
بسم الله الرحمن الرحيم

اداره دیابت نوع یك و دو و تغییرات رژیم درمان در رمضان

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Management of Type 2 diabetes when fasting during Ramadan

- **STEP 1: PRE-RAMADAN ASSESSMENT**
- **STEP 2: MEDICATION ADJUSTMENTS**

WHAT IS KNOWN?

- A pre-Ramadan assessment is very important for all individuals seeking to fast during Ramadan.
- The majority of people with type 2 diabetes mellitus (T2DM) can safely fast during Ramadan.
- Individuals taking metformin, sulphonylureas (SUs), insulin secretagogues or insulin will need to make treatment adjustments to reduce the risk of hypoglycaemia.
- A post-Ramadan Assessment is recommended.

- Dose modifications alongside stricter schedules of self-monitoring of blood glucose (SMBG) are important tools to ensure safe fasting with good glycaemic control during Ramadan.

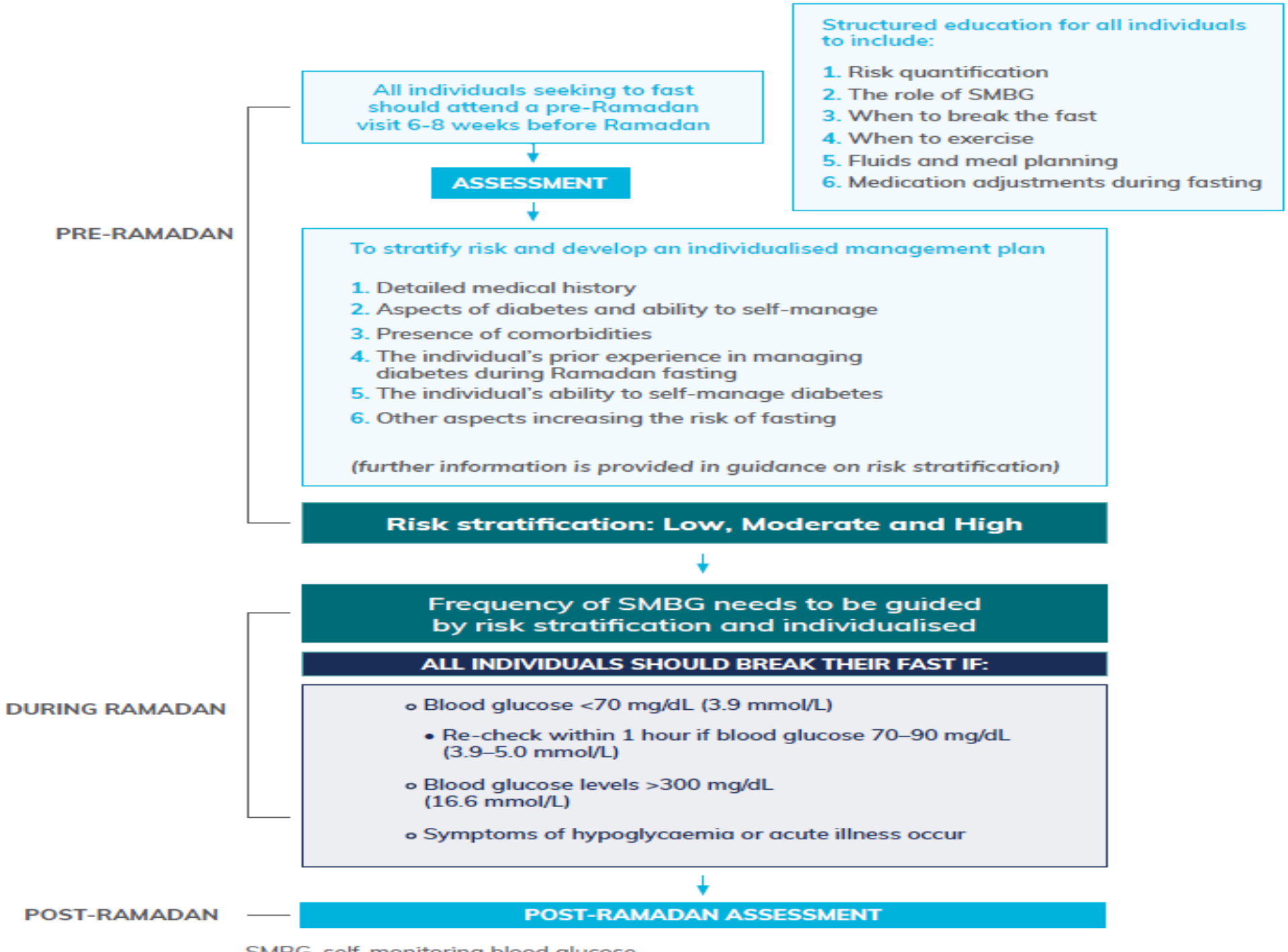
- Individuals on multiple antidiabetic therapies need *individualised* dose reductions to avoid additional risks of hypoglycaemia or hyperglycaemia when fasting during Ramadan.

WHAT IS MISSING?

- Further randomized controlled trials for different antidiabetic therapies are required to provide more specific treatment recommendations.

PRE-RAMADAN ASSESSMENT

- All people with diabetes seeking to fast during Ramadan should have a pre-Ramadan assessment with their healthcare provider, ideally, 6–8 weeks before the start of Ramadan.
- Healthcare professionals (HCP) can obtain a detailed medical history on individuals seeking to fast and review their glycaemic control and capability to self-manage their diabetes.
- Among other things, the HCP can apply the new risk scoring process to stratify the individual seeking to fast as “high”, “moderate” or “low” and provide advice on whether fasting is safe.



SMBG, self-monitoring blood glucose

STEP 2:
MEDICATION ADJUSTMENTS

- **Metformin :**
- Metformin is the most commonly used, first-line, oral antidiabetic drug (OAD) and works by ***preventing the liver from producing new glucose***.
- It comes in an ***immediate release*** preparation which may be taken up to three times per day, and a ***prolonged release*** formulation which is typically taken just once a day.

