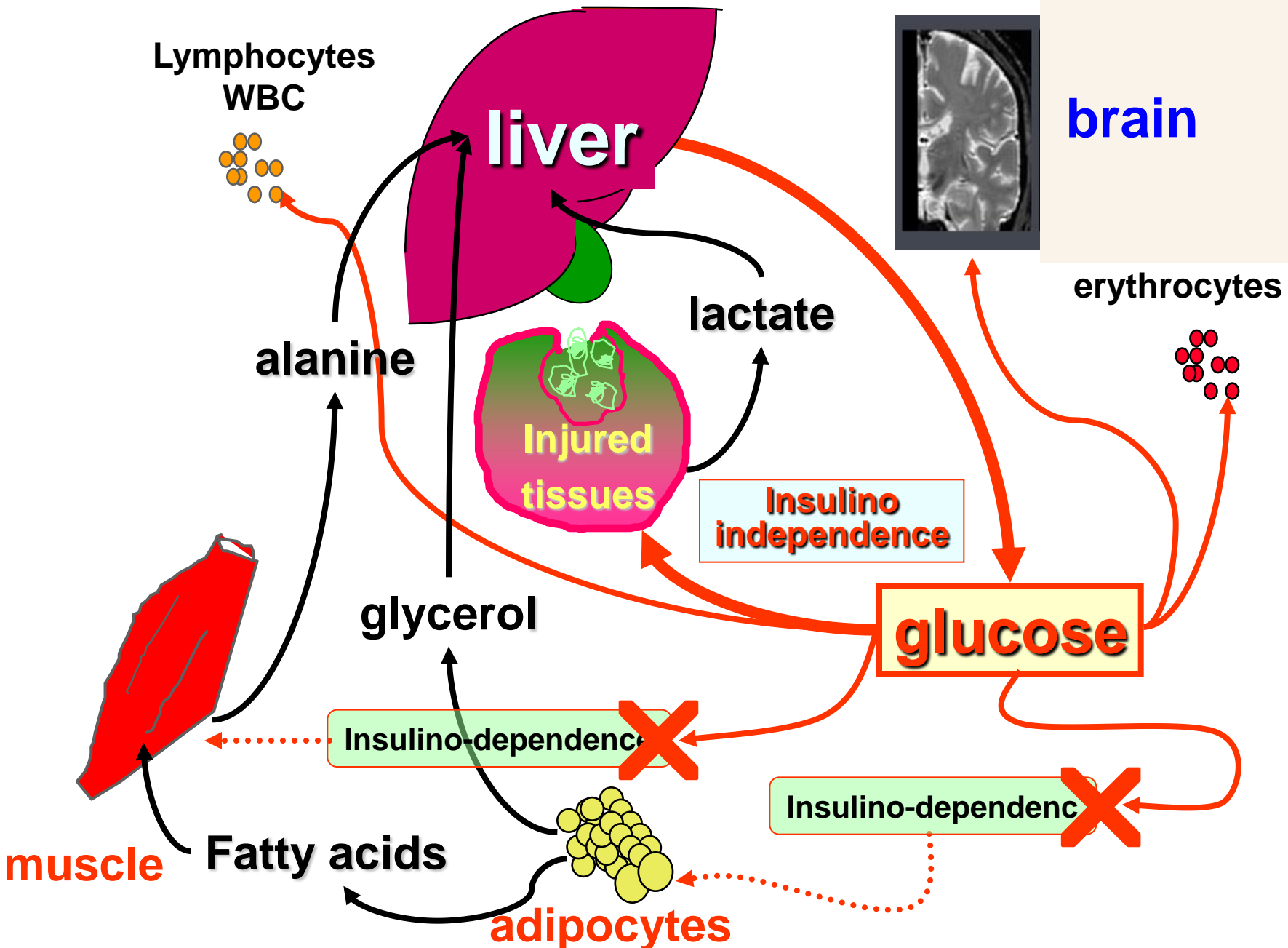
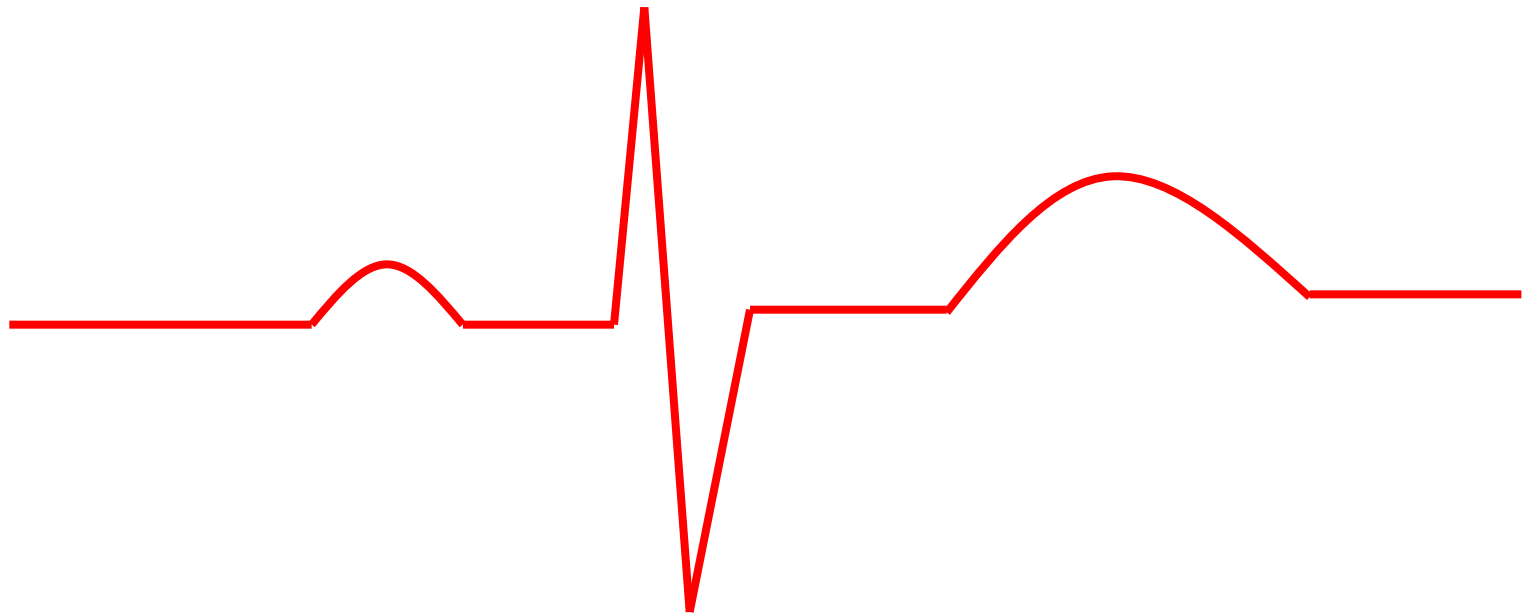

« FAST HUGS »
Contrôle glycémique

Valérie Schittekatte
Jean-Charles Preiser
USI – Hôpital Universitaire Erasme
XXXII SYMPOSIUM SIZ nursing – 15 avril 2014

