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Diabetes and Ramadan: Practical guidelines 2021☆

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ABSTRACT

Fasting during Ramadan is one of the five pillars of Islam and is obligatory for all healthy Muslims from the age of puberty. Though individuals with some illness and serious medical conditions, including some people with diabetes, can be exempted from fasting, many will fast anyway. It is of paramount importance that people with diabetes that fast are given the appropriate guidance and receive proper care. The International Diabetes Federation (IDF) and Diabetes and Ramadan (DaR) International Alliance have come together to provide a substantial update to the previous guidelines. This update includes key information on fasting during Ramadan with type 1 diabetes, the management of diabetes in people of elderly ages and pregnant women, the effects of Ramadan on one's mental wellbeing, changes to the risk of macrovascular and microvascular complications, and areas of future research. The *IDF-DAR Diabetes and Ramadan Practical Guidelines 2021* seek to improve upon the awareness, knowledge and management of diabetes during Ramadan, and to provide real-world recommendations to health professionals and the people with diabetes who choose to fast.

1. Introduction

In Islam, Ramadan is the holy month of fasting and falls on the ninth month of the lunar calendar and varies in its timing from year to year. It is one of the five main pillars of Islam and is obligatory for all healthy adult Muslims. Fasting during Ramadan involves not eating or drinking anything from dawn to sunset, and in some parts of the world this can last up to 20 h. There are two main meals eaten on each day of Ramadan: *Suhoor* is the meal eaten before dawn before fasting commences, and *Iftar* is the meal served at the end of day to mark the end of the day's fast. However, not all Muslims can fast during Ramadan; people that are ill or unwell can be exempted from fasting and can participate in Ramadan through giving charity to those that are less fortunate. Nevertheless, there is a strong desire to participate in fasting during Ramadan, even amongst those that are deemed ill or unwell.

Muslims comprise almost a quarter of the world's population and in 2010 there were nearly 1.6 billion followers of Islam worldwide [1]. The geographic regions that contain the highest Muslim populations are Middle East-North Africa (93% Muslim) [2], Central Asia (83% Muslim) [3], Southeast Asia (42% Muslim) [4] and Sub-Saharan Africa (29–31% Muslim) [5], other regions of Oceania, Europe and the Americas all have estimated Muslim populations of 5% or under [6-8]. Crucially, we note that the current and future prevalence of diabetes in these regions are high [9]. Consequently, projections point towards a large number of people with diabetes seeking to fast during Ramadan. Indeed, Hassanein *et al.* highlighted the motivation among people with diabetes seeking to fast during Ramadan in a recent review [10].

Fasting during Ramadan may provide enduring benefits. It can be an opportunity for a better lifestyle, weight loss and the cessation of unhealthy habits such as smoking [11]. For people with diabetes who choose to fast, Ramadan may also help to strengthen the therapeutic alliance with physicians and may help to improve general diabetes management.

However, people with diabetes and Healthcare Professionals (HCPs) face challenges during Ramadan. For those that fast, the onset of Ramadan can lead to a sudden change to one's usual lifestyle — this can include a shift in mealtimes and diet, changes to usual sleeping schedules and adjustments to physical activity patterns. For people with diabetes further changes are also required, these may involve a need for education, a knowledge of diabetes management plans and adaptations to self-monitoring of blood glucose (SMBG) schedules and medication regimens. Moreover, due to the varying and metabolic nature of diabetes, people living with it are also at greater risk of complications from large changes in food and fluid intake. Potential health hazards include hypoglycaemia, hyperglycaemia, dehydration and acute metabolic complications such as diabetic ketoacidosis (DKA) [12].

For HCPs the challenges involve ensuring that individuals with diabetes that are seeking to fast can do so safely. In order for HCPs to help provide safety, a greater evidence-based understanding of diabetes and Ramadan is required and an established set of guidance to help inform the best management strategies for during Ramadan are needed.

It is clear that with the increasing number of people participating in Ramadan with diabetes, there is a greater need for effective guidance. The International Diabetes Federation (IDF) and the Diabetes and Ramadan (DAR) International Alliance have once again come together to provide guidance on fasting during Ramadan with diabetes. The *IDF-*

DAR Diabetes and Ramadan Practical Guidelines 2021 will help to provide real-world recommendations to both individuals with diabetes that are seeking to fast and to HCPs that provide care. This update includes the addition of new guidance based on a greater and more recent body of evidence and the introduction of a novel clinical risk calculator to assist physicians in classifying risk. This new information comprises the impact of fasting during Ramadan on both one's physical and mental wellbeing; the management of type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM); the management of diabetes in special populations such as in pregnant women and the elderly; fasting during Ramadan and changes to the risk of comorbidities such as cardiovascular disease, stroke and renal impairment. Key revisions include updates to the risk stratification of individuals with diabetes that are seeking to fast; further evidence on the changes that can occur to the body with Ramadan fasting; new information on pre-Ramadan education and Ramadan Nutrition Plans (RNP).

2. Methods

The IDF and DAR International Alliance approached experts in diabetes from across the world to jointly develop this update to the *IDF-DAR Practical guidelines*. The IDF-DAR writing held several meetings to discuss and identify the revisions to the previous guidelines. An extensive literature review was performed for studies that were related to people with diabetes and fasting during Ramadan. Relevant studies were identified, and the key results and messages were extracted (further details are available in the full version of the guidelines). Following this, information was collated together and used to develop the recommendations presented in this article.

The DAR writing group has critically appraised and given grades to the recommendations and scored the level of evidence that were used in each case, see Tables 1 and 2. These grades have been presented throughout and will help to identify gaps within the literature and areas for future research.

3. What happens to the body? Physiology of fasting during Ramadan

Ramadan fasting (RF) represents a major shift from normal ways of eating as well as in sleep and wakefulness patterns. Feeding Patterns [13] and the accompanying changes in glucose variability [14] in RF differ significantly from non-fasting days and from other common forms of fasting due to the absolute abstinence from food and drink. This has important implications for physiology, with ensuing changes in fluid and energy balance, and in the rhythm and magnitude of fluctuations in several homeostatic and endocrine processes. In people with diabetes, the effects on glucose homeostasis are particularly important and are discussed separately. The duration of fasting impacts the physiological changes and is of particular relevance when Ramadan falls during longer summer days or in higher latitudes countries.

Table 1
Criteria for assigning levels to evidence used in developing guidance.

Level	Criteria
Level 1A	Systematic review or *meta*-analysis of high quality Randomized Controlled Trials (RCTs) a) Comprehensive search of evidence. b) Authors avoided bias in selecting articles for inclusion. c) Authors assessed each article for validity. d) Reports clear conclusions that are supported by the data and appropriate analyses. OR Appropriately designed RCT with adequate power to answer the question posed by the investigators. a) Participants were randomly allocated to treatment groups. b) Follow up at least 80% complete, (no>20% missing data). c) Participants and investigators were blinded to the treatment where applicable. d) Participants were analysed in the treatment groups to which they were assigned. e) The sample size was large enough to detect the outcome of interest.
Level 1B	Non-randomised clinical trial or cohort study with indisputable results.
Level 2	RCT or systematic review that does not meet Level 1 criteria above.
Level 3	Non-randomised clinical trial or cohort study; systematic overview or *meta*-analysis of Level 3 studies.
Level 4	Other

Table 2
Criteria for assigning grades to recommendations.

Grade	Criteria
Grade A	The best evidence was at Level 1.
Grade B	The best evidence was at Level 2.
Grade C	The best evidence was at Level 3.
Grade D	The best evidence was at Level 4 or consensus by IDF-DAR writing group

The full version of the *IDF-DAR Diabetes and Ramadan Practical Guidelines 2021* is available to freely download from the IDF website (http://www.idf.org/guidelines/diabetes-in-ramadan) and the DAR International Alliance website (http://www.daralliance.org/daralliance).

3.1. Changes to energy balance and weight

With major changes to meal times and content and sleeping times, there are also changes in activity patterns during Ramadan. Daytime and overall activity are reduced, although there does not appear to be significant changes in resting metabolic rate [13,15]. As sleeping time also decreases, there is no significant change in total (24 h) daily energy expenditure [15]. There is, on average, a reduction in total daily energy intake and a net weight loss of around 1 kg by the end of Ramadan [16,17]. Though weight loss is not a universal outcome and weight change with Ramadan shows a great deal of inter-individual variability.

3.2. Changes to circadian and hormonal rhythms

Changes during RF can impact circadian rhythm and epigenetic studies have shown alterations occurring to CLOCK circadian rhythm-controlling genes during Ramadan [18]. These can affect hormones [19-23], including cortisol, which can in turn affect insulin sensitivity and thus glucose levels. Generally, rises in cortisol are associated with rises in blood glucose levels. It was also found that the typical high morning to evening cortisol ratio reduced from 2.55 to 1.22 during Ramadan fasting [21]. Other hormonal changes associated with RF include much higher leptin in the morning, probably reflecting meal time changes; evening levels are, however, similar to that of pre-Ramadan [24]. Likewise RF can affect adiponectin; higher levels of adiponectin are associated with increased insulin sensitivity [25]. Adiponectin levels are reported to decrease in the morning days of Ramadan [26], but there is conflicting information on how levels change after fasting, during Ramadan with some proclaiming an increase [24] and others a decrease [27]. Ghrelin is an important hormone involved in the regulation of appetite, but no differences in Ghrelin levels among individuals of a healthy weight were observed during the RF [28]. In contrast, overweight and obese individuals show a marked reduction in ghrelin in the last week of Ramadan [19]. Growth hormone is also important in regulating fat metabolism and can affect insulin sensitivity; a study of 23 healthy individuals found that levels of both morning and evening growth hormone may decrease during RF [24]. Other hormonal changes reported in RF include a modest reduction in testosterone in single men, towards the end of Ramadan period [29].

3.3. Insulin sensitivity

As the Ramadan day time fasting hours progress, there is a gradual shift from carbohydrates to lipids as the main source of fuel [30]. An increase in insulin resistance in RF has been shown in several studies [24]. This, together with insulin deficiencies can lead to excessive glycogen breakdown and increased gluconeogenesis among people with diabetes. Eating large quantities at and after *Iftar* can cause further rises in blood glucose levels. As a result, the risks facing people with diabetes are heightened during Ramadan. These include hypoglycaemia, hyperglycaemia, diabetic ketoacidosis (DKA), dehydration and thrombosis [31,32].

