# Going beyond $HbA_{1c}$: glycaemic variability in people with T1DM and T2DM

## Understanding the important role of glycaemic variability in effective diabetes management

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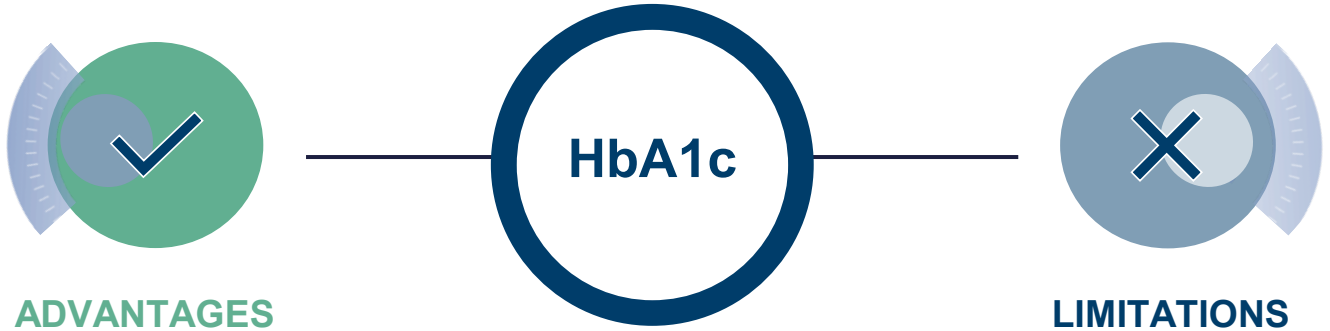
# Beyond $HbA_{1c}$: defining glycaemic variability

# Advantages and limitations of HbA1c




## ADVANTAGES

Easy to measure

Relatively cheap

Predictive of vascular complications

Helps management decisions

## LIMITATIONS

Only provides an approximate measure of glycemia

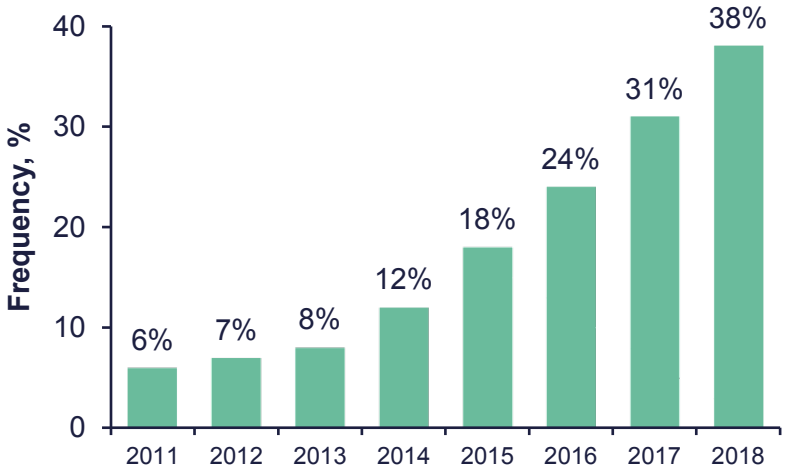
Unable to address GV or hypoglycemia

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

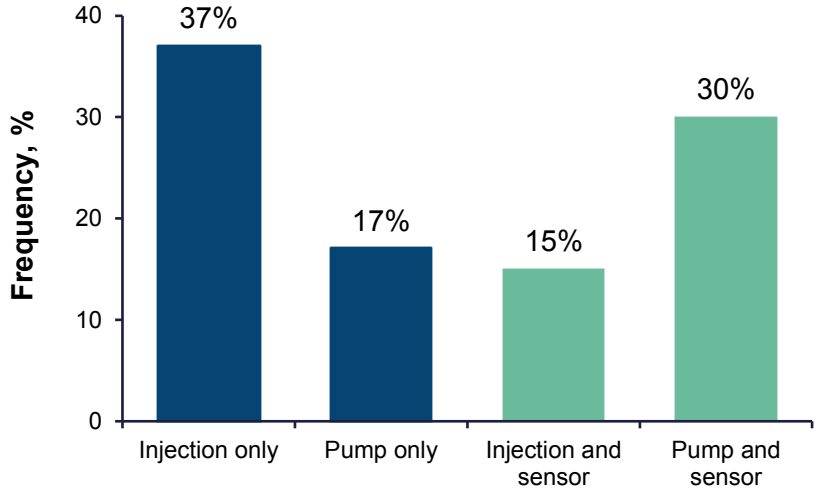
GV, glycemic variability; Hb, hemoglobin
Ajjan RA, Diabetes Technol Ther 2017;19(S2):S27–36

# Prevalence of CGM use

## Frequency of CGM use among adults in the T1D Exchange registry




## Frequency of CGM use among children and adolescents with T1D in the SWEET registry



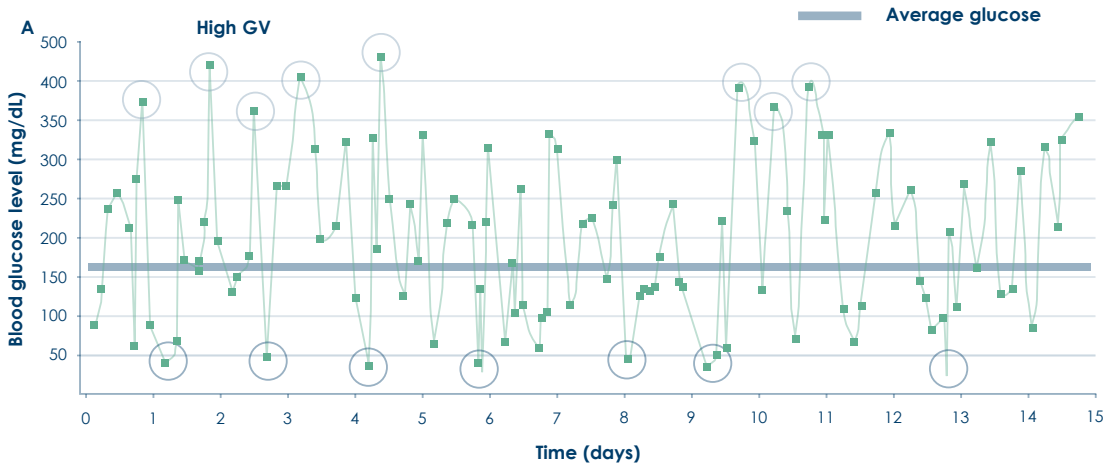

In the T1D Exchange Registry, data from 22,697 registry participants (age 1-93 years) were collected between 2016–2018 and compared with data collected in 2010–2012 for 25,529 registry participants (data from adults only is shown); in the SWEET registry, data from 25,654 children and adolescents with T1D were analyzed during 2017–2019.

