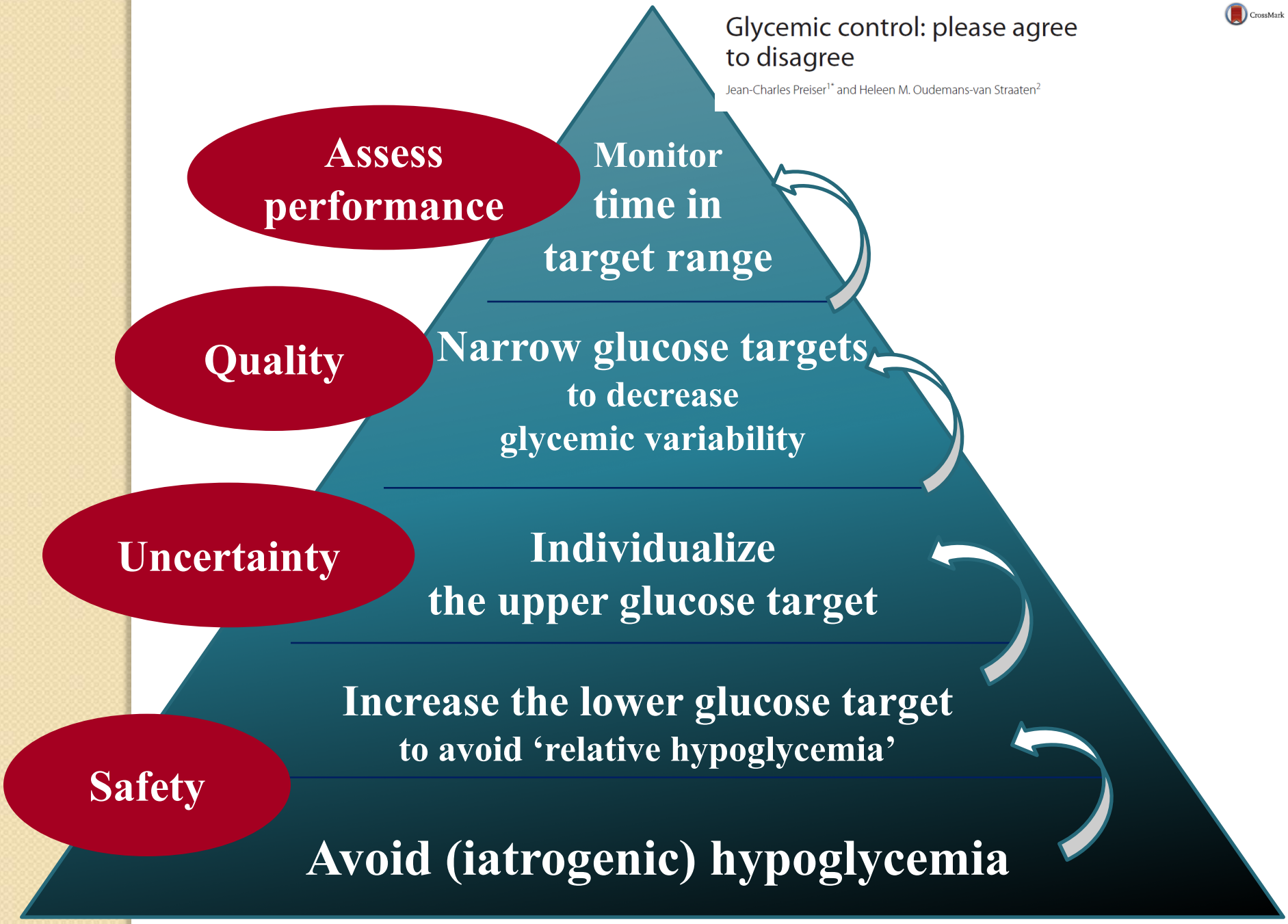
Critical Care 2010, 14**: R166**

A glucose target of less than 10 mmol/L is strongly suggested, using intravenous insulin following a standard protocol, when spontaneous food intake is not possible.

WHAT'S NEW IN INTENSIVE CARE

Glycemic control: please agree to disagree

Jean-Charles Preiser[1*] and Heleen M. Oudemans-van Straaten[2]




DEMAIN

In terms of insulin treatment: One size does not fit all

Endocrine and metabolic considerations in critically ill patients 1

Glucose management in critically ill adult

Lancet Diabetes Endocrinol 2015; 3: 723–33

Dieter Mesotten, Jean-Charles Preiser, Mikhail Kosiborod*

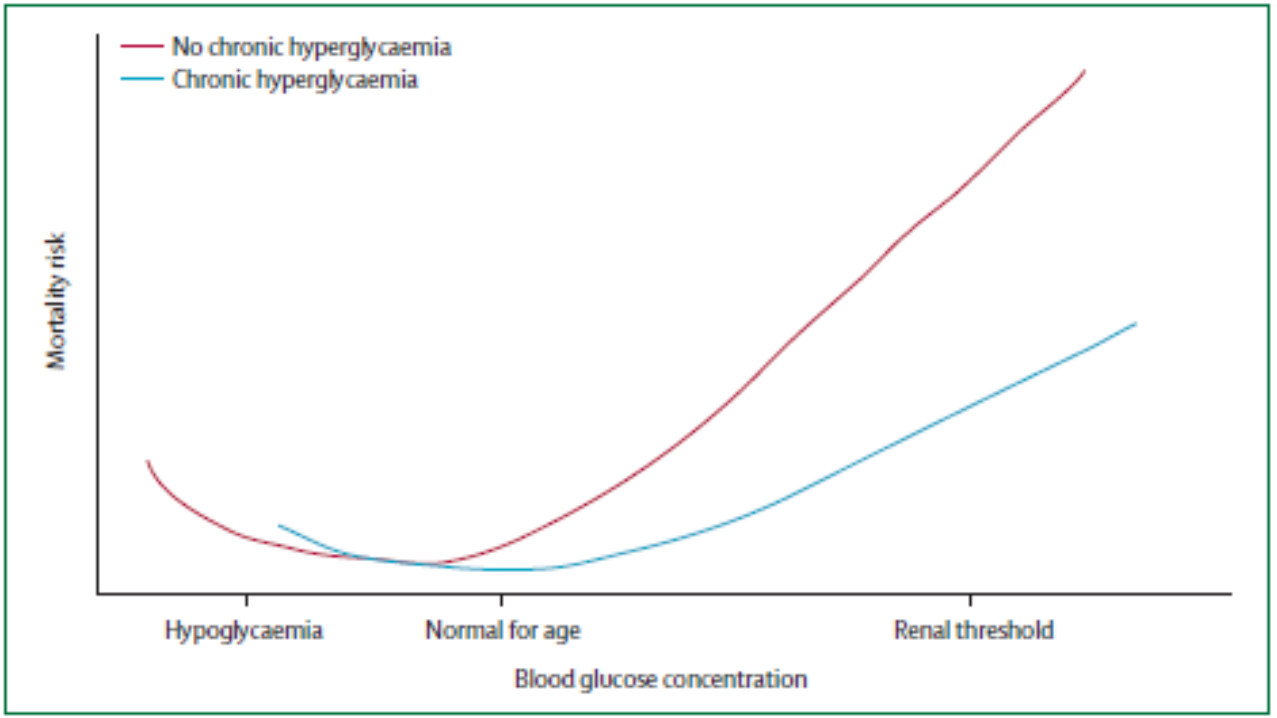


Figure: **J-shaped association curve between blood glucose concentrations and mortality in critically ill patients**
Lowest risk zone for mortality in adults, represented by the red line, is 3·9–8·0 mmol/L. Renal threshold for glucosuria is about 12 mmol/L. Patients with chronic hyperglycaemia, such as in established diabetes, have a blunted association curve represented by the blue line. This figure is based on the results from Falciglia and colleagues,[9] Kosiborod and colleagues,[12] and Egi and colleagues.[13]