3.4. Glucose variability and Ramadan fasting in diabetes

Data generated in continuous glucose monitoring (CGM) studies in Ramadan report stable blood glucose levels in healthy individuals (without diabetes) during fasting hours, with no significant differences in glycaemic marker exposure and in average, highest or lowest glucose sensor readings. At *Iftar*, a modest rise in interstitial glucose (and therefore blood glucose) is observed, but this increase remains within normal ranges (Fig. 1). The *Iftar* glucose peak is exaggerated in diabetes and is thought to represent the response to a carbohydrate rich meal at *Iftar*, possibly enhanced by the hormonal changes in Ramadan with patients on insulin and sulphonylureas showing excursions of higher magnitudes [14]. Although there is much intra- and inter-individual variability in glycaemic profile changes with RF, there are no overall significant differences in markers of glycaemic control between Ramadan and non-Ramadan periods [14]. Likewise, no significant differences in the number of high or low glucose excursions, time spent in range, hypoglycaemia, and hyperglycaemia have been observed [14,32]. In individuals on multiple antidiabetic medication, an increase in the mean amplitude of glycaemic excursions (MAGE) has been observed in the early stages of Ramadan compared to that of before Ramadan ($p = 0.006$) but not in late-Ramadan and post-Ramadan periods [32]. An important concern among fasting individuals on insulin or its secretogogues is hypoglycaemia during the daylight hours and this is discussed in more detail in the full version of the *IDF-DAR Diabetes and Ramadan Practical Guidelines 2021*.

3.5. Other medical considerations; relevance to Ramadan fasting and diabetes

Several other common conditions can be affected by RF and many can be present in people with diabetes. For instance, hypothyroidism and its treatment can be affected by changes to meal times. Thyroxine absorption can be affected and lead to suboptimal control of hypothyroidism [33]. It has been proposed that the best time to take thyroxine is later at night provided that no additional heavy food is eaten between Iftar and the late night hours [34]. These recommendations have used Level 3 evidence and a **Grade D** by the IDF DAR writing group. As such, specialised advice is required among individuals with diabetes and

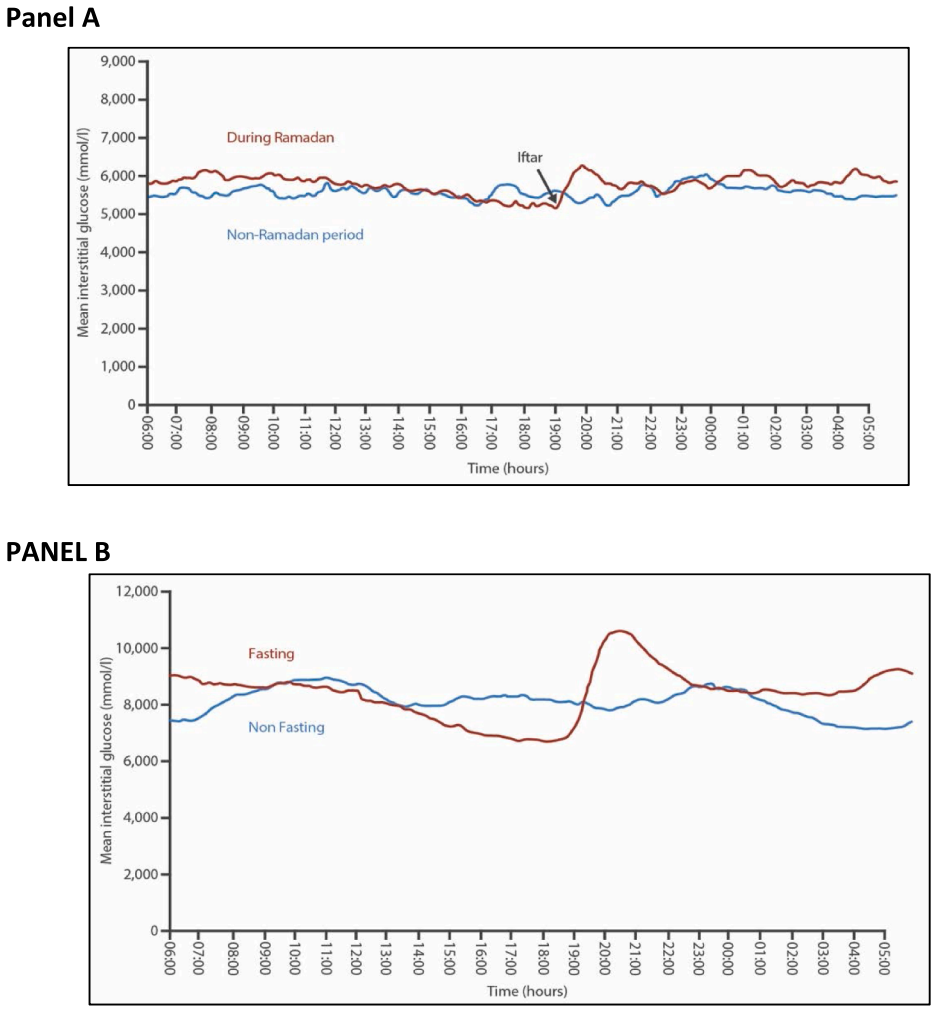

Fig. 1. Changes in glycaemic variability during Ramadan Fasting periods. Mean Continuous glucose monitoring (CGM) profiles before and during Ramadan from healthy ($n = 7$) individuals (PANEL A) and individuals with diabetes ($n = 56$, PANEL B) (adapted from Lessan et al, Diabetes Metab,2015. 41(1): p. 28–36).

hypothyroidism that seek to fast during Ramadan. Other conditions affected by RF include hyperlipidaemias, hypertension, chronic kidney disease (CKD), ischaemic heart disease (IHD) and vitamin D deficiency. For some of these, only an adjustment of timing of medication during RF is needed. For others, such as CKD and IHD, advice from a specialist and if available multi-disciplinary management is recommended and is discussed in chapter 13 of the full version of the *IDF-DAR Diabetes and Ramadan Practical Guidelines 2021*.

3.6. Effects of RF on mental wellbeing

There are many spiritual and mental benefits of Ramadan – an opportunity to self-reflect on aspects of life that need improving, the ability to grow spiritually through prayers, a time where there is an emphasis placed on good deeds and a chance to spend more time with loved ones and people within the community. Actively participating in Ramadan can lead to declining rates of depression, anxiety, stress and improvements in memory [35,36] and overall mental wellbeing [37].

The act of fasting during Ramadan itself has also been associated with alleviating feelings of anxiety and a reduction in stress among healthy individuals [38,39] and people with diabetes [40]. A study conducted in healthy Muslim graduate students showed fasting led to improvements in self-acceptance, self-sufficiency, social relations and personal growth [37]. Moreover, a longitudinal study conducted in people with T2DM has shown that fasting during Ramadan could help alleviate feelings of depression and that this could perhaps be linked to the spiritual and emotional benefits of fasting during Ramadan [41]. These benefits play a huge role in the motivation to fast during Ramadan and need to be understood by HCPs.

Other studies have found the opposite. A systematic review found RF to be associated with a negative impact to mental wellbeing [42]. People with pre-existing feelings of depression might also experience poorer glycaemic control when fasting during Ramadan [43]. The changes that occur to energy intake during RF has also been linked to fatigue, deteriorated mood and greater irritability [44]. A fear of complications, particularly hypoglycaemia, is also an important issue among people seeking to fast during Ramadan [45].

Altogether, the effects of fasting during Ramadan on one's overall mental wellbeing can be varied. Both healthy individuals and people with diabetes can experience opposing outcomes for different reasons including the changes that accompany RF or due to pre-existing circumstances. HCPs should aim to understand these reasons in pre-Ramadan assessments and ensure individuals are aware of both the potential benefits and risks to their overall physical and mental wellbeing, see Fig. 2.

4. Risk stratification of individuals with diabetes for fasting during Ramadan

Risk stratification is an important step in the process of providing guidance to individuals with diabetes seeking to fast during Ramadan. It forms the basis of all subsequent guidance and decision making. The Risk stratification process has gradually evolved from the 4 tier categories in the 2005 and 2010 American Diabetes Association (ADA) recommendations to the three-tier traffic light system in the IDF-DAR guidelines in 2016 [46]. However, in light of emerging evidence showing people previously categorised as "high-risk" as being able to safely conduct RF, and with a high proportion of individuals conducting the fast despite these risk categorisations [47], many felt that the previous risk scoring systems were too rigid.

Therefore, the IDF-DAR writing group has investigated the different components of risk stratification and has assigned a score for every risk element in accordance with the available evidence in the literature and best clinical judgement. Furthermore, these risk criteria were assessed using multiple case scenarios and presented in a survey to 350 experienced physicians within the regions of North Africa, Middle East, South Africa, Gulf region, Indian sub-continent, South East Asia and UK. The key benefit of this new risk criteria is that more people will receive better, more applicable, guidance. This will help empower individuals that were going to fast anyway, to do so safely. A greater depth of thought and consideration has gone into the development of these risk criteria compared to the previous IDF-DAR guidelines of 2016, and HCPs will be able to account for the concerns of more individuals and provide more well-founded advice.

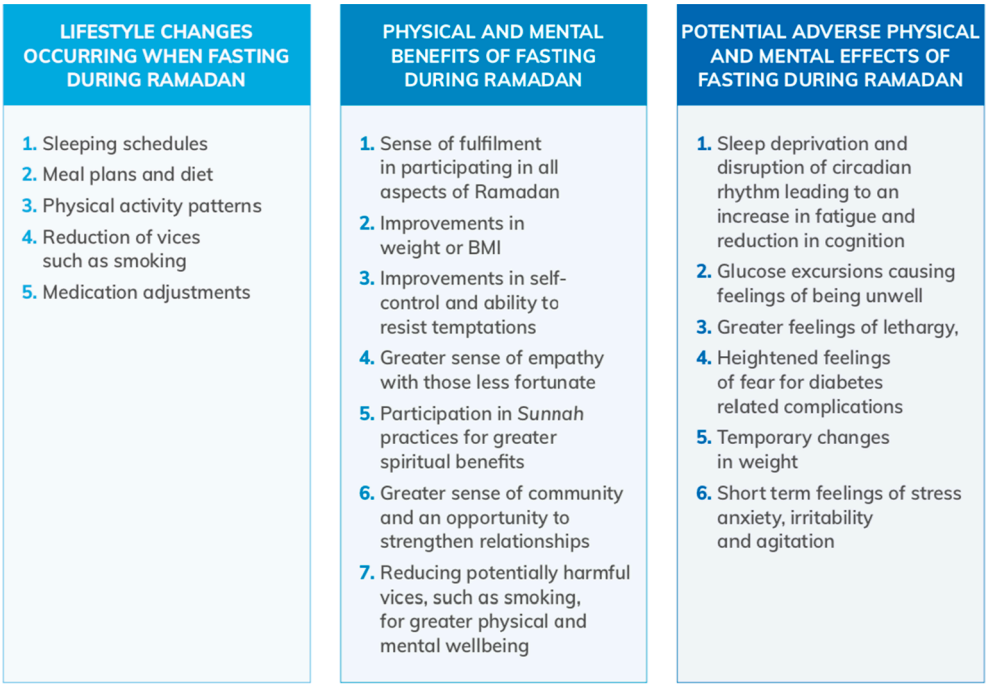

Fig. 2. Lifestyle, physical and mental changes that can occur during Ramadan.

