

QUALI EVIDENZE PER TITR?

Congresso

La tecnologia oggi e...domani

Aula Magna - ASST Grande Ospedale Metropolitano Niguarda

7 Giugno 2025

Dott. Matteo Conti

Università degli Studi di Milano-Bicocca

Dichiarazione sul Conflitto di Interessi

Io sottoscritto Dott. Matteo Conti
in qualità di Relatore dell'evento

La tecnologia oggi e ...domani
dichiaro

di NON aver avuto rapporti di finanziamento
con soggetti portatori di interessi commerciali
in campo sanitario negli ultimi due anni.

TITR: definizione

Time

In

70-180 mg/dl

Tight

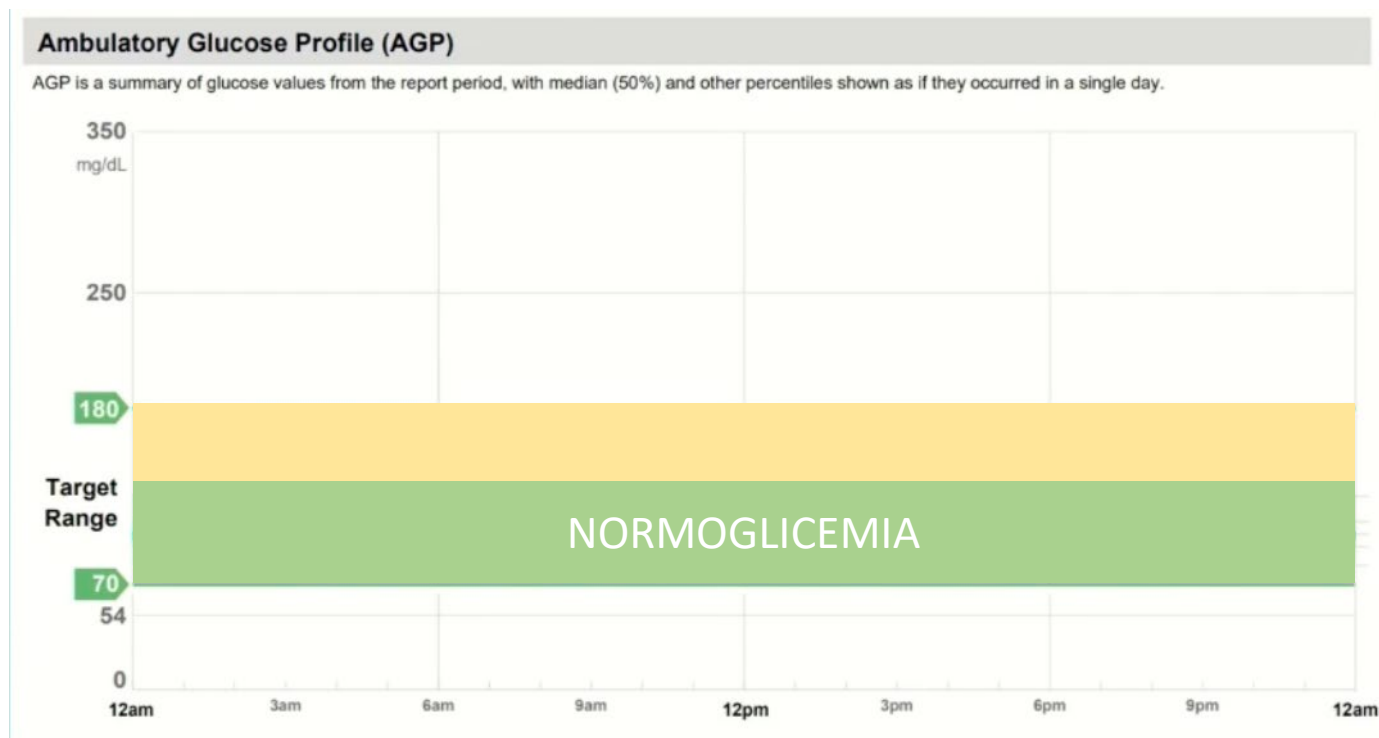
70-140 mg/dl

Range

DATI CGM DI 153 SOGGETTI SENZA DIABETE

Table 2. Summary of Glucose Metrics Over a 24-h Period (n = 153)

	All Participants	Age Group				
		6 to <12 y	12 to <18 y	18 to <25 y	25 to <60 y	≥60 y
Percentage of glucose sensor values, median (IQR)						
>180 mg/dL	0.0 (0.0–0.2)	0.0 (0.0–0.1)	0.0 (0.0–0.0)	0.0 (0.0–0.4)	0.0 (0.0–0.2)	0.1 (0.0–0.5)
>160 mg/dL	0.3 (0.1–0.9)	0.2 (0.1–0.8)	0.2 (0.0–0.2)	0.4 (0.2–1.1)	0.4 (0.2–0.9)	0.6 (0.1–2.9)
>140 mg/dL	2.1 (0.9–3.9)	1.7 (0.8–2.9)	1.2 (0.3–2.0)	2.4 (1.3–4.4)	2.1 (1.1–3.1)	4.1 (1.3–8.6)
70–140 mg/dL	96 (93–98)	97 (94–97)	97 (95–98)	95 (91–97)	97 (94–98)	93 (89–96)
70–120 mg/dL	89 (82–92)	90 (83–92)	92 (86–93)	87 (82–90)	89 (86–91)	81 (71–86)
<70 mg/dL	1.1 (0.3–2.9)	1.1 (0.3–3.3)	1.7 (0.6–2.6)	1.3 (0.5–3.6)	1.0 (0.3–2.3)	1.4 (0.2–3.4)
<60 mg/dL	0.2 (0.0–0.6)	0.2 (0.0–0.3)	0.2 (0.0–0.8)	0.2 (0.0–0.7)	0.2 (0.0–0.4)	0.3 (0.0–0.7)
<54 mg/dL	0.0 (0.0–0.2)	0.0 (0.0–0.2)	0.0 (0.0–0.4)	0.1 (0.0–0.4)	0.0 (0.0–0.2)	0.1 (0.0–0.2)



