

Supplementary Online Content

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eTable 1. Methodology Employed by the APACHE Algorithm to Report Day 1 Blood Glucose

eTable 2. Time Trends in Tight Glycemic Control Comparing Day 1 and Day 2 Glucose Data

eFigure 1. Bland-Altman Plots Assessing Agreement Between Physiologically Most Extreme Day 1 Glucose (GLUC₂₄) and Mean Glucose During the First Week of ICU Admission (GLUC_{TOT})

eFigure 2. Time Trends In Tight Glycemic Control When Glycemic Control Is Defined Using Day 2 Glucose (n = 167,797 Admissions, 72 ICUs)

eFigure 3. Time Trends in Measures Of Glucose Control in Patients Admitted to Subgroup of ICUs That Contributed Data Every Year During the Study (n = 46,718 Admissions, 10 ICUs)

eFigure 4. Time Trends in Tight Glycemic Control for Patients Admitted to Individual ICUs That Contributed Data Every Year During the Study (n = 46,718 Admissions, 10 ICUs)

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Methodology Employed by the APACHE Algorithm to Report Day 1 Blood Glucose

Blood Glucose Range		APACHE Points	Prioritization for Recording in APACHE Database ^a
mg/dL	mmol/L		
≤ 39	≤ 2.16	8	2
40 – 59	2.22 – 3.27	9	1
60 – 199	3.33 – 11.04	0	5
200 – 349	11.10 – 19.37	3	4
≥ 350	≥ 19.42	5	3

- a. The APACHE database contains actual blood glucose values. Priority for recording glucose data on a given day of ICU admission is such that preference is given to values that provide the most APACHE points.
- b. Source: Knaus WA, Wagner DP, Draper EA, et al. The APACHE III prognostic system. Risk prediction of hospital mortality for critically ill hospitalized adults. *Chest*. 1991;100(6):1619-1636.

eTable 2. Time Trends in Tight Glycemic Control Comparing Day 1 and Day 2 Glucose Data

Tight Glycemic Control Marker ^a	Start of Study ^b (%)	Post-Leuven I ^c		Pre-NICE-SUGAR	Post-NICE-SUGAR ^c		End of Study ^b (%)
		Immediate Change (%) ^d	Change in Trend (% per quarter) ^e		Immediate Change (%) ^d	Change in Trend (% per quarter) ^e	
Glucose ICU day one ^f	17 (16 to 18)	-4.2 (-11 to 3.1)	1.7 (1.2 to 2.3) ^g	20 (19 – 22)	-3.3 (-8.1 to 1.8)	0.28 (-0.26 to 0.83)	28 (26 to 29)
Glucose ICU day two ^f	19 (17 to 20)	3.7 (-4.8 to 13)	1.8 (1.3 to 2.3) ^g	26 (24 – 27)	-4.1 (-11 to 3.3)	0.27 (-0.63 to 1.2)	28 (25 to 29)

a: Tight glycemic control, physiologically most extreme glucose between 80 and 110 mg/dL (4.4 – 6.1 mmol/L)

b: Data are provided as (unadjusted) proportion (95% CI) of ICU admissions with the given glycemic control measure.

c: Adjusted (APACHE III/IV score, proportion with septic admission diagnosis, and proportion with diabetes mellitus) change in relative proportion of admissions with given measure of glycemic control as obtained from multi-level segmented linear regression analyses

d: Immediate change in relative proportion of ICU admissions with glycemic control measure in the quarter that followed publication.