4.1. The process of risk stratification

For a given individual with diabetes seeking to fast during Ramadan, each risk element should be assessed, and the score should be totalled. The resulting score will determine the overall risk level (Table 3). The risk levels are high risk, moderate risk and low risk. Individuals who insist on fasting, despite their risk category, must follow the relevant guidance and recommendations throughout.

The scores that equate to these risk levels and recommendations are shown in Figs. 3 and 4. It is important to highlight that risk stratification is an ongoing process and circumstances can often change. It is, therefore, necessary that individuals have an assessment annually prior to Ramadan.

Based on risk scoring, people with diabetes can be categorised as (Fig. 3):

- High risk, where fasting is probably unsafe
- Moderate risk, where the fasting safety is uncertain
- Low risk, where fasting is probably safe

These new risk stratification criteria should be used during the pre-Ramadan assessment. HCPs must ensure that people with diabetes that want to fast understand all the risks associated with doing so. It is important to note that these risk stratification criteria and the process of categorising risk levels is a new development. Though there have been case scenarios and survey studies used in its development, it is primarily based on expert opinion and experience and a **Grade D** is the highest level that can be given for this recommendation (see Tables 1 and 2). Further research is yet needed for the validation of this risk stratification tool.

An important aspect of these risk criteria is that they been approved by the Mofty of Egypt, the highest religious regulatory authority in Egypt. Further religious advice from the Mofty of Egypt is available in the full version of the *IDF-DAR Diabetes and Ramadan Practical Guidelines 2021*. Fig. 4 has summarised the religious recommendations from the Mofty of Egypt alongside the IDF-DAR risk categories. It should be noted that this opinion may not reflect the religious rulings in all countries and, therefore, further regional discussions are required when offering guidance based on these recommendations.

5. Pre-Ramadan education and guidance for nutrition during Ramadan

Structured diabetes education is about empowering individuals to make informed decisions regarding their behaviour and enabling them to effectively self-manage their condition [48]. Ramadan-focused diabetes education is an extension of this and provides additional knowledge on the necessary adjustments needed during the month of Ramadan [31,50-53].

The need for pre-Ramadan education remains high; it has been shown that only 30–67% physicians used Ramadan-focused educational programmes [49,53], and only 47.5% of individuals with diabetes attended such programmes [54]. Ramadan-focused education aims to raise awareness of the risks associated with diabetes and fasting and to provide strategies to minimise them [54,55]. Education should be simple, engaging, and delivered in a culturally sensitive manner by well-informed individuals [55,56]. The key components of any Ramadan focused educational programme are Risk Quantification; SMBG; medical management of diabetes; fluid, dietary and physical activity advice; recognition of complications; and understanding when to break the fast, (see Fig. 5). Importantly, Ramadan focused education should target HCPs, the people with diabetes that are seeking to fast and the wider public [57].

Table 3
Elements for risk calculation and suggested risk score for people with diabetes mellitus (DM) that seek to fast during Ramadan.

Risk Element	Risk Score
1. Diabetes type and duration	
Type 1 diabetes	1
Type 2 diabetes	0
2. Duration of Diabetes	
A duration of ≥ 10	1
A duration of < 10	0
3. Presence of hypoglycaemia	
Hypoglycaemia unawareness	6.5
Recent Severe hypoglycaemia	5.5
Multiple weekly Hypoglycaemia	3.5
Hypoglycaemia < 1 time per week	1
No hypoglycaemia	0
4. Level of glycaemic control	
HbA1c levels > 9% (75 mmol/mol)[1]	2
HbA1c levels 7.5–9% (58.5–75 mmol/mol)[2]	1
HbA1c levels < 7.5% (58.5 mmol/mol)[3]	0
5. Type of treatment	
Multiple daily mixed insulin Injections	*3*
Basal Bolus/Insulin pump	2.5
Once daily Mixed insulin	2
Basal Insulin	1.5
Glibenclamide	1
Gliclazide/MR or Glimepride or Repeglanide	0.5
Other therapy not including SU or Insulin	0
6. Self-Monitoring of Blood Glucose (SMBG)	
Indicated but not conducted	2
Indicated but conducted sub-optimally	1
Conducted as indicated	0
7. Acute complications	
DKA/ HHS in the last 3 months	3
DKA/ HHS in the last 6 months	2
DKA/ HHS in the last 12 months	1
No DKA or HHS	0
Risk Element	**Risk Score**
8 MVD Complications/Comorbidities	
Unstable MVD	6.5
Stable MVD	2
No MVD	0
9. Renal Complications/Comorbidities	
eGFR < 30 mL/min	6.5
eGFR 30–45 mL/min	4
eGFR 45–60 mL/min	2
eGFR >60 mL/min	0
10. Pregnancy[4]	
Pregnant not within targets	6.5
Pregnant within targets	3.5
Not pregnant	0
11. Frailty and Cognitive function	
Impaired cognitive function or Frail	6.5
> 70 years old with no home support	3.5
No frailty or loss in cognitive function	0
12. Physical Labour	
Highly Intense physical labour	4
Moderate Intense Physical Labour	2
No physical labour	0
13. Previous Ramadan Experience	
Overall negative experience	1
No negative or positive experience	0
14. Fasting hours (location)	
≥ 16 h	1
< 16 h	0

DKA—Diabetic Ketoacidosis.
HHS— Hyperosmolar Hyperglycaemic Syndrome/.
Hyperglycaemic Hyperosmolar Nonketotic Coma (HONC).
MVD—Macrovascular disease (Cardiac-cerebral or peripheral).
eGFR—Estimated glomerular filtration rate.
[1]This measure is equivalent to 11.7 mmol/L average blood glucose.
[2]This measure is equivalent to 9.4–11.7 mmol/L average blood glucose.
[3] This measure is equivalent to 9.4 mmol/L average blood glucose.
[4]Pregnant and breastfeeding women have the right to not fast.
regardless of whether they have diabetes or not.

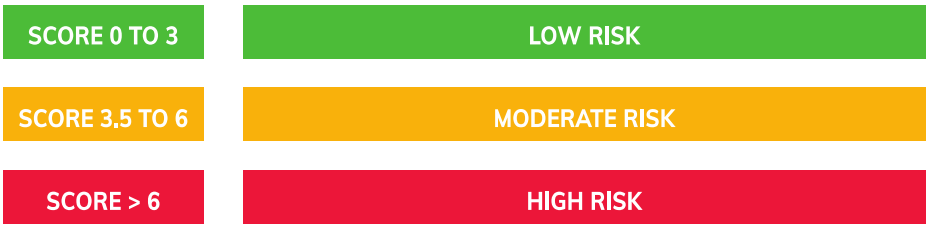

Fig. 3. Risk score and associated categories.

Risk score/level	Medical Recommendations	Religious Recommendations
Low Risk 0-3 points	Fasting is probably safe 1. Medical Evaluation 2. Medication adjustment 3. Strict monitoring	1. Fasting is obligatory 2. Advice not to fast is not allowed, unless patient is unable to fast due to the physical burden of fasting or needing to take medication or food or drink during the fasting hours
Moderate Risk 3.5-6 points	Fasting safety is uncertain 1. Medical Evaluation 2. Medication adjustment 3. Strict monitoring	1. Fasting is preferred but patients may choose not to fast if they are concerned about their health after consulting the doctor and taking into account the full medical circumstances and patient's own previous experiences 2. If the patient does fast, they must follow medical recommendations including regular blood glucose monitoring
High Risk >6 points	Fasting is probably unsafe	Advise against fasting

Fig. 4. Medical and religious risk score recommendations from the Mofty of Egypt.

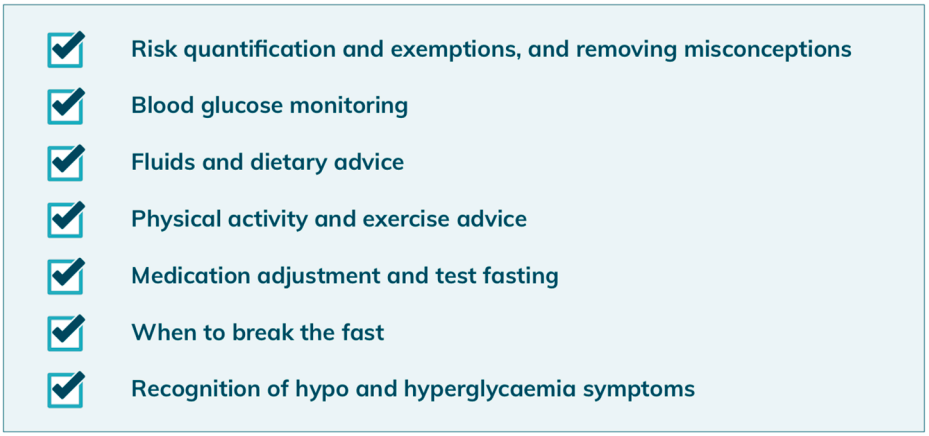

Fig. 5. Key Components of a Ramadan-focused Educational Programme.