TITR



Time In NormoGlycemia (TING)

Time

In

70-180 mg/dl

> 70%

Tight

70-140 mg/dl

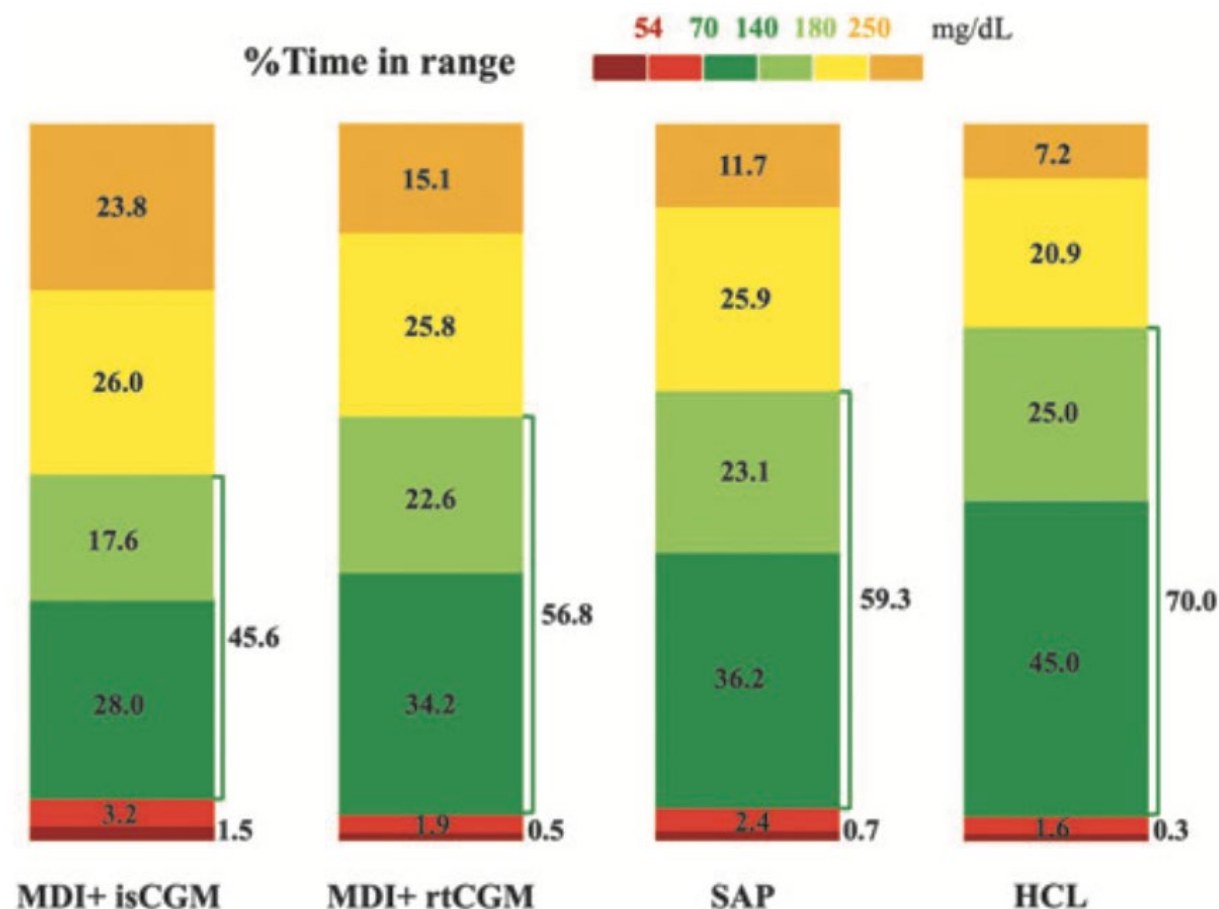
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Range

TITR: obiettivo realistico?

Aiming for the Best Glycemic Control
Beyond Time in Range:
Time in Tight Range as a New Continuous Glucose
Monitoring Metric in Children and Adolescents
with Type 1 Diabetes Using Different
Treatment Modalities

Stefano Passanisi, MD,^{1,*} Claudia Piona, MD,^{2,*} Giuseppina Salzano, PhD, MD,¹
Marco Marigliano, PhD, MD,² Bruno Bombaci, MD,¹ Anita Morandi, MD,² Angela Alibrandi, PhD,³
Claudio Maffei, PhD, MD,^{2,†} and Fortunato Lombardo, MD^{1,†}



