

TITLE: Acute glycaemic management before, during and after exercise for cardiac rehabilitation participants with diabetes mellitus: A joint statement of the British and Canadian Associations of Cardiovascular Prevention and Rehabilitation, the International Council for Cardiovascular Prevention and Rehabilitation, [oxford comma] and the British Association of Sport and Exercise Sciences

A joint scientific statement of the British Association for Cardiovascular Prevention and Rehabilitation^a, the Canadian Association of Cardiovascular Prevention and Rehabilitation^b, and the British Association of Sport and Exercise Sciences^c

Endorsed by the International Council for Cardiovascular Prevention and Rehabilitation

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ABSTRACT

Type 1 (T1) and Type 2 (T2) Diabetes mellitus (DM) are significant pre-cursors and co-morbidities to cardiovascular disease and prevalence of both types is still rising globally. Currently, ~25% of participants (and rising) attending cardiac rehabilitation in Europe, North America and Australia have been reported to have DM (>90% have T2DM). Whilst there is some debate over whether improving glycaemic control in those with heart disease can independently improve future cardiovascular health related outcomes, for the individual patient whose blood glucose is well controlled, it can aid the exercise programme in being more efficacious. Good glycaemic management not only helps to mitigate the risk of acute glycaemic events during exercising, it also aids in achieving the requisite physiological and psycho-social aims of the exercise component of CR. These benefits are strongly associated with effective behavior change, including increased enjoyment, adherence, and self-efficacy. It is known that CR participants with DM have lower uptake and adherence rates compared to those without DM. This expert statement provides CR practitioners with nine recommendations aimed to aid in the participant's improved blood glucose control before, during and after exercise so as to prevent the risk of glycaemic events that could mitigate their beneficial participation.

INTRODUCTION AND AIMS

This guidance statement is aimed at helping front-line practitioners better manage the growing number of cardiac rehabilitation participants who have diabetes.(1) It has been developed and written by a group of practitioner-academics with a special interest in how diabetes management interacts with their practices in cardiology (3 authors), dietetics (1 author), rehabilitation therapy (1 author) or exercise science applied to metabolic care (2 authors). All of the authors have previous experience in contributing to national and international practice guidelines/standards in either cardiac rehabilitation and/or diabetes. They have been brought together to combine their expertise to represent the multi-professional CR associations of the UK and Canada, who are partnered with 38 other countries that make up the International Council of Cardiovascular Prevention and Rehabilitation (ICCPR). This means that the statement has also been reviewed and endorsed by doctors, nurses, physiotherapists, exercise physiologists, dietitians and psychologists representing health professionals and groups from around the world. The statement is laid out in two parts; Part 1 is a summary table (Table 1) of nine key recommendations on managing glycaemic control in and around exercise, and Part 2 provides the evidence-based consensus that underpins these recommendations.

Part 1.

The summary guidance statements in Table 1 include scores (+ sign in brackets) from the GRADE* system (2) for evidence quality, which was used in the development of the recent Diabetes UK Nutritional Guidelines (3, 4)

Table 1. A summary of nine key statements for managing glycaemic control in cardiac rehabilitation participants before, during and after exercise

Guidance point	Recommendation
1	<p>More than 25% of cardiac rehabilitation (5) participants will have diabetes mellitus (DM) and over 90% of these will be Type 2 diabetes mellitus (T2DM). Participants should be categorized into one of three levels of observation for exercise related to dysglycaemia risk,</p> <ul style="list-style-type: none">a. Participants with Type 1 diabetes mellitus (T1DM), have the greatest risk of exercise-related dysglycaemia (i.e. hypo- or hyperglycaemia) and require the greatest level of individualised management to maintain stable glycaemic levels. (+++)b. Participants with T2DM on-insulin secretagogues (sulfonylureas, meglitinides) are the next level of risk to warrant moderate to similar levels of observation for dysglycaemia as those with T1DM (+++), andc. Participants with T2DM on non-insulin medications and/or managed with nutrition and lifestyle, usually require little additional observation compared to CR participants without diabetes (NR).
2	<p>Exercise should only to be contraindicated for CR participants with DM when one of the following states persists:</p> <ul style="list-style-type: none">a. Recent history of 'brittle'/unstable glycaemic control (i.e. 4 or more episodes of severe hypoglycaemia and hyperglycaemia with diabetic ketoacidosis, without obvious or apparent causes and requiring emergency response and/or hospitalization, over the last 12 months). These individuals are typically on exogenous insulin and have a T1DM diagnosis (NR).b. Low glucose level (<5 mmol/l) that is not reversed by nutritional supplementation in a short period of time (<30 minutes) (NR).c. In participants with T1DM, where hyperglycaemia is >15 mmol/L and ketones > 1.5 mmol/L (NR).d. In T2DM, where there are ketones > 1.5 mmol/L (++).
3	<p>CR services should now possess glucose and ketone monitoring devices, and where the team includes practitioners skilled in taking these measures, in an</p>

	equivalent standard to monitoring blood pressure, measuring ECG and providing cardiac life support (NR) .
4	For CR participants with DM, the value of regular physical activity is of even greater value than for those participants without DM, as it has significant influences these two key independent and interdependent morbidities (+++) .(6) Unfortunately, uptake, adherence and completion of a CR programme has been found to be poorer in CR participants with DM versus those without DM (++) . Participants with DM on insulin therapy are typically more fearful of glucose exertion related events (both during or for several hours after the exercise session has ended) and therefore need greater individualised attention, support and guidance to optimise management. CR programme managers therefore need to adopt strategies to overcome both the service and psychological motivation challenges of this large and increasing sub-group of CR participants (NR) .
5	For those participants managing their DM with insulin, the following guidance is recommended: <ul style="list-style-type: none"> a. Before exercise, prandial insulin, if administered just before the activity, should be injected into the abdomen or upper buttock. Ideally, the bolus (prandial) insulin dose should be reduced by 25-50% if an exercise session is within the time action period for that insulin (i.e. within 2-hours of prandial insulin). Consider up to a 50% reduction to prandial insulin with next post-exercise meal and, if engaging in regular exercise, a 20% reduction to daily basal insulin dose (MDI only). For those on pump therapy, basal rates can be reduced by 50-80% 60-90 minutes before the onset of exercise and rates can be resumed after the exercise is done (++). b. Participants with less stable T1DM should be on continuous glucose monitoring and the CR team should support needs to pursue more vigilant care in working with the participant's Diabetes care-team (++).
6	Risk management related to chronicity, should respect that: <ul style="list-style-type: none"> a. Increased age is associated with greater risk of hypoglycaemia (+++). b. Over the longer term, unlike T2DM, exercise in T1DM does not typically improve glycaemic control substantively, but is associated with reduced risk for diabetes-related complications (+++).
7	In all cases and to promote the value of exercise, all should be done to reverse a contra-indicated state before deciding to cease the exercise opportunity. Even if it means cutting the exercise session short while waiting for glycaemia and ketones to return to acceptable levels as detailed in sections 6 and 7 of the full report. Mild to moderate aerobic exercise can be started if blood ketones are low (<0.6 mmol/L) or the urine ketone dipstick is less than 2+ (or < 4.0 mmol/L). Blood glucose concentrations should be monitored during exercise to help detect whether glucose concentrations increase further. Strategies for preventing hyper or hypoglycaemia include: <ul style="list-style-type: none"> a. Lighter intensity aerobic activity (walking, light cycling, etc.) for those starting in a hyperglycaemic state (++).