5.1. *Evidence supporting the use of Ramadan focused education*

Various studies from the last decade have demonstrated the benefits of Ramadan focused education on outcomes during Ramadan, for people with diabetes. Recently, El Toony *et al.* compared individuals attending structured 30-minute education sessions 6–8 weeks prior to Ramadan to controls. It was found that education sessions were associated with a decrease in the incidence of hypoglycaemia and HbA1c levels when compared to controls. Interestingly, education sessions prior to Ramadan were also associated with improvements in HDL and LDL profiles [58]. These benefits can also be effective in helping higher risk individuals as shown by Hassanein *et al.* who investigated people with diabetes that included individuals with chronic kidney disease (CKD), ischaemic heart disease and pregnant women with gestational diabetes. Education sessions were 90 min in duration and took place 4–6 weeks prior to Ramadan. Overall, there were marked improvements in glycaemic control after Ramadan [59]. These results were also confirmed by a recent *meta*-analysis [60].

The key components to any Ramadan focused education programme are listed in Fig. 5. These should act as a guide in the development of programmes and allow for appropriate individualisation for people with diabetes that have other more important or applicable areas of concern.

5.2. *Self-Monitoring of blood glucose (SMBG)*

An extremely important aspect of fasting during Ramadan for people

with diabetes is SMBG. There needs to be a greater rate of SMBG in order to keep on top of any changes to glycaemia so that hyperglycaemia or hypoglycaemia can be prevented. People with diabetes need to be given education on when and how to monitor their blood glucose levels.

It is important to emphasise that pricking the skin to test blood glucose levels DOES NOT break the fast.

A useful guide that can be used to monitor blood glucose during RF is shown in Fig. 6. This example of a 7 point SMBG guide can be adapted for individuals with better controlled diabetes or those using continuous measurement methods (CGM/FGM). However, it is essential that some similar form of strategy for SMBG is followed as it is vital in managing the risk of complications of diabetes such as glucose excursions and also in medical management.

Pre-Ramadan focused education plays a vital role in assuring safety during Ramadan for people with diabetes. It is essential that HCPs are trained adequately, and educational programmes are given to individuals well in advance of Ramadan; Level 3 evidence, **Grade C** (See Tables 1 and 2).

5.3. Dietary changes and guidance during RF

Ramadan marks a dramatic change to one's usual eating patterns. Dietary recommendations to people with diabetes need to be individualised, accounting for an individual's personal preferences, lifestyle, age, ability to manage their diabetes and other medical needs. Importantly dietary recommendations need to be culturally adapted to maximise access.

It is important that adequate nutrition is received during Ramadan so that individuals that are fasting stay properly nourished. There should be a pre-Ramadan assessment where individuals with diabetes can seek individualised nutrition advice. This can help address any targets or goals such as weight maintenance or weight loss.

To this end, the DAR International Alliance has developed the Ramadan Nutrition Plan (RNP), a web and digital-based tool designed to help HCPs in delivering patient-specific medical nutrition therapy (MNT) during Ramadan fasting (www.daralliance.org or DAR SaFa application). This tool should be used by HCPs when providing nutrition related guidance.

The recommended use of the RNP has been given a **Grade D** by the IDF-DAR writing group (based on the criteria set out in Tables 1 and 2). The development of the RNP is largely based on expert opinion and further research assessing the efficacy of the RNP in studies of higher levels is still needed (see Table 1). However, the RNP is an extremely useful tool that can provide the basis for any nutrition advice for people with diabetes seeking to participate in RF across the world. There are several culturally adapted menus that have been reviewed for suitability and are accessible to HCPs and individuals with diabetes (See supplementary figures A-B). Moreover, the RNP includes an algorithm and a toolkit to provide meal plans specific for one's caloric targets. Further details are provided in the full version of the *IDF-DAR Diabetes and Ramadan Practical Guidelines 2021*.

6. Management of individuals with diabetes when fasting during Ramadan

Guidance on the management of diabetes must be provided prior to Ramadan. A pre-Ramadan assessment needs to take place, ideally, 6–8 weeks before the start of Ramadan. Here, HCPs will be able to obtain a detailed medical history and perform a risk assessment. This risk assessment will form the basis of all recommendations thereafter, these include advice on whether fasting is safe, strategies for dose modifications and treatment regimen adjustments, the provision of Ramadan focused education and nutrition advice. Following this, individuals that decide to fast will need to adhere to guidance on the management of their diabetes during RF including changes to glycaemia monitoring schedules and dosing adjustments of medication. Finally, after Ramadan ends it is advised that a post-Ramadan follow up is performed. A follow up after Ramadan will help HCPs obtain crucial information about the individual's successes and challenges during Ramadan and will ensure that RF the following year can be more successful. This process must be undertaken each Ramadan as safely fasting one year does not guarantee the same the next year. (See Fig. 7.)

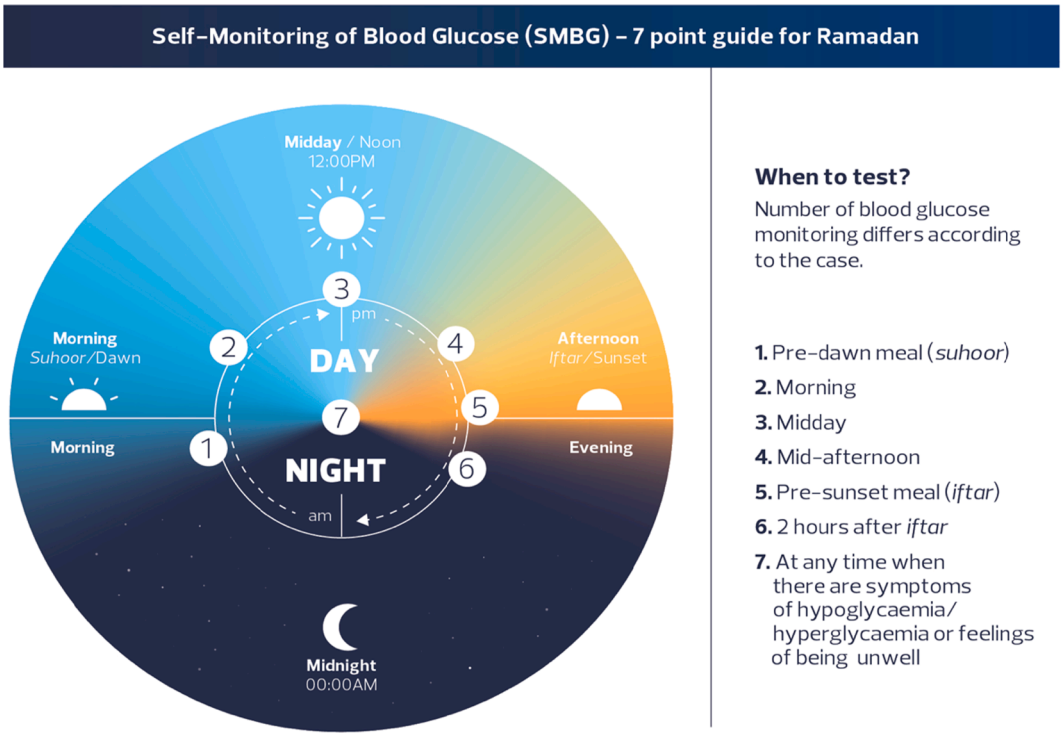

Fig. 6. Self-monitoring of blood glucose (SMBG) guide for people with diabetes fasting during Ramadan.

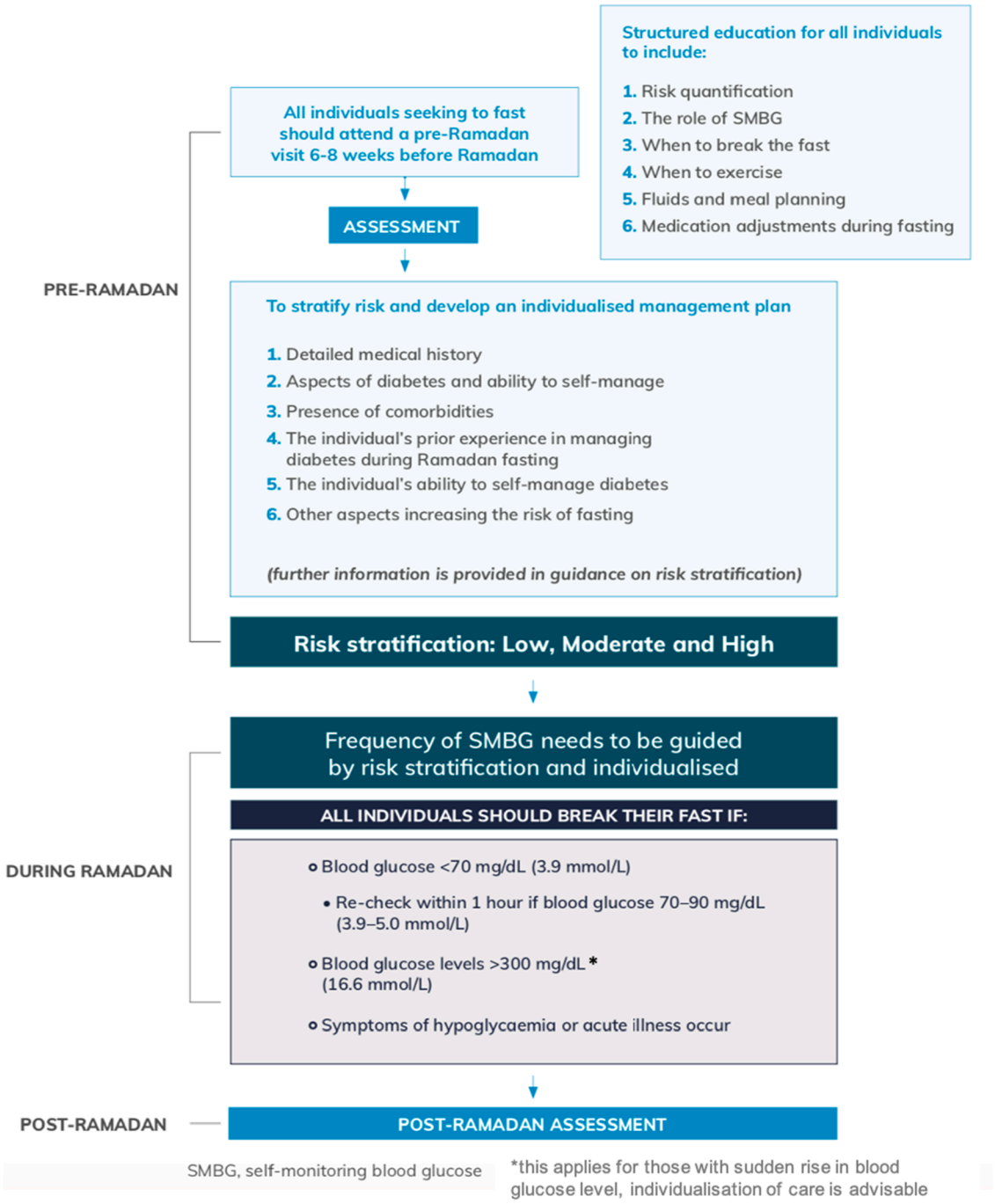

Fig. 7. Assessment overview for people with diabetes fasting during Ramadan.