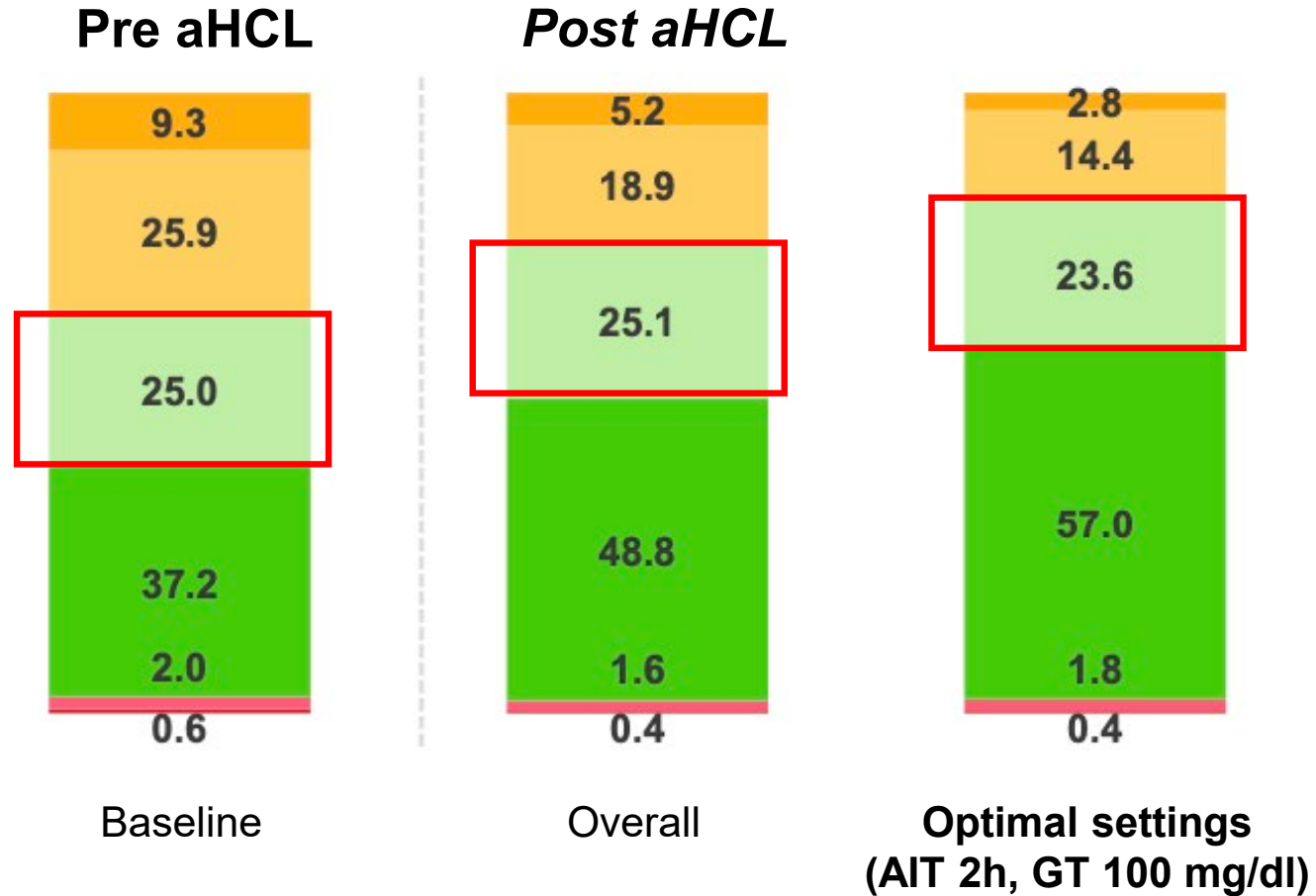
854 pazienti DM1

TITR > 50%

3.3% MDI+isCGM group
VS.
34.4% HCL group

TITR: obiettivo realistico?

13.461 pazienti con DM1



TITR: obiettivo realistico?

Table 1—Optimal TITR targets associated with GMI targets of <7%, <6.8%, and <6.5%

Metric	Age ≤15 years		Age >15 years	
	Value	95% CI	Value	95% CI
<u>GMI <7%</u>				
Optimal TITR target, %*	>46.3	46.2–46.8	<u>>45.4</u>	45.2–45.8
Sensitivity	0.93	0.9–0.94	0.93	0.92–0.94
Specificity	0.92	0.89–0.94	0.92	0.91–0.94
Accuracy	0.92	0.91–0.94	0.93	0.92–0.94
AUC	0.98		0.98	
<u>GMI <6.8%</u>				
Optimal TITR target, %*	>50.7	50.1–51.2	<u>>50.7</u>	50.2–50.7
Sensitivity	0.9	0.87–0.93	0.94	0.92–0.95
Specificity	0.9	0.88–0.92	0.93	0.92–0.94
Accuracy	0.9	0.88–0.92	0.93	0.93–0.94
AUC	0.98		0.99	

Overall population:

65% dei pazienti > **45% TITR**

46% dei pazienti > **50% TITR**

Optimal settings:

93% dei pazienti > **45% TITR**

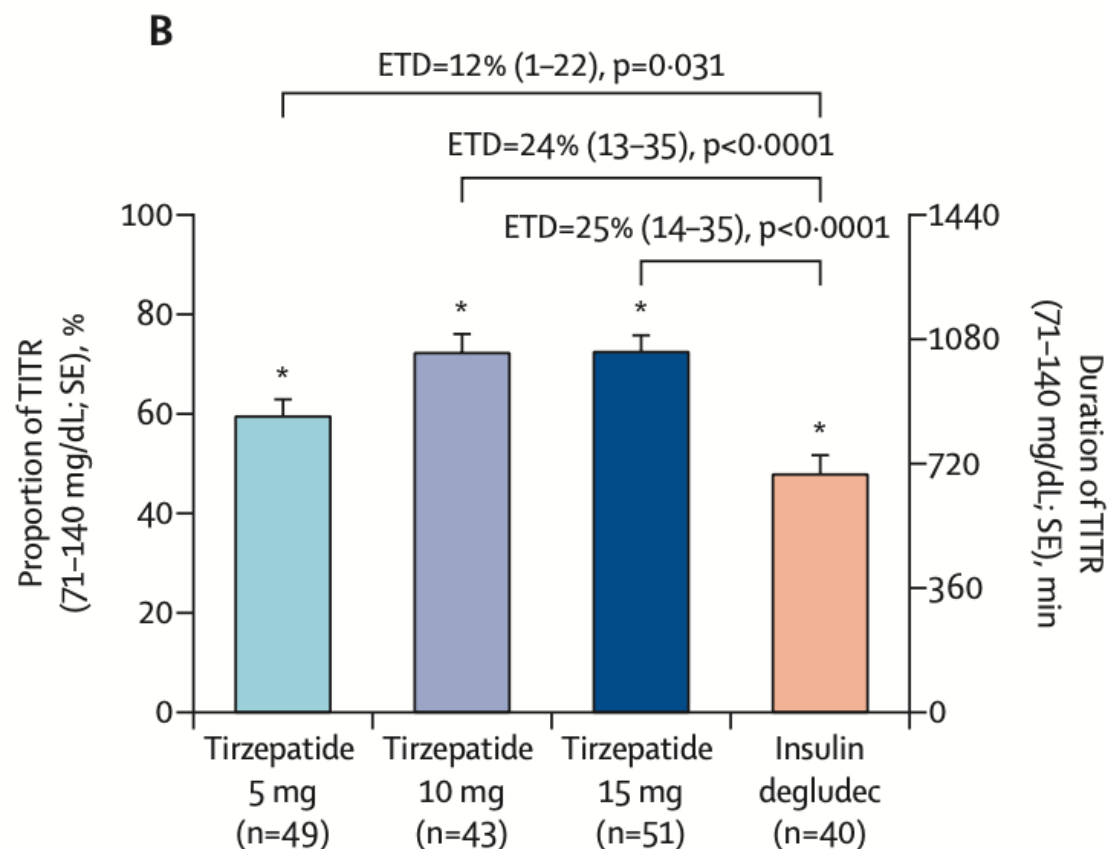
81% dei pazienti > **50% TITR**

TITR ottimale: > 50%

TITR: obiettivo realistico?

Efficacy of once-weekly tirzepatide versus once-daily insulin degludec on glycaemic control measured by continuous glucose monitoring in adults with type 2 diabetes (SURPASS-3 CGM): a substudy of the randomised, open-label, parallel-group, phase 3 SURPASS-3 trial

Tadej Battelino, Richard M Bergenstal, Angel Rodriguez, Laura Fernández Landó, Ross Bray, Zhentao Tong, Katelyn Brown



243 pazienti con DM2

Terapia baseline: metformina, SGLT2i

Media TITR Degludec: 48%

Media TITR Tirzepatide 15 mg: 73%

Maggiore TBR (circa +1.5%) in Degludec

Time

In

70-180 mg/dl

> 70%

Tight

70-140 mg/dl

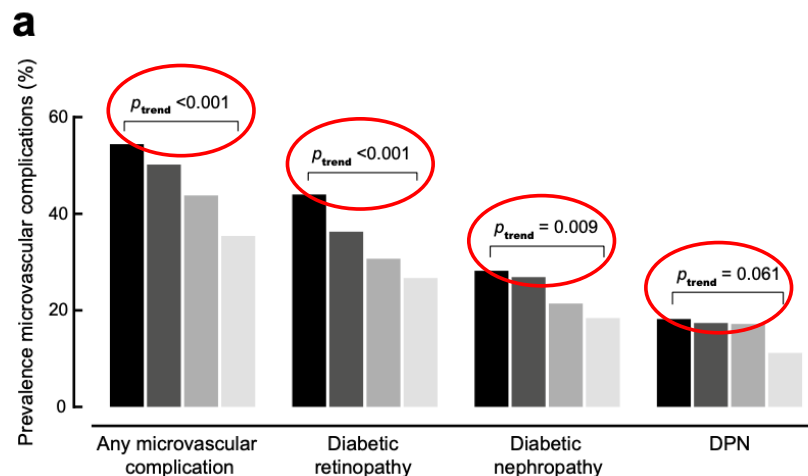
> 50%

Range

TITR e complicitanze: DM1

The association of chronic complications with time in tight range and time in range in people with type 1 diabetes: a retrospective cross-sectional real-world study

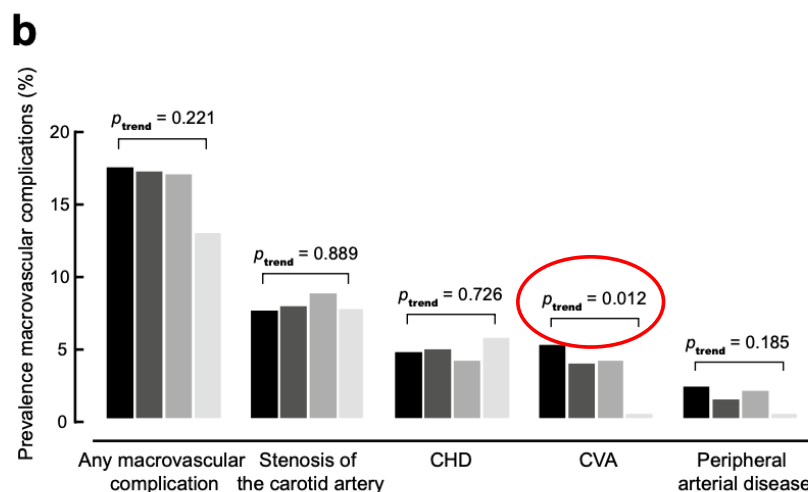
Jolien De Meulemeester¹ · Sara Charleer¹ · Margaretha M. Visser¹ · Christophe De Block² · Chantal Mathieu¹ · Pieter Gillard^{1,3}