Relationship between A1C and average glucose (AG) levels

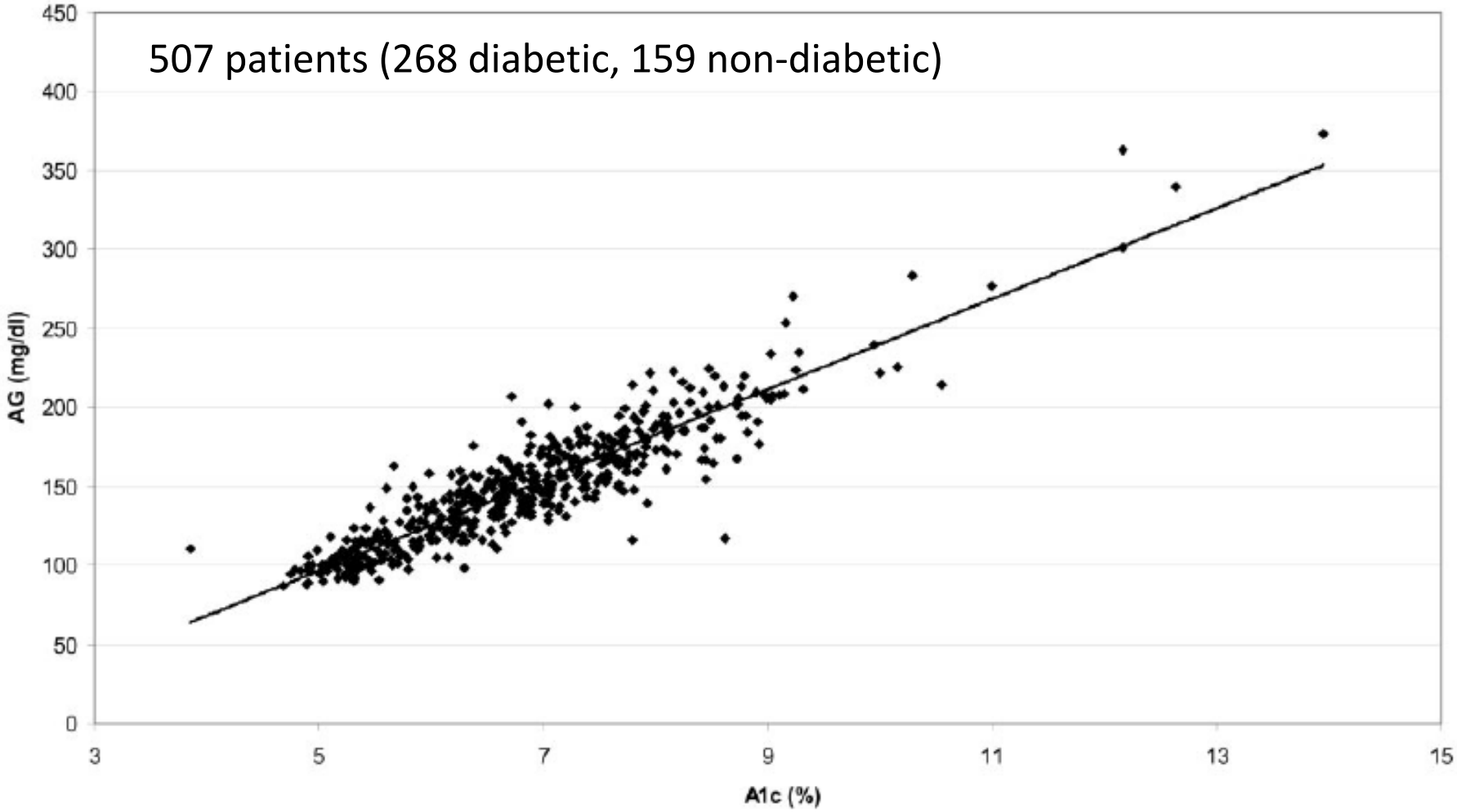
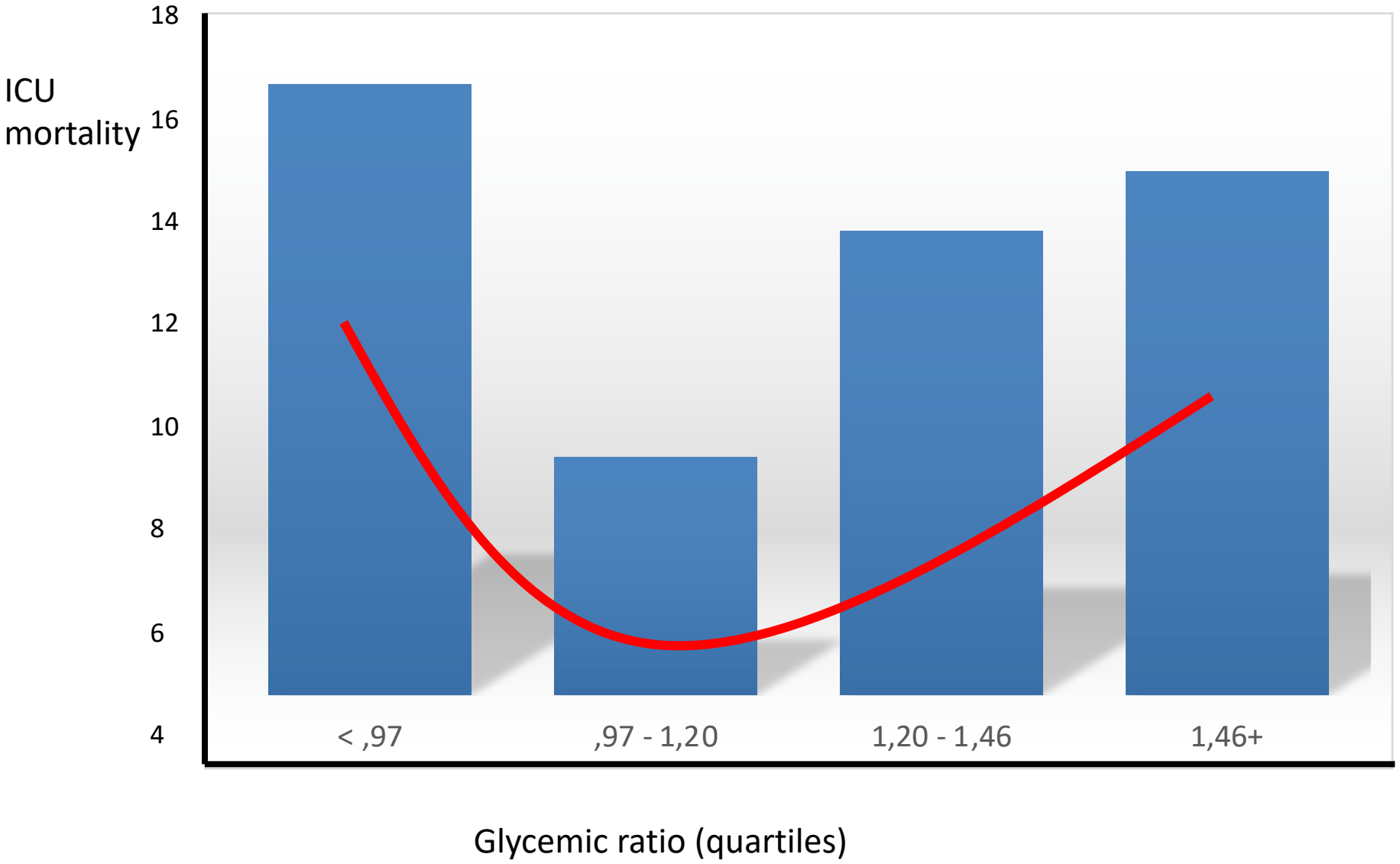


Figure 1—*Linear regression of A1C at the end of month 3 and calculated AG during the preceding 3 months. Calculated* $AG_{mg/dl} = 28.7 \times A1C - 46.7$ ($AG_{mmol} = 1.59 \times A1C - 2.59$) ($R^2 = 0.84$, $P < 0.0001$).