	<ul style="list-style-type: none"> b. For participants with T1DM, if glucose is > 10 mmol/L, then it is recommended to perform the aerobic exercise component of the session first before the strength and/or more anaerobic type activities (+) c. Performing resistance-type activities before aerobic type exercise is better suited to prevent hypoglycemia, including those starting in a euglycaemic state d. For those in a lower glycaemic state (< 5.0 mmol/l), nutritional supplements of simple carbohydrates of 15-30 g, 30 minutes pre-exercise + 25-30g for every additional 30 minutes of activity (+). e. Hypoglycemia during exercise should be treated with 15-30 grams of rapid acting carbohydrate (glucose tabs, juice, etc.). Exercise can be resumed once glucose levels rise > 5.0 mmol/L (+.) f. For T1DM and T2DM individuals on insulin, Section 6 provides the full details of recommendations for participants in one of five pre-exercise glycaemic categories: < 5 mmol/L; 5 – 6.9 mmol/L; 7 – 10 mmol/L; 10.1 – 15 mmol/L; and > 15 mmol/L (NR).
8	<p>There are a number of interactions between exercise and cardiovascular and non-insulin glycaemic management medications see Table 2 (Part 2).</p> <ul style="list-style-type: none"> a. These medications do not cause a need for extra carbohydrates to be taken with exercise: Biguanides (e.g. metformin), Incretin-based therapies of GLP1-RA, DPP-4 inhibitors (+). b. These medications do require the monitoring of blood glucose and risk of hypoglycaemia and the need for taking of extra carbohydrate: Sulphonylureas, Glinides (++). c. A more recent medication for diabetes is the Sodium-glucose co-transporter-2 (SGLT-2) inhibitor mainly prescribed for individuals with T2DM, and sometimes in T1DM under very specific circumstances. These glucose lowering agents are principally seen as an add-on therapy when metformin alone is not sufficient to reach the glycaemic target. The SGLT-2 inhibitors have shown benefits in patients with cardiovascular disease, however, ketoacidosis, has been reported in the absence of hyperglycaemia. Interactions with exercise are unknown, but recommendations already given for vigilance in monitoring of hypo and hyperglycaemic prevention and management would seem prudent (see section 4.1 Part 2) (++). d. For participants prescribed beta blocking agents, DM also attenuates the heart-rate response to exertion (and similarly for oxygen uptake responses) when either exercise commences or when exercise intensity is increased. It would seem prudent for CR participants with diabetes on beta-blockers to expect a further reduction in heart rate responsiveness to any given change in exercise intensity compared to beta-blocked CR participants without diabetes (NR).

9	c. The time of day (circadian effects) of exercise also influences glycaemic regulation in both T1DM and T2DM. In those who are at risk of post-exercise hypoglycaemic events, morning exercise is recommended and for those more prone to hyperglycaemia, afternoon and evening exercise (including High Intensity Interval Training [HITT] in T2DM) has been demonstrated as preferable (NR) .

*GRADE system scores of evidence quality

++++: strong recommendation based on high-quality evidence.

+++ : moderate recommendation based on moderate-quality evidence.

++ : low-strength recommendation based on low-quality evidence.

+ : very-low strength recommendation based on very-low quality evidence.

NR: not rated

Part 2

1.0 BACKGROUND

1.1 Evidence Search and Review

The search and review strategy involved using health and medicine databases (CINAHL, Pubmed, Medline, Embase, and TRIP). Initial searches commenced by reviewing existing key position statements and guidelines from other national and international associations that combined the topics of exercise, cardiovascular health/rehabilitation, diabetes and glycaemic management. The only statement which was most closely allied to this same focus was the 2012 position statement of the American Association of Cardiovascular and Pulmonary Rehabilitation. (7, 8) More recently (2019), the European Association of Preventive Cardiology (EAPC)(6) produced guidelines but these focused on principles of exercise prescription and outcomes in Type 2 Diabetes Mellitus (T2DM), as opposed to our focus on mitigating acute risks from exercise of glycaemic events in cardiac rehabilitation (CR) (5) participants with either Type 1 Diabetes Mellitus (T1DM) and T2DM. Following this, we searched and reviewed landmark review and consensus statements reporting on acute glycaemic management during exercise in people with diabetes from the past 10 years.(9-21). In noting the dates of the cited evidence in these statements, our final search involved the reference lists of the cited evidence and then searching and reviewing individual studies beyond the last date where guidelines did not yet exist. Our review and consensus not only included the efforts of the authors but also a second level checking by the council members of the multi-professional societies of the British and Canadian Associations of Cardiovascular Prevention and Rehabilitation, the British Association of Sport and Exercise Sciences and the International Council of Cardiovascular Prevention and Rehabilitation (ICCPR). In considering

evidence quality, the authors wish to emphasise that this consensus statement focuses on pragmatic acute matters of safety and behavioural efficacy of completing individual exercise sessions. The systematically reviewed guidance on following appropriate risk stratification published by one of our authors on exercise safety in T1DM and T2DM (22) provides a key example of our underpinning rationale in translating applications into the arena of CR. Furthermore each of the Guidance notes in Table 1 have been scored with the GRADE system for evidence quality (2) as applied in recent Diabetes UK guidelines led by another one of our authors. (3) If the guidance in this new statement can aid practitioners in reassuring CR participants with DM that they are safe to exercise and this positively influences their participation behaviour, then it has fulfilled its aims. As a result, it has been realised that much future research is required to evaluate the efficacy of these recommendations in terms of participant behaviour and education efficacy. As always, the largest challenge to outcomes in physical activity and exercise, whether in public health or rehabilitation/secondary prevention, is not simply biomedical or physiological, they are the complex behavioural interactions influenced by society, psychology, genetics and lifestyle impositions.