808 pazienti con DM1

65.5% in MDI

34.5% in AID



TITR

**Complicitanze microvascolari
Eventi cerebrovascolari**

Time in tight range ■ Q1 (≤26%) ■ Q2 (>26 to ≤33%) ■ Q3 (>33 to ≤41%) ■ Q4 (>41%)

TITR e complicanze: DM1

Time in Range Is Associated with Incident Diabetic Retinopathy in Adults with Type 1 Diabetes: A Longitudinal Study

Viral N. Shah, MD,¹ Lauren G. Kanapka, MSc,² Halis K. Akturk, MD,¹ Sarit Polsky, MD, MPH,¹ Gregory P. Forlenza, MD,¹ Craig Kollman, PhD,² Roy W. Beck, MD, PhD,² and Janet K. Snell-Bergeon, PhD¹

163 pazienti con DM1
Follow-up mediano 6.5 anni

TABLE 3. ASSOCIATION OF GLYCATED HEMOGLOBIN AND CONTINUOUS GLUCOSE MONITORING METRICS WITH DIAGNOSIS OF INCIDENT DIABETIC RETINOPATHY

Metric	Unit of change for calculation of OR	Unadjusted ^a		Adjusted ^a	
		OR (95% CI)	P	OR (95% CI)	P
HbA1c	0.5% Increase	1.38 (1.18–1.62)	<0.001	1.24 (1.05–1.48)	0.01
	0.4% Increase	1.30 (1.14–1.47)		1.19 (1.04–1.37)	
Time in range 70–180 mg/dL	5% Decrease	1.26 (1.13–1.42)	<0.001	1.18 (1.03–1.35)	0.02
	10% Decrease	1.60 (1.27–2.01)		1.39 (1.06–1.82)	
Time in tight range 70–140 mg/dL	5% Decrease	1.37 (1.19–1.59)	<0.001	1.28 (1.08–1.51)	0.004
Mean glucose	10 mg/dL Increase	1.31 (1.15–1.48)	<0.001	1.22 (1.05–1.41)	0.008
Time >180 mg/dL	5% Increase	1.27 (1.14–1.42)	<0.001	1.20 (1.06–1.36)	0.005
Time >250 mg/dL	5% Increase	1.33 (1.14–1.55)	<0.001	1.19 (0.99–1.43)	0.06
Time >300 mg/dL	1% Increase	1.08 (1.03–1.14)	0.002	1.04 (0.98–1.10)	0.21

^aORs and *P* values are calculated from a logistic regression model unadjusted and adjusted for potential confounders. The adjusted model includes age, duration of T1D, and CGM sensor type as covariates. CIs and *P* values are not adjusted for multiplicity.
CI, confidence interval.

TITR e complicanze: DM2

2518 pazienti con DM2
Follow-up mediano 5.4 anni

TABLE 2 Hazard ratios (HR) for incident diabetic retinopathy according to time in tight range (TITR) quartiles.

	TITR quartiles			
	Q1 (<19%)	Q2 (19% ~ 37%)	Q3 (38% ~ 57%)	Q4 (≥58%)
No. of participants	617	635	622	644
No. (%) with outcome	199 (32.3)	166 (26.1)	159 (25.6)	122 (18.9)
Unadjusted HRs (95%CI)	2.16 (1.73, 2.71)	1.66 (1.31, 2.09)	1.56 (1.23, 1.97)	1.00
Adjusted HRs (95%CI) ^a	1.93 (1.53, 2.43)	1.52 (1.20, 1.93)	1.47 (1.16, 1.87)	1.00

^aAdjusted for sex, age, diabetes duration, family history of diabetes, current smoking status, body mass index, systolic blood pressure, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and estimated glomerular filtration rate.