Foster NC, et al. Diabetes Technol Ther 2019;21:66-72; Cardona-Hernandez R, et al. Diabetes Care 2021;44:1176–1184

# Managing glycaemia based on $HbA_{1c}$ tells us little about the variability of blood glucose in individual people with diabetes

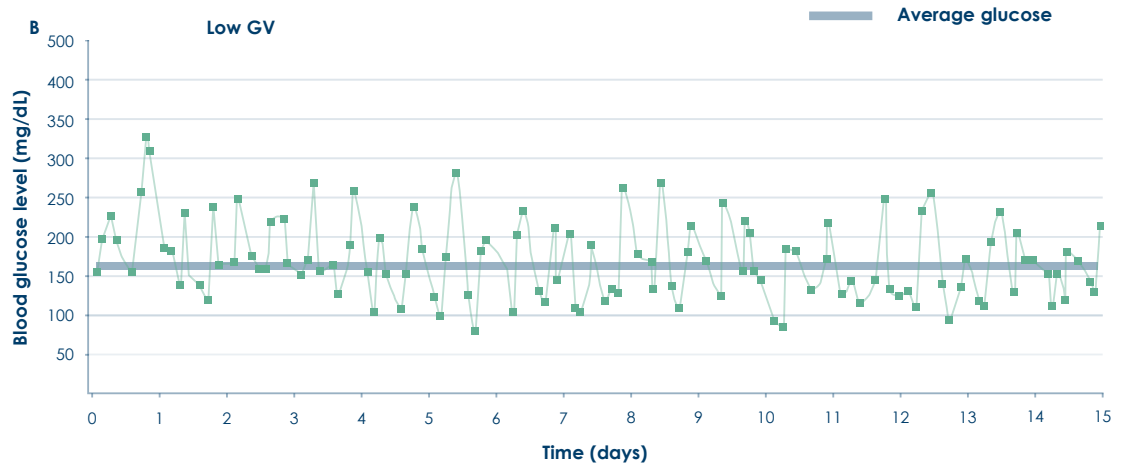
## Two people who have identical $HbA_{1c}$ of 8.0% can have different degrees of glycaemic variability (GV):*[1]

### Subject 1: $HbA_{1c}$ 8.0%




Adapted from Kovatchev and Cobelli. (2016)

### Subject 2: $HbA_{1c}$ 8.0%




Adapted from Kovatchev and Cobelli. (2016)

**Glycaemic variability may be a useful clinically relevant marker of daily glucose control and hypoglycaemia risk alongside $HbA_{1c}$, to provide meaningful data to inform therapeutic decisions[1–5]**

*15-day glucose traces of two subjects who had identical $HbA_{1c}$ of 8.0% but different degrees of GV. High GV in subject 1 was reflected by numerous episodes of both hypo- and hyperglycaemia (A), whereas low GV in subject 2 resulted in no such episodes (B).[1]
GV, glycaemic variability

1. Kovatchev B and Cobelli C. Diabetes Care. 2016;39:502–510; 2. Krishna SV, et al. Indian J Endocrinol Metab. 2013;17:611-619; 3. Wilmot EG, et al. Diabetes Obes Metab. 2019;21:2599–2608; 4. Monnier L and Colette C. Diabetes & Metabolism. 2018;44:97–100; 5. Rayman G. Br J Diabetes. 2016;16(Suppl1):S3–S6.

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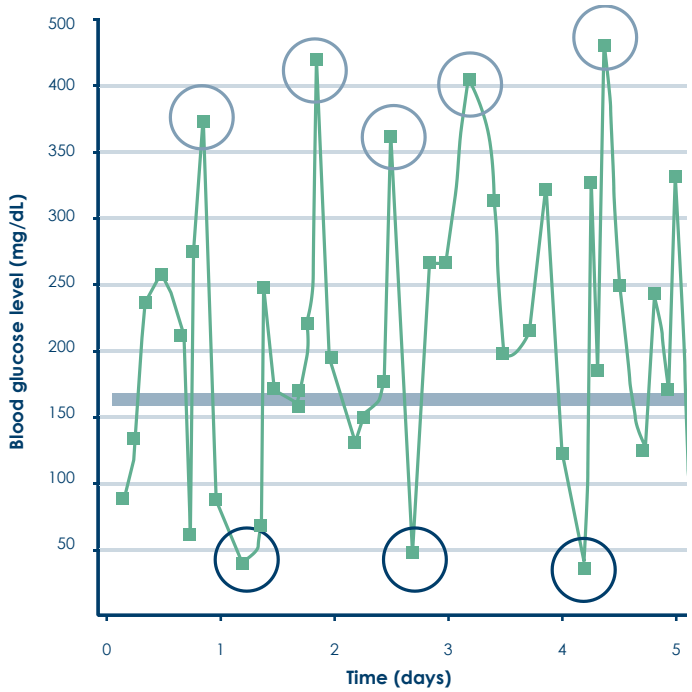
# GV is the measurement of fluctuations of glucose or other related parameters of glucose homoeostasis over a given interval of time




GV is one of a suite of CGM metrics, which include time-in-range, that offer a snapshot of a person's daily glycaemic excursions including episodes of **hyperglycaemia** and **hypoglycaemia**[1–3]

Adapted from Kovatchev and Cobelli. (2016)

GV can be divided into **short-term and long-term** glucose fluctuations[3–5]

| Short-term | Long-term |
|---|---|
| Within-day (intra-day) glucose fluctuations | Serial determinations over longer period of time e.g. $HbA_{1c}$, FPG and PPG measurements |
| Between-day (inter-day) glycaemic variability | |

**Excessive GV can have substantial negative impact on the lives of people with diabetes[1,2]**

CGM, continuous glucose monitoring; FPG, fasting plasma glucose; GV, glycaemic variability; PPG, post prandial glucose

1. Kovatchev B and Cobelli C. Diabetes Care. 2016;39:502–10; 2. Krishna SV, et al. Indian J Endocrinol Metab. 2013;17:611–619; 3. Wilmot EG, et al. Diabetes Obes Metab. 2019;21:2599–2608; 4. Monnier L and Colette C. Diabetes & Metabolism. 2018;44:97–100; 5. Monnier L, et al. Diabetes & Metabolism. 2018;44:313–319.