- Severe hypoglycaemia in non-fasting individuals receiving metformin is rare, and while there are no randomised controlled trials (RCTs) on the use of metformin in people with T2DM that fast during Ramadan, *it is considered safe* for individuals on metformin monotherapy to fast.
- Dose adjustments are shown in **Figure 2**.

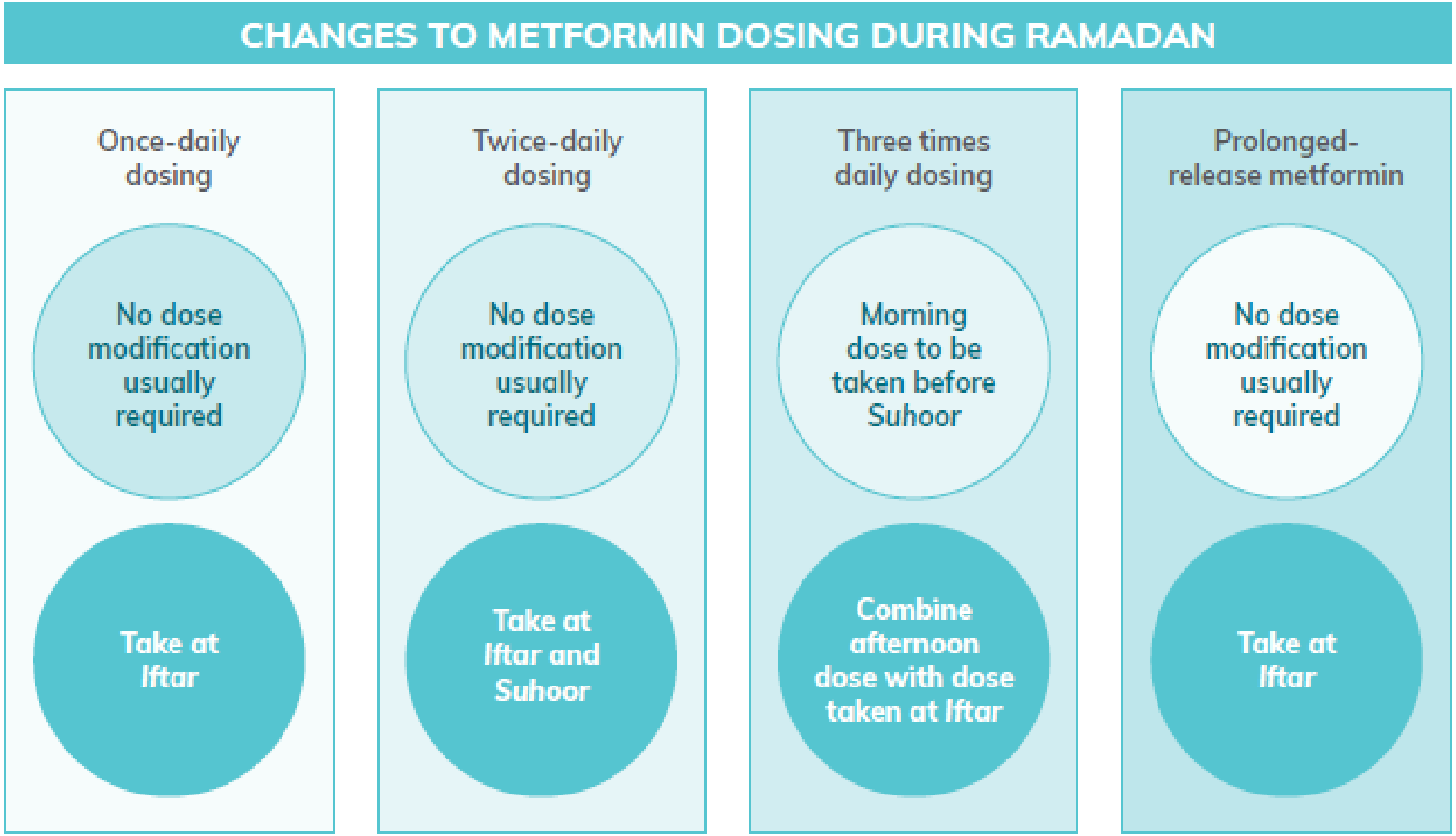


FIGURE 2

Dose adjustments for metformin

Acarbose :

- **While no RCTs have been conducted on acarbose in people with T2DM that fast during Ramadan, NO DOSE MODIFICATION is considered necessary as the risk of hypoglycaemia is low.**

Thiazolidinediones :

- Thiazolidinediones (TZDs) *improve the insulin sensitivity of fat, muscle, liver* and peripheral tissue cells by specifically activating the peroxisome proliferator-activated receptor (PPAR)-γ.
- This receptor controls the level of proteins involved in glucose regulation and uptake; activation of PPARγ via TZDs *can increase glucose uptake and utilisation, particularly in adipose tissue*.
- An increase in glucose uptake will subsequently *lower glucose levels* in the blood **[4]**. As TZDs function without increasing insulin secretion, *the risk of hypoglycaemia in non-fasting people on TZD monotherapy is very low* **[5]**.

- **Due to the low risk of hypoglycaemia with pioglitazone, NO DOSE MODIFICATION is required during Ramadan, but dose should be taken with *Iftar*.**

Short-acting insulin secretagogues :

- Short-acting insulin secretagogues such as **repaglinide** and nateglinide *stimulate pancreatic β cells to secrete more insulin* and are usually *taken before meals*.