6.1. *Type 1 diabetes mellitus*

Fasting becomes obligatory for children or adolescents from the age of puberty, however, much like in adults those with medical conditions that can be compromised by fasting are exempt from this obligation. Generally, all people with T1DM have been discouraged from fasting [47,61] but despite this many, even the younger individuals, insist on fasting against HCP advice [31,62].

6.1.1. *Safety of fasting among adolescents and adults with T1DM*

Over the past decade, several studies have shown that with the right support and management, many adolescents with T1DM can fast for at least 15 days with some studies showing that 60% of study participants fasting for the whole month of Ramadan [45,63]. Studies of CGM data taken from adolescents during Ramadan did not show any differences in interstitial glucose (IG), or in glucose fluctuation to periods before or after Ramadan [64]. However, others have found the opposite, with wide IG fluctuations and even periods of unrecognised hypoglycaemia [63]. A recent cross-sectional global survey showed that 1 in 10 adolescents did not change their behaviour after discovering hypoglycaemia [47].

In general, the body of research that has been conducted on adults with T1DM fasting during Ramadan is relatively small but in recent times some new studies have showed that people with T1DM on multiple insulin regimens could safely fast, with no differences in the frequency of hypoglycaemia during Ramadan when compared to before Ramadan [65]. However, there have been studies finding worse outcomes in adults with T1DM. In a multi-centre study, Malek *et al.* found that people

previously categorised as high or very high risk were likely to experience hypoglycaemia and break their fast. It was also found that SMBG levels were reduced during Ramadan among this cohort [66]. Though there is limited research in older age groups, the risks and concerns are broadly similar between adults and adolescents. Studies that solely investigated adolescents can still be informative for adults with T1DM. The findings from research studies that have been discussed thus far apply to individuals with access to advanced medical care, good education programmes and appropriate support. We believe that people with T1DM who have these privileges and wish to fast during the month of Ramadan can be allowed to do so, after proper risk scoring, a pre-Ramadan assessment and individualisation of care as mentioned above.

The IDF-DAR guidelines experts feel that the allowance to fast cannot be generalised across to all individuals with T1DM, especially those are considered as high risk. We acknowledge that data on the safety of fasting is incomplete and may be prone to selection-bias in that individuals that are not willing to fast or those that show poor glycaemic control are not represented in these studies. It is therefore not possible to quantify or be assured of the exact risk related to fasting, and an individualised risk assessment remains the most appropriate method.

Though there are several longitudinal studies demonstrating safety for fasting during Ramadan with T1DM but there needs to be larger, randomised studies confirming these findings to achieve higher evidence grades for these recommendations. For adults with T1DM there are no real specific studies assessing this age group and, greater evidence is needed. This recommendation has been given a level 3 for evidence and **Grade C** (Table 1 and 2).

6.1.2. *Insulin regimens in people with T1DM*

Most studies that have looked into the efficacy and safety of insulin regimens in adolescents and adults have been of an observational design and with relatively small sample sizes, making evidence-based guidance on regimens more difficult. It is, therefore, recommended that an individualised approach is taken and decided upon in the initial pre-Ramadan assessment.

6.1.3. *Insulin regimens and blood glucose monitoring among adolescents with T1DM*

The most widely used insulin regimens in adolescents are basal-bolus regimens; continuous subcutaneous insulin infusion (CSII) with or without sensors; conventional, twice daily NPH/Regular short acting (human) insulin; and premixed insulins.

For adolescents using non CSII therapies for T1DM management the following is recommended:

- Basal-bolus regimen is preferred over conventional twice daily regimens in adolescents with T1DM, recommended changes are shown in Fig. 8
- Premixed insulin regimens do not provide the necessary flexibility for fasting due to the rigidity in nutrition that is often required with these therapies.
- SMBG must be performed regularly throughout the fasting hours and whenever there are feelings of being unwell. If accessible and available, CGM or FGM are the preferred methods for monitoring blood glucose levels.

Where circumstances provide, CSII/insulin pump therapies should be used with adolescents with T1DM. Numerous studies have shown promising results with insulin pimp usage when compared to other insulin therapies [45,67,68]. The advent of the Low Glucose Suspend (LGS) function, has allowed insulin to be automatically suspended for up to 2 h when sensors detect a fall in glucose levels below a pre-set

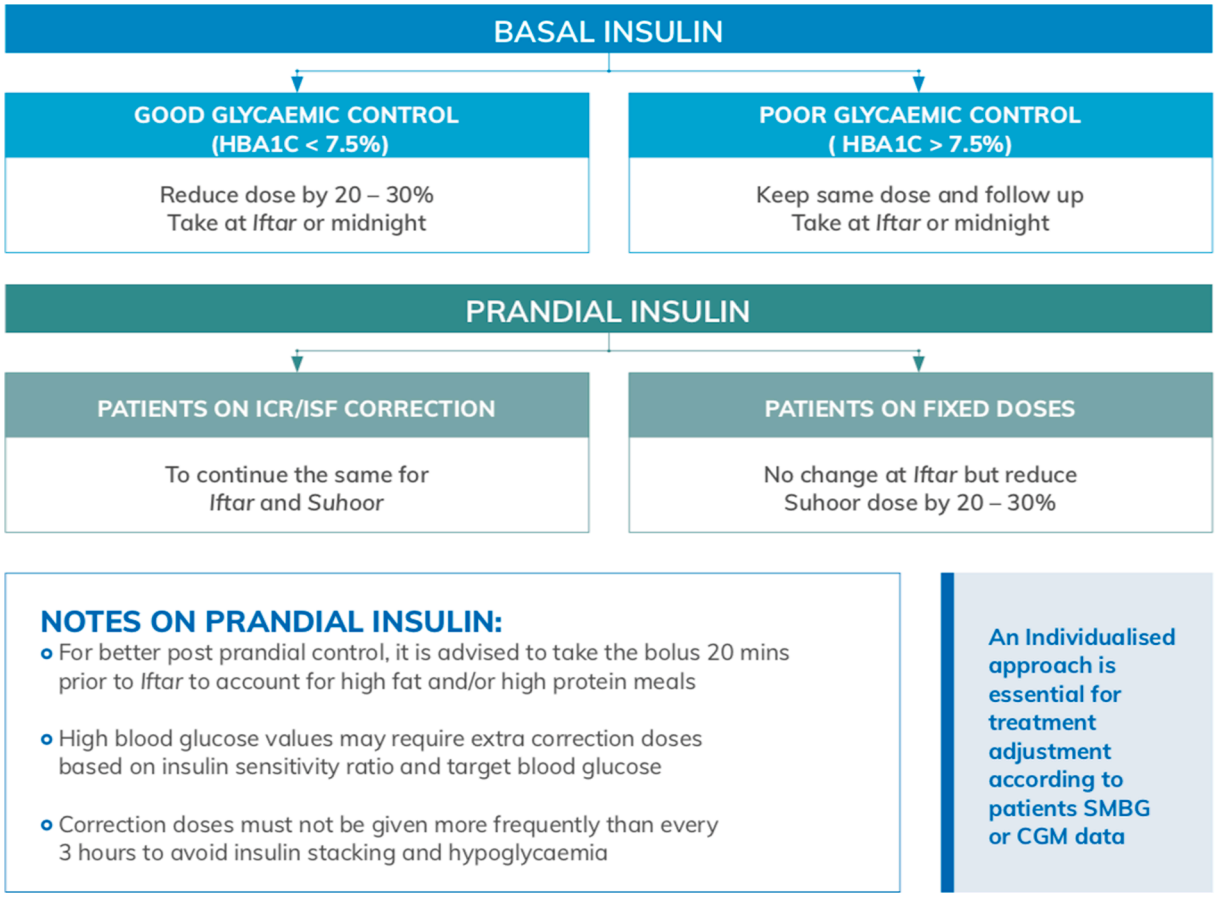

Fig. 8. Recommended use of MDI therapy in adolescents with T1DM undergoing RF.

threshold [69]. Elbarbary was able to show the effectiveness of LGS among adolescents that fasted during Ramadan [70]. Moreover, the use of Predictive Low Glucose Suspend (PLGS) pumps have also demonstrated favourable outcomes [71,72]. These therapies have been shown to reduce the risk of glucose excursions and, importantly, the risk of hypoglycaemia when fasting. Further research is yet needed to fully assess the effectiveness of these therapies during RF and to provide more specific recommendations, currently the recommended use is shown in Fig. 9.

It is important that access to such therapies is increased and education programmes include guidance on the use of these newer more complicated technologies to ensure maximum safety during RF.

6.1.4. *Insulin regimens and blood glucose monitoring among adults with T1DM*

There have been relatively few studies conducted on the use of insulin therapy among adults with T1DM that fast during Ramadan. Some studies have included adults in their total sample, but direct research into these individuals is scarce. Caution should be taken when fasting and the recommended changes to insulin regimens are shown below in Table 4.

6.2. *Type 2 diabetes mellitus*

RF among people with T2DM can present many challenges. The key concerns relate to uncontrolled blood glucose levels that can lead to hyperglycaemia and/or hypoglycaemia. Appropriate and effective blood glucose monitoring and medical management of T2DM is crucial to ensure safety during Ramadan. The overall guidance for people with T2DM that want to fast during Ramadan can be summarised into a number of steps including a pre-Ramadan assessment, medication adjustments during Ramadan and a post-Ramadan follow-up (see Fig. 7).

6.2.1. *Medication adjustments*

The type of medication the individual is taking for the management of their diabetes influences the potential risks that fasting during Ramadan may lead to and, therefore, requires careful attention when formulating the treatment plan. The primary concern relating to these medications are their risk towards hypoglycaemia. Particular care must be taken when individuals are on multiple antidiabetic therapies and HCP advice need to account for this when making dose modifications during the pre-Ramadan assessment.

