Monitoraggio in continuo della glicemia e nuove metriche glicemiche

- Paolo di Bartolo
- UO di Diabetologia
- Dip Medicine Specialistiche Ravenna
- AUSL della Romagna

Paolo Di Bartolo Disclosure

Board Member/Advisory Board

Abbott Diagnostic Italy, Boehringer Ingelheim Italy, Eli Lilly International, Novartis Italy, Novo Nordisk Italy, Astra Zeneca

Speaker's Bureau

Abbott Diagnostic Italy, Astra Zeneca BMS Italy, Eli Lilly Italy, Novartis Italy, Novo Nordisk Italy, Sanofi Aventis Italy, Sigma-Tau Italy, Ypsomed Italy.

Ai sensi dell'art. 3.3 del Regolamento applicativo dell'Accordo Stato-Regioni 05.11.2009, dichiaro che negli ultimi due anni ho avuto i seguenti rapporti anche di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:

Box 1
Key definitions

Real-time continuous glucose monitoring (CGM)	Wearable technology that provides real-time continuous glucose measurements with the options of alerts for hyperglycemia, hypoglycemia, or projected glucose out of target ranges
Flash glucose monitoring (FGM)	Glucose monitoring system in which data are stored in a wearable sensor and obtained by scanning the sensor with dedicated receiver or smartphone
Automated insulin delivery, artificial pancreas system, closed-loop system, bionic pancreas	Terms that refer to an insulin delivery system that uses mathematical algorithms that can adjust insulin delivery based on CGM input
Threshold suspend	Automated insulin suspension when glucose level drops less than a specified threshold
Predictive low glucose suspend	Automated insulin suspension when glucose level is predicted to be less than a specified glucose threshold (eg, 70 mg/dL) in a specific period of time (eg, 30 min)
Hybrid-closed loop system	An automated insulin delivery system that modulates insulin delivery but still requires quantitative announcement of carbohydrate intake by the user
Fully closed-loop system	Automated insulin delivery not dependent on user input
Bihormonal (dual hormone) system	An artificial pancreas technology that uses insulin plus an additional hormone (eg, glucagon) intended to achieve better glycemic control than possible with an insulin-only system

Endocrinol Metab Clin N Am 49 (2020) 667–678
https://doi.org/10.1016/j.ecl.2020.07.006

New and Emerging Technologies in Type 1 Diabetes

Jordan S. Sherwood, MD, Steven J. Russell, MD, PhD,
Melissa S. Putman, MD, MSc*

Linee Guida AMD-SID Diabete Tipo 1

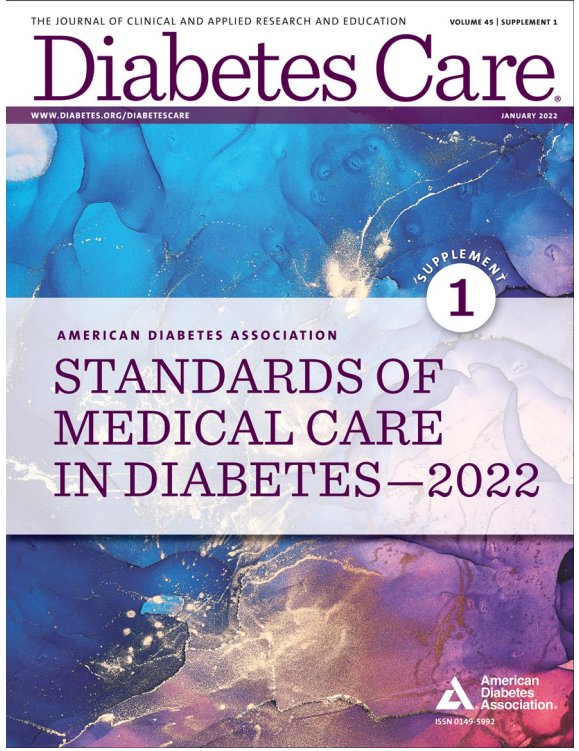
2.2 In soggetti con diabete mellito di tipo 1 è preferibile l'utilizzo di un monitoraggio intermittente del glucosio (FGM, Flash Glucose Monitoring) o di automonitoraggio glicemico capillare (SMBG)?

In soggetti con diabete mellito di tipo 1 in buon controllo si suggerisce l'opzione di utilizzare sistemi di monitoraggio intermittente del glucosio (FGM, Flash Glucose Monitoring) rispetto ai sistemi di autocontrollo capillare della glicemia.

Raccomandazione condizionata a favore dell'intervento

Qualità delle prove: moderata.

https://snlg.iss.it/wp-content/uploads/2022/04/LG_La-terapia-del-diabete-di-tipo-1_rev.pdf



Recommendations

7.11 Real-time continuous glucose monitoring **A** or intermittently scanned continuous glucose monitoring **B** should be offered for diabetes management in adults with diabetes on multiple daily injections or continuous subcutaneous insulin infusion who are capable of using devices safely (either by themselves or with a caregiver). The choice of device should be made based on patient circumstances, desires, and needs.

7.12 Real-time continuous glucose monitoring **A** or intermittently scanned continuous glucose monitoring **C** can be used for diabetes management in adults with diabetes on basal insulin who are capable of using devices safely (either by themselves or with a caregiver). The choice of device should be made based on patient circumstances, desires, and needs.

7.13 Real-time continuous glucose monitoring **B** or intermittently scanned continuous glucose monitoring **E** should be offered for diabetes management in youth with type 1 diabetes on multiple daily injections or continuous subcutaneous insulin infusion who are capable of using the device safely (either by themselves or with a caregiver). The choice of device should be made based on patient circumstances, desires, and needs.

7.14 Real-time continuous glucose monitoring or intermittently scanned continuous glucose monitoring should be offered for diabetes management in youth with type 2 diabetes on multiple daily injections or continuous subcutaneous insulin infusion who are capable of using devices safely (either by themselves or with a caregiver). The choice of device should be made based on patient circumstances, desires, and needs. **E**

https://diabetesjournals.org/care/issue/45/Supplement_1

DIABETES RESEARCH AND CLINICAL PRACTICE 177 (2021) 108917

Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International Diabetes Federation

Review

Time-in-range for monitoring glucose control: Is it time for a change?

Virginia Bellido [a,*], *Pedro José Pinés-Corrales* [b], *Rocío Villar-Taibo* [c], *Francisco Javier Ampudia-Blasco* [d,e,f,g]

- The HbA1c value has been the gold standard for evaluating glucose control for decades. However, it has limitations such as the lack of information on glycemic variability or the risk of hypoglycemia.
- The increasing use of continuous glucose monitoring has provided patients and healthcare professionals with a range of useful metrics for the management of diabetes.
- Among them, Time in Range (TIR) is a simple and intuitive metric that gives information regarding the quality of glucose control.
- TIR is strongly correlated with HbA1c, and it has been linked to the risk of developing microvascular and macrovascular complications.
- The International Consensus on Time in Range has recently set targets for different diabetes populations.
- Nowdays we have data for strogly support the use of TIR as an essential parameter in the management of diabete

