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Article type : Review

Title: Diabetic Medicine

Created by: Maria Davie

Email proofs to: emma.wilmot2@nhs.net

Article no.: DME-2020-00497

Accepted date: 01 October 2020

Short title/*Authors running head*: Time in range: a best practice guide for UK diabetes HCPs • E. G. Wilmot *et al.*

# **Time in range: a best practice guide for UK diabetes healthcare professionals in the context of the COVID-19 global pandemic**

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/dme.14433

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### **What's new?**

- The aim of this best practice guide was to clarify the intent and purpose of international consensus recommendations on time in range (TIR) and to provide practical insights for their implementation in UK diabetes care.
- We highlight the unmet need for awareness of the consensus recommendations regarding TIR in UK diabetes care and the benefits of improved application of TIR targets for people with diabetes.
- The strengths of TIR are clearly identified, along with important checks and balances for understanding and using TIR in UK clinical practice.
- Challenges for implementation in UK clinical practice are discussed, including the need for education both of healthcare professionals and people with diabetes.
- Evidence-based learnings from the provision of diabetes care at a distance during the period of COVID-19 social distancing are identified.
- This best practice guide covers type 1 and type 2 diabetes, including people at increased risk of hypoglycaemia as well as pregnant women with type 1 diabetes.

## **Abstract**

The emergence of continuous glucose monitoring has driven improvements in glycaemic control and quality of life for people with diabetes. Recent changes in access to continuous glucose monitoring systems within UK health services have increased the number of people able to benefit from these technologies. The COVID-19 pandemic has created an opportunity for diabetes healthcare professionals to use continuous glucose monitoring technology to remotely deliver diabetes services to support people with diabetes. This opportunity can be maximized with improved application and interpretation of continuous glucose monitoring-generated data. Amongst the diverse measures of glycaemic control, time in range is considered to be of high value in routine clinical care because it is actionable and is visibly responsive to changes in diabetes management. Importantly, it is also been linked to the risk of developing complications associated with diabetes and can be understood by people with diabetes and healthcare professionals alike. The 2019 International Consensus on Time in Range has established a series of target glucose ranges and recommendations for time spent within these ranges that is consistent with optimal glycaemic control. The recommendations cover people with type 1 or type 2 diabetes, with separate targets indicated for elderly people or those at higher risk from hypoglycaemia, as well as for women with type 1 diabetes during pregnancy. The aim of this best practice guide was to clarify the intent and purpose of these international consensus recommendations and to provide practical insights into their implementation in UK diabetes care.

## **Introduction**

Continuous glucose monitoring (CGM) has emerged as a powerful tool in helping people with diabetes achieve better glucose control. Two types of CGM systems are currently available: real-time (rtCGM) and intermittently scanned CGM (isCGM), also called flash glucose monitoring, each of which measure glucose in the interstitial fluid. rtCGM systems

measure glucose every few minutes and actively transmit data wirelessly from the sensor to a reader or smartphone app, whereas isCGM systems transmit data only when the user scans their sensor with a reader or smartphone app.

A key benefit of CGM systems is the ability to transmit data to the 'cloud'. This can be done automatically from a mobile phone or uploaded from a dedicated reader. In either case, it allows data to be simultaneously viewed by people with diabetes and healthcare professionals (HCPs), supporting virtual consultations. As diabetes services emerge from the COVID-19 pandemic in the UK, there is a realization that it will be necessary to mould and adapt our services to the 'new normal'. People with diabetes appear to be particularly vulnerable to the adverse effects of COVID-19 and, as such, social distancing will remain desirable for some time. Virtual consultations remove the need for face-to-face contact. Shared access to detailed glucose data during these consultations will support goal-setting and planning, leading to improved outcomes. More importantly, evidence clearly shows that remote consultations and availability of rtCGM or isCGM data can maintain or improve glycaemic control for many people with type 1 diabetes who use rtCGM or isCGM systems during a period of restricted access to regular diabetes services (see later).

Numerous studies have proven the clinical benefits of rtCGM and isCGM in people with type 1 or type 2 diabetes treated with different intensive insulin regimens, including multiple daily insulin injections and continuous subcutaneous insulin infusion or insulin pump therapy [1–9]. In recent years, the improved accuracy of a number of these systems (Dexcom G5 and G6, FreeStyle Libre) means that they can be used safely to make therapeutic decisions, including decisions about insulin dosing, without the need to confirm readings using an adjunct self-monitored blood glucose (SMBG) fingerprick test [10,11].

Continuous glucose monitoring systems allow a different understanding of glycaemia from that previously established. Historically, HbA<sub>1c</sub> has been considered the 'gold standard' measurement for assessing glycaemia in clinical practice. It is widely available and is clearly associated with the risk of developing complications associated with diabetes, both in type 1 and type 2 diabetes [12,13]. However, HbA<sub>1c</sub> also has limitations because it can be affected by external factors unrelated to blood glucose [14]. Furthermore, it does not provide information about clinically important measures, such as day-to-day glycaemic variability and the frequency of hyper- and hypoglycaemia, which impact on the health and well-being of people with diabetes. The glucose data reported by rtCGM and isCGM systems provide a means of expressing these important measures for standardized reporting and analysis. This is reflected in international consensus recommendations that endorse a move beyond HbA<sub>1c</sub> as the most useful marker of individual glycaemia [11,15]. Currently available rtCGM and isCGM systems are able to report on a large number of glycaemic variables, summarized in Table 1. At the heart of these measures is time in range (TIR).

### **International consensus on time in range: aims, scope and purpose**

Each rtCGM and isCGM system requires that the user specify the upper and lower limits of a target glucose range, within which they should aim to maintain their glucose readings across the day. It is important to note that this target range may differ from the target range set in a bolus calculator or an insulin pump that are used to calculate bolus doses. The target range set within each CGM device is not intended to manage targets for glucose corrections but is used to calculate their TIR and also provide visual cues on the display. We recommend that individuals use the recommended settings. As use of rtCGM and isCGM systems becomes widespread, it is clear that standardization of this target glucose range is necessary in order to provide consistent and effective reporting of outcomes in routine clinical care and for clinical research. A number of metrics have been adopted for interpreting the wealth of data provided

by rtCGM systems (Table 1) and, from these, an international consensus panel has concluded that TIR is a glycaemic measure that has high value in routine clinical care [14]. This is a measure that is easily understandable by people with diabetes and by HCPs, whilst also being rapidly responsive to changes in diet, lifestyle and medication in day-to-day diabetes management.

The percentage of TIR (%TIR) refers to the proportion of each day that a person with diabetes spends with glucose readings in each of three defined glucose ranges (Table 1). The %TIR reports on the amount of time each day that glucose readings are within the upper and lower limits of the target glucose range 3.9–10 mmol/l (or 3.5–7.8 mmol/l during pregnancy).

The percentage of time below range (%TBR) is the amount of time that readings are below the target glucose range of 3.9 mmol/l (3.5 mmol/l during pregnancy) and the percentage of time above range (%TAR) refers to the amount of time that glucose readings are above the target glucose range 10.0 mmol/l (>7.8 mmol/l during pregnancy). As will be discussed later, TBR and TAR can be divided further into low/very low and high/very high ranges, depending on the profile of the person with diabetes.

In terms of implementing these metrics in day-to-day clinical practice, the International Consensus on Time in Range [14] has defined a series of clinical targets for %TIR, %TBR and %TAR that can be applied to people with type 1 or type 2 diabetes. Separate recommendations have also been made for women with type 1 diabetes during pregnancy and for people with type 1 or type 2 diabetes who are at higher risk of hypoglycaemia as a result of age, duration of diabetes, duration of insulin therapy or impaired awareness of hypoglycaemia. These consensus recommendations also emphasize the importance of setting individual goals for time spent within any defined glycaemic range, which is an essential part of implementing %TIR, %TBR and %TAR in clinical practice.

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It is important to state that, for the purposes of the present guide, we are focusing only on TIR as measured by rtCGM or isCGM systems. Although the principles of %TIR, %TBR and %TAR can apply to glucose readings taken by multiple daily SMBG tests [16,17], the accuracy of SMBG tests is dependent on individual technique and the timing of testing, so %TIR outcomes based on SMBG may not be comparable with those generated by rtCGM or isCGM [18].

### **International consensus on time in range: current UK status**

To date, awareness of %TIR amongst UK diabetes HCPs has been low [8]. Reimbursement and access both to rtCGM and isCGM technologies has been restricted to a small number of qualifying individuals with type 1 diabetes. National Institute of Health and Care Excellence (NICE) guidance NG17 for type 1 diabetes in adults and NG18 for treatment of diabetes in children and young people both recommend the use of rtCGM in certain defined circumstances when SMBG testing is unable or unlikely to meet the need for safe and effective glucose monitoring [19,20].