1.2 Identifying the need

Type 1 (T1) and Type 2 (T2) Diabetes mellitus (DM) are significant pre-cursors and co-morbidities to cardiovascular disease and the prevalence of both types is still rising globally.(23-25) Pan-European data show that over 25% of people with established coronary heart disease (CHD) have a history of DM, where >90% have T2DM.(6, 26-28) Compared to T2DM, T1DM has a greater overall cardiovascular disease risk .(29) Risk factor analyses have also identified specific DM associations for heart failure, stroke and peripheral vascular

disease.(30, 31) Therefore, modern programmes of CR need to have their staff able to manage additional exercise considerations for DM. A recent Position Paper from the European Association of Preventive Cardiology (EAPC) provides guidance on exercise prescription for people with T2DM participating in cardiovascular disease (CVD) prevention and rehabilitation programmes.(6) The prevalence of type 1 diabetes mellitus (T1DM) is also increasing globally (32, 33) and a majority of this population also develop macrovascular disease at rates similar to what is observed in T2DM.(34) Although the glycemic control of individuals with T1DM(35) and T2DM (36) remains a major challenge in both developed and developing countries, considerable evidence supports the concept that regular physical activity and exercise programming benefits both T1DM and T2DM groups in the prevention of micro- and macrovascular disease progression.(10, 11, 13)

2.0 RATIONALE, AIMS AND FRAMEWORK OF THIS STATEMENT

Although the debate continues on whether improved glucose control in those with cardiovascular disease (CVD) actually helps to prevent further DM progression,(37) it is clear that poor glycaemic management will mitigate the performance of optimally safe, effective and enjoyable physical activity for the CR participant.(38) As noted earlier, key statements on the guidance and numerous health benefits that exercise confers in individuals with diabetes already exist from a number of international authorities from Canada, Europe and the United States of America.(6, 8-10, 13, 15, 39) This current Statement neither aims to review the physiological and long-term health benefits of increased physical activity in people with cardiovascular and metabolic disease nor to supersede these other published guidelines. *This current consensus statement specifically aims to focus on guidance for managing the acute glycaemic needs before, during and after an exercise session in CR*

participants with diabetes. The objectives for meeting the aims of this statement include the following elements:

- Factors influencing physical activity behavior influenced by concerns around blood glucose management
- Preventing incidences and/or managing hypo- or hyperglycaemic events
- Preventing accidents, injury or symptoms from neuropathies leading to sensory-motor deficiencies, and
- Considering interactions between exercise and medications for the CR participant with diabetes.

The above elements will be covered in three main sections:

- 1) overarching considerations for all participants with DM (Sections 3 - 5);
- 2) specific glycaemic risk and management in T1DM (Section 6);
- 3) specific glycaemic risk and management in T2DM (Section 7).

Section 8, provides some brief notes regarding exercise intensity interactions with obesity and Section 9 the conclusion.

3.0 OVERARCHING CONSIDERATIONS; BEHAVIOUR, SCREENING AND ACTIVITY INTENSITY

3.1 Behavioural considerations

Globally, it is estimated that the behaviour of physical inactivity is a cardiovascular disease risk factor found in up to ~45% of individuals, for whom many have cardiovascular disease, T2DM or cancer (breast and colon); in some western higher-income countries the prevalence of inactivity rises to 70%.^(40, 41) It is therefore likely that many people entering

a CR programme, including participants with diabetes, will have a history of physical inactivity and naturally requiring a staged approach of targeted lifestyle behavioural-change strategies. It is a large enough challenge to get CR participants more physically active to any degree, let alone achieving the minimum targets recommended for an exercise-based rehabilitation programme (i.e. > 60 minutes per week at an intensity ≥ 2.5 metabolic equivalents; METS).(42-44) One of the key challenges to CR participation is the perceived health risk to participation.(45, 46) This fear is further compounded in those with DM, especially those with T1DM , where there is an added fear of hypoglycaemia and its consequences.(13, 47, 48) Even if CR participants with diabetes take up participation in CR, their physical activity goal attainment is poorer compared to participants without diabetes.(1, 6, 49) Hypoglycemia is also a barrier for engagement in exercise for those individuals with T2DM who are on insulin therapy or sulfonylureas.(50) In some settings, high intensity exercise may promote a rise in glucose resulting in hyperglycemia in patients with T1DM and some with T2DM,(51, 52) and this may also be perceived as a barrier to participate. For example, if a CR participant arrives to join an exercise group whose blood glucose is at a relatively contra-indicated level for exercise of too high or too low a level (i.e. > 15 mmol/L or < 5.0 mmol/L) and is turned away, he/she may leave with the wrong perception, which has been reinforced by the rehabilitation or healthcare practitioner; exercise is risky and something to be avoided (see specific guidance later for contraindication differences between T1DM and T2DM).

Whilst many individuals with T2DM may not be provided with self-monitoring devices for blood glucose, it seems prudent for cardiac rehabilitation practitioners, in the pursuit of participant safety, education and achievement, to invest in capillary blood glucose and

ketone level monitoring devices in a similar way to having the use of blood pressure monitors.(43) Qualitative evidence has reported, on balance, that continuous monitoring in T1D led to improved exercise management.(53) Furthermore, patient education on how exercise can acutely and chronically influence changes to blood glucose management has been demonstrated to be efficacious.(54-56) Whilst specific evidence for CR participants with DM is needed in evaluating blood glucose monitoring, in T2DM such monitoring before and during the exercise session as part of tailoring the mode, intensity and type of exercise has been shown to minimise acute glycaemic disturbances and improve chronic glycaemic control in T2DM.(57-59) As an example, if glucose levels tended to be on the higher end (> 8.0 mmol/L), then milder intensity aerobic exercise could be initiated first, while if glucose levels were on the lower end (i.e. < 5.0 mmol/L), a carbohydrate snack could be provided and/or more intensive but brief aerobic activity or resistance training could be initiated first (see guidance and evidence in specific sections on risk management in Sections 6 and 7 on T1DM and T2DM, respectively). Overall, having glucose and ketone monitoring available can aid in more personalised exercise safety and efficacy.