- **The daily dose of short-acting insulin secretagogues (based on a three-meal dosing) may be REDUCED or REDISTRIBUTED to two doses during Ramadan according to meal sizes.**

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) :

- GLP-1 RAs mimic the incretin hormone and decrease glucose levels in the blood by *increasing insulin secretion* in a glucose-dependent manner. Like endogenous GLP-1, drugs in this class *reduce glucagon secretion, increase glucose uptake and storage in muscle, decrease glucose production by the liver, reduce appetite and retard gastric emptying* **[12, 13]**.
- As they act in a glucose-dependent manner, *the risk of severe hypoglycaemia is low* when used as monotherapy, but this risk may be higher when given with sulphonylureas (SUs) or insulin **[14]**.

- **As long as liraglutide, lixesenatide, exenatide have been appropriately DOSE-TITRATED prior to Ramadan (at least 2–4 weeks), NO FURTHER TREATMENT MODIFICATIONS are required.**

Dipeptidyl peptidase-4 (DPP-4) inhibitors :

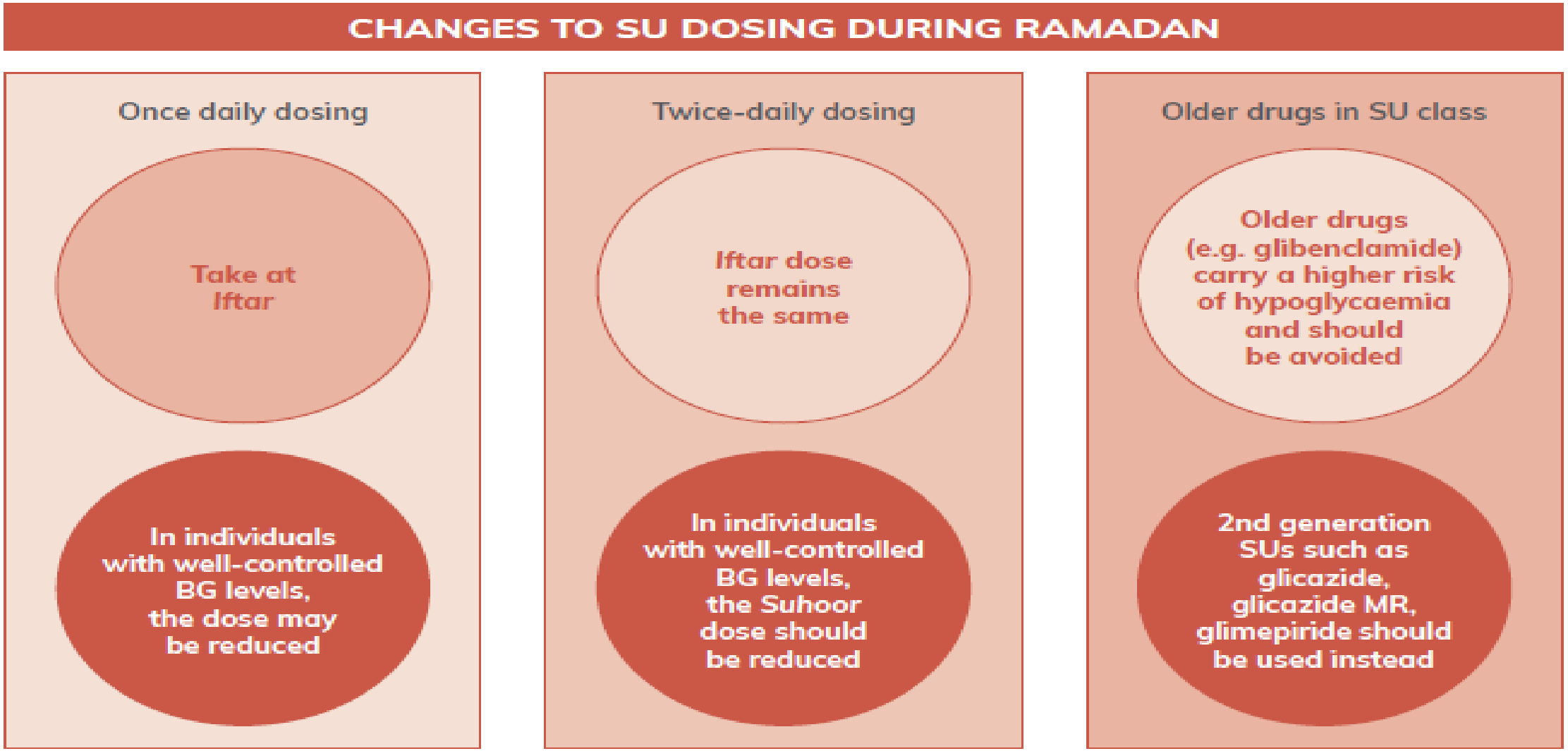
- DPP-4 is an enzyme that rapidly metabolizes GLP-1, thereby regulating the activity of the hormone. By blocking this action, DPP-4 inhibitors *effectively increase the circulating levels of GLP-1*, which in turn *stimulates insulin secretion* in a glucose-dependent manner **[13]**.

- Currently available DPP-4 inhibitors include *sitagliptin*, vildagliptin, saxagliptin, alogliptin and *linagliptin*, which *are administered orally once or twice a day* and are considered one of the best tolerated antidiabetic drugs *with low risk of hypoglycaemia* in non-fasting patients **[2]**.

- A recent meta-analysis of 16 RCTs and 13 observational studies in people with T2DM who fasted during Ramadan suggested, in a pooled analysis, *DPP-4 inhibitors were associated with the lowest incidence of hypoglycaemic events* compared with SU **[30]**.
- **DPP4-I do NOT REQUIRE TREATMENT MODIFICATIONS during Ramadan.**

Sulphonylureas (SUs) :

- SUs are *widely used as second-line treatment for T2DM* after metformin and so there is a wealth of evidence and experience with this low cost efficacious drug class.
- SUs *stimulate insulin secretion* from pancreatic β cells in a glucose-independent process. Because of this, SUs are associated with a *higher risk of hypoglycaemia* compared with other OADs, which has raised some concerns about their use during Ramadan. However, this risk varies across medications within this class due to differing receptor interactions, binding affinities and durations of action.