In recent years, the UK has seen increased access to CGM, in particular isCGM, with almost one-third of people with type 1 diabetes in England now having access to this technology [21]. Consequently, there is an immediate need for diabetes HCPs to apply TIR and associated glycaemic measures to routine clinical practice. In order to make the most of this opportunity, there is a need for increased awareness on how HCPs and people with diabetes can use this measure, how to understand the targets and implications of changes in TIR, and how to agree strategies to improve the health and well-being of people with diabetes by supporting the attainment of these targets. This guideline is part of this drive.

## **Time in range: definitions, outcomes and relationship with HbA<sub>1c</sub>**

Time in range refers to the amount of time that a person with diabetes spends within the target glucose range. TBR and TAR are also important measures that quantify the periods when glucose levels are not in range, and are critical to assessing the overall glycaemic profile. The time spent in any of these ranges can be described either as the percentage of glucose values recorded each day or as the number of minutes or hours per day spent in that range. Throughout this guide we will provide both points of reference for TIR.

### **Time in range 3.9–10 mmol/l**

The international consensus recommendations on TIR have proposed that a target glucose range of 3.9–10 mmol/l is an appropriate standard against which to assess %TIR for people with type 1 or type 2 diabetes, both in clinical practice and in clinical trials [14]. Overall, the target that people with type 1 or type 2 diabetes should aim for is TIR >70% (16 h 48 min/day). This is modified for those aged <25 years with type 1 diabetes when the HbA<sub>1c</sub> goal is 58 mmol/mol (7.5%), in which case the TIR target should be set to approximately 60% (Table 2a, Fig. 1). Achieving mean %TIR of >70% is comparable to the American Diabetes Association /European Association for the Study of Diabetes glycaemic HbA<sub>1c</sub> target of 53 mmol/mol (7.0%).

In moving towards a standard of care that emphasizes %TIR, it is important to maintain the connection with long-term outcomes. Although HbA<sub>1c</sub> is a more abstract and hard-to-visualize measure of individual glycaemic control, it remains the gold standard for understanding population-based risks for developing macrovascular and microvascular complications [12,13]. SMBG data from the Diabetes Control and Complications Trial (DCCT) in type 1 diabetes [12] have been reanalysed to calculate the %TIR 3.9–10 mmol/l of participants with and without microvascular complications in the DCCT [16]. Seven-point SMBG testing was performed by 1440 DCCT participants on 1 day every 3 months during

more than 6 years of the DCCT, allowing the SMBG-based %TIR to be calculated. This showed a significant difference in TIR of 10–12 percentage points (2.5–3.0 h/day) between participants who did and did not develop complications. For each 10% fall in TIR (2 h 24 min less each day with glucose levels in the target range), the risk of progression of retinopathy was increased by 64% and risk of developing microalbuminuria was increased by 40% (Fig. 2). In a separate study that used retrospective CGM to measure glucose control in 3262 people with type 2 diabetes, %TIR was again inversely correlated with the prevalence and severity of diabetic retinopathy, so that a higher %TIR was associated with less or less-severe retinopathy [22]. Subsequently, further analyses of blinded CGM in 2983 people with type 2 diabetes have also demonstrated a relationship between %TIR and carotid intimal thickness [23].

These reports demonstrate that %TIR is directly correlated with risk of retinopathy, microalbuminuria or coronary artery disease, which aligns with the association between HbA<sub>1c</sub> and risk of complications in the DCCT [12] and the UK Prospective Diabetes Study (UKPDS) [13]. However, some caution must be exercised in this regard. An analysis from the REPLACE-BG study in type 1 diabetes has shown that the correlation between %TIR and outcomes reported for the DCCT based on SMBG may be different for data generated by rtCGM [18]. Similarly, targets for %TIR based on SMBG data may need to be different from those indicated by recommendations based on rtCGM or isCGM, which underscores that the present guide is centred only on interpretation of rtCGM and isCGM data.

### **Time below range <3.9 mmol/l**

Hypoglycaemia is a major limiting factor in the glycaemic management of people with type 1 or type 2 diabetes [24]. Reducing both the occurrence of hypoglycaemia and the risk of hypoglycaemia is a central tenet of optimal diabetes care. Minimizing hypoglycaemia includes acknowledging the problem, considering each risk factor, and applying the

principles of intensive glycaemic therapy, including education, drug selection and selective application of diabetes treatment technologies [24].

Real-time CGM and isCGM data have been used to define two objective measures of time in hypoglycaemia, each of which indicates different degrees of urgency for clinical action [11,14]: level 1 hypoglycaemia, with glucose 3.0–3.9 mmol/l (54–69 mg/dl), and level 2 hypoglycaemia, with glucose <3.0 mmol/l (54 mg/dl). Level 1 hypoglycaemia is clinically important, independent from any acute symptoms, and HCPs and people with diabetes should monitor time spent in level 1 hypoglycaemia in order to minimize the risk of severe hypoglycaemia episodes and/or development of impaired awareness of hypoglycaemia. Level 2 hypoglycaemia, with a glucose level of <3.0 mmol/l (54 mg/dl), with or without symptoms, is considered clinically significant and likely to trigger counterregulatory responses. As such, level 2 hypoglycaemia is deemed as requiring immediate attention.

In cases of level 1 or level 2 hypoglycaemia, the episode is considered relevant if it lasts  $\geq 15$  min before returning above 3.9 mmol/l. People meeting glucose control targets [HbA<sub>1c</sub> 48 mmol/mol (6.5%) or TIR >70%/16 h 48 min] may experience mild hypoglycaemic events. However, more-extended periods of hypoglycaemia [ $>4\%$  (1 h/day) below 3.9 mmol/l or  $>1\%$  (15 min/day) below 3.0 mmol/l], should be avoided as this can impair the counterregulatory hormonal response to low glucose [25] and increase the risk of severe hypoglycaemia requiring third-party intervention. To date, studies have shown a link between TBR and severe hypoglycaemia [26] and, more recently, an association between TBR and impaired awareness of hypoglycaemia has been demonstrated in rtCGM users [27]. A recent study has shown that people with good awareness of hypoglycaemia may be unaware of up to 60% of low sensor-glucose events [28], but the clinical significance of these asymptomatic episodes, especially overnight, is unclear. This emphasizes that the sensor data must always be interpreted in the wider context.

The International Consensus on Time in Range [14] therefore proposes that people with type 1 or type 2 diabetes should spend <4% (1 h/day) of time in level 1 hypoglycaemia each day and <1% (15 min/day) of time in level 2 hypoglycaemia (Table 2a, Fig. 1).

Recommendations for pregnancy in type 1 diabetes and for people at high risk of hypoglycaemia are discussed separately below.

### **Time above range >10.0 mmol/l**

Exposure to high glucose is a major risk factor for microvascular and macrovascular complications of diabetes, as confirmed in the DCCT [12] and the UKPDS [13]. To date, these risks have been correlated with HbA<sub>1c</sub> as a long-term marker of glucose exposure, but the impact of short-term hyperglycaemia is not well understood. rtCGM and isCGM data provide the opportunity to look at both long-term and short-term hyperglycaemia.

In common with the classification of hypoglycaemia, CGM-defined hyperglycaemia has been set at two levels that indicate different degrees of urgency for clinical action [11,14]: level 1 hyperglycaemia: glucose 10.0–13.9 mmol/l (180–250 mg/dl); and level 2 hyperglycaemia: glucose >13.9 mmol/l (250 mg/dl). The percentage of time at level 1 hyperglycaemia again cautions the user to monitor their glucose and take action only if needed, whereas level 2 urges immediate action to lower the high glucose and to minimize risk of ketoacidosis in people with type 1 diabetes.

Time in level 1 hyperglycaemia is only moderately correlated with HbA<sub>1c</sub> and an individual %TAR can be associated with a wide range of HbA<sub>1c</sub> levels. An analysis by Beck *et al.* [29] suggests that a 10% decrease (2 h 24 min/day) in TAR 10–13.9 mmol/l is associated with an average HbA<sub>1c</sub> reduction of approximately 7 mmol/mol (0.6%). Also, the higher the baseline HbA<sub>1c</sub>, the greater the benefit derived from reducing TAR.

The International Consensus on Time in Range [14] recommends that people with type 1 or type 2 diabetes aim to spend <25% of time in level 1 (10–13.9 mmol/l) or level 2 (>13.9 mmol/l) hyperglycaemia, of which <5% should be in level 2 hyperglycaemia (Table 2a, Fig.1). Recommendations for pregnancy in type 1 diabetes and for people at high risk of hypoglycaemia are discussed separately.