METABOLIC ADAPTATION TO STRESS

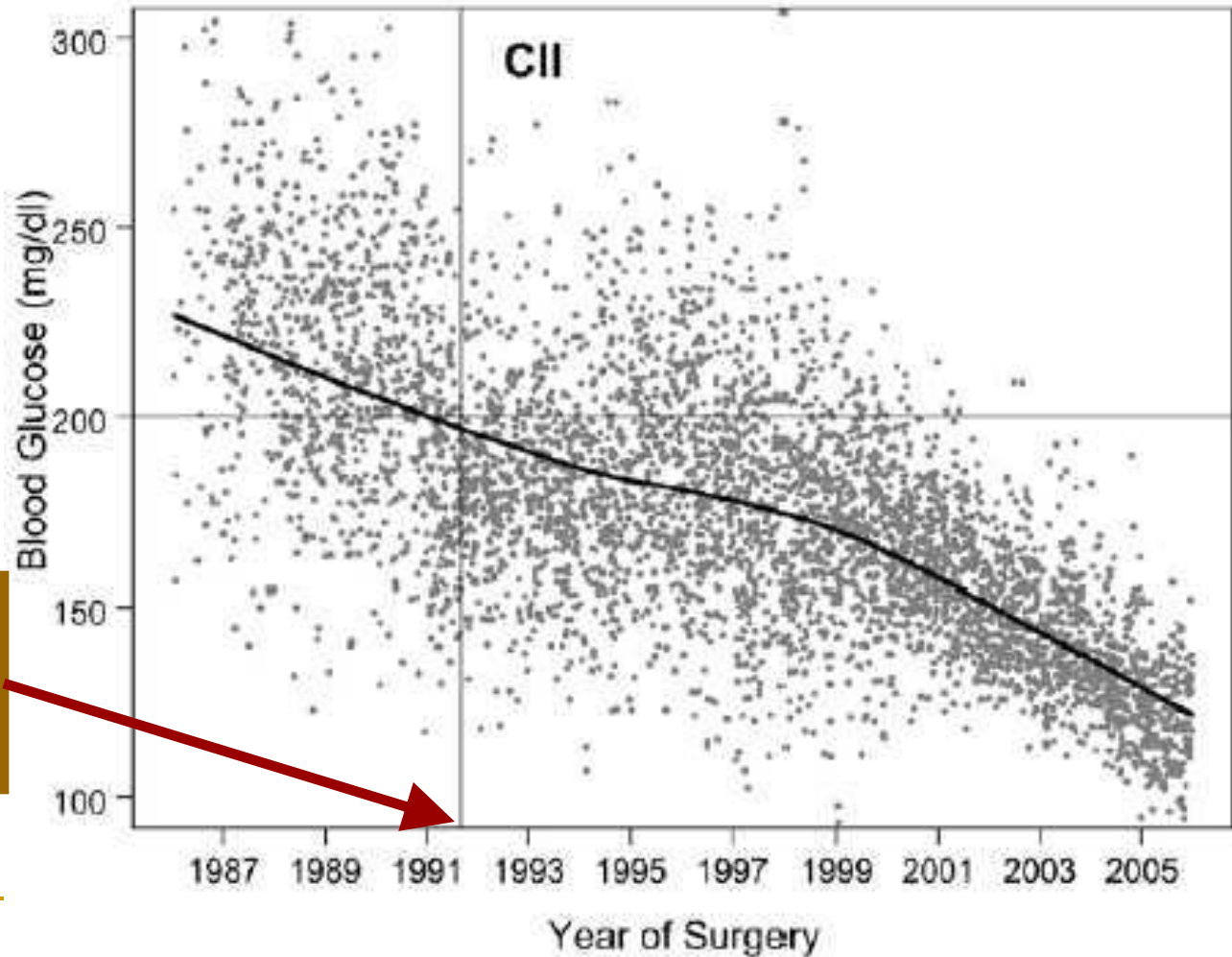




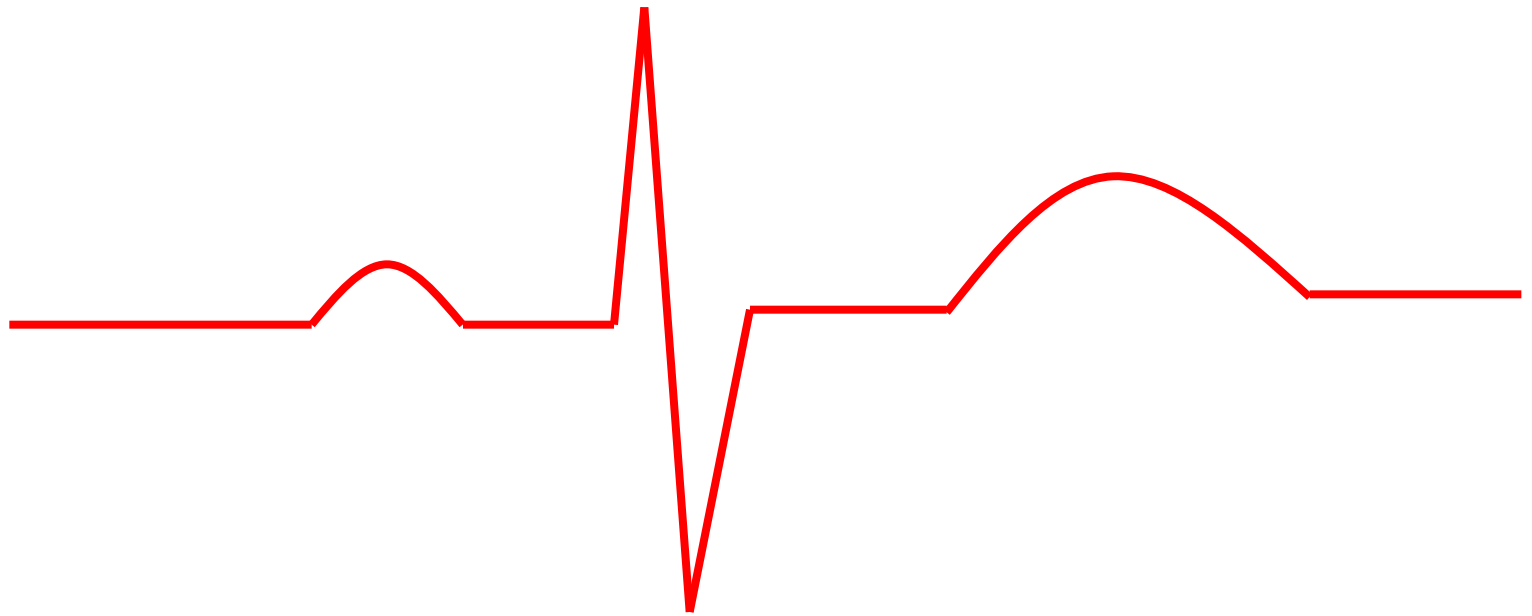
Period 1 : 1970-2000

Progressive Decline In Blood Glucose with Portland Protocol

Furnary Semin Thorac Cardiovasc Surg. 2006;18:302



Introduce
Portland
Protocol



—
Period 2
2001



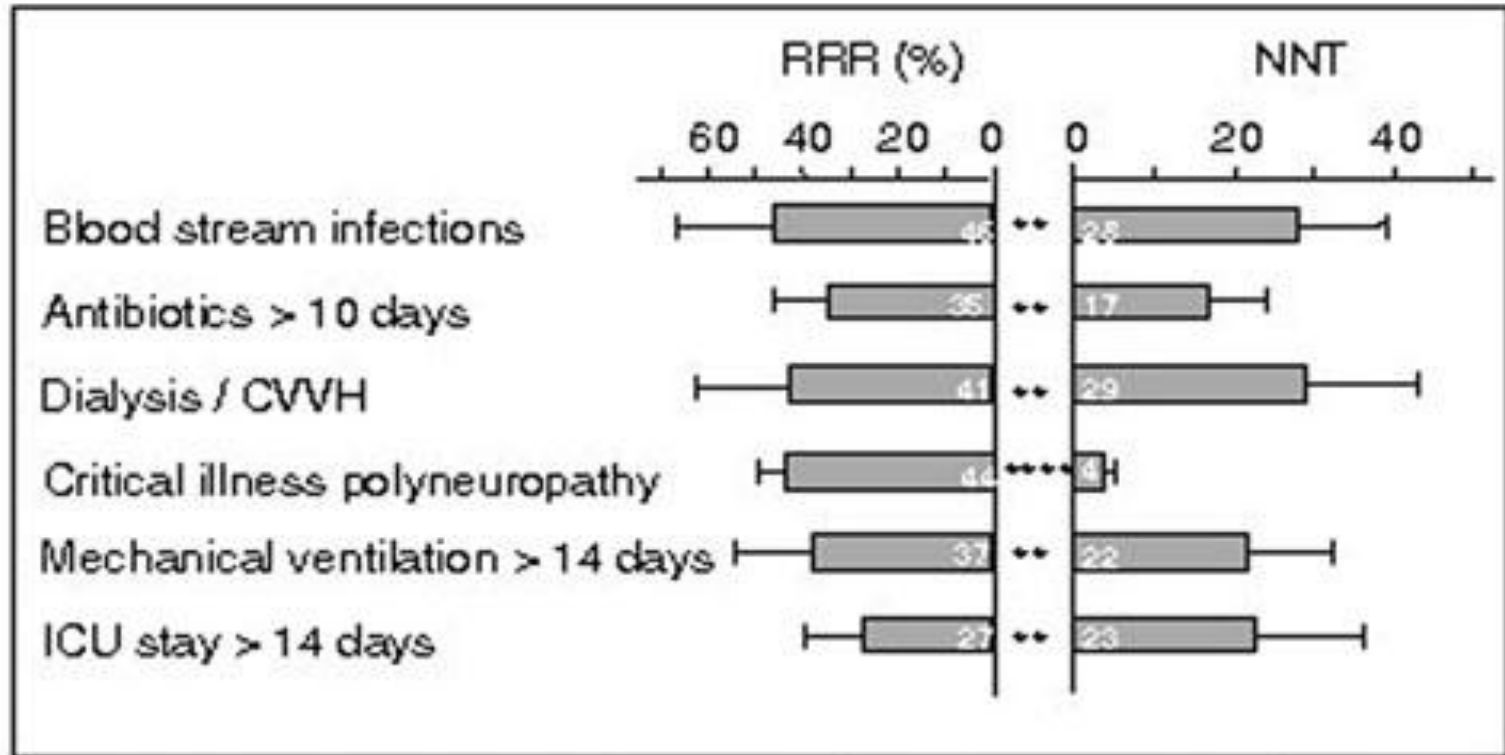
Intensive insulin therapy : Mortality

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

<u>Result</u>	<u>Control</u>	<u>Intensive</u>	<u>%.</u>	<u>p</u>
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

SECONDARY OUTCOME VARIABLES



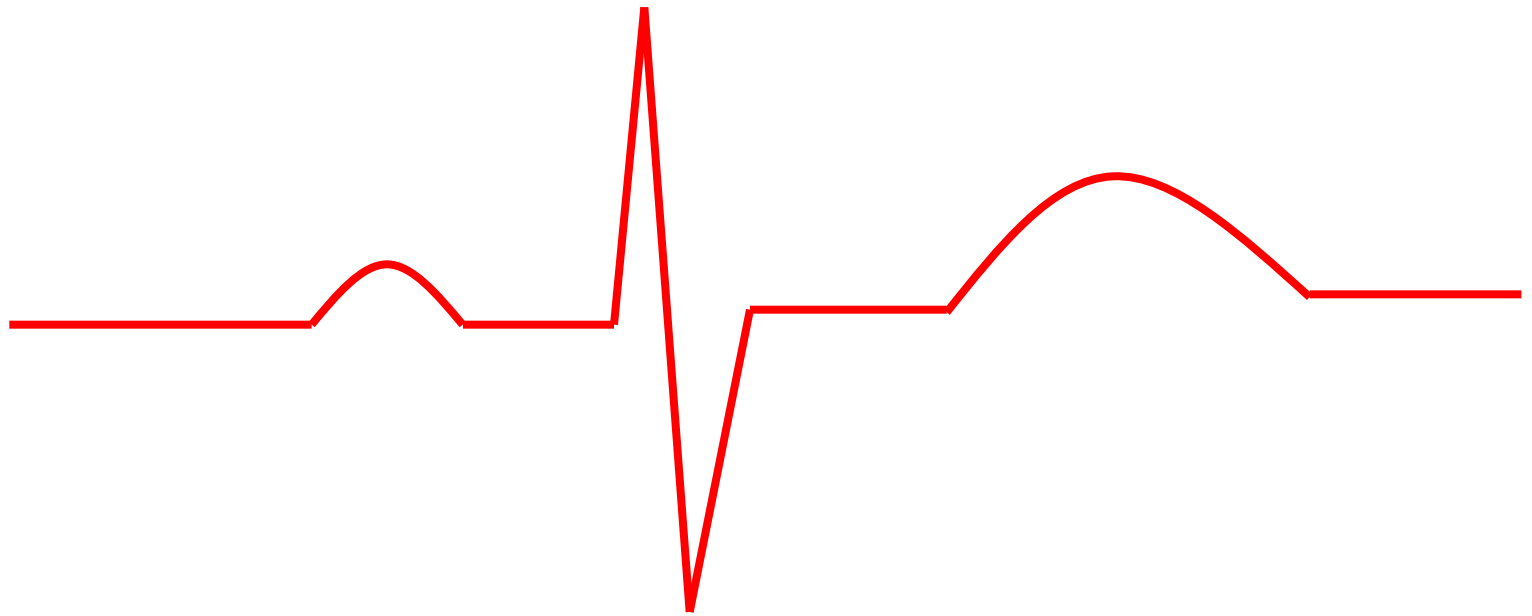
** $P \leq 0.01$ *** $P < 0.0001$

(error bars: 95% confidence intervals)

Critical Care

RRR = Relative risk reduction

NNT = Number needed to treat



Period 3
2006-2009





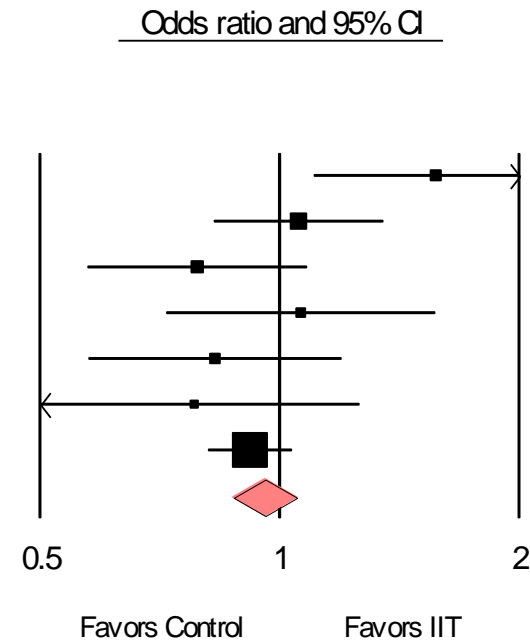
Toward Understanding Tight Glycemic Control in the ICU