Nathan, Diabetes Care 2008;31:1473

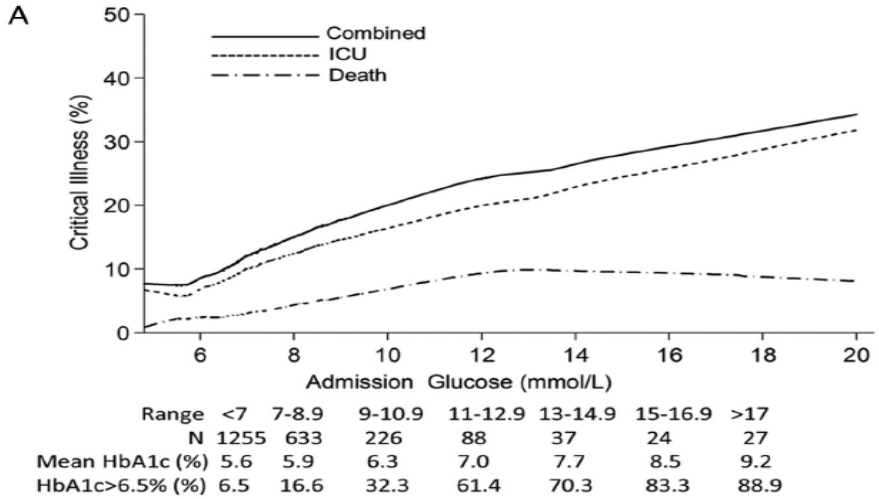
A step towards personalized glycemic control.

JC Preiser, D Prevedello, O Lheureux Crit Care Med 2018

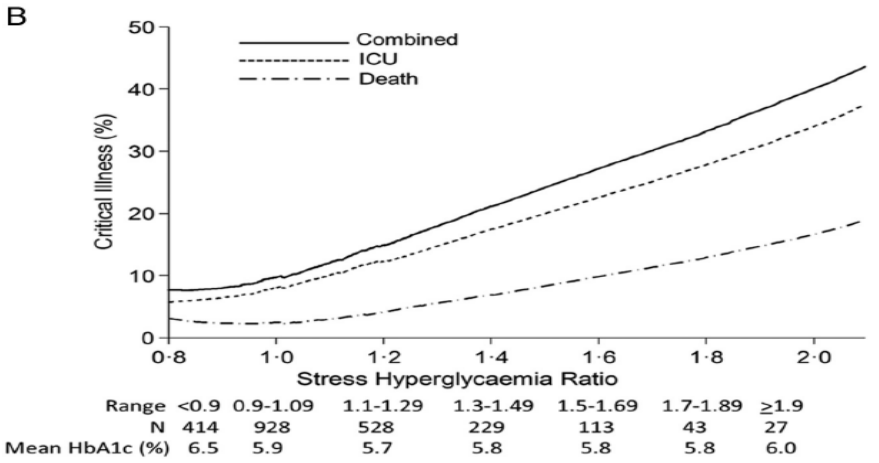


Relative Hyperglycemia, a Marker of Critical Illness: Introducing the Stress Hyperglycemia Ratio

Gregory W. Roberts, Stephen J. Quinn, Nyoli Valentine, Tariq Alhawassi, Hazel O'Dea, Stephen N. Stranks, Morton G. Burt, and Matthew P. Doogue



Range	<7	7-8.9	9-10.9	11-12.9	13-14.9	15-16.9	>17
N	1255	633	226	88	37	24	27
Mean HbA1c (%)	5.6	5.9	6.3	7.0	7.7	8.5	9.2
HbA1c>6.5% (%)	6.5	16.6	32.3	61.4	70.3	83.3	88.9



Range	<0.9	0.9-1.09	1.1-1.29	1.3-1.49	1.5-1.69	1.7-1.89	≥1.9
N	414	928	528	229	113	43	27
Mean HbA1c (%)	6.5	5.9	5.7	5.8	5.8	5.8	6.0

J Clin Endocrinol Metab, December 2015, 100(12):4490–4497

Safety and efficacy of personalized glycemic control in critically ill patients: A 2 year before and after interventional trial

James S Krinsley , Jean-Charles Preiser, Irl B. Hirsch

Endocrine Practice 2017;23:318

- This investigation includes 1,979 patients admitted to a single intensive care unit between September 16, 2013 and September 15, 2015. The BG target was 90-120 mg/dL in the PRE era and 80-140 mg/dL for patients without diabetes (NON) and diabetes patients (DM) with A1C < 7% and 110-160 mg/dL for DM with A1C $\geq$ 7% in the POST era. The primary efficacy outcome were the observed:expected mortality ratios.

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- Among NON, mean BG was slightly lower in the POST era: 118 (106-132) vs 115 (101-120) mg/dL (p=0.0003). Among DM, mean BG was 139 (123-160) mg/dL in the PRE era vs 136 (119-149) and 159 (138-171) mg/dL for TIGHT and LOOSE in the POST era (p=0.0668 and 0.0001, respectively). 11.0% and 11.8% of the patients had at least one BG level < 70 mg/dL in the 2 eras (p=0.68). Observed:expected mortality for NON and DM for the 2 eras were 0.75 vs. 0.74 (p=0.51) and **0.69 vs 0.52 (p<0.001)** respectively, and **among DM with A1C ≥ 7% was 0.74 vs 0.52 (p=0.004) .**

Mortality rate in case of severe hypoglycemia

Jacobi et al Crit Care Med 2012

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
Arabi 2008	76	266	8	257	9.9%	12.45 [5.87, 26.42]
De La Rosa 2008	21	254	2	250	6.8%	11.18 [2.59, 48.19]
Glucontrol 2009	44	536	13	542	10.5%	3.64 [1.94, 6.84]
Krinsley 2006	61	2699	40	2666	11.3%	1.52 [1.02, 2.27]
NICE-SUGAR	206	3016	15	3014	10.9%	14.66 [8.66, 24.82]
Toft 2006	19	136	5	135	8.7%	4.22 [1.53, 11.67]
Treggiari 2008	156	8108	24	2366	11.2%	1.91 [1.24, 2.95]
Van den Berghe 2001	39	765	6	783	9.4%	6.96 [2.93, 16.53]
Van den Berghe MICU 2006	111	595	19	605	11.0%	7.07 [4.28, 11.68]
VISEP 2008	42	247	12	290	10.3%	4.75 [2.44, 9.24]
Total (95% CI)		**16622**		**10908**	**100.0%**	**5.18 [2.91, 9.22]**
Total events	775		144			

Heterogeneity: Tau² = 0.72; Chi² = 76.82, df = 9 (P < 0.00001); I² = 88%

Test for overall effect: Z = 5.59 (P < 0.00001)

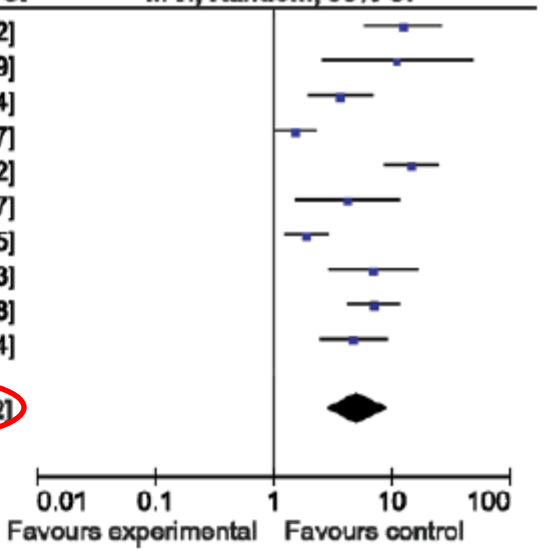


Figure 3. Forest plot of severe hypoglycemia (1, 14–19, 25, 26, 29). *CI*, confidence interval; *MH*, Mantel-Haenszel.