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# Monitoring glycaemic variability and time-in-range to avoid negative consequences for your patients

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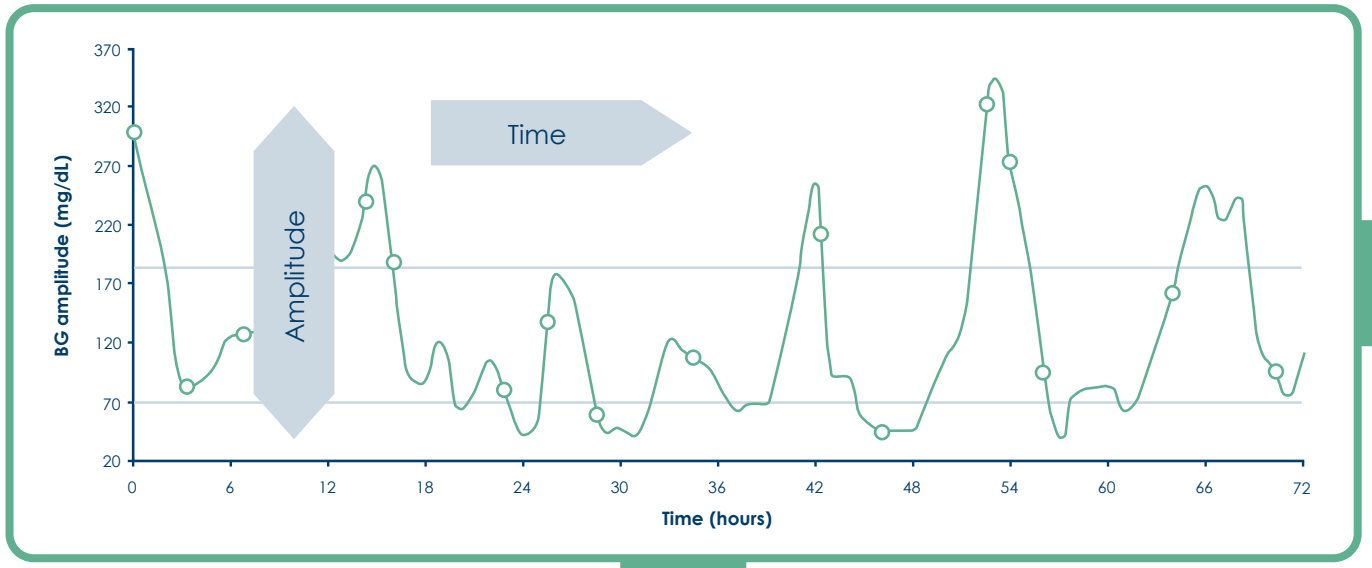
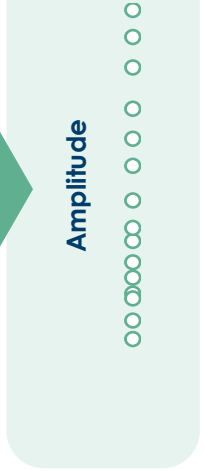
# Amplitude and timing of glucose excursions are two useful measures of glycaemic variability

## Glucose fluctuations are a process in time with two principal dimensions: amplitude and time[1]

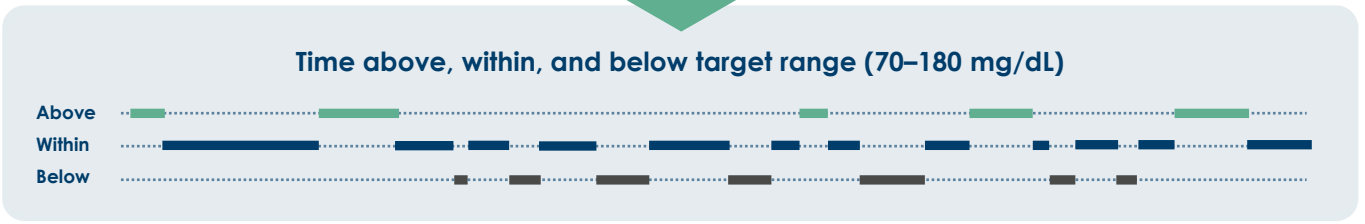



**Amplitude of glucose excursions**

Projected along the y-axis, this process is measured by metrics such as

**SD**, **%CV** or **MAGE**[1,2]




**Timing of glucose excursions**

Projected along the time x-axis, this metric is measured by the **time a person spends within, above and below the target blood glucose range**[1]

Adapted from Kovatchev and Cobelli. (2016)

%CV, percentage coefficient of variation for glucose; GV, glycaemic variability; MAGE, mean amplitude of glucose excursions; SD, standard deviation

1. Kovatchev B and Cobelli C. Diabetes Care. 2016;39:502–510; 2. Krishna SV, et al. Indian J Endocrinol Metab. 2013;17:611–619.

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# Coefficient of variation (%CV) is an important metric for measuring amplitude of glycaemic variability

| Metrics for assessing amplitude of glycaemic variability[1–4] | |
|---|---|
| 01 | Standard deviation (SD) = variation around the mean blood glucose |
| **02** | **Coefficient of variation (%CV) = magnitude of variability relative to a mean level (SD/mean)*** |
| 03 | High blood glucose index (HBGI) |
| 04 | Low blood glucose index (LBGI) |
| 05 | Mean of daily differences (MODD) |
| 06 | Continuous overlapping net glycaemic action (CONGA) |
| 07 | Mean Amplitude of Glycaemic Excursions (MAGE) |

Current guidelines (2019 CGM consensus and ADA 2020 guidelines) mention **%CV as a preferred measure of GV[1,2]**

For **stable glycaemic control, a %CV of**

**≤36%**

is considered a suitable target[1,2,4]