Antidiabetic drugs such as metformin, acarbose, Thiazolidinediones (TZDs), Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and Dipeptidyl peptidase-4 (DPP-4) inhibitors work in a glucose dependent manner and generally have a low risk of hypoglycaemia. These drugs generally don't require any dose modifications during Ramadan. Studies have also shown Short-acting insulin secretagogues to be safe for use during Ramadan [32]. It is recommended that the normal three meal dosing is redistributed to accommodate the eating patterns of *iftar* and *Suhoor* during Ramadan.

HCPs should also be aware that drugs such as modern Sulphonylureas (SUs) carry a slightly higher risk of hypoglycaemia and account for this in the pre-Ramadan assessment. Studies have demonstrated the efficacy of modern SUs (glimepiride, gliclazide and gliclazide modified release) and the use of these are preferred [73-76].

Data regarding the safe use of Sodium-glucose co-transporter-2 (SGLT2) inhibitors were not well established in the previous guidelines and indeed, there have been some safety concerns relating to dehydration and this can be particularly important among higher risk individuals [46]. However, recent data during RF are now available and the results of these studies prompted [76-79] the following recommendations:

- For stabilisation, SGLT2Is should be initiated at least two weeks to one month prior to Ramadan. SGLT2Is are recommended to be administered at the time of evening meal (*Iftar*). However, if the indication for SGLT2I initiation is cardiovascular or renal protection, then the pre-Ramadan initiation should be conducted with a lower dose.
- Increasing fluid intake during the non-fasting hours of Ramadan is recommended.
- SGLT2I do not require treatment modifications during Ramadan, however if an individual is on multiple medications a review of the doses should be made to avoid the risk of hypoglycaemia.

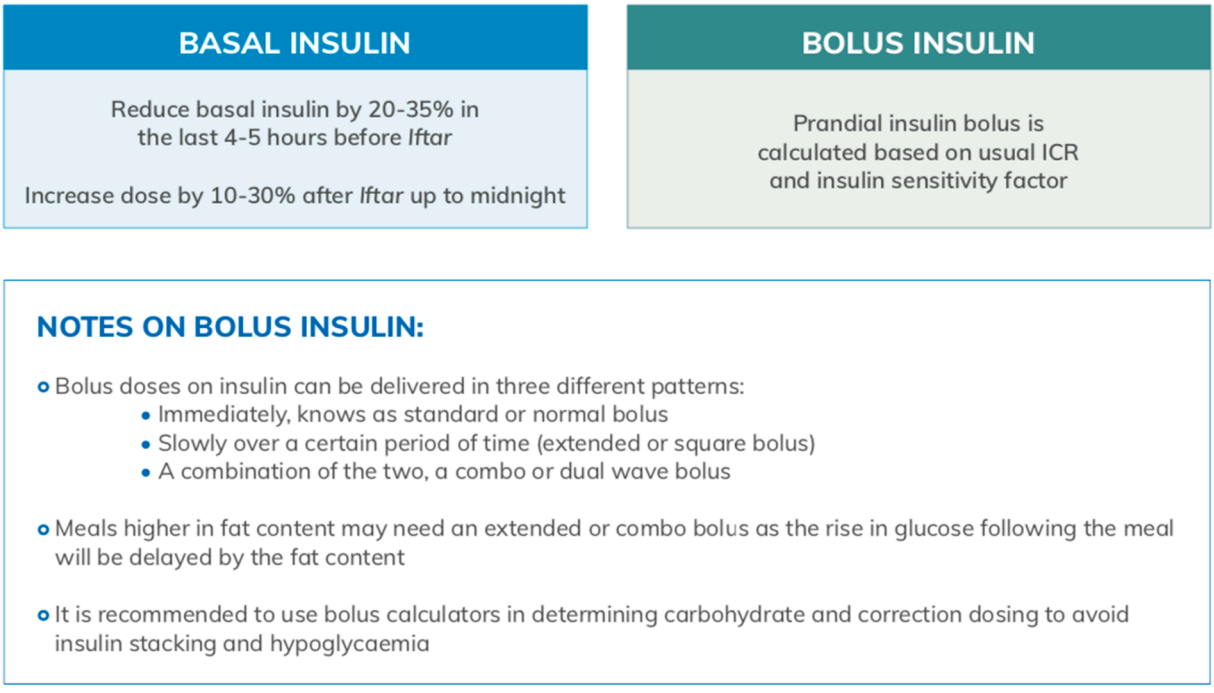

Fig. 9. Recommendations for insulin pump therapy usage among adolescents with T1DM that are fasting during Ramadan.

Table 4
Recommendations for Insulin Dose Adjustments based on type of regimen.

Type of Insulin Regimen	Adjustment for fasting during Ramadan	Methods of monitoring during Ramadan
CSII / Insulin Pump	Basal rate adjustment - 20–40% decrease for the last 3–4 h of fast - 10–30% increase for the first few hours after *Iftar* Bolus doses - Same principles as prior to Ramadan	CGM
MDI (basal bolus) with analogue insulin	Basal insulin - 30–40% reduction in dose and to be taken at *Iftar* Rapid Analogue Insulin - Dose at *Suhoor* to be reduced by 30–50% - Pre-lunch dose to be skipped - The dose around *Iftar* to be adjusted based on the 2-hour post-*Iftar* glucose reading	7-point glucose monitoring
MDI (Basal bolus) with conventional insulin	NPH insulin - The usual pre-Ramadan morning dose to be taken in the evening during Ramadan - 50% of the pre-Ramadan dose to be taken at *Suhoor* Regular insulin - Dose at evening meal remains unchanged - *Suhoor* dose to be 50% of the pre-Ramadan evening dose - Afternoon dose to be skipped	7-point blood glucose monitoring or 2–3 staggered readings throughout the day
Premixed (analogue or conventional)	- Shift the usual pre-Ramadan morning dose to *Iftar* - 50% of the pre-Ramadan evening dose at *Suhoor*	At least 2–3 daily readings and whenever any hypoglycaemic symptoms develop

- SGLT2I use when fasting during Ramadan should be in accordance with the usual safety and prescribing measures as recommended by each drug SMP.

Full guidance on individual antidiabetic drugs for people with T2DM that fast during Ramadan is available in the full version of the *IDF-DAR Diabetes and Ramadan Practical Guidelines 2021*. The recommended use of antidiabetic drugs during Ramadan have been summarised in Table 5.

6.2.2. *Insulin treatment for T2DM*

Many individuals with T2DM are on insulin therapy to control their diabetes and a variety of insulin regimens can be used [79]. Insulin use during fasting carries a risk of hypoglycaemia, especially when more complex insulin regimens are used and so extra care and caution must be taken when developing Ramadan medication regimens.

It needs to be emphasised that the administration of insulin via the subcutaneous, intramuscular or intravenous routes do not cause a breaking of the Ramadan fast.

All recommended dose adjustments for people with T2DM should be guided by SMBG. These aspects of management need to be integrated into pre-Ramadan focused education programmes so that individuals can self-titrate their doses. The usage of long long/intermediate or short-acting insulins and premixed insulins have been demonstrated in Figs. 10 and 11. These recommendations have largely been based on expert opinion and have, therefore, been given a **Grade D**, consensus by the IDF-DAR writing group (see Tables 1 and 2).

Table 5
Recommended dose and regimen modifications for non-insulin based antidiabetic medications during Ramadan fasting.

Antidiabetic Medications	Regimen/Dose modifications	Level of evidence supporting recommendation and grading from IDF-DAR writing group (Table 1 and 2)
Metformin	Once daily No dose modifications Take at *Iftar* Twice daily No dose modifications Take at *Iftar* or Suhoor Three times daily Morning dose taken before *Suhoor* Combine afternoon dose with *Iftar* dose Prolonged release No dose modifications Take at *Iftar*	Level 4 and Grade D
Acarbose	No dose modifications	Level 4 and Grade D
TZDs	No dose modifications but doses can be taken with *Iftar* or *Suhoor*	Pioglitazone - Level 2 Grade B Other TZDs Grade D
Short acting insulin secretagogues	Three meal dosing can be redistributed to two doses according to meal sizes	Repaglinide - Level 2 Grade B Gliclazide, Gliclazide MR. and Glimepiride – level 3 Grade C
GLP-1 RAs	No dose modifications after appropriate dose titrations have been achieved	Exenatide, Liraglutide, Lixisenatide Level 2 Grade B Other GLP-1 RAs Grade D
DPP-4 inhibitors	No dose modifications	Vildagliptin, Sitagliptin - Level 1A/B Grade A Other DPP-4 inhibitors Grade D
SUs	Use newer drugs e.g. Glicazide, Glicazide MR, Glimepiride Once daily: Reduce dose in well controlled individuals Take at *Iftar* Twice daily Reductions of *Suhoor dose* in well controlled individuals	Level 3 and Grade C
SGLT2 inhibitors	No dose modifications Extra fluids to maintain hydration	Dapagliflozin, Canagliflozin - level 3 Grade C Other SGLT2 inhibitors Grade D

6.2.3. *Multiple antidiabetic therapies*

Due to the increasing availability of newer glucose lowering therapies, it is common for individuals with T2DM to be prescribed multiple drug regimens to manage their diabetes. Importantly, the risk of hypoglycaemia can be amplified in these circumstances and care must be taken.

Generally, people on multiple antidiabetic therapies are more likely to be of an older age and with multiple comorbidities to their diabetes and this further heightens the risk of complications during RF [81] . This can be particularly concerning among more active people [82]. Indeed, those participating in *Taraweeh* prayers (additional ritual prayers performed at night) need to be cautious and increase the frequency of blood glucose monitoring.