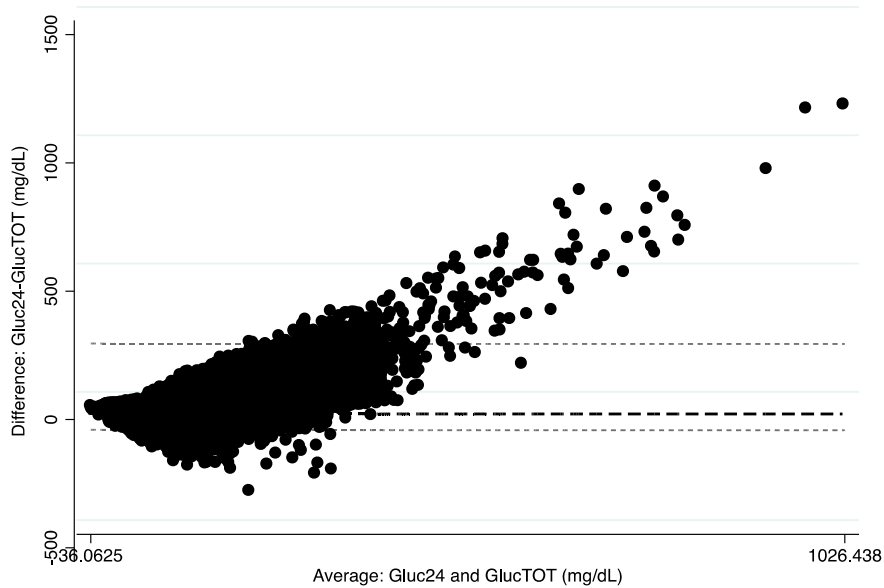
e: Quarterly change in relative proportion of ICU admissions with glycemic control measure.

f: ICU Day one glucose: 377,861 admissions to 113 ICUs; ICU Day two glucose: 167,797 admissions to 72 ICUs

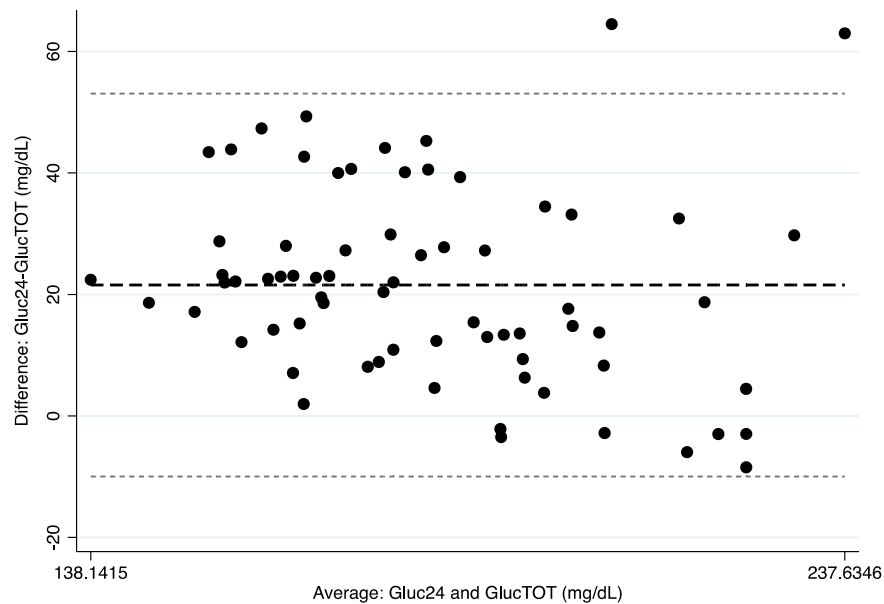
g: $p < 0.01$

eFigure 1. Bland-Altman Plots Assessing Agreement Between Physiologically Most Extreme Day 1 Glucose (GLUC₂₄) and Mean Glucose During the First Week of ICU Admission (GLUC_{TOT})