BG, blood glucose; SU, sulphonylurea

FIGURE 3

Dose adjustments for sulphonylureas in people with T2DM fasting during Ramadan

Sodium-glucose co-transporter-2 (SGLT2) inhibitors :

- SGLT2 inhibitors including dapagliflozin, canagliflozin, empagliflozin and ertugliflozin are the newest class of OADs.
- SGLT2 inhibitors have a unique mode of action whereby *they increase the excretion of glucose by the kidneys* by reducing reabsorption in the proximal tubule, consequently decreasing blood glucose **[36]**.
- SGLT2 inhibitors have demonstrated effective improvements in *glycaemic control and weight loss* and are associated with a *low risk of hypoglycaemia*. Because of this, it has been proposed that they can be a *safe treatment option for people with T2DM that fast during Ramadan.*

- However, ***some safety concerns*** were raised, such as *an increased risk of dehydration* in vulnerable patients, which may be a particularly pertinent issue during Ramadan.

- The previous 2016 IDF-DAR guidelines were in favour of using SGLT2I, but there remains a need for ***caution during among those on loop diuretics, the elderly and those with renal impairment*** **[37]**.

- Over the last 5 years, a greater number of studies assessing the use of SGLT2I have been published. Cardiovascular outcome trials (CVOTs) including CANVAS, EMPA-REG OUTCOME, and DECLARE-TIMI 58 provided evidence of **cardiovascular benefits** in people with diabetes that took SGLT2I **[38-42]**.
- These information were used to important diabetes related guidance such as that of the ADAs, *where SGLT2I and GLP1-RA showed cardiovascular benefit and were placed ahead of other classes of drugs in people with cardiovascular disease (CVD) or chronic kidney disease (CKD)* or people at risk of these issues **[40]**.

- Meanwhile, the use of SGLT2I in people with T2DM that fast during Ramadan have also been *studied recently*.

- The results of these studies, alongside the importance of SGLT2I as a class for people with or at risk of CVD/CKD, prompted the authors of the Canadian diabetes and Ramadan guidelines to advise on *withholding SGLT2I only in circumstances of significant volume depletion such as frequent vomiting or diarrhoea and in situations where medications such as ACE-I and diuretics are used* **[43]**.

Current recommendations for the use of SGLT2-I during Ramadan fasting :

- For stabilization, *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.

- **SGLT2 inhibitors have a low risk of hypoglycaemia.**
- **NO DOSE ADJUSTMENTs are required during Ramadan.**

Individuals on multiple antidiabetic therapy

3.9.1 CONSIDERATIONS AND RECOMMENDATIONS:

1. Many individuals on multiple antidiabetic agents have a long duration of diabetes, multiple comorbidities and renal impairment. Hence, they are at higher risk of hypoglycaemia when fasting during Ramadan.
2. 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.
3. 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.
4. Newer technologies including continuous glucose monitoring and activity monitoring need to be harnessed through AI to reduce the risk of hypoglycaemia in people with diabetes that are on multiple antidiabetic agents and fast during Ramadan.

Insulin treatment for T2DM :

- Many individuals with T2DM are on insulin therapy to control their diabetes and a variety of insulin regimens are used.
- These include ***long/intermediate basal insulins*** (insulin glargine, insulin detemir, insulin degludec or neutral protamine Hagedorn insulin) that are often combined with oral agents; basal insulin with bolus prandial ***rapid or short-acting insulins*** (lispro, glulisine,aspart or regular human insulin); and ***premixed insulins*** (fixed ratio combinations of short and intermediate acting insulins) **[55]**.

- ***Insulin*** use during fasting carries a risk of ***hypoglycaemia***, especially when more complex insulin regimens are used.
- Although a small number of randomised trials and observational studies have been conducted to assess some insulin regimens during Ramadan, however ***information from large RCTs in this area are lacking.***

CHANGES TO LONG AND SHORT-ACTING INSULIN DOSING DURING RAMADAN

Long/intermediate-acting (basal) insulin

NPH/detemir/glargine/glargine 300/degludec
ONCE-DAILY
Reduce dose by 15-30%
Take at *Iftar*

NPH/detemir/glargine
TWICE-DAILY
Take usual morning dose at *Iftar*
Reduce evening dose by 50% and take at *Suhoor*