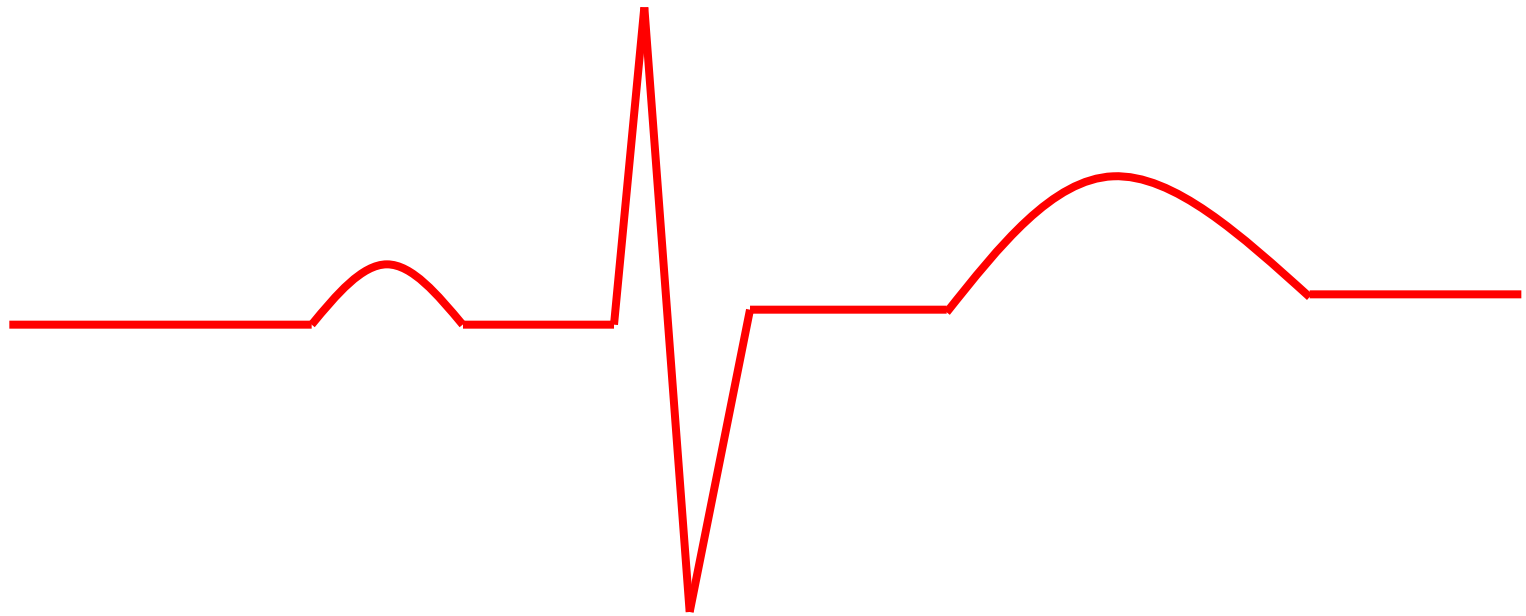
A Systematic Review and Metaanalysis

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

CHEST 2010; 137(3):544–551

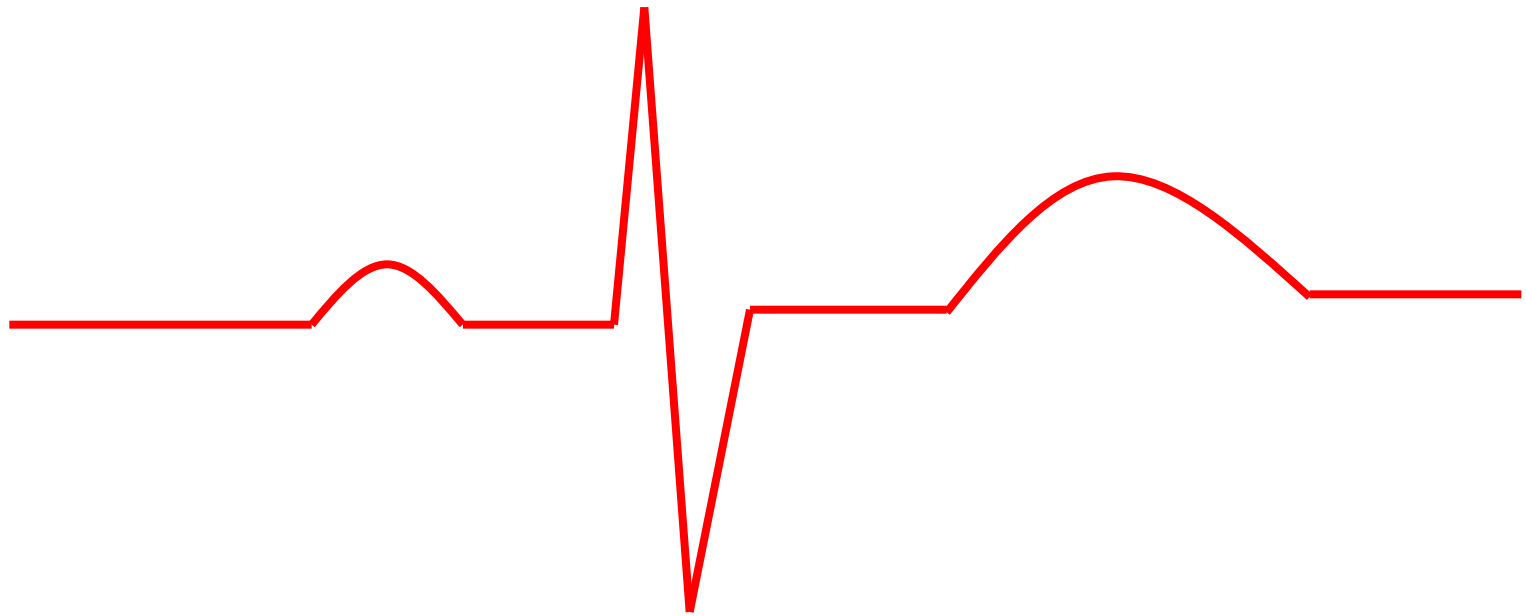
Study name	Statistics for each study				
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Van den Berghe-2001	1.572	1.102	2.242	2.498	0.012
Van den Berghe-2006	1.057	0.826	1.353	0.441	0.659
Glucotrol-2006	0.788	0.573	1.085	-1.460	0.144
WISEP-2008	1.064	0.720	1.572	0.310	0.757
De La Rosa-2008	0.830	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





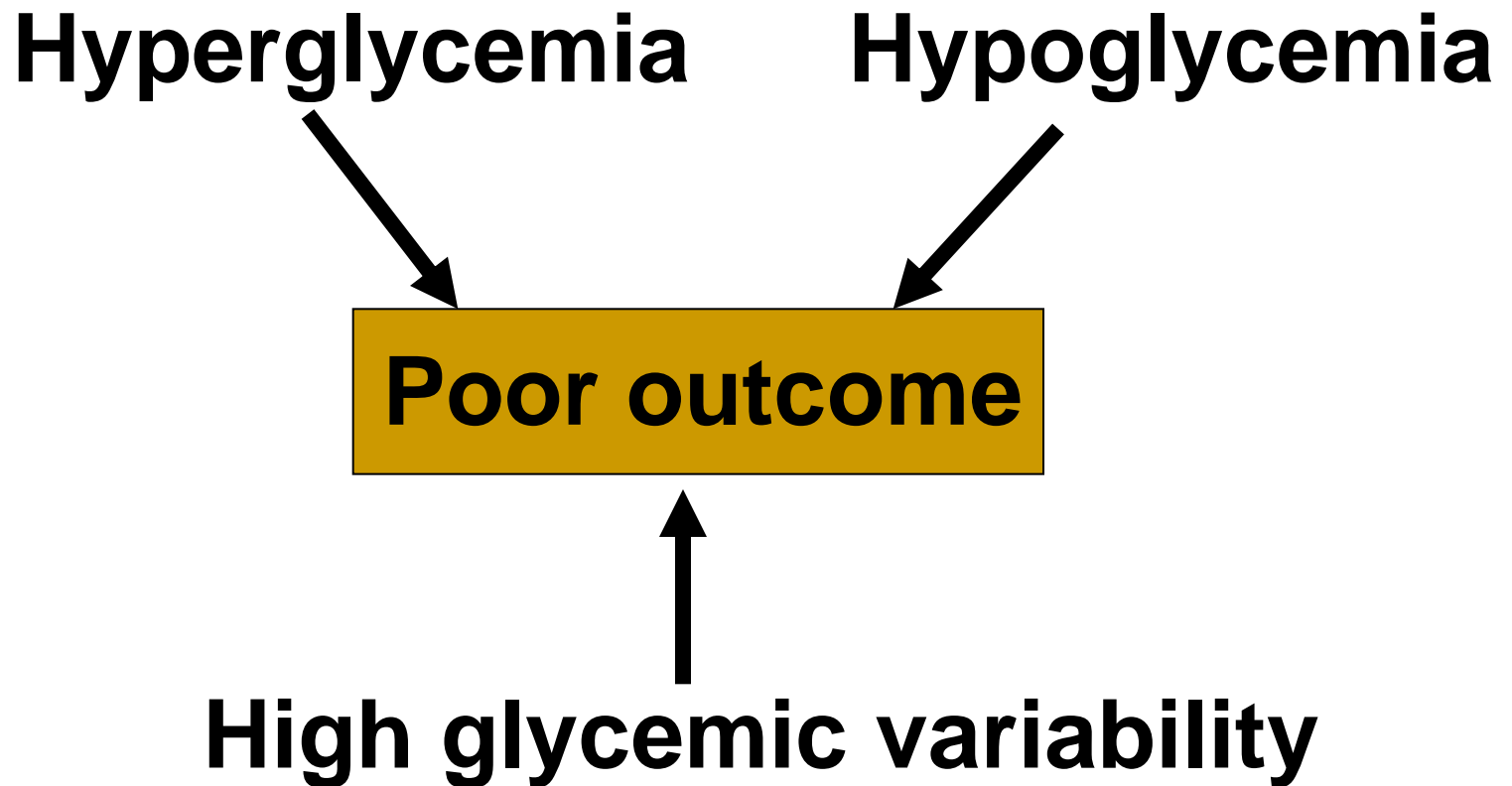
Period 4
2009-

Enthusiasm - interest



Understanding

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

	<80 mg/dL	80-110 mg/dL	110-150 mg/dL	150-180 mg/dL	180-240 mg/dL	>240 mg/dL
<40 mg/dL						
40-60 mg/dL						
60-80 mg/dL	2.2 (1.2-3.9)	1.6 (1.1-2.2)	1.9 (0.6-5.5)			
80-110 mg/dL		1.0 (0.7-1.4)	1.7 (1.5-2.1)	4.2 (2.1-8.5)		
>110 mg/dL			2.3 (1.9-2.7)	4.2 (3.3-5.3)	2.7 (0.6-12.1)	

GV < 25%

	<80 mg/dL	80-110 mg/dL	110-150 mg/dL	150-180 mg/dL	180-240 mg/dL	>240 mg/dL
<40 mg/dL			1.1 (0.1-9.4)			
40-60 mg/dL		3.4 (1.3-9.4)	2.7 (1.1-6.6)	1.8 (0.2-15.1)		
60-80 mg/dL	1.1 (0.2-8.5)	2.1 (1.6-2.6)	2.3 (1.8-2.8)	3.5 (2.1-5.6)	5.3 (1.1-26.5)	
80-110 mg/dL		1.1 (0.8-1.6)	1.9 (1.6-2.2)	3.5 (2.9-4.3)	5.0 (3.3-7.5)	
>110 mg/dL			2.4 (1.9-3.1)	4.5 (3.7-5.5)	8.3 (6.2-11.0)	

GV 25-50%

	<80 mg/dL	80-110 mg/dL	110-150 mg/dL	150-180 mg/dL	180-240 mg/dL	>240 mg/dL
<40 mg/dL		1.9 (0.2-16.8)	2.6 (1.3-5.5)	6.3 (2.8-14.1)	5.3 (1.3-22.5)	
40-60 mg/dL	5.7 (1.6-20.6)	4.4 (2.6-7.3)	2.7 (1.9-3.7)	3.6 (2.5-5.4)	5.6 (2.8-11.2)	26.0 (1.5-445.8)
60-80 mg/dL		2.5 (1.9-3.2)	2.5 (2.1-3.0)	3.6 (3.0-4.5)	5.9 (4.3-7.9)	20.0 (4.0-99.7)
80-110 mg/dL		1.6 (0.9-2.9)	2.0 (1.7-2.3)	3.6 (3.0-4.3)	5.7 (4.7-6.9)	6.6 (3.0-14.5)
>110 mg/dL			1.4 (0.7-2.6)	4.0 (3.0-5.3)	6.0 (4.8-7.5)	21.5 (12.2-38.0)

GV 50-75%

	<80 mg/dL	80-110 mg/dL	110-150 mg/dL	150-180 mg/dL	180-240 mg/dL	>240 mg/dL	
<40 mg/dL			24.0 (14.1-40.7)	10.8 (8.1-14.3)	10.6 (7.7-14.6)	13.2 (9.8-17.8)	10.5 (7.0-15.6)
40-60 mg/dL	3.4 (0.4-31.7)	5.2 (3.5-7.8)	4.5 (3.6-5.6)	6.5 (5.2-8.1)	6.6 (5.3-8.2)	8.2 (6.2-10.8)	
60-80 mg/dL		1.9 (1.3-2.9)	2.6 (2.2-3.2)	4.0 (3.3-4.8)	5.5 (4.6-6.6)	7.1 (5.8-8.7)	
80-110 mg/dL		1.2 (0.3-5.2)	1.6 (1.3-2.0)	3.1 (2.5-3.7)	5.2 (4.4-6.2)	7.8 (6.4-9.5)	
>110 mg/dL			2.2 (0.5-9.3)	4.0 (2.4-6.9)	5.2 (4.0-6.8)	11.5 (8.9-14.9)	

GV > 75%

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).

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.



simplicity versus complexity of implementation of potentially important factors of SGC

easy, simple, distinct and/or clear ←

→ obscure, indistinct, complex and/or difficult

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

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

insulin delivery

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)

algorithm

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*

Comment mesurer ?