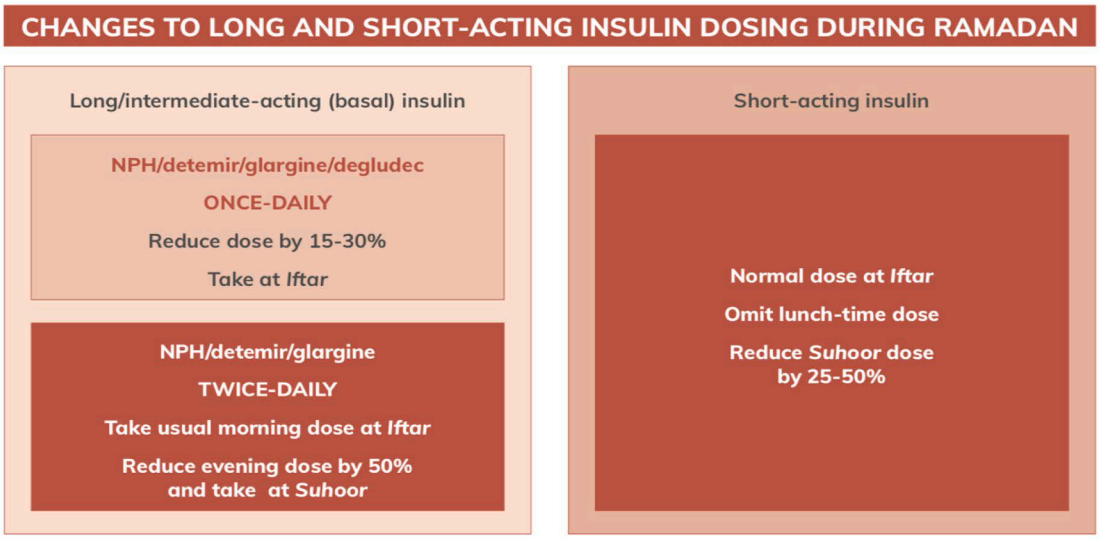

Fig. 10. Dose adjustments for long or short-acting insulins and pre-mixed insulins. *Reduce the insulin dose taken before *Suhoor*; **Reduce the insulin dose taken before iftar. Information adapted from Hassanein *et al.* (2014) [80].

Fasting/pre-Iftar/pre-Suhoor blood glucose	pre-Iftar	pre-Iftar*/post-Suhoor**
	Basal insulin/Pre-mixed	Short-acting insulin
<70 mg/dL (3.9 mmol/L) or symptoms	Reduce by 4 units	Reduce by 4 units
<90 mg/dL (5.0 mmol/L)	Reduce by 2 units	Reduce by 2 units
90-126 mg/dL (5.0-7.0 mmol/L)	No change required	No change required
>126 mg/dL (7.0 mmol/L)	Increase by 2 units	Increase by 2 units
>200 mg/dL (16.7 mmol/L)	Increase by 4 units	Increase by 4 units

Fig. 11. Dose titrations for long and short acting insulins and pre-mixed insulins based on blood glucose levels. For those on a high dose of insulin, an adjustment of 10–20% is recommended.

- Individuals with T2DM on 3 or more antidiabetic agents who fast during Ramadan, should receive counselling and comprehensive advice on diet, lifestyle and drug dose modifications prior to Ramadan.
- Individuals on 3 or more drug combinations, especially those on both insulin and SU should be considered at an increased risk of hypoglycaemia. An approximate 25–50% reduction in the dose of insulin is advised, depending on the subsequent risk score after risk stratification. A reduction in the dose of SUs is also advocated in these individuals.

These recommendations have been based on level 3 information and

given a **Grade C** by the IDF-DAR writing group. This approach should help to mitigate the risk of hypoglycaemia and is a better approach than not making any dose adjustments at all.

6.3. Special populations

6.3.1. Pregnant women

All pregnant women have the right not to fast regardless of whether they have diabetes or not. Nevertheless, many pregnant women still participate in fasting against medical and religious advice [83,84]. In some communities, the social pressure to fast during the Holy month of Ramadan is so strong that medical advice against doing so might be ignored. For those that do fast, expert support and guidance is needed in order to improve safety for both the mother and foetus.

Studies among healthy pregnant women, without diabetes, indicate that fasting during Ramadan might be safe [85-88] but others have found increased risks to both the mother and the baby [88,89]. The long-term effects of fasting to the new-born have not been assessed and further research it still needed. In any case, the potential risks of fasting among pregnant women with gestational diabetes mellitus (GDM) [90-93], pre-existing T1DM or T2DM is high. Currently, there is lack of research in the area of RF in pregnant women with pre-existing diabetes (T1DM or T2DM). As such, it is recommended that pregnant women with diabetes not to fast until further research is available to support fasting, (see Section 4 for Risk stratification) [92].

As with all individuals with diabetes, there should be a pre-Ramadan assessment alongside individualised Ramadan focused education. There needs to be an increase in the rate of SMBG throughout the day — including before *Iftar*, after meals, during fasting and anytime there are feelings of being unwell (see Fig. 6).

Pregnant women that are fasting during Ramadan will need to follow the RNP, as with all other individuals with diabetes, but also make further changes. Each individual's specific circumstances must be discussed at the pre-Ramadan assessment, but it is recommended that caffeine, sugar and salt should be limited, and the eating of fibrous foods should be encouraged. There needs to be a greater effort made to stay hydrated and pregnant women should aim to drink 2–3 L of water a day.

Many pregnant women will be treated with insulin to manage their condition, but currently research on the best dosing regimens is scarce. The IDF-DAR guidelines have recommended insulin dose and blood glucose monitoring regimen modifications to be aligned with that mentioned above for those with type 1 or type 2 diabetes.

These recommendations have primarily been based on expert opinion and, as such, have been given a ***Grade D*** (see Tables 1 and 2). Further research studies are needed on pregnant women that fast during Ramadan in order to understand the potential risks and assess different dosing regimens.

6.3.2. Elderly individuals with diabetes

Previously, elderly individuals with diabetes have been placed among the higher risk categories and advised against fasting. Indeed, the DAR global survey showed that a greater proportion of those aged < 65 (87%) intended to fast than ≥ 65 (71%) [93]. It is important to recognise that age in and of itself is not a good reason to categorise individuals as high risk for fasting during Ramadan, but rather it is the associated implications of old age that need consideration. Many elderly individuals have enjoyed fasting during Ramadan for many years and should be allowed to continue if their health is stable [46]. The new risk stratification presented in these guidelines have accounted for these issues and provide a better assessment of the health of elderly individuals with respect to the safety of fasting (see Section 4).

Elderly individuals are at a higher risk of having comorbidities. These comorbidities can include dementia, recurrent falls, hip fractures, amputation and visual impairment [94] — these all have important implications on the safety of fasting during Ramadan. Likewise, many elderly individuals generally have a longer duration of diabetes and will also be more likely to suffer from diabetes related complications such as hypertension, hyperlipidaemia, retinopathy and neuropathy, among others. Fig. 12 compares the proportions of diabetes related complications among elderly and younger individuals with T2DM and highlights the increased risk among elderly individuals [93].

The DAR Global survey found those aged ≥ 65 were more likely not to fast than those aged < 65 years; 28.8% compared to 12.7% respectively ($p < 0.001$) [93].

It is vital that pre-existing comorbidities and any history of diabetes related complications are identified by HCPs during the pre-Ramadan assessment and risk stratification process. Understanding each individual's circumstances will help provide the best, most appropriate guidance. Importantly, HCPs must also consider an elderly individual's degree of independence as this is crucial in understanding what kind of support may be needed during Ramadan such as with feeding, taking medications and checking blood glucose levels.

The primary concern among elderly individuals is the risk of developing hypoglycaemia during Ramadan. It has been found that the risk of hypoglycaemia [93,95] is increased among the elderly and may often present with neuroglycopenic manifestations in the form of dizziness, delirium and confusion. These can all lead to periods of unawareness in hypoglycaemia which can be extremely dangerous. Hyperglycaemia is also an important issue and has been seen to be higher among the elderly than in younger individuals with T2DM [93]. It is recommended that individuals with hypoglycaemia unawareness or a history of unawareness do not fast.

A key component to avoiding hypoglycaemia is SMBG and it must be conducted frequently. The seven-point guide for SMBG should be used as a guide and can be adapted, see Fig. 7. Moreover, medication doses should also be adjusted appropriately. As there are a limited number of studies investigating elderly individuals with diabetes that fast during Ramadan and the fact that elderly individuals often present with other health problems, the development of specific dosing recommendations are very difficult to make. Any dose adjustments that are made need to be set prior to Ramadan, ideally during the pre-Ramadan assessment. Ramadan focused education also needs to be adapted and individualised to account for these issues.

The IDF-DAR guidelines have provided specific guidance that HCPs and elderly individuals should aim to follow when providing advice for fasting during Ramadan. Specific guidance for the elderly with diabetes include the following:

Medications and regimens

- Have an assessment and discussion prior to Ramadan.
  - o Choose medications that have a lower risk towards hypoglycaemia.
  - o Make dose adjustments to lower the risk of hypoglycaemia.

SMBG

- Increase the frequency of SMBG when fasting during Ramadan than before Ramadan.
- Consider using a continuous means of monitoring blood glucose levels if available.

Diet

- There needs to be an emphasis on staying properly hydrated, particularly in individuals prone to diabetes related comorbidities.
- It is important to have an adequate intake of nutrients when breaking the fast.
- An individualised nutrition plan should be made prior to Ramadan and adhered to during the Ramadan fast.

Physical Activity

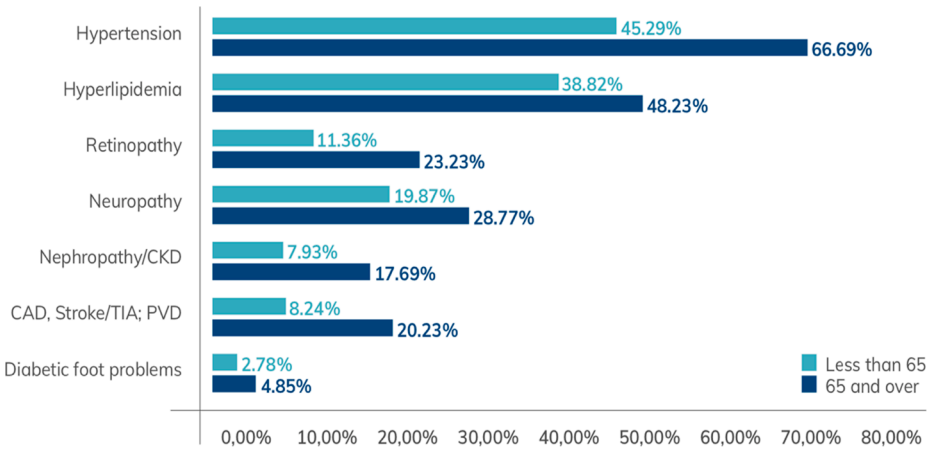

Fig. 12. Reported complications among individuals with T2DM aged ≥ 65 and < 65; data adapted from the DAR 2020 Global Survey [93].

- Physical activity levels should be curtailed but not halted during fasting hours.
- Activities should be planned ahead of time and thought of holistically — i.e., in conjunction with nutrition plans and medication regimens.

Social considerations and community support

- Adequate support mechanisms should be in place to ensure that elderly individuals with diabetes wishing to fast receive support from family members, friends, carers or community members. This should provide greater levels of safety and confidence.