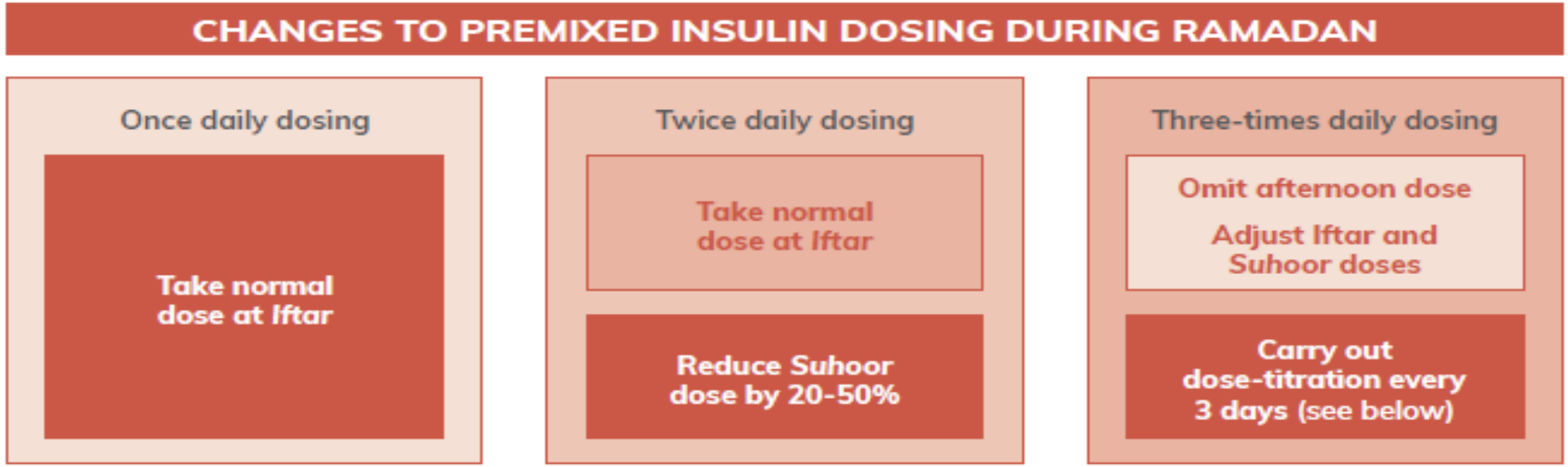
Short-acting insulin

Normal dose at *Iftar*
Omit lunch-time dose
Reduce Suhoor dose by 25-50%

Fasting/pre-*Iftar*/pre-Suhoor blood glucose	pre-*Iftar*	pre-*Iftar**/post-Suhoor**
	Basal insulin	**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

*Reduce the insulin dose taken before Suhoor; **Reduce the insulin dose taken before *Iftar*

FIGURE 4
Dose adjustments for long or short-acting insulins



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

Table adapted from Hassanein et al. (2014) [66].

FIGURE 5

Dose adjustments for premixed insulin

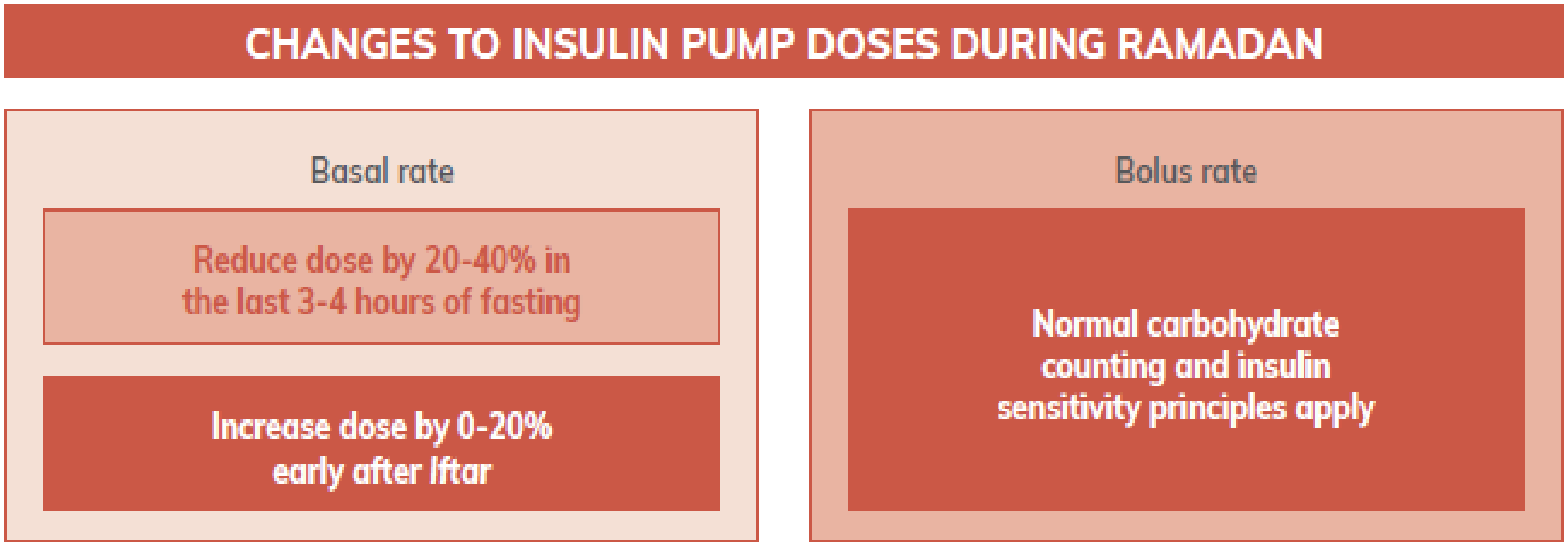


FIGURE 6

Dose adjustments for insulin pump therapy

SUMMARY

- A pre-Ramadan assessment is vital for any Individual with T2DM that intends to fast in order to evaluate the risks, educate the patient in self-management of the condition during Ramadan and to produce a patient-specific treatment plan.
- There are advantages and disadvantages associated with the different treatment options for people with T2DM that seek to fast during Ramadan.
    - Individuals taking metformin, SUs, insulin secretagogues or insulin will need to make dose adjustments to reduce the risk of hypoglycaemia.
- Individuals on multiple antidiabetic therapies will find themselves at a greater risk of hypoglycaemia
    - Counselling is recommended to individuals on 3 or more antidiabetic agents
    - Dose reductions need to be made to accommodate for the increased risk of hypoglycaemia.
- Artificial intelligence in the form of machine learning prognostic modelling can be a useful tool for future use in risk stratification and planning strategies for dose modifications.
- A post-Ramadan follow-up consultation is recommended to reassess treatment regimens and discuss fasting experiences during Ramadan.
- With the correct advice and support from HCPs most people with T2DM can fast safely during Ramadan.