RESEARCH

Open Access

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

Carole Ichai¹, Jean-Charles Preiser^{2*}, for the Société Française d'Anesthésie-Réanimation (SFAR)³, Société de Réanimation de langue Française (SRLF) and the Experts group⁴

- 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.
-

Accuracy of blood glucose measurements using glucose meters and arterial blood gas analyzers in critically ill adult patients: systematic review

Shigeaki Inoue, Moritoki Egi , Joji Kotani and Kiyoshi Morita

- Type of central laboratory machine (reference) is highly variable
 - Accuracy of blood glucose and a glucose meter using arterial blood were significantly more accurate than a glucose meter using capillary blood
 - Blood glucose monitoring by ABG analyzers tends to be more accurate than that by glucose meters using arterial blood
 - Blood glucose monitoring in the hypoglycemic range is less accurate than that in the non-hypoglycemic range
 - Unstable hemodynamics and insulin infusion might increase the risk of errors in blood glucose monitoring using a glucose meter
-

Cible glucose en réanimation

- Il n'y a pas de cible universelle (cela dépendra des ressources).
 - Il est fortement suggéré d'éviter **l'hyperglycémie sévère** (> 10 mmol/L / 180mg/dl) chez les patients adultes en réanimation.
 - Il est fortement suggéré d'éviter de grandes variations dans les niveaux de glucose.
 - **L'hypoglycémie sévère** est considérée à un seuil de glucose $< 2,2$ mmol/L / 40mg/dl.
-

Administration de l'insuline

- IV ou SC ?
- Insuline rapide ou lente ?

RESEARCH

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Carole Ichai¹, Jean-Charles Preiser^{2*}, for the Société Française d'Anesthésie-Réanimation (SFAR)³, Société de Réanimation de langue Française (SRLF) and the Experts group⁴

- **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.**
-

RESEARCH

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

Carole Ichai¹, Jean-Charles Preiser^{2*}, for the Société Française d'Anesthésie-Réanimation (SFAR)³, Société de Réanimation de langue Française (SRLF) and the Experts group⁴

- Il est suggéré d'interrompre la perfusion d'insuline par voie intraveineuse lorsque le patient a repris une prise alimentaire et de continuer à surveiller sa glycémie pendant au moins trois contrôles par jour avant le repas.
-

SLIDING vs DYNAMIC SCALES

- **Échelle statique/
sliding scales**

1 Blood glucose



1 Insulin rate

One simple algorithm

White (1982) – Bode (2004)

- Insulin dose (U/h) = multiplier*[BG (mg/dl)-60]
 - Multiplier = 0.03
 - + 0.01 if BG > 200 or
 - 0.01 if BG < low threshold
 - 0.02 if BG < 60
 - + IV glucose
-

SLIDING vs DYNAMIC SCALES

- **Échelle statique/
sliding scales**

1 Blood glucose



1 Insulin rate

- **Échelle dynamique/
dynamic scales**

1 Blood glucose



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

RESEARCH

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

Carole Ichai¹, Jean-Charles Preiser^{2*}, for the Société Française d'Anesthésie-Réanimation (SFAR)³, Société de Réanimation de langue Française (SRLF) and the Experts group⁴

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


Iwan A. Meynaar
Lilian Dawson
Peter L. Tangkau
Eduard F. Salm
Lode Rijks

Introduction and evaluation of a computerised insulin protocol

Fig. 1 The insulin protocol –
computer interface

<u>Input</u>	
Give <u>current</u> glucose	<input type="text" value="7"/> mmol/L
Give <u>old</u> glucose (no older than 8 hours)	<input type="text" value="5"/> mmol/L
Give current insulin dose per hour	<input type="text" value="2"/> U/hr
What is the hourly rate of feeding?	<input type="text" value="> 25 ml/hr"/>

Calculate

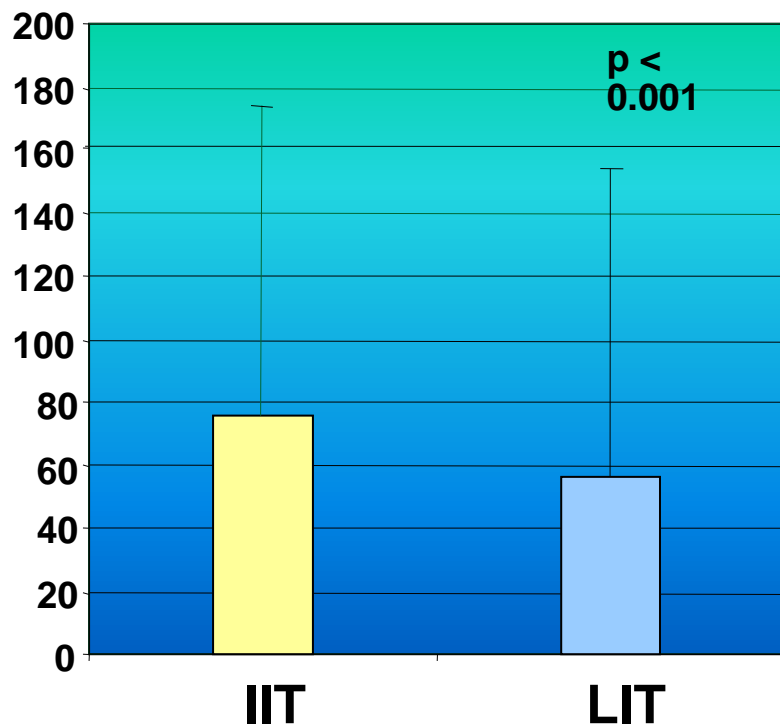
Intensive Care
Reinier de Graaf Groep


<u>Output</u>	
Give insuline bolus	0 U
The new hourly insulin rate is	2.5 U/hr
Measure glucose again	in 4 hrs

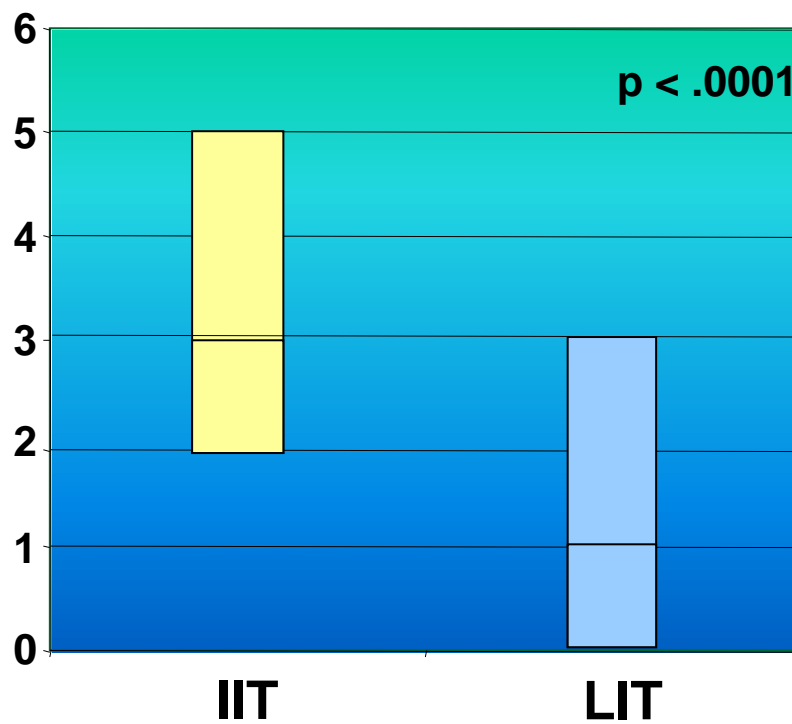
Effects of TGC on nursing workload

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

Glucose Monitoring is Labor Intensive and Prone to Error

4.72 Minutes/measurement

~ 2,500 Hours/month

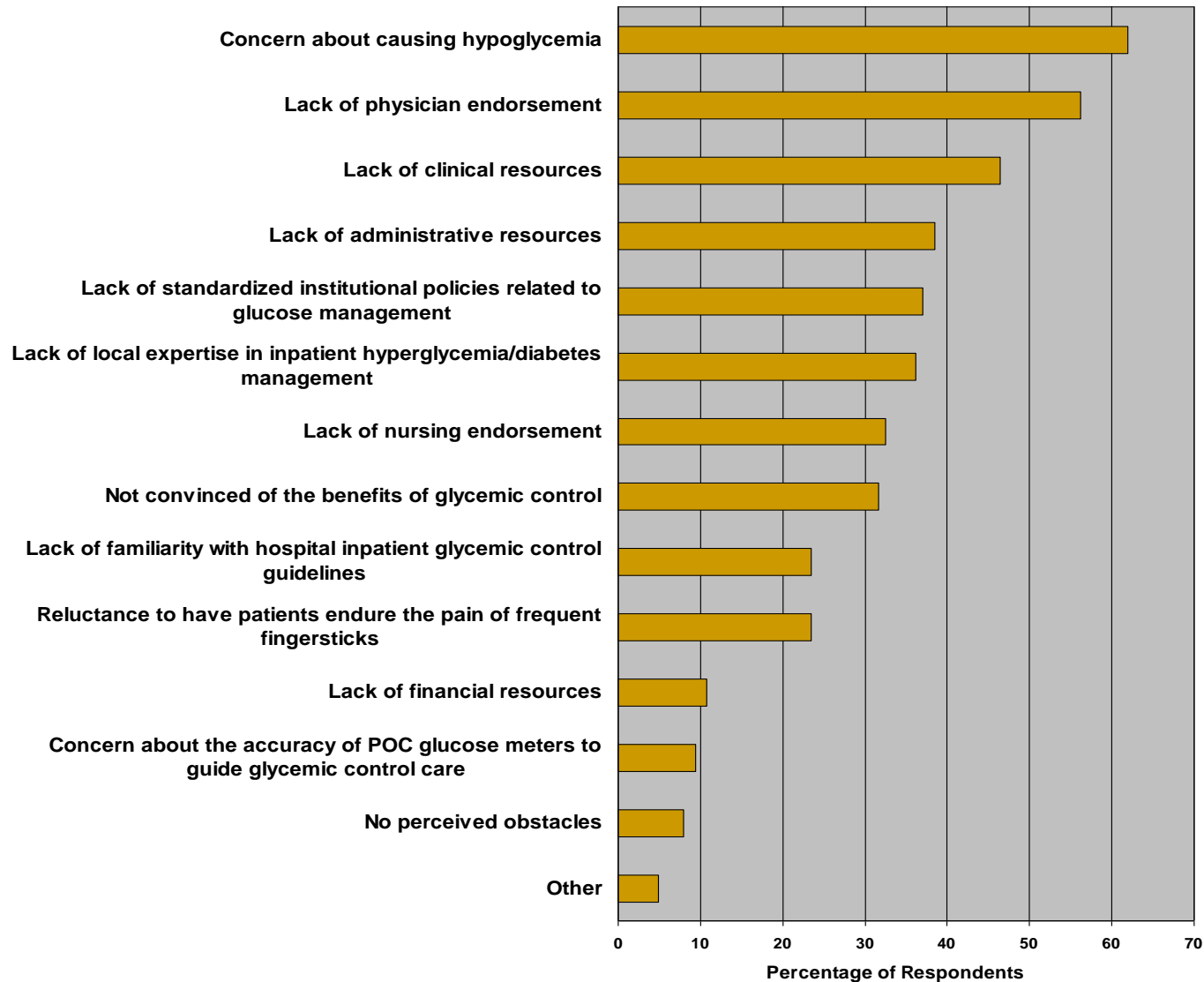
Aragon D. Evaluation of Nursing Work Effort and Perceptions about Blood Glucose Testing in Tight Glycemic Control. American Journal of Critical Care. 15(4):370-377, 2006.