RESEARCH Open Access

Severe and multiple hypoglycemic episodes are associated with increased risk of death in ICU patients

Pierre Kalfon[1*], Yannick Le Manach[2], Carole Ichai[3], Nicolas Bréchot[4], Raphaël Cinotti[5], Pierre-François Dequin[6], Béatrice Riu-Poulenc[7], Philippe Montravers[8], Djilalli Annane[9], Hervé Dupont[10], Michel Sorine[11], Bruno Riou[12,13] and on behalf of the CGAO-REA S

Kalfon *et al. Critical Care* (2015) 19:153
DOI 10.1186/s13054-015-0851-7

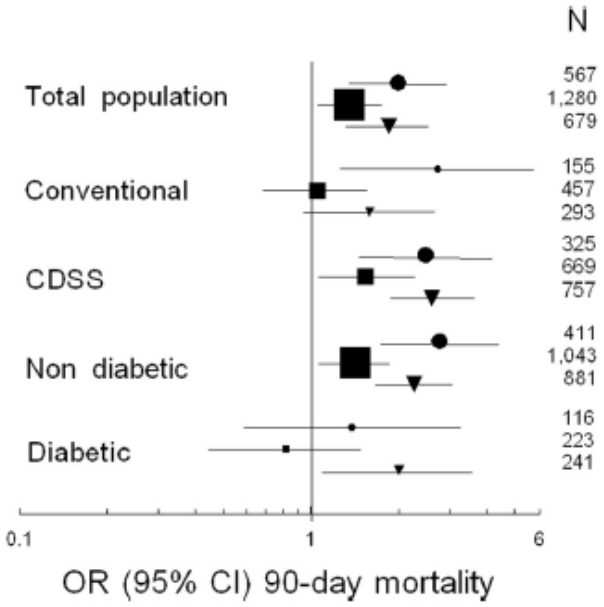
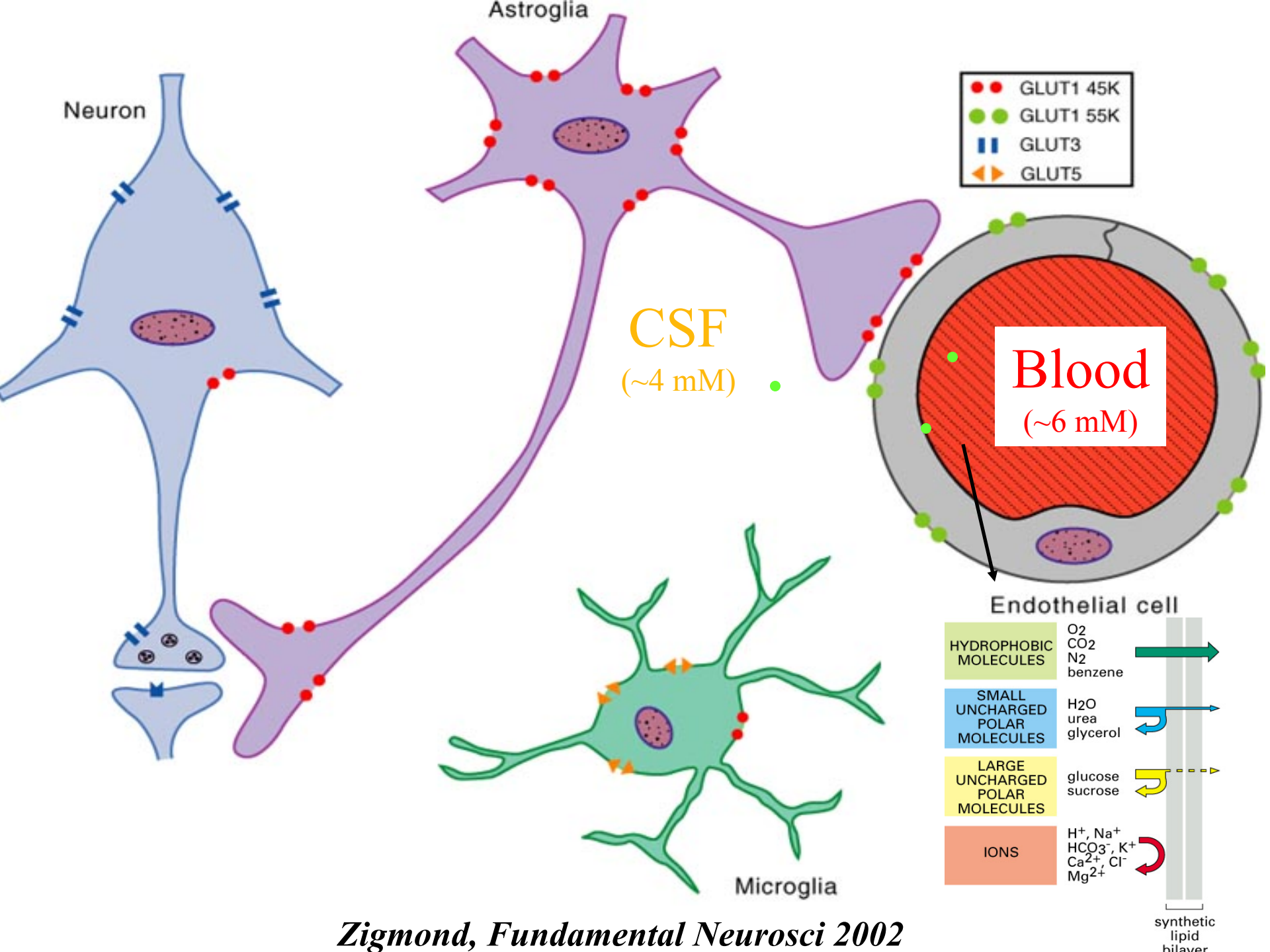