**Increased GV (%CV) can lead to serious consequences, including hypoglycaemia[3–5]**

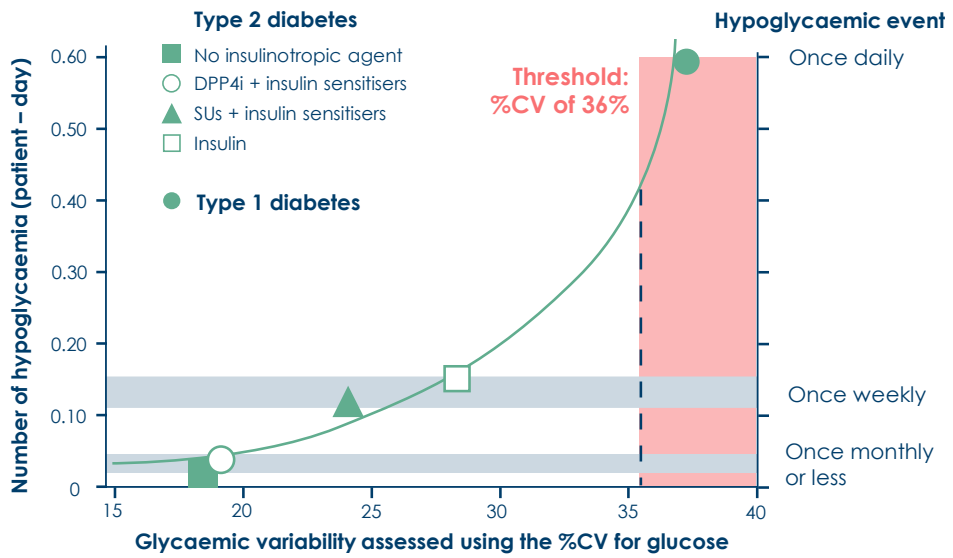
*%CV is calculated as: ([SD of glucose]/[mean glucose]) x 100.[4]

ADA, American Diabetes Association; CGM, continuous glucose monitoring; %CV, percentage coefficient of variation for glucose; GV, glycaemic variability; SD, standard deviation; SMBG, self-measured of blood glucose

1. Battelino T, et al. Diabetes Care. 2019;42:1593–1603; 2. ADA. Diabetes Care. 2020;43(Suppl 1); 3. Krishna SV, et al. Indian J Endocrinol Metab. 2013;17:611–619; 4. Monnier L, et al. Diabetes & Metabolism. 2018;44:313–319; 5. Qu Y, et al. Diabetes Technol Ther. 2012;14:1008–12.

# A %CV above 36% is associated with significantly increased frequency of hypoglycaemia in people with T1DM and T2DM[1,2]

**Frequency of hypoglycaemia* in 5 populations of people with diabetes and according to their %CV**[2]**




Adapted from Monnier L, et al. (2018)

**Glycaemic variability was greater in people with T1DM vs those with T2DM[1,2]**

**GV steadily increased across the T2DM treatment groups** from those on diet +/- insulin sensitisers and those treated with DPP-4 inhibitors to those receiving sulphonylureas and finally those receiving insulin[2]

**Experiencing hypoglycaemia can have a substantial negative impact on your patients' diabetes self-management[3]**

**Frequency of hypoglycaemia* increased exponentially with increasing GV[1,2]**

*Hypoglycaemia was defined as 3 consecutive interstitial glucose levels <56 mg/dL (3.1 mmol/L) with time spent ≥15 min;[1] **From an observational study conducted at the outpatient clinic of the University Hospital of Montpellier (France) between 2003 and 2012. 376 people with T1DM (n=122) or T2DM (n=254) underwent ambulatory CGM for 3 consecutive working days, avoiding the weekend, using the same technology during 2003 to 2012. Participants with T2DM were divided according to treatment received. Percentage CV and frequency of hypoglycaemia were calculated.[1]

%CV, percentage coefficient of variation for glucose; CGM, continuous glucose monitoring; DPP-4, dipeptidyl peptidase 4; GV, glycaemic variability; SU, sulphonylurea; T1DM, Type 1 diabetes mellitus; T2DM, Type 2 diabetes mellitus

1. Monnier L, et al. Diabetes Care. 2017;40:832–838; 2. Monnier L, et al. Diabetes & Metabolism. 2018;44:313–319; 3. Khunti K, et al. Diabetes Res Clin Pract. 2017;130:121–129.

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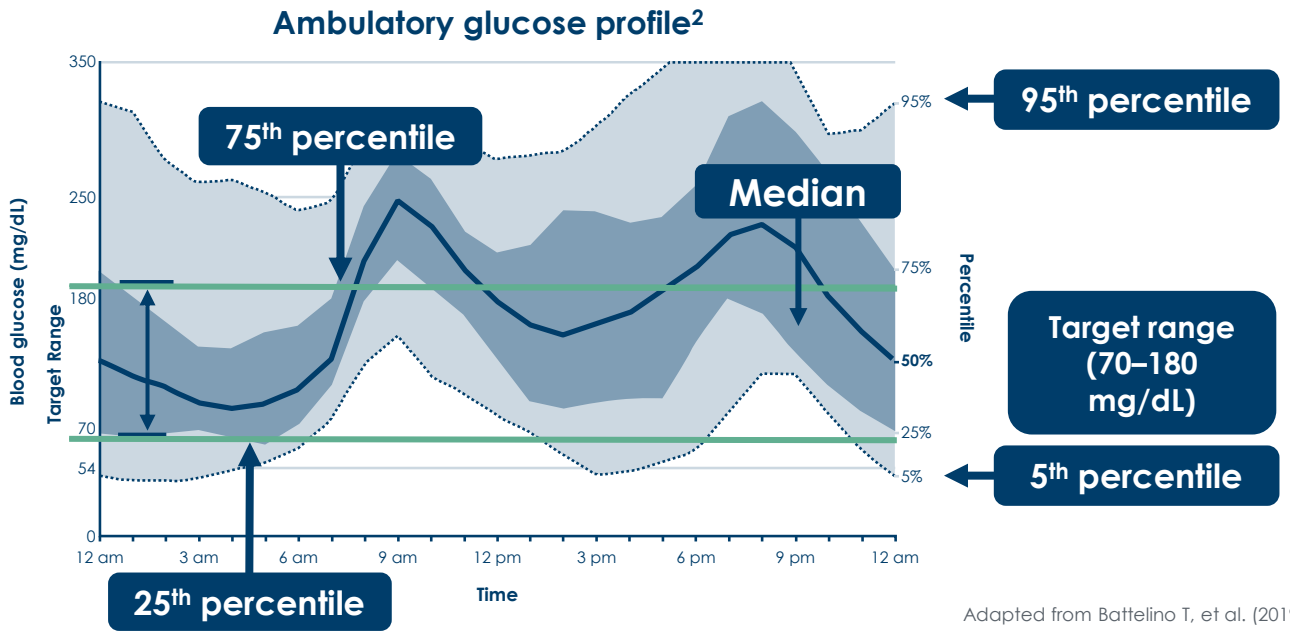
# Time-in-range is also an important clinical glucose metric of glycaemic control

## Time-in-range (TIR) is the percentage of time over a 24-hour period when glucose is within a target range: usually 70–180 mg/dL (3.9–10.0 mmol/L)[1–4]




Adapted from Battelino T, et al. (2019)

### Why is TIR useful?

**TIR can aid understanding of whether hypoglycaemia** (time-below-range) **or hyperglycaemia** (time-above-range) **improves with treatment over time**[1,4]