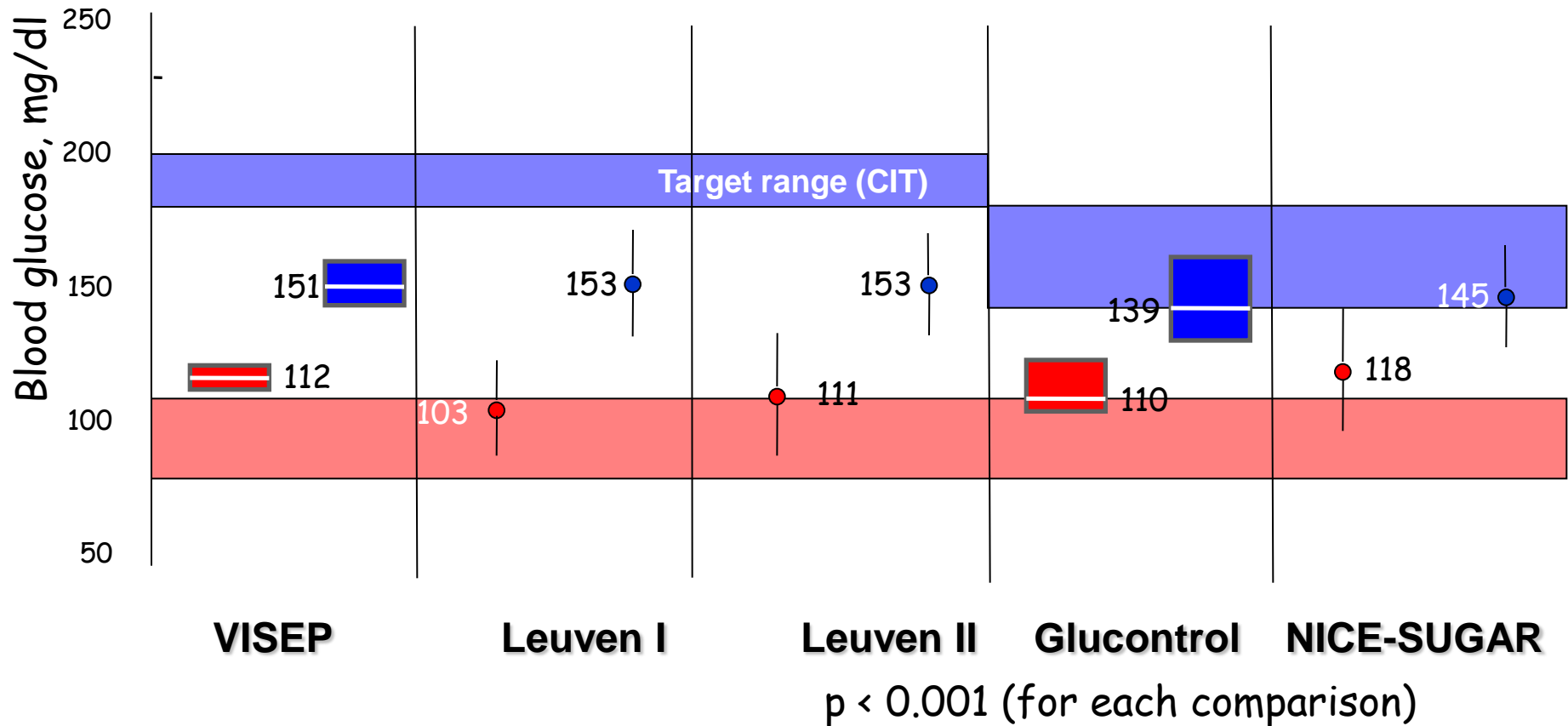
Perceived obstacles to the implementation of TGC

US survey

Cook BC et al SCCM congress (poster #282)



BG TARGET IS NOT ALWAYS REACHED !



RESEARCH

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

Carole Ichai¹, Jean-Charles Preiser^{2*}, for the Société Française d'Anesthésie-Réanimation (SFAR)³, Société de Réanimation de langue Française (SRLF) and the Experts group⁴

- L'hypoglycémie (même modérée <à 70mg/dl) doit être corrigée même en l'absence de signe cliniques.
- Dans la stratégie de contrôle strict de glycémie, il est recommandé de surveiller de près le niveau de glucose sanguin pour une détection précoce de l'hypoglycémie sévère.

RESEARCH

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

Carole Ichai¹, Jean-Charles Preiser^{2*}, for the Société Française d'Anesthésie-Réanimation (SFAR)³, Société de Réanimation de langue Française (SRLF) and the Experts group⁴

- Il n'y a pas de recommandations générale de quantités maximales ou minimales de glucides par voie IV et/ou entéral devant être administré à des patients gravement malades, quel que soit le type, la gravité de la pathologie et de son délais d'apparition.
-

Research

Open Access

A systematic review on quality indicators for tight glycaemic control in critically ill patients: need for an unambiguous indicator reference subset

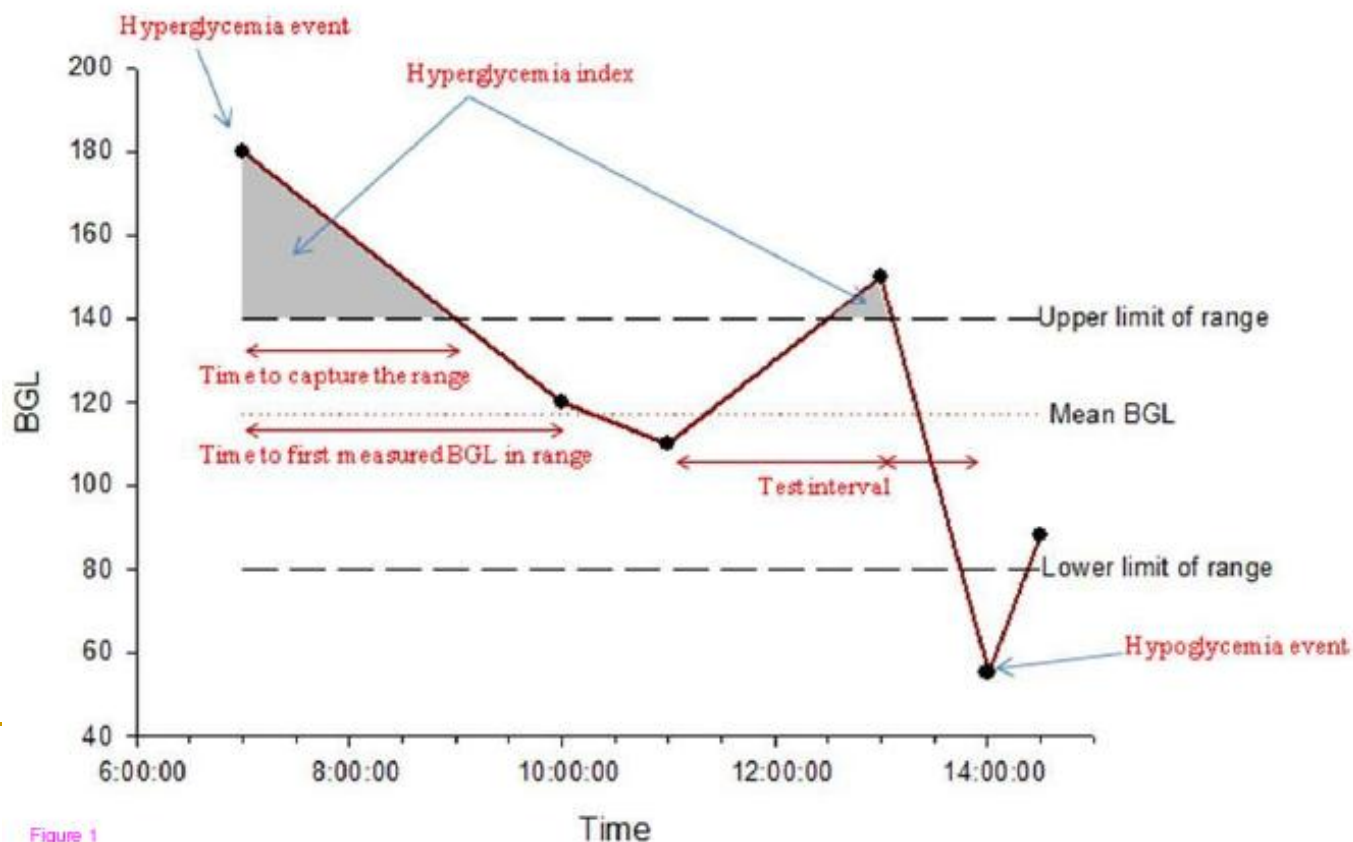
Saeid Eslami¹, Nicolette F de Keizer¹, Evert de Jonge², Marcus J Schultz² and Ameen Abu-Hanna¹

Figure 1

Try to use the same language!



The logo features a grey silhouette of a person with a question mark on their chest, standing to the left of the word "ASK" in large, bold, red letters. Below "ASK" is the word "the" in a smaller, black, lowercase font, and below that is the word "EXPERTS" in a black, italicized, uppercase font.

ASK the EXPERTS

Intensivists
Clinical chemists
Pharmacists
Healthcare providers
Involved in ICU care



REVIEW

Consensus recommendations on measurement of blood glucose and reporting glycemic control in critically ill adults

Simon Finfer¹, Jan Wernerman², Jean-Charles Preiser^{*3}, Tony Cass⁴, Thomas Desaive⁵, Roman Hovorka⁶, Jeffrey I Joseph⁷, Mikhail Kosiborod⁸, James Krinsley⁹, Iain Mackenzie¹⁰, Dieter Mesotten¹¹, Marcus Schulz¹², Mitchell G Scott¹³, Robert Slingerland¹⁴, Greet Van den Berghe¹¹ and Tom Van Herpe^{11,15}

1. How should we measure and report glucose control when intermittent BG measurements are used?

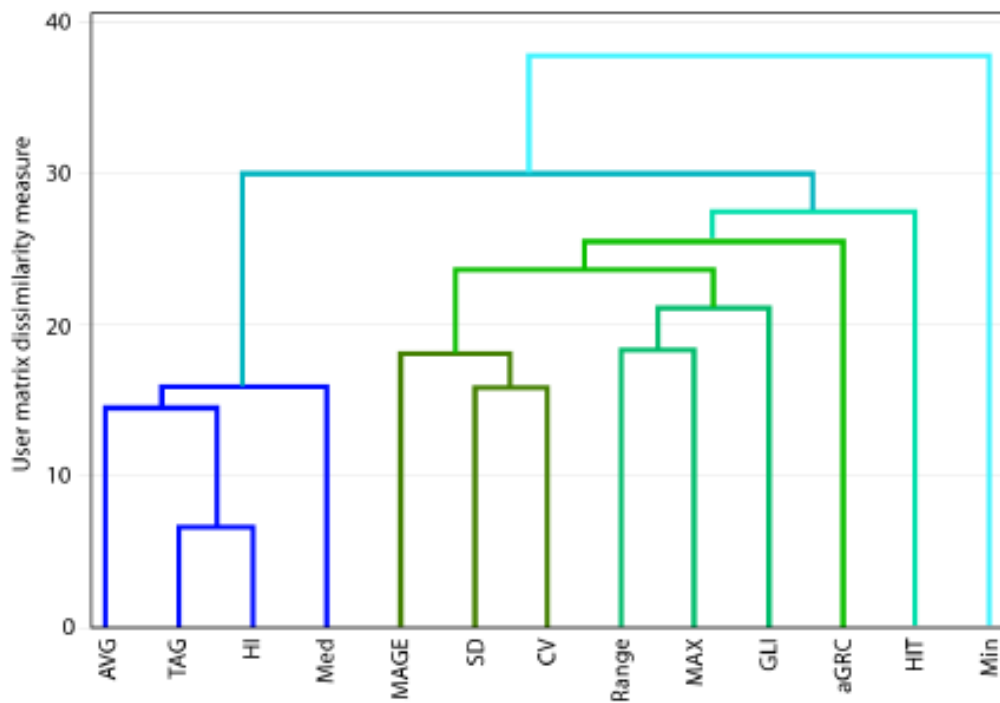


Figure 1. Cluster analysis dendrogram of the metrics of glycaemic control.

1. How should we measure and report glucose control when intermittent BG measurements are used?

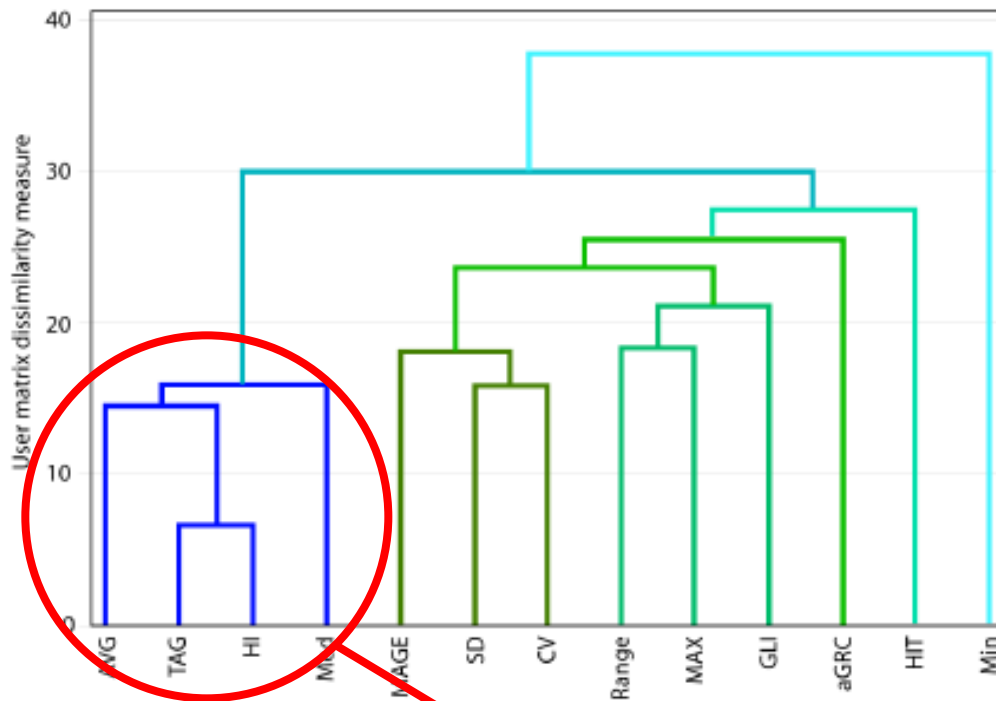


Figure 1. Cluster analysis dendrogram of the metrics of glycaemic control.