### **Time in range and HbA<sub>1c</sub>**

It is important to emphasize that %TIR is not a surrogate for HbA<sub>1c</sub> and has a clinical utility that is different from HbA<sub>1c</sub>, since %TIR reflects the combined influence of glucose exposure and the degree of glycaemic variability [30]. The correlation between %TIR and HbA<sub>1c</sub> is therefore important to understand in this context. Using the retrospective rtCGM data from four randomized controlled trials in type 1 diabetes, Beck *et al.* [29] examined a variety of CGM metrics and their correlation with long-term glycaemia, as measured by HbA<sub>1c</sub>. They included 6 months of CGM data from 545 participants from the following trials: JDRF CGM [31]; DIAMOND [3], REPLACE-BG [2] and HypoDE [32]. Despite a moderate correlation between %TIR and HbA<sub>1c</sub>, it was clear that a given %TIR could be associated with a wide range of HbA<sub>1c</sub> levels and vice versa. However, the established place of HbA<sub>1c</sub> in diabetes management means that it is helpful to create a rule of thumb for long-term glycaemia that correlates %TIR with HbA<sub>1c</sub>. Thus, on average, a TIR of 50% (12 h/day) is associated with an HbA<sub>1c</sub> of approximately 63 mmol/mol (7.9%), a TIR of 60% (14 h 24 min/day) is associated with an HbA<sub>1c</sub> of 57 mmol/mol (7.4%) and a TIR of 70% (16 h 48 min) is associated with an HbA<sub>1c</sub> of 53 mmol/mol (7.0%; Table 3a). The 95% CIs shown in Table 3 reiterate that a given TIR can be associated with HbA<sub>1c</sub> values that differ widely among individuals. Although a TIR of 50% (12 h/day) is associated with an average HbA<sub>1c</sub> of 63 mmol/mol (7.9%), the true value for any person with diabetes may lie anywhere between 49 mmol/mol (6.6%) and 77 mmol/mol (9.2%).

A separate analysis by Vigersky and McMahon [33] looked at paired %TIR and HbA<sub>1c</sub> data from participants with either rtCGM ( $n = 1137$ ) or SMBG ( $n = 1440$ ) measurements, from 22 studies, including 18 in people with type 1 diabetes and four in people with type 2 diabetes.

These data across type 1 and type 2 diabetes suggested a slightly lower HbA<sub>1c</sub> for a given %TIR as compared with Beck *et al.* [29] in type 1 diabetes. These two analyses also differ in that the study by Beck *et al.* used individual participant-level data to calculate the link between TIR and HbA<sub>1c</sub>, whereas Vigersky and McMahon [33] used study-level data.

However, overall, both studies show that a TIR of 60–70% (14 h 24 min to 16 h 48 min/day) should correlate to an average HbA<sub>1c</sub> of between 48 and 58 mmol/mol (6.5–7.5%).

These %TIR targets are broadly aligned with national guidelines for glycaemia in adults and children with type 1 diabetes [19,20]. However, for someone with a starting HbA<sub>1c</sub>  $\geq 64$  mmol/mol (8.0%), each 10% (2 h 24 min/day) increase in TIR is associated with an approximate 11-mmol/mol (1%) reduction in HbA<sub>1c</sub>, whereas a person with a baseline HbA<sub>1c</sub> of 53–63 mmol/mol (7.0–7.9%) will see, on average, a 4-mmol/mol (0.4%) reduction in HbA<sub>1c</sub> with each 10% (2 h 24 min/day) increase in TIR [29]. Since a therapeutic intervention is considered effective if the reduction in HbA<sub>1c</sub> is  $\geq 4$  mol/mol (0.4%), the importance of setting small, achievable goals for improvements in %TIR is underlined. For someone with an HbA<sub>1c</sub>  $\geq 64$  mmol/mol (8.0%), even a 5% (1 h 15 min/day) increase in TIR can potentially result in a clinically relevant reduction in HbA<sub>1c</sub> of 9 mmol/mol (0.85%)[29]. The much greater impact of change in %TIR for individuals with a higher starting HbA<sub>1c</sub> may reflect that each 5% or 10% incremental improvement in TIR can be a result of reductions in TAR, whereas those with a lower starting HbA<sub>1c</sub> will probably need to reduce TBR as well.

Estimates of change in HbA<sub>1c</sub> for different incremental improvements in %TIR at different baseline HbA<sub>1c</sub> values are indicated in Table 3b, based on the analysis by Beck *et al.* [29].

Again, the important 95% CIs should be noted.

Both HbA<sub>1c</sub> and %TIR will continue to be important markers of glycaemic health with important roles to play in clinical decision making. However, %TIR is more meaningful for understanding day-to-day glycaemia and is responsive to changes in diabetes management.

A recent Association of British Clinical Diabetologists (ABCD) audit of %TIR measures for people with diabetes using the FreeStyle Libre system has shown substantial variation in target glucose ranges used by clinicians [8], with only 15% of 2191 cases using the recommended 3.9–10 mmol/l range. As remote consultations become the ‘new normal’, access to TIR measures which do not require a face-to-face visit may replace laboratory HbA<sub>1c</sub> measurements [19]. Thus, the need to standardize our approach to the interpretation of rtCGM/isCGM data has never been greater.

### **Time in range in elderly people with diabetes and those at high risk from hypoglycaemia**

Some people with diabetes are at higher risk of severe hypoglycaemia due to age, duration of diabetes, duration of insulin therapy and/or greater prevalence of hypoglycaemia unawareness [34–39]. This increased risk of severe hypoglycaemia can be exacerbated by cognitive and physical impairments, as well as other comorbidities (e.g. renal disease, joint disease, osteoporosis, fracture and/or cardiovascular disease), and people requiring assisted care [36,39].

The International Consensus on Time in Range recommendations for high risk and elderly people emphasize the need to be conservative and to individualize targets for %TIR, with a clear focus on reducing the %TBR <3.9 mmol/l (<70 mg/dl) while preventing excessive hyperglycaemia (Table 2a, Fig. 3). Thus, the recommended target range for high-risk and elderly individuals is still 3.9–10 mmol/l, but the daily goal is for >50% (>12 h/day) TIR, rather than >70% (>16 h 48 min/day). Because of the need to closely manage the risk of

hypoglycaemia in this group, the recommendation is to keep %TBR (<3.9 mmol/l) below 1% or <15 min/day. Similarly, the recommendations for %TAR are streamlined to focus on keeping levels >13.9 mmol/l to <10% (2 h 24 min/day; Table 2a, Fig. 3).

### **Time in range in pregnancy**

During pregnancy, the goal for women with diabetes is to safely increase %TIR as quickly as possible, while reducing %TAR, %TBR and glycaemic variability. Early studies using rtCGM in women with pregestational type 1 or type 2 diabetes show that, during the critical stages of early pregnancy, women with diabetes on average spend only 50% (12 h/day) with glucose levels in a target range of 3.9–7.8 mmol/l [40]. This rises to almost 60% (14 h 24 min/day) during the third trimester for women with type 1 diabetes and to almost 80% (19 h 12 min/day) for women with type 2 diabetes. Women with type 1 diabetes spend 40% (9 h 36 min/day) of time in hyperglycaemia (TAR >7.8 mmol/l) at the end of the first trimester, falling to 33% (7 h 55 min/day) at the end of the third trimester. For women with type 2 diabetes, TAR was 33% (7 h 55 min/day) at the end of the first trimester, falling to 12% (2 h 53 min/day) at the end of the third trimester. However, it should be noted that at 8 weeks' gestation, women with type 1 diabetes or type 2 diabetes spend 40% (9 h 36 min/day) of the time with a glucose level >7.8 mmol/l [39]. Women with type 1 diabetes also spent more time (~4% or 1 h/day) with CGM glucose levels below 3.9 mmol/l than women with type 2 diabetes [40].

Data from the CONCEPTT trial [41] in pregnancy in type 1 diabetes used the target glucose range of 3.5–7.8 mmol/l, but confirmed that TIR increased by approximately 10% (2 h 24 min/day) from the first to the third trimester. It also showed that use of rtCGM helps women with type 1 diabetes improve their %TIR during pregnancy compared to a control group using SMBG (68% vs 61%; 16 h 19 min vs 14 h 38 min/day), as well as reducing %TAR

(27% vs 32%; 6 h 29 min vs 7 h 41 min/day) at 34–35 weeks. The improvement in glycaemia was achieved without increased maternal hypoglycaemia. Indeed, the %TBR at 4% (1 h/day) was lower in the CONCEPTT study than previously reported during type 1 diabetes pregnancy [40], even accounting for the lower 3.5-mmol/l threshold for low glucose. This indicates that the international consensus recommendation of <4% (1 h/day) time below 3.5 mmol/l for women with type 1 diabetes during pregnancy [14] is safely achievable. The CONCEPTT trial was not powered to examine whether the use of rtCGM impacted on either TBR or the number of episodes of severe hypoglycaemia.