DIABETES RESEARCH AND CLINICAL PRACTICE 177 (2021) 108917

Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

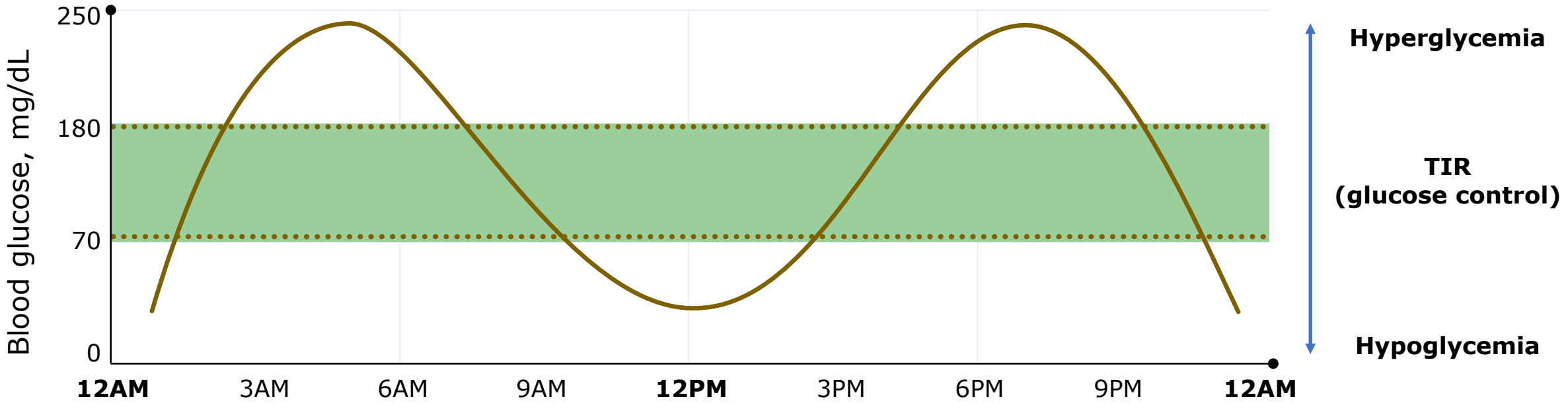
Review

Time-in-range for monitoring glucose control: Is it time for a change?

Virginia Bellido [a,*], *Pedro José Pinés-Corrales* [b], *Rocío Villar-Taibo* [c], *Francisco Javier Ampudia-Blasco* [d,e,f,g]

- TIR was defined as the time spent in an individual's target glucose range.
- It can be expressed as a percentage (%) of CGM readings, the average time (hours and minutes) spent in the range per day, or both.
- It can also be individualized, reporting the amount of time the patient remains within a certain goal selected as appropriate for each case, taking several individual factors into consideration, such as type of diabetes, age, pregnancy o intention to be pregnant and comorbidities

CGM metrics can help to provide an improved understanding of glycemic control and variability compared with HbA1c



CGM, continuous glucose monitoring; TIR, time-in-range.
Battelino T, et al. Diabetes Care 2019;42:1593–603.

HbA1c (%)	2019	2020
<=6,0	5,6	5,5
6,1-6,5	8,7	8,8
6,6-7,0	14,6	15,2
7,1-7,5	19,1	18,1
7,6-8,0	17,0	16,9
8,1-8,5	13,3	13,5
8,6-9,0	8,8	8,8
> 9,0	13,0	13,2

https://aemmedi.it/wp-content/uploads/2022/05/AMD-Annali-diabete-tipo-1-2022-prot.pdf

Such factors are connected to clinical unmet needs, such as hypoglycemia

38%* of people with diabetes report **≥1 severe hypoglycemia event per year**

2.42** events per person year are reported (similar rates by diabetes type)[1]

People experiencing hypoglyemia are at **greater risk of:**

Hospitalization[2]

Emergency care visits[3]

Physical morbidity[4] or death[5,6]

Hypoglycemia risk can translate into **hypoglycemia fear**

Psychosocial implications, e.g.:

Impaired daily living (e.g. driving/work)[7]

Depressive symptoms and anxiety[7]

Strained relationships[8]

*95% CI: 35.7–40.4; **95% CI: 2.36–2.49. CI, confidence interval.

1. Ratzki-Leewing A, et al. Oral presentation at IDF 2021; 2. Dalal M, et al. Adv Ther 2017;34:2083–92; 3. Leiter L, et al. Can J Diabetes 2005;29:186–92;
4. Frier BM. Nat Rev Endocrinol 2014;10:711–22.; 5. Bonds D, et al. Brit Med J 2010;340:b4909; 6. Cryer P. Diabetes Care. 2012;35:1814–6;
7. Barendse S, et al. Diabet Med 2012;29:293–302; 8. Ratzki-Leewing A, et al. Diabetes Ther 2019:10:2305–11.

Hypoglycemia can result in clinical inertia, which is a major obstacle to optimal glycemic control

49%

of people with T2D experience **hypoglycemia** during the **titration period**[1]

79%

of people with T2D who experience hypoglycemia **discontinue basal insulin** within 12 months of initiation[2,*]

60% and 79%

of people with T2D and T1D, respectively, intentionally **reduce their insulin dose** to lower their risk of hypoglycemia[3,4]

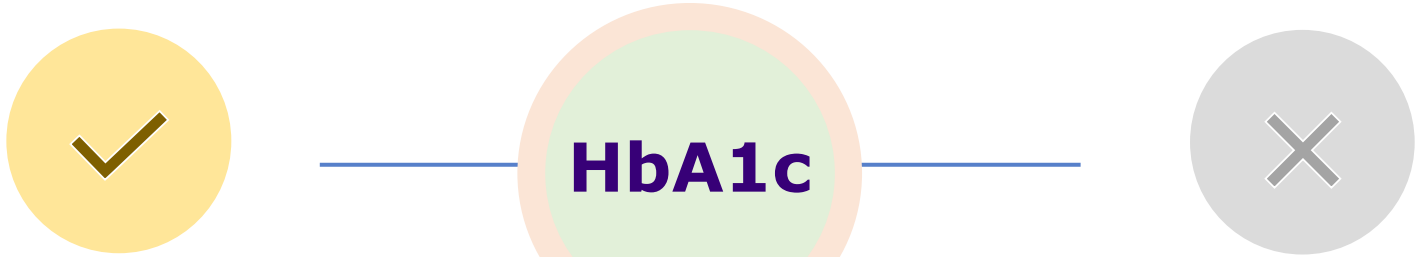
76%

of physicians would treat people with **diabetes more aggressively** if not for concerns about hypoglycemia[5]

*Using a definition of discontinuation of a greater than 45-day gap in insulin prescription coverage.

1. Harris S, et al. Poster presented at 19th Annual World Congress Insulin Resistance Diabetes & Cardiovascular Disease 2021 #0093;
2. Dalal M, et al. Adv Ther 2017;34:2083–92; 3. Leiter L, et al. Can J Diabetes 2015;39:19–25; 4. Leiter LA, et al. Can J Diabetes 2005;29:186–92;
5. Peyrot M et al. Diabet Med 2012;29:682–9.

Reviewing the gold standard for glycemic control assessment



ADVANTAGES

Easy to measure

Relatively cheap

Predictive of vascular complications

Helps management decisions

LIMITATIONS

Only provides an approximate measure of glycemia

Unable to address glucose variability or hypoglycemia

Unreliable in certain conditions (renal failure, Hb abnormalities, other)

Hb, hemoglobin. Aijan RA. Diabetes Technol Ther 2017;19:S27–36.