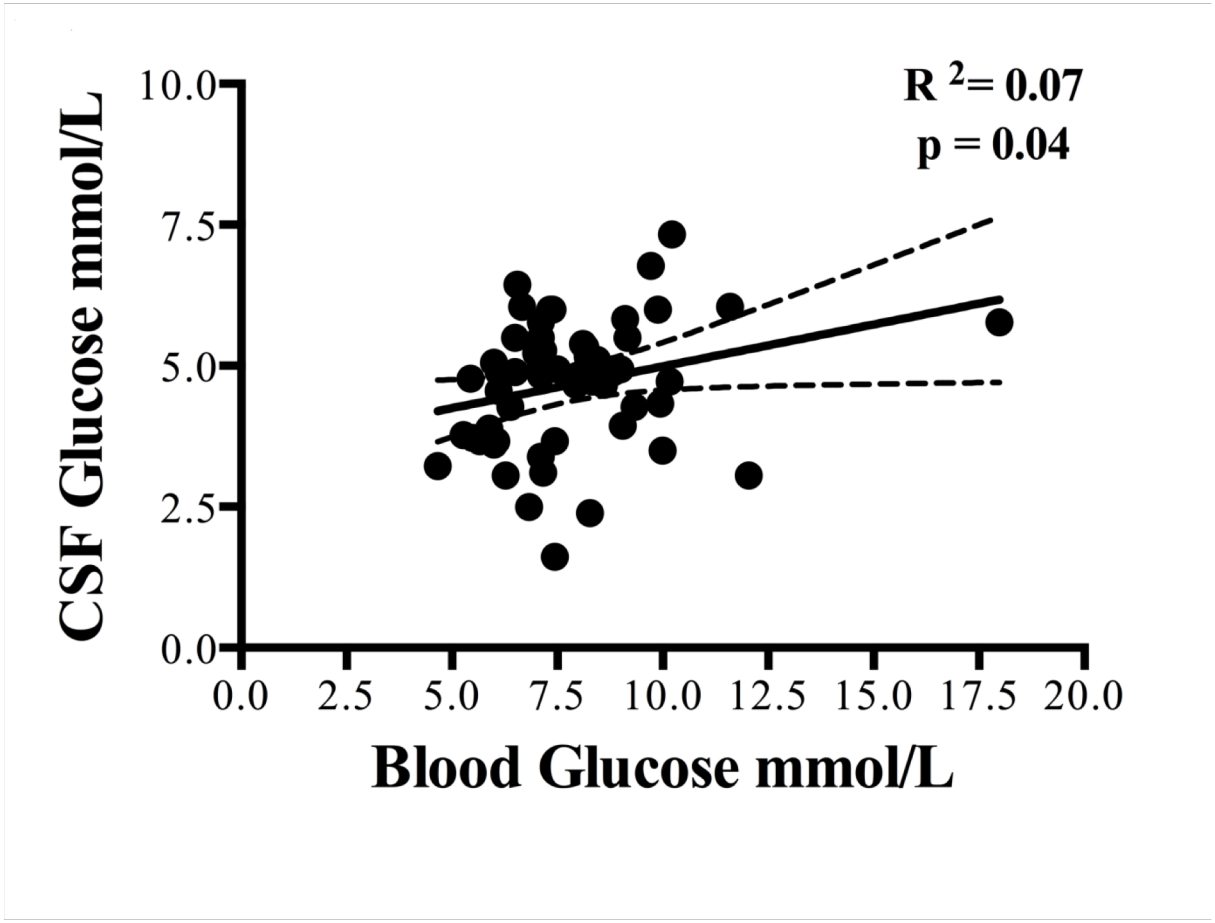
Figure 3 Subgroup analysis. Odds ratio (OR) and 95% confidence interval (CI) for death at 90 days associated with moderate (filled squares) or severe (filled circles) hypoglycemia or multiple (n ≥3) hypoglycemic (filled triangles) events in the total population and in matched subgroups according to treatment assignment (conventional vs. computerized decision support system (CDSS)) and diabetes status (diabetic vs. non-diabetic). Matching was performed using propensity score and a ratio of 2:1 for severe hypoglycemia and 1:1 for moderate hypoglycemia and multiple hypoglycemic events. The size of symbols is related to the number of patients (N) retained in the matching process.



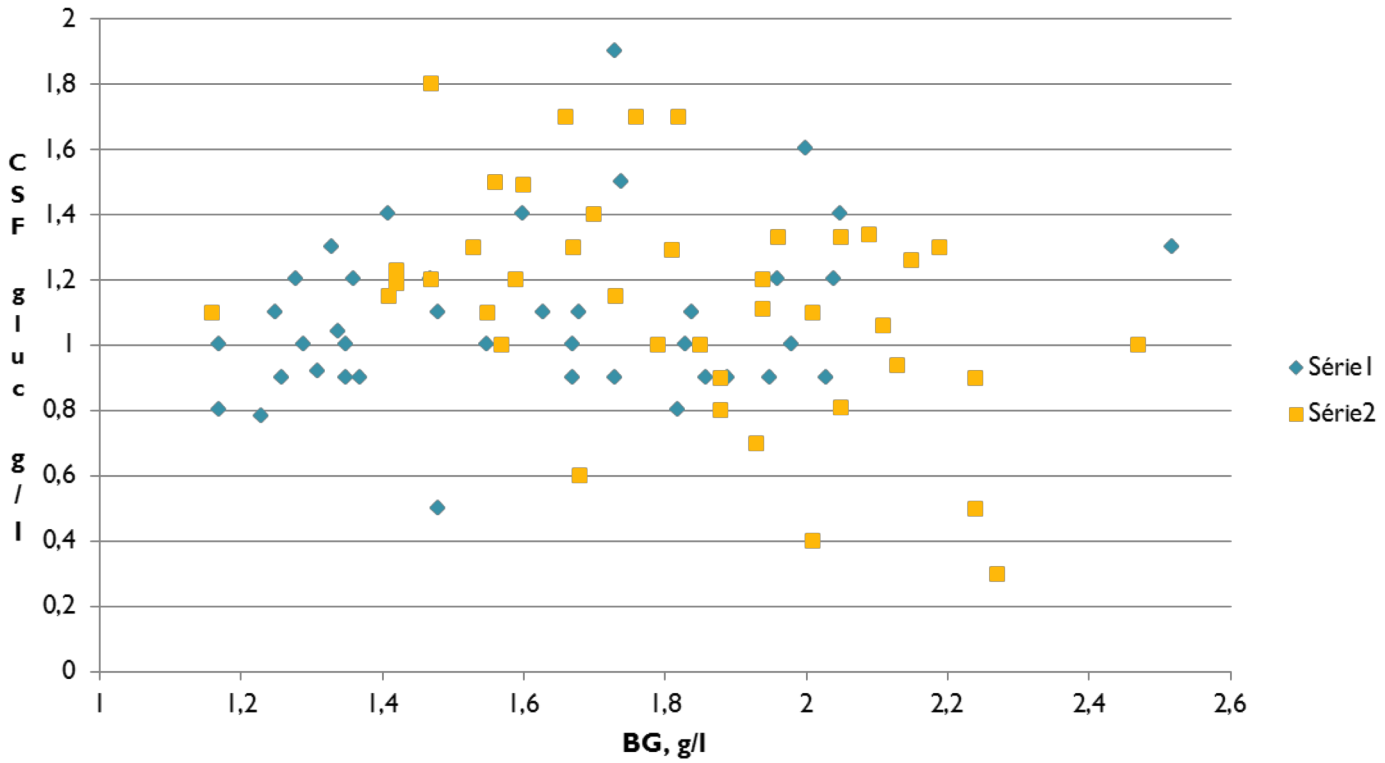
Zigmond, Fundamental Neurosci 2002

Glucose in CSF and BG

Lozano et al. J Neurosurg Anesthesiol (in press)



Glucose in CSF and BG



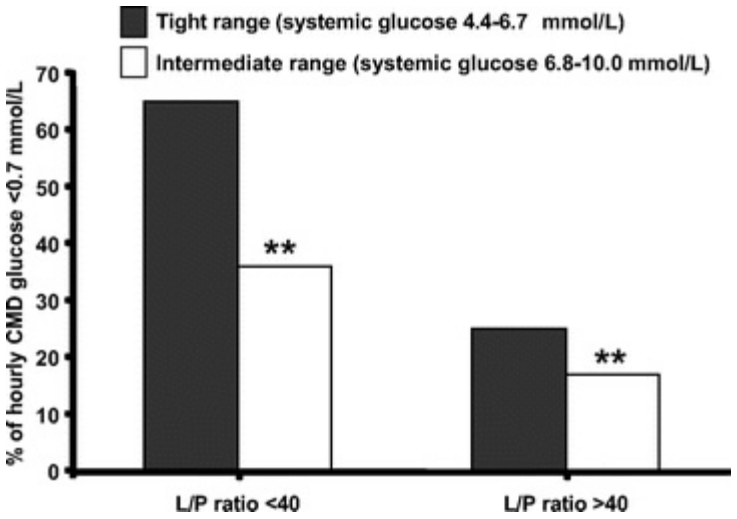
Cerebral microdialysis, n=2 (SAH - vasospasm)