Another important observation from CONCEPTT and other recent studies in type 1 diabetes pregnancy [41,42] is that a 5–7% (72–100 min/day) increase in TIR during the second and third trimester is associated with significantly improved neonatal health outcomes, with lower incidence of large-for-gestational-age infants and other complications, such as neonatal hypoglycaemia, and neonatal intensive care admissions lasting more than 24 h.

The International Consensus on Time in Range recommends a target glucose range of 3.5–7.8 mmol/l for women with type 1 diabetes during pregnancy and a %TIR of >70% (16 h 48 min/day; Table 2b, Fig. 4). However, data from CONCEPTT and real-world data from Sweden suggest that this was only achieved in the final 3–4 weeks of pregnancy in type 1 diabetes, which is too late for optimal neonatal outcomes [41,42]. In practice, women with type 1 diabetes should therefore be encouraged to aim for a TIR of >70% (16 h 48 min/day) and a daily TAR >7.8 mmol/l of <25% (6 h/day; Table 2b), from as early as possible during pregnancy. Accepting that this target for TIR of >70% (16 h 48 min/day) in the second and early third trimester may not be realistic for all women, it is important to reiterate that even a 5% increase in TIR during this important part of the pregnancy is associated with clinically relevant improvements in neonatal health [43]. This means a target of an extra 72 min/day in range, which is worth striving for.

On a practical level it can be productive to document average glucose, %TIR, %TBR and %TAR, and a one-line summary of what their profile is showing for women with diabetes during pregnancy each time they are reviewed. This provides additional structure in the notes to easily assess progress against targets for all multidisciplinary team members who may be responsible for a review.

To manage the risk of low glucose during pregnancy, the International Consensus on Time in Range recommends that women with type 1 diabetes should aim for a %TBR <3.5 mmol/l of <4% (1 h/day), and <1% (15 min/day) for TBR <3.0 mmol/l (Table 2b, Fig. 4). The observations from the CONCEPTT study indicate that these should be achievable [41].

The International Consensus on Time in Range recommendations for %TIR, %TBR and %TAR are for pregnancy in women with type 1 diabetes. Women with type 2 diabetes spend one-third less time in hyperglycaemia during pregnancy than women with type 1 diabetes and can achieve up to 20% (4 h 48 min/day) higher %TIR throughout pregnancy [40]. Because of the lack of evidence on CGM targets for women with type 2 diabetes or with gestational diabetes mellitus, no firm recommendations for %TIR, %TBR or %TAR for these two groups have been established. However, because of the data on neonatal health outcomes, a target glucose range of 3.5–7.8 mmol/l is recommended for women with type 2 diabetes or gestational diabetes during pregnancy.

The practicalities of using CGM data in pregnancy, including the value of meeting targets for %TIR within the range 3.5–7.8 mmol/l, are covered extensively in a series of educational videos created by the UK Diabetes Technology Network (DTN-UK; <https://abcd.care/dtn/CGM>).

## Strengths of time in range

Percentage of time in range is a dynamic measure of short-term and medium-term glycaemic control. Compared to established markers of glycaemic health, such as HbA<sub>1c</sub> or frequency of symptomatic hypoglycaemia, %TIR is easy to track, can be visualized in a meaningful way and can be personalized. Importantly, in contrast to HbA<sub>1c</sub>, %TIR provides information that is directly actionable and responsive to changes in diabetes management that can be viewed on demand by the person with diabetes or their healthcare team. Consequently, using %TIR allows SMART objectives to be agreed when goal-setting, each of which can be more accessible and achievable than targets set for improvements in HbA<sub>1c</sub>.

As previously discussed, %TIR can be visualized and interpreted either as a % figure or as an absolute number of hours per day. This increases accessibility for patients, who can choose the format that best suits their own preference for interpreting their %TIR targets and performance. This also improves the quality of the conversation between a person with diabetes and their HCP during a review, since %TIR better reflects the day-to-day experience of living with diabetes than does HbA<sub>1c</sub>.

From a clinical perspective, %TIR is influenced by all of the known factors that affect daily glucose patterns. These include: glucose excursions and peaks associated with mealtimes; carbohydrate counting and carbohydrate content and glycaemic index of food; insulin doses and timings throughout the day, especially around mealtimes; stress and anxiety; exercise and physical health. This means that all of the established clinical behaviours for managing unwanted high or low glucose can be brought to bear in making decisions about how best to improve %TIR in line with agreed targets.

An important strength is that %TIR provides for different and more positive messaging for people with diabetes, a key objective in effective diabetes consultations. Awareness and

understanding of %TIR allows day-by-day monitoring of the achievement of glycaemic goals. By including %TBR as an active measure, the focus can also be directly moved to the risk of hypoglycaemia and objective management of low glucose. This is not possible with HbA<sub>1c</sub>, which masks the reality of glucose variability and potential hypoglycaemia.

The consensus target of 70% (16 h 48 min/day) TIR also makes it explicit that readings may stray above or below the target range for approximately 7 hours (~ 30% of time) each day and still be considered a 'good' performance. Equally, in a real-world setting, a 70% (16 h 48 min/day) target for TIR may be unrealistically aspirational, but %TIR also allows for incremental improvements that have real impact. For example, depending on their current HbA<sub>1c</sub>, a 10% (2 h 24 min/day) step-change in TIR for a person with diabetes can result in a 4–11 mmol/mol (0.4–1.0%) fall in HbA<sub>1c</sub>, a change that can be directly linked to a genuine reduction in risk of microvascular and macrovascular complications [29,33].

Each of these attributes is summarized in Box 1.

### **Learning from COVID-19: the role and impact of remote monitoring and care**

As a consequence of strategies to prevent the spread of COVID-19, the ABCD has issued guidance for the management of people with diabetes during the pandemic that minimizes attendance at clinics and encourages remote consultations in secondary/primary care [44].

This has been accompanied by guidance that recognizes the need to reorganize diabetes services to provide advice and support at a distance, whilst ensuring proactive care for people with diabetes at high risk. This ultimately means using telehealth and digital services for consultations, self-management and remote monitoring [45]. In this context, both rtCGM and isCGM technologies have allowed many clinicians and people with diabetes to view and discuss glucose downloads together. In the absence of routine laboratory HbA<sub>1c</sub> testing,

several studies since the start of the COVID-19 pandemic have shown the value of TIR and other CGM-derived metrics in demonstrating that glucose control need not suffer while access to regular diabetes clinical services is interrupted.

In the largest of these studies, Dover *et al.* [46] evaluated sensor-glucose data from 572 people in Scotland with type 1 diabetes between early March, prior to shielding, and May 2020. %TIR over this period increased from 53% to 56%, with associated improvements in glycaemic variability and estimated HbA<sub>1c</sub> (eA<sub>1c</sub>). Importantly, these differences were not seen for the comparable period in 2019. A similar study on 307 adults with type 1 diabetes in Spain [47] compared data from 14-day periods before the start of shielding and 8 weeks afterwards. In this case %TIR increased from 58% to 62% and eA<sub>1c</sub> declined from 7.4% to 7.1%. In both these studies, %TBR increased slightly. Further studies in smaller groups of people with type 1 diabetes across Europe have shown improvements or no change in %TIR during enforced shielding [48–50], and either improvement or no change in %TBR over the same period, including for groups at higher risk of hypoglycaemia [51,52].

These studies confirm that, despite the lack of access to regular diabetes services, glycaemic control can improve for many people with type 1 diabetes who are using rtCGM or isCGM systems. It may be that having more time for diabetes self-management may help improve glycaemic control in the short term. Given that a future return to so-called ‘normal’ services cannot be predicted or guaranteed, the need for wider application and interpretation of remote glucose monitoring seems clear. However, the Scottish study [46] also showed that deterioration in TIR and eA<sub>1c</sub> was more likely in people with higher levels of socio-economic deprivation. This must be included in learnings from the COVID-19 lockdown in order to ensure that a care gap does not emerge as we optimize the value of diabetes care that emphasizes technology and treatment at a distance, even after the COVID-19 pandemic is over.

## **Important checks and balances for understanding and using time in range**

The strengths of implementing %TIR in daily practice are accompanied by some important caveats. The first is to accept that there is a need for more rigorous data regarding the relationship between %TIR and health outcomes for people with diabetes. In contrast to HbA<sub>1c</sub>, data that link improved %TIR with reduced occurrence of complications of diabetes are only starting to emerge. This is why HbA<sub>1c</sub> and the link with %TIR continues to be an essential part of assessment of the longer-term risk of diabetes complications.