**TIR provides actionable information**, and can **identify the magnitude and frequency of intra- and inter-day GV** vs using $HbA_{1c}$ alone[1–4]

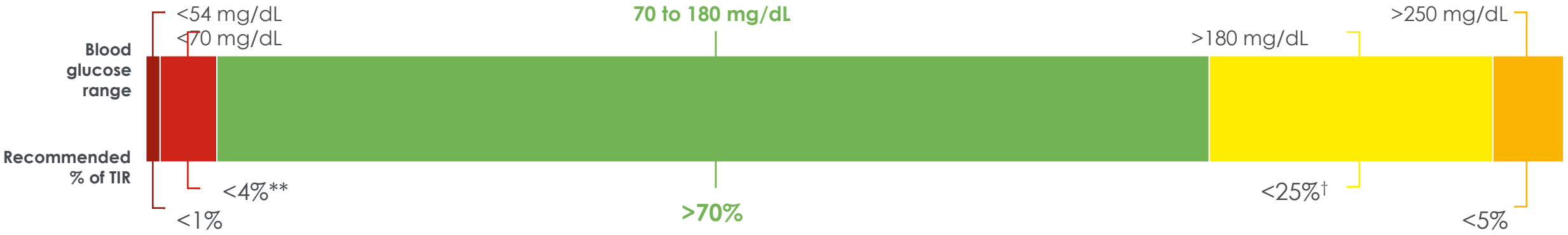
## International clinical guidelines recommend time-in-range targets for people with T1DM and T2DM[4]

GV, glycaemic variability; T1DM, Type 1 diabetes mellitus; T2DM, Type 2 diabetes mellitus; TIR, time-in-range

1. Danne T, et al. Diabetes Care. 2017;40:1631–1640; 2. Battelino T, et al. Diabetes Care. 2019;42:1593–1603; 3. Beck RW, et al. Diabetes Care. 2019;42:400–405; 4. ADA. Diabetes Care. 2020;43(Suppl 1).

# International clinical guidelines recommend adults with T1DM and T2DM spend >70% of time in-range (70 to 180 mg/dL)[1,2]

## People with T1DM* and T2DM should aim for the following blood glucose profile[1]




Adapted from Battelino T, et al. (2019)

**Hypoglycaemia**

**<1 hour per day**
with blood glucose <70 mg/dL

**<15 minutes per day**
with blood glucose <54 mg/dL

**TIR**

**>16.48 hours per day**

**Hyperglycaemia**

**<1.12 hours per day**
with blood glucose >250 mg/dL

**<6 hours per day**
with blood glucose >180 mg/dL

**Each incremental 5% increase in TIR is associated with clinically significant benefits for adults with T1DM or T2DM[1]**

*For people with T1DM aged <25 years, if the $HbA_{1c}$ goal is 7.5%, then TIR target is approximately 60%;[1] **Includes percentage of values <54 mg/dL (3.0 mmol/L);[1] †Includes percentage of values >250 mg/dL (13.9 mmol/L).[1]

T1DM, Type 1 diabetes mellitus; T2DM, Type 2 diabetes mellitus; TIR, time-in-range

1. Battelino T, et al. Diabetes Care. 2019;42:1593–1603; 2. ADA. Diabetes Care. 2020;43(Suppl 1).

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# Glycaemic variability is a common challenge for people with diabetes and has a range of serious consequences

## GV and time spent outside target range are continuous issues for people with T1DM and T2DM:[1,2]

**~56%**

of people with T1DM were found to have excess GV (%CV of >36%)*[1]

**19%**

of people with T2DM receiving insulin were found to have excess GV (%CV of >36%)*[1]

**~9 h/day**

are spent outside target range (in hyper- or hypoglycaemia) for an average person with T1DM[2]

## GV is linked to:

- Microvascular complications[3–5]
- Macrovascular complications[3–6]
- Severe hypoglycaemia[7]
- ↓ QoL and negative emotions[4,8,9]
- Increased mortality rates[10]

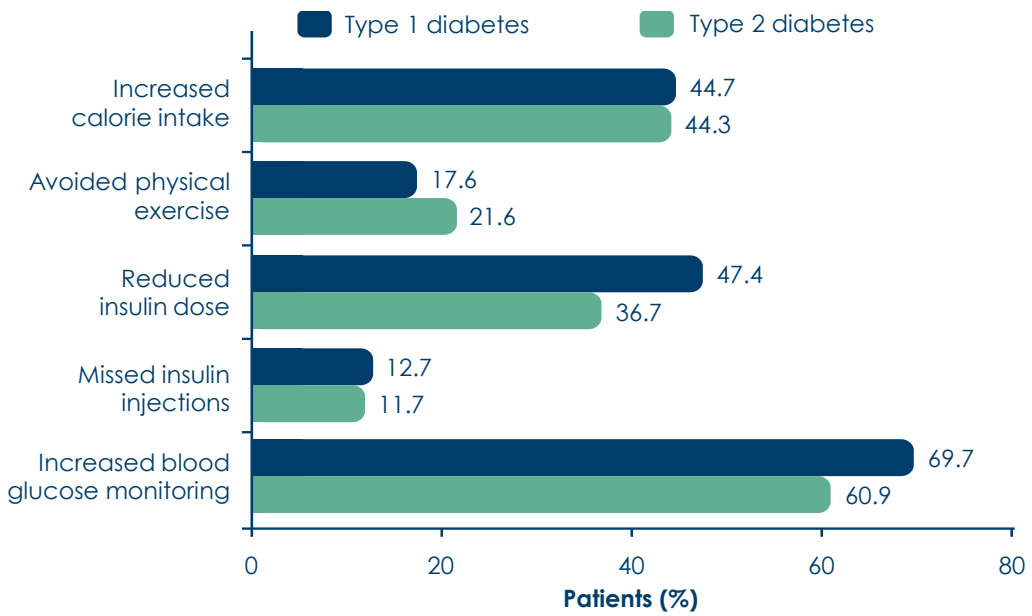
*Of the 376 persons who were included in the study, 122 had T1DM, 79 had T2DM and were receiving insulin treatment. Subjects underwent CGM at the University Hospital of Montpellier between 2003 and 2012. %CV = [(SD of glucose)/(mean glucose)] × 100).[1]

%CV, percentage coefficient of variation for glucose; CGM, continuous glucose monitoring; GV, glycaemic variability; QoL, quality of life; SD, standard deviation; T1DM, Type 1 diabetes mellitus; T2DM, Type 2 diabetes mellitus

1. Monnier L, et al. Diabetes Care. 2017;40:832–838; 2. Agiostratidou G, et al. Diabetes Care. 2017;40:1622–1630; 3. Cardoso CRL, et al. Cardiovasc Diabetol. 2018;17:33; 4. Krishna SV, et al. Indian J Endocrinol Metab. 2013;17:611–619; 5. Hirsch IB. Diabetes Care. 2015;38:1610–1614; 6. Monnier L, et al. Diabetes & Metabolism. 2018;44:313–319; 7. Cox DJ, et al. Diabetes Care. 2007;30:1370–1373; 8. Cox D, et al. Int J Clin Pract Suppl. 2002;20–26; 9. Penckofer S, et al. Diabetes Technol Ther. 2012;14:303–310; 10. Lu J, et al. Diabetes Care. 2020; dc201862.doi:10.2337/dc20-1862 (Online ahead of print).