Impact of TGC on cerebral glucose metabolism

Oddo et al Crit Care Med 2008;36:3233

- Twenty patients monitored with microdialysis after severe brain injury
- TGC (target 80-120 mg/dl)
- Cerebral glucose and lactate/pyruvate ratio collected hourly

- ***Outcome variables*** :
  - ranges of BG :
    low (< 80) - tight : (80-120),
    intermediate (120-180) - high (>180)
  - L/P ratio :
    > 25 : abnormal
    > 40 : brain energy failure
    ➢40 + brain glucose < 13 :
    Brain energy crisis



Predictors of brain energy crisis
(multivariate logistic regression adjusted for ICP and CPP) :
Serum glucose and dose of insulin

Impact of TGC on cerebral glucose metabolism

Oddo et al Crit Care Med 2008;36:3233

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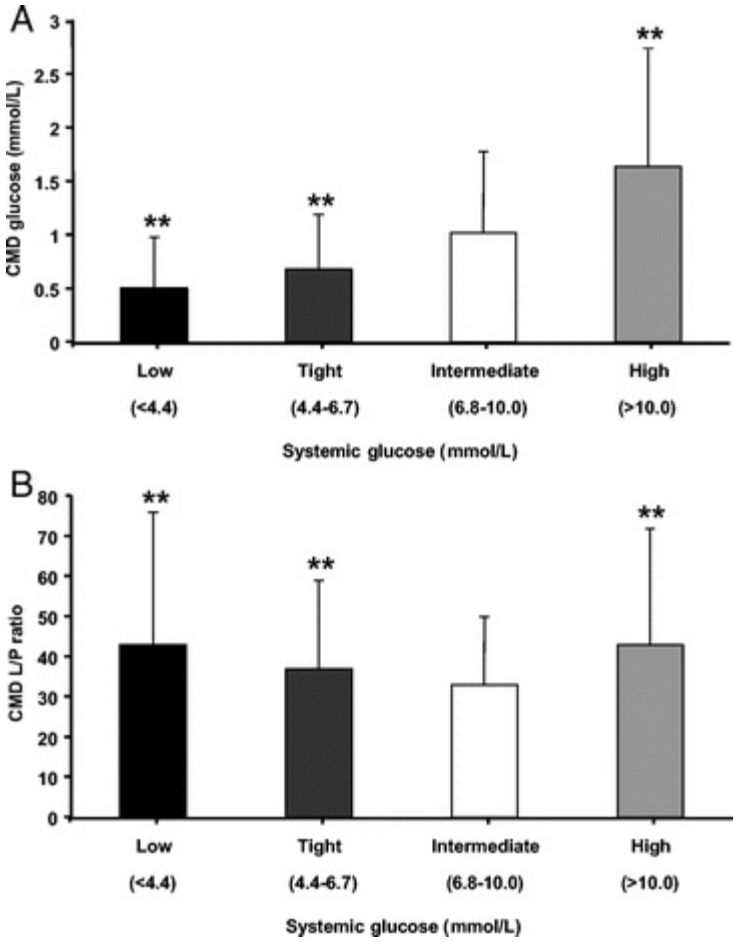

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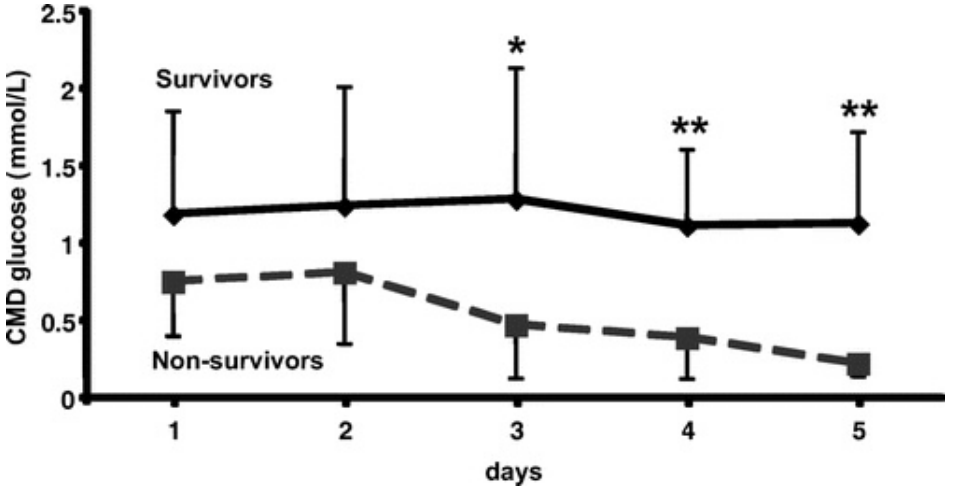

Predictors of hospital mortality (logistic regression)

Brain energy crisis 7.4 (1.4-39.5)*
Glasgow Coma scale 1.1 (.96-1.3)
CPP 1.01 (.97-1.04)
ICP 1 (0.99-1.01)

Hypoglycemia Aggravates Critical Illness–Induced Neurocognitive Dysfunction

Thomas Duning, MD[1]
Ingeborg van den Heuvel, MD[2]
Annabelle Dickmann[2]
Thomas Volkert, MD[2]
Carola Wempe, MD[2]
Julia Reinholz, MD[1]
Hubertus Lohmann, MD[1]
Hendrik Freise, MD[2]
Björn Ellger, MD, PhD[2]

Diabetes Care 33:639–644, 2010

	Hypo group			Control group			
	Score (percentile)	Evaluation	Z scores	Score (percentile)	Evaluation	Z scores	*P*
Dementia screening			0.006			−0.003	0.969
Mini-mental state examination	28.4	Close below average		28.8	Close below average		0.909
Boston Naming Test	13.8	Normal		13.9	Normal		0.871
Attention and working memory			−0.039			−0.045	0.774
Nuernberg Gerontopsychological Inventory							
Digit symbol substitution	30.0 (56.7)	Normal		31.1 (60.7)	Normal		0.770
Color word interference task (reading)	39.8 (10.2)	Far below average		40.0 (12.5)	Far below average		0.861
Color word interference task (color naming)	53.3 (28.4)	Close below average		52.8 (26.6)	Close below average		0.608
Wechsler Memory Scale (revised)							
Digit span forward	11.6 (51.7)	Normal		12.6 (54.4)	Normal		0.156
Digit span backward	10.7 (40.6)	Close below average		11.6 (42.0)	Close below average		0.892
Trail-making test (A)	60.1 (13.9)	Far below average		59.6 (13.0)	Far below average		0.270
Executive function			−0.001			−0.007	0.991
Color word interference task (interference condition)	17.5 (47.9)	Normal		19.5 (51.3)	Normal		0.421
Regensburg Word Fluency Test (letter fluency) (S)	14.2 (28.4)	Close below average		14.2 (28.4)	Close below average		1.000
Trail-making test (B)	117.0 (27.8)	Close below average		110.8 (25.6)	Close below average		0.792
Visuospatial skills			−2.084			−0.145	0.001
Rey Osterrieth Complex Figure Test							
Copy	20.4			24.7			0.007
Delayed recall	9.4 (22.8)	Close below average		14.5 (29.9)	Close below average		0.002
Difference copy (delayed)	−54.3%			−41.9% (4.2)			0.043
Verbal learning and memory			−0.027			−0.064	0.807
Auditory verbal learning test (German)							
Recall trial 1	4.9 (30.2)	Close below average		5.5 (38.4)	Close below average		0.503
Recall trial 5	10.7 (31.1)	Close below average		10.5 (28.8)	Close below average		0.543
Total trials 1–5	38.0 (30.4)	Close below average		38.7 (32.1)	Close below average		0.527
Delayed recall	8.5 (13.8)	Far below average		9.0 (15.0)	Far below average		0.240
Recognition (true positives, false positives)	10.9 (30.5)	Close below average		10.9 (30.5)	Close below average		1.000

Many questions and hypotheses to be answered:

Commentary

Moving beyond tight glucose control to safe effective glucose control

James S Krinsley[1] and Jean-Charles Preiser[2]

Near-Continuous Glucose Monitoring Makes Glycemic Control Safer in ICU Patients

Jean-Charles Preiser, MD, PhD[1]; Olivier Lheureux, MD[1]; Aurelie Thooft, MD[1];
Serge Brimioulle, MD, PhD[1]; Jacques Goldstein, MD[2]; Jean-Louis Vincent, MD, PhD, FCCM[1]

Crit Care Med 2018 Aug;46(8):1224

Design

- Single-centre, clustered-randomized, prospective
- Medico-surgical ICU of Erasme Hospital
- From july 2014 to june 2015

Cluster randomized study

Period 1 (1 month)

- Included patients of ICU 1 & 2 → Unblinded group
- Included patients of ICU 3 & 4 → Blinded group

Period 2 (1month)

- Included patients of ICU 3 & 4 → Unblinded group
- Included patients of ICU 1 & 2 → Blinded group

Near-Continuous Glucose Monitoring Makes Glycemic Control Safer in ICU Patients

Jean-Charles Preiser, MD, PhD[1]; Olivier Lheureux, MD[1]; Aurelie Thooft, MD[1];
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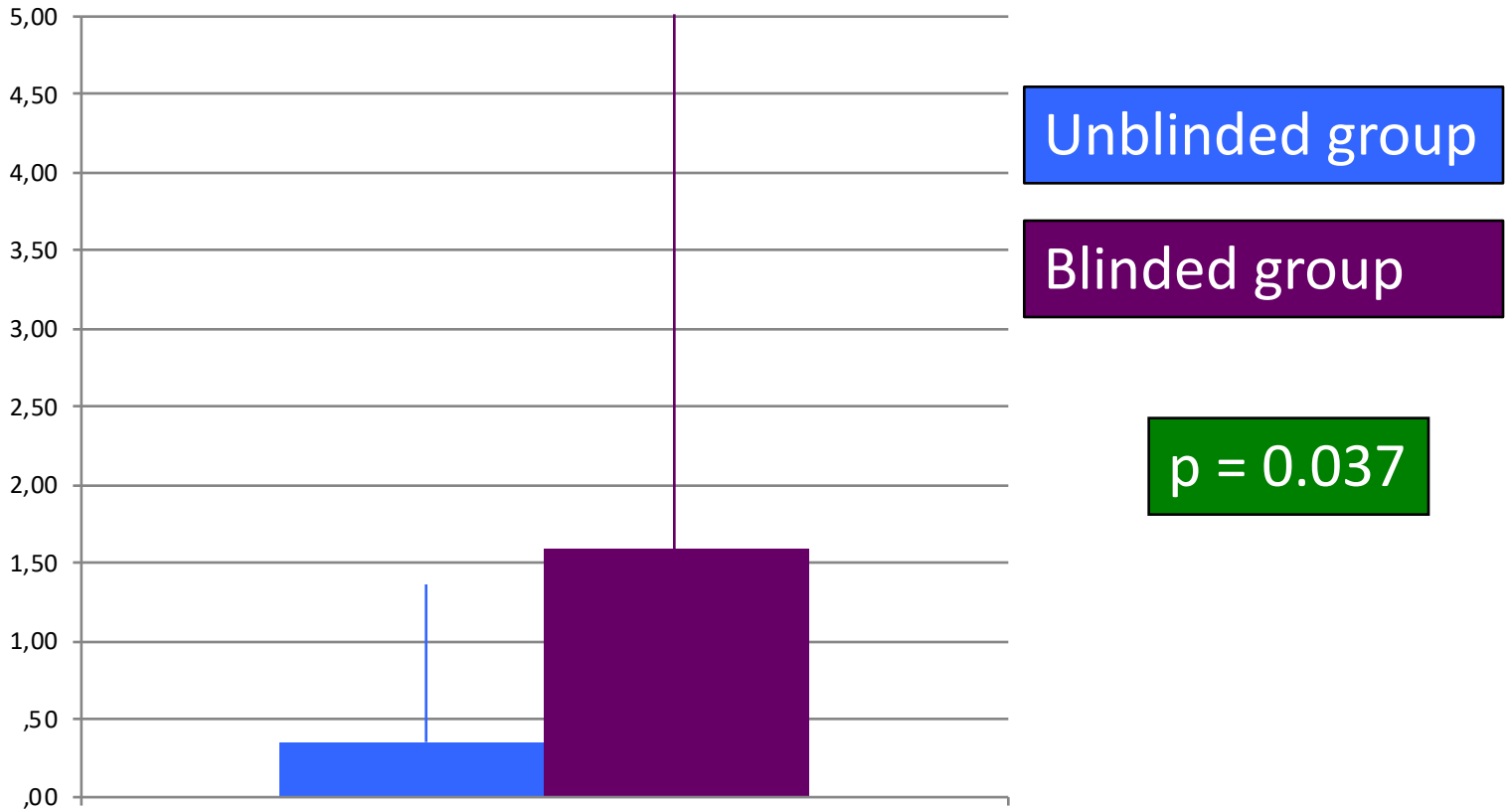
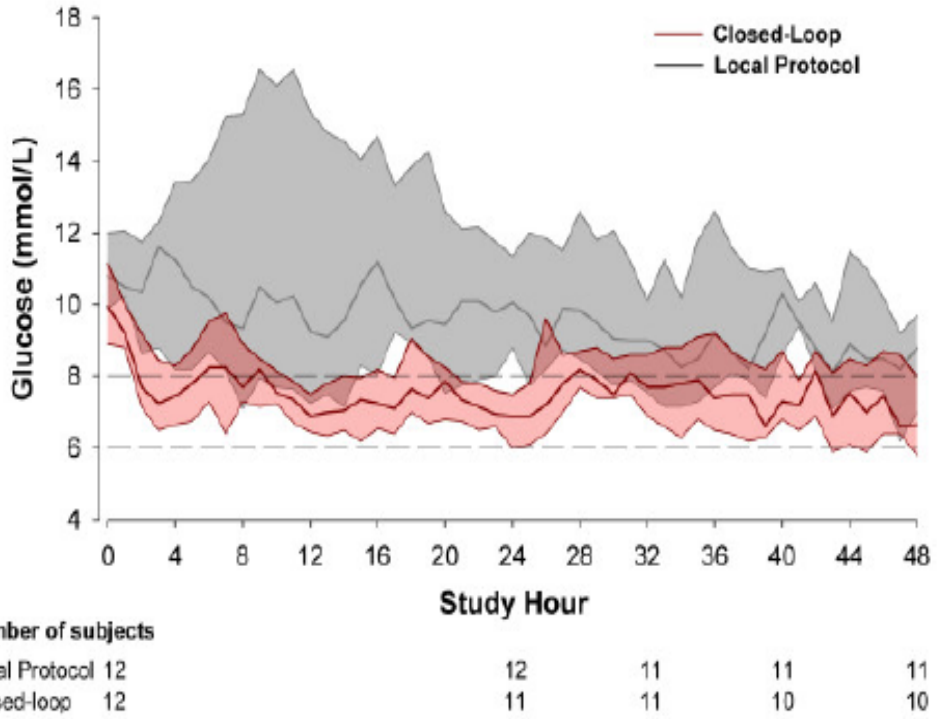


Percentage in time blood glucose below 70mg/dl

Feasibility of fully automated closed-loop glucose control using continuous subcutaneous glucose measurements in critical illness: a randomized controlled trial

Lalantha Leelarathna[1], Shane W English[2], Hood Thabit[1], Karen Caldwell[1], Janet M Allen[1], Kavita Kumareswaran[1], Malgorzata E Wilinska[1], Marianna Nodale[1], Jasdip Mangat[1], Mark L Evans[1], Rowan Burnstein[2] and Roman Hovorka[1*]



Leelarathna et al. Crit Care 2013

The evaluation of the ability of closed-loop glycemic control device to maintain the blood glucose concentration in intensive care unit patients*

Tomoaki Yatabe, MD; Rie Yamazaki, MD; Hiroyuki Kitagawa, MD, PhD; Takehiro Okabayashi, MD, PhD; Koichi Yamashita, MD, PhD; Kazuhiro Hanazaki, MD, PhD; Masataka Yokoyama, MD, PhD

- Retrospective analysis (n=208)
- STG-22 closed-loop system (NIKKISO, Tokyo, Japan):
  - Continuous venous sampling (2ml/u)
  - Glucose/insulin infusion adjusted per minute
  - Automatic internal recalibration every 4h
- Target 90-110 mg/dl
- 90% surgical ICU + early PN
- Device used for mean 33h

- **49.5% within 70-110 mg/dl**
- No hypoglycemic events (<70 mg/dl)

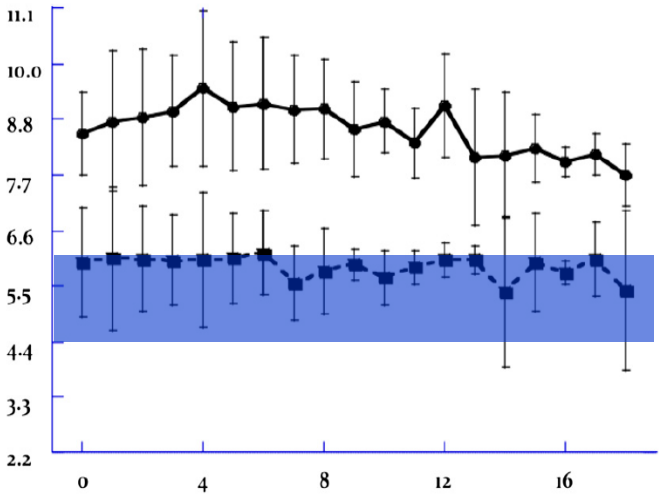
Yatabe al. Crit Care Med 2011

Intensive Versus Intermediate Glucose Control in Surgical Intensive Care Unit Patients

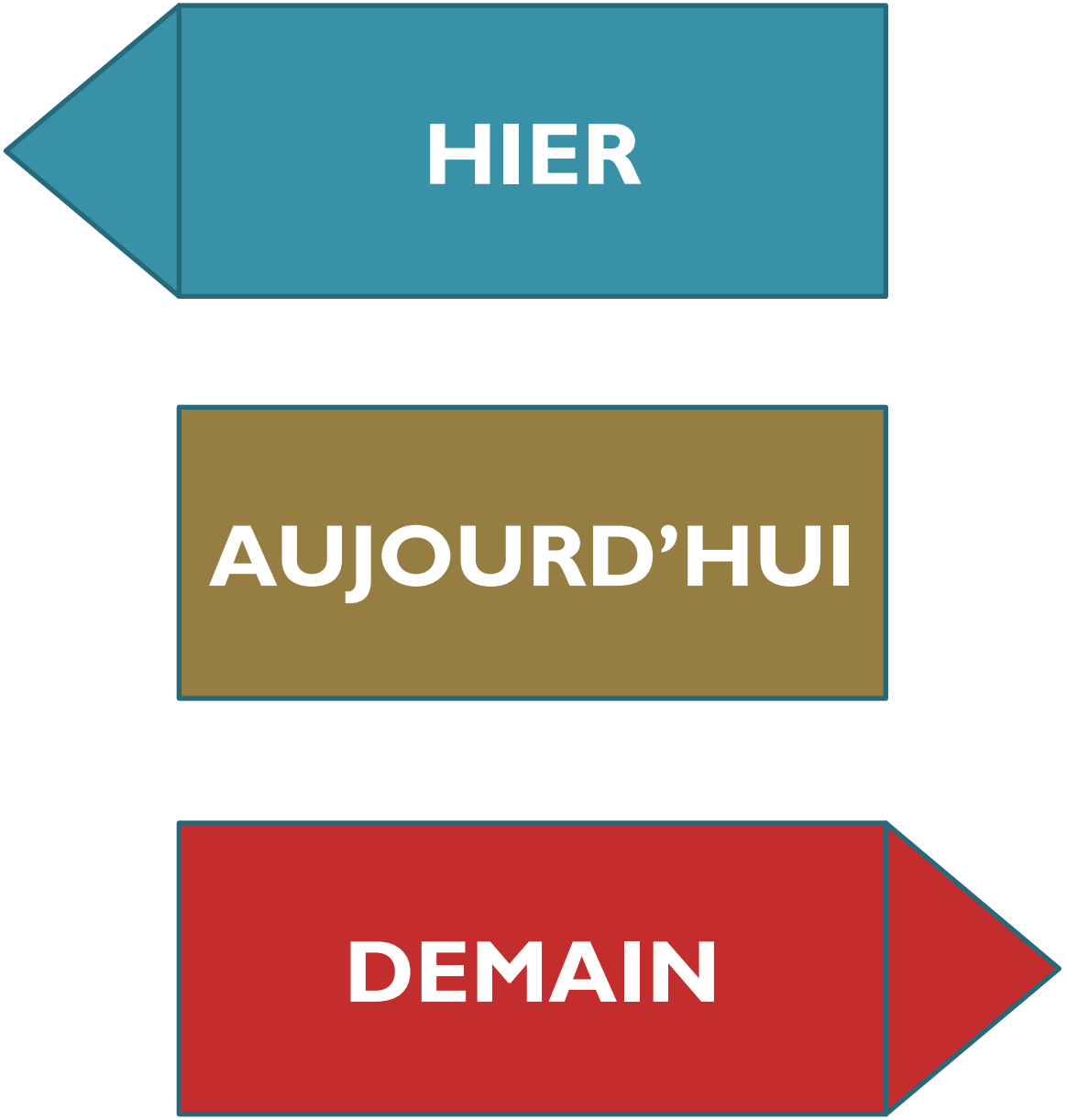
Takehiro Okabayashi,[1,2] Yasuo Shima,[2] Tatsuaki Sumiyoshi,[2] Akihito Kozuki,[2] Teppei Tokumaru,[2] Tasuo Iiyama,[3] Takeki Sugimoto,[1] Michiya Kobayashi,[1] Masataka Yokoyama,[4] and Kazuhiro Hanazaki[1]

Diabetes Care 2014;37:1516–1524 | DOI: 10.2337/dc13-1771

- RCT (n=447)
- **STG closed-loop system for 18 hours: target 80-110 vs. 139-180 mg/dl**
- Day 1: sliding-scale insulin, target 149-200 mg/dl
- Hepatic or pancreatic surgery
- Early PN



- **85.8% within 80-110 mg/dl during ICU stay**
- No hypoglycemic events (<40 mg/dl)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AUJOURD'HUI
DEMAIN

Review Article

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