Glycaemic management in diabetes: old and new approaches

Antonio Ceriello, Francesco Prattichizzo, Moshe Phillip, Irl B Hirsch, Chantal Mathieu, Tadej Battelino

Lancet Diabetes Endocrinol
2022; 10: 75–84

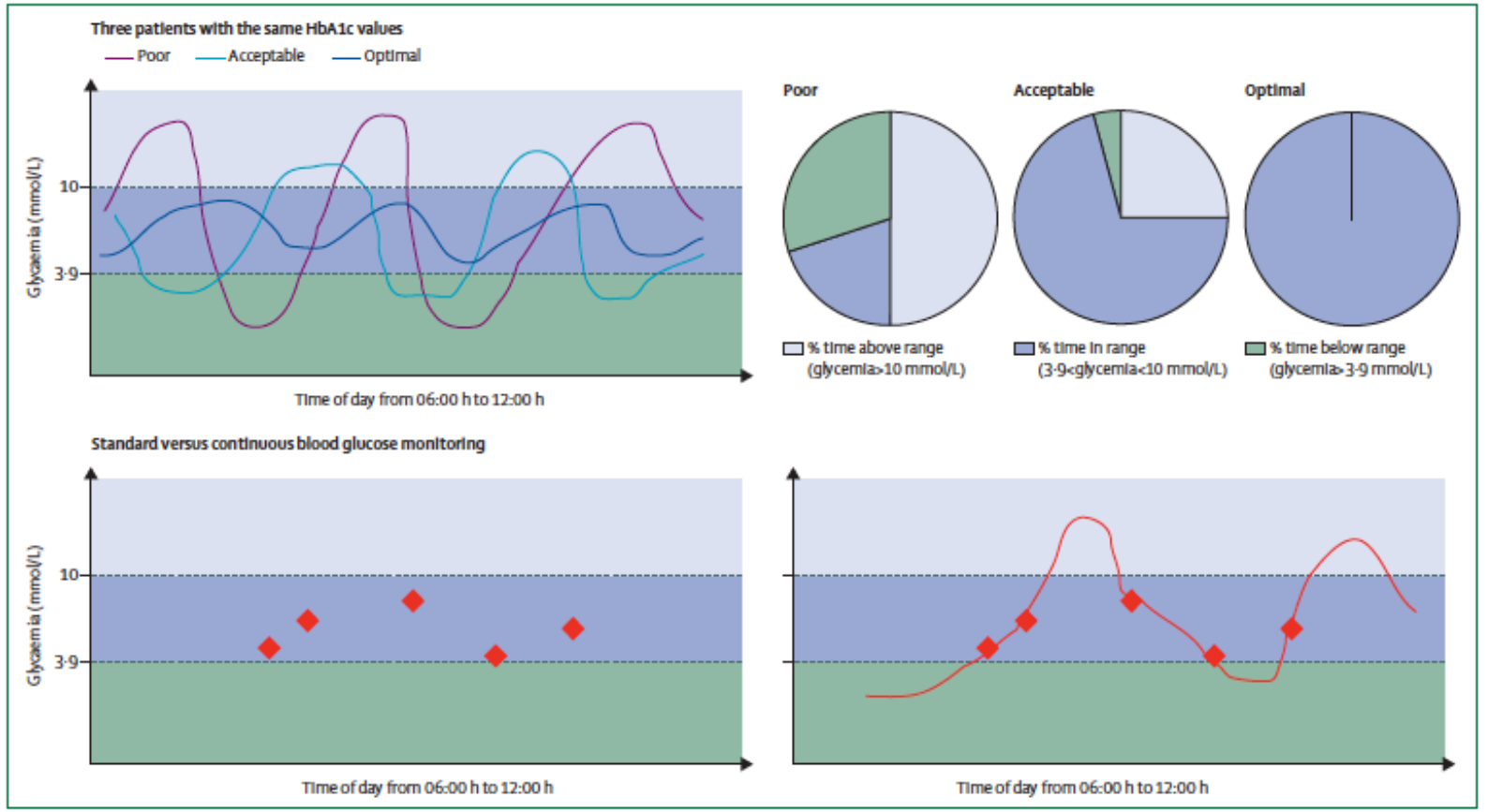
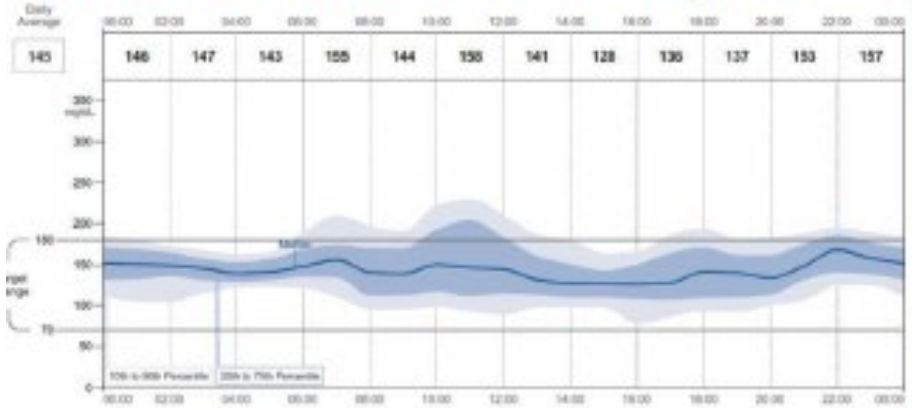
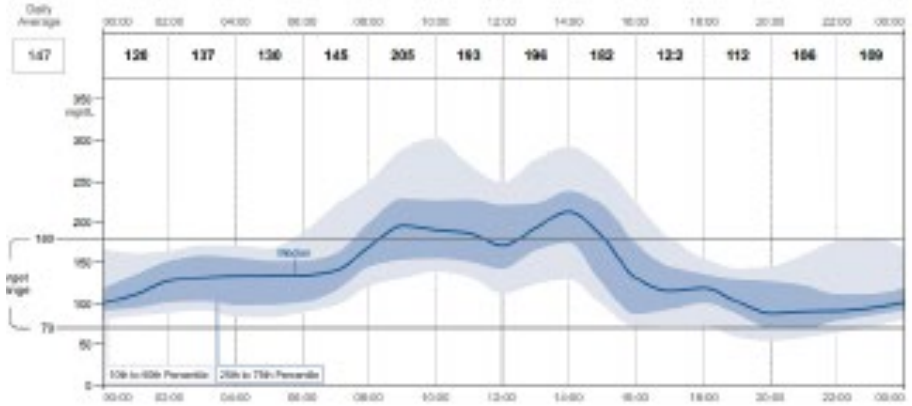
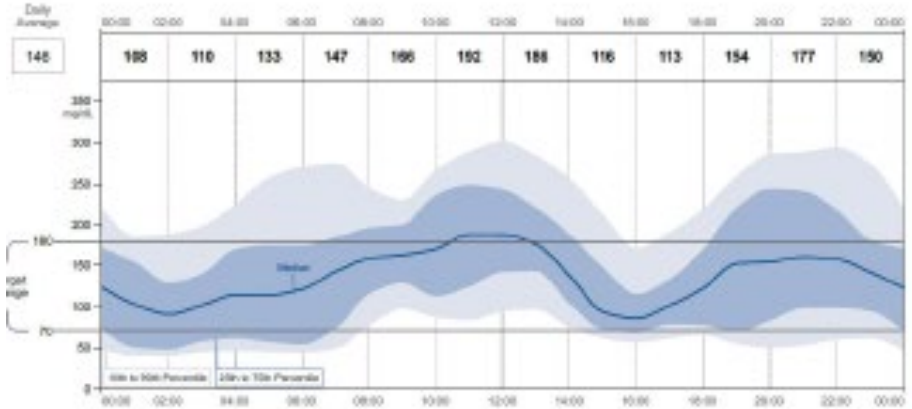


Figure 2: **Possible different patterns of glycaemia in people with the same HbA_{1c} evaluated by self-monitoring blood glucose and continuous glucose monitoring**
In people with diabetes and with the same HbA_{1c}, exact glycaemic control can be very different. For example, some people can have excellent glycaemic control, spending the whole day with glucose concentrations between 3·9 mmol/L and 10 mmol/L; in contrast, some patients' glucose concentrations could range from 2·3 mmol/L to 14 mmol/L. Self-monitoring blood glucose cannot fully capture actual glycaemic fluctuations like continuous glucose monitoring.