(a) Patient-level data

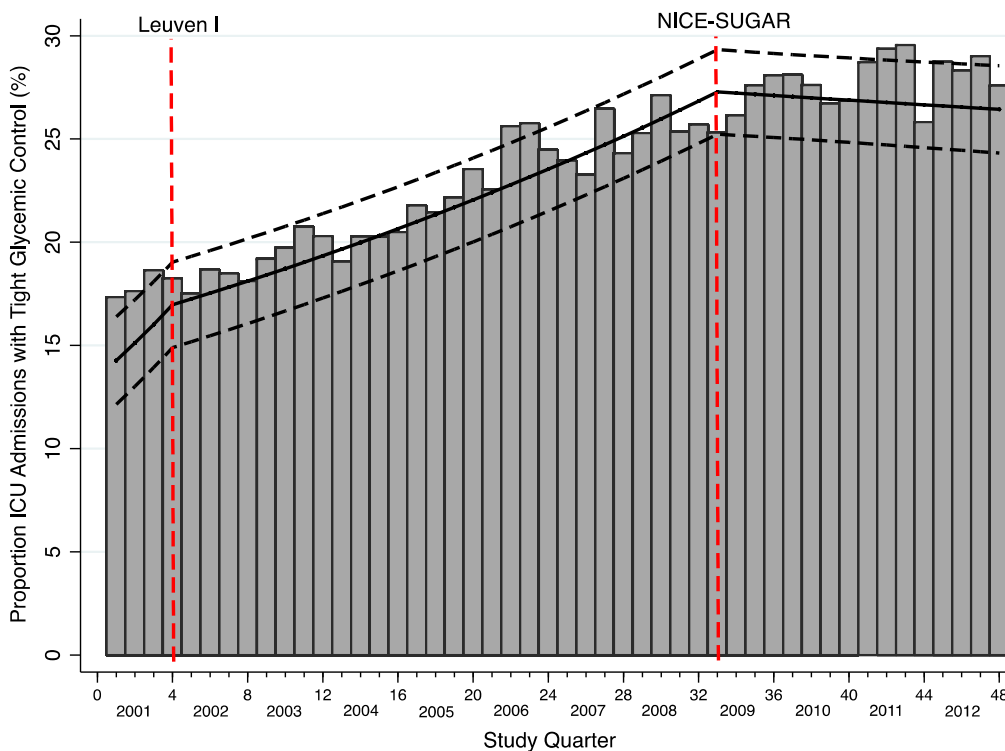


(b) Aggregate ICU-level data



(a) GLUC₂₄ and GLUC_{TOT} for each individual ICU admission (n = 26,766). Note: 96% of the study population had GLUC₂₄ < 360 mg/dL (20 mmol/L); (b) GLUC₂₄ and GLUC_{TOT} for aggregate ICU-level data. GLUC_{TOT} is the mean blood glucose during the first eight days of ICU admission. For each plot, the middle dashed line is the overall mean difference between GLUC₂₄ and GLUC_{TOT}, and the outer dashed lines represent the mean difference +/- two standard deviations (limits of agreement) respectively.

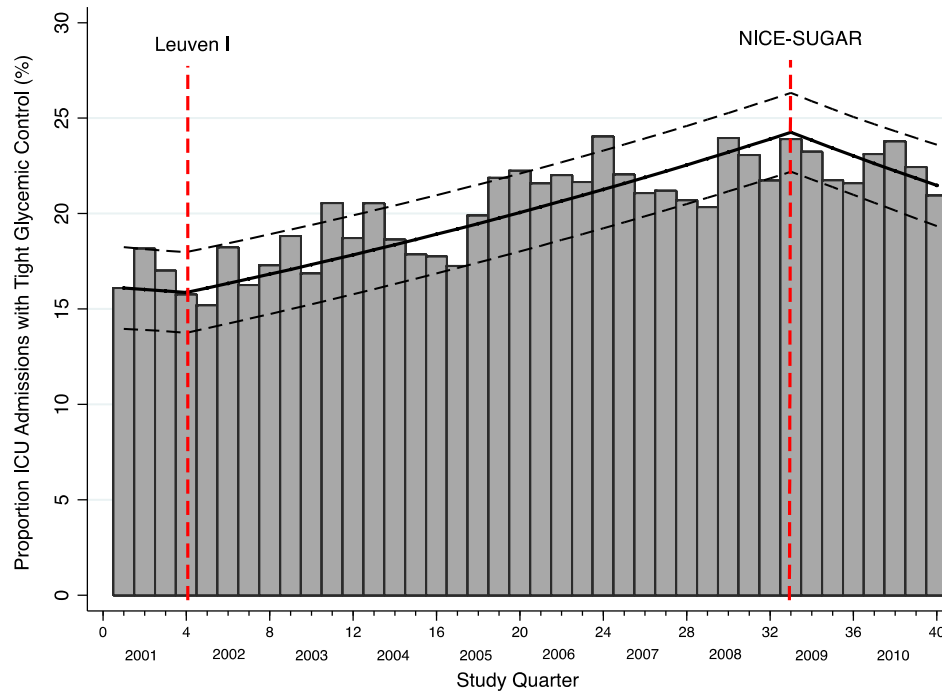
eFigure 2. Time Trends In Tight Glycemic Control When Glycemic Control Is Defined Using Day 2 Glucose (n = 167,797 Admissions, 72 ICUs)