TITR e complicanze: DM2

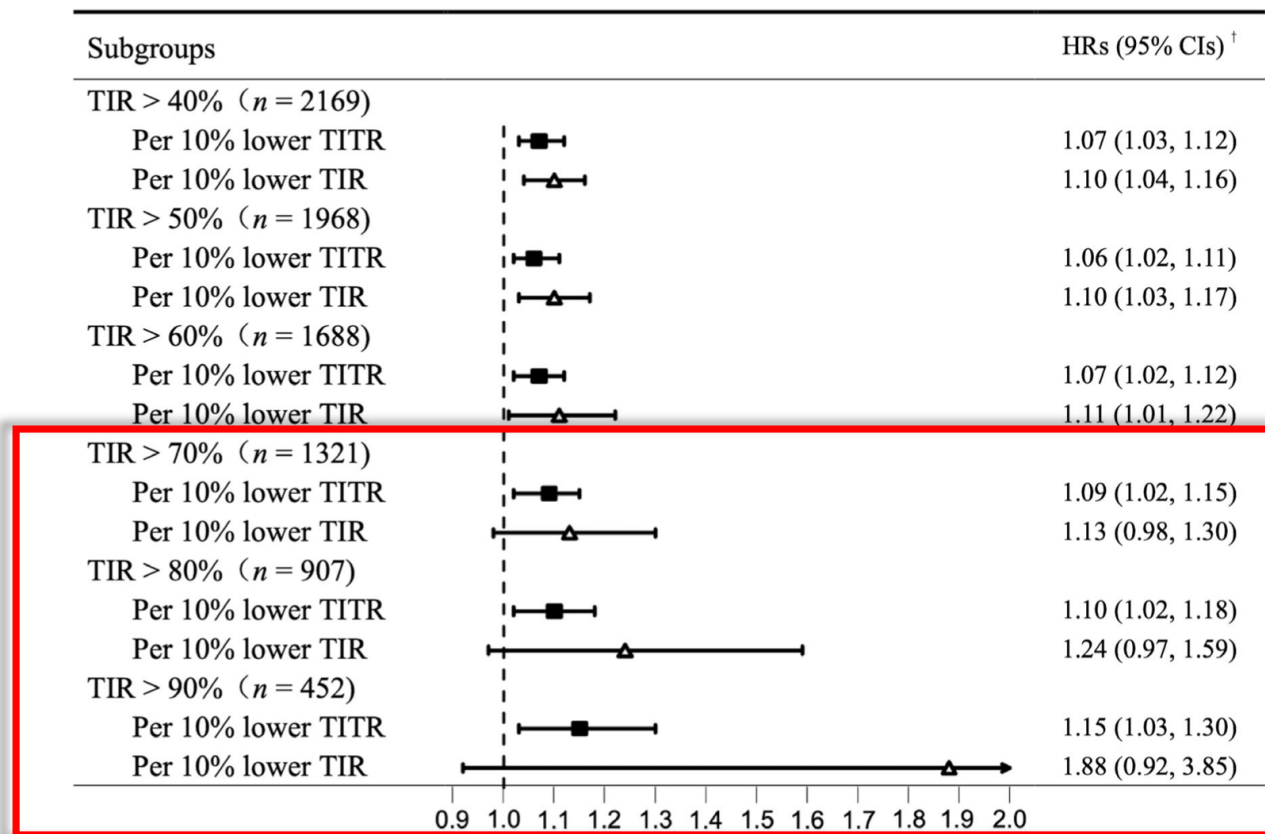


FIGURE 1 Hazard ratios for incident diabetic retinopathy according to time in tight range (TITR) and time in range (TIR) in different TIR subgroups. [†]Adjusted for sex, age, diabetes duration, family history of diabetes, current smoking status, body mass index, systolic blood pressure, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and estimated glomerular filtration rate. TIR and TITR were included in the models as continuous variables (per 10% decrease). HR, hazard ratio.

TITR e mortalità

6061 pazienti con **DM2**
Follow-up mediano **10.9** anni

	TITR (%)				TITR as a continuous variable (each 10% decrease)
	≥55.0	35.0–54.9	17.0–34.9	<17.0	
All-cause mortality					
Number of participants	1554	1517	1501	1489	
Number of deaths	356	479	526	537	
Person-years	17 817.4	16 623.8	15 490.2	15 212.9	
HR (95% CI)					
Model 1	1.00	1.25 (1.09–1.44)**	1.55 (1.35–1.77)***	1.65 (1.44–1.88)***	1.09 (1.07–1.11)***
Model 2	1.00	1.19 (1.04–1.37)*	1.42 (1.24–1.63)***	1.54 (1.34–1.77)***	1.08 (1.05–1.10)***
Model 3	1.00	1.09 (0.95–1.26)	1.29 (1.12–1.49)***	1.36 (1.18–1.57)***	1.06 (1.04–1.08)***
Model 4	1.00	1.03 (0.89–1.19)	1.17 (1.01–1.35)*	1.21 (1.04–1.40)*	1.04 (1.01–1.06)**
Cardiovascular mortality					
Number of deaths	121	169	200	199	
HR (95% CI)					
Model 1	1.00	1.25 (0.99–1.58)	1.69 (1.35–2.12)***	1.73 (1.37–2.17)***	1.09 (1.05–1.12)***
Model 2	1.00	1.18 (0.94–1.50)	1.54 (1.22–1.94)***	1.60 (1.27–2.02)***	1.07 (1.04–1.11)***
Model 3	1.00	1.13 (0.88–1.43)	1.48 (1.17–1.87)**	1.50 (1.18–1.90)**	1.06 (1.03–1.10)**
Model 4	1.00	1.07 (0.84–1.36)	1.34 (1.05–1.71)*	1.34 (1.04–1.72)*	1.04 (1.00–1.08)*

HOT TOPIC: TITR-TIR DEBATE

Is It Time to Move Beyond TIR to TITR? Real-World Data from Over 20,000 Users of Continuous Glucose Monitoring in Patients with Type 1 and Type 2 Diabetes

Editorial > [Diabetes Technol Ther.](#) 2024 Mar;26(3):147-150. doi: 10.1089/dia.2023.0602.

Is It Time to Replace Time-in-Range with Time-in-Tight-Range? Maybe Not

[Roy W Beck](#) ¹

Time in Tight Range for Patients With Type 1 Diabetes: The Time Is Now, or Is It Too Soon?

Vala Hamidi and Jeremy H. Pettus

Diabetes Care 2024;47:782–784 | <https://doi.org/10.2337/dci23-0092>

COMMENT ON CASTEÑEDA ET AL.

The Time in Tight Range for People With Type 1 Diabetes Debate Presents a False Dichotomy

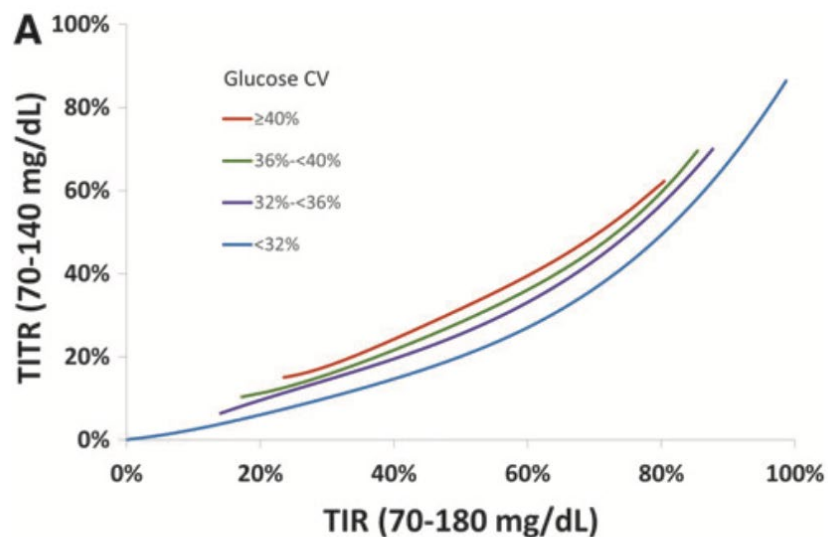
Diabetes Care 2025;48:e28 | <https://doi.org/10.2337/dc24-1006>