A1C or CGM for Management?







A1C (%)	% Time Hypo (< 70 mg/dL)	Glu. Variability (CV %)	% Time TIR (70-180 mg/dL)
6.7%	1%	26%	83%
6.7%	6%	42%	69%
6.7%	9%	53%	51%

CV= coefficient of variation

DIABETES RESEARCH AND CLINICAL PRACTICE 177 (2021) 108917

Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International Diabetes Federation

Review

Time-in-range for monitoring glucose control: Is it time for a change?

Virginia Bellido [a,*], *Pedro José Pinés-Corrales* [b], *Rocío Villar-Taibo* [c], *Francisco Javier Ampudia-Blasco* [d,e,f,g]

Table 3 – Relationship of TIR and chronic complications.

Study	Population	Metrics	Outcome	Results
Beck et al. [46]	T1D (DCCT) N = 1440	7-point SMBG Derived TIR	Retinopathy, albuminuria	HRs for retinopathy and albuminuria (each 10% decrease in TIR): 1.64 (1.51–1.78) and 1.40 (1.25–1.56)
Bergenstal et al. [55]	T2D (DEVOTE) N = 5644	8-point SMBG Derived TIR	MACE, microvascular events	HR for MACE and microvascular events (TIR >10% vs TIR <50%): 0.69 (0.52–0.91) and 0.60 (0.43–0.85)
Cutruzzola et al. [56]	T1D N = 70 T1D, 35 controls	CGM 6 months before	Carotid artery wall thickness and endothelial function	No significant relationship between IMT, FMD and TIR
Li et al. [52]	T2D N = 740	rtCGM (3 days)	Peripheral nerve conduction	OR for risk of slowing conduction velocity. TIR tertiles (TIR medium tertile OR = 0.44; TIR high tertile OR 0.26)
Lu et al. [48]	T2D N = 3262	Retrospective CGM (3 days)	Retinopathy	OR for any retinopathy (each 10% increase in TIR): 0.92 (0.88–0.96)
Lu et al. [53]	T2D N = 2215	Retrospective CGM (3 days)	Carotid intima-media thickness	OR for carotid intima-media thickness (each 10% increase in TIR): 0.936 (0.878–0.998)
Lu et al. [54]	T2D, inpatients N = 6225	Retrospective CGM (3 days)	All-cause and cardiovascular mortality	HR for all-cause mortality and cardiovascular mortality (each 10% decrease in TIR): 1.08 (1.05–1.12) and 1.05 (1.00–1.11)
Yoo et al. [49]	T2D N = 866	Retrospective CGM (3–6 days)	Albuminuria	OR for albuminuria (each 10% increase in TIR): 0.94 (0.88–0.99)
Yang et al. [51]	T2D N = 364	FGM (14 days)	Painful diabetic polyneuropathy	OR for painful diabetic polyneuropathy (Q1 of TIR compared with Q4): 2.66 (1.16–6.10)
Mayeda et al. [50]	T2D N = 105	Retrospective CGM (12 days)	Diabetic peripheral neuropathy	OR for diabetic peripheral neuropathy (each 10% decrease in TIR): 1.25 (1.02–1.52)
Ranjan et al. [57]	T1D on SAP N = 26	rtCGM for 1 year	Albuminuria	HR for albuminuria (each 10% increase in TIR): 0.81 (0.72–0.90)

CGM, continuous glucose monitoring; FGM, flash glucose monitoring; FMD: flow-mediated dilation; HR, hazard ratio; IMT: intima media thickness; MACE, major adverse cardiovascular events; OR, odds ratio; rtCGM, real time continuous glucose monitoring; SAP, sensor augmented pump; SMBG, self-monitoring of blood glucose; TIR, time in range; T1D, type 1 diabetes; T2D, type 2 diabetes.

The value of TIR as a predictor of diabetes-related complications

Each 10% drop in TIR was associated with increased frequency of:

In people with T1D

+64%
increased risk of retinopathy*

(95% CI: 51–78)

In people with T1D

+40%
increased risk of microalbuminuria**

(95% CI: 25–56)

Re-analysis of DCCT data in adults with T1D (N=1440) collected between 1983–1993[1]

In people with T2D and chronic kidney disease

+25%
increased odds of peripheral neuropathy

(95% CI: 2–52)

A control-matched study of 105 people with T2D and CKD[2†]

In people with T2D

+8%
increased risk of all-cause mortality
(95% CI: 5–12)

+5%
increased risk of cardiovascular mortality
(95% CI: 0–11)

A single-center cohort study of 6225 people with T2D[3]

More TIR (>70%)
vs
less TIR (≤50%)
was associated with a reduced risk of developing:‡

Severe hypoglycemia	**-46%**
Microvascular complications	**-40%**
MACE	**-31%**

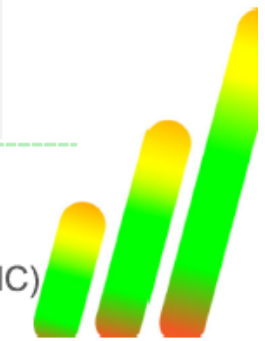
Post hoc analyses from the DEVOTE study in people with T2D (n=5644)[4]

*For assessment of retinopathy, DCCT definitions of primary prevention were used: no retinopathy at baseline (n=726) and retinopathy at baseline (n=714). **For assessment of microalbuminuria, 1283 participants with an AER <30 mg/24 h were included in the analysis. †Out of 105 participants, 81 were participations with moderate-to-severe CKD (eGFR <60 ml/min/1.73m^2) and 23 were matched control participants with eGFR ≥ 60 ml/min/1.73m^2. ‡HR: 0.54 (CI: 0.40–0.73), for time to first severe hypoglycemia when TIR is >70% (vs TIR ≤50%); HR: 0.60 (CI: 0.43–0.85), for time to first microvascular complication when TIR is >70% (vs TIR ≤50%); HR: 0.69 (CI: 0.52–0.91), for time to first MACE when TIR is >70% (vs TIR ≤50%). CI, confidence interval; CKD, chronic kidney disease; DCCT, Diabetes Control and Complications Trial; MACE, major adverse cardiac events.

1. Beck RW, et al. Diabetes Care 2019;42:400–5; 2. Mayeda L, et al. BMJ Open Diab Res Care 2020;8:e000991;
3. Lu J, et al. Diabetes Care 2021;44:549–55; 4. Bergenstal R, et al. Presented at ADA 2020 (21-LB).