Mackenzie et al, ICM 2011;37:435-43

Central tendency

1. How should we measure and report glucose control when intermittent BG measurements are used?

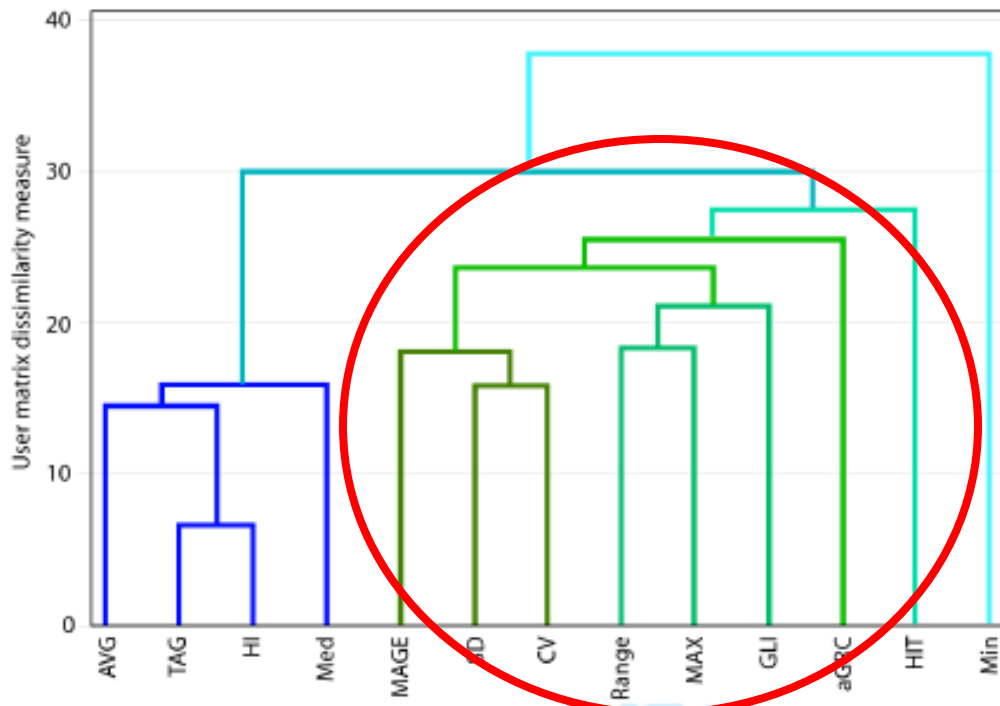


Figure 1. Cluster analysis dendrogram of the metrics of glycaemic control.

Mackenzie et al, ICM 2011;37:435-43

Dispersion

1. How should we measure and report glucose control when intermittent BG measurements are used?

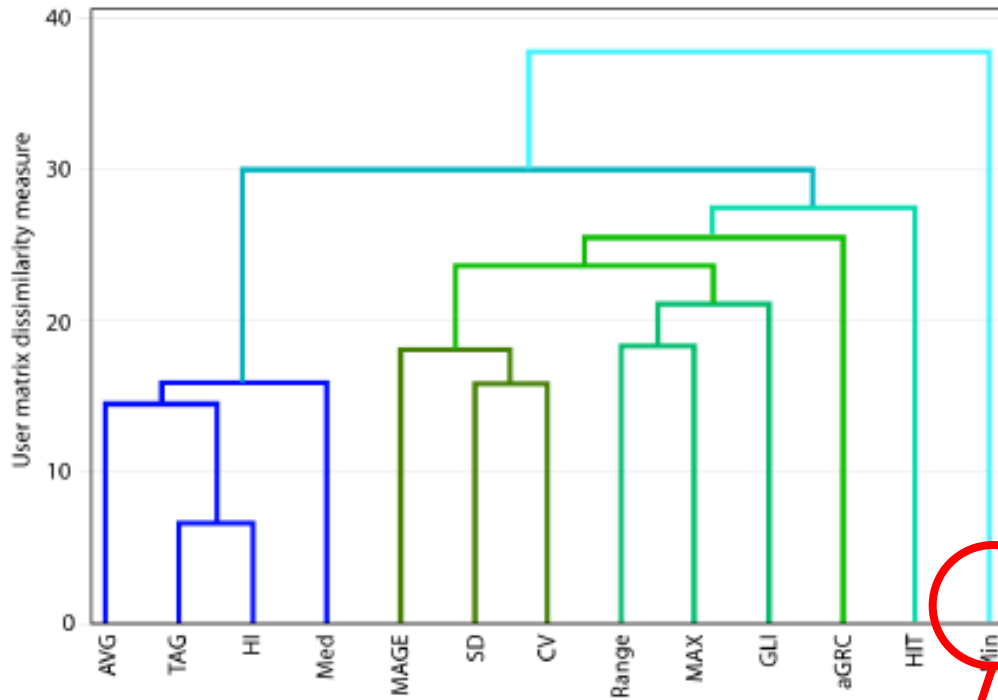


Figure 1. Cluster analysis dendrogram of the metrics of glycaemic control.

Mackenzie et al, ICM 2011;37:435-43

Hypoglycemia

A 5-year view Glycemic control in ICU



(Expert review Endocrinol Metab 2011;6:681)

- ***Better delineation of the risks associated with tight glucose control***
- ***What is the most appropriate glycaemic target?***
- ***Blood glucose measurement***
- ***Continuous glucose monitoring***
- ***Insulin algorithms***
- ***Closed-loop systems***

Why would we use CGM?

- Research tool
 - **Improved quality of glucose control**
 - **Ease of glucose control**
 - **Decreased nursing workload**
 - **Decreased costs**
-

The current market

	Glucose oxidase	Mid-infrared	Fluorescence
Interstitial tissue	Sentrino Navigator Dexcom 7 Symphony		
Intravascular			
Microdialysis	Eirus MicroEye Glucoday		Diramo
Venous	Glucoclear (p) Glucoscout	Optiscanner	Glysure
Arterial			Glucath

Monitoring sites

- Glucose can be measured in
 - whole blood
 - plasma (gold standard)
 - interstitial fluid
 - microdialysis fluid.
-

Interstitial versus plasma

- Interstitial fluid glucose levels depend on the rate of glucose diffusion from plasma to the interstitial fluid and the rate of uptake by subcutaneous tissue cells.
-

Microdialysis

- Microdialysis fluid measurements use a probe with a membrane impermeable to macromolecules but permeable to low molecular weight compounds, such as glucose and lactate. Flow of isotonic fluid within the membrane enables a degree of equilibrium to be reached between the surrounding fluid and the dialysate fluid
-

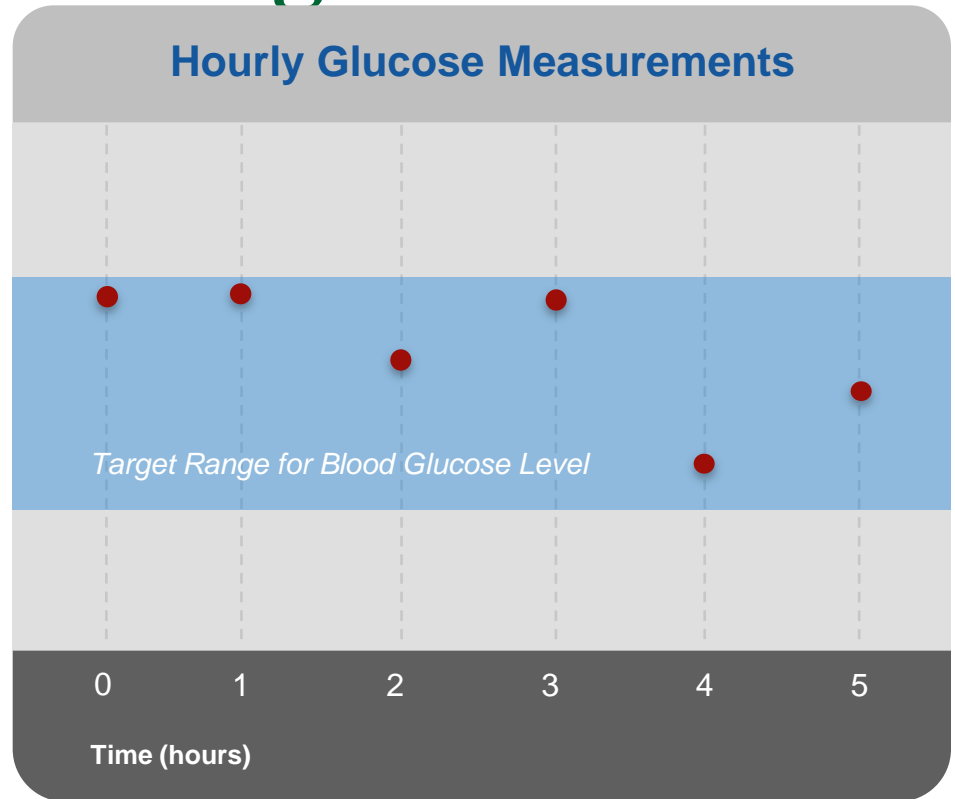
Development and validation of near-continuous glucose monitoring an hurdle race....

- Site →
- Calibration →
- Lifespan →
- Interferences →



The Complete Picture in Glucose Monitoring

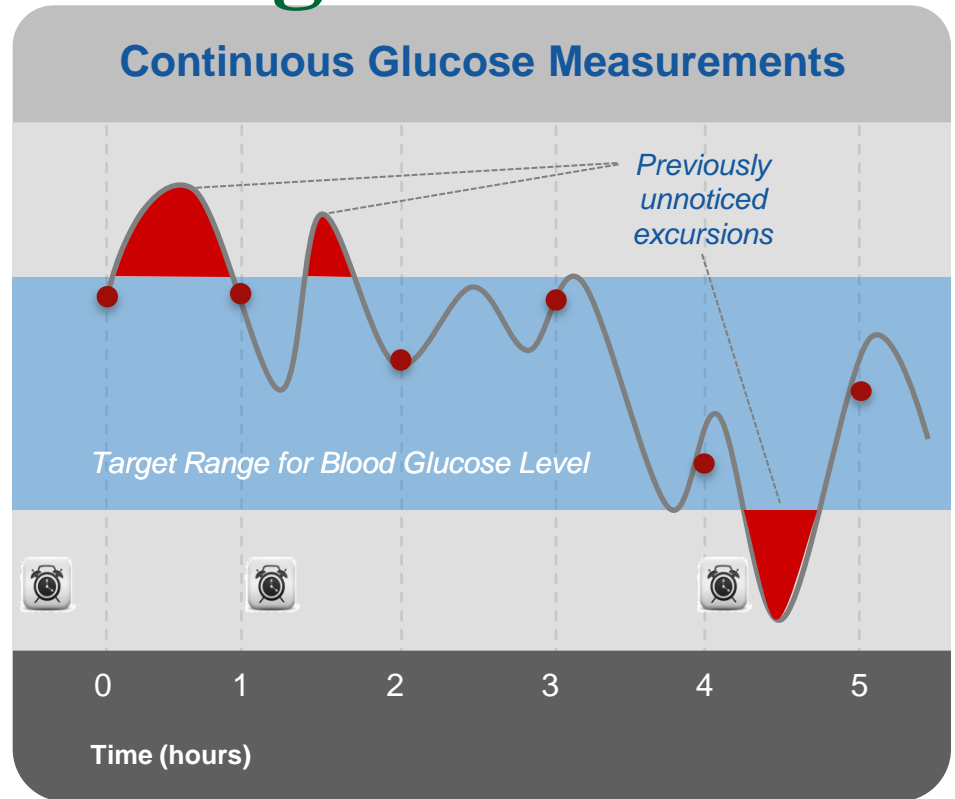
See What You've Been Missing!