Assessing and managing participants' risk, as per the next sections, must be performed in a manner that clearly highlights the benefits to metabolic and cardiovascular health of being more physically active. Following an appropriate behavioural evaluation of the CR participant, the practitioner needs to carefully determine whether a typical bio-psycho-social approach can be taken or if there is a need for a more specialised psycho-biological approach.(60, 61) The former approach focuses on the usual adapting behavior to meet an "ideal" prescription as outlined by the EAPC(6), whereas the latter approach requires adapting the exercise prescription to the current psycho-social state (including perceived

barriers) of the participant. In this latter case, the participant needs to be supported to move towards agreed goals of optimised (but sometimes still not ideal) achievable behavioral and physiological targets. A place to start behavior change could be in something as simple as considering ways to avoid sedentary behaviour; i.e. avoiding time spent sitting or by breaking up prolonged periods of sitting with any non-exercise activity in a standing position or light activity.(10, 62) In T2DM, simply reducing sedentary time that encourages even increased amounts of daily light activity (starting with standing), improves glycaemic control.(63) These benefits have been shown to be independent, but not as a substitute, of recommended levels of physical activity and are increasingly being shown to favourably influence cardio-metabolic profile in people with diabetes.(62, 64-66) A whole consensus statement on improving CR participant behaviour affected by other co-morbidities, such as diabetes, beyond current recommendations (43, 67) is certainly warranted

3.2 General considerations for monitoring, screening and managing acute risk

3.2.1 Record keeping and monitoring glycaemic changes

Given that there are many CR participants with DM, practitioners are recommended to create an specific section in their records on DM glucose and medication management. In order to determine acute blood glucose (and ketones if required) interactions before, during and after sessions (up to 24 hours for T1DM), levels should be recorded to identify trends that could either help improve glucose and related symptom management or demonstrate chronic improvements or declines in control. The specific factors requiring recording should be identified in each of the key sections to follow, including: contra-indicatory events; sensory motor function; DM medication side-effects exacerbated by exertion; DM and heart disease medication interactions occurring/exacerbated; times of day of glycaemic events

occurring; management strategies (acute and chronic nutrition and medication factors) implemented.

3.2.2 Screening and managing risk

Most CR participants with diabetes are likely to be T2DM, by noting that ~10% of all people with diabetes are T1DM (Diabetes UK; www.diabetes.org.uk). The main acute risks before, during or after exercise include: 1) hypoglycaemia, 2) hyperglycaemia with ketoacidosis, 3) adverse events related to neuromotor, visual or sensory insufficiencies, and/or 4) fatigue relating to other co-morbidities e.g. renal disease and dehydration.(10, 14, 38) CR participants with T1DM, as compared to T2DM participants, are at much greater risk of an exertion-related glycaemic event from acute exercise (e.g. hypoglycaemia, hyperglycaemic or ketoacidosis), along with having a greater challenge in achieving consistent “optimal in-range” glucose levels.(13, 16)

Glycaemic stability and reducing the risk of undesirable exertion-related glycaemic events during an exercise session are recommended to be best achieved through performing a mixture of aerobic, strength and interval-type training activities.(10) Overall, the glycaemic responses to exercise in general is highly variable in T1DM, although some reproducibility does exist within patients.(51, 68) To help limit hypoglycaemia risk, performing resistance-type activities before aerobic type exercise is better suited for those patients with T1DM who are relatively euglycemic before exercise onset.(69) In contrast, if individuals with T1DM (or T2DM) have mild hyperglycemia (defined here as a glucose between 9.0 to 15

mmol/L), then initiating a session with some aerobic exercise (e.g. walking, jogging, cycling) will tend to reduce blood glucose levels toward a euglycaemic level.(13) Recent evidence in T1DM participants suggests that blood glucose levels increase significantly with high intensity exercise as compared with moderate continuous intensity exercise.(70) Post exercise hypoglycemia is also common in T1DM,(13) and may result in nocturnal hypoglycemic seizures, particularly if post exercise insulin dose reductions have not been managed properly.(71) Specialist diabetes clinicians, who are already working with the CR participant, should be informed from the CR team of any events that occur in and around physical activity or exercise sessions. This will ensure that patient records are updated and adapted to the best possible individualised care-plan.

3.3 Putting contra-indications into context for light-to-moderate and vigorous physical activity

The key priority of all CR professionals is to provide advice and education to patients on the actions that should be taken if and when a participant is relatively contra-indicated to performing physical activity. The guidance notes to follow must not be confused with standard contra-indications for “maximal exercise testing” typically outlined by the British Association of Sport & Exercise Sciences (BASES) and the American College of Sports Medicine(17, 39) where glycaemic dynamics to specific incremental maximal exercise test protocols are distinctly different to the types of exercise which occur in most CR settings. Though, some may challenge this thinking, with the increasing number of studies involving repeated maximal bouts of High-Intensity-Interval-Training (HIIT). A key difference, however, between a maximal exercise test and HITT training, is the former normally applies a relentless incremental staged or ramped protocol towards maximum, where the latter

involves regular intervals of active recovery at low to moderate intensity. More research is thus required on comparing the glycaemic dynamics involved in these two forms of maximally achieved exertion.

The level of contra-indication decision-making criteria and actions, in order of priority, should be as follows:

- Participants should not perform exercise if presenting with any significant signs and symptoms of a potential acute diabetes event, such as a recent episode of severe hypoglycemia or ketoacidosis (blood ketone levels >1.5 mmol/L before exercise onset in individuals with T1DM) which requires urgent medical attention/intervention(13). Though not common in T2DM, ketoacidosis can occur, and the same urgent attention should be given for blood ketones levels > 1.5 mmol/L.(72)
- Participants should not perform exercise if they have described a recent history of unstable (sometimes called “brittle”) diabetes where they experience wide unpredictable swings between hyper- and hypoglycaemia, especially where this is often linked with psycho-social difficulties; it needs the input of an expert multidisciplinary team.(73) In this case, any form and intensity of physical activity could potentially exacerbate the risk of an acute adverse glycaemic event. The specific target levels for hypo- and hyperglycaemia and related management are outlined in each of the sections 6 and 7 for T1DM and T2DM, respectively.

- Before excluding a participant from exercise, all should be done to rectify signs and symptoms of potential relative or absolute hypo- or hyperglycaemic contraindications and to get the patient to be active, even if only at light intensities.

Specific details on this issue are described in sections 6 and 7.