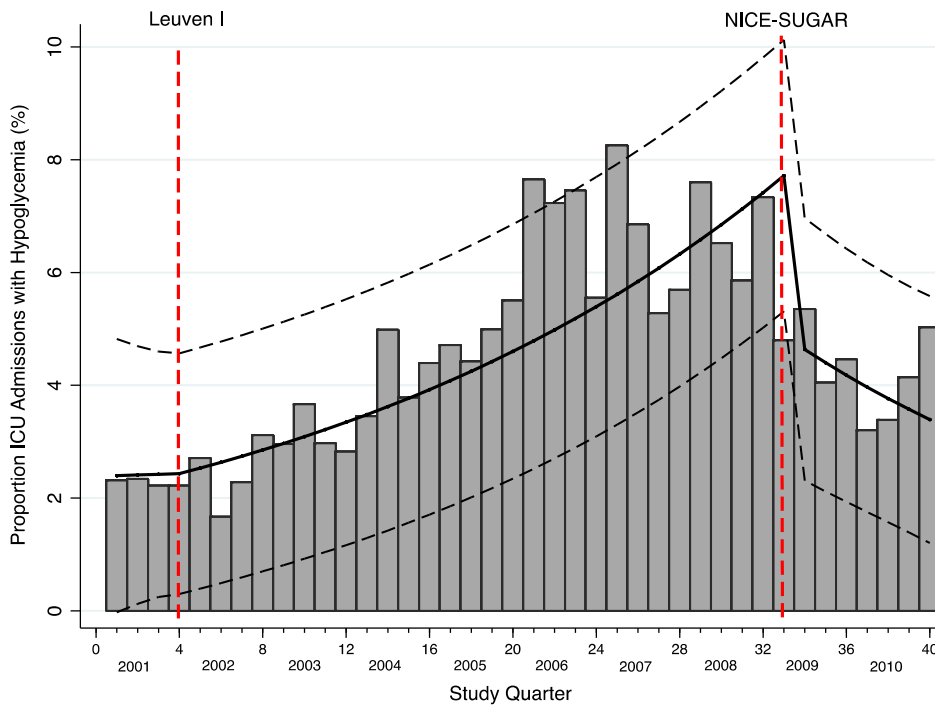
Tight glycemic control defined as physiologically most extreme day two glucose between 80 and 110 mg/dL (4.4 – 6.1 mmol/L). Bars are the unadjusted overall mean, and the solid line represents the multivariable adjusted overall mean (dotted lines are 95% CI). The two vertical lines denote the quarter of publication of Leuven I and NICE-SUGAR.

eFigure 3. Time Trends in Measures Of Glucose Control in Patients Admitted to Subgroup of ICUs That Contributed Data Every Year During the Study (n = 46,718 Admissions, 10 ICUs)

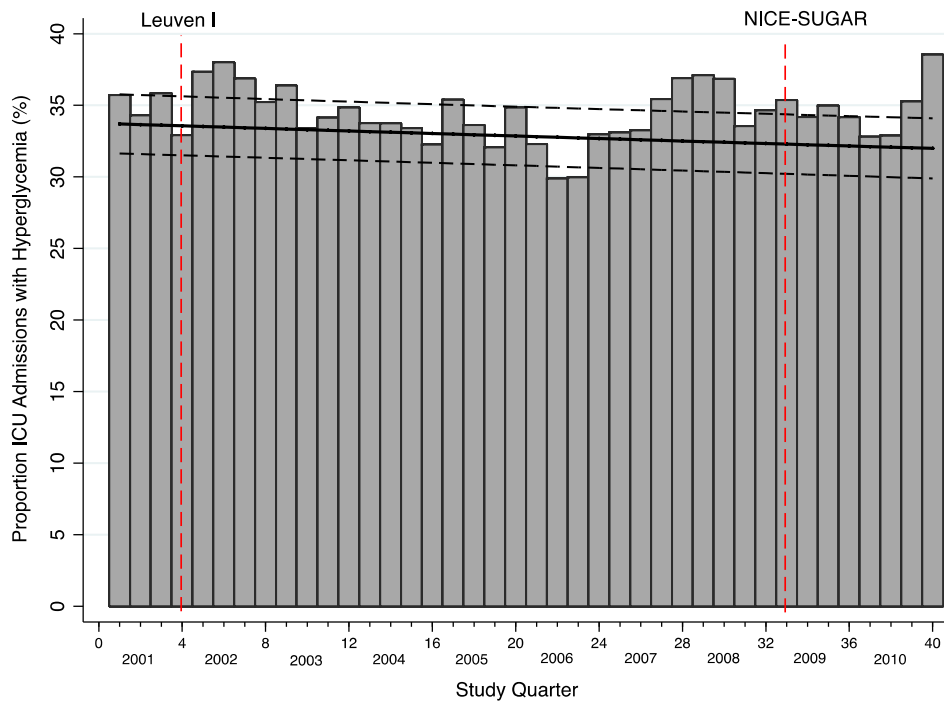
(a) Tight glycemic control, day one glucose 80 – 110 mg/dL (4.4 – 6.1 mmol/L)