*Gijsbert Stoet*¹ and
Richard I.G. Holt^{2,3}

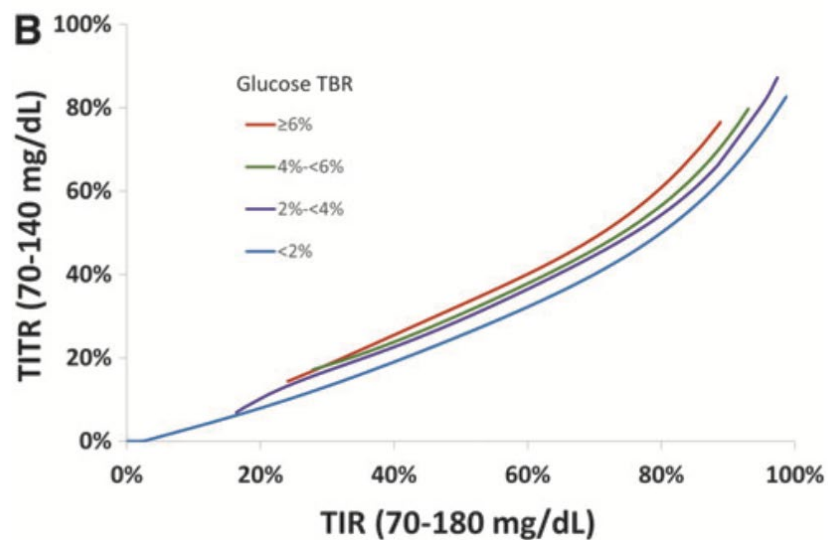
A Comparison of Continuous Glucose Monitoring-Measured Time-in-Range 70–180 mg/dL Versus Time-in-Tight-Range 70–140 mg/dL

Roy W. Beck, MD, PhD,¹ Dan Raghinaru, MS,¹ Peter Calhoun, PhD,¹ and Richard M. Bergenstal, MD²

TITR-TIR quale relazione?



912 pazienti DM1
184 pazienti DM2

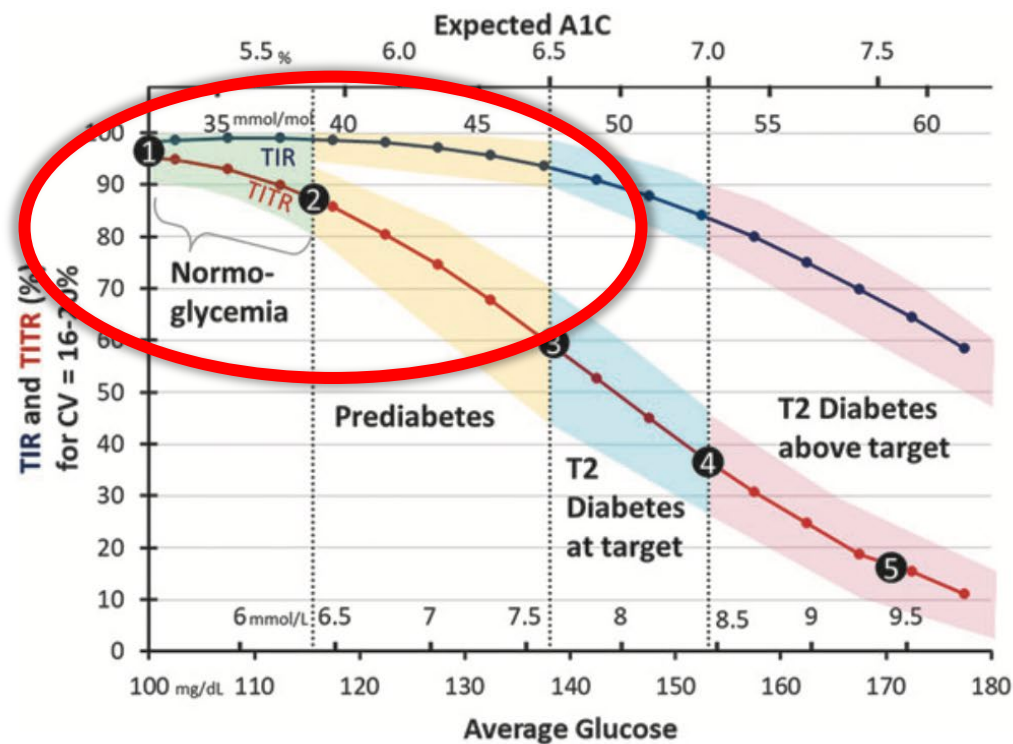


TITR-TIR Spearman correlation:
 $r = 0.94$

TIR-TIR quale relazione?