### **Using %TIR in conjunction with the ambulatory glucose profile**

Understanding %TIR is fundamental to assessing the overall glycaemic profile for an individual with diabetes. However, it is important to acknowledge that %TIR is a summary statistic, and not on its own sufficient for managing therapy and making treatment decisions.

It needs to be used in conjunction with information on blood glucose patterns, such as ambulatory glucose profile. Ambulatory glucose profile is an internationally agreed standard for summarizing and interpreting CGM data in a visually impactful format that allows diabetes HCPs and people with diabetes to identify patterns and trends in daily glucose control, including those that raise clinical concerns [53]. When used properly, ambulatory glucose profile can be used to target changes to daily diabetes care and to aspects of lifestyle that can improve overall glucose control and optimize the health and well-being of someone with diabetes [54]. Understanding %TIR is an important part of this wider process. Concerns raised by analysis of %TIR should always be checked with a review of the ambulatory glucose profile data and daily traces for the period in question [54].

Equally, it is important to keep each element of the TIR picture in focus. Achieving a good %TIR outcome for 3.9–10 mmol/l is to be encouraged, but it should not come at the cost of

an increase in %TBR. Avoidance of hypoglycaemia is central to optimizing outcomes in diabetes, so minimizing %TBR must be a key focus of all consultations.

Lastly, %TIR has high value for people with diabetes who have a level of glycaemia that can be assessed realistically using the measures that accompany CGM data management tools.

For anyone with diabetes who has persistent hyperglycaemia at a level that is above the visualizable limits of TIR, with chronically high glucose well above 13.9 mmol/l (250 mg/dl), there is little benefit in setting %TIR goals. In such cases, HbA<sub>1c</sub> remains the principal measure to focus on, along with managing the risks for the adverse consequences of hyperglycaemia, such as diabetic ketoacidosis.

Each of these key recommendations are summarized in Box 1.

### **Challenges for implementation in UK clinical practice**

Implementation of %TIR as standard across all diabetes healthcare services will require several strands of activity and awareness. Frequent face-to-face HbA<sub>1c</sub> blood tests are not desirable when alternative, easily accessed and remotely viewed surrogate markers such as %TIR and eA<sub>1c</sub>/glucose management indicator (GMI) are available to view in the cloud.

Potential barriers include technical issues and data management, and the requirement to change the knowledge, attitudes and behaviours of HCPs as they move away from the familiar approach of supporting consultations using HbA<sub>1c</sub>.

The technical issues start with setting up the rtCGM or isCGM device in line with the target range agreed with the person with diabetes. The International Consensus on Time in Range recommends a target glucose range of 3.9–10 mmol/l in type 1 and type 2 diabetes [14].

However, at first time of use, different CGM devices have default target glucose ranges that do not necessarily reflect this standard. As newer or updated CGM systems are launched onto the market, the default target range settings should start to adopt the 3.9–10 mmol/l

consensus range. Some systems currently do not allow target setting below 3.9 mmol/l which presents challenges to their use in pregnancy with a recommended target glucose range of 3.5–7.8 mmol/l.

The next key barrier to overcome is ensuring data sharing with the clinic has been established, assuming the individual is happy to share their data. This process is quickest and easiest using smartphone apps that are able to act both as the data reader and the data upload system. This requires the device to link to the cloud through an appropriate connection and, where this does not occur, the data will not be available in the cloud for review at future consultations. It is also common that device-specific hand-held readers are used to upload glucose data to a data management interface using a micro-USB cable connected to a computer. Data collection in this way happens only when the user chooses to do so, which can have an impact on the completeness of the glucose data available for review. Appropriate data governance needs to be followed. For example, according to General Data Protection Regulation, multidisciplinary teams should have individual log-ins rather than team log-ins.

A common theme in services caring for users of rtCGM/isCGM and insulin pump systems is the need for integrated in-clinic software and data visualization tools that can be adopted as standard across diabetes services. These should provide data capture and management capability without the need for complex systems administration support or end-user training.

Interoperability of systems is critical, able to accept data from rtCGM/isCGM and insulin pump systems, without the need for device-specific interfaces or third-party support. This need is paramount, given that the number of different devices available for rtCGM, isCGM and insulin pump management for people with diabetes is proliferating, along with the number of possible product-specific user interfaces. Currently, it is not uncommon for a diabetes clinic to have up to five data management systems open at one time to enable effective download of data.

## Education, awareness and behaviour

Along with the technical aspects of working in a data-heavy clinical space, there is the need both for clinical education on each aspect of emerging diabetes technologies and also the greater need for skills that enable HCPs to help each person using rtCGM or isCGM to optimize their own diabetes self-management. Ultimately, the emerging emphasis on %TIR will make assessing and managing glucose control easier, not harder.

As sensor-augmented care becomes widespread, it is evident that use of rtCGM/isCGM can be used to improve %TIR and reduce the occurrence of hypoglycaemia as measured by %TBR. However, these important outcomes can be further improved with additional education that can optimize the benefits of rtCGM and isCGM technologies. A study across 26 secondary care centres in Germany showed that a structured education and treatment programme for people on an intensive insulin regimen and using isCGM can improve HbA<sub>1c</sub> and %TIR at 6 months, compared to users of isCGM who did not undertake the education [55]. This educational programme was designed both to provide skills and knowledge to make use of the glucose data provided by the isCGM system, and also to address the psychosocial issues that are associated with the use of isCGM technology, such as coping with the sheer amount of glucose information generated and the exaggerated expectation it can create about glucose management [56]. The need for more-widespread educational programmes with this focus is underscored by at least one study that has shown that adolescents may be unable to make full use of rtCGM data systematically to problem-solve or reduce the frequency of hypoglycaemic events [57].

Along with their established clinical skills involved in managing unwanted high or low glucose, HCPs must therefore learn how improvements in %TIR can be driven by better use of the technology itself, and deploy these insights in support of their patients. This will mean understanding the most impactful use of trend arrows, daily scan rates, % data capture and

the various reporting tools that filter and distil the large amounts of glucose data that are generated by CGM and isCGM systems.

In clinical practice, it will become important to include mean glucose, %TIR, %TBR and %TAR into our clinical consultation templates. Post-COVID-19, as many appointments become remote, we must learn to rely more on %TIR and mean glucose or eA<sub>1c</sub>/GMI to assess and monitor progress of our patients.

More fundamentally, HCPs must learn how to have a confident and constructive consultation with each person with diabetes, that uses each aspect of %TIR, %TBR and %TAR. This will mean both education and a change in culture. Ultimately, as much as reviewing objective numbers for %TIR, there is a need to empower people with diabetes to use these new concepts and targets effectively in their daily life with diabetes.

## **Summary**

The aim of this best practice guide to %TIR is to assist clinicians and other HCPs to support people with diabetes in achieving and maintaining glucose levels that minimize their risk of complications and also improve their well-being and quality of life. This need is more pressing given that remote consultations will be an established feature of diabetes care in the future and experience from the period of COVID-19 shielding has demonstrated their efficacy. We have interpreted the recommendations provided by the International Consensus on Time in Range and provided relevant practical insights that clarify the derivation and rationale for using the different TIR measures in a safe and effective manner for the growing number of people with diabetes who use rtCGM or isCGM technology. In a clinical practice setting, TIR values are emerging as important outcome measures that can be monitored in day-to-day diabetes care. Because of what it offers in addition to HbA<sub>1c</sub> and mean glucose, TIR is now an integral component of diabetes risk assessment and therapy.

## **Funding sources**

The authors acknowledge writing support from Bite Medical Consulting, through an educational grant from Abbott Diabetes Care, who were not otherwise involved in the development of this manuscript.

## **Competing interests**

E.G.W. has received speaker honoraria from Abbott Diabetes Care, Diasend, Dexcom, Eli Lilly, Minimed Medtronic, Novo Nordisk and Sanofi Aventis, has served on advisory panels for Abbott Diabetes Care, Eli Lilly, Medtronic and Sanofi Aventis, and has received grants to attend educational meetings from Boehringer Ingelheim, Diasend, Novo Nordisk, Roche and Sanofi Aventis. P.H. has received personal fees from Abbott Diabetes Care, Medtronic, Insulet, Lilly, Novo Nordisk and Sanofi Aventis. H.R.M. has received speaker honoraria from Novo Nordisk, Roche, Medtronic and Abbott Diabetes Care. H.R.M. sits on the Medtronic European Scientific Advisory Board and has received research support from Dexcom, Medtronic, Abbott Diabetes Care and Johnson & Johnson outside the submitted work. E.S. has received speaker honoraria from Abbott Diabetes Care and Eli Lilly. F.G. has received speaker fees from Abbott Diabetes Care and advisory board fees from Dexcom. P.C. has received personal fees from Abbott Diabetes Care, Dexcom, Medtronic, Insulet, Roche, Novo Nordisk, Lilly, Sanofi and Novartis.