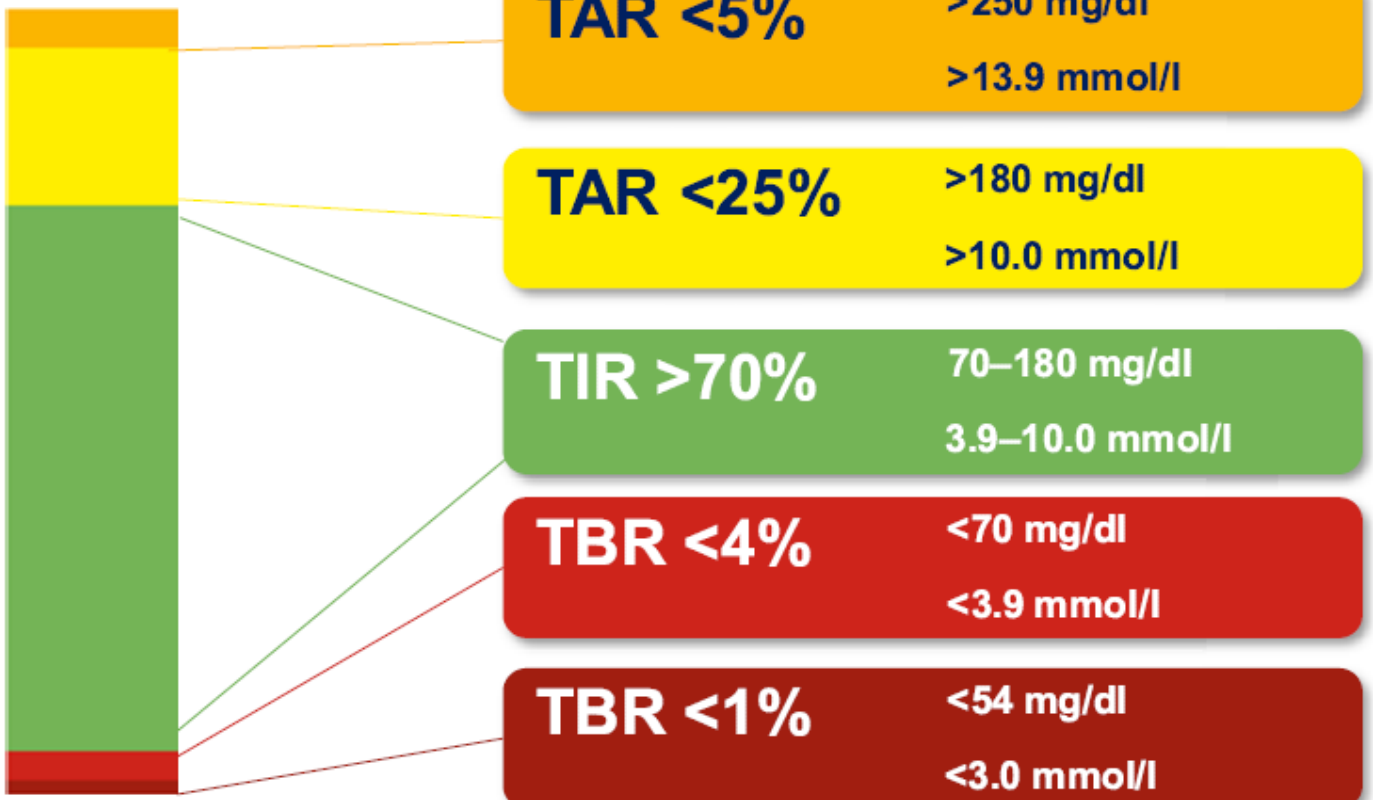
Standardizing CGM metrics and reporting

2000–2006	CGM Introduced and Approved in US	
2012	First proposal of a **Standardized** CGM Report: **AGP**	**Recommendations for Standardizing Glucose Reporting and Analysis to Optimize Clinical Decision Making in Diabetes: The Ambulatory Glucose Profile (AGP)** Bergenstal, Beck, Mazze et al. DTT and JDST 2013
2013–2017	International Consensus on CGM **Metrics including TIR**	International Consensus on Use of Continuous Glucose Monitoring Danne, Nimri, Battelino, Bergenstal, Close et al. Diabetes Care
2019	International Consensus On CGM **TIR Targets**	Clinical Targets for Continuous Glucose Monitoring Data Battelino T, Danne T, Bergenstal R et al Diabetes Care 2019
JAN 2020	**Standards of Diabetes Care** 10 Core Metrics, TIR Targets and **AGP Report**	
JUN 2021	**IDC integrates CGM (AGP) into EHR (EPIC)**	ADA Scientific Sessions, June, 2021 Criego A. for IDC, successful integration of discreet CMG metrics and AGP into EHR (EPIC)



CGM TIR targets for most with T1D and T2D

T1D and T2D



Level 2 Hyperglycemia

Level 1 + Level 2 Hyperglycemia

In target

Level 1 + Level 2 Hypoglycemia

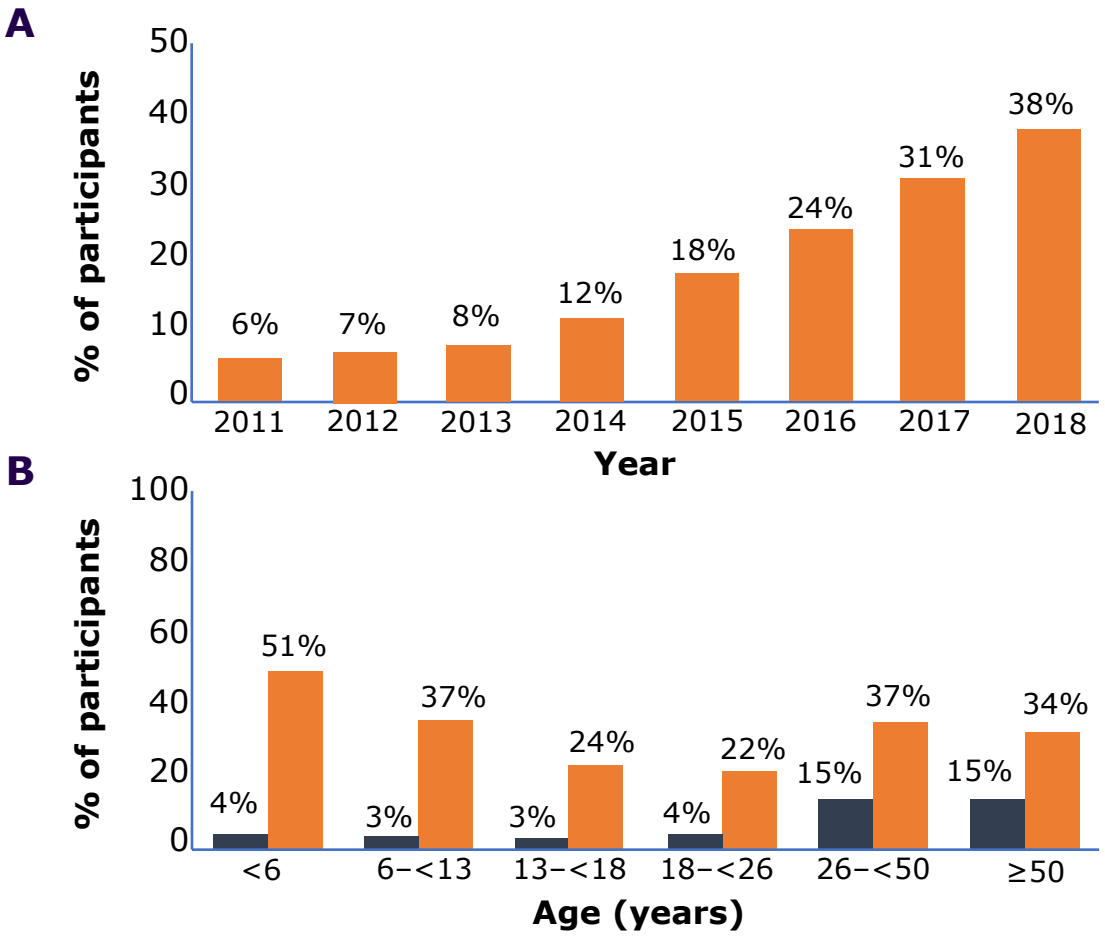
Level 2 Hypoglycemia

High risk individuals (with complications or comorbidities & pregnancy) have different targets