# Hypoglycaemia is a major barrier to glycaemic control in people with T1DM and T2DM

## Patient responses to hypoglycaemia…*[1]




Adapted from Khunti K, et al. (2017)

## …can negatively impact glycaemic control…[1–8]

- Maintaining higher than recommended $HbA_{1c}$ levels
- Negative impact on QoL, and physical, mental and social functioning
- Reduced treatment adherence
- Fear of future hypoglycaemic episodes

The impact of hypoglycaemia on blood glucose control could **further exacerbate poor glycaemic control and its negative consequences[1–8]**

*In the 4 weeks following baseline. Results shown are from a non-interventional, multicentre, 4-week prospective survey using self-assessment questionnaires and patient diaries of hypoglycaemic events conducted across 2004 sites in 24 countries from 2012 to 2013. 27,585 subjects were ≥18 years of age at the time of enrolment, with T1DM (n=8,022) or T2DM (n=19,563), treated with insulin for >12 months.[1]

QoL, quality of life; T1DM, Type 1 diabetes mellitus; T2DM, Type 2 diabetes mellitus

1. Khunti K, et al. Diabetes Res Clin Pract. 2017;130:121–129; 2. Russell-Jones D, et al. Diabetes Obes Metab. 2018;20:488–496; 3. Willis WD, et al. Expert Rev Pharmacoecon Outcomes Res. 2013;13:123–130; 4. Sakane J, et al. J Diabetes Investig. 2015;6:567–570; 5. Leiter LA, et al. Can J Diabetes. 2005;29:00–00; 6. Fidler C, et al. J Med Econ. 2011;14:646–655; 7. Aronson R, et al. Diabetes Res Clin Pract. 2018;138:35–43; 8. Diabetes Canada. 2018; Clinical Practice Guidelines. Available from: http://guidelines.diabetes.ca/docs/CPG-2018-full-EN.pdf [Accessed October 2020].

# Time-in-range is an important physical and emotional measure of success for people with T1DM and T2DM

**Up to 57%** of people with T1DM and T2DM ranked TIR as the measurable therapy outcome that had the **biggest impact on daily life with diabetes***

**Up to 57%** ranked TIR as the **highest driver of a positive mindset****

**More daily TIR** may give patients **greater feelings of personal or therapeutic success with their diabetes,** whereas $HbA_{1c}$ is not likely to have the same impact on feelings of success

*Online survey of 3,461 people with T1DM (n=1,026) or T2DM (n=1,154 on insulin; n=1,281 not on insulin). The survey presented respondents with 25 questions investigating patients' perceptions of the success of current diabetes drugs and devices; which factors have the biggest impact on patients' daily lives and which changes would have the biggest positive impact on diabetes management and mindset; and mental well-being, QoL, desired improvements for future therapies, relationships with health care providers, and the concerns of loved ones. The survey was conducted from 17–22 August;[1] **Food choices were rated by all groups (range 63% to 67% of the groups) as the greatest factor having an impact on daily life with diabetes, but TIR emerged as the **measurable therapy outcome** that had the biggest impact on daily life with diabetes for all groups of respondents (range 41% to 57%).[1]

QoL, quality of life; T1DM, Type 1 diabetes mellitus; T2DM, Type 2 diabetes mellitus; TIR, time-in-range

Runge AS, et al. Clin Diabetes. 2018;36:112–119.

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# Glycaemic variability can impact diabetes-related quality of life and treatment satisfaction, independent of $HbA_{1c}$

**Although there are no definitive conclusions around a link between GV and QoL, use of CGM is associated with improved QoL and reduced GV may be the mediator[1,2]**

## In people with T1DM and T2DM:

Independent of reductions in daily glucose and $HbA_{1c}$…*

**…decreased glycaemic variability** was associated with improvements in patient satisfaction and perceived health[3]**

**Time-in-range is an important physical and emotional measure of success**, whereas $HbA_{1c}$ is not likely to have the same impact on feelings of success†[4]

**Greater treatment satisfaction is associated with better disease outcomes.[5,6] This could potentially lead to better treatment adherence and self-care behaviours in people with diabetes[5,6]**

*Based on a multicentre, randomised, crossover trial at 52 US centres in adults with T1DM (n=82) and T2DM (n=306). Subjects received basal-bolus regimen of insulin glargine plus premeal insulin glulisine (n=192) or premix analogue insulin (n=196). Participants were then crossed over to the other treatment at 12 weeks and continued for another 12 weeks;[3] **Including intra-day mean glucose, glycaemic variability, and excursions >140 mg/dL;[3] †Online survey of 3,461 people with T1DM (n=1,026) or T2DM (n=1,154 on insulin; n=1,281 not on insulin). The survey presented respondents with 25 questions investigating patients' perceptions of the success of current diabetes drugs and devices; which factors have the biggest impact on patients' daily lives and which changes would have the biggest positive impact on diabetes management and mindset; and mental well-being, QoL, desired improvements for future therapies, relationships with health care providers, and the concerns of loved ones. The survey was conducted from 17–22 August. Food choices were rated by all groups (range 63% to 67% of the groups) as the greatest factor having an impact on daily life with diabetes, but TIR emerged as the measurable therapy outcome that had the biggest impact on daily life with diabetes for all groups of respondents (range 41% to 57%).[6]

CGM, continuous glucose monitoring; GV, glycaemic variability; QoL, quality of life; T1DM, Type 1 diabetes mellitus; T2DM, Type 2 diabetes mellitus

1. Polonsky WH, et al, Diabetes Care. 2017;40:736–774; 2. Wilmot EG, et al. Diabetes Obes Metab. 2019;21:2599–2608; 3. Testa J Clin Endocrinol Metab. 2012;97:3504–3514; 4. Runge AS, et al. Clin Diabetes. 2018;36:112–119; 5. Dex T, et al. Presented at the 53rd Annual Meeting of the European Association for the Study of Diabetes; September 11–15, 2017. 801; 6. Rodbard H, et al. Diabetes Care. 2017;40:171–180.