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**Table 1** Objective measures of glycaemic control derived from real-time continuous glucose monitoring (CGM) and intermittently scanned CGM data

| Metric                             | What does it measure?   |
|------------------------------------|---|
| Percentage of sensor data captured | Proportion of possible readings captured by the rtCGM or isCGM device. Provides a measure of confidence in the other data-derived outcomes. |
| TIR measures                       |   |
| TIR                                | Percentage of time spent in the target glucose range set on the rtCGM or isCGM system: defined as 3.9–10.0 mmol/l.                          |
| TBR                                | Percentage of time spent below the target glucose range set on the rtCGM or isCGM system: defined as below 3.9 mmol/l.                      |
| TAR                                | Percentage of time spent above the target glucose range set on the rtCGM or isCGM system: defined as above 10.0 mmol/l.                     |
| eA <sub>1c</sub> /GMI              | Short-term glucose exposure that can be used in conjunction with long-term HbA <sub>1c</sub> in setting goals.                              |
| Mean glucose                       | Average glucose level calculated across the recorded glucose readings over a defined period.  |
| Standard deviation                 | Variability (highly influenced by mean glucose).  |
| CV                                 | Variability that is less influenced by mean glucose. Expressed as %CV, calculated as $100 \times (SD/\text{mean glucose})$                  |

CGM, continuous glucose monitoring; CV, coefficient of variation; eA<sub>1c</sub>, estimated HbA<sub>1c</sub>; GMI, glucose management indicator; isCGM, intermittently scanned CGM (flash glucose monitoring); rtCGM, real-time CGM; TAR, time above range; TBR, time below range; TIR, time in range.

Each of these measures of glycaemia can be derived and reported by isCGM or rtCGM systems. They are all endorsed by international consensus guidance on use of CGM systems in the management of diabetes [11,14,15].

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**Table 2** (a) Consensus recommendations for percentage of time in range, percentage of time below range and percentage of time above range for adults, children and young people with type 1 or type 2 diabetes, and people at high risk of hypoglycaemia

| Diabetes group                    | TIR                               |                             | TBR                       |                             | TAR                          |                             |
|-----------------------------------|-----------------------------------|-----------------------------|---------------------------|-----------------------------|------------------------------|-----------------------------|
|                                   | Target range                      | % of readings: time per day | Below target level        | % of readings: time per day | Above target level           | % of readings: time per day |
| Type 1/type 2                     | 3.9–10.0 mmol/l<br>(70–180 mg/dl) | >70%:<br>>16 h 48 min       | <3.9 mmol/l<br>(70 mg/dl) | <4%:<br>< 1 h               | >10.0 mmol/l<br>(>180 mg/dl) | <25%:<br><6 h               |
|                                   |                                   |                             | <3.0 mmol/l<br>(54 mg/dl) | <1%:<br>< 15 min            | >13.9 mmol/l<br>(>250 mg/dl) | <5%:<br><1 h 12 min         |
| Older/high-risk type 1 or type 2* | 3.9–10.0 mmol/l<br>(70–180 mg/dl) | >50%:<br>>12 h              | <3.9 mmol/l<br>(70 mg/dl) | <1%:<br>< 15 min            | >13.9 mmol/l<br>(>250 mg/dl) | <10%:<br><2 h 24 min        |

TAR, time above range; TBR, time below range; TIR, time in range.

\*People with type 1 or type 2 diabetes at high risk of hypoglycaemia because of age, duration of diabetes, duration of insulin therapy or impaired awareness of hypoglycaemia.

%TIR in pregnancy are based on limited evidence. No consensus recommendations for %TIR, %TBR or %TAR in pregnancy in type 2 diabetes or in gestational diabetes are available.

**Table 2** (b) Consensus recommendations for percentage of time in range, percentage of time below range and percentage of time above range for diabetes during pregnancy

| Diabetes group                 | TIR                              |                                | TBR                       |                                | TAR                         |                                |
|--------------------------------|----------------------------------|--------------------------------|---------------------------|--------------------------------|-----------------------------|--------------------------------|
|                                | Target range                     | % of readings:<br>time per day | Below target level        | % of readings:<br>time per day | Above target level          | % of readings:<br>time per day |
| Pregnancy, type 1 <sup>+</sup> | 3.5–7.8 mmol/l<br>(63–140 mg/dl) | >70%:<br>>16 h 48 min          | <3.5 mmol/l<br>(63 mg/dl) | <4%:<br>< 1 h                  | >7.8 mmol/l<br>(>140 mg/dl) | <25%:<br><6 h                  |
|                                |                                  |                                | <3.0 mmol/l<br>(54 mg/dl) | <1%:<br>< 15 min               |                             |                                |
| Pregnancy, type 2<br>and GDM   | 3.5–7.8 mmol/l<br>(63–140 mg/dl) |                                | <3.5 mmol/l<br>(63 mg/dl) |                                | >7.8 mmol/l<br>(>140 mg/dl) |                                |
|                                |                                  |                                | <3.0 mmol/l<br>(54 mg/dl) |                                |                             |                                |

GDM, gestational diabetes; TAR, time above range; TBR, time below range; TIR, time in range.

\*%TIR in pregnancy are based on limited evidence. Consensus recommendations are provided for %TIR, %TBR and %TAR for women with type 1 diabetes during pregnancy or planning pregnancy. During pregnancy the %TIR should be considered in conjunction with mean daily glucose, aiming for a mean glucose of 6.0–6.5 mmol/l.

No consensus recommendations for %TIR, %TBR or %TAR in pregnancy in type 2 diabetes or in GDM are available.

**Table 3** (a) Predicted HbA<sub>1c</sub> for a specified percentage of time in range\*

| <b>TIR, %</b> | <b>Predicted HbA<sub>1c</sub><sup>†</sup></b> |                 |
|---------------|---|-----------------|
|               | <b>mmol/mol</b>                               | <b>%</b>        |
| 90            | 42 (28, 56)                                   | 6.0 (4.7, 7.3)  |
| 80            | 48 (33, 62)                                   | 6.5 (5.2, 7.8)  |
| 70            | 53 (38, 67)                                   | 7.0 (5.6, 8.3)  |
| 60            | 57 (43, 73)                                   | 7.4 (6.1, 8.8)  |
| 50            | 63 (49, 77)                                   | 7.9 (6.6, 9.2)  |
| 40            | 68 (54, 83)                                   | 8.4 (7.1, 9.7)  |
| 30            | 74 (60, 88)                                   | 8.9 (7.6, 10.2) |
| 20            | 78 (64, 93)                                   | 9.4 (8.0, 10.7) |

TIR, time in range.

\*Correlations of %TIR with HbA<sub>1c</sub> for target glucose range 3.9–10 mmol/l. Analysis by Beck *et al.*

[29] is based on data in type 1 diabetes only.

<sup>†</sup>Data are presented as change in HbA<sub>1c</sub> (95% CI). The 95% CI for the predictive value represents the range within which the true value for an individual's value is likely to be. For example, a TIR of 50% (12 h/day) is associated with an average HbA<sub>1c</sub> of 63 mmol/mol (7.9%), the true value for any individual with diabetes may lie anywhere between 49 mmol/mol (6.6%) and 77 mmol/mol (9.2%).

**Table 3** (b) Predicted change in HbA<sub>1c</sub> for incremental improvements in percentage of time in range\* for different baseline HbA<sub>1c</sub> values in type 1 diabetes

| Increase in %TIR | Starting HbA <sub>1c</sub> <sup>†</sup> |                      |                      |                    |                   |                    |
|------------------|---|----------------------|----------------------|--------------------|-------------------|--------------------|
|                  | <7.0%                                   | 7.0–7.9%             | ≥8%                  | <53 mmol/mol       | 53-63 mmol/mol    | ≥64 mmol/mol       |
| +5.0%            | -0.06% (-1.06, 0.93)                    | -0.26% (-1.25, 0.73) | -0.85% (-1.84, 0.14) | -0.7 (-11.7, 10.2) | -2.9 (-13.8, 8.0) | -9.4 (-20.2, 1.5)  |
| +10.0%           | -0.21% (-1.20, 0.79)                    | -0.40% (-1.39, 0.59) | -0.99% (-1.99, 0.00) | -2.3 (-13.2, 8.7)  | -4.4 (-15.3, 6.5) | -10.9 (-21.9, 0.0) |

TIR, time in range.

\*Correlations of %TIR with HbA<sub>1c</sub> for target glucose range 3.9–10 mmol/l. Analysis by Beck *et al.* [29] is based on data in type 1 diabetes only.