The Complete Picture in Glucose Monitoring

See What You've Been Missing!

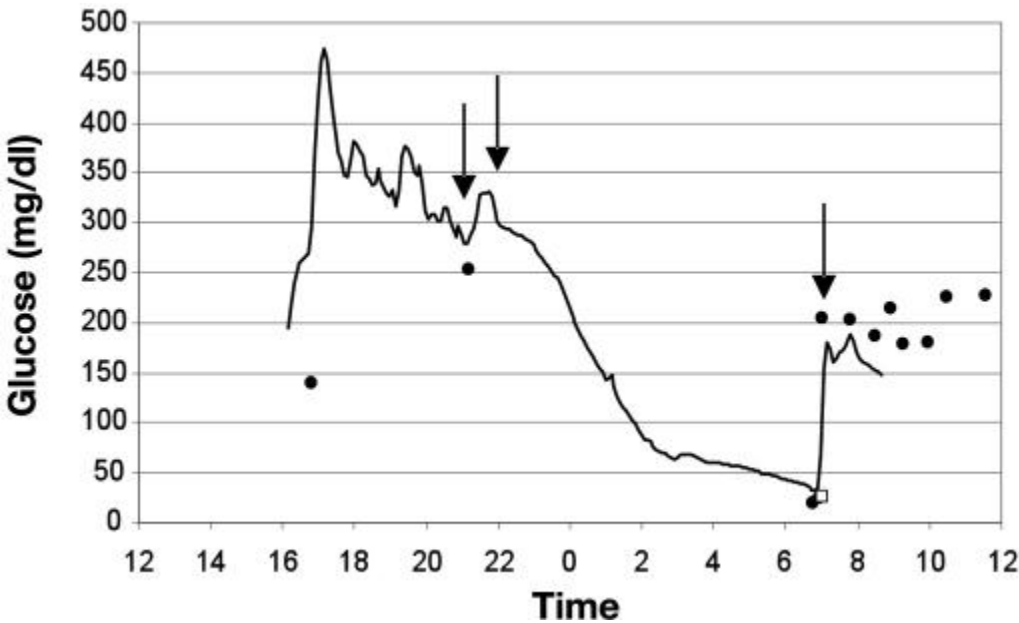
- Continuous image vs. snapshots in time
 - Predicts trends prior to excursions
 - Helps manage “time in target”
 - Helps safely avoid hypoglycemic events
- ...all of these help eliminate nurse burden**



 Predictive alarms

Clinical Need for Continuous Glucose Monitoring in the Hospital

Jeffrey I Joseph, D.O

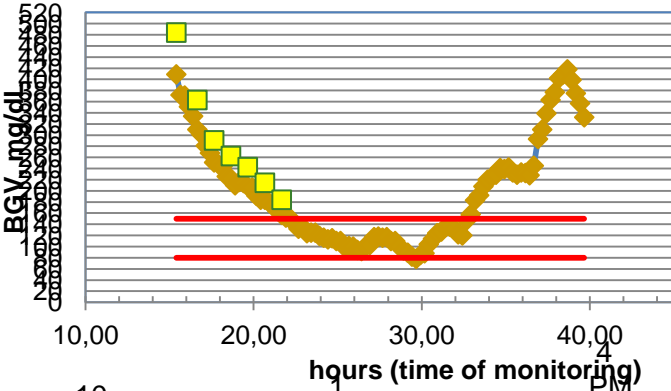
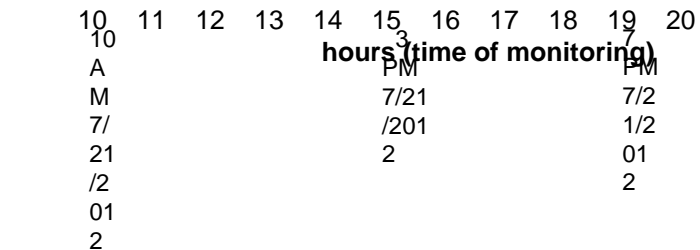
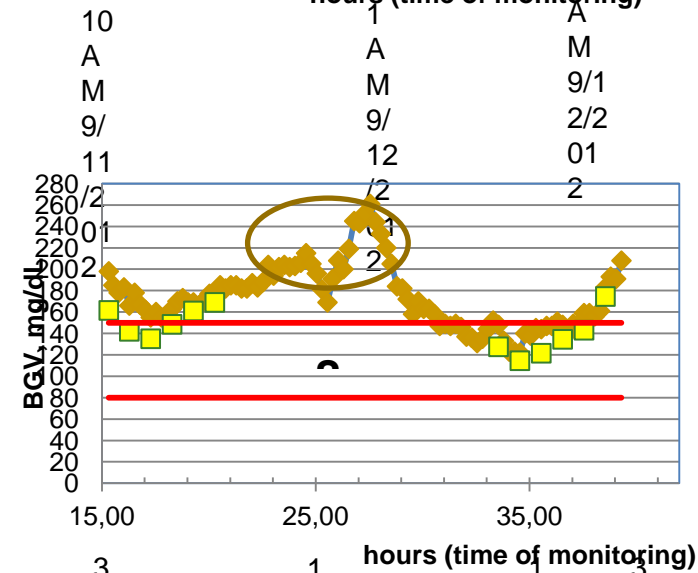
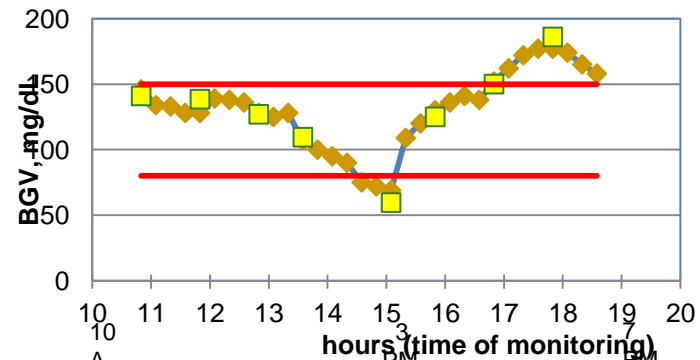
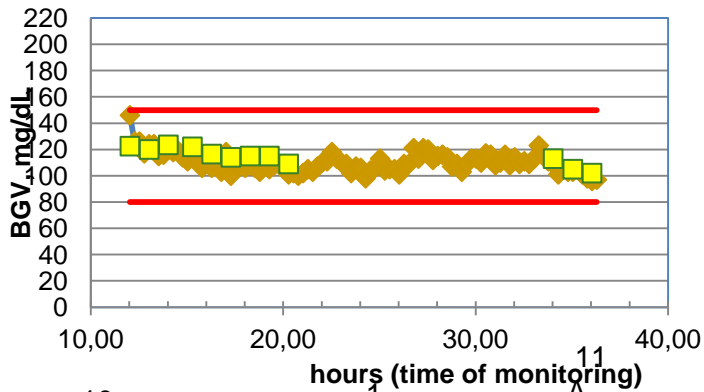


Severe hypoglycemia recorded in a hospitalized patient with type 1 diabetes 1 day after orthopedic surgery. The interstitial fluid glucose concentration (solid line) was measured and recorded every 5 minutes using a CGMS iPro Continuous Glucose

J Diabetes Sci Technol. 2009 ; 3 : 1309

Some runcharts from MANAGE II

Optiscanner – Erasme Hosp - Brussels



10	1	11
A	A	M
M	M	9/1
9/	9/	2/2
11	12	01
12	12	2

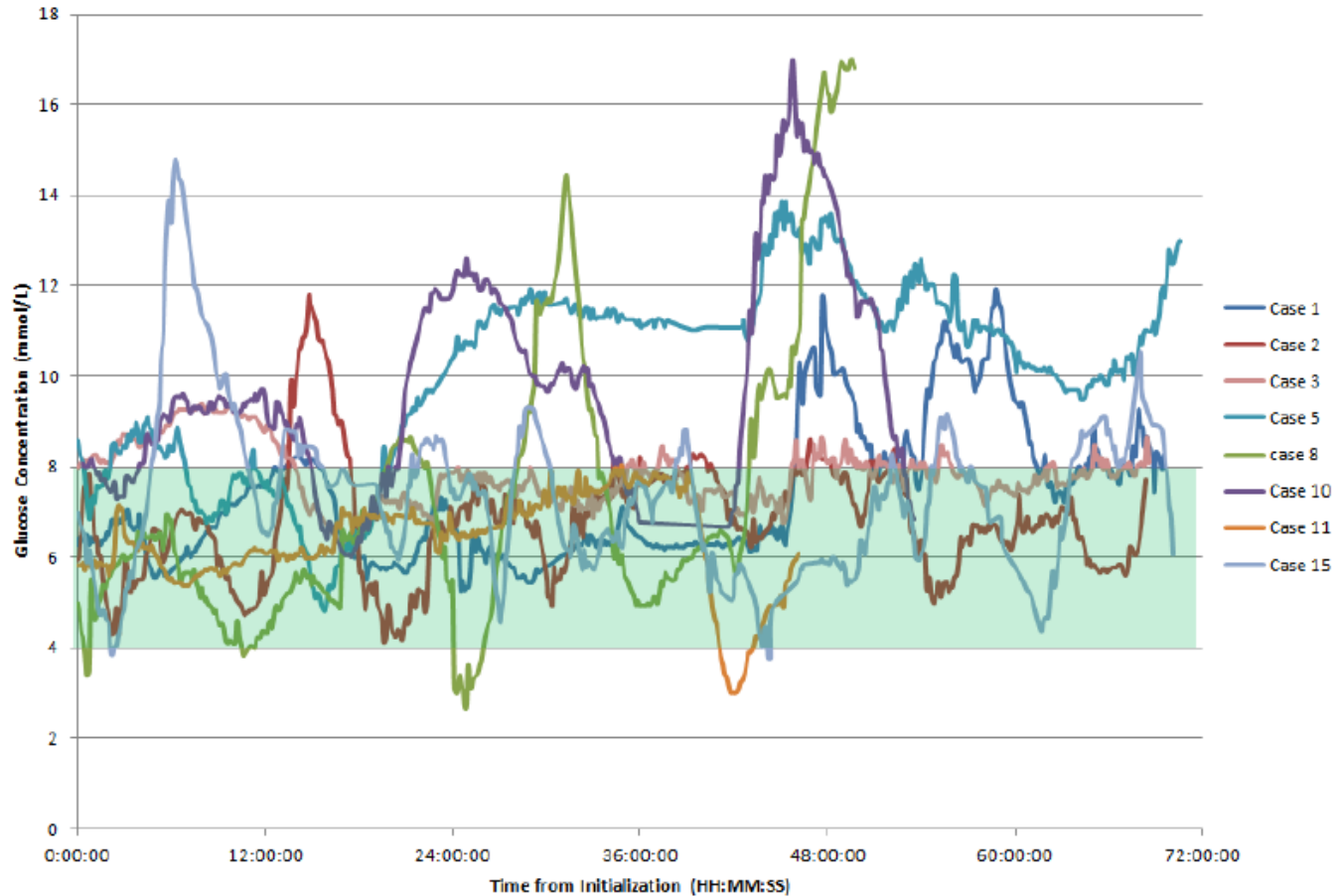
3	1	3
P	A	P
M	M	M
8/	8/	8/

10	4
A	PM
M	M
11	11
/2	/2

A	11/
M	22/
11	20
/2	12

Cardiothoracic patients from Liverpool (N Scawn)

Summary of Liverpool MPE Patients Monitored with GlucoClear



Computerized protocols



- Very suitable :
 - Mathematical formula with several entries (previous measures, rates of infusion, BMI, changes in insulin resistance/sensitivity etc..)
 - Repetitive, systematic
 - Decision tree in binary language