Risks of complications and awareness

- There needs to be an active effort to increase the awareness of symptoms of hypoglycaemia and hyperglycaemia
  - o Symptoms and events should be documented to help with recognition.
- The effects of fasting in people with comorbidities such as dementia, impaired renal function, CVD and others should be seriously considered and discussed prior to conducting Ramadan fasting.

The guidance provided for elderly individuals with diabetes have primarily been based on expert opinion and experience. Future studies assessing diabetes during Ramadan must consider this higher risk group and understand what specific dosing strategies are required to ensure safety. A **Grade D** has been assigned to this by the IDF-DAR writing group.

Further guidance on the management of the elderly is available in the full version of the *IDF-DAR Diabetes and Ramadan Practical Guidelines 2021*.

7. Complications of diabetes when fasting during Ramadan

People with diabetes that have unstable macro- or microvascular complications, and choose to fast during Ramadan, could exacerbate these complications, and therefore these individuals are classified as high risk [96] (see Section 4).

7.1. Macrovascular disease (MVD)

Diabetes is frequently associated with an increased risk of cardiovascular disease [97,98] and a heightened risk of stroke [99]. Studies have shown that the practice of unsafe fasting including a high intake of carbohydrates, low levels of activity, poor sleeping patterns, inadequate hydration, and missing doses of essential medicines could have an impact on the risk of CVD or stroke in people with diabetes [100,101].

7.1.1. Fasting during Ramadan and congestive heart failure (CHF)

Congestive heart failure (CHF) has been investigated by several studies during Ramadan. A multi-centre study conducted in the Gulf region found no difference in the proportion of patients that were hospitalised for heart failure with diabetes during Ramadan and outside of Ramadan, 52% and 48.4% respectively [102]. A retrospective review of clinical data also found that there were no differences in the number of hospitalisations when comparing the month prior to Ramadan, the period of Ramadan and the month after Ramadan [101].

7.1.2. Fasting during Ramadan and acute coronary syndrome (ACS)

Evidence suggests that there is no clear association between fasting during Ramadan and an increase in acute cardiac events [103,104]. Some have also identified improvements in the number of ACS events. Temizhan *et al.* found a significant reduction in the number of ACS events during Ramadan when compared to times outside of Ramadan [105]. Likewise, Burazeri *et al.* found protective associations between a composite measure of religiosity and ACS in a cross-sectional study [106]. However, these studies need to be replicated through randomised longitudinal studies and among individuals with diabetes.

7.1.3. Fasting during Ramadan and stroke

Diabetes is an independent risk factor for stroke and the effect of fasting during Ramadan in people with diabetes needs to be established. There have been several studies that have investigated this, and the evidence is conflicting.

Assy *et al.* in a cross-sectional designed study found that people with type 2 diabetes mellitus (T2DM) were no more likely to be hospitalised for ischaemic or haemorrhagic stroke during Ramadan than in the months before or after Ramadan [107]. Moreover, El-Mitwalli *et al.* confirmed these results in a longitudinal study in Egypt [108]. Conversely, others found the opposite, with Ramadan fasting being associated with a significantly higher risk of stroke. Yazdeen *et al.* found, in a cohort that were primarily middle aged, that there was evidence showing that fasting was associated with a higher risk towards stroke ($p = 0.03$) [109].

Those that insist on fasting despite having macrovascular complications must adhere to the recommendations mentioned in Table 6.

The studies that have investigated the safety of fasting during Ramadan among people with macrovascular health issues have limitations. It is recommended that individuals with diabetes that have unstable macrovascular complications should remain classified as high risk. Further research is still needed, and these individuals should be discouraged from fasting, as such this recommendation has been given a level 3 and a **Grade D**; consensus (see Tables 1 and 2).

Table 6
Macrovascular complications and safety of fasting during Ramadan.

Macrovascular complication	Recommendations
Congestive heart failure (CHF), Acute coronary syndrome (ACS), Stroke	• Receive a thorough risk assessment from their diabetes specialist, cardiologist and/or neurologist well in advance of Ramadan • Receive pre-Ramadan education and understand how to properly conduct safe fasting with diabetes (See Section 5). • Obtain individualised advice based on their current health status and treatment regimes • Practice safe fasting as discussed in these guidelines wherever applicable. • Make appropriate adjustments to therapies in accordance with their symptoms. For example, diuretics, antihypertensives, anti-diabetes medication and insulin regimens will need adjusting to give the greatest chance of achieving safe fasting during Ramadan. • Make a concerted effort to stay hydrated and get an adequate amount of sleep and nutrition prior to conducting fasting.

Table 7
Microvascular complications and safety of fasting during Ramadan.

Microvascular complication	Recommendations
Renal impairment, Dialysis, Renal transplant	● All individuals with diabetes (both T1DM and T2DM) and chronic kidney disease (CKD) or with any other renal issues should discuss their intentions to fast during Ramadan with diabetes and renal specialists at least three months prior to Ramadan and attend Ramadan focused education. ● Individuals with diabetes (both T1DM and T2DM) and CKD of stages 3-5, or on dialysis should be considered high-risk, and fasting ought to be discouraged. ● Those that are considered high risk and still choose to fast must: o be carefully monitored and have weekly reviews during Ramadan o make a concerted effort to stay hydrated outside of fasting periods o monitor electrolyte and creatinine levels at various points during Ramadan to ensure safe fasting is being conducted and whether it should continue o avoid foods with high potassium or phosphorous content.

7.2. Chronic kidney disease

An important microvascular complication that can arise as a result of diabetes can be chronic kidney disease (CKD) [110]; CKD can be categorised into different stages reflecting the severity of the disease, this classification has been described elsewhere [111]. The International Diabetes Federation and Diabetes and Ramadan International Alliance (IDF – DAR) guidelines stratify people with diabetes that have CKD by risk. People with diabetes and CKD of stage 3 and above ought to adhere to the advice provided in Table 4 [46].

7.2.1. Fasting during Ramadan and renal function

Some studies have shown that fasting during Ramadan can worsen renal function. Mbarki *et al.* also showed that individuals with CKD that fasted during Ramadan could experience deterioration in renal function, particularly in those with an estimated glomerular filtration rate (eGFR) of<60 mL/min/1.73 m2 [112]. Bakhit *et al.* also showed that the higher the stage of CKD the worse the renal outcomes during Ramadan [113]. However, others have shown that fasting during Ramadan may not be associated with any less bad outcomes or even finding improvements. Bernieh *et al.* showed an improvement in eGFR during and after Ramadan with no significant changes to biochemical measures such as urinary electrolytes, protein or osmolarity [114]. A *meta*-analysis conducted on the mean difference of the eGFR before and after Ramadan among several different studies; no clear or meaningful difference was found (mean difference 0; 95% CI −0.19 – 0.19) [115].

7.2.2. Fasting during Ramadan after renal transplants

There have been several studies that have investigated the outcomes of individuals that had previously a kidney transplant and fasting during Ramadan. The overall outlook is that these circumstances do not make fasting unsafe. Further research in the form of longitudinal and randomised trials are still needed to support this recommendation. The IDF-DAR guidelines have given recommendations related to renal transplants a *level 3* and a ***Grade D***, (see Table 1 and Table 2).

Currently the risk for fasting remains high in cases of unstable renal impairment and these individuals should not fast. This is also true of individuals with poorly controlled diabetes where fasting could be unsafe. Individuals with diabetes that have microvascular health issues or those that insist on fasting against the advice of HCPs must consider the recommendations listed in Table 7.

Further guidance on fasting and micro/macrovascular complications are available in the full version of the *IDF-DAR Diabetes and Ramadan Practical Guidelines 2021*.

8. Strengths and weaknesses of the guidelines

The current guidelines are the first diabetes and Ramadan guidelines to combine the input of a large number of experts from 6 continents, including 53 authors and the religious opinion represented by the Mufti of Egypt. The quality of the evidence for all aspects of the guidelines is graded throughout and clearly indicated.

The area of religious fasting and diabetes is under-served by the diabetes research community. Consequently, many aspects of the guidelines are not based on large randomised controlled trials. Indeed, various sections are based wholly upon consensus opinion, which is level 4/Grade D evidence. A good example for this is the new risk scoring, which represents a significant departure from the older three-tier table that was considered too rigid by many and adjusted accordingly. This section is considered by the authors to be Grade 4 evidence. Studies to validate this new risk assessment method are eagerly awaited. Indeed, since the publication of the full version of the guidelines, the new risk score has led some to express a different opinion to the current method and has raised concerns[116]. Such scientific discussion is welcome. Open debate and future clinical studies are needed to improve the level of evidence underpinning practical guidance for those living with diabetes who wish to observe Ramadan. Sections with a low level of evidence should be considered genuine opportunities for researchers with an interest in diabetes and Ramadan fasting. This is a rich area for potential research and any new research will provide welcome contribution to the evidence base and help DaR and IDF to deliver the best possible guidance.

The authors are aware of the huge variations in opinion among many regions and cultures in the field of Ramadan fasting and acknowledge that strong evidence-based guidance will be at the heart of a robust process to catalyse further scientific contribution and nourish the wide-held interest of the global diabetes community in the topic of diabetes and Ramadan fasting.

9. Conclusions and considerations

It is of the utmost importance that HCPs, and individuals with diabetes understand the risks of fasting during Ramadan so that more informed decisions can be taken.

A pre-Ramadan assessment should be the initial step for every individual seeking to fast during Ramadan. This allows HCPs to perform a risk quantification and stratify individuals seeking to fast. At this stage, Ramadan focused education can also be planned and given so that those

that decide to fast understand the strategies to manage their diabetes and any complications that may arise. Likewise, expert nutrition advice can be provided so that individuals with diabetes stay properly nourished and do not experience any diet related issues during or after Ramadan. All individuals with diabetes may need to modify their treatment regimens. Those who are considered at a heightened risk of fasting during Ramadan ought to accept the medical and religious advice.

It is necessary that religious leaders, such as Imams, and members of the community assist in promoting awareness and in overcoming potential hurdles such as previous belief systems and cultural practices that can impede the implementation of these guidelines. Technology such as mobile phones and social media can also play an important role in guideline usage, particularly where access can be an issue. Taken together, a collective approach is needed in order to ensure all, that choose to do so, can safely fast during Ramadan.

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Declaration of Competing Interest

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Appendix A. Supplementary material

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