TAR = Time Above Range
TIR = Time In Range
TBR = Time Below Range

Battelino T, Danne T, Bergenstal RM, et al. Diabetes Care 2019;42:1593–1603

The increasing use of CGM technology is paving the way for new metrics of glycemic control



(A) CGM use over time. (B) CGM use in 2010–2012 versus 2016–2018.[4]

1. Lawton J, et al. BMC Endocr Disord 2018;18:12; 2. Martens T, et al. JAMA 2021;325:2262–2;
3. Karter A, et al. JAMA 2021; 325:2273–84; 4. Foster N, et al. Diabetes Technol Ther 2019;21:66-72.

The additional value of CGM

Provides individuals with a means of **accessing detailed blood glucose data**[1]

Allows individuals to **better understand** how **insulin, activity** and **food impact their diabetes**[1]

Use is associated with significant **improvements** in **HbA1c**[2]

Initiation is associated with **significant reductions** in **emergency department visits** and **hospitalizations** for **hypoglycemia**[3]

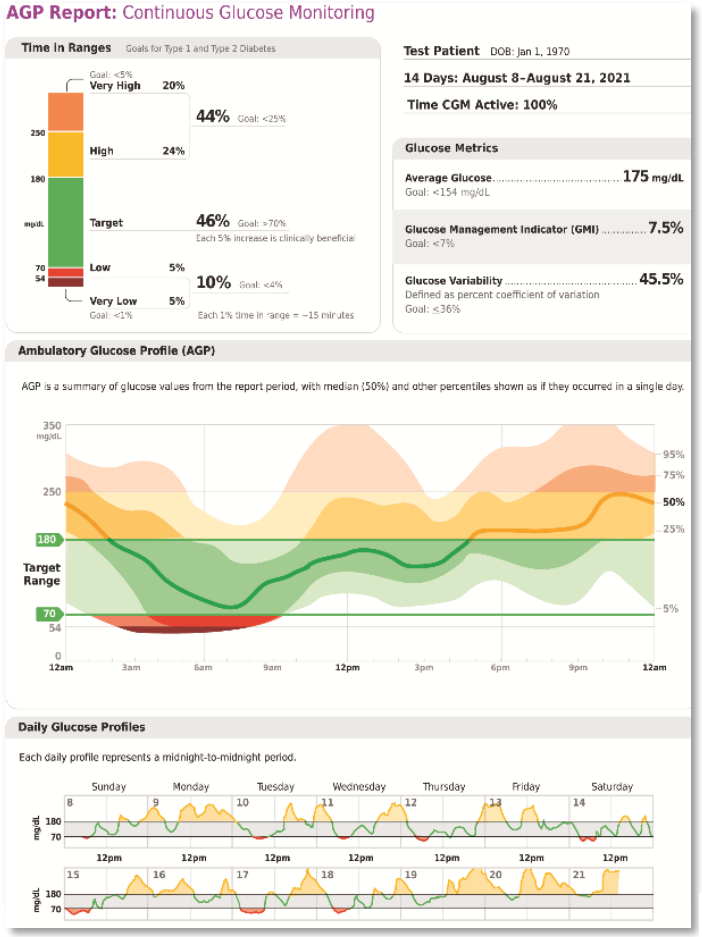
Presenting core metrics through the Ambulatory Glucose Profile (AGP)

- AGP includes all core metrics & 14-day composite glucose profile
- Helps to identify trends[1] and visually represent glycemic patterns[2]

Recognized in ATTD CGM consensus[3]

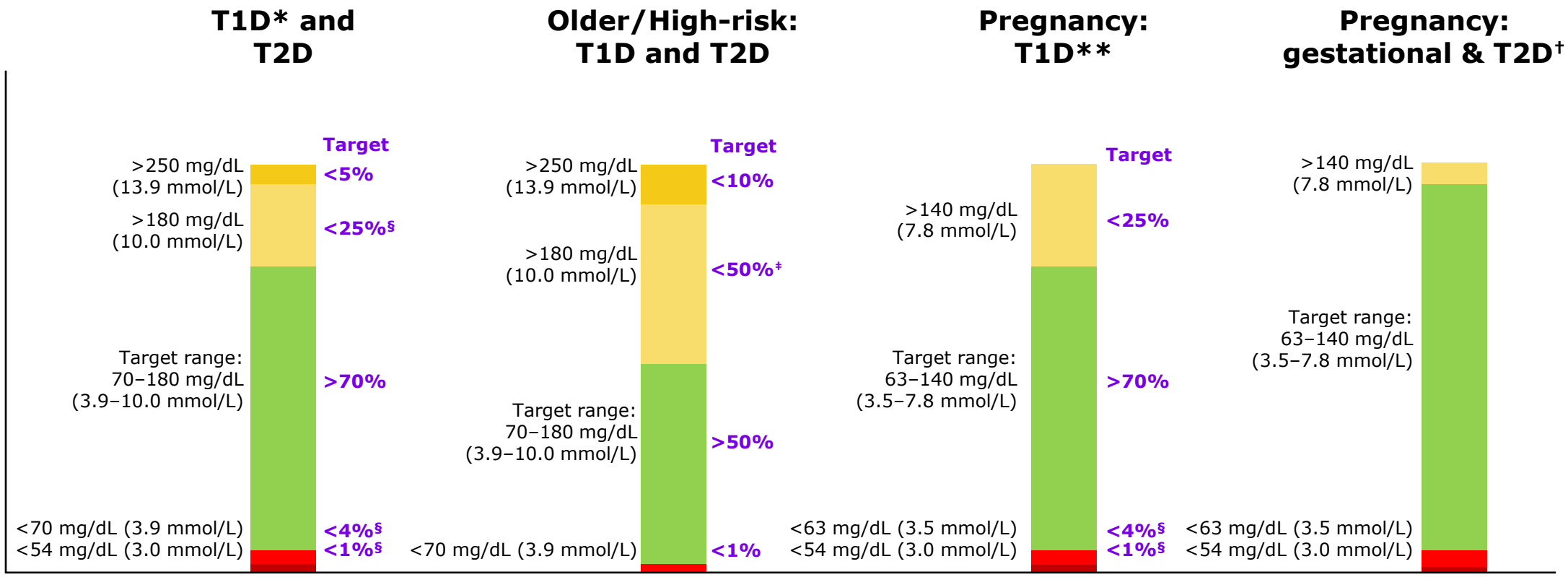
Recommended in ADA "Standards of Medical Care in Diabetes"[4]

Included in update to AACE CGM consensus[5]



AACE, American association of clinical endocrinologists; ADA, American diabetes association.
1. Hammond P. Br J Diabetes 2016;16(S1):S10–5; 2. Bergenstal R, et al. J Diabetes Sci Technol 2013;7:562–78; 3. Battelino, T, et al. Diabetes Care. 2019;42:1593–603;
4. American Diabetes Association Professional Practice Committee. Diabetes Care 2022;45:S83–96; 5. Fonseca V and Grunberger G. Endocr Pract 2017;23:629–32.