<sup>†</sup>Data are presented as change in HbA<sub>1c</sub> (95% CI). The 95% CI for the predictive value represents the range within which the true value for an individual's value is likely to be. For example, a TIR of 50% (12 h/day) is associated with an average HbA<sub>1c</sub> of 63 mmol/mol (7.9%), the true value for any individual with diabetes may lie anywhere between 49 mmol/mol (6.6%) and 77 mmol/mol (9.2%).

**Box 1** Using percentage of time in range in clinical practice: checks and balances. AGP, ambulatory glucose profile; TBR, time below range; TIR, time in range.

| <b>Strengths</b>  | <b>Key considerations</b>  |
|---|--|
| <ul style="list-style-type: none"><li>• %TIR is a dynamic measure of short-term and medium-term glycaemia.</li><li>• Easy to track.</li><li>• Can be visualized in a meaningful way.</li><li>• Can be personalized.</li><li>• Provides information that is directly actionable.</li><li>• Responsive to changes in diabetes management that can be viewed in real-time.</li><li>• Allows SMART objectives to be agreed when goal setting.</li><li>• Can be visualized and interpreted either as a % figure or as an absolute number of hours/minutes per day.</li></ul> | <ul style="list-style-type: none"><li>• Limited data to link improved %TIR with reduced risk of microvascular and macrovascular complications of diabetes.</li><li>• It is important to acknowledge that small improvements of 5–10% in TIR can deliver significant glycaemic benefits.</li><li>• Women with type 1 diabetes who are pregnant or planning a pregnancy must be supported to reach %TIR targets as early as possible during pregnancy.</li><li>• During pregnancy the %TIR should be considered in conjunction with mean daily glucose, aiming for a mean glucose of 6.0–6.5 mmol/l.</li><li>• %TIR should be used in conjunction with AGP data for a fuller</li></ul> |

|   |  |
|---|--|
| <ul style="list-style-type: none"><li>• Better reflects the day-to-day experience of living with diabetes than HbA<sub>1c</sub>.</li><li>• Provides for different and more-positive messaging for people with diabetes.</li></ul> | <p>picture of glycaemic health and as a basis for managing therapy and making treatment decisions.</p> <ul style="list-style-type: none"><li>• Achieving a good %TIR outcome for 3.9–10 mmol/l should not come at the cost of an increase in %TBR.</li></ul> |
|---|--|

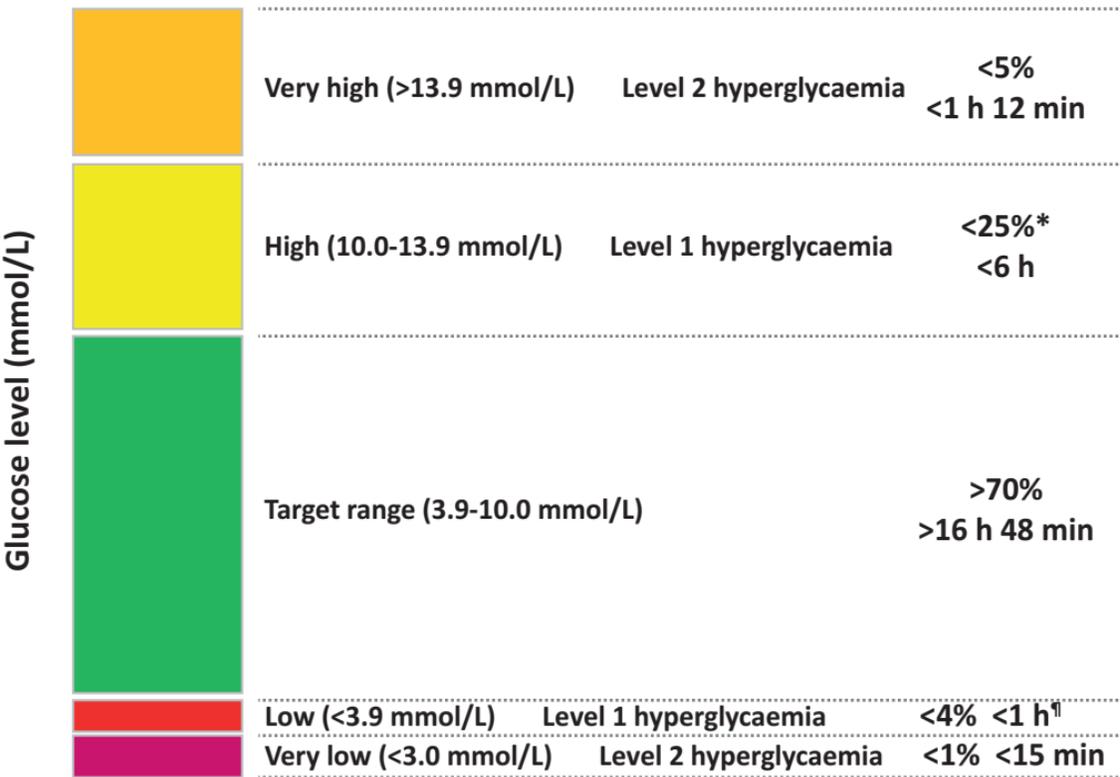
FIGURE 1 Time in ranges: targets for people with type 1 or type 2 diabetes. TAR, time above range; TIR, time in range.

FIGURE 2 Associations of time in range with risk factors for microvascular complications.

FIGURE 3 Time in ranges: targets for older people with type 1 or type 2 diabetes and those at high risk from hypoglycaemia. TBR, time below range.

FIGURE 4 Time in ranges: targets for women with type 1 diabetes who are pregnant or planning pregnancy. TAR, time above range; TBR, time below range; TIR, time in range.

# Figure 1. Time in Ranges: targets for people with type 1 or type 2 diabetes



\* Readings >13.9 mmol/L are also included in the <25% target  
 Readings <3.0 mmol/L are also included in the <4% target

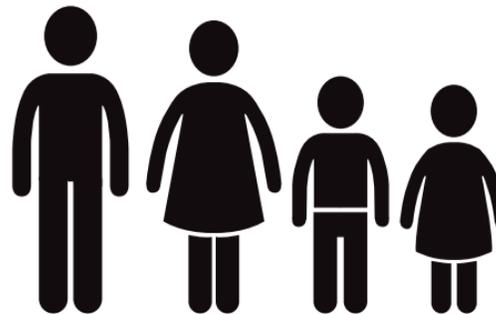
## Thinking about individualised targets

A person with HbA1c of 53-63 mmol/mol (7.0-7.9%) will see on average a 4 mmol/mol (0.4%) reduction with each 10% (2 h 24 min) increase in TIR

A person with HbA1c of ≥64 mmol/mol (≥ 8.0%) can see on average a 11 mmol/mol (1.0%) reduction in HbA1c with each 10% (2 h 24 min) increase in TIR

A 10% (2 h 24 min) decrease in TAR can be associated on average with a reduction in HbA1c of approx 7 mmol/mol (0.6%)