Risk stratification for a person with type 1 diabetes wishing to fast should be individualised and dependent on a range of different factors including:

- Pre-Ramadan glucose control
- The duration of T1DM – for example those newly diagnosed may be within the 'honeymoon period'
- Hypoglycaemia risk
- Level of hypoglycaemia awareness
- The level of diabetes related education
- Motivation for self-monitoring of blood glucose (SMBG)
- The ability to take appropriate decision making
- The feasibility of, and access to, continuous glucose monitoring and advanced insulin delivery technology
- The presence of diabetes related complications and/or associated autoimmune disorders such as Coeliac disease and thyroid disorders

Criteria for Fasting during Ramadan in people with T1DM :

- **A pre-Ramadan clinical evaluation and a full review of an individual's glucose profile should be completed.**
- **If poor glycaemic control is found (HbA1c >9% and or wide glucose fluctuation), the insulin treatment regimen should be adjusted as necessary and re-evaluated once again before the start of fasting.**

Criteria for Fasting during Ramadan in people with T1DM :

- **Individuals with T1DM, regardless of their age, and their carers or guardians should be taught about the potential adverse effects of fasting, including hypoglycaemia,hyperglycaemia and dehydration, and appropriate preventative measures to minimise the risks of these occurring.**

Criteria for Fasting during Ramadan in people with T1DM :

- **There should be a nutritional assessment reviewing carbohydrate (CHO) intake and recommendations about the proper food options for the two main meals of the day.**
- **Carbohydrate counting techniques should also be discussed. An emphasis needs to be placed on the importance of a scheduled time for meals rather than following a looser erratic and frequent eating pattern.**
- **Also, an adequate intake of sugar-free beverages, especially with the pre-dawn meal, should be stressed.**

Criteria for Fasting during Ramadan in people with T1DM :

- **While there is still a debate about the best insulin regimen for during fasting, a basal insulin dose reduction by 10-30% has been recommended by the majority of experts and medical societies.**
- **More importantly, an individualised regimen should be considered and based on a review of the individual's glucose profile within the first few days of fasting.**

Criteria for Fasting during Ramadan in people with T1DM :

- **Frequent glucose testing is fundamental to ensure early recognition of abnormal glucose readings and that the proper measures in controlling them are taken.**
- **The use of CGM or FGM is superior to the traditional BG monitoring and should be the method of choice if available.**

Criteria for Fasting during Ramadan in people with T1DM :

- **Fasting should be broken immediately with hypoglycaemia (< 70 mg/dL; 3.9 mmol/L) in individuals using MDI, both symptomatic or asymptomatic.**
- **Those using CSII may try suspending the pump if glucose drops below 90mg/dL (5 mmol/L) but should also break the fast if glucose is < 70 mg/dL (3.9 mmol/L).**

The allowance to fast cannot be generalised across to all individuals with T1DM, especially those where the aforementioned criteria are not met. 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.**

- Frequent glucose testing is fundamental to ensure safe fasting.
- The use of CGM or FGM is superior to SMBG monitoring, and should be the method of choice if feasible.
- Fasting should be broken immediately with hypoglycaemia (glucose < 70mg/dL; 3.9 mmol/L).

Taken together, it is essential to design an individualised meal plan well before Ramadan. The plan should be to help individuals maintain an adequate caloric intake and help avoid excessive weight changes. Furthermore, this meal plan should take into account the insulin regimen, the type of food consumed, and meal timing. During Ramadan continuous glucose monitoring and daily adjustments are required to achieve good glucose control and avoid excursions.