Is It Time to Move Beyond TIR to TITR? Real-World Data from Over 20,000 Users of Continuous Glucose Monitoring in Patients with Type 1 and Type 2 Diabetes

Timothy C. Dunn, PhD;¹ Ramzi A. Ajjan, MD, PhD;² Richard M. Bergenstal, MD;³ and Yongjin Xu, PhD¹



	①	②	③	④	⑤
A1C, %	5.1	5.7	6.5	7.0	7.5
AG, mg/dL	100	117	138	154	170
CV, %	18	18	18	18	18
TIR, %	98	99	94	84	67
TITR, %	95	86	60	37	18
TIR-TITR, %	3	13	34	47	49

- ① → ② Normoglycemia → Prediabetes
- ② → ③ Prediabetes → T2 diabetes
- ③ → ④ T2 diabetes → In target zone
- ④ → ⑤ In target zone → Above target zone

TITR vs. TIR

TABLE 1. HAZARD RATIOS FOR THE DEVELOPMENT OR PROGRESSION OF RETINOPATHY

	<i>HR per change of 1 or 0.5 SD</i>	<i>Unadjusted HR (95% CI)^a</i>	<i>Adjusted HR (95% CI)^a</i>
0.5 SD change			
Measured HbA1c			
Mean HbA1c	0.72%	1.39 (1.33, 1.46)	1.54 (1.46, 1.63)
Virtual CGM metrics			
Time-in-range 70–180 mg/dL	–9.0%	1.50 (1.41, 1.59)	1.63 (1.53, 1.75)
Time-in-tight-range 70–140 mg/dL	–7.5%	1.53 (1.43, 1.64)	1.66 (1.54, 1.78)
Mean glucose	19.9 mg/dL	1.45 (1.37, 1.53)	1.60 (1.51, 1.70)

TITR: patient's point of view

‘We’re taught green is good’: Perspectives on time in range and time in tight range from youth with type 1 diabetes, and parents of youth with type 1 diabetes

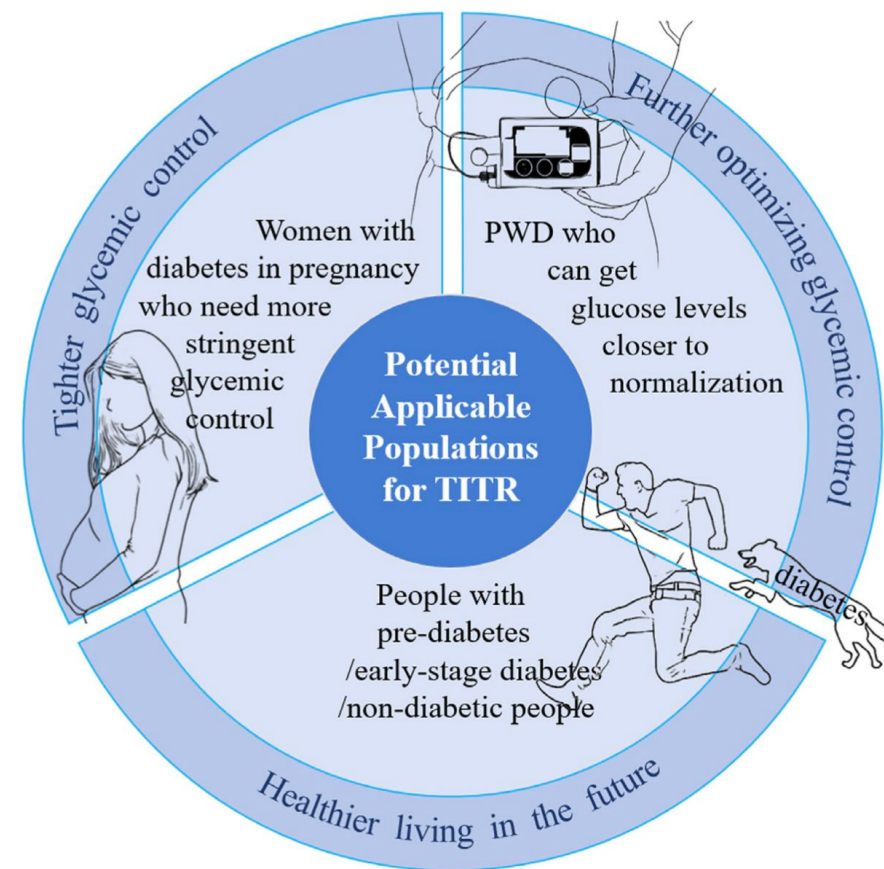
Molly L. Tanenbaum^{1,2,3} | Erica Pang² | Rachel Tam² | Franziska K. Bishop² |
Priya Prahalad^{2,3} | Dessi P. Zaharieva² | Ananta Addala^{2,3} | Jessie J. Wong² |
Diana Naranjo² | Korey K. Hood^{2,3} | David M. Maahs^{2,3}

- **Frustrazione** per il mancato raggiungimento dei target
TIR percepito come un voto sulla propria salute o su quella dei propri figli
- **TITR possibile motivo di conflitto** familiare, associato a **maggiore peso** di malattia e **maggiore rischio** di ipoglicemia
- **Richiesta di maggiore assistenza** e maggiori **evidenze** a supporto dell'utilizzo del **TITR**
- **TITR** visto da alcuni **come stimolo** per migliorare il proprio controllo glicemico

TITR vs. TIR? Maybe not

Time in tight range: A key metric for optimal glucose control in the era of advanced diabetes technologies and therapeutics

Ziyi Zhang BM¹ | Yaxin Wang MD^{2,3} | Jingyi Lu PhD^{2,3} | Jian Zhou PhD^{2,3} 



STRENGTHS	LIMITATIONS
Mantenimento di livelli glicemici vicini al range fisiologico	Possibile aumento del rischio ipoglicemico
Riduzione del rischio di complicanze e mortalità	Evidenze ancora limitate rispetto al TIR
Possibile stimolo a migliorare il compenso glicemico	Possibile aumento del peso di malattia per pazienti e caregiver