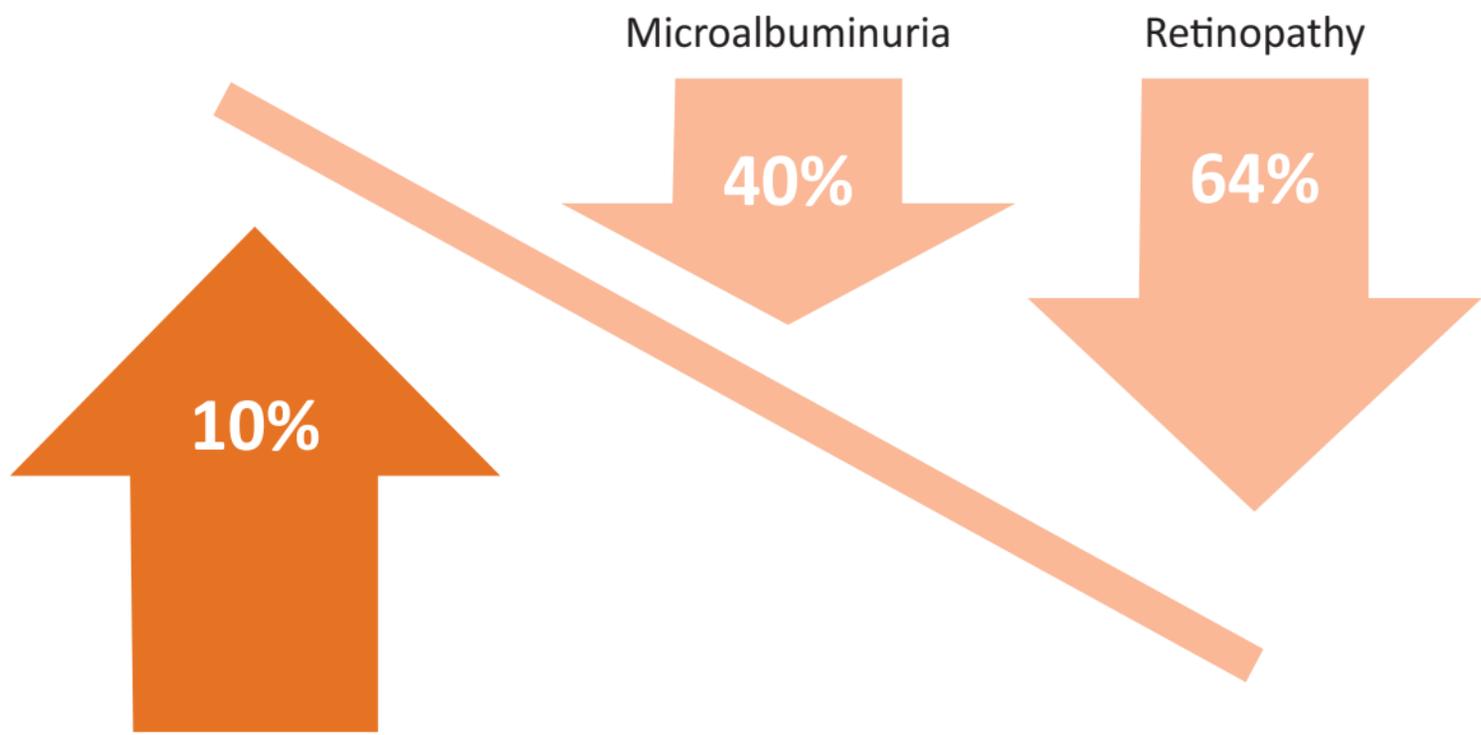
For age <25 years with type 1 diabetes, if the HbA1c goal is 58 mmol/mol (7.5%), set TIR target to approx 60%



**Figure 2. Time in range is associated with risk for microvascular complications of diabetes**

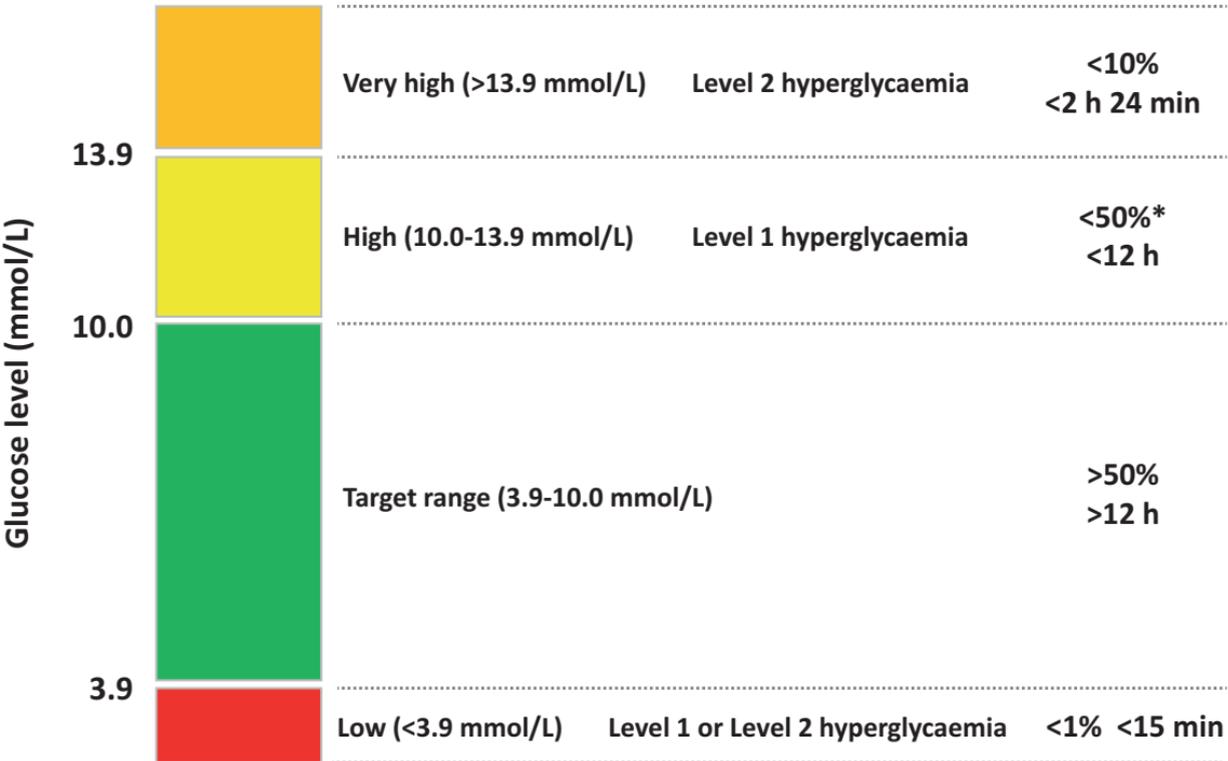
**EVERY 10% increase in TIR**

**REDUCED RISK**



Adapted from: Beck RW et al. *Diabetes Care* 2018;42:400–405; Lu J et al. *Diabetes Care* 2018;41:2370–2376

**Figure 3. Time in Ranges: targets for older people with type 1 or type 2 diabetes and those at high-risk from hypoglycaemia**



**Thinking about individualised targets**

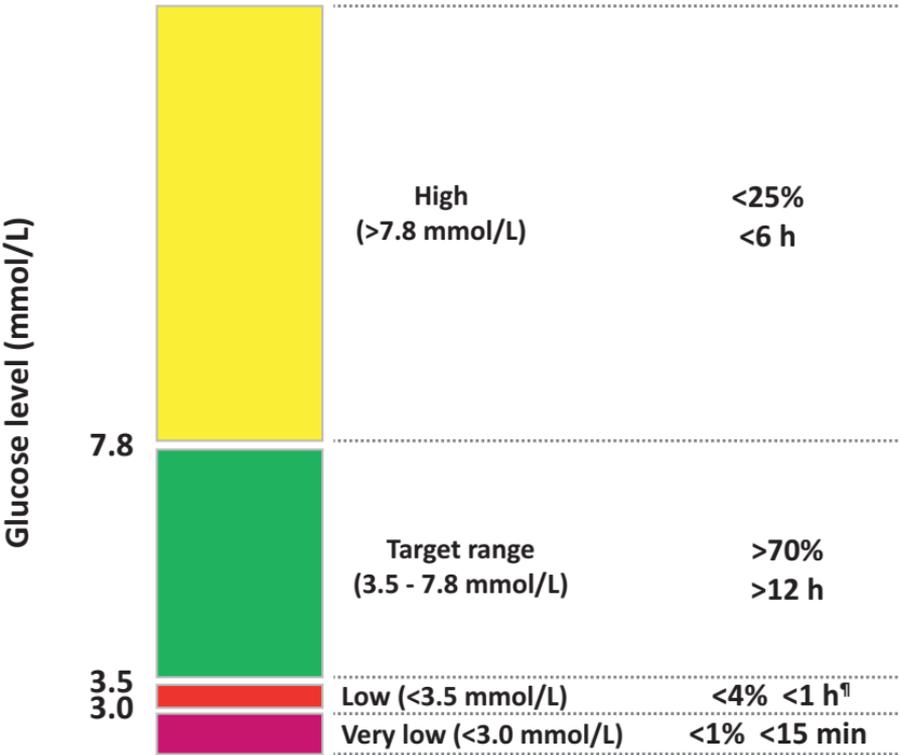
Emphasise the need to **prioritise hypoglycaemia avoidance, reducing the %TBR <3.9 mmol/L**

Remommendation is to keep %TBR <3.9 mmol/L to **<1% or 15 min per day**



\* Readings >13.9 mmol/L are also included in the <50% target

**Figure 4. Time in Ranges: targets for women with type 1 diabetes who are pregnant or planning pregnancy\***



### Thinking about individualised targets

Women with T1D should aim for a **daily TIR of >70% (16 h 48 min)** from as early as possible during pregnancy

Women with T1D should aim for a **daily TAR >7.8 mmol/L of <25% (<6 h)**, from as early as possible during pregnancy

A **5% (1 h 12 min) increase in TIR** during the **2nd and early 3rd trimester** is associated with **clinically relevant improvements in neonatal health**

During pregnancy the %TIR should be considered in conjunction with mean daily glucose, aiming for a **mean glucose of 6.0 - 6.5 mmol/L**



\* %TIR, %TBR and %TAR are based on limited evidence. More research is needed.

¶ Readings <3.0 mmol/L are also included in the <4% target