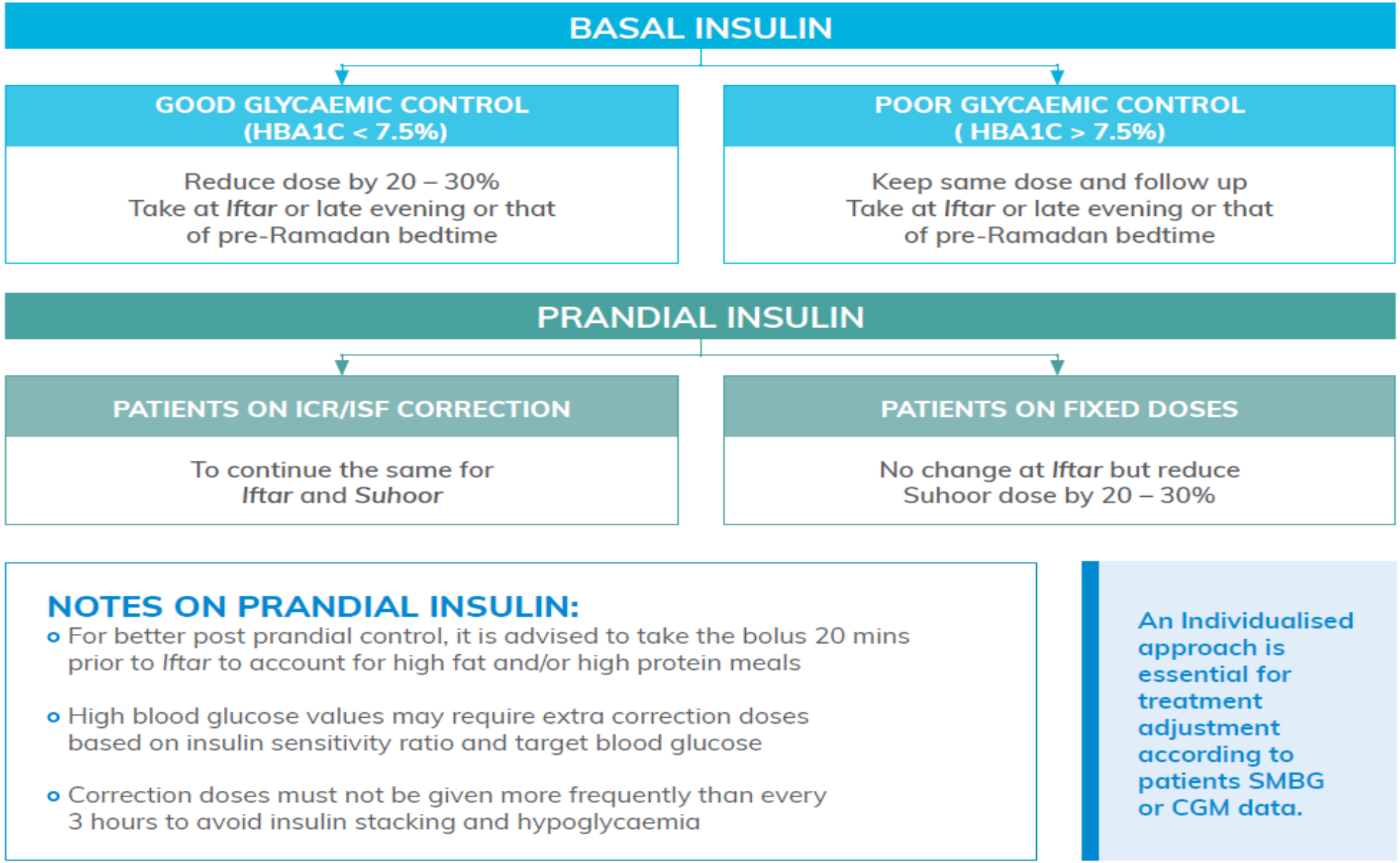


FIGURE 1

The recommended use of MDI therapy in adolescents with T1DM that are fasting during Ramadan

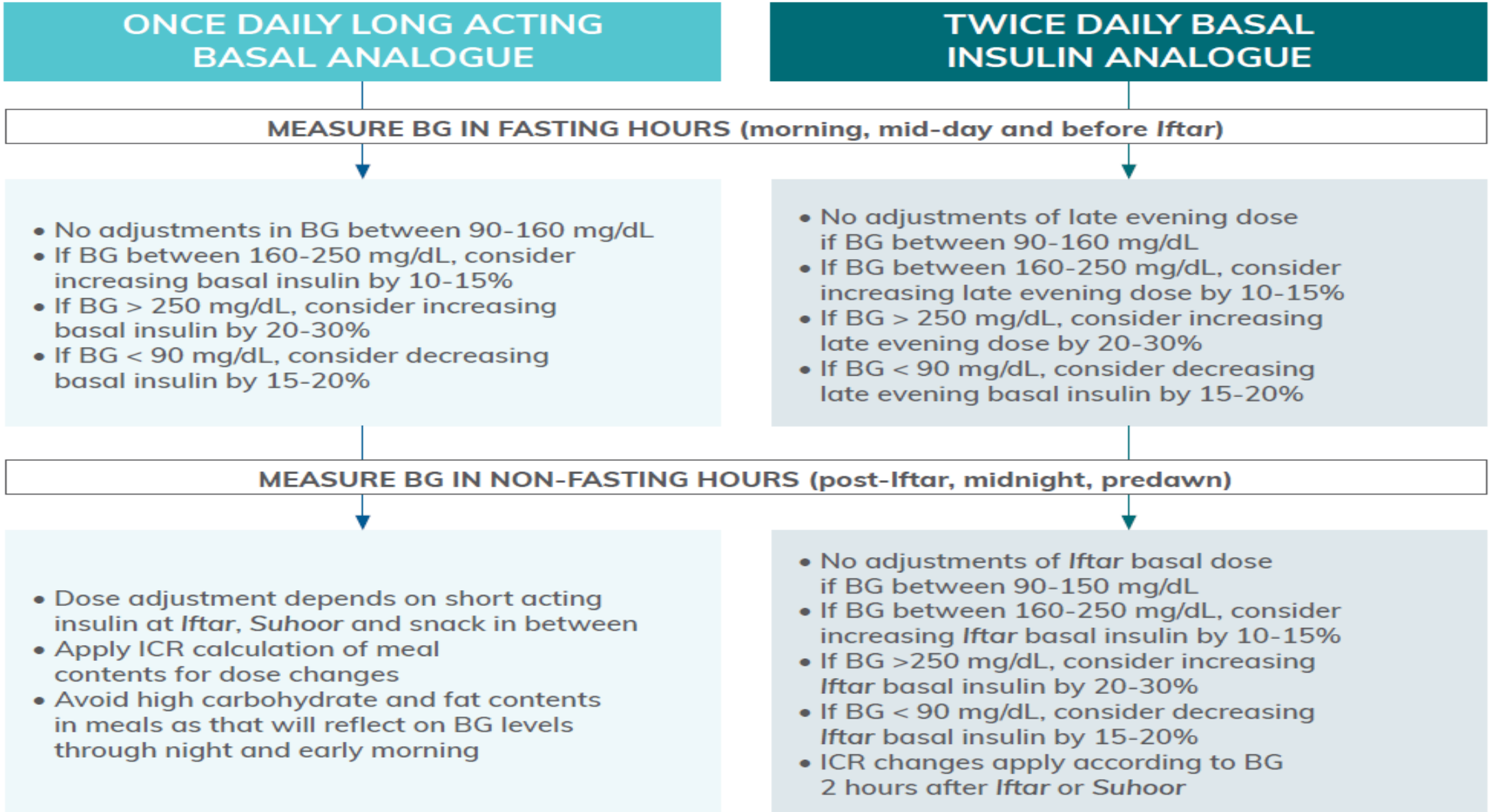


FIGURE 2

Schematic adjustments of insulin and/or food considerations during fasting and non-fasting hours

- **Basal-bolus regimen is preferred** over conventional twice daily regimens in adolescents with T1DM.
- **Basal** insulin should be adjusted according to fasting blood glucose levels, to reduce hypoglycaemia during fasting.
- **Bolus** insulin before *Iftar* and *Suhoor* using ICR and ISF-based corrections are recommended in order to control postprandial and evening hyperglycaemia.
- ***Premixed insulin regimens are incompatible with safe fasting*** and should be discouraged.