3.4 Sensory-motor considerations

Sensory and motor disturbances in diabetes are common and may increase the risk for falls and injury.(74) Care should be taken to maximize safety and minimize foot injuries associated with increased levels of physical activity in these patients, including balance assessment and regular foot exams.(75) Whilst not directly related to acute glycaemic management, many complications of diabetes can compound the problems associated with hypo or hyperglycaemia, which thus limit the ability of participants performing physical activity. These include: renal disease, where raised urea level is known to lead to fatigue(76); retinopathy with concerns over activities that increase intraocular pressure; peripheral neuropathy linked with hand/foot ulcers and loss of motor sensation; autonomic neuropathy that affects recognizing symptoms of angina and hypoglycaemia; reducing the ability of the heart rate to increase and reduced thermoregulation.(14) If a CR participant with diabetes has known complications or appears to have symptoms suggesting loss of neuro or motor function, it is vital that immediate advice from specialists is sought. It is important to note however, that patients with advanced disease can still exercise if certain precautions are made including the supervision of exercise sessions by a qualified exercise specialist and a modified training program.(77, 78)

4.0 DIABETES INTERACTIONS WITH CARDIOVASCULAR MEDICATIONS

4.1 Beta blockers, heart rate and oxygen-uptake kinetics

Beta-blocker medication, commonly taken by most CR participants, attenuates heart rate response and oxygen uptake kinetics during exercise.(79) Diabetes also reduces the responsiveness of the heart-rate to increased work demands (and similarly for oxygen uptake responses) when either exercise commences or when exercise intensity is increased.(80) The potential mechanisms for this have been reported to be, but not yet fully agreed, either neuro-chronotropic (80) and/or a result of lower activity/fitness levels linked with lowered left ventricular function.(81, 82) Until the evidence is clearer on the combined effect of diabetes and beta-blockade, it would seem prudent for CR participants with diabetes on beta-blockers to expect a further reduction in heart rate responsiveness to any given change in exercise intensity compared to beta-blocked CR participants without diabetes.

In individuals who manage their glycemia with insulin administration (basal and/or bolus insulin) as well as considering any adjustments to doses with their diabetes specialist team; the site of injection should also be considered.(13) It is thought that the increased blood flow associated with exercise in the legs or arms may increase the rate of uptake of insulin as compared to other insulin administration locations (abdomen, upper buttock). This could increase the risk of hypoglycaemia with exercise. It is generally advised that insulin administration should be limited to the abdomen or upper buttock if an exercise session is to be initiated post-insulin administration.(83) However, this may not fully protect against exercise-associated hypoglycemia and other preventative actions may be required (i.e. insulin dose reduction, carbohydrate snacking).(52, 84-87)

Statins, traditional thiazides and some beta blockers can reduce glycaemic control in diabetes(88-92) and in some patients metformin can reduce the benefits of atorvastatin.(93) In relation to the interactions between medications, exercise and diabetes, there is much literature on beta-blockers either affecting liver glucose output, insulin release, muscle glucose uptake, and reductions in hypoglycaemic symptom sensations (e.g. tachycardia blunted).(92, 94, 95) Non-vasodilating beta-blockers (metoprolol, bisoprolol, atenolol and bucindolol) can negatively impact on glucose control but vasodilating beta-blockers (carvedilol and nebivolol) are reported to have little deleterious effect on glucose control.(96) It is therefore important to check which beta-blocker the CR participant is taking, and to enquire with the medical team of the potential benefits of using a vasodilating beta-blocker.

It has also been reported that there are two negative effects of the blood glucose lowering medications from the sulfonylurea glibenclamide on normal exercise responses, which are important to CR participants:

- I. the benefit of “the warm-up” to prevent subsequent ischaemia during moderate to higher intensity exercise is impaired in those with stable angina,(97, 98) thus increasing the chances of exertion related angina during a typical exercise session, and
- II. the normal effect that exercise has on acutely reducing blood insulin during higher intensity exercise is significantly impaired,(99) which means that higher intensity exercise could contribute to hypoglycaemia in those treated with gliclazide and other sulphonylureas.

Table 2. provides a summary of the interactions between common medications used in diabetes management and exercise.

Table 2. Acute exercise interactions with diabetes medications (adapted from Nagi and Gallen(18); Eckstein et al.(19))

Medicine	Effect on glucose	Extra CHO with exercise
Biguanides (e.g. metformin)	In people with T2DM, metformin can reduce the decline in blood glucose during acute aerobic exercise but the glycaemic effects of metformin whilst performing exercise in people at risk of or with T2DM appear transient and minor	No
Sulphonylureas (e.g. glibenclamide or gliclazide) / Glinides (e.g. nateglinide)	Sulphonylureas should be taken with caution during acute exercise as the combined influence of both can rapidly decrease blood glucose levels and lead to hypoglycaemia. There is little evidence to detail the impact of glinides on physical exercise and metabolic outcomes.	Check glucose with exercise and take extra CHO during exercise
Thiazolidinediones (e.g. pioglitazone)	No noted effect on blood glucose with acute exercise	No
Sodium Glucose like Transporter (SGLT) Inhibitors (e.g. Empagliflozin or canagliflozin)	Largely unknown, studies needed	Unknown
Incretin-based therapies GLP1-RA: liraglutide DPP-4 inhibitors: sitagliptin or saxagliptin	GLP1-RA: No noted effects on blood glucose with acute exercise DPP-4 inhibitors: unknown	No
Insulin (e.g. Tresiba or Aspart)	Promote hypoglycaemia with exercise; may need to reduce dose before planned exercise	Check glucose before, during and after exercise and take extra CHO if needed during exercise

*CHO = carbohydrate

4.2 Euglycaemic ketoacidosis with SGLT-2 Inhibitors

Sodium-glucose co-transporter-2 (SGLT-2) inhibitors are mainly prescribed in T2DM, but can also be used in T1DM under very specific circumstances.(100-102) They are principally seen as an add-on therapy when biguanides (e.g. metformin) alone are not sufficient to reach the glycaemic targets. The SGLT-2 inhibitors have shown benefits in patients with cardiovascular disease,(103) making it an interesting choice in that population. However, ketoacidosis, even in the absence of hyperglycaemia, has been reported in patients taking

SGLT-2 inhibitors.(7) Although rare, this euglycemic ketoacidosis is serious and could potentially be fatal if not recognised.(100, 102) In light of this evidence, any patients on SGLT-2 inhibitors should be asked to report if and when they have experienced symptoms of nausea, vomiting or malaise, and also other typical symptoms of ketoacidosis (increased urination frequency, thirst, abdominal pain, confusion, “pear-drop breath”, flushed face, fatigue, rapid breathing, dry mouth and skin). A concomitant decline in exercise performance would be a key sign of any of these symptoms of ketoacidosis and exercise would sensibly be contra-indicated for a number of reasons in these instances anyway. The effects of SGLT2 antagonism on hypoglycemia risk associated with exercise are unknown, but these medications typically result in lower glucose concentrations in general and more vigilant glucose and ketone monitoring (using portable ketone meters) around exercise seems prudent.