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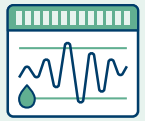
# Glycaemic variability and time-in-range targets for your clinical practice

# In summary: international clinical guidelines recommend glycaemic variability and time-in-range targets for adults with T1DM and T2DM

## ADA Standards of Medical Care and International Consensus on TIR Guidelines recommend:[1,2]



**Glycaemic variability (%CV)** **≤36%***

**TIR (70 to 180 mg/dL)** **>70%**** (>16.8 hours per day)

**Additional recommended % of time in blood glucose ranges:**

>250 mg/dL: <5% >180 mg/dL: <25% <70 mg/dL: <4% <54 mg/dL: <1%

**Helping people with T1DM and T2DM to reduce their glycaemic variability and maximise their TIR is a key aspect of effective diabetes management[1,2]**

*Some studies suggest that lower %CV targets (<33%) provide additional protection against hypoglycaemia for those receiving insulin or sulphonylureas;[2] **For age <25 years, if the $HbA_{1c}$ goal is 7.5%, set TIR target to approximately 60%.[2]

%CV, percentage coefficient of variation for glucose; T1DM, Type 1 diabetes mellitus; T2DM, Type 2 diabetes mellitus; TIR, time-in-range

1. ADA. Diabetes Care. 2020;43(Suppl 1); 2. Battelino T, et al. Diabetes Care. 2019;42:1593–1603.

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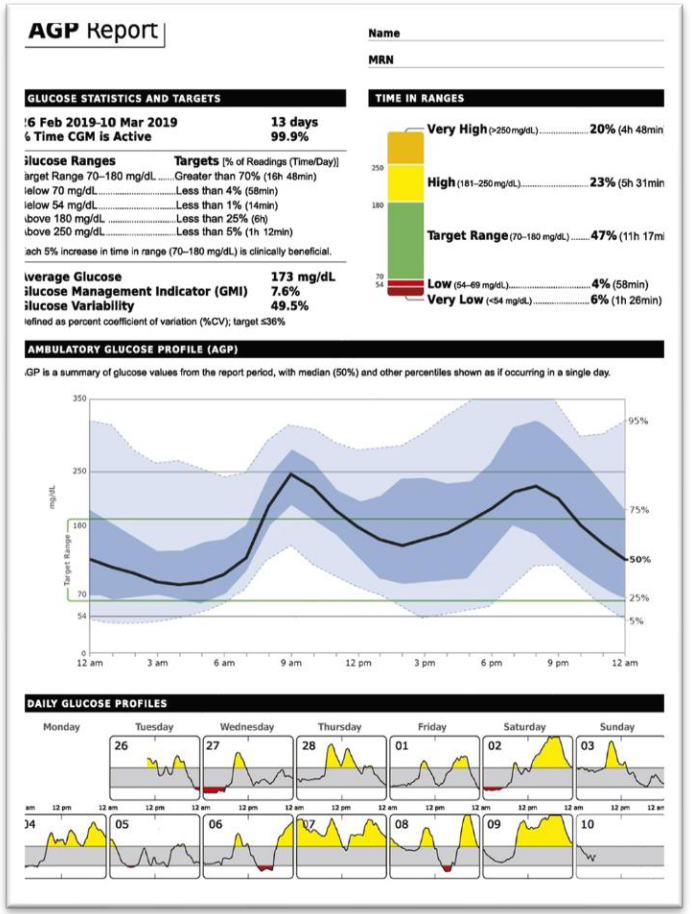
# Presenting core metrics through the Ambulatory Glucose Profile (AGP)

**AGP includes all core metrics & 14-day composite glucose profile**

**Helps to identify trends1 and visually represent glycemic patterns[2]**

- **Recognized in ATTD CGM consensus[3]**
- **Referenced 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; ATTD, Advanced Technologies and Treatments for Diabetes

1. Hammond P. Br J Diabetes 2016;16(S1):S10–S15; 2. Bergenstal RM, et al. J Diabetes Sci Technol 2013;7:562–78; 3. Battelino, T, et al. Diabetes Care. 2019;42: 1593–603; 4. ADA. Diabetes Care. 2019; 42(Suppl 1):S71–S80; 5. Fonseca VA, et al. Endocr Pract 2016;22:1008–1021

# Time-in-range targets should be tailored to a person's individual needs

| Diabetes mellitus group | TIR | Time in hypoglycaemia | Time in hyperglycaemia |
|---|---|---|---|
| | % of readings (target range) | % of readings | % of readings |
| **T1DM* and T2DM** | >70% (70–180 mg/dL) | <4% below 70 mg/dL† <1% below 54 mg/dL | <25% above 180 mg/dL§ <5% above 250 mg/dL |
| **T1DM and T2DM older/high-risk**** | >50% (70–180 mg/dL) | <1% below 70 mg/dL | <50% above 180 mg/dL§ <10% above 250 mg/dL |
| **T1DM pregnancy** | >70% (63–140 mg/dL)† | <4% below 63 mg/dL‡ <1% below 54 mg/dL | <25% above 140 mg/dL |
| **Gestational DM & T2DM pregnancy** | There are no specific recommendations for these conditions given the limited evidence, but recent data suggest that even more stringent targets may be required. | | |

The **primary goal** for effective and safe control when using CGM
**is to increase the TIR while reducing the time below range**

*For people with T1DM aged <25 years, if the $HbA_{1c}$ goal is 7.5%, then set TIR target to approximately 60%; **High-risk individuals include those with a higher risk of complications, comorbid conditions (e.g., cognitive deficits, renal disease, joint disease, osteoporosis, fracture, and/or cardiovascular disease), and those requiring assisted care, which can complicate treatment regimens. Older and/or high-risk individuals with diabetes are at notably higher risk for severe hypoglycaemia due to age, duration of diabetes, duration of insulin therapy, and greater prevalence of hypoglycaemia unawareness; †Percentages of TIR in pregnancy are based on limited data; more research is needed. ‡Includes percentage of values <54 mg/dL; §Includes percentage of values >250 mg/dL.