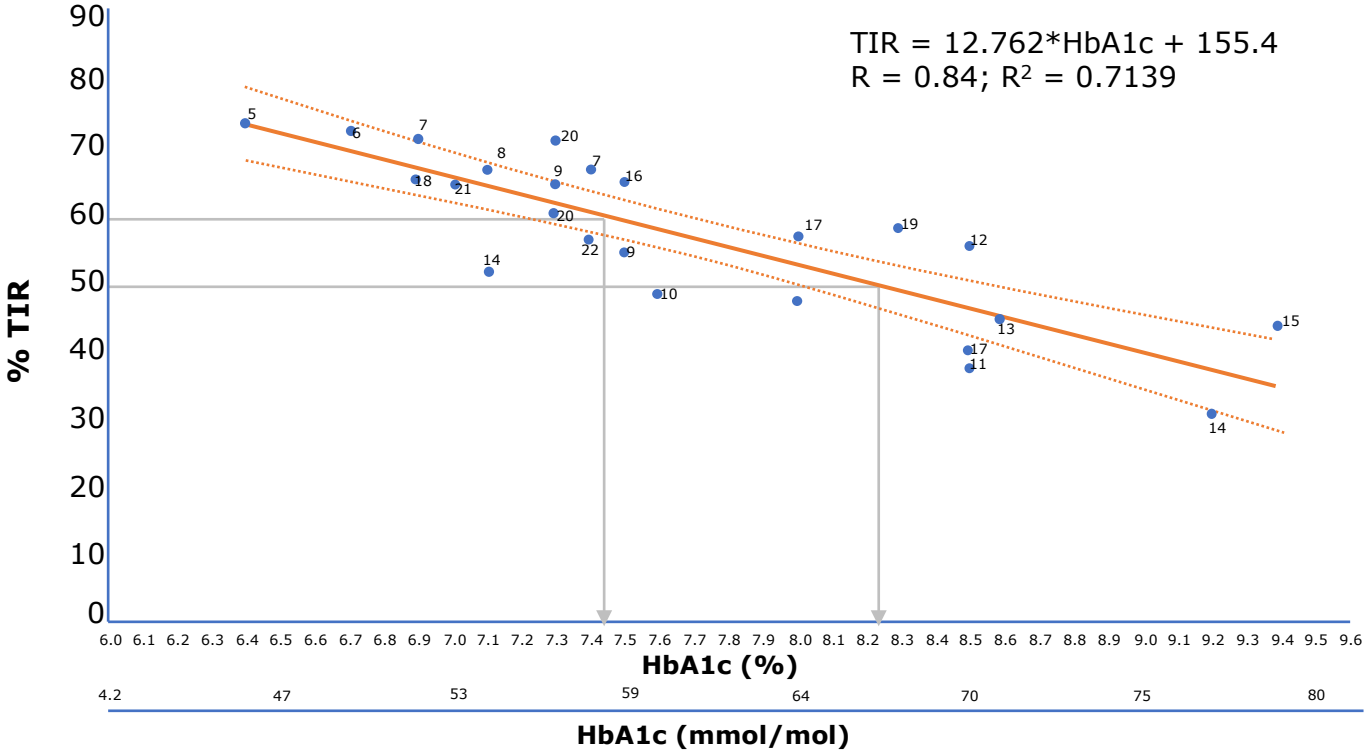
Current consensus on CGM TIR targets for most people with T1D and T2D



High-risk individuals (with complications or comorbidities & pregnancy) have different targets.

*For age <25 years, if the HbA1c goal is 7.5% then set TIR target to approximately 60%. **Percentages of time-in-ranges are based on limited evidence – more research is needed. †Percentages of time-in-ranges have not been included because there is very limited evidence in this area – more research is needed. ‡Includes percentage of values >250 mg/dL (13.9 mmol/L). §Includes percentage of values <54 mg/dL (3.0 mmol/L). Battelino T, et al. Diabetes Care 2019;42:1593–603.

Linear correlations have been observed between TIR and HbA1c



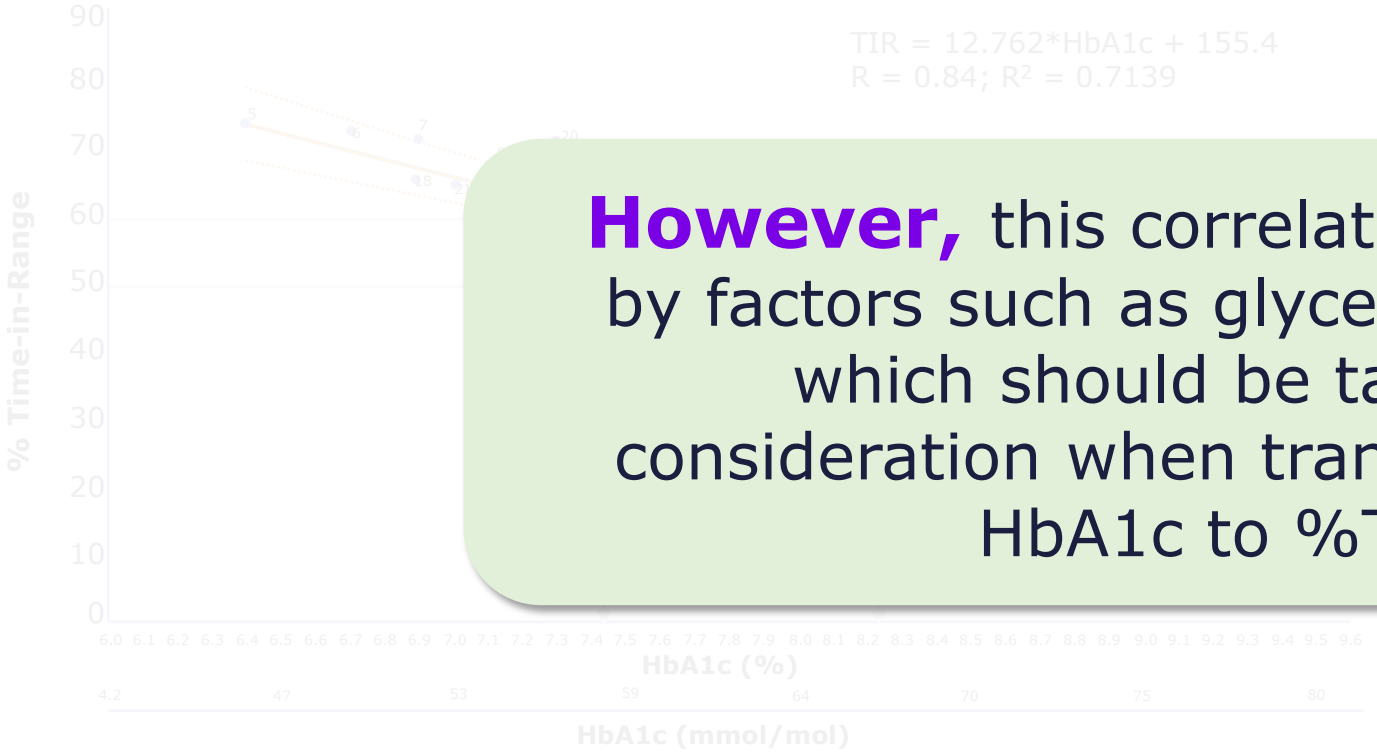
In a meta-analysis of 18 studies across both T1D and T2D populations, there was a **0.8% change in HbA1c for every absolute 10% change in %TIR**

TIR may represent a suitable alternative metric to HbA1c when assessing glycemic control

A meta-analysis of 18 recent studies in people with T1D and T2D using CGM as a therapeutic intervention alone or with an insulin pump. The relationship of %TIR to HbA1c was determined using linear regression analysis and Pearson's correlation coefficient.