5.0 TIME OF DAY OF EXERCISE INFLUENCES

In addition to the effects of the timing of eating around exercise on glycaemic control, the time of day (circadian effects) of exercise also influence glycaemic regulation in both T1DM and T2DM.(20, 104-106) In those patients to whom it is of concern to reduce the risk of post-exercise hypoglycaemic events, morning exercise is recommended and for those more prone to hyperglycaemia, afternoon and evening exercise (including HIIT in T2DM) have been demonstrated as preferable.(104, 106-109) In these noted studies of morning exercise before breakfast (~7 am), the post-breakfast glucose levels were actually more normal compared to having breakfast before exercise, with fewer hypos’ in the subsequent 15 – 24 hours. However, fasted morning HIIT may promote a significant rise in glucose concentration in both T1DM and T2DM.(106, 110) It is also important to note that post-

exercise hypoglycaemic events can be delayed up to 15 hours,(71, 111) so it is important to inform CR participants to monitor their blood glucose levels more carefully in this period.

6.0 SPECIFIC CONSIDERATIONS FOR TYPE 1 DIABETES

A general rule is that those with T1DM are at higher risk of an exertion-related glycaemic event compared to those with T2DM.(12) Managing blood glucose levels in and around exercise in people with T1DM is therefore more challenging and crucial than in T2DM. The guidance on glucose management summarised in Table 1 is of most pertinence to this group of CR participants. Whilst more evidence is required on efficacy, it would seem prudent for CR practitioners to now be skilled in using and include glucose and ketone monitoring devices as part of their standard equipment, in a similar way to having blood pressure, heart rate and ECG monitors.

Aerobic endurance type exercises (walking, jogging, light to moderate cycling) are likely to contribute to hypoglycaemia, whereas activities involving short bursts of higher intensity activity (sprints, weight training and circuit training) can contribute to hyperglycaemia.(13) Unlike T2DM, where glycaemic control can be improved over time with increased levels of physical activity, in T1DM such improvements do not usually ensue.(11, 112) Risk of severe hypoglycemia increases markedly with age and disease duration in this population.(113) In light of such a benefit paradox for T1DM, it is important to reinforce with CR participants that their main gain from the exercise is significant improvements in cardiovascular health and fitness.(114, 115) Specific to diabetes, the CR participant can be informed that increasing levels of physical activity and improved fitness can help in reducing the risk of retinopathy and moderately increased albuminuria.(13, 116) For those people with T1DM

and poorer glycaemic control, there is an increased chance of an atypically accelerated heart rate response at higher exercise intensities (>75% maximal heart rate) and it is important to observe the intensity of exercise at this point to determine if the participant is over-exerting themselves.(117) Poor glucose control is also associated with a greater risk for diabetic ketoacidosis in T1DM.(113)

Whilst the recent advances in glucose management with continuous subcutaneous insulin infusion (pump) or closed-loop insulin pumps have reduced some of the burden of diabetes self-care, through allowing freer independent care and freer living, the individualised nature of T1DM remains a challenge.(118, 119) This is especially true when setting individual insulin delivery levels in and around exercise, sports participation and nutrition. A tripartite team approach between the individual patient, the diabetes specialist (physician and/or nurse) and the exercise practitioner thus continues to remain an important factor in achieving quality, safe and effective care for the individual participant. Insulin treatment is essential as part of the management of T1DM, therefore when planning physical activity, the type and amount of insulin (affected by time of last injection and dose) as well as the time of the last carbohydrate containing meal (including quality and quantity) needs to be considered. The overarching considerations are whether the exercise is planned or unplanned, and the intensity and duration of the exercise.(13) In general, lowering insulin pump basal rates needs to be made in advance of aerobic exercise by approximately 60-90 minutes, if possible, to be effective in limiting hypoglycemia.(86) Insulin pumps can be beneficial for improving glucose control after exercise as compared to multiple daily injections (120), because they likely allow for temporary basal rate reductions to prevent post-exercise hypoglycemia and bolus or basal rate corrections for post-exercise hyperglycemia.(13)

6.1 Contra-indications for T1DM hypo- and hyperglycaemia levels and related management

A comprehensive consensus statement by a group of international sport & exercise and diabetes experts(13) provides initial guidance on encouraging the participation in physical activity. The guidance takes a proactive approach to mitigating, where possible, potential contraindications with the aim “to do all that is possible” to increase physical activity and exercise participation in patients with T1DM. They state that the target blood glucose zone during exercise should be between 7 to 10 mmol/L (126 – 180 mg/dL) and to quote the guidance directly from this consensus statement,(13) the following systematic steps should be employed:

“Blood glucose concentrations before exercise commencement and recommended glucose management strategies

The carbohydrate intakes shown here aim to stabilise glycaemia at the start of exercise. Blood glucose at the start of exercise must also be viewed within a wider context. Factors to consider include directional trends in glucose and insulin concentrations, patient safety, and individual patient preferences based on experience. Carbohydrate intake will need to be higher if circulating insulin concentrations are high at the onset of exercise.

Starting glycaemia below target (< 5 mmol/L; < 90 mg/dL)

- Ingest 15–30 g of glucose before starting exercise
- Delay exercise until blood glucose is ≥ 5 mmol/L (≥ 90 mg/dL) and monitor closely for hypoglycaemia.

Starting glycaemia near target (5–6.9 mmol/L; 90–124 mg/dL)

- Ingest 10 g of glucose before starting aerobic exercise
- Anaerobic exercise and high intensity interval training sessions can be started.

Starting glycaemia at target levels (7–10 mmol/L; 126–180 mg/dL)

- Aerobic exercise can be started

- Anaerobic exercise and high intensity interval training sessions can be started, but glucose concentrations could rise.

Starting glycaemia slightly above target (10.1–15.0 mmol/L; 182–270 mg/dL)

- Aerobic exercise can be started
- Anaerobic exercise can be started, but glucose concentrations could rise.

Starting glycaemia above target (> 15 mmol/L; > 270 mg/dL)

- If the hyperglycaemia is unexplained (not associated with a recent meal), check blood ketones levels. If blood ketones levels are modestly elevated (up to 1.4 mmol/L), exercise should be restricted to a light intensity for only a brief duration (< 30 minutes) and a small corrective insulin dose might be needed before starting exercise. If blood ketones levels are elevated (≥ 1.5 mmol/L), exercise is contraindicated and glucose management should be initiated rapidly as per the advice of the healthcare professional team.
- Mild to moderate aerobic exercise can be started if blood ketones are low (< 0.6 mmol/L) or the urine ketone dipstick is less than 2+ (or < 4.0 mmol/L). Blood glucose levels should be monitored during exercise to help detect whether glucose levels increase further. Intense exercise should be initiated only with caution as it could promote further hyperglycaemia.”