TABLE 7: **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 o 20-40% decrease for the last 3-4 hours of fast o 10-30% increase for the first few hours after *Iftar* Bolus doses o Same principles as prior to Ramadan	**CGM**
MDI (basal bolus) with analogue insulin	Basal insulin o 30-40% reduction in dose and to be taken at *Iftar* Rapid Analogue Insulin o Dose at *Suhoor* to be reduced by 30-50% o Pre-lunch dose to be skipped o 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 o The usual pre-Ramadan morning dose to be taken in the evening during Ramadan o 50% of the pre-Ramadan dose to be taken at *Suhoor* Regular insulin o Dose at evening meal remains unchanged o *Suhoor* dose to be 50% of the pre-Ramadan evening dose o Afternoon dose to be skipped	**7-point blood glucose monitoring or 2-3 staggered readings throughout the day**
Premixed (analogue or conventional)	o Shift the usual pre-Ramadan morning dose to *Iftar* o 50% of the pre-Ramadan evening dose at *Suhoor*	**At least 2-3 daily readings and whenever any hypoglycaemic symptoms develop**

1.9 When to break the fast during Ramadan – all people with T1DM

In general, it should be recommended that all people with T1DM fasting during Ramadan monitor their blood glucose levels closely and carefully.

ALL INDIVIDUALS SHOULD BREAK THEIR FAST IF:
◦ **Blood glucose <70 mg/dL (3.9 mmol/L)** – re-check within 1 h if blood glucose 70-90 mg/dL (3.9 - 5.0 mmol/L)
◦ **Blood glucose >300 mg/dL (16.7 mmol/L)****
◦ **Symptoms of hypoglycaemia or acute illness occur**

** In people with previously well controlled diabetes, these targets can be adapted and individualised.

SUMMARY

- Fasting Ramadan for people with T1DM is generally associated with a high risk of hypoglycaemia and hyperglycaemia.
- With well-structured pre-Ramadan education programmes, the risks of fasting can be reduced, and suitable individuals can be allowed to fast under strict monitoring and after appropriate insulin dose adjustments.
- Approaches to treatment adjustments should be individualised. The following should be considered: pre-Ramadan diabetes control; previous Ramadan experience; availability of recourses; the level of education; and the motivation for self-care.
- Different demographic characteristics affecting duration of fast, access to insulin and glucose monitoring must be considered in any risk assessment for the safety fasting.
- Insulin analogues are preferred over conventional insulin regimens if fasting is considered.
- Frequent SMBG is essential and if feasible, through CGM or FGM.
- Advanced insulin technology seems very promising in allowing for safe fasting.
- There is a lack of research and guidance for adults with T1DM that are seeking to fast during Ramadan and further research needs to be conducted in this age group.
- Overall, further research, including randomised clinical trials, are needed to assess clinical outcomes during fasting in Ramadan to help produce the best treatment options for adolescents and adults with T1DM.

SUMMARY

- Many pregnant women with pre-existing diabetes or GDM are considered as high-risk group for fasting during Ramadan.
- Multiple factors influence the risk assessment of a pregnant women with hyperglycaemia and these should be carefully reviewed prior to Ramadan.
- Patient education prior to Ramadan is essential to ensure mother and fetus safety regardless of fasting decision.
- Regular SMBG should be conducted and at the very least once before the sunset meal; 1-2 hours after meals; once while fasting; anytime feeling unwell.
- Pregnant women must break their fast if they feel unwell; BG levels drop below 70 mg/dL (3.9 mmol/L); or identify a reduction in fetal movement.
- Patients treated with insulin should have doses adjusted according to their insulin regimen.

SUMMARY

- Lower proportions of elderly individuals fast than their younger counterparts.
- Diabetes related complications such as hypoglycaemia and hyperglycaemia can be more frequent in elderly individuals than in younger individuals during the Ramadan fast.
- Greater and more careful planning pre-Ramadan is needed in elderly individuals to ensure a safe fast during Ramadan can be achieved.
- There must be a greater emphasis on SMBG in elderly individuals during the Ramadan fast to ensure safety.
- Antidiabetic drugs with lower risks of hypoglycaemia are preferred in elderly individuals.
- There is a significant need for more research into elderly individuals with T1DM, T2DM and differing comorbidities that fast during Ramadan.

- All individuals with diabetes (both T1DM and T2DM) and CKD 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 (see **chapter 7: Pre-Ramadan Assessment and Education**). As a pre-requisite, the recommendations for the practice of safe fasting discussed in these guidelines must also be met where applicable.

- Individuals with stable renal transplants and diabetes (both T1DM and T2DM) may be able to fast safely providing they are monitored carefully by their transplant team before, during, and after Ramadan, and given careful advice on how to take immunosuppressive and anti-diabetes medication.

- Individuals with diabetes (both T1DM and T2DM) and CKD of stages 3-5, or on dialysis should be considered high-risk, and fasting should be discouraged.

- Those that are considered high risk and still choose to fast must:
    - be carefully monitored and have weekly reviews during Ramadan
    - make a concerted effort to stay hydrated outside of fasting periods
    - monitor electrolyte and creatinine levels at various points during Ramadan to ensure safe fasting is being conducted and whether it should continue
    - avoid foods with high potassium or phosphorous content.

SUMMARY

- Fasting during Ramadan with stable CVD does not increase hospitalisations or worsening of the underlying heart condition. However further research is needed into individuals with diabetes and pre-existing CVD to carry any specific recommendations to individuals with diabetes and CVD.
- Studies investigating the risks of fasting on stroke are conflicting and greater research is needed in individuals with diabetes with pre-existing stroke.
- Fasting during Ramadan with stable CKD or having undergone a kidney transplant does not increase eGFR and any biochemical changes are transient. This may also apply to individuals with diabetes, but further research is needed into individuals with pre-existing diabetes and CKD.
- Individuals that have undergone a kidney transplant or have stage 3-5 CKD are at high-very high risk of fasting during Ramadan. These will require careful monitoring and specialised tailored advice before fasting during Ramadan. The conditions required to safely fast in other chapters of these guidelines must be met as a pre-requisite.
- Larger prospective studies are needed; these include randomised trials and studies assessing the effect of fasting in individuals with diabetes and its complications on microvascular and macrovascular complications.

با تشکر از توجه شما