Vigersky R & McMahon C. Diab Technol Ther 2019;21:1–5.

Linear correlations have been observed between TIR and HbA1c



However, this correlation is impacted by factors such as glycemic variability, which should be taken into consideration when transitioning from HbA1c to %TIR

TIR may represents a suitable alternative metric to HbA1c when assessing glycemic control

CGM data from 2559 individuals with T2D were included. Glycemic variability was assessed using the glucose coefficient of variation. Estimated HbA1c was calculated via mean sensor glucose. While a strong correlation between TIR and estimated HbA1c was observed (r=−0.908), regression slopes differed significantly based on glucose coefficient of variation. Lu J, et al. Diabetes Res Clin Pract 2020;161:108032.

DIABETES RESEARCH AND CLINICAL PRACTICE 177 (2021) 108917

Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

Review

Time-in-range for monitoring glucose control: Is it time for a change?

Virginia Bellido [a,*], *Pedro José Pinés-Corrales* [b], *Rocío Villar-Taibo* [c], *Francisco Javier Ampudia-Blasco* [d,e,f,g]

TIR to be included in future clinical trials

- For many years, HbA1c has been used as an outcome in clinical trials and a predictor of long-term diabetic complications, resulting in large amounts of data.
- However, given the limitations of HbA1c in characterizing daily glycemic fluctuations or in accurately reflecting mean blood glucose levels, there is a need to incorporate outcomes beyond HbA1c into regulatory decisions and clinical care .
- The question is whether it is possible to use TIR as an alternate endpoint for clinical trials, including those for regulatory purposes.
- Further prospective studies are required to obtain a definitive role of TIR in the onset and progression of chronic complications. In the meantime, the data available so far suggest that TIR could be an acceptable end point for clinical trials.

Glycaemic management in diabetes: old and new approaches

Lancet Diabetes Endocrinol
2022; 10: 75–84

Antonio Ceriello, Francesco Prattichizzo, Moshe Phillip, Irl B Hirsch, Chantal Mathieu, Tadej Battelino

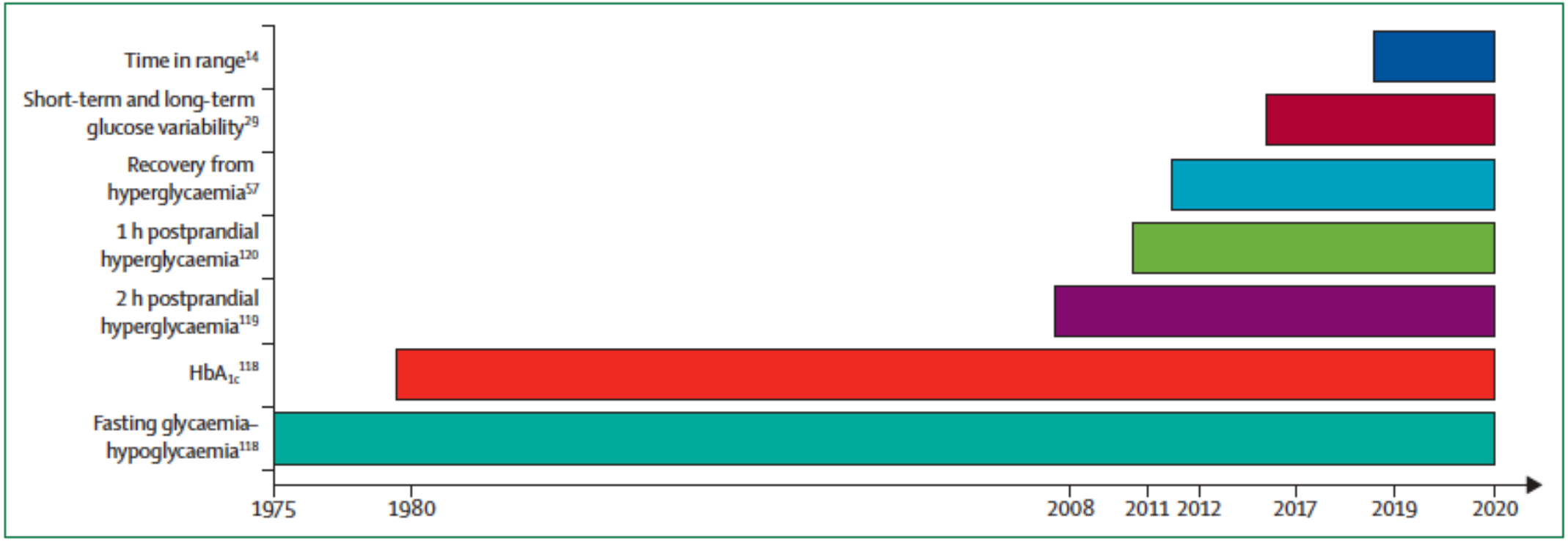


***Figure 3*: Milestones of glycaemic management in diabetes—understanding the history (1975–2021)[14,29,40,118–120]**
The figure reports a timeline of when the various aspects of glycaemic management were formally proposed.

SDC e Glucometria

Esami di laboratorio

Periodo

2 anni | Tutti | Seleziona Periodo 04/10/2020 - 04/10/2022

Gruppo

Glucometria

MMG Altra diabetologia

Descrizione	2022			
	27/09	03/08	08/06	11/05
Nessun sottogruppo				
N. giorni calcolo	14	14	14	14
Glicemia media [%]	125	118	121	116
TAR > 250 mg/dL [%]	1	0	0	0
TAR > 181 e < 250 mg/dL [%]	13	8	10	7
TIR > 70 e < 180 mg/dL [%]	83	91	88	93
TBR > 54 e < 69 mg/dL [%]	3	1	1	0
TBR < 54 mg/dL [%]	1	0	0	0
CV [%]	36	27	29	24
Tempo di utilizzo del sensore...				
Insulina media giornaliera [UI]				
Insulina [U/kg/die]				
Insulina basale [%]				
Insulina boli [%]				
N° episodi di ipoglicemia grave				
N° episodi di chetoacidosi				
N° glicemie/die				

The evolving frontier of diabetes therapy: The renaissance of glycemology

Antonio Ceriello [a,b,*], *Stefano Genovese* [b], *Emanuele Bosi* [c]

- ….To some extent, this is a renaissance of "glycemology", the science of measuring and interpreting glucose values, the "core" of diabetology, and is now, more than ever, at the center of diabetes management