As part of symptom management in and around exercise, it is important to highlight and ensure that the patients learn the sensations of how they feel during exercise when their blood glucose levels are in the requisite safest exercise target zone (7 – 10 mmol/L), including: heart rate, rating of perceived exertion (muscles and breathing), muscle fatigue, and levels of perspiration. If patients lack this perception, then increased glucose monitoring is warranted. Especially for participants unaccustomed to exercise, individuals need to be able to differentiate between these normally raised responses during “glycaemic safe exercise” compared to those same but often more noticeable responses which ensue from a state of hypoglycaemia.

Exercise that is longer in duration (> 60 minutes) or at intensities likely to significantly lower muscle and liver glycogen stores (including interval or intense resistance training) can increase risk of late-onset (i.e. nocturnal) hypoglycaemia. In such cases, consumption of 10-30 g of carbohydrate during and within 30 minutes after completing this type of exercise is recommended.(13, 14) An alternative strategy could be to reduce the prandial insulin dose with a pre-exercise meal and at the next meal by ~50% and/or reduce the basal (background) insulin by ~20 % in those on MDI, especially if performing exercise on multiple days.(121, 122) Basal dose reductions can also be made if the participant is performing multiple acute physical exercise sessions over successive days.(84) Such strategies are important for a supportive environment for weight maintenance or loss while reducing risk of hypoglycaemia. Those on pump therapy should be advised to lower basal insulin rates overnight by 20%, starting at bedtime for 6 hours, after an intensive exercise session that occurs in the afternoon or evening to help limit post-exercise nocturnal hypoglycemia.(13) This should be done in conjunction with the diabetes specialist team as individuals may vary in the effect of exercise on tissue insulin sensitivity. However, such strategies may be important for a supportive environment for weight maintenance or loss while reducing risk of hypoglycaemia.

7.0 SPECIFIC CONSIDERATIONS FOR TYPE 2 DIABETES

As noted, most CR participants with diabetes will be T2DM. For the large majority of T2DM participants, they will either be managed conservatively through diet or on medications such as metformin or sulphonylureas (Table 1.). Sulphonylureas increase activity-related hypoglycemia risk.(123) As noted in section 5, for those with T2DM undertaking morning

exercise before 0900 hrs in a fasted state, appears to reduce the risk of post-exercise hypoglycaemia.(105)

For people with T2DM on insulin and in some cases on a continuous subcutaneous insulin infusion device (i.e. insulin pump), the guidance for T1DM participants should suffice. For those on multiple daily injections (MDI), some evidence suggests a reduced risk of hypoglycemia with insulin degludec vs. insulin glargine in patients with T2DM,(124), although in a randomised controlled trial with T1DM participants, there was an equivalent incidence of hypoglycaemia from acute exercise.(125) It is noted that in T1DM, insulin degludec is somewhat more difficult to titrate down for a planned exercise event, as compared to other basal insulins, because of its very long half-life.(122) If from this evidence in T1DM is applicable to T2DM, a basal rate reduction of insulin degludec by 20% may be warranted if patients are generally becoming much more physically active with CR.

Another somewhat paradoxical area of nutritional management has been the effects of sugar-free foods sweetened with aspartame conspiring with exercise to cause hypoglycaemia in T2DM.(126) Traditional physiology is challenged here in explaining this phenomenon but the “metabolic-conditioning survival instinct” from sensory psychobiological anticipatory responses to taste, smell or sight of “sweet food” is the hypothesised explanation of these rises in endogenous insulin secretion.(126)

7.1 Contra-indications for type 2 participants, with hyperglycaemia and related management

For participants with T2DM, in a hyperglycaemic state where blood glucose is > 17 mmol/L, without ketosis and without symptoms, is not a contra-indication to exercise but the exercise practitioner should have the patient proceed with some caution.(107) Milder forms of exercise intensity are likely to promote a beneficial reduction in glycaemia. In respecting these American College of Sports Medicine (127) recommendations, and more recent recommendations on the value of performing light activity to reduce blood glucose levels,(10) the following approach is recommended:

- If the participant has no symptoms and feels well, they can perform 10-15 minutes of low intensity light activity, such as walking (< 40% VO₂max or heart rate reserve, Borg RPE < 11 or Borg CR-10 < 2.0), then blood glucose levels should be re-checked with the following guidance:
 - i. If blood glucose level has risen, then the participant needs to see a specialist to review, as this is not the expected response.
 - ii. If blood glucose level has fallen to 13 - 15 mmol/L then the light intensity activity should continue, and review at next session to see if a more favourable response has occurred; if not then review with diabetes specialist is recommended
 - iii. If blood glucose level has fallen < 12 mmol/L then gradually progress towards completion of the normal exercise programme for that day and re-check at the end of the exercise session to see it has not risen again. As hyperglycaemia increases urine output, encouraging extra fluid intake may be prudent. They should be reviewed as soon as

possible with the diabetes specialist to prevent this from becoming a common occurrence. If it is a new occurrence of such hyperglycaemia, a cautious approach may be to check blood glucose levels during subsequent exercise sessions.

iv. In all the above cases, the CR team must note this in the participant records, inform the participant's diabetes specialist clinician and review and check on the next visit.

- In keeping with recommendations for effective participant education and the development of self-management skills (42, 128, 129), the CR team and the diabetes specialists should aim for the participant to learn, understand and be able to employ the above decisions and actions independently. This will ensure that the participant can become independently physically active safely and effectively.

7.2 Management of type 2 participants with hypoglycaemia

Overall, for asymptomatic T2DM participants being managed conservatively and not on medication or insulin, they should proceed similar to people without diabetes. In T2DM, preventable hypoglycaemia is the most common risk from physical activity, which is usually a function of inadequate nutrition and/or timing of taking medication, especially insulin and sulphonylureas.(14, 21, 38, 130) Pre-exercise low blood glucose levels is only a contraindication if it cannot be raised to > 5.5 mmol/L through an acute nutritional intervention (i.e. treated with 15-30 grams of fast acting carbohydrate such as dextrose).

Please note earlier statements about counter-intuitive effects of sugar-free foods sweetened with substitutes such as aspartame.