(b) Hypoglycemia, day one glucose < 70 mg/dL (4.0 mmol/L)

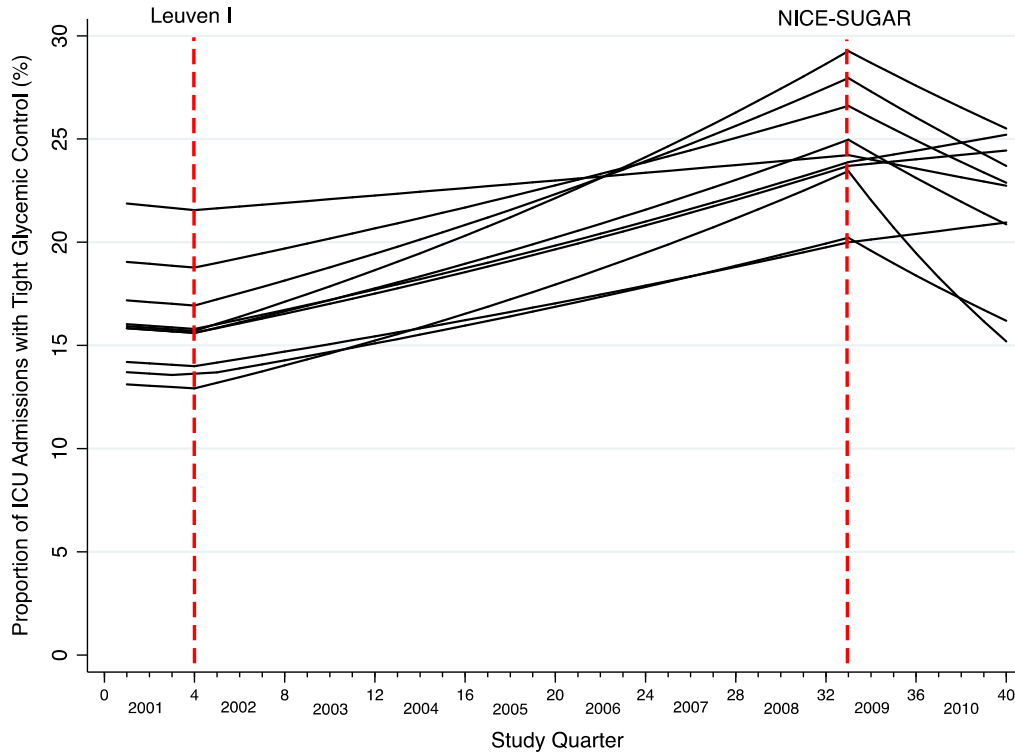


(c) Hyperglycemia, day one glucose ≥ 180 mg/dL (10.0 mmol/L)



Bars are the unadjusted overall mean, and the solid line represents the multivariable adjusted overall mean (dotted lines are 95% CI). The two vertical lines denote the quarter of publication of Leuven I and NICE-SUGAR.

eFigure 4. Time Trends in Tight Glycemic Control for Patients Admitted to Individual ICUs That Contributed Data Every Year During the Study (n = 46,718 Admissions, 10 ICUs)



Tight glycemic control defined as day one glucose 80 – 110 mg/dL (4.4 – 6.1 mmol/L). Each solid line represents the multivariable adjusted overall mean for an individual ICU. The two vertical lines denote the quarter of publication of Leuven I and NICE-SUGAR.