CGM, continuous glucose monitoring; T1DM, Type 1 diabetes mellitus; T2DM, Type 2 diabetes mellitus; TIR, time-in-range

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

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# Optimising glycaemic variability and time-in-range are fundamental to effective diabetes management and in helping to reduce the risk of negative consequences for your patients

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

### Retinopathy*[1]

**In people with T1DM**

**+64%**

increased risk of retinopathy

### Microalbuminuria*[1]

**In people with T1DM**

**+40%**

increased risk of microalbuminuria

### Neuropathy**[2]

**In people with T2DM and CKD**

**+25%**

increased risk of peripheral neuropathy

### Mortality†[3]

**In people with T2DM**

**+8%** increased risk of all-cause mortality

**+5%** increased risk of CV mortality

**More TIR** was associated with **reduced risk of severe hypoglycaemia, MACE** and **microvascular complications** vs less TIR‡[4]

**In people with T2DM**

**Risk of a severe hypoglycaemia event decreased by up to**

**−46%**

(TIR >70% vs ≤50%)

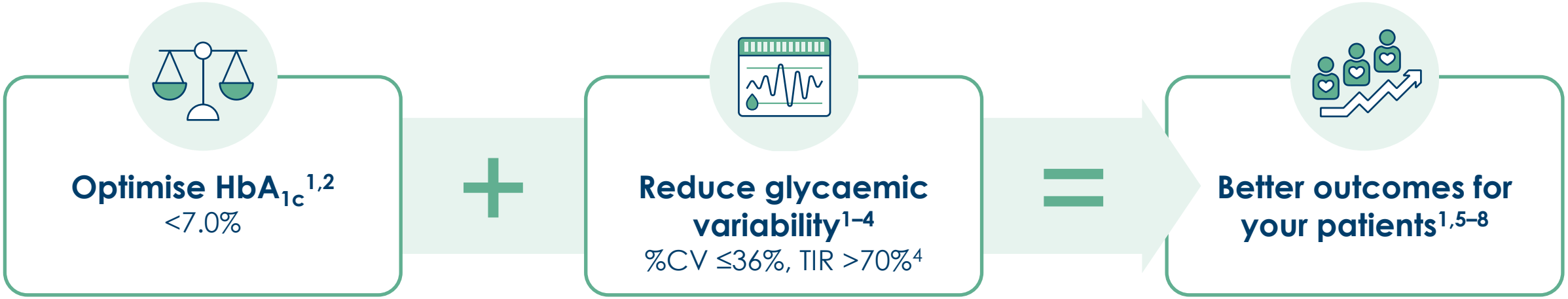
**Greater treatment satisfaction** is linked to **better disease outcomes in diabetes**[5,6]

**Decreased glycaemic variability§** was associated with improvements in **patient satisfaction** and **perceived health**[7]

**International guidelines recommend a %CV ≤36% and a target of >70% TIR (70 –180 mg/dL) for most patients**[8,9]
Adhering to these can help improve outcomes for your patients and promote better diabetes management

*Post hoc* analysis using the DCCT dataset to evaluate the association of TIR of 70–180 mg/dL (3.9–10 mmol/L) with the development or progression of retinopathy and microalbuminuria to validate TIR as a metric. Criteria for the retinopathy outcome were met by n=271/1,440 (19%), and for the microalbuminuria outcome were met by n=116/1,283 (9%). Mean TIR for 7-point profiles for 1,440 people was 41 ± 16%;[1] **Data from a prospective observational cohort study which evaluated the association of TIR of 70–180 mg/dL (3.9–10 mmol/L) with microvascular diabetes outcomes, including peripheral neuropathy; 62 out of 105 participants with a total MNSI questionnaire score ≥2 were defined as having distal peripheral neuropathy;[2] †A prospective cohort study evaluating the link between TIR of 70–180 mg/dL (3.9–10 mmol/L) with all-cause and cardiovascular mortality, with the objective of validating TIR as surrogate marker of long-term adverse clinical outcomes.[3] ‡*Post hoc* study using data from the DEVOTE study from 5,644 people with T2DM who had an 8-point glucose profile. Individual TIR was derived as the proportion of the 8-point glucose profile within range (derived TIR). A Cox model was used to estimate the association between derived TIR and time to first MACE, severe hypoglycaemic episode and microvascular event (retinopathy and CKD);[4] §Including intra-day mean glucose, glycaemic variability, and excursions >140 mg/dL;[7] CKD, chronic kidney disease; CV, cardiovascular; DCCT, Diabetes Control and Complications Trial; MACE, major adverse cardiovascular event; MNSI, Michigan Neuropathy Screening Instrument; T1DM, Type 1 diabetes mellitus; T2DM, Type 2 diabetes mellitus; TIR, time-in-range. 1. Beck RW, et al. Diabetes Care. 2019;42:400–405; 2. Mayeda L, et al. BMJ Open Diab Res Care. 2020;8:e000991; 3. Lu J, et al. Diabetes Care. 2020; dc201862.doi:10.2337/dc20-1862 (Online ahead of print); 4. Bergenstal RM, et al. Presented at the American Diabetes Association, 80th Scientific Sessions; June 12–16, 2020. 21-L; 5. Dex T, et al. Presented at the 53rd Annual Meeting of the European Association for the Study of Diabetes; September 11–15, 2017. 801; 6. Rodbard H, et al. Diabetes Care. 2017;40:171–180; 7. Runge AS, et al. Clin Diabetes. 2018;36:112–119; 8. Battelino T, et al. Diabetes Care 2019;42:1593–1603; 9. ADA. Diabetes Care. 2020;43(Suppl 1).

# Reducing glycaemic variability is a fundamental element of effective T1DM and T2DM management




**Balance hyperglycaemia reduction** while **avoiding hypoglycaemia**

**Increasing TIR** and **decreasing %CV**

**Reducing the risk of complications and mortality** and **improving patient QoL**

%CV, percentage coefficient of variation for glucose; QoL, quality of life; T1DM, Type 1 diabetes; T2DM, Type 2 diabetes; TIR, time-in-range

1. ADA. Diabetes Care. 2020;43(Suppl1); 2. Monnier L, et al. Diabetes Metab. 2018;44:97–100; 3. Rayman G. Br J Diabetes. 2016;16(Suppl1):S3-S6; 4. Battelino T, et al. Diabetes Care. 2019;42:1593–1603; 5. Runge AS, et al. Clin Diabetes. 2018;36:112–119; 6. Beck RW, et al. Diabetes Care. 2019;42:400–405; 7. Bergenstal RM, et al. Presented at the American Diabetes Association, 80th Scientific Sessions. June 12–16, 2020. 21-LB; 8. Lu J, et al. Diabetes Care. 2020; dc201862.doi:10.2337/dc20-1862 (Online ahead of print).