Key guidelines and reviews highlight that hypoglycaemia will occur either as a result of commencing activity with too low a blood glucose level prior to exercise or as a result of prolonged exercise (> 30 minutes), which may be manifested during or post activity and can be delayed up to 15-24 hours.(10) A key education point that should be noted for the CR participant is that regular aerobic exercise training will reduce the risk of endurance related hypoglycaemia as a result of enhanced fatty acid oxidative energy metabolism.(14) In light of the ACSM recommendations,(10, 14) hypoglycaemia, in some ways is akin to hyperglycaemia where all individuals treated with insulin and insulin secretagogues (both sulphonylureas and meglitinides) are at risk of hypoglycaemia and therefore at an increased risk of exercise-induced hypoglycaemia. For patients on metformin alone, it is unlikely to cause hypoglycaemia, whereas those taking sulphonylureas either on their own or in combination with metformin increases the risk of hypoglycaemia exacerbated by exercise. Please also note the previous cautionary notes on the effects of diabetes impairing the “warm-up effect” combined with reducing blood-insulin clearance caused by the sulfonylureas group of medications.

The risk of hypoglycaemia and how it is managed, in part, depends on whether the activity is planned or unplanned. In the formal CR setting, it is considered that all physical activity is planned. Additionally, when planning to manage hypoglycaemia risk, the duration and intensity of physical activity need to be considered. In individuals managed with treatments

(insulin and/or insulin stimulated agents) that increase the risk of hypoglycaemia the following precautions should be taken:

- Consider the duration of action of the medications, some insulins have short half-lives e.g. rapid acting insulin analogues, whereas some sulphonylureas and some forms of basal insulins (e.g. insulin glargine, insulin degludec) have very long half-lives.
- Discuss with the patients and ask them to speak to their diabetes specialist about the potential effect of their medication on physical activity. If pre-exercise blood glucose level is $< 5\text{mmol/l}$ in individuals treated with insulin or sulphonylureas additional carbohydrate containing foods should be consumed (i.e. 15-30 grams in the form of sugar cubes, dextrose, sugared drinks). If the exercise duration is > 30 minutes, additional carbohydrate may be needed at a rate of about 25-30 grams per hour of exercise.(13)
- Exercise that is longer in duration or at intensities likely to deplete glycogen stores (including interval or intense resistance training) can increase the risk of later-onset hypoglycaemia. In such cases, consumption of 10-30 grams of carbohydrate during and within 30 minutes after completing this type of exercise is recommended.(14) An alternative strategy could be to reduce insulin dose by $\sim 25\%$ at the next meal and/or reduce the basal (background) insulin by $\sim 20\%$ for at least 6 hours.(13) This should be done in conjunction with the diabetes specialist team as individuals may vary in the effect exercise has on their insulin sensitivity.

8.0 CONSIDERATIONS FOR THE DOSE AND TYPES OF PHYSICAL ACTIVITY

Generally, for participants whose blood glucose level is well controlled and within the target range noted early in the management recommendations, then normal CR intensities, durations and modes should be employed. Intensities and durations should be adjusted as noted by the guidance given. As this position statement has focused on acute glycaemic management, further information on exercise design and prescription as emphasised earlier are well described in statements by the AACVPR, ACSM and EAPC.(6, 8, 10)

Potential exercise risks with obesity

An important exercise consideration is the strong concomitance of obesity and diabetes and their links with bone and joint conditions.(131, 132) The significant positive curvilinear relationship between the prevalence of diabetes and obesity,(133) where over 80% of the risk of T2DM is associated with obesity,(134) means that many diabetes patients' programmes may need adapting to prevent either joint pain or potential fractures in older patients. With some participants having sensory-motor deficits from diabetes, they are at increased acute risk of falls and potentially reduced senses of acute angina during exercise. Poor skin health in the hands and feet linked with neuropathy and poorer circulation increase problems with gripping, and loss of awareness of blister formation on the feet.

High intensity training

More recently high intensity "burst" interval training (e.g. HIIT) has shown increased efficacy for aerobic fitness and muscle metabolic endurance improvements, compared to traditional moderate-vigorous continuous aerobic exercise, in CR and for people with T1DM and T2DM.(70, 135-139) However, caution is advised, for those at risk of or having

musculoskeletal comorbidities but more importantly in those with T1DM where hyperglycemia and a post-exercise increased ketosis levels may occur, therefore monitoring including ketone testing is recommended.

9.0 CONCLUSIONS

With the prevalence of diabetes in the general population and its strong association with CVD, up to one third of CR participants will need additional exercise considerations because of diabetes. Current incidence rates of diabetes would predict this programme and service challenge will continue to increase in the future. It is however important that for all with diabetes and especially those enrolled in a CR programme that every effort should be made to promote physical activity, when properly managed, as a vital component of a healthy lifestyle (cardio-metabolic, circulatory, sensory-neuro-motor and psychologically).

Behaviourally, the concomitance of diabetes with CVD increases the challenge for CR practitioners to impact positively behavior change. Patients with T1DM, compared to T2DM, pose a much greater challenge to the CR practitioner in relation to both motivation and to guide and adapt exercise, including the greater risk of an exertion-related event (hypoglycaemia, hyperglycaemia and ketoacidosis). However, due to the much smaller prevalence of T1DM, most CR participants with diabetes will be T2DM, albeit the T2DM participants may be on insulin therapy which complicates slightly blood glucose management strategies around exercise. Important risk management considerations specific to the CR participant with diabetes include interactions between CVD and diabetes medications which can include loss of effect of some medications, augmenting chances of hypo- or hyperglycaemia. Diabetes also affects neuro-sensory function that can reduce symptom recognition during exercise along with the reduction of heart rate and oxygen

uptake response kinetics. The time of day of exercise can modulate the reduction or the increase in risk of hypo or hyperglycaemic events along with the type and intensity of exercise. In T2DM, afternoon sessions of HIIT are preferred over morning sessions of HIIT for glucose improvements. In contrast, for T1DM, morning sessions of any exercise format may be safer than afternoon or evening sessions since the later often result in nocturnal hypoglycemia. A combination of muscular strength activities and aerobic endurance activities (perhaps in that given order) within any given session appears to be preferable in preventing acute and latent hypoglycaemia. For most CR participants with T2DM, they should be able to participate in the typical exercise programme unhindered. Glycaemic control in T2DM improves with increased physical activity levels but this is not necessarily the case for those with T1DM. There is a small proportion of T2DM participants that will need closer monitoring and more bespoke glucose managing in a similar way to the minority of CR participants who have T1DM.

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