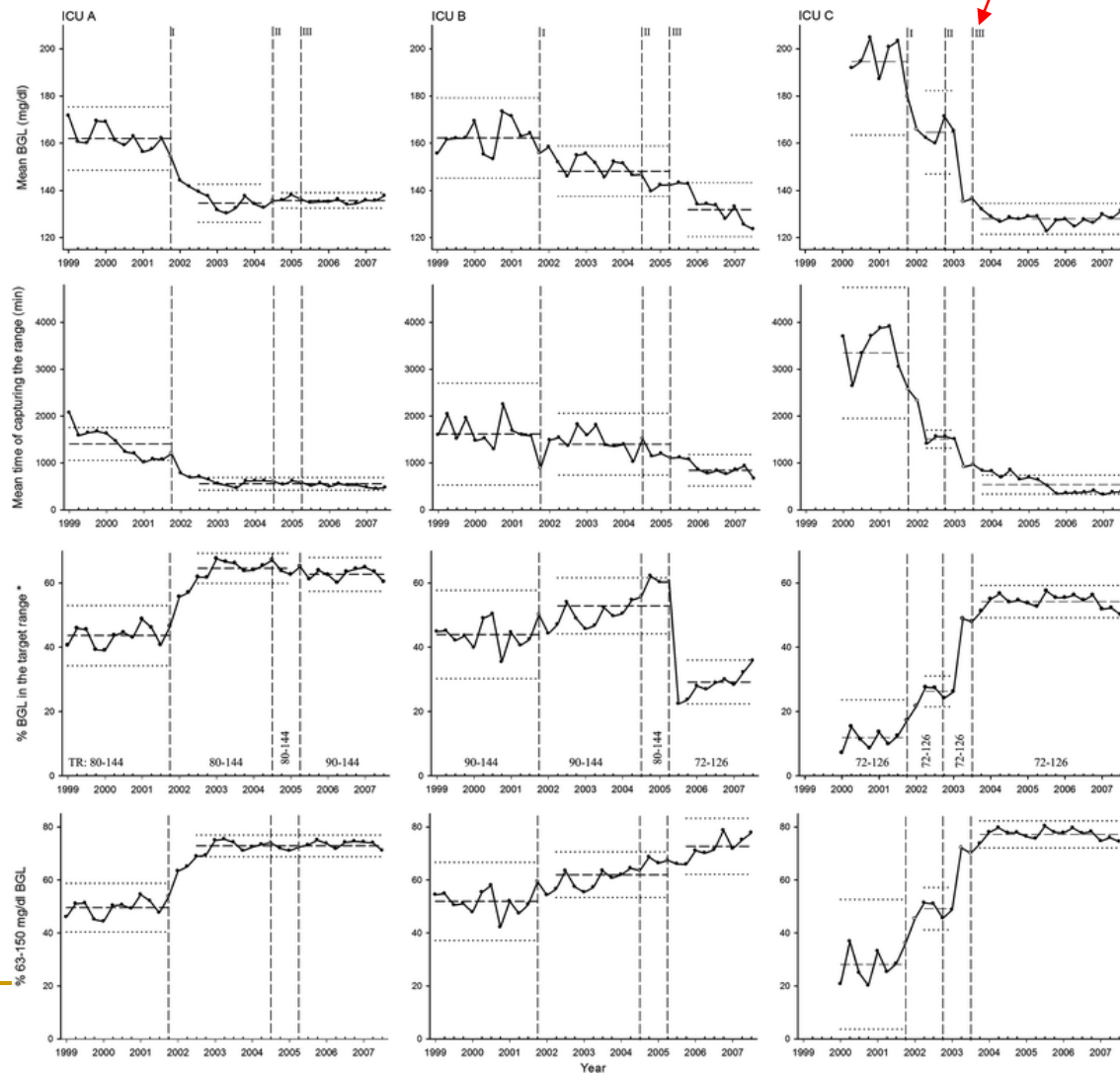
Implementing glucose control in intensive care.

Eslami Intensive Care Med 2010;36:1556

CDSS

Efficiency/effectiveness indicators

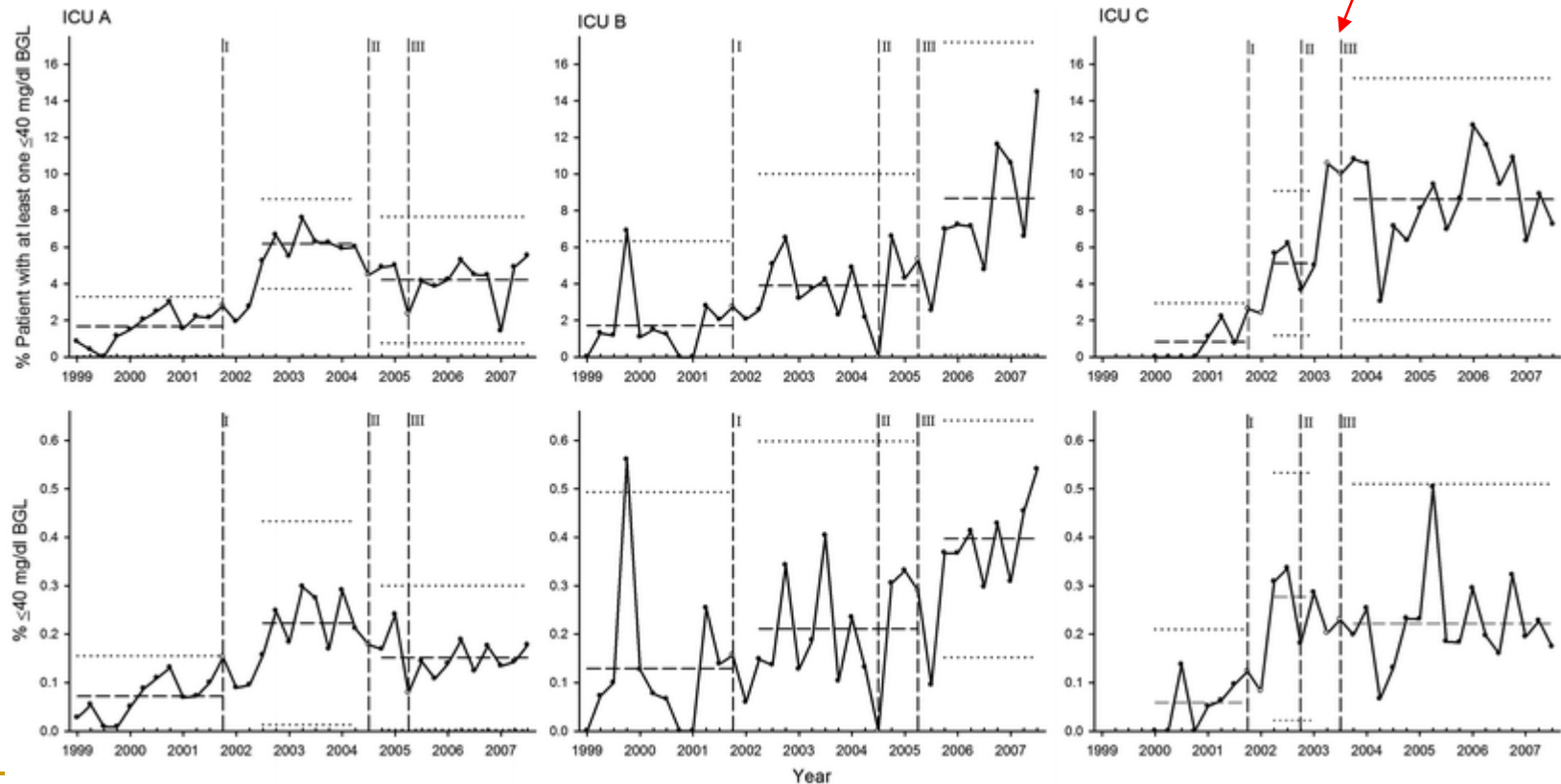
Data of 17,111 patient admissions were evaluated, with 714,141 available blood glucose levels (BGL) measurements. Mean BGL, time to reach target, hyperglycemia index, sampling frequency, percentage of hyperglycemia events, and in-range measurements statistically changed after introducing GC in all ICUs.. Various revisions were implemented to reduce hypoglycemia events, but levels never returned to those from pre-implementation. More intensive implementation strategies including the use of a decision support system resulted in better control of the process.



Implementing glucose control in intensive care.

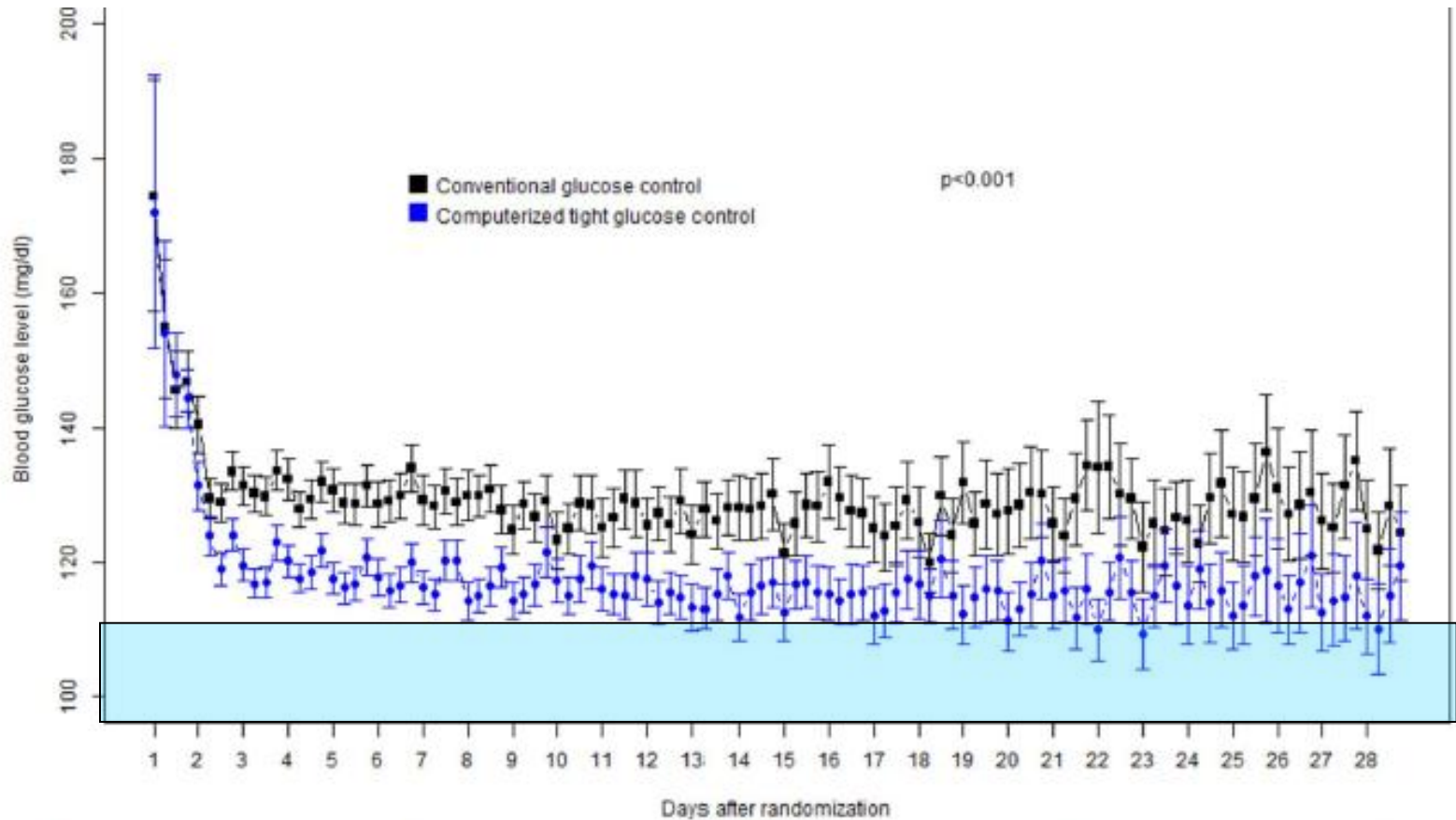
Eslami Intensive Care Med 2010;36:1556

Safety indicators



CGAO-rea study

Kalfon et al Intensive Care Med 2014 (in press)



No. of patients					
Conventional glucose control	1190	603	292	168	103
Computerized tight glucose control	1251	678	322	165	94



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**Programme détaillé en ligne
Mai 2014**

**Ouverture des inscriptions et
de la soumission des abstracts
Mai 2014**

**Date limite de soumission
des abstracts
12 